FROM THE NEWEST TWIGS TO THE ANCIENT LIMBS OF THE "TREE OF LIFE," RESEARCHERS TRACE THE CONNECTIONS BETWEEN ALL LIVING THINGS.

/ BY DANNY FREEDMAN /

'ENDLESS FORMS MOST BEAUTIFUL AND MOST WONDERFUL'

CAPITON TK

WRITING THE WORDS WAS "LIKE CONFESSING A MURDER."

But, Charles Darwin continued in an 1844 letter, he had come to believe that species are not "immutable." They change, they evolve.

Fifteen years later, though still as heretical as it was revolutionary, the famed naturalist outlined his theory of evolution by natural selection in a book. He wrote lyrically of a "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."

Biologists since have sought to find, describe, and assemble its twigs and branches and illuminate the connections between all living things. In turn, that knowledge has nourished other sciences from medicine and agriculture to engineering and climate studies.

"If you're interested in nature and you want to know about the fundamental questions," says GW biologist Guillermo Orti, "then this is your roadmap to understand it."

More than 150 years of work has produced vast catalogues of the planet's biodiversity, limb by limb. At GW, where sketching the tree is the main focus of about one third of the biology faculty and a core group from anthropology, the research spans the evolution of things big and small, from dinosaurs to single-celled organisms, plants to people.

GW biologists have led or co-led some of the many arms of a high-profile National Science Foundation project to map large branches, among a variety of other investigations. And even as they continue to fine tune the resolution in sections of the tree, others among them are part of an ambitious plan to piece together the whole megillah: a behemoth of some 2 million branches representing every known animal, plant, fungus, and microbe species.

It won't be the cultural cold shower that was Mr. Darwin's theory. It will be, the researchers say, akin to the first glimpse of Earth from space: a chance to see all at once the fragile sum of existence, a fountainhead of new questions and, perhaps, some answers.

"A HUNDRED YEARS of received wisdom and hundreds of papers and articles." That's been the result, Alex Pyron says, of conventional knowledge on the oldest ancestor of lizards and snakes. That's what he's about to disrupt.

In research published online this summer, the GW biologist and a colleague suggest that the oldest ancestor of lizards and snakes probably gave birth to live young, rather than laying eggs.

That wouldn't be unheard of—around 20 percent of lizards and snakes operate that way, Dr. Pyron says—but it reframes the way we look at their world.

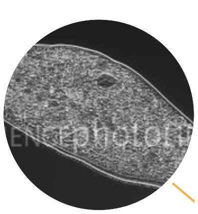
"It's a pretty major overturn of an accepted school of thought," he says.

The study required a framework for slogging through 170 million years of evolution, accounting for as many subgroups as possible. And Dr. Pyron had just the thing. This year he and two colleagues published an evolutionary tree of lizards and snakes—

Alex Pyron

Robert F. Griggs Assistant Professor of Biology

FOCUS: Snakes
SPECIALTY: Colubroids, the group that includes all the dangerously venomous snake species, as well as non-venomous ones



Diana Lipscomb

Ronald L. Weintraub Chair of the Department of Biological Sciences and professor

FOCUS: Protozoa
SPECIALTY: Ciliates, single-celled organisms with hair-like organs that propel them

Guillermo Orti

Louis Weintraub Professor of Biology

FOCUS: Fish
SPECIALTY: Characiformes, a fish order that includes piranhas, an area of particular expertise

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together, known as squamates—that covers 25 times the number of species as the next-largest genetic analysis of squamates.

Two years ago he did much the same for amphibians. And it's not an unfamiliar accomplishment around Bell Hall.

Last year researchers published the largest tree for the group of spiders called orb weavers, which comprise a third of all spiders, tracing them back to a common ancestor that lived 230 million years ago.

This year GW researchers published the largest evolutionary study of "bony fish," a group that makes up the majority of the world's fish, and likewise for anomurans, a class of crustaceans that includes hermit crabs and king crabs.

They have published a comparative study of muscle evolution in primates, the first to be based on anatomical evidence, and reported two new species that help fill in the fossil record: a 161-million-year-old dinosaur of the same ilk as T. Rex, and the closest relative to the group that gave rise, eventually, to modern crocodiles and alligators. The coming months also promise the largest evolutionary timeline for plants.

For two decades the university has been cultivating an expertise in systematics, or the classification of living things, and evolutionary history, nature's relentless tinkering that results in "endless forms most beautiful and most wonderful," as Mr. Darwin put it.

"This is one of the more revolutionary ideas in science in the last 200 years, that pond scum to killer whales can all be put into this big Tree of Life," says Diana Lipscomb, chair of the biological sciences department.

