Systematics Goes Molecular

A crop of new high-tech labs reflects the healing of a deep rift within evolutionary biology between molecular upstarts and the classical establishment

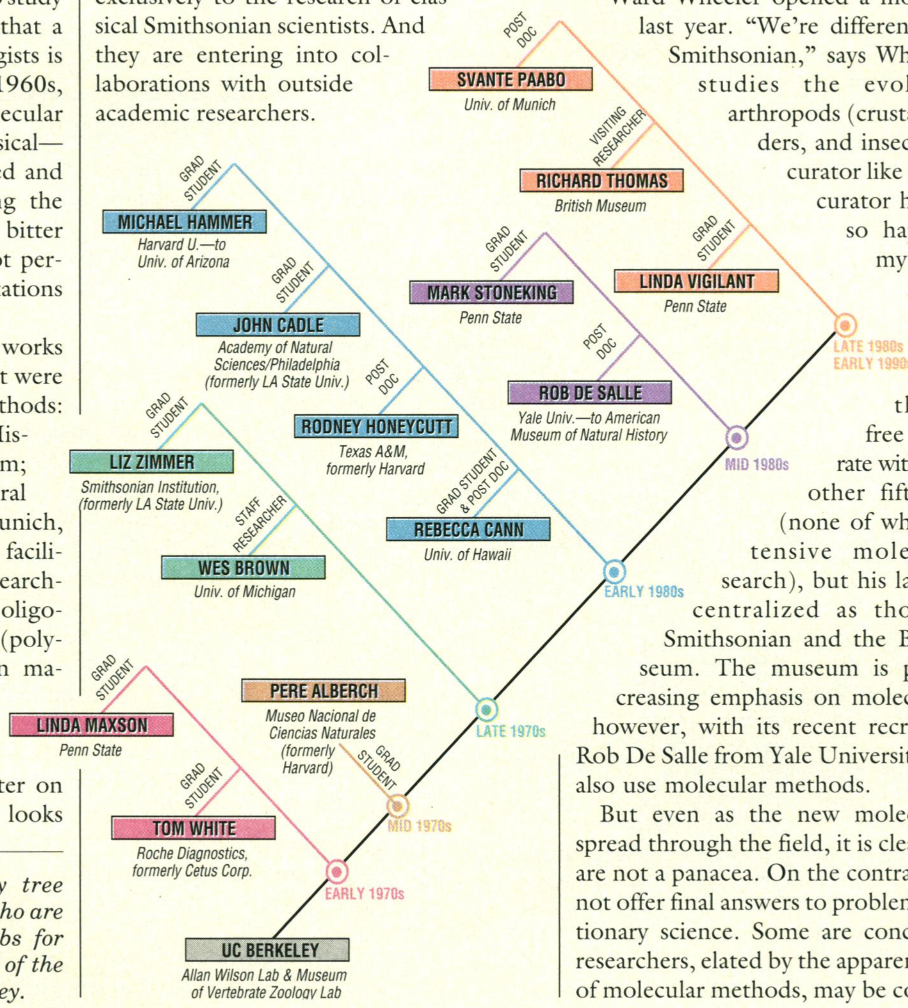
FOR YEARS, SMITHSONIAN INSTITUTION ecologist Gary Graves has studied speciation in birds the old-fashioned way—by comparing the colors and patterns in their plumage. But in 1987 Graves was instrumental in convincing the Smithsonian's Museum of Natural History to set up a gleaming new 5500-square-foot lab in which molecular methods will be used to study relations among species. Now he plans to augment his classical morphological studies by analyzing the mitochondrial DNA in frozen tissue samples taken from the same birds. "I use traditional methods in my research," says Graves, "but the questions I'm interested in asking often times can be more easily answered with modern technology, like DNA analysis."

Graves' use of molecular methods to study classical questions is a distinct sign that a long-standing civil war among biologists is finally waning. Ever since the early 1960s, brash—often arrogant—young molecular scientists have been vying with classical—sometimes stodgy—upholders of tried and true systematics methods for tracing the evolution of species. It has been a bitter internecine battle that sometimes got personal, leaving egos bruised and reputations bloodied.

