How Technique Is Changing Science

The late 20th century is witnessing an explosion of techniques that may be unparalleled since Galileo and van Leeuwenhoek shook the 17th century to its intellectual foundations

With its Big Bang, black holes, and gravity waves, astronomy in the latter part of the 20th century no doubt seems to most mere mortals a highly sophisticated, theoretical adventure. But consider the insider's perspective of Harvard astrophysicist Patrick Thaddeus, who likes to say: "Behind every great discovery in astronomy there's a guy with a soldering gun." Therein lies an instructive tale that is applicable in many, if not every, state-of-the-art corner of scientific research these days. Take, as one case in point, the tinkerings of Stephen A. Shectman, whose overworked little "2-D Frutti Detector" is helping to measure the distribution of matter in the universe.

Science Innovations
Beginning on this page, Stephen S. Hall describes the renaissance in technique that is transforming every branch of science. Beginning on page 350, Robert P. Crease discusses historical examples that show how scientific techniques develop and mature.

When Shectman travels down to Las Campanas Observatory in Chile for an observing run, much of the crucial work has already been done at a machine shop on Hope Street in South Pasadena, California. There, Shectman, who works out of the Pasadena headquarters of the Observatories of the Carnegie Institution of Washington, oversees a process that owes as much to industrial arts as it does to astrophysical theory. One by one, a set of 12-pound aluminum disks, 3 feet in diameter and an eighth of an inch thick, are bolted onto a computer-driven milling machine. Then each "plug plate," as they are known, is drilled full of holes.

Strip-mining the sky

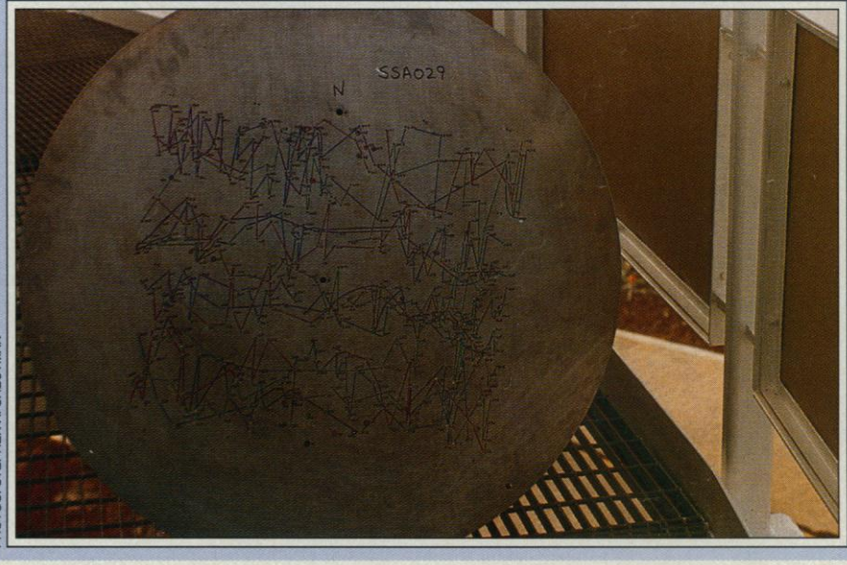
Each hole measures 2.3 millimeters in diameter; Shectman typically drills about 500 in each plate—and then draws in a series of connecting lines in colored inks, the end product resembling a kind of occult cartography. The size of the plug plate matches the optical field of Las Campanas's wide-field 2.5-meter telescope, and every hole corresponds to the spot where a particular galaxy will appear in the night sky over South America months later. Once at Las Campanas, Shectman clamps the aluminum disk on the telescope and begins to insert optical fibers into each hole, the fiber's business end near the telescope encased in bicycle-brake cable, its entire length sheathed in stainless steel hypodermic tubing. The fibers drip from the plate like metallic spaghetti, carrying the ancient light of distant galaxies from the telescope to the slit of a spectrograph, at the back of which lies a two-dimensional photon counter that intensifies and registers the light. Since this particular electronic detector goes by the name of "2-D Frutti," Shectman refers to the whole shebang as the "Fruit and Fiber" system. In the literature, the technique is known more soberly as fiber-optic spectroscopy. In conversation, Shectman tends to speak of it as "my gadget."

