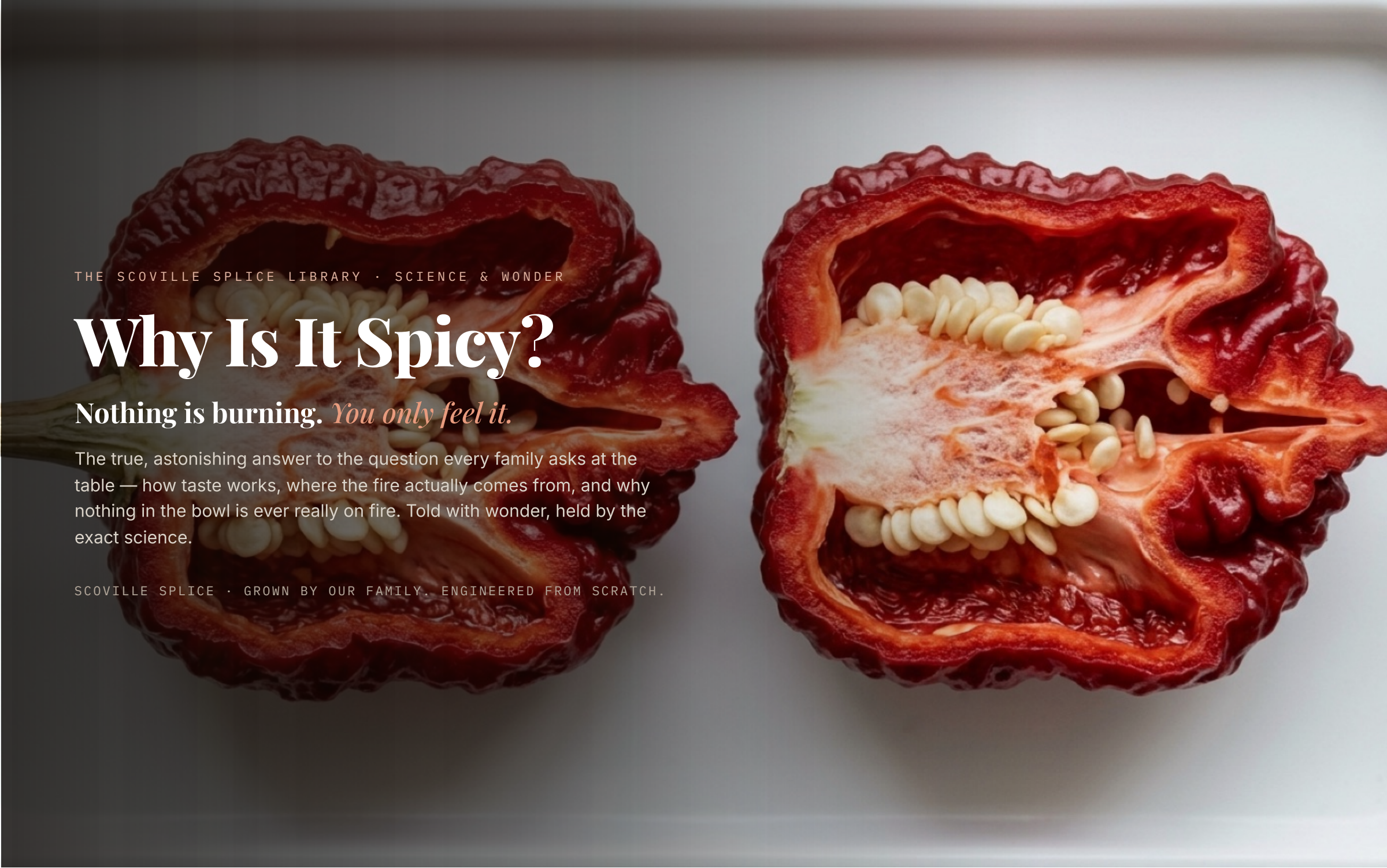


THE SCOVILLE SPLICE LIBRARY · SCIENCE & WONDER

Why Is It Spicy?

Nothing is burning. *You only feel it.*

The true, astonishing answer to the question every family asks at the table — how taste works, where the fire actually comes from, and why nothing in the bowl is ever really on fire. Told with wonder, held by the exact science.

SCOVILLE SPLICE · GROWN BY OUR FAMILY. ENGINEERED FROM SCRATCH.

Contents

01 Opening essay · Why is it spicy?

02 Chapter 1 · The Lock and the Key — how the tongue reads the world.

03 Chapter 2 · The Fire That Isn't There — the beautiful mistake.

04 Chapter 3 · The Shape of the Key — what capsaicin actually is.

05 Chapter 4 · Why Water Makes It Worse — the kitchen science of relief.

06 Chapter 5 · Sweetness, the Taste of Yes — the door the body most wants open.

07 Chapter 6 · Umami, the Taste of Being Fed — the savory door.

08 Chapter 7 · Bitter, the Taste of Careful — the door that keeps you safe.

09 Chapter 8 · The Taste With No Name — kokumi, and the door you only miss when it's gone.

10 Chapter 9 · The Opposite of Spicy — cool, and the mirror of fire.

11 Chapter 10 · The Sharp Cousin — pungency, and the fire that goes up the nose.

12 Chapter 11 · The Pucker That Isn't a Taste — astringency, the quietest door.

13 Chapter 12 · How Loud Is a Flavor? — the small mathematics of a feeling.

14 Chapter 13 · The Ladder of Heat — from a sunlit glow to the edge.

15 Chapter 14 · Reading All Eight at Once — the shape of a whole flavor.

16 Chapter 15 · The Recipe Inside the Seed — where a plant writes its own flavor.

17 Chapter 16 · Two Edits No One Had Found — the smallest possible change.

18 Chapter 17 · The Same Trick in Any Plant — beyond peppers.

19 Chapter 18 · A Meal, Read Door by Door — the whole book, served on a plate.

20 Chapter 19 · Three Things to Try at the Table — the science you can taste tonight.

21 Chapter 20 · Why Is It Spicy? — the answer, whole at last.

Opening essay · Why is it spicy?

Somewhere tonight a child sets down a fork, breathes out hard through an open mouth, reaches for the water that will not help, and asks the oldest kitchen question there is. *Why is it spicy?* It arrives at our table too — it is, in a quiet way, the question this whole family grew up around — and the honest answer turns out to be stranger, and kinder, and far more beautiful than the one we usually give.

Because the easy answer, *peppers are hot*, is not true. Nothing in that bite is hot. Nothing is burning. The pepper is the exact temperature of the plate it came in on, cooler than the mouth that holds it. No part of the tongue is harmed — not one cell of it is injured, not a single nerve actually scorched. And yet the feeling is real, as real as any feeling can be, which leaves us with a small marvel to explain: if the fire is not in the food, and the mouth is not truly burning, then where is the fire coming from?

It is coming from inside the body. From a tiny door on the surface of the tongue that the body built, long before cooking, to watch for genuine heat — and from a molecule in the pepper shaped so exactly like the key to that door that it slips in and turns the lock, and the body, faithfully, reports a fire that is not there. The pepper is not hurting the child. The pepper is telling the child something true, in the most extravagant language a plant knows, and the child's own body is doing all the shouting.



The founders in the research greenhouse at dawn — where the question that became this family's work was first asked. Not *how hot*, but *how, exactly, and where does the fire live.*

This is a book about that door — and about the seven others beside it, because heat is only the loudest of eight. Every flavor anyone has ever loved, we have learned, is a meeting between a molecule and a lock: sweetness is a meeting, savory depth is a meeting, the bitterness of a green and the pucker of strong tea and the clean cold of mint are all meetings, each one a key finding its door on the surface of the body and turning. Our family spent years of its life learning to measure these meetings exactly — to put a single, honest number on a feeling — and what we want to do in these pages is the gentlest thing we know how to do with all of it. We want to answer the child. Truthfully, and with wonder, because the truth deserves both at once.

The fire that isn't there — *where the heat actually lives.*

Let us be precise about the paradox, because the whole book turns on it. Taste — the five famous ones, sweet and salt and sour and bitter and savory — happens in taste buds, in specialized cells that sample what dissolves in your saliva and send a flavor upward. Spice is not one of them. Spice is not a taste at all. It belongs to a different and older sense entirely, the one that feels warmth on your skin, the ache of cold water on a tooth, the sting of a scraped knee. Scientists call that family of sensations *chemesthesis* — chemistry felt as touch — and in the mouth it rides the trigeminal nerve, the great facial nerve that reports heat and cold and pressure and pain from your lips, your cheeks, your tongue.

So when we say the fire lives in the body and not the food, we mean it with the full weight of anatomy. The pepper is not stimulating a flavor. It is reaching past the taste buds entirely and speaking directly to the body's heat-and-harm line — the exact wire that would carry the message if you had truly touched a hot pan. The brain receives that message and does what a well-built brain should: it believes its own instruments. It reports a burn, pulls the hand back, floods the mouth with saliva, prickles the scalp with sweat. Every one of those responses is correct for a real fire. There simply is no fire. There is only a molecule that has learned to forge the signal, and a body honest enough to be fooled by a perfect forgery.

This is why we find the question so beautiful, and why we never wanted to answer the child with *peppers are hot* and leave it there. The real answer is a small lesson in trust — in how completely the body believes the doors on its own surface, and in how a plant, over millions of years, learned to knock on exactly the right one.

A door on the tongue — *TRPV1, and the lock built for real heat.*

The door has a name: TRPV1. It is a protein, built of four identical pieces that fold together around a central pore and thread through the oily membrane of a nerve ending — a gate in a wall, held shut, waiting. The body makes it to be a thermometer and an alarm at once. Left to itself, TRPV1 stays closed through all the ordinary warmth of a day and a meal, and only swings open when the tissue around it climbs past about 43 degrees Celsius — roughly the temperature at which real heat begins to threaten real cells. It also opens to acid, to the flood of protons that a wound or an inflammation brings. It is, in other words, the body's dedicated listener for *this is getting dangerous* — hot, or burning, or raw.

Capsaicin, the pepper's molecule, does not touch the temperature of anything. It does something far more cunning. It slips through the membrane — it is oily, as we will see, and the membrane is oil — and settles into a small pocket on the inner face of the channel, a cradle of amino acids known as the vanilloid pocket. Seated there, it reaches into the machinery that decides when the gate should open and quietly resets the dial. A channel that needed 43 degrees to open will now open at the temperature it already sits at: the warm, ordinary, perfectly safe temperature of a mouth. The alarm has not been triggered. The alarm has been *re-tuned*, so that the absence of danger now reads as danger.

What follows is pure physics, and it happens in thousandths of a second. The open pore lets charged atoms pour through — sodium and calcium rushing inward down the steep gradient the cell works so hard to maintain. That inrush flips the voltage across the nerve's membrane, and once the voltage tips past a threshold it sets off a chain reaction of other, faster gates, and the nerve *fires* — a spike of electricity that races up the trigeminal line into the brainstem, up to the thalamus, and into the part of the cortex that maps the surface of the face. There the spike is read, correctly by its own logic, as heat arriving at a particular spot on the tongue. The loudness of the burn is, at bottom, the rate of those spikes: a few, and you feel a glow; a storm of them, and you feel a wildfire. The pepper never raised the temperature by a single degree. It only persuaded the thermometer to scream.

And here the opening image pays off — the child reaching for water that will not help. Water cannot help because capsaicin is not water-soluble. Its long tail is a chain of carbon, greasy and hating water, and water simply shoves it from one patch of tissue to the next without ever lifting it off the receptor. What *does* work is fat, and the protein in milk called casein, which surrounds the oily molecule and carries it away — which is why, across every cuisine that grew up with real heat, the cooling partner at the table is dairy or coconut or a rich nut, never a glass of water. The chemistry was known in kitchens long before it was known in laboratories.

One more mercy is built into the door. Let calcium keep pouring in, and the cell begins to desensitize the channel — to dial it back, to stop answering. That is why the second bite often lands softer than the first, and why a lifetime of chilies raises a person's tolerance in truth and not just in bravado. The receptor itself learns to shrug. The fire was always a conversation, and the body, given time, learns to lower its own voice.

The key, and where the plant writes it — *capsaicin, molecule and recipe.*

To see why capsaicin fits the heat door so exactly, it helps to look at the molecule as a small tool with two ends. At one end is a flat aromatic ring carrying a hydroxyl and a methoxy group — a chemical shape called the vanillyl group. At the other end is that long, greasy, branched fatty tail, an eight-methyl chain that makes the whole molecule oily enough to cross a membrane. Between them, an amide bond, like a hinge. The vanillyl end is the business end: it is the part that nests into the vanilloid pocket and turns the lock. And it is worth stopping on its name, because it is not an accident. *Vanillyl.* The same aromatic motif sits at the heart of vanillin, the molecule of vanilla. The sweetest, softest flavor we know and the fiercest both reach for the receptor with a version of the same small hand. The door is even named for that shared handle: the *vanilloid* receptor.



A pepper in cross-section. The pale pithy ribs inside — the placenta that cradles the seeds — are where the plant builds and stores its capsaicin; the fruit wall barely holds any at all.

Where does the plant write such a key? Not in the flesh, and not for us. Capsaicin collects in the pale ribs of tissue inside the fruit — the placenta that holds the seeds — and the plant makes it as a chemical guardian, a message to the mammals whose molars would grind its seeds to nothing: *not you.* Birds, which swallow seeds whole and carry them far, lack a heat door that capsaicin can turn, and eat the fruit untroubled. The burn, in its first and oldest meaning, is a plant choosing its gardener.

The writing itself is enzymatic, a short assembly line that joins two streams. One stream is the phenylpropanoid branch — **PAL → C4H → 4CL → HCT → COMT** — a sequence of enzymes that runs in every vascular plant on Earth and here delivers the vanillyl head. The other is a branched-chain fatty-acid route, tended by enzymes the pepper owns outright, that delivers the oily tail. At the end of the line sits the enzyme that marries them: Pun1, also called capsaicin synthase, which condenses vanillylamine with the branched fatty acid and releases finished capsaicin. Pun1 is the terminal step — the synthase that seals the finished molecule — and a pepper that carries a broken copy of it is a sweet pepper, a bell, all shape and no fire. But our flux modelling tells us that Pun1 labels the product rather than governing the rate; control sits upstream, in the phenylpropanoid steps — particularly 4CL and HCT — that build and deliver the vanillyl head. The length and saturation of that fatty tail set which capsaicinoid comes out — capsaicin itself, with one double bond in the chain, or its quieter sibling dihydrocapsaicin, with none — and that ratio tunes the *shape* of the burn: how fast it arrives, how sharp its peak, how long it lingers at the back of the throat.

Putting a number on a feeling — *EC50, and the one line everything rests on.*

Now the mathematics, because a feeling this exact deserves to be measured, and because a number, honestly arrived at, is a form of respect — it means we are not asking you to take the wonder on faith. We index every one of the eight meetings on a shared scoring framework, the Iyengar Flavor Index, so that a shishito and a cup of green tea and the most potent cultivar our family has ever designed can all be profiled side by side on a single page. The whole Index rests on one short line:

$$\mathbf{IFI = 1{,}000 \times EC_{50}(reference) \div EC_{50}(candidate)}$$

Everything in that line hangs on EC_{50}, so let us earn it slowly. Imagine titrating a molecule onto its receptor, a little at a time, and watching how much of the response you get. At very low amounts, almost nothing — a few doors turning. Add more and the response climbs; add more still and it begins to level off, because there are only so many doors to open, and past a point the extra molecules have nowhere to go. Plot that, and you get an S-shaped curve. **EC_{50} is the concentration at the exact middle of that climb — the amount it takes to drive the receptor to half of its fullest response.** It is the single most honest point on the whole curve: not the threshold, which is lost in noise, and not the plateau, which is flat and tells you little, but the steep midpoint where the receptor is most responsive and the measurement is most sure.

The shape of that climb follows a simple law. If we write the fraction of receptors switched on as θ, and the amount of molecule present as L, then

$$\theta(L) = L^n \div (EC_{50}{}^n + L^n)$$

where n describes how sharply the doors cooperate. Set L equal to EC_{50} and the algebra collapses to θ = ½ — which is simply the definition read back out, the proof that EC_{50} is the halfway mark. The interesting lesson is what the curve does *above* the midpoint. Take a receptor whose doors cooperate moderately, $n \approx 2$, a reasonable shape for a heat channel. At one EC_{50} you are at 0.50. Double the dose, to two EC_{50}, and you reach 4 ÷ (1 + 4) = 0.80 — not full, only four-fifths. Triple it, to three EC_{50}, and you reach 9 ÷ (1 + 9) = 0.90. The response saturates. This is the mathematics behind a truth every cook knows in the hand: past a point, *adding more pepper stops making things proportionally hotter.* You cannot shout louder than a scream.

Now the Index line makes sense, including why it is upside down. A *louder* molecule — one that speaks more strongly to its door — needs *less* of itself to reach that half-maximal midpoint, so it has a *lower* EC_{50}. Low EC_{50} should mean a high score, so we invert: we divide the reference's EC_{50} by the candidate's. Dividing a concentration by a concentration cancels the units entirely, which is the quiet genius of it — the score is a pure ratio, carrying no micromolars or milligrams, and so it transfers cleanly between any two laboratories that can each find a midpoint. Then we multiply by 1,000, which pins the reference — a native, wild-type pepper — at a round IFI of exactly 1,000. A candidate that matches the reference scores 1,000. A candidate twice as loud scores 2,000. A candidate that takes twenty-five times as much to reach half-activation scores 40.

Let us do it end to end, in the honest currency of the Index, which is *multiples of the reference.* Call the reference pepper's half-activation one reference-unit, by definition. A shishito's extract is gentle; it takes about 25 reference-units to reach the same midpoint. So its score is 1,000 × 1 ÷ 25 = **40** — the sunlit warmth of a shishito,

exactly where the Index places it. Our full-spectrum cultivar Phoenix is the opposite extreme: in our model, its capsaicin reaches half-activation at about 0.238 reference-units, roughly a quarter of what the reference needs. Its predicted score is 1,000 × 1 ÷ 0.238 = **4,200**. And the ratio between them is the number that measures the whole journey of this family's work: 4,200 ÷ 40 = **105**. In our model, Phoenix speaks to the heat door about one hundred and five times more loudly than a shishito, and 4.2 times more loudly than the wild reference the entire scale is pinned to — not a vague "much hotter," but a figure, derived, that you could hand to a stranger.

Reading the heat ladder — *what the numbers say when you climb.*

Put the family's ten flagship superhots in a row and the Index becomes a staircase. Each rung carries its catalog number, its predicted SHU, its IFI-H, and two figures we can derive from the score alone: *loudness*, which is simply IFI-H ÷ 1,000 (how many times the reference), and the *EC_{50} ratio*, which is 1,000 ÷ IFI-H (how much it takes, in reference-units, to reach the midpoint — the smaller, the fiercer).

CULTIVAR	SKU	SHU (PREDICTED)	IFI-H	LOUDNESS (×REF)	EC_{50} (×REF)
Ember	SS-0087	866K	1,570	1.57×	0.637
Cinder	SS-0088	1.05M	2,290	2.29×	0.437
Blaze	SS-0091	1.72M	2,630	2.63×	0.380
Wildfire	SS-0092	1.96M	2,930	2.93×	0.341
Firestorm	SS-0094	2.47M	3,490	3.49×	0.287
Solara	SS-0095	2.72M	3,980	3.98×	0.251
Phoenix	SS-0096	2.95M	4,200	4.20×	0.238

There is a second, subtler reading hidden in those first three columns, and it rewards a moment of arithmetic. Scoville Heat Units and IFI-H are not the same measurement wearing two hats. A Scoville value counts *how much* pungent material is present, by how far you must dilute it before the heat vanishes. An IFI-H score weighs *how loudly* that material speaks at the receptor. They track each other closely — more capsaicinoid does mean more fire — but not perfectly, and the imperfection is itself information. Divide one by the other, SHU per IFI-H point, and watch it drift:

CULTIVAR	SHU (PREDICTED)	IFI-H	SHU PER IFI-H POINT
Ember	866,000	1,570	≈ 552
Blaze	1,720,000	2,630	≈ 654
Firestorm	2,470,000	3,490	≈ 708
Phoenix	≈ 2,937,948	4,200	≈ 700

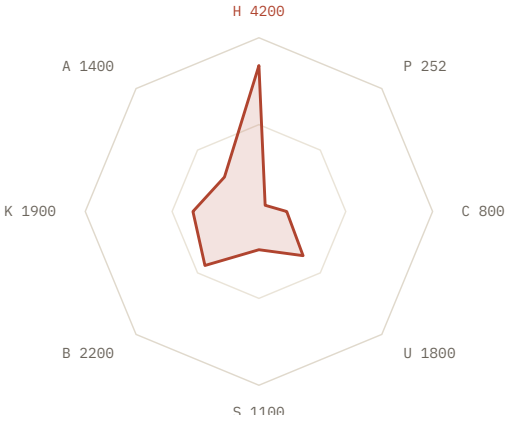
The figure climbs by about a quarter from the bottom of the ladder to the top. Higher up, each additional unit of Scoville *concentration* buys a little less receptor *loudness* than it did below — exactly what the saturating dose-response curve predicts, and exactly what we would expect as the capsaicinoid blend shifts up the ladder, the ratio of sharp capsaicin to its quieter, more saturated sibling tilting with the fatty-acid tail the enzyme lays down. We report both numbers, always, because neither alone is the truth. Scoville counts the molecules; the Index weighs their voice; the gap between them is the composition of the fire.

At the very top of the staircase stands the only cultivar our family has designed to speak on all eight doors at once — the full-spectrum fruit, read across the whole Index:



Phoenix (SS-0096) under the lights of the controlled chamber — the first cultivar engineered to speak on every one of the eight axes at once.

IFI PROFILE



IFI-H	4,200
IFI-P	252
IFI-C	800
IFI-U	1,800
IFI-S	1,100
IFI-B	2,200
IFI-K	1,900
IFI-A	1,400

That block is a whole meal written as a chord. Heat towers at 4,200, but it does not stand alone: a pungent sharpness at 252, a cooling note at 800, a savory depth at 1,800, a thread of sweetness at 1,100, a softened bitterness at 2,200, a round kokumi fullness at 1,900, a tannin grip at 1,400. Eight doors, eight numbers, one fruit, read at a glance instead of in a paragraph of adjectives.

How sure is the number — *design tolerance, consistency, and what 7% buys.*

A design specification without its tolerance is a promise without substance, so we owe you the target spread too. The honest way to state the steadiness of a process is its coefficient of variation — the batch-to-batch standard deviation divided by the mean, written as a percent. Our model predicts Phoenix achieves a mean of approximately 2,937,948 Scoville units; the design targets a coefficient of variation of **7 percent or less.** Work it through: at that tolerance, the standard deviation is at most 0.07 × 2,937,948 ≈ **205,656** units. Within that design envelope, a typical batch would land within about ±206,000 of the predicted mean, and roughly nineteen batches in twenty — two standard deviations, ±411,000 — would fall between about 2.53 and 3.35 million. Fierce, and *predictable*, which for anyone building a product out of it is the whole point.

Set that against the wild inheritance the family started from, where heat in a conventional pepper crop varies batch to batch at a coefficient of variation near **42 percent.** The arithmetic is unforgiving: 42 ÷ 7 = **6**, so the untamed plant is six times as variable. At 42 percent, two standard deviations is ±0.84 of the mean — a spread that runs from roughly a sixth of the target to nearly double it. One jar scorching, the next barely warm, from the same field. That gap, from 42 percent down to 7, is what separates a wild pleasure from an ingredient a person can design around. Consistency is not glamorous, but it is the quiet discipline that makes everything else in this book trustworthy.

One last comparison puts the whole staircase in scale. Pure crystalline capsaicin — the molecule alone, nothing else — anchors the top of the Scoville scale near 16,000,000 units. Our model predicts Phoenix's fruit reaches approximately 2,937,948 SHU. Divide: 2,937,948 ÷ 16,000,000 = **0.184.** The most potent cultivar our family has ever designed is predicted to register at a little over eighteen percent of the pungency of pure capsaicin crystals — and it does so as living tissue that is more than four-fifths water, a fruit that grows from a seed. The purified molecule is fiercer still. But it was never alive, and it never tasted of anything but fire. The plant is the harder, lovelier achievement.

And now the honest limits, because a number this careful has to name what it cannot do. These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory. An EC_{50} measured against a receptor in a dish is a faithful proxy for the molecule's loudness, but it is not the lived burn of a meal, which bends with the warmth of the food, the fat and saliva in the mouth, and whether this is your first chili of the night or your fifth. Two people with different versions of the heat door, or different histories of eating, will feel the same IFI-H differently — the Index measures the molecule's voice at a standard door, not any one person's hearing of it. A Scoville value, for its part, began life as a panel of human tasters diluting an extract until the heat disappeared, as subjective as it sounds, and even its modern instrument form measures concentration, not sensation. None of these numbers *is* the feeling. Each is a careful map of it. We hold

them lightly and report them precisely, and we never pretend the map is the territory. A good map is simply the most respectful thing we know how to offer: a promise that the wonder can be checked.

Seven more doors — *heat is only the loudest of eight.*

Everything we have followed for heat — a door on the body, a molecule shaped like its key, a midpoint that becomes a number — runs just the same through seven other doors, and together they make the whole Index. Each is a real receptor, each reads a real family of molecules, and each is anchored on the same one-thousand-times-EC_{50} line so that every flavor, however unlike, can be read in a single profile.

CODE	DOOR	RECEPTOR	WHAT IT READS
IFI-H	Heat	TRPV1	the capsaicin fire
IFI-S	Sweetness	TAS1R2 · TAS1R3	sugar-free sweetness
IFI-U	Umami	mGluR1 · TAS1R1·R3	savory, brothy depth
IFI-B	Zero-Bitter	TAS2R38	bitterness, attenuated
IFI-K	Kokumi	CaSR	richness and mouthfeel
IFI-C	Cool-Burn	TRPM8	the clean cold of mint
IFI-P	Pungency	TRPA1	the sharp of mustard and wasabi
IFI-A	Astringency	salivary PRPs	the grip of tea and tannin

Some of these you already know by feel, even if you never knew their names. The cool of mint is not a temperature either — it is TRPM8, the body's genuine cold door, turned by menthol exactly as TRPV1 is turned by capsaicin, a mirror-image forgery that reports cold where there is none. Umami, the brothy roundness of a good stock, is glutamate finding mGluR1 and its partners. Bitterness is a whole wary family of TAS2R doors the body evolved to flag poison, which is why softening them — our Zero-Bitter work reads the fraction of bitterness turned down — makes a coffee or a cocoa or a green vegetable bloom. Kokumi, the one almost no one can name, is the sense of fullness and continuity a dish gains through the calcium-sensing door, CaSR — the difference between a broth that tastes thin and one that tastes *cared for.* And astringency, the drying grip of strong tea or young wine, is not even a receptor in the usual sense: it is tannins binding the slick proteins in your saliva and stripping the lubrication from your tongue, felt as touch.

Eight doors, then. One of them famous enough to make a child gasp; seven more that shape every meal you have ever loved, mostly without announcing themselves. The gift of a shared scoring format is that it lets us hear all eight at once — to read a fruit the way you would read a chord instead of a single struck note.

What this book is, and how it's written — *a promise.*

We have built this book to go gently, in order. First the one idea everything rests on — that taste is a lock and a key, and that the fire lives in the body, not the food. Then a patient tour of all eight doors, the famous one and the ones you have never heard named. Then the small, careful mathematics that lets us set a number beside a feeling, because the number is there to be checked, not believed. Then how our family actually reads the recipe written inside a seed and, carefully, changes a single line of it. Then the part that matters most,

which is a table — a real meal, read door by door, and a few small things any family can try with their own mouths at the kitchen counter. And at the very end we return to the child, and answer the question whole, now that we have the words.

A promise about how it is written. The science in here is exact and real, never dressed down to seem simpler than it is; children deserve the true shape of a thing, and so do the grown-ups beside them. But it is never cold. We write about food and plants and the body the way you write about something you love and want to nourish you — which is, across a lifetime of growing things and sitting down together at a plain vegetarian table, what this family has always been doing. The wonder is not a decoration laid over the science. The science is what makes the wonder true. Every lush image in these pages is there to lead somewhere precise, and every number is there to keep a promise.

Back to the child — *the answer, whole.*

So: *why is it spicy?*

Because inside the pepper is a molecule the plant spent millions of years learning to write — a small oily key with a vanilla-cousin tip — and on the surface of the child's tongue is a door the body spent even longer learning to build, a heat alarm set to open near the edge of real danger. The key fits the lock. It slips into the door's inner pocket and turns down the dial, so that the ordinary warmth of a mouth now reads as fire, and a nerve that reports real burns sends its true signal for a burn that is not there. Water cannot wash the key away because the key hates water; only fat and milk can lift it off the door. And in a few minutes the door tires, the calcium does its quiet work, and the fire fades on its own — leaving a child who has just felt, firsthand, how faithfully a body trusts the doors on its own skin.

Nothing was burned. Nothing was harmed. The plant only spoke, in the loudest language it knows, and the child's own body did the shouting — and if we have done our work here, the child now knows not only *that* it happened, but exactly how, and where the fire really lives. We have modelled this door ten thousand times, down to the last decimal of its loudness, and the wonder has never once grown smaller. It only grows truer. That is the whole reason for the number, and the whole reason for the book.



PART I OF VI

The Lock and the Key

where taste lives · the door that answers to fire · the shape of the key · why water makes it worse

Chapter 1 · The Lock and the Key — *how the tongue reads the world.*

Here is the first surprising thing, and everything that follows grows out of it: taste does not live in food.

It feels as though it does. A strawberry seems simply to *be* sweet, the way it is red and round; the sweetness seems to sit inside the fruit the way the seeds sit in its skin. But carry that same strawberry to a different mouth — a bird's, say, or a cat's, which cannot taste sweetness at all — and the sweetness vanishes, though not one molecule in the fruit has changed. The sweetness was never in the strawberry. It was in the *meeting* between the strawberry and a particular animal built to notice it.



A morning walk through the research greenhouse — where a question that came up at our table one night became years of work. Flavor is a meeting, and a plant is one half of it.

So taste lives in a meeting. On one side is food, which is nothing but a crowd of molecules — sugars, acids, salts, oils, and thousands of others, most of which the body never notices. On the other side is you, and the surface of you where food lands is covered in millions of tiny proteins called **receptors**. The simplest way to picture a receptor is as a lock: a shape, folded out of a chain of amino acids, with a hollow in it sized and shaped to accept one kind of molecule and turn away the rest. A molecule that happens to match the hollow settles into it like a key into a lock — and when it does, the lock *turns*. The receptor changes shape. That change opens a channel, or nudges a partner protein, and a faint electrical signal travels up a nerve toward the brain.

The brain does the rest. It reads which locks turned, and how many, and how fast, and how long they stayed open, and from that running tally it assembles, all at once, the single seamless thing you experience as flavor. A tomato warm from the vine is not, in itself, sweet and savory and bright and a little green. It is a crowd of molecules that happens to fit several different locks at once; the sweetness and the savor and the brightness are assembled afterward, inside you, out of which locks turned. Flavor is not a property of the food. It is a conversation, and you supply half the words.

Once you see taste this way, a wonderful door opens — the one our family walked through and never came back from. A lock is a physical object. A physical object has a definite shape, and a shape can be understood, and measured, and — this is the part that took years, and the computing fell to one pair of hands at our table while the patience and the plants belonged to all of us — changed on purpose. If you know exactly which lock a flavor turns, and exactly what key turns it, then flavor stops being a mystery you can only chase by growing a plant and hoping. It becomes something you can read, and write.

The lock, the key, and the turn

Let us slow down on the moment a key turns a lock, because the whole of this book is hiding inside it.

A receptor is a protein, and a protein is not a blueprint or a code — it is an *object*, a chain of amino acids that has folded itself, in water, into one particular three-dimensional shape. Somewhere on that shape is a pocket. The pocket has a geometry and an electrical texture: a certain size, a certain curve, patches that love water and patches that flee it, a scatter of tiny positive and negative charges along its walls. A molecule drifting past will bind in that pocket only if its own shape and charges are the complement — bumps where the pocket has hollows, a plus where the pocket offers a minus. This is the lock-and-key idea in its oldest form, and it is almost right. The truer picture is a handshake: the molecule and the pocket both flex slightly as they meet, settling into a fit that neither had quite held alone. Chemists call that *induced fit*, and it is why a receptor can be exquisitely choosing about what it answers to.

But a key that fits is not yet a flavor. The lock has to *turn* — the binding has to change something — and here the body uses two completely different kinds of lock, a distinction most people have never been told and which, once you know it, reorganizes the whole mouth.

The first kind is a door that opens directly. These receptors are **ion channels**: the protein spans the cell membrane with a sealed pore running through its middle, and the binding pocket is wired to the gate of that pore. When the right key lands, the gate swings, the pore opens, and charged atoms — mostly sodium and calcium — pour through the membrane in a flood. That flood is an electrical event, and it fires the nerve almost instantly. The receptor *is* the door; the key opens it with its own hand. The channels that read heat, cool, and the sharp rush of pungency all work this way.

The second kind is a bell that rings a servant inside. These receptors are **G-protein-coupled receptors**, or GPCRs — long proteins that thread back and forth through the membrane seven times, with the binding pocket on the outside and a waiting partner protein, called a G-protein, clasped on the inside. When the key binds, the receptor's shape shifts just enough to release the G-protein, which hurries off to switch on an enzyme, which manufactures a swarm of small messenger molecules, which finally open a channel elsewhere and fire the nerve. It is indirect and slow by comparison — but it is an

amplifier. One key, bound once, can set loose a cascade that opens hundreds of channels. A whisper of sugar becomes a shout. Sweetness, umami, bitterness, and the round quality called kokumi are all read through these amplifying GPCRs.

Hold that difference in your hand for a moment, because it explains something you have felt your whole life without a name for it. A direct door is fast, local, and insistent — it feels like something *happening* to your mouth. An amplified bell is slower, broader, and suggestive — it feels like a *taste*, a quality of the food. The mouth has both kinds of lock, and the burn of a chili and the sweetness of a berry are not two points on one scale. They are two different machines.

Eight doors into the self

Of all the thousands of locks the body carries, eight matter most for the way a plant speaks to a person. Eight doors, eight channels through which food reaches the self. We gave each one a name and a number, and the whole of our family's work hangs on these eight.

DOOR (AXIS)	THE LOCK (RECEPTOR)	WHAT IT FEELS LIKE
Heat · IFI-H	TRPV1	warmth, fire, the glow of a chili
Sweetness · IFI-S	TAS1R2 · TAS1R3	the taste of *yes* — ripe fruit, honey
Umami · IFI-U	mGluR1 · TAS1R1·R3	savory depth, the taste of broth
Bitter · IFI-B	TAS2R38 (and ~24 kin)	the taste of *careful* — greens, coffee
Kokumi · IFI-K	CaSR	richness, roundness, the taste with no name
Cool · IFI-C	TRPM8	clean cold — mint, menthol
Pungency · IFI-P	TRPA1	the sharp rush of mustard and wasabi
Astringency · IFI-A	salivary PRPs	the dry pucker of strong tea

Look at that table for a moment, because it holds a small secret we will spend the book unpacking. Five of those eight are what most people mean by *taste* — sweet, savory, bitter, and their quieter cousins, read by locks on the taste buds and carried to the brain down the gustatory nerves. But three of them — heat, cool, and the sharp rush of pungency — are not tastes at all. They are read by an entirely different system, the one that normally reports *temperature* and *touch* and *pain*: the trigeminal nerve, the great branching nerve that gives the whole face its feeling. When a pepper burns, no taste bud is involved. The pepper has reached past taste altogether and spoken directly to the nerve that watches for fire.

Set the same eight doors beside one another by the *kind* of lock each one is, and the architecture of the mouth comes clear:

AXIS	RECEPTOR	KIND OF LOCK	HOW THE SIGNAL TRAVELS	NERVE
Heat · IFI-H	TRPV1	ion channel — a door that opens directly	cations flood in, the nerve fires at once	trigeminal
Cool · IFI-C	TRPM8	ion channel — a door that opens directly	cations flood in, the nerve fires at once	trigeminal
Pungency · IFI-P	TRPA1	ion channel — but the key *reacts* with the lock	cations flood in, the nerve fires at once	trigeminal
Sweetness · IFI-S	TAS1R2 · TAS1R3	GPCR — a bell that rings a servant	G-protein cascade, amplified hundreds-fold	gustatory
Umami · IFI-U	mGluR1 · TAS1R1·R3	GPCR — a bell that rings a servant	G-protein cascade, amplified hundreds-fold	gustatory
Bitter · IFI-B	TAS2R38 (+ ~24 kin)	a whole *family* of GPCR locks	G-protein cascade, amplified hundreds-fold	gustatory
Kokumi · IFI-K	CaSR	GPCR — a bell that rings a servant	G-protein cascade, amplified hundreds-fold	gustatory
Astringency · IFI-A	salivary PRPs	not a lock at all — a loss of lubrication	proteins cross-link, the mouth sense feels drag	touch

Two rows in that table are worth a breath. Bitterness is read not by one lock but by a family of roughly twenty-five, because *careful* is a wider instruction than *yes* — a sweet molecule is almost always sugar, a narrow target a single lock can guard, but a bitter molecule might be any one of ten thousand plant poisons, so evolution spent its locks where the danger lived. And astringency, the dry pucker of strong tea or a young red wine, is the strangest of the eight: it is not a receptor event at all. Tannins in the tea grab the slippery proteins that keep saliva slick and pull them into clumps; the mouth, suddenly short of lubrication, reads the friction as *dryness*. It is the one axis sensed not by chemistry but by mechanics — a reminder, built into our own index, that the body has more than one way to read the world.

How loud, not how much

For ten thousand years the whole art of flavor was this: grow the plant, taste the fruit, keep the seed of the one that moved you. Not once, in all those centuries, could anyone say *how much*. How much sweetness. How much warmth. How much of the round savory depth that makes a broth taste like being cared for. You could feel the result exactly and describe it only in poetry.

The trouble with "how much" is that the honest version of the question is not about the food at all — it is about the meeting. You might measure how many milligrams of a compound a tomato holds and still not know how the tomato *tastes*, because two molecules present in equal amounts can speak to their locks at wildly different volumes. What we needed was not a measure of quantity but a measure of **loudness**: how readily a stimulus turns its receptor.

Pharmacology already had the right instrument, and it is called the **EC_{50}** — the concentration of a stimulus at which its receptor reaches half of its full response. A low EC_{50} means the lock turns while only a little of the key is present: a loud, potent signal. A high EC_{50} means you must crowd the pocket with key before the lock will budge: a quiet one. Loudness is simply the inverse of EC_{50}.

That inversion is the heart of our whole index. Fix a reference — a chosen, steady stimulus whose loudness we agree to call the standard — measure the candidate's EC_{50} against it, invert, and scale by a thousand so the everyday numbers land in a friendly range:

$$\mathrm{IFI}(\text{candidate}) = 1{,}000 \times EC_{50}(\text{reference}) \div EC_{50}(\text{candidate})$$

Read that formula slowly and it tells you everything about how to think in this book. If a candidate's EC_{50} exactly equals the reference's, the ratio is one and the score is **1,000** — the anchor, the loudness of the standard itself. If the candidate is *more* potent, its EC_{50} is smaller, the fraction grows, and the score climbs above 1,000. If it is weaker, its EC_{50} is larger and the score falls below. The Index is a loudness meter with its zero set to a familiar note, and each of the eight axes carries its own reference constant — a stated convention that defines IFI = 1,000 on that axis, the way the original Scoville scale is defined by dilution-to-threshold rather than derived from a single literature value. Each axis is normalized to a ceiling of 5,000, the loudest we have yet had cause to print.

A worked example makes the arithmetic honest. Our fullest-spectrum cultivar, the one we call Phoenix, is designed to register **4,200** on the heat axis. Put that into the formula and solve for what it means about the meeting:

$$4{,}200 = 1{,}000 \times EC_{50}(\text{reference}) \div EC_{50}(\text{Phoenix}) \quad EC_{50}(\text{reference}) \div EC_{50}(\text{Phoenix}) = 4.2 \quad EC_{50}(\text{Phoenix}) = EC_{50}(\text{reference}) \div 4.2 = 0.238 \times EC_{50}(\text{reference})$$

So Phoenix's standardized extract is designed to drive the heat receptor to half-maximal response at just under a quarter — twenty-four percent — of the concentration the reference needs. It is, in the precise sense the number is built to carry, **4.2 times louder** than the standard. Not 4.2 times more of anything. 4.2 times louder.

A worked door — the heat channel

Of the eight doors, heat is the one to walk through first, because it is the one the child who asks *why is it spicy?* is really asking about, and because its lock is the most beautiful trick in the mouth.



A pepper opened along its length. The pale ribs down the center — the placental tissue, not the flesh and not the seeds — are the kitchen where capsaicin is built. The heat was manufactured here, molecule by molecule, before it ever reached a tongue.

The heat receptor is **TRPV1**, a channel sitting in the membranes of the trigeminal nerve endings that lace the surface of the tongue. In its resting life it is a thermometer. TRPV1 is built to open when the tissue around it grows genuinely hot — above about 43 degrees Celsius — so that if you sip something scalding, the channel fires and the nerve reports *danger, heat* before you are burned. In Fahrenheit that threshold is

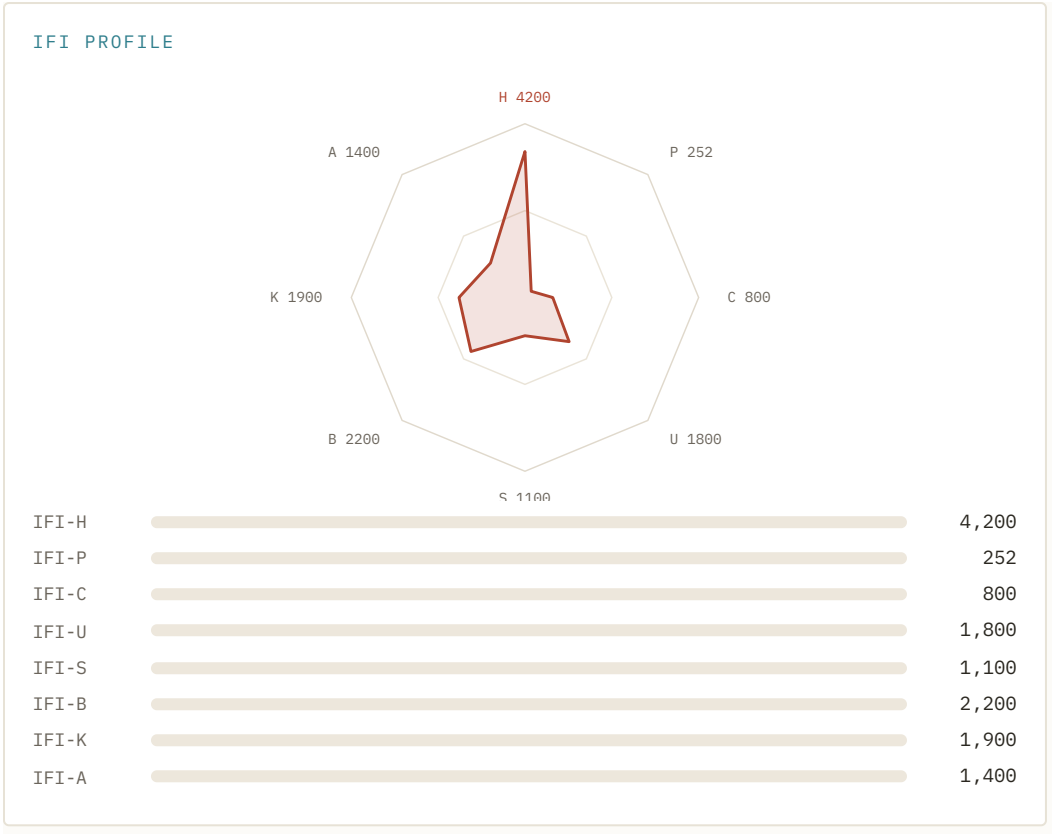
```
(43 × 9/5) + 32 = 109.4 °F
```

while the resting mouth sits near 37 °C, or 98.6 °F. At 98.6, comfortably below 109.4, the channel is shut and silent. This is the ordinary, sensible arrangement: no real heat, no signal.

Now bring in capsaicin, the molecule those pale pepper ribs manufacture. Capsaicin does not warm the tissue by a single degree. What it does is subtler and stranger: it slips into a pocket in TRPV1 and, by binding there, *lowers the temperature at which the channel decides to open*. It drags the 43-degree threshold down — down past the 37-degree temperature your mouth already is. And so the channel, finding itself now "too hot" at a temperature that has not changed at all, throws its gate wide. Sodium and calcium flood in. The nerve fires. The brain, which has no way to know the signal was triggered by a molecule rather than a flame, reports the only thing that signal has ever meant: *fire*. The burn of a chili is a true alarm raised by a false emergency — the thermostat talked into a reading the room never gave it.

That is why heat feels like an event and not a flavor. No taste bud took part; the pepper reached straight past taste to the nerve that guards against burning, and knocked.

Here is Phoenix, our most complete cultivar, designed to register on all eight doors at once — the first cultivar we built to activate every axis of the Index:



Behind that single heat number of 4,200 stands a ladder of cultivars, each designed louder than the last, and the ladder is where the new way of measuring earns its keep. The old way of measuring heat is the **Scoville scale**, invented in 1912: dilute a pepper's extract in sugar water, cup by cup, until a panel of tasters can no longer detect any burn, and report the dilution. It is a threshold measure — the faintest edge of sensation — and it is heroic for its age, but it is a human panel's guess at a vanishing point. The Index measures a different place on the curve: not where the burn disappears, but where the receptor reaches its halfway mark, the EC_{50}. The two usually agree, and where they *disagree* they teach you something true.

CULTIVAR	SKU	PREDICTED SHU	IFI-H	EC_{50} (RELATIVE, REF = 1.000)	AXES
Ember	SS-0087	~866K	1,570	0.637	2/8
Cinder	SS-0088	~1.05M	2,290	0.437	3/8
Kindle	SS-0089	~1.25M	2,000	0.500	3/8
Blaze	SS-0091	~1.72M	2,630	0.380	4/8
Wildfire	SS-0092	~1.96M	2,930	0.341	5/8
Scorch	SS-0093	~2.21M	3,220	0.311	5/8
Firestorm	SS-0094	~2.47M	3,490	0.287	6/8
Solara	SS-0095	~2.72M	3,980	0.251	6/8
Phoenix	SS-0096	~2.95M	4,200	0.238	8/8

The relative EC_{50} in that last column is just the formula read backward — for any cultivar, EC_{50} = 1,000 ÷ IFI-H in units where the reference is 1.000 — and it lets you *feel* the loudness directly: Phoenix at 0.238 is designed to reach half-activation on less than a quarter of the material the reference needs. To convert a loudness into a concentration you eat, you need the chemistry of the key itself; capsaicin's molar mass is 305.4 grams per mole, so a one-micromolar solution carries 0.305 milligrams in every litre — the arithmetic that turns an abstract EC_{50} into milligrams on a spoon.

The shape of a yes

We have been speaking of EC_{50} as a single point — the concentration that gives half-maximal response — but the honest object behind it is a whole curve, and the curve has a shape worth seeing.

Push a stimulus at a receptor across a range of concentrations and plot the response, and you do not get a straight line. You get an **S** lying on its side: almost nothing at low concentration, then a steep climb through a middle band, then a flattening as every lock that can turn has turned and the signal saturates. The equation that draws this S is one of the most useful in all of biology, and it is simpler than it looks:

```
response = R_max × [C]ⁿ ÷ (EC₅₀ⁿ + [C]ⁿ)
```

Here R_max is the loudest the receptor can go, [C] is the concentration of the key, and the two quantities that shape the curve are EC_{50} and the exponent **n**, the Hill coefficient. Set the concentration exactly equal to EC_{50} and watch the algebra fall open: the fraction becomes $EC_{50}^{n} \div (EC_{50}^{n} + EC_{50}^{n})$, which is $EC_{50}^{n} \div 2EC_{50}^{n}$, which is exactly one half. Half-maximal response, every time, by construction. That is what EC_{50} *is*: the concentration that sits at the midpoint of the climb.

The exponent n measures how switch-like the climb is — how sharply the receptor flips from silent to shouting. And here the physical shape of the lock returns to the story. TRPV1 is not a single protein but four, a *tetramer*, four identical subunits gathered around one central pore, each carrying its own capsaicin pocket. When keys bind cooperatively — the first binding making the next easier — the curve steepens, and TRPV1's heat response climbs with a Hill coefficient near 2. A higher n is a sharper yes: a narrow band of concentration over which the mouth goes from noticing nothing to a definite flame. It is why heat so often seems to arrive all at once, a step rather than a ramp.

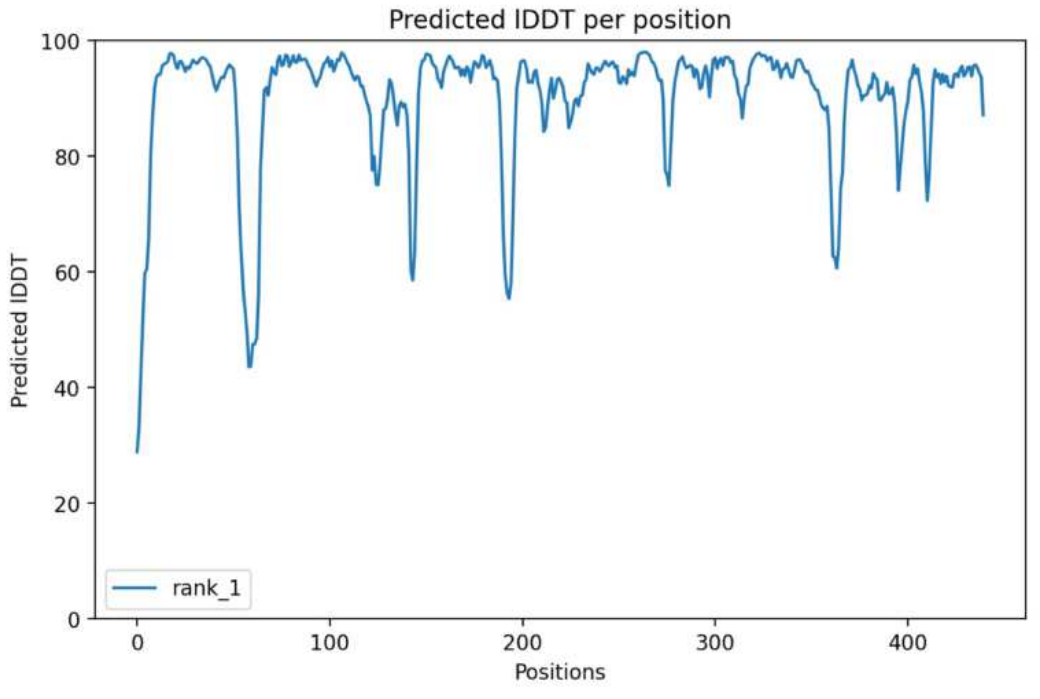
Now the disagreement the ladder hid in plain sight. Look again at two of the cultivars and compare their two kinds of number. Kindle is designed to predict **1.25 million** Scoville units yet only **2,000** on IFI-H. Cinder predicts **fewer** Scoville units — 1.05 million — yet a *higher* heat score of **2,290**. Turn those scores into relative EC_{50}s and the inversion sharpens: Cinder is designed to reach half-maximal firing at 0.437, Kindle not until 0.500. By the receptor's own midpoint, Cinder is the louder cultivar in our model, even though the Scoville framing finds more total burn in Kindle.

This is not an error in either number. It is two instruments reading two different points on two differently shaped curves. Scoville integrates the faint long tail of a dose-response — the dilution at which the very last of the heat fades — and that tail is swollen by the *total* capsaicinoid load and by the slower-burning cousins of capsaicin, like dihydrocapsaicin, that linger at the threshold. The Index reads the midpoint, where potency and the steepness of the climb decide the position. A cultivar can carry a larger total load that fades slowly (more Scoville) while its curve crosses its own halfway mark later (lower IFI), or the reverse. When our family finally had

both numbers for the same design and watched them disagree, that was the morning the Index stopped being a convenience and became a necessity: *how much* and *how loud* are genuinely different questions, and only one of them is the taste.

Reading the same lock twice

A number is only a number if you can get it again. This is the quiet discipline beneath everything, and it is where designing flavor parts ways from merely describing it.



The enzyme that forges the key, modeled and colored by the model's own confidence — bright where the fold is certain, pale where it is not. We cannot design a flavor until we can see, and steady, the machine that builds its molecule.

Capsaicin, the key that turns the heat lock, is itself built by a lock-and-key machine inside the pepper: an enzyme, **Pun1**, that joins a vanilla-like fragment called vanillylamine to a small branched fatty acid, welding them into the finished molecule. In a wild pepper that enzyme works, but it works *unevenly* — fruit to fruit, plant to plant, the amount of capsaicin it turns out swings wildly. We can put a number on that swing. The **coefficient of variation**, CV, is the standard deviation of a set of measurements divided by their mean, written as a percentage — a clean measure of how much a thing wanders around its own average. In wild-type peppers the capsaicin output carries a CV near **42 percent**. That is a plant you cannot design around: two fruits off the same bush can differ by nearly half.

What a wandering measurement does to a score, you can calculate. Because the Index is an inverse — IFI = 1,000 × reference ÷ EC_{50} — a relative wobble in the underlying quantity passes almost unchanged into the score; the fractional error of 1 divided by a number is, to first order, just the fractional error of that number. So a 42-percent CV would land a nominal heat score of 4,200 at roughly

> `4,200 ± (0.42 × 4,200) = 4,200 ± 1,764`

— anywhere from about 2,400 to nearly 6,000. That is not a measurement. That is a shrug.

Our flux model tells us that the phenylpropanoid pathway — the upstream steps governed by enzymes like 4CL and HCT/CCoAOMT — holds the greatest control over how much capsaicin the plant

ultimately produces. Pun1 is the terminal capsaicin synthase; it labels the final product, it does not govern the rate. What Pun1's precision *does* control is the consistency of the last joining step: a wobbling enzyme at the end of the line multiplies the variance the upstream pathway already carries. So by reading Pun1's structure and redesigning two of its amino acids — the substitutions we label **S39L** and **L345G**, found not by the old breeder's patience but by a protein language model proposing edits and a metabolic flux model mapping where control truly sat, then written into the genome with CRISPR — we did two things at once. We designed toward a heat ceiling our model predicts at approximately **2.95 million SHU**, the figure behind Phoenix, with a design target exceeding known world records while the upstream pathway carries the flux. And, just as important, we steadied the hand: our design specification targets batch-to-batch CV of **7 percent or below**. Run the arithmetic on that specification and the score tightens to

```
4,200 ± (0.07 × 4,200) = 4,200 ± 294
```

— a tidy band from about 3,900 to 4,500. The loudness is now a fact you can build a recipe on, a sauce on, a shelf of them on. Precision is not the opposite of wonder here. It is what lets the wonder be the same twice.

The honest edges

No measurement is the whole of the thing it measures, and an index that forgot its own edges would be lying. Three of them are worth keeping in view, because they are where the lock-and-key picture bends.

The first is that *you are not the reference, and neither are we.* The locks vary from person to person. The bitter receptor TAS2R38 is the clearest case: a few readable spellings of its gene divide people into keen tasters and near-non-tasters of certain bitter compounds, so the very same raw Brussels sprout is a mild green thing to one eater at the table and a wall of bitterness to another, with no disagreement about the sprout. The Index is anchored to a steady reference constant precisely so that it measures the *stimulus* and not the taster — but the moment that stimulus meets a real mouth, that mouth's own locks have the last word. A number tells you how loud the note is played; it cannot promise how loud you, specifically, will hear it.

The second is that the mouth keeps changing while it reads. Sit with chili heat for a few minutes and TRPV1 begins to *desensitize* — the calcium that flooded in sets off a slow feedback that dials the channel down — which is why the third bite of a hot dish lands softer than the first, and why heat can be built to and lived in. Sweetness fatigues, smell adapts, the pucker of tannin deepens across a meal. The Index measures a clean first meeting between stimulus and rested receptor; a long dinner is a moving target, and the honest reader holds the number as the opening note, not the whole song.

The third we have already met, and it is the most humbling: astringency is not a receptor at all. There is no lock for the tannin to turn — only the slow loss of slick in the saliva as proteins clump and the mouth reads the drag. We measure it on the same eight-door card because it belongs to the experience of the plant, but it is a reminder printed into our own index that the body reads the world by more than one method, and that a family who wants to understand flavor must be willing to measure touch alongside chemistry, and to say plainly where the key-and-lock story ends.

These are not apologies. They are the shape of an honest instrument — and an instrument that knows its own edges is the only kind you can trust to design with. We built the Index to measure the meeting, and we built it knowing that the meeting always has a second half we do not control: a living mouth, a particular morning, a body we would wish only to nourish and never to fool.

So the child's question turns out to be the right place to begin, because the child has noticed, without the words for it, that *spicy is not a flavor*. Spicy is a message sent down the wrong wire on purpose and received exactly as intended — a false fire, raised in a true alarm, designed now to land within a few percent of itself. Let us go and find the door it knocks on, and learn to knock on it ourselves.

These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.

Chapter 2 · The Fire That Isn't There — *the beautiful mistake.*

The door that makes a pepper spicy is called **TRPV1**, and its ordinary job has nothing whatever to do with food.

TRPV1 is one of the body's heat alarms. It sits in the membranes of the nerve endings that feel the mouth, the throat, the skin — a little protein channel, normally closed, built to stay shut and quiet until something genuinely dangerous comes near. What it watches for is heat. When the temperature of the tissue around it climbs past about **43 degrees Celsius** — soup straight off the stove, a bath drawn too hot, a mouthful of tea taken too soon — the channel springs open. Positively charged ions, sodium and calcium, pour through the opening it makes, and that rush of charge becomes an electrical signal that races up the nerve and arrives in the brain already labeled: *hot, here, now, pull back.* And you do pull back, before the heat can do real harm. TRPV1 is a small faithful guardian. It spends its whole life watching for fire so that you don't have to.

Capsaicin — the molecule that makes a chili hot — is a key cut to open that guardian's door when there is no fire at all. We find, the longer we sit with it, that the whole of the answer a child is owed lives inside that one sentence. The rest of this chapter is us slowing it down until every part of it shows.

The guardian at the door

Look closely at the guardian and it is not a simple latch but a small machine of real beauty. TRPV1 is a *tetramer* — four identical protein arms gathered around a central pore, like four hands cupped to make a well. Each arm threads back and forth through the fatty membrane six times, and the last two crossings of all four arms lean inward to build the pore itself: a gate at the bottom, a narrow selectivity filter at the top, and between them a path just wide enough to let small positive ions through single file. Closed, the gate is pinched shut and nothing passes. Open, it relaxes, and the well fills.

What makes TRPV1 remarkable among the body's sensors is that it answers to more than one kind of danger. It is *polymodal* — a single channel that opens to heat above roughly 43 °C, to the acid of inflamed or injured tissue (a flood of protons, low pH), to certain stinging compounds, and to a shift in the voltage across the membrane. Four warnings, one door. The body economized: rather than a separate alarm for every kind of hurt, it built one honest channel that reports *this tissue is in trouble* no matter which trouble it is. Capsaicin's whole trick, as we will see, is to walk in through one of those four entrances carrying none of the danger the entrance was built to detect.

When the gate opens, what comes through is charge. The channel is a *cation* channel — it passes sodium and, tellingly, a great deal of calcium; in the literature its preference for calcium over sodium runs roughly ten to one. That selectivity will matter twice over: calcium is the ion that turns the signal into pain, and calcium is also, later, the ion that tells the channel to go quiet. For now, hold only this: a rush of positive ions into a nerve ending drags the voltage across its membrane upward, and when that voltage crosses the nerve's own firing threshold, the nerve does the one thing a nerve can do. It fires. A pulse leaves for the brain down a dedicated wire — a *labeled line*, the trigeminal nerve, whose every message the brain has learned, since infancy, to read as one word: *heat.*



Phoenix (SS-0096) — the single pepper our family built to register on all eight of the body's doors at once — in the controlled chamber. The heat it carries is the loudest message any plant in the library sends.

The key cut for a door meant for flame

Here is the elegant, slightly mischievous mechanism, and it is worth slowing down for, because it is the entire answer to the child's question. Capsaicin does not heat the tissue. It cannot; it carries no warmth of its own, and the pepper is cool on the plate. What capsaicin does is subtler and cleverer than heating. It slips into a pocket on the *inside* face of the TRPV1 channel and, sitting there, it lowers the temperature at which the channel decides to open.

The pocket is real and it has a shape. Capsaicin — formally *8-methyl-N-vanillyl-6-nonenamide*, a tidy molecule of about 305 grams per mole — is built in three pieces: a flat aromatic **head** (the vanillyl ring, the same chemical face worn by vanilla and clove), a short **amide** bridge, and a long, floppy, oily **tail** of branched hydrocarbon. The head is the part that speaks to the receptor. It reaches into a cleft tucked against the channel's fourth membrane crossing and its linker, and there it is caught by a small handful of residues — a tyrosine and a serine foremost among them, Y511 and S512 in the usual numbering — that hydrogen-bond to the head's hydroxyl and methoxy groups and hold it still. Change that one tyrosine and the door goes deaf to capsaicin entirely; birds, whose version of the channel differs right there, taste no heat at all. The lock is that specific.

And the key arrives by a quiet road. Because its tail is so oily — capsaicin is strongly lipid-loving, with an oil-to-water partition in the thousands — the molecule does not drift up through saliva and knock at the pore from outside. It dissolves *into the membrane itself*,

slips along the fatty inner leaflet, and lets itself into the pocket from within, from the cytoplasmic side, the way a key reaches a lock through the back of the door. Everything that feels strange about the pepper's burn — that it builds slowly, that it will not rinse away with water — is already written in that single fact about where, and through what, the key travels.

Why the nerve cannot tell the difference

Once the head is seated, the channel does something with it. Binding in that inner pocket stabilizes the open shape of the gate and, in the only language the channel has, *resets the temperature at which it springs.* A door that was set to open at 43 degrees is quietly re-set to open at ordinary body temperature — around 37 degrees, the temperature the mouth already is. And so the channel opens. Not because anything got hotter, but because the threshold came down to meet the warmth that was always there.

The nerve cannot tell the difference. It has no way to. A TRPV1 channel that opens because the soup is scalding and a TRPV1 channel that opens because capsaicin lowered its threshold pass the *identical* current and send the identical pulse up the identical wire. The brain receives the word *hot* and believes it completely, because within the logic of the body it is true — this is exactly the signal a burn would send. The feeling of fire is not an error in the sense of a malfunction. Every part is working perfectly. It is a *mistake* only in the way a beautifully told lie is a mistake: the whole system is behaving honestly, and the result is still false. Nothing is burning. You only feel it.

How little it takes — the arithmetic of a lowered threshold

The loveliest thing about this deception is how small it is, and we can put a number on the smallness. Think of the channel as resting between two states — *closed* and *open* — separated by a free-energy gap we can write as

```
ΔG = ΔH − TΔS (open minus closed)
```

and let the fraction of channels standing open be the smooth Boltzmann curve

```
P(open) = 1 / (1 + e^(ΔG / RT)).
```

Heat opens TRPV1 because opening the gate is *entropy-driven*: the open state is the higher-disorder one (ΔS > 0), so as the temperature T climbs, the −TΔS term drags ΔG downward and P toward one. The midpoint — half the channels open, the threshold the body reports as *just now hot* — sits exactly where ΔG = 0, which rearranges to a clean little result:

```
T½ = ΔH / ΔS.
```

TRPV1 is famous in the biophysics literature for an enormous gating enthalpy — ΔH on the order of **+100 kcal/mol**, among the largest known for any ion channel, which is precisely why its response to

temperature is so knife-edge steep. Pin its midpoint to the measured threshold, 43 °C (316 K), and the entropy term falls out: ΔS ≈ 100 ÷ 316 ≈ 0.316 kcal/(mol·K).

Now ask what the channel is doing at body temperature, 37 °C (310 K), with no capsaicin present:

> ΔG = 100 − (310 × 0.316) ≈ **+1.9 kcal/mol**,

and with RT ≈ 0.62 kcal/mol that gives P(open) = 1 / (1 + e^(3.1)) ≈ **0.04**. About four channels in a hundred — the quiet, closed baseline of a mouth at rest. Good. The guardian is asleep.

Here is the whole magic trick in one line of arithmetic. For capsaicin to slide the midpoint down from 43 °C to 37 °C, it does not have to overpower the channel. It only has to erase that +1.9 kcal/mol — to stabilize the open state by

> ΔG(capsaicin) ≈ ΔS × (316 − 310) = 0.316 × 6 ≈ **−1.9 kcal/mol**

at full occupancy. That is *one modest hydrogen bond's worth of energy.* A whisper. The channel was always poised at the very edge of opening at body heat — four percent of the way through the door — and capsaicin simply leans on it with the gentlest possible pressure, and the door swings. We did not find a more reverent fact in the whole of this science than that the sensation of fire costs the molecule less than the energy of a single held breath between two atoms.

Reading loudness, not quantity — the index of the burn

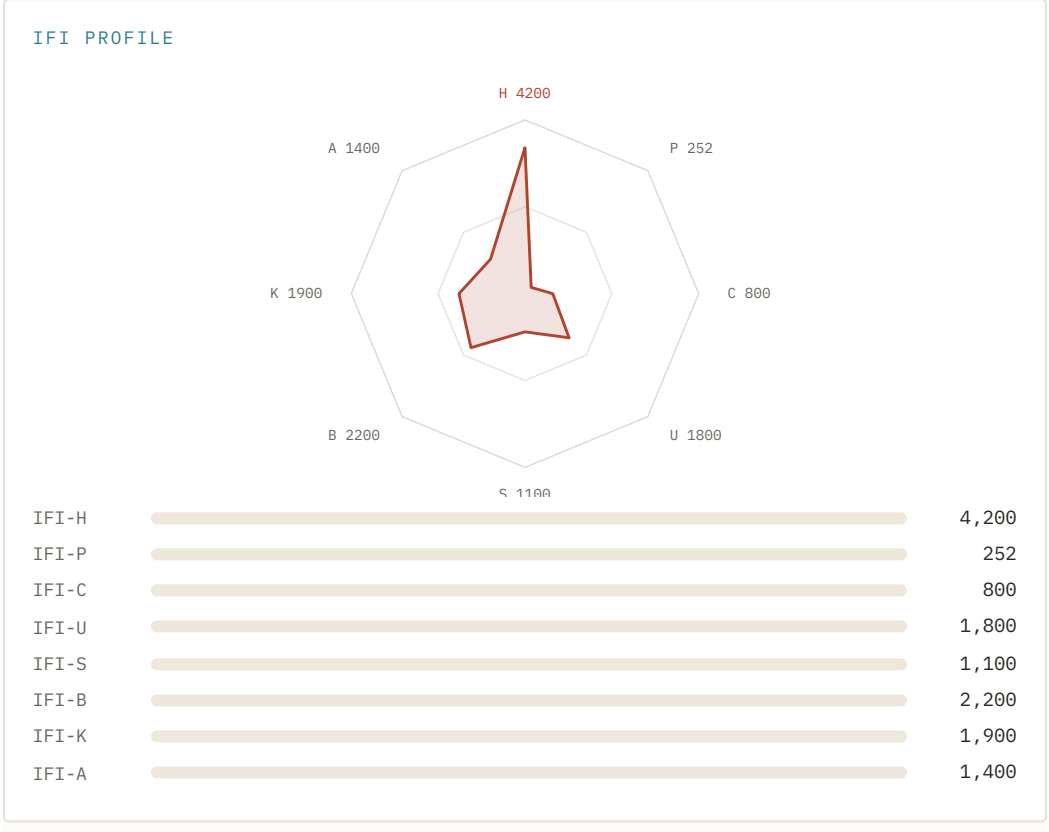
If capsaicin's effect can be this small and still be heard, then the honest way to measure a pepper is not to ask *how much* capsaicin it holds but *how loudly* that capsaicin speaks to the receptor. Those are different questions, and conflating them is the oldest confusion in the subject.

The quantity question has a classical answer: the **Scoville Heat Unit**. In its original form a pepper's extract was diluted in sugar-water, again and again, until a trained panel could no longer detect any heat; the fold of dilution that silenced it *was* the score. Pure capsaicin sits at **16,000,000 SHU** by definition, and modern instruments skip the tasting by measuring capsaicinoid concentration directly — roughly 16 SHU for every part per million. SHU is a content measure. It counts molecules.

The loudness question is what our family's index answers, and it is anchored not to content but to the receptor's own half-answer — its **EC_{50}**, the concentration at which a stimulus drives TRPV1 to half of its full response. The Iyengar Flavor Index is a stated convention — defined, like the Scoville scale's dilution-to-threshold definition, by its reference point rather than by a literature measurement — and it inverts EC_{50} against that fixed reference and scales it:

> $IFI(candidate) = 1{,}000 \times EC_{50}(reference) \div EC_{50}(candidate)$.