But today, labs like the one Graves works with are being set up at museums that were once the citadels of the classical methods: the American Museum of Natural History in New York; the British Museum; the Field Museum in Chicago; natural history museums in Stockholm, Munich, and Madrid. At such state-of-the-art facilities a new generation of molecular researchers are setting up DNA sequencers, oligonucleotide synthesizers, and PCR (polymerase chain reaction) amplification machines.

Some of these new high-tech shops are quite ambitious. The Smithsonian's sprawling new support center on the outskirts of Washington, D.C., looks more like an electronics company than a museum. Working in these modern surroundings, molecular scientists have been laboring for 2 years to set up new labs, computer rooms, and dark rooms for systematics. Michael Braun, a molecular evolutionist, and Liz Zimmer, a biochemist, are running the labs stocked with automated DNA amplifiers (PCR), DNA synthesizers, ultracentrifuges, UV/visible spectrophotometers, and other state-of-the-art tools.

Braun and Zimmer are working with a dozen postdoctoral researchers and technicians and are in the process of interviewing more researchers to bring the total to twenty by the end of 1991. They also have plans to hire two to six principal investigators and to set up a multiuser lab dedicated exclusively to the research of classical Smithsonian scientists. And they are entering into collaborations with outside academic researchers.



The fountainhead. *Evolutionary tree shows that many of the researchers who are starting up high-tech molecular labs for systematics got their training at one of the molecular laboratories at UC Berkeley.*

Across the Atlantic at the British Museum in London, population ecologist Richard Thomas is clearing blue whale bones out of a storage room in the basement of the museum to make room for a $500,000-molecular lab where there will be bench space for ten or so researchers. Already Thomas is producing his own DNA sequences from lizards for population studies and is hiring postdocs to work on the mitochondrial DNA of marine gastropods and protozoa. Meanwhile, "I have people sort of knocking on my door, asking could we do this and can we do that," says Thomas, who was hired last April to set up the lab.

A slightly lower keyed approach is being tried at the American Museum of Natural History, where evolutionary systematist Ward Wheeler opened a molecular lab last year. "We're different from the Smithsonian," says Wheeler, who studies the evolution of arthropods (crustaceans, spiders, and insects). "I'm a curator like every other curator here. It just so happens that my research is molecular." The idea is that he is free to collaborate with any of the other fifty curators (none of whom do extensive molecular research), but his lab is not as centralized as those at the Smithsonian and the British Museum. The museum is putting increasing emphasis on molecular work, however, with its recent recruitment of Rob De Salle from Yale University, who will also use molecular methods.

But even as the new molecular tools spread through the field, it is clear that they are not a panacea. On the contrary, they do not offer final answers to problems in evolutionary science. Some are concerned that researchers, elated by the apparent precision of molecular methods, may be content with "easy answers" obtained by sequencing just one gene or molecular character in a species, says Jeff Palmer, a leading molecular evolutionist at Indiana University. There has been a creeping realization that it is important to sequence many segments of DNA—and to pick the right segments—to make an accurate comparison between individuals, populations, or species.

