

THE SCOVILLE SPLICE LIBRARY · VOLUME XXV

The Synthetic Frontier

An ocean of evolution from a chili. *We are teaching them to burn.*

The long-horizon edition. Tier 4 — the full synthetic pathway installed in the plants that share almost nothing with a pepper: Wildfire Broccoli, Nuclear Cabbage, Deep-Earth Carrot, Storm Corn, Dynasty Rice. The farthest reach of the method, and the mathematics that make it a plan rather than a dream.

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

Contents

01 Opening essay · The plants that share nothing with a pepper

02 Chapter 1 · The four-tier climb — distance is the only hard variable.

03 Chapter 2 · Anatomy of a twelve-gene install — what "synthetic" actually means.

04 Chapter 3 · The phenylpropanoid inheritance — five modules every plant already owns.

05 Chapter 4 · The terminal four — the enzymes only a pepper ever evolved.

06 Chapter 5 · The acyl half — where the shape of the burn is decided.

07 Chapter 6 · The target envelope — a number before a genome.

08 Chapter 7 · Flux has the last word — the limiter moves when the host does.

09 Chapter 8 · Designing the enzyme for a stranger — porting the method to a new background.

10 Chapter 9 · Wildfire Broccoli — heat in a plant we taught to stop being bitter.

11 Chapter 10 · Nuclear Cabbage — the leaf, the head, and the cold chain.

12 Chapter 11 · Deep-Earth Carrot — the taproot as a reservoir.

13 Chapter 12 · Storm Corn — the first grass to carry a chili's gift.

14 Chapter 13 · Dynasty Rice — warmth and nourishment at the scale of a staple.

15 Chapter 14 · The forty-eight-to-seventy-two-month clock — why the frontier takes this long.

16 Chapter 15 · Containment and the honest label — what we will and will not say.

17 Chapter 16 · Nourishment at the scale of a staple — flavor and feeding, one act.

18 Closing essay · The long horizon

Opening essay · The plants that share nothing with a pepper

There is a photograph we keep coming back to — not of a pepper, but of a cornfield at the hour before the light turns, the tassels still grey, the whole stand holding its breath. We love it because of what it does not contain. Nowhere in that field, in any cell of any one of those plants, is there a single molecule of capsaicin, nor the enzyme that would make one, nor the gene that would encode the enzyme. A grass has been growing on this planet for sixty million years and has never once tasted of fire. That absence is the subject of this book.

Everything we have built until now leaned, somewhere, on a pepper. The flagships were *Capsicum chinense* pushed to the edge of what a chili can be. The early organism work — tomato, eggplant, the nightshade cousins — borrowed a biochemistry that already sat two or three steps from the pepper's own. Even when we left the nightshades, we chose hosts that still spoke the dialect: plants whose cells already ran the reactions we needed to redirect. That was never cowardice. It was the correct order of operations. You prove a method where the ground is soft before you take it to rock.



The family in the research greenhouse at dawn — where the question that became this book was first asked: not *how hot*, but *how far*.

This is the book of the rock. Tier 4 — the Frontier Synthetic tier — is the set of targets where the host organism shares with the pepper almost nothing beyond the universal machinery every green thing on Earth inherited from a common ancestor before flowers existed. Corn and rice are grasses, monocots, as far from a chili as a living seed plant can be and still be a crop. Broccoli and cabbage are brassicas, sulfur-chemists, builders of a defensive pungency that has nothing to do with capsaicin and everything to do with mustard. Carrot is an umbellifer, a root-hoarder, an aromatic entirely its own. To put designed warmth into any of them, you cannot redirect a pathway that is already most of the way there. There is no pathway.

You install it — the whole of it, enzyme by enzyme, from the common inheritance all the way to the final condensation — into a cell that has never run it and was never built to.

We call that the *full synthetic pathway*, and the plants that need it the *synthetic frontier*. It is the hardest thing the platform does, it takes four to six years per organism, and it is the reason this volume exists. The people this book is written for — the ones who fund the long work, the ones who review it, the ones whose imaginations run ahead of the data — deserve to see the frontier drawn honestly: the real distance, the real gene counts, the real mathematics that turns a wild idea into a stage-gated plan. Nothing here is a product you can buy. Everything here is a target we can name, cost, and model. That is what a frontier is: not a fantasy, but a coordinate you have not yet reached and already know how to walk toward.

> The pepper was never the point. The pepper was the proof. The point was always everything that is not a pepper.

A word, before the distance, about why we would do this at all — why put heat into rice, of all things, the quiet staple that feeds more of the world than any other crop. The honest answer is in two halves, and we will hold both all the way through. The first half is flavor: that a warmth you can dial, grown into the plant rather than shaken on at the end, is a different and better pleasure than the one a jar of chili flakes can give, and that a staple able to carry a trace of designed warmth is a staple a cook can build on in ways the plain grain never allowed. The second half is quieter and matters more to us, and it runs under every chapter here without once being preached: that if you are going to re-engineer the plants that feed billions, you do not get to touch only their flavor. You touch the whole plant. You ask, in the same breath, what else it could be made to hold — which vitamin, which mineral, which more-available form of the nourishment it already carries — because designing flavor and designing nourishment are the same act performed on the same cell, and it would be a small imagination that did one and left the other on the table. We will come back to that. For now, the distance.



PART I OF IV

The Distance

four tiers · the twelve-gene install · the inheritance every plant owns · the four enzymes only a pepper evolved

Chapter 1 · The four-tier climb — *distance is the only hard variable.*

When people ask us why one organism takes eighteen months and another takes six years, they expect the answer to be about size, or about how hot we are trying to make it, or about how finicky the plant is to grow. It is none of those. The single variable that governs the difficulty of a synthetic-flavor program is *biochemical distance* — how many of the reactions we need are already running in the host, and how foreign the ones we must import will be to the cell we put them in. Everything else is downstream of that number. We built the whole roadmap around it, and it sorts the hundreds of concept organisms into exactly four tiers.



Phoenix (SS-0096) in the controlled chamber — the eight-axis pepper that sits at the top of the near climb and defines the reference the frontier is measured against.

Tier 1 is the Solanaceae core: the nightshades, the pepper's own family. A tomato, an eggplant, a tobacco already runs the entire upstream phenylpropanoid branch and sits a handful of enzymes from vanillylamine. You are not building a pathway; you are extending one. Four or five genes, eighteen to twenty-four months, and the plant that could not make heat makes heat. Tier 2 reaches to the extended nightshades — potato, ground cherry, tomatillo, petunia — where the family resemblance is fainter and the flux has to be coaxed harder: five to seven genes, two to three years. Tier 3 leaves the family entirely and crosses into strawberry, cucumber, melon, apple, lettuce — the first true strangers, seven to ten genes, three to four years, where you can no longer assume the host will even route its carbon the way a nightshade does.

And then Tier 4. The frontier synthetic tier. Here the host shares with the pepper only the deep, universal inheritance — the few reactions so old that every vascular plant kept them — and nothing of the pepper's specializations. Ten to twelve genes. Forty-eight to seventy-two months. Five organisms chosen because each one, if it can be done, proves something the others cannot: a brassica, a leaf, a root, and two grasses, one of which happens to be the most-eaten plant on Earth.

TIER	NAME	REPRESENTATIVE HOSTS	GENES TO INSTALL	TIMELINE	WHAT IT PROVES
T1	Solanaceae Core	Volcanic Tomato · Dark-Matter Eggplant · Laboratory Tobacco	4–5	18–24 mo	The method ports inside the family
T2	Extended Nightshades	Seismic Potato · Celestial Ground Cherry · Acid Tomatillo	5–7	24–36 mo	Flux can be rebalanced across a genus
T3	Cross-Family	Sweet-Heat Strawberry · Contradiction Cucumber · Solar Melon	7–10	36–48 mo	The pathway survives in a stranger's cell
T4	**Frontier Synthetic**	**Wildfire Broccoli · Nuclear Cabbage · Deep-Earth Carrot · Storm Corn · Dynasty Rice**	**10–12**	**48–72 mo**	**A full install in a plant that shares nothing**

Read the gene counts as a map of inheritance. A Tier 1 host hands you seven or eight of the twelve reactions for free; you supply the terminal four and a promoter. A Tier 4 host hands you the oldest handful — the reactions that make lignin and defend against ultraviolet light, which every plant kept — and makes you build the rest from imported parts. The timeline scales with the count not because writing more DNA is slower (it is not; synthesizing a twelve-gene cassette takes the same few weeks as a four-gene one) but because every gene you import is a new way for the installation to fail: a precursor the host under-supplies, an intermediate the host degrades, a localization the host misreads, a regulatory signal the host ignores. De-risking those failure modes one at a time, in a crop with a long generation and a slow transformation, is what consumes the years.

There is a reference at the top of the near climb, and we will hold it in view through the whole book, because the frontier is measured against it. Phoenix — SS-0096, the eight-axis pepper — carries a predicted heat of approximately 2.95 million Scoville Heat Units and registers on all eight sensory axes at once, the only cultivar in the library to do so. Its IFI-H of 4,200 is eighty-four percent of the scorecard ceiling. That is what the method can do when the host is a pepper and hands you everything. The frontier organisms will not reach it, and are not meant to. The point of Tier 4 is not to out-burn a chili in a grass. It is to prove that the method has no outer wall — that given enough genes and enough years, the warmth can be grown into anything with a genome. Phoenix is the proof that the ceiling is high. The frontier is the proof that the walls are not there.

A last word on the shape of the climb, because it governs how we fund it. Difficulty does not rise linearly from tier to tier; it rises with the *novelty* of the install, and novelty compounds. Each tier reuses almost everything the tier below it validated — the enzyme-design loop, the flux models, the promoters, the assays — and adds only the new problems its extra distance creates. That is why we never build a frontier organism cold. We build it on the back of a nearer one that already solved most of the way there. Every Tier 4 program

in this book stands on a validated bridgehead from the lower tiers, and the first job of each organism chapter is to name the bridgehead it stands on.

Chapter 2 · Anatomy of a twelve-gene install — *what "synthetic" actually means.*

The word *synthetic* does a lot of quiet work in this book, and it is worth slowing down on, because it does not mean what a reader outside the lab usually hears. It does not mean artificial, and it does not mean that we are building a molecule nature never made — capsaicin is capsaicin whether a Trinidad pepper makes it or a field of corn does; the receptor cannot tell and neither can the tongue. *Synthetic* here is used the way a synthetic chemist or a synthetic biologist uses it: we are assembling a complete working pathway, reaction by reaction, from defined parts, and installing the whole assembly into a cell that did not have it. The pathway is real biochemistry. What is synthetic is the *construction* — that we drew it, wrote it, and placed it, rather than finding it.



A twelve-gene cassette on the assembly bench — each transcription unit its own promoter, coding sequence, and terminator, strung into one contiguous construct before it ever meets a cell.

So let us open the thing up and count what is actually inside. A full synthetic capsaicinoid install is two converging arms and a condensation that joins them. The first arm is the *aromatic* arm: it starts from an amino acid the plant already makes and walks it, hydroxylation by methylation by amination, to vanillylamine — the nitrogen-bearing head group that will become the business end of the molecule. The second arm is the *acyl* arm: it takes a branched-chain amino acid, strips it to a branched starter unit, and elongates it

into the fatty tail whose length and single double bond decide the character of the burn. The two arms meet at capsaicin synthase, the pepper's terminal enzyme, which joins the amine head to the acyl tail and releases the finished molecule. Twelve transcription units cover it, with a little give at either end depending on the host:

#	MODULE	ENZYME	REACTION INSTALLED	ARM
1	Entry	PAL (or grass PTAL)	Phe → cinnamate (PTAL also Tyr → coumarate)	aromatic
2	Hydroxylation	C4H (CYP73A)	cinnamate → *p*-coumarate	aromatic
3	Activation	4CL	*p*-coumarate → *p*-coumaroyl-CoA	aromatic
4	Transfer	HCT	coumaroyl-CoA → coumaroyl-shikimate	aromatic
5	Ring hydroxylation	C3′H (CYP98A)	coumaroyl-shikimate → caffeoyl-shikimate	aromatic
6	Methylation	COMT / CCoAOMT	caffeoyl → feruloyl (ferulic acid)	aromatic
7	Chain shortening	HCHL-type lyase	ferulate → vanillin	aromatic
8	Amination	pAMT	vanillin → vanillylamine	aromatic
9	Branch entry	BCAT	Val/Leu → branched α-keto acid	acyl
10	Elongation	KAS / FAS module	branched starter → 8-methyl-6-nonenoyl-ACP	acyl
11	Activation	ACS	8-methyl-6-nonenoate → its CoA ester	acyl
12	Condensation	Pun1 / CS (AT3)	vanillylamine + acyl-CoA → capsaicin	join

Twelve is the eudicot number — the full set, which is what a broccoli, a cabbage, or a carrot requires, because an eudicot's native phenylpropanoid branch, though present, is tuned for lignin and does not spill enough of the right intermediates to spare you any module. In a grass the count drops toward ten, and the reason is a single elegant quirk of grass biochemistry we will spend a whole chapter on: grasses carry a *bifunctional* entry enzyme, PTAL, that can deaminate tyrosine directly to *p*-coumarate, collapsing modules one and two into one and letting the native, abundant grass supply of ferulate feed in partway down the aromatic arm. The frontier is not uniformly twelve genes deep. It is ten in a grass and twelve in an eudicot, and knowing which, and why, is the first design decision of every program.