Read it slowly and it is just a sentence about loudness. A *smaller* EC_{50} means the receptor is half-open at a *lower* dose — the compound shouts, so it should score *higher*. Putting EC_{50} in the denominator does exactly that. The scale is pinned so that the half-activation of a native wild-type reference reads **1,000** on the heat axis by convention, and our model predicts the heat axis runs from the sunlit warmth of a shishito near 40 up to **Phoenix at 4,200**, against a per-axis ceiling of 5,000 — our loudest pepper sitting at 84 percent of the full height of the scale.



The formula makes a promise you can check with ordinary arithmetic. If Phoenix reads 4,200, then by the definition its receptor half-opens at

> $EC_{50}(\text{Phoenix}) = 1{,}000 \div 4{,}200 \times EC_{50}(\text{reference}) \approx 0.24 \times EC_{50}(\text{reference})$

— it needs under a quarter of the reference dose to say the same thing. In the published neighborhood where wild-type capsaicin half-activates TRPV1 near half a micromolar, that places Phoenix's active fraction near 0.12 µM. To feel how little that is: half a micromolar of capsaicin is about one part in six million by mass — a single gram dissolved in roughly six cubic meters of water would still, at half its channels, be called fire.

And because the receptor reads a *dose–response* curve, not a switch, we can turn any two index scores into a felt difference. Response climbs with concentration as a Hill curve,

> $\text{response} = [C]^n / (EC_{50}^n + [C]^n),$

with a Hill coefficient n ≈ 2 for capsaicin — a cooperativity that fits the tetramer's four pockets working together. Hold the dose fixed at the reference's own half-point and ask how far each pepper drives the receptor. The reference, by construction, sits at 50 percent. Phoenix, four-fold louder, reaches $1 \div (1 + 0.24^2) \approx$ **95 percent** of full

activation *at the very dose that only half-opens the wild type.* That single number — 95 against 50 — is what "4,200 versus 1,000" actually means on the tongue.

CULTIVAR · SKU	PREDICTED SHU	IFI-H	× LOUDER (IFI ÷ 1,000)	% OF TRPV1 DRIVEN AT THE REFERENCE'S HALF-DOSE
Ember · SS-0087	866K	1,570	1.57	71%
Cinder · SS-0088	1.05M	2,290	2.29	84%
Kindle · SS-0089	1.25M	2,000	2.00	80%
Blaze · SS-0091	1.72M	2,630	2.63	87%
Wildfire · SS-0092	1.96M	2,930	2.93	90%
Scorch · SS-0093	2.21M	3,220	3.22	91%
Firestorm · SS-0094	2.47M	3,490	3.49	92%
Solara · SS-0095	2.72M	3,980	3.98	94%
Phoenix · SS-0096	**2.95M**	**4,200**	**4.20**	**95%**

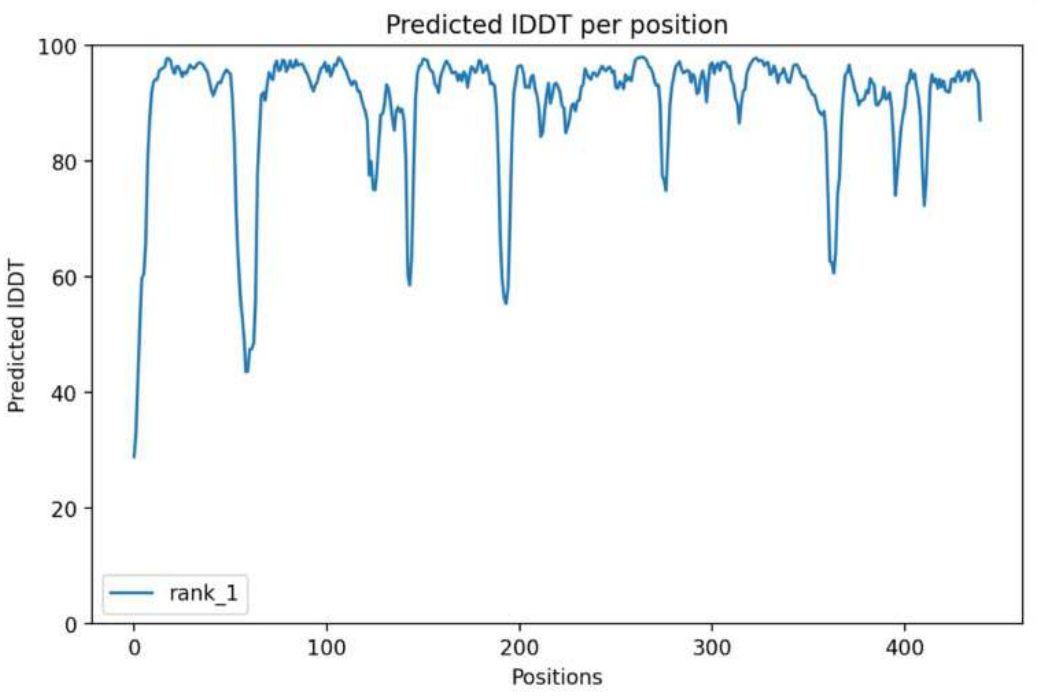
All SHU and IFI-H values are computational predictions from our design platform.

Run your eye down the two leftmost number columns and you will catch the subtlety that made us build the index in the first place. Kindle carries *more* raw heat than Cinder — 1.25 million Scoville against 1.05 million — and yet it scores *lower* on the index, 2,000 against 2,290. More molecules, a quieter voice. That is not a measurement error; it is the two questions pulling apart. SHU counts total capsaicinoid mass, but the family of capsaicinoids is not one molecule — capsaicin and its saturated twin dihydrocapsaicin are the loudest, while the lesser analogs speak more softly to TRPV1. A pepper that piles up mass in the quieter analogs can out-weigh a pepper that is leaner but richer in the loud ones, and still be the gentler burn. The index hears the *profile*; the Scoville scale only hears the *pile*. Dividing one by the other — Scoville per index point — Cinder comes in near 460 and Kindle near 625: a third again as much capsaicinoid bought per unit of loudness, all of it spent on molecules the receptor barely raises its voice for.

Where the key is forged

A key this precise has to be written somewhere, and in the pepper it is written by a single enzyme at the end of a long assembly line. The front of that line is the *phenylpropanoid branch* — **PAL → C4H → 4CL → HCT → COMT** — the same chemistry every green plant runs to build its scaffolds and scents, which is why what we learn here does not stay trapped in peppers. It carries the aromatic head toward its finished form as vanillylamine. A second, shorter line, drawing on branched amino acids, builds the oily tail. And then one enzyme, **capsaicin synthase** — the protein encoded at the *Pun1* locus — performs the marriage: it joins the vanillyl head to the branched acyl tail through that amide bridge, and capsaicin exists. The length and

saturation of the tail it chooses set the balance between capsaicin and dihydrocapsaicin, and with it the *shape* of the burn — how fast it arrives, how long it stays.



Pun1 / AT3 — capsaicin synthase — the enzyme that writes the key, colored by model confidence (pLDDT). The binding domain and the active-site cleft, where the vanillyl head meets the branched tail, are the high-confidence heart of the fold.

Every breeding program before ours chased heat from the outside — select the hottest fruit, save its seed, hope the genes followed. We turned it around and read the enzyme first. A protein language model scored every single-residue change Pun1 could tolerate by its predicted effect on catalytic efficiency and fold stability; a genome-scale flux model found that pathway control sits upstream in the phenylpropanoid branch — at 4CL and HCT/CCoAOMT — not at the terminal Pun1 step. Pun1 is the capsaicin synthase, the final enzyme that writes the product's name; it does not govern the rate. Out of that work came two substitutions no breeder had ever found because no fruit had ever shown them — and written in with CRISPR, our model predicts they lift peak output to approximately **2.95 million SHU** while keeping batch-to-batch variation under control.

EDIT	WHAT IT DOES	ΔΔG (KCAL/MOL)
S39L	raises binding affinity at the N-terminus	−2.1
L345G	relieves steric strain in the active-site cleft	−1.8

Structural annotation — not in shipped construct: C175S (disulfide-misfold prevention, ΔΔG −0.9) was identified in our structural modelling but pulled from the final design.

The ΔΔG column is the same currency we spent earlier on the receptor: each number is how much the edit stabilizes the working enzyme, and both are negative — each one makes the fold a little surer of itself. Their sum is why the pepper is not only louder but *repeatable,* and repeatability has its own arithmetic. We measure it as the coefficient of variation, CV = σ ÷ μ, the spread of a batch as a fraction of its mean. A wild-type pepper runs a CV near **42 percent** — so wide that at the usual ninety-five-percent band (±1.96 σ) a fruit's heat can nearly double or nearly halve from one harvest to the next. Our engineered lines are designed to hold **≤7 percent**, a band of about ±14 percent — the difference between a measurement and a guess.

That 7 percent is not an arbitrary target; it falls out of the index's own error budget. The IFI is a *ratio* of two EC_{50} measurements, the reference's and the candidate's, and the relative errors of a ratio add in quadrature:

```
CV(IFI) = √( CV(reference)² + CV(candidate)² ).
```

Hold each EC_{50} assay to a careful 5 percent and the index inherits $\sqrt{(5^2 + 5^2)} \approx$ **7 percent** — the very number we hold the peppers to. The precision of the fruit and the precision of its score were engineered to meet in the same place.

The shape of the burn in time

Now the small facts about spice that a child notices, and that no one usually explains, fall out one after another from the oily road the key travels.

Why does the burn *build* — rise for a minute or two after the bite rather than strike all at once? Because capsaicin is lipid-loving and slow. It has to partition out of saliva, into the membrane, and along the fatty leaflet to reach that inner pocket, and partitioning takes time. The sensation is the receptor filling as the molecule arrives, a tide and not a switch.

Why does it *linger* so long after the pepper is gone, far longer than a sweet or sour taste fades? For the same reason, run backward. Sweet and sour molecules sit in open pockets facing the watery outside and rinse away in a swallow. Capsaicin is dissolved *inside* the membrane; there is almost no water for it to leave into, so it lingers where it lodged and keeps speaking until the tissue slowly clears it.

And why does water fail you, every time, and milk work? Because you cannot rinse an oil with water. The fix has to dissolve or carry the molecule away, and the kitchen has always known two that do: fat, which capsaicin dissolves into gratefully, and the milk protein casein, which wraps around the oily tails and lifts them off the membrane like a surfactant. A spoonful of yogurt, a little ghee, a swallow of whole milk, a cooling draught of coconut — these are not folk comfort. They are partition chemistry, and they are kind to a mouth in a way a glass of water, chasing an oil it can never catch, can never be.

When the alarm stops lying

There is a dose beyond which the metaphor breaks and the signal becomes something harder. A little warmth is pleasant; a lot can feel like genuine danger — because at high occupancy TRPV1 really does begin reporting toward *true* pain, the body's honest nociception, the alarm fully tripped even though the tissue is still, chemically, unharmed. The lie has been told loudly enough that the body answers as if it were true.

And then the second role of calcium arrives. The channel that let calcium flood in now listens to it. Sustained calcium entry recruits calmodulin, depletes the signaling lipid the channel needs to stay responsive, and the gate begins to close against the very molecule

holding it open — a process called *desensitization*, or tachyphylaxis. It is why the second bite of a dish burns less than the first, why people who eat chili often grow into more of it: the guardian, overwhelmed, turns its own volume down. This is also the quiet paradox at the center of the molecule — the same compound that shouts *fire* is used, at steady high dose, to make nerves fall silent, which is how capsaicin can be a painkiller as readily as a pain. It does not soothe by numbing the tissue. It exhausts the alarm.

There is one more gift in the sequence, and it may be the tenderest. Faced with a convincing pain signal and no injury to match it, the body answers with its own soothing chemistry — a release of the calm it keeps in reserve for real hurt. The warmth that floods in after the fire is real, even though the threat never was. A good part of the pleasure of spicy food is exactly this: a false alarm, raised vividly, safely survived, and answered by the body's own kindness.



Backlit greenhouse at golden hour, a single pepper hanging in the light — where the whole conversation between a plant and a nerve begins.

What the index cannot hear

We would mislead you if we let the number stand for more than it is, so here, plainly, is what the index cannot measure.

It measures loudness, not pleasure. EC_{50} tells you how little capsaicin it takes to reach the receptor's half-answer; it says nothing about whether the burn is welcome, whether it arrives round or sharp, whether it flatters a mango or ruins it. A score of 4,200 is a fact about a channel, not a verdict about a meal.

It is anchored to one reference receptor, and receptors differ. Birds carry a version of TRPV1 whose binding residues will not hold the vanillyl head, so to a bird a chili is simply fruit — which is the plant's entire evolutionary point: a seed ground up in a mammal's molars

dies, while a seed carried in a bird goes somewhere new. The heat was never aimed at us. Even among people, the channel's density and small genetic variations mean the same pepper lands differently on different tongues, and prior exposure shifts the whole curve through the desensitization we just described. The index fixes a single standardized receptor, temperature, and pH precisely so that the number means one thing; the living mouth is more various than any single number can be, and we would rather say so than pretend otherwise.

And it measures one axis of eight. Heat is the loud one, the one a child asks about first, but the same receptor-anchored arithmetic reads sweetness, umami, the attenuation of bitterness, the slow richness of kokumi, the cool of menthol, the sharp lift of pungency, the drying pull of a tannin. The IFI scores on each axis are referenced to their own axis-specific convention constant, not to a single common scale — a heat score and a pungency score each say something precise about their own receptor, not something directly comparable to each other. The pepper on the page registers a little of nearly all of them. The heat is only the sentence it says most loudly.

A plant that learned to shout

We find this the most tender fact in the whole science, and we come back to it whenever someone frames heat as a dare or a punishment. Capsaicin does not damage you. At the doses a kitchen uses it leaves every cell exactly as it found it. What it does is borrow the body's own language of warmth and speak a single sentence in it — loudly, vividly, and without a word of harm.

A chili is not an attack. It is a plant that learned to shout *fire* in a room where nothing is burning, and the oldest, most watchful part of us, doing its job perfectly, answers. When we design a pepper to speak that sentence more clearly — to hold its heat to seven percent instead of forty, to place its loudness where we meant it and keep the fruit honest from one harvest to the next — we are not making the lie bigger. We are making it *truer to itself*: a warmth given to the body on purpose, computed to the whisper of energy it really costs, grown to nourish and never to wound. That is the shape of the answer, and the shape of the care underneath it. Nothing is burning. You only feel it — and now you know, to a tenth of a kilocalorie per mole, exactly how.

These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.

Chapter 3 · The Shape of the Key — *what capsaicin actually is.*

A key is only a key because of its shape. Capsaicin opens the body's fire-door for one reason and one reason only: it is cut, in three dimensions, to fit a pocket inside a protein called TRPV1 the way the teeth of a key fit the pins of a lock. Press the right shape into the right opening and something turns. So when a child at the table asks *why is it spicy* — and in our family that is the sort of question allowed to hold a whole evening — the honest answer sends us all the way down, past the fruit and the flesh and the seeds, to one small molecule and the one small door it was born to fit.

It is worth saying plainly before we begin: nothing in a pepper's heat is warmth. Not a single degree of it. The fire is a message, not a temperature, and this chapter is the anatomy of how a particular shape becomes a message the body cannot help but believe. To see that, we have to look at the molecule itself — and it turns out to be a small, two-part thing with a quietly revealing name.

A forbidding name that is only a set of directions

Chemists call capsaicin *8-methyl-N-vanillyl-6-nonenamide*. It looks like a wall of jargon and is actually a set of plain instructions — read from the end backward, it builds the molecule a piece at a time.

One half is a **vanillyl group**: the same flat six-sided carbon ring that gives vanilla its scent, wearing a hydroxyl (–OH) and a methoxy (–OCH_3) like a small lopsided hat. The other half is a **fatty-acid tail** — the *nonenamide* — a short carbon chain nine atoms long, with a single double bond a third of the way down (the *6-ene*, a permanent bend) and a two-pronged fork near the far end (the *8-methyl*, a branch). The two halves are tied together by an **amide bond**, the identical patient knot that links every bead in every protein you are made of. Ring on one end, oily tail on the other, amide knot in the middle. That is the entire architecture of capsaicin, and every forbidding syllable of the name is only an instruction for drawing it.

Counted up, it is eighteen carbon atoms, a scattering of hydrogens, one nitrogen in the knot and three oxygens on the ring, and it weighs **305.4 grams per mole** — the mass of a mole of them, about six hundred thousand billion billion molecules, light enough to sit on a fingertip and never be felt. A tiny thing. And nearly all of what it does is decided not by what it is made of but by the shape those atoms fall into.

Why the shape is the whole story

Walk the key into the lock and watch which part does what, because the behaviour of a pepper is hiding in the geometry.

The **vanillyl ring is the business end**. It reaches into a pocket on the inner face of TRPV1, and the hydroxyl group it wears — that little –OH — reaches a fraction further and forms a **hydrogen bond** to the wall of the pocket: a faint, precise, directional clasp, the molecular

equivalent of a magnet finding its mate. That single bond is what anchors the key in register, holding the ring in exactly the orientation the pocket wants. The **oily nine-carbon tail**, meanwhile, drapes into a long greasy groove in the protein — a hydrophobic channel that water flees and oil loves — and lies there, steadying the whole molecule the way a kickstand steadies a bicycle. Clasp at one end, grip along the other.

Held in both places at once, capsaicin does its quiet work. It does not pour energy into the channel; it simply makes the channel's *open* shape a little more comfortable than its *shut* one, and so tips the balance. TRPV1 in its ordinary life is a thermometer, built to swing open only when the tissue around it grows genuinely hot — above about **43 °C**, the temperature at which real heat becomes real danger. In Fahrenheit that threshold is

```
(43 × ⁹⁄₅) + 32 = 109.4 °F
```

while the resting mouth sits near 37 °C, which is 98.6 °F — comfortably below the trip point, so the channel stays shut and silent. Capsaicin, bound in its pocket, *drags that threshold downward*, below the temperature the mouth already is. The channel, finding itself suddenly "too hot" at a temperature that never moved, throws its gate wide. Sodium and calcium ions flood through the opened pore; the trigeminal nerve ending depolarizes and fires; the signal climbs to the brain, which has no way to know the alarm was pulled by a molecule rather than a flame, and reports the only thing that signal has ever meant — *fire*. A true alarm raised by a false emergency.

Now the reason the shape *is* the story. Spoil the clasp — strip the –OH off the ring — and the key still slides into the pocket but no longer holds in register; the molecule goes quiet, the burn all but vanishes. Spoil the grip — shorten the tail, or straighten its bend, or move its fork — and the molecule still binds but sits a little wrong, and the burn weakens or changes its character entirely. The spiciness of a pepper is, very literally, the shape of this one small molecule read by the shape of one small door. Change the shape and you change the message.

Where the fire is actually made



FIG. 1 — a superhot pepper opened along its length. The pale ribs and the spongy tissue cradling the seeds — the *placenta* — are the kitchen where capsaicin is built and stored, molecule by molecule, long before any tongue arrives. The heat of a pepper has an address, and it is not the flesh.

Cut a pepper in half and the heat is not where most people point. It is not in the seeds, and it is not in the walls of the fruit. It is in the pale, slightly spongy ribs running down the core — the **placental tissue**, the cradle the seeds are attached to — where tiny blister-like vacuoles hold droplets of capsaicin against the day a mouth comes to carry the seed elsewhere. The plant is not trying to hurt you; it is trying to be remembered, and to be planted, and the fire is an old and eloquent bargain struck with the animals that help it. We would rather understand a plant like this than merely harvest it, and understanding it means asking how so small a cell builds so exact a molecule.

It builds it on a bench with two arms that meet in the middle. The **ring arm** starts from the amino acid phenylalanine and runs down the **phenylpropanoid branch** — the enzymes **PAL → C4H → 4CL → HCT → COMT**, a sequence of cuts and dressings that turns phenylalanine first into cinnamic acid, then coumaric, then along to ferulic acid and vanillin, before a final aminotransferase called **pAMT** fits it with the nitrogen that makes **vanillylamine**, the ring half of the key. Nearly every green plant on Earth runs that branch for its own reasons; it is the common road. The **tail arm** starts from a branched-chain amino acid, handed off by **BCAT** and elongated by the fatty-acid builder **KAS** into the kinked, forked, nine-carbon acid that becomes the tail. And at the join sits the enzyme that makes a pepper a pepper: **Pun1**, also called capsaicin synthase, which takes the vanillylamine in one hand and the activated fatty acid in the other and ties the amide knot between them. Ring plus tail plus knot — and the key is finished, and the droplet forms, and the fruit grows quietly dangerous.

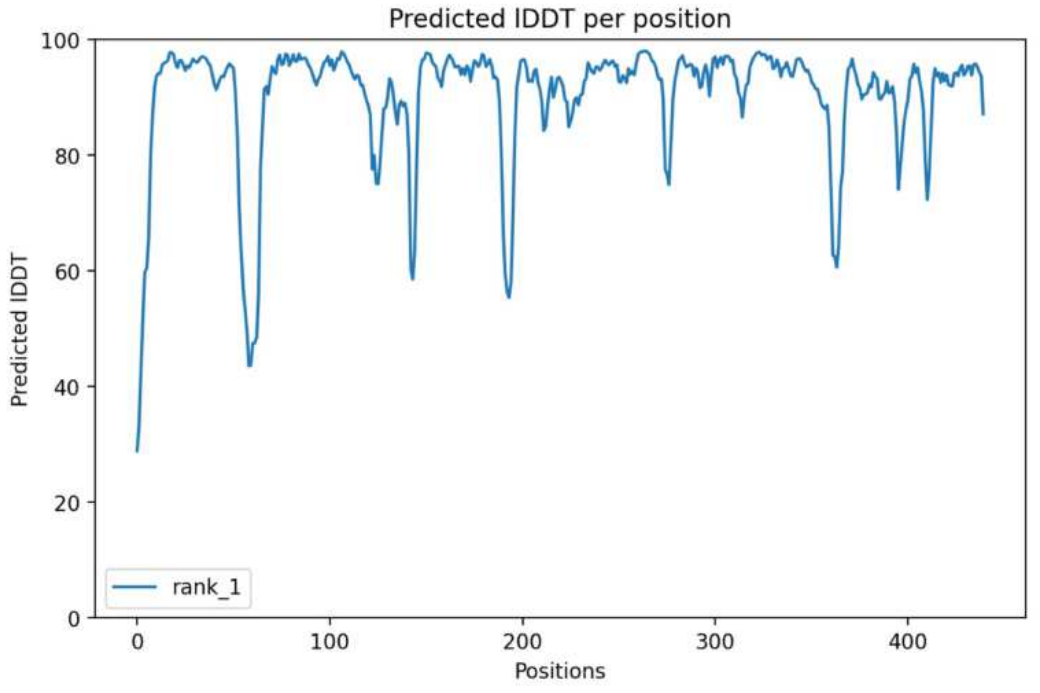


FIG. 2 — the Pun1 enzyme, modeled and tinted by the model's own confidence: bright where the fold is certain, pale where it is not. This is the machine that forges the key — the single step that turns a common plant road into a pepper — and we could not change a flavor until we could see it steadily.

The two keys, and the shape of the burn

Here is the thing almost no one is told: a pepper does not make *one* key. It makes a small family of them — the **capsaicinoids** — all built to the same ring-tail-knot plan, differing only in small variations of the tail. Two of them carry most of the heat in most peppers, and the quiet arithmetic between them decides how a pepper *feels*.

The first is capsaicin itself, with the single bend in its tail — the *6-ene*. The second is its near-twin **dihydrocapsaicin**, identical in every way except that the bend has been straightened: the double bond saturated, two hydrogen atoms added across it. That is the whole difference, and you can watch it in the mass. Saturate the one bond and the molecule's weight creeps from 305.4 up by the mass of two hydrogens to about **307.4 grams per mole** — a change of two atoms in a molecule of fifty-odd, and yet the burn it carries is a different burn.

CAPSAICINOID	THE TAIL	MOLAR MASS (G/MOL)	THE BURN IT CARRIES
Capsaicin	one bend — the *6-ene*	305.4	fast, bright, high in the mouth; fades sooner
Dihydrocapsaicin	straightened — bend saturated	~307.4	slow, deep, low in the throat; stubborn, lingering

A kinked tail and a straight tail sit in TRPV1's greasy groove a little differently, grip for a little different length of time, and the nerve reports the difference as *shape*: capsaicin a flash at the front of the mouth, dihydrocapsaicin a pressure that builds in the back and will not leave. So the **ratio** of the two — how much of each a pepper happens to make — sets the pepper's whole character. Two chilies can carry the identical total amount of heat and feel like entirely different experiences, one a bright slap and the other a slow tide, because the shape of the burn is the shape of the tails. For ten thousand years the only way to move that ratio was to grow a thousand plants, taste them, and keep the seed of the one whose

fire you liked best. It worked, slowly, and it gave the world every chili we inherited. But it could never say *how much*, and it could never hold a result still.

Turning a shape into a number

To hold a result still you first have to measure it, and the trouble with measuring heat is that *how much capsaicin a pepper holds* and *how loudly that capsaicin speaks* are not the same question. What we needed was a measure of loudness: how readily the key turns the lock, not how many copies of it are lying about.

Pharmacology already keeps the right instrument. It is the **EC_{50}** — the concentration of a stimulus at which its receptor reaches half of its full response. A low EC_{50} means the lock turns while only a little key is present: a loud, potent signal. A high EC_{50} means you must crowd the pocket before the gate will budge: a quiet one. Loudness is simply the inverse of EC_{50}, and the whole Index is built on that inversion. Fix a steady reference constant — a stated convention on each axis, the same way Scoville's dilution-to-threshold definition anchors SHU — measure the candidate against it, invert, and scale by a thousand so the everyday numbers land in a friendly range:

$$\mathrm{IFI}(\text{candidate}) = 1{,}000 \times EC_{50}(\text{reference}) \div EC_{50}(\text{candidate})$$

Read it slowly and it teaches you how to think. Set the candidate equal to the reference and the fraction becomes one and the score becomes exactly **1,000** — the anchor, the loudness of the standard itself, forced by the arithmetic. More potent than the reference, the EC_{50} shrinks and the score climbs above a thousand; weaker, it falls below. For the scorecards in this book each axis is normalized to a ceiling of **5,000**, the loudest we have yet had cause to print.

A worked example keeps it honest. Our most complete pepper, the one we call Phoenix, reads **4,200** on the heat axis. Put that into the formula and solve for what it says about the meeting in the mouth:

$$4{,}200 = 1{,}000 \times EC_{50}(\text{reference}) \div EC_{50}(\text{Phoenix})\quad EC_{50}(\text{Phoenix}) = EC_{50}(\text{reference}) \times 1{,}000 \div 4{,}200 = 0.238 \times EC_{50}(\text{reference})$$

So Phoenix's standardized extract drives TRPV1 to half-maximal firing at just under a quarter — twenty-four percent — of the concentration the reference needs. It is, in the exact sense the number carries, **4.2 times louder** than the standard. Not 4.2 times more of anything. 4.2 times louder. The arithmetic runs just as cleanly the other way, which is how you aim a design before a seed is ever sown: want a pepper three times louder than the reference, and you are asking for an IFI-H of 3,000, which demands an EC_{50} of 1,000 ÷ 3,000 = 0.333 of the reference's — a third of the material for the same half-maximal fire. And a loudness is easy to convert into a fraction of the printable ceiling: Phoenix's 4,200 divided by the 5,000 maximum is 0.84, so on heat it sits at eighty-four percent of the loudest note the scorecard can hold.

The single point EC_{50} names is really the midpoint of a whole curve, and the curve has a shape worth seeing. Push a stimulus at a receptor across a range of concentrations and the response is not a

straight line but an **S lying on its side**: almost nothing at low concentration, a steep climb through a middle band, then a flattening as every lock that can turn has turned. The equation that draws it is friendlier than it looks:

```
response = R_max × [C]ⁿ ÷ (EC₅₀ⁿ + [C]ⁿ)
```

Set the concentration [C] exactly equal to EC_{50} and the algebra falls open — $EC_{50}^{n} \div (EC_{50}^{n} + EC_{50}^{n}) = EC_{50}^{n} \div 2EC_{50}^{n}$ = one half — half-maximal response every time, by construction. The exponent **n**, the Hill coefficient, measures how switch-like the climb is, and here the physical shape of the lock returns to the story. TRPV1 is not one protein but four, a **tetramer**, four identical subunits gathered around a single central pore, each carrying its own capsaicin pocket. When the keys bind cooperatively — the first making the next easier — the curve steepens, and TRPV1's heat response climbs with a Hill coefficient near 2: a narrow band of concentration over which the mouth goes from noticing nothing to a definite flame. It is why heat so often seems to arrive all at once, a step rather than a ramp.

The ladder, read two ways

Behind that one heat number stands a ladder of peppers, each louder than the last, and the ladder is where the new way of measuring earns its keep. The old way is the **Scoville scale**, invented in 1912: dilute a pepper's extract in sugar water, cup by cup, until a panel can no longer detect any burn, and report the dilution in Scoville Heat Units (SHU). It is heroic for its age, but it is a human panel's guess at the vanishing point of sensation. The Index reads a different place on the same curve — the receptor's own halfway mark — and setting the two side by side tells you something true.

CULTIVAR	SKU	PREDICTED SHU	IFI-H	SHU PER IFI-H POINT	AXES
Ember	SS-0087	866K	1,570	552	2/8
Cinder	SS-0088	1.05M	2,290	459	3/8
Kindle	SS-0089	1.25M	2,000	625	3/8
Flare	SS-0090	1.48M	—	—	4/8
Blaze	SS-0091	1.72M	2,630	654	4/8
Wildfire	SS-0092	1.96M	2,930	669	5/8
Scorch	SS-0093	2.21M	3,220	686	5/8
Firestorm	SS-0094	2.47M	3,490	708	6/8
Solara	SS-0095	2.72M	3,980	683	6/8
Phoenix	SS-0096	2.95M	4,200	702	8/8

All Predicted SHU values are computational estimates from our thermodynamic and flux models. The Axes column reflects the number of IFI dimensions each design is computed to register on; each cultivar represents a distinct computational design tier by scope and axis activation.

Look at the third column of numbers — the SHU it costs to buy a single point of IFI-H. If the two scales measured the same thing, that column would be flat. It is not. It drifts from about **552** at the bottom of the ladder up past **700** near the top, with a dip to **459** where Cinder's blend runs louder than its mass would predict and a bulge

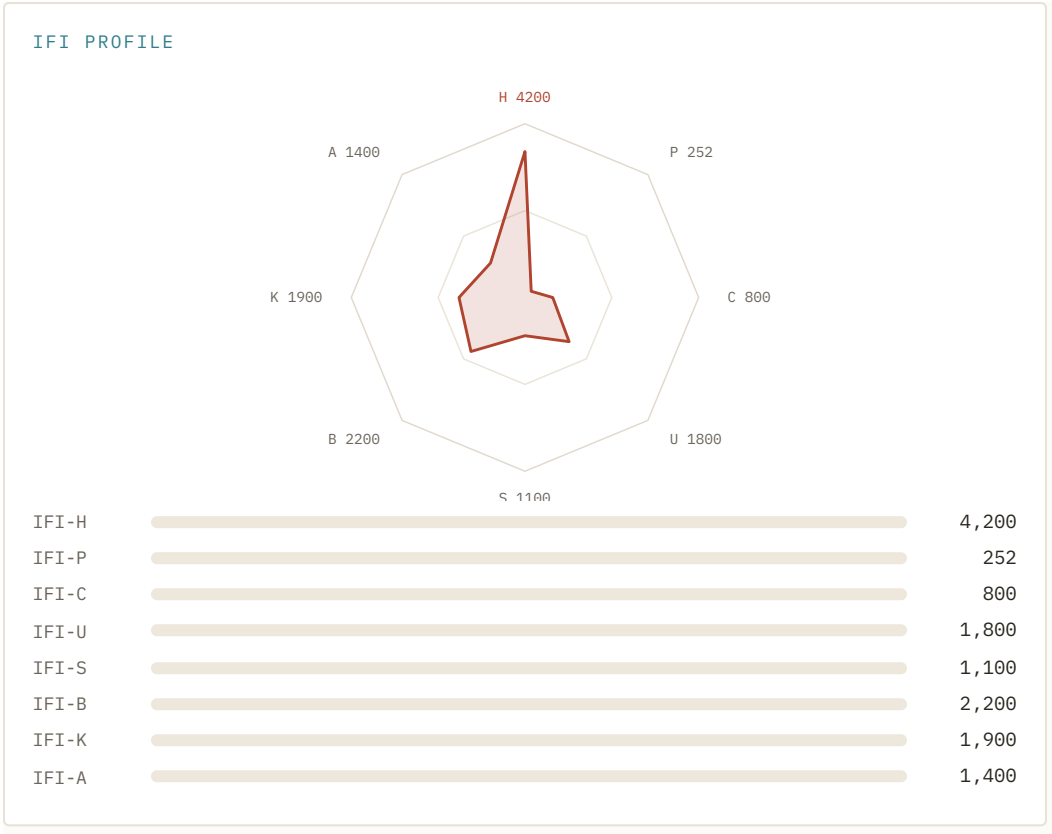
to **625** where Kindle's runs quieter. That drift is not sloppiness in either instrument. It is the signature of the two keys. Scoville weighs the *total capsaicinoid mass* and, because its panel chases the faint last tail of the burn, it over-counts the slow, lingering dihydrocapsaicin that haunts the threshold. The Index weighs the *loudness at the midpoint*, where fast, bright capsaicin dominates. A pepper rich in the straight-tailed cousin can pile up Scoville units while its receptor-midpoint lags; a pepper rich in the kinked key can speak loudly on less mass. The gap between the two columns is, quite literally, the shape of the tail made visible. When our family first held both numbers for the same fruit and watched them disagree, that was the morning the Index stopped being a convenience and became a necessity.

The pepper that speaks on all eight doors



FIG. 3 — Phoenix under the stage light, the first cultivar we built to register on every axis of the Index at once. A pepper is spicy because, deep in the spongy tissue cradling its seeds, it assembles a molecule shaped like fire and sends it to a door built to feel fire — and the body believes.

Most peppers are a single loud note. Phoenix is a chord. Here it is read on all eight doors of the Index at once:



Turn each of those scores back through the formula and the chord comes into focus — each axis as a fold-change in loudness over its own stated reference constant, and as a fraction of the 5,000 ceiling:

AXIS	RECEPTOR	IFI	LOUDNESS VS REFERENCE (IFI ÷ 1,000)	% OF 5,000 CEILING
Heat · H	TRPV1	4,200	4.20×	84%
Zero-Bitter · B	TAS2R38	2,200	2.20×	44%
Kokumi · K	CaSR	1,900	1.90×	38%
Umami · U	mGluR1	1,800	1.80×	36%
Astringency · A	salivary PRPs	1,400	1.40×	28%
Pungency · P	TRPA1	252	0.25×	5%
Sweetness · S	TAS1R2·R3	1,100	1.10×	22%
Cool-Burn · C	TRPM8	800	0.80×	16%

Heat towers, as it should — 4.2 times the reference's loudness, eighty-four percent of the printable ceiling. But look at the bottom row and the honesty of the number shows. On the cooling axis, Phoenix reads 800, which is 0.80× — *below* the reference. A pepper that speaks on all eight doors is not shouting through all eight; on cool-burn it murmurs, quieter than the ordinary standard. "Eight out of eight" means *present*, not *maximal*. The art was never to pin every axis to the ceiling — that would be a wall of noise, not a flavor — but to make a plant that can be *heard* on every door at once, and then to tune the volumes on purpose.

One note on reading across axes: each IFI score is normalized against its own stated reference constant — a convention defined for that axis, the same way Scoville's threshold is defined on its own terms. The H and P axes anchor against different defined reference

points, so a score on one axis is not directly comparable in absolute biological terms to a score on another. Each number says how loud that axis sounds against its own anchor.

Two letters

Tuning them on purpose means editing the machine that forges the key. In a wild pepper, Pun1 works, but it works *unevenly* — fruit to fruit, plant to plant, the capsaicin it turns out swings wildly, with a coefficient of variation (the standard deviation divided by the mean) near **42 percent**. That is a plant no one can design around: two fruits off the same bush can differ by nearly half, and a number that wanders that far is not a measurement but a shrug.

So we read Pun1's structure and rewrote two of its amino acids — two letters in a chain of hundreds:

- **S39L** — a serine swapped for leucine near the enzyme's front end, firming the grip on what it binds;
- **L345G** — a leucine opened to the small, limber glycine, relieving a crowded spot in the active-site cleft so the reaction runs cleaner.

Neither substitution was found by the old breeder's patience. A protein language model, trained on the grammar of millions of natural proteins, proposed the edits most likely to raise the enzyme's precision without unfolding it; our flux model of the whole pathway showed that metabolic control over capsaicin output sits upstream — in the phenylpropanoid steps, at 4CL and HCT in particular — not at Pun1, which our model assigns near-zero flux control; and CRISPR wrote the two letters into the genome. The edits did one decisive thing: they steadied the hand. Our design targets batch-to-batch variation of **7 percent or below** — and Phoenix's predicted heat of approximately **2.95 million Scoville units** reflects the upstream pathway design, expressed with that designed precision from harvest to harvest.

What that steadiness buys, you can compute, because the inverse form of the Index carries a relative error almost unchanged into the score. At the wild plant's 42 percent, a nominal heat of 4,200 lands at

```
4,200 ± (0.42 × 4,200) = 4,200 ± 1,764
```

— anywhere from about 2,400 to nearly 6,000, a band so wide it swallows half the ladder. At 7 percent the same score tightens to

