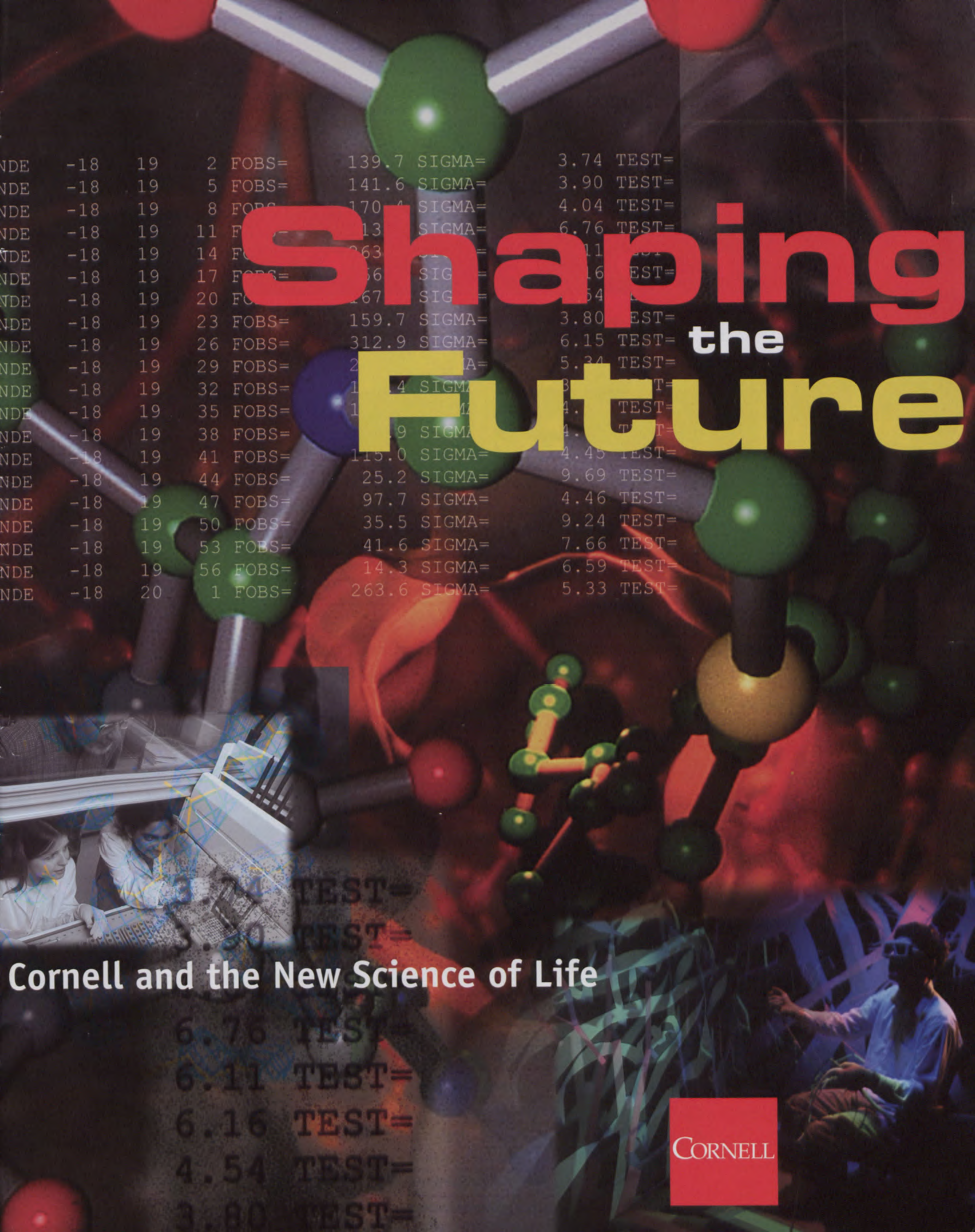
Shaping the Future

Cornell and the New Science of Life



CORNELL

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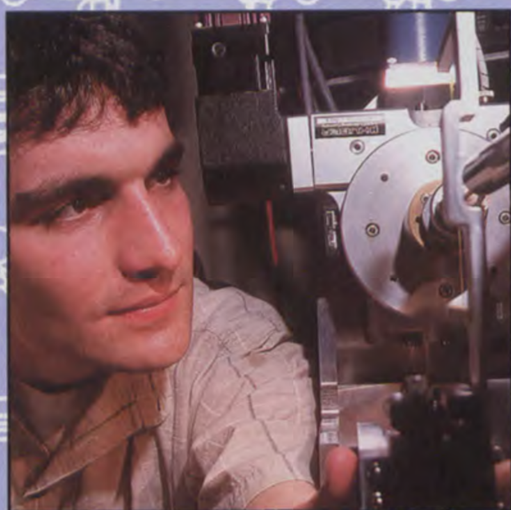

