

The
TANGLED
TREE

A RADICAL
NEW HISTORY
of LIFE

DAVID
QUAMMEN

AUTHOR OF *SPILLOVER* AND *THE SONG OF THE DODO*

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Illustration Credits

*To Dennis Hutchinson and David Roe, my
attorneys of the soul*

THREE SURPRISES



An Introduction

Life in the universe, as far as we know, and no matter how vividly we may imagine otherwise, is a peculiar phenomenon confined to planet Earth. There's plenty of speculation and probabilistic noodling, but zero evidence, to the contrary. The mathematical odds and chemical circumstances do seem to suggest that life should exist elsewhere. But the reality of such alternate life, if any, is so far unavailable for inspection. It's a guess, whereas earthly life is fact. Some astounding discovery of extraterrestrial beings, announced tomorrow, or next year, or long after your time and mine, may disprove this impression of Earth's uniqueness. For now, though, it's what we have: life is a story that has unfolded here only, on a relatively small sphere of rock in an inconspicuous corner of one middling galaxy. It's a story that, to the best of our knowledge, has occurred just once.

The shape of this story, in its broad outlines as well as its finer details, is therefore a matter of some interest.

What happened, over the course of roughly four billion years, to bring life from its primordial origins into the fluorescence of diversity and complexity we see now? How did it happen? By what concatenation of accident and determination did it yield creatures so

wondrous as humans—and blue whales, and tyrannosaurs, and giant sequoias? We know there have been crucial transitions in evolutionary history, improbable incidents of convergence, dead ends, mass extinctions, big events, and little ones with big consequences—including some fateful contingencies that have left behind evidence of their occurrence embedded subtly throughout the fossil record and the living world. Alter those few contingencies, as a thought experiment, and everything would be different. We wouldn't exist. Animals and plants wouldn't exist. Why did it happen as it did, and not some other way? Religions have their responses to such questions, but for science, the answers must be discovered and then supported with empirical evidence, not received in a holy trance.

This book is about a new method of telling that story, a new method of deducing it, and certain unexpected insights that have flowed from the new method. The method has a name: molecular phylogenetics. Wrinkle your nose at that fancy phrase, if you will, and I'll wrinkle with you, but, in fact, what it means is fairly simple: reading the deep history of life and the patterns of relatedness from the sequence of constituent units in certain long molecules, as those molecules exist today within living creatures. The molecules mainly in question are DNA, RNA, and a few select proteins. The constituent units are nucleotide bases and amino acids—more definition of those to come. The unexpected insights have fundamentally reshaped what we think we know about life's history and the functional parts of living beings, including ourselves. In particular, there have come three big surprises about who we are—we multicellular animals, more particularly we humans—and what we are, and how life on our planet has evolved.

One of those three surprises involves an anomalous form of creature, a whole category of life, previously unsuspected and now

known as the archaea. (Their name gets uppercased when used as a formal taxonomic category: Archaea.) Another is a mode of hereditary change that was also unsuspected, now called horizontal gene transfer. The third is a revelation, or anyway a strong likelihood, about our own deepest ancestry. We ourselves—we humans—probably come from creatures that, as recently as forty years ago, were unknown to exist.

The discovery and identification of the archaea, which had long been mistaken for subgroups of bacteria, revealed that present-day life at the microbial scale is very different from what science had previously depicted, and that the early history of life was very different too. The recognition of horizontal gene transfer (HGT, in the alphabet soup of the experts) as a widespread phenomenon has overturned the traditional certitude that genes flow only vertically, from parents to offspring, and can't be traded sideways across species boundaries. The latest news on archaea is that all animals, all plants, all fungi, and all other complex creatures composed of cells bearing DNA within nuclei—that list includes us—have descended from these odd, ancient microbes. Maybe. It's a little like learning, with a jolt, that your great-great-great-grandfather came not from Lithuania but from Mars.

Taken together, these three surprises raise deep new uncertainties—and carry big implications about human identity, human individuality, human health. We are not precisely who we thought we were. We are composite creatures, and our ancestry seems to arise from a dark zone of the living world, a group of creatures about which science, until recent decades, was ignorant. Evolution is trickier, far more intricate, than we had realized. The tree of life is more tangled. Genes don't move just vertically. They can also pass laterally across species boundaries, across wider gaps, even between different kingdoms of life, and some have come sideways into our

own lineage—the primate lineage—from unsuspected, nonprimate sources. It’s the genetic equivalent of a blood transfusion or (different metaphor, preferred by some scientists) an infection that transforms identity. “Infective heredity.” I’ll say more about that in its place.

And meanwhile, speaking of infection: another result of this sideways gene movement involves the global medical challenge of antibiotic-resistant bacteria, a quiet crisis destined to become noisier. Dangerous bugs such as MRSA (methicillin-resistant *Staphylococcus aureus*, which kills more than eleven thousand people annually in the United States and many more thousands around the world) can abruptly acquire whole kits of drug-resistance genes, from entirely different kinds of bacteria, by horizontal gene transfer. That’s why the problem of multiple-drug-resistant superbugs—unkillable bacteria—has spread around the world so quickly. By such revelations, both practical and profound, we’re suddenly challenged to adjust our basic understandings of who we humans are, what has gone into the making of us, and how the living world works.

This whole radical reset of biological thinking arose from several points of origin in space and time. One among them, maybe the most crucial, deserves mentioning here: the time was autumn 1977; the place was Urbana, Illinois, where a man named Carl Woese sat with his feet on his desk, before a blackboard filled with notes and figures, posed jauntily for a photographer from the *New York Times*. The accompanying *Times* story for which the photo was shot, announcing that Woese and his colleagues had discovered “a separate form of life” constituting a “third kingdom” of biological forms in addition to the recognized two, ran on November 3, 1977. It was front page, above the fold, shouldering aside items on the kidnapped heiress Patty Hearst and an arms embargo against the apartheid regime in South Africa. Big news, in other words, whether

or not the average *Times* reader could grasp, from such a lean telling, just what was meant by “a separate form of life.” That article marked the apex of Woese’s fame, his Warhol moment: fifteen minutes of limelight, then back to the lab. Woese brought radical changes—to his own field, to the story of life—and yet he remains unknown to most people outside the rarefied corridors of molecular biology.

Carl Woese was a complicated man—fiercely dedicated and very private—who seized upon deep questions, cobbled together ingenious techniques to pursue those questions, flouted some of the rules of scientific decorum, made enemies, ignored niceties, said what he thought, focused obsessively on his own research program to the exclusion of most other concerns, and turned up at least one or two discoveries that shook the pillars of biological thought. To his close friends, he was an easy, funny guy; caustic but wry, with a love for jazz, a taste for beer and scotch, and an amateurish facility on piano. To his grad students and postdoctoral fellows and laboratory assistants, most of them, he was a good boss and an inspirational mentor, sometimes (but not always) generous, wise, and caring.

As a teacher in the narrower sense—a professor of microbiology at the University of Illinois—he was almost nonexistent as far as undergraduates were concerned. He didn’t stand before large banks of eager, clueless students, patiently explaining the ABCs of bacteria. Lecturing wasn’t his strength, or his interest, and he lacked eloquent forcefulness even when presenting his work at scientific meetings. He didn’t like meetings. He didn’t like travel. He didn’t create a joyous, collegial culture within his lab, hosting seminars and Christmas parties to be captured in group photos, as many senior scientists do. He had his chosen young friends, and some of them remember good times, laughter, beery barbecues at the Woese home, just a short walk from the university campus. But those friends were

the select few who, somehow, by charm or by luck, had gotten through his shell.

In later years, as he grew more widely acclaimed, receiving honors of all kinds short of the Nobel Prize, Woese seems also to have grown bitter. He considered himself an outsider. He was elected to the National Academy of Sciences, an august body, but tardily, at age sixty, and the delay annoyed him. He became, by some reports, distant from his family—a wife and two children, seldom mentioned in published accounts of his scientific labors. He was a brilliant crank, and his work triggered a drastic revision of one of the most basic concepts in biology: the idea of the tree of life, the great arboreal image of relatedness and diversification. For that reason, Woese's moment of triumph in Urbana, on November 3, 1977, has its place near the core of this book.

Other scientists and other discoveries are connected to Woese and his tree. A little-known British physician named Fred Griffith, for instance, in the mid-1920s, while researching pneumonia for the Ministry of Health, noticed an unexpected transformation among bacteria: one strain changing suddenly into another strain, presto, from harmless to deadly virulent. This was important in terms of public health (bacterial pneumonia was in those days a leading cause of death) but also, as even Griffith didn't realize, a clue to deeper truths in pure science.

The mechanism of Griffith's perplexing transformation remained obscure until 1944, when a quiet, fastidious researcher named Oswald Avery, at the Rockefeller Institute in New York, identified the substance, the "transforming principle," that can cause such sudden change from one bacterial identity to another. It was deoxyribonucleic acid. DNA. Less than a decade later, Joshua Lederberg and his colleagues showed that this sort of transformation, relabeled "infective heredity," is a routine and

important process in bacteria—and, as later work would show, not just in bacteria. Meanwhile, the corn geneticist Barbara McClintock, discovering genes that bounce from one point to another on the chromosomes of her favorite plant, worked with very little support or recognition through the prime years of her career—and then accepted a Nobel Prize at age eighty-one.

Lynn Margulis, a Chicago-educated microbiologist unique in almost every way, shared at least one thing with McClintock: the frustrations of being dismissed by some colleagues as an eccentric and obdurate woman. In Margulis's case, it was for reviving an old idea that had long been considered wacky: endosymbiosis. What she meant by the term was, roughly, the cooperative integration of living creatures within living creatures. That is, not just tiny creatures within the bellies or noses of big creatures, but cells within cells. More specifically, Margulis argued that the cells constituting every creature in the more complex divisions of life—every human, every animal, every plant, every fungus—are chimerical things, assembled with captured bacteria inside nonbacterial receptacles. Those particular bacteria, over vast stretches of time, have become transmogrified into cellular organs. Imagine an oyster, transplanted into a cow, that becomes a functional bovine kidney. This seemed crazy when Margulis proposed it in 1967. But she was right about the matter, mostly.