The concept behind the gadget isn't "his," but that is one of the beauties of a scientific technique: It belongs to no one—and can be improved by anyone. John M. Hill of the University of Arizona first tried multifiber optics in 1979, but Shectman has probably taken the idea further than anyone else in the field. When his "gadget" is performing well, a single telescope exposure can record up to 112 new red shifts in 2 hours; the red shifts provide crucial information about the three-dimensional position of galaxies in the universe. Shectman says he can measure about 400 a night now, a process he calls "strip-mining" the sky. To get an idea of how this combination of techniques is changing astronomy, Shectman can in 8 typical nights snag 2200 red shift spectra, probably more than were recorded by all astronomers on Earth between 1925 and 1975. "By the mid-1970s there were a couple of thousand red shift measurements," he says. "The number of red shifts in the largest database to date is about 46,000. They are being added at a rate of about 10,000 a year, and my impression is that this instrument alone is producing one-third to one-half of the total."

The remarkable speedup in data collection has made possible a dramatic intellectual advance: the first three-dimensional maps

Astronomy's "Fruit and Fiber" Diet

This sequence of photographs shows some of the preparations for an observing run at Las Campanas Observatory near La Serena in Chile by astrophysicist Stephen A. Shectman's team. A key step is the drilling of hundreds of holes in an aluminum "plug plate," shown below.



PHOTOS: STEPHEN A. SHECTMAN

of the universe. "Going from photographic plates to solid-state detectors, and now from the solid-state detectors to fiber optics, has made it possible to do the galaxy surveys that are now being done," says astrophysicist Margaret Geller, who with colleague John Huchra of the Harvard-Smithsonian Center for Astrophysics produced one of the most startling maps in 1986. And those surveys, with their bubbles and "Great Wall" and unimaginably large voids, have perturbed astrophysics enormously in recent years, challenging theorists to ever more daring speculations about the roots of matter and the evolution of the universe.

Shectman's "gadget"—the marriage of nitty-gritty engineering to an important intellectual question—shows just how clearly technique is connected to the soaring superstructure of scientific theory. And yet the "Fruit and Fiber" system is but a small gadget in a burgeoning warehouse of methods, instruments, and technical tricks that is transforming contemporary science. Indeed, at the end of the 20th century, science is enjoying a burst of technical imagination that may be unrivaled since Galileo's telescopes and van Leeuwenhoek's microscope shook 17th-century conceptions of the world to their intellectual roots.

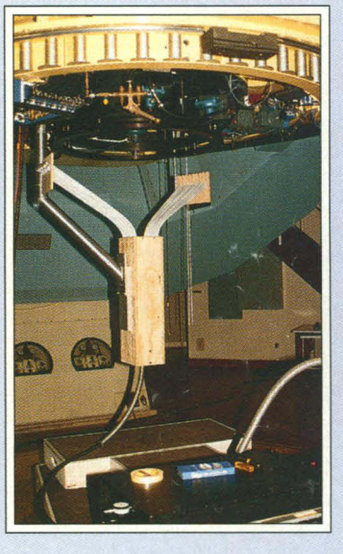
"In biology," says molecular biologist Sydney Brenner, speaking as well for all the sciences, "I have said before that in a strong sense all the answers exist in nature. All we need is the means to look them up, and that's what the techniques give us." Today, techniques are helping scientists look up the answers in a staggering array of fields.

Transforming power

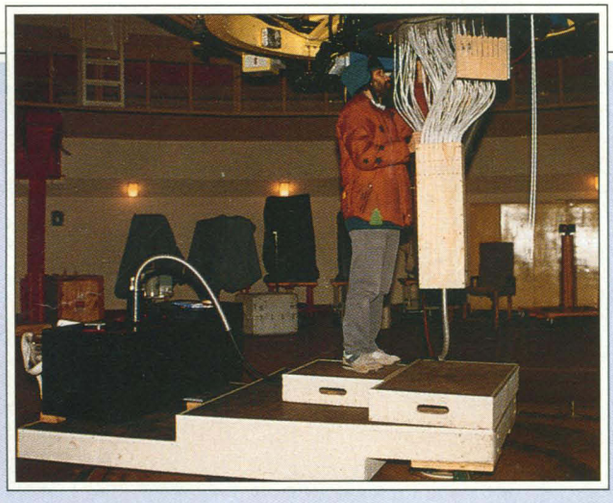
To cite only a few examples, Brenner's own field of molecular biology has been revolutionized by the invention of gene cloning (reported by Herbert Boyer and Stanley Cohen in 1973) and sequencing (independently reported by Frederick Sanger in England, and Walter Gilbert and Allan Maxam in the United States); the two techniques have allowed biologists to produce pharmaceuticals like growth hormone and interferon and also to begin assembling a complete atlas of human genetics. Patch-clamping, introduced in 1976 by Erwin Neher and Bert Sakmann, has allowed neurobiologists to study the crucial traffic of ions across cell membranes and obtain whole-cell recordings of synaptic currents in neural tissue. Physical chemistry and physics are being dramatically altered by the stunning power and sensitivity of the scanning tunneling microscope and its progeny instruments, first described by Gerd Binning and Heinrich Rohrer in 1982, which permit glimpses of atomic landscapes and even allow scientists to manipulate individual atoms.