Dr. Lipscomb, who studies single-celled organisms, was the only systematist at the university when she arrived in the early 1980s, amidst what she describes as a decades-long lull for the field. "People didn't really understand how central this all was."

Now there's little mistaking it. In medicine and public health, evolutionary trees are used to identify diseases, such as the SARS outbreak in 2003; to help determine which flu strain to vaccinate against; to find ways to attack antibiotic-resistant bugs; and to prospect drugs from plants and animals. Venoms, for instance, are studied for their potential to treat conditions like heart attack, stroke, pain, and cancer. And trees can predict wider uses of antivenoms by pointing to animals that may be close cousins, despite looking like perfect strangers.

In agriculture, evolutionary trees are used to bolster crops and combat invasive species. They help engineers understand natural marvels, like adhesives that let geckos walk upside down on glass and the aerodynamic design of fins and wings.

"It's like man has a warehouse of things and we don't know 90 percent of what's in the warehouse," says Dr. Lipscomb. "How dumb is that?"

The systematics program at GW began to bud in the early 1990s. It was a practical leap, she says, based on the strength of what was already a century of collaboration between the Smithsonian Institution and GW's biology department and the limitations of its home, Bell Hall, which dates to 1935.

Graduate students already were taught by GW faculty and curators at the Smithsonian's National Museum of Natural History. Then in 1993 the program received a game-changing boost when Professor Emeritus of Botany and three-time alumnus Robert Weintraub and his wife, Frances, endowed five professorships in systematics. (Since then the program has been named for Dr. Weintraub—as have a handful of species.)

Around the same time, Dr. Lipscomb had been part of a small group of scientists lobbying to shift attention back to evolutionary studies. The effort helped spur the National Science Foundation's

Amy Zanne

Assistant Professor of Biology

FOCUS: Plants
SPECIALTY: Angiosperms and conifers, respectively, flowering plants and the group of trees and shrubs that deliver seeds via cones, like pines, spruces, and firs

Bernard Wood

University Professor of Human Origins, Department of Anthropology

FOCUS: Primates
SPECIALTY: Hominins, the lineage that led to our own species, Homo sapiens

A sample of faculty members who study evolution is set against the outline of a model evolutionary tree. Living species sit at the outermost tips, atop branching connections that trace back billions of years, in theory, to a single common ancestor.

Catherine Forster

Associate Professor of Biology

FOCUS: Dinosaurs
SPECIALTY: Ornithopods, the group of bipedal herbivores that typically had horned beaks or duck bills, and large teeth for eating plants

James Clark

Ronald Weintraub Professor of Biology

FOCUS: Dinosaurs and Crocodylomorpha
SPECIALTY: Crocodilians, which burst into an array of forms during the Jurassic and Cretaceous periods, and include modern-day crocodiles, alligators, and gharials.

Assembling the Tree of Life program, which launched in 2002 with Dr. Lipscomb serving a two-year stint at NSF as one of the program's administrators.

Geared toward large-scale, multi-institutional projects, the program started with a $17 million bang. It funded a handful of studies, including one on the connection between birds and their dinosaur relatives, led by GW paleontologist James Clark, and another on the evolutionary track of spiders, co-led by GW biologist Gustavo Hormiga.

Since then the NSF's program has invested millions more into dozens of tree studies, including two other GW-led trees: one for "bony fish," a group that comprises most of the world's fish, and another for decapod crustaceans, which includes crabs, shrimp, crayfish, and lobsters.

Beyond those projects, the biology department continued to leverage its Smithsonian bond and endowed professorships to attract faculty members who have put the department on the map. They've forged collaborative relationships with New York's American Museum of Natural History, among other institutions, and established track records for winning funding for evolutionary studies year after year—in some cases now for two decades.

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> **— DIANA LIPSCOMB, CHAIR OF GW'S BIOLOGICAL SCIENCES DEPARTMENT**

FOR MUCH OF THE HISTORY of evolutionary trees, and very much still today, connections have been made by comparing the physical characteristics of organisms. Over the past 50 years or so, genetic analysis has offered a deepening data goldmine for studying younger life forms—those dating back perhaps several hundred thousand years, if their DNA has been preserved.

At its most basic level, DNA from two species is combed for differences; the more differences they have, the further apart they are from each other on the Tree of Life. Genetic differences can also help scientists estimate how long ago changes occurred.

The steady sprint of advances in sequencing technology and computing muscle have made possible studies on a large scale, which might analyze a dozen—or dozens—of genes, or other biological markers, across thousands of species.