Fred Sanger, Francis Crick, Linus Pauling, Tsutomu Watanabe, and other scientists played crucial parts in this chain of events too, sometimes by force of personality as well as by scientific brilliance. Slightly deeper in the past lie obscure figures such as Ferdinand Cohn, Edward Hitchcock, and Augustin Augier, as well as more famous ones, including Ernst Haeckel, August Weismann, and Carl Linnaeus. The ghost of Jean-Baptiste Lamarck rises here again to skulk along inescapably in the shadows of evolutionary thinking.

Such people, all contributors to a scientific upheaval, are of additional interest for the ways their works grew from their lives. They serve as good reminders that science itself, however precise and objective, is a human activity. It's a way of wondering as well as a way of knowing. It's a process, not a body of facts or laws. Like music, like poetry, like baseball, like grandmaster chess, it's something gloriously imperfect that people do. The smudgy fingerprints of our humanness are all over it.

Humans aren't the only important characters in this book. There are also a lot of other living creatures, whose unique histories and foibles illustrate points in the story I'm trying to tell. Many of them are microbes—those bacteria I've mentioned, those archaea, and other teeny things. Please don't be fooled by their smallness; their implications and impacts are big. And don't be daunted by their names, which are mostly expressed in scientific Latin: *Bacillus subtilis* and *Salmonella typhimurium* and *Methanobacterium ruminantium* and other monstrous tongue twisters. The reason I call them by those names is not because I like arcane language but because no other labels exist. Microbes generally don't get the courtesy of common names at the species level, casual monikers such as southern giraffe, olive bunting, monarch butterfly, and Komodo dragon. If the bacterium known as *Haemophilus influenzae* could be accurately called Fleming's nose-tickler, I promise you I would do it.

One other featured character, of the human sort, should be introduced here. He's a bearded American microbiologist with a penchant for philosophical musing, tucked away at a university in Nova Scotia. This man has linked Carl Woese, Lynn Margulis, and much of the new work in molecular phylogenetics into a pungent challenge against biology's central metaphor. His name is Ford Doolittle. He's tall, diffident in manner though not in thought, and

enjoys causing a little intellectual discomfort. At the turn of the millennium, Doolittle published an essay titled “Uprooting the Tree of Life,” which helped release a cascade of arguments. I caught wind of him through that essay and his related writings, notably those in which he discussed horizontal gene transfer and its implications. “Horizontal what?” was my earliest thought. Then I pilgrimed to Halifax and camped for days in his office. Doolittle is semiretired, still guiding graduate students, still well funded with a prestigious research grant, but no longer growing radioactive bacteria in a lab in order to deduce bits of their genomes (the totality of their DNA) from images on chest X-ray films. He’s no longer pulling chopped molecules through electrophoretic gels, as he did in the pioneer days. He reads, he thinks, he writes, he draws. (He takes art photographs, mainly for his own amusement, and occasionally mounts a gallery show, but that’s another realm of enterprise entirely.) In fact, part of what has made Ford Doolittle so influential is that, in addition to his qualifications in biology, he writes far better than most scientists—and he draws deftly, turning big concepts into graceful, cartoony shapes. Doolittle’s father was a painter and an art professor. Young Ford considered an art career himself, though his father called that “a terrible way to make a living.” Then, when he was fifteen years old, in 1957, the Soviets put Sputnik into space, persuading Ford and many other Americans that science and engineering were the more urgent, forceful pursuits. He went to Harvard College and studied biochemistry. The artistic impulse never left him. Nowadays, to illustrate his subversive thinking and his genial provocations, he draws trees that aren’t trees.

Woese, Doolittle, Margulis, Lederberg, Avery, Griffith, and the others—they all have their roles in this story. But a more natural starting point is much earlier: London, 1837, with a very different scientist, in a very different situation.

PART I

Darwin's Little Sketch

1



Beginning in July 1837, Charles Darwin kept a small notebook, which he labeled “B,” devoted to the wildest idea he ever had. It wasn’t just a private thing but a secret thing, a record of his most outrageous thoughts. The notebook was bound in brown leather, with a tab and a clasp; 280 pages of cream-colored paper, compact enough to fit in his jacket pocket. Portable, but no toss-away pad. Its quality of materials and construction reflected the fact that Darwin was an affluent young man, living in London as a naturalist of independent means. He had arrived back in England just nine months earlier from the voyage of HMS *Beagle*.

That journey, consuming almost five years of Darwin’s life, on sea and land, mostly along the South American coastline and inland to the plains and mountains, though with notable other stops on the roundabout way home, would be the only major travel experience of his sheltered, privileged life. But it was enough. A mind-awakening and transformative opportunity, it had given him some large ideas that he wanted to pursue. It had opened his eyes to an astonishing phenomenon that demanded explanation. In a letter to his biology professor and friend John Stevens Henslow, back at Cambridge University, written from Sydney, Australia, Darwin mentioned his puzzling observations of the mockingbirds (not the finches) of the Galápagos Archipelago, a set of volcanic nubs in mid-Pacific. These gray, long-beaked birds differed from island to island but so subtly

that they seemed to have diverged from one stock. Diverged? Three kinds of mockingbird? Varying slightly, this island to that? Yes: they appeared distinct but similar, in a way that suggested relatedness. If that impression were true, Darwin confided to Henslow, confessing an intellectual heresy, “such facts would undermine the stability of species.”

The stability of species represented the bedrock of natural history. It was taken for granted, and important, not just among clergy and pious lay people but scientists too. That all the varied forms of creatures on Earth had been fashioned by God, in special acts of creation, and are therefore immutable, was an article of faith to the Anglican scientific establishment of Darwin’s era. This tenet is known as the special-creation hypothesis, though at the time, it seemed less hypothesis than dogma. It had been embraced and supported by prominent naturalists and philosophers of the scientific culture within which Darwin had been educated at Cambridge. He was now home from his wildcat voyage, a youthful adventure with a bunch of rough English sailors, about which his stern father had been skeptical at the start. The experience had altered him—though not in the ways his father may have feared. He hadn’t become a drunk or a libertine. He didn’t curse like a bosun. Darwin’s wanderlust, satisfied physically, was now intellectual. He intended to investigate, very discreetly, a radical alternative to scientific orthodoxy: that the forms of living creatures *weren’t* eternally stable, as God had created them, but instead had changed over time, one into another—by some mechanism that Darwin didn’t yet understand.

It was a risky proposition. But he was twenty-seven years old and deeply changed by what he had seen and, in a quiet way, very gutsy.

So he had set himself up in the big city, with lodgings on Great Marlborough Street, a convenient location for his visits to the

British Museum. This was just a few doors down from the house where his elder brother, Erasmus, had already settled. Darwin joined scientific clubs, the Geological Society, the Zoological Society, but had no job. Didn't need one. The same formidable father who had first disapproved of the *Beagle* voyage—Dr. Robert Darwin, a wealthy physician up in the town of Shrewsbury—was now rather proud of his second son, the young naturalist well regarded within British scientific circles. Grumpy on the outside, generous within, Dr. Darwin had made supportive arrangements for both brothers. And Charles was single. He sauntered around London, he handled follow-up tasks on his specimens from the voyage, he worked on rewriting his *Beagle* diary into a travel book, and—very privately—he ruminated about that radical alternative to special creation. He read widely, scribbling facts and phrases into various notebooks. The “A” notebook was devoted to geology. The B notebook was first of a series on what, to himself only, he called “transmutation.” You can guess what that meant. Darwin had begun thinking his way toward a theory of evolution.

He opened the B notebook, in July 1837, with a few phrases alluding to a book titled *Zoonomia; or the Laws of Organic Life*, published decades earlier by his own grandfather, another Erasmus Darwin. *Zoonomia* was a medical treatise (Erasmus was a physician), but it contained some provocative musings that sounded vaguely evolutionary. All warm-blooded animals “have arisen from one living filament,” according to *Zoonomia*, and they possess “the faculty of continuing to improve” in ways that could be passed down across the generations, “world without end!” Improvement across generations? Heritable change throughout the history of the world? That was contrary to the special-creation hypothesis, but not too surprising from a gouty, libidinous freethinker and sometime poet such as old Erasmus. Darwin had read *Zoonomia* during his

student days and shown little sign of giving his grandfather's daring ideas much credit. But now, on revisiting, he took them as a point of departure. Page one, entry one, in the B notebook: his grandfather's title, *Zoonomia*, followed by reading notes.

Then again, those wild suggestions didn't lead anywhere. Erasmus Darwin had offered no material mechanism for "the faculty of continuing to improve," and a material mechanism was what young Charles wanted, though he may not have fully realized that yet. As reflected in the B notebook, he now went from his grandfather's work to other readings, other speculations and questions, jotting down clipped phrases, often in bad grammar and punctuation. He wasn't writing to publish. These were messages to himself.

"Why is life short," he asked, omitting the question mark in his haste. Why is reproduction so important? Why do animals of a given kind tend to be constant in form across an entire country but to differ at least slightly on separate islands? He remembered the giant tortoises on the Galápagos, where his stopover had lasted only thirty-five days but catalyzed an upheaval in his thinking. He remembered the mockingbirds too. And why had he seen two distinct kinds of "ostriches" (his label for big, flightless birds now known as rheas) on the Argentine Pampas, one living north of the Rio Negro, one south of it? Did creatures somehow become different when isolated? Put a pair of cats on an island, let them breed and inbreed there for generations, with a little pressure from enemies, and "who will dare say what result," Darwin wrote. He dared. The descendants might come to look different from other cats, might they not? He wanted to understand why.

Another important question: "Each species changes. does it progress." Do the cats become *better* cats, or at least better cats for catting on that particular island? If so, how long would it take? How

far would it go? What are the logical limits, if “every successive animal is branching upwards” and with “different types of organization improving,” new forms arising, old forms dying out? That one word, *branching*, was freighted with interesting implications: of directional growth, of divergence, of an arboreal form. And these questions Darwin asked himself, they applied not just to cats and ostriches but also to armadillos and sloths in Argentina, to marsupials in Australia, to those huge Galápagos tortoises, and to the wolflike Falkland Islands fox, all peculiar in certain ways, all unique to their isolated places, but recognizably similar to their correlatives—other cats and tortoises and foxes, etcetera—elsewhere. Darwin had seen a lot. He was an acutely observant and reflective young man. He sensed that he had seen patterns, not just particulars. It almost seemed, he wrote, that there was a “law of adaptation” at work.