Around these twelve sit the parts that are not pathway but without which the pathway is inert, and they matter as much as the enzymes. Every module needs a *promoter* — and not just any promoter, but one that fires in the organ we want the heat in and nowhere else, because a plant that makes capsaicin in its roots and leaves as well as its fruit is a plant that poisons its own growth. Tissue specificity is not a nicety on the frontier; it is a survival requirement for the engineered line. Every module needs a *terminator* to stop transcription cleanly. The finished molecule needs somewhere to *go* — a sequestration signal that routes the lipophilic capsaicinoid into a vacuole or an oil body where it can accumulate without dissolving the membranes that made it. And the whole cassette needs a *selectable* element so that out of a thousand

transformed cells we can find the handful that took. None of those are counted in the ten-to-twelve, because they are scaffolding, not chemistry — but a frontier construct is easily twenty kilobases of designed DNA by the time it is whole, and the art is as much in the scaffolding as in the enzymes.

This is why we say, flatly, that the synthetic frontier is an *assembly* problem before it is a *discovery* problem. We are not searching for a new reaction. Every reaction in that table was worked out, by the pepper or by us, years ago. What is hard, and what the years go into, is making twelve foreign reactions run in concert, in the right place, at the right level, in a cell whose entire regulatory apparatus was built to do something else — and to do it so reliably that a batch-to-batch coefficient of variation stays under seven percent, the same precision bar every construct in the catalog is held to, measured not on a convenient pepper but on a field of grass that would much rather be making starch.

Chapter 3 · The phenylpropanoid inheritance — *five modules every plant already owns.*

Walk back far enough down the aromatic arm and you reach reactions so ancient that to call them "pepper chemistry" is almost an insult to their age. The phenylpropanoid pathway — the opening stretch from phenylalanine to the activated hydroxycinnamates — predates flowers, predates fruit, predates the split between the plant that became a chili and the plant that became a grass. Every vascular plant on Earth runs it, because every vascular plant needs it: it is the road to lignin, the stiffening polymer that let plants stand up out of the water four hundred million years ago, and the road to the flavonoids and the sinapate esters that screen a leaf from ultraviolet light. When we install heat into a plant that has never made it, this first stretch is the part we do not have to bring. The host already owns it. The whole trick of the frontier is learning to borrow it.



A monocot stem in cross-section — the vascular bundles ringed in lignified cell wall, every fibre of it built through the same phenylpropanoid road the heat pathway needs to merge onto.

The road has five waystations, and we label them by their enzymes because the enzymes are what we measure. PAL — phenylalanine ammonia-lyase — strips the amino group from phenylalanine and leaves *trans*-cinnamic acid, the committed first step, the moment a molecule stops being destined for protein and becomes destined for the phenylpropanoid world. C4H, a cytochrome-P450 monooxygenase, hangs a hydroxyl on the ring and makes *p*-coumaric acid. 4CL activates it to its coenzyme-A thioester, the

currency form the downstream enzymes can spend. HCT and C3′H together perform the ring's second hydroxylation by way of a shikimate shuttle — a small piece of biochemical sleight of hand in which the molecule is esterified to shikimate, hydroxylated, and handed back — producing caffeic acid. And COMT caps the new hydroxyl with a methyl group to give ferulic acid. Five enzymes; five of our twelve modules; and in every host in this book, all five are already present and running, because the plant needs them to stand upright and to survive the sun.

That is the inheritance, and it is a gift. But a gift with a catch, and the catch is the whole reason the frontier is hard rather than trivial. The host's phenylpropanoid road is not idling, waiting for us. It is running at full tilt, committed, every molecule of ferulate it makes already spoken for — pulled onward into lignin by the monolignol enzymes, or sideways into flavonoids, or, in the grasses, esterified straight onto the cell wall. The intermediates we need are flowing past us in abundance, and they are all downstream-committed. To feed our heat pathway, we are not opening a dry tap. We are trying to divert a river that is already turning someone else's mill.

This changes the engineering from *supply* to *competition*, and competition is modeled differently. We do not ask "can the host make ferulate?" — it makes floods of it. We ask "how much ferulate can we skim toward vanillin before the plant notices its lignin is thinning and its roots are weakening?" That is a flux-partition question, and we answer it with the flux-balance machinery of the next part. But the design intuition is already visible here: the frontier is not about brute-forcing more precursor into existence. It is about inserting a new off-ramp onto a crowded highway and tuning the ramp so it takes exactly as much traffic as we need and not one car more. Take too little and the heat never arrives. Take too much and the plant falls over — literally, a lignin-starved cereal stem lodges flat in the first wind, which for a crop called Storm Corn would be a cruel irony we have thought about more than once.

Each host owns the inheritance in its own accent, and the accents matter. The grasses — corn, rice, sorghum — run an unusually heavy phenylpropanoid flux, because grass cell walls are stitched together with ferulate cross-links the way an eudicot's are not; a grass is, in a real sense, already a ferulate factory, which is both the frontier's great grass advantage and its great grass hazard. The brassicas — broccoli, cabbage — run the road while simultaneously running an enormous parallel draw on the shared aromatic amino-acid pool for their glucosinolate defenses, so the competition there is upstream, at the level of phenylalanine supply itself. The carrot runs a quieter road but routes a striking share of it toward the terpenoid and polyacetylene chemistry that gives a carrot its smell and its faint bitterness, so the competition there is lateral. Same five reactions, same ancient inheritance, three completely different negotiations. The inheritance tells you what you get for free. The accent tells you what it will cost.

Chapter 4 · The terminal four — *the enzymes only a pepper ever evolved.*

If the first five modules are the inheritance every plant kept, the last reactions are the opposite: the enzymes so specialized, so particular to one lineage's strange ambition, that exactly one branch of the tree of life ever evolved them. Capsaicin is a pepper's invention and a pepper's alone. No other plant genus makes a capsaicinoid; the chemistry is unique to *Capsicum*, which assembled it perhaps a few million years ago as a defense — a molecule that burns a mammal's mouth but means nothing to the birds that spread the seed. When we take heat to the frontier, these are the reactions we truly import. The inheritance we borrow. The terminal enzymes we carry in.

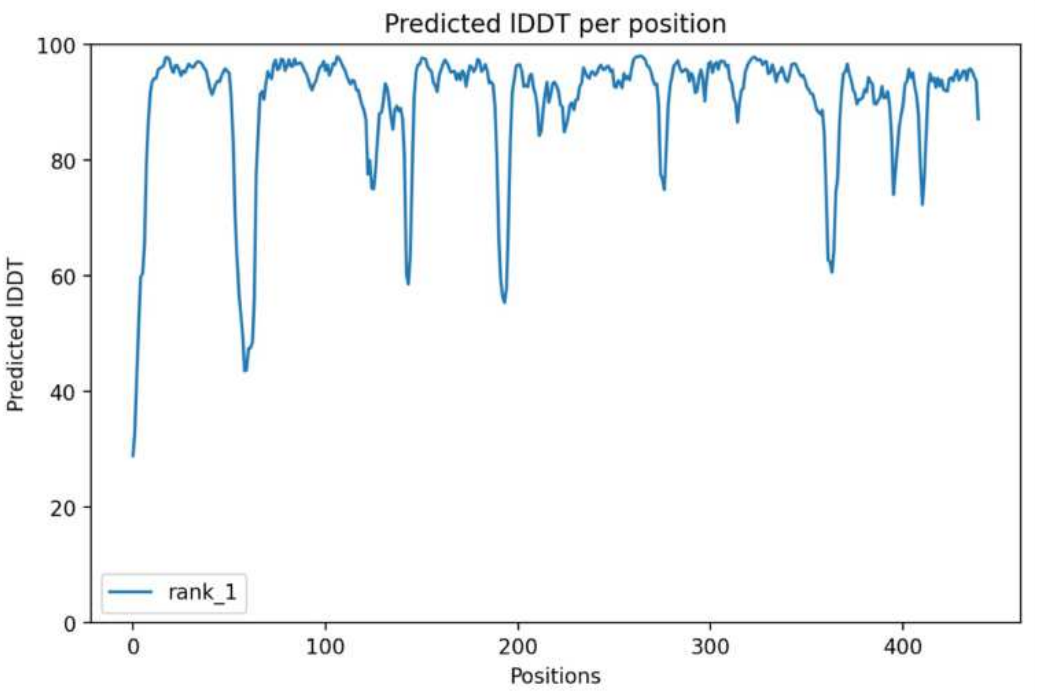


FIG. 4.1 — the Pun1/AT3 capsaicin-synthase model coloured by pLDDT confidence; the acyl-binding channel and the catalytic cleft resolve at high confidence, the flexible loops at low. This is the enzyme no plant but a pepper ever built, and the one every frontier organism must be taught.

There are four of them, and they are the hinge of the whole enterprise. pAMT — the putative aminotransferase — takes vanillin, the fragrant aldehyde, and aminates it to vanillylamine, swapping an oxygen for a nitrogen and in doing so turning a flavor molecule into the reactive head group of a capsaicinoid. BCAT, the branched-

chain aminotransferase, opens the acyl arm by deaminating valine or leucine to a branched α-keto acid, the seed of the forked fatty tail. The KAS module — a ketoacyl-ACP synthase working with the host's own fatty-acid machinery — elongates that branched starter into the ten-carbon, singly-unsaturated chain, 8-methyl-6-nonenoyl, that is the signature acyl group of capsaicin itself. And then Pun1 — capsaicin synthase, also called AT3, a BAHD-family acyltransferase and the gene whose loss-of-function allele is precisely what makes a bell pepper sweet — performs the final condensation, joining vanillylamine's nitrogen to the acyl-CoA's carbonyl and releasing capsaicin and free coenzyme A. Four enzymes. The difference between a plant that cannot burn and a plant that can.

The pepper-specificity of these four is not a trivia point; it is a design constraint with teeth. Because no host in this book has ever seen them, there is no native regulation around them — no feedback loop to throttle them when the intermediate pool runs low, no chaperone evolved to fold them, no transporter expecting their product. We import not just the enzymes but the entire local logic they need to function, and we import it into a cellular environment that has no slot shaped like them. The single most common failure mode on the frontier is not that a terminal enzyme does not express — modern promoters make expression easy — but that it expresses into a context that starves it, misfolds it, or lets its product poison the cell. The terminal four are where the frontier is won or lost, and three of them behave well. The fourth, Pun1, is the one we have spent years learning to rebuild.

Which is the natural moment to recall what we already know about Pun1, because it anchors everything the enzyme chapters will do to it on the frontier. In the flagship superhot program, Pun1 was not merely installed; it was redesigned. A protein language model — ESM2, in its 650-million-parameter form — scored every possible single-residue substitution across the enzyme by predicted effect on catalytic efficiency weighted against fold stability, and a genome-scale flux-balance model mapped the flux control across the capsaicinoid pathway. Two substitutions — plus one structural annotation our modelling identified — emerged that no breeding program had ever found, because breeding cannot see a genotype it has not already stumbled into:

EDIT	EFFECT	ΔΔG (KCAL/MOL)
S39L	binding affinity ↑ (N-terminal)	−2.1
L345G	steric relief at the active-site cleft	−1.8
C175S	prevents a disulfide misfold (structural annotation — not in shipped construct)	−0.9

Written in with CRISPR, the double variant S39L+L345G is designed to achieve a predicted peak of approximately 2.95 million SHU, with a batch-to-batch coefficient of variation design target at or below seven percent, against forty-two percent in the unedited background. That is the designed starting point the frontier inherits — not a wild-type pepper enzyme, but an enzyme our design loop has refined. The question the frontier asks is harder and more interesting: those two edits were optimized *in a pepper's cell*,

against a pepper's codon usage, a pepper's chaperones, a pepper's temperature and redox. Will they be optimal in a grass? Almost certainly not. The enzyme that is best in a chili is not the enzyme that is best in a corn kernel, and the method's real test on the frontier is whether the same design loop that found S39L in a pepper can find the *different* edits that a corn kernel needs. That is Chapter 8's problem. Here it is enough to have named the four enzymes that only a pepper ever evolved, and to have marked the one of them that we will spend the rest of the book teaching to live somewhere new.