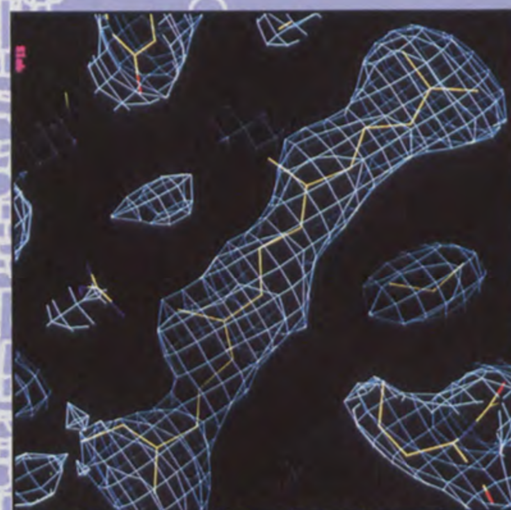

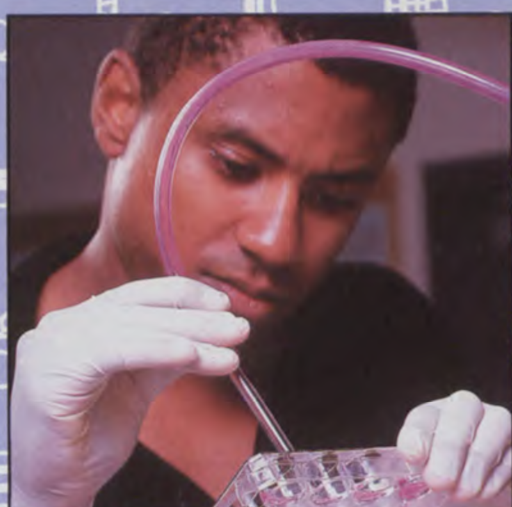

Photo by Dede Hatch

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Shaping the Frontiers of Science and Engineering

by President Hunter Rawlings

Three years ago, the Research Futures Task Force, a faculty group led by Dean John Hopcroft of the College of Engineering and Professor Norman Scott, then vice president for research and advanced studies, identified three "strategic enabling research areas"—genomics and integrative molecular biology, information sciences, and advanced materials—in which Cornell would need superb programs in order to remain a top-ranked university. These research areas, the task force noted, are "characterized by the breadth of their impact in basic and applied research throughout the sciences, the social sciences, and the humanities," and it emphasized that "a university needs to be world class in these areas because the science developed in these areas supports so many other disciplines across the entire university."

The Research Futures report focused our attention on these fields and on the power of selection. It has guided many of Cornell's recent investments in faculty, programs, and research facilities. It has also stimulated deep thinking by faculty committees in other fields, including the

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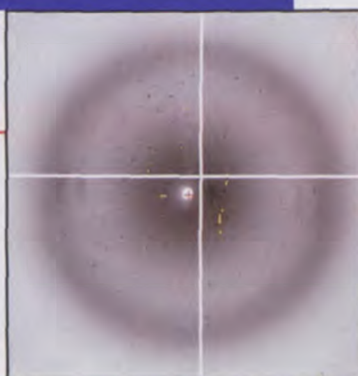
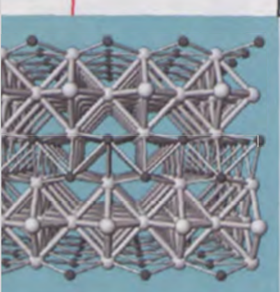
"It is becoming increasingly clear that society
expertise and careful policy analysis in order