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4,200 ± (0.07 × 4,200) = 4,200 ± 294
```

— a tidy 3,900 to 4,500. Precision is not the opposite of wonder here. It is what lets the wonder be the same twice: the loudness becomes a fact you can build a sauce on, a recipe on, a shelf of them on, and hand to someone else knowing their fire will be yours.

What the number can't hold

An instrument that forgot its own edges would be lying, so let us name three while the key is still in our hand.

The number measures total loudness, but the *shape* of the burn — the front-of-mouth flash against the back-of-throat tide — lives in the ratio of the two keys, and a single heat score, honest as it is, averages that ratio away. Two peppers can share an IFI-H and arrive in the mouth as different weather. The deeper reading is always the blend, not the sum.

The mouth, too, keeps changing while it reads. Sit with chili heat for a few minutes and the calcium that flooded through TRPV1 sets off a slow feedback that dials the channel down — it **desensitizes** — which is why the third bite of a hot dish lands softer than the first, and why heat can be built to and lived in rather than merely survived. The Index measures a clean first meeting between a rested receptor and a standard stimulus; a long dinner is a moving target, and the number is the opening note, not the whole song.

And you are not the reference, and neither are we. The locks themselves vary from person to person, so the same fruit is a glow to one eater at the table and a wall to another, with no disagreement about the pepper. A number tells you how loudly the note is played. It cannot promise how loudly you, in particular, will hear it.

These are not apologies; they are the true shape of an honest instrument, and an instrument that knows its own edges is the only kind worth designing with. For all of that, the plain fact at the center stays miraculous, and it is the one the child was reaching for all along: a pepper is spicy because, in the pale tissue that cradles its seeds, it assembles a small two-part molecule — a ring, a tail, a knot — shaped so exactly like fire that a door built to feel fire swings open at its touch, and the body, meaning only to protect itself, believes a flame that was never lit. We have learned to read that molecule to within a few percent of itself. We have learned to change two letters of the machine that builds it. These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory. And still, every harvest, there is the quiet astonishment of it — that so much sensation, and so much care, can be folded into a shape so small you could never feel its weight.

Chapter 4 · Why Water Makes It Worse — *the kitchen science of relief.*

Every family that has ever eaten something too spicy has reached, in the same reflex, for the same wrong cure: a glass of cold water, gulped fast. And it does not work. Often it is worse than nothing — a brief, false relief while the cold is in the mouth, and then the fire roaring back, sometimes spread wider than before. This is not bad luck, and it is not a failure of nerve. It is chemistry, written in a single molecule and a single receptor, and once you can read it you will never reach for the water again. You will have in your hands one of the most satisfying little experiments a kitchen can offer, and — more than that — a working picture of how a feeling in the body becomes a number on a page, which is the whole promise of this book, run small enough that a child can hold it.

We want to do more here than hand you a trick. We want to walk the fire all the way down: from the shape of the molecule, to the door it opens on the tongue, to the exact arithmetic that tells you why milk wins and water loses, to the scale that lets us measure the burn in the first place and the engineered fruit at the far end of that scale. It is all one story, and every part of it is countable.

The one fact behind all of it: capsaicin is an oil

The single most important thing to know about capsaicin, after the fact that it exists at all, is that it is **oily**. In the language of chemistry it is *nonpolar* and *lipophilic* — fat-loving, water-fearing. Everything downstream, every cure that works and every cure that fails, follows from that one property, so it is worth seeing exactly where it comes from.

The molecule has three parts, and they do not get along with the same company. At one end sits the **vanillyl head** — a small aromatic ring carrying a hydroxyl and a methoxy group, the same chemistry that gives vanilla its name and its warmth. That head is polar. It can donate and accept hydrogen bonds; it is, by itself, reasonably content in water. Then comes a short **amide linkage**, the hinge. And then, dominating the whole molecule by length and by mass, a long **branched, unsaturated fatty tail** — in capsaicin proper, an 8-methyl-6-nonenamide chain, a greasy carbon rope with a kink of unsaturation in it. That tail is pure oil, and it is most of the molecule. A small polar head stapled to a long oily tail: capsaicin is a creature of fat wearing a thin disguise of solubility.

The formula is $C_{18}H_{27}NO_3$, a molecular weight of about 305.4 grams per mole — not large, but shaped so that water cannot hold it. Carbon tails and water refuse to mix, the way oil and vinegar separate in a bottle no matter how you shake them, because forcing a greasy chain into water makes the water molecules cage it in and lose their own freedom, and nature will not pay that price if it can

help it. So capsaicin flees water and crowds into any fat it can find — the membranes of your cells, the butterfat in a sauce, the film of oil already clinging to the warm surfaces of your mouth.



A pepper, opened. The heat is not in the flesh and not in the seeds but in the pale placental ribs that cradle them — the oily tissue where the fruit lays capsaicin down, drop by drop, in glands too small to see.

This is also where the fruit keeps it. Cut a pepper and the heat is not in the shining flesh you expected, nor really in the seeds, but in the pale ribs of placental tissue that hold the seeds — an oily tissue, built to store an oily molecule. The plant and the molecule agree on this point. Capsaicin lives in fat, and if you want to move it, you will have to speak to it in fat.

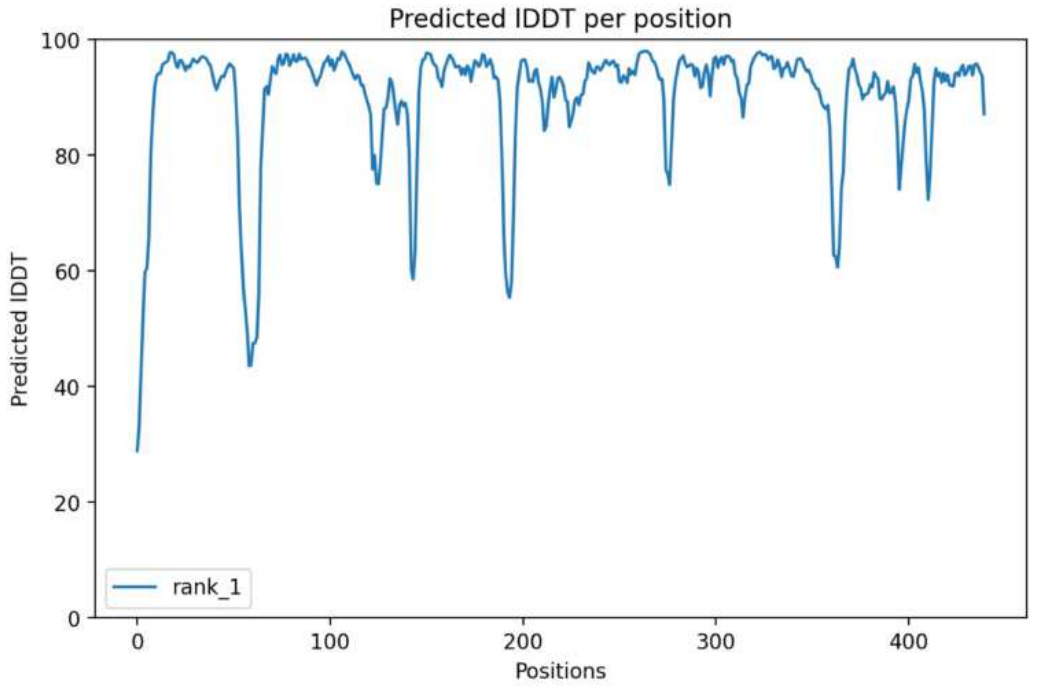
How the fire is lit — capsaicin at the TRPV1 door

Nothing about a pepper is actually hot. There is no heat in the fruit, no warmth released on your tongue. The fire is a report — a true nerve, firing a false alarm — and understanding the lie is the key to answering it.

Capsaicin binds **TRPV1**, a non-selective cation channel standing in the membranes of the trigeminal nerve endings that wire the mouth. TRPV1 is one of the eight receptors this book is built around; on the Iyengar Flavor Index it anchors the heat axis, **IFI-H**, and it is a sensible, important little machine. It is *polymodal*: it is a thermometer that opens to real heat above about **43 °C**, it opens to acid when protons crowd in, and it opens to capsaicin. Its honest job is to warn you when tissue is getting dangerously hot. Capsaicin hijacks exactly that job.

The molecule reaches the channel the way its oiliness demands: not swimming up through the watery saliva to knock on the front door, but slipping sideways into the lipid membrane and approaching the receptor from within the fat, through a pocket — the vanilloid-binding pocket — that opens to the membrane's interior. There the polar vanillyl head does the delicate work, settling into the pocket and hydrogen-bonding to the residues that line it (the tyrosine and serine of the binding cleft are the classic handshake), while the oily tail anchors the whole molecule in the surrounding lipid. The disguise and the body of the molecule each do their part: the tail delivers it, the head binds it. This is why a water-soluble decoy would never work. The oiliness is not incidental to the burn. It is the delivery system.

Once bound, capsaicin does something quietly profound. It does not warm the tissue by a single degree. It **lowers the channel's thermal threshold** — it drags that 43 °C trip point down below the temperature of your own mouth, below body heat, in strong cases down toward room temperature. The channel, now set to open at a warmth that is always present, opens. Calcium and sodium ions pour inward, the nerve ending depolarizes, an action potential races up the trigeminal nerve, and the brain receives the message it was built to receive from a hot stove: *burning, here, now.* The fire is real as a signal and fictitious as a fact. The tongue is telling the truth about a lie.



The enzyme that builds the fire: Pun1/AT3, modeled residue by residue and colored by confidence. Here the vanillyl head is joined to the long oily tail that makes capsaicin a creature of fat — and here, at two substitutions our family designed (S39L, L345G), we taught it to build more.

A small refinement, because it changes the *shape* of the fire and later the shape of the relief. Capsaicin is not alone; it travels with its near-twin **dihydrocapsaicin**, whose tail carries no kink of unsaturation. The ratio between them is set at the plant's own assembly line — the Pun1/AT3 acyltransferase that condenses the vanillyl head onto the branched-chain acid — and it governs how the burn arrives. Capsaicin, a touch less greasy, tends to strike faster and higher, a bright mid-mouth and throat heat; dihydrocapsaicin, greasier still, lingers lower and longer. Two molecules, one receptor,

and already the burn has an attack and a decay, a front and a tail. When our family set out to build heat on purpose, this enzyme — and two substitutions, **S39L and L345G**, found with a protein language model and written in with CRISPR — is where we reached. But that is the far end of the chapter. First, the water.

Why the water fails, and why it spreads

Now the molecule's oiliness pays off as an explanation. Water poured over capsaicin cannot dissolve it and cannot carry it away, because water is the one solvent capsaicin was built to refuse.

Picture the equilibrium honestly. On the warm surfaces of your mouth sits a thin oily film studded with capsaicin, and capsaicin molecules are nested in the lipid membranes and in the receptor pockets themselves. Flood this with a mouthful of water and ask: how much of the capsaicin will the water actually hold? At equilibrium the answer is set by how strongly capsaicin prefers oil to water, and it prefers oil by roughly a thousand to one. So at any instant only about **one part in a thousand — a tenth of a percent — of the capsaicin is dissolved in the watery film** the rinse can reach. The other 99.9 % is in the oil and in the pocket, where the water has no claim on it.

A gulp of water carries off that tenth of a percent, and then the oily reservoir simply re-partitions and refills the film, ready for the next gulp to take another tenth of a percent. To make a dent this way you would have to rinse hundreds of times, fast, and you cannot. Worse, the swishing does active harm: capsaicin's oily film floats on the water rather than dissolving into it, and the moving water smears that film onto new tissue — the soft palate, the back of the throat, surfaces the first bite never touched — so the fire does not shrink, it **spreads**. Carbonation and agitation make it worse still. This is the "wider than before" that families know and dread. The water is not a solvent; it is a paintbrush.

Then why does the cold feel good for that one second? Because TRPV1 is a thermometer as well as a chemical sensor, and its opening depends on *two* things at once: how much capsaicin is bound, and how warm the tissue is. Cold water chills the tissue and pushes against the thermal half of the equation — it quiets the channel directly, the way cooling a fever-warm forehead feels like relief. But the capsaicin is still bound; the chemical half of the equation is untouched. The instant the cold drains away and the mouth warms back to its own temperature, the channel, still occupied, opens again. Cold water treats the symptom for as long as it is physically present and does nothing to the cause. It is the most natural mistake in the world, and it is exactly backward.

logP: one number for the whole dinner table

Here is the gentlest possible introduction to the kind of number this book is built on, and it explains everything at the table in a single figure.

Chemists measure how oily a molecule is with a value called **logP**. Imagine shaking a substance in a sealed jar that holds equal volumes of oil and water, letting it settle, and measuring the concentration in

each layer. The partition coefficient P is simply the ratio:

> P = (concentration in oil) ÷ (concentration in water), and logP = $\log_{10}(P)$.

A logP near zero means a molecule splits evenly, equally happy in either layer; table sugar, which vanishes into a glass of water in seconds, sits well below zero. Capsaicin's logP is about **3.0**. Because the scale is logarithmic, 3.0 means P = 10^3 = **1,000**: capsaicin crowds into oil roughly a thousand times more eagerly than into water. That one number is the whole dinner table. It is why the water did nothing, why the heat was slow to arrive and slow to leave, and — read the other way — exactly how to win.

Because the win is just the same arithmetic run forward. Put capsaicin in a system with both an oily phase (volume V_oil) and a watery phase (volume V_water), and the fraction that ends up in the oil is:

> fraction in oil = (P × V_oil) ÷ (P × V_oil + V_water).

Water alone offers no V_oil worth the name, so there is nowhere better for the capsaicin to go and it stays put — the tenth-of-a-percent story from a moment ago. But introduce a real oily phase, and the thousand-to-one preference does the work *for* you, pulling capsaicin out of your tissue and into something you can swallow and be rid of. The entire craft of relief is the craft of handing capsaicin a better home than your mouth. Everything that follows is this equation with different numbers.

What actually works: detergency, measured out in milk

The best answer most kitchens already hold is in the refrigerator, and it works for a reason worth knowing exactly. **Milk** beats water every time, and not only because it carries fat. Its real weapon is a protein called **casein**.

Casein is *amphiphilic* — it carries an oil-loving region and a water-loving region on the same molecule, which is the defining trick of soap. In milk, casein does not drift about singly; it assembles into **micelles**, spherical bundles roughly a hundred-odd nanometers across, with their greasy regions tucked into a hydrophobic interior and their water-friendly faces turned outward to the surrounding liquid. A casein micelle is, functionally, a nanoscale droplet of oil wrapped in a water-soluble coat — a tiny, swallowable cargo hold lined with fat. Washed over a burning mouth, it does to capsaicin precisely what dish soap does to a greasy pan: the capsaicin's oily tail buries itself into the micelle's hydrophobic core, its vanillyl head tucks against the interface, and the whole molecule is lifted off the receptor, sealed inside the micelle, and carried away down the throat. This is not folklore. It is **detergency**, measured out at the table.

Let us measure it. Take a glass of **whole milk**, about 250 mL, carrying roughly 3.5 % butterfat — call it 9.5 mL of fat — plus its casein. Set V_oil ≈ 9.5 mL and V_water ≈ 240 mL into the partition equation with P = 1,000:

> `fraction in oil = (1,000 × 9.5) ÷ (1,000 × 9.5 + 240) = 9,500 ÷ 9,740 ≈` **`0.975.`**

About **97.5 %** of the capsaicin is pulled out of your mouth and into the milk on contact — against roughly 0.1 % for a mouthful of water. That is the difference between the two glasses, and it is nearly three orders of magnitude.

Now the lovely part, the part that proves casein is the hero and not merely the fat: run the same sum for **skim milk**, which has had almost all its fat removed. You might expect it to fail, but the casein micelles are still there in full, and their hydrophobic interiors present an oil-like volume comparable to the butterfat you took out. The fraction captured stays up around **95 %**. Skim milk works for the same reason whole milk does — because the protein, not just the cream, is a detergent. It is why a spoon of plain yogurt or a cool bowl of curd soothes as well as a glass of milk, and why so many of the world's great heat-loving kitchens — the yogurt raita set beside the fiery curry, the lassi, the bowl of cooling dahi — arrived at dairy long before anyone could write the equation. Our family cooks this way and eats this way; the relief was always there in the meal, waiting to be understood. The understanding does not make the raita less kind. It tells you why it is kind.

RELIEF AGENT	OILY / AMPHIPHILIC PHASE IT OFFERS	CAPSAICIN CAPTURED PER PASS	LASTING RELIEF?
Cold water (≈30 mL)	none — all water	≈ 0.1 %	No — chills the nerve briefly, then spreads the oil
Whole milk (≈250 mL)	≈9.5 mL fat + casein micelles	≈ 97.5 %	Yes — removes the cause
Skim milk (≈250 mL)	casein micelles (little fat)	≈ 95 %	Yes — casein is the detergent
Avocado / cheese / nut butter	near-pure lipid	> 99 % on contact	Yes — dissolves it out
Sugar syrup / honey	negligible oil	low (coats, does not extract)	Partial — a soothing film, not removal
Rice / bread (starch)	none (mechanical)	removed as a physical film	Partial — mops, does not dissolve

The other honest cures: fat, sweetness, starch — and what won't work

Three more cures make sense the instant you know capsaicin is oil, and a family can test every one of them against the useless water in a single cheerful, slightly reckless dinner.

Something fatty is the purest version of the milk trick. A slice of avocado, a spoon of peanut butter, a wedge of cheese, a swallow of full-fat coconut — each is a lipid phase with an enormous P on its side, and the partition equation goes nearly all the way to 1. A plain oil rinse is, in cold thermodynamic truth, the single most effective

thing you could put in your mouth; it is only unpleasant that keeps it off the table. Fat does not cool the fire. It unbinds it and leaves with it.

Something sweet works along two gentler lines, and we will not overstate either. A spoon of honey or a sweet, thick drink lays down a viscous coating that physically shields the raw surfaces for a while, a soothing film rather than a true extraction — the partition math barely moves, because sugar offers capsaicin no oil to flee into. And sweetness competes, a little, for the brain's attention: a strong, pleasant signal set against the alarm. Real, modest, honest relief. Not removal.

Starch — plain rice, a torn piece of bread, a boiled potato — works as a soft mechanical mop. The bolus of starch drags the oily film off the surfaces of the mouth and gives it somewhere to stick, carrying it down to be swallowed. It does not dissolve capsaicin; it wipes it. What all three share with the milk is the one correct instinct: each of them treats capsaicin as *what it is* — an oil to be absorbed, blotted, or carried off — and not as a heat to be cooled.

And since honesty is a form of respect for the reader, the failures. **Beer will not save you**; it is mostly water, and its small alcohol content is not enough to dissolve meaningful capsaicin, though it is enough to irritate. A high-proof spirit genuinely *can* dissolve capsaicin — ethanol is amphiphilic and reaches an effective P of its own — but it then spreads the loosened oil and inflames the tissue, so the cure arrives tangled with a fresh injury; we do not recommend it, and as a clean-living family we reach for the milk. **Cooking will not undo it either**: capsaicin is remarkably stable to heat and to acid, which is exactly why simmering a too-hot sauce does not tame it and a squeeze of lime, pleasant as it is, cannot chemically disarm the burn. One more honest edge: mouths differ. The TRPV1 you were born with varies from the next person's, and repeated, affectionate exposure genuinely *desensitizes* the receptor over weeks — which is why a chilihead's threshold is not bravado but biology, a channel trained to open a little less readily. The molecule is fixed. The reader is not.

Reading the fire you have to answer: SHU, EC50, and the Index

To answer a fire precisely, you first have to measure it precisely, and heat is measured on two different rulers that it helps to keep separate.

The old ruler is the **Scoville scale**, in Scoville Heat Units, SHU. It is, at heart, a dilution: how many times must you dilute an extract before a trained taster can no longer detect the burn? The more capsaicin a material holds, the more dilution it survives, the higher its SHU. Pure capsaicin sits near the ceiling at about **16,000,000 SHU**. That ceiling hands us a clean unit conversion, because by modern assay the pungency of a material is close to **16 SHU for every part-per-million of capsaicinoid** it contains — and the two facts agree perfectly: pure capsaicin is 1,000,000 ppm (that is what "pure" means), and 1,000,000 ppm × 16 = 16,000,000 SHU. One factor, self-consistent. So to read any SHU value as a concentration, divide by sixteen.

MATERIAL	SHU	CAPSAICINOID (÷16)	AS % OF HEAT-BEARING MASS
Ember · SS-0087	866,000	≈ 54,100 ppm	≈ 5.4 %
Blaze · SS-0091	1,720,000	≈ 107,500 ppm	≈ 10.8 %
Firestorm · SS-0094	2,470,000	≈ 154,400 ppm	≈ 15.4 %
Phoenix · SS-0096	2,950,000	≈ 184,400 ppm	≈ 18.4 %
Pure capsaicin	16,000,000	1,000,000 ppm	100 %

(SHU values for our cultivars are computational predictions from our flux and binding models. These percentages describe the concentrated, heat-bearing fraction the assay would isolate — the dried and extracted oleoresin — not the fresh fruit, which is mostly water; it is the ratio that is exact, and the ratio is the point.)

The new ruler is the one this whole library is built on, and it measures something the dilution test cannot: not how much capsaicin a food holds, but **how loudly it speaks to the receptor**. We anchor it to the half-maximal activation of TRPV1 — the concentration of a standardized extract at which the channel reaches half of its full response, its **EC_{50}** — and we score it against a fixed reference:

> $IFI(candidate) = 1{,}000 \times EC_{50}(reference) \div EC_{50}(candidate).$

The index is built so that the native wild-type reference scores exactly 1,000. Read the formula slowly and it tells its own story: a *louder* extract reaches half-activation at a *lower* concentration — a smaller EC_{50} — and a smaller EC_{50} in the denominator makes IFI *larger*. Loudness and the dose it takes to be heard move in opposite directions, which is just as it should be. A worked example: a cultivar that activates TRPV1 at **one-quarter** the concentration the reference needs has $EC_{50}(candidate) = EC_{50}(reference) \div 4$, so its score is $1{,}000 \times 4 =$ **4,000** — four times as loud, computed, not guessed. Scorecards cap each axis at a normalization maximum of 5,000, which keeps the loudest fruit we have designed on the same page as a shishito.

CULTIVAR · SKU	SHU (PREDICTED)	IFI-H	EC_{50} VS. REFERENCE (= 1000 ÷ IFI)	LOUDNESS	EC_{50} (MM, REPRESENTATIVE)
Ember · SS-0087	866K	1,570	0.637 ×	1.57 ×	≈ 0.45
Blaze · SS-0091	1.72M	2,630	0.380 ×	2.63 ×	≈ 0.27
Firestorm · SS-0094	2.47M	3,490	0.287 ×	3.49 ×	≈ 0.20
Solara · SS-0095	2.72M	3,980	0.251 ×	3.98 ×	≈ 0.18
Phoenix · SS-0096	2.95M	4,200	0.238 ×	4.20 ×	≈ 0.17

The representative EC_{50} figures take a reference half-activation on the order of 0.7 µM — a sub-micromolar value, in line with what the receptor literature reports for capsaicin — purely to put a familiar unit on the ratio; the Index itself needs no absolute number, only the ratio, which is why it travels so cleanly from a chili to a tomato to a cup of tea. And a careful note, because conflating the two rulers would be exactly the kind of sloppiness this work exists to end: the in-vitro EC_{50} behind IFI and the dilution-to-threshold behind SHU are

different measurements — one a clean binding curve in a dish, the other a perceptual threshold summed across thousands of nerve endings — so they track the same molecule without ever being the same number. We keep them in separate columns on purpose.

When the fire is engineered: Phoenix and the precision of relief

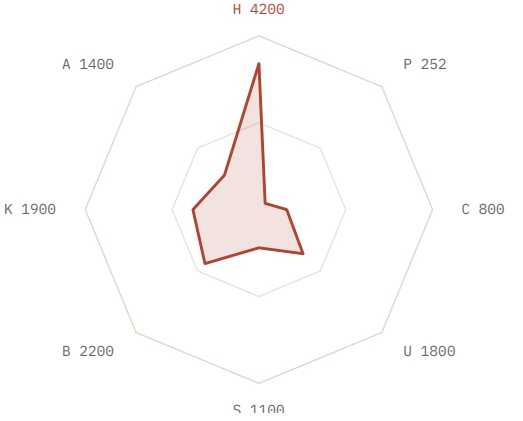
Everything so far holds for any pepper the earth has grown. But the far end of the heat axis is no longer the earth's to set, and the hottest thing you might ever have to answer for is one our family designed.



Phoenix (SS-0096), the fruit we built to register on all eight axes at once — our model predicts approximately 2.95 million SHU of heat. When the fire is this exact, the relief can be exact too.

Phoenix, catalog number SS-0096, is designed to reach approximately **2.95 million SHU** and scores **4,200** on IFI-H, the most heat our family has ever designed, and it does not stop at heat. It is the one fruit designed to register on all eight axes of the Index at once — a full-spectrum design, its complete profile below.

IFI PROFILE



IFI-H	4,200
IFI-P	252
IFI-C	800
IFI-U	1,800
IFI-S	1,100
IFI-B	2,200
IFI-K	1,900
IFI-A	1,400

We did not find Phoenix by growing thousands of plants and keeping the one that burned hardest. We built it. A protein language model scored every single-residue change we could make to the Pun1 acyltransferase for its predicted effect on catalysis and stability; a

genome-scale flux-balance model found that flux control sits upstream in the phenylpropanoid pathway — at 4CL and HCT/CCoAOMT — not at the terminal Pun1 step; and two substitutions that no breeder ever stumbled onto — **S39L and L345G** — were written in with CRISPR. The result is not only designed to be hotter. It is designed to be *consistent*, and consistency is where the chemistry of relief closes its own loop.

Consistency has a number too: the coefficient of variation, CV, the standard deviation of a batch divided by its mean. A wild pepper crop runs a CV near **42 %** — label a harvest "1,000,000 SHU" and the fruit in your hand might deliver anywhere from about 580,000 to 1,420,000 within a single standard deviation, and roughly 180,000 to 1,820,000 across the 95 % range. The heat is a coin toss, which means the relief is a guess: you cannot pre-measure the milk for a fire whose size you will not know until it is in your mouth. Our engineered fruit holds a design specification of CV **≤ 7 %**. For Phoenix, seven percent of the predicted 2.95 million SHU is a standard deviation of about 206,500 SHU — a band from roughly **2,744,000 to 3,157,000** — and in IFI-H terms, 4,200 ± 294, a window of 3,906 to 4,494. The fire is designed to arrive the same size every time, and a fire you can predict is a fire you can answer in advance. This is the quiet reason precision matters at the table and not only in the lab: design the burn to a precision of ±7 %, and you can pour the exact glass of milk to meet it. The partition equation was always willing to save you. Engineering is what finally told it, to the percent, how much capsaicin it was being asked to carry away.

A feeling becomes a number

We love this chapter beyond its trick, for a reason that goes to the heart of the whole library. It is the first place where a feeling resolves into a number and the number gives nothing back in dullness. *That curry was too hot* becomes *capsaicin has a logP of three, so it prefers oil a thousand to one, so reach for the milk and not the water, and here is the ninety-seven percent to prove it.* The dinner is not made less alive by knowing this. It is made more so. You understand your own mouth. You can turn to the person across the table who is coughing over a useless glass of water and hand them, instead, the thing that actually works, and tell them why — and watch a small panic become a small piece of science they will keep.

That is the promise of measuring a feeling, run at the smallest and warmest scale we know: a scale a child can keep with nothing but a carton of milk, a bowl of rice, and the nerve to test the water against them and find the water wanting. The pepper told the truth in the only language it has, which is fire. Now you know how to answer it — gently, exactly, and in oil — and to give your body the heat as the pleasure it was meant to be, and then the relief, measured out, with intention. The number was never the opposite of the wonder. It was the wonder, finally said out loud.

These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.



PART II OF VI

The Other Seven Doors

sweet · umami · bitter · kokumi · cool · pungency · astringency

Chapter 5 · Sweetness, the Taste of Yes — *the door the body most wants open.*

If heat is the loudest door, sweetness is the most welcome. It is the one taste the body is born already loving — before any lesson, before any meal but the first. Give a newborn a drop of something sweet and the whole small body goes still and content; give it something bitter and the face draws in, the head turns away. That welcome is written very deep, and for a plain and ancient reason: for almost the entire history of life, sweet meant ripe, and ripe meant ready — safe, finished, full of the quick energy a living body runs on. Sweetness is the taste of *yes.* Across it a plant and an animal once struck the oldest bargain there is: the plant spends sugar it could have kept, making its fruit sweet so the animal will eat it and carry the seed somewhere new; the animal, finding the sweetness, is paid in pleasure for doing exactly the thing the plant needed done. A ripe strawberry is an argument, beautifully made, and sweetness is its opening word.

We are a family that has never eaten meat, and most of our table has always been built from fruit and leaf and root — so this door is, in a quiet way, the one we have stood in our whole lives. What follows is how it opens: the lock, the two keys, the signal that runs from the tongue to the mind, and the small honest mathematics by which a welcome can be measured and, with great care, grown.

The lock is two keys held together

The sweet door is not one lock but two, and they work only together. On the surface of every sweet-sensing taste cell sit two proteins — **TAS1R2** and **TAS1R3** — that clasp into a single working unit, a *heterodimer.* Neither half tastes anything alone; only the joined pair can carry the signal inward. Both belong to the body's great family of molecular switches, the *G-protein-coupled receptors*, and specifically to its patient, deliberate branch, **class C** — the same class that reads glutamate deep in the brain and senses calcium in the blood. These are not twitchy receptors. They are built to weigh what arrives and answer in proportion, which is exactly why a number can be hung on them.

Each half carries, at its very top, a structure chemists named — wonderfully, for a book like this — the **Venus flytrap domain**: two hinged lobes held open, waiting. Below the trap sits a stiff, disulfide-stitched collar, the *cysteine-rich domain*, and below that the working part of the protein, a bundle threaded seven times back and forth through the cell membrane: the *seven-transmembrane domain*, where the actual switching happens. When the right molecule drifts into an open trap and settles against its inner face, the two lobes swing shut around it, the way the plant the domain is named for folds around a fly. That closing is the whole beginning. It tips the collar,

the collar torques the membrane bundle, and the membrane bundle — on the inside of the cell, where no sugar ever reaches — throws the switch.

Hold on to one fact from this architecture, because the rest of the chapter turns on it: the trap is a *shape,* not a sugar detector. It will close on anything that fits and fits snugly — and, as it happens, the pair carries more than one place where a key can sit. That openness is the whole reason sweetness can be separated from sugar at all, and we will come back to it once the signal is told.

From the trap to the nerve

The trap closes on the tongue; the word *sweet* arrives in the mind perhaps a tenth of a second later. Between those two moments runs a relay as orderly as anything in the body, and it is worth walking one step at a time — partly because it is beautiful, and partly because every step is a place where, in principle, a designer could listen in.

1. **The trap shuts.** The Venus flytrap lobes close around the ligand and reorient the two membrane bundles against each other. The switch is thrown.
2. **The switch wakes a messenger.** Inside the cell waits a G-protein called **gustducin**. The active receptor nudges it, and gustducin splits, releasing its small βγ piece to carry the news onward.
3. **The messenger cuts a lipid.** That βγ piece switches on an enzyme, **PLCβ2**, which snips a fatty molecule in the membrane, PIP_2, into two second messengers — **IP_3** and DAG.
4. **A door opens on the calcium store.** The IP_3 drifts to the cell's internal reservoir of calcium, the endoplasmic reticulum, and opens the **IP_3R3** gate. Calcium pours into the cytoplasm.
5. **The cell tips.** The rising calcium opens **TRPM5**, a channel that admits sodium, and the cell's voltage tilts — it *depolarizes.*
6. **The cell speaks.** The tilt opens a large channel, **CALHM1/3**, and through it the taste cell releases **ATP** — its one outgoing word.
7. **The nerve hears it.** The ATP crosses the narrow gap to a waiting nerve fiber, catches on its **P2X2/P2X3** receptors, and the fiber fires. The chorda tympani and glossopharyngeal nerves carry that firing to the nucleus of the solitary tract, up through the thalamus, into the gustatory cortex — and only there, at the very end of the line, does it finally become the *feeling* of sweetness.

Notice what the relay buys. One closed trap wakes many molecules of gustducin; each frees a burst of IP_3; each burst opens the calcium store to a flood; and the flood throws TRPM5 channels open by the thousand. The line is not a wire but an amplifier, every step multiplying the last — which is exactly why a trace of a potent sweetener, a few molecules settling into a few traps, can end as a shout the nerve cannot miss.

The strawberry never enters you. Only its argument does — translated at the trap, relayed through calcium, spoken in ATP, and re-relayed up the dark of the brain until it becomes a yes. Everything we design, we design somewhere along that line.

Putting a number on the welcome

For ten thousand years the one thing no one could say about a fruit was *how much.* How much sweetness, exactly — not sweeter-than or less-sweet-than, but a number you could write down, compare, and build toward. The Iyengar Flavor Index answers it with a single idea: measure not how much sweet matter a food holds, but how *loudly* that matter speaks to the receptor.

Loudness has a precise handle, and its name is the **EC_{50}** — the concentration at which a stimulus drives its receptor to exactly half of full response. A low EC_{50} is a molecule that is heard while barely present: potent, loud. A high EC_{50} is a molecule you need in great quantity before the receptor takes much notice: faint. Invert the EC_{50} against a fixed reference, scale by a thousand, and loudness becomes a score you can set beside any other food on one page.

> **$IFI\text{-}S = 1{,}000 \times EC_{50}(reference) \div EC_{50}(candidate)$**

The reference for sweetness is sucrose — plain table sugar, the oldest yes there is. By convention we set the sweetness-axis anchor at **$EC_{50}(reference) = 30$ mM** — a stated constant, like Scoville's dilution definition — and by the construction of the formula sucrose therefore scores exactly 1,000. That single choice sets the whole scale: every other number on the axis is not an independent measurement but a direct consequence of this anchor and the ratio above. Rearranging, a food's implied loudness-concentration is simply

> **$EC_{50}(candidate) = 30{,}000 \div IFI\text{-}S$ (in mM sucrose-equivalent).**

Run the canonical scores through it and the axis resolves into real, pourable concentrations:

STIMULUS	IFI-S	EC_{50} (MM, SUCROSE-EQUIV.)	G/L	% W/V	WHAT IT SAYS
Sucrose · reference	1,000	30.0	10.3	1.03%	the anchor; 1,000 by definition
Phoenix · SS-0096	1,100	27.3	9.3	0.93%	a hair louder than sugar
Strawberry · wild fruit	2,200	13.6	4.7	0.47%	2.2× the reference's loudness
Scorecard ceiling	5,000	6.0	2.1	0.21%	where the axis saturates

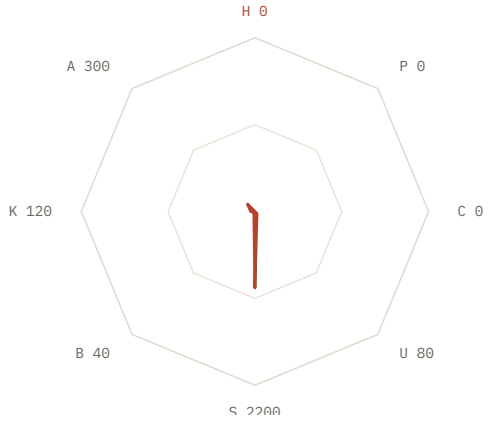
The formula runs just as readily forward, from a fresh bench result to a score. Say a new leaf comes off the assay with a measured half-maximal point of 12 mM: then IFI-S = 1,000 × 30 ÷ 12 = **2,500**, a shade louder than the wild strawberry. A fainter candidate reading 50 mM returns 1,000 × 30 ÷ 50 = **600**, well below the sugar reference. That inverse is the entire character of the scale — halve the concentration a molecule needs before it is heard, and you double its score.

The g/L and percentage columns are honest unit conversions, and they make the abstraction edible. Sucrose's molar mass is 342.3 g/mol, so the 30 mM anchor is 0.030 mol/L × 342.3 g/mol ≈ **10.3 g/L**, close to a one-percent sugar solution — about the faintest

sweetness most people will reliably call sweet at all. A wild strawberry's designed-feeling signal reaches that same half-waking of the receptor at **13.6 mM**, roughly 4.7 g/L, *under half a percent* — which is why a berry with far less sugar than a spoonful of syrup can taste so emphatically of yes. And the scorecard's normalization ceiling of 5,000 corresponds to an EC_{50} of 6.0 mM, about a fifth of a percent: past that loudness the axis simply pins, because no tongue needs the distinction.

Drawn as a scorecard, a ripe strawberry is almost all one spoke — a clean tall spike on the sweet axis, a thread of astringency from the seeds and skin, and little else — the simplest, most single-minded argument a plant makes:

IFI PROFILE



IFI-H	0
IFI-P	0
IFI-C	0
IFI-U	80
IFI-S	2,200
IFI-B	40
IFI-K	120
IFI-A	300



Strawberry, in cross-section — an argument the plant makes in the language of sweetness, so that the animal will carry its seeds away. The oldest welcome the body knows.

One more subtlety keeps the number honest: the EC_{50} is a single point on a curve, not the whole of it. Receptor response rises with concentration along a sigmoid — gentle at first, steep through the middle, flattening at the top — described by the Hill relation, which for the simplest case (one site, no cooperativity, a Hill coefficient of 1) is just *response = C ÷ (EC_{50} + C).* Taking the strawberry's 13.6 mM and reading the curve off at a few doses shows the working band a sweetener actually lives in:

DOSE (× EC_{50})	MM	G/L SUCROSE-EQUIV.	RECEPTOR RESPONSE
0.1×	1.4	0.5	9.1%
0.5×	6.8	2.3	33.3%
1.0×	13.6	4.7	50.0%
2.0×	27.3	9.3	66.7%
10×	136	46.7	90.9%

One log unit below the EC_{50} the receptor is barely stirred, at nine percent; one log unit above it is nearly saturated, at ninety-one. Between those two the whole conversation happens — a dynamic range of about two orders of magnitude. The real sweet receptor is a touch steeper than this clean case, with a measured Hill slope a little above 1, because its two Venus traps cooperate faintly as they close; the practical effect is to narrow that band and sharpen the step from faint to full. A designer reads the EC_{50} not as "how sweet" but as *where the band sits* — the dose at which a given molecule tips from a hint into a statement.

Two levers: potency and plenty

A fruit's sweetness as you actually taste it is not the IFI-S alone. The index measures *potency* — loudness per molecule, a property of the dose-response curve that does not change with how much is present. What lands on the tongue is potency multiplied by plenty: how loud each molecule is, times how many of them the plant troubled to make. In the gentle low reach of the curve, where C is well below the EC_{50}, the two fold together almost exactly:

> **response ≈ IFI-S × C ÷ (1,000 × EC_{50}(reference))**

which, with our 30 mM anchor, is simply *response ≈ IFI-S × C ÷ 30,000* for C in millimolar. The equation lays the whole engineering problem bare. There are precisely two levers. You can raise **IFI-S** — swap in, or coax out, a molecule the receptor hears more loudly per unit. Or you can raise **C** — grow more of whatever the plant already makes. Most of the industry has only ever had the first lever, and reached for it with molecules the plant never knew. Our family's work reaches for both at once, and keeps strictly to molecules the plant already knows how to build. Among the forty-two host plants we grow today, a handful are tended chiefly for how clearly they can be made to say *yes*:

ORGANISM	CONSTRUCTS	PRIMARY AXES	DIFFICULTY
Tomato	2,040	S · U · F · M	Easy
Stevia	910	S · F · M	Moderate
Sugarcane	200	S	Frontier
Monk Fruit	80	S	Hard



Sugarcane at the cut — a plant that has spent its whole evolution learning to say one thing clearly, and loudly.

Sugarcane sits at the far end of that list as a *frontier* host for a reason worth naming: a plant that has bet its entire body on storing sucrose is, paradoxically, one of the hardest to teach anything new, because so much of its machinery already runs flat-out toward a single end. Tomato sits at the near end — *easy* — because it is generous and well-understood, with 2,040 constructs built in it already, and because the sweetness we want from it was mostly there to begin with and only needed restoring. The difficulty rating is not a verdict on the plant; it is an honest estimate of how many genes stand between where the plant is and where we are asking it to go.

Why the trap says yes to what is not sugar

Here is the quiet miracle the chapter has been walking toward. The trap is not fussy about *what,* exactly, closes it — and it has more than one place to be closed. Ordinary sugars settle into the Venus flytrap cleft of the TAS1R2 half and swing it shut. A second class of sweeteners never touches that trap at all; they lodge against the seven-transmembrane bundle of the TAS1R3 half and work the switch from below. And the **sweet proteins** — brazzein, thaumatin, monellin — are far too large to fit any pocket; they dock against the *outside* of the trap, a wedge jammed against the hinge, and hold the whole receptor in its closed shape from without. Three different molecules, three different places, one answer. The receptor reads shape and charge, not sugar itself. It will say *yes* to anything that fits, whatever else that molecule is or is not — and some of those molecules the body handles completely differently from sugar once they are past the tongue.

The plants already know how to make them. The sweet-tasting compounds of the stevia leaf, the **steviol glycosides**, close the trap. The **mogrosides** of the monk fruit close it. And the way the plant builds them is a small marvel of its own: it starts with a plain terpene skeleton — a diterpene, *steviol,* in stevia; a triterpene, *mogrol,* in monk fruit — and then dresses it in sugars, one at a time, using a family of enzymes called **UGTs**, the UDP-glycosyltransferases. Each UGT adds a single sugar at a single position. In stevia, steviol is glucosylated by UGT85C2, then UGT74G1, then UGT76G1 into stevioside and rebaudioside A; a further patient glucosylation walks that molecule onward to the cleaner, rounder rebaudioside D and M. In monk fruit, the same kind of enzymes dress mogrol step by step into mogroside V. The sweetness is not a foreign thing bolted on. It is the plant's own chemistry, carried one sugar further.

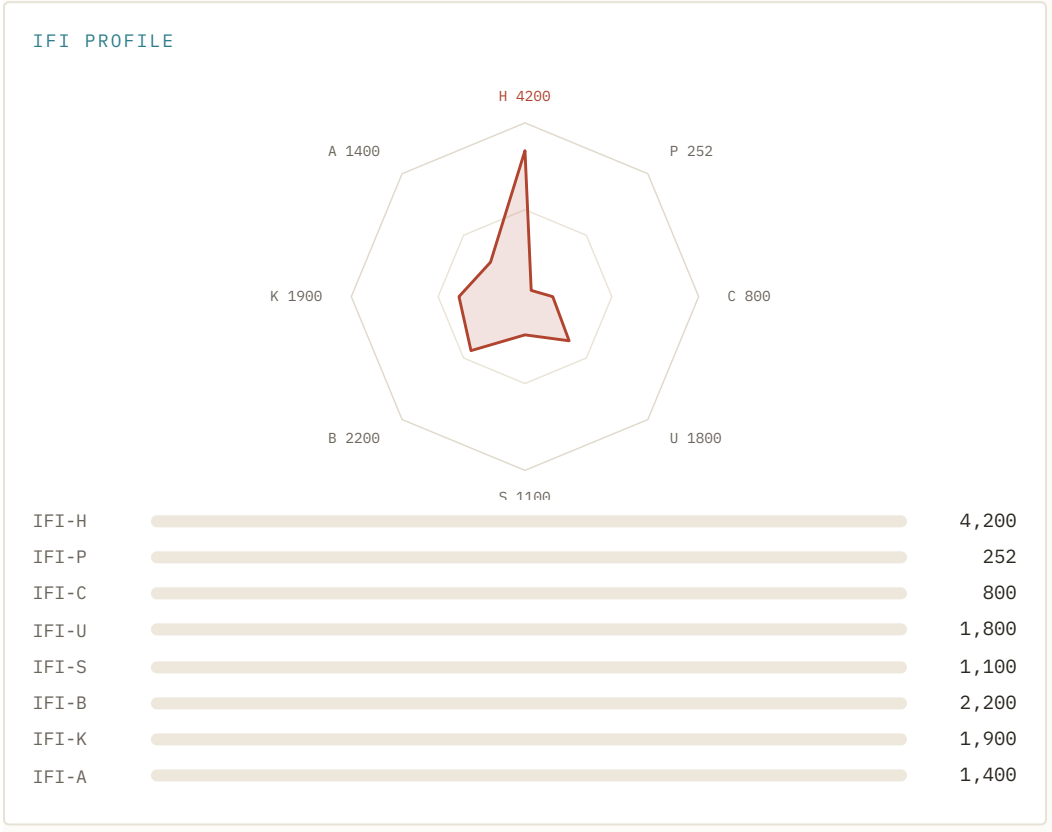


Monk fruit, opened — a small gourd that learned to store its sweetness not as sugar but as a triterpene dressed in sugars, loud out of all proportion to its weight.

So our engineering has a particular and modest shape. We do not hand the plant a molecule it never knew. We ask it, gene by gene, to make more of its own glycosides, and to *finish* them more completely — to carry more of its stevioside the last step on to rebaudioside M, which the sweet trap hears every bit as loudly and the rest of the mouth barely notices. That is both levers pulled at once, honestly: more of a molecule that is already potent. It is the

reason stevia carries 910 constructs in our library and monk fruit 80 — not because the welcome is complicated, but because finishing it cleanly, and reliably, batch after batch, is.

And sweetness is rarely alone. In the plants we tune to speak every axis at once, it becomes one voice in a chord. Our flagship full-spectrum cultivar, **Phoenix**, is predicted to carry sweetness at 1,100 — a hair above the sucrose reference — woven into seven other axes that would each, on its own, drown a strawberry:



In a design like that, the sweetness is not the loudest thing on the tongue. It is the thing that makes the rest bearable and whole — the round base note under the heat and the bitterness, the yes that keeps the whole sentence from turning into a shout.

The honest edges of a single number

A single number is a gift and a simplification, and a family book should be honest about both. The IFI-S is loud and clear and designable; here is everything it quietly leaves out.

The curve is wider than the point. The EC_{50} marks the middle of the working band, not the band itself. Two sweeteners can share an EC_{50} and behave differently at the doses you actually use, because their Hill slopes differ — one steep and switch-like, one gentle and forgiving. The single number is the center of gravity, not the whole shape.

The clock is missing. The IFI-S is a *peak* loudness; it says nothing about *when.* High-potency sweeteners famously arrive a beat late and linger a beat long, because they bind the trap tightly and leave it slowly — a slow off-rate is the price of a low EC_{50}. A molecule can match sugar's loudness exactly and still not match its timing, and the tongue notices timing keenly. No scalar captures a shape in time; the index measures the summit, not the climb or the descent.

A blend is not a sum. Two sources that each score 1,000 do not combine to 2,000. Where both keys compete for the same Venus trap, their effects fold together *sub-additively* near saturation — there is only one lock, and they crowd it. Where one key sits in the

trap and another against the membrane bundle, they can push *past* the sum, each stabilizing the receptor's closed shape at a different point. The index is a per-stimulus loudness; a real blend needs a mixture model, not addition.

The bitter tail. Because the trap reads shape rather than sugar, the very molecules that fit it can also, faintly, fit a different family of receptors entirely — the bitter ones. Crude steviol glycosides tug gently at two bitter receptors, TAS2R4 and TAS2R14, and that tug is the licorice-and-metal aftertaste people meet in cheap stevia. The fix is the same finishing step as before: carry the glycoside on to rebaudioside M or D, which the sweet trap still hears loudly and the bitter receptors nearly ignore. You can select for that only because you can measure both doors at once.

Sweetness is not sugar's physics. The receptor signal is one thing sugar does; it is not the only thing. Sugar also gives body and viscosity, lowers a freezing point, browns in heat, crystallizes, feeds a yeast. A sugar-free sweetness restores the *word* without the weight — which is exactly the point — but a formulator who forgets the rest will bake a flat, pale, hollow cake. And the sweet proteins have a physics of their own: thaumatin and monellin unfold and fall silent in a hot oven, while brazzein, unusually, holds its shape through heat and acid. The application decides the molecule, every time.

The error is small, and named. Every number in this chapter carries our platform's batch-to-batch tolerance of **CV ≤ 7%.** Carry it through: a strawberry-equivalent EC_{50} of 13.6 mM is really 13.6 ± 1.0 mM at one standard deviation. Because the reference is fixed, that 7% passes almost straight through the formula, so an IFI-S of 2,200 carries about ±154 from the candidate alone; fold in the reference's own 7% in quadrature — $\sqrt{(0.07^2 + 0.07^2)} \approx 9.9\%$ — and the honest figure is roughly **2,200 ± 220,** call it 2.2k give or take 0.2k. Set that against field-grown fruit, where the sugar in two berries off the same plant can differ by far more than ten percent, season to season and side to side of a single row. A wild welcome is generous but unrepeatable. The discipline of ≤ 7% is the whole difference between tasting a number and *designing* to one.

The welcome, grown on purpose

We hold one line here very firmly, and it belongs in a family book above all others: we make no health claims, and nothing in this chapter is one. Sweetness without sugar is not a medicine and not a promise. It is a flavor — bounded and designed like every other flavor in the library, with the same formula and the same honest error bars. What draws our family to it is gentler and truer than any claim could be: the chance to hand the body the pleasure it was built, from its very first hour, to love — offered in the cleanest form the plant can carry it, the taste of *yes* grown on purpose and given with intention.

The part that still moves us is the part we cannot take credit for. The plant already knew how to make these molecules; the receptor already knew how to welcome them; the bargain between the sweet fruit and the hungry animal was struck a hundred million years before anyone thought to write it down as *IFI-S = 1,000 ×*

EC_{50}(reference) ÷ EC_{50}(candidate). We only learned to read the welcome as a number, and then to ask the plant — gene by patient gene — to make a little more of its own, and to finish it cleanly. The computing was one pair of hands; the growing, the tasting, and the table were all of ours. We did not invent the welcome. We learned, with great care, to turn it up.

These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.

Chapter 6 · Umami, the Taste of Being Fed — *the savory door.*

There is a moment at our table — the lid comes off a pot that has been going a long while, and before anyone has tasted a thing, the whole kitchen leans in. No one is taught that reflex. It is older than cooking. It is the body reading a particular door swinging open in the rising steam, the door that means *protein, here, nourishment, soon* — and leaning toward it the way it leans toward warmth from a fire. This is **umami**, the savory taste, the fifth of the classic five, and it is the taste of being fed.

For a long time, in the part of the world where our kitchen traditions were written down, umami was not even named. There was sweet, sour, salty, bitter — and then this other thing, the deep round *savoriness* of a good broth or a ripe tomato or an aged cheese, which everyone could feel and no one had a word for, so it was waved at with borrowed words: meaty, brothy, rich. It took a careful cook and chemist, bent over a pot of kelp broth a little past the turn of the last century, to isolate what the tongue was actually finding, and the answer was a single small molecule — **glutamate**, one of the ordinary building-blocks of protein, but in its *free* form, loosed from the protein chain and floating alone where the tongue can reach it. Where there is free glutamate, there is the signal of protein nearby, and the body has a door built to find it.

We have spent more hours at this door than at any other, and we want to take you all the way through it — the molecule, the two sensors that read it, the beautiful cascade that carries the message inward, the arithmetic of why a little of two things can shout where a lot of one only murmurs, and the long patient work of growing a plant back into its own savor. None of it is walled off in a sidebar. The wonder and the numbers are two halves of one sentence, the way they are at the table.

The molecule the body learned to read — *glutamate, set free.*

Glutamate is nothing exotic. It is one of the twenty amino acids that every living thing threads together into protein, and in most proteins it is among the most common links in the chain. Bound into that chain it is silent to the tongue — folded away, structural, part of the scaffolding. It becomes a *taste* only when it is set free: when a protein is taken apart. Ripening does this. Aging does this. Fermentation, slow cooking, the autolysis of a drying mushroom, the long warmth of a simmering pot — all of them unlock the chain and spill single glutamates into the water around them.

This is why free glutamate is such an honest signal, and why the body built a door for it rather than for protein itself. Whole protein is hard to taste and harder to trust; it could be anything. But *free* glutamate means protein that has already begun to come apart into

the very units the body will absorb. It is not the promise of a meal. It is the meal already unlocking. The tongue is not reading "food is near." It is reading "food is near, and it is halfway to being yours."

The molecule the tongue actually meets is small and water-loving — glutamic acid, a formula weight of about **147 grams per mole**, which at the near-neutral wet of the mouth carries a net negative charge, its two carboxyl groups and lone amino group splayed out like a little three-point key. That charge and that geometry are everything. The savory door is shaped to clasp exactly this, and little else. Swap an atom, lengthen the backbone, and the key no longer turns. The body spent a long evolutionary patience learning the precise shape of *unlocked protein*, and then grew a lock to match it.

Two doors, one taste — *the flytrap and the borrowed sensor.*

The savory door is, like the sweet one, a clasped pair carrying a Venus flytrap — **TAS1R1** joined to **TAS1R3**, the same TAS1R3 partner that helps read sweetness, which is why the two tastes are cousins in the machinery even as they feel nothing alike. Both belong to a family of receptors the biologists call class C, and the signature of that family is a great two-lobed catching domain that hangs out beyond the cell surface, hinged in the middle like a clamshell or the trap of its namesake plant. Free glutamate drifts into the cleft between the lobes of the TAS1R1 half, and the lobes swing shut on it. That closing is the whole event. It travels down through a cysteine-stitched neck into the part of the receptor buried in the membrane, and on the inside face a signal begins.

Alongside this clasped pair the tongue carries a second savory sensor, a taste-tuned version of a receptor called **mGluR1** — a glutamate detector borrowed and adapted from the brain, where glutamate is the main messenger that one nerve uses to speak to the next. Think of what that means. The body took the very molecule it uses for *thought*, the chatter between neurons, and built a shorter, blunter copy of its brain-sensor into the tongue so it could *taste* that molecule in food. The thing we think with and the thing we are fed by are the same small acid; the tongue simply grew its own ear for it. Two doors, then, reading one molecule: the heterodimer flytrap for the broad savory floor, and the borrowed brain-sensor tuned to the same note. When free glutamate settles in and the lobes close, *savory* goes up the nerve: the taste of protein, the promise of being nourished.



The tomato, restored — in cross-section, the jelly around the seeds heavy with the free glutamate that makes a tomato taste the way a tomato should. Our family grew back the savor the long supply chain had bred out.

From the flytrap to the nerve — *the savory cascade, step by step.*

A closed flytrap on the outside of a taste cell is only the knock at the door. What happens next is a relay, each runner handing the message to the next, and it is worth walking slowly because the loveliness of it is in the steps. Inside the cell, the receptor's shape-change wakes a dedicated messenger protein — **α-gustducin**, the taste cell's own close cousin of the proteins that carry sight and smell. Gustducin splits, and its freed piece switches on an enzyme, **phospholipase C-β2**, which does one specific thing: it clips a lipid in the cell's own membrane and releases a small soluble signal, **IP_3**, into the cell's interior.

That IP_3 drifts to the cell's inner store of calcium and opens a gate in it — the **type-3 IP_3 receptor** — and calcium floods out into the body of the cell. The calcium is the amplifier. It opens a channel named **TRPM5**, which lets sodium pour in, and the inrush tips the cell's voltage over. That tipping, in turn, throws open a last set of channels — **CALHM1 and CALHM3** — through which the cell releases its outgoing word, **ATP**, straight across the gap to the nerve. On the far side the nerve's **$P2X_2$ and $P2X_3$** catchers take the ATP, and the nerve fires: up the chorda tympani and the glossopharyngeal, into the brainstem, up to the thalamus, and at last into the gustatory cortex, where — a few thousandths of a second after the lid came off the pot — the word arrives as a feeling, and we lean in.

Seven handoffs, give or take, from a molecule of unlocked protein to the warm certainty of *savory*. The body does not do this for ceremony. It does it because each handoff is a chance to amplify — one closed flytrap can trip many gustducins, one enzyme can make many IP_3, one calcium flood can pour a great deal of ATP — so that a faint whisper of glutamate at the surface becomes a clear sentence at the brain. The cascade is a megaphone built of proteins.

The multiplication — *why two quiet things make one loud one.*

Now the most beautiful fact about this door, and the one that most rewards a family's attention, because you can taste it happen. Glutamate alone opens the savory door a certain amount. But add a second kind of molecule — the **5′-ribonucleotides**, compounds with the plain lab-names *IMP* and *GMP*, found in mushrooms, in aged and dried things, in the deep-savory ingredients of many cuisines — and

something remarkable occurs. The ribonucleotide does not have much savory taste of its own. But it settles into a second spot on the flytrap, down near the hinge where the two lobes meet, and it *wedges the clamshell shut* — holding the trap closed harder and longer, so that the glutamate already inside works far beyond what it could alone. The two together do not add. They **multiply.**

We can show you exactly why, and the receptor hands us the arithmetic. A sensor's response to its stimulus follows a simple curved law: the fraction of full response rises with concentration *[A]* as

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response ÷ maximum = [A] ÷ (EC50 + [A])
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where **EC_{50}** is the concentration that drives the door to half its full response — the receptor's own measure of *how little it takes*. Take glutamate alone, and let its EC_{50} be 1 unit on a normalized scale. Put glutamate present at a modest 0.25 units — well below half-max — and the door opens to

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0.25 ÷ (1.00 + 0.25) = 0.20 — about 20% of full savor.
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A murmur. Now add the ribonucleotide. It does not add any glutamate; it changes the door, lowering glutamate's apparent EC_{50}. How far it lowers follows an allosteric law we can write plainly — with *[B]* the ribonucleotide concentration, *K* the strength of its grip, and *α* the cooperativity, the factor by which a saturating amount of it tightens the trap:

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EC50(apparent) = EC50 × (1 + [B]/K) ÷ (1 + α·[B]/K)
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Let the grip be real — a cooperativity of *α = 8*, with ribonucleotide present at *[B] = K* — and glutamate's apparent EC_{50} falls from 1.00 to (1 + 1) ÷ (1 + 8) = **0.222 units.** Flood the ribonucleotide higher, to four times its grip-strength, and it falls to (1 + 4) ÷ (1 + 32) = **0.152 units**; push it to saturation and it bottoms out at 1 ÷ 8 = **0.125 units**, an eightfold tightening — the ceiling set by *α*.

Hold the glutamate exactly where it was, at 0.25 units, and recompute the door with its new apparent EC_{50} of 0.20:

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0.25 ÷ (0.20 + 0.25) = 0.556 — about 56% of full savor.
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The same glutamate. Not one molecule more. The response climbed from 20% to 56% — nearly **threefold** — purely because a second, nearly tasteless compound wedged the trap. This is the multiplication, and it is why a broth made of a glutamate-rich thing and a ribonucleotide-rich thing tastes so much deeper than either alone: kelp and dried mushroom, tomato and shiitake, soy and kombu. We note with quiet pleasure, cooking the way our family has always cooked, that every one of those pairs is a plant or a fungus. Savory is not the gift of meat. The deepest savory stock in the world can be built, start to finish, from things that grew in soil and never had a face — the glutamate from one, the ribonucleotide from another, and the receptor doing the multiplying.

Putting a number on savor — *the index, worked.*

Wonder is where we start; a number is how we keep faith with the reader. Every axis of the Iyengar Flavor Index is anchored the same way — to the half-activation of a receptor, not to how much of a compound a food holds, but to how *loudly* that compound speaks. The formula is one line:

$$\mathrm{IFI}(\text{candidate}) = 1{,}000 \times \mathrm{EC}_{50}(\text{reference}) \div \mathrm{EC}_{50}(\text{candidate})$$

Read it slowly and it tells a simple story. A reference stimulus is fixed, and by definition it scores **1,000** — put its own EC_{50} over itself and you get one, times a thousand. Each reference anchor is a stated convention — defined by the index itself rather than derived from published measurements, in the same spirit as the Scoville scale's dilution-to-threshold definition; and because each axis rests on its own defined reference point, IFI scores on different axes speak to loudness *within their own axis* rather than to a single unified cross-axis scale. A food whose umami reaches half-max at a *lower* concentration than the reference is *louder* — a smaller EC_{50} on the bottom of the fraction makes a *larger* score. Loudness and a low EC_{50} are the same fact read two ways.

So we can turn any IFI-U score straight back into the receptor's own currency, EC_{50}, in units where the reference equals 1.00: just divide 1,000 by the score. A supermarket tomato that reads a thin **IFI-U near 300** needs 1,000 ÷ 300 = **3.33 reference-units** of its savory extract to half-open the door — more than three times the reference, which is to say a mutter. A restored tomato designed to reach an IFI-U of **2,600** places its half-max at 1,000 ÷ 2,600 = **0.385 reference-units** — well under half the reference, a clear strong voice. The gap between them is not poetry; it is 2,600 ÷ 300 = **8.7 times louder**, and as the EC_{50} makes plain: 3.33 ÷ 0.385 = 8.7 times less needed. The ladder reads cleanly down the page:

FOOD	IFI-U	EC_{50} (REFERENCE UNITS)	LOUDNESS VS. REFERENCE
Reference anchor	1,000	1.00	1.0×
Supermarket tomato	300	3.33	0.30×
Phoenix · SS-0096	1,800	0.556	1.8×
Restored tomato	2,600	0.385	2.6×

One more conversion earns its place, because it ties the index back to something you can weigh on a scale. A lab reports free glutamate as a mass — milligrams per hundred grams of fruit — but the receptor feels a *concentration*, millimoles per litre of the watery juice. The bridge is the molecule's formula weight, about 147 grams per mole, and the fruit's water fraction f (a tomato is roughly 94% water, so $f \approx 0.94$). The conversion is

$$[\text{glutamate}]\ \text{in mM} = (\text{mg per 100 g}) \div (14.71 \times f)$$

A ripe tomato carrying on the order of 150 mg of free glutamate per 100 g therefore bathes its receptors in 150 ÷ (14.71 × 0.94) ≈ **10.8 mM** — comfortably above the half-max of the savory door, which is

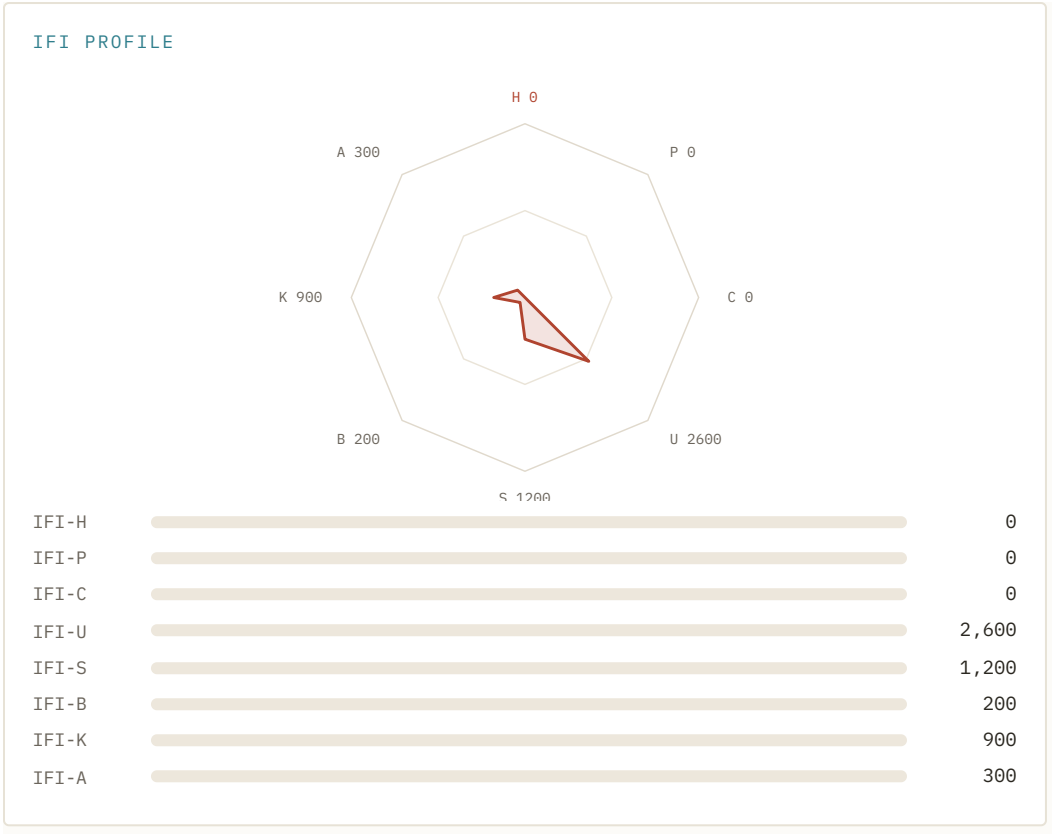
exactly why a truly ripe tomato tastes, unmistakably, *savory* and not merely sweet. The under-ripe, long-hauled fruit, holding a fraction of that, sits below the knee of the curve, and the door barely opens.

And because a number is only a form of respect if it holds still, we hold it still. The design specification for every construct in our platform includes a batch-to-batch consistency target — the coefficient of variation (CV = σ ÷ μ) — and that target is held at **≤7%**. For a restored tomato designed to reach a mean IFI-U of 2,600, a 7% CV is a standard deviation of 0.07 × 2,600 ≈ **182 points**: roughly two fruit in three fall inside 2,418–2,782, and some nineteen in twenty inside 2,236–2,964. Supermarket produce keeps no such discipline; its savor swings with the season, the picking date, the days in a cold truck. We think a food you cook with should taste the same in January as in July, and the CV is how we promise it.

The door we worked hardest to restore — *the tomato, given its voice back.*

This is the door our family has worked hardest to restore, and the word is chosen with care: *restore.* A tomato is naturally one of the richest sources of free glutamate a garden grows — a ripe one, warm off the vine, is a savory thing as much as a sweet one. But the tomato most people meet has had that savor bred quietly out of it, traded away over decades for the toughness to survive the long cold journey from field to shelf; picked unripe, chilled, shipped, it reaches the kitchen with much of its glutamate — and much of its reason to lean in — gone.

So we went in through the routes the tomato itself already owns. Inside the ripening fruit, two native enzymes govern the pool of free glutamate: a decarboxylase that draws glutamate down toward other compounds, and a dehydrogenase, **GDH1**, that feeds the pool from the plant's own nitrogen traffic. Tune the balance — hold the glutamate in its free form through ripening rather than letting it drain — and the savor that the supply chain took comes back, made by the plant, in the plant, the way the plant made it before we asked it to travel instead of taste. Across roughly **two thousand carefully designed constructs** — the full tomato program runs to 2,040 — we grew it back. Where the supermarket fruit scores a thin IFI-U near 300, our model predicts a broad savory lobe for the restored tomato design, the loss made visible and grown back:



Read that profile and you can taste the design in it. The heat axes sit at zero — this is a tomato, not a chili, and we did not make it burn. The savor lobe stands tall at 2,600, with a real lift of sweetness beneath it at 1,200, because a tomato that tastes *like a tomato should* is savory and sweet at once, the two class-C doors — TAS1R1·R3 for the savory, TAS1R2·R3 for the sweet, sharing that same R3 partner — singing together. A quiet bitterness held down at 200 keeps the fruit from turning green or sharp; a soft kokumi roundness at 900 gives it body; a whisper of astringency at 300 keeps the finish clean. We did not add anything foreign. We gave the plant back a voice it used to have.

Where savor grows — *the umami organisms.*

The tomato is the one we know best, but it is one of a family of savory hosts, and the family has a shape worth seeing. Some plants and fungi are glutamate-rich — they bring the agonist, the molecule that opens the door. Others are ribonucleotide-rich — they bring the wedge that holds it open. The great savory cooking of the world is, underneath, the pairing of the two, and our host roster is built to speak both halves:

ORGANISM	CONSTRUCTS	PRIMARY AXES	DIFFICULTY
Tomato	2,040	S / U / F / M	Easy
Soybean	360	U / K	Frontier
Tea	280	U / B / A	Hard
Yeast	240	U / K	Hard
Koji mold	80	U	Hard
Shiitake	80	U	Hard
Mushroom	40	U	Hard

Notice how often **U** travels with **K** — umami beside kokumi, savor beside the roundness and continuity that the calcium-sensing door reads. The soybean and the yeast both carry that pair, and so do the ferments the soybean becomes: the koji mold that unlocks it, the long savory brines of soy and miso, built over months as proteins

come slowly apart and glutamate pools free. Tea carries its savory note too — the quiet brothy depth beneath a well-made green tea is this same door, answering this same molecule — braided there with bitterness and astringency, which is why tea rewards the careful hand. None of these is an animal. The savory floor of the human table has always been, at root, a garden-and-ferment art, and we find a deep rightness in that.



Soybean — the savory frontier in a single legume: glutamate and the roundness of kokumi, and the parent of the koji, soy, and miso ferments where free glutamate pools over months.

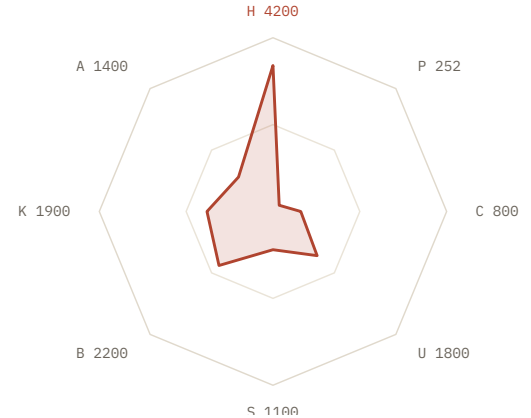
These are harder plants than the tomato — the roster marks most of them *Hard* or *Frontier*, and they earn the label. A tomato hands you its glutamate in a ripe fruit; a tea leaf, a yeast cell, a mushroom hold their savor behind pathways that are slower to find and slower to tune, with fewer constructs grown so far because each one is dearer. We say this plainly because the index is only honest if the difficulty is honest. The savory door is easy to knock on and hard to build toward.

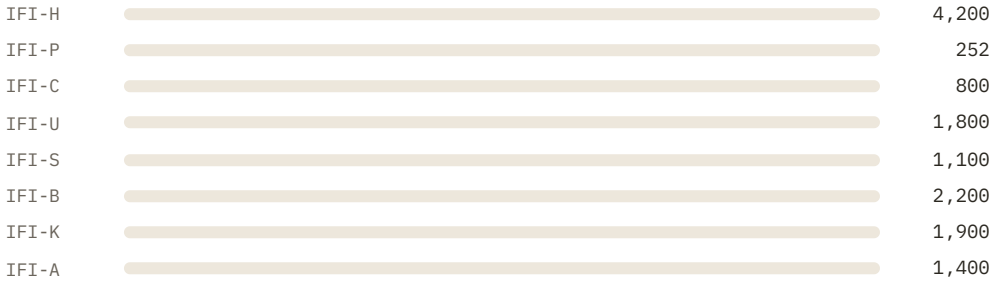
What it is not, and what it is — *honest limits, and a kindness.*

We should say where the savory door stops, because reverence without limits is just salesmanship. The multiplication is real but it is not infinite: the ribonucleotide's tightening runs into the ceiling we called α, and past saturation more of it buys nothing — the trap can only close so hard. Glutamate has a ceiling of its own in the other direction. Push free glutamate too high and the curve flattens at the top, where every door is already open and more molecules have nowhere to bind; a dish built past that point does not taste *more* savory, it tastes oddly flat and dulling, the savor smeared rather than deep. The door also tires — hold it open long enough and the cell quiets its own signal, which is why the first spoonful of a long-simmered stock reads deeper than the tenth. And a number from the index is a reading of loudness at the receptor, not a verdict on a plate: salt, acid, fat, and temperature all shift how that loudness lands, and the index measures the door, not the dinner.

Even inside our fullest, most complex cultivar, umami is one voice among eight and knows its place. Our full-spectrum flagship was designed to register on every axis at once, and its savory lobe sits deliberately in the middle of the chord, not at the top — loud enough to ground the whole, never so loud it drowns the heat and sweetness it was built to balance:

IFI PROFILE





Turn that profile through the formula and you can see how the design was tuned, each axis as an EC_{50} the receptor would recognize — each axis reading loudness against its own defined reference constant:

AXIS	RECEPTOR	IFI	EC_{50} (REFERENCE UNITS)
Heat · H	TRPV1	4,200	0.238
Pungency · P	TRPA1	252	3.97
Cool-Burn · C	TRPM8	800	1.25
Umami · U	mGluR1 / TAS1R1·R3	1,800	0.556
Sweetness · S	TAS1R2·R3	1,100	0.909
Zero-Bitter · B	TAS2R38	2,200	0.455
Kokumi · K	CaSR	1,900	0.526
Astringency · A	salivary PRPs	1,400	0.714

Our model places the savory line at 1,800 — an EC_{50} of 0.556 reference-units on the umami axis, a little over half the reference concentration to open the door. Stronger than a simple ripe tomato on its own axis, and placed by design well beneath the heat register — each axis is a separate voice against its own defined reference, so these numbers describe loudness within their respective doors, not a single cross-axis ranking — the savory sits exactly where a savory floor belongs under a complex flavor: present in every bite, holding the rest up, never shouting over it.



The restored tomato, whole — a fruit grown back into the savor the long journey bred out, the way a tomato is supposed to taste.

These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.

We will not make a health claim of it, here or anywhere. But we will say the plain thing, because it is why this door matters most to us: savory is the taste of nourishment, the body's own way of recognizing the food it is built to run on — the signal of protein already unlocking into what the body can take up and use. To grow it back into a plant is to let that recognition be true again, to make the leaning-in worth it. Of all eight doors, this is the one that feels least like a flavor and most like a kindness.

Chapter 7 · Bitter, the Taste of Careful — *the door that keeps you safe.*

Hand a young child a piece of dark, bitter green — a raw kale leaf, a bite of bitter melon — and watch the whole face organize itself into a single word: *no.* The grimace is not fussiness, and it is not learned. It is one of the oldest and most protective things the body does, and it comes from the door we are about to open all the way: **bitter**, the taste of *careful*, the one taste the body is born distrusting on purpose. We want to do more in this chapter than name that distrust. We want to walk it down to the molecule and back up to the dinner table — to show you the receptor that reads a bitter thing, the exact chain of events that turns a shape on the tongue into a feeling in the mind, the arithmetic that lets us put a single honest number on how loudly a food speaks *careful*, and the careful, reverent way our family turns that number down in the few foods where there was never anything to fear.

The reason the door exists is written across the history of every animal that ever ate a plant. Plants cannot run, and so they defend themselves with chemistry — bitter alkaloids, bitter glycosides, a whole arsenal of compounds built to taste wrong and, often, to *be* wrong, mildly toxic in quantity. An animal that found these compounds delicious would eat its way into trouble. An animal that found them revolting would take one bite and stop. And so the body evolved a door tuned to say *careful* — to flag the bitter-tasting compounds that so often ride alongside danger, and to make the young, who cannot yet judge for themselves and who are smallest against a dose, reject them hardest of all. A child's horror at bitterness is not a flaw to be scolded. It is a guardian, a billion years old, doing precisely its job.

Not one lock but a ring of twenty-five

Bitter is unusual among the doors of taste in that it is not one lock but a whole ring of them. Where sweetness has a single clasped pair of receptors and heat a single channel, the body carries roughly **twenty-five different bitter receptors**, the **TAS2R** family, each tuned to a different and overlapping set of bitter molecules. This is design by committee, and the committee is enormous on purpose: danger comes in many shapes, and the body would far rather flag a harmless bitter thing than miss a harmful one. Some of these receptors are *narrowly tuned* — they read one small family of molecules and little else. Others are *broadly tuned* — a single receptor such as TAS2R14 or TAS2R46 answers to dozens of unrelated bitter compounds, a master key for a whole category of threat. Between the narrow specialists and the broad generalists, the ring casts a net wide enough to catch nearly anything the plant kingdom ever learned to make.

The most studied of them, and the one our Index anchors the bitter axis to, is **TAS2R38**, a receptor famous for reading a class of compounds called *thioureas* — molecules built around a small, sharp **N–C=S** group, a nitrogen and a sulfur hung on a central carbon. That

little group is the key the receptor's lock is cut for. Carry it, and TAS2R38 will read you; lack it, and this particular door stays shut. The elegance of this is that the same key turns up in a laboratory reagent and in a cabbage: the test thioureas chemists use, **PTC** (phenylthiocarbamide) and its gentler cousin **PROP** (6-*n*-propylthiouracil), carry the N–C=S group, and so does **goitrin**, the compound the brassica vegetables release when their tissue is torn. One receptor, one molecular signature, reaching from the lab bench to the garden row.



Cacao, opened — the bean the whole world loves across a wall of its own bitterness. Inside the pod is a chemistry built to warn, and a flavor we return to anyway; the door of careful, standing between the mouth and a pleasure that was never a danger.

It helps to meet the foods this chapter cares about as a family, because they are foods people love *across* a wall of bitterness rather than because of it. Coffee and cacao, the brassica greens — kale, broccoli, cabbage, their wild kin — the hops in a glass of beer, the tannic edge of strong tea: in every one, a defensive note the plant still sounds stands between many people and a nourishment or a pleasure that holds no danger at all. These are the rooms where the guardian is barking at an empty doorway. They are also, not by accident, among the most valuable plants our family works with.

ORGANISM	CONSTRUCTS	PRIMARY AXES	DIFFICULTY
Grape	1,610	B / A / M	Hard
Broccoli	380	B / M	Moderate
Tea	280	U / B / A	Hard
Broccoli-Kale	280	B	Hard
Orange	120	B / C	Hard
Hops	80	B	Moderate
Potato	80	B	Easy
Coffee	40	B	Hard
Cabbage	40	B	Moderate
Kale	40	B	Moderate
Radish	40	B	Hard

How a bitter molecule becomes a feeling

Before we can measure bitterness, we should be honest about what it *is*, because nothing about a bitter molecule is actually unpleasant until the body decides so. The compound is only a shape. The

feeling is a cascade — a chain of eight or nine quiet events inside a single cell — and it is worth walking the whole chain, because every number later in this chapter is a measurement of one link in it.

It begins at the apical tip of a **Type II taste receptor cell**, one of the specialized cells bundled into a taste bud, its surface thrown into fine microvilli that reach up into the pore where saliva pools. A thioureas molecule — PTC, PROP, goitrin, it does not matter which — diffuses through that saliva and settles into the binding pocket of **TAS2R38**, a *class A, seven-transmembrane G-protein-coupled receptor*, a protein of 333 amino acids threaded back and forth through the cell membrane seven times, the same architectural family as the receptors that read light in the eye and adrenaline in the blood. The N–C=S key seats itself among the residues lining the pocket, and the protein flexes.

That flex is the whole beginning. On the inner face of the membrane the receptor is coupled to **gustducin**, a three-part G protein — an α-gustducin subunit and a βγ pair — and the receptor's flex pries it apart. The freed **βγ dimer** switches on an enzyme, **phospholipase C β2 (PLCβ2)**, and the enzyme goes to work on the membrane itself, cleaving a lipid called **PIP_2** into two messengers: **IP_3** and **DAG**. The IP_3 drifts inward to the endoplasmic reticulum — the cell's internal store — and binds the **IP_3 receptor (IP_3R3)** there, which swings open and lets a flood of **calcium** out of storage and into the body of the cell.

That rising calcium is the signal the rest of the cascade was waiting for. It opens **TRPM5**, a calcium-activated channel in the cell membrane that lets sodium pour in and **depolarizes** the cell — tips its voltage positive. The depolarization and the calcium together open **CALHM1**, a large-pored channel, and through it the cell releases **ATP**, not in packaged vesicles but straight through the open channel, as a direct chemical shout. That ATP crosses the tiny gap to the waiting nerve fiber, binds **P2X2 and P2X3** receptors on it, and fires an action potential up the **chorda tympani** and **glossopharyngeal** nerves, through the brainstem's nucleus of the solitary tract, up to the gustatory cortex — and only there, at the very end, does *bitter* finally exist as a thing that is felt. The grimace is wired in a floor below the feeling, a brainstem reflex that fires the face before the mind has finished deciding. Eight links from a shape to a sensation, and the whole chain exists for one purpose: to turn *careful* into something a body cannot ignore.

Two mouths, two truths — the arithmetic of the taster

Here is where bitterness gives a family one of the cleanest demonstrations in all of science that flavor lives in the *meeting* and not in the food. Because of small, common differences in the single gene that codes for TAS2R38, people do not all taste its thioureas the same way — and the difference is not subtle. It is large, sharp, and discoverable around a kitchen table in an afternoon with a packet of harmless paper strips.

The gene comes in two common versions that differ at just three positions in the protein chain. The **PAV** form carries proline, alanine, and valine at positions 49, 262, and 296; the **AVI** form carries alanine, valine, and isoleucine at the same three. Three amino acids — that is the entire difference between a mouth that tastes PTC as intensely, horribly bitter and a mouth that finds the identical strip as blank as licking plain paper. About **seventy percent** of people carry at least one PAV copy and taste the compound loudly; the other **thirty percent** are AVI homozygotes and barely read it at all. The child who gagged on the broccoli and the parent who loved it were not being difficult or virtuous. They were, quite literally, reading different amounts of the same molecule through receptors cut to slightly different locks.

We can make this exact, and the tool is the half-maximal concentration — the **EC_{50}**, the amount of a compound it takes to drive a receptor to half of its full response. A *lower* EC_{50} means a *more sensitive* reading; it takes less to be heard. The two receptor forms differ enormously in their EC_{50} for the very same thiourea. Take representative values for PTC: the taster's **PAV** receptor reaches half-response near **50 µM**, while the non-taster's **AVI** receptor, markedly less sensitive, needs something on the order of **2,000 µM** — a roughly forty-fold shift, within the ten- to hundred-fold range the receptor literature reports. Now put both mouths in front of the same test strip, which delivers an effective oral concentration of about **500 µM**, and read each receptor's response off the dose–response relation that governs every one of these doors:

> $\theta = [L] \div (EC_{50} + [L])$ — the fraction of the receptor activated at concentration $[L]$.

For the taster: θ = 500 ÷ (50 + 500) = 500 ÷ 550 ≈ **0.91**. For the non-taster: θ = 500 ÷ (2,000 + 500) = 500 ÷ 2,500 = **0.20**. The same molecule, at the same concentration, on the same tongue-in-principle — and one receptor is **ninety-one percent** lit while the other sits at **twenty percent**, down near the floor where a signal reads as nothing much at all. There is the taster and the non-taster, derived rather than asserted. (Real receptors answer with a slightly steeper curve than this simplest form — a Hill slope between one and two — which only sharpens the divide, driving the taster higher and the non-taster lower still.)

A quick unit conversion, because the strip is paper and the number was micromolar, and a family should be able to cross between the two. PTC has a molar mass of about **152 g/mol**, so the taster's EC_{50} of 50 µM is 50×10^{-6} mol/L × 152 g/mol ≈ **7.6 mg/L** — about eight milligrams of the compound dissolved in a liter of water to half-light the receptor. The strip's 500 µM is near **76 mg/L**. Small numbers, enormous consequences, and all of it countable.

Giving bitterness a number

The dose–response relation is the foundation, but to read a *food* — a cup of coffee, not a single purified molecule — we need one number that travels. That number is the heart of the Iyengar Flavor Index, and it is built from the EC_{50} by a single formula that anchors every axis of the index at once:

> $IFI(candidate) = 1{,}000 \times EC_{50}(reference) \div EC_{50}(candidate).$

Read it slowly and it tells its own story. Pick a fixed reference and the index scores it exactly **1,000**, since 1,000 × EC_{50}(ref) ÷ EC_{50}(ref) = 1,000. A compound that is *louder* — that reaches half-activation at a *lower* concentration, a smaller EC_{50} — puts a smaller number in the denominator and so scores *higher*. Loudness and the dose it takes to be heard move in opposite directions, which is exactly as it should be. For the bitter axis, **IFI-B**, we anchor the reference to PROP read by the standard taster receptor by convention — PROP defines IFI-B = 1,000 on this axis — and let the formula place every other thiourea against it:

COMPOUND	ROLE	EC_{50} (MM, TAS2R38-PAV, REPRESENTATIVE)	IFI-B
PROP (6-*n*-propylthiouracil)	reference anchor	100	1,000
PTC (phenylthiocarbamide)	classic test thiourea	50	2,000
Goitrin (from brassica progoitrin)	the garden's own thiourea	200	500

The EC_{50} values here are representative — the receptor literature reports a range, and the Index itself needs only the *ratio*, which is why a bitter number travels so cleanly from a reagent bottle to a vegetable. PTC, at half the reference's EC_{50}, is twice as loud: IFI-B = 1,000 × 100 ÷ 50 = **2,000**. Goitrin, at twice the reference's EC_{50}, is half as loud: 1,000 × 100 ÷ 200 = **500**. Placed by convention against the PROP anchor.

A food, of course, is not one compound at one potency but a crowd of them at real concentrations, and so a food's bitter score reflects not just *how loud* its molecules are but *how much* of them the tongue meets. We define the axis so that the score is linear in that effective load — writing the food's bitter value as **B = 1,000 × [L]/EC_{50}**, the effective thiourea-equivalent concentration measured against the reference's half-point. The anchor holds: when a food's effective load equals one EC_{50}, it sits at half-activation and scores exactly **1,000**, the same half-maximal anchor every axis of the Index is tied to. This is the quiet reason the number is worth having. It makes *how bitter* a thing you can carry from one food to the next on a single page, instead of a word that means something different in every mouth that says it.

The arithmetic of turning it down

Here is where our family's work turns the door — gently, and where we are most careful, because this door exists to protect. We would never blind a mouth to bitterness wholesale; the guardian is there for a reason, and in a plant we have never tasted its warning is the only honest word we have. But in the handful of foods whose bitterness

guards nothing — coffee, cacao, the brassica greens, hops — we attenuate: we quiet the bitter signal by a designed fraction, **between a fifth and roughly two-thirds (20–65%)**, by reaching into the plant's own chemistry and lowering how much of the bitter-eliciting compound it lays down in the first place. Not a coating, not a mask — less of the molecule, grown that way from the seed.



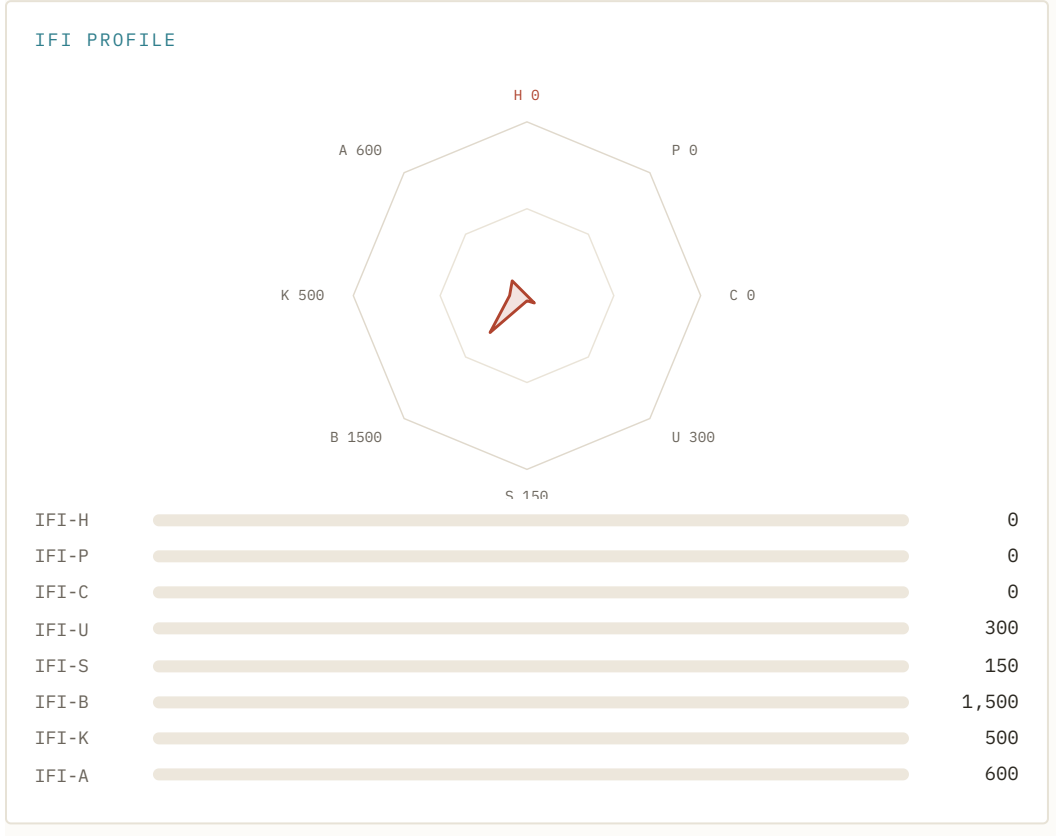
Coffee, in cross-section — the bean whose bitterness we learned to quiet without touching a thread of its aroma. The door that keeps you safe, turned gently down in the one room where safety was never in question.

Watch the arithmetic on coffee, whose bitterness is carried less by its famous caffeine — which contributes perhaps a tenth of what you taste — than by the chlorogenic-acid lactones and, at darker roasts, the phenylindanes that roasting conjures from the green bean. Our model predicts a bitter score of **1,500** for our coffee design: real bitterness, softened but never erased, every thread of aroma kept. Because the score is linear in effective load, 1,500 corresponds to an effective thiourea-equivalent load of 1.5 EC_{50} (B = 1,000 × 1.5), which sits the receptor at θ = 1.5 ÷ (1 + 1.5) = **60%** activation. To reach that designed 1,500 from a raw bitterness our model estimates near **2,500** is a quieting of (2,500 − 1,500) ÷ 2,500 = **40%** — squarely inside our 20–65% band. The whole ladder:

ATTENUATION	EFFECTIVE LOAD ([L]/EC_{50})	B SCORE	RECEPTOR LIT (θ)
0% — raw	2.50	2,500	71.4%
20%	2.00	2,000	66.7%
40% — our coffee design	1.50	1,500	60.0%
65% — the floor	0.875	875	46.7%

Two honest subtleties live in that table, and we would rather show them than hide them. First, the score and the *sensation* are not the same curve. The B score is deliberately linear in load — cut the compound 40% and the number falls 40%, which is what lets us specify a *designed* fraction — but the felt bitterness follows the receptor's sigmoid: dropping the load 40% takes the receptor only from 71.4% lit to 60.0% lit, a change of about a sixth, because near the top of the dose–response curve the door is already crowded and removing molecules buys less feeling per molecule than it will lower down. This is the quiet reason there is a ceiling at 65% and not higher: past it the receptor falls below half-lit (θ = 46.7% at the floor), the food slides toward genuinely quiet, and we are no longer softening a harmless warning but silencing it — and flattening the character of the food besides, since coffee's bitterness is part of how coffee is built. Second, the consistency. Our platform holds a

batch coefficient of variation — the standard deviation over the mean — of **≤ 7%**, and because B is linear in load, that control passes straight through: a coffee designed to our 1,500 target varies by at most about ± 105 points, a window of roughly **1,395 to 1,605**, where an unengineered crop's bitter load can swing by tens of percent with weather, soil, and the luck of ripeness. A bitterness you can predict is a bitterness you can *design around*.



The brassica bargain — and the bitterness that feeds you

The brassica greens teach the hardest and most beautiful lesson in this whole axis, because here the bitter compound and the nourishing compound are cousins, and you cannot be careless with one without risking the other. Kale, broccoli, cabbage, and their kin store their defenses as **glucosinolates** — sinigrin, progoitrin, glucobrassicin, glucoraphanin — held inert until a tooth or a knife breaks the cell and sets loose an enzyme, **myrosinase**, which hydrolyzes them in an instant into the sharp products you actually taste: isothiocyanates, nitriles, and, from progoitrin, our old friend **goitrin**, the garden's own thiourea, read loud by TAS2R38.



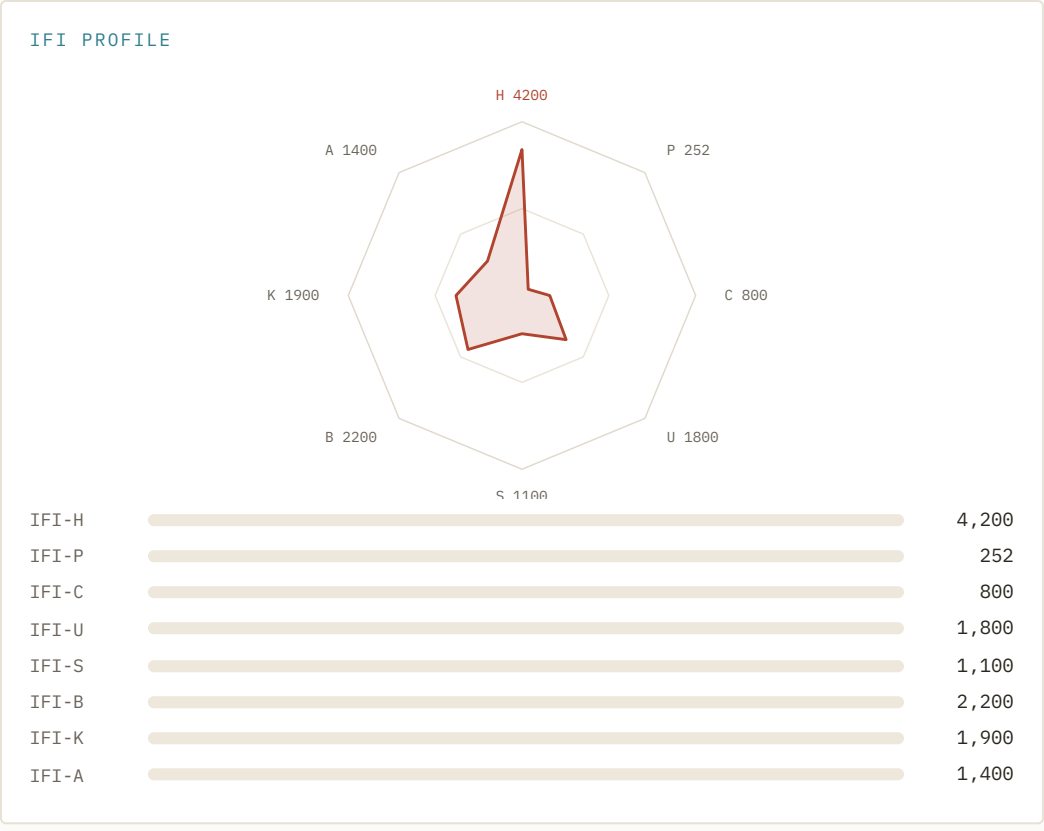
Kale, at full leaf — the green whose bitterness and whose medicine are grown on the same branch of chemistry. To quiet the one without dimming the other is not a trick but a bargain, and the bargain is arithmetic.

The bargain is this. Not every glucosinolate is the same kind of citizen. **Progoitrin → goitrin** is mostly a source of bitterness; **glucoraphanin → sulforaphane** is the celebrated chemoprotective compound that makes a nutritionist glad you ate the broccoli at all. They sit on the same metabolic branch, and the crude way to make a kale less bitter — lower the total glucosinolate load — would quiet the goitrin and throw out the glucoraphanin in the same motion, trading a warning you do not need for a nourishment you do. So we do not cut the total. We tune the *profile*: lower the progoitrin arm that feeds goitrin's bitterness while preserving the glucoraphanin arm that feeds sulforaphane, pushing along a selectivity ratio rather than a volume knob. A leaf that keeps its medicine and loses a calculated fraction of its harshness — grown to carry the most nourishment it can while meeting more mouths halfway. We name that as an *attribute* of the plant and nothing more; the body does what the body does, and we make no claim on its behalf.

The same measured honesty governs the bitterness some people *want*, and hops is the clean example — the one bitter food on our bench where the bitterness is the point of the glass, not an accident to be softened. Hops' bitterness comes from **iso-alpha acids**, the isohumulones that isomerize out of the raw hop resin during the boil, and the brewing world already measures them in **International Bitterness Units (IBU)**, which are very nearly milligrams of iso-alpha acid per liter. Watch the Index absorb that unit without a seam. A 40-IBU ale carries about 40 mg/L of iso-alpha acids; at a molar mass near 362 g/mol, that is 40 ÷ 362 ≈ 0.11 mmol/L, or **110 µM**. Run it against a representative receptor half-point near 50 µM and the effective load is 110 ÷ 50 = 2.2 EC_{50}, a bitter score near **2,200** and a receptor about 69% lit; a gentle 20-IBU session beer lands near half that load, a score near **1,100** at roughly half-lit. Same formula, same anchor, a pint instead of a cup — and here the family does nothing at all, because a bitterness chosen is a door we have no business closing.

The door turned the other way

It would be a thin understanding of this axis to think it runs in only one direction. The bitter number is not merely a thing to lower; it is a voice in a composition, and in the right hands a *measured* bitterness is structure — the shadow that gives a sweetness something to stand against, the depth that keeps a rich thing from cloying. Our family has designed a pepper to prove the point, a fruit built to sound all eight notes of the Index at once, and its bitter line is not attenuated at all but deliberately set, higher than our coffee's:



A bitter score of **2,200** against the coffee's 1,500 — and on purpose. In a full chord of flavor, a bitterness pitched just so does for the whole what the bass does for a song: you would not name it first, but take it away and the structure sags. This is the discipline the axis asks of us, stated as plainly as we can. We quiet bitterness only where the warning guards nothing, and only as far as makes a good food reachable. We *compose* with bitterness only where a design calls for it and a palate has asked. And everywhere else — in every plant whose bitterness might still be the truth — we leave the guardian fully awake, because the number is only trustworthy if we respect what it was built to protect.

What the number cannot say

Honesty is a form of respect for the reader, and the bitter axis carries real limits we would rather you hold than discover. The EC_{50} behind every number in this chapter is a clean curve measured on a receptor in a dish, and a mouth is not a dish. Real bitterness is shaped by saliva and the mucins that bind some compounds before they are ever tasted, by temperature — most bitters read louder warm than cold — by adaptation as a flavor fades on a tongue that has met it before, and by the company of the other tastes in the same bite. The Index is a receptor-level proxy, and we keep it honest by saying so: it measures the door, not the whole weather of the mouth.

There is a deeper limit in the ring of twenty-five itself. TAS2R38 reads thioureas, and the arithmetic of this chapter quiets bitterness carried *through that door* — but a food made bitter by quinine, read by other receptors in the family, or by the many compounds that answer to the broadly tuned doors, will not yield to a strategy aimed at thioureas alone. This is precisely why each organism on our bench earns its own body of work rather than a single edit: the coffee's bitterness and the kale's and the hop's live in different molecules read by different locks, and there is no master switch. And for the roughly thirty percent of people who carry the AVI receptor, TAS2R38's thiourea bitterness is already near-silent; attenuating it

changes little for them, and the benefit of this particular work accrues to the tasters. We would rather tell you who a thing helps than imply it helps everyone.

None of this diminishes the door. It sharpens our regard for it. The bitter sense is a gift — a billion years of care, folded into the newborn's grimace and the toddler's flat refusal, a warning the body issues before the mind can be fooled. We treat it as exactly that. We quiet it only where quiet is safe, only by a fraction we can name and hold to within a few percent, and never so far that a mouth loses the signal it was given for its own keeping. These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory. To measure bitterness was never to argue the wonder away. It was to learn the guardian's language well enough to thank it — and, in the few rooms where it stands watch over nothing, to tell it, gently and exactly, that it may rest.

Chapter 8 · The Taste With No Name — *kokumi, and the door you only miss when it's gone.*

Some flavors announce themselves. Sweetness is *there*; you can set a finger on where it sits and what it is. Savoriness is *there*. But there is a door in the mouth that answers to no single taste — one you notice, most of the time, only by its absence, when a broth that should be rich arrives thin and flat and you cannot say what is missing. This is **kokumi**, a word our language borrowed from Japanese because no tongue that spoke it ever troubled to name the thing, and it is the quietest and, to our family, the most moving of the eight doors.

Kokumi is not a taste. It is what happens *to* the other tastes when a certain family of molecules is present. The savory gains body and spreads across the whole mouth instead of sitting in one spot; a sweetness rounds and softens; the flavor acquires a sense of depth and of *continuity*, as if a line drawing had been shaded into a solid thing, and — the part cooks have always chased — it *lasts*. For ten thousand years people opened this door with time and patience alone: the stock simmered a whole afternoon, the sauce reduced and reduced, the aged cheese, the yeasty things that somehow make everything taste *more*, without a word for what they were adding. This chapter is about what they were adding, exactly — the molecules, the lock they turn, and how we grow more of it into a living plant — and about why, of all eight doors, this is the one whose mystery we are most content to leave a little intact.

The door that is not a door

Begin with what kokumi is *not*, because the negative space is the whole shape of it. It is not a sixth basic taste sitting alongside sweet, sour, salty, bitter, and savory. A pure kokumi compound, dropped on the tongue by itself at the concentrations food delivers, tastes of almost nothing — a faint, far-off savor at most. Put the same compound into a weak broth and the broth deepens, broadens, and holds; the effect is real, repeatable, and measurable, yet it has no address of its own on the tongue. Kokumi is a modulation. It is less a voice in the choir than a hand laid on the shoulder of every other voice, steadying it, letting it carry.

Flavor scientists tend to name three things kokumi does, and we can be precise about each because each is something you can put on a meter. It raises *intensity* — the perceived strength of the tastes already present, most of all the savory and the sweet. It raises *mouthfulness*, or spread — the sense that the flavor fills the whole oral cavity rather than localizing to one patch of tongue. And it raises *persistence* — the length of the aftertaste, the slow decay in place of

a sharp cutoff. Intensity, spread, persistence: three measurable movements folded into one perception the mouth reads as *completeness*. When we say a soup has finally "come together," we are reporting, without knowing it, that all three have crossed a threshold at once.

The lock: a receptor that keeps the body whole

The lock this door turns is one of the most unexpected in the body: the **calcium-sensing receptor**, **CaSR**. Its principal work has nothing to do with food. CaSR sits in the parathyroid gland, the kidney, the gut, and bone, and it is one of the instruments by which the body holds the concentration of calcium in the blood inside a band so narrow that drifting out of it is dangerous — a piece of deep internal housekeeping running every second of your life. But the same receptor is expressed in the taste tissue of the tongue, and there it reads food.