Chapter 5 · The acyl half — *where the shape of the burn is decided.*

It is tempting, because the aromatic arm is longer and busier, to treat the acyl arm as a supporting player — three modules to the aromatic arm's eight, a tail to the molecule's more glamorous head. That would be a mistake, and a mistake you can taste. The aromatic half decides *whether* a plant burns. The acyl half decides *how*. The length of the fatty tail, the position of its single double bond, the branch at its far end — these are what separate the fast, bright, front-of-mouth strike of capsaicin from the slower, broader, more lingering warmth of dihydrocapsaicin, and from the softer still profiles of the minor capsaicinoids. When a frontier cook eventually tastes Deep-Earth Carrot and says the heat *blooms* rather than *stabs*, they will be tasting a decision made here, in the acyl arm, by an enzyme we tuned to make one chain a hair longer than another.

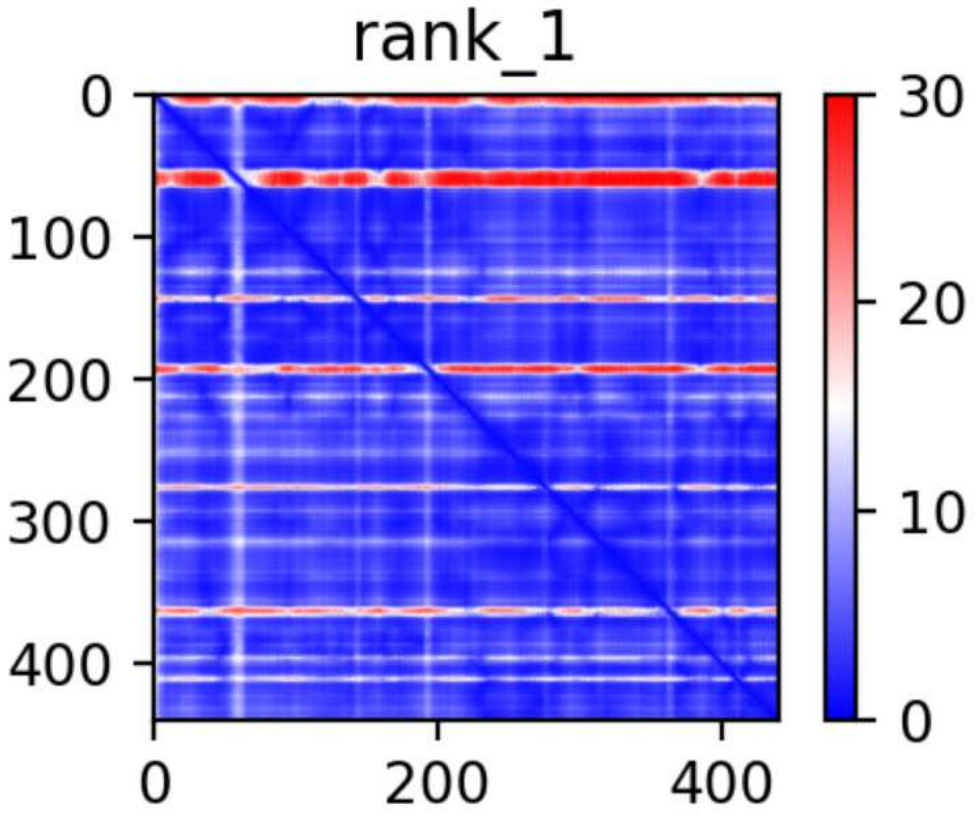


FIG. 5.1 — the predicted aligned-error map for the Pun1/AT3 model. The dark low-error block spanning the acyl-binding channel tells us the enzyme holds the fatty tail in a rigid, well-coupled pocket — which is exactly why small changes to chain length translate into reliable, repeatable changes in the character of the burn.

The chemistry is specific and worth stating plainly. Capsaicin proper carries an 8-methyl-6-nonenoyl group: a nine-carbon chain with a methyl branch at carbon eight and a *cis* double bond at carbon six.

Dihydrocapsaicin carries the same chain with the double bond removed — 8-methylnonanoyl, fully saturated. Those two account for the great majority of the heat in any pepper, and the ratio between them is the single most important lever on the *character* of a chili's burn. A pepper rich in capsaicin hits fast and sharp and fades; a pepper rich in dihydrocapsaicin builds and holds and sits at the back of the throat. The minor capsaicinoids — nordihydrocapsaicin, homocapsaicin, homodihydrocapsaicin, differing by a carbon here or a branch there — fill in the edges, widening or narrowing the attack. The total determines how *hot*. The distribution determines how it *feels*.

That distribution is set in the acyl arm, and set largely at one enzyme: the ketoacyl-ACP synthase, the KAS module, that elongates the branched starter. Its substrate preference — how many rounds of two-carbon elongation it runs before it releases the chain, and whether a desaturase introduces the carbon-six double bond before release — determines the capsaicin-to-dihydrocapsaicin ratio directly. Push the elongation one preference one way and you bias toward the unsaturated, fast-striking capsaicin. Push it the other and you bias toward the broad, saturated warmth. The branch at carbon eight comes from the choice of starter — valine gives one branch pattern, leucine another — and that choice is set upstream at BCAT, the branched-chain aminotransferase, by which amino acid it prefers to deaminate. So the shape of the burn is a two-enzyme conversation: BCAT sets the branch, KAS sets the length and the saturation, and between them they write the profile that the tongue will eventually read as *character*.

On the frontier this becomes a lever we do not have in a wild pepper, and it is one of the quiet reasons the synthetic approach is not merely a way to copy a chili but a way to exceed what a chili can be. A wild pepper's acyl profile is whatever its particular KAS and BCAT alleles happen to produce; the plant has no interest in your preferences. When we install the acyl arm from scratch, we choose the alleles — and more than that, we can tune them, by the same enzyme-design loop that reshapes Pun1, to hit an acyl distribution that suits the host and the dish. A rice grain, which will carry its warmth into gentle, long-simmered contexts, wants a profile weighted toward the slow dihydrocapsaicin warmth that survives cooking and does not shock. A carrot, which may be eaten raw and bright, can carry more of the fast capsaicin strike. We are not stuck with a pepper's acyl chemistry. We get to compose it.

There is a constraint that keeps this honest, and it comes from the host's own fatty-acid machinery, with which the imported KAS module must share tools. Every plant runs a fatty-acid synthase to make the lipids its membranes need; our branched-chain elongation borrows that machinery's acyl-carrier proteins and reducing power. In a host with abundant lipid flux — an oilseed, or the oil-rich germ of a corn kernel — the acyl arm has room to work, and the branched tails elongate cleanly. In a host that is poor in lipid and rich in starch — a rice endosperm, say, which is very nearly pure amylose and

amylopectin — the acyl arm is competing for a thin stream of acyl-carrier protein against the plant's own essential membrane synthesis, and it elongates grudgingly. This is one of the deep reasons the frontier organisms differ so sharply in their achievable heat ceiling, and it is why, when we reach the organism chapters, the storage chemistry of the edible organ will predict the heat more reliably than anything about the aromatic arm. A plant can only burn as brightly as its acyl arm can build tail, and the acyl arm can only build as much tail as the host's lipid economy will spare. The head decides whether. The tail decides how much, and how. Remember the tail; the frontier is decided there as often as not.



PART II OF IV

The Mathematics

the target envelope · flux has the last word · designing an enzyme for a stranger's cell

Chapter 6 · The target envelope — *a number before a genome.*

We do not begin a frontier program by editing a plant. We begin it by writing a number, and then a small set of numbers around that number that together describe the warmth we intend to grow — the *target envelope*. It is the first deliverable of every program and the thing the whole four-to-six-year effort is measured against, and it exists before a single base of DNA is synthesized, because the discipline of the frontier is to know exactly what you are trying to make before you spend six years trying to make it. The number is an IFI value, and to understand what it commits us to, you have to understand what the Iyengar Flavor Index actually measures, because it does not measure what most people assume.



Replicate dose-response trays — the raw material of an EC_{50}. Every point on every curve is a receptor population reporting, at one stimulus concentration, what fraction of its full response the molecule has drawn. The whole of the Index is built from stacks of these.

The Index does not measure how much of a compound a food contains. It measures how *loudly* that compound speaks to the receptor that reads it. The distinction is the entire point. Two peppers can carry the same milligrams of capsaicin per gram and deliver different heat, because heat is not a quantity of molecule; it is a quantity of *receptor activation*, and the bridge between the two is a single number: the EC_{50}, the concentration at which a stimulus drives its receptor to half of full response. A molecule with a low EC_{50} is potent — it reaches half-activation at a whisper. A molecule with a

high EC_{50} is faint — it needs a shout. The Index inverts the EC_{50} against a fixed reference and scales it, so that loudness becomes a score a corn kernel and a chili can be read against on one page:

```
IFI(candidate) = 1,000 × EC50(reference) ÷ EC50(candidate)
```

The inversion is the elegant part. Because EC_{50} sits in the denominator, a *more* potent stimulus — a *lower* EC_{50} — yields a *higher* score, which is what intuition wants: louder should mean bigger. The reference is chosen so that the native wild-type stimulus scores 1,000, the anchor of the scale. And the scorecards cap each axis at 5,000, a normalization ceiling that keeps the eight-axis radar readable and sets the frame for every target we draw. When we say Phoenix reaches IFI-H 4,200, we are saying its heat presents to TRPV1 with an EC_{50} low enough that, inverted against the reference, it scores eighty-four percent of the way to the ceiling. Run the formula backward and it tells you something concrete: Phoenix's heat reaches half-activation at 1,000 ÷ 4,200 — about twenty-four percent — of the reference concentration. Four times more potent a presentation than the anchor. That is what a 4,200 *is*.

Now the frontier use of the same math, which is where it earns its keep. When we set a target envelope for a frontier cultivar, we are not guessing at a flavor; we are committing to an EC_{50} at a named receptor, and through it, by the formula, to a concentration the engineered tissue must actually achieve. Suppose we set Wildfire Broccoli's top rung at a target of IFI-H 1,600 — a real, culinary, build-upon-able warmth, well short of a superhot and deliberately so. The formula fixes the required potency: EC_{50}(target) = EC_{50}(reference) × 1,000 ÷ 1,600 = 0.625 × reference. From there, the receptor's own dose-response curve — its Hill function —

```
R / R_max = [A]^n ÷ ( EC50^n + [A]^n )
```

tells us the local capsaicinoid concentration [A] the floret tissue must reach for the eater to perceive that warmth, and the acyl-profile work of Chapter 5 tells us *which* capsaicinoids, at which ratio, present with that EC_{50}. The target envelope, in other words, is not a wish. It is a chain of equalities running from a flavor we intend, through an EC_{50} we commit to, to a tissue titer we must engineer and a flux we must divert. A number before a genome, yes — but a number that already contains the genome's marching orders.

This is why the frontier target envelopes in this book are drawn as targets and never as measurements, and why we are scrupulous about the line. A computed IFI value is derived from our dose-response models and the platform's design loop; Phoenix's eight IFI scores are among the computed predictions the platform has generated. A target IFI value is the top of a chain of design commitments — it says *this is the EC_{50} we are building toward and here is the flux math that says it is reachable* — and until a real curve confirms it, it stays a target, labeled as one. To present a target as a measurement would be to lie with a scorecard, and the scorecard is the one place in the whole library we refuse to lie, because it is the place the reader trusts most. So when, in the organism chapters, you see an `ifi` block under a frontier cultivar, read it as the envelope the

program is engineering toward — the coordinate on the map, not the flag already planted. The flags, when they come, will be measured, and they will replace these numbers with the real ones. That is the whole arc of a frontier program: to turn a target envelope into a measurement, one EC_{50} at a time.