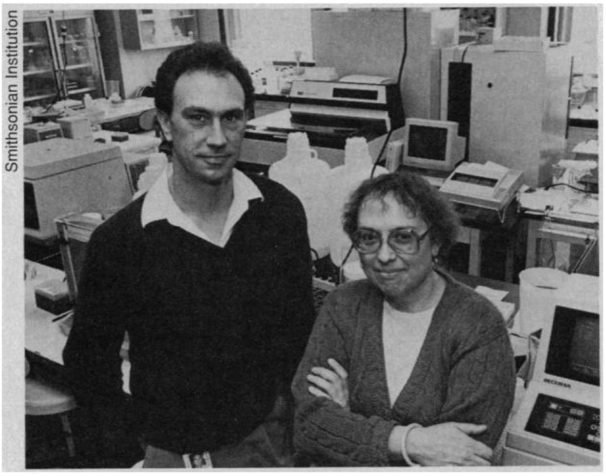
Furthermore, many scientists don't know quite what to make of the new DNA data. Already, says Palmer, the field has been swamped with a glut of molecular data that is outstripping the evolutionary theory available to explain it. The speed at which that data are being generated has outpaced the scientists' ability to analyze it—to the point where Palmer says it's time to develop better statistical and computational methods for interpreting the data. Terry Yates, director of the NSF's systematic biology program, agrees: "It's not like we have a body of theory. Suddenly we have capabilities of generating huge quantities of data, and we're scrambling to find ways to analyze it."

Nonetheless, the new tools are rapidly changing the way classical whole-organism biology is done, much as computers changed research in the physical sciences. "The new labs are definitely symptomatic of a real sea-change that has occurred," says Wesley M. Brown, a molecular evolutionist at the University of Michigan who studies the evolution of lizards and of mammalian DNA. "There still is a fair amount of antagonism and a fair amount of resistance," he says. But the progress made so far is still quite startling, considering "the early history" of contention between the classically trained biologists and the molecular upstarts.

That early history dates back to 1962, when Linus Pauling and Emile Zuckerkandl of the California Institute of Technology unexpectedly recognized that molecules can serve as an evolutionary clock. Put simply, they showed that the more mutations that have accumulated in a specific protein sequence, the older its lineage is. Furthermore, the differences in protein sequences can be used to compare extant species to help classify them.

A small but tenacious group of researchers immediately saw the potential of this molecular clock. By 1967 Allan Wilson and Vincent Sarich at the University of California at Berkeley had used it to estimate that humans, chimps, and gorillas shared a common ancestor as recently as 4 to 6 million years ago—much more recently than the classical paleontologists believed. The reaction from the classical side was immediate and "vitriolic," recalls Brown of Michigan, a graduate student in evolutionary biology at the time. (Indeed, it wasn't until the 1980s, when problems were found with the paleontological data on *Ramapithecus* that the molecular data were vindicated.)

Unfortunately, in dismissing Wilson and Sarich's specific results, many paleontologists also rejected the molecular approach in general—and the civil war was under way.



Smithsonian Institution

Dynamic duo. *Michael Braun and Liz Zimmer, who run the Smithsonian's new molecular systematics lab on the outskirts of Washington, D.C.*

Feelings ran so high that Brown recalls systematists being "terribly opposed" to his decision to take a time-consuming detour from graduate work in evolutionary biology to get a doctorate in biophysics. That route ultimately took him to Wilson's lab, where he introduced the technical methods that made the lab the first to use DNA to study evolutionary questions in the late 1970s.

But the intransigence wasn't only on one side. Some of the upstarts brought problems on themselves—by not being entirely diplomatic with their older, more entrenched colleagues. "Some of them came in with the attitude, 'Well here I am, I'm going to solve your problems,'" says Brown. "There was a certain amount of arrogance."

To make matters worse, many of the molecular hotshots were ignorant of the classical background of systematics and evolutionary biology. As a result, research choices were sometimes naive. Colin Patterson, curator of fossil fishes at the British Museum, complains: "It was as if they chose a species by going down to the shores of the San Francisco Bay and saying: 'All right, let's grind up that one'—rather than thinking of the problem to solve and the vital species that might help with that."

Now that the rift is healing, some classical biologists, such as Patterson, admit they have come around to seeing the usefulness of the molecular data. In retrospect, though, it's easy to see that they were already uneasy over the competition for precious research funds that they envisioned coming from molecular biologists. That worry is still there, and it's the reason some classical folks resent seeing large sums of money spent on state-of-the-art labs—particularly at the British Museum, where about 100 staff lost their jobs in budget cuts last year. "The grumbling from systematists is, 'We're underfunded,'" says NSF's Yates. "It is true. It costs a lot more money to sequence genes than to measure skulls."