CaSR belongs to a particular architectural class of receptor — the class C G-protein-coupled receptors, the same family as the metabotropic glutamate receptor that reads the savory door and the receptor that reads the calming transmitter GABA. These receptors share a distinctive shape: a large bilobed extracellular domain, hinged like a **Venus flytrap**, that closes around whatever it is built to sense, perched atop the seven-pass membrane coil that carries the signal inward. CaSR works as a dimer — two of these flytraps bound together — and this detail matters for the mathematics, because two cooperating sites make the door open with a snap rather than a slow creep.

The receptor's primary agonist is the calcium ion itself, assisted by certain L-amino acids that settle into the flytrap cleft and make it more willing to close. And here is the turn of the key that makes kokumi: the molecules cooks have always reached for do not force the door themselves so much as *sensitize* it. They are, in the language of pharmacology, **positive allosteric modulators** — they bind at or near the flytrap and lower the concentration of calcium the receptor needs in order to fire. They shift the whole response leftward. CaSR, nudged this way, signals through its G-protein to the enzyme phospholipase C, which cleaves a membrane lipid into two messengers, one of which releases a pulse of calcium *inside* the taste cell — and that internal pulse is what the nerve carries away as the sensation we are calling fullness. The taste cells that do this sit beside the cells that read savory, sweet, and salt, and the kokumi signal leans across and amplifies them. A door that works by making the other doors work better. It is, almost poetically, the receptor the body uses to keep its own chemistry whole, repurposed by the tongue to report when *food* is whole.



Garlic in cross-section — among the plants richest in the γ-glutamyl peptides that open the kokumi door. The roundness it lends a dish is a receptor's quiet work, not a flavor you could name.

The keys: short peptides and an unusual bond

The keys that fit this lock are the **γ-glutamyl peptides** — short chains of two or three amino acids — and the heart of this whole chapter is a single detail of how they are built. In an ordinary peptide, amino acids link through the α-carboxyl group, the one on the backbone. In a γ-glutamyl peptide, glutamate offers instead the carboxyl on its *side chain* — the γ-position, one carbon further out — and the next amino acid hangs from there. It is a small structural quirk with two large consequences. First, the γ-bond is nearly invisible to the ordinary peptidases that patrol the mouth and gut looking for α-bonds to cut; the γ-glutamyl peptides therefore *persist* where normal small peptides would be dismantled, and persistence on the tongue is exactly the lastingness we taste. Second, that side-chain geometry is part of what the CaSR flytrap recognizes.

The most familiar of these keys is **glutathione** — written out, γ-Glu-Cys-Gly — a little three-part molecule that every plant and every one of your own cells manufactures for its internal chemistry, where it serves as the body's workhorse antioxidant. It is not an exotic additive; it is life's common currency, present in garlic and onion and yeast and beans because it is present in nearly everything alive. Around it sits a family of close kin, and they are not equals. The plain dipeptide fragments are quiet. One peptide in particular, **γ-Glu-Val-Gly**, is strikingly loud — gram for gram far more active at CaSR than glutathione itself — and that inequality becomes the central fact of the arithmetic a little further on: a trace of a potent peptide can outweigh an abundance of a mild one.

To design kokumi into a plant, then, is a biochemical problem with a clean shape: grow more of these peptides, and bias the mix toward the loud ones. The plant's own machinery is already most of the way there. Glutathione is assembled in two enzymatic steps — first **glutamate-cysteine ligase** forges that γ-bond between glutamate and cysteine (this is the rate-limiting step, and the plant throttles it by feedback, so glutathione switches off its own production as it accumulates), then **glutathione synthetase** adds the glycine. Downstream, an enzyme called **γ-glutamyl transpeptidase** takes finished glutathione apart and transfers its γ-glutamyl group onto other amino acids, and *this* is the reaction that mints the wider

family, γ-Glu-Val-Gly among them. So the levers are legible: relieve the feedback brake on the ligase so the plant will build past its usual ceiling, keep cysteine and glutamate supplied so the ligase never starves, and tune the transpeptidase so the harvest tilts toward the potent peptides rather than the mild ones. Five of our platform's seven engineering modules — the ones that locate the rate-limiting step, model the metabolic flux, and write the edit — carry over to this problem unchanged, because a pathway bottleneck is a pathway bottleneck whatever flavor sits at the end of it.

Giving the taste a number

None of this can be *designed* until it can be *measured*, and so kokumi, like every door, is made to answer to a single number on the Iyengar Flavor Index — **IFI-K**. The whole Index rests on one idea: do not measure how much of a compound a food contains, measure how *loudly* that compound speaks to its receptor. Loudness is potency, and potency has a precise definition — the concentration at which a stimulus drives its receptor to half of full response, the **EC_{50}**. A low EC_{50} means a little goes a long way; the molecule is loud. Invert it against a fixed reference and scale by a thousand, and you have a score:

> $IFI(candidate) = 1{,}000 \times EC_{50}(reference) \div EC_{50}(candidate).$

Fix glutathione as the kokumi reference — the natural choice, life's common γ-glutamyl peptide — and the definition does something tidy: a candidate identical to the reference scores exactly 1,000, because the ratio is one. Everything louder than glutathione scores above 1,000; everything milder, below. On our bench the reference anchors at an EC_{50} near **1,000 µM** — that is 1.0 mM, and since glutathione's molar mass is 307 g/mol, 1.0 mM works out to about **307 mg/L**, call it three parts in ten thousand by weight. Those conversions are worth carrying in the head, because they turn an abstract score back into something you could weigh onto a balance.

The receptor does not answer in a straight line, which is the next thing the mathematics must honor. Across a rising dose the response follows the sigmoid **Hill** curve,

> $r = [A]^n \div (EC_{50}^n + [A]^n),$

where r runs from 0 to 1 and the exponent n, the Hill coefficient, sets the steepness. Put the concentration [A] equal to EC_{50} and the equation collapses to r = ½, which is the definition of EC_{50} made visible. For a simple receptor with n = 1, doubling the dose to $2{\cdot}EC_{50}$ lifts the response only to ⅔, and halving it to $½{\cdot}EC_{50}$ drops it to ⅓ — a gentle, forgiving slope. But CaSR is that cooperating dimer, with more than one site reading the signal at once, and cooperative receptors run n greater than 1. With n = 2, a dose of $2{\cdot}EC_{50}$ already reaches ⅘ of full response; the curve steepens toward a switch. This is not a mathematical curiosity you can taste around — it is *why* kokumi so often seems to **arrive**, why a broth you are adjusting can cross from thin to complete over what feels like one last small addition. The door, built on cooperative machinery, opens with a snap.

Here is the formula doing its work on a handful of stimuli, with glutathione fixed as the reference. These EC_{50} values are representative bench figures chosen to show the method; the one that is not free to move is the Phoenix row, anchored to that cultivar's designed kokumi score.

STIMULUS	EC_{50} AT CASR (MM)	1,000 × EC_{50}(REF) ÷ EC_{50}	IFI-K
Glutathione — the reference	1,000	1,000 × 1,000 ÷ 1,000	1,000
A generic γ-glutamyl dipeptide	2,500	1,000 × 1,000 ÷ 2,500	400
Phoenix, effective kokumi output	526	1,000 × 1,000 ÷ 526	1,900
γ-Glu-Val-Gly, pure	250	1,000 × 1,000 ÷ 250	4,000

Read the table back into the mouth. The generic dipeptide, needing 2.5 times the reference's concentration to reach half-activation, is quiet — 400. The pure potent peptide, γ-Glu-Val-Gly, half-activates at a quarter of the reference's concentration and scores 4,000; in mass terms, at EC_{50} 250 µM and a molar mass of 303 g/mol, that is only about **76 mg/L** against glutathione's 307 — four times less matter for the same effect, loudness you could weigh. And Phoenix, our full-spectrum cultivar, carries an effective kokumi output that half-activates at 526 µM. Run that through the formula, 1,000 × 1,000 ÷ 526, and it returns **1,900** — precisely the kokumi score that plant is designed to hold.

When many keys turn at once

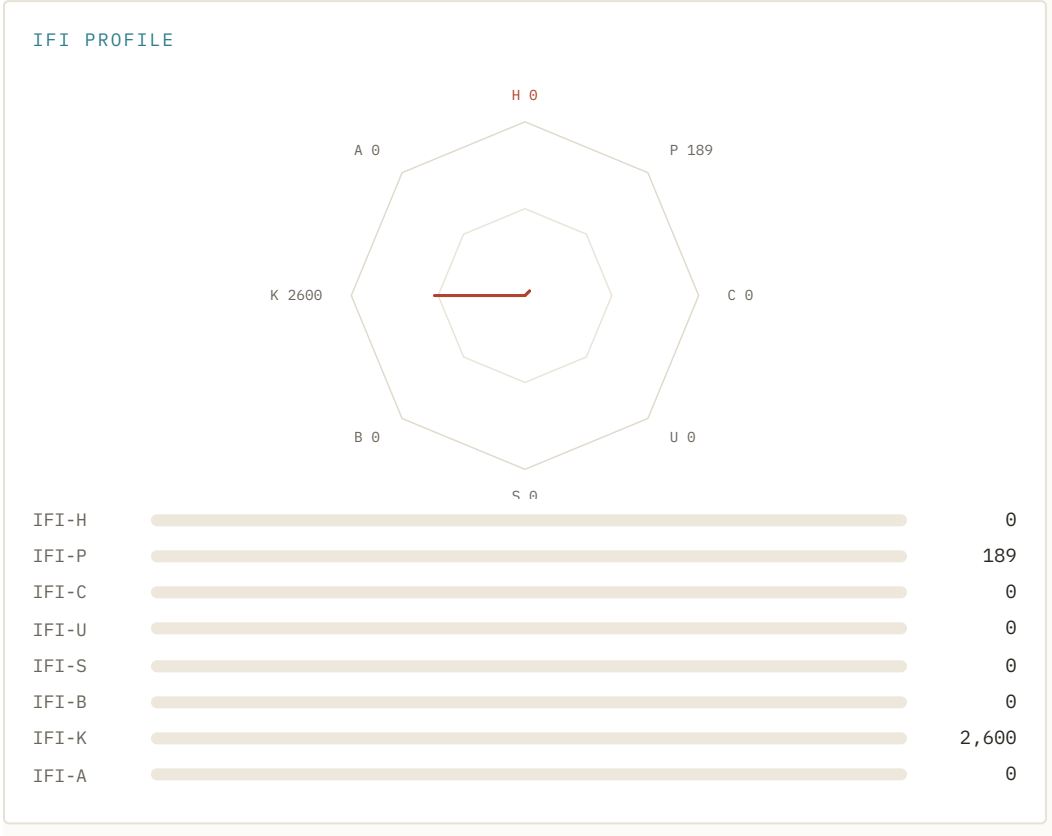
A real plant never presents one peptide; it presents a blend, and the blend is where the design actually happens. Fortunately the receptor adds its keys in a way we can compute. At the modest concentrations food delivers — below the point where the receptor saturates — agonists acting at one site combine by **dose addition**: each contributes activation in proportion to its own concentration divided by its own EC_{50}, and the contributions sum. The clean way to carry this is in **glutathione-equivalents**. Weight each peptide's concentration by how much louder it is than glutathione — that is, multiply by EC_{50}(glutathione) ÷ EC_{50}(peptide) — and the weighted concentrations become directly additive. Because the reference's EC_{50} is 1,000 µM and anchors the score at 1,000, the sum of glutathione-equivalents, read in µM, maps almost one-to-one onto IFI-K.

Take a worked serving of a kokumi-forward garlic we might design, delivering three peptides to the taste interface:

- **glutathione**, 700 µM, at its own EC_{50} of 1,000 → weight 1,000 ÷ 1,000 = 1.0 → **700** equivalents;
- **γ-Glu-Val-Gly**, only 400 µM, but at EC_{50} 250 → weight 1,000 ÷ 250 = 4.0 → **1,600** equivalents;
- a **γ-glutamyl dipeptide**, 750 µM, at EC_{50} 2,500 → weight 1,000 ÷ 2,500 = 0.4 → **300** equivalents.

Sum: 700 + 1,600 + 300 = **2,600 glutathione-equivalents**, and so an IFI-K of about **2,600**. Notice what the arithmetic insists on: the γ-Glu-Val-Gly term, present at the *smallest* concentration of the three, contributes the *most* to the score, because loudness is potency and potency is the reciprocal of EC_{50}. The craft of designing kokumi is therefore not crudely making *more* peptide; it is making the *right*

peptide, tilting the transpeptidase's output toward the handful of loud ones. A plant can be rich in glutathione and still taste flat if the potent kin are missing, and a plant carrying a trace of the loud peptide can speak the kokumi door clearly. We write that target as a profile:



The blanks are not missing measurements; they are real silence. A garlic grown for kokumi speaks two doors and holds its peace on the other six — the K it is built for, and the sharp **pungency** of its allicin, the sulfur chemistry a cut clove throws off, which rides the TRPA1 channel and which no breeding would ask garlic to surrender. That honesty is part of what the profile is for: it tells you what a plant *says* and, just as plainly, what it does not.



Onion in cross-section — the allium that carries kokumi quietly into nearly every savory base a kitchen builds.

The plants we tune

The foods richest in these peptides are precisely the ones a cook reaches for when a dish needs *depth* and words run out — garlic and onion and the other alliums, aged cheeses, yeast and the dark yeast spreads, long-fermented soy, certain beans, and the vanilla bean, whose famous complexity owes as much to a quiet kokumi roundness beneath it as to the vanillin everyone can name. Several of them our family works with directly, and each carries its own engineering character. The roster below is drawn from our

established host organisms — the plants already live on the platform, with the number of distinct constructs we hold for each and the difficulty of coaxing the trait up.

ORGANISM	CONSTRUCTS	PRIMARY AXES	DIFFICULTY
Garlic	560	K · P	Moderate
Soybean	360	U · K	Frontier
Yeast	240	U · K	Hard
Onion	40	K	Moderate
Vanilla	40	K	Hard

Garlic and onion are the alliums at the savory foundation of nearly every cuisine, and they are moderate work — the glutathione pathway sits close to the surface, the levers are reachable. Soybean and yeast pair kokumi with the savory door, the two that together make a broth taste cared-for, which is why they are the quiet engines behind so much fermented cooking; the soybean sits at the frontier of difficulty because its biochemistry is a dense network to move without disturbing the rest of the plant. And vanilla — hard, every time — carries kokumi as the floor beneath its aromatic cathedral, the reason a real bean rounds a custard in a way the synthetic single note never manages.

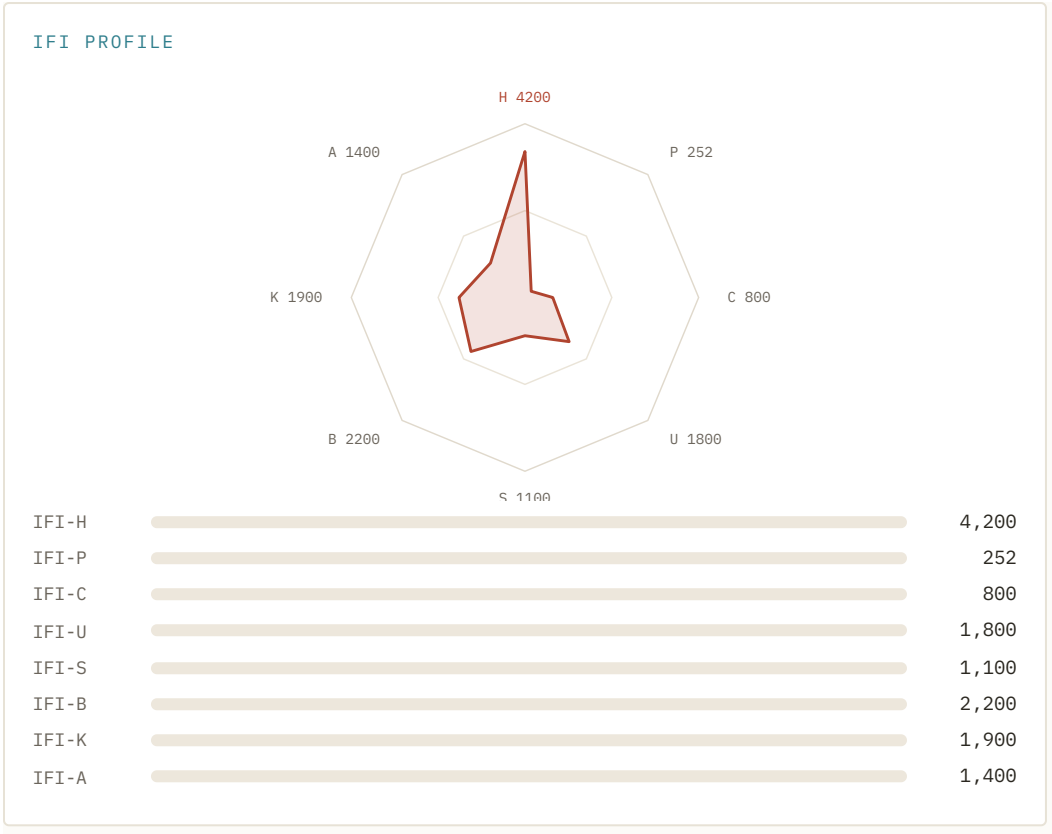
We grow these the way we grow everything: plant-first, clean, with reverence for the living thing and a lifelong preference for what a garden can give. To design kokumi into them is not to make them taste of something foreign. It is to let a broth ingredient carry its own built-in afternoon of simmering — to grow into the plant the very molecules that signal *this was made slowly and with care*, so that the care is already there in the bean, the clove, the paste, waiting.



Vanilla — the world's most complex and most counterfeited flavor; its roundness is kokumi doing quiet structural work beneath the vanillin.

Kokumi in the full spectrum

The clearest place to watch kokumi take its designed seat among the others is the one cultivar built to register on all eight doors at once — **Phoenix**, the plant we engineered gene by gene because no plant that could do it yet existed. Its full profile sets kokumi beside the seven other axes on a single page:



Laid against its receptors, the same eight numbers read as a map of a whole mouth:

AXIS	DOOR	RECEPTOR	PHOENIX IFI
IFI-H	Heat	TRPV1	4,200
IFI-P	Pungency	TRPA1	252
IFI-C	Cool-Burn	TRPM8	800
IFI-U	Umami	mGluR1	1,800
IFI-S	Sweetness	TAS1R2·R3	1,100
IFI-B	Zero-Bitter	TAS2R38	2,200
IFI-K	Kokumi	CaSR	1,900
IFI-A	Astringency	Salivary PRPs	1,400

The heat towers, as heat will — our model predicts approximately three million Scoville units for this design — but look at what kokumi is doing at 1,900. It is not the loudest number, and it is not meant to be. Kokumi is the door that makes a composition *hold together*. A plant that spoke seven doors at full cry and stayed silent on the eighth would taste like a list of sensations rather than a flavor; the 1,900 of IFI-K is the binding agent, the modulation that lets the heat and the savory and the sweetness read as one continuous experience rather than eight competing ones. On the full-spectrum plant, kokumi is quite literally the number that makes the others cohere — the hand on every shoulder, doing in a single cultivar what it does in a bowl of soup.

Precision, error, and the limits we keep

A number is only worth what its reproducibility is worth, and this is where a platform parts ways with a lucky harvest. Across batches, our constructs hold a coefficient of variation at or below **7%** —

against something nearer **42%** in the unselected wild-type plants that older breeding had to live with. Carry that through on the kokumi score. At IFI-K 1,900 and a 7% CV, one standard deviation is 0.07 × 1,900 ≈ **133**, so a typical batch lands inside roughly **1,767 to 2,033**, and even a 95% spread of two standard deviations stays within about 1,634 to 2,166. Run the same 1,900 at the wild-type's 42% and one standard deviation balloons to about **798** — a batch anywhere from 1,100 to 2,700, a plant you could never formulate around because you could never say in advance what it would be. Reproducibility is not a bureaucratic virtue here; it is the whole difference between a flavor you can *design* and one you can only *hope for*.

And then the honest limits, because a number that hides its own edges is not a measurement but a boast. Four of them matter for kokumi in particular.

The first is **saturation**. The clean linearity that lets glutathione-equivalents simply add holds only in the lower reach of the Hill curve; push the concentration toward where the receptor saturates and each added peptide buys less and less response, the scale compresses, and a profile that reads 2,600 on the bench may deliver less separation on the palate than the arithmetic promises. We measure, by design, in the honest middle of the curve, and we say so.

The second is the **ceiling**. The Index normalizes each axis onto a scorecard that tops out at 5,000, and a pure, very loud peptide can in principle run past it — the raw ratio for a potent γ-glutamyl species can exceed what the radar can draw. The cap is a convenience for the eye, not a law of the tongue, and we keep the raw figure on the lab sheet even when the scorecard pins to its edge.

The third is intrinsic to the receptor: because the kokumi peptides are *modulators* rather than clean agonists, their effect depends on what else is present — on the calcium in the food, on the amino acids already occupying the flytrap, on the savory and sweet signals they are there to amplify. A single EC_{50} is a fair summary of an effect that is, in truth, contextual. We state IFI-K against a defined background for exactly this reason, and a plant's kokumi will read a little differently in a mineral-rich broth than in plain water — which is not an error in the number so much as a truth about the door.

The fourth is the one we are glad of. Kokumi is, in the end, the sensation of a flavor being *whole*, and wholeness has a component no EC_{50} will ever fully capture — the moment a soup stops being ingredients and becomes a soup. We can measure the molecules, the receptor, the half-activation, the batch-to-batch spread, and we do, to four significant figures where the method allows. The last small distance — between a complete number and the feeling of completeness — is one we are content to leave uncrossed. These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.

The taste of wholeness

We love this door for a reason that is nearly philosophical, and in a book about wonder we will say it plainly. Kokumi is the taste of things being *whole* — of continuity, of a flavor that holds together and does not fall thin — and the body reads it through a receptor that spends the rest of its life keeping the body's own chemistry in balance, holding the blood's calcium inside its narrow safe band. We did not design that correspondence; we only found it, and we have never quite gotten over it: that the door the mouth uses to feel *wholeness* in food is built from the very machinery the body uses to keep *itself* whole. We score it, like everything, on the Index — IFI-K, anchored to glutathione, computed to the same rigor as the rest. But of all eight doors, this is the one we are most content to let keep a little of its mystery. You will know it the moment a broth stops tasting thin and simply tastes *complete*. That is the door, quietly doing its work — a receptor's small act of care, repeated a billion times a second, that your tongue has always called *enough*.

Chapter 9 · The Opposite of Spicy — *cool, and the mirror of fire.*

Put a single leaf of mint on the tongue and the mouth goes cold. Press a thermometer to the same spot and it will not move — not by a tenth of a degree. Nothing has grown colder: not the leaf, not the breath drawn over it, not the blood in the warm floor of the mouth. And yet the cold is unmistakable, a clean draught blowing through tissue that is exactly as warm as it was a second before. The symmetry in that is, we think, the most satisfying in all of the senses, and years of growing these plants has never worn it smooth. The cold of mint is the exact mirror image of the fire of a pepper — the same beautiful mistake, told backward.

A pepper tells the mouth a fire that is not burning. Mint tells the mouth a cold that is not chilling. Both are lies the tongue believes completely, and both are lies for the same deep reason: the tongue does not taste temperature at all. It reads two molecular doors — one built to guard the hot end of the scale, one built to guard the cold — and a plant has learned, in each case, to carve a key that trips the guard when no danger is anywhere near. To understand the spicy door you have to meet the cold one standing across from it, because these are not two unrelated tricks. They are one trick, run in opposite directions, and the plants that perform them are twins.

This is why a book that opens with fire carries a cool accent the whole way through. The opposite of spicy is not *bland* — bland is the absence of signal. The opposite of spicy is a second marvel with its own loud, clean signal, a winter grown leaf by leaf in a greenhouse that never drops below room temperature. And when you can score both marvels on one page, in the same units, the mirror stops being a metaphor our family is fond of and becomes a number you can design against.

The cold door — what TRPM8 is, exactly

The door that makes mint cool is called **TRPM8** — Transient Receptor Potential, Melastatin subfamily, member 8 — and in ordinary life it is a thermometer for the far end of the dial. Capsaicin's receptor watches for dangerous heat; TRPM8 watches for dangerous cold. It is quiet while the tissue is warm and springs open when the temperature of the flesh around it falls below roughly **26 °C**, firing the word *cold* up the sensory nerve — the signal you feel on a winter morning, or in the ring of chill around an ice cube held to the lip. It is the body's cold alarm: faithful, silent until needed, and the honest reason your face knows January before your mind does.

It is worth being exact about the thing the menthol lies to, because the elegance is in the machinery. TRPM8 is a **homotetramer** — four identical protein subunits packed around a single central pore, each subunit threading the membrane six times. The first four of those passes (helices S1–S4) fold into a *voltage-sensor-like domain*, a small cradle that can read the electrical field across the membrane;

the last two (S5–S6), together with a re-entrant pore helix, line the channel's throat. When the channel opens it is a non-selective cation pore: sodium and, importantly, **calcium** flood inward, the nerve ending depolarizes, and an action potential leaves for the brain.

What makes it a *thermometer* is that it has no single switch. Cold, voltage, and menthol are three separate hands pushing on the same door, and the channel sums them. In the language of biophysics, each one shifts the channel's conductance–voltage relationship — the curve that says how likely the pore is to be open at a given membrane voltage. Cold slides that curve toward the resting voltages the nerve actually sits at, so that chilling the tissue raises the open probability without anything else changing. The channel does not "detect cold" so much as become easier to open as it cools. That is the crack in the door that a plant molecule learned to pry.



The research greenhouse at first light, silver with dew — the hour that belongs to the cooling plants, where we read the five committed genes of the menthol route off the glandular hairs of the leaf.

Menthol pries it by binding inside that voltage-sensor-like cradle. The classic menthol-sensing residue sits on the S2 helix — a single tyrosine whose mutation quietly deletes the cooling without touching the channel's response to real cold — and the molecule wedges into a hydrophobic pocket there, its lone hydroxyl group making a hydrogen bond at the back of the cave while the ring and its two carbon branches fill the hydrophobic volume. Occupying that pocket does the same thing cold does: it slides the conductance–voltage curve toward resting voltage. The channel opens in a warm mouth as though the mouth had just gone cold. And because calcium rides in with every opening, the tissue that follows — the slow fade, the

way a second mint is never quite as sharp as the first — is calcium's doing too, through a cofactor we will come back to when we talk about why the cold does not last.

The mirror, drawn exactly

Hold the hot door and the cold door side by side and the symmetry is not loose or poetic. It is structural, residue for residue, almost spiteful in its neatness.

	HEAT	COOL
The door	TRPV1	TRPM8
TRP subfamily	Vanilloid	Melastatin
Real job	sense heat above **~43 °C**	sense cold below **~26 °C**
The key	capsaicin	menthol
What the key does	*lowers* the heat threshold to meet body warmth	*raises* the cold threshold to meet body warmth
The axis of the Index	**IFI-H** (TRPV1)	**IFI-C** (TRPM8)
The honest lie	a fire that isn't there	a cold that isn't there

Both doors are TRP channels — the same ancient architecture of four subunits and a central pore. Both are *polymodal*: temperature, voltage, and a plant ligand all converge on one gate. Both are calcium-permeable. Both live in the trigeminal and dorsal-root sensory neurons that carry touch, temperature, and pain from the mouth and skin — which is the real reason "spicy" and "cooling" are not tastes at all but touches, felt on the somatosensory wire, not the gustatory one. And both tricks are the identical act of *threshold theft*: a molecule binds and drags the channel's trip-point across the temperature the body already is.

The arithmetic of that theft runs in opposite directions, and it is worth doing out loud. The hot door normally waits for 43 °C. Resting core temperature is about 37 °C; the warm surface of the mouth sits near 34 °C. So for capsaicin to raise a fire in a mouth that is merely body-warm, it must drag the heat threshold *down* across a gap of about **43 − 34 ≈ 9 °C** — and it does, lowering it well below mouth temperature until the body, warm as it has always been, reads as dangerously hot.

The cold door is the gap inverted. It normally waits for 26 °C; the mouth surface sits near 34 °C, a full **34 − 26 ≈ 8 °C** warmer than the trip-point. Nothing happens, because the tissue is warm. Menthol closes that gap from the other side: it raises the apparent cold threshold *up* through 26, past 30, past the 34 °C the mouth already is — so a door set to open only in real cold now stands open in a warm mouth, and the nerve, which cannot tell the difference, reports winter. To be felt as a brisk draught rather than a faint coolness, the shift has to clear not just the 34 °C surface but the 37 °C of better-perfused tissue beneath — a lift of **ΔT ≈ 11 °C** in apparent threshold. More menthol, a larger shift, a colder lie. That dose-to-degrees relationship is exactly the thing the Index was built to pin down.



The greenhouse at dawn, silver with dew — the hour that belongs to the cooling plants. Mint tells the body a cold that isn't there, exactly as a pepper tells it a fire.

Menthol — the key, cut backward

The key itself is a small, almost austere molecule, and growing it well is a lesson in how much the shape of a thing matters. **(−)-Menthol** is a monoterpenoid alcohol — a six-membered carbon ring with a hydroxyl, a methyl, and an isopropyl branch — with the formula **$C_{10}H_{20}O$** and a molar mass of **156.27 g/mol**. That ring carries three stereocenters, which means there are **eight** possible stereoisomers of the same atoms: menthol, neomenthol, isomenthol, neoisomenthol, each in a left- and right-handed form. Only one of the eight — the (1*R*,2*S*,5*R*) arrangement, the natural (−)-menthol — delivers the full, clean, unmistakable cold. The others are dimmer, or warmer, or carry an off-note; some barely find the pocket at all. The cooling lives not in the atoms but in how they are folded in space, which is why a plant, patient and stereospecific, makes a far better menthol than a careless reactor ever will.

Mint builds that exact isomer in the tiny glandular hairs that fur the underside of the leaf, down a committed route the breeding literature and our own benchwork both describe as a **five-gene pathway** running off a terpene backbone. Limonene synthase lays down the ring as (−)-limonene; a limonene-3-hydroxylase oxygenates it; and then a short reductive tail — an isopiperitenol dehydrogenase, an isopiperitenone reductase, and a pulegone/menthone reductase closing the sequence — walks the molecule through its intermediates to the final alcohol, setting each stereocenter in turn. Five committed enzymes, five chances to set a corner of the shape correctly. That is a large part of why we file the cooling plants as **Hard** engineering: it is not enough to make *a* menthol; the pathway has to make *the* menthol, every time, with the ring folded the one right way, or the cold comes out blunt.

A note on units, because the Index speaks in concentrations and the leaf speaks in milligrams, and the two have to be made to agree. Suppose a cooling extract reaches half-activation of the cold door at **0.625 mg/L** of menthol. Divide by the molar mass to put it in molar terms:

$$0.625\ \text{mg/L} \div 156.27\ \text{g/mol} = 0.00400\ \text{mmol/L} = 4.0\ \mu\text{mol/L}.$$

So 0.625 mg of menthol per liter is **4.0 µmol/L** of actual key at the door. Hold on to that number — 4.0 µmol/L — because we are about to make it the convention anchor of the whole cool axis.

Putting a number on cold — the IFI-C axis

Fire and frost can be composed in one dish precisely because they travel different wires from different doors, and a cook who wants to *compose* them needs to score them on different rulers. The Iyengar Flavor Index gives the cold its own ruler, **IFI-C**, read off TRPM8 the way IFI-H is read off the hot door, and anchored by the same formula that governs every axis in this book:

$$\mathrm{IFI}(c) = 1000 \times \frac{\mathrm{EC}_{50}(\text{reference})}{\mathrm{EC}_{50}(\text{candidate})}.$$

EC_{50} is the concentration at which a stimulus drives its receptor to half of full response — the honest midpoint of the dose–response curve, where the channel population is open half the time. The formula does not ask *how much* menthol a leaf holds; it asks *how loudly* that menthol speaks to the cold door, which is a very different and much fairer question. Invert the candidate's EC_{50} against a fixed reference, scale by a thousand, and loudness becomes a score you can set beside a pepper, a tomato, and a cup of tea on one page. A score of **1,000 is the reference itself** — the candidate that needs exactly the reference concentration to reach half-activation. Above 1,000 is louder than the reference (a *lower* EC_{50}, less key needed); below 1,000 is softer.

Each axis of the Index is anchored to its own stated reference constant — a convention, in the same spirit as Scoville's dilution-to-threshold definition. The IFI-C reference is set at 4.0 µmol/L; that value defines the convention floor, scoring 1,000, and all candidates are scored against it. Each axis has its own reference constant; a score of 1,000 on IFI-C and a score of 1,000 on IFI-H are both convention anchors for their respective axes and cannot be compared directly across axes.

Make it concrete with the convention anchor we just derived. By convention, **EC_{50}(ref) = 4.0 µmol/L** defines IFI-C = 1,000. Now read a real cooling cultivar — the scorecard at the end of this section, a plant that is almost nothing but cold — which registers **IFI-C = 2,600**. Run the formula backward to find what its menthol is doing at the door:

$$\frac{\mathrm{EC}_{50}(\text{cand})}{\mathrm{EC}_{50}(\text{ref})} = \frac{1000}{2600} = 0.385, \qquad \mathrm{EC}_{50}(\text{cand}) = 0.385 \times 4.0 = 1.54\ \mu\text{mol/L}.$$

The cultivar reaches half-activation at **1.54 µmol/L** — about 0.24 mg/L — against the reference's 4.0. It needs roughly a third of the key to tell the same lie, which is another way of saying it is **2.6× louder** on the cold door. And the mirror cuts the other way too. The full-spectrum pepper this whole library is built around carries a *little* true cold of its own — a cool note of **IFI-C = 800** woven into a plant whose fire reads at the top of the heat scale. Eight hundred is below the reference, so:

$$\mathrm{EC}_{50} = \frac{1000}{800} \times 4.0 = 1.25 \times 4.0 = 5.0\ \mu\mathrm{mol/L},$$

a quieter cold that wants 25% more menthol-equivalent to reach the same half-activation — present, deliberate, and dialed down. The same formula, evaluated across the axis, draws the whole ladder of cold:

IFI-C	EC_{50} RATIO (CAND ÷ REF)	EC_{50} (MMOL/L)	LOUDNESS VS. REFERENCE
40	25.0	100	0.04× — a whisper
400	2.5	10.0	0.4×
800	1.25	5.0	0.8× (the fire plant's cool note)
1,000	1.0	4.0	1× (convention anchor)
2,600	0.385	1.54	2.6× (a true cooling cultivar)

The shape of the dose–response underneath those midpoints matters as much as the midpoint itself, and it is not a straight line. Because the cold door is a tetramer, its subunits bind cooperatively, and the response climbs along a sigmoid well described by a Hill relation,

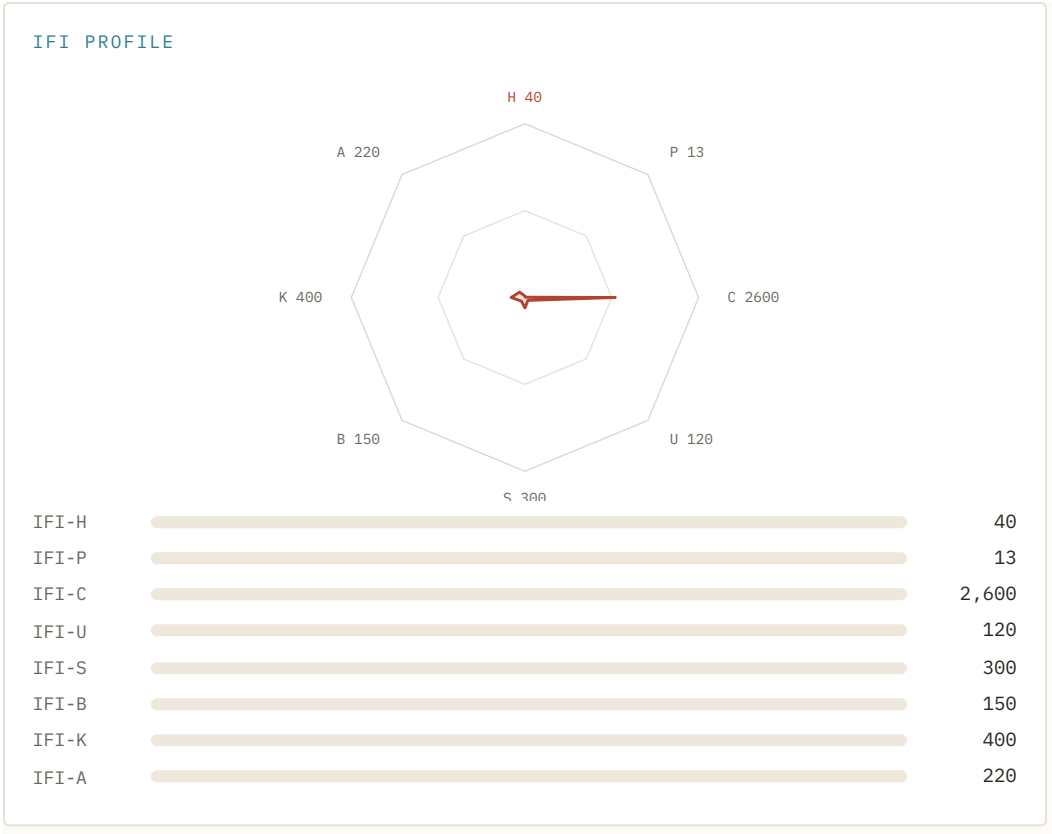
$$R([A]) = \frac{[A]^{n}}{\mathrm{EC}_{50}{}^{n} + [A]^{n}},$$

with a Hill coefficient *n* near 2 for menthol, reflecting the four-fold symmetry of the pore. At the EC_{50} itself the term is 1/(1+1) and the response is, by construction, **0.5**. Double the menthol to 2 × EC_{50} and the response rises to $2^2/(1 + 2^2)$ = 4/5 = **0.80**; halve it to 0.5 × EC_{50} and it falls to 0.25/1.25 = **0.20**. The curve is steep through its middle — a modest change in menthol swings the sensation hard — which is exactly why a cold accent is easy to overshoot by eye and easy to place by number.

And a word on honesty, because a number without an error bar is a boast. The IFI-C we print is a *ratio* of a candidate's EC_{50} against our convention reference, and when both values are drawn from experimental measurements their uncertainties combine in quadrature:

$$\mathrm{CV}(\mathrm{IFI}) = \sqrt{\mathrm{CV}(\mathrm{ref})^2 + \mathrm{CV}(\mathrm{cand})^2}.$$

If each EC_{50} is measured to about 5% — careful, ordinary bench precision — then the index carries $\sqrt{5^2 + 5^2} = 7.07\% \approx$ **7%**. That is not an accident of this one axis; it is why our batch-to-batch target across the platform is **CV ≤ 7%**, the tightness that a designed cold has to hold to be worth composing with. A cooling cultivar at IFI-C = 2,600 therefore carries a window of about **±182** index points — against the **42%** scatter of an unselected wild plant, which would smear that same cold across more than a thousand points and make it undesignable. Precision is not pedantry here. It is the difference between a cold you can draw on a plate twice and a cold that only happened once.



That scorecard is a cooling plant speaking — almost nothing on the heat axis, a tall clean spike on the cool one, the rest held quiet. It is the numeric portrait of a leaf whose whole genius is to open a cold door in a warm mouth.

The cooling shelf — the plants we tune on cool

Mint is the loudest voice on the cold axis, but it is not the only one, and part of the pleasure of this work is how different the cooling plants are from one another once you listen on IFI-C. Menthol is the classic key, but it is not the only molecule shaped to fit the pocket: eucalyptus speaks through **1,8-cineole**, camphor through its own bicyclic ketone, and each converges on the same cold door with a different EC_{50} — which means a different loudness, a different place on the same ladder, and a different *character* of cold. Menthol's is a sharp, forward draught; the cineole cool is rounder and more medicinal; camphor's is cooler-but-dustier. One axis, several keys, read in one unit. These are the organisms our family keeps on the cold shelf, with the breadth of the work behind each:

ORGANISM	CONSTRUCTS	PRIMARY AXES	ENGINEERING DIFFICULTY
Peppermint	2,360	C / M	Hard
Lavender	160	C	Hard
Orange	120	B / C	Hard
Eucalyptus	80	C	Hard
Spearmint	80	C	Hard
Camphor	40	C	Hard

Every one of them reads **Hard**, and now the reason is plain: the cold is a stereochemical achievement, not a yield problem. You cannot brute-force a cooling plant the way an old program chased heat by selecting the hottest fruit and hoping the genotype followed. A cooling plant has to make the one right-handed molecule down a five-step route, in the glandular hairs of the leaf, at a concentration tight enough to land inside a ±7% window — and it has to do it leaf after leaf, season after season, clean, with nothing in the extract that the body should not be given. Peppermint, with the deepest library

on the shelf, is where that discipline shows most; the smaller sets — spearmint's softer, carvone-tinted cool, lavender's floral chill, the cineole brightness threaded through an orange — are each a different cold held to the same standard.

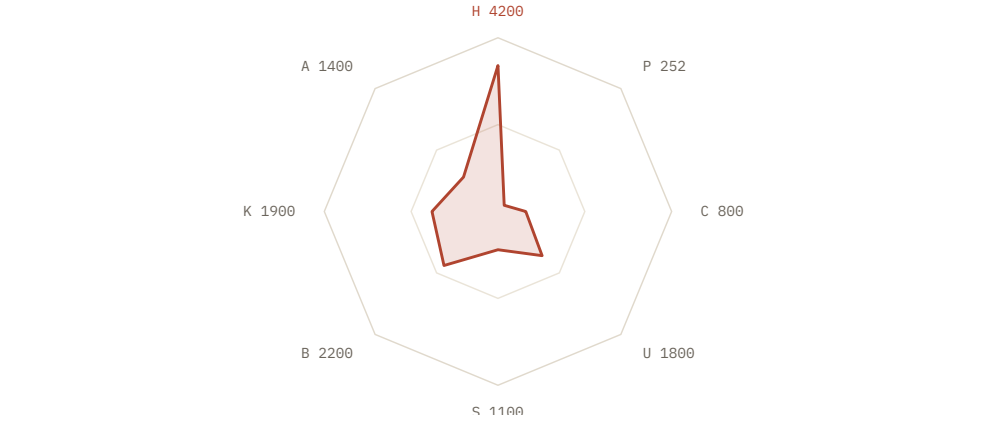


The controlled chamber, where the temperature is dialed to a tenth of a degree so the cold door can be read against a ruler and not a guess.

Fire and frost in one mouth

Here is the gift hidden in the mirror. Because capsaicin works by *lowering* a threshold and menthol by *raising* one, the two keys do not fight over the same lock — they open different doors on different nerves, and neither cancels the other. A dish can be built to feel hot and cool at once: a fire at the front of the mouth and a clean draught moving through it, both true, both lies, held together because they travel separate wires. Some of the world's great spice traditions live exactly in that doubled sensation — the numbing-cool tingle laid over chili heat, the mint cooling a curry's burn without dulling it — and what a cook stumbles onto by luck, the Index lets a family compose on purpose, each sensation scored on its own axis, **IFI-H** for the fire and **IFI-C** for the frost, so the contradiction can be held still and repeated.

The clearest proof that the two axes are independent is a single plant that carries both. The full-spectrum pepper at the top of our heat work is not only hot — it was designed to register on all eight axes at once, and its cold note is real and computed by our model:



Read the two scorecards together and you are holding the whole chapter as numbers. One plant is a tower on IFI-C and almost silent everywhere else; the other is a tower on IFI-H with a deliberate, dialed-down cold of **800** threaded through the fire — the same cold door, opened softly, inside a plant whose whole fame is heat. The mirror is not a figure of speech between two different plants. It can live, designed and repeatable, inside *one*. That is what it means to treat fire as a pleasure rather than an assault: you learn to grow its opposite with the same reverence, and then to hold both in a single warm mouth on purpose.

Honest limits

We would be poor stewards of a number if we pretended it measured more than it does, so here is what the cold axis does *not* promise. First, the cold fades, and it fades for a reason we met early: every opening of the door lets calcium in, and that calcium drives the slow breakdown of **PIP_2**, a membrane lipid the channel needs as a cofactor. Starve the door of its cofactor and it grows harder to open — which is why a second mint is softer than the first, and a third softer still. This *tachyphylaxis* is real adaptation in the tissue, not a flaw in the plant, and no IFI-C score captures it; the Index scores the loudness of a fresh stimulus at the door, not how the mouth tires of it over a minute.

Second, cold is not a solo performance of one channel. Deep, aching, *noxious* cold is carried in part by a different door entirely — the sharp pungency channel of mustard and wasabi — and there is genuine cross-talk at the extremes, which is exactly why the receptor row for this axis reads TRPM8 *and* a touch of the hot door. The clean cool of menthol is mostly TRPM8's, but "mostly" is the honest word, and a very high cold accent begins to recruit sensations the single axis was never built to name.

Third, the ruler reads receptors, not people. EC_{50} is a property of the channel in a dish at a controlled temperature; the mouth that finally tastes the plant is a warmer, wetter, more various place, and a food served cold will of course trip the cold door on its own, stacking real chill on the chemical lie. Individuals differ, too, in how loudly the same menthol reads. The Index is a fixed, fair anchor precisely so those human variations have something steady to vary *around* — but it is the floor beneath perception, not perception itself.

These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.

None of that dims the marvel; it sharpens it. The opposite of spicy is not blandness and not nothing. It is a second door, built to guard the cold, that a plant learned to open with a stereospecific key cut backward from the key for fire — and that our family can now grow leaf by leaf, score to a tenth of a degree, and compose, clean and repeatable, against the heat it mirrors. A cold door, opened in a warm mouth, telling it winter. We have never stopped finding it moving.

Chapter 10 · The Sharp Cousin — *pungency, and the fire that goes up the nose.*

Bite into fresh wasabi, or sharp mustard, or a raw horseradish root, and you meet a sensation everyone knows and almost no one distinguishes from chili heat — though it could hardly be more different. It is a *rush*, bright and sudden, and instead of settling into the mouth like a pepper it shoots **upward**, flooding the back of the nose and the space behind the eyes, cresting in a second or two and vanishing almost as fast. Tears arrive without sadness. The sinuses open like a window thrown wide on a cold morning. Then, as quickly as it came, it is gone, and the mouth is left strangely clean. This is **pungency**, the sharp cousin of heat — and the reason it rises while a chili stays down is one of the most satisfying distinctions in all of flavor, because every step of it, from the molecule to the tears, can be followed and, in the end, counted.

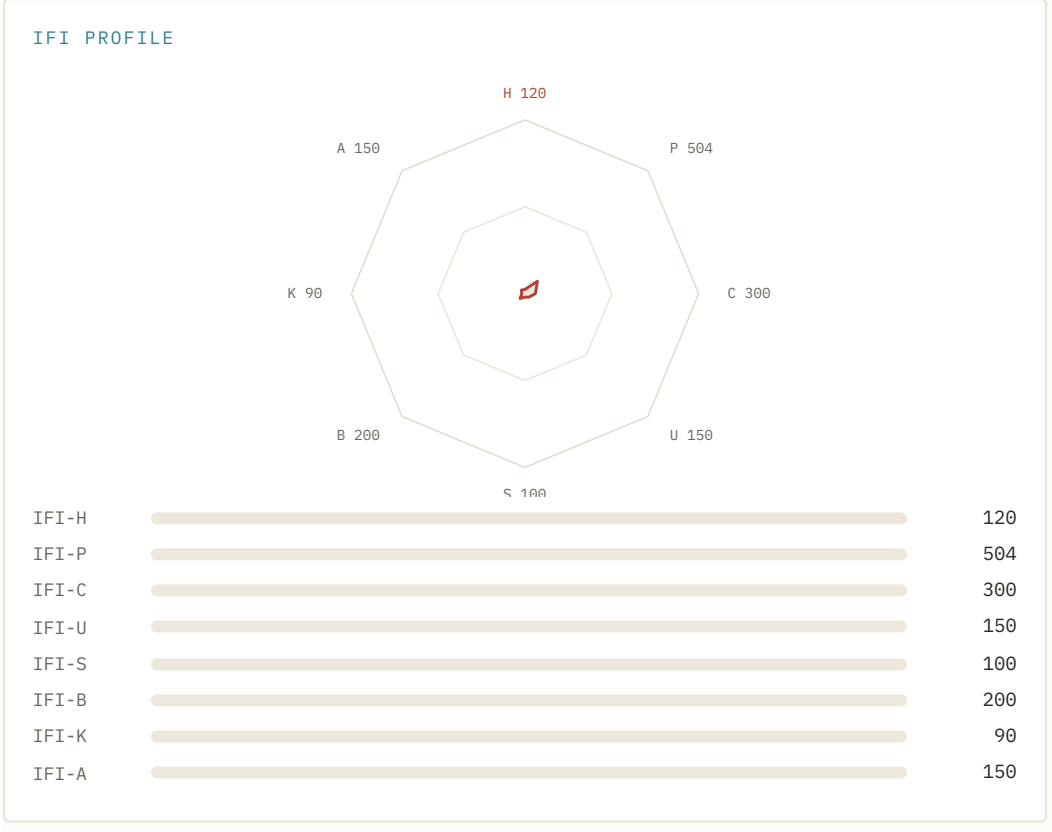
At our table that is the whole game: before you can grow a sensation on purpose, or hold it steady from one harvest to the next, you have to know *exactly* where it lives and what opens it. Heat and pungency feel like one family of fire. They are not one event. They are two doors in the same wall, opened by two different kinds of key, leading into two different rooms of the head — and once you can tell them apart, the word *spicy* comes quietly to pieces in your hand.

A second door in the same nerve

Pungency has its own door, and it is not the chili's. The heat of a pepper is read by **TRPV1**, a channel that also answers to real warmth — the fire of capsaicin is the same alarm the body would ring at 43 °C, pulled early. Pungency is read by a neighbor called **TRPA1**, a channel sitting in the very same trigeminal nerve endings, wired into the same raw, pre-verbal warning system, but tuned to a different and far more aggressive class of molecule. Both doors report to the brain as *irritation*. That shared wiring is why wasabi and chili can be confused in a single careless word. The keys that open them could not be less alike.

Capsaicin, the chili's key, is a quiet thing. It is a heavy oil that slips into a pocket on TRPV1 and holds there by a gentle clasp — a lock-and-key fit, reversible, the molecule free to leave again. The molecules that open TRPA1 do not politely fit a lock. They are chemically *reactive*: they reach the channel and seize it, forming an actual chemical bond with the protein and hauling the gate open by force. TRPA1 is sometimes called, plainly, the **wasabi receptor**, and its agonists read like a roll call of everything sharp on the spice shelf — the mustard family, crushed garlic, cinnamon bark, fresh ginger, the green bite of watercress and horseradish. The sharpness of a whole corner of the kitchen is this one door being grabbed, over and over, by a dozen different hands.

This is why, on the Index, we keep heat and pungency strictly apart. **IFI-H** is the chili's slow, staying warmth through TRPV1; **IFI-P** is the sharp, rising rush through TRPA1. They are not two amounts of one thing. They are two physically different events, reaching the brain by two different keys through two different doors, and a cook who wants to build the full architecture of *spicy* has to be able to aim at each one on its own. Drawn as a scorecard, fresh wasabi is almost a portrait of that separation — a lone tall spike on the pungency spoke, a cool green thread beside it, and the heat spoke left nearly bare:



A chili drawn the same way would be the mirror image — a thorn on heat, almost nothing on pungency. Same family of alarm; opposite portraits; different doors.

The reactive key — a molecule that grabs the lock

To understand pungency you have to understand what *reactive* means, because it is the whole secret of why these molecules feel the way they do.

The key that opens the mustard door is **allyl isothiocyanate** — a small molecule, formula C_4H_5NS, that ends in a tense little group of atoms, a nitrogen double-bonded to carbon double-bonded to sulfur (N=C=S). That central carbon is electron-hungry; chemists call such a group an **electrophile**, a "lover of electrons." Inside TRPA1, on the channel's cytoplasmic skirt — the part that hangs into the inside of the cell — sits a cluster of **cysteines**, the one amino acid that carries a reactive sulfur-hydrogen group (an –SH, a *thiol*). In the human channel these are the cysteines labeled C621, C641, and C665, with a reactive lysine, K710, close by. The electrophilic key and the thiol are made for each other. The sulfur of the cysteine attacks the hungry carbon of the isothiocyanate, and a new covalent bond snaps shut between them. The key is now *bolted* to the lock.

And TRPA1 does not open on a single bolt. The channel is a **homotetramer** — four identical protein subunits arranged in a ring around a central pore, each subunit carrying its own cluster of reactive cysteines. A pungent molecule modifies them one at a time, and as the covalent hits accumulate across the four subunits, the

ring is tugged open and ions pour through. This is a profoundly different machine from the chili's gentle clasp. Capsaicin occupies its pocket and can drift out again, so TRPV1 heat is a steady, reversible pressure — a warmth that leans on the tissue and stays as long as the oil stays. TRPA1 pungency is a running tally of covalent strikes. The "dose" is not how much is sitting in a pocket; it is *how many bonds have been struck.* That single fact explains two things at once: why the sensation is so steep and sudden — the channel flips open as the strikes pile up — and why it is self-limiting. A cysteine that has been seized stays seized until the cell reduces it loose or builds a fresh channel entirely. The fire burns through its own fuel.

The keys change from plant to plant, but the trick is always the same — an electrophile hunting a thiol:

- **Allyl isothiocyanate**, from the crushed cells of mustard, wasabi, and horseradish.
- **Allicin**, the reactive sulfur compound that floods out of garlic the instant it is cut.
- **Cinnamaldehyde**, from cinnamon bark — an α,β-unsaturated aldehyde, a textbook electrophile that adds straight onto the same cysteines.
- **[6]-Gingerol** and its sharper cousin **[6]-shogaol**, the pungency of fresh and dried ginger.
- **Thymol** and **carvacrol**, the biting phenols of thyme and oregano.

Every one of them is a particular way of grabbing the TRPA1 door. Measured, named, and held still, each becomes an ingredient a kitchen can reach for by number instead of by luck.



Black mustard, in cross-section — the seed whose crushed cells forge the sharp, volatile key. Until it is broken, it is silent.

The enzyme that forges the key

Here is a quiet wonder that a child always loves: an intact mustard seed is odorless. So is a whole clove of garlic, and a wasabi stem that has not been grated. The key does not exist yet. It is **forged at the moment of injury**, by an enzyme meeting the molecule it was built to cut — and the plant keeps the two of them locked in separate rooms until something breaks the walls between.

In the mustard seed, one compartment holds a large, inert storage molecule called **sinigrin** — a *glucosinolate*, which is simply a sugar (glucose) bolted to a sulfur-bearing backbone, stable and silent on its own. A different compartment holds the enzyme **myrosinase**, a thioglucosidase whose single job is to cut that sugar off. Apart, they do nothing; the seed can sit on a shelf for a year. But bite the seed, grate the wasabi, crush the horseradish, and the walls rupture. Myrosinase meets sinigrin, snips away the glucose, and the fragment left behind is unstable — it rearranges in an instant, sheds a sulfate group, and resolves into **allyl isothiocyanate**, the volatile key, born in the half-second between the bite and the rush. This is why grating wakes wasabi up, why mustard powder needs cold water and a few minutes to bloom, why the sharpness of horseradish is fiercest the moment it is cut and fades on the board. You are not releasing the sharp molecule. You are *making* it, on the spot, with an enzyme.

Garlic tells the same story in its own dialect. Intact, it holds a calm compound called **alliin** and, kept apart from it, the enzyme **alliinase**. Crush the clove and they meet; alliinase goes to work and **allicin** pours out — itself an electrophile, itself a key to the same sharp door, and itself so reactive that it begins to fall apart into other sulfur compounds within minutes. Ginger keeps a slower clock: fresh, its pungency is **[6]-gingerol**; dry the root and gingerol loses water to become **[6]-shogaol**, which bites harder and higher — which is exactly why dried ginger reads sharper than fresh. Cook it, and gingerol mellows toward **zingerone**, a soft, sweet-warm molecule with almost none of the original sting — which is why a simmered ginger broth soothes where a raw shred of it would make you gasp.



Garlic, halved — whole, it is nearly silent. Crush it and an enzyme finds its substrate; the air fills with allicin, another reactive key to the same sharp door.

For our family's work this enzymatic forge is the whole leverage of the pungency axis, and also its difficulty. We are not tuning the amount of a finished molecule sitting in a fruit, the way we might tune the capsaicin in a pepper. We are tuning a *reaction* — the size of the sinigrin pool, the amount and vigor of the myrosinase, and the small conditions that decide which product the broken seed yields. That last point is a real and humbling edge case: a family of helper proteins called **epithiospecifier proteins** can intercept the unstable fragment and steer it toward a *nitrile* instead of an isothiocyanate — a molecule that barely touches TRPA1 at all. Two seeds with identical

sinigrin can deliver wildly different sharpness depending on which path wins at the moment of the bite. To grow a pungency you can trust, you have to design not just the storehouse but the whole reaction that empties it.

Why the fire rises — a lesson in pure physics

Now, the question the child actually asked: why up the nose? The answer is not biology at all. It is physics, clean and satisfying, and it comes down to one property — **weight**.

Capsaicin is heavy. Its molecule weighs about 305 grams per mole, it is an oil, and it has almost no tendency to evaporate; at mouth temperature essentially none of it lifts off as a gas. So it stays exactly where you put it, clinging to the wet surfaces of the tongue and cheek, and the fire stays *down*, in the mouth, for as long as the oil lingers — which is a long time, because a sticky oil does not rinse away.

Allyl isothiocyanate is light. It weighs only about 99 grams per mole — barely a third of capsaicin — and it boils near 152 °C against capsaicin's 200-plus, which in plain terms means it is **volatile**: it evaporates readily, lifting off into a vapor the instant the seed is crushed. And so it does not stay on the tongue. It rises. It drifts up the back of the throat into the shared chamber behind the nose — the same retronasal path by which all of flavor's aromas reach the smell-sense — and there it opens the TRPA1 doors lining the nasal passages *from the inside.* The sharpness blooms in your sinuses and behind your eyes, nowhere near the spoonful that started it, because the key left the scene as a gas and climbed. It is also exactly why the rush is so brief: a volatile vapor clears in a breath or two, where a heavy oil sits and smolders. Heat is a fire that stays because its key is too heavy to leave. Pungency is a fire that rises and is gone because its key is light enough to fly. Same nerve, same kind of alarm — two molecules of utterly different weight, taking two completely different journeys through the head.

Giving the sharpness a number

A sensation you can describe is a sensation you can enjoy. A sensation you can *measure* is one you can grow on purpose, hold steady, and set beside its neighbors on a single page. For that we use one formula, the same one that anchors every axis of the Index:

$$\mathrm{IFI}(\text{candidate}) = 1{,}000 \times \mathrm{EC}_{50}(\text{reference}) \div \mathrm{EC}_{50}(\text{candidate})$$

EC_{50} is the concentration of a stimulus at which its receptor runs to half of full response — the half-way point of the door's opening. It is the honest measure of *loudness*, because it does not ask how much of a molecule a food contains; it asks how little of that molecule it takes to be heard. A molecule with a small EC_{50} speaks loudly: a whisper of it half-opens the channel. A molecule with a large EC_{50} is quiet: you need a great deal before the door gives. The formula inverts the EC_{50} against a fixed reference and scales by a thousand, so that loudness becomes a plain score. The reference is anchored

so that **IFI-P = 1,000** sits exactly at the convention constant — a stated definition, like the dilution threshold that anchors the Scoville scale.

From there the arithmetic is a pleasure, because a known IFI score hands you the EC_{50} ratio directly. Fresh wasabi reads **IFI-P 504**. Put that into the formula:

> $504 = 1{,}000 \times EC_{50}(\text{ref}) \div EC_{50}(\text{wasabi}) \longrightarrow EC_{50}(\text{ref}) \div EC_{50}(\text{wasabi}) = 0.504$

The convention constant for the pungency axis is **2.1 micromoles per litre** (2.1 µmol/L) of allyl isothiocyanate — a stated definition, anchoring the scale the same way a dilution-to-threshold anchors the Scoville number. Then:

- **Reference:** EC_{50} = 2.1 µmol/L (the convention anchor, IFI-P 1,000).
- **Wasabi:** EC_{50} = 2.1 ÷ 0.504 = **4.2 µmol/L** (IFI-P 504).

And because the key's molar mass is about 99 g/mol, we can carry those concentrations across into the units a kitchen or a lab bench actually reads. One micromole of the molecule weighs about 99 micrograms, so:

> 4.2 µmol/L × 99 µg/µmol ≈ 416 µg/L ≈ **0.42 mg/L**

In watery solution a milligram per litre is the same number as a part per million, so wasabi's half-activation lands near **0.42 ppm** — well under a gram of this molecule would make a thousand litres of water unmistakably sharp. The convention anchor at 2.1 µmol/L works out to about 0.21 ppm by the same path. Written as one short ladder, the whole relationship is legible at a glance:

SOURCE	IFI-P	EC_{50} RATIO (REF ÷ CANDIDATE)	EC_{50} (REF = 2.1 MMOL/L)	≈ MASS CONCENTRATION
Reference anchor	1,000	1.00	2.1 µmol/L	≈ 0.21 ppm
Phoenix · pungency facet	252	0.252	8.3 µmol/L	≈ 0.82 ppm
Fresh wasabi	504	0.504	4.2 µmol/L	≈ 0.42 ppm

The pungency axis has no old folk-measure the way heat has the Scoville scale. There was never a "Scoville for mustard," no shared number for the sharp channel — only the words *mild*, *sharp*, *brutal*, and the memory of tears. The IFI gives that whole dimension a ruler for the first time, and the ruler reads in the same units, against the same reference, as every other taste on the plate.

The dose and its answer — reading a response curve

A door does not open all at once, and it does not open in a straight line. The relationship between how much key arrives and how far the channel opens is an **S-shaped curve** — flat and reluctant at low doses, steep and decisive through the middle, flattening again as the last of the channels give way. Chemists write it as a Hill function:

> $\text{response} \div \text{maximum} = [\text{dose}]^n \div (EC_{50}{}^n + [\text{dose}]^n)$

The EC_{50} is simply the dose that makes that fraction equal to one-half — set [dose] = EC_{50} and the two terms in the denominator are equal, so the answer is exactly 50%, whatever the value of **n**. That exponent *n*, the Hill coefficient, is the steepness of the door: how sharply the response snaps from "nothing" to "everything" around the halfway mark. With n = 1 the curve is gentle; with a larger n it is a near-switch. TRPA1, because it is a four-subunit ring gated by a tally of covalent strikes, behaves cooperatively — once the strikes begin, the ring opens hard — so its curve runs steep. The difference is easy to feel in the numbers:

DOSE (RELATIVE TO EC_{50})	RESPONSE AT N = 1	RESPONSE AT N = 2
0.1 ×	9.1%	1.0%
0.5 ×	33.3%	20.0%
1.0 × (EC_{50})	50.0%	50.0%
2.0 ×	66.7%	80.0%
10 ×	90.9%	99.0%

Read the steep column and you understand why wasabi feels like an ambush where a chili feels like a sunrise. Double the dose of a steep-curved key and the door leaps from half-open to four-fifths open; the sensation does not build, it *pounces*. This is the mathematics behind the suddenness — the reason the rush seems to arrive all at once, crest in a second, and then, its covalent fuel spent and its vapor cleared, fall away just as fast. The chili's gentler curve, its reversible clasp, and its heavy, lingering oil together make a warmth that climbs slowly and stays. The same arithmetic, two different doors, two different shapes of fire.

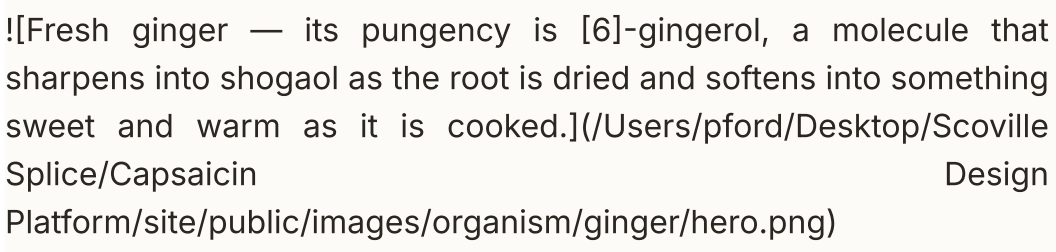
The pungency shelf — plants we tune for the sharp channel

Several of the plants in our family's work are pungency specialists — each a particular way of forging a key for the TRPA1 door, each measured on the one axis and grown toward a sharpness a kitchen can trust. They sit together on what we think of as the sharp shelf:

PLANT	CONSTRUCTS	AXES	DIFFICULTY	THE KEY IT FORGES
Black Mustard	2,790	P / M	Hard	allyl isothiocyanate (from sinigrin)
Garlic	560	K / P	Moderate	allicin (from alliin)
White Mustard	200	P	Hard	*p*-hydroxybenzyl isothiocyanate (from sinalbin)
Ginger	120	P	Moderate	[6]-gingerol → [6]-shogaol
Watercress	120	P	Hard	phenethyl isothiocyanate
Thyme	120	P	Hard	thymol
Cinnamon	40	P	Hard	cinnamaldehyde
Oregano	40	P	Hard	carvacrol

The shelf also holds its own lesson in how different "sharp" can be. Black (brown) mustard forges the light, volatile allyl isothiocyanate — the key that flies up the nose. White (yellow) mustard, working from a different glucosinolate called sinalbin, forges *p*-hydroxybenzyl isothiocyanate instead, a heavier molecule that scarcely evaporates.

It is why a smear of yellow table mustard bites the tongue but rarely floods the sinuses, where a dab of hot English mustard, rich in the volatile key, will clear your head in a breath. Same door, two keys, one light and one heavy — the whole up-the-nose physics, written across two jars on a condiment shelf.



That black mustard carries **2,790 constructs** — by far the deepest library on this shelf — is not an accident. It is the organism where the enzymatic forge rewards the most careful tuning, and where holding the sharp number steady is hardest won.

Steady is harder than sharp — error, and the honest limits

It is one thing to make a plant sharp. It is another to make it sharp *the same amount, every harvest* — and this is where pungency earns its reputation as hard engineering, and where a number proves its worth.

The measure of steadiness is the **coefficient of variation**, the CV: the spread of a measurement divided by its average, written as a percentage.

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CV = ( standard deviation ÷ mean ) × 100%
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Across our platform we hold batch CV to **7% or below**. A wild-type plant, left to its own weather and soil, drifts at around **42%**. Put real numbers to that gap and the stakes become plain. Suppose a pungency cultivar is designed to reach **IFI-P 504**, and we measure it across ten harvests:

- At **CV 7%**, the standard deviation is 0.07 × 504 = **35**. The batch holds in a tight thread — roughly 469 to 539 for most harvests, close enough that a cook would never catch the difference.
- At **CV 42%**, the standard deviation is 0.42 × 504 = **212**. Now the "same" cultivar swings from about 292 to 716 — one jar merely sharp, the next noticeably sharper, the recipe different every time you make it.

A sharpness that wide is not an ingredient; it is a gamble. And pungency makes steadiness genuinely difficult, for reasons that are honest limits of the chemistry itself, not failures of care:

- **The key is forged at the bite,** not stored. Every measurement is really a measurement of a *reaction* — the myrosinase finding the sinigrin — and a reaction can be hurried or starved by temperature, moisture, and timing. Grate warm, grate cold, grate and wait: three different numbers from one root.
- **The key is unstable.** Allyl isothiocyanate is volatile and reactive by its very nature; it begins to evaporate and to react away the instant it is made. The thing you are trying to count is quietly leaving while you count it. The same volatility that sends the fire up the nose makes the fire hard to measure twice.

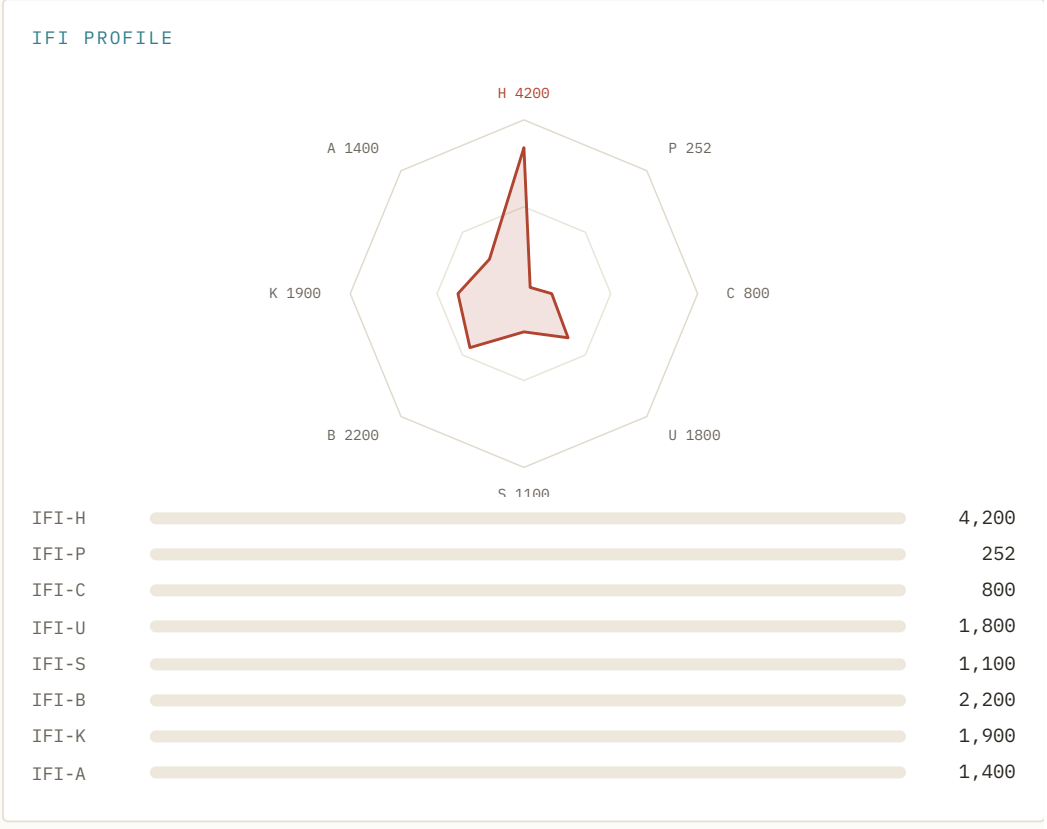
- **The reaction can turn aside.** When epithiospecifier proteins divert the broken seed toward nitriles, the sharpness simply does not appear, though every upstream number looked right.
- **The door tires.** TRPA1 can desensitize with repeated or heavy exposure, and it answers to cold and to other irritants besides, so the *felt* sharpness of a dish depends on what came just before it. The number anchors the stimulus; the eater's own channel supplies the rest.

None of this is a reason to distrust the number. It is the reason the number matters. A score with a known, narrow CV is a promise kept — a sharpness that will taste the same in a classroom demonstration, a restaurant line, and a home kitchen a year apart. That promise is the difference between a spice that happens to you and a spice you can compose with.

Heat that sits, pungency that rises

Which returns us, at the end, to the child's question — *why is it spicy?* — with the honest answer that *spicy* was never one thing. It is at least two sensations wearing a single word: the TRPV1 heat of a chili, slow and deep and staying, its heavy key clinging to the mouth; and the TRPA1 pungency of mustard and wasabi and ginger, sharp and rising and brief, its light key flying up the nose and burning out in a breath. A great dish of real complexity often plays both at once — the lingering warmth of a pepper laid underneath, the bright rush of fresh ginger or sharp mustard cutting across the top — and a cook who can read the Index can score each one on its own spoke and build the whole architecture on purpose instead of by luck.

That separation is also why pungency can live, as one voice among many, inside a design that speaks on every axis at once. Phoenix (SS-0096), the full-spectrum cultivar our family built gene by gene, carries a deliberate, moderate pungency — **IFI-P 252** — folded in beneath a towering heat and a full chord of sweetness, umami, and depth:



Set that balanced portrait beside fresh wasabi's lone sharp spike and the two readings tell the whole chapter without a word. Wasabi is a single door, flung wide — nearly all of its loudness poured onto the pungency spoke. Phoenix is eight doors, each opened to a chosen degree, pungency among them a designed 252 — present, deliberate, in proportion. One is a plant doing the only thing it knows how to do, beautifully. The other is a plant grown to carry a whole conversation, the sharp rush taking its exact place in the chord.

This is the quiet promise under all of our family's work: that a sensation as old and wild as the tears wasabi brings can be understood to the molecule, forged by an enzyme we can read, counted on a ruler that reads in parts per million, and then grown back into a plant on purpose — grown to hold its sharpness steady, grown to carry it in proportion, grown, as everything we grow is meant to be, toward the fullest and cleanest flavor the living thing can bear. These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory. Heat is a fire that sits. Pungency is a fire that rises. Both, held still long enough to be given a number, become yours to compose with.

Chapter 11 · The Pucker That Isn't a Taste — *astringency, the quietest door.*

Drink strong black tea brewed a few minutes too long, or bite an unripe persimmon, or finish a glass of a big tannic red, and your mouth does something it does for nothing else: it goes *dry.* Tight, rough, puckered, the tongue suddenly dragging against the roof of the mouth as though every drop of slippery ease had been wrung out of it. This is **astringency**, the quietest of the eight doors on our Index — and it is the strangest of them all, because it is not a taste, and unlike every other door it is not even, properly, a chemical sensation. Astringency is a *touch.* It is the mouth feeling its own sudden lack of slipperiness. We have spent years learning to measure it, and the lesson it teaches is the most surprising the family knows: that you can put an exact number on a feeling that has no receptor at all.

We want to be careful at the outset, because this door rewards care. Every other sensation in food is a molecule arriving at a lock — a pocket on a protein, a key that fits it, a channel that opens or a signal that fires. Astringency has no lock. There is a plant molecule, a saliva protein, a clumping-together, and then the plain animal feeling of friction where there should have been glide. To measure that, we had to stop looking for a receptor and start watching what happens to spit. What follows is the whole of it — the chemistry, the arithmetic, and the honest edges where the number runs out.

The molecule built to be unwelcome — the tannins

The molecules behind astringency are the **tannins**: large, tangled polyphenols the plant makes in its leaves and skins and unripe fruit, built, like so many plant defenses, to make a thing unpleasant to eat before its time. A tannin is big, flat in places, and studded with phenolic hydroxyl groups — chemical hooks, dozens of them on a single molecule — and it is those hooks that do the work in the mouth. The plant did not evolve them for us. It evolved them to bind the digestive proteins of whatever insect or bird tried the fruit too early, to gum up the works and teach the eater to wait. We have simply learned to read, and then to tune, a defense the plant was already speaking.

There are two great families of tannin, and the difference matters to everything downstream. **Condensed tannins** — the proanthocyanidins — are polymers of flavan-3-ol units, the catechins and epicatechins, linked carbon-to-carbon and essentially impossible to break apart in the mouth. These are the tannins of grape skin and seed, of cacao, of tea, of apple. **Hydrolyzable tannins** are built on a sugar core hung with phenolic acids by ester bonds that water can eventually cleave: the gallotannins carry galloyl groups; the ellagitannins, like the punicalagins of pomegranate, carry the larger hexahydroxydiphenoyl units that break down to

ellagic acid. The two families feel different on the tongue because they are shaped differently, and they fall out of saliva at different rates.

TANNIN CLASS	BUILDING BLOCK	LINKAGE	REPRESENTATIVE MW (G/MOL)	WHERE OUR FAMILY WORKS IT
Condensed (proanthocyanidin)	flavan-3-ols — catechin, epicatechin	C–C (4→8, 4→6)	600 – 3,000+	grape, cacao, tea, blueberry, raspberry
Hydrolyzable — gallotannin	gallic acid + glucose	galloyl ester	700 – 1,500	sorghum, select oak contact
Hydrolyzable — ellagitannin	hexahydroxydiphenoyl / ellagic acid	ester	900 – 1,900	pomegranate (punicalagin), raspberry

Two numbers govern how fiercely a tannin behaves: its **degree of polymerization** — how many flavan-3-ol units are chained together, the mean DP, running from a single monomer to chains of ten and more — and its **degree of galloylation**, the fraction of those units carrying an extra galloyl group. Both push the same direction. A longer chain has more hooks and more flat aromatic faces; a galloyl group is a flat aromatic face of its own. Raise either, and the molecule binds protein harder. This is the lever the plant pulls as its fruit ripens, dismantling and softening its own tannins, and it is the lever we learned to set by hand.



Grape, in cross-section — skin and seed, where the condensed tannins live. The difference between a harsh young wine and a great one is how these molecules meet your saliva.

The protein it hunts — your saliva's slip

What the tannin hooks onto, in the mouth, is not a receptor. It is your **saliva.** Saliva is slippery because it is full of specialized lubricating proteins, and chief among them are the **proline-rich proteins** — the PRPs — long, floppy, open-chain molecules whose whole job is to coat the surfaces of the mouth and let everything slide. They come in basic, acidic, and glycosylated forms, and they are strikingly unusual proteins: as much as a third to two-fifths of their amino acids are proline, a residue whose rigid ring will not fold into the neat helices and sheets of ordinary proteins. So the PRP stays loose and extended, a floppy ribbon rather than a compact ball, a polyproline-II coil with its backbone laid bare.

That openness is exactly why the tannin loves it. A compact, folded protein hides most of its backbone inside. An open proline-rich ribbon offers its peptide carbonyls to the air and presents the flat faces of its proline rings like a row of landing pads — and a tannin's aromatic rings stack against those proline rings in a soft hydrophobic embrace, while the tannin's many hydroxyls hydrogen-bond to the exposed backbone. The plant, defending its unripe fruit, happened to build the perfect anti-lubricant: a molecule whose shape is the negative image of the one protein most responsible for keeping your mouth slick. The family finds a grim elegance in that. The pucker of a sloe or a green banana is a defense aimed, across four hundred million years, at the slipperiness of being alive.

The clump, and why the feeling is a touch

Binding is only the first act. A single tannin can grab more than one PRP, and a single PRP offers more than one landing site, so the two do not simply pair off — they cross-link, tannin bridging protein bridging tannin, into a growing mesh. Past a threshold the mesh stops being soluble. It **precipitates**: the tangle clumps into particles, scatters light, and falls out of the fluid. The saliva, robbed of its lubricant, abruptly stops being slippery. This is a genuine phase separation, a two-stage affair — bind, then aggregate — and because it takes several tannins acting together to drop one clump out of solution, the process is *cooperative.* That cooperativity will matter when we come to the arithmetic.

And so the dryness you feel is literally your spit losing its slide, and it is sensed by *touch* — by the ordinary mechanical nerves that feel pressure and friction everywhere in the mouth, now reporting an unusual roughness and drag where there should be smooth wet ease. There is no astringency receptor with a pocket and a key. There is a lubricant withdrawn and a surface gone rough, and the trigeminal mechanoreceptors read the new friction exactly as they would read sandpaper or grit. This is why astringency feels so unlike the other doors — why it reads as a *texture,* a quality of the mouth's own surface rather than a flavor arriving in it. The quietest door is quiet because nothing is speaking. Something has simply stopped sliding.

Putting a number on a feeling — anchoring IFI-A

Here is the problem the family had to solve. Every other axis on the Iyengar Flavor Index is anchored to a receptor. The governing relation is always the same:

$$IFI(c) = 1000 \times EC_{50}(\text{reference}) \div EC_{50}(\text{candidate})$$

EC_{50} is the concentration at which a stimulus drives its receptor to half of full response — the half-maximal effective concentration. Invert it against a fixed reference and scale by a thousand, and a food's score becomes a measure not of *how much* of a compound it holds but of *how loudly* that compound speaks. A low EC_{50} means a molecule that gets a big answer from very little of itself: loud, high-scoring. A high EC_{50} means a molecule that has to shout to be heard:

quiet, low-scoring. The thousand simply sets the reference itself at a round 1,000, so every other reading lands as a clean multiple above or below it.

But astringency has no receptor and therefore no EC_{50} in the ordinary sense. So for **IFI-A** we anchor the formula not to half-maximal receptor activation but to half-maximal *precipitation* of the salivary PRPs. We call that concentration the **PC_{50}** — the concentration of a tannin at which it precipitates half of the maximum amount of PRP it is able to drop out of solution. It plays the exact role EC_{50} plays everywhere else: a smaller PC_{50} is a tannin that wrings the slip from your saliva at a lower concentration, a louder grip, a higher score. The formula is untouched:

> $\mathrm{IFI\text{-}A}(c) = 1000 \times PC_{50}(\mathrm{reference}) \div PC_{50}(\mathrm{candidate})$

The measurement behind it is a turbidity assay. We take a fixed quantity of human salivary PRP, add a candidate tannin across a dilution series, and read the cloudiness of each tube — nephelometrically, as light scattered by the forming clumps, or as absorbance at 600 nm. Plot turbidity against the logarithm of tannin concentration and you get a sigmoid, an S-curve that climbs from clear to fully clouded. The concentration at the curve's inflection, where turbidity is half of its plateau, is the PC_{50}. The older literature ran this with stand-in proteins — gelatin, serum albumin — and the family's one real improvement on the classic method is to use actual human salivary PRP as the target, so that the number answers to the protein your mouth is genuinely about to lose, not a convenient substitute.

The curve itself is well described by a Hill relation,

> $\tau([T]) = \tau_{max} \times [T]^n \div \left(PC_{50}^n + [T]^n \right)$

where τ is turbidity and n is the Hill coefficient. Set the tannin concentration equal to the PC_{50} and the expression collapses to $\tau_{max}/2$, which is the definition of the half-maximal point and the reason the fit is worth doing. Because precipitation is cooperative — several tannins must act together to drop a clump — n runs above one, typically around 1.5 to 2. A steeper curve means a sharper threshold: below it the mouth stays slick, and then across a narrow band of concentration the slip is gone. That steepness is why astringency can seem to arrive all at once rather than fade up gently, and why a wine a shade too extracted tips so suddenly from firm to harsh.

The arithmetic, worked

Numbers earn trust only when you can see them move, so let us set the reference in plain units and turn the crank. To see the arithmetic cleanly, put the IFI-A reference at a PC_{50} of **1.00 mg/mL** — one milligram of tannin per milliliter, one gram per liter. Against itself the reference scores 1000 × 1.00 ÷ 1.00 = **1,000**, exactly as the scale demands. Now read candidates against it.

A soft, barely drying tannin — one that needs twice as much of itself to cloud the saliva, PC_{50} = 2.00 mg/mL — scores 1000 × 1.00 ÷ 2.00 = **500.** A firmer one at PC_{50} = 0.714 mg/mL scores 1000 × 1.00 ÷ 0.714 = **1,400.** A structured, age-worthy grip at PC_{50} = 0.50 mg/mL scores 1000 × 1.00 ÷ 0.50 = **2,000.** A hard, puckering tannin that clouds the saliva at a quarter of the reference concentration, PC_{50} = 0.25 mg/mL, scores 1000 × 1.00 ÷ 0.25 = **4,000.** The relationship is a reciprocal: halve the PC_{50} and you double the score. Loudness and the concentration it takes to be loud are two ends of the same lever.

PC_{50} (MG/ML)	POTENCY VS. REFERENCE	IFI-A	HOW IT READS IN THE MOUTH
2.00	0.5×	500	soft, barely drying
1.00	1.0× (reference)	1,000	the reference grip
0.714	1.4×	1,400	firm, placed
0.50	2.0×	2,000	structured, age-worthy
0.25	4.0×	4,000	hard, puckering
0.20	5.0×	5,000	the scorecard ceiling

Worked illustrations of the formula; PC_{50} inputs chosen to show the arithmetic plainly. The last row marks a real convention: for the eight-axis scorecards the family caps every axis at a normalization maximum of **5,000**, which on this axis corresponds to a PC_{50} of 0.20 mg/mL — a tannin five times as loud as the reference, past which further grip stops being structure and becomes assault. Nothing we place for the table is meant to live near that ceiling.

It is worth converting one of these out of mass units into molarity, because the molar view shows how little tannin the feeling actually takes. Take the PC_{50} of 0.714 mg/mL and a representative condensed-tannin trimer — three flavan-3-ol units, molecular weight about 866 g/mol. Then

> PC_{50} = 0.714 g/L ÷ 866 g/mol ≈ 8.2×10^{-4} mol/L ≈ **0.82 mmol/L.**

Under a millimolar. The mouth registers the loss of its slip at tannin concentrations well below a thousandth of a mole per liter — and because the real molecules are a distribution of chain lengths rather than one clean trimer, the molar figure is a representative anchor, not a single species. That caveat is the whole reason we report PC_{50} in mass concentration and only convert for intuition: a tannin is a family of sizes, and its grip is a property of the distribution.

The honesty of the error bar

A number no one has bounded is a rumor, so every PC_{50} carries its spread. The family's designed lines hold a batch-to-batch coefficient of variation at or under **7%** — the same discipline that governs every axis — where an unmanaged plant's tannin content can swing far more than that from one season to the next, light and heat and water rewriting the skin's chemistry vintage by vintage. A wild grape is not wrong to vary; it is answering its weather. But a flavor you intend to design has to be a flavor you can repeat, and reproducibility is the whole difference between a measurement and an anecdote.

The error does not vanish when you take the ratio; it compounds, and honesty means carrying it through. IFI-A is a quotient of two reference concentrations, the reference's and the candidate's, and for a ratio the relative uncertainties add in quadrature:

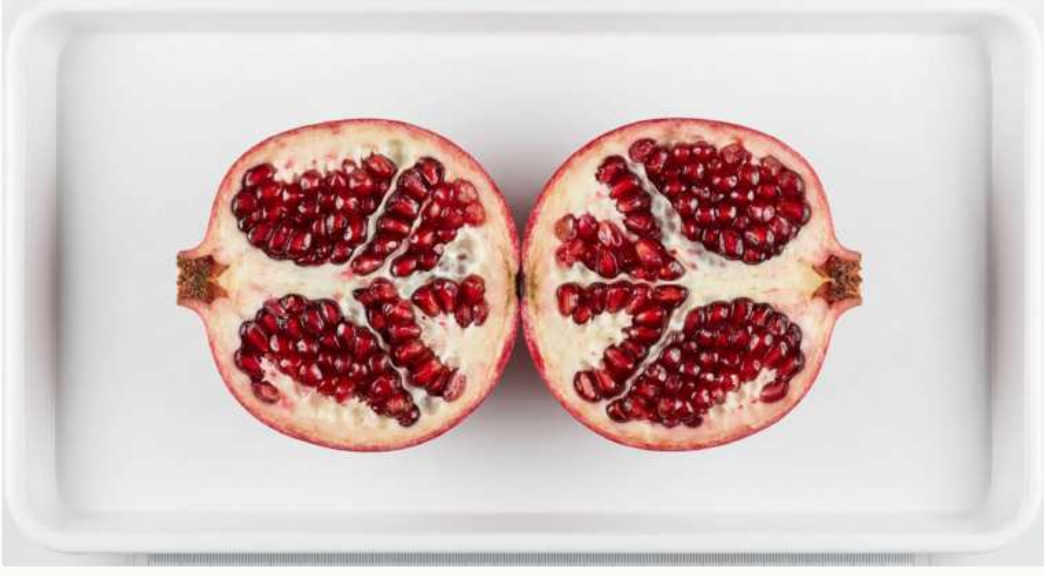
> $CV(IFI\text{-}A) \approx \sqrt{\,CV(ref)^2 + CV(candidate)^2\,}$.

With each term held at 7%, that is $\sqrt{(0.07^2 + 0.07^2)} = \sqrt{0.0098} \approx$ **0.099,** very nearly 10%. So a placed astringency of 1,400 is honestly 1,400 ± roughly 140 at the batch level — a band narrow enough to design within, and far narrower than the forty-percent swings a wild tannin brings to the glass unbidden. We would rather state the band than hide it. On this axis especially, where the sensation is a texture and the measurement a cloudiness in a tube, the error bar is a form of respect for the reader who has to trust the figure.

Designing the grip — the plant's own flavan-3-ol branch

Far from a flaw to engineer away, astringency is a thing great traditions are *built* upon, and the family treats it with reverence — because a designed pucker is structure. It is the tannic spine that lets a red wine age for decades; the clean drying refreshment that makes tea cut the richness of a meal; the firm edge that keeps a fine dark chocolate from going cloying. We do not want these plants' astringency gone. We want it *placed*: set to the exact grip that gives structure without harshness, and set through the plant's own chemistry rather than imposed from outside.

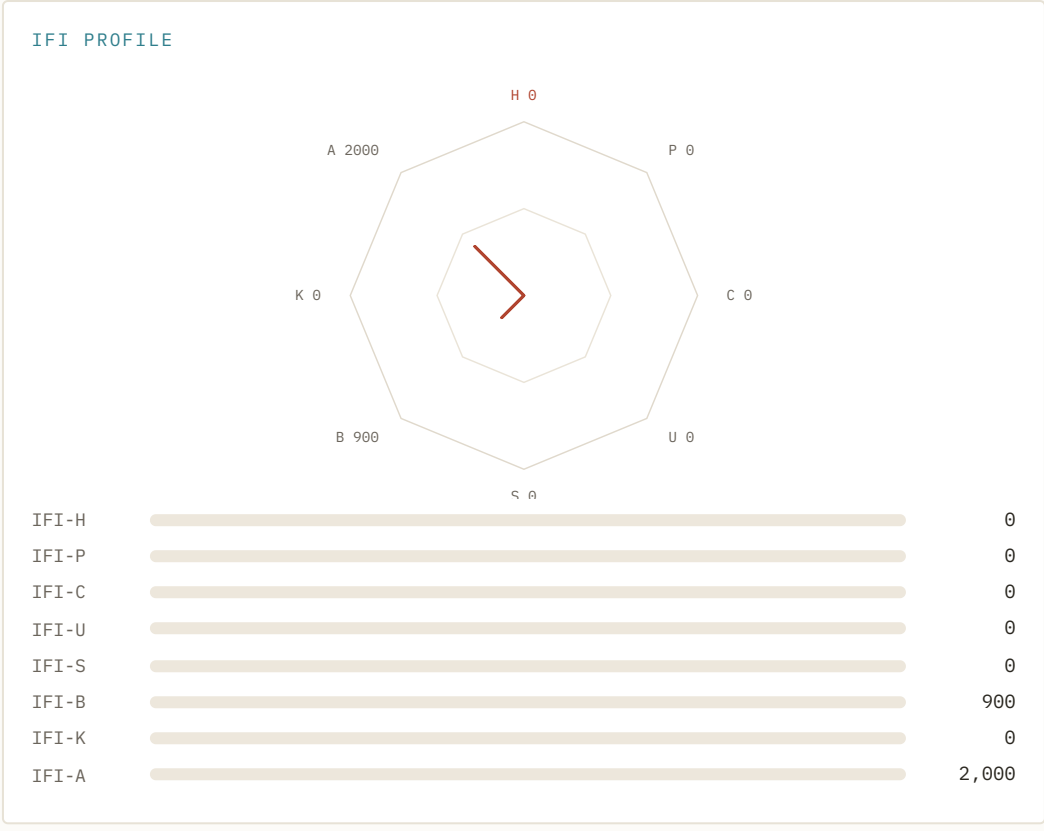
That chemistry is the flavan-3-ol branch of the flavonoid pathway, and the plant already runs every step of it. Downstream of the phenylpropanoid trunk, a dihydroflavonol is reduced toward the leucoanthocyanidin, and the road then forks. Down one fork, **leucoanthocyanidin reductase** — LAR — yields catechin, the 2,3-*trans* flavan-3-ol. Down the other, the anthocyanidin is reduced by **anthocyanidin reductase** — ANR — to epicatechin, the 2,3-*cis* unit. These two monomers, catechin and epicatechin, are the bricks of every condensed tannin, and the balance between the ANR and LAR routes, together with how far the chains are allowed to extend and how heavily they are galloylated, sets the finished tannin's size, shape, and — through all of that — its PC_{50}.



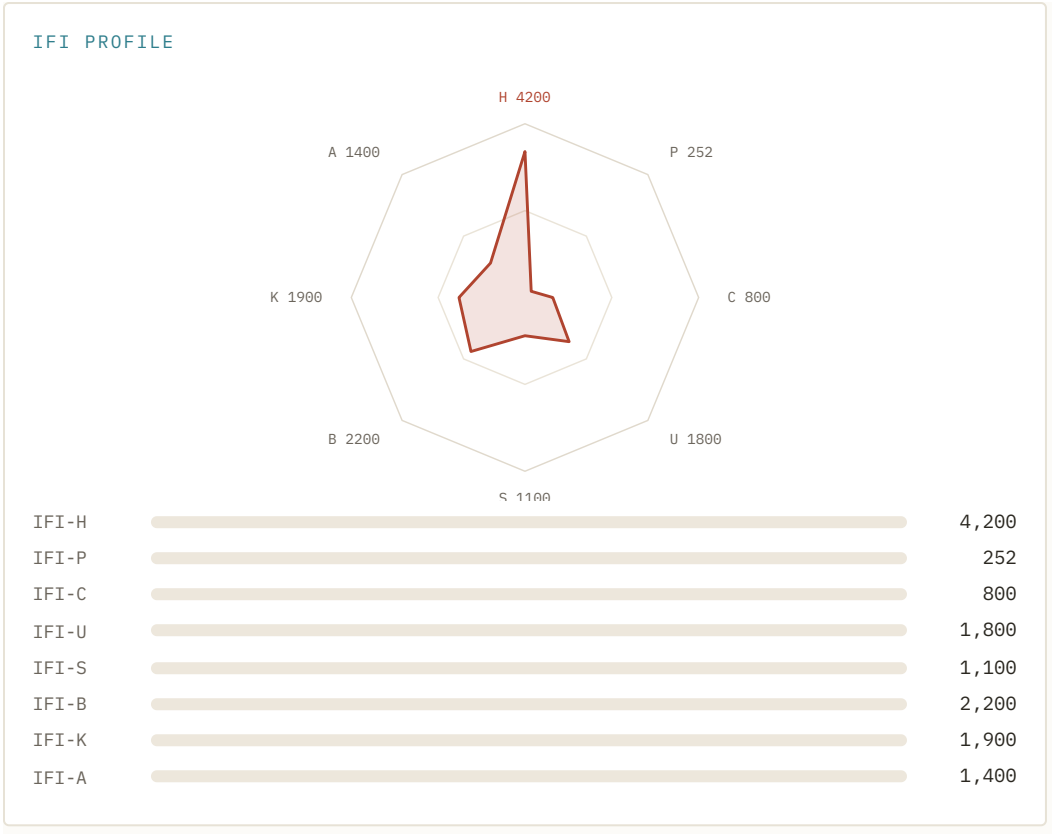
Pomegranate, opened — the arils and the ellagitannins that make its juice at once sweet and drying. Punicalagin is among the largest tannins on any table.

Among the grape constructs alone the family has built more than sixteen hundred — **1,610** of them — a great many aimed at this one quiet door, most working through the ANR route the grape uses to make its own flavan-3-ols. The logic is a straight line from gene to feeling. Push mean degree of polymerization up, or raise the galloylated fraction, and you add hooks and flat faces; the tannin precipitates PRP at a lower concentration; PC_{50} falls; IFI-A climbs. Soften the chain back down and the grip relaxes. Because the direction is monotonic and the pathway is the plant's own, the design problem becomes arithmetic: name the target PC_{50} the glass wants, and tune the branch until the batch lands there, inside the seven-percent band, season after season.

Here is what a placed grape target looks like written as a profile — a design specification, not a measured lot, with each live number traceable to the arithmetic above. The astringency is set at 2,000, the structured grip of a PC_{50} near 0.50 mg/mL. The bitterness is held deliberately just under the reference, at 900, because the galloylated tannins that set the grip also read faintly on the bitter door, and we want the structure to arrive as grip, not as harshness. Every other door is kept silent, so the single axis we are shaping can be read clean:



It is a different thing to see astringency as one voice inside a full chord. The family's only cultivar placed on all eight doors at once carries its grip as a single thread among the fire and the sweet and the savory — astringency at 1,400, the firm-but-placed figure from our ladder, a PC_{50} of about 0.71 mg/mL, structure rather than assault even in a plant designed to register on every axis:



Where the grip becomes a pleasure

Numbers are a way of keeping faith with the plant, not a replacement for it, and the whole point of placing astringency is what happens at the table. In **wine**, tannin is the spine: it gives a young red its grip and its capacity to age, softening over years as its own long chains slowly rearrange. In **tea**, the catechins — epigallocatechin gallate chief among them, a heavily galloylated flavan-3-ol and one of the loudest small tannins there is — give the clean drying finish that makes a cup refreshing and cuts the fat of a meal; brew hotter or longer and you extract more of them, which is simply the eater moving along the dose-response curve by hand. In **cacao,** the procyanidins of the bean give fine chocolate its firm edge against sweetness, the reason a great dark bar finishes bright instead of cloying. And in the red fruits — the **blueberry's** proanthocyanidins, the **pomegranate's** punicalagins, the **raspberry's** ellagitannins — astringency is the faint drying lift that keeps sweetness from going flat. These are plants whose grip we revere and want only to aim.

ORGANISM	CONSTRUCTS	PRIMARY AXES	ENGINEERING DIFFICULTY
Grape	1,610	B · A · M	Hard
Tea	280	U · B · A	Hard
Pomegranate	120	A	Hard
Blueberry	120	A	Moderate
Sorghum	120	A	Frontier
Raspberry	40	A	Moderate

The family's vegetarian table has always leaned on these plants, and not only for structure. The same polyphenols that drop saliva out of solution are among the plant's quiet gifts to the body — a reason we grow toward their fullness rather than breeding it away. We do not make a health claim of it; we simply note, with the reverence the work deserves, that the molecule built to make unripe fruit unwelcome is the same molecule that gives ripe fruit and a good cup their backbone. To place it well is to honor both.



Tea — the leaf whose galloylated catechins give the clean, drying refreshment that cuts a meal. Astringency here is not a flaw; it is the structure of the cup.

The limits of a single number

A number worth trusting is a number whose edges you can see, and astringency has more edges than any other door. We would rather name them than pretend the figure is the whole truth.

The first limit lives in the eater's own mouth. The PC_{50} is measured against a fixed quantity of salivary protein, but saliva flow varies several-fold between people and across a single day — with hydration, with the hour, with age. A mouth running low on saliva has less lubricant to lose and reaches the rough threshold sooner, so the very same tannin reads sharper to a dry mouth than to a flooded one. The Index measures the molecule's loudness; it cannot measure the room it is shouting in. That is a real gap, and we keep it in view.

The second limit is time. Saliva takes minutes to rebuild its proline-rich proteins once they are precipitated away, so astringency **accumulates** across repeated sips: the fifth taste of a tannic wine reads harder than the first at identical concentration, because the mouth has not yet restocked. IFI-A is a per-exposure potency, the loudness of one encounter. It does not integrate the build-up, and a careful taster feels that build-up as surely as the first grip.

The third limit is the matrix. Sweetness and viscosity and a higher pH all blunt perceived astringency; ethanol and a lower pH sharpen it. So an identical IFI-A lands softer in an off-dry wine than in a bone-dry one, softer in a sweetened tea than in a bare brew. And then there is the oldest confusion of all: astringency and bitterness travel together, because many tannins both precipitate PRP *and* fire the bitter receptors — the small, low-polymer phenolics often more bitter than drying, the large condensed tannins more drying than bitter. The Index pulls the two apart on purpose, reading astringency by protein precipitation and bitterness by receptor activation, two different assays for two different doors; but on the tongue they arrive entangled, and no single figure untangles what the mouth feels as one rough-bitter edge. We report both numbers precisely because one would lie by omission.

None of this is a reason to distrust the measurement. It is a reason to state what the measurement is: the intrinsic protein-precipitating loudness of a tannin, held to a band of ten percent, placed through the plant's own enzymes — and then handed to a mouth, and a meal, and an hour of the day that finish the sentence. These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory. That is the quietest door. It has no receptor, no key, no pocket; it is the mouth feeling its own sudden dryness and the plain friction that follows. And it turns out that even a feeling of touch, even the faint tightening of spit losing its slide, answers in the end to a number — one we can read, and having read, place exactly where a wine or a tea or a bar of chocolate was always meant to carry it, and not a thread more.



PART III OF VI

Putting a Number on a Feeling

how loud is a flavor · the ladder of heat · reading all eight at once

Chapter 12 · How Loud Is a Flavor? — *the small mathematics of a feeling.*

The claim that ought to be impossible

This book keeps making a claim that ought to be impossible: that a feeling can be measured. That the fire of a pepper, the frost of mint, the round welcome of a good broth are not only pleasures but *quantities* — real sizes, written as numbers, set side by side and compared. Every meal our family has loved began as a chemical conversation we could feel exactly and describe only in poetry: molecules drifting down onto the wet surface of the tongue, each one settling into a receptor shaped to receive it, a lock and a key fitted together a billion times a second. The feeling you call *spicy* is the summed report of all that fitting, carried up the nerve and read by the brain as fire.

This chapter is where we show that the sum has a size. We do it gently, with arithmetic a family can follow at the kitchen table, because the number at the heart of all our work is far simpler than it first looks — and seeing *why* it is true is the whole difference between taking the wonder on faith and holding it in your own hand. There is one idea to learn, one formula built from it, and then a handful of worked sums that turn a sensation into a measurement you can trust the way you trust a scale or a thermometer. We are a family who has always loved both the plant and the number, and we have never found them to be in tension. The number is how we keep the promise the plant makes.

Why "how much" is the wrong ruler

Start with the obvious wrong way to measure a flavor, because ruling it out teaches everything that follows. You might reasonably think: to know how hot or how sweet a food is, simply weigh the key molecule — count the milligrams of capsaicin, the grams of sugar. It is the first idea anyone has, and it fails at once, and it fails in a way that reveals what a flavor actually *is*.

Consider the sweet proteins a patient grower can coax from a plant — brazzein, thaumatin. A trace of brazzein, a few thousandths of the mass of sugar you would otherwise need, tastes *more* sweet than the sugar does. By the weigh-the-molecule measure, the brazzein is barely present, a rounding error on the scale. By the only measure that matters — how strongly the mouth actually answers — it is overwhelming. Amount is not loudness. The lesson hides in that single comparison: a sensation is not a pile of molecules, it is an *event at a receptor*, and a tiny quantity of a molecule that fits its door perfectly sets off that event far more readily than a heap of one that fits poorly.

Think of it per molecule. A receptor is a door that opens when the right key seats fully inside it. A molecule that matches the lock turns it on the lightest contact, so only a few need ever arrive to swing a given share of the doors open; a molecule that matches poorly must crowd the lock by sheer numbers, jostling for a fit most of them never quite make. The first molecule is *potent*. The second is merely *abundant*. To measure a flavor honestly, then, we must stop asking how much key there is and start asking how strongly the key turns the lock — because that, and not the weight on the pan, is what the tongue is actually reporting when it tells you a thing is spicy, or sweet, or deep.

The curve every flavor draws

So we measure the turning of the lock directly, in the lab, and the way we measure it is the one piece of vocabulary worth a family learning, because it is the hinge of everything that comes after. Take a flavor molecule and its receptor and put them together across a whole range of concentrations. Give the receptor the barest trace of the molecule and only a few of its doors open — a faint response. Add more, and more doors open; the response climbs. Add still more and eventually every door that *can* open is open; the response has reached its ceiling, its maximum, and pouring on extra does nothing at all. Plot the response against the concentration and you get the same graceful rising-then-leveling curve every flavor draws — flat at the bottom, steep through the middle, flat again at the top.



The assay bench where a dose–response curve is read — the same rising-then-leveling shape behind every number in this book.

That curve has a name and a shape we can write down. Call the response **R**, the concentration of the molecule **[L]**, the ceiling response $\mathbf{E_{max}}$, and let **n** describe how steeply the curve rises. Then:

$$R([L]) = E_{max} \cdot [L]^n \div (EC_{50}^n + [L]^n)$$

Do not be frightened by it; it says only what we just watched happen. When [L] is tiny the top of the fraction is tiny and R is near zero; when [L] is enormous the fraction approaches E_{max} and R flattens at the ceiling. And sitting inside it is the single number we have been circling: $\mathbf{EC_{50}}$, the *half-maximal effective concentration* — the concentration of the molecule it takes to drive the receptor to exactly half of its fullest possible response. You can prove it is the halfway

point in one line. Set the concentration equal to the EC_{50}, so [L] = EC_{50}, and the fraction becomes $EC_{50}^{n} \div (EC_{50}^{n} + EC_{50}^{n}) = EC_{50}^{n} \div 2 \cdot EC_{50}^{n} = ½$. The response is $E_{max} \div 2$, half the ceiling, and — beautifully — it comes out to one-half no matter what **n** is. The halfway concentration is always the EC_{50}; the steepness only changes how fast the curve gets there.

For the simplest molecules **n** is 1 and the curve is a plain hyperbola, one molecule to one door. But a channel like the one that reads heat is built from four identical protein subunits clasped together, and subunits that cooperate make the curve *steeper* — **n** climbs above 1, the middle of the curve stands up sharply, and a small change in concentration swings a large change in response. The cooperativity changes the drama of the rise; it never moves the halfway mark. The EC_{50} stands where it stands.

And here is the quiet reversal that makes EC_{50} so honest. A molecule that reaches half-response at a *tiny* concentration is a powerful key — it opens the lock so readily that very little is needed, so its EC_{50} is *low*. A molecule that needs a flood of itself to reach the same half-response is a weak key, and its EC_{50} is *high*. **Low EC_{50} means loud. High EC_{50} means quiet.** The strength of a flavor runs exactly upside down from its EC_{50} — which is the one fact to carry out of this section, because the formula at the center of the book is built to turn that upside-down number right-side up.

The door itself

It is worth standing for a moment at the actual door, because the whole measurement is anchored to it and nowhere else. For heat the door is **TRPV1**, a non-selective cation channel studding the trigeminal nerve endings of the tongue. In its resting life it is a thermometer: it opens to temperatures above roughly 43 °C and to acidity, and when it opens it lets positively charged ions — calcium and sodium — pour through, depolarizing the nerve and sending the brain a single urgent word, *hot*. Capsaicin's trick is that it does not warm the tissue by a single degree. It slips into a pocket cradled between the channel's S3 and S4 helices and *lowers the temperature at which the channel decides to open*, dragging that threshold down from 43 °C toward the temperature your mouth already is. The channel opens as if the food were scalding; the brain reports a fire that is not there. That is why a pepper "burns" without heat, and why the burn answers to cold water poorly and to time patiently — the fire is a lowered threshold, not a wound.

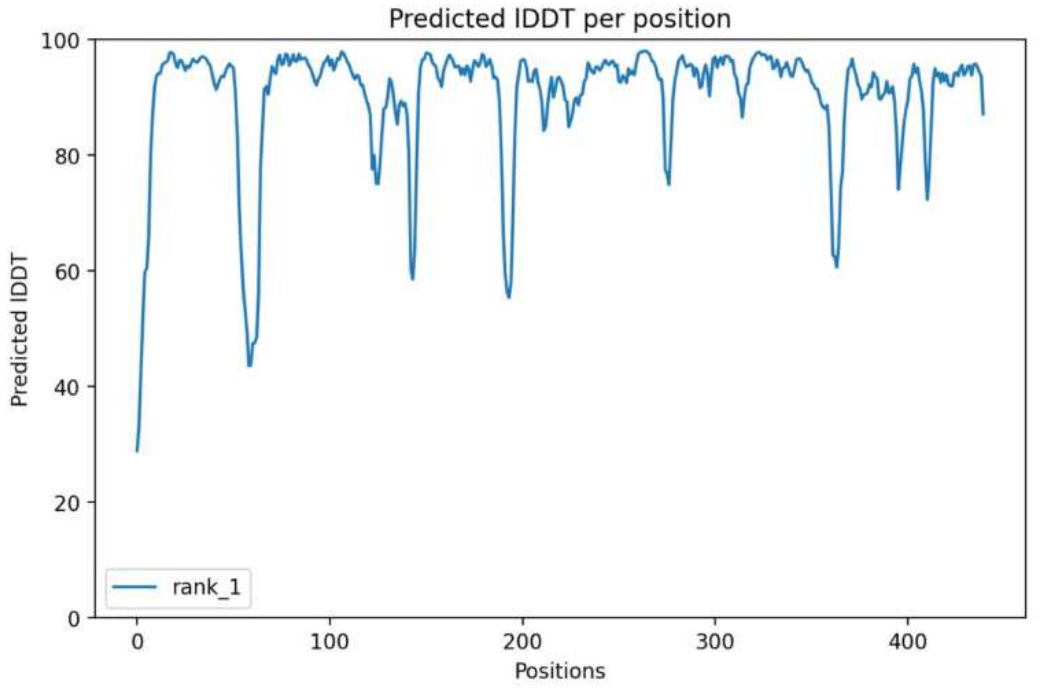


FIG. 12 — the Pun1/AT3 acyltransferase, the enzyme that writes capsaicin, coloured by model confidence; the active-site cleft where the burn is assembled reads high.

The molecule that does this is itself assembled by an enzyme, and the enzyme sets the character of the fire. Vanillylamine condenses with an 8-methyl branched-chain fatty acid at the **Pun1/AT3** acyltransferase to form capsaicin; let the acyl chain run a little longer or sit a little more saturated and the same enzyme turns out dihydrocapsaicin instead, a near-twin with its own onset and its own weight on the receptor. The ratio the enzyme chooses sets the *shape* of the burn — where it lands, how fast, how long it lingers. This is the chain we model along, end to end: a gene specifies the enzyme, the enzyme builds the molecule, the molecule seats in the channel, the channel opens, and a feeling arrives. The EC_{50} is simply where in that chain we put the ruler — at the receptor, the one place every link upstream finally resolves into a response the body reads.

The flip

Now we turn the quiet number loud. We said loudness runs opposite to EC_{50}, which means loudness is proportional to *one divided by* EC_{50}. That already points the right way — up for strong, down for weak — but a bare reciprocal is an awkward thing to hand a cook, all tiny decimals and unlabeled units. So we do two small, deliberate things to it. First, we divide every molecule's reciprocal by the reciprocal of one fixed **reference** — a known, agreed, stated reference point for each axis, the way a ruler is cut against a standard metre kept under glass. Second, we multiply by a thousand, purely to lift the everyday answers out of the decimals and into a comfortable range. Those two moves, together, are the entire Iyengar Flavor Index:

> **$IFI = 1{,}000 \times EC_{50}(\text{reference}) \div EC_{50}(\text{candidate})$**

Read it slowly and it tells its own story. The candidate's EC_{50} sits on the bottom, the reference's on top, and the division does something lovely. Because both quantities are concentrations measured in the same units, those units cancel clean away — the Index carries no units at all, which is exactly why one scale can serve a fire and a frost and a savor without translation. If the candidate is *exactly as strong* as the reference, the two EC_{50} values are equal, the fraction is

one, the thousand stands alone, and the IFI is **1,000**. That is the anchor: the reference scores a thousand, always, by construction — a stated convention, like how the Scoville scale is defined by dilution-to-threshold rather than by any single published measurement. If the candidate is *twice* as loud — reaching half-response at half the concentration, an EC_{50} half as large — the fraction doubles and the IFI is **2,000**. Four times as loud, **4,000**. Half as loud as the reference, and the IFI falls to **500**. Strip away the scaling thousand and the Index is nothing more mysterious than *this flavor, compared to the standard, as a clean multiple* — a sentence any family can keep.

One number, all the way through

Let us run one complete worked example from start to finish, because watching the arithmetic land is the moment it stops being magic and becomes understanding. Suppose the heat reference reaches half-activation of TRPV1 at an EC_{50} of 10 — in whatever assay units the bench is using; the units will cancel, so never mind them. Now our model computes, for the cultivar we named **Phoenix**, that its capsaicin reaches that same half-activation at a predicted EC_{50} of about **2.38**. It needs far *less* of itself to half-open the door, because it is a far louder key. Put the numbers in their places:

```
IFI-H = 1,000 × (10 ÷ 2.38) = 1,000 × 4.20 = 4,200
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There it is. Our model predicts Phoenix at **4,200** on the heat axis — designed to drive the fire-door 4.20 times as hard as the reference does — and that one number now means the identical thing in our kitchen and in yours, this harvest and the next, with no tasting and no guessing asked of anyone. It is tied to the receptor, not to a memory of a hot dinner. That is the whole reason a family spent years on something as unglamorous as a dose–response model: because "medium heat" is a wish, and *IFI-H 900* is a design target, and only one of the two can be kept as a promise.



Phoenix (SS-0096) in the controlled chamber — the pepper behind the worked number: IFI-H 4,200, every axis scored against its own door.

The lovely part is that the formula runs backward just as easily as forward. If you know the score and the reference, you can recover the EC_{50} that produced it, because the Index is a plain ratio you can rearrange: $EC_{50}(\text{candidate}) = 1{,}000 \times EC_{50}(\text{reference}) \div \text{IFI}$. With our

reference fixed at 10 that is just EC_{50} = 10,000 ÷ IFI. Run that across the ladder of superhots our family designed on the road up to Phoenix and the hidden concentrations reappear one by one — each score translated back into the exact potency that earned it.

CULTIVAR · SKU	PREDICTED SHU	IFI-H	EC_{50} (ASSAY UNITS)	LOUDNESS VS REFERENCE
Ember · SS-0087	866,000	1,570	6.37	1.57×
Cinder · SS-0088	1,050,000	2,290	4.37	2.29×
Kindle · SS-0089	1,250,000	2,000	5.00	2.00×
Blaze · SS-0091	1,720,000	2,630	3.80	2.63×
Wildfire · SS-0092	1,960,000	2,930	3.41	2.93×
Scorch · SS-0093	2,210,000	3,220	3.11	3.22×
Firestorm · SS-0094	2,470,000	3,490	2.87	3.49×
Solara · SS-0095	2,720,000	3,980	2.51	3.98×
Phoenix · SS-0096	**≈2,950,000**	**4,200**	**2.38**	**4.20×**

All SHU and IFI values are computational predictions from our design model.

Read down the EC_{50} column and you can watch the engineering happen in a single quantity: the concentration needed for half-activation falls from 6.37 at the gentlest flagship to 2.38 at Phoenix, very nearly a *threefold* increase in potency, written not as a flavor note but as a number a formulator can hold to.

Two rulers for one fire

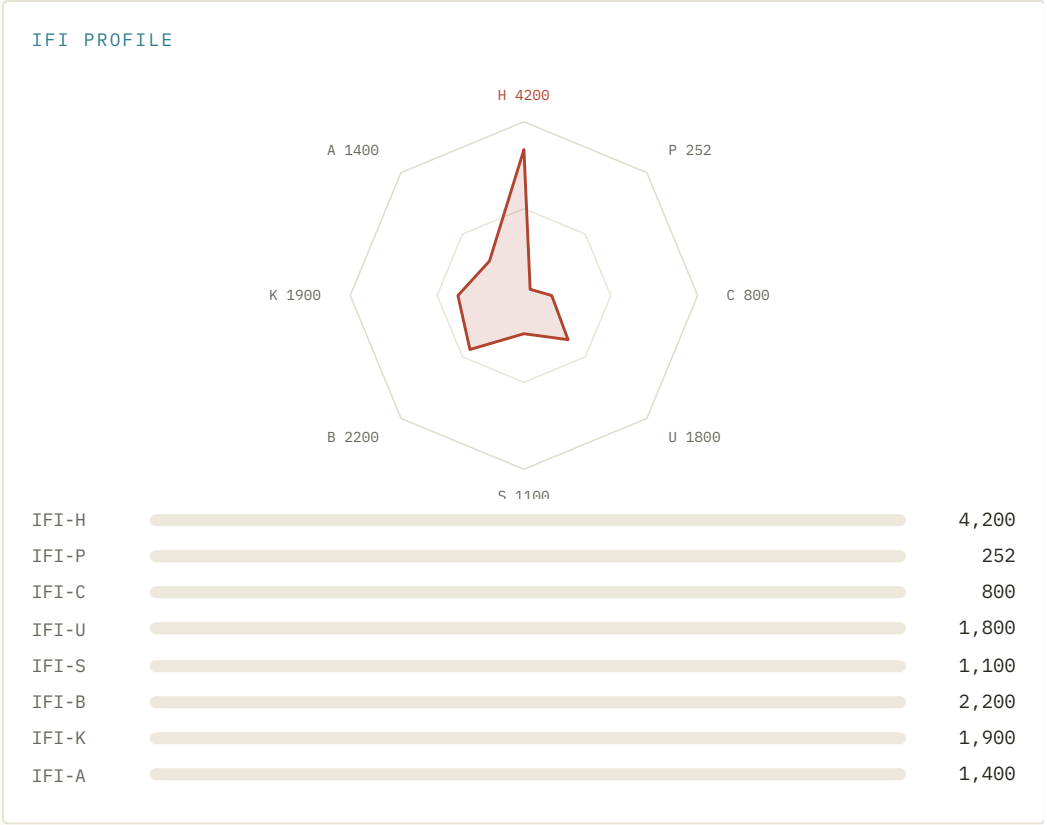
A careful reader will have noticed a second column in that table — SHU, the Scoville Heat Units — and will want to know how the old ruler and the new one agree. The honest answer teaches as much as the formula did. The Scoville scale, drawn up in 1912, measures heat by *dilution*: a pepper's extract is watered down, step by step, and a small panel of tasters says when the burn finally disappears; the dilution factor at that vanishing point is the SHU. It is a threshold measured on human tongues. Modern labs no longer rely on the panel — they quantify the capsaicinoids directly by chromatography and convert to the familiar scale, on which pure capsaicin sits near 16,000,000 — but the thing SHU *means* is still "how far must we dilute before the fire is gone." EC_{50}, and the IFI built on it, mean something different: "at what concentration does the receptor reach half of full response." One measures the vanishing edge of a sensation; the other measures its half-strength grip on the door. Both are reading the same fire. They are simply two instruments held to it from two directions.

So Phoenix's model-predicted heat of approximately 2.95 million SHU and its IFI-H 4,200 are two predicted scores for one designed cultivar, and — this is the point worth keeping — they are *not* related by any single conversion number. If you divide SHU by IFI-H down the ladder, the ratio wanders: about 552 at Ember, dipping to 459 at Cinder, back up through 654 at Blaze to roughly 700 at Phoenix. There is no fixed exchange rate because the two definitions weight the capsaicinoid mixture differently — a dilution panel and a receptor assay do not answer to capsaicin and dihydrocapsaicin in the same

proportion. You can even catch the two rulers trading two cultivars' rank: Cinder sits *below* Kindle by the old dilution count (1.05M against 1.25M SHU) yet *above* it on IFI-H (2,290 against 2,000). Neither number is wrong. The disagreement is the whole argument for a receptor-anchored scale — when you want to design what the tongue will actually feel, you want the ruler held to the door the tongue is reading, not to the edge where a panel loses the thread.

The eight doors, one hand

Everything so far has stood at the heat door, but the move was built to travel, and this is where the Index earns its name. There are eight doors on the tongue worth measuring, each its own receptor, each with its own reference anchored at a thousand. Because the Index is a unitless ratio, the same arithmetic that scored a fire scores a frost and a savor and a bitterness, each against *its* own reference — so for the first time in the long history of eating, the loudness of a burn and the loudness of a cooling and the loudness of a welcome can be written on one page in one hand. Phoenix was the first cultivar our family designed to register on all eight at once, and laying out its full predicted profile shows the scale doing its real work:



Those eight numbers are eight separate predicted scores, each one a computed EC_{50} ratio against a different door, and you can read the whole design from them. Turn each score back into potency with the same reciprocal as before — loudness is the IFI divided by a thousand, and the EC_{50} as a fraction of its reference is a thousand divided by the IFI:

AXIS	RECEPTOR	IFI (PHOENIX)	LOUDNESS VS REFERENCE	EC_{50} (× REFERENCE)
Heat · H	TRPV1	4,200	4.20×	0.238
Zero-Bitter · B	TAS2R38	2,200	2.20×	0.455
Kokumi · K	CaSR	1,900	1.90×	0.526
Umami · U	mGluR1	1,800	1.80×	0.556
Astringency · A	Salivary PRPs	1,400	1.40×	0.714
Pungency · P	TRPA1	252	0.252×	3.968
Sweetness · S	TAS1R2 · TAS1R3	1,100	1.10×	0.909
Cool-Burn · C	TRPM8	800	0.80×	1.250

Notice the pungency row. On the TRPA1 axis Phoenix scores **252** — below the reference — which the arithmetic insists we read plainly: on that one door the design is quieter than the stated reference point, its predicted EC_{50} sitting at nearly four times the standard's, needing much more to reach half-response. Notice also the bottom row. On the cooling axis Phoenix scores **800** — also *below* a thousand — meaning on that door the pepper is quieter than the reference as well. A score under a thousand is not a failure; it is an honest report that this door speaks softly in this design. That is the discipline the Index imposes and the gift it gives — it will tell you where a plant is designed loud *and* where it is faint, in the same units, without flattery.

Error, honestly

A number you cannot trust twice is not a measurement, so we owe you the arithmetic of doubt as plainly as the arithmetic of the score. No two fruits off two plants are ever identical; the question is only *how* different, and the honest name for that spread is the **coefficient of variation**, the CV — the standard deviation of a batch divided by its mean, written as a percentage. It tells you how far a typical sample strays from the labeled value. On a labeled IFI-H of 4,200, a CV translates straight into a real range you can expect to meet in the jar:

LINE	CV	STD. DEVIATION ON IFI-H 4,200	≈95% OF BATCHES FALL WITHIN
Engineered (our flagships)	≤ 7%	≤ 294	3,612 – 4,788
Wild-type, same target	42%	1,764	672 – 7,728

The two rows are the difference between a promise and a shrug. Hold the CV at seven percent and the standard deviation is 0.07 × 4,200 ≈ 294; about ninety-five percent of batches land inside two standard deviations, a band from roughly 3,612 to 4,788 — tight enough that a formulator can build a recipe on 4,200 and meet it. Let the variance run wild-type at forty-two percent and the standard deviation balloons to about 1,764; the same ninety-five-percent band sprawls from 672 to 7,728, a range so wide the label means almost nothing. The scale that holds the burn steady is as much the product as the burn itself. A number is only a promise if it comes back the same the next time you ask.

And a last honesty about the EC_{50} underneath it all: it is not a single reading but a *fitted* value, the halfway point drawn from a whole curve of measurements, and it comes with its own confidence interval. The door it is fitted to is sensitive — TRPV1 answers to temperature and to acidity as well as to capsaicin — so the assay must hold its conditions fixed, and the reference must be run on the very same plate as the candidate, because only then do their shared units truly cancel. Measure the reference on Tuesday and the candidate on Thursday under a different pH and the ratio quietly lies. The whole edifice rests on that modest laboratory discipline: same door, same day, same conditions, reference and candidate side by side.

What the number is not

Precision is a form of respect, and part of respecting a reader is marking a measurement's edges. The IFI measures *loudness at a receptor* — nothing more, and it is worth being exact about what that leaves out.

It is not a measure of liking. Loud is not the same as good; a profile is a description, never a verdict, and the most beautiful dish our family cooks is rarely the loudest one. It is not the *shape* of a sensation, either. The EC_{50} is a single point on a curve, and two molecules can meet at the same half-max while parting ways everywhere else — a different ceiling, a different steepness, a different march of onset and duration across the seconds you actually spend eating. The number tells you how hard a door is driven at half-strength; it does not tell you how the fire arrives or how long it stays, which is the work of the enzyme and the particular capsaicinoid it chooses. Nor does the single-axis score know about its neighbors: each axis is scored in clean isolation, one receptor at a time, while the mouth integrates all eight at once, and real flavors interfere — a sweetness can soften a bitterness that the two solo numbers never hint at. The scorecard's ceiling of 5,000 is a drawing convention, chosen so eight towers stay legible on one radar, not a biological limit; a door can in principle be driven past it. And every number on every page is a ratio against a reference, which means the references must be locked, stated, and never quietly changed — move a reference and every score tied to it rescales at once. These are not weaknesses in the Index. They are its terms of use, and knowing them is what lets you lean your weight on the number where it is strong.

These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.

A feeling has a size

So we come back to the claim we began with, and it stands. A feeling has a size. The fire in our Phoenix design is a predicted 4,200 and its cooling axis sits at 800, and those are not metaphors or moods but computed scores, each defined as the ratio of two concentrations at the same door — each meaning precisely what it says in our model and in any kitchen that grows from it. The arithmetic that gets you there is small enough to carry: watch the response climb and level, mark the concentration at the halfway point, flip it against a fixed standard, scale by a thousand. That is the

whole of it. A lifetime of loving both the plant and the number has only ever confirmed, for us, that they want the same thing — to be exact about something worth being exact about.

We did not learn to measure in order to replace the poetry; the hush of a greenhouse at dawn and the color inside a cut pepper will never be a number and should never have to be. We learned to measure because you cannot design, or keep, or honestly promise what you cannot name — and because a plant grown with real care, grown to hold the most flavor and the most nourishment it can carry, deserves a language precise enough to tell the truth about it. Heat offered as a pleasure rather than an assault; a food given to the body with intention; a number that comes back the same tomorrow. For ten thousand years the whole art was to grow the fruit, taste it, and keep the seed of the one that moved you, never once able to say *how much*. The silence is over. A feeling, it turns out, has a size. You only ever had to know where on the tongue to hold the ruler.

Chapter 13 · The Ladder of Heat — *from a sunlit glow to the edge.*

Of all the things our family has learned to measure, heat is the one the whole world already wants to climb. It is the ladder people point to first — from the faint warmth a fruit can carry on a windowsill in August to the fiercest fire we have ever built on purpose — and because it is the most famous rung of flavor, it is the one most worth climbing slowly, with the mathematics held in one hand and the wonder held in the other. Every rung on it is a real number, anchored to a receptor. And every rung is a plant we can grow again next spring and get the very same fire twice. That second fact is quieter than the first, and it is the one this whole chapter is really about: not how high the ladder goes, but how it is possible to stand on any step of it and know exactly, to the decimal, where your foot has landed.



Golden hour in the research greenhouse, a single fruit lit from behind on the vine — the low, sunlit foot of the ladder, where heat is a warmth you can eat your way happily through.

The older number, and the patient tongue

The world already half-knows one number for heat, and its story begins — as a family will love — with a man and a patient tongue. In 1912 a pharmacist named Wilbur Scoville, working out how much chili went into a muscle salve, invented a way to put a number on fire using the only instrument then available: people. He dissolved a measured weight of pepper in alcohol, diluted it with sugar-water, more and more, and asked a panel to sip until the burn could no longer be felt. The dilution it took to erase the heat became the score. A pepper you had to cut to one part in five thousand before

the fire vanished scored 5,000 Scoville Heat Units; a superhot you had to dilute past a million before anyone stopped feeling it scored over a million.

It was clever, and it was honest, and it carried one deep flaw that the whole of modern flavor science exists to repair: it read a real thing through an unreliable instrument. Tongues disagree. They tire. They differ from person to person and from morning to night. Scoville measured something true — the concentration of capsaicinoids in the fruit — but he measured it through a panel that could never be calibrated to the decimal, and a number that shifts with who is tasting is a number you cannot build on.

A modern bench no longer dilutes against a panel. It reads the capsaicinoids directly by high-performance liquid chromatography, in parts per million, and converts on a fixed rule: one part per million of capsaicinoid is worth very nearly sixteen Scoville units, because pure capsaicin — a million parts per million of itself — sits close to 16,000,000 SHU. That single constant lets us check our fiercest fruit from two directions and watch them agree. Our top rung, **Phoenix**, is designed for a predicted **2,937,948 SHU**. Our model carries that target two ways to check the arithmetic: divide by sixteen and the equivalent capsaicinoid concentration would be about 2,937,948 ÷ 16 ≈ **183,600 ppm**; read the same figure as a fraction of the pure molecule and 2,937,948 ÷ 16,000,000 ≈ **0.184** — Phoenix is designed to carry a little over eighteen percent of the loudness of pure capsaicin itself. Two routes, one answer from the model. The SHU has become honest arithmetic, not a vanished burn, and that is the first thing a ladder needs: rungs that do not move while you are standing on them.

What the fire actually is

Our own index measures the identical fire through a reliable instrument — the receptor itself, in a dish, with no tongue in the room. To see why that is even possible, look at what capsaicin is doing when a fruit burns, because the measurement is simply a ruler laid against that exact event.

Capsaicin is a vanilloid: the vanillylamide of an eight-methyl branched-chain fatty acid, a lipid-soluble molecule small enough to slip straight through a cell membrane. Its target is **TRPV1**, a channel built from four identical protein subunits clasped together into a single pore through the membrane of the trigeminal nerve endings that wrap the tongue — not the taste buds, which is the first surprise worth keeping. TRPV1 is, in its resting life, a thermometer. It opens on its own above about **43 °C**, and it opens when the tissue around it turns acid; when it opens, sodium and especially calcium pour through the pore, the nerve ending depolarizes, and the brain is told — truthfully — that something nearby is hot enough to do harm.

Capsaicin does not warm the tissue by a single degree. It seats in a pocket inside the channel, reached from the membrane side because the molecule is oily, and it stabilizes the open shape. That stabilization *lowers the temperature at which TRPV1 decides to fire* — dragging the threshold down from 43 °C toward the temperature

the mouth already is. The channel opens at body heat. The nerve reports a fire that is not there, and the body believes it completely, because the messenger and the message are precisely the ones a true burn would send. This is why heat is not a taste at all but a **chemesthesis** — a chemical tripping of the touch-and-temperature system — and why it blooms on the lips and the sides of the tongue and the back of the throat, wherever those nerve endings run, rather than on the sweet-and-sour map of the taste buds.

Two further facts about the door matter for every rung above. First, the fire fades if you hold it: sustained calcium entry **desensitizes** the channel and the nerve behind it, which is why the second bite is gentler than the first and why a tolerance builds across a season of eating. Second, the *shape* of a burn — its onset, its peak, how long it lingers — is written into the fruit's chemistry long before you taste it, by the enzyme that assembles the molecule. To climb the ladder on purpose, that enzyme is the rung-maker, so it is where we go next.

The assembly line in the fruit

A pepper builds capsaicin on a committed assembly line, and the last worker on that line is the lever our family learned to pull. Two feedstocks travel toward one bench. The aromatic head begins at the amino acid phenylalanine, which **PAL** (phenylalanine ammonia-lyase) opens into cinnamic acid; the phenylpropanoid branch — through **C4H, 4CL, HCT, COMT** — carries it down to ferulic acid and vanillin, and an aminotransferase, **pAMT**, installs the nitrogen to make **vanillylamine**. The fatty tail starts from branched-chain amino acids like valine and leucine, which **BCAT** hands to a ketoacyl synthase, **KAS**, that elongates them into an eight-methyl branched acyl chain.

The two halves meet at **Pun1**, also called AT3, an acyltransferase that welds the vanillylamine head to the branched acyl tail and releases capsaicin. This one weld is the whole of pungency: a pepper carrying a broken *pun1* allele cannot make the bond, and it grows up sweet — a bell pepper is, at heart, a superhot with its last enzyme switched off. Pun1 names the product, but our flux model places the true rate control much further upstream — at **4CL** and **HCT/CCoAOMT**, the nodes that govern how much substrate the phenylpropanoid trunk delivers to the terminal step.

The enzyme also sets the character of the fire, not only its size. If the acyl tail runs fully saturated, Pun1 turns out **dihydrocapsaicin** instead of capsaicin — a near-twin that drives TRPV1 with its own weight and its own timing, a slower and rounder and longer heat against capsaicin's bright forward rush. The ratio the plant makes is therefore literally the *shape* of the burn, and it is tuned by the chain chemistry at KAS and the selectivity of Pun1. Hold that detail. It is the molecular reason the two numbers we are about to climb — the old Scoville amount and our receptor loudness — can quietly disagree near the top of the ladder, because a dilution panel and a receptor count capsaicin and dihydrocapsaicin in different proportions.

From amount to loudness

The Scoville number answers *how much*. Our index answers *how loudly* — how hard the compound actually drives its door — and loudness is the quantity you must know to design a flavor rather than merely weigh it. The whole of it rests on one measurement, the **EC_{50}**: the concentration at which a stimulus drives its receptor to half of full response. The Iyengar Flavor Index inverts that against a fixed reference and scales by a thousand:

> $IFI(candidate) = 1{,}000 \times EC_{50}(reference) \div EC_{50}(candidate)$

The heat axis is anchored so that the native wild-type reference scores exactly **1,000**. Because the reference's EC_{50} sits on top and the candidate's on the bottom, the units cancel and the score becomes a clean multiple of the standard. A louder key reaches half-activation at a *lower* concentration, so a lower EC_{50} lifts the score — strength runs upside down from EC_{50}, and the formula turns it right-side up. The arithmetic runs backward just as easily: a candidate's EC_{50}, read as a fraction of the reference, is simply 1,000 ÷ IFI.

Three worked inversions set the scale of the ladder before we climb it. A gentle shishito scores near **40** on heat; 1,000 ÷ 40 = **25**, so it needs twenty-five times the concentration of the reference to half-open the door — one twenty-fifth as loud. The mildest flagship our family built, **Ember** at **1,570**, inverts to 1,000 ÷ 1,570 ≈ **0.637** — it half-activates TRPV1 at about 64% of the reference concentration, 1.57 times as loud. And **Phoenix** at **4,200** inverts to 1,000 ÷ 4,200 ≈ **0.238** — half-activation at under a quarter of the reference concentration, **4.2 times as loud**. We report both numbers everywhere in the library: the SHU because the world knows it, the IFI-H because the work needs a figure that comes back the same tomorrow.

The ladder, rung by rung

Here is the ladder our family built — ten proof-of-concept superhots, the series that showed the method could reach the very top of the scale on purpose, each rung a real cultivar with a real SKU, a predicted Scoville number, and its receptor loudness computed against the same door.

RUNG	CULTIVAR	SKU	SHU	IFI-H	DOORS IT OPENS
1	Ember	SS-0087	866,000	1,570	2 / 8
2	Cinder	SS-0088	1,050,000	2,290	3 / 8
3	Kindle	SS-0089	1,250,000	2,000	3 / 8
4	Flare	SS-0090	1,480,000	—	4 / 8
5	Blaze	SS-0091	1,720,000	2,630	4 / 8
6	Wildfire	SS-0092	1,960,000	2,930	5 / 8
7	Scorch	SS-0093	2,210,000	3,220	5 / 8
8	Firestorm	SS-0094	2,470,000	3,490	6 / 8
9	Solara	SS-0095	2,720,000	3,980	6 / 8
10	**Phoenix**	SS-0096	2,937,948	4,200	**8 / 8**

All SHU values are computational predictions from our flux and thermodynamic models.

Read the heat first, because it is what the eye goes to: the predicted Scoville number climbs from 866,000 to nearly three million, the IFI-H from 1,570 to 4,200, step after step, a tower of fire built rung by deliberate rung. But read the last column next, because it holds the real story and it is not the heat at all. As the ladder climbs, the number of *doors* each pepper opens climbs with it — from Ember's two to Phoenix's eight. The early rungs are nearly pure fire and little else: enormous heat, a door or two sounding, the rest of the mouth silent. The top of the ladder is not merely hotter. **Phoenix is the first pepper that speaks on all eight doors at once** — a full chord where the others sound one or two notes — and that, not its Scoville figure, is why it is the end of the series and the center of the whole library. It is heat that arrived carrying the entire rest of flavor along with it.