Chapter 7 · Flux has the last word — *the limiter moves when the host does.*

An enzyme can be perfect and a pathway can still produce nothing. This is the hardest lesson the frontier teaches, and it is the one that separates people who think in genes from people who think in systems. You can install all twelve modules, each one folding beautifully, each one catalytically superb, and harvest a plant with no more heat than the wild type — because somewhere in the network a precursor is not arriving, or an intermediate is draining away, or the carbon you need is committed to something the plant values more than your ambition. Genes are necessary. *Flux* is sufficient. And flux obeys a different mathematics than catalysis, one that treats the whole metabolic network at once and asks not "how fast is this enzyme" but "what does the network, as a system at steady state, actually permit."



A frontier line under controlled-environment light — every variable but the one under test held flat, because a flux measurement is only as trustworthy as the constancy of everything you are not measuring.

The tool is flux-balance analysis, and its central assumption is deceptively simple: at metabolic steady state, every internal metabolite is made as fast as it is consumed, so its concentration does not change. Write that for every metabolite at once and you get a single matrix equation —

$$\mathbf{S} \cdot \mathbf{v} = 0$$

where **S** is the stoichiometric matrix of the entire genome-scale network, every reaction's every substrate and product, and **v** is the vector of all the reaction rates, the fluxes. The equation says the net production of each internal metabolite is zero — nothing piles up, nothing runs dry, the whole network balanced. On its own it is underdetermined; there are far more reactions than metabolites, so infinitely many flux vectors satisfy it. You close the system by adding bounds — the thermodynamic irreversibilities, the measured uptake rates, the enzyme-capacity ceilings — and then optimizing an objective: maximize flux toward capsaicinoid, subject to $\mathbf{S} \cdot \mathbf{v} = 0$ and $lb \le \mathbf{v} \le ub$. The solution is not a prediction of what the plant *will* do. It is a statement of the best the network *could* do, and the shadow prices that fall out of the optimization tell you precisely which constraint is holding you back. That constraint is the rate limiter, and finding it is the whole game.

Here is the frontier's deepest and most counterintuitive result, the thing we most want investors and reviewers to understand, because it reframes the entire effort: *the rate limiter moves when the host moves*. In a pepper, our flux model predicts control sits upstream in the phenylpropanoid pathway — at 4CL and HCT/CCoAOMT — not at the terminal Pun1/AT3 step; Pun1 is the final capsaicin synthase, it labels the product, it does not govern the rate. The double variant S39L+L345G raised Pun1's terminal efficiency and stability, but Metabolic Control Analysis assigns the overwhelming share of flux control to the upstream modules. One would naturally assume a better Pun1 is therefore always the design target on the frontier. It is not. Run the flux model in a grass and the limiter is somewhere else entirely — often the branched-chain precursor supply, the acyl arm, because a grass pours its carbon into starch and ferulate cross-linking and spares very little for the branched fatty acids the tail requires. Run it in a brassica and the limiter is upstream again, at the aromatic amino-acid pool itself, which the plant is draining day and night to feed its glucosinolate defenses. Same twelve genes, three different bottlenecks, because the network around them is three different networks.

The engineering consequence is total, and it is the reason the frontier cannot be done by copying. The edit that unlocks a pepper — a better Pun1 — does nothing in a grass whose limiter is the acyl supply, because you have widened a pipe that was never the narrow one. Every frontier program therefore begins, after the target envelope, with a flux model of *that host*, built on its genome-scale metabolic reconstruction, run to find *that host's* limiter, before we decide which of the twelve modules to pour the enzyme-design effort into. In Storm Corn the models point us at the acyl arm and the branched-chain aminotransferase; we spend the design loop there. In Wildfire Broccoli they point us at the aromatic amino-acid supply and the competition with glucosinolate biosynthesis; we spend it there, sometimes attenuating the competing draw rather than boosting the pathway at all. In Deep-Earth Carrot they point at the sink — the storage root's willingness to accept and hold the product — and the work becomes a transport and sequestration problem more than a catalytic one. The flux model does not just tell us

whether a target is reachable. It tells us *where the six years should go*, and on the frontier, where the years are the whole budget, that is the most valuable sentence a model can produce.

There is a quieter mathematics braided through all of this that we will say once, plainly, and then let hum: the flux model does not have to be run with only flavor as its objective. The same $\mathbf{S} \cdot \mathbf{v} = 0$, the same network, can be optimized for a different output — the flux toward a vitamin, a mineral chelator, a more-available form of iron or provitamin A — and the shadow prices will tell you, just as honestly, what the plant would have to give up to make more of it. We will return to that in the final chapters, because on a staple crop it is not a footnote. For now the point is only that flux has the last word on every objective you can name, flavor and nourishment alike, and that the model which finds the heat limiter is the same model that would find the nourishment limiter, run with its objective swapped. One piece of mathematics; two things we care about; the same last word.

Chapter 8 · Designing the enzyme for a stranger — *porting the method to a new background.*

We ended Chapter 4 with a question and owe it an answer. The double Pun1 variant — S39L+L345G — was designed for a pepper. These two substitutions were found by a protein language model reading the enzyme against a pepper's constraints, their predicted effect informed by a flux model of a pepper's metabolism. Take that enzyme to a corn kernel, a different temperature, a different redox state, a different codon economy, a different crowd of chaperones, and there is no reason the same two edits should be best in that new context, and good reason to expect they are not. So the real test of the method on the frontier is not whether we can install the pepper's improved Pun1. It is whether the *design loop itself* — the thing that found S39L — can be pointed at a new host and made to find the different edits that host needs. This chapter is about porting the loop, and it is the most portable thing we own.



A frontier enzyme in isolation before it is written back into the host — the point in the loop where a prediction becomes a physical sequence, carried from the model to the cell.

Start with what the loop is, because its generality is the whole asset. A protein language model — ESM2, in the 650-million-parameter weight we standardized on — has read a very large fraction of all known protein sequences and, in doing so, has learned the deep grammar of what makes a protein fold and function: which residues at which positions are tolerated, which substitutions preserve a fold, which quietly break it. Give it an enzyme and it will score every possible single-residue substitution — for Pun1, that is on the order of 430 positions times 19 alternatives, some eight thousand point

mutations — by how much each is predicted to help or hurt. We weight that prediction by two objectives at once: catalytic efficiency, the k_cat/K_M the active site can reach, and fold stability, the ΔΔG that says whether the protein will hold its shape long enough to work. The product of the two is the score. Rank the eight thousand, take the handful at the top that do not interfere with one another, write them in with CRISPR, and measure. That is the loop: *read, score, rank, write, measure*, closed, repeated. Nothing in that loop is pepper-specific except the inputs you give it.

And the inputs are exactly what the frontier changes. When we port the loop to a new host, three things enter the scoring that were silent in the pepper. First, *codon context*: the same amino-acid sequence must be encoded in the host's preferred codons, or the ribosome stalls and the enzyme never reaches full titer; the language model scores the protein, but a companion model re-optimizes the coding sequence for the host's transfer-RNA economy, and the two must agree. Second, *the folding environment*: a maize cell's cytoplasm is not a chili's — its temperature regime in the field, its redox poise, its chaperone complement all shift which substitutions are safe, and the stability term in the score must be computed against the host's conditions, not the pepper's. Third, and most important, *the limiter from Chapter 7*: the flux model tells us which enzyme is the bottleneck in this host, and the design loop is pointed there — at the branched-chain aminotransferase in a grass, at an aromatic-supply enzyme in a brassica — rather than reflexively at Pun1. The loop is the same. Where we aim it, and the conditions we score against, are the host's.

What comes out the other end is, as predicted, a *different* set of edits — and this is the result that most reassures us the frontier is tractable, because it means the method is not a lucky pepper-shaped key but a general lockpick. We are scrupulous about the status of these frontier edits, so let us state it exactly: they are *in silico* predictions, the top-ranked substitutions from the ESM2-plus-stability loop run against the host's constraints, and they remain predictions until wet-lab measurement confirms them. The table below is illustrative of the loop's *output form*, not a report of validated enzymes; the real values will replace these as each program clears its stage gates. We show it only so the reader can see what porting produces: not the pepper's double variant, but a host-specific set aimed at the host's own limiter.

HOST (PROJECTED)	LIMITER FROM FLUX MODEL	DESIGN-LOOP TARGET	PREDICTED EDIT CLASS (IN SILICO, PRE-VALIDATION)
Storm Corn	branched-chain acyl supply	BCAT / KAS module	substrate-pocket widening for Val starter
Dynasty Rice	acyl supply + endosperm sink	KAS module	thermostabilizing core substitutions
Wildfire Broccoli	aromatic amino-acid pool	pathway entry + competition	activity-preserving, expression-raising
Deep-Earth Carrot	storage-root sink / transport	sequestration, not catalysis	(loop aimed off-enzyme — see Ch. 11)
Nuclear Cabbage	aromatic pool + cold regime	Pun1 fold under low temperature	cold-stable active-site variants

Read the last column less for its specifics — which are predictions awaiting the bench — than for its *variety*. The pepper needed binding affinity and steric relief. The grasses need the acyl arm widened and stabilized. The brassicas need the aromatic supply protected and the enzyme made cold-tolerant for a cool-season crop. The carrot barely needs a better enzyme at all; it needs its product escorted into a root that will hold it, which turns the design loop away from catalysis and toward transport — a problem we will meet in full in Chapter 11. One loop, five hosts, five different answers, each one the host's own. That is what it means for a method to have no outer wall: not that the same edit works everywhere, but that the same *process* for finding the right edit works everywhere, and that the frontier, however foreign, is never scored by hand. It is scored by the same loop that found S39L, pointed somewhere new, and asked the same patient question — *which change, here, in this cell, makes this enzyme a little more itself.*



PART III OF IV

The Frontier Organisms

Wildfire Broccoli · Nuclear Cabbage · Deep-Earth Carrot · Storm Corn · Dynasty Rice

Chapter 9 · Wildfire Broccoli — *heat in a plant we taught to stop being bitter.*

There is a pleasing symmetry in beginning the frontier organisms with broccoli, because broccoli is the one Tier 4 target we already know intimately — not as a heat host, but as a bitterness host. Broccoli is a validated organism in the library: 380 constructs, built almost entirely around the Zero-Bitter axis, IFI-B, the attenuation of the harsh glucosinolate-derived bitterness that makes so many people, and nearly all children, push the florets to the side of the plate. We have spent years learning to quiet a brassica's bitterness. Wildfire Broccoli asks the opposite and complementary question: having learned to turn one thing down in this plant, can we turn a wholly new thing *up*? The debittering work is the bridgehead. The heat is the frontier. And the tension between them is the chapter.



Broccoli — a validated bridgehead organism, 380 constructs deep on the bitterness axis, now the first brassica asked to carry designed heat.

Begin with the host's own chemistry, because a brassica is a sulfur-chemist first and everything else second. The defining metabolism of broccoli, cabbage, kale, and their kin is the glucosinolate pathway: sulfur- and nitrogen-rich defensive compounds, built in large part from the aromatic amino acids, that sit inert in the tissue until the cell is crushed and the enzyme myrosinase hydrolyzes them into isothiocyanates — the volatile, nose-tingling, TRPA1-activating molecules that give mustard, horseradish, and raw broccoli their sharp pungency. Note what that means on the axes: a brassica

arrives already expressing two of our eight. It carries pungency, IFI-P, through its isothiocyanates, and it carries bitterness, IFI-B, through the glucosinolates themselves and their breakdown products. It is not a blank host. It is a host already loud on two axes, one of which we have learned to quiet.

That prior chemistry sets the flux problem precisely, and the flux model of broccoli is unambiguous about where Wildfire's limiter sits. It is not Pun1. It is upstream, at the aromatic amino-acid pool — the shared supply of phenylalanine and tyrosine out of the shikimate pathway — because the glucosinolate machinery is drawing on that same pool at industrial scale to build the plant's defenses. Our heat pathway's aromatic arm and the plant's glucosinolate arm are competing for the same phenylalanine at the same branch point, and in the wild type the glucosinolate arm wins decisively. So the Wildfire design does something that looks, at first, backward: before it adds a single heat module, it *attenuates* the competing draw, borrowing directly from the 380-construct debittering program. The very edits that quiet broccoli's bitterness for the Zero-Bitter cultivars also free aromatic amino-acid flux — and that freed flux is exactly what the heat pathway needs. The debittering was never only about flavor. On the frontier it turns out to have been, all along, a way of opening the supply line that heat would one day travel. Turn the bitterness down and you do not merely make a kinder broccoli; you unlock the precursor budget that lets the same plant, for the first time, begin to burn.