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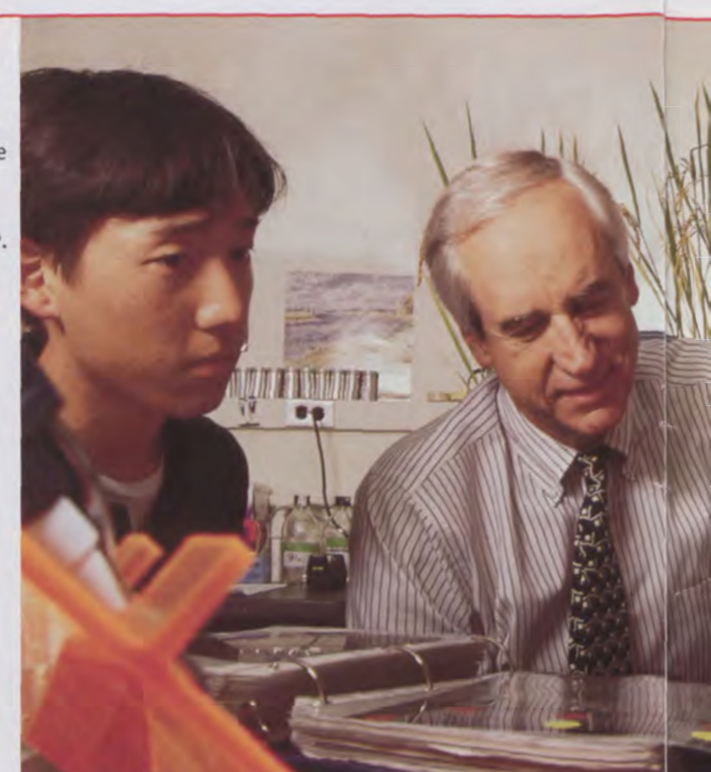
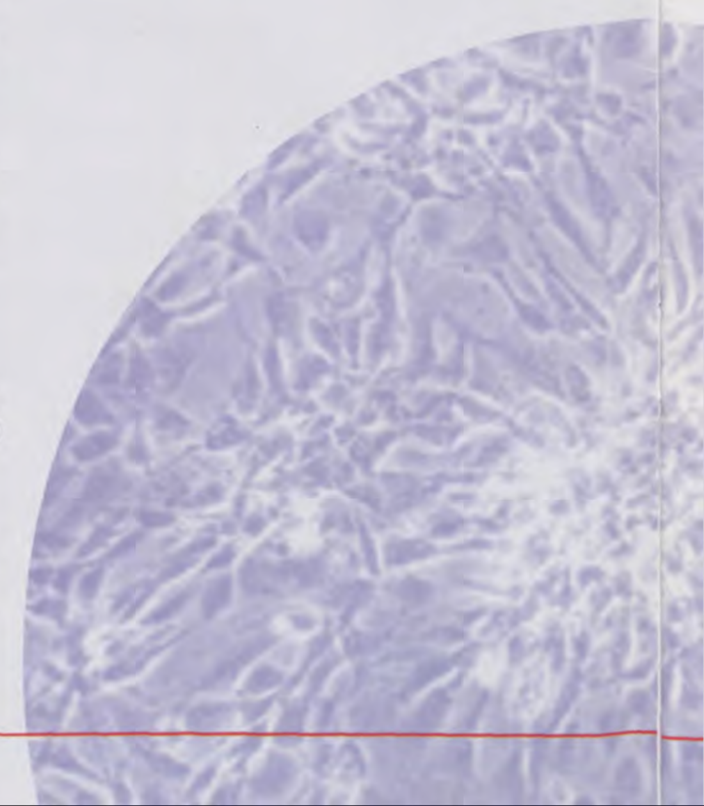
humanities and, more recently, the social sciences, on how to mobilize the university's resources for the best results possible. And it has positioned Cornell for leadership in the remarkable convergence of the physical and biological sciences that promises to be the most exciting intellectual development of the early 21st century.



There are four main reasons, each sufficient by itself, why Cornell must continue to be a major player in this revolution. The first of these is intellectual promise. The revolution that's occurring is ripe with opportunities for new discoveries, analogous in its potential impact to quantum mechanics in the 20th century. Of that earlier revolution, Daniel Kleppner and Roman Jackiw wrote, "quantum mechanics forced physicists to reshape their ideas of reality, to rethink the nature of things at the deepest level, and to revise their concepts of position and speed, as well as their notions of cause and effect."

"Cornell is extremely well positioned for leadership in these converging fields, with a formidable array of facilities and a strong tradition of successful interdisciplinary research."