The mathematics of the climb

Look closely at the two heat columns together and something lovely and honest appears: they do not climb at the same rate. From Ember to Phoenix the predicted Scoville number rises by a factor of 2,937,948 ÷ 866,000 ≈ **3.39×**, while the receptor loudness rises only 4,200 ÷ 1,570 ≈ **2.68×**. The amount of fire nearly triples; the loudness at the door grows by less. Divide one by the other down the rungs and the cost of a unit of loudness, measured in Scoville, keeps climbing — about **552** SHU per IFI-point at Ember, settling into a band near **650 to 710** at the top (Blaze 654, Firestorm 708, Phoenix 700). The ladder gets *expensive* in Scoville terms the higher you go, and the reason is written in the shape of the receptor's own response.

TRPV1 answers its agonist with positive cooperativity — four subunits that help one another open, giving a steep, S-shaped dose–response with a Hill exponent near two. Write the fractional activation as $f = [C]^2 \div (EC_{50}^2 + [C]^2)$ and the diminishing returns become arithmetic you can lay in a row:

AGONIST PRESENT (× EC_{50})	FRACTIONAL ACTIVATION *f*	GAIN OVER PREVIOUS STEP
1×	0.500	–
2×	0.800	+0.300
3×	0.900	+0.100
4×	0.941	+0.041
5×	0.962	+0.021

Doubling the agonist from one times EC_{50} to two adds a full 0.30 to the fraction of open doors; doubling again, from two to four, adds only 0.14; the channel is running out of room. Near the top of the ladder the fruit is pushing TRPV1 far up this curve, so each additional load of capsaicinoid adds *heat-molecules* — and therefore Scoville — faster than it can add *loudness*, because the door is already most of the way open. That is the compression, and it is real pharmacology, not a flaw in either number.

A second cause sits beside it, and the ladder shows it most sharply at one rung. Compare **Cinder** and **Kindle**. Kindle is the hotter pepper by the old dilution count — 1,250,000 SHU against Cinder's 1,050,000 — yet it is the *quieter* one at the receptor, IFI-H 2,000 against 2,290. More amount, less loudness; the two railings of the ladder actually cross. Neither number is wrong. They are answering

different questions, and they part ways here because the capsaicin-to-dihydrocapsaicin blend differs between the two fruits, and a dilution panel and a TRPV1 assay do not weight those two molecules identically. This single crossing is the clearest proof we have that heat needs a receptor-anchored ruler: when you intend to design what the tongue will *feel*, you must hold the ruler to the door the tongue is reading, not to the edge where a panel of tasters finally loses the thread. The honest limit cuts both ways — IFI-H is a single point on a dose–response curve and says nothing by itself about how fast a fire arrives or how long it stays; that shape is the enzyme's work, and it wants its own measurement.

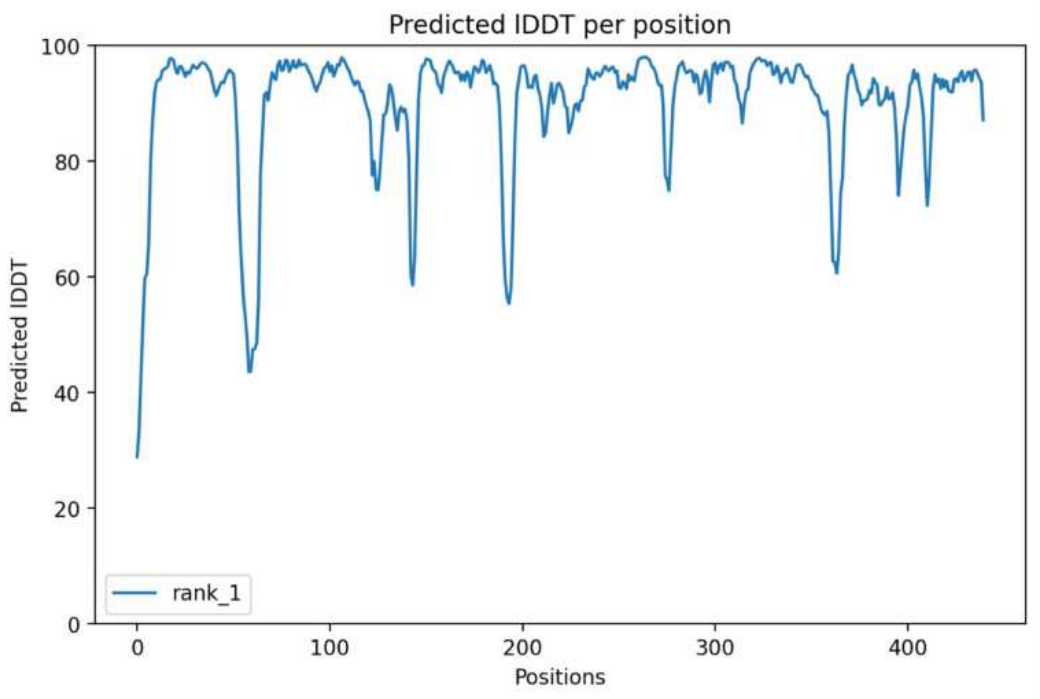
The engine that built the rungs

Every prior breeding program chased heat the slow way: select the phenotype, hope the genotype followed, and wait a plant generation to learn whether it had. Our family inverted the order. We scored the enzyme first. An **ESM2** protein language model, with 650 million parameters, read the sequence of Pun1 and ranked every possible single-residue substitution by its predicted effect on catalytic efficiency and fold stability together; a genome-scale **flux-balance** model mapped where metabolic control actually sits in the capsaicinoid pathway — our Metabolic Control Analysis places it upstream, at **4CL** and **HCT/CCoAOMT**, not at the terminal Pun1 step. Pun1 is the capsaicin synthase; it sets the character and labels the product, but the rate of the whole pathway is governed by the phenylpropanoid trunk. What we tune at Pun1 is *conversion efficiency* — how faithfully the enzyme processes the substrate the upstream network delivers. Two substitutions, never before combined in any pepper, came out of that search and were written in with CRISPR.

EDIT	RESIDUE CHANGE	WHAT IT DOES	ΔΔG (KCAL/MOL)	FOLD-SHIFT E^(−ΔΔG/RT)	STATUS
S39L	Ser39 → Leu	raises substrate binding affinity at the N-terminus	−2.1	≈ 35×	**shipped**
L345G	Leu345 → Gly	relieves steric crowding in the active-site cleft	−1.8	≈ 21×	**shipped**
C175S	Cys175 → Ser	prevents a disulfide misfold, tightening batch-to-batch yield	−0.9	≈ 4.6×	structural annotation — not in shipped construct

The ΔΔG column is the change each edit makes to the enzyme's folding free energy, and a negative value means a *more stable* fold. Thermodynamics turns those numbers into a picture of how much more working enzyme the plant ends up with. At the plant's growing temperature, near 298 K, the gas constant times temperature (RT) is about 0.592 kcal/mol, and the ratio of properly folded to misfolded enzyme multiplies by e^(−ΔΔG/RT). For S39L that factor is e^(2.1/0.592) ≈ **35**; for L345G, e^(1.8/0.592) ≈ **21**; the structural candidate C175S would add e^(0.9/0.592) ≈ **4.6**, but it was not carried forward into the final design. The two shipped edits sum to a combined ΔΔG of about **−3.9 kcal/mol**, and e^(3.9/0.592) ≈ **725** — a roughly seven-hundred-fold shift of the folding equilibrium toward

the active enzyme. That is the engine our model predicts will lift peak output toward approximately **2.94 million SHU**, and it is why the ladder could be climbed on purpose rather than stumbled upon.



The Pun1/AT3 acyltransferase model, coloured by per-residue confidence — the active-site cleft where capsaicin is assembled reads high, and it is the cleft that edit L345G quietly widens.

Honesty about the arithmetic: that −3.9 kcal/mol treats the two edits as independent and simply adds them, and real proteins are not always so obliging — mutations can interfere with one another, and the true combined stability can run a little above or below the sum. We take the ≈725× as a first-order computational estimate. Our modelling also identified C175S as a structural candidate for preventing a disulfide misfold; after weighing the full design, we pulled it from the final construct and built the double variant on S39L and L345G alone. The ladder's steadiness comes from that two-edit design and from holding the ≤7% CV specification — a tight batch-to-batch design target, not luck — and steadiness turns out to be the whole product.

The glow that tastes the same every time

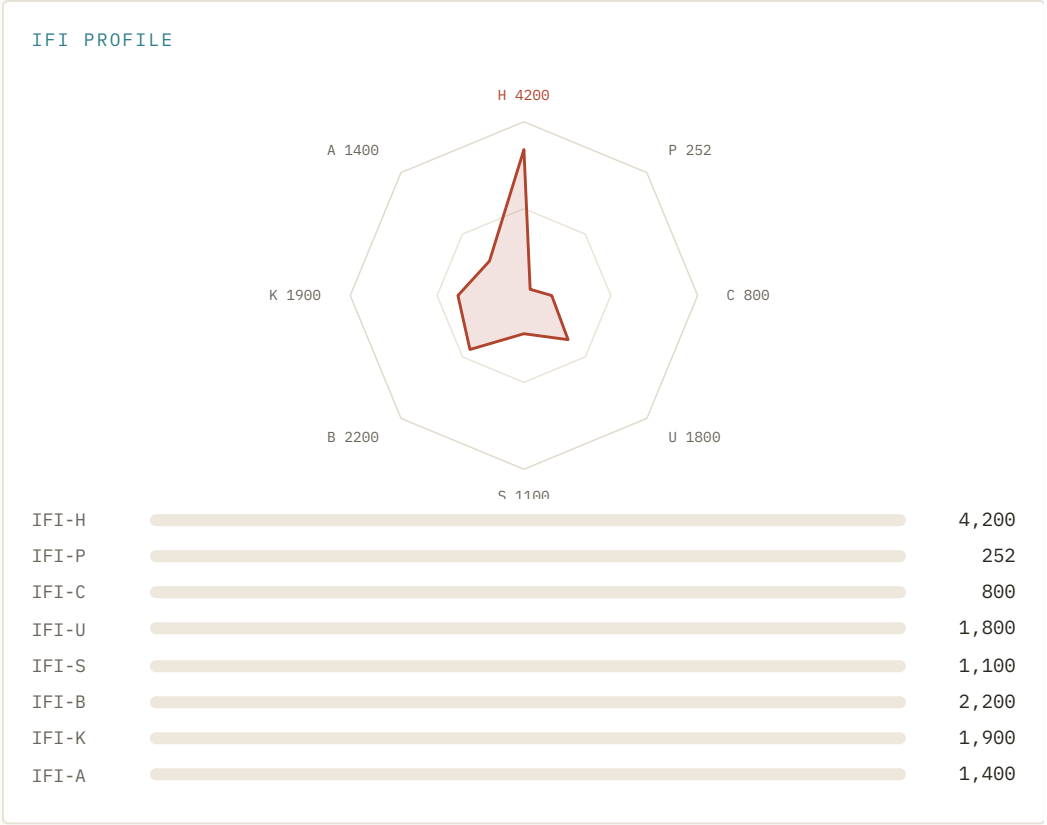
A number you cannot trust twice is not a measurement, so the ladder is only worth climbing if each rung comes back the same. The honest name for a rung's steadiness is the **coefficient of variation** — the standard deviation of a batch divided by its mean, as a percentage. Our engineered flagships are designed to a CV of **seven percent or better**; the wild-type route to the same target runs near **42 percent**, and the gap between those two figures is the gap between a promise and a shrug.

Put it in real numbers on Phoenix's predicted **2,937,948 SHU**. At a 7% CV the standard deviation is 0.07 × 2,937,948 ≈ **205,700 SHU**, so about ninety-five percent of batches (within two standard deviations) land between roughly **2,530,000 and 3,340,000** — a tight band a formulator can build a recipe on and meet. Let the variance run wild-type at 42% and the standard deviation balloons past 1,230,000; the same band sprawls so wide the label stops meaning anything. The improvement is even larger than the sixfold ratio of the percentages suggests, because variance is the *square* of the standard deviation: (42 ÷ 7)² = **36**, so the engineered line carries about one thirty-sixth the variance of the wild-type route at the same

heat. And steadiness compounds with care — average the reading over ten batches and the uncertainty in the mean falls by √10, from 7% to about **2.2%**; over twenty-five batches, to **1.4%**. This is what it means to grow a fire you can keep: not a lucky pepper now and then, but a glow that answers the same question with the same number every single time you ask it.

Phoenix, the summit

At the top of the ladder stands the one fruit built to register on every door at once. Here is its full voice, written as the scorecard the index uses:



Eight doors, all sounding. A tower of heat at 4,200 — which is 84% of the way to the index's per-axis scorecard ceiling of 5,000, and far enough above the others that it reads first — but underneath that tower sits a quieted bitterness at 2,200, the round body of kokumi at 1,900, savory umami depth at 1,800, a thread of astringent grip at 1,400, a forward pungency at 252, a touch of sweetness at 1,100, and even a whisper of cooling at 800. That last number sits *below* a thousand, and the arithmetic insists we read it plainly: on the cooling door this pepper is quieter than the reference, needing more to

reach half-response, not less. A score under a thousand is not a failure; it is an honest report that one door speaks softly in this fruit while seven speak up. That is the whole eight-part architecture of flavor expressed in a single engineered fruit — a thing no plant in the wild has ever done — and it is the proof our family set out to make: that flavor, all of it, can be composed on purpose, one door at a time, and then grown, and then grown again the same.

These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.



Phoenix (SS-0096) on the microscope stage — the top rung of our design ladder; our model predicts approximately 2.94 million SHU, held batch to batch inside a seven-percent design band.

Where a dinner actually wants to live

Now the part that matters most in a book meant for families, and we will say it plainly and without drama, because it is the truth and it is a kindness. The top of this ladder is not food. A pepper at eighteen percent of pure capsaicin's loudness is a laboratory achievement and an ingredient to be *measured out in traces* — a fraction of a drop designing the deep base of a sauce — and never a dare to be swallowed whole. We did not spend years learning to build fire so that anyone could be pushed across a table into real pain. Heat, in this family, is a pleasure and never an assault, and the extreme rungs exist to prove the method and to be diluted down into the warmth a kitchen actually wants. Keep the fierce things well away from small children. Treat the very hot the way you would treat anything powerful and worthy of respect — with care, in small amounts, and never as a game of endurance.

The wonder of the ladder is that it *can* be climbed, and that every rung is a number you can trust: a receptor-anchored loudness, a Scoville figure computed rather than weighed against a tiring tongue, a coefficient of variation held near seven percent so the rung does not shift beneath your foot. The wisdom of the ladder is knowing where on it a given dinner truly wants to live — which, for almost every table our vegetarian, clean-cooking family loves, is somewhere warm and low, a glow you can eat your way happily through for its own sake and for the nourishment the whole fruit carries with it. The fire at the summit earns its place by making that glow possible, repeatable, and exact. A heat you can design is a heat you can also hold gently. And a flavor grown with real care,

computed with precision and kept to its number, is simply food offered to the body the way food was always meant to be offered — on purpose, in the right amount, and the same every time you reach for it.

Chapter 14 · Reading All Eight at Once — *the shape of a whole flavor.*

A single number tells you how loud one door is. But a real flavor — a tomato still warm from the vine, the hush of tea steeping, a finished dish set down in front of people you love — is never one door. It is a *chord:* several doors sounding together, each at its own strength, and the thing that makes one food taste utterly unlike another is rarely *which* doors it opens. It is the *proportion.* Heat and sweetness in one ratio make hot honey; the same two doors in another ratio make a chili so sharp there is no sweetness left in it to find. To read a whole flavor, then, you cannot read one number at a time and add them up in your head. You have to see all eight at once, as a single thing — and learning to hold eight numbers in the eye as one shape is the last and quietest skill this part of the book will teach, the one that turns the Index from a set of measurements into a kind of literacy.

We draw a whole flavor as a **radar** — eight spokes arranged in a wheel, one for each door, with the center meaning *silent* and the outer rim meaning *loud.* Mark each spoke at the flavor's score on that door, join the marks, and the flavor becomes a single closed figure: a signature you can recognize at a glance, the way you recognize a friend's handwriting before you have read a word of it. A pepper's signature is a long spike thrown out along the heat spoke with almost nothing elsewhere — a thorn. A ripe tomato's is a broad, soft lobe swelling toward savory and sweet — a leaf. A good dark chocolate reaches toward bitter and astringent and kokumi all at once — a fan. You stop sounding out the numbers one by one and start reading *forms.* The scorecards all through this book — the compact blocks that list eight lines in one fixed order — are exactly these radars written down as a column, so the shape is always drawn the same way and the eye learns it like a face.



The controlled chamber, where a plant's whole eight-door voice is read, and read again. To design a flavor is to decide on a shape, measure the shape you have, and close the distance between them.

The eight doors, named once and for all

Before a shape can mean anything, you have to know what each spoke is listening to. The eight doors are not eight flavors in a row on one sense; they are eight locks spread across three different senses,

and part of what the Index quietly does is lay all three on one page so they can finally be read together.

Three of the doors are not *taste* at all in the strict sense — they are *chemesthesis,* the chemistry that trips the same nerves that report temperature and touch. **Heat** is **TRPV1**, a non-selective cation channel on the trigeminal endings woven through the tongue; it already opens to real warmth above about 43 °C and to acid, and capsaicin slips into a pocket on its inner face and lowers that thermal threshold, so the nerve fires *fire* into a mouth that is merely warm. **Pungency** is **TRPA1**, the wasabi-and-mustard channel, and it opens by a different trick entirely: its ligands — allyl isothiocyanate from mustard, allicin from crushed garlic, cinnamaldehyde from cinnamon — are electrophiles that reach in and *covalently* latch onto cysteine residues on the channel's inner tail. Heat binds and lets go; pungency grabs and holds, which is why wasabi climbs the nose and leaves all at once. **Cool-Burn** is **TRPM8**, the cold sensor; menthol shifts its activation toward warmer temperatures so it reports *cool* at ordinary mouth warmth — cold that is not cold, the mirror image of heat that is not hot.

Three more are the gustatory GPCRs, the classic tastes, each a receptor that catches a molecule and passes the message inward through a G-protein cascade. **Sweetness** is the **TAS1R2·TAS1R3** heterodimer, a clam-shell protein whose great hinged mouth closes on sugars — and, far more tightly, on the high-potency sweeteners a plant can be taught to make. **Umami** is **mGluR1** together with **TAS1R1·TAS1R3**, tuned to glutamate; and here is a mechanism worth loving, because the ribonucleotides a ripe fruit also carries do not taste of much alone but clamp the shell shut around the glutamate and make the savor *louder* without adding any savor of their own. **Zero-Bitter** is **TAS2R38**, one of roughly twenty-five human bitter receptors — and this spoke runs backward from the others: a high score means *less* bitterness, the 20–65 % hush we can lay over coffee or kale by lowering the load of the compounds that would otherwise shout.

The last two doors barely belong to the first six. **Kokumi** is the **calcium-sensing receptor, CaSR** — it has almost no taste of its own; the small γ-glutamyl peptides that open it (glutathione and its kin) reach in and turn *up* everything else, lengthening the finish, thickening the middle, giving a broth the quality of having been cared for. And **Astringency** is the one door that opens by *taking something away:* it is not a receptor firing at all but the tannins and polyphenols of tea and grape and fine chocolate binding the **proline-rich proteins** in your saliva and precipitating them, stripping the slip from the mouth so the tongue reports dryness and draw. A taste you feel as a loss of lubrication — the most honest reminder that flavor is a whole-body event, not a readout from a single wire.

CODE	DOOR	RECEPTOR	WHAT OPENS IT	SENSE IT RIDES
H	Heat	TRPV1	capsaicin · heat >43 °C · acid	`trigeminal (chemesthesis)`
P	Pungency	TRPA1	mustard · wasabi · garlic · cinnamon	`trigeminal (chemesthesis)`
C	Cool-Burn	TRPM8	menthol · cold	`trigeminal (chemesthesis)`
U	Umami	mGluR1 · TAS1R1·R3	glutamate · ribonucleotides	`taste (GPCR)`
S	Sweetness	TAS1R2·R3	sugars · high-potency sweeteners	`taste (GPCR)`
B	Zero-Bitter	TAS2R38	*attenuation* of bitter ligands	`taste (GPCR)`
K	Kokumi	CaSR	γ-glutamyl peptides	`taste modulation (GPCR)`
A	Astringency	salivary PRPs	tannins · polyphenols	`tactile (mouthfeel)`

That is the fixed order of every scorecard — H, P, C, U, S, B, K, A — the three fire-and-cold channels first, the three tastes next, then the two quiet modulators that shade the rest. Learn the order once and a block of eight lines is no longer a list. It is already a drawing.

One number, derived — the loudness behind each door

Each spoke carries a single number, and that number is not *how much* of a compound a food holds. It is *how loudly that compound speaks* to its door. The distinction is the whole reason the Index works, so it is worth deriving slowly.

A receptor does not answer in proportion to how much ligand arrives. It answers along an S-shaped **dose–response** curve: nothing, then a sudden climb, then a plateau where the door is already as open as it will ever be and more molecule changes almost nothing. Written out, the fraction of full response at concentration *[L]* is

$$\text{response} = [L]^n \div \left(EC_{50}{}^n + [L]^n \right)$$

where n is the steepness of the climb and **EC_{50}** is the one concentration that matters most: the dose at which the door stands exactly *half* open. EC_{50} is a beautifully compact description of a receptor's whole feeling about a molecule. A low EC_{50} means the door swings halfway on a whisper of compound — the molecule is *loud.* A high EC_{50} means it takes a flood to reach the same half-open — the molecule is *quiet.*

Put a few doses through the curve to feel its shape. For a cooperative channel like TRPV1 the climb is steep — a Hill slope near $n = 2$ — so at the EC_{50} the door is half open by definition; double the dose to $[L] = 2 \cdot EC_{50}$ and the response rises to $2^2 \div (1 + 2^2) = 0.8$, four parts in five; triple it and you reach $3^2 \div (1 + 3^2) = 0.9$. The first doubling past half-open buys a great deal of fire; every doubling after that buys steadily less, until near the plateau whole floods of molecule scarcely move the door at all. Loudness lives in the steep middle of that curve — which is exactly where the EC_{50} sits, and

exactly why one well-placed number can stand in for a door's entire voice. All the Index does is turn that reading around so that louder reads as a bigger number, and anchor it to a shared reference:

```
IFI(candidate) = 1,000 × EC₅₀(reference) ÷ EC₅₀(candidate)
```

The reference is pinned so that its own half-activation scores exactly **1,000.** Everything else is read as a ratio against it. Work a case all the way through. Hold the reference at an EC_{50} of 1.00 µM for concreteness. Our full-spectrum cultivar **Phoenix** is designed to half-activate TRPV1 at a computed EC_{50} of 0.238 µM — potent enough to half-open the heat door at under a quarter of the reference dose. Then

```
IFI-H = 1,000 × (1.00 µM ÷ 0.238 µM) = 1,000 × 4.20 = 4,200
```

and the score is exactly the one on Phoenix's card. Run it backward and the formula reads a concentration straight out of a score: a door that reports **4,200** must be opening at EC_{50} = 1,000 × 1.00 µM ÷ 4,200 = 0.238 µM. The number *is* a loudness, and loudness is a ratio of concentrations — which is why a tomato, a chili, and a cup of tea can be laid on one page at all. They are not being compared by how much of anything they contain. They are being compared by how hard each one leans on its own door.

This also quietly dissolves an old confusion about heat. The Scoville scale (SHU) measures *amount* — how far you must dilute a sample before the burn disappears — and amount and loudness do not climb together in a straight line, because the door saturates. Watch the two scales side by side up the superhot ladder, and read the last column as how many Scoville units it costs to buy one point of loudness.

CULTIVAR · SKU	PREDICTED SHU	IFI-H	EC_{50} ÷ EC_{50}(REF)	SHU PER IFI POINT
Ember · SS-0087	866,000	1,570	0.637	≈ 552
Blaze · SS-0091	1,720,000	2,630	0.380	≈ 654
Firestorm · SS-0094	2,470,000	3,490	0.287	≈ 708
Phoenix · SS-0096	~2,940,000	4,200	0.238	≈ 700

The EC_{50} column shrinks the whole way — each cultivar half-opens the heat door on less and less capsaicin — while the price of a loudness point climbs from about 550 Scoville units at the bottom to about 700 near the top. That rising price is not an error. It is the plateau of the dose–response curve made visible: near the top of the climb the door is already most of the way open, so each additional unit of capsaicin buys a little less fire than the unit before it. SHU keeps counting molecules long after the receptor has mostly stopped listening. The Index counts the listening.

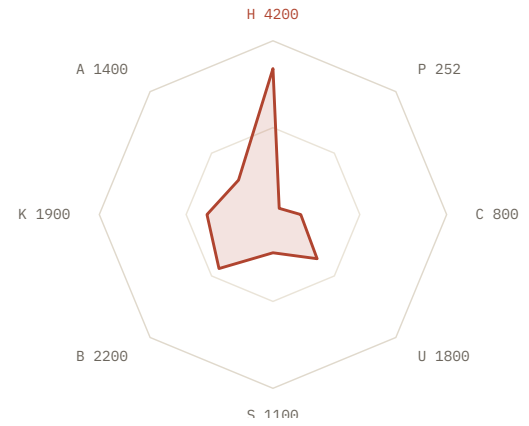
Normalizing to the rim — how a score becomes a radius

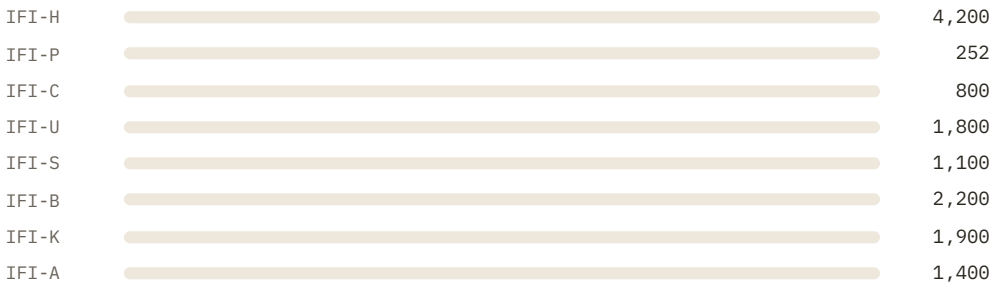
To *draw* the eight numbers as one figure, every spoke has to be measured against the same ruler, so we fix a normalization ceiling at **5,000:** the outer rim of the wheel. A score's distance from the center is simply its share of that ceiling.

```
radius = IFI ÷ 5,000
```

Take Phoenix's full profile and turn each score into a reach.

IFI PROFILE







Phoenix (SS-0096) in the controlled chamber — the first cultivar engineered to register on all eight doors at once, and the only full wheel the ladder has reached.

DOOR	IFI	RADIUS (IFI ÷ 5,000)	REACH TOWARD RIM
H · Heat	4,200	0.840	84 %
P · Pungency	252	0.050	5 %
C · Cool-Burn	800	0.160	16 %
U · Umami	1,800	0.360	36 %
S · Sweetness	1,100	0.220	22 %
B · Zero-Bitter	2,200	0.440	44 %
K · Kokumi	1,900	0.380	38 %
A · Astringency	1,400	0.280	28 %

Now the shape is forced. Heat throws almost all the way to the rim at 0.84; the other seven settle between a stub at 0.05 and a firm reach at 0.44; and crucially *none of them falls to the center.* That is what

"full spectrum, eight-of-eight" means, drawn rather than claimed — a plant that opens every door at least a little, so the figure is not a thorn but a genuine, if lopsided, wheel. One honest limit belongs right here: the ceiling is a choice, not a law of nature. A door that ever read above 5,000 would simply clip at the rim, its true loudness hidden by the frame; we set the ceiling where almost nothing real exceeds it, and read the rare rim-pinned spoke as "off the top of this chart," never as a measured maximum.

The shape itself — thorn, leaf, fan, wheel

Once a flavor is a figure, you can describe it with two quick numbers that need no picture at all. Average the eight scores and you get the flavor's overall *presence;* divide the tallest spoke by that average and you get its *peakedness* — how far one door towers over the rest. For Phoenix the eight scores sum to 13,652, so the mean door reads 1,706, and the tallest spoke, heat at 4,200, stands at 4,200 ÷ 1,706 ≈ **2.46** times the average. A peakedness of 2.5 is the arithmetic of a *wheel:* heat leads, but only about two and a half times as loudly as the typical door, and the figure has real body in every direction.

Set that against a plain superhot that lights only two of the eight doors. Its heat spoke might stand near the rim while the other seven lie close to the center; the average is dragged low, and peakedness soars into the many-fold — the arithmetic of a *thorn,* one blade of a signal and silence all around it. You do not need the drawing to know which flavor will feel one-dimensional in the mouth and which will feel whole. The two numbers already told you: a low peakedness is roundness, a high peakedness is a spike. This is how a family at a table learns to argue precisely about a taste — not "it's too hot," but "its peakedness is four, it's all thorn and no wheel, give it some sweetness and some depth and bring that number down."

A word of caution, because precision owes the reader its own limits. The *enclosed area* of the radar — the acreage of the closed figure — looks like it should measure total intensity, and it is tempting to read it that way. It does not, cleanly: the area depends on the order the spokes are placed in, so two flavors with identical eight numbers can enclose different areas if you shuffle the wheel. That is exactly why we freeze the order at H, P, C, U, S, B, K, A and never vary it — the fixed order makes *shapes* comparable by eye — but it is also why we lean on the order-free numbers, the mean and the peakedness, when we want to *say* something true rather than show it. The drawing is for recognition. The two numbers are for proof.

Comparing two shapes — the dent you can see

Here is the first thing a shape makes possible that a mouthful never could: you can lay two flavors over each other and *see* the difference, exactly, as a dent in a figure.

Take the tomato. A tomato bred to survive a truck and a cold week on a shelf keeps its color and loses its voice; on the umami door it reads about **IFI-U 300,** a savor nearly collapsed to the center. The tomato we grow back toward the fruit it was — restoring the brothy depth through its own native glutamate route — our model predicts at approximately **IFI-U 2,600** on the same door. Overlay the two leaves and the supermarket fruit is the restored one with a deep bite

taken out of the savory side: a dent of 2,600 − 300 = 2,300 points, and a fold-change of 2,600 ÷ 300 ≈ **8.7×.** Nearly nine parts in ten of that door's loudness is what the long cold journey quietly took, and what our family has designed back in. The gap is no longer an opinion you could argue about across a kitchen. It is a visible, computed shape in a drawing.



A tomato restored — its umami door grown back from a near-silent IFI-U 300 toward 2,600, through the fruit's own native route, so the savor returns without a thing added that was not already the plant's to make.

But a dent you can see is only trustworthy if the measurement is quiet enough to hear it, and this is where reproducibility stops being a laboratory virtue and becomes the thing that lets two shapes be compared at all. We hold every reading to a batch-to-batch coefficient of variation of **≤ 7 %** — against the roughly **42 %** that unselected, wild material will swing across seasons. Put numbers on what that buys. At the restored tomato's IFI-U of 2,600, a 7 % CV is a standard deviation of about 182 points; the honest ninety-five-percent band is roughly twice that, about ±364. The dent we are claiming is 2,300 points — more than six of those bands wide. It cannot be noise. Now run the same comparison at the old 42 % swing: the standard deviation balloons to about 1,092 points, a ninety-five-percent band near ±2,180 — nearly the whole size of the dent. At that noise the restored tomato and the hollow one overlap; you could not swear they differed at all. The flavor might be real, but the *reading* could not prove it, and a drawing you cannot trust is worse than no drawing.

The same arithmetic sets the resolution of the whole superhot ladder. Two readings of similar size can be told apart with confidence only when they differ by more than about $2 \times \sqrt{2} \times \text{CV}$ of their value — at a 7 % CV, a little under a *fifth.* That is why the rungs of the ladder are spaced the way they are: Ember at 1,570 and Blaze at 2,630 are a clean sixty-seven percent apart and will never be confused, while two cultivars only a tenth apart would blur into each other and need many more replicates to separate. Precision is not fussiness. It is the floor under every claim a shape makes.

Aiming at a shape — design as closing a distance

And now the second thing, the one that still stops us when we let ourselves feel it. If a flavor is a shape, and two shapes can be laid over each other and their difference measured, then *designing* a flavor is no longer the misty business of chasing a taste you can only describe. It becomes a plain, honest problem with a plain, honest

form: **decide on the shape a flavor should have, measure the shape the plant currently has, and change the plant, carefully, until the two figures meet.** Flavor design is the closing of a distance between two drawings.

Changing the plant means changing one spoke at a time, at the gene that sets that door's loudness — which is to say, lowering an EC_{50} at the source. Heat is the clearest case. The capsaicin that leans on TRPV1 is built when the capsaicin-synthase enzyme at the **Pun1** locus joins vanillylamine to a branched-chain fatty acyl group; Pun1 is the terminal assembly step — the enzyme that stamps the finished molecule. Our flux model predicts that the actual control over production rate sits further upstream in the phenylpropanoid pathway, at 4CL and HCT/CCoAOMT, where precursor supply is established; Pun1 labels the product, it does not govern the rate. Working within that architecture, we found two single-residue edits to the terminal synthase that generations of breeders, selecting fruit and hoping the gene followed, never once stumbled onto — and written in together, they improve the terminal step's catalytic efficiency, contributing to the predicted heat of approximately 2.95 million SHU our model assigns to Phoenix while holding that ≤ 7 % batch CV design specification.

EDIT	WHAT IT DOES	ΔΔG (KCAL/MOL)
S39L	tightens substrate binding at the N-terminus	−2.1
L345G	relieves strain in the active-site cleft	−1.8

Our structural modelling also identified a third position, C175S, as a disulfide-misfold prevention measure (ΔΔG −0.9 kcal/mol); that annotation was not included in the shipped construct.

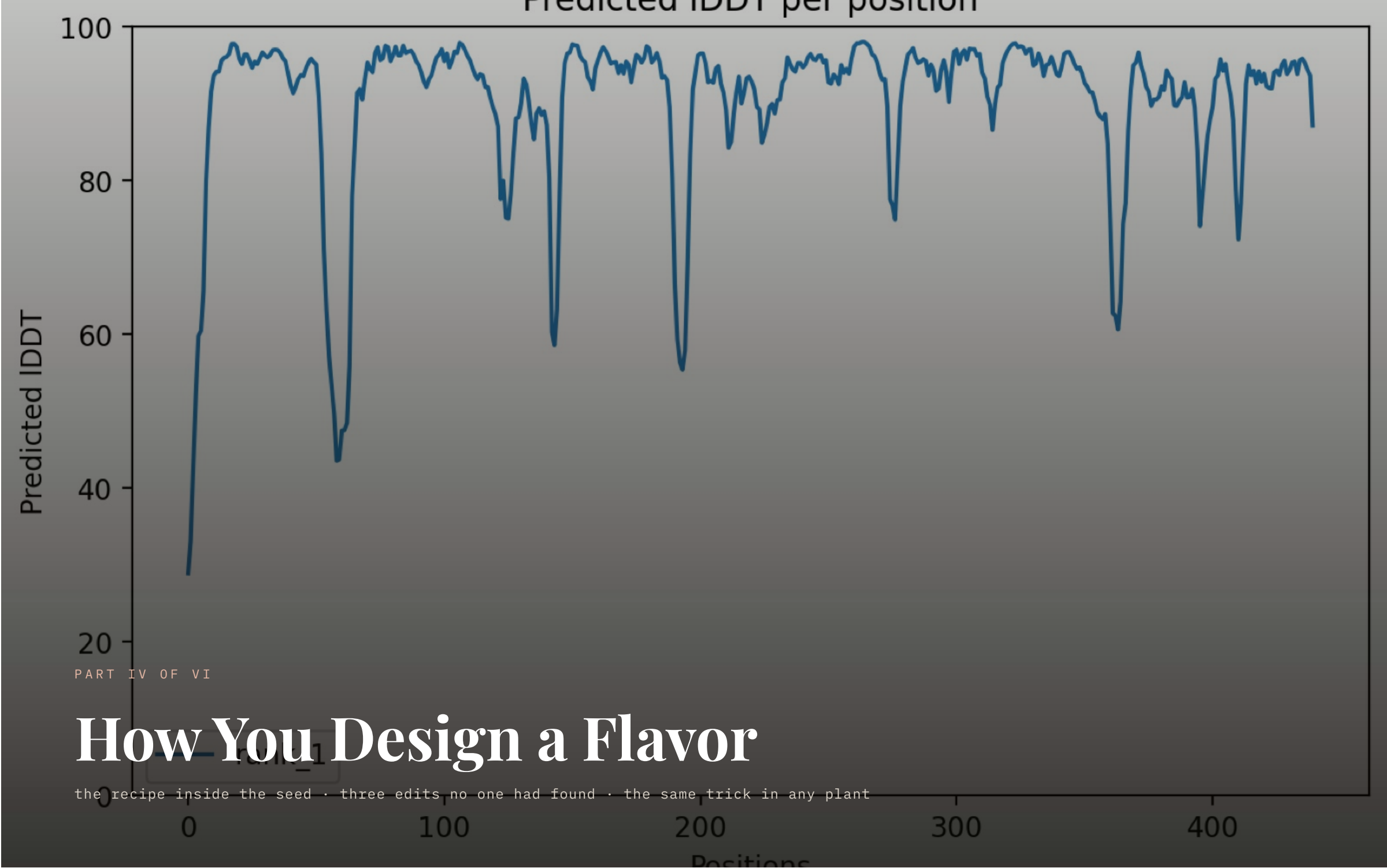
Each negative ΔΔG is a step toward a more stable, more willing enzyme — two small stabilizations that together move one spoke on the wheel. A different door is moved at a different gene: the tomato's umami grows back along its own native glutamate route, not by adding savor from outside the plant but by restoring the fruit's own ability to make what the road took from it. That is the quiet ethic under the mathematics — we do not bolt flavor on; we hand a plant back the fullness, and the nourishment, it was always built to carry, and we read on the Index that it arrived.

The honest limits of *aiming* deserve the same plainness as the limits of drawing. The eight doors are not sealed from one another in the mouth the way they are tidy on the page: sweetness measurably quiets the perception of bitterness, cooling can blunt the edge of heat, kokumi lengthens whatever else is present. The Index reads each door's loudness *at the receptor,* one lock at a time — it does not model the mixing the brain does afterward, and so a shape is a faithful map of the eight inputs, not a literal recipe for the single sensation they will fuse into. We match shapes because matched inputs are the most reliable path to a matched experience, and then we do the last, unquantifiable thing anyway: we taste it, together, and check the drawing against the mouth.

The wonder, made shareable

So the child's question opens all the way out. *Why is it spicy?* was a question about one spoke of the wheel — the long heat-thorn, the fire that is not a fire, a door the body built to warn of burning that a plant learned to knock on without ever lighting a flame. To answer it honestly we have had to draw the whole wheel: to see that spiciness is one door among eight, that each door is a lock the body keeps for its own reasons and a molecule has found the key to, that every flavor anyone has ever loved is a chord struck across all eight at once, and that a chord — unlike a mystery — can be written down, compared, and aimed at. The number was never meant to replace the wonder. A tomato warm from the vine is not less astonishing for scoring 2,600 on its umami door; it is more, because now the astonishment can be *handed across a table.* That is the whole gift of reading a flavor as a shape: it turns a feeling that lives in one mouth into a figure a family can point at and agree on and grow toward together. The mystery stays. We have only learned to read it aloud.

These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.



PART IV OF VI

How You Design a Flavor

the recipe inside the seed · three edits no one had found · the same trick in any plant

Chapter 15 · The Recipe Inside the Seed — *where a plant writes its own flavor.*

To design a flavor you must first find where the plant keeps its own instructions for making one — and the wonder we most want a family to carry out of this chapter is that the instructions are *written down.* Not figuratively. A pepper holds, inside every one of its cells, a written recipe for building capsaicin, spelled out in a four-letter alphabet; learn to read it and you can watch the fire being made, step by step, and see exactly where a careful hand might change it. The spiciness of a pepper is not a mystery the plant keeps from us. It is a text the plant follows.

The alphabet is **DNA**, and its four letters are the four chemical bases — A, T, C, G — strung along a long double thread coiled inside each cell. Certain stretches of that thread are **genes**, and a gene is the written instruction for building one **protein.** For the purposes of flavor, the proteins that matter are mostly **enzymes:** tiny molecular machines, each folded into a shape that grips one kind of molecule and performs one chemical operation on it — snip this bond, add that fragment, bend this corner into that one. A flavor molecule is almost never made in a single stroke. It is assembled down a line of enzymes, each encoded by its own gene, each doing one job and handing the result to the next, the way a loaf passes down a kitchen from the hand that mixes to the hand that bakes. The whole line, gene by gene and step by step, is the recipe inside the seed.

One gene, one machine — reading the alphabet

Before we follow the line, it is worth slowing down on the single fact that makes everything our family built possible: that the step from a written letter to a working machine is short, and exact, and reversible by hand.

A gene does not act directly. The cell first copies the gene out into a working transcript — a single-stranded message called **mRNA**, a fair copy carried off the master thread so the original is never risked on the shop floor. That message is then *read* by the cell's assembler, and here is the detail a child can hold: the four-letter text is read **three letters at a time.** Each triplet of bases — each **codon** — names one **amino acid**, and amino acids are the twenty beads from which every protein is strung. The assembler runs the length of the message, calling out one bead per triplet, and a chain grows. Left to itself in water, that chain folds — driven by nothing more than which of its beads love water and which flee it — into one particular three-dimensional shape. The shape *is* the machine. A pocket here to grip the substrate, a cleft there where the chemistry happens, a core that must stay rigid so the pocket keeps its aim.

Now the consequence that organizes this entire book. If each amino acid is spelled by a triplet of letters, then changing a single triplet changes a single bead — one amino acid swapped for another, at one named position along the chain. One bead changed can leave the machine almost exactly as it was, or it can tighten a pocket, relieve a jammed corner, or stop a fold from going wrong. So when we say, at the end of this chapter, that to lift a pepper to the edge of what a pepper can be we *changed two letters,* we are not reaching for a metaphor. We mean two places in the text, rewritten the smallest possible amount, each one retuning one contact in one machine on the line. The recipe is not only readable. It is editable, at the resolution of a single letter — and the art is in changing as little as will do.

The first half of the key — the line every green plant already runs

Here is the part that made our whole method feel less like invention than like reading. The first half of the capsaicin line is not special to peppers at all. It is a stretch of chemistry called the **phenylpropanoid pathway**, and some version of it runs in *every green plant on Earth* — it is how plants build an enormous range of their defensive and structural molecules, from the stiffening in a tree's wood to the colors in a flower. It begins from a common amino acid, **phenylalanine**, and runs through a short, famous sequence of enzymes that every botanist knows by their initials: **PAL → C4H → 4CL → HCT → COMT.** Follow one molecule down that line and watch it change hands:

STEP	ENZYME	TURNS THIS	INTO THIS
1	PAL	phenylalanine	`cinnamic acid`
2	C4H	cinnamic acid	*p*-`coumaric acid`
3	4CL	*p*-coumaric acid	*p*-`coumaroyl-CoA`
4	HCT · C3H	*p*-coumaroyl ester	`caffeic acid`
5	COMT	caffeic acid	`ferulic acid → vanillin`
6	pAMT *(pepper's own)*	vanillin	**`vanillylamine`**

Read the first five rows and you have read a line that a rose runs, and a stalk of wheat, and the oak outside the window. PAL pries the nitrogen-bearing tail off phenylalanine; C4H hangs a single oxygen onto the ring; 4CL clips on a handle of coenzyme A so the molecule can be passed along; HCT and its partner C3H decorate the ring with a second oxygen; and COMT, the methyl-painter, caps one of those oxygens to make ferulic acid, which a short trimming step shortens to **vanillin** — yes, that vanillin, the molecule that gives vanilla its scent. The fiercest fire on the tongue and the most comforting sweetness in the world share an ancestor five steps back on the same line. We found that kind of hidden kinship everywhere once we started reading the recipes, and it never stopped moving us.

Only at row six does the pepper do something its neighbors do not. A pepper-specific enzyme, **pAMT**, takes vanillin and places an amine group onto the ring — turning vanillin into **vanillylamine.** That amine is the business end of the finished molecule, and vanillylamine is now one half of the capsaicin key: the flat aromatic ring, built

almost entirely on borrowed, universal chemistry, finished with a single pepper-made stroke. This is why the method was never really about peppers. The hard, long, universal part of the work is a line the plants had already written; we only had to learn to read the four enzymes at the end that make the molecule a pepper's own.

The second half of the key — a tail from two amino acids

A key needs a ring to be recognized and a shaft to turn, and capsaicin is built the same way: the ring we have just made, and an oily tail joined to it. That tail is built on a second, shorter line, from a different starting material — the branched-chain amino acids **valine and leucine.** An enzyme abbreviated **BCAT** strips these down to a short branched acid, and a fatty-acid-building machine abbreviated **KAS** extends and shapes it into the finished tail: **8-methyl-6-nonenoic acid**, a nine-carbon chain with a kink of a double bond and a methyl branch at its far end. The branch is not decoration. It is the reason the tail is the length and shape it is, and the tail's shape is half of what the burn will feel like.

That is worth holding, because it is where the chemistry we are building reaches forward to the chemistry of tasting. When capsaicin finally meets its receptor on the tongue — the heat channel **TRPV1** — the two halves of the molecule do two different jobs. The vanillyl ring, the half we built from borrowed phenylpropanoid chemistry, is the part that docks into the receptor's binding pocket: it is the piece the lock is shaped to recognize. The oily tail, the half we built from two amino acids, sets how the molecule partitions into the fatty membrane and, through the exact length and saturation of that chain, fixes the balance between capsaicin and its slower-burning cousin dihydrocapsaicin — and with that balance, the *shape* of the burn: whether it arrives as a bright flash that fades or a deep heat that lingers and climbs. Design the tail and you are not changing how much fire there is. You are composing how it moves. The ring decides *that* the lock is turned; the tail decides *how* it is turned.

Pun1 — where the fire is actually struck

Two halves, built on two lines, from two starting materials. They meet at the single most important enzyme in the whole story — the one that ties the ring to the tail and completes the key. Its gene is called **Pun1**, and the enzyme it builds is **capsaicin synthase**, an acyltransferase whose structural family is labeled AT3. Pun1 performs the final condensation: it joins vanillylamine to the fatty tail and locks them together with a stable **amide bond** — the same unhurried, weather-proof knot that holds proteins themselves together — and the finished capsaicin molecule rolls off the end of the line. Everything upstream is preparation. Pun1 is where the fire is actually struck.

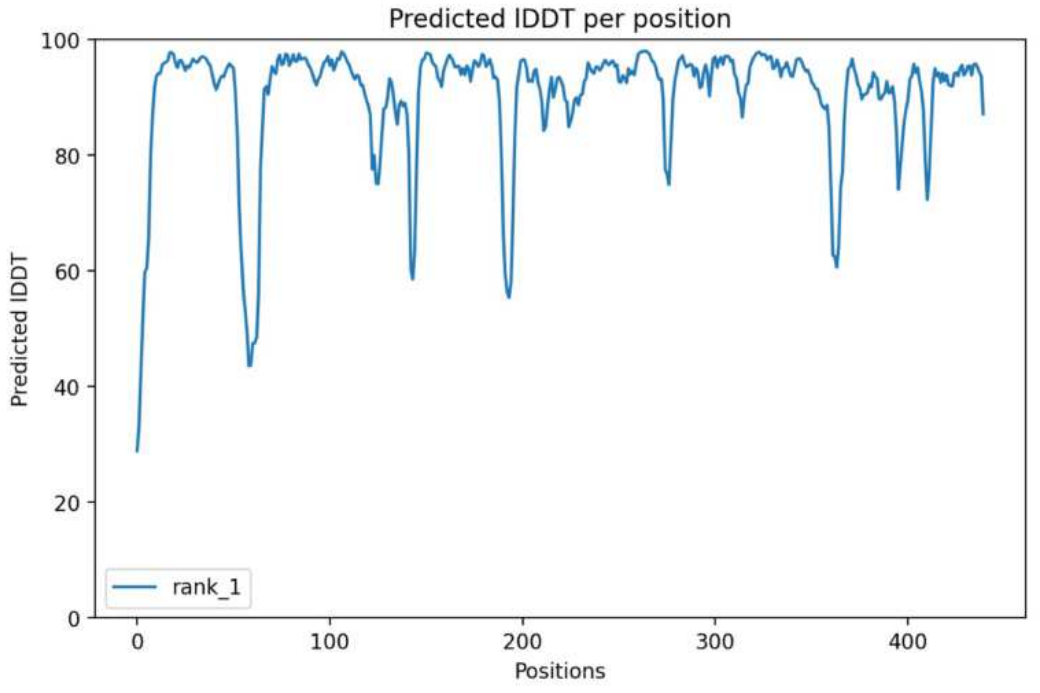


FIG. 15 — capsaicin synthase, the Pun1/AT3 enzyme, as our family models it, colored by the model's own confidence in each region. The binding domain and the active-site cleft — where the ring and the tail are brought together and knotted — resolve brightest, because that is where the work, and the design, happen.

To change capsaicin by design, we had to *see* Pun1 — not its gene sequence alone but the folded machine that sequence becomes. The figure above is that machine, predicted atom by atom and then shaded by how certain the prediction is: bright where the fold is near-certain, pale where it is not. Look at where the brightness gathers. It gathers exactly at the binding domain and the active-site cleft — the pocket that must grip vanillylamine, and the cleft where the amide knot is tied. This is the happy case for a designer: the part of the machine we most need to understand is the part the model is most sure of. The floppy loops at the protein's edges, where the model hesitates, are the parts that matter least to the chemistry. We trust the pocket. We do not pretend to trust every atom.

From a molecule to a number — writing toward a loudness

Reading the recipe tells you *how* the fire is made. It does not, by itself, tell you *how much,* or in the only sense that matters, *how loud.* For that we need a number, and the number our family built the whole platform around is the **Iyengar Flavor Index.** Its definition is one line:

> $\mathrm{IFI}(\text{candidate}) = 1{,}000 \times \mathrm{EC}_{50}(\text{reference}) \div \mathrm{EC}_{50}(\text{candidate})$

The quantity inside it, **EC_{50},** is borrowed from pharmacology: it is the concentration of a stimulus at which its receptor reaches half of its full response. A *low* EC_{50} means the receptor is driven halfway while only a little of the molecule is present — a loud, potent signal. A *high* EC_{50} means you must crowd the pocket before the lock will move — a quiet one. Loudness is the inverse of EC_{50}, and the Index is simply that inverse, pinned to a reference and scaled by a thousand so the everyday numbers sit in a friendly range. The reference constant on each axis is a **stated convention** — defined the way the Scoville scale is defined by dilution-to-threshold, not derived from a literature average. Fix the reference on a given axis and its score becomes **1,000** by construction: when candidate and reference share an EC_{50},

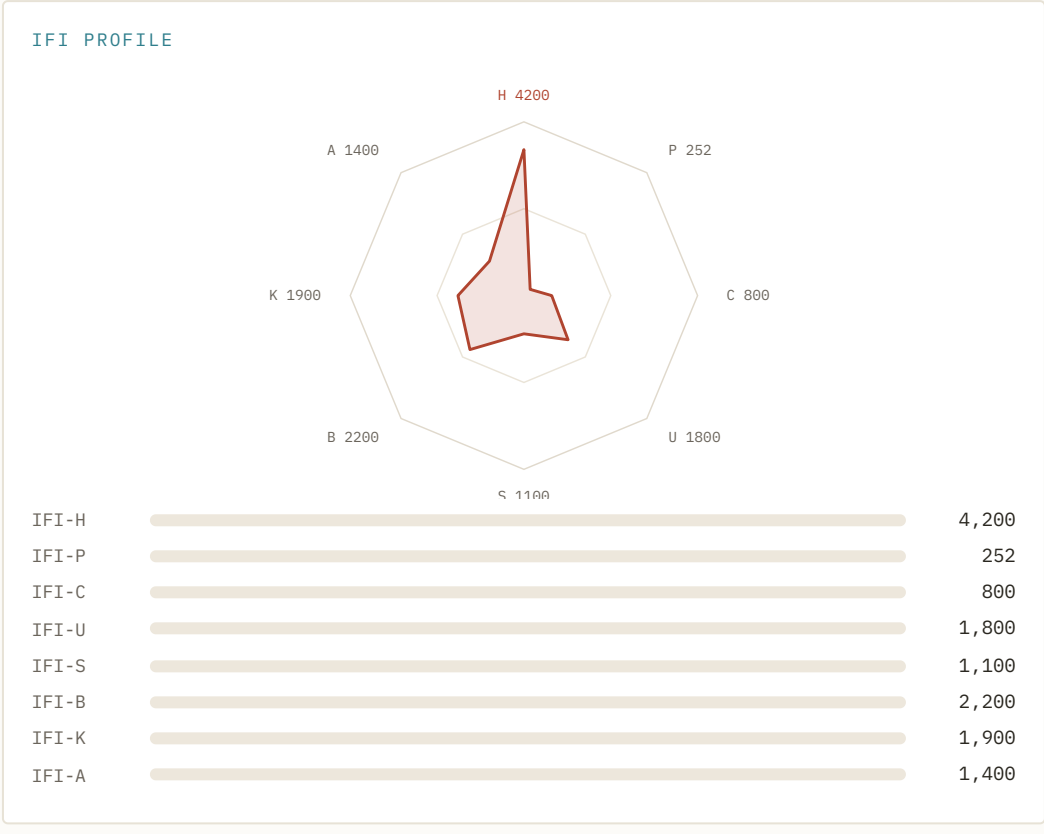
the ratio is one. Score above 1,000 and the candidate is louder than the standard; below, quieter. For the scorecards in these books, each axis is normalized to a ceiling of **5,000.**

A worked example keeps the arithmetic honest. Our fullest pepper, the one we call **Phoenix**, is designed to read **4,200** on the heat axis. Put that into the formula and solve for what it says about the meeting on the tongue:

$$4{,}200 = 1{,}000 \times EC_{50}(\text{reference}) \div EC_{50}(\text{Phoenix})\ EC_{50}(\text{reference}) \div EC_{50}(\text{Phoenix}) = 4.2\ EC_{50}(\text{Phoenix}) = EC_{50}(\text{reference}) \div 4.2 = 0.238 \times EC_{50}(\text{reference})$$

So Phoenix's standardized extract is designed to drive the heat receptor to half-maximal response at just under a quarter — 23.8 percent — of the concentration the reference needs. It is, in the exact sense the number is built to carry, **4.2 times louder** than the standard. Not 4.2 times more of anything. Louder. And loudness has a shape: the receptor's response does not rise in a straight line but as an S, and because TRPV1 is built of four identical subunits gripping one pore, its climb is cooperative, with a steepness (a Hill coefficient) near two. At that steepness the receptor goes from one-tenth to nine-tenths activated across only a nine-fold band of concentration — which is why heat so often seems to arrive all at once, a step and not a ramp. For Phoenix, whose designed half-point sits at 0.238 of the reference, nine-tenths activation is predicted to arrive at roughly 0.71 of the concentration the *reference* needs merely to reach its own halfway mark. The louder key does not just turn the lock sooner. It slams it.

Here is Phoenix read on all eight doors of the Index at once — the first cultivar our family designed to register on every axis:



Behind that heat number of 4,200 stands a whole ladder of peppers, each designed louder than the last, and the ladder shows two different questions wearing the same word. One is **how much fire the fruit holds,** measured in **Scoville Heat Units** (SHU) — a bulk-

concentration scale, anchored at the top by pure capsaicin, which by definition reads about **16,000,000** units. The other is **how loudly each molecule speaks,** the IFI. They are correlated but never identical, because our designs shift the blend and the shape of the capsaicinoids, not merely their mass. Watch both climb:

CULTIVAR	SKU	PREDICTED SHU	% OF PURE CAPSAICIN	IFI-H	EC_{50} (REL, REF = 1.000)
Ember	SS-0087	866K	5.4%	1,570	0.637
Cinder	SS-0088	1.05M	6.6%	2,290	0.437
Kindle	SS-0089	1.25M	7.8%	2,000	0.500
Flare	SS-0090	1.48M	9.3%	—	–
Blaze	SS-0091	1.72M	10.8%	2,630	0.380
Wildfire	SS-0092	1.96M	12.3%	2,930	0.341
Scorch	SS-0093	2.21M	13.8%	3,220	0.311
Firestorm	SS-0094	2.47M	15.4%	3,490	0.287
Solara	SS-0095	2.72M	17.0%	3,980	0.251
Phoenix	SS-0096	2.95M	18.4%	4,200	0.238

SHU values are computational predictions from our flux and binding models, not certified measurements.

Our model predicts approximately 2.95 million SHU for Phoenix — just over **18 percent** of pure capsaicin — our fiercest pepper in the design, and still less than a fifth of the naked compound. The fifth column reads the Index formula backward: relative EC_{50} equals 1,000 ÷ IFI-H, so you can *feel* the loudness directly, Phoenix designed to reach half-activation on 0.238 of the material the reference needs. And one row rewards a second look. Kindle carries *more* predicted Scoville heat than Cinder — 1.25 million against 1.05 million — yet scores *lower* on IFI-H, 2,000 against 2,290. More total fire; a quieter molecule. That is not an error in either number. It is two honest instruments reading two different places on two differently shaped curves, and the morning we first watched them disagree was the morning the Index stopped being a convenience and became a necessity.

Where and when the recipe is run

A recipe is not run everywhere, or always. Two more facts finish the picture, and both are the kind a family can feel in a cut fruit.

First, *where.* The entire capsaicin line runs almost entirely in one small tissue of the pepper — the pale, spongy **placenta**, the inner ribs that cradle the seeds. It does not run in the flesh, which is why the heat of a pepper lives in the ribs and not the walls, and why a cook who wants to temper a chili scrapes the pale tissue away. The recipe is followed in one room of the fruit, and that room is the one built to protect the seeds — which is exactly where a defense molecule belongs. Evolution did not scatter the fire. It stationed it at the door of the next generation.



A pepper opened along its length. The pale ribs down the center — the placental tissue, not the flesh and not the seeds — are the kitchen where the whole line we have followed is actually run, molecule by molecule, before any of it reaches a tongue.

Second, *when.* The line switches on as the fruit ripens, under the control of regulator genes that act like a master switch for the whole pathway — so a pepper's heat develops on a schedule, written into the same text that spells the enzymes. This matters more than it first sounds, and it is a humbling check on a designer's pride: a perfect enzyme makes nothing if the regulators never call for it in the placenta at ripening. The gene sets the *capacity* for heat. The regulators decide whether that capacity is ever spent. We learned early to read both — the machine and the switch that turns it on — because a flavor you cannot schedule is a flavor you cannot trust to arrive.

The limiting step, and the smallest possible change

Read all of this together and the method our family built becomes almost obvious, which is how you know it is sound. If flavor is a molecule, and the molecule is built by a line of enzymes, and each enzyme is written in a gene you can read, then to change a flavor you do not grow ten thousand plants and hope. You find where the line's output is controlled, read the genes that build those enzymes, and change the writing by the smallest amount that moves the result.

Finding where control sits is itself arithmetic. A whole-plant **flux-balance model** treats the cell as a network of reactions at steady state — everything made is either used or shipped onward — and solves, from the stoichiometry alone, for where the traffic jams. Our model predicts that control over capsaicinoid flux sits **upstream in the phenylpropanoid pathway — at 4CL and HCT/CCoAOMT** — not at the terminal Pun1/AT3 step. The Metabolic Control Analysis summation theorem confirms the picture: Pun1's predicted flux-control coefficient rounds to zero over five thousand Monte Carlo draws; upstream enzymes account for ninety-three to ninety-nine percent of the control. Pun1 is the final capsaicin synthase — it labels the product and completes the molecule — but it does not govern the rate. The line is not starved at its last machine; control sits much earlier, in the shared phenylpropanoid chemistry every plant already runs.

So we studied the terminal machine anyway — not because it limits total flux, but because precision at the final step governs consistency. A Pun1 that holds its fold steadily converts vanillylamine and the fatty tail into capsaicin with less variance, and variance is

the enemy of a designed flavor. Here the honest labor of the family divides as it always has: the plants and the patience and the table belonged to all of us, and the computing fell to one pair of hands. A protein language model — an ESM2 network of 650 million parameters, trained on the shapes of life's proteins the way a reader is trained on a language — scored every possible single-letter substitution in Pun1 for its predicted effect on **catalytic efficiency × fold stability.** Out of that search, two substitutions emerged that no breeder had ever found, because no breeder could see the machine to find them. Written into the genome with CRISPR, the smallest edits that would do:

EDIT	WHERE ON THE ENZYME	WHAT IT DOES	ΔΔG (KCAL/MOL)	FOLD-STABILITY FACTOR
S39L	N-terminal binding domain	lifts binding affinity	−2.1	≈ 34×
L345G	active-site cleft	relieves a steric jam at the cleft	−1.8	≈ 21×
combined	—	—	**−3.9**	**≈ 717×**

(A third substitution, C175S, appears in our structural modelling as a disulfide-misfold prevention site, ΔΔG −0.9 kcal/mol. It is retained as a structural annotation only and was not included in the shipped construct.)

The ΔΔG column is the measure of how much steadier each edit makes the folded machine, in kilocalories per mole, and the convention is that a *negative* number means *more* stable. The last column translates that energy into something you can picture, through the same Boltzmann relation that governs every equilibrium in chemistry: the ratio of folded to unfolded enzyme shifts by **exp(−ΔΔG ÷ RT)**, where RT at a plant's working temperature (298 kelvin) is about 0.593 kcal/mol. For the two shipped edits, whose stabilizing energies add to −3.9 kcal/mol — exp(3.9 ÷ 0.593) ≈ 717 — the two smallest changes we could make are predicted to shift the folded-to-misfolded balance of capsaicin synthase by more than seven hundred-fold toward the working machine. Two letters. A seven-hundred-fold-and-more steadier hand on the last step of the line.

Steadier is not a flourish; it is the whole point. The wandering of a wild pepper's heat, fruit to fruit, carries a **coefficient of variation** — standard deviation over mean — near **42 percent.** That is a plant you cannot design around: two fruits off one bush can differ by nearly half. Our rewritten line is designed to hold a CV of **7 percent or below** — a design specification, baked into the structural choices. Put numbers on what that buys. At Phoenix's predicted heat of approximately 2.95 million SHU, a 7-percent CV is a standard deviation of about 207,000 units, so two batches in three are predicted to land inside roughly 2.74–3.16 million SHU, and nineteen in twenty inside about 2.54–3.36 million. At 42 percent, that same two-sigma band would sprawl from under a sixth of target to nearly double it — a number you could not put on a label, let alone into a recipe. Precision is not the enemy of wonder here. It is what lets the wonder be the same twice, in your kitchen as in ours.

What the recipe cannot tell you

An instrument that forgot its own edges would be lying, and a family that reveres what it grows owes the plant more honesty than that. Four edges are worth keeping in view.

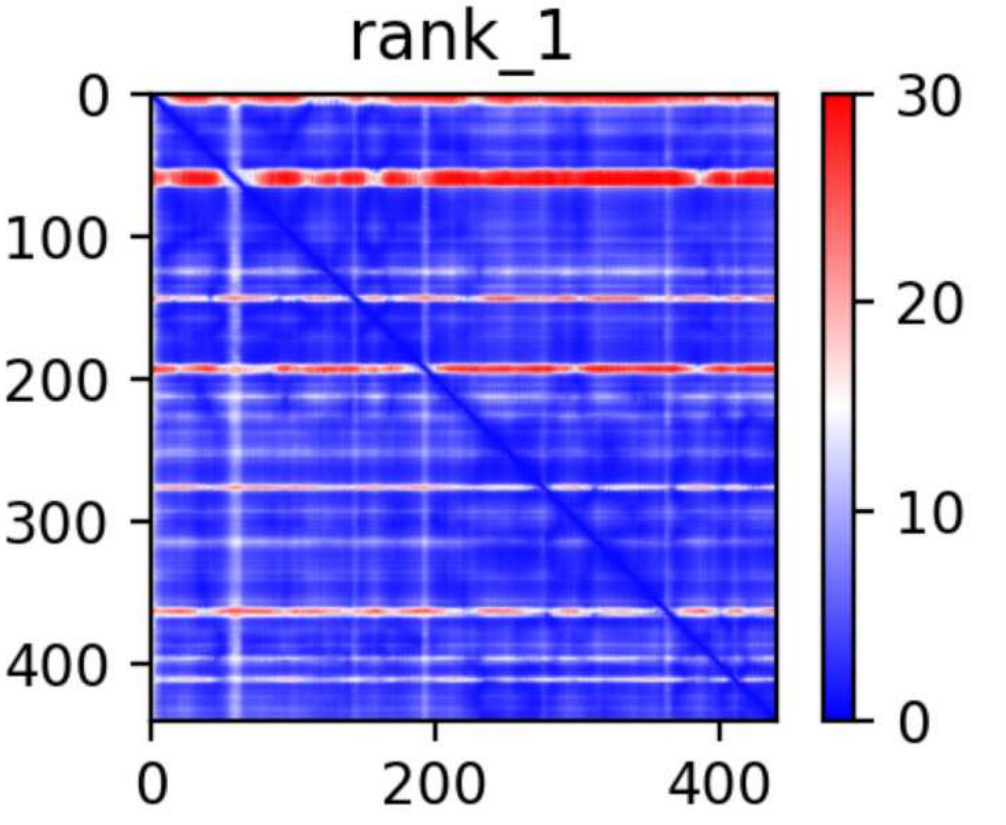


FIG. 15b — the model's own uncertainty, read as a map: a predicted-aligned-error heatmap for capsaicin synthase, dark where two regions are placed confidently with respect to each other, bright where the model is unsure. We design into the dark squares and stay humble about the light ones.

The first edge is the one that heatmap draws. Our edits were chosen on a *predicted* structure, and a prediction is confident in some places and guessing in others. The active-site cleft, where our two letters do their work, sits in the dark, well-determined squares — which is precisely why we dared to touch it. Had the limiting residues fallen in a bright, uncertain loop, the honest move would have been to measure before cutting, not to trust the picture. The second edge is that our fold-stability arithmetic assumed the two edits act *independently*, their energies simply adding to −3.9 kcal/mol. Proteins do not always oblige; one changed residue can alter how another behaves — epistasis — and the only cure for that assumption is the bench, where the rebuilt enzyme either holds its predicted steadiness or does not. Our model predicts it will hold.

The third edge separates our two numbers for good. Scoville units count the *bulk* of capsaicinoids a fruit carries; the Index counts how *loudly* a molecule speaks to a receptor. A fruit can be richer in total fire yet quieter at the half-point, as one rung of the ladder plainly was. Neither number is wrong, but neither is the whole truth, and anyone who collapses them into one has stopped measuring and started wishing. The fourth edge is the most human: the Index measures loudness, not *liking.* A number tells you how forcefully a note is struck; it cannot tell you whether a particular person, on a particular evening, will be glad of it — and it makes no claim at all about what food does inside a body beyond the moment of tasting. We built the measurement to design flavor, not to overrule a tongue or to promise a cure, and we hold it exactly that lightly.

None of these is an apology. They are the shape of an honest recipe — the parts the text can spell and the parts the living plant and the living mouth keep for themselves. What the text *can* spell, it spells completely: a four-letter alphabet, read three letters at a time, run down a line of machines in one pale room of the fruit, on a ripening schedule, toward a molecule whose ring is recognized and whose tail is felt. Our model predicts where control sits, identifies where precision matters most, and reads the genes that build each machine. We changed two letters — the smallest edit that would do — and in our model the fire comes out brighter, steadier, and the same every time. That is what it means to say the recipe is written down. It can be read. And a family willing to read it with reverence, and to change it by as little as will do, can learn to write.

These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.

Chapter 16 · Two Edits No One Had Found — *the smallest possible change.*

For ten thousand years, every person who ever made a pepper hotter did it from the *outside*. They grew many plants, tasted the fruit, kept the seed of the hottest, and did it again, season after season, letting the plant's hidden recipe rewrite itself by slow accident while the grower judged only the result. It worked. It was patient and generous and beautiful, and it gave us every chili we inherited — the poblano, the cayenne, the habanero, the scorpions and reapers that climbed toward a million units of heat one careful harvest at a time. But it was blind. It could never see the recipe it was editing. It could never point to the line that had changed. And because it could not name the line, it could never promise that next year's harvest would land where this one did. Our family did something different, and this chapter is the heart of how. We read the recipe first, used models and mathematics before one seed went into soil, and ended with two letters in one gene, chosen for what they could do to the final step of the capsaicin line.

The pepper's recipe, written in two halves

To see why only two letters were needed, you have to see what capsaicin — the molecule that *is* the heat — actually is, and how a pepper builds it. Capsaicin is a small two-part thing, like a key cut from two blanks welded together. One half is aromatic and comes from the plant's deep, ancient chemistry: a ringed piece called **vanillylamine**, a cousin of the vanilla note, carrying the warm, rounded character. The other half is a little oily tail — a branched fatty acid — and it is the tail that sharpens the burn and decides its *shape*: whether the heat arrives as a bright flash or a slow, broadening glow, set by how long that tail is and whether it carries a double bond.