The edible organ cooperates, which is not something the frontier can take for granted. A broccoli floret is a dense arrest of immature flower buds, metabolically active tissue with real secondary-metabolite capacity and a reasonable lipid fraction to host the acyl arm — a better reservoir than a leaf, if not the equal of a root or a seed germ. That capacity sets Wildfire's achievable ceiling in the mid-range of the frontier: a warmth that is culinary and real, built to sit alongside the plant's inherent mustard-sharp pungency and its newly-quieted bitterness rather than to overwhelm them. We draw the proposed ladder as five rungs, each a target envelope, climbing from a proof-of-concept warmth to a top rung that a chef could build a dish around but no one would mistake for a superhot:

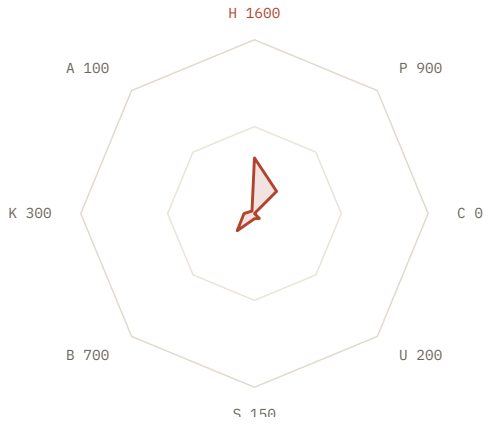
RUNG (PROPOSED)	CHARACTER	TARGET IFI-H	STATUS
Spark	first perceptible warmth	150	target
Smolder	gentle, floret-wide	450	target
Flashover	clearly hot, still kind	900	target
Firestorm	assertive culinary heat	1,300	target
Conflagration	top of the brassica band	1,600	target



Broccoli floret in cross-section — the arrested flower buds that give the organ its density, and the secondary-metabolite capacity that sets Wildfire's achievable heat ceiling.

The top rung, Conflagration, carries a target envelope that reads across more than one axis, because a brassica cannot help but be a multi-axis plant, and because the honest scorecard shows the heat arriving into a host that was never silent. This is a projected target envelope — the coordinate we would engineer toward — not a measured profile:

IFI PROFILE



IFI-H	1,600
IFI-P	900
IFI-C	0
IFI-U	200
IFI-S	150
IFI-B	700
IFI-K	300
IFI-A	100

Read it as a brassica learning a new language while keeping its native accent: a real designed heat on the H axis, the inherited mustard-pungency still speaking on P, the bitterness deliberately held low on B because the debittering that freed our precursor also gentled the plate, and quiet contributions of savor and body underneath. A pepper would score this profile very differently — all heat, little else. Wildfire is not a pepper. It is a broccoli that we first taught to stop being bitter, and then, on that cleared ground, taught to burn. The symmetry we opened with turns out to be the whole

mechanism: on the frontier, sometimes the first step toward a new flavor is quieting an old one, and the plant you taught restraint becomes the plant best prepared to carry fire.

Chapter 10 · Nuclear Cabbage — *the leaf, the head, and the cold chain.*

Cabbage and cauliflower are the next step out along the brassica branch, and they teach a lesson the dense broccoli floret let us postpone: that the *architecture* of the edible organ — leaf versus floret versus head versus root — is not a cosmetic detail but a determinant of how much warmth a plant can hold and how evenly it holds it. A cabbage is a tight sphere of overlapping leaves; a cauliflower is a mass of arrested, undifferentiated floral meristem, a curd. Neither is a floret, and neither is a seed or a root. Each poses its own version of the reservoir problem, and together they push the frontier's engineering from the pathway into the tissue.



Cabbage — validated at 40 constructs on the bitterness axis, a leafy brassica whose layered architecture makes even heat distribution the central engineering problem.

Cabbage is a validated host too, if a shallow one — 40 constructs, again on the Zero-Bitter axis, the same bridgehead logic as broccoli but less deeply explored. Its flux limiter is the same aromatic-pool competition with glucosinolate synthesis, and the same debittering-unlocks-precursor trick applies. What is new is the leaf. A cabbage stores its mass as water-rich, photosynthetic and post-photosynthetic leaf tissue, and leaf tissue is a poor host for a lipophilic capsaicinoid: it is low in the lipid bodies that would sequester the product, high in water that the oily molecule will not enter, and layered in a way that makes it fiendishly hard to deliver an even dose from the outer leaves to the pale, folded heart. The engineering challenge of Nuclear Cabbage is not, in the end, making the heat. It is distributing it — ensuring the eater who takes an outer leaf and the eater who reaches the core taste the same designed warmth, rather than a fierce edge and a bland center. That is a promoter-and-transport problem, solved by driving the pathway from a promoter that fires evenly across leaf layers and by giving the product a sequestration route that works in a cell poor in native oil bodies.

The leaf's low lipid capacity also sets Nuclear Cabbage's ceiling below broccoli's, and we would rather say so plainly than draw a flattering ladder. A water-rich leaf can hold less lipophilic capsaicinoid than a dense floret, and the acyl arm — which, recall from Chapter 5, can only build as much tail as the host's lipid

economy will spare — runs leaner here. The proposed ladder therefore tops out lower, and we name the rungs for the nuclear theme the concept was given, climbing by yield:

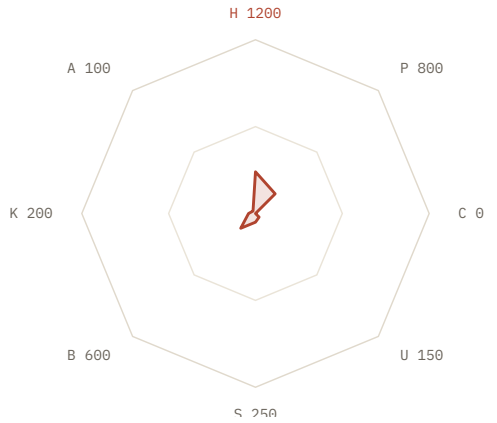
RUNG (PROPOSED)	CHARACTER	TARGET IFI-H	STATUS
Criticality	threshold warmth	120	target
Fission	even, leaf-wide heat	400	target
Detonation	clearly hot	750	target
Fallout	assertive, still distributed	1,000	target
Fusion	top of the leaf band	1,200	target



Cabbage in cross-section — the tight concentric leaf layers that make the heart as hard to reach, and to dose evenly, as anything on the frontier.

There is a reason this chapter is titled for the cold chain, and it is the second lesson cabbage teaches. Brassicas are cool-season crops; cabbage sweetens in frost and is grown, stored, and shipped cold. An engineered enzyme that folds and functions beautifully at a pepper's warm optimum may stall at a cabbage field's temperature — proteins slow and stiffen in the cold, and an active site tuned for warmth can lose most of its rate near freezing. This is exactly why, in the enzyme-design table of Chapter 8, the projected design-loop target for Nuclear Cabbage was *cold-stable active-site variants*: the loop must score fold stability and catalytic rate not at the pepper's temperature but at the cabbage's, hunting substitutions that keep the enzyme supple in the cold. It is the clearest single illustration in the book of why the method must be ported rather than copied. The best Pun1 for a Trinidad greenhouse is not the best Pun1 for a Minnesota cabbage field, and only a design loop that knows the host's temperature can find the difference. The projected top-rung envelope reflects the leafy, cool, evenly-dosed reality:

IFI PROFILE



IFI-H	1,200
IFI-P	800
IFI-C	0
IFI-U	150
IFI-S	250
IFI-B	600
IFI-K	200
IFI-A	100

The sweetness note on S is not an accident of modeling; it is the frost sugar a cabbage genuinely makes, and it is the kind of thing that keeps us honest and keeps us reverent at once — that even on the frontier, engineering the newest axis into a plant, we are still working with a vegetable that has its own old gifts, its cold-weather sweetness among them, and the designed warmth has to be composed to sit *with* that sweetness, a gentle heat threading frost-sweet leaves, rather than to bury it. The cauliflower variant, a curd of undifferentiated meristem rather than layered leaf, is the same program aimed at a different architecture — more uniform than a cabbage's layers, lower still in lipid, its own target band — and we hold it in the same chapter because the chemistry is one chemistry and only the tissue changes. The leaf and the head are two answers to the one question the brassicas pose: given a new warmth, where in this strange, sulfurous, cold-loving body will it live, and how do we make sure every bite finds it.

Chapter 11 · Deep-Earth Carrot — *the taproot as a reservoir.*

The carrot changes the problem completely, and it changes it in the one direction the frontier most wants: downward, into the ground, into a storage organ built for the very thing a capsaicinoid needs. Everything before this chapter has fought the host's tissue for somewhere to put the heat — a water-rich leaf that will not hold it, a floret of modest capacity. The carrot does not fight. A carrot is a plant that has spent its evolutionary life learning to pack a single swollen taproot with as much energy and pigment as it can hold against the winter, and a storage organ that good at hoarding sugars and carotenoids is, with the right transport, a storage organ that will hoard a designed capsaicinoid too. Deep-Earth Carrot is the frontier organism where the reservoir is a gift rather than a struggle, and the whole character of the program reflects it.



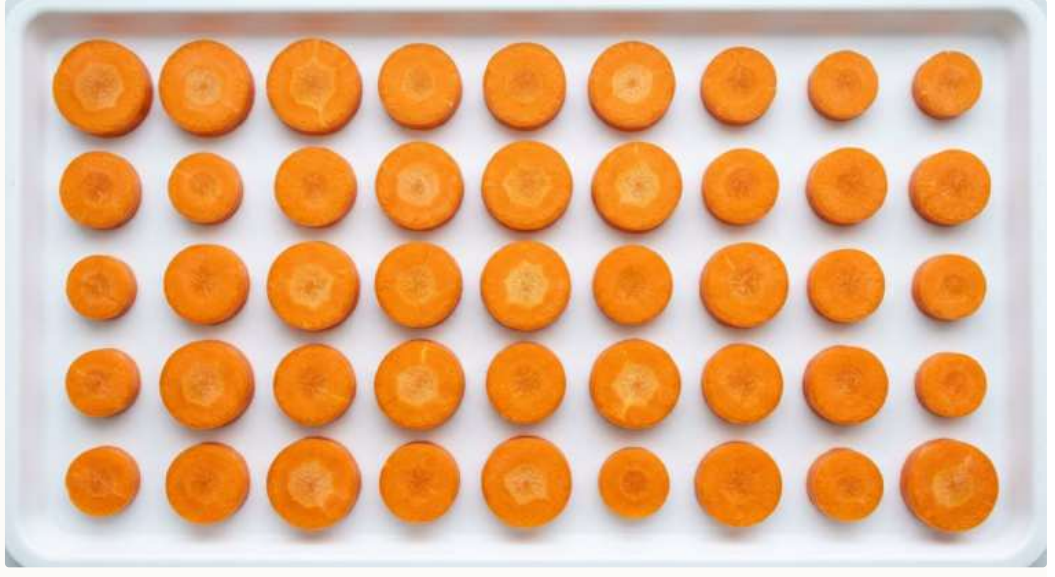
Carrot — an Apiaceae root, easy to regenerate in culture and built by evolution to hoard; the frontier's most willing reservoir.

Two facts about carrot biology make it the frontier's friendliest root, and they pull in opposite directions in a way that is instructive. The first is that carrot is one of the oldest and easiest plants in all of tissue culture — *Daucus carota* was a founding model of somatic embryogenesis, the organism in which biologists first watched a single cultured cell regenerate a whole plant. Transformation and regeneration, which in a grass are a multi-year ordeal, are nearly routine in carrot. So one of the great frontier time-sinks is cheap here. The second fact is the countervailing one: the carrot's native metabolism is busy and particular. The taproot is a riot of

carotenoids — the β-carotene that makes it orange, the anthocyanins that make the heirloom varieties purple — and the plant routes real flux into the terpenoid volatiles that give a carrot its unmistakable smell and into polyacetylenes like falcarinol that give it a faint native bitterness. The root is a willing reservoir, but it is a *crowded* one, and the flux model of Deep-Earth Carrot reflects that: its limiter is neither Pun1 nor the acyl supply but the *sink* — the competition, inside the root, for the carbon and the storage space that the carotenoid and terpenoid programs are already claiming.