The Research Futures Task Force foresaw several interrelated revolutions: the computing revolution, which is enabling us to model systems and manipulate data on a scale that would have been inconceivable a generation ago; the molecular biology and genetics revolution, which, less than fifty years after Watson and Crick revealed the structure of DNA, has sequenced the three billion "letters" in the human genetic code, as well as the DNA sequences of other species, and is beginning to identify the function of individual genes and the structure and function of proteins; the chemical biology revolution, which uses new techniques to address biological problems, such as structure-based drug design; and the nanotechnology revolution, which is enabling us to manipulate matter at the level of individual atoms.



Cornell is extremely well positioned for leadership in these converging fields, with a formidable array of facilities and a strong tradition of successful interdisciplinary research. The university has superb programs in physics, chemistry, chemical biology, engineering, and computer science, and the breadth of Cornell's biological science programs is unmatched among its peers. We now have the additional advantage of a $160-million partnership formed by Cornell's Weill Medical requires scientific to weigh the opportunities and the risks inherent in this research into nature's deepest properties and processes."

>> President Hunter Rawlings and Susan McCouch, professor of plant breeding, discuss research with undergraduate Presidential Research Scholars Vincent Lee, left, and Christopher Maher. Lee works on computational approaches to genome analysis and on understanding sequence information. Maher is developing a virtual science center with the Cornell Theory Center and, with McCouch, is writing materials for high school and junior high school students.

College in New York City with The Rockefeller University and the Memorial Sloan-Kettering Cancer Center. Together, these outstanding institutions will recruit a dozen new faculty members and develop core facilities in fundamental technologies—such as high-performance computing, physical analysis of molecular structure, light and electron microscopy, and DNA sequencing—and acquire other tools for genetic analysis and the broad range of chemical techniques that are applied to biology.

A second reason Cornell must move swiftly along these research frontiers is that they offer a tremendous opportunity for improving human life. Better medical diagnosis and treatment, improved drug design and drug delivery, higher-yielding food crops with improved nutritional value, bioremediation techniques to remove toxic substances from the environment, and the use of biotechnology to reduce reliance on pesticides are some of the benefits that can be expected from the new research. As the land grant university for the state of New York, Cornell has a strong tradition of applying its research to meet human needs. With our growing capability in distance learning, we will be in an ideal position to disseminate the products and processes that result from our research to those who can use them in New York State and around the world.

Some of the new research, such as the creation of genetically modified foods and the development of genetic profiling techniques, is already controversial elsewhere in the world and right here in Ithaca, New York. I am pleased that among our strong new faculty members are several from nonscientific disciplines who can contribute to thoughtful campus discussion of these issues, as well as to public debate in national and international fora. It is becoming increasingly clear that society requires scientific expertise and careful policy analysis in order to weigh the opportunities and the risks inherent in this research into nature's deepest properties and processes.

Third, Cornell must be a leader in the new research because it is essential to the education of our students, graduate as well as undergraduate. Cornell students will learn from faculty members who are leading the scientific and technical revolutions of the 21st century. They will have access to powerful facilities, such as the Cornell Nanofabrication Facility, the Nanobiotechnology Center, the Cornell Electron Storage Ring, the Cornell High Energy Synchrotron Source, the Cornell Center for Materials Research, and the Cornell Theory Center.

Many Cornell students will go on to scientific and technical careers that build on the skills they learn at Cornell. But students in all fields will benefit from Cornell's leadership in the biophysics revolution and from our attention to the ethical, social, and political issues involved in it. By combining specialized knowledge with a broad understanding of the issues, Cornell graduates—scientists and nonscientists alike—will be better able to participate actively in public-policy debates and to carry out the responsibilities of citizenship.

And finally, the convergence of the biological and physical sciences with engineering holds great potential for economic development, since many of the products and processes created by faculty and students will have substantial commercial applicability. At least eighty small businesses in our region have already emerged as a result of Cornell's academic resources, with substantial impact on local employment and the tax base of Tompkins County. We know we have entered the era of the "knowledge economy." By investing in these potent new fields, Cornell also will be investing in our region's financial future.

In the biological and physical sciences and engineering, as in other areas of intellectual endeavor, faculty initiative and institutional investment combine to enable Cornell to continue its tradition of leading research and education. In the fields of genomics, computation, and advanced materials, we expect to assume positions of leadership in the new century. I invite you, with this publication, to learn more about Cornell's work at the frontiers of science and technology. <<

Top faculty, new labs, and technology transfer help science pay off for society and Cornell

Multimillion-Dollar Investment Advances Cornell

by David Brand

>> Steve Harvey, project manager for the College of Agriculture and Life Sciences, left, shows Walter De Jong, assistant professor of plant breeding, blueprints for a refurbished laboratory. Harvey recently completed renovating office and laboratory space in Bradfield Hall for De Jong's lab, which was carefully designed and tailored for the scientist's research needs.