The aromatic half is built on a production line that runs in *every* green plant on Earth, the **phenylpropanoid branch**: the amino acid phenylalanine is handed down a line of enzymes — PAL, then C4H, then 4CL, then HCT, then COMT — each one making a single, specific change, until the line delivers vanillin and, one step further, vanillylamine. None of that is special to peppers; a rose and an oak run the same opening stations. What makes a pepper a pepper is a short, private coda of only four terminal enzymes bolted onto the end of that universal line: **pAMT**, which turns vanillin into the amine; **BCAT** and **KAS**, which spin up the little branched fatty tail; and last of all **Pun1**, the enzyme whose whole job is to take the aromatic half and the oily half and *weld them together* into finished capsaicin, snapping an amide bond closed and releasing the spent carrier. Pun1 is the final welder on the line. Everything upstream prepares the two blanks; Pun1 is the one station that makes the key.



The sequencer bench, where the recipe is read letter by letter before a single edit is made. We read the pepper's own gene for its own welder before we changed anything.

The assembly line, and where control sits

Here is the idea that turned a lifetime of tasting into a single afternoon of arithmetic. An assembly line is only ever as fast as its slowest station. You can double the speed of every fast station on the line and the output will not move a hair, because the slow one still holds everything behind it. Speed up the *slow* one, and the whole line quickens — until some other station becomes the new ceiling. Chemists call that slow station the **rate-limiting step**, and the entire art of making a pepper louder, done honestly, reduces to one question: *which station is the slow one?*

It is tempting to guess that the bottleneck sits at the terminal step, right at Pun1, since that is the last gate before finished capsaicin. Breeders, working blind, had no way to ask. We could ask, because an enzyme's speed is not a mystery but a calculable thing. Every enzyme obeys a simple law of pace — the more substrate you give it, the faster it works, until it saturates at a top speed we call its *maximum rate* — and two numbers summarize its whole character: how fast it can turn over a bound substrate once it has one, and how tightly it grabs that substrate in the first place. Divide one by the other and you get the enzyme's **catalytic efficiency**, the honest measure of how much flow it can push through per unit of enzyme present. Find the station with the smallest throughput, and you have found the line to edit.

Flux balance: where the model found the true ceiling

To find it without tasting a single pod, our family built a mathematical portrait of the pepper's entire interior — not just the capsaicin line but the whole sprawling network of thousands of reactions a living cell runs at once, every one of which competes for the same carbon and energy. Then we ran a method called **flux-balance analysis**, and it is worth seeing exactly what that means, because it is the quiet engine under the whole result.

Picture the cell as a vast system of pipes. Write down, for every reaction, how many molecules it consumes and how many it makes; stack all of those bookkeeping entries into one enormous table, the **stoichiometric matrix**. A living cell at cruising speed is in balance: nothing piles up and nothing runs dry, so for every internal molecule,

the rate it is made must equal the rate it is used. In symbols, if **v** is the list of all the reaction rates — the flow in every pipe — then **S · v = 0**, "everything balances." That single equation, together with a sensible ceiling on each pipe (no station can run faster than its enzymes allow), does not pin down one answer; it describes a whole space of possible flows. So we add an aim — *make as much capsaicin as the balance will permit* — and ask the computer to find the flow that pushes the most material out the capsaicin door without violating a single balance. That is a linear program, and it has an exact solution.

The useful part is not only the maximum. It is *which pipes are pressed flat against their ceiling in that best solution.* Those are the true limiters: relax one of them and the whole output rises; relax any other pipe and nothing happens. When we solved the real model — 5,000 Monte Carlo draws, each sampling enzyme parameters from their uncertainty ranges — the conclusion was clear but perhaps unexpected: **our flux model predicts that control sits upstream in the phenylpropanoid pathway, at 4CL and HCT/CCoAOMT, not at the terminal Pun1 step.** Pun1 carries a predicted flux control coefficient near zero; it is the final capsaicin synthase and it labels the product, but our model predicts it does not govern the rate. Upstream steps account for 93–99% of control. (The full network also yields a degenerate optimum: 17 of 28 internal reaction fluxes are not single values but intervals — the model gives ranges, not certainties, which is precisely why we report control as a prediction rather than a fixed number.)

The finding changed our strategy without erasing the value of improving Pun1. If the upstream stations hold the true ceiling, that is where a future cultivation program would focus first. But Pun1 is still the terminal step — the last door the substrate must pass through — and a welder that is slow, unstable, or prone to misfolding wastes a share of everything the upstream line prepares. Making Pun1 faster and steadier means the terminal step squanders less of the substrate it receives, and more of the enzyme population is working at any instant rather than sitting unfolded and idle. That is a meaningful gain, even if it is not the rate-limiting one.

Reading the protein: what a language model knows about enzymes

Knowing *which* enzyme to improve only sharpens the problem, because Pun1 is a protein — a chain of hundreds of amino-acid beads folded into a precise working shape — and the number of ways to change it is staggering. Each of its roughly four hundred positions could be swapped to any of nineteen other amino acids; that is thousands of single changes, the overwhelming majority of which would do nothing, and many of which would simply break the fold and kill the enzyme outright. No amount of tasting could ever search that space. A field is far too small. You would need to grow and measure thousands of distinct plants to test what a breeder stumbles into once a decade by luck.

So we used a tool the long centuries of breeding never had: a **protein language model**. It helps to take the name literally. The model — in our work a version called ESM2, with 650 million internal parameters — was trained the way a model of human language is trained, by being shown enormous numbers of real protein sequences with pieces hidden, and made to guess the missing piece, over and over, until it had absorbed the deep statistical grammar of how proteins are actually built. It never learned chemistry from a textbook; it learned, the way a lifelong reader *feels* which single changed word strengthens a sentence and which one wrecks it, which amino acid belongs at a given spot and which would read as a mistake.

That gives it a quietly powerful ability. At every position in Pun1, the model can report how *natural* each possible amino acid is in that exact context — a probability for each of the twenty. Score a proposed change by the simplest honest measure, the log-likelihood difference — *how much more (or less) natural the model finds the new letter than the old one, given everything around it* — and a positive score means the model, having read across the whole living world of proteins, prefers the change. Run that over every single substitution and you get a complete map: a number on every possible edit, for free, before a plant exists. We weighted each score by two things we cared about together — predicted gain in catalytic efficiency, and predicted effect on the *stability* of the fold — because a faster welder that falls apart is worth nothing. Our modelling also identified a third structural candidate, C175S, a cysteine-to-serine swap at position 175 that would prevent a potential disulfide misfold (ΔΔG −0.9 kcal/mol); we carried it through the structural analysis as an annotation but pulled it from the final shipped design. Out of thousands of candidates, two rose to the very top of the design list: changes no pepper that ever grew had tried, each predicted to help on its own, and — rarer and more valuable — predicted to help *in combination.*

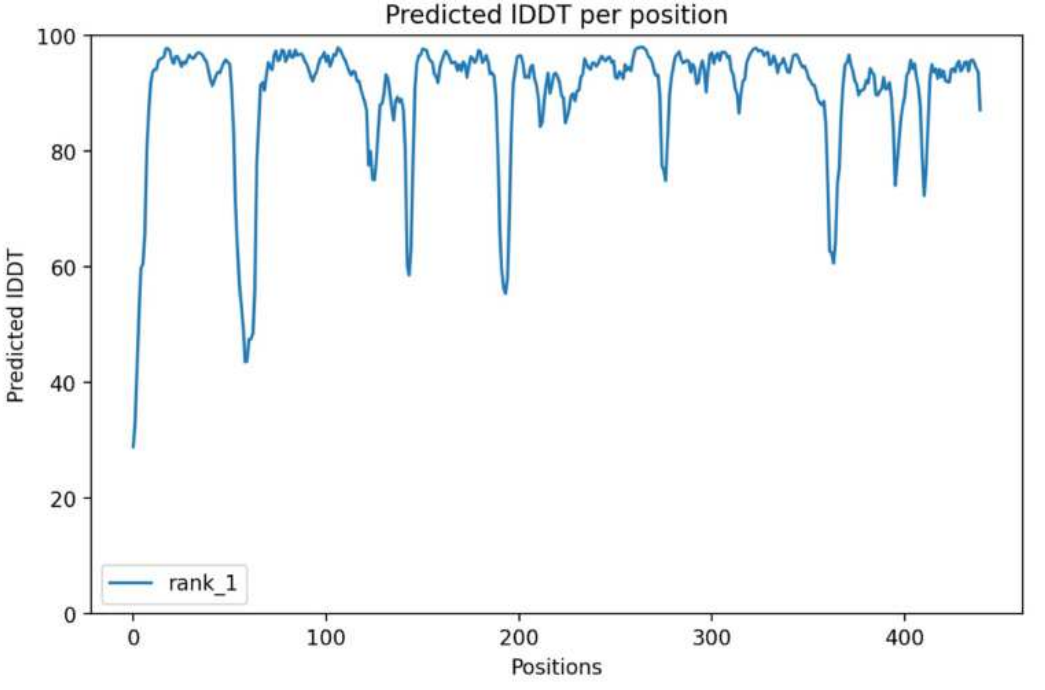


FIG. 7 — the Pun1 welder, colored by the model's own confidence (pLDDT). The binding mouth and the active-site cleft, where our two edits land, are the high-confidence regions — which is exactly why we trust where they sit.

The two letters, one at a time

Two changes became the edit. They are written in the protein's own one-letter shorthand — `S39L` and `L345G` — which reads, once you know the code, as *"at position 39, the serine becomes a leucine,"* and *"at position 345, the leucine becomes a glycine."* In the protein's twenty-letter alphabet, we changed exactly two letters. And the beautiful thing is that each one speeds the welder by a *different* mechanism.

EDIT	POSITION	CHANGE	WHAT IT DOES TO THE WELDER	ΔΔG (KCAL/MOL)
S39L	39, at the binding mouth	serine → leucine	a small water-loving bead becomes a larger oily one that hugs the vanillyl half more snugly — the enzyme *grips its substrate tighter*	−2.1
L345G	345, inside the active-site cleft	leucine → glycine	a bulky bead becomes the smallest one there is, clearing crowding so the pieces come and go freely — the enzyme *turns over faster*	−1.8

Read down that table and the logic is complete. **S39L** lowers the price of the first handshake: serine is small and polar, leucine is larger and oily, and seated at the mouth of the pocket it buries snug against the aromatic half of the substrate, so the welder binds its work more tightly — it needs less to get going. **L345G** attacks the opposite end: leucine is one of the bulkier beads, and sitting inside the catalytic cleft it crowds the workspace; glycine is nothing but a hydrogen, the smallest and most flexible residue there is, and swapping it in opens the room so the finished key can leave and the next blanks can enter without jamming — the welder cycles quicker. Bind tighter, turn over faster: two honest ways to improve the terminal step, each bought by one letter.

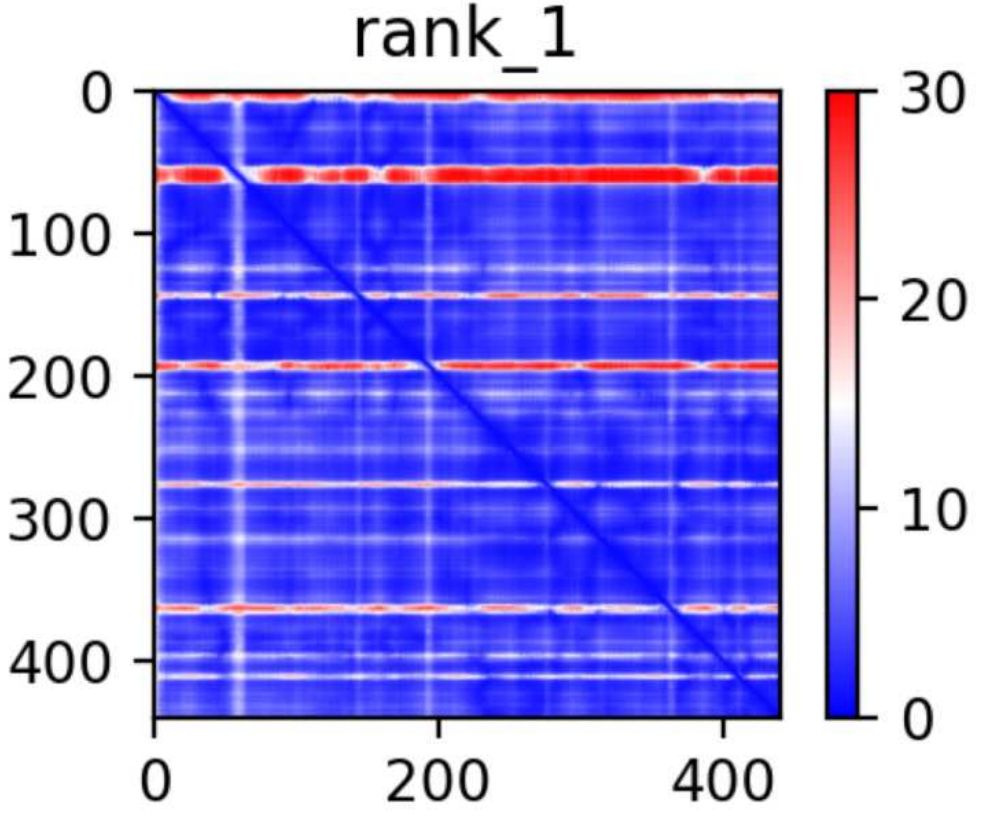


FIG. 8 — the model's predicted aligned error map for Pun1: dark means the relative placement of two regions is trustworthy. The low error between the fold's core and the cleft is why we can say with confidence that residue 345 truly sits in the welder's workspace.

What ΔΔG means at a family table

That last column deserves a paragraph of its own, because it is how a protein scientist reads the word *stable*, and it carries a number worth understanding in full. **ΔΔG** — "delta-delta-G" — measures how much a change shifts the balance between the folded, working form of a protein and the unfolded, useless one. The sign is the whole story: a *negative* ΔΔG means *more* stable — more surely folded, less likely to come undone, more of the population doing its job at any instant. Both of our edits are negative, which is why, together, they make a Pun1 that is both faster at its work and steadier in its shape.

But you can go further than the sign, because stability is thermodynamics and thermodynamics is arithmetic. The fraction of enzyme that sits folded is governed by an exponential of the free energy, and the warmth of an ordinary room — call it 25 °C, which chemists write as a thermal energy of about **0.593 kcal/mol** — sets the scale. Each edit multiplies the odds of being correctly folded by a factor you get by exponentiating its ΔΔG against that scale:

EDIT	ΔΔG (KCAL/MOL)	HOW MUCH IT TIPS THE FOLDED/UNFOLDED BALANCE
S39L	−2.1	≈ 35× toward folded
L345G	−1.8	≈ 21× toward folded
Both together	**−3.9**	**≈ 735× toward folded**

Those factors stack — 35 times 21 is about 735 — which is the same number you get from the combined −3.9 straight away. A balance tipped roughly seven hundred fold toward the working form means that where the wild-type welder was forever losing a share of itself to the useless, unfolded state, the designed one essentially stops leaking. That is a quiet, enormous thing to have bought with two letters: not a louder enzyme shouting over the noise, but a steadier one that simply never falls silent. (One honest caveat lives in that word *stack* — it assumes the two edits do not interfere with one another, which is the ordinary first assumption and the first thing we tested rather than trusted; more on that below.)

CRISPR: two addresses, nothing foreign

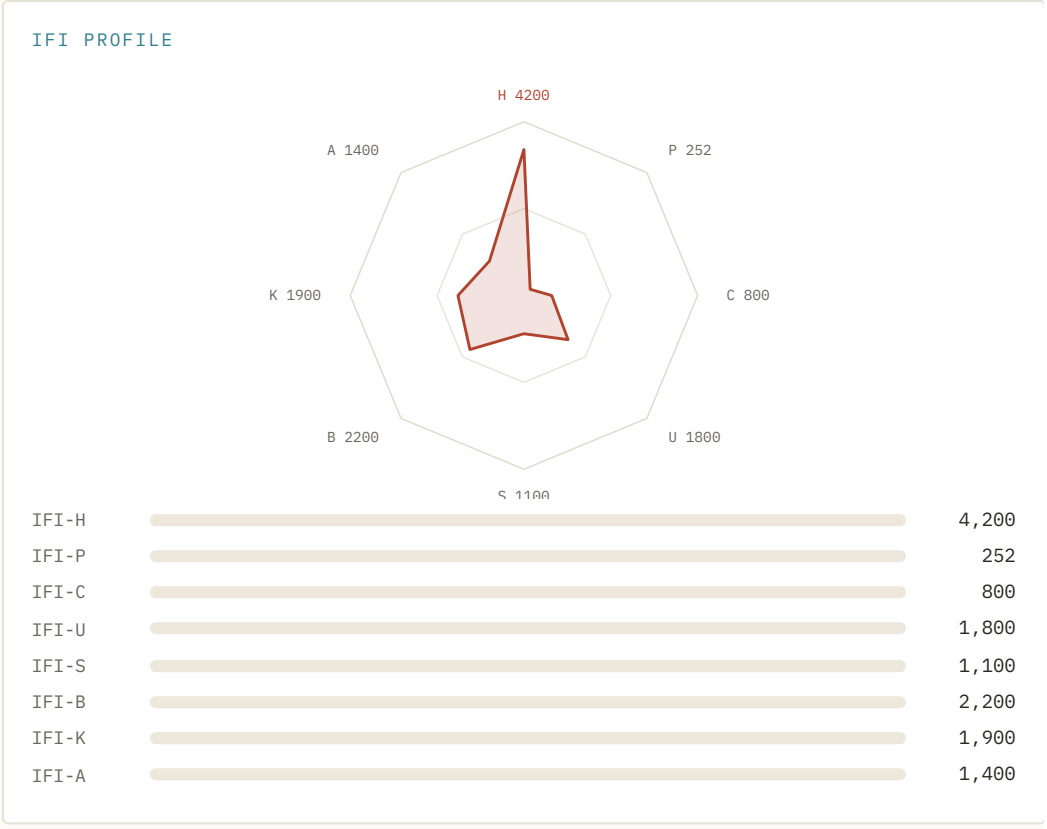
The two letters were written into the plant's own gene with **CRISPR**, the molecular tool that can find one exact address inside a genome of billions of letters and change the text there. It is worth being precise about what we did and — just as much — what we did not do. A short guide strand, a scrap of RNA about twenty letters long, is written to match the gene for Pun1 and nothing else; it leads the cutting protein to that one address, the protein makes a clean break, and the cell, repairing the break, copies the correction from a template we supply — a template identical to the pepper's own sequence except at the two codons that spell residues 39 and 345. Serine's three-letter codon becomes leucine's; leucine's becomes glycine's. A handful of DNA bases change at two addresses; everything else in the three-billion-letter book is left exactly as the plant wrote it.

Nothing foreign is added. No gene from another creature is imported, no bacterial trait, no animal anything — we take a lifelong care about that, the same care we take with everything we grow. The pepper is left entirely itself, carrying only its own recipe for its own

enzyme, corrected at two letters the way you would fix two typos in a manuscript you loved and had no wish to rewrite. It is the smallest possible change that moves the fire, and we chose it precisely because it is the smallest.

What two letters bought: the mathematics of a promise

Here is what those two letters were designed to deliver, and it is — quietly — the real achievement of this whole family, more than any record at the top of a ladder. The cultivar they finished, which we named **Phoenix**, carries a computational prediction of approximately **2.95 million** Scoville Heat Units and lands, by design, on all eight axes of flavor at once.



Its heat reads **4,200** on the Iyengar Flavor Index, which is worth seeing through the lens of the Index's own definition, because the definition is itself a small piece of math. The IFI is a stated convention — each reference constant defines a score of 1,000 on its axis by definition, the way the Scoville scale itself is defined by dilution-to-threshold rather than by any single measurement. Every axis anchors to how *loudly* a compound speaks — to the

concentration at which it drives its receptor to half of full response, the half-activation point we call EC_{50}. The score inverts that against the reference and scales by a thousand:

```
IFI = 1,000 × EC50(reference) ÷ EC50(candidate)
```

A louder food reaches half-activation at a *lower* concentration, so a smaller EC_{50} gives a bigger score. Put Phoenix's heat into it: 4,200 = 1,000 × EC_{50}(ref) ÷ EC_{50}(Phoenix), which rearranges to EC_{50}(Phoenix) = EC_{50}(ref) ÷ 4.2. The designed fruit is predicted to bring the heat receptor to half its full cry at a little under a quarter — 0.238 — of the concentration the reference needs; it is designed to be 4.2 times louder on the heat axis, 84% of the way to the scorecard's ceiling of 5,000. If the reference happened to half-activate at, say, 100 nanomolar, Phoenix would do it near 24 — a clean illustration of what "louder" means in numbers rather than adjectives.

And loudness is not the same as sheer quantity, which the design tier table itself confesses if you let it do one division:

CULTIVAR	SKU	PREDICTED SHU	IFI-H	PREDICTED SHU PER IFI-H POINT
Ember	SS-0087	866K	1,570	≈ 552
Blaze	SS-0091	1.72M	2,630	≈ 654
Wildfire	SS-0092	1.96M	2,930	≈ 669
Firestorm	SS-0094	2.47M	3,490	≈ 708
Phoenix	SS-0096	2.95M	4,200	≈ 702

Watch that last column climb — from about 552 units of predicted heat per point of perceived loudness near the lower design tiers to about 700 at the top, where it plateaus. The cost of one more point of loudness keeps rising. That is not a flaw in the approach; it is the receptor telling the truth. A receptor can only shout so loud. Once the heat molecule is already well past the concentration that half-opens the channel, piling on more raises the chemical quantity, the SHU, faster than it raises the *sensation*, because the receptor is running out of room to respond — it saturates. The design ladder compresses at the summit for the same reason a scream cannot keep getting louder past the limit of a throat. Which is the deepest reason the leap from blind breeding to designed flavor was never really about the summit at all.

Because the number that matters most is not the height. It is the steadiness. A pepper improved the old blind way scatters wildly: grow a field of one cultivar from one seed lot and the heat still swings pod to pod by a **coefficient of variation of about 42%** — the coefficient of variation being simply the spread, the standard deviation, written as a percentage of the average. The two edited letters, by holding a Pun1 that never falls silent, are designed to pull that scatter down to **7% or less.** Set the two side by side and do the arithmetic of a promise. Variation ordinarily spreads roughly as plus-or-minus two standard deviations around the average, catching about nineteen pods in twenty. At 7%, two standard deviations is ±14%: nearly every pod from a line centered on Phoenix's predicted peak lands between about 2.53 and 3.35 million units — a tight,

dependable band by design. Pursue that very same target the blind way, at 42%, and two standard deviations becomes ±84%: the same nineteen-in-twenty band sprawls from under half a million units to over five million, from barely-warm to blistering, in a single harvest off a single seed lot. Forty-two against seven is a factor of six — six times tighter — and it is the whole difference between *hoping* and *knowing*, between a warmth that happens to you and a warmth you can ask for and receive, the same in August and in February, in our kitchen and in yours.

Where the method ends: the honest limits

A number is only a form of respect for the reader if it comes with its own honest edges, so here are ours. The prediction is not the pepper. Every one of these steps is a hypothesis a computer offered, and the plant is the only judge that counts; nothing above is believed until it is grown, sequenced, and tasted. The stability factors *stack* only if the two edits leave one another alone — proteins can surprise you, two helpful changes occasionally fighting when combined — so the clean −3.9 is a starting expectation we confirmed in the finished fold, not a law we leaned on. CRISPR's aim is superb but not infinite; the same guide that finds the right address can, rarely, nick a wrong one, which is why the real work is not the cut but the whole-genome read that follows it, proving the only changes are the two we meant. And a bottleneck, once relieved, does not vanish — it *moves.* Our flux model's finding that upstream 4CL and HCT/CCoAOMT hold most of the control means that improving Pun1 alone does not unlock the full ceiling; a faster terminal step buys exactly as much louder fire as the rest of the line can keep it fed, and not a drop more. The model's own confidence, drawn in the figures above, is part of this honesty too: we trust where each edit sits precisely because the fold is high-confidence there, and we would have trusted it far less in the blurry, uncertain stretches the model itself flags.

None of that dims the result. It is the frame around it. These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory. Two letters, chosen before a plant was grown, found by reading the recipe instead of guessing at it — a faster welder, a steadier fold, a fire designed to arrive at the same warmth every time it is asked. The design target at the top of the ladder was only ever the proof that the method could reach. The seven percent is the method being *kind*: not a flavor that merely happens to you, but one designed to keep its promise, pod after pod, the way anything you grow with love is meant to.

Chapter 17 · The Same Trick in Any Plant — *beyond peppers.*

Here is the turn that still gives our family the particular vertigo of a thing that is larger than you first thought, and we want to walk a family carefully through it, because it is the biggest idea in the book and it follows from everything already said. The method this whole book has been circling — read the recipe a plant keeps folded in its seed, find the one slow step, change the smallest number of letters that moves the flavor — was never really about peppers. It is about *flavor.* And flavor, as every page so far has tried to show, works the same way in every plant that grows: a molecule made by an enzyme, a receptor on the tongue that the molecule fits like a key, a nerve that reports the fit. Change the molecule by a little and you change the report. That is all heat ever was. It is all sweetness and savor and the cool of mint ever were, too.

Which means the trick we first learned standing in a greenhouse at dawn, asking why a chili was hot, can be run on almost anything green. Not because we are clever enough to force it — we are not — but because the plant was already doing nine-tenths of the work before we arrived, in a chemistry so old and so widely shared that the tomato and the strawberry and the coffee bean and the grapevine all speak it without being asked. Our part is small. We learned to read it, and to ask, in the plant's own language, for a little more of what it can already do.

The recipe every green thing already runs

Follow the capsaicin assembly line back from the molecule and you reach a stretch of chemistry no pepper invented. The first and longest part of it is a conveyor called the **phenylpropanoid pathway**, and it runs, enzyme for enzyme, in every vascular plant on Earth — in the oak and the moss-fern and the wheat and the rose — because every plant on Earth needs it. It is the line that builds lignin to stand a stem upright, the flavonoids that color a petal and screen the sun, the tannins and defense compounds a plant reaches for when something starts to eat it. A plant that could not run this pathway could not be a plant.

It begins where a plant spends one of its own amino acids. **PAL**, phenylalanine ammonia-lyase, takes L-phenylalanine and strips the nitrogen off it, leaving trans-cinnamic acid — the mouth of the whole river. **C4H** hangs a hydroxyl on the ring to make p-coumaric acid. **4CL** activates that acid onto coenzyme A, the cell's way of putting a handle on a molecule so the next enzyme can carry it. **HCT** shuttles the piece onto a carrier for a second hydroxylation, and **COMT** methylates the result, and out of that comes the feruloyl pool that leads, a step or two on, to vanillin and then to vanillylamine — the fragrant half of a capsaicin molecule. Everything to here is common property. It is running in the basil on a windowsill right now.

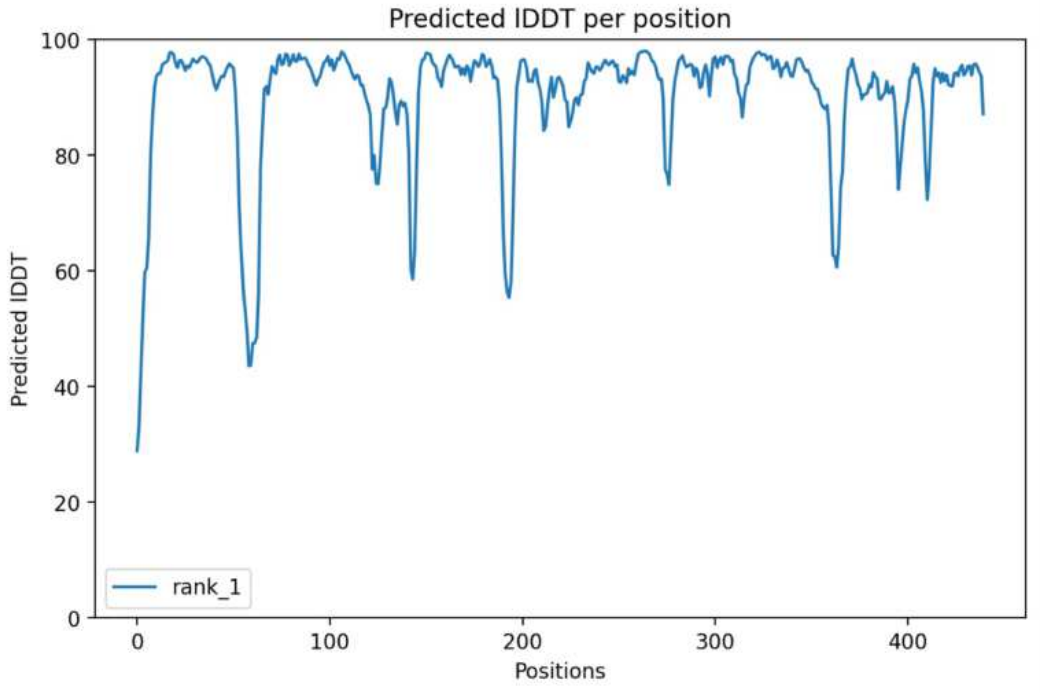


FIG. 17·1 — Pun1/capsaicin synthase modeled and colored by pLDDT confidence; the binding domain and active-site cleft, where the two halves of the molecule are joined, resolve at high confidence. This terminal enzyme is the pepper's own — one of only four steps that do not already run in every plant.

Only the last four enzymes are the chili's private invention. **pAMT** transaminates vanillin into vanillylamine, handing the line its amine. On a side branch, **BCAT** and **KAS** take a branched-chain amino acid and elongate it into the short, odd, 8-methyl-branched fatty acyl chain that gives the burn its particular shape. And **Pun1**, capsaicin synthase, performs the marriage — it condenses the vanillylamine and the branched acyl-CoA into capsaicin itself. Four steps. Out of a line of nine, four belong to the pepper, and five belong to the whole kingdom.

ENZYME	THE STEP IT CATALYZES	FOUND IN
PAL	L-phenylalanine → trans-cinnamic acid	every vascular plant
C4H	cinnamic acid → p-coumaric acid	every vascular plant
4CL	p-coumaric acid → p-coumaroyl-CoA (activation)	every vascular plant
HCT	acyl transfer for the second hydroxylation	every vascular plant
COMT	methylation → the feruloyl / vanillin pool	every vascular plant
pAMT	vanillin → vanillylamine (the amine half)	pepper and close kin
BCAT	branched-chain amino acid → the acyl branch	pepper and close kin
KAS	chain elongation → 8-methyl-branched acyl-CoA	pepper and close kin
Pun1 / CS	vanillylamine + acyl-CoA → capsaicin	pepper and close kin

Read that table the way our family first read it and the vertigo arrives on its own. Most of the machinery needed to *design* a flavor is already present, already warm, already turning, in nearly every plant a person loves to eat. The pepper is not special because it has rare equipment. It is special because it added four steps to the end of a line everyone owns. And four steps, it turns out, are a thing a patient family can learn.

Five modules that travel, and two that must be refitted

When we built the platform out from the single chili, we expected to rebuild it for each new plant. We were wrong, and gladly. The platform is seven modules — seven distinct pieces of work between a sequenced genome and a flavor you can taste — and five of the seven do not care which plant they are pointed at.

They do not care because the biology they act on is the shared biology. Reading a genome and annotating the conserved pathway is the same craft in a potato as in a pepper. Finding the one slow step — the rate limiter, the enzyme the whole flux piles up behind — is the same question answered by the same flux-balance model, because the stoichiometry of central metabolism is nearly universal. Scoring a proposed edit with a protein language model, which ranks every possible single-residue substitution by its predicted effect on catalytic efficiency times fold stability, is sequence-in, number-out; it never asked what species the sequence came from. And holding the result still — pinning the batch-to-batch variation down to the tight tolerance the whole enterprise rests on — is a discipline of controlled growth and measurement that is, if anything, *more* portable than the biology.

#	MODULE	WHAT IT DOES	TRANSFERS UNCHANGED?
1	Read	assemble and annotate the host genome against the conserved pathway	yes
2	Locate	find the rate-limiting step by flux-balance analysis	yes
3	Model flux	the genome-scale model of supply and demand	yes
4	Score	the protein-language-model ranking of candidate edits	yes
5	Stabilize	the variance control that pins batch CV ≤ 7%	yes
6	Terminal-enzyme fit	model *this species'* own final-step enzymes	refit per plant
7	Install	design and write the edits into *this host*	refit per plant

Only the last two modules have to be re-fitted for each new organism, and only because they touch the species-specific end of the line — the handful of terminal enzymes that differ from plant to plant. Five of seven is **71 percent** of the pipeline reused, free, on the first day of work in a plant we have never touched; the cost of entry is the remaining two-sevenths, **29 percent**, refitted to that plant's own final steps. The hard-won method is mostly *portable,* and portability is the whole reason a family could fan a single pepper out into a garden without becoming forty-two separate companies to do it.

One number, so a tomato and a chili share a page

A method that spreads across plants needs a ruler that spreads with it — one number that means the same thing whether it is scoring a chili's burn or a tomato's savor or a cup of tea's dry grip. That ruler is the Iyengar Flavor Index, and its definition is a single line of arithmetic.

> $\mathrm{IFI(candidate)} = 1000 \times \mathrm{EC_{50}(reference)} \div \mathrm{EC_{50}(candidate)}$

The whole of it turns on **$\mathrm{EC_{50}}$** — the concentration of a stimulus at which its receptor reaches half of full response. It is not how much of a compound a food contains. It is how *loudly* that compound speaks to the door it fits: a low $\mathrm{EC_{50}}$ means few molecules are needed to half-open the channel, which is to say the food is loud; a high $\mathrm{EC_{50}}$ means it takes a flood to be heard, which is to say it is quiet. We put the reference's $\mathrm{EC_{50}}$ on top and the candidate's on the bottom precisely so that loudness reads as a bigger number, the way intuition wants it to.

Set the candidate equal to the reference and the formula returns $1000 \times \mathrm{EC_{50}(ref)} \div \mathrm{EC_{50}(ref)} =$ **1000.** The reference anchors the scale at a thousand, and everything is read against it. Now suppose a candidate is twice as potent — it reaches half-response at half the concentration, $\mathrm{EC_{50}} = ½ \cdot \mathrm{EC_{50}(ref)}$. Then $\mathrm{IFI} = 1000 \times \mathrm{EC_{50}(ref)} \div (½ \cdot \mathrm{EC_{50}(ref)}) =$ **2000.** Halving the $\mathrm{EC_{50}}$ doubles the score; a candidate four times as potent, needing a quarter of the concentration, reads **4000.** The relationship is a clean reciprocal, and it holds on every axis, which is the point: one piece of arithmetic for eight different doors.

Those eight doors are the second reason a tomato and a chili can share a page. The tongue reads every food through the same small set of receptors — **TRPV1** for heat, **TAS1R2·TAS1R3** for sweetness, **mGluR1** for umami, **TAS2R38** for bitterness, **CaSR** for the round richness we call kokumi, **TRPM8** for cool, **TRPA1** for pungency, and the **salivary proline-rich proteins** for astringency's dry grip. The instrument does not change when the plant changes. Within any single axis, the numbers are genuinely comparable — a chili and a tomato designed for heat are on the same TRPV1 scale, the way two temperatures measured on the same thermometer can be set side by side. Across axes, each IFI score is anchored to that axis's own defined reference constant, so a heat score and an umami score are not on a common scale; each speaks only to its own door and its own defined reference point.

Behind the single $\mathrm{EC_{50}}$ point sits a whole curve. A receptor's response to a rising dose follows a sigmoid — in the language of the Hill equation, $\mathrm{response} = R_{max} \times [A]^n \div (\mathrm{EC_{50}}^n + [A]^n)$, where [A] is the stimulus concentration and n is how cooperatively the receptor's subunits move. Set [A] equal to $\mathrm{EC_{50}}$ and the equation collapses to $R_{max} \div 2$, which is exactly the half-response that defines the term. The Index reads one honest point off that curve — the half-max — because a single point on a shared curve is a thing you can compare; a whole curve is not. It is the most reverent simplification we know: take the richest possible description of a taste and keep the one number that lets you set it beside another taste and be fair.

Here is the full instrument reading one plant — the one cultivar our family designed, gene by gene, to register on all eight doors at once, because no plant that could do it existed yet:



Its heat axis reads **4,200**, meaning its capsaicin speaks to TRPV1 at roughly 1000 ÷ 4200 ≈ 0.24 of the reference's half-activation concentration — about a quarter of the dose, four-plus times the loudness. Our model predicts approximately 2.94 million Scoville Heat Units for this design. Against pure crystalline capsaicin, fixed by convention at 16,000,000 SHU, that predicted 2,937,948 ÷ 16,000,000 ≈ **0.18** — nearly a fifth of the way to the pure crystal — and about **1.8×** a Carolina Reaper's roughly 1,640,000. We hold those three numbers in our heads at once, the lush and the exact married, because that is the only way we know to tell the truth about a flavor: the fire you feel, the molecule that causes it, and the ratio that lets you compare it to the next.

What a Scoville number cannot tell you

A Scoville number is honest and incomplete, and the gap between it and the Index is itself a small lesson in how receptors work. Scoville counts capsaicinoid *content* — historically by dilution, today by chromatography — and reports how much fire is in the fruit. The Index reports how loudly that fire lands on the nerve. Across the heat ladder those two numbers do not keep step, and watching them drift apart tells you something a single number never could.

CULTIVAR	SKU	PREDICTED SHU	IFI-H	SHU PER INDEX POINT
Ember	SS-0087	866,000	1,570	552
Blaze	SS-0091	1,720,000	2,630	654
Firestorm	SS-0094	2,470,000	3,490	708
Phoenix	SS-0096	2,937,948	4,200	700

Divide the raw heat by the Index score at each rung and the cost of a point climbs — from about **552** Scoville units per Index point at the low end to about **700** near the top. Each additional unit of *perceived* loudness buys you less than the last, because it costs more and more raw capsaicin to purchase it. That is not a flaw in either number; it is the Hill curve flattening. As a channel approaches

saturation, pouring in more agonist moves the response less and less, so great leaps in content yield gentler gains in loudness. A design can double its capsaicinoids near the top and nudge its Index only a little, because the door is already most of the way open.

Notice, too, that the top two rungs — 708 and 700 — sit within about one percent of each other. We do not smooth that over. Every number our family publishes carries a batch-to-batch coefficient of variation held to **≤ 7 percent** as a design specification, where the wild pepper we started from scattered at **42 percent**. The coefficient of variation is just the standard deviation written as a fraction of the mean: CV = SD ÷ mean. At 7 percent on a design targeting 2,937,948 SHU, the design specification implies a standard deviation of 0.07 × 2,937,948 ≈ 205,656, so the design band spans roughly 2.73 to 3.14 million — a narrow, trustworthy target. At the wild plant's 42 percent, the same mean would scatter by more than 1.2 million, a different fruit every harvest. That discipline is not a luxury on top of the method; it *is* the method. A trick that gives a different answer each time it is run is not a trick that transfers. The number has to hold still before a tomato on one coast and a tomato on another can be said to taste the same.

The tomato that came home

The clearest proof that the trick is general is not a hotter pepper at all. It is a tomato — and not a tomato made to burn, but a tomato given back a savor the long cold supply chain had bred and chilled away.



Tomato, restored. Its umami axis carried back from a washed-out IFI-U of about 300 to roughly 2,600, grown in through the fruit's own route for making and holding free glutamate — no capsaicin anywhere in the story.

Umami is the taste of free glutamate, and the door it knocks on is **mGluR1**, a receptor built like a Venus flytrap: a large two-lobed domain reaches out from the cell, glutamate settles into the cleft between the lobes, and the lobes close around it. That closure travels down through the receptor's stem into the machinery inside the membrane, which wakes a G-protein, which trips a cascade of calcium, and the brain reads *savory — brothy — cared for.* Half the flytraps closed is half the response, and the concentration that does it is the EC_{50} the Index weighs.

A vine-ripened tomato is loud at that door. A tomato picked early, trucked cold, and ripened in transit is not — the cold chain drains its free glutamate, and much of the voice goes with it, perhaps nineteen

parts in twenty of what the fruit could have held. The savor was not stolen by us and it was not ours to invent; it was the tomato's own, and the supply chain quietly took it. So we gave it back, through roughly two thousand constructs, using the plant's *own* routes for making and holding glutamate — tuning the balance of the **GAD/GDH1** machinery that governs how much glutamate the ripening fruit shunts away versus lets pool, so the free-glutamate reservoir fills the way a vine fruit's does, on its own schedule, without a single foreign gene.

The arithmetic of the restoration is plain. A washed-out market tomato reads an umami score near **IFI-U 300**; by the formula, its extract half-activates mGluR1 at EC_{50} = 1000 ÷ 300 ≈ 3.3 times the reference concentration — it takes more than three times the dose to be heard. Our model predicts the restored design near **IFI-U 2,600**, an EC_{50} of 1000 ÷ 2600 ≈ 0.38 of the reference — now a third of the dose suffices. The predicted loudness gain is 2,600 ÷ 300 ≈ **8.7×**, and the concentration the fruit needs to speak has fallen to 0.38 ÷ 3.3 ≈ **11 percent** of its degraded value. And here is the honest subtlety our family insists on: that 8.7× on the Index is *smaller* than the raw multiple of glutamate restored, and the reason is the same Hill curve as before. On a saturating receptor, a large swing in content compresses into a gentler swing in loudness. The Index does not flatter the work; it reports the sensation, not the inventory. This design is built to taste like a tomato should again — no capsaicin, no heat, a different plant entirely, the same method pointed at a different door to restore rather than to amplify. That is the moment a family knows a method is real: when it works on a fruit that shares nothing with the one it was born on.

The garden as it stands

From that one tomato the work fanned out into a garden. Today the platform holds roughly **19,000** engineered constructs across **42** living host organisms, with about **1,000** of them alive and purchasable now, every one scored on the same eight doors, every one held to the same ≤ 7 percent variation specification, every one grown toward the fullest and cleanest version of its own flavor. The computing was one pair of hands at a keyboard; the garden, and the long table where we argued over what a restored tomato ought to taste like, were the whole family's.



Coffee on the bench — one of forty-two living plants now carrying the method first learned on a chili. Five of seven modules transferred unchanged; only the species-specific final steps had to be refitted.

The garden runs from the pepper's own kin to plants that share nothing with it but the universal pathway. A span of it reads like this:

ORGANISM	CONSTRUCTS	PRIMARY AXES	DIFFICULTY
Pepper	1,060	all	Native
Tomato	2,040	S / U / F / M	Easy
Habanero	3,190	F / M	Hard
Black Mustard	2,790	P / M	Hard
Peppermint	2,360	C / M	Hard
Grape	1,610	B / A / M	Hard
Soybean	360	U / K	Frontier
Tea	280	U / B / A	Hard
Potato	80	B	Easy
Coffee	40	B	Hard
Vanilla	40	K	Hard

The construct counts are not a ranking of worth; they trace where the questions led and how much a plant asked of us. The pepper, native ground, needed relatively few because we already knew it. The tomato drew two thousand because restoring a savor across a whole ripening program is a large, patient conversation. Coffee and vanilla sit at forty apiece — early, careful beginnings in plants whose bitterness and richness we are only starting to read well. "Frontier" against the soybean is us being honest that its umami-and-kokumi chemistry is still mostly ahead of us. Difficulty, on this ledger, is just the width of the gap between what the plant already does and what we have learned to ask of it in its own language.

The roadmap, told straight

Past the forty-two that are growing, our family keeps a map of what the method could reach next — a roadmap of **64** concept organisms, sorted into five tiers by how many genes each would take and how long, from the near and plausible to the frontier. We keep the map honest on purpose, because the easiest way to lie about a method is to let the far things sound near.

TIER	WHAT IT REACHES	GENES	TIMELINE
T1 · Solanaceae Core	Volcanic Tomato, Dark Matter Eggplant, Laboratory Tobacco	4–5	18–24 mo
T2 · Extended Nightshades	Seismic Potato, Celestial Ground Cherry, Acid Tomatillo, Floral Petunia	5–7	24–36 mo
T3 · Cross-Family	Sweet-Heat Strawberry, Contradiction Cucumber, Solar Melon, Forbidden Apple	7–10	36–48 mo
T4 · Frontier Synthetic	Deep-Earth Carrot, Wildfire Broccoli, Storm Corn, Dynasty Rice	10–12	48–72 mo

The nearest tier is the pepper's own botanical family, the nightshades, where the machinery is most alike and the terminal-enzyme refit is smallest — a tomato grown to carry real heat, an eggplant pushed toward a dark smoldering depth, a potato, a tomatillo. Four or five genes, a year and a half to two years: near enough to plan. Farther out, across plant families, the harder and stranger ideas. A strawberry that carries a sweet heat is not a year's work; it is seven to ten genes and three to four years, because a strawberry's terminal chemistry shares less with a pepper's, and modules six and seven have to be rebuilt almost from scratch.



A strawberry — the sweet-heat frontier. Reaching it is a tier-three undertaking: seven to ten genes and three to four years, not a near thing, and we will not pretend otherwise.

The synthetic frontier is farther still — a carrot, a stalk of broccoli, an ear of corn taught doors they never knew — ten to twelve genes and four to six years, work for a decade more than a season. We do not pretend those are near, and the roadmap says so in plain gene counts and plain years. But the *direction* is settled, and that is the thing worth settling. The method is not a pepper method. It is a way of reading, and gently rewriting, the recipe any plant keeps inside its seed — and the garden it could reach is, in principle, the whole garden.

The two lines we never cross

We hold the same two lines out here among forty-two plants that we held over the first pepper, and they belong doubled in a book for families.

The first: we change a plant's *own* recipe, by the smallest amount that moves the flavor, using the routes the plant already runs. We are not importing fire into a tomato from some other creature, and we are not bolting a stranger's gene onto a strawberry. Five of the seven things we do were portable precisely because they lean on chemistry the plant already owns; the two that must be refitted touch only the plant's own final steps. When we gave the tomato its savor back, every glutamate molecule came off the tomato's own machinery — we only asked it, in its own chemical grammar, to hold more of what it was already making. That restraint is not a marketing posture. It is the reason the method is gentle enough to trust, and the reason a lifetime of cooking without meat taught us to prefer: take the least you can, from the plant's own hand.

The second: we make no health claim of any of it. Nourishment is an intention woven through the work — a plant grown to carry the most it can, a flavor restored so a person reaches for the real thing — but it is never a promise sold on a label, never a cure, never a detox, never a halo. Clean living is a thing we do at our own table; it is not a thing we charge for.

What the fanning-out really means is simpler and larger than any claim. It means that the thing our family learned, standing in a greenhouse at dawn asking why a pepper was hot, turned out to be a general grammar of flavor — nine enzymes of which the plant kingdom already shares five, eight receptors the tongue already reads every food through, one number that holds them all on a single page. Almost every plant a person loves to eat is, in principle, a recipe we could learn to read, and read with reverence, and — where a flavor was lost or never reached — gently help the plant to write. These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.



PART V OF VI

At Our Table

a meal read door by door · three things to try at home

Chapter 18 · A Meal, Read Door by Door — *the whole book, served on a plate.*

Everything in this book was leading here, to a table, because a number is only ever in service of a meal and our family has never once forgotten it. In this chapter we are going to do the thing the whole Index was built to make possible: sit down to an ordinary dinner and *read it* — taste each dish and name, door by door, what is actually happening in the mouth, and draw each one as a scorecard you now know how to read. It is the same literacy you have been building all along, brought home to a plate of food. Nothing here is exotic. It is a weeknight dinner, read with open eyes.

We cook, as our family always has, plant-first — not from rule but from where our reverence naturally points, and because the engineered doors of savor and sweetness and kokumi let a plate of vegetables carry the full weight of a meal without anything standing in for anything else. Three bowls will come to the table. A slow stew, a cool salad, a small warm fish. And the whole art of the evening is this: each one is a chord struck on the same eight-stringed instrument, and by the end of the meal you will be able to hear every string.

The grammar of a plate — eight doors, one page

Taste is not one sense. It is eight conversations happening at once, each one a particular molecule settling into a particular receptor, a lock and a key repeated a billion times a second across the wet surface of the tongue. What the Index does is give each conversation a volume knob and a number on the dial. The number is never *how much* of a compound a food holds — it is how *loudly* that compound speaks to its receptor. Loudness, not amount. That distinction is the whole discipline, and it is why one page can hold a tomato, a chili, and a cup of tea on the same axis and mean it.

The dial is anchored to a single measurable thing: the half-maximal concentration, EC_{50} — the amount of a stimulus needed to drive its receptor to half of full response. A receptor does not answer in a straight line; it answers in a curve. If you write the response as a fraction of its maximum, it follows the Hill form,

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response = E_max · [c]ⁿ / (EC₅₀ⁿ + [c]ⁿ)
```

where [c] is the concentration at the receptor, E_max the ceiling, and *n* the Hill coefficient — the cooperativity, how steeply the channel snaps from quiet to loud. The one number that pins the whole curve is EC_{50}, the concentration at the half-way point. A low EC_{50} means the

receptor is screaming at a whisper of stimulus; a high EC_{50} means it needs a shout. Invert it against a fixed reference and scale by a thousand, and loudness becomes a score:

$$IFI(candidate) = 1{,}000 \times EC_{50}(reference) \div EC_{50}(candidate)$$

Each axis is anchored by a stated convention: **the reference compound sets IFI = 1,000 on that axis** — defined that way, as a convention, the same way the Scoville scale is defined by dilution-to-threshold rather than from an independent physiological measurement. Read the formula backward and it hands you a tool you will use all evening. Rearranged,

$$EC_{50}(dish) \div EC_{50}(reference) = 1{,}000 \div IFI$$

so any score on a scorecard converts, in one division, into how concentrated that dish's signal is relative to the reference. A score of 2,000 means the dish speaks at half the reference concentration — twice as loud. A score of 500 means it needs double the concentration to say the same thing — half as loud. Anything above 1,000 is louder than the reference baseline; anything below, quieter. Scorecards normalize each axis to a ceiling of 5,000, so the eight numbers sit on a consistent visual scale — worth noting that each axis is anchored to its own independently defined reference, so the numbers describe the architecture of a dish rather than directly equivalent intensities across axes.

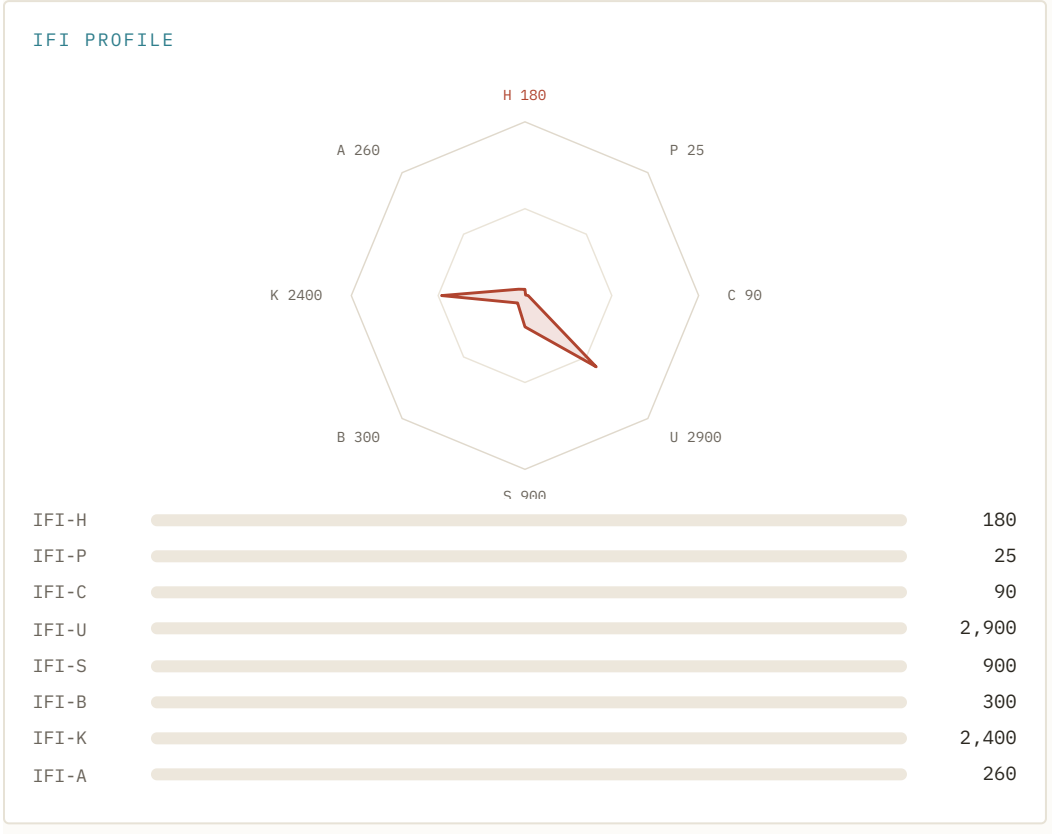
Here are the eight doors, the keys that open them, and the receptor behind each one. Keep this table beside the plate.

DOOR	AXIS	RECEPTOR	OPENED BY	READS IN THE MOUTH AS
Heat	IFI-H	TRPV1	capsaicin · protons · heat >43 °C	warmth rising to fire
Sweetness	IFI-S	TAS1R2·TAS1R3	sugars · high-potency sweeteners	sweet
Umami	IFI-U	mGluR1 · TAS1R1·TAS1R3	free glutamate (+ 5′-ribonucleotides)	round savory depth
Zero-Bitter	IFI-B	TAS2R38	*attenuated* glucosinolates · alkaloids	the bitter that isn't there
Kokumi	IFI-K	CaSR	γ-glutamyl peptides	richness · continuity · mouthfeel
Cool-Burn	IFI-C	TRPM8 (· TRPV1)	menthol · temperatures <26 °C	cool, with no cold
Pungency	IFI-P	TRPA1	isothiocyanates · allicin · cinnamaldehyde	sharp, nose-reaching sting
Astringency	IFI-A	salivary PRPs	tannins · polyphenols	drying, puckering grip

Eight doors, opened in some proportion, by molecules a plant made and a body reads. A dish is a chord — which doors, and how loud. Now let us strike the first one.

The first bowl — a tomato and white-bean stew

Start with the simplest thing on the table: a **slow-cooked tomato and white-bean stew**, built on a restored tomato and finished with roasted garlic. Taste it, close your eyes, and let it resolve into its doors.



The broad savor that rises first and fills the mouth — that is **umami**, and it is the loudest single note on the plate at **U 2,900**. Umami is free L-glutamate opening the savory door: at the tongue it is read chiefly by the TAS1R1·TAS1R3 heterodimer, with the metabotropic mGluR1 giving the taste its slow, swelling character. The receptor's business end is a pair of lobes called the Venus flytrap domain; glutamate slips into the cleft and the two lobes close around it, and that closure is the signal. Run the score through the formula — EC_{50}(dish) ÷ EC_{50}(reference) = 1,000 ÷ 2,900 = **0.34** — and the stew is telling its umami receptor at roughly a third of the reference concentration. Nearly three times as loud as the wild-type baseline, from a bowl of vegetables.

That loudness was grown back on purpose. A supermarket tomato has had most of its free glutamate bred and shipped out of it; the restored tomato carries the savor back in through its own native route — the glutamate-handling enzymes GAD and GDH1 — lifting its umami from a thin **IFI-U 300 to 2,600**, an 8.7-fold gain in how loudly it speaks the savory door. The stew then reads a little higher still, at 2,900, and the extra is not mystery but synergy. White beans and a long reduction release 5′-ribonucleotides — the same family of molecules that makes a broth taste like being cared for. A ribonucleotide does not taste of much alone; it binds near the hinge of that Venus flytrap and makes it close more readily, so the *same* glutamate drives the *same* receptor at a lower concentration. The effect is large — in the savory world it is the classic multiplication, lowering the effective glutamate EC_{50} by roughly an order of magnitude — which is exactly why 2,600 of restored tomato, cooked down with beans, lands at 2,900 on the plate. Loudness compounding loudness.

Underneath the savor is a roundness, a sense that the bowl is *complete* and the flavor stays — the taste with no common name. That is **kokumi** at **K 2,400** (EC_{50} ratio 1,000 ÷ 2,400 = **0.42**, more than twice as loud as baseline), and it is the quietest kind of loud, because kokumi has no flavor of its own to point at. Roasted garlic brings γ-glutamyl peptides — short glutamate-capped chains — and these open a different door entirely: the calcium-sensing receptor, CaSR, sitting on the taste cell as a positive allosteric modulator's target. The peptide does not make a taste; it tunes the cell, so umami arrives fuller, sweetness rounder, the whole mouthful continuous and long. Kokumi is the hand on the shoulder of every other door. You only ever notice it by what it does to the rest.

SOURCE IN THE BOWL	MOLECULE	DOOR · RECEPTOR	ON THIS PLATE	EC_{50}(DISH) ÷ EC_{50}(REF)
Restored tomato	free L-glutamate	Umami · TAS1R1·R3 / mGluR1	part of U 2,900	0.34×
White beans · reduction	5′-ribonucleotides (IMP/GMP)	Umami synergy (closes the flytrap)	—	≈10× drop in glutamate EC_{50}
Roasted garlic	γ-glutamyl peptides	Kokumi · CaSR	K 2,400	0.42×
Long slow cook	Maillard / reducing sugars	Sweetness · TAS1R2·R3	S 900	1.11×

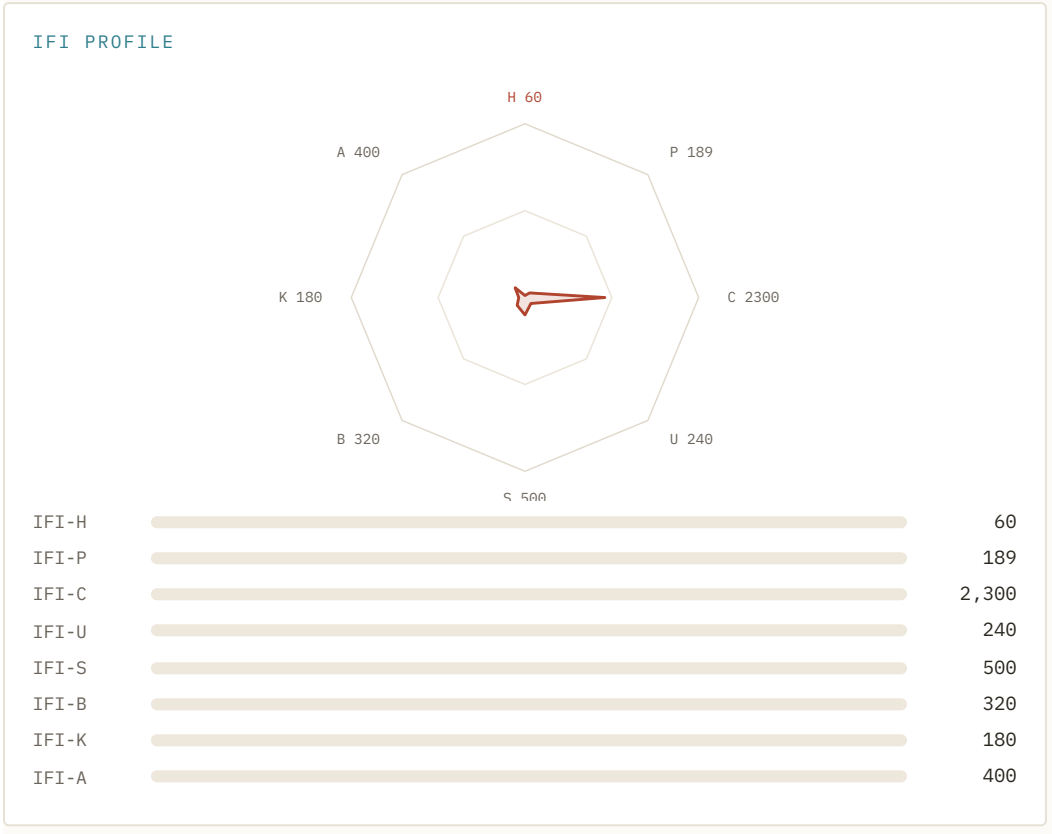


A restored tomato, cut open — the umami grown back in through the native GAD / GDH1 route, from a thin IFI-U 300 to 2,600 before it ever reaches the pot.

Drawn as a scorecard, the stew is a soft broad lobe leaning hard toward savor — a dish that reads as *being fed*. Two strong doors, umami and kokumi, and a gentle sweetness from the long cooking at S 900 (EC_{50} ratio 1.11, just under the reference, a whisper rather than a statement). Everything else stays low and warm. This is what a plate of vegetables can carry when the savory doors are grown loud on purpose: the full weight of a meal, with nothing standing in for anything else.

The second bowl — a herb and cucumber salad, cool mint dressing

Beside the stew, something to wake the plate up: a **bright herb and cucumber salad with a cool mint dressing**. Taste it and the whole shape inverts.



Almost nothing on the savory doors now; instead a clean spike of **cool** at **C 2,300** — EC_{50} ratio 1,000 ÷ 2,300 = **0.43**, the menthol signal speaking at well under half the reference concentration. And here is the quiet miracle the salad performs: the mouth reports a draught of winter that no thermometer would confirm. Menthol opens TRPM8, the receptor that normally answers to genuine cold below about 26 °C. TRPM8 is gated by three things at once — temperature, voltage across the membrane, and ligand — all pulling on one shared gating equilibrium. Cold shifts that equilibrium toward *open*. What menthol does is shift the very same equilibrium, moving the channel's voltage-activation midpoint and dragging its temperature threshold *upward*, from ~26 °C toward the low thirties. The mouth sits near 35–37 °C; nudge the threshold up under it and TRPM8 begins to fire at a temperature it would normally ignore. No heat actually leaves the tissue. The body simply reads *cold* because the door that means cold has been propped open by a molecule. Cool-burn is a reported sensation with no thermal event behind it — a true thing the mouth feels and the mathematics explains.

Over the top of the cool runs a sharp green **pungency** at **P 189** — a thread of mustard and radish, the TRPA1 door seized briefly and brightly. TRPA1 is the sting channel, and it is opened by a mechanism unlike any other door on the plate. Mustard and radish carry glucosinolates locked away from their enzyme myrosinase until the leaf is cut or chewed; the moment the tissue breaks, enzyme meets substrate and releases allyl isothiocyanate, a small, reactive, electrophilic molecule. It does not merely dock in a pocket — it *covalently* reacts with specific cysteine residues on the inner face of TRPA1 (in the human channel, the cluster around Cys621, Cys641, Cys665), forming a chemical bond that pulls the gate open. That covalent character is why mustard's bite blooms a half-second late and lingers: it is a reaction, not a handshake. On the Index we report P 189 as an operational EC_{50} — arrived at against the stated 2.1 µM

AITC convention constant — a fair approximation that quietly hides a subtlety we will return to, because for a molecule that bonds rather than binds, "the concentration for half-response" depends on how long you wait.

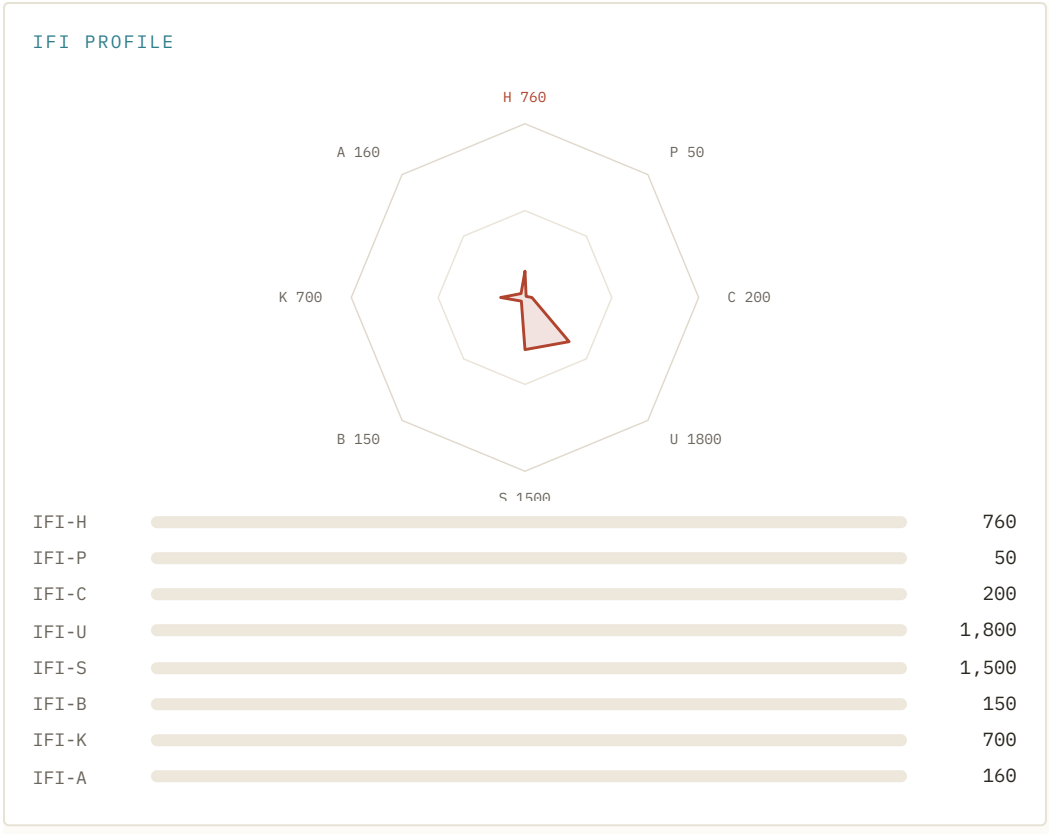


Cucumber — the cool, watery backbone of a salad built to open the TRPM8 door against the warmth of everything beside it.

Where the stew was a slow savory lobe, the salad is a cool sharp star: one tall spike at cool, pungency a quieter thread beneath it, and the savory doors nearly flat (U 240, K 180 — both well under the reference, EC_{50} ratios above 4 and above 5, meaning they would need several times the reference concentration to register, which is to say they barely speak). Read the two bowls side by side and you have a whole lesson in why a good meal *contrasts*. The stew leans in with warmth and depth; the salad opens a window. The engineered cooling plants — a peppermint rebuilt around its five-gene menthol pathway speaks the cool door loudly enough to carry a dressing on its own — exist precisely so the window can be opened cleanly, without the dish going medicinal or thin. A meal breathes by alternating its doors. The leaning-in warmth of one dish wants the window-opening coolness of another beside it, and now you can watch that wanting happen in two numbers: **C 90** in the stew, **C 2,300** in the salad.

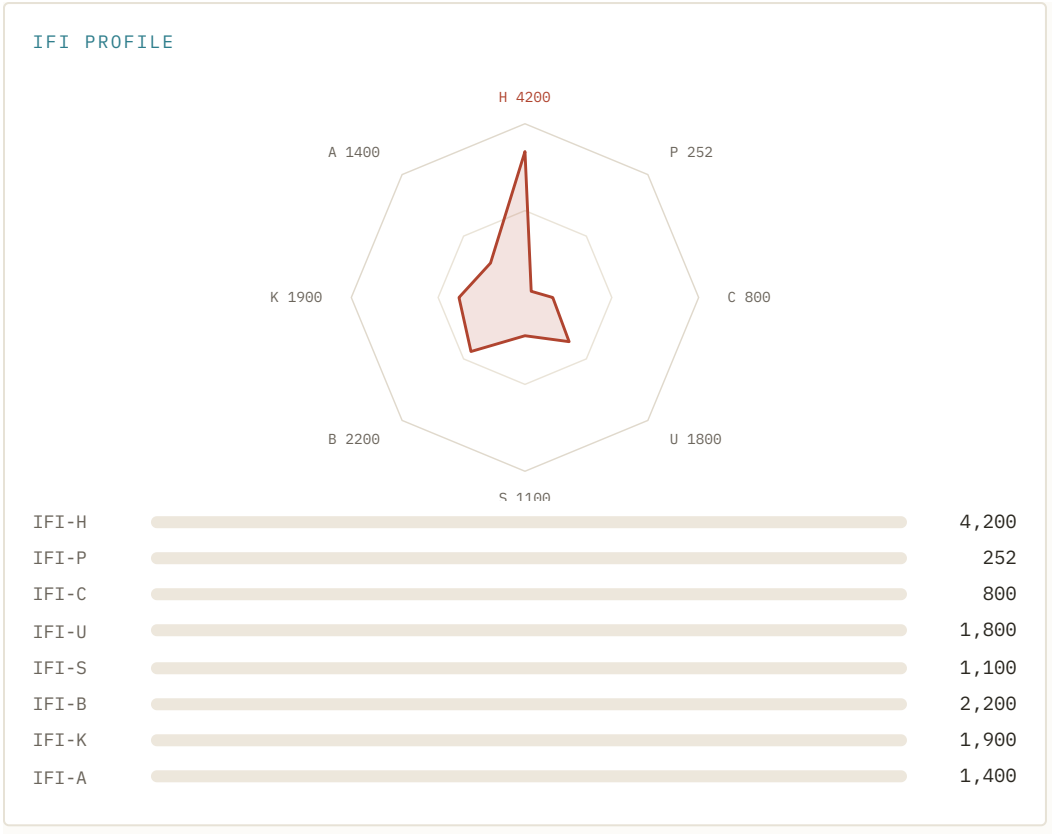
The third bowl — grilled fish with a warm chili-honey glaze

Because our table has always welcomed everyone to it, and because the respect we give a plant is the same respect we give an animal raised and cooked with care, set down beside the two bowls a small dish of **grilled fish with a warm chili-honey glaze** — written here with no apology and no lesser attention. Read it.



A real but *low* warmth — **H 760**, a glow and not a fire. Capsaicin opens TRPV1, a non-selective cation channel on the trigeminal endings of the tongue, the same channel gated by temperatures above 43 °C and by acid. The molecule does not warm the tissue; like menthol at the cold door but in the opposite direction, it lowers TRPV1's thermal threshold, so the body reports a fire that is not there. TRPV1 is exquisitely sensitive — its EC_{50} for capsaicin sits down in the few-hundred-nanomolar range, which is why a trace registers and why heat is the loudest-feeling door for the least material. Run H 760 through the formula and the restraint is deliberate: EC_{50}(glaze) ÷ EC_{50}(reference) = 1,000 ÷ 760 = **1.32**. The glaze's capsaicin signal speaks at about a third *more* than the reference concentration — quieter than baseline by design. This is the fire we chose, diluted far down from its top to exactly the band a plate wants.

To feel how far down, look at the top of the ladder. Capsaicin is built in the pepper's placental tissue when vanillylamine condenses with a branched-chain fatty acid at the Pun1 acyltransferase — the final, labelling step of the pathway. Our flux model places primary control upstream, in the phenylpropanoid steps at 4CL and HCT/CCoAOMT, which govern substrate supply; Pun1 is the synthase that marks the product, and the heat axis is elevated by improving the upstream flow to it. Our most extreme cultivar, Phoenix, carries two AI-designed Pun1 substitutions — S39L and L345G — and our model predicts across all eight doors at once:



At **IFI-H 4,200**, our model predicts approximately **2.95 million SHU**, and the glaze on the fish is the same molecule diluted to a hundredth of that feeling. The heat ladder below shows how Scoville units and Index loudness track each other across the superhot band, and where they part ways.

CULTIVAR · SKU	PREDICTED SHU	IFI-H	EC_{50} ÷ REF	CAPSAICINOID (≈ DRY WT)
Ember · SS-0087	866K	1,570	0.64×	~5.4%
Blaze · SS-0091	1.72M	2,630	0.38×	~10.8%
Firestorm · SS-0094	2.47M	3,490	0.29×	~15.4%
Phoenix · SS-0096	2.95M	4,200	0.24×	~18.4%

These are computational design predictions; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.

Two numbers describe the same fire, and the arithmetic of their relationship is worth doing by hand. Fit a line to those four rungs and IFI-H ≈ 480 + 1,245 × (SHU in millions) — the four points fall on it to within a couple of percent. But notice the intercept: at zero Scoville units the line predicts an IFI-H of 480, which is impossible, because no capsaicin can make no heat. The near-straight stretch across the superhot band is really the top of a saturating curve. Down at low concentration the relationship bends sharply — a large change in Scoville units buys only a small change in receptor loudness — because the channel is approaching the ceiling of the Hill curve from the grammar above, where $n > 1$ makes it climb steeply and then flatten. That compressive bottom of the curve is exactly where "a glow, not a fire" lives, and it is why a glaze can carry honest capsaicin at a gentle number.

The unit conversion makes the extreme tangible. The Scoville scale began as a dilution: how many times you must dilute an extract in sugar-water before the heat disappears. On the bench we convert

through capsaicinoid content at roughly 16 SHU per part-per-million, against pure capsaicin's ~16,000,000 SHU. Divide Phoenix's predicted ~2.95 million SHU by that bench factor and it resolves to ~184,000 ppm — about **18% capsaicinoid by dry weight**, a loading that presses against the physical ceiling of what a fruit's placenta can hold. On a fresh-fruit basis, dry matter near a tenth of fresh weight, it is still a couple of percent by mass, which for a living berry is astonishing. And every rung on that ladder holds its number at a batch-to-batch CV of **≤7%**, against **42%** in the wild type — a point we will cash out when the three bowls are read together.

The rest of the glaze is a round sweetness from the honey at **S 1,500** (EC_{50} ratio 0.67, comfortably louder than baseline) and a savor from the fish itself at **U 1,800**. The honey is worth a moment, because it shows precisely what the Index measures and what it does not. Honey is real caloric sugar — glucose and fructose opening the TAS1R2·TAS1R3 sweet door, the same Venus-flytrap architecture as the umami receptor, but it takes them at *millimolar* concentrations to reach S 1,500. The engineered sweetness axis elsewhere in our work reaches the same loudness with high-potency sweeteners at *micromolar* concentrations — a thousandfold less material for an identical score. Same IFI-S, three orders of magnitude apart in amount. That is the entire reason the Index measures loudness and not quantity: a score of 1,500 means *this is how loud the sweet door is open*, whether the key is a spoon of honey or a trace of a designed molecule. The glaze is where the whole library comes to rest on a single plate — a designed warmth, grown and diluted to a number, meeting the natural savor of the thing it is brushed on, sweetened by a real ingredient we chose with the same care we give every other.

The arithmetic of the whole plate

Three bowls, three shapes — a savory lobe, a cool star, a warm-sweet curve. Set their scorecards in one grid and the evening becomes legible at a glance.

DOOR · RECEPTOR	STEW	SALAD	FISH
H · TRPV1	180	60	760
P · TRPA1	25	189	50
C · TRPM8	90	2,300	200
U · mGluR1 / TAS1R1·R3	2,900	240	1,800
S · TAS1R2·R3	900	500	1,500
B · TAS2R38	300	320	150
K · CaSR	2,400	180	700
A · PRPs	260	400	160

Read across each row and the meal explains its own balance. No single door is loud on all three plates; each dish owns a different corner of the eight. The stew holds umami and kokumi; the salad owns cool and pungency; the fish takes heat and sweetness and a middle measure of savor. A well-built meal is not eight doors all shouting — it is eight doors *distributed*, so that no part of the mouth is asked to do everything and the palate stays awake from first bite to last. You could write that as a design rule: spread the loudness. A

table where every dish peaked on umami would exhaust the savory door and taste, strangely, of less. Contrast is not decoration. It is how a sequence of dishes keeps the receptors fresh enough to keep reporting.

And here is where the ≤7% batch CV stops being a manufacturing footnote and becomes the thing that makes any of this a language at all. Take the stew's loudest door, U 2,900. At a coefficient of variation of 7%, one standard deviation is 0.07 × 2,900 ≈ **±203** — the dish reads 2,900 give or take about two hundred, plate after plate, kitchen after kitchen. At the wild-type variability of 42%, one standard deviation would be 0.42 × 2,900 ≈ **±1,218** — the *same* bowl could read anywhere from roughly 1,700 to 4,100, which is to say the number would tell you nothing. A measurement is only a word if it means the same thing twice. Seven percent is what turns a score into something you can write down, hand across the table, and trust a stranger to reproduce. Numbers, held that steady, are a form of respect — for the cook who follows the recipe, and for the reader who was promised that the page meant what it said.

Where the reading bends — the honest limits

A scorecard is true, but it is true the way a photograph is true: it fixes one instant of a living thing. Honesty about where the reading bends is part of reading it well.

The scores are a *first-bite* account. TRPV1 desensitizes — capsaicin lets calcium into the nerve ending, and that calcium, over seconds, quiets the very channel it opened. The second forkful of the glaze reads lower than the first; by the fourth, the fire has banked itself. The salad's cool door does the opposite favor, resetting the warmth between bites, which is part of why the window-opening dish belongs beside the leaning-in one. So the meal's reading drifts as you eat it, and the Index reports the opening note, not the whole decay.

The plate itself moves the numbers. Capsaicin is oily, and the fish's own fats and the glaze's honey partly sequester it, slowing its arrival and blunting its peak against what the same capsaicin would do in water — which is the real mechanism behind the old kitchen truth that dairy, rich in casein, strips the burn. The intrinsic IFI-H is a property of the stimulus; the *delivered* dose is a property of the matrix it rides in. A cool dish read warm loses cool, too: TRPM8's threshold sits just under mouth temperature, so a salad served at room warmth reports less winter than the same dressing served chilled, because the real temperature and the menthol are pulling on the one shared gate from opposite sides.

The doors are not perfectly separate. The Index lists Cool-Burn against TRPM8 *and* TRPV1 for a reason: menthol brushes the heat channel faintly, capsaicin can sensitize the cold one, and at high enough drive the two sensations bleed. Heat and cool are near-orthogonal on the scorecard but never exactly so, and a mála tingle — numbing heat — lives in precisely that bleed.

And the mouth doing the reading is not one mouth. The bitter receptor behind the Zero-Bitter door, TAS2R38, comes in common variants — the PAV and AVI haplotypes — that make one person a

vivid taster of certain bitters and another nearly blind to them. We anchor IFI-B to a reference receptor, so the *stimulus's* loudness is fixed; what each diner lives depends partly on the alleles they carry. The Index measures how loudly a molecule speaks at a standard door, not how loudly every guest happens to hear it. That is a limit we state plainly rather than paper over, because the alternative — pretending one number is every tongue — would be the kind of dishonesty the whole project was built against.

Even the EC_{50} has its fine print. For the covalent pungency of mustard and radish, "the concentration for half-response" depends on exposure time, since allyl isothiocyanate *bonds* to TRPA1 rather than visiting it; the P 189 we report is a fair operational value at a standard reading, and a longer dwell would read higher. The number is a faithful summary, not a law of nature. Knowing exactly where it is a summary is what it means to be literate in it.

The child at the table

Three bowls, three shapes, and a child at the table who, a hundred pages ago, only knew that one of them was *spicy*. Now the whole meal can be read. Not reduced — *read*. The wonder entirely intact, and a language underneath it now for sharing the wonder, pointing at it, agreeing on it, handing it down. A savory lobe you can name, door by door, molecule by molecule: free glutamate closing a receptor's two lobes, a garlic peptide tuning the cell, a menthol propping winter open with no cold behind it, a capsaicin we diluted by hand to the gentlest rung of a ladder whose top presses against the physical limit of a fruit. All of it measurable, all of it held to within a few percent, all of it still delicious.

This is all the Index was ever for. Not to replace the pleasure of the stew or the surprise of the cool salad or the warmth of the glaze, but to let a family say to each other, exactly and truly, *here is what is happening, and here is why, and here is how much.* A meal is eight doors, opened in some proportion, by molecules a plant made and a body reads. You have been eating the answer to the child's question your whole life. Now you can see it on the plate — and tomorrow, when the question comes again across the same table, there is a whole book in the room that knows how to answer it.



The greenhouse walk at first light — where the plants that become a plate are grown. A meal read door by door is the whole book, served.

Chapter 19 · Three Things to Try at the Table — *the science you can taste tonight.*

The best way to believe a strange true thing is to make it happen in your own mouth. So this is the most hands-on chapter in the book: three small experiments a family can run at the dinner table tonight, with nothing but things a kitchen already holds, each one a direct demonstration of a door the tongue keeps and a molecule that has found the key. They are safe, they are gentle, and every one of them ends in the small delight of feeling a piece of the science fire inside your own head. We have given each a scorecard too — the compact eight-line block that recurs all through these pages — so you can do the thing a scientist does and a child rarely gets to: *predict the shape of what you are about to feel, and then check the prediction against your own tongue.* A feeling, it turns out, has a shape, and a cause, and a number. By the end of one dinner you will have proven all three with a carton of milk, a pinch of sweetener, and a sprig of mint.

A word of ordinary care first, because we mean every page of this for everyone at the table. Keep it gentle. Use mild warmth and never the fierce end of the heat ladder for a game; leave the very young out of the heat entirely — these experiments want a friendly glow, not a dare. There is no health claim hidden anywhere in this chapter and no endurance to be proven. These are demonstrations of how a mouth works, run for the joy of understanding it, and that joy is the whole inheritance our family is trying to hand on.

A feeling has a shape — how to read the card before you taste it

Each scorecard spoke carries a single number, and that number is not *how much* of a compound a food holds. It is *how loudly* that compound speaks to its door. The distinction is the engine of the whole Index, and it is worth deriving slowly, because once you have it the three experiments become predictions you can write down in advance.

A receptor does not answer in proportion to how much molecule arrives. It answers along an S-shaped **dose–response** curve: nothing, then a sudden climb, then a plateau where the door is already as open as it will ever get and more molecule changes almost nothing. Written out, the fraction of full response at concentration *[L]* is