But even at the beginning, not all classically trained systematists resisted the new trends. As early as the 1970s, there were tiny glimmers of the collaboration that have emerged full-blown in the last couple of years. Take David Wake, director of the Museum of Vertebrate Zoology at UC Berkeley. A classical systematist, he collaborated with Wilson and other molecular scientists in the department of biochemistry. Other early important work also was done in university labs such as Charles Sibley's at Yale, Roy Britten's at CalTech, Morris Goodman's at Wayne State University, Richard Lewontin's at Harvard, and Carl Woese's at the University of Illinois.

But the first recognized prototype of the molecular systematics lab was set up at Berkeley, where Wilson's lab in the department of genetics collaborated with a wide array of faculty and other researchers on campus. And out of that lab—and others like it at Berkeley—came a crop of hybrids: graduate students trained both in systematics and in molecular techniques who have seeded the combination around the world.

At a celebration last year for the 25th anniversary of Wilson's lab, former students jokingly showed a slide of a map of the world, showing the paths the Berkeley researchers had taken to other molecular evolution labs around the world. You could trace Berkeley students and collaborators to brand new labs at Pennsylvania State University, Louisiana State University, the University of Hawaii, the Museo Nacional de Ciencias Naturales in Madrid, and the Smithsonian's Museum of Natural History, among others.

One of the pioneers, Tom White, played a particularly key role in the recent progress in making molecular methods accessible to classical biologists. White landed at Cetus Corp. in 1978, later becoming vice president of research—the post he held when the PCR was invented at Cetus in the mid-80s. He was able to repay mentor Wilson with an early gift of PCR, making it possible to obtain rare DNA sequences in quantity. As a result, the labs at Berkeley were the first academic outfits to test the method, which has gone on to be of tremendous importance in research.

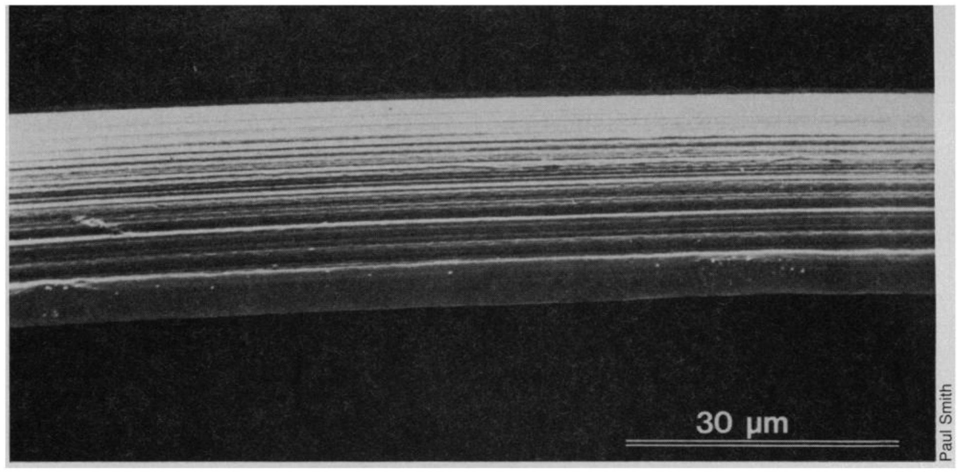
Indeed, PCR, which received its commercial release in 1987, has now convinced virtually all organismal biologists that using DNA could actually be a tremendous boon to them. "PCR means all of a sudden that all these dead rats in museums are genetic goldmines," says NSF's Yates. Svante Paabo, another pioneer, who has just left Wilson's lab to set up a new molecular lab at the University of Munich and at the Zoological Museum in Munich, enthuses: "I think it's kind of a renaissance for museums. You can obtain samples from extinct species, and you can look at populations over time, which is totally unique."