When Calient Networks Inc. of San Jose, California, announced that it was acquiring Kionix Inc. of Lansing, New York, the deal was not only a victory for researchers who had poured years of work into the development of microscopic mechanical switches. It also was a major payoff for Cornell's substantial efforts to exploit the fruits of the university's research.

In the early 1990s, Cornell Research Foundation (CRF), the university arm charged with transferring Cornell technology to the public sector, began talking with Greg Galvin, formerly deputy director of the Cornell Nanofabrication Facility. In 1993 Galvin formed a startup company to develop tiny micro-electromechanical (MEMS) devices with an exclusive license from CRF. Since then, Cornell has added other patents to Kionix's portfolio.

Now Cornell will be receiving a handsome payoff from the sale to Calient, based on CRF's equity position in Kionix.

"It takes a significant commitment on the part of the university to run an office like ours," says James Severson, president of CRF. "And it will take a significant amount of income to make the commitment pay off."

Indeed, that statement typifies the Cornell administration's farsighted approach to research, whether it be microscopic electronic devices, new drug-delivery systems, DNA chips, or biosensors: make research pay off for the benefit of society and financially for the benefit of the university.

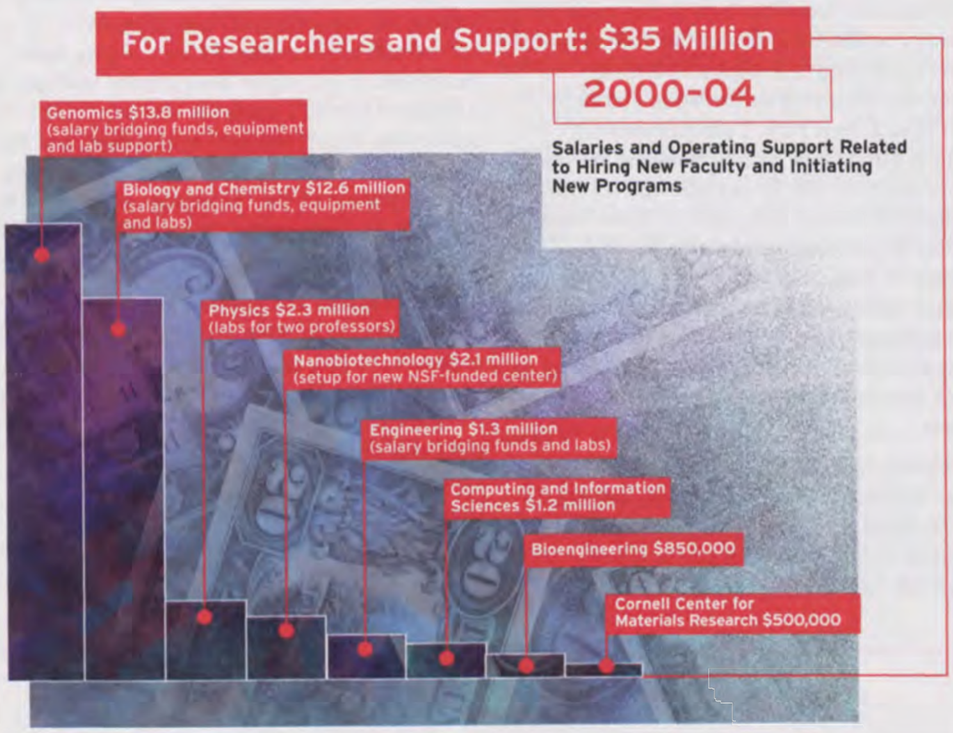
Cornell-developed technology, says Robert Richardson, vice provost for research, "should not sit on the shelf, but should be developed for the public good and, in the process, should profit the university and involve education at the graduate and undergraduate level, the advancement of basic knowledge, and the furthering of faculty research careers."