All this and more, facts and speculations, crammed into the first twenty-one pages of notebook B. The pages are mostly undated, so we can’t know how many days or weeks passed in the opening burst of effort. Anyway, he didn’t yet have his theory. Big ideas were coming at him like diving owls. He needed some order as much as he needed the jumble of tantalizing clues. Maybe he needed a metaphor. Then, on the bottom of page 21, Darwin wrote: “organized beings represent a tree.”

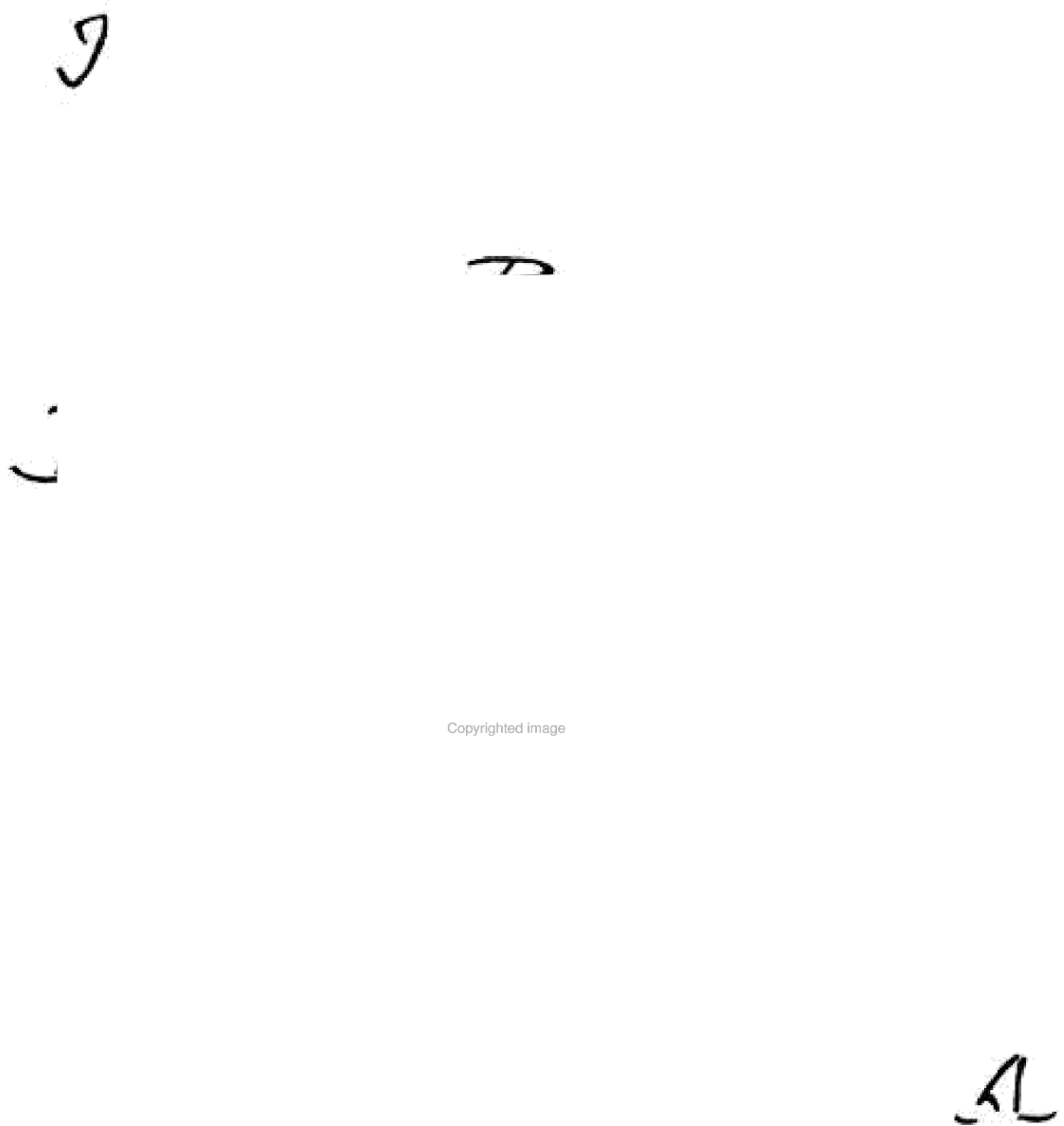
2



We don't know whether Darwin sat back after writing that statement and breathed deep with a new sense of clarity, but he might have. And he was entitled.

Then he scribbled on. The tree is “irregularly branched,” he told the B notebook, “some branches far more branched.” Each branch diverges into smaller branches, he wrote, and then twigs, “Hence Genera,” the next higher category above species, which would be the twiglets or terminal buds. Some buds die away without yielding further growth—species extinction, end of a line—while new buds appear, somehow. Although the very idea of extinction had once been problematic among naturalists and philosophers, doubted as a possibility or rejected outright on grounds that God's acts of special creation couldn't be undone, Darwin recognized that there's “nothing stranger in death of species” than in death of an individual. In fact, extinction was not just natural but necessary, making space for new species as old ones die away. He wrote: “The tree of life should perhaps be called the coral of life, base of branches dead,” ancestral forms gone. Darwin knew something about coral, having seen reefs at Keeling Atoll in the eastern Indian Ocean and elsewhere during the *Beagle* voyage. They fascinated him; he concocted a theory of how reefs are formed; and in 1842, five years after this notebook entry, he would publish a book about coral reefs. Coral seemed apt—branching coral, not brain coral or table coral, was what he had in mind—because the lower limbs and base are lifeless calcitic skeleton, left behind like extinct forms of ancient lineages as the soft polyps advance upward

like living species. But even he seems to have sensed that “the coral of life” didn’t have the same memorable ring. He drew a feeble pen sketch, on page 26 in the B notebook, of a three-branched coral of life, with dotted lines depicting the inanimate lower sections. And then he let the coral idea slide, abandoning that metaphor.



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Darwin’s 1837 sketch, redrawn by Patricia J. Wynne.

The tree of life was better. It was already a venerable notion in 1837, and Darwin could adapt it to his purposes as an evolutionary theorist—easier than inventing a new trope from scratch. Of course, to make that adaptation was to alter its meaning radically. Never mind, he took the step. Ten notebook pages along, he sketched a much livelier and more complex figure in bold strokes, with a trunk rising into four major limbs and several minor ones, each major limb diverging into clusters of branches, one branch within each cluster labeled A, B, C, D. The branches B and C were near neighbors in the treetop, within adjacent clusters, indicating close relationships among the creatures on those branches. The letter A was far away, on the opposite side of the tree’s crown, signaling a more distant relationship—but still a relationship. The letters were placeholders, meant to represent living species, or maybe genera. *Felis*, *Canis*, *Vulpes*, *Gorilla*. We don’t know exactly what he had in mind, and maybe it was nothing so specific. Anyway, this was a thunderous assertion, abstract but eloquent. You can look at the little sketch today, with its four labeled branches amid the limbs and the crown, and imagine the evolutionary divergence of all life from a common ancestor.

Just above the sketch, as though gesturing toward it bashfully, Darwin wrote: “I think.”

3



Darwin didn't invent that phrase, "the tree of life," nor originate its iconic use, though he put it to new purpose in his theory. Like so many other metaphors embedded deep in our thinking, it came down murkily, modified and reechoed, from early versions in Aristotle and the Bible. (Why do these things always go back to Aristotle? Well, that's why he's Aristotle.) In the Bible, it's a grand bookend motif, invoked in Genesis 3 just as Adam and Eve are booted out of the Garden, and reappearing at the end of Revelation, on the very last page of the King James version—excellent placement for a launch into Western culture. There in Revelation 22, verses 1–2, the authorial prophet describes his ecstatic vision of the "water of life," flowing out like a pure river from the throne of God, and beside which grows "the tree of life," bearing fruit every month, plus leaves "for the healing of the nations." This tree possibly represents Christ, supplying his leafy and fruity blessings to the world; or maybe it's grace, or the Church. The passage is opaque, and differences in translations (one tree or many?) have confused things further. The point here is simply that the "tree of life" is an ancient poetic image, a resonant phrase, variously construable, with a long presence in Western thought.

In Aristotle's *History of Animals*, written during the fourth century BCE, the tree of life is not yet a tree. It's more like a ladder of nature or—as later Latinized from his Greek—a *scala naturae*. According to Aristotle, the diversity of the natural world "proceeds" from lifeless things such as earth and fire to living creatures such as animals "little by little," in a progression so incremental that it's impossible to draw absolute lines

between one form and another. This idea remained useful throughout the Middle Ages and beyond, turning up in woodcuts during the sixteenth century as a *Great Chain of Being* or a *Ladder of Ascent and Descent of the Intellect*, which typically rose step-by-step from inanimate substances such as stone or water, to plants and then beasts, then humans, then angels, and finally to God. By that point it was a “Stairway to Heaven,” almost five centuries before Led Zeppelin.

The Swiss naturalist Charles Bonnet reverted to this linear, stair-step model as late as 1745, even while other Enlightenment thinkers and artists were allowing images of nature’s diversity to burgeon sideways with limbs and branches. Bonnet’s treatise on insects, published that year, included a foldout diagram of his “Idea of a Scale of Natural Beings,” arranged in vertical ascent from fire, air, and water, through earth and various minerals, upward to mushrooms, lichens, plants, and then sea anemones, followed by tapeworms and snails and slugs, upward further to fish and then flying fish in particular, and then birds, above which came bats and flying squirrels, then four-legged mammals, monkeys, apes, and lastly man. See the logic? Flying fish are superior to other fish because they fly; bats and squirrels exist on a higher level than birds because bats and squirrels are mammals; orangutans and humans are the best of mammals, and humans are more best than anybody. Bonnet made his living as a lawyer but much preferred studying insects and plants. He was a lifelong citizen of the Republic of Geneva, his French ancestors having been chased out of France by religious persecution, and so maybe it’s no accident that his ladder diagram culminated in people, not God.