Yet not everybody appreciates the importance of technique. Many scientists, in fact, are "theory snobs" who dismiss technique as a kind of blue-collar suburb of science (see story on page 346. But the Nobel Prize committee doesn't agree: All of the techniques mentioned, except for gene cloning, received science's ultimate award. The reason, clearly, is the enormous transforming power of techniques. In the absence of an essential technique, a researcher or a field flounders, developing elegant theories that cannot be decisively accepted or rejected—no matter how many intriguing circumstantial observations are available. But with a key technique in hand, the individual and field move ahead at almost terrifying speed, finding the right conditions to test one hypothesis after another. Conversely, new techniques often uncover new phenomena that demand new theories to explain them. Almost all great techniques were invented by people in a hurry to get someplace else scientifically, and a researcher's ability to answer important scientific questions successfully often depends on how closely theory is tethered to technique.

The story of how radioimmunoassays, or RIA, provided a way to measure the presence of insulin is a classic example of the way a new technique can provide the opportunity to accept or reject a specific hypothesis—the kind of test Francis Crick, codiscoverer of the structure of DNA, calls a "decisive experiment." As in many cases, before the innovation in technique, a hypothesis had been advanced, but it couldn't be readily proved or disproved. Specifically, the physician Arthur Mirsky had hypothesized that

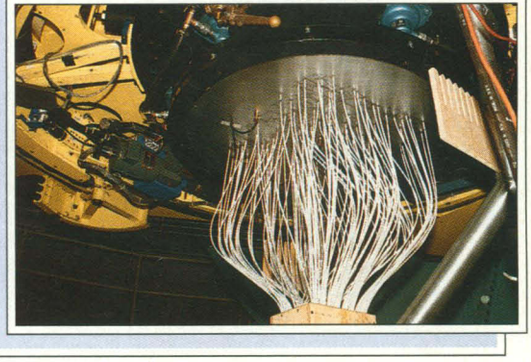


The plug plate fits onto the back of Las Campanas's 2.5-meter-wide field telescope. Each hole matches the point where a galaxy will appear in the heavens over the southern hemisphere.



After the plug plate is put in place, optical fibers are inserted into 128 of the plug plate's holes for each exposure *(left)*. Every fiber carries light from one galaxy to a spectrograph, where a two-dimensional photon counter records the light's spectrum.

Shectman's two-dimensional photon detector is known as "2-D Frutti," and he calls the entire setup his "Fruit and Fiber" system. Known in more technical terms as fiber-optic spectroscopy, this technique is adding data to measurements of distant galaxies at a remarkable pace.



individuals with type II (adult-onset) diabetes produced sufficient amounts of insulin but somehow degraded the crucial hormone in the bloodstream before it could be used, leading to diabetic symptoms.

The highly sensitive RIA technique grew accidentally out of work by Rosalyn Yalow and Solomon Berson of the Bronx Veterans Administration Hospital in the mid-1950s. By attaching a radioisotope to insulin, they developed a test-tube method that could measure insulin concentrations in the bloodstream with 1000 times more sensitivity than existing methods. The technique showed that Mirsky was wrong: Type II diabetics didn't degrade insulin rapidly; they made plenty of insulin but failed to utilize it efficiently. That discovery led to the use of radiolabeled antigen in competitive assays to measure concentrations of many biologically sensitive molecules. "Just look at the original Mirsky hypothesis," says Yalow, who won a Nobel Prize in 1977 for developing RIA. "He had a perfectly good theory. Trouble with the theory is they had the wrong conclusion. To me, the bottom line is: If you want to study what's going on physiologically, you have to *measure* what's going on. It's all right to be theoretical, but unless you can make measurements, your theories can be wrong."