In the 1999–2000 fiscal year the university spent $396 million on scientific research (which included $114 million for Weill Cornell Medical College). Of this, more than 60 percent came from federal sources, such as the National Science Foundation and the Department of Health and Human Services, and 24 percent from non-federal sources, including foundations and the New York State government. But Cornell, through the support of donors, funded the balance of 16 percent, or $58 million.

"Cornell is paying out more and more for research, even though the federal government is a major funding source for research here," states Kraig Adler, vice provost for life sciences. The question is, Adler says, where should this growing portion of university research costs not funded by Washington come from?

Tuition is frowned on as a source, particularly by parents, even though undergraduate research is becoming increasingly common on campus. That forces the administration to rely on internal funds, such as college funds and endowments, and on donations, largely from alumni. Most of this alumni support goes to cover new faculty appointments and to provide startup money for researchers, says Inge Reichenbach, vice president for alumni affairs and development.

The primary sources of this gift money are two academic initiatives funds, the first of which was launched in 1996 with an $8-million gift. The second fund was initiated in 2000 with a gift of $22 million. An additional $80 million has been given (and a further $80 million is being sought) to support a collaborative program between Cornell and its Weill Medical College, Memorial Sloan-Kettering Cancer Center, and The Rockefeller University in New York City.



Research

The future of scientific research at Cornell will largely be guided by two forces, says Bruce Ganem, the Franz and Elizabeth Roessler Professor in the Department of Chemistry and Chemical Biology, and a leader in collaborative research at Cornell. "Those are the external discovery of new fields, where we become players through new faculty hires, and the internally generated new directions, which Cornell must nurture in some way. Both efforts involve dollars."

What part of the Cornell research machine does the university have to fund? Basically it can be broken down into researchers and laboratories, bricks and mortar, and technology transfer.

>> Hiring the best faculty

Adler noted: "If you hire the best faculty, external research funding will follow. If you hire the best faculty, the best students will follow. Fundamental to everything is a first-class faculty."

Over the two years 1999 and 2000, thirty-one new tenure-track appointments were made in chemistry and chemical biology, ecology, molecular biology and genetics, neurobiology and behavior, physics, computer science, electrical engineering, materials science, mechanical and aerospace engineering, theoretical and applied math, microbiology, plant breeding and pathology, biomedical science, and molecular medicine.

For 2000 through 2004, says Carolyn Ainslie, vice president for financial planning and budget management, the university has committed about $35 million in salary and operating support for new faculty in these areas (see the accompanying charts). In addition, roughly one third of that amount is being invested in these new researchers by their colleges.

Bidding for potential academic stars is highly competitive, a fact illustrated by a number of recent faculty hires who have received gift money and college funds for bridging salaries (i.e., salaries and benefits, sometimes for several years, until budgeted payroll funds become available, and for staff costs before federal funding is received), laboratories, and equipment. One physicist hired as an associate professor a year ago drew more than $1 million from an academic initiatives fund plus additional funds from the College of Arts and Sciences. And several negotiations are under way to bring researchers in the field of genomics to Cornell, each at a cost of more than $1 million.

The belief that all new researchers come to Cornell with a clutch of federal research contracts is far from reality. Many new faculty hires are post-doctoral researchers coming to their first faculty job. That means they come without any research funding from government or foundations and depend on the university to set up their first laboratory and hire support staff.

"We do the heavy lifting. We make the investment in new faculty," says Adler. "We spend startup money to get the laboratory set up and to hire personnel for the first year or two, giving the new faculty member time to get grants submitted so they can get onto external funds. For those first two years, Cornell is carrying these costs."

And those costs have been rising sharply. Adler estimates that the hiring of a post-doctoral researcher as a tenure-track professor in scientific research typically costs about $300,000, and some hiring costs go over $1 million. "That was not an unusual figure for a full professor some years ago because that person would bring a staffed lab. But now we're talking about one person," Adler says.

Partly this increase is being driven, he adds, by biological research. "Biologists used to be relatively inexpensive compared to physicists, whose equipment is a lot more expensive on the average. But that has changed dramatically as many biologists are using molecular techniques that require very expensive equipment."

>> Building new research facilities

New research buildings and extensions to existing buildings, those under construction or planned, have a mix of possible funding sources including university reserve funds, New York State grants, and gifts. For example, the entire $62.5-million cost of Duffield Hall, the planned multidisciplinary research center, and landscaping of the surrounding Engineering Quad is being raised from donations, while the $5.3-million renovation that will make Emerson Hall the physical center for plant genomics research on campus is coming from the College of Agriculture and Life Sciences and the State University Construction Fund. The new $3-million G-Line Facility building at the Cornell High Energy Synchrotron Source is being funded entirely by unrestricted gifts to the university (with $2.5 million provided by the NSF to fund the X-ray beam line equipment in the new building), and phase one of the building of transgenic mouse facilities is being funded by a single gift of $6.2 million (see the story on page 8).