The other notable absence from Bonnet’s scale of natural beings, besides God, are microbes. He paid no attention to microorganisms, although the pioneering Dutch microscopist Antoni van Leeuwenhoek had discovered the existence of bacteria, protozoans, and other tiny “animalcules” about seventy years earlier. We all know Leeuwenhoek’s name from our reading in high school of Paul de Kruif’s *Microbe Hunters* (a terrible book full of concocted dialogue and bogus detail, but an

influential doorway to the subject) or other storybook histories of science, though we might not remember that Leeuwenhoek was a draper in Delft who started making his own magnifying lenses in order to better inspect the thread-count of textiles. Then he turned the lenses onto other materials, out of sheer curiosity, and made astonishing discoveries: he found menageries of tiny creatures living in lake water, in rain water, in water from drain pipes, even in scrapings of crud from his own teeth.

Leeuwenhoek's revelatory observations of microbial life were reported in the journal of the Royal Society of London and became famous in scientific circles throughout Europe, but Charles Bonnet wasn't interested enough in those "very wee animals" to fit them into his rising scale—not even where they might dismissively have been slotted, somewhere between asbestos and truffles. That omission presages a lasting discomfort with placing microbes on the ladder of life or, harder still, arranging their diverse forms on the tree—and it's a discomfort to which I'll return, because it became acute in 1977.

The linear approach to depicting life's diversity was on the way out, notwithstanding Charles Bonnet's scale of nature, and being replaced by its more complicated and dimensional successor, the tree. By the late eighteenth century and the start of the nineteenth, natural philosophers (we'd call them scientists, but that word didn't yet exist) tried to classify and arrange living creatures into distinct groups and subgroups, reflecting their similarities and differences and some sort of organizing schema. The linear alignment, in order of what passed for increasing sublimity, the ladder raised toward God, was no longer satisfactory. There had been a knowledge explosion in Europe since the great age of sailing explorations began—knowledge of diverse animals, plants, and other creatures from all over the world—and scholars wanted to set that explosive abundance of new facts within hierarchical categories so that it could be easily accessed and used.

This wasn't evolutionary thinking; it was just data management. The knowledge would fill volumes (one man alone, the German naturalist

Alexander von Humboldt, published a thirty-volume account of his travels in South America), making all the more necessary an overview, an organizing principle, that could be apprehended at a glance: an illustration. But the illustrators now needed two dimensions, not one, and so the ladder turned into a trunk, and the trunk sprouted limbs, and the limbs diverged into branches. This offered more scope, sideways as well as up and down, for arranging the varied abundance of known creatures.

The tree of life was an old symbol by then, an old phrase, dating back at least to those mentions in Genesis and Revelation. The tree had also served as a model for family histories—the genealogical tree or pedigree of a German duke, for instance. Now the secularized tree became useful for organizing biology. Among the first to embrace this convention was another Frenchman, Augustin Augier, who wrote in 1801 that “a figure like a genealogical tree appears to be the most proper to grasp the order and gradation” of what concerned Augier: the diversity of plants.

Augier was an obscure citizen of the French Republic, living in Lyon, working on botany part-time; his real profession was unknown, his biographical details lost, even to a historian of Lyonnais botanists writing a hundred years later. Augier disappeared. But he left behind a book, a little octavo volume, in which he proposed a new classification of plants, “according to the order that Nature appears to have followed.” That is, a “natural order,” as opposed to an artificial classification system based merely on human whim or convenience. And in the book was a figure representing that system: his *arbre botanique* (botanical tree). Its trunk and limbs look almost as orderly and stiff as a menorah, but its sideways branching and copious leafing suggest a rife multiplicity of plant forms.

Again, this didn't imply any heretical ideas about origins. Augier was no evolutionist before his time. His natural order wasn't meant to suggest that all plants had descended from common ancestors by some sort of material process of transformation. God was their maker, shaping the varied forms individually: “It appears, and one can hardly doubt it, that

the Creator, when making flowers, followed certain proportions and progressions in the number of their different parts.” Augier’s contribution, as he saw it, was discovering those proportions and progressions—design principles that had satisfied the Deity’s neat sense of pattern—and using them after the fact to organize botanical knowledge into a tidy system.

Augier wasn’t the first naturalist to hanker for a natural order of nature’s diversity. Aristotle had classified animals as “bloodless” and “blooded.” In the first century of our era a Greek physician named Dioscorides, attached to the Roman army, gathered lore on more than five hundred kinds of plants, arranging them in a compendium mainly on the basis of their medicinal, edible, and perfumatory uses. That book, in various reprints and translations, served as a trusted botany text for the next fifteen hundred years. Toward the end of its run, around the time of the Renaissance, as people traveled more widely and paid closer attention to the empirical details of nature, old Dioscorides gave way to newer illustrated herbals. These were essentially field guides to botany, graced with better illustrations based on improvements in drawing and woodcut techniques, but still organized for convenience of use, not natural order. In the sixteenth century, Leonhart Fuchs produced one of those books, an herbal cataloging hundreds of plants, beautifully illustrated and arranged in alphabetical order. Two centuries later, the great systematizer Carl Linnaeus described a genus of plants with purplish red flowers, naming it *Fuchsia* in honor of Leonhart Fuchs (and hence we got also the color, fuchsia). Linnaeus himself, a Swede who traveled widely as a young man and then took up a professorial life in Uppsala, emerged from this herbalist tradition but went beyond it.

Augier's *Arbre Botanique*, 1801.

Linnaeus's *Systema Naturae*, as first published in 1735, was a unique and peculiar thing: a big folio volume of barely more than a dozen pages, like a coffee-table atlas, in which he outlined a classification system for all the members of what he considered the three kingdoms of nature: plants, animals, and minerals. Notwithstanding the inclusion of minerals, what matters to us is how Linnaeus viewed the kingdoms of life.

His treatment of animals, presented on one double-page spread, was organized into six columns, each topped with a name for one of his classes: Quadrupedia, Aves, Amphibia, Pisces, Insecta, Vermes. Quadrupedia was divided into several four-limbed orders, including Anthropomorpha (mainly primates), Ferae (doggish forms such as wolves and foxes, plus cat forms such as lions and leopards, in addition to bears), and others. His Amphibia encompassed reptiles as well as amphibians, and his Vermes was a catchall group containing not just worms, leeches, and flukes but also slugs, sea cucumbers, starfish, barnacles, and other sea animals. He divided each order further into genera (with some recognizable names such as *Leo*, *Ursus*, *Hippopotamus*, and *Homo*), and each genus into species. Apart from the six classes, Linnaeus also gave a half column to what he called Paradoxa: a wild-card assemblage of mythic chimeras and befuddling but real creatures, including the unicorn, the satyr, the phoenix, the dragon, and a certain giant tadpole (*Pseudis paradoxa*, under its modern label) that, strangely, paradoxically, shrinks during metamorphosis into a much smaller frog. Across the top of the chart ran large letters: CAROLI LINNAEI REGNUM ANIMALE. His animal kingdom. It was a provisional effort, grand in scope, integrated, but not especially original, to make sense of faunal diversity based on what was known and believed at the time. Then again, animals weren't Linnaeus's specialty.

Plants were. His classification of the vegetable kingdom was more innovative, more comprehensive, and more orderly. It became known as the "sexual system" because he recognized that flowers are sexual

structures, and he used their male and female organs—their stamens and pistils, those delicate little stems sticking up to present and receive pollen—for characterizing his groups. Linnaeus defined twenty-three classes, into which he placed all the flowering plants, based on the number, size, and arrangement of their stamens. Then he broke each class into orders, based on their pistils. To the classes, he gave names such as Monandria, Diandria, and Triandria (one husband, two husbands, three husbands), and, within each class, ordinal names such as Monogynia, Digynia, and Tryginia (numbers of wives, yes, you get the idea), thereby evoking all sorts of polygamous and polyandrous ménages that must have caused lewd smirks and disapproving scowls among his contemporaries. A plant of the Monogynia order within the Tetrandria class, for instance: one wife with four husbands. Linnaeus himself seems to have enjoyed the sexy subtext. And it didn't prevent his botanical schema from becoming the accepted system of plant classification throughout Europe.

Our man Augustin Augier, coming along a half century later with his botanical tree of classification, seems to have seen himself challenging Linnaeus's overly neat sexual system. "Stamen number is a striking character," Augier conceded, but "not when it comes to the examination of plants"—that is, not always unambiguous and therefore not reliable as a basis for organizing the great jumble of botanical life. He nodded respectfully to Linnaeus—also to the French botanist Joseph Pitton de Tournefort, who had sorted plants into roughly seven hundred genera based on their flowers, their fruits, and other bits of their anatomy—and offered his own system, using multiple characters for different levels of sorting and to resolve the ambiguities and fine gradations. "This figure, which I call a *botanical tree*, shows the agreements which the different series of plants maintain amongst each other, although detaching themselves from the trunk; just as a genealogical tree shows the order in which different branches of the same family came from the stem to which they owe their origin." All discrete, yet all connected: bits of the same tree.

But they weren't connected, in Augier's mind, by descent from shared ancestors. Despite the hint he gave to himself in his language about family trees—all branches divergent from “the stem to which they owe their origin”—there is no evidence in Augier's writing or his tree figure that he had embraced, or even imagined, the idea of evolution.



That idea was coming soon, and, with its arrival, the tree of life would change meaning. The change was drastic, soul shaking to many people who lived through it, because it reflected a challenge to faith, and it met strong resistance. Jean-Baptiste Lamarck, France's great early evolutionist, and Edward Hitchcock, an American who prided himself a "Christian geologist," are the two scientists whose works—and whose graphic illustrations—best reflect how tree thinking shifted during the decades before Darwin unveiled his theory of evolution.