As Yalow's comment suggests, there is nothing like a decisive experiment to put a hypothesis in its proper place—be it on a pedestal or in the wastebasket. The flip side of such power is that a hypothesis or a field still awaiting its essential technique is consigned to an intellectual purgatory: uncertainty, supposition, impatience, and hand-waving. Crick, now at the Salk Institute in La Jolla, California, thinks neurobiology is currently in that realm. As Crick points out, vision researchers have a map of the different cortical areas involved in vision in the macaque and increasing information about its internal neural connections—but there is no equivalent chart for humans. "Until recently there were no methods with which we could get that sort of map for the human visual system," says Crick, "let alone for language or something like that, where they desperately need a technique because they don't have an experimental animal that they can argue with by analogy."

Indeed, Crick thinks that, in general, neurobiology is a field that is still searching for the right techniques to bridge the chasm between theoretical speculation and hard data. "The theory is so remote from the real thing that there's no way of checking the theory," he says with a chuckle. "If there comes a difficulty, they don't think of some way of testing it experimentally which will go to the crux of the matter. They tend to think with their models. That's what we didn't do in molecular biology. When we had ideas, we wanted to know what was the crucial feature of this idea and how could we think of a decisive experiment in which you would have to be right or wrong. And of course," he adds, still laughing, "sometimes it was quite wrong."

Enabling researchers to perform a decisive experiment is not the only way scientific innovation can help bring a field out of the purgatory of hand-waving. A related benefit is that a new battery of techniques can make concrete an entire intellectual framework that had previously been populated only by abstractions. And, in so doing, it may validate fundamental scientific intuitions that simply could not be borne out in an earlier period because of technical limitations. A striking example is provided by the ideas of Thomas Hunt Morgan, the prominent early 20th-century Columbia University geneticist.

Morgan spent many years investigating the factors that influence the early, orderly spatial development of frog embryos and other organisms. He suspected that there were biological substances arrayed in a gradient that determined head-tail polarity. But the lack of molecular tools for sorting out these factors led Morgan to fall back on names such as "head stuff" and "tail stuff" for the substances in question—his frustration at not being able to get down to the molecular level of detail evident in his fuzzy terminology. Within the past decade, Morgan's frustrations have been overcome by a later generation of researchers armed with the techniques of molecular biology.

Many researchers have contributed to this work, cloning and sequencing a host of genes that are involved in the spatial organization of the embryo. One of the techniques that has enabled them to do so is the use of anti-

Scientists as "Theory Snobs"

Among researchers, "technique," if not quite a dirty word, is a begrimed and almost blue-collar term. To twist Edison's famous dictum, technique reeks too much of perspiration and not enough of inspiration, at least according to this rarely discussed but pervasive view. Molecular biologist Sydney Brenner ruefully acknowledges what he calls "a kind of scientific snobbism" that separates the gentleman scientist from the lumpen technician.

"I'm very keen on technique, but my colleagues aren't," admits Brenner, who splits his time these days between the Medical Research Council in Cambridge, England and the Scripps Research Institute in La Jolla, California. Brenner, 65, has been dealing with genes long enough to still speak with awe of such antique high-tech devices as the ultracentrifuge and the chromatograph. "And it may be the idea that 'technique' means 'technician'—that is, not as *intellectual* a thing. But of course that doesn't matter at all. The thing is to find the answer. That's the *only* thing that matters."

The aristocratic attitude toward technique is not new. It goes back at least to Archimedes. The Greek mathematician made a valiant effort (almost succeeding) to save his native Syracuse from being sacked by the Romans during the Second Punic Wars in the 3rd century B.C. by devising ingenious machines of war. Yet it is said that he felt such mean inventions were beneath the dignity of pure science and never described them in his treatises. Many scientists, however, attribute the modern primacy of theory to the brilliance of Albert Einstein and the ability of theoretical physics to explain everything from the fundamental components of matter to the history of the universe. "Theory has become so dominant," says Harvard biologist Walter Gilbert, "that you feel that, yes, you can almost predict everything."

In a kind of sociological pecking order, Brenner says, the bias runs something like this: "Pure mathematicians are a cut above applied mathematicians, who are a cut above theoretical physicists, who are a cut above applied physicists, and so on." The "wet" sciences, like chemistry and biology, seem to lie in the marshy margins of theory.