Other major building projects under consideration are a $75-million renovation of Baker Laboratory and Olin Chemistry Research Laboratory to include the construction of new laboratories, approximately $70 million for a Life Sciences Technology Building, and new research facilities for physics and for the College of Veterinary Medicine.

>> Supporting technology transfer

The university's commitment to promoting research that benefits society is embodied in the entrepreneurial spirit at CRF. The foundation exploits Cornell's research through startup companies or licensing agreements, often taking founders' stock or a promise of royalties in lieu of a fee.

During the 1990s, CRF took an equity position in twenty-two startup companies and received royalties of nearly $25 million from licensing agreements. Of that amount, the foundation retained $5.6 million to fund its operation and distributed $11.2 million to the university (including the colleges and departments involved) and $7.4 million to the inventors. In return, the university provided a loan of $10 million to support CRF's deficit.

"Technology transfer is a business of champions," CRF's Severson says. "Universities with significant income from licensing usually have had just one or two big hits. We think that Cornell's big opportunities lie in the areas of nanobiotechnology, materials science, genomics, software and information technology, veterinary medicine, and human health care." <<

University Builds a Mouse House

Alexis Wenski-Roberts/College of Veterinary Medicine

Alexis Wenski-Roberts/College of Veterinary Medicine

>> The Core Transgenic Mouse Facility, a 12,000-square-foot center to genetically transform and breed the most-used animal model in biomedical research, is scheduled to open in spring 2001. In the new facility, located in the College of Veterinary Medicine, Michael Kotlikoff, left, chair of the Department of Biomedical Sciences, takes a mouse out of a cage for viewing, assisted by Ke-Yu Deng, director of transgenic services.

by Roger Segelken

They will never replace the Big Red Bear mascots, but little mice of varied colors and genetic makeups are becoming symbols of life sciences research progress at Cornell.

Studies employing transgenic mice—those with added genes from other species as well as the so-called knockout mice with certain genes deleted—have been under way at Cornell on a limited basis. Soon, researchers will have an on-campus source of made-to-order mice from the university's first specific-pathogen-free mouse facility to genetically transform and breed the most-used animal model in biomedical research.

Located in the College of Veterinary Medicine, the 12,000-square-foot core "mouse house" will serve satellite mouse facilities around campus. In total, $6.2 million, all from a single gift, is being spent on building, upgrading, and outfitting transgenic mouse facilities in existing buildings, including the Biotechnology Building and in the Division of Nutritional Sciences. The second phase of the program, which includes a facility in the proposed life sciences technology building, is budgeted at $15 million.

Mice are a highly regarded asset in research, according to Michael Kotlikoff, professor of biomedical sciences in the veterinary college and director of the Cornell Core Transgenic Mouse Facility. That's because they are the only species in which the full range of genetic manipulations are currently available and can be used to efficiently determine mammalian gene function. "Mice are an important tool in the effort to understand genetic factors that underlie diseases, such as cancer and obesity; to determine the function of individual genes in mammals, including humans; and to better understand complex traits and physiological processes," Kotlikoff explains.

In addition to Kotlikoff's laboratory, numerous investigators across campus will take advantage of the new facility. As part of Cornell's Genomics Initiative, departments in the colleges of Veterinary Medicine, Arts and Sciences, and Agriculture and Life Sciences are recruiting faculty members who require transgenic mouse facilities. Estimates suggest that within five years more than forty faculty members at Cornell will be significant users of the Core Transgenic Mouse Facility.

Kotlikoff also stresses the importance of these facilities in providing the most up-to-date undergraduate, graduate, and professional training in biology.

"Gain-of-function" transgenic mice are produced by microinjecting fertilized mouse eggs with a "transgene," an artificial gene cloned in the laboratory by recombinant DNA technology. "Loss-of-function" or knockout mice are produced by genetically altering an embryonic stem cell in the laboratory and then injecting that cell into a developing embryo early in its development. The eggs or embryos are transferred to a foster mother for gestation. Soon after birth, the young animals are genetically screened to determine which are truly transgenic—that is, those in which the desired genes are expressed and are likely to be transmitted to subsequent generations of mice.