These studies corroborate much of what had been surmised based on anatomy and fossils, but they also offer surprising insights.

Genetic analyses for the recent GW-led "bony fish" evolutionary tree turned up this tidbit: Although the warm-blooded tunas, mackerels, swordfish, and billfish, like the marlin, had been lumped together based on physical characteristics, researchers found that tunas and mackerels actually are more closely related to seahorses, and billfish and swordfish are closer to the Picaso-esque flatfishes, like flounder.

"They don't resemble each other at all," says GW post-doctoral researcher Ricardo Betancur, "but according to DNA they are more closely related." Given that finding, it now appears that warm-bloodedness evolved independently at least twice among fish.

But DNA is also pointing to physical similarities that simply had gone unnoticed. Spider expert Gustavo Hormiga recently

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Keith Crandall

Director of the Computational Biology Institute and Professor of Biology

FOCUS: Crustaceans

SPECIALTY: Freshwater crayfish, lobster-like crustaceans that across some 600 species vary widely in color and size, ranging from under an inch long to more than 15 inches

Gustavo Hormiga

Ruth Weintraub Professor

FOCUS: Spiders

SPECIALTY: Orb weavers, the spiders known originally for their classic, wheel-and-spoke shaped webs, though its now known that their web-building can take many forms, and some don't produce webs at all

was studying an obscure group that was known to belong to the sprawling family of orb-weaving spiders, but scientists had "absolutely no clue" where they fit in, he says.

A genetic analysis suggested the closest relative, and once Dr. Hormiga got them side-by-side the mystery became a head-slapper. "This makes a lot of sense," he says, "but nobody actually had that vision."

Despite the tidal wave of new genetic and anatomical data, resulting in thousands of new trees being published each year in scientific journals, the notion of a singular Tree of Life has remained simply a metaphor.

That could change beginning this fall. A research team is anticipating the release a so-called first draft of the Tree of Life. The immense architecture, built by grafting together existing data, will include a spot for each of the roughly 2 million known species across more than 3 billion years of life.

"It will be a fundamentally different way to do systematics," says Keith Crandall, director of GW's Computational Biology Institute, who is one of the project's 11 leaders from 10 institutions.

The nearly $6 million project, called the Open Tree of Life, is one part of a three-pronged, $13 million initiative launched last year by the NSF that aims to produce an open-source tree and the analytical tools needed to explore it.

The task, Dr. Crandall says, is possible now because of advances in computing power and the recent work to bring the branches into better focus. The framework will include classification details for each species and, where available, evolutionary connections.

The researchers ultimately envision a tree that updates automatically as new data becomes available. But they're finding that the trees and genetic data found in studies overwhelmingly are not reusable, bound in formats like PDFs that can't be meshed with other datasets. Resolving that will require a shift in the field toward seeing branching diagrams assembled for studies "as data, and not as a result," Dr. Crandall says.

The Open Tree of Life, however, also will bloom through crowdsourcing. The team is relying on scientists to upload their data, enticed by analytical tools capable of searching across the big picture and mining it for new perspectives and opportunities. Researchers will be able to see across life and through time at the emergence of specialized characteristics, booms and lulls in species formation, and how species historically have responded to climate change.

But, Dr. Crandall says, one of the most significant things the Tree of Life will show is precisely what isn't known; the pinholes and chasms in the collective knowledge.

And there are plenty—even in the number of species that are formally known to science.

It's "somewhere between 1.8 million and 2.2 million, depending on who you talk to," Dr. Crandall says. "That's part of the irony: Not only do we not know how many species are on Earth, we don't even have a reasonable handle on how many we've described."

And saying a species is known or described is relative: Diana Lipscomb, the biology chair, who researchers singled-celled organisms, says she deals with "big chunks of tree" in which living species are called simply "Undescribed from the Atlantic Ocean," or "Undescribed from the Great Lakes."

Genes have been sequenced, she says, "but nobody knows what any of those things look like, what they're eating, how they're functioning."

How much else is out there that may have no name at all? Guesses range from another million species to a hundred million.

The unknown weighs on Dr. Hormiga, the spider researcher, while collecting in remote locales, like a recent trip to an island 400 miles off the coast of Chile.

"Think of actually running through a library that's on fire," he says. "You're going to try to pull out as many books as possible before you get out of the building."

"The reality is that a lot of these places are going fast," he says. "The extinction rates are episodic. So it's not unthinkable that many of the places where I've collected will be gone, and the only evidence those species ever existed is what was deposited in a museum."

The trips, he says, are exhausting. "Because you know well there's not much time to sleep."