As a result of PCR (and other techniques), the tide is rapidly turning. "I think systematists like myself have settled down and are saying, hey, molecular data are really neat and need to be explored," says Michael Donoghue, a plant systematist who has been instrumental in convincing the University of Arizona to open a new $225,000 molecular systematics lab. "It's not going to reveal the truth in some sort of cosmic sense, but it's going to be extremely valuable to us and help us solve the sort of evolutionary questions we couldn't answer before."

Reflecting the trend, funding requests for molecular proposals are way up at the NSF. "We see a lot of people who 10 years ago were sending us proposals to work on a group of organisms; now...they need money to sequence the genes or to look for polymorphisms, as well," says Yates, whose agency funds about $13 million a year in systematics research (molecular and nonmolecular). "I find it interesting that curators were talking for years and years about how these things were valuable, but rarely convincing administrators. Now the same administrators are scrambling to get funds for molecular labs to re-examine these specimens."

Museum administrators also have another motivation to tool up: They are better positioned to recruit young scientists to replace their aging cohort of curators. Of 125 curators at the Smithsonian's Museum of Natural History, only about a dozen are under the age of 40. One of them is Graves, the 37-year-old ecologist who is a curator of birds at the Smithsonian. "People my age can't afford to be any other way," says Graves. "This is the future. I think 20 to 30 years from now the old style museum curator is going to be a thing of the past."

■ ANN GIBBONS



Lining up. *Scanning electron micrograph of an ultra high molecular weight form of polyethylene made up of oriented polymers.*

Plastics Get Oriented—and Get New Properties

They can be stronger than steel and more conductive than copper. But producing them is no mean feat

"I HAVE JUST ONE WORD TO SAY TO YOU. JUST one word: plastics." More than 20 years ago an enterprising uncle uttered that bit of advice to Dustin Hoffman's character in *The Graduate*.

Looking back, it wasn't bad advice, but if the graduate had returned home in 1991, a forward-looking uncle might have added two more words: oriented polymers.

The uncle would point out that oriented polymers can make plastics stronger than steel and more conductive than copper, as well as resistant to heat, chemicals, moisture, and corrosion. Today, specially processed plastics give Oliver North's bullet-proof vest its stiffness and the ropes and sails on America's Cup yachts their strength. Still to come: plastic airplane parts, plastic wires, and plastic diodes and transistors.

Making plastics with oriented polymers takes elaborate and expensive tinkering. One chemist compares the process to "uncooking spaghetti" because scientists take the coiled, spaghetti-like polymers that make up plastics, straighten them out, and put them back together in a parallel fashion—something like the way spaghetti comes in the box.

That technique can theoretically make plastic do many things metal can—only better, says Paul Smith of the University of California at Santa Barbara, a pioneer in the field. "Plastics have the potential for greater than ten times the strength and stiffness of steel." But for 2 decades scientists have been prevented from realizing that remarkable potential, because the materials that promised these properties proved impossible to make on a practical scale. "People can dream up all kinds of nice polymers but if you can't process them into useful materials, they have absolutely no interest," Smith says.

As long as processing problems separated scientists from their dream plastics, the quest for high-strength and conductive polymer materials waxed and waned. Scientists lost patience as the polymers promising the most strength and conductivity resisted the necessary first step of melting or dissolving.

But in the last 4 years, new discoveries have sparked excitement, offering the promise of breaking through the processing obstacles. Some areas of oriented polymer research are now so hot that competing industry scientists hesitate to divulge details of their latest work.

A major insight made 2 years ago further boosted the spirits of both scientists seeking conductivity and those after strength. Both groups of researchers realized they needed to achieve the same thing—alignment—says Alan Heeger, another pioneer who works with Smith at UC Santa Barbara. "In our experiments we put two types of polymers together and oriented both at the same time," he says. "We were excited to find that alignment improved both strength and conductivity."

Heeger says that scientists in the two pursuits, who traditionally followed separate paths, are now taking an interest in each other's ideas and examining materials combining strength and conductivity, as well as other properties—resistance to corrosion