Lamarck was a protean figure: a soldier from a family of soldiering minor nobility who transformed himself into a botanist, then into a professor of zoology at the Muséum National d'Histoire Naturelle in Paris, to which he was appointed in 1793, on the eve of the Reign of Terror. His title at the museum put him in charge "of insects, of worms, and microscopic animals," three categories of life he had never studied, but he adapted fast, and even invented the word *invertebrates* to cover them. He abandoned plants and studied his invertebrates through the grimmest days of the French Revolution, earning a measly salary but at least keeping his head, as other scientists such as Antoine-Laurent Lavoisier went to the guillotine. Lamarck had probably helped his standing among the revolutionaries back in 1790 while employed at what was then the Jardin du Roi, when he urged dropping the royal label and renaming

that institution the Jardin des Plantes. Clearly, he had good political instincts. He held the conventional view of species—that they were fixed forever and created by God—until 1797, but then his views changed, possibly as a result of his study of fossil and living mollusks, which seemed to show patterns of gradual transformation. He came out as an evolutionist on May 11, 1800, in his first lecture for the year's course on invertebrates. After that, he published three major works on evolutionary zoology, the most influential being his *Philosophie Zoologique* in 1809.

Lamarck outlived four wives and three of his seven children, living beyond the revolution, through the Napoleonic era and most of the Bourbon Restoration, a handsome man with a downturned mouth, balding slowly across his pate, blind for his final ten years, his faithful daughter, Cornélie, giving her life to him and reading him French novels. He died at eighty-five and was eulogized by important colleagues such as Geoffroy St. Hilaire, after which things didn't go so well: his remains were interred at the Montparnasse Cemetery in a common trench, not a permanent individual plot, and because such burial trenches were regularly recycled, his bones may have ended up in the Paris catacombs, along with those of thousands of paupers and other neglected folk. There was no Lamarck grave to visit. He became, according to one biographer, rather quickly “forgotten and unknown.” His fame would return, if not immediately, but still it was a cold finish for the world's first serious evolutionary theorist.

Lamarck nowadays is commonly associated with what his name came to represent: Lamarckism, an easy but imprecise label for the idea of the inheritance of acquired characteristics. Many people are vaguely aware of him as a predecessor to Darwin; he is seen as a forerunner whose theory was provocative but wrong, refuted by later evidence because it depended, as Darwin's did not, on that

Oiseaux.

Monotrèmes.

M. Amphibies.

M. Cétacés.

M. Ongulés.

M. Onguiculés.

Lamarck's tree of dots, 1809.

It came back into fashion during the late nineteenth century, when the general idea of evolution gained acceptance but the crucial details of Darwin's particular theory, offering natural selection as the primary mechanism, were widely rejected. Natural selection just seemed too mechanistic, too stark and unguided, and many evolutionists found it unpalatable. This situation went on for decades—the world accepting Darwin's idea of evolution but not his explanation of how it occurs—though only historians remember that now. Lamarckism became neo-Lamarckism and seemed a less nihilistic alternative. It has continued to linger as a dubious but ineradicable notion—embodied in that single tenet, the inheritance of acquired characteristics—enjoying small surges of reconsideration even down to the present day.

But that single tenet was never Lamarck in totality. He had other ideas, some even worse. He believed in spontaneous generation. He disbelieved in extinction, at least as a natural process. He argued that “subtle fluids,” surging through the bodies of living creatures, helped reshape them adaptively.

In one of his earlier botanical works, before the shift to animals and the epiphany about evolution, Lamarck had arranged plants in what he called “the true order of gradation”: from least perfect and complete to most, ascending along an old-fashioned ladder of life. He matched that with a separate ladder for animals, a “counterpart” arrangement, showing an ascending series of forms: from worms, through insects, through fish and amphibians and birds, to mammals. Neither of those ladders hinted at divergence from common ancestors or transformation. But in the 1809 book *Philosophie Zoologique*, he included a different sort of figure, subtle yet dramatic, depicting animal diversity. It was a branched diagram, descending down the page, with major animal groups connected by dotted lines, like one of those connect-the-dots games for kids on the paper placemats at a pancake house. Connect the dots and discover that the secret shape is . . . an airplane! Or . . . an elephant! Or . . . George Washington’s head! In Lamarck’s dotted figure, the secret shape was a tree.

Birds sat perched on a branch divergent from reptiles. Insects had diverged from the main trunk before it yielded mollusks. Walruses and other marine mammals lay farther along that trunk, beyond which still other branches led to whales, then to hoofed mammals, and finally to all other mammals. Wrong though it was about the particulars, and despite being upside down, this figure marked an important transition in scientific thought. Scholars tell us that it was the earliest evolutionary tree.

5



Edward Hitchcock stands as a counterpoint to Lamarck, with that first evolutionary tree, in that Hitchcock offered a last *pre*-evolutionary tree in the decades before Darwin changed everything. In fact, Hitchcock presented two separate trees of life, one for animals, one for plants, in his 1840 book *Elementary Geology*, which became a successful and often-reprinted text in the mid-nineteenth century. Hitchcock's trees were also innovative—among the first based on deep knowledge of fossils, not just close observation of living creatures. He called his illustration a “Paleontological Chart,” and what it shows is diversification of the animal and plant kingdoms charted against geological time, from the Cambrian period (beginning about 540 million years ago) to the present.

Hitchcock's trees weren't classically tree shaped, spreading outward into a canopy like a maple or an oak. Each of the two, the one for animals and the one for plants, looks more like a windbreak of tightly placed Lombardy poplars grown to maturity along a roadway. The base of each windbreak is a thick, solid trunk from which rise slender stems, fluffy with foliage but without much branching as they ascend. Vertical, parallel, they seem independent: crustaceans, worms, bivalves, vertebrates. The vertebrate stem does branch into several shafts. The shaft leading up to modern mammals culminates in the word *Man*, atop which sits a regal crown adorned by a cross.

The crowned “Man,” with its cross, tells us what we need to know about Hitchcock’s sense of hierarchy in the living world. He grounded his geology firmly within the tradition known as natural theology, meaning science purposed to illuminate the power and wisdom of God as creator of all, with humans as the culmination of that divine creativity. He was a devout, driven New England Yankee, and his “Paleontological Chart” reflected his view of humans as the apogee of creation, as well as his findings in geology.

Hitchcock was born to a poor family in Deerfield, Massachusetts, his father a Revolutionary War veteran and a hatter by trade, with debts and three sons, who found just enough money to see his boys through primary school and some time at the local academy. After that, as Hitchcock recalled, “nothing was before me but a life of manual labor.” He balked at the idea of apprenticing as a hatter, to his father, or in any other trade. Instead he worked on a farm—it was rented land, cropped by one of his brothers—for a period that stretched on so long, or what felt like so long, that later he claimed not to remember how many years. With his free time, especially rainy days and evenings, young Edward studied science and the classics. Ambitious and hungry, he thought he was preparing himself for Harvard. Under the influence of an uncle, he took up astronomy. Then came the great comet of 1811, a celestial passerby that reached its peak of brightness in the north sky during autumn that year, when Hitchcock was eighteen. He borrowed some instruments from Deerfield Academy and spent night after night measuring its progress. “I gave myself to this labor so assiduously that my health failed,” he wrote later.

The health crisis brought on a religious conversion: from Unitarianism, into which he had drifted, back to the Congregationalism of his father. That passed for a drastic rethink in Edward Hitchcock’s life. In lieu of Harvard, he returned to

Deerfield and somehow got hired, at age twenty-three, as principal of the academy. Then he studied for the ministry, was ordained, and became pastor of a Congregationalist church in Conway, Massachusetts, just up the road from Deerfield. Throughout these years and for the rest of his life, Hitchcock remained an invalid in self-image if not bodily, obsessed with his own fragility, continually complaining that he felt death nearby, although he lived to be seventy. One scholar, having looked into his life and work, called him “a hypochondriac of the first rank.”

Hitchcock’s “Paleontological Chart,” 1857 version.

Conveniently for his scientific career, he was “dismissed” from the Conway pastorate in autumn 1825 on the grounds of impaired health and imminent death if (according to his own worried judgment) he didn’t stop preaching, circuiting the parish, and running revivals. Amherst College, recently founded, hired him to teach chemistry and natural history, and he stayed there the rest of his life, serving later as professor of natural theology and geology, and for one nine-year stretch also as president. The early years of Hitchcock’s career at Amherst spanned the period when Charles

available niches. If that doesn't quite make sense, don't blame Charles Lyell or me.

Hitchcock's *Elementary Geology* was a hit. Between 1840 and the late 1850s, it went through thirty editions, to which he made minor revisions of language and data. Throughout all those editions, the trees figure remained—unchanged except for color adjustments. Then something happened. As a consequence of that something, or else by improbable coincidence, the thirty-first edition of Hitchcock's book, in 1860, contained a notable difference. An omission. No trees.

What happened was that in 1859 Charles Darwin published *On the Origin of Species*. His book also contained a tree, but one with dangerous new meaning.

6



By that point, Darwin had incubated his theory in secret for half a lifetime. After sketching his little tree into the B notebook in 1837, he had continued reading, gathering facts, pondering patterns, trying out phrases, brainstorming fervidly for another sixteen months in a series of such notebooks, labeled “C” and “D” and “E,” like a man pushing puzzle pieces around on a table. Then suddenly, in November 1838, as recorded in the E notebook, he solved the puzzle of *how* species must evolve. Combining three pieces in his mind, he hit upon an explanatory mechanism for evolution.

The first piece was hereditary continuity. Offspring tend to resemble their parents and grandparents, providing a stable background of similarity throughout time. The second factor, a countertrend to the first, was that variation does occur. Offspring don't *precisely* resemble their parents. Brown eyes, blue eyes, taller, shorter, differences of hair color or nose shape among humans; wing markings in a butterfly, beak size in a bird, length of neck in a giraffe. Reproduction is inexact. Likewise, siblings, as well as parents and offspring, differ from one another. Darwin saw that these two pieces, heredity and variation, stand together in some sort of dynamic tension.