This bias shows up almost everywhere that big scientific projects are under way, if they are heavily dependent on technology. "One anomaly is that the biomedical world in general, and the genome project in particular, suffers from the fact that people are uncomfortable with research projects designed to improve technology as opposed to a research project designed to extract a few facts," says Stanford biologist David Botstein. "It's very hard to convince people of the value of technology. We're very poor at that."

Yet, like most forms of snobbery, the scientific hauteur toward technique is misplaced: It is impossible to imagine science without technique, and the health of any scientific discipline can be measured by how quickly and easily researchers in the field can prove or disprove a theory. Says Brenner: "In general, techniques have been absolutely important. We couldn't have got anywhere without them." And he adds—with a twinkle—that those who prefer the airy realm of theory to the grimy arena of the decisive experiment aren't necessarily doing so by choice: "I always say it's important to distinguish between chastity and impotence."

–S.H.

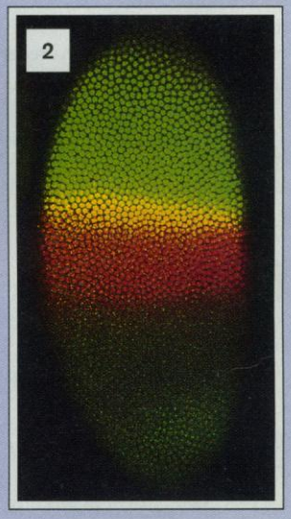
bodies tagged with fluorescent or chemical markers, which enables investigators to locate and time the appearance of specific nucleic acids and proteins in the early embryo. Using a sophisticated optical technique known as laser-scanning confocal fluorescent microscopy, investigators like Sean Carroll of the University of Wisconsin can identify and literally "light up" key developmental genes and proteins as they come into play in embryonic development. The resulting images, showing where in the embryo the genes and proteins operate, reveal beautiful, precise patterns of stripes, bands, and compartments that could never before have been visualized. And with the use of related immunohistological techniques and optical techniques has come the means of making Morgan's intuitions concrete: Developmental biologist Christiane Nüsslein-Volhard of the Max Planck Institute in Tübingen has shown that messenger RNA molecules passed from the mother fruit fly to the egg congregate in the pole that inevitably becomes the

Heads–We Win!

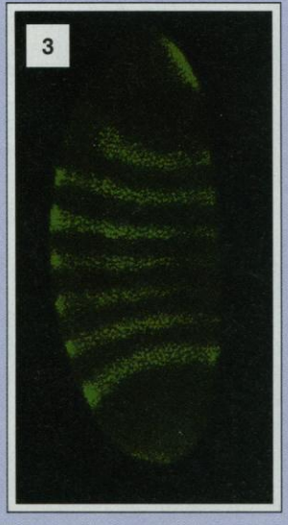
CHRISTIANE NÜSSLEIN-VOLHARD

A gene called *bicoid* controls the development of the anterior, or head, end of the fruit fly embryo, as Christiane Nüsslein-Volhard and her colleagues have shown. This image shows a gradient of the protein produced by *bicoid* shortly after fertilization in the *Drosophila* embryo. High concentrations of the protein *(yellow through red)* mark areas where the head and thorax will develop.

The *bicoid* gene doesn't act alone. Two and a half hours after fertilization, it turns on two other genes–*Krüppel (red)* and *hunchback (green)*. The overlap between the two regions is yellow in this image, which, like numbers 3, 4, and 5, was produced in the laboratory of Sean Carroll using immunofluorescence and laser scanning confocal microscopy.



IMAGES 2, 3, 4, 5: JAMES LANGELAND, STEPHEN PADDOCK, SHERWIN ATTAI, SEAN CARROLL



Not long after *hairy* is expressed, *engrailed*, a "segment polarity" gene, divides each of the previous units into anterior and posterior compartments. The 14 narrow compartments correspond to specific segments of the embryo: three head segments, three thoracic segments, and eight abdominal segments.

The latest method–a combination of triple-label immunofluorescence and laser scanning confocal microscopy–shows three gene products at once. The genes are *hairy (green)*, *Krüppel (red)*, and *giant (blue)*. A separate color appears where two genes overlap. The overlap of *hairy* and *Krüppel* is yellow.

Half an hour later, a gene called *hairy*, regulated by *Krüppel* and *hunchback*, switches on, yielding seven transient stripes. The stripes act as boundaries that begin to divide the embryo into 14 segments.

head; this RNA encodes a protein known as bicoid that diffuses as a gradient and determines the anterior-posterior axis of the embryo. Morgan's "head stuff," in short, is a gradient of the protein produced by the *bicoid* gene.