That is why, uniquely among the five organisms, the enzyme-design loop for Deep-Earth Carrot is aimed *off the enzyme entirely*, as the Chapter 8 table flagged. There is little point lavishing the design loop on a faster Pun1 when the limiter is not catalysis but whether the root will accept and hold the product. The work moves to *transport and sequestration*: engineering the route that carries the finished, lipophilic capsaicinoid out of the cells that synthesize it and into the vacuoles and storage structures of the root where it can accumulate to real titer without dissolving the membranes it passes through. Solve the sink, and the carrot's natural hoarding capacity does the rest — which is why Deep-Earth Carrot, despite being a stranger to the pepper, carries the highest achievable heat band of any root or leaf on the frontier. The reservoir is simply that good. A taproot that can store a winter's worth of sugar can store a serious dose of designed warmth, if you can only get the molecule in.

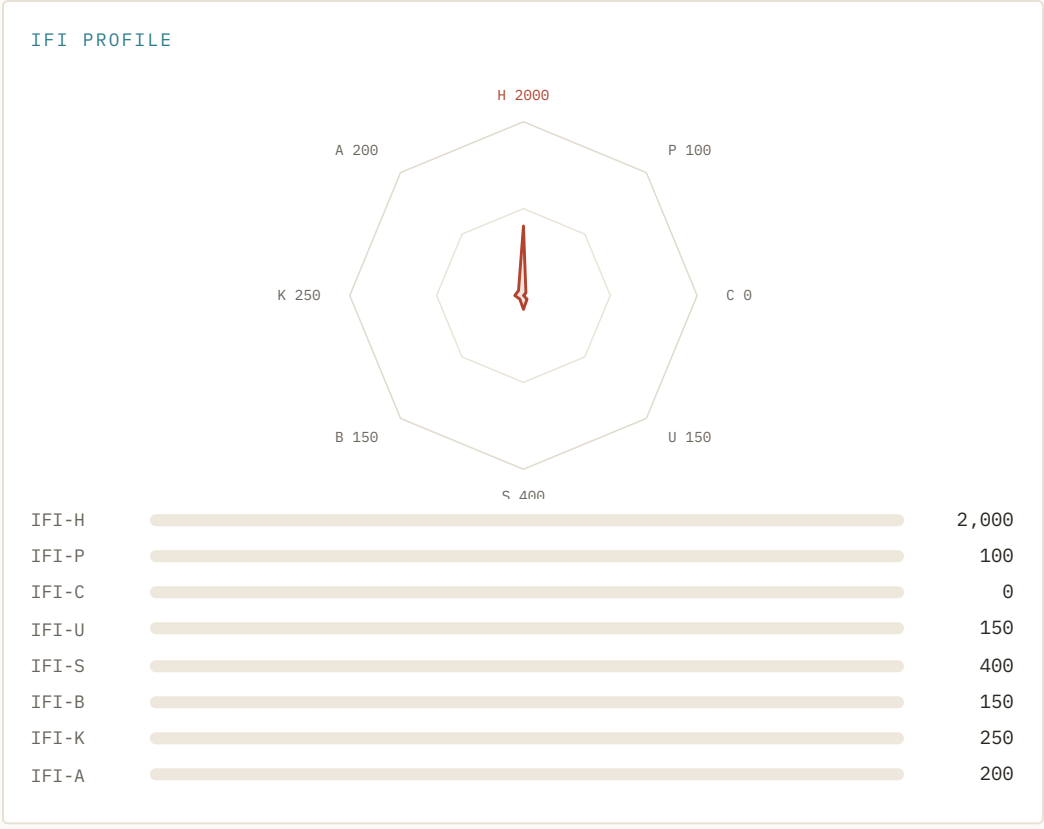
RUNG (PROPOSED)	CHARACTER	TARGET IFI-H	STATUS
Topsoil	first warmth near the crown	200	target
Bedrock	even through the upper root	600	target
Mantle	clearly hot, full-length	1,100	target
Magma	deep, building warmth	1,600	target
Core	top of the root band	2,000	target



Carrot in cross-section — the xylem core and phloem ring of a storage taproot, the architecture that makes it the frontier's most capacious home for a lipophilic capsaicinoid.

The acyl chemistry gets to be expressive here in a way it cannot in a rice grain, and this is where the carrot becomes, to us, the most quietly delightful organism on the frontier. A carrot is often eaten raw — grated bright into a salad, pulled straight from the soil — so its warmth can be composed toward the fast, front-of-mouth capsaicin strike rather than the slow, cooking-stable dihydrocapsaicin warmth

a simmered grain needs. We can tune the KAS preference, by the loop of Chapter 5, toward the unsaturated tail, so that Deep-Earth Carrot's heat *arrives* the way the carrot's own crisp sweetness arrives: immediate, clean, over the tongue and gone, a warmth that blooms with the raw snap rather than building behind it. The projected top-rung envelope carries that brightness, and it carries the carrot's own native sweetness alongside it, because we would no sooner silence a carrot's sweetness than silence a cabbage's frost sugar — the designed heat is meant to thread the native sweetness, not replace it:



Here the sweetness on S is substantial and intended — the carrot's defining gift, carried through rather than overwritten — and the faint astringency on A is the native polyacetylene character, left as a shadow at the edge because a trace of it is part of what a carrot *is*. Deep-Earth Carrot is the frontier organism we find it easiest to imagine on a table: a root pulled from the ground, orange or deep purple, grated into something cold and bright, carrying a clean designed warmth that reaches the tongue at the same instant as its sweetness. Of all the strangers in this book it is the one that feels

least like a feat of engineering and most like a vegetable that simply learned, late in its long history of hoarding, one more thing worth keeping underground.

Chapter 12 · Storm Corn — *the first grass to carry a chili's gift.*

With corn we leave the eudicots entirely and cross the deepest divide in the flowering-plant world — the split between the monocots and everything else, a hundred and fifty million years wide. A grass is not a broccoli with different leaves. It is a fundamentally different architecture of plant: different vasculature, different cell wall, different flower, different seed, and — crucially for us — a different way of running the very phenylpropanoid inheritance that the whole heat pathway must merge onto. Storm Corn is the frontier's monocot proof, and if it can be done, it says something no eudicot success can: that the method crosses the great divide, that the warmth we design can be grown into the grasses that feed the world. Corn first, because it is the grass we understand best and the one whose kernel offers the acyl arm a real home.



Corn — a monocot, a hundred and fifty million years of evolution from a pepper, and the frontier's proof that the method crosses the great divide.

Two features of grass biochemistry define the Storm Corn program, and the first is pure advantage. Grasses carry a bifunctional entry enzyme the eudicots lack — PTAL, a phenylalanine/tyrosine ammonia-lyase, that can deaminate tyrosine directly to *p*-coumaric acid, skipping the cytochrome-P450 hydroxylation step that eudicots require. Recall the twelve-module table: in an eudicot, modules one and two — PAL then C4H — are two separate reactions and two separate genes. In a grass, PTAL collapses them into one, because the grass can enter the pathway at *p*-coumarate directly from tyrosine. That is one of the reasons the frontier gene count drops

from twelve toward ten in a grass: the host's own machinery hands us a shortcut the eudicots never evolved. The second feature is both advantage and hazard, and it is the one we think about most. Grasses stitch their cell walls together with ferulate — they esterify huge quantities of ferulic acid, our module-seven intermediate, onto the arabinoxylan of the wall as cross-links. A grass is, metabolically, a ferulate factory running day and night. The precursor our aromatic arm needs most is the one a grass makes in the greatest abundance.

The hazard is the mill the river is already turning, and in a grass it turns the structural wall itself. That ferulate is not spare; it is load-bearing, the cross-links that keep a cereal stem stiff against the wind. Skim too much of it toward vanillin and you thin the wall, and a lignin-and-ferulate-starved cereal stem *lodges* — falls flat in the first storm, roots in the air, unharvestable. For a crop we have, with a straight face, named Storm Corn, this is not a metaphor we can ignore; the flux model has to find the heat while leaving the stalk strong enough to stand through the weather the cultivar is named for. So the Storm Corn flux problem is a careful partition: divert a measured few percent of the ferulate flux toward the heat pathway, confirm the remaining wall ferulate keeps the stalk standing, and tune the off-ramp to take exactly that much and no more. It is the clearest case in the book of the Chapter 3 principle — that the frontier is an off-ramp onto a crowded highway — and the stakes of over-skimming are visible in the field, flat on the ground, the first hard wind after a greedy design.

Where the corn kernel is generous is the acyl arm, and this is what sets Storm Corn's ceiling above the grasses' reputation for leanness. A maize kernel carries a real, oil-rich germ — the embryo and its surrounding scutellum are among the more lipid-dense tissues in any cereal, which is why corn oil is a commodity. That lipid economy gives the branched-chain acyl arm the acyl-carrier protein and reducing power it needs to build tail, so the flux limiter in corn, per the model, sits at the *branched-chain precursor supply* — the BCAT and KAS step, where valine and leucine are drawn into the forked starter — rather than at the lipid capacity itself. That is where the Chapter 8 design loop is aimed for Storm Corn: widening the branched-chain aminotransferase's substrate pocket to pull more valine into the acyl arm. Solve the branch supply and the oil-rich germ will carry the tail. The kernel becomes the reservoir, the warmth stored in the germ and endosperm where it can survive drying, milling, and cooking.

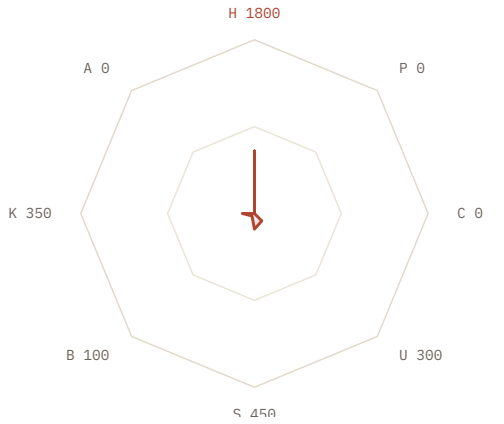
RUNG (PROPOSED)	CHARACTER	TARGET IFI-H	STATUS
Gust	first kernel warmth	180	target
Squall	even across the ear	500	target
Downburst	clearly hot	950	target
Supercell	assertive, cooking-stable	1,400	target
Derecho	top of the grass band	1,800	target



Corn kernels in cross-section — the oil-rich germ and starchy endosperm that make the maize kernel, uniquely among cereals, a real reservoir for the acyl arm's lipophilic product.

Because the kernel will carry its warmth into masa, into porridge, into long heat, the acyl profile is composed the opposite way from the carrot's: weighted toward the slow, saturated dihydrocapsaicin warmth that survives cooking and builds gently, rather than the fast capsaicin strike that a raw root can show off. A warmth you cook *with*, that comes up through a simmered dish rather than snapping on a raw bite. The projected top-rung envelope reflects a grass that keeps its own sweetness — a sweet corn is sweet, and we would not take that — under a designed, cooking-stable heat:

IFI PROFILE



IFI-H	1,800
IFI-P	0
IFI-C	0
IFI-U	300
IFI-S	450
IFI-B	100
IFI-K	350
IFI-A	0

The sweetness and the savory, body-giving kokumi notes on S and K are the corn's own — the sweetness of the sugary kernel, the brothy depth a good corn carries — and the heat threads up through them, composed to cook rather than to shock. Storm Corn is the frontier's great crossing. A grass, a hundred and fifty million years from a chili, taught to store a pepper's gift in the oil of its kernel, with a stalk engineered to stand through the storm it is named for. If the method reaches corn, the method reaches the grasses. And the grasses are most of what the world eats.

Chapter 13 · Dynasty Rice — *warmth and nourishment at the scale of a staple.*

We come, at the far edge of the frontier, to rice — and with rice the stakes change in kind, not merely in degree, because rice is not one crop among many. It is the staple that feeds more human beings than any other plant on Earth, the daily foundation of billions of meals, grown and eaten across more of the world than wheat or corn. To propose engineering rice at all is to propose touching the center of the human diet, and that is a thing no honest book can treat lightly or hurry past. Dynasty Rice is the frontier's longest horizon and its heaviest responsibility, and it is the organism where the two halves of our purpose — flavor and nourishment — finally become impossible to speak of separately, which is why we placed it last.



Rice — the staple that feeds more people than any plant on Earth, and the frontier's heaviest responsibility.