The third puzzle piece, which he had begun considering just recently, having been alerted to it by his eclectic reading, was that population growth always tends to outrun the available means of

subsistence. Earth is always getting too full of life. One female cat may give birth to five kittens; one rabbit may deliver eight bunnies; one salmon may lay a thousand eggs. If all those offspring were to survive, and reproduce in their turns, there would soon be a very great lot of cats and bunnies and salmon. Whatever the litter size, whatever the lifetime fecundity, whatever the kind of organism, including humans, we all tend to multiply by geometric progression, not just by arithmetic increase—that is, more like 2, 4, 8, 16 than like 2, 3, 4, 5. Meanwhile, living space and food supply don't increase nearly so quickly, if at all. Habitat doesn't replicate itself. Places get crowded. Creatures go hungry. They struggle. The result is competition and deprivation and misery, winners and losers, unsuccessful efforts to breed and, for the less fortunate individuals, early death. Many are called, but few are chosen. The book that awakened Darwin to this reality was *An Essay on the Principle of Population*, by a severely logical clergyman and scholar named Thomas Malthus.

Malthus's gloomy treatise was first published in 1798. It went through six editions in the next three decades and influenced British policy on welfare. (It argued against the relatively easy charity of the contemporary Poor Laws, which were soon changed.) Darwin read it in early autumn 1838—"for amusement," as he recalled later. Seldom is amusement more productive. He came away with the population piece, combined that with his two other pieces, and scribbled an entry in his D notebook about "the warring of the species as inference from Malthus." Yes, this "warring" applied not just to humans, Darwin realized, but also to other creatures. Competition was fierce, and opportunities were finite. "One may say there is a force like a hundred thousand wedges," Darwin wrote, all trying to "force every kind of adapted structure" into the gaps in the economy of nature. "The final cause of all this wedgings," he

added, “must be to sort out proper structure & adapt it to change.” By “final cause,” he essentially meant final result: the struggle yielded well-adapted forms. That was the essence, though still inchoate and crudely stated.

Darwin seemed to leave Malthus behind as he finished the D notebook, but returned to him soon in the next. That one, labeled E, begun in October 1838, was bound in rust-brown leather, with a metal clasp. It’s one of the true relics in the history of biology. In its earlier pages, Darwin ruminated further about “the grand crush of population” and alluded repeatedly to what he now called “my theory.” He was growing more confident and clear. Then, on or soon after November 27, with his usual clipped grammar and eccentric punctuation, he wrote:

Three principles, will account for all

1. Grandchildren, like, grandfathers
2. Tendency to small change . . . especially with physical change
3. Great fertility in proportion to support of parents

Inheritance, variation, overpopulation. He saw how they fit. Put those three together and turn the crank: you’ll get differential survival, based on something or other. Based on what? Based on which variations turn out to be most advantageous. And those variations will tend to be inherited. The result will be gradual transmutation of heritable forms, and adaptation to circumstances, by a process of selective culling. Eventually he gave the crank a name: natural selection.

Twenty years passed after the E notebook entry. The world heard nothing about natural selection.



It was a perplexingly long delay, almost two decades, between the writing of those four lines in his secret E notebook and the first public announcement of Darwin's theory. Longer still, twenty-one years, to publication of the theory in book form—*On the Origin of Species* appeared in November 1859. The reasons for that delay, which were both scientific and personal, both anxious and tactical, have been minutely examined in other works (including some of mine). We can skip over them here except to note that, when Darwin finally went public with his theory, it was because a younger naturalist had forced his hand by coming forward with the same idea.

Alfred Russel Wallace, after four years of fieldwork in the Amazon and four more in the Malay Archipelago, had hit upon the notion of natural selection (framed in his own language, not that pair of words) and written it up in a short paper. As recounted by Wallace long afterward, the idea came during a layover in his collecting travels through the northern Moluccas. He suffered a bout of fever (maybe malarial), and, amidst it, he had this extraordinary insight. Variation plus overpopulation, minus the unsuccessful variants, would yield heritable adaptation. When the fever broke, and the sweat dried, and the dreamy brainstorm still seemed cogent, Wallace composed his manuscript and then tried to get it considered.

evolution (though not to natural selection as the prime mechanism). It was translated and embraced in other countries, especially Germany. That's why Darwin is still history's most venerated biologist and Alfred Russel Wallace is a cherished underdog, famous for being eclipsed, to the relatively small subset of people who have heard of him.

The crux of the "one long argument" comes in chapter 4 of *The Origin*, titled "Natural Selection," in which Darwin describes the central mechanism of his theory. It's the same combination of three principles that he had scratched into his notebook two decades earlier, plus the turned crank. "Natural selection," he wrote in the book, "leads to divergence of character and to much extinction of the less improved and intermediate forms of life." Lineages change over time, he stated. You could see that in the fossil record. Different creatures adapt to different niches, different ways of life, and thereby diversify into distinct forms and behaviors. Transitional stages disappear. Then he wrote: "The affinities of all the beings of the same class have sometimes been represented by a great tree. I believe this simile largely speaks the truth."

8

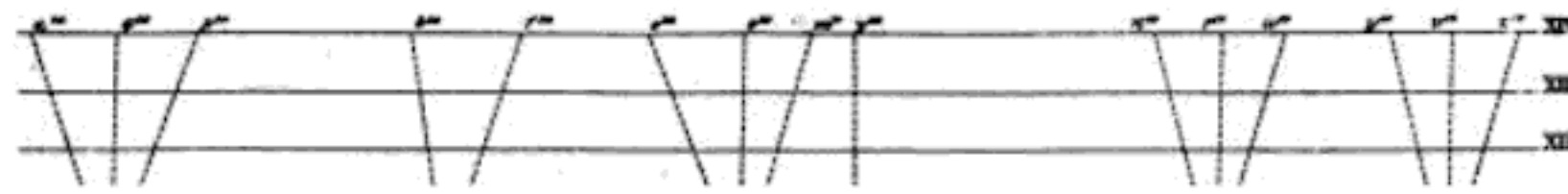


Darwin explored the tree simile in one extended paragraph, ending that chapter of *The Origin*. “The green and budding twigs may represent existing species,” he wrote. From there he worked backward: woody twigs and small branches as recently extinct forms; competition between branches for space and for light; big limbs dividing into branches, then those into lesser branches; all ascending and spreading from a single great trunk. “As buds give rise by growth to fresh buds,” Darwin wrote, and those buds grow to be twigs, and those twigs grow to be branches, some vigorous, some feeble, some thriving, some dying, “so by generation I believe it has been with the great Tree of Life, which fills with its dead and broken branches the crust of the earth, and covers the surface with its ever branching and beautiful ramifications.” There’s a nice word: *ramifications*.

It’s especially good in this context because, while the literal definition is “a structure formed of branches,” from the Latin *ramus*, of course the looser definition is “implications.” Darwin’s tree certainly had implications.

Furthermore his book, like Edward Hitchcock’s, included a treelike illustration. This was the *only* illustration, the only graphic image of any sort, in the first edition of *The Origin*. It appeared between pages 116 and 117, amid his discussion of how lineages diverge over time. A foldout, again like Hitchcock’s, but published

in simple black and white. It was a schematic figure, not an artfully drawn tree, not even so lively as the little sketch in his notebook long ago. Darwin called it a diagram. It showed hypothetical lineages, proceeding upward through evolutionary time and diverging—that is, dotted lines, rising vertically and branching laterally. Darwin was no artist, but, even lacking such talent, he could have laid out this diagram with a pencil and a ruler. In its draft version, as sent to the lithographer, he probably had. But it made the arboreal point.



Darwin's diagram of divergence, from *On the Origin of Species*, 1859.

Each increment of vertical distance on the ruled page, Darwin explained, stood for a thousand generations of inheritance. Deep time. Eleven major lineages began the ascent. Eight of those came to dead ends—meaning, they went extinct. Trilobites, ammonites, ichthyosaurs, and plesiosaurs had all suffered such ends, leaving no descendants of any sort. One lineage rose through the eons without splitting, without tilting, like a beanstalk—meaning that it persisted through time, unchanged. That's much the way horseshoe crabs, sometimes called living fossils, have survived relatively unchanged (at least externally, so far as fossilization can show) over 450 million years. The other two lineages, dominating the diagram, branched often and spread horizontally—as well as climbed vertically. Their

branching and horizontal spread represented the exploration of different niches by newly evolved forms. So there it all was: evolution and the origins of diversity.

Back in Massachusetts, Edward Hitchcock read Darwin's book, and it stuck in his craw. This wasn't his first exposure to the idea of transmutation (he knew of Lamarck's work and some other wild speculations), but it was the latest statement of that idea, the most concrete and logical, and therefore the most dangerously persuasive. Like some other pious scientists who chose to see God's hand acting directly in the fossil record—Louis Agassiz at Harvard, François Jules Pictet in Geneva, and Adam Sedgwick, who had been Darwin's mentor in geology at Cambridge—Hitchcock wasn't pleased.

Into the 1860 edition of his *Elementary Geology*, he inserted his rejoinder to Darwin's book, based mainly on proof by authority. He noted that Pictet saw no evidence for transmutation in the fossil record of fishes. Agassiz said that the resemblances among animals derive from—where?—the mind of the Creator. "It is well to take heed to the opinions of such masters in science," Hitchcock wrote, "when so many, with Darwin at their head, are inclined to adopt the doctrine of gradual transmutation in species."

That was mild but firm, a dismissive shrug. Hitchcock would ignore Charles Darwin and encourage his readers to do likewise. More telling, more defensive, was his other response: he removed the trees figure from his own book. No more Paleontological Chart. It seems never to have appeared in another edition of *Elementary Geology*.

Darwin and Darwin's followers owned the tree image now. It would remain the best graphic representation of life's history, evolution through time, the origins of diversity and adaptation, until the late twentieth century. And then rather suddenly a small group of scientists would discover: oops, no, it's wrong.

PART II

A Separate Form of Life

acids, and proteins—often collectively called the molecules of life. Proteins might be the most versatile, serving a wide range of structural, catalyzing, and transporting functions. Their piecemeal production, and the controls on the process of building and using them, are encoded in DNA. Every protein consists of a linear chain of amino acids, folded upon itself into an elaborate secondary structure. Although about five hundred amino acids are known to chemistry, only twenty of those serve as the fundamental components of life, from which virtually all proteins are assembled. But what sequences of the four bases determine which amino acids shall be added to a chain? What combination of letters specifies leucine? What combination produces cysteine? What arrangement of A, C, G, and T delivers its meaning as glutamine? What spells tyrosine? This fundamental matter—how do bases designate aminos?—became known as “the coding problem,” to which Francis Crick addressed himself in the late 1950s. Solving it was a crucial step toward understanding how organisms grow, live, and replicate.