Making the abstract concrete isn't the only benefit that technical innovation confers on science. One consequence of improved technique—as shown so clearly in the work of Stephen Shectman—is a remarkable speeding up in the pace at which data is gathered. Crick, as always one of the shrewdest observers of scientific trends, comments that it's possible to discern the speed of work in a given field by the way researchers use the term "recently." "'Recently' in neurobiology means the last 2 or 3 years," he says, "but in molecular biology it usually means the last 2 or 3 weeks!"

One publication in particular neatly parallels the technique-driven explosion that characterized the field of molecular biology during the 1980s: the well-thumbed, much-traveled "cookbook" of recombinant DNA techniques known as *Molecular Cloning: A Laboratory Manual*. That book grew out of a summer course at Cold Spring Harbor Laboratory in 1980 and, like a technical samizdat, first made the rounds the following year in photocopied versions. So great was the demand that Cold Spring Harbor Laboratory Press published the first edition in 1982, a second in 1989, and has sold, according to one of its editors, something like 150,000 copies, with a third edition in the works. As for impact, authors Joe Sambrook, Tom Maniatis, and E. F. Fritsch note that when the first edition came out in 1982, there were fewer than 350 gene sequences on file in the GenBank database; by 1986, there were 5000; by 1988, there were 15,000. By last month the total had reached 72,000.

And as the rate of data gathering accelerates, it does not just alter the field as a whole—its influence is soon felt in the career trajectory of individual researchers. Take x-ray crys-

Two Techniques Converge on One Problem

To understand how contemporary scientific methods develop and spread, consider the fate of two landmark techniques. In their lecture accepting the 1986 Nobel Prize, IBM scientists Gerd Binnig and Heinrich Rohrer, inventors of the scanning tunneling microscope, cheerfully acknowledged hearing rumors that colleagues in the field had wagered cases of champagne in the belief that their scanning technique, first described in a 1982 article in *Physical Review Letters*, had actually produced nothing more than computer simulations of atomic surfaces. If the wild proliferation of $100,000 scanning probe microscopes is any indication, the technique has surmounted those initial doubts.

No such fate befell the development of fast sequencing of DNA, a technique that spread rapidly through the biology community in the mid-1970s. Although starting from very different points, the stories of rapid DNA sequencing and the scanning tunneling microscope reveal what might be called a "natural history" of methods and instruments. Ironically, the later chapters of these stories demonstrate how seemingly unrelated techniques may begin, long after they are first used, to converge from different directions on a significant scientific problem.

No matter how chilly its initial reception, a new technique soon triggers widespread optimism if it works and is demonstrably useful. Within the limits of competition and patent protection, news of a novel technique will spread instantly. The DNA sequencing technique devised by Allan Maxam and Walter Gilbert of Harvard University was widely discussed at seminars and shared through photocopied method sheets at least a year before publication in the February 1977 *Proceedings of National Academy of Sciences*. By the time a technique is published in a refereed journal, it will probably have passed through shakedown cruises in several labs.

Researchers tend to greet a new technique with the delight a child feels at receiving a new toy—and gene sequencing was no exception—but the combination of cloning and sequencing rapidly produced intellectual convulsions in molecular biology. Says Gilbert: "Every question we know how to phrase in biology is phrased in terms of genes, and every question about genes can be phrased in terms of the DNA sequences and how they compare." Among the first fundamental answers to be obtained in this way was the discovery that genes are made up of expressed portions (exons) and unexpressed intervening sequences (introns). The enormous interest in the splicing mechanisms whereby the introns are removed and the exons stitched together created the equivalent of an intellectual landrush.