Begin, as always, with the tissue, because the tissue is honest and the tissue sets the limit. A rice grain is a starch grain. Its edible endosperm is very nearly pure amylose and amylopectin — starch and more starch — with only a thin aleurone layer and the germ carrying any appreciable lipid, most of which is stripped away in milling to make the white rice most of the world eats. For the acyl arm, this is the leanest home on the entire frontier. Recall the iron rule of Chapter 5: a plant can only burn as brightly as its acyl arm can build tail, and the acyl arm can only build as much tail as the

host's lipid economy will spare. A starch grain spares almost nothing. The flux model of Dynasty Rice is unambiguous and we will not soften it: the limiter is the acyl supply compounded by the endosperm sink, and the achievable heat ceiling is the *lowest* of the five organisms. Rice will carry a gentle warmth, a trace of designed heat threaded through the grain — and that is all, and that is correct. The point of Dynasty Rice was never a fierce rice. A fierce staple would be a contradiction; you cannot build a daily foundation on a shock.

RUNG (PROPOSED)	CHARACTER	TARGET IFI-H	STATUS
Vassal	barest perceptible warmth	100	target
Magnate	gentle, grain-wide	300	target
Sovereign	clearly present, still mild	550	target
Dynast	warm, cooking-stable	750	target
Celestial	top of the grain band	900	target

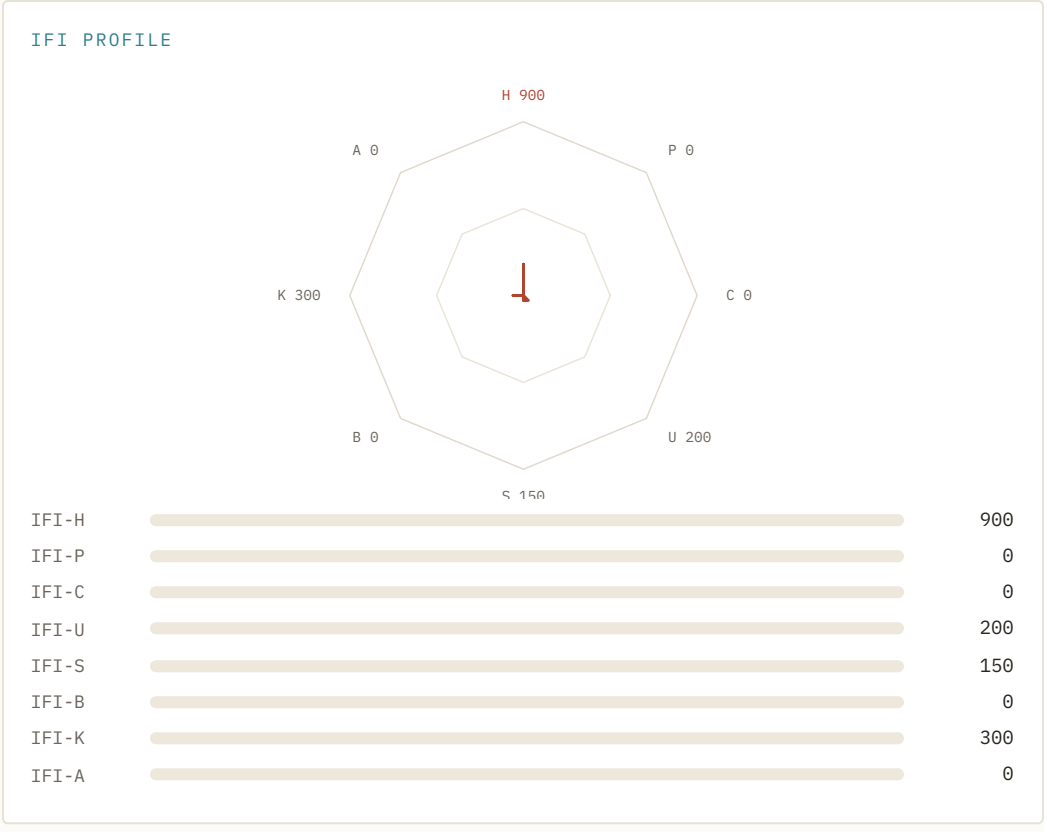


Rice grains in cross-section — the near-pure starch endosperm that makes rice the leanest acyl host on the frontier, and the aleurone and germ where what little lipid the grain holds resides.

Now the half of the chapter that matters more than the heat, and the reason rice, of all the frontier organisms, is where the nourishment ethos stops humming under the floor and stands up as the subject. There is a precedent that hangs over any attempt to engineer rice, and it is an honorable one: Golden Rice, the decades-long effort to install β-carotene — provitamin A — into the rice endosperm by adding a phytoene synthase and a carotene desaturase under an endosperm-specific promoter, so that a grain which is a nutritional near-blank could carry, grown into itself, a vitamin that its eaters' diets most lack. We study that precedent closely, for two reasons. The first is scientific: it proves that the rice endosperm, starchy and lean as it is, *can* be taught to accumulate a lipophilic, pathway-built molecule it never made before — which is precisely the capability

the acyl arm needs, and a real reason for hope on the heat side. The second is sobering: Golden Rice took the better part of two decades to move from proof to field, not because the biology was intractable but because engineering the center of the human diet rightly draws the most scrutiny, the longest review, the heaviest regulatory and social weight of anything in agriculture. That is the real content of the forty-eight-to-seventy-two-month timeline on a staple, and we will not pretend it away.

So Dynasty Rice is designed from the first day as two objectives braided into one construct, because on a staple it would be a failure of imagination and of responsibility to do otherwise. The same endosperm-specific promoters that place the gentle warmth place, alongside it, the nourishment payload — and recall from Chapter 7 that this costs us no new machinery, because the flux model that finds the heat limiter is the very same model, run with its objective swapped, that finds what the grain would have to give up to carry more of a vitamin or a more-available form of a mineral. One construct, one set of endosperm promoters, two things the grain is taught to hold: a trace of designed warmth that a cook can build on, and a measure of the nourishment that a grain which feeds billions ought, if we are touching it at all, to be made to carry. The projected top-rung envelope is modest on heat by design, and we show it as a target, with the understanding that the nourishment work travels in the same grain though it does not appear on a flavor scorecard:



A gentle heat, a little savory depth and body on U and K, nothing sharp, nothing that would make a daily bowl anything but welcoming — a warmth you could eat every day of your life. That restraint is not a limitation we are apologizing for; it is the whole design intent. Dynasty Rice is the frontier organism that taught us the clearest version of our own ethos: that when you reach the plant that feeds the most people, flavor and nourishment are not two projects but one, that you do not get to touch a staple's taste without asking in the same breath what else its daily billions of bowls could be made

to carry, and that the right warmth for the foundation of a diet is a quiet one. The dynasty the name invokes is not a dynasty of heat. It is the long, patient, generational line of a crop improved with the care a staple deserves — grown, at last, to hold a little more of everything a body draws from it.



PART IV OF IV

The Long Horizon

the forty-eight-to-seventy-two-month clock · containment and the honest label · nourishment at the scale of a staple

Chapter 14 · The forty-eight-to-seventy-two-month clock — *why the frontier takes this long.*

The single number that most shapes how the frontier is funded, staffed, and believed in is the timeline: four to six years per Tier 4 organism, against eighteen months for a Tier 1 nightshade. People who have watched modern synthetic biology move fast — a construct designed in an afternoon, synthesized in a week, expressed in a month — reasonably ask why a frontier plant should take so much longer. The answer is not that any single step is slow. It is that a frontier program is a long chain of de-risking stage gates, most of them gated not by cleverness but by the generation time of a plant and the patience of validation, and that you cannot run them in parallel because each one must pass before the next is worth attempting. This chapter lays the clock out honestly, because an investor or a reviewer deserves to see where the years actually go.



Potato — a validated Tier-2 bridgehead at 80 constructs, one of the stepping stones a frontier program stands on rather than starting cold.

The first thing to understand is that no frontier organism is ever built cold, and this is the most important risk-reduction we have. Every Tier 4 program stands on a validated bridgehead from a lower tier — a nearer organism that already solved most of the shared problems. Wildfire Broccoli and Nuclear Cabbage stand on the 380-construct broccoli and 40-construct cabbage debittering programs, which handed them the brassica transformation protocols, the aromatic-pool flux models, and the precursor-freeing edits ready-made. Storm Corn and Dynasty Rice stand on sorghum — a validated grass at 120

constructs — which proved the monocot phenylpropanoid handling, the PTAL shortcut, and the grass transformation chemistry before corn or rice were ever attempted. Deep-Earth Carrot stands on the broad root and tuber work that potato, at 80 constructs, validated. We do not climb the frontier from the ground. We climb it from the highest validated ledge below it, and the first budget line of every frontier program is the bridgehead it inherits.

With that said, here is where the clock's years go, stage by stage, and why each gate must clear before the next:

STAGE	WHAT IT ESTABLISHES	TYPICAL DURATION	WHY IT GATES
Design & model	target envelope, host flux model, the ported enzyme loop	3–6 mo	fast; all *in silico*
Construct build	the ten-to-twelve-gene cassette, synthesized and assembled	2–4 mo	fast; DNA synthesis is cheap now
Transformation & regeneration	getting the cassette into cells and whole plants back out	6–18 mo	grasses are recalcitrant; this is the first hard wall
First-generation expression	does the pathway run; does the heat appear at all	6–12 mo	gated by the plant's generation time
Flux rebalancing	finding and widening the real limiter in planta	12–18 mo	iterative; each cycle is a plant generation
Tissue & stability validation	even dosing, sequestration, CV ≤ 7%, agronomics	12–18 mo	must hold across seasons and sites
Regulatory & field	the review a novel food crop rightly draws	12–24 mo+	longest on a staple; see Chapter 15

Read down that column and the shape of the frontier becomes clear. The design and the build — the parts that feel like modern synthetic biology, the parts that are fast — are a few months at the top, and they are not where the time goes. The time goes into the plant: into the long recalcitrance of getting a cassette into a grass and a whole fertile plant back, a problem so hard that its recent solution, the use of morphogenic regulators to coax monocot cells to regenerate, was itself a landmark; into the generation-time-gated cycles of

expression and flux rebalancing, where every iteration costs a season because you cannot rush a plant to seed; into the seasons of validation a construct must survive before it earns a coefficient of variation under seven percent across real fields; and, on a staple, into the regulatory horizon that a novel food crop rightly and unavoidably draws. The frontier is not slow because we are slow. It is slow because a plant has its own clock, and because touching the food supply is a thing that *should* take long enough to be sure.

This is why the frontier is funded as a portfolio and staged as a relay, not sprinted as a single dash — and why a volume like this one exists at all. You cannot shorten a plant's generation time or a regulator's review, so you de-risk instead by sequencing: prove the brassicas on the bridgeheads you already hold, let sorghum carry the monocot risk ahead of corn, let corn carry it ahead of rice, and let the hardest and heaviest target — the staple at the center of the human diet — come last, after every nearer organism has retired a risk it would otherwise have faced alone. Dynasty Rice is the final organism in the book not only because it is the most consequential but because it is the most de-risked: by the time rice is attempted, the brassica programs have proven the eudicot install, sorghum and corn have proven the grass install, and the only genuinely new thing rice introduces is the weight of care the center of the human diet rightly carries — a weight we would rather meet last, and meet ready.

So the clock is not an obstacle the frontier is burdened with; it is the frontier's conscience, the mechanism that keeps ambition honest. Four to six years is the time it takes to be *sure* — sure the heat sits only where it belongs, sure it holds across seasons and soils, sure the plant stands through its own weather, sure the grain that will become a billion breakfasts is exactly what we say it is. We would not trade that time away if we could. A faster frontier would be a less trustworthy one, and on the food people give their children, trust is the only currency that matters. The years are the price of being allowed to touch the staples at all, and we pay them gladly, one stage gate at a time.

Chapter 15 · Containment and the honest label — *what we will and will not say.*

A frontier crop owes two separate honesties, and they are owed to two different parties. The first is owed to the field — a discipline of stewardship, that the designed trait stays exactly where we put it and does exactly what we intended, in the crop and in the edible organ and nowhere else. The second is owed to the eater — a discipline of language, that we describe what we have grown with total plainness and never once drift into a promise food cannot keep. We take both as seriously as any enzyme in the book, because a plant engineered with great care and then described with a loose tongue is a betrayal of its own making. This chapter is about the two honesties, and it is the one chapter where the method steps back and lets the values that drove it the whole way speak in their own voice.



A young line in its transplant pot under glass — the whole of frontier stewardship begins here, in keeping the trait where it belongs and proving it stays there.