There were questions within questions. Do the bases work in combinations? If so, how many? Two-base clusters, selected variously from the group of four and in specified order (CT, CG, AA, and so on) would allow only sixteen combinations, not enough to code twenty amino acids. Then maybe clusters of three or more? If three (such as CTC, CGA, AAA), do those triplets overlap one another, or do they function separately, like three-letter words divided by commas? If there are commas, are there periods too? Four letters, in every possible combination of three, yield sixty-four variants. Are all sixty-four possible triplets used? If so, that implies some redundancy; different triplets coding for the same amino acid. Does the code include a way of saying “Stop”? If not, where does

one gene end and another begin? Crick and others were keen to know.

Crick himself had also started thinking beyond that problem, to the question of how proteins are physically assembled from the coded information, with one amino acid brought into line after another. How does the template strand find or attract its amino acids? How do those units become linked? He wanted to learn not just the language of life—its letters, words, grammar—but also the mechanics of how it gets spoken: its equivalent of lungs, larynx, lips, and tongue.

Crick was back in England by the mid-1950s, after a sojourn in the United States, and based again at the Cavendish Laboratory in Cambridge, where he had worked with Jim Watson. He had a contract with the Medical Research Council (MRC), a government agency with some mandate for fundamental as well as medical research. Solving the DNA structure, though it had brought scientific fame to Crick and Watson and would eventually bring the Nobel Prize, provided no immediate cure for Crick's dicey financial situation, all the more acute since the birth of his and his wife Odile's third child. He had to work for pay: a modest salary from the MRC and whatever small change the occasional radio broadcast or popular article might bring. Now he was sharing his office, his pub lunches, his fevered conversations, and his blackboard with another scientist, Sydney Brenner, rather than with Watson. One colleague at the Cavendish, upon early acquaintance with Crick, concluded that "his method of working was to talk loudly all the time." When not talking, or listening to Brenner, he spent his time reading scientific papers, rethinking the results of other researchers, combing through such bodies of knowledge for clues to the mysteries that engaged him. He was not an experimentalist, generating data. He

was a theoretician—probably the century’s best and most intuitive in the biological sciences.

Sometime in 1957 Crick gathered his thoughts and his informed guesses on this problem—about how DNA gets translated into proteins—and in September he addressed the annual symposium of the Society for Experimental Biology, convened that year at University College London. His talk “commanded the meeting,” according to one historian, and “permanently altered the logic of biology.” The published version appeared a year later, in the society’s journal, under the simple title “On Protein Synthesis.” Another historian, Matt Ridley, in his short biography of Crick, called it “probably his most remarkable paper,” comparable to Isaac Newton’s *Principia* and Ludwig Wittgenstein’s *Tractatus*. It was a commanding presentation of insights and speculations about how proteins are built from DNA instructions. It noted the important but still-fuzzy hypothesis that RNA (ribonucleic acid), the *other* nucleic acid, which seemed to exist in DNA’s shadow, is somehow involved. Might RNA play a role in manufacturing proteins, possibly by helping express the order (coded by DNA) in which amino acids are linked one to another? Amid such ruminations, Crick threw off another idea, almost parenthetically: ah, by the way, these long molecules could also provide evidence for evolutionary trees.

As published in the paper: “Biologists should realize that before long we shall have a subject which might be called ‘protein taxonomy’—the study of the amino acid sequences of the proteins of an organism and the comparison of them between species.”

He didn’t use the words “molecular phylogenetics,” but that’s what he was getting at: deducing evolutionary histories from the evidence of long molecules. Comparing slightly different versions of essentially the same protein (such as hemoglobin, which transports

oxygen through the blood of vertebrates), as found in one creature and another, could allow you to draw inferences about degrees of relatedness between them. Those inferences would be based on assuming that the variant hemoglobins had evolved from a common ancestral molecule and that, over time, in divergent lineages, small differences in the amino sequences would have crept in, by accident if not by selective advantage. The degree of such differences between one hemoglobin and another should correlate with the amount of time elapsed since those lineages diverged. From such data, Crick suggested, you might draw phylogenetic trees. Humans have one variant of hemoglobin, horses have another. How different? How long since we shared an ancestor with horses? It could be argued, Crick added, that protein sequences also represent the most precise observable register of the physical identity of an organism, and that “vast amounts of evolutionary information may be hidden away within them.”

Having tossed off this fertile suggestion, Crick returned in the rest of the paper to his real subject: how proteins are manufactured in cells. That was his way. A passing thought, with the heft of a beer truck. Essentially he had said: Look, *I'm* not pursuing this protein taxonomy business, but *somebody* should.

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Somebody did, though not immediately. Seven years passed, during which several other scientists began noodling along various routes that would lead to a similar idea. Two of them were Linus Pauling and Emile Zuckerkandl, who gave their own fancy name to the enterprise—they called it “chemical paleogenetics”—and they converged on it by very different trajectories.

Zuckerkandl was a young Viennese biologist whose family had escaped Nazi Europe via Paris and Algiers. He got to America, did a master’s degree at the University of Illinois (long before Carl Woese would arrive there), then returned to Paris after the war for a doctorate. He found work at a marine laboratory on the west coast of France and studied the molting cycles of crabs, which involve a molecule analogous to hemoglobin. His interest drifted from crustacean physiology to questions at the molecular level, and he hankered to return to America. In 1957 Zuckerkandl finagled a chance to meet Pauling, who by then was a celebrated chemist with the first of his two Nobel Prizes already won. The prize had given Pauling some latitude to expand his own range of concerns, from lab chemistry at the California Institute of Technology to the wider world, and some leverage in pursuing those concerns. He had two in particular: genetic diseases such as sickle cell anemia and the threats posed by thermonuclear weapons, including radioactive fallout from testing. By the late 1950s, Pauling was raising his voice. He

lineages split, what the ancestral molecules must have looked like, and what were the lines of descent. The first of those three kinds of information became known as the molecular clock, although Zuckerkandl and Pauling hadn't yet named it. The third kind implied trees.

Zuckerkandl continued reworking and developing these ideas, with Pauling as his coauthor and sponsor. In September 1964, before a distinguished and argumentative symposium audience at Rutgers University, he delivered a long paper that became the definitive version of their shared ideas and that, despite Zuckerkandl having done most of the writing, has been called the “most influential of Pauling’s later career.” In this paper, the two authors offered their memorable metaphor: if the minor changes in molecular variants are proportional to elapsed time over the eons, they said, what you have is “a molecular evolutionary clock.”

It was tentative, a hypothesis. The hypothesis was disputed at the Rutgers symposium and would be controversial in coming years, but it captured attention, it focused thought, and it promised a whole new way of measuring life’s history, if it was right. The molecular clock has since been called “one of the simplest and most powerful concepts in the field of evolution,” and also “one of the most contentious.” Crick himself later judged it “a very important idea” that turned out to be “much truer than people thought at the time.”

Emile Zuckerkandl, meanwhile, moved back to France. Along with Pauling and just a few others, he had helped launch a new scientific enterprise, and when a *Journal of Molecular Evolution* came into being, in 1971, he was its first editor in chief. His name isn't familiar to the wider world, as Pauling's is, but if you say “Zuckerkandl and Pauling” to a molecular biologist today, he or she will think “molecular clock.” Fitting as that may be, it overlooks the

other important point: the other metaphor embedded in the long Rutgers paper, where Zuckerkandl wrote that “branching of molecular phylogenetic trees should in principle be definable in terms of molecular information alone.” This was a whole new way of sketching those trees, which rose and spread their branches as the clock ticked.



Carl Woese came to the University of Illinois, in Urbana, in 1964, the same year Zuckerkandl delivered the paper at Rutgers. The enterprise that would become molecular phylogenetics—back then bruted under other names, such as Crick’s protein taxonomy, and Pauling and Zuckerkandl’s chemical paleogenetics—had begun to attract interest. Woese saw its deepest possibilities more clearly than anyone else. Molecular sequence information, he realized, could be used to read the shape of the past.

Woese was thirty-six years old and was hired with immediate tenure, which gave him some latitude to undertake risky, laborious research projects without need to worry about quick publications. His professorship was in the Department of Microbiology, though he had trained as a biophysicist, not a microbiologist, and had spent little time if any peering through microscopes at bacteria and other tiny bugs. He was more interested in molecular biology, then still in its early phase. It was a thrilling new branch of science, its methods just being invented, its cardinal principles just taking shape, and he wanted to be part of that. But the molecular clock wasn’t Woese’s topic, and the prospect of a molecular tree of life hadn’t yet captured his imagination. He was focused instead on the genetic code—and not just what he called the cryptographic aspect: the matter of which bases in which combinations specified which amino acids for

building proteins. He wanted to go deeper in time and meaning; he wanted to understand how the code had evolved.

He was well aware that Francis Crick and others, including the eclectic Russian physicist George Gamow, had been working on the cryptographic aspect as a theoretical problem, treating it like an abstract intellectual game. That problem had been illuminated, but not solved, since Crick's 1958 paper, by a new recognition of RNA's role, as a messenger molecule somehow carrying DNA instructions to the site in a cell where proteins are built. But what was the structure of RNA, and how did it play that role? Gamow and the others were puzzled, and to them the puzzle was a thrilling game. They had even formed an elite, semifacetious little club—limited to twenty members, reflecting the twenty amino acids of life—for the private exchange of ideas about how coding and protein synthesis might work. They called it the RNA Tie Club—*RNA* because that molecule was still the mysterious intermediary; *Tie* because such neckwear evoked, and mocked, the clubby bond of an old school tie. As tokens of club membership, these scientists had embroidered neckties, all alike. They had individual tiepins, each representing one amino acid. They embraced their respective amino identities, at least jocularly: Serine and Lysine and Arginine, etcetera. Cute. Woese wasn't a member.

The cryptographic riddle, so intriguing to Gamow and Crick and the others, was this: How could the four bases of DNA—represented by those four cardinal letters, A, C, G, and T—be combined in groups of at least three, with or without commas, to produce the twenty different amino acids? Woese addressed it alone. He knew that a team led by Marshall Nirenberg, a young biochemist at the US National Institutes of Health, had made better progress with an experimental approach than the RNA Tie Club was making with collegial theorizing. But he wanted to go deeper.