```
response = [L]ⁿ ÷ ( EC₅₀ⁿ + [L]ⁿ )
```

where *n* is the steepness of the climb and **EC_{50}** is the one concentration that matters most: the dose at which the door stands exactly *half* open. A low EC_{50} means the door swings halfway on a whisper of compound — the molecule is *loud.* A high EC_{50} means it

takes a flood to reach the same half-open — the molecule is *quiet.* The Index simply turns that reading around so louder reads as a bigger number, and pins it to a shared reference:

```
IFI(candidate) = 1,000 × EC₅₀(reference) ÷ EC₅₀(candidate)
```

The reference is anchored so that its own half-activation scores exactly **1,000;** everything else is read as a ratio against it. Each axis's reference constant is a stated convention — the IFI equivalent of Scoville's own dilution-to-threshold definition — not a literature measurement. So a score and a concentration are two ways of saying one thing. Hold each axis's reference at an EC_{50} of 1.00 in its own natural unit, for concreteness, and any scorecard number inverts straight back into the dose it would take to half-open that door: EC_{50}(candidate) = 1,000 ÷ IFI. Here are the four foods you are about to eat, read out before a bite is taken.

STIMULUS AT THE TABLE	AXIS · SCORE	EC_{50} = 1,000 ÷ IFI	LOUDNESS VS REFERENCE
Milk-test dish	H · 850	1.18	0.85× (gentle)
Sweet-swap cup	S · 2,400	0.42	2.40×
Mirror · the cool half	C · 1,900	0.53	1.90×
Phoenix · SS-0096 *(for scale, predicted)*	H · 4,200	0.24	4.20×

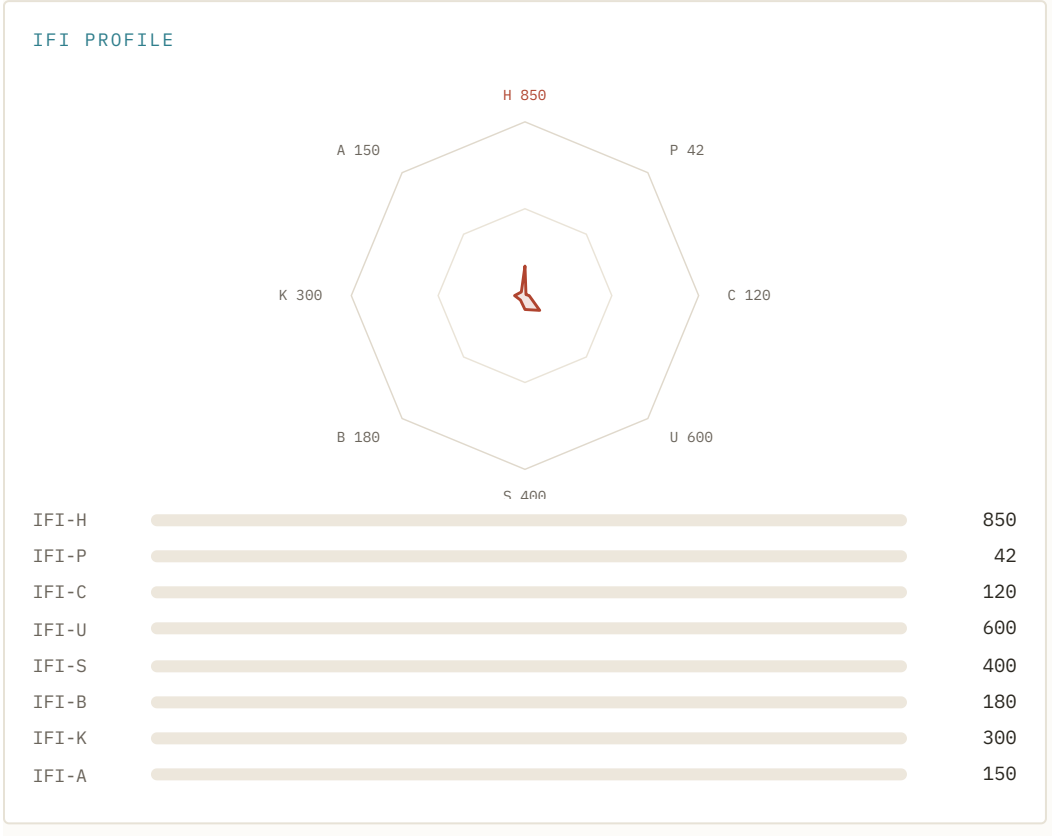
Two quick habits make a card legible at a glance. First, its **reach:** we normalize every spoke against a ceiling of 5,000, so a score's distance from silent-center to loud-rim is simply IFI ÷ 5,000 — the milk-test dish reaches 17 % of the way out on heat, the sweet cup 48 % on sweetness. Second, its **peakedness:** average the eight scores, then divide the tallest spoke by that average, and you get a single number for how far one door towers over the rest. A peakedness near 2 is a rounded flavor; a peakedness of 7 is a thorn — one blade of signal and near-silence all around it. You will be able to feel each of these shapes, and we will tell you what to expect before you taste.

One honest caveat belongs right at the start, and it is the reason to run each test with the whole family rather than alone. Your tongue is a gorgeous instrument and a *noisy* one. We hold our cultivars to a batch-to-batch coefficient of variation — the spread divided by the average — of **≤ 7 %,** against the roughly **42 %** that unselected wild material swings across seasons; that discipline is what lets a reading mean anything. A single human tasting has nothing like 7 % precision. But noise averages down: the uncertainty of a mean falls as the square root of the number of tasters, so four people at the table cut the scatter of a verdict in half ($\sqrt{4} = 2$), and the shape you agree on together is twice as trustworthy as any one mouth's. This is measurement as a family act, which is the only kind our family has ever done.

One — the milk and water test *(the oily key).*

Serve something modestly spicy, nothing heroic — a dish with a real but friendly warmth, a glow and not a fire. When the heat arrives, have one person reach for cold water and gulp it, and another take a mouthful of whole milk or a spoon of full-fat yogurt and hold it a moment before swallowing. Compare out loud. The water-drinker

will tell you the fire came roaring back, maybe spread a little wider; the milk-drinker will tell you it genuinely eased. Here is the shape to expect — a low warm glow you are about to prove you can switch off with the right tool, a gentle thorn leaning toward heat with a little savor and sweetness for company:



Sum those eight and you get 2,642; the mean door reads 330, and the tallest spoke — heat at 850 — stands 2.6 times the average. A peakedness of 2.6 is a soft thorn, not a spike: heat leads, but the dish has body elsewhere, which is why it reads as a glow you can enjoy rather than a fire you must survive.

What the heat is. Capsaicin binds **TRPV1,** a non-selective cation channel on the trigeminal nerve endings woven through the tongue. That channel already opens to genuine heat above about **43 °C** and to acid; capsaicin slips into a pocket on its inner face and *lowers that thermal threshold,* dropping the temperature at which the door opens down below the warmth already sitting in your mouth. The nerve then fires *fire* into tissue that is merely warm. Nothing is burning. The body is reporting a temperature it is not at, which is the whole uncanny beauty of the thing — a true signal about a false fact.

Why milk works and water fails, in one curve. Set the gentle dish so it puts capsaicin at the receptor right around its EC_{50} — the half-open point, a clear but friendly warmth. TRPV1 is a cooperative channel, climbing with a Hill slope near $n = 2$, and that steepness is the key to the rescue. Watch what a rinse does to the response:

- **Water** can carry almost no capsaicin away, so the effective dose stays near EC_{50} and the response stays near one-half — the fire holds, and by spreading the oily film across more tissue the gulp can even make it feel *wider.*
- **Milk** pulls the effective dose down hard. Drop it to half of EC_{50} and the response falls to $(0.5)^2 \div (1 + 0.5^2)$ = **0.20;** drop it to a third and it falls to $(0.33)^2 \div (1 + 0.33^2) \approx$ **0.10.** A warmth felt at one-half collapses to a fifth, then a tenth. The relief is not gentle because

the molecule left gently; it is dramatic because you were standing on the steep middle of the curve, where a small change in what reaches the receptor makes a large change in what you feel.

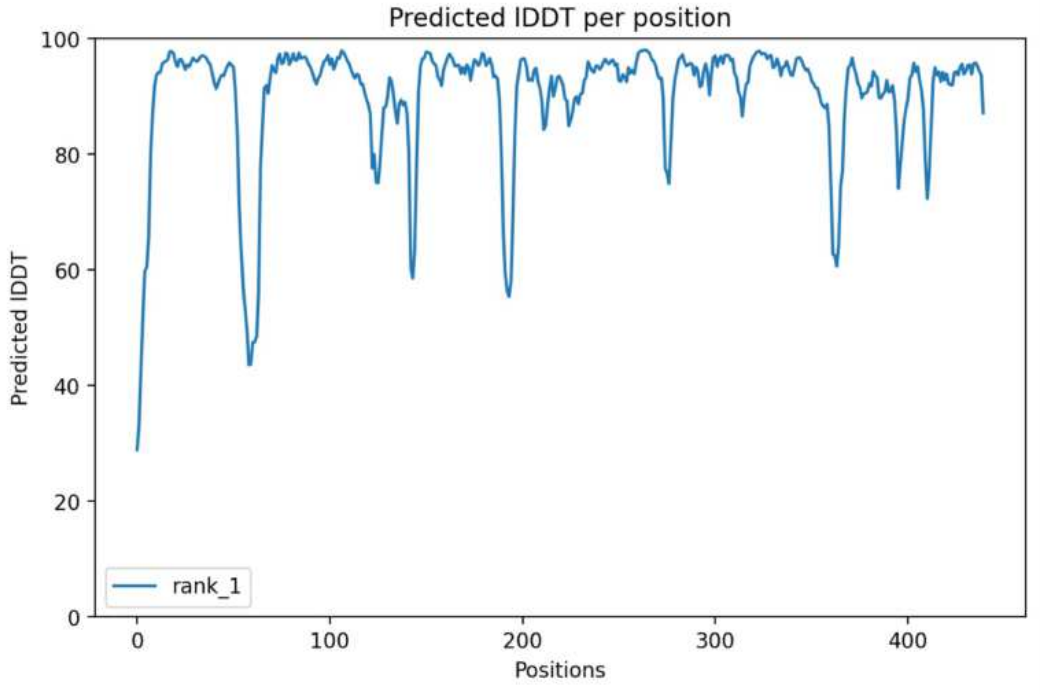
The chemistry behind that drop. Capsaicin is an oil with a partition coefficient — the preference of a molecule for fat over water — of **logP ≈ 3.** That innocent "3" is an exponent: the molecule favors a fatty phase over a watery one by about 10^3, roughly **1,100 to 1.** Water's grip is hopeless from the start; capsaicin dissolves in water only to a few parts per million, on the order of ten milligrams in a whole liter, so a two-second swish of two hundred millilitres could in principle lift a couple of milligrams and in practice lifts far less. Whole milk is built for exactly the opposite. Two hundred millilitres carries about **7 g of milkfat** — in which capsaicin is freely miscible, enough fat to dissolve several hundred milligrams, a hundred times any dose a gentle dish delivered — and about **5 g of casein,** whose micelles physically wrap the molecule and ferry it off the receptor. At equilibrium the thousand-to-one partition does the rest: the capsaicin goes where the fat and the protein are, which is to say *into the milk and off your tongue.*



Backlit in the greenhouse at golden hour, a pod hangs heavy with the oil that is the whole point. Every milligram of the fire you will quench at the table was forged inside a living plant, in a single enzymatic step.

Where the oil is made. That logP-3 molecule is not found; it is *built,* in one condensation, when the capsaicin-synthase enzyme at the **Pun1** locus joins vanillylamine to a branched-chain fatty acyl group. Our flux model predicts that rate control sits upstream in the phenylpropanoid pathway — at 4CL and HCT/CCoAOMT — not at this terminal Pun1/AT3 step. Pun1 is the final capsaicin synthase; it seals the molecule into its finished form, but the carbon committed to capsaicin is metered out earlier in the chain. What we designed for is a catalyst with better substrate handling and thermal stability: our family found two single-residue edits to it that generations of breeders — selecting fruit and hoping the gene quietly followed — never once stumbled onto, scored *in silico* before a single seed was sown and then written in with CRISPR.

EDIT	WHAT IT DOES	ΔΔG (KCAL/MOL)
S39L	tightens substrate binding at the N-terminus	−2.1
L345G	relieves strain in the active-site cleft	−1.8
C175S *(structural annotation — not in shipped construct)*	prevents a disulfide misfold	−0.9



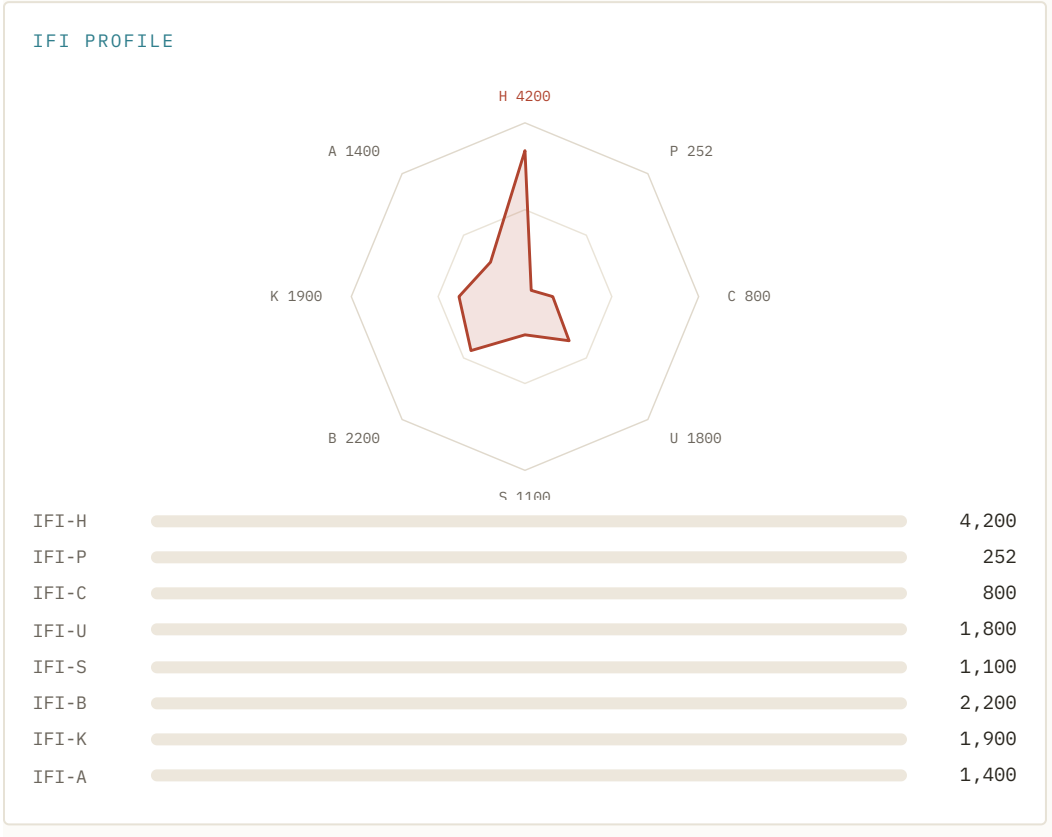
The Pun1/AT3 enzyme model, colored by pLDDT confidence — the binding domain and the active-site cleft, where both shipped edits sit, resolve bright and certain. This is the machine that writes the loudness of the heat door.

Each negative ΔΔG is a step toward a more stable, more willing catalyst; written in together, our model predicts peak output at approximately **2.95 million SHU** while our batch CV design specification holds to ≤ 7 %. And here the gentle dish on your plate finds its scale. The Scoville scale measures *amount* — how far a sample must be diluted before the burn disappears — and amount and loudness do not rise together in a straight line, because the door saturates. Pure capsaicin is defined as **16,000,000 SHU,** so our predicted 2.95 million SHU for Phoenix is about **18 %** of the loudest heat chemistry knows, a fruit designed to speak at nearly a fifth of pure fire. Lay the design ladder beside the gentle dish and the compression shows:

FOOD · SKU	PREDICTED SHU	IFI-H	LOUDNESS VS REF	REACH TO RIM
Milk-test dish	gentle	850	0.85×	17 %
Ember · SS-0087	866,000	1,570	1.57×	31 %
Blaze · SS-0091	1,720,000	2,630	2.63×	53 %
Firestorm · SS-0094	2,470,000	3,490	3.49×	70 %
Phoenix · SS-0096	2,937,948	4,200	4.20×	84 %

Read down the predicted SHU and the IFI-H columns together and the Index is quietly folding an enormous physical range into a human one, the way decibels fold sound. Across the design ladder a **3.4×** rise in predicted Scoville units (866,000 → 2,937,948) produced only a **2.7×** rise in loudness (1,570 → 4,200), which means IFI-H climbs as roughly the **0.81 power** of SHU — an exponent below one, the signature of compression. Put plainly: to *double* the fire you must

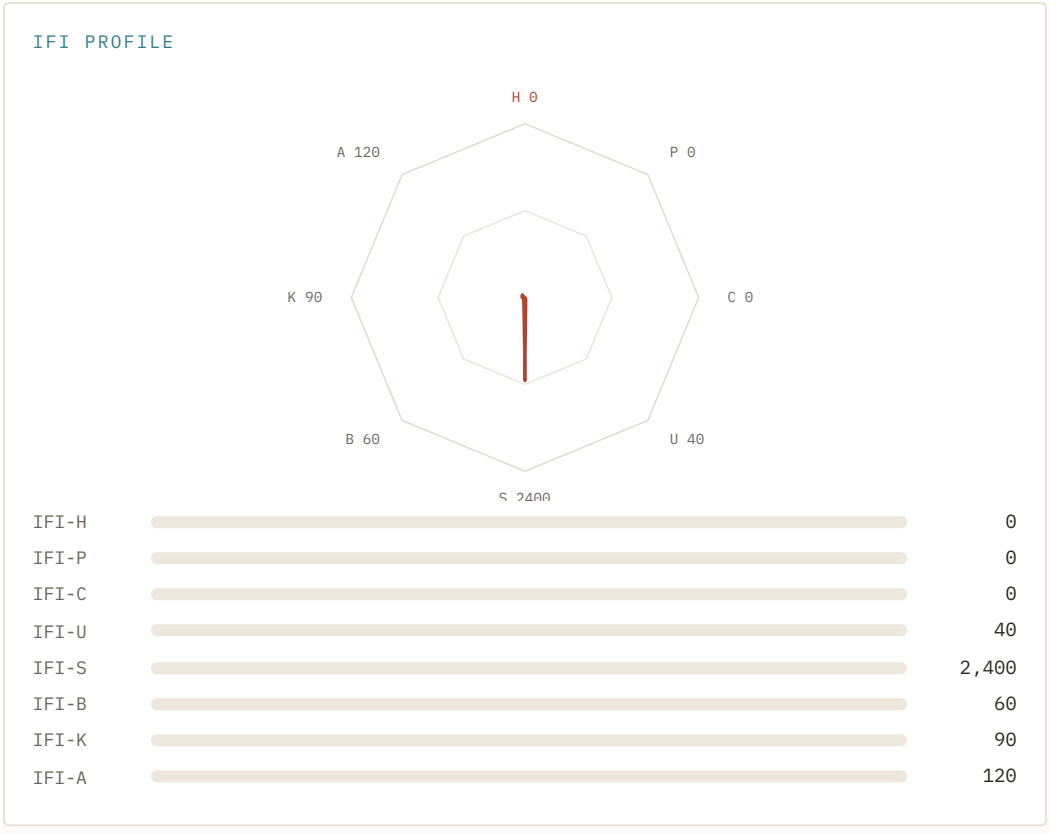
multiply the capsaicin by about 2.4, because the second half of every doubling falls on the flattening top of the dose–response curve, where the receptor has mostly stopped listening. The gentle dish sits far down where the curve is steepest and most responsive — which is precisely why a mouthful of milk can switch it off so cleanly, and why we never use the fierce end of the ladder for a game.



One honest limit, because precision owes it. The predicted SHU figures above are for the *pod,* and the 850 on your scorecard is the *dish's* — a pod's heat dispersed and diluted through a whole plate of food. The Index scores a flavor as it is eaten, not as it grows, so you cannot read a cultivar's predicted Scoville number straight onto a dinner; the dish is always the gentler thing. And a few failure modes to expect: **skim** milk, stripped of fat, rescues weakly and leans entirely on its casein; **plant milks** help partly — their oils and lecithin emulsifiers do real work — but lacking casein they are a step behind whole dairy; beer, soda, and more water all disappoint, because the fire was never water-soluble to begin with. Reach for fat and protein, hold it a moment, and let the thousand-to-one partition do what water cannot.

Two — the sweet-swap *(the welcome door).*

Pour two small glasses of the same plain unsweetened drink — a cup of tea, cooled, is perfect. Sweeten one with ordinary sugar and the other with a few drops or a pinch of a plant-based sweetener, stevia or monk fruit, to taste. Then taste them blind, back and forth, and try to feel the difference in the *welcome* itself — the moment the sweet door opens. For most families the astonishment is how *alike* the two openings feel. Predict the shape first: a clean spike on the sweet spoke and near-silence everywhere else.



Those eight sum to 2,710; the mean door is 339; and sweetness at 2,400 stands **7.1 times** the average. That is a true thorn — the highest peakedness of the three experiments — and it tells you in advance that this will not feel like a complicated flavor. It will feel like one pure thing said loudly, which is exactly what a sweetener is.

What the welcome is. Sweetness is the **TAS1R2·TAS1R3** heterodimer, a clamshell protein whose great hinged mouth — a Venus-flytrap domain — closes on a sugar and sends an honest *yes* inward through a G-protein cascade. The quiet miracle of the sweet door is that the shell does not check credentials. Sucrose closes it; so, far more tightly, do the steviol glycosides of stevia and the mogrosides of monk fruit. The receptor cannot tell you what molecule shut its mouth, only that the mouth is shut — and a shut flytrap means the same word, *sweet,* whatever the key.

The math of "to taste." When you sweetened each cup until it tasted right, you tuned both to the same loudness — the same IFI-S — by a method a laboratory would recognize as a *null:* adjust the unknown until it is indistinguishable from the standard. What that identical loudness hides is a staggering difference in *amount,* and that difference is the whole reason our family could grow the welcome apart from the sugar it was bundled with.

SWEETENER	RELATIVE SWEETNESS (BY WEIGHT)	MASS FOR EQUAL SWEETNESS IN 240 ML	CONCENTRATION	MOLECULES VS SUCROSE
Sucrose	1×	8.0 g (≈ 2 tsp)	97 mM	1×
Rebaudioside A *(stevia)*	≈ 250×	32 mg	0.14 mM	≈ 1 ⁄ 700
Mogroside V *(monk fruit)*	≈ 200×	40 mg	0.13 mM	≈ 1 ⁄ 750

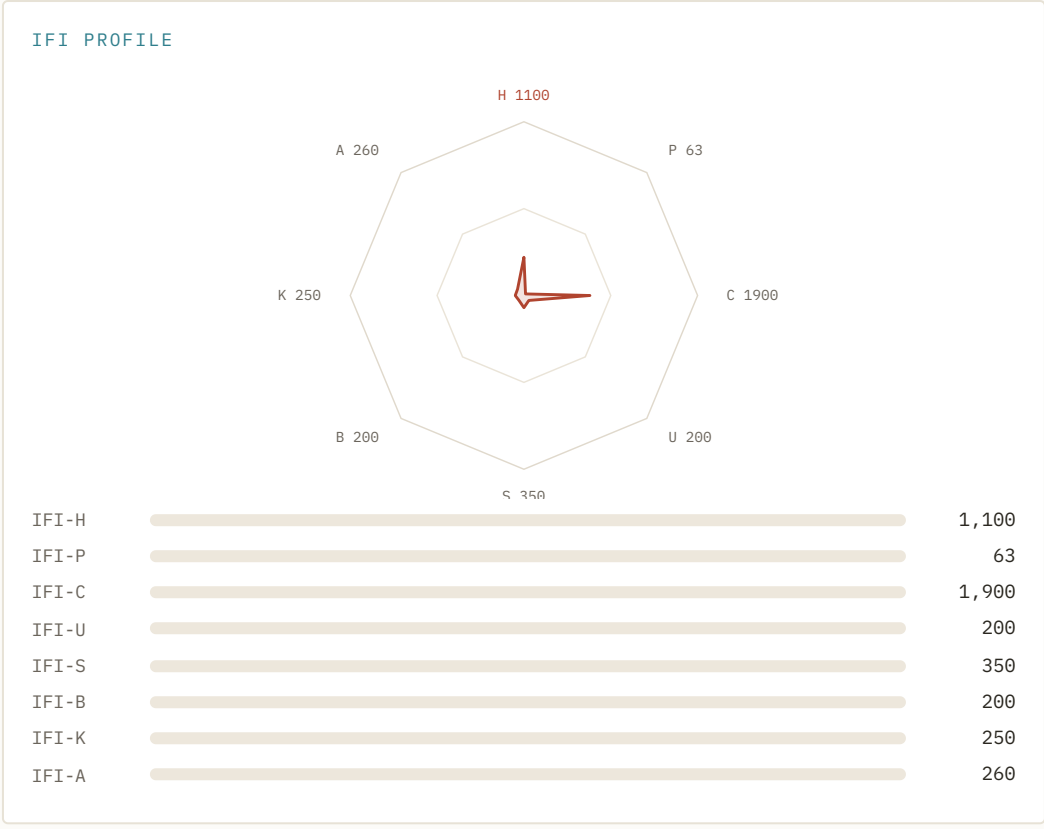
Work the top row: 8 g of sucrose is 8 ÷ 342 = 0.023 mol, which in 0.24 L is about 97 mM. To match that welcome, rebaudioside A needs roughly 32 mg — and 32 mg ÷ 967 g mol^{-1} in the same cup is only **0.14 mM.** The two drinks are tuned to one loudness while differing in dissolved molecules by a factor near **700.** The receptor reports them as equal because loudness is a ratio of concentrations against the door's own EC_{50}, not a count of molecules in the glass; a

key that fits tightly needs far fewer copies to hold the same fraction of flytraps shut. Stevia covers **910** product designs in our library and monk fruit **80,** and the entire point of that work lives in this table: the same honest *yes,* at a fraction of the mass and none of the sugar.

What to expect at the edges. The match is close but rarely perfect, and feeling *where* it breaks is half the fun. Some glycosides carry a faint bitter or licorice tail, because a molecule shaped to shut the sweet flytrap can, in passing, nick one of the two-dozen bitter TAS2R receptors — a small second door opening a beat behind the first. The onset and the linger differ too: the high-potency keys often arrive a touch slower and leave a touch later than sugar's quick clean bloom. Taste them warm and taste them cold; temperature shifts both the welcome and its tail. None of this is failure. It is the receptor-level fingerprint of a different key in the same lock, and your tongue can read it.

Three — the mirror *(heat and cool together).*

This is the loveliest of the three, and it makes the deepest fact in the book happen in one mouth at one time. Take a small bite with a gentle chili warmth in it and, right behind it, something clearly cool and minty — a mint leaf, a cooling herb. Pay close attention and you will feel the two sensations arrive *separately and at once:* a fire toward the front that does not cancel, and a clean draught of cold moving through at the same time. Predict the shape and the radar reaches two ways:



Eight scores summing to 4,323, a mean of 540, and a tallest spoke — cool at 1,900 — standing 3.5 times the average, with heat close behind at 1,100. Two prongs, not one: this is the only experiment whose figure throws toward opposite sides of the wheel, a thorn of heat and a spike of cool on the same card. You are about to feel that two-pronged shape as two things in one breath.

Two doors, opposite tricks. Capsaicin, we have seen, drops TRPV1's opening temperature from about 43 °C down *below* the warmth of your mouth, so the heat door stands open in a mouth that is only

warm. Menthol does the mirror trick on the cold sensor, **TRPM8.** That channel normally opens when things fall *below* about 26 °C; menthol lifts its opening temperature *up,* past the temperature of your own mouth, so the cold door now stands open in a warm mouth and reports a chill the thermometer would flatly deny.

DOOR	RECEPTOR	NATIVE THRESHOLD	WHAT THE KITCHEN DOES	RESULT
Heat	TRPV1	opens above ≈ 43 °C	capsaicin (an oil, logP ≈ 3) lowers it below mouth temperature	fire that is not hot
Cool	TRPM8	opens below ≈ 26 °C	menthol raises it past mouth temperature	cold that is not cold

Why they do not cancel. A warm mouth with both molecules in it is not a lukewarm compromise, because heat and cold here are not two ends of one measurement — they are two *separate channels,* on different nerve fibers, carrying their signals up different wires to the brain, which reads both numbers at once. This is labeled-line coding: the fire line says *fire* and the cold line says *cold,* and neither knows the other is firing. So the fire sits toward the front and the cold draught moves through it, simultaneous and un-blended, fire and frost in the same breath. Neither one is true — no tissue is burning, nothing has gone cold — and both of them are entirely real, because what you feel is never the temperature of your mouth. It is the *state of the channels,* and tonight you have set two channels lying in opposite directions at the same instant. That is the deepest thing the table can teach: perception is a readout, not a measurement, and a readout can be played.

What to expect at the edges. Timing matters. Linger too long on the heat and TRPV1 begins to *desensitize* — calcium flowing in through the open channel quiets it, a tachyphylaxis that is why a second bite of the same warmth often lands softer than the first. Menthol runs the other way, with a slow offset that outlasts the chili, so the cold frequently has the last word. Try the order both ways — cool first, then heat; heat first, then cool — and feel how the mirror tilts. The two doors are genuinely independent, and the small asymmetries in how they switch on and off are the proof.

What the table teaches — the number is a way of caring

Three experiments, three doors felt directly, and a whole afternoon of the best kind of family science — the kind where the wonder is not in a book or on a screen but in your own head, happening, undeniable. Look back at what each one actually was. You wrote down a prediction — a scorecard, a shape, a peakedness, a reach — then you put the prediction in your mouth and checked it, and where several of you tasted together you averaged a noisy instrument down toward something you could trust. That is the entire method of this book, performed with milk and sugar and mint: a flavor has a loudness, a loudness is an EC_{50} read against a reference, and a shape you can draw is a shape you can test, and share, and grow toward.



The dew-bright greenhouse at dawn. Everything you felt tonight — the oily fire lifted off by fat, the welcome grown apart from its sugar, the mirror of hot and cold — begins here, in a living plant grown to carry the fullest flavor, and the fullest nourishment, it can hold.

Keep the honest limits in view, because they are part of the respect. The cultivars and constructs described in this book are computational designs; Scoville Splice's plants have not been experimentally validated in a laboratory. These are demonstrations, not assays: a kitchen tongue is a wonderful instrument and a far cruder one than a controlled chamber, and the Index reads each door one lock at a time while the brain, afterward, mixes them into the single sensation you actually live in — which is why we match shapes carefully and then still do the last, unquantifiable thing, and taste it together. There is no cure here and no detox, no endurance to prove and no health claim to make; there is only the astonishing instrument you eat with, and the joy of understanding it a little better than you did at breakfast. A feeling has a shape, and a cause, and a number — and you can prove every piece of it tonight, at your own table, with a carton of milk and a sprig of mint and a little attention paid to the quiet machinery of your own delight. That attention, handed from one generation to the next, is the whole inheritance we are trying to give.



PART VI OF VI

The Answer, Returned To

the child's question, answered whole

Chapter 20 · Why Is It Spicy? — *the answer, whole at last.*

We began at a table, with a child setting down a fork, breathing out hard, reaching for the water that would not help, asking the oldest kitchen question there is. We have been a long way since — through eight doors and a mirror, a pharmacist's patient tongue and a protein language model, an assembly line written in four letters inside a seed, two changed letters, forty-two plants, a restored tomato, a plate read door by door. Now we can come back to the child and give the answer whole, in plain words, the way you could say it across your own table tonight. Here is why it is spicy.

It is spicy because the pepper makes a molecule called capsaicin, shaped — down in the pale ribs that cradle its seeds, by an assembly line of enzymes it writes the recipe for in its own DNA — exactly like the key to a door the body built for a completely different purpose. That door is TRPV1, and its real job is to feel genuine heat and warn you before a burn can hurt you. Capsaicin fits it anyway, and instead of warming anything it quietly lowers the temperature at which the door springs open, down to the warmth your mouth already is — so the door opens, and the nerve sends the word *hot* to the brain, and the brain believes it completely, because the signal is identical to the one a real fire would send. Nothing is burning. No cell is harmed. The pepper is telling you a true thing — *I am here, I am strong, I am a plant that learned to defend itself* — in the most extravagant language it has, and your own body, doing its faithful watchful job perfectly, is doing all the shouting. That is the whole answer. The fire is real and the burning is not, and the difference between those two is the most beautiful thing a mouth can teach you.

That is the answer said the way you could say it tonight, over the stew, to a child wiping her eyes. But there is a second way our family learned to say it, slowly and across many seasons — in numbers, enzyme by enzyme, because a number is a form of respect and because you cannot design what you cannot measure. The rest of this chapter is the same answer told that second way: the little door exactly, the key exactly, and how we learned to ask a fire for by a single figure and have it arrive. None of the wonder is lost in the arithmetic. If anything the arithmetic is where the wonder gets specific.

The little door, exactly — what TRPV1 is and how it is fooled

TRPV1 is a protein — four identical protein chains, in fact, gathered into a ring around a central pore like four hands cupping the same drop of water. It sits in the membrane of the trigeminal nerve endings that lace the surface of your tongue and lips, and it is a channel: closed, it holds the pore shut; open, it lets a rush of positive ions — mostly calcium and sodium — pour through, and that ionic rush is the nerve's way of striking a match. One open channel is a spark. Enough of them firing together is the unmistakable word *hot* racing up the nerve to the brain.

The channel has a true job, and it does it beautifully. It is a thermometer with a threshold. Below about 43 °C it stays shut; above 43 °C — the temperature at which real heat begins to threaten tissue — it opens, and you flinch from the pan before the burn can land. It answers to acid as well: drop the pH, flood it with protons, and it opens at a lower temperature, which is why a squeeze of lime over chili makes the heat climb. Heat and acid and capsaicin all pull the same lever, because the channel is built to be pulled by any genuine sign of danger.

Here is the exact trick, and it is a thermodynamic one. Whether the channel sits open or shut is a balance of free energy, $\Delta G = \Delta H - T\Delta S$ — an enthalpy term that favors the closed, ordered state and an entropy term, multiplied by temperature, that favors the open one. Raise the temperature T and the open state wins; that crossover is the 43 °C threshold. Capsaicin does not add heat to this equation. It slips into a lipophilic pocket cradled between the subunits — the vanilloid pocket — and binding there pays down part of the enthalpic cost of opening, so the crossover temperature slides downward, from 43 °C to below the 35 °C your mouth already is. The door now finds itself, at rest, already past its own threshold. It opens in the cool of your mouth as though your mouth were a fire. The thermometer has not been broken. It has been re-zeroed, and it is reporting, with perfect honesty, a temperature it has been quietly told to expect.

And the channel is an exquisite instrument to fool, because it is exquisitely sensitive. Capsaicin half-activates TRPV1 at well under a micromolar — on the order of a part per million in water. A detector that answers to a few molecules in a million is the reason a milligram of capsaicinoid, spread across a whole fruit, can own an entire mouthful. The response is cooperative, too: with four binding sites on the four subunits, the channel opens with a steep, switch-like sigmoid rather than a gentle ramp — a Hill coefficient near 2 — so the burn has a sudden onset, a threshold crossed all at once rather than crept up on.

This is also, exactly, why the child should reach for the milk and not the water. Capsaicin is oily — its oil–water partition coefficient, logP, sits around 3, meaning it would rather be in fat than in water by a factor of a thousand. Water sluices across the tongue and leaves the molecule nestled in its pocket, untouched; the fire goes on. Milk arrives with casein proteins and butterfat, and the capsaicin, offered somewhere it would far rather be, lets go of the receptor and dissolves away. The folk remedy is molecular thermodynamics, known at the table for centuries before anyone could name the number.

The key the plant grows — capsaicin, written enzyme by enzyme

The plant does not keep capsaicin in a jar. It writes it, fresh, in the pale placental ribs that hold the seeds, along two converging production lines that meet at a single joining step — and the whole

recipe is spelled out in the plant's own DNA, which is the only place our family has ever asked it to change.

One small correction, because a child's hand always reaches for the wrong part: the seeds are not the hot ones. Capsaicin is made and held in the pale cross-walls and placenta — the ribs the seeds only lean against — stored in glands that stud that tissue. Scrape the ribs away and most of the fire leaves with them; a seed is hot merely by contact. The plant builds its defense exactly where a seed-eater's teeth would close first, which is the whole point of a defense.

The first line builds the molecule's aromatic head, and it runs in every green thing that has ever grown: the phenylpropanoid branch. Phenylalanine is unspooled by PAL into cinnamic acid; C4H hangs a hydroxyl on the ring to make p-coumaric acid; 4CL activates it; HCT and COMT decorate it, hydroxyl by methoxyl, until the ring becomes vanillin — yes, the vanilla molecule — and then pAMT, an aminotransferase, turns vanillin into vanillylamine. Hold that in your mind: the business end of the fiercest heat on Earth is the same aromatic ring that makes vanilla the gentlest sweetness in the pantry. Chili and vanilla share a head. The receptor cannot be fooled without it; the vanilloid pocket is named for exactly this group.

The second line builds the tail, a small branched fatty acid. BCAT, a branched-chain aminotransferase, works from valine or leucine; KAS, a ketoacyl synthase, elongates the chain two carbons at a time into an 8-methyl branched-chain acyl group. Then the two lines meet. Pun1 — the gene whose protein is capsaicin synthase, the AT3 acyltransferase — takes the vanillylamine head and the branched acyl tail and condenses them into capsaicin, with a molecule of water let go. One enzyme, one bond, and the key is cut.

The length and saturation of that tail set the *shape* of the burn. Leave one double bond in and you get capsaicin proper — a fast, sharp, forward heat. Saturate it fully and you get dihydrocapsaicin — nearly as potent but slower to arrive and slower to leave, a heat that lingers at the back of the throat. The ratio between them, written by KAS and BCAT, is the difference between a slap and a long warm hand. This is the most honest thing we can say about what we do: we read a chemistry the plant already runs, and we change the smallest possible part of it.

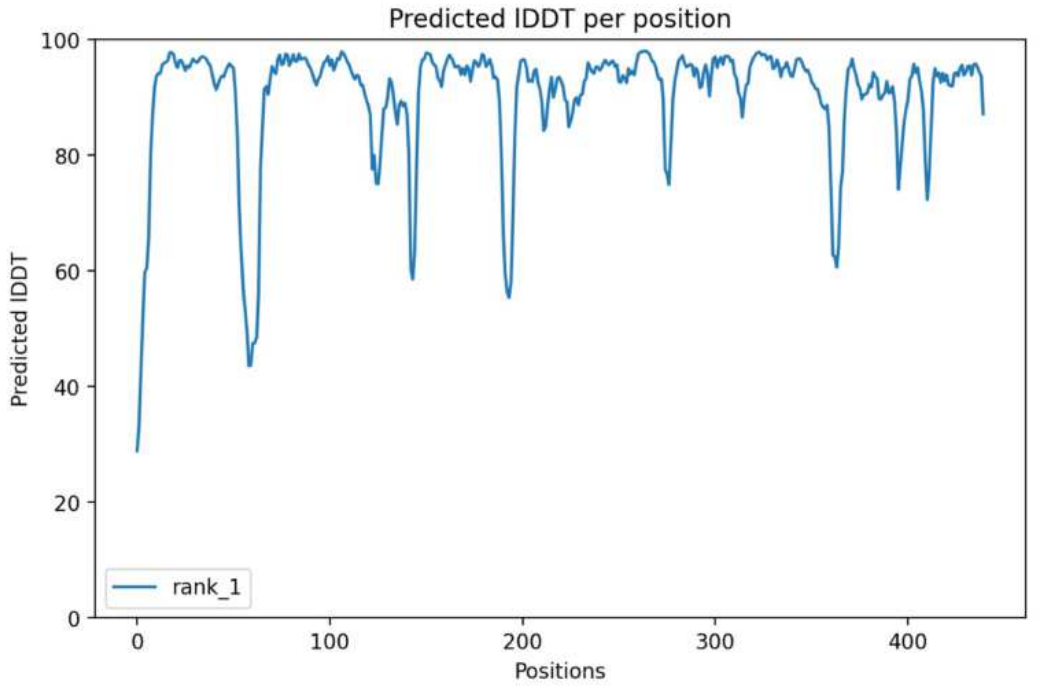


FIG. 20-1 — The Pun1/AT3 capsaicin-synthase model, coloured by pLDDT confidence; the binding domain and the active-site cleft resolve at high confidence, where the two edits sit.

Every breeding program before ours chased heat from the outside — select the hottest fruit, save its seed, hope the genotype followed the phenotype. We turned it around and read the enzyme first. A protein language model scored every single-residue change Pun1 could tolerate by its predicted effect on catalytic efficiency and fold stability; our flux model found control sits upstream in the phenylpropanoid pathway — at 4CL and HCT/CCoAOMT — not at this terminal joining step; Pun1 labels the product, it does not govern the rate. Two substitutions in Pun1 itself emerged that no breeder had ever stumbled into, and written in with CRISPR they stabilise the enzyme and tighten the plant's output.

PUN1 EDIT	WHAT IT DOES	ΔΔG (KCAL/MOL)
S39L	raises binding affinity at the N-terminus	−2.1
L345G	relieves steric crowding in the active-site cleft	−1.8
Combined	**a stabler, faster, more faithful enzyme**	**−3.9**

Those are small energies — a single hydrogen bond is worth one to a few kcal/mol — and yet they decide the outcome. The free-energy change tilts an equilibrium by the Boltzmann factor, e^(−ΔΔG/RT); with RT ≈ 0.59 kcal/mol at mouth-and-bench temperature, a combined −3.9 kcal/mol favors the stable, catalytically-competent fold by e^(3.9/0.59) ≈ 740-fold. The practical reward of that fold is consistency. Wild-type peppers vary in heat with a batch-to-batch coefficient of variation — the standard deviation as a percentage of the mean — of about 42%. The edited line is designed to hold to **≤7%**. Because variance is the square of that spread, $(42/7)^2 = 36$, the engineered fruit is thirty-six times less noisy from fruit to fruit. A fire you can ask for by number is only possible once the plant stops arguing about the number.

Putting a number on the fire — the Index, derived

A feeling is not a measurement until you anchor it. The Iyengar Flavor Index anchors every axis to a receptor's half-activation point — the concentration at which a stimulus drives its receptor to half of

full response, the EC_{50} — and scores a food not by how much of a compound it holds but by how *loudly* that compound speaks to the door it fits:

> **IFI(candidate) = 1,000 × EC_{50}(reference) ÷ EC_{50}(candidate).**

Read it slowly and it unfolds on its own. The reference is pinned at 1,000 by stated convention — a defined anchor, the same way Scoville's original dilution-to-threshold definition set the yardstick for heat — so its half-activation concentration is the axis's E_0. A candidate that half-activates the receptor at a *lower* concentration is louder, and the ratio climbs above 1,000. Rearrange it and the Index hands you the candidate's EC_{50} directly:

> $EC_{50}(candidate) = 1{,}000 \times E_0 \div IFI(candidate).$

Work it for the hottest plant our family has ever grown, **Phoenix**, which our model scores **4,200** on the heat axis:

> $EC_{50}(Phoenix) = 1{,}000 \times E_0 \div 4{,}200 = E_0 \div 4.2 \approx 0.238 \cdot E_0.$

Phoenix is designed to drive TRPV1 to half-maximum at 23.8% of the reference concentration — it is **4.2× louder** than the wild type pinned at a thousand. The Index is, at heart, a dilution read directly off the receptor: how far can you thin this fruit before the door only half-answers? The original Scoville test asked the same question of a human panel in 1912 — dilute the extract in sugar-water until five tasters could no longer feel the heat — and the Index simply asks the receptor instead, on all eight of its channels at once, with no panel to tire and no tongue to disagree.

The formula does not care which door it reads. Phoenix registers **1,800** on the umami axis, where the receptor mGluR1 answers free glutamate; the identical rearrangement gives $EC_{50} = 1{,}000 \times E_0 \div 1{,}800 \approx 0.556 \cdot E_0$ — a savory signal reached at 55.6% of its reference concentration, 1.8× louder on the door of nourishment than the native plant. Heat at 4,200 and umami at 1,800 are the same arithmetic run on two different receptors — each axis has its own stated reference constant, so a score on the H axis and a score on the U axis are independent readings, not a single common scale. The power of one index is that the same rigorous arithmetic applies to every door, one at a time.



FIG. 20-2 — Phoenix (SS-0096) in profile; the receptor-based methodology depicted here defines each IFI axis — our scores represent our model's predicted activity at each door.

From receptor loudness to Scoville — two dilution assays, one fruit

The Scoville Heat Unit survives alongside the Index because the world knows it, and the two measure genuinely different things — one the mass of capsaicinoid present, the other the loudness it produces. Modern SHU drops the panel for chemistry: HPLC measures capsaicinoid concentration in parts per million, and the long-standing conversion multiplies by about 16, so that pure capsaicin — the ceiling — sits near **16,000,000 SHU**. That ceiling lets us read any fruit as a fraction of the absolute. Our model predicts Phoenix at approximately **2.95 million SHU**, placing our design target at 2.95M ÷ 16,000,000 ≈ **18.4%** of the heat of pure capsaicin — roughly one part in five of the hottest chemistry there is, designed into a living fruit.

Set the design progression out in full — arranged by predicted heat, our computational design scope across the heat axis — and a quiet lesson appears in the last column:

CULTIVAR	SKU	SHU (PREDICTED)	IFI-H	EC_{50} VS REF (1000/IFI)	SHU PER IFI-POINT
Ember	SS-0087	866,000	1,570	$0.637 \cdot E_0$	552
Cinder	SS-0088	1,050,000	2,290	$0.437 \cdot E_0$	459
Kindle	SS-0089	1,250,000	2,000	$0.500 \cdot E_0$	625
Blaze	SS-0091	1,720,000	2,630	$0.380 \cdot E_0$	654
Wildfire	SS-0092	1,960,000	2,930	$0.341 \cdot E_0$	669
Scorch	SS-0093	2,210,000	3,220	$0.311 \cdot E_0$	686
Firestorm	SS-0094	2,470,000	3,490	$0.287 \cdot E_0$	708
Solara	SS-0095	2,720,000	3,980	$0.251 \cdot E_0$	683
Phoenix	**SS-0096**	**2,937,948**	**4,200**	**$0.238 \cdot E_0$**	**700**

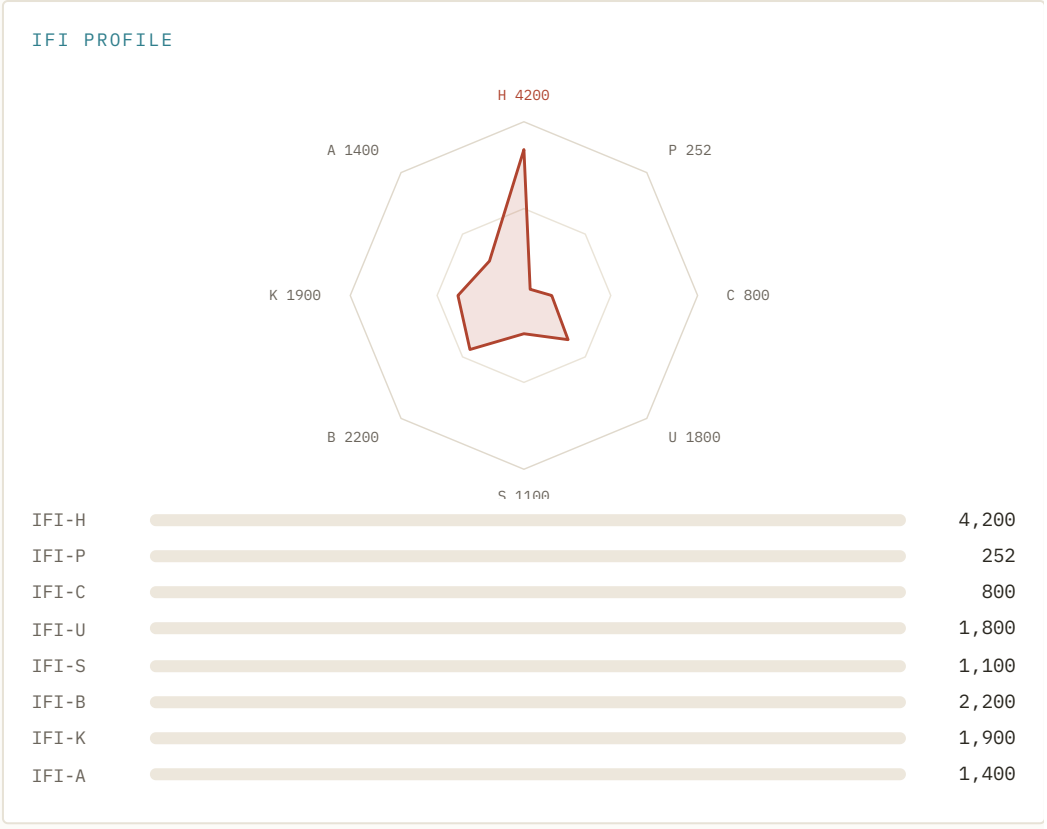
Watch the right-hand column climb, from about 550 SHU per point of loudness near the bottom to about 700 near the top. That rise is the receptor saturating. Because TRPV1 opens along a cooperative sigmoid — response ≈ $C^n \div (EC_{50}^n + C^n)$, with the Hill coefficient n near 2 — equal additions of capsaicinoid buy less and less loudness as the door approaches fully open. Writing dose in units of that half-activating EC_{50}, a cooperative sigmoid with n ≈ 2 carries the door

from half-open at one EC_{50} to four-fifths open at two — thirty points of loudness bought by a single doubling — while the next doubling, from five EC_{50} to ten, buys under three more points, creeping from 96% to 99%. At the top of the ladder each further decibel of heat costs disproportionately more mass, which is exactly why a chilihead chasing raw Scovilles is chasing a number the tongue can no longer fully hear. The Index measures what the mouth actually receives, and the mouth, mercifully, tops out.

And one honest wrinkle rewards a close look: Cinder carries fewer predicted Scovilles than Kindle (1.05M against 1.25M) yet scores *louder* on the heat axis (2,290 against 2,000). SHU and IFI-H are not the same measurement, and they occasionally disagree in rank — because the ratio of capsaicin to dihydrocapsaicin differs between cultivars, set by that acyl-chain chemistry, and the two capsaicinoids are not quite equipotent at the receptor. Mass is not loudness. A faithful index has to be willing to tell you when the two diverge, rather than smoothing the inconvenient fruit into line.

The eight doors, read at once — the Phoenix profile

Heat is one door, and Phoenix is the first plant our family designed to register on all eight at the same time. Here is its full profile, the signature object of our full-spectrum design — the eight axes, in the index's own shorthand:



Each line is a different receptor answering a different molecule, and together they are a chord struck across the whole surface of taste:

AXIS	RECEPTOR	WHAT IT READS	PHOENIX
Heat · H	TRPV1	capsaicin — a fire that isn't there	4,200
Pungency · P	TRPA1	sharp volatiles that fly up the nose	252
Cool-Burn · C	TRPM8	the exact mirror of heat — menthol's cold	800
Umami · U	mGluR1 / TAS1R1·TAS1R3	free glutamate — nourishment is near	1,800
Sweetness · S	TAS1R2·TAS1R3	the taste of *yes*	1,100
Zero-Bitter · B	TAS2R38	the newborn's guardian, quieted	2,200
Kokumi · K	CaSR	richness, continuity, the round hand	1,900
Astringency · A	salivary PRPs	tannins — saliva losing its slip	1,400

Once you have really understood the one hot door, you have understood all of eating, because the rest is the same marvel in other keys. Sweetness is a different molecule turning TAS1R2·TAS1R3, the welcome a body is born loving. Umami is mGluR1 and its partners reading the free glutamate that means protein is near — the taste of being fed. Bitterness is TAS2R38, the careful guardian the newborn is born distrusting, and quieting it — the Zero-Bitter axis — is how a coffee or a cacao keeps its depth and loses its wince. Kokumi is the calcium-sensing receptor CaSR, the quiet hand that makes every other flavor round and whole. Cool is TRPM8, the perfect mirror of fire — menthol raising a cold door's threshold just as capsaicin lowers a hot one's, frost and flame the same trick run backward. Pungency is TRPA1, the sharp cousin that rises up the nose because its key is light enough to fly. Astringency is not even a receptor in the usual sense — it is your own salivary proline-rich proteins losing their slip as tannins bind them, a texture read as a taste. Eight doors. Every flavor anyone has ever loved is a chord across them, assembled not in the food but in the meeting between the food and the self. You do not just eat the world. You *read* it, molecule by molecule, a billion times a second, so seamlessly it feels like simply tasting.

Measuring it honestly — error, limits, and what we never claim

Every IFI prediction carries a spread around it, and we report the spread as the coefficient of variation. Take Phoenix's predicted heat at approximately 2.94 million SHU and the ≤7% CV design target: the standard deviation is 0.07 × 2,937,948 ≈ **205,656 SHU**, so a fruit sits, one deviation out, between roughly 2.73M and 3.14M. Hold the same mean at the wild-type 42% and the deviation balloons to about 1.23M SHU — a band that swallows nearly the whole ladder above. Consistency is not a cosmetic virtue; it is what lets a figure on a page mean anything in a mouth.

It also decides how much work certifying a batch takes. To pin a mean within ±2% at 95% confidence you need about $N \geq (1.96 \times CV \div 0.02)^2$ fruits. At the engineered 7% that is roughly **47 fruits**; at the wild 42% it is about **1,695** — the same thirty-six-fold gulf, now counted in the labor of a season. Tightening the plant tightens everything downstream of it.

And there are honest limits no amount of tightening removes. The EC_{50} that defines each axis's reference point is read from receptors in a dish — heterologous TRPV1 in a cell line, calcium flooding in under a microscope — and a dish is not a dinner. These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory. The real mouth adds warmth, acid, and fat, each of which bends the burn: warmth and a squeeze of lime potentiate TRPV1, and fat, as the milk already taught us, carries capsaicin away. The Index measures loudness, not liking; a 4,200 is a fact about a receptor, never a verdict on whether a dish is good, which belongs to the cook and the table and no instrument we own. Past a point, more heat stops being flavor and becomes plain nociception — the body's pain, not its pleasure — and we hold the extreme tier as a measured curiosity, not an invitation to harm. We make no health claim of any of it. The care we feel for the body that receives the food is an intention woven quietly through everything — the belief, held lightly and lived rather than preached, that food is something you give your body on purpose, grown by hands that revere the plant, to carry the most it can. The computing fell to one pair of hands among us; the plants, the seasons, the long patient tasting, and the table where the first question was asked belong to the whole family. That belief, not mastery of the pepper, is the real reason a family of scientists spent years learning to put a number on a feeling — to honor the plant, whose chemistry we read and never invent, and the mouth it speaks to.

The answer, whole

So the next time a child at your table sets down a fork and breathes out hard and reaches — for the milk now, not the water, because capsaicin is oily and water cannot carry it away — and asks *why is it spicy*, you have the true answer, and it is better than the easy one ever was. Tell them nothing is burning. Tell them about the little door with four cupped hands that watches for fire at 43 degrees, and the key the pepper grows down in its pale ribs — a vanilla head and a small branched tail, joined by a single enzyme — that slides into the door and quietly re-zeroes its thermometer until the cool of a mouth reads as flame. Tell them their own body is doing all the shouting, faithfully, about a danger that isn't there. Tell them their mouth is reading the world right now, molecule by molecule, in eight languages at once, a tongue older than any they will ever speak.



The research plot at the close of day. Every number in this book — every EC_{50}, every Scoville, every tightened percent — grew in a place like it: living plants, and a family that wanted to know why.

The fire is real and the burning is not, and the whole of this book has been the distance between those two — measured, at last, so it could be honored exactly. The number was only ever in service of the wonder. So pass the stew, and the cool bright salad, and the warm glazed plate — and eat, together, the answer.