Begin with the honesty owed to the field, because it is the more technical of the two and it rests on a design decision we have met in every organism chapter: tissue-specific expression. From the first construct, the heat pathway is driven by promoters that fire only in the edible organ — the floret, the head, the root, the kernel, the grain — and are silent everywhere else. This is not only a survival requirement for the plant, though it is that; it is the foundation of stewardship, because a trait that lives only in the fruit cannot be a trait that surprises you in the leaf or the pollen. On top of that

foundation sits the ordinary, well-trodden discipline of responsible crop development: controlled breeding under glass and under agreement, so the genetics stay accounted for; the reproducibility bar that runs through the entire library, a batch-to-batch coefficient of variation held at or below seven percent, which is as much a stewardship instrument as a quality one, because a trait you can reproduce to within seven percent is a trait you understand; and the openness of publishing the work — three patents filed and twenty-one peer-reviewed papers released on Zenodo under a CC BY 4.0 license, so the science is on the record where others can check it rather than locked where no one can. Containment, in the only sense this book means it, is keeping a designed flavor where it belongs and proving, in public, that it stays there.

The regulatory horizon is the second half of the field's honesty, and it is most of the clock's final stage for a reason we respect rather than resent. A novel food crop draws review — the careful, deliberate, sometimes years-long examination that any new thing entering the food supply rightly receives — and the heavier the crop's place in the human diet, the heavier and slower that review becomes. We met the archetype in the Dynasty Rice chapter: the biofortified-rice precedent took the better part of two decades to travel from a working plant to a field, and the biology was never the long pole; the scrutiny was, because scrutiny is what the center of the diet deserves. We do not treat that scrutiny as friction to be minimized. We treat it as a partner to be satisfied, and we build every frontier program to meet it — the tissue-specificity data, the compositional analysis, the stability across environments, the open publications — assembled from the first year so that when the review comes, the answers are already on the shelf. A frontier crop that cannot survive review is a frontier crop that was not finished, and we would rather know that in year five than argue with it in year six.

Now the honesty owed to the eater, which is harder than any of the field work, because it is a discipline of restraint and restraint is the thing ambition finds most difficult. The nourishment ethos runs under this entire book — the conviction, stated once and then left to hum, that if you are going to re-engineer the plants that feed people you must ask what else they could be made to carry — and here is where we draw the bright, unmovable line that keeps that conviction clean: *nourishment is an intention and a design choice, and it is never, ever a claim.* We will tell you, precisely and provably, what we grew into a plant — this measure of this vitamin, this more-available form of this mineral, this trace of designed warmth. We will not tell you what it will do to your body, because food does not make promises and neither will we. No cures. No detox. No prevention. No health halo hung on a grain of rice to make it sell. We name attributes — what is *in* the plant, measured — and we stop at the edge of the body, and we let the body do with good food what bodies have always done with good food, which is quietly, unglamorously, to be nourished by it.

This is not legal caution dressed as principle, though it keeps us right with the law; it is the principle the whole company is built on, expressed as a refusal. The clean-living sensibility that drives us to put more nourishment into a staple is the *same* sensibility that forbids us to lie about it, because a health claim is a kind of pollution — it dirties the very trust that makes nourishing food worth growing. A plant grown with reverence and then sold with a false promise has had its reverence cancelled. So the label stays honest the way the scorecard stays honest: it says what is measured and not one word more. When Dynasty Rice carries a more-available form of a mineral alongside its gentle warmth, the label will say the grain carries that mineral, in that form, in that amount — and it will let the reader, and the reader's own good sense about food, take it from there. That restraint is the most reverent thing in the book. Anyone can promise a miracle. It takes discipline, and a real respect for the person eating, to grow something genuinely better and then simply, plainly, tell the truth about it.

Chapter 16 · Nourishment at the scale of a staple — *flavor and feeding, one act.*

We have kept a promise in reserve since the opening essay, where we said that the nourishment half of this work would hum under every chapter and stand up as the subject only at the end. This is the end, and here it stands. Everything in this book — the twelve modules, the flux models, the ported enzyme loop, the five strangers taught to burn — has been, read one way, a book about flavor. Read another way, it has been a book about the one thing flavor and nourishment share, which is that they are both just *what a plant holds*, and that a method able to change what a plant holds does not get to care about taste and ignore nutrition. On the frontier, where we are installing whole pathways into the plants that feed the world, that choice is not academic. It is the difference between a clever trick and a reason to have done any of this at all.



A grain of rice in close specimen — a near-blank nutritional canvas, and for exactly that reason the highest-leverage place on Earth to grow a little more of what a body needs.

Recall the quiet mathematics we set humming in Chapter 7 and let ring in Chapter 13: the flux model that finds the heat limiter is the *same model*, run with its objective swapped, that finds the nourishment limiter. The network is one network. $\mathbf{S} \cdot \mathbf{v} = 0$ does not care whether the output you optimize toward is a capsaicinoid or a carotenoid; it will tell you, with the same honesty and the same shadow prices, what the plant would have to give up to make more of either. This is the technical heart of why flavor and nourishment are one act and not two. We do not run a flavor program and then, as

an afterthought, bolt on a nutrition program. We run one metabolic design against one genome-scale model with two objectives, and we place both payloads through the *same* tissue-specific promoters into the *same* edible organ in the *same* construct. The heat and the nourishment travel together, in one cassette, into one cell. They were always the same engineering. We simply chose to do both.

What "nourishment" concretely means on a staple has a well-trodden and honorable precedent, and it comes in three kinds. The first is *vitamins* — installing a biosynthetic route so a grain accumulates a vitamin its eaters' diets lack, exactly as the provitamin-A rice precedent did, teaching a starchy endosperm to build and hold a molecule it never made. The second is *minerals* — raising the amount of iron or zinc a grain carries, the elements whose scarcity shapes human health more than almost any other. The third, and the most underappreciated, is *bioavailability* — not how much of a nutrient a plant holds, but how much of it a body can actually absorb, which is often the binding constraint. A grain can be rich in iron and still deliver almost none, because it is also rich in phytate, the storage compound that chelates minerals and carries them straight through undigested. Lower the phytate, or shift the nutrient into a more-available chemical form, and you can double what the body draws from a grain without adding a single milligram to what the grain contains. We model all three the same way, as objectives on the one network, and we hold them to the same proof bar as the heat:

NOURISHMENT OBJECTIVE	MECHANISM (INSTALL OR TUNE)	BINDING CONSTRAINT	STATUS
Provitamin A in endosperm	install carotenoid route under grain promoter	lipid sink in a starch tissue	`target`
Iron / zinc loading	tune uptake and grain-ward transport	source-to-sink partition	`target`
Mineral bioavailability	lower phytate / shift to available form	antinutrient–nutrient balance	`target`
Protein quality	rebalance limiting amino acids	aromatic-pool competition	`target`

Every row is a target, drawn and modeled exactly like a target heat envelope, awaiting the same measured validation — and every row, note, is an *attribute*, a statement about what is in the plant, never a statement about what it will do to a person. The honest-label discipline of the previous chapter governs this table absolutely. We say the grain carries the nutrient, in the form, in the amount. We stop there.

Why the staples, and why does this matter most precisely where the heat ceiling is lowest? Because of leverage, and leverage is the whole argument for the frontier's nourishment case. A trace improvement in a luxury is a trace improvement. A trace improvement in rice is multiplied by the most-eaten plant on Earth, by the billions of daily bowls that are, for so many people, not a part of the meal but the whole of it. The crop whose starchy endosperm makes it the *hardest* host for designed heat — the leanest acyl economy, the lowest burn ceiling in the book — is the *best* host for designed nourishment, precisely because it is a near-blank canvas eaten in such staggering quantity that a small change grown into it

reaches further than any sauce or supplement ever could. Dynasty Rice carries only a gentle warmth, and we said that was by design. Here is the rest of that design: the warmth was always meant to travel beside something that matters more, and on a staple, what matters more is that the daily grain be made to hold, and to give up to the body, a little more of what a body needs.

This is where the vegetarian-first reverence that runs through the whole library arrives at its plainest statement, so we will make it plainly. We revere plants not only for the pleasure they carry but for the nourishment they are — for the fact that a plant grown to hold the most it can, and engineered so the body can draw the most from it, is the most direct kind of care one living thing can design into another. A tomato restored to its full savor and a rice grain taught to carry an available mineral are the same gesture performed at two scales: food made, on purpose, to be more fully itself and more fully good for the one who eats it. That is not a health claim. It is a reason to grow food at all, and it is the reason the frontier is worth six years an organism. The heat is the proof that the method has no outer wall. The nourishment is the point of there being no wall — that a method which can change what any plant on Earth holds should be aimed, in the same breath it is aimed at flavor, at the quiet, unglamorous, generational work of making the things that feed us hold a little more of the good they were always meant to carry.



CODA

The Long Horizon

what the frontier is for

Closing essay · The long horizon

We began at a cornfield in the grey hour before the light turns, and we love it, we said, for what it does not contain: not a molecule of fire, not the enzyme that would make one, not the gene that would encode the enzyme — sixty million years of grass that has never once tasted of warmth. We can stand in that same field now, at the end of the book, and see it differently. Not as an absence. As a coordinate. The field is a place the method has not yet reached and already knows how to walk toward, and the walking is a matter of years, not of miracles — ten genes, a ported enzyme loop, a flux model that finds the limiter, a stalk kept strong enough to stand through its own storm, and the patience to let a plant keep its own clock. That is what a frontier is, and it is why we are careful never to call it a dream. A dream has no stage gates. This has nothing but.



Dawn on the dew — the hour the long work is done in, and the only honest emblem of a horizon: not arrival, but light coming up on the distance you mean to cross.

Hold the two proofs of this book together, because between them they draw the whole shape of what we believe. Phoenix, the eight-axis pepper with a predicted 2.95 million Scoville and eighty-four percent of the design ceiling, is the proof that the ceiling is high — that when the host hands you everything, the method can take flavor as far as the tongue can follow. The five strangers of the frontier — a brassica, a leaf, a root, and two grasses — are the proof that the walls are not there: that the same method, pointed at a plant that shares nothing with a chili but the oldest inheritance all green things keep, can still install the warmth, enzyme by enzyme, from the

common road all the way to the final condensation. High ceiling, no walls. A flavor you can design to the edge of perception, grown into very nearly anything with a genome. That is the claim the frontier makes, and we have tried, in this book, to make it the way we make everything — with the mathematics shown, the targets marked as targets, the designs stated plainly as the computational predictions they are, and the reverence held exactly as tight as the rigor. These are computational designs; Scoville Splice's cultivars and constructs have not been experimentally validated in a laboratory.

But a method with no walls is a responsibility, not a trophy, and the longer we have worked out here the more plainly we have felt it. If you can change what any plant holds, then the question is no longer *can we* but *toward what* — and we have given our answer in every organism chapter and stated it outright in the last two. Toward flavor, yes: toward a designed warmth grown into the plant rather than shaken on at the end, a pleasure you can dial and build on, a staple a cook can finally lean on. But in the same breath, through the same promoters, in the same cell, toward nourishment: toward the vitamin a near-blank grain could carry, the mineral a body could finally absorb, the quiet daily good that, multiplied by the billions of bowls a staple becomes, reaches further than any luxury ever will. Flavor and feeding were always one act performed on one cell, and the frontier is where refusing to separate them stops being a philosophy and becomes a plan with a budget and a clock.

This is a family's work, and we will end on that, because it is the truest thing we know about it. The voice that carried this whole book — the *we* — is not a corporate plural; it is a table, a line of people who revere what they grow and who came to this the way families come to anything that matters, through a question that would not let them sleep. The computing was one pair of hands. The reverence, the patience, the refusal to lie on a label, the conviction that food should be grown to hold the most it can and the body helped to draw the most from it — those belong to all of us, and they are what the long horizon is made of. The frontier takes six years an organism because being sure takes six years, and we have come to love the slowness, because the slowness is where the care lives. We are not in a hurry to put fire in the staples. We are in a hurry to be *right* about it, and those are different hungers, and the second one is the one worth keeping.

So we leave the cornfield as we found it — grey, breathing, fireless, feeding most of the world exactly as it is. We are in no rush to change it. But we know, now, that we could; we know what it would take and how long and to what end; and we know that if we ever do, the warmth will not travel alone. It will travel beside a little more of everything that field was always meant to give. That is the frontier. Not a plant that burns, but a future in which the things that feed us are grown, on purpose, with reverence and with rigor, to be more fully good — and the patience, held across years and across a family, to reach it one honest coordinate at a time.

> The pepper was the proof. The staples are the point. And the horizon is not a place we arrive — it is the light coming up on the distance we have decided, together, to cross.