“I differed from the whole lot of them,” Woese wrote decades later, “in perceiving the nature of the code as inseparable from the problem of the nature and origin of the decoding mechanism.” The decoding mechanism? By that, he meant whatever organ or molecule translated the DNA information into real, physical proteins. Its origin? To him, at that time, this was *the* central biological concern. He wanted to understand not just how that decoding mechanism worked but also how it had come into being roughly four billion years ago. He recognized, more clearly than anyone else, that life could not have progressed beyond its simplest primordial forms without a translation system for applying the information in DNA.

No statement from Woese is more telling of his character, his cantankerous self-image as a scientific outsider, than the beginning of that sentence just quoted: “I differed from the whole lot of them . . .” He was a loner by disposition. He took a separate path. Not in the club. No RNA tie. He published a few papers in *Nature* on the coding question, and a comment in *Science*—all under his sole authorship, suggesting ideas, critiquing what others had done. He offered his own view in full, an evolutionary view, in a 1967 book, *The Genetic Code*, which was visionary, ambitious, closely reasoned, and mostly wrong. But in science, wrong doesn’t mean useless. Trying to imagine the origins of the genetic code brought Woese around, almost reluctantly, to the tree of life.

He needed some such universal diagram, Woese realized, as a framework for understanding the evolution of that one crucial system at life’s core—the translation system, turning DNA-coded information into proteins. Deep biology required deep history. This conundrum has been nicely expressed by Jan Sapp, a plant geneticist who became a historian of biology and came to know Woese well: “A universal tree would therefore hold the secret to its own

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On June 24, 1969, Woese in Urbana wrote a revealing letter to Francis Crick in Cambridge. He had struck up an acquaintance with Crick about eight years earlier when Woese was an obscure young biologist at the General Electric Research Laboratory in Schenectady, New York, and Crick was already world renowned for the DNA structure discovery. It had begun as a tenuous exchange of courtesies, through the mail—Woese requesting, and receiving, a reprint of one of Crick’s papers on coding—but by 1969, they were friendly enough that he could be more personal and ask a larger favor. “Dear Francis,” he wrote, “I’m about to make what for me is an important and nearly irreversible decision,” adding that he would be grateful for Crick’s thoughts and his moral support.

What he hoped to do, Woese confided, was to “unravel the course of events” leading to the origin of the simplest cells—the cells that microbiologists called prokaryotes, by which they meant bacteria. Eukaryotes constituted the other big category, the other domain, and all forms of cellular life (that is, not including viruses) were classified as one or the other. Prokaryotes (*pro* being the Greek for “before,” *karyon* the Greek for “nut” or “kernel”) are cells without nuclei. Eukaryotes (*eu* for “true”) are the more complicated creatures, including multicellular animals, and plants, and fungi, plus certain single-celled but complex organisms such as amoebae, whose cells contain nuclei (hence the name, meaning “true kernel”).

Prokaryotes (“before kernel”) seem to have existed on Earth before eukaryotes. Although bacteria are still around and still vastly successful, dominating many parts of the planet, they were thought in 1969 to be the closest living approximations of early life-forms. Investigating their origins, Woese told Crick, would require extending the current understanding of evolution “backward in time by a billion years or so,” to that point when cellular life was just taking shape from . . . something else, something unknown and precellular.

Oh, just a billion years further back? Woese was always an ambitious thinker. “There is a possibility, though not a certainty,” Woese told Crick, “that this can be done using the cell’s ‘internal fossil record.’” What he meant by that term was merely the evidence of long molecules, the linear sequences of units in DNA, RNA, and proteins. Comparing such sequences—variations on the same molecule, as seen in different creatures—would allow him to deduce the “ancient ancestor sequences” from which those molecules had diverged, in one lineage and another. And from such deductions, such ancestral forms, Woese hoped to glean some understanding of how creatures had evolved in the very deep past. He was talking about molecular phylogenetics, still without using that phrase, and he hoped by this technique to look back at least three billion years.

But which molecules would be the most telling? Which would represent the best internal fossil record? Frederick Sanger, a humble but visionary biochemist in England, had sequenced the amino acids of bovine insulin, and insulins are a fairly old family of molecules in animals and other eukaryotes, but they don’t go back nearly as far as Woese wanted. Other scientists had sequenced a protein called cytochrome c, also crucial in cell biochemistry among many creatures. But those didn’t satisfy Woese. He wanted something

more basic, more universal—something that went *all* the way back, or nearly all the way, to the beginnings of life.

“The obvious choice of molecules here lies in the components of the translation apparatus,” he told Crick. “What more ancient lineages are there?” By “translation apparatus,” Woese meant the decoding mechanism, the system that turns DNA information into proteins—the same system that Crick had groped toward understanding in his 1958 paper “On Protein Synthesis.” Investigating the translation apparatus would in turn bring Woese around toward his starting point: his desire to learn how the genetic code itself might have evolved. Now, eleven years after Crick’s protein paper, the system was much better understood.

The components Woese had in mind were pieces of a tiny molecular mechanism common to all forms of cellular life. It’s called the ribosome. Nearly every cell contains ribosomes in abundance, like flakes of pepper in a stew, and they stay busy with the task of translating genetic information into proteins. Hemoglobin, for instance, that crucial oxygen-transporting protein. Architectural instructions for building hemoglobin molecules are encoded in the DNA, but where is hemoglobin actually produced? In the ribosomes. They are the core elements of what Woese called the translation apparatus.

Crick hadn’t used that phrase, “translation apparatus,” in his paper. He hadn’t even used the word *ribosomes*, but he touched upon them vaguely under their previous name, *microsomal particles*. These particles had only recently been discovered (in 1956, by a Romanian cell biologist using an electron microscope) and at first no one knew what they did. Then they became recognized as the sites where proteins are built, but a big question remained: how? Some researchers suspected that ribosomes might actually *contain* the recipes for proteins, extruding them as an almost autonomous

process. That notion collapsed in 1960, almost with a single flash of insight, when Crick's brilliant colleague Sydney Brenner, during a lively meeting at Cambridge University, hit upon a better idea. Matt Ridley has described the moment in his biography of Crick:

Then suddenly Brenner let out a “yelp.” He began talking fast. Crick began talking back just as fast. Everybody else in the room watched in amazement. Brenner had seen the answer, and Crick had seen him see it. The ribosome did not contain the recipe for the protein; it was a tape reader. It could make any protein so long as it was fed the right tape of “messenger” RNA.

This was back in the days before digital recording, remember, when sound was recorded on magnetic tape. The “tape” in Brenner's metaphor was a strand of RNA—that particular sort called messenger RNA (one of several forms of RNA that perform various functions) because it carries messages from the cell's DNA genome to the ribosomes. A ribosome consists of two subunits, one large, one small, fitted together and performing complementary functions. The small subunit reads the RNA message. The large subunit uses that information to join the appropriate amino acids into a chain, constituting the protein. The ribosomes and the messenger RNA, plus a few other pieces, constitute what Woese called the translation apparatus. By 1969, when Woese wrote to Crick, their crucial roles were appreciated.

Every living cell, including bacteria, including the cells of our own bodies, including those of plants and of fungi and of every other cellular organism, contains many ribosomes. They function as assembly mechanisms, taking in genetic information, plus raw material in the form of amino acids, and producing those larger

physical products: proteins. In plainer words: ribosomes turn genes into living bodies. Because the proteins they produce become three-dimensional molecules, a better metaphor than Brenner's tape-reader, for our own day, might be this: the ribosome is a 3-D printer.

Ribosomes are among the smallest of identifiable structures within a cell, but what they lack in size they make up for in abundance and consequence. A single mammalian cell might contain as many as ten million ribosomes; a single cell of the bacterium *Escherichia coli*, better known as *E. coli*, might get by with just tens of thousands. Each ribosome might crank out protein at the rate of two hundred amino acids per minute, altogether producing a sizzle of constructive activity within the cell. And this activity, because it's so basic to life itself, life in all forms, has presumably been going on for almost four billion years. Few people, in 1969, saw the implications of that ancient, universal role of ribosomes more keenly than Carl Woese. What he saw was that these little flecks—or some molecule within them—might contain evidence about how life worked, and how it diversified, at the very beginning.

Another of Woese's penetrating insights, back at this early moment, was to focus on a particular portion of ribosomes: their *structural* RNA. Usually we think of RNA in the role I mentioned above—as an information-bearing molecule, single stranded rather than double helical like DNA, carrying the coded genetic instructions to the ribosomes for application. Transient in space (through the cell) and transient in time (used and discarded). But that's only one kind of RNA, messenger RNA, performing one function. There's more. RNA can serve as a building block as well as a message. Ribosomes, for instance, are composed of structural RNA molecules and proteins, just as an espresso machine might be made of both steel and plastic. "I feel," Woese confided to Crick in



The mechanics of this effort in Woese's lab, during Mitch Sogin's time and for much of the next decade, were intricate, laborious, and a little spooky. They involved explosive liquids, high voltages, radioactive phosphorus, at least one form of pathogenic bacteria, and a loosely improvised set of safety procedures. Every boy's dream. Courageous young grad students, postdocs, and technical assistants, under a driven leader, were pushing their science toward points where no one, not even Fred Sanger or Linus Pauling, had gone before. The US Occupational Safety and Health Administration (OSHA), though recently founded, was none the wiser.

The fundamental goal was to sequence variants of a molecule from the deepest core of all cellular life, compare those variants, and deduce the history of evolutionary relationships since the beginning. Woese had already settled on that one universal element of cellular anatomy, the ribosome, the machine that turns genetic information into proteins, but there remained a crucial decision: *Which* ribosomal molecule should he study? Ribosomes comprise two subunits, as I've mentioned—a small one snuggled beside a larger one, like an auricle and a ventricle of the heart, each constructed of both RNA and proteins. The RNA fractions include several distinct molecules of different lengths. At first, Woese targeted a short RNA molecule from the large subunit, known as 5S ("five-S") for obscure