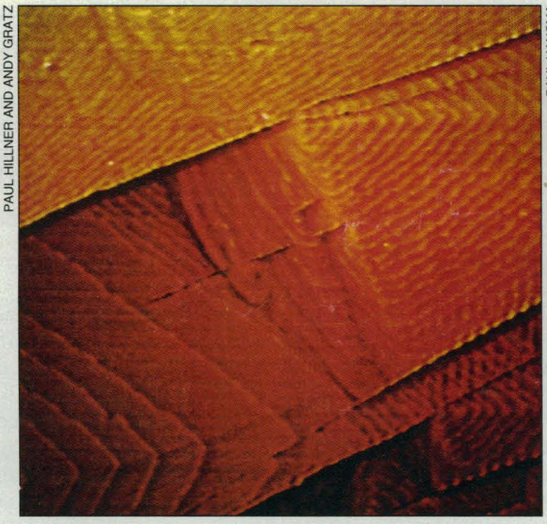
Once the details of a new technique become known, tinkerers and tamperers will soon be at the bench, bending the rules, changing the conditions, refining protocols and dreaming up novel applications. Within a few years of the invention of the scanning tunneling microscope, for example, many labs, including Binnig and Rohrer's, were modifying the device, keeping its superstructure—sensitive piezoelectric controls of nanometer precision—while scrapping its tunneling stylus. This process inspired at least half a dozen spinoffs, among them the atomic force microscope, which has demonstrated how molecules of fibrin join to form a blood clot, and the magnetic force microscope, which can be used to detect the magnetization patterns of computer hard disks and floppy disks.

By the time a critical mass of data accumulates (and probably no technique has extruded more sheer mass than sequencing), a technique may have changed the way science is conducted: A recent report identifying sequence similarity between a gene defect involved in human leukemia and a developmental gene in fruit flies would not have been possible 15 years ago. Indeed, comparisons of DNA sequences are leading to a different, more theoretical, kind of biology, according to Gilbert: "I think biology will develop a mathematical side and an algorithmic side that will turn it into a much more conceptual science, one that will be predictive."

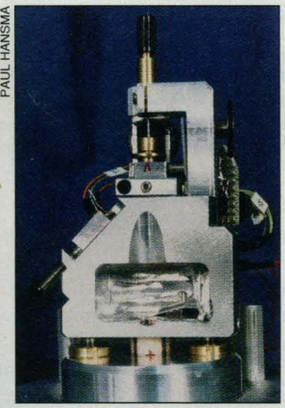
Later, beyond the stage of intellectual fireworks, someone inevitably thinks about automation. For sequencing, one of those people was molecular immunologist Leroy Hood, whose team at the California Institute of Technology developed an automated machine to sequence DNA. Since 1986 Applied Biosystems Inc. of Foster City, California, has marketed a version of the automated sequencer, and the company has sold more than 800 (the current list price is about $110,000). The result of this development is a prodigious increase in the speed of data collection: Sequencers in the 1970s struggled to do several hundred nucleotides a year; Applied Biosystems now claims 18,000 uncorrected nucleotides a day.

Finally, new techniques in unrelated fields have a surprising habit of coming together, as a technique from a distant domain attempts to reinvent the wheel in a familiar field. Even as the Human Genome project has placed a premium on ever more rapid DNA sequencing, the scanning tunneling microscope, that dubious instrument on whose failure physicists were wagering cases of champagne, is edging in from the wings. Biologists at the University of California, Santa Barbara, notably Helen G. Hansma, are experimenting with the use of an atomic force microscope to read the letters of the genetic alphabet "tactilely"—simply by visualizing their shapes—rather than chemically, as is done now. "It's reasonable to assume that this will be possible," says Hansma, "although...it's a long ways in the future still." Nevertheless, the current explosion of scientific technique suggests that the possible becomes actual in an ever shorter period of time.

–S.H.



PAUL HILLNER AND ANDY GRATZ



PAUL HANSMA

Forceful imagery. A prototype atomic force microscope (AFM) built in the lab of Paul Hansma was the basis of the commercial instruments that followed. AFMs can be used to examine processes in living or inorganic systems; the image at left is of a forming calcite crystal.

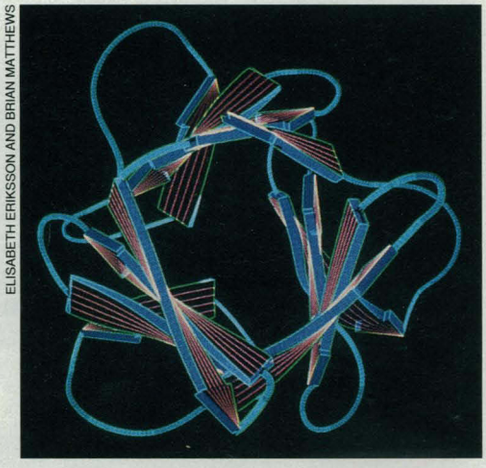
tallography. A generation ago, a scientist embarking on a career in this Sisyphean field had to be resigned to the fact that his or her scientific lifetime would probably be devoted to the elucidation of a single, three-dimensional molecular structure: "Recently" in x-ray crystallography used to mean the past 20 years. No more. "In many cases, the time from the start of the project to the completion of the structure now is substantially less than 12 months," says Brian Matthews, Howard Hughes Medical Institute investigator and director of the Institute of Molecular Biology at the University of Oregon. "I'm not saying that's always the case, but there are many examples of that." Matthews' group recently solved and refined the structure of fibroblast growth factor in several months, and Thomas A. Steitz's group at Yale University solved the polypeptide backbone of a large viral enzyme, reverse transcriptase, in about a year.

Matthews attributes the change to a combination of techniques. "There's not been a single, radical new technology that's had a major impact, but there have been a number of substantial increases in efficiency of a number of different techniques, and in combination they've had a large impact," he says. One is that ubiquitous method, gene cloning, which has allowed crystallographers to obtain large, remarkably pure amounts of previously rare biological molecules; another is the use of two-dimensional electronic detectors that register x-ray beams after the beams are diffracted by crystals. Yet another is the power and speed of computers that run the huge calculations needed to make sense of the diffraction patterns. Finally, many x-ray crystallographers have turned to the increased intensity of synchrotron beams to study biological materials that diffract weakly. "With a synchrotron source," Matthews explains, "the main advantage is that the intensity of the source is orders of magnitude brighter, so it is possible in less time to determine the diffraction pattern." The results are apparent in the proliferation of full-color, three-dimensional images of molecules that have, like fresh-cut flowers on a gray table, enlivened the pages of many journals.

The great leveller

As technique changes the face of a field it doesn't merely alter the career paths of individual researchers, it may also have a fundamental influence on competitive relations among groups in a field. A new technique can, for example, act as a democratic influence, bringing parity into a field where individuals were separated widely by their technical skills. What was once enormously difficult, and could be done only by the most highly skilled scientists, can now be done by almost anyone. "Cloning was a real great leveller," observes Joseph Sambrook of the University of Texas Southwestern Medical Center in Dallas. "All these great techniques are. You take people who are terrifically clever and original, and people who are camp followers and tend to do repetitive work 2 years later, and when a new technique like cloning comes along, everyone goes back to the starting line together. And sure enough, good labs and good people move ahead in the field, until the next great leveller comes along."

Perhaps the subtlest effect of innovations in technique, however, is not on the field, or on the researchers, or the speed of data collection but on something that is both more tangible and often less consciously appreciated: images of the natural world. One benefit that is rarely associated with technique—but that is definitely correlated with it—is beauty. "Beautiful" and "elegant" may well be the most coveted scientific adjectives, more coveted, it sometimes seems, than "accurate" or "true."



ELISABETH ERIKSSON AND BRIAN MATTHEWS

Crystal clear. A combination of unrelated technical innovations has made it possible to produce x-ray crystallographic structures, such as this one of fibroblast growth factor, far more rapidly than would have been possible only a few years ago.

Those adjectives are generally applied to ideas and to theories. Yet anything within a physical domain that can be measured can also be imaged or mapped, and computers have made the distance from data to pictures even shorter. The recent coupling of techniques of measurement with techniques of visualization has produced images of unexpected beauty. Consider the quantum stylus of the scanning tunneling microscope riding the surface of silicon or germanium, its single-atom tip probabilistically bouncing on clouds of electrons, each bump feeding a frail but amplifiable signal back to computers. Out of that fragile signal can be conjured, via digital manipulation and massage, splendid, vibrant landscapes of packed atoms.

Consider the crashing wave of data generated by the remote sensing instrument known as the Thematic Mapper aboard Landsat 5, measuring each geographical scene 705 kilometers below in seven wavelengths, firing off 85 megabits of data per second toward ground-based computers that can, when tweaked and nudged by human engineers, assemble scenes of familiar geography into unfamiliar yet informative beauty—corn crops succumbing to blight in Iowa, oil-well fires staining the landscape of Kuwait.

This beauty is not an end in itself; little in science is. The remarkable patterns in these images are interesting to the researcher not for their beauty alone but because they suggest regularities, themes, even physical laws and new questions to ask. Such images inspire admiration for human ingenuity and awe for the intrinsic beauty with which nature organizes herself, to be sure, but they also encourage an optimism that the unknown can be, and will continue to be, knowable. That, of course, is akin to the fundamental optimism that fires the scientific enterprise.

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