The core mouse house will be operated as a barrier facility to keep disease pathogens away from the mice, not because the animals have diseases they could transmit to humans, the director emphasizes. "The spread of infectious disease, such as mouse viruses, in mouse colonies is a particular problem," he adds. Specially designed mechanical and air-handling systems—as well as a quarantine requirement for animals shipped to campus—will keep the mice isolated from disease. Even individual mouse cages, which are cleaned in high-capacity, cage-washing machines and sterilized in special autoclaves, have their own micro-ventilation systems.

It is critical for many faculty research programs to have the capability to produce genetically altered mice at Cornell—commercial facilities are expensive and slow, requiring long quarantine times before mice can be used in research.

The university's new veterinary college core mouse facility is expected to house up to 30,000 mice. "That may sound like a lot, but a single researcher using mice intensively in his or her research can require 2,000 or 3,000 animals," Kotlikoff says.

The Core Transgenic Mouse Facility is scheduled to open in the spring, with Ke-Yu Deng serving as the director of transgenic services. But already the presence of mice is attracting humans. At least six new researchers in specialties such as murine pathology and functional genomics are joining the faculty. <<

At Weill Cornell Medical College, a Strategic Plan for Research

by Victor Chen and Jonathan Weil

Alan B. Arellano/Weill Medical College of Cornell University

>> **Three of the faculty members at Weill Cornell Medical College involved in the institution's comprehensive Strategic Plan for Research are, from left, Craig Basson of the Cardiology Division in the Department of Medicine, who is in the Program in Genetic Medicine and specializes in cardiac genetics and developmental biology; Hao Wu, an X-ray crystallographer in the Department of Biochemistry, who is in the Program in Structural Biology; and Neil Harrison, a researcher with an international reputation for his work in the molecular neuropharmacology of general anesthetics, who is in the Department of Anesthesiology.**

Weill Cornell Medical College has developed a comprehensive Strategic Plan for Research to expand on its existing strengths, while creating greater opportunities for interdisciplinary collaboration aimed at ultimately improving patient care. The plan, which is likely to lead to major advances in biomedicine, is the result of a consensus of faculty views and of cooperation with the medical college's partners and neighbors, New York-Presbyterian Hospital, Memorial Sloan-Kettering Cancer Center, and The Rockefeller University.

The strategic plan, under the leadership of Weill Cornell dean Antonio M. Gotto Jr., M.D., already has markedly expanded and improved the school's overall research effort. Weill Cornell has enlarged its total research area and renovated existing space, increased the dollar amount of federal research grants awarded to the college by about twenty percent annually, and opened new housing for faculty and postdoctoral fellows.

Above all, Gotto was determined to expand the college's cutting-edge basic research, which involved recruiting thirty new tenure-track faculty members and providing them with new, state-of-the art research laboratories. The question was, how much would this cost?

The answer so far is $316 million, the total cost of Gotto's strategic plan. About half of this, or more than $160 million, has been raised from private gifts, including a major leadership gift of $100 million from Sanford I. Weill '55, chairman and chief executive of Citigroup, and his wife, Joan. The remainder of the plan's cost is covered by medical college funds, sponsored grants, borrowing, and other sources. The program represents the largest expansion of research initiatives in Weill Cornell's century-long history.

The strategic plan focuses on the development of major scientific programs in three fields.

Genetic medicine investigates the genetic factors responsible for such major health problems as cancer, diabetes, AIDS, and cardiovascular disease. It aims to develop treatments using the techniques of gene therapy, a new and rapidly progressing medical treatment in which genetic material (usually in the form of DNA) is administered to patients and used to modify the genetic repertoire of cells to treat or prevent disease.

Ronald G. Crystal, M.D., director of the Institute of Genetic Medicine, and his colleagues have developed an innovative application of gene therapy—essentially blood vessels on demand. They have injected copies of the gene responsible for the production of a specific protein—vascular endothelial growth factor—directly into targeted areas of heart muscle. The researchers hope the newly inserted gene will stimulate the heart to grow brand new blood vessels. The results to date have been promising.

Neuroscience studies the intricate functions of the brain and nervous system, promising to revolutionize the treatment of neuropsychiatric and neurodegenerative disorders such as depression and Alzheimer's disease, among many others.

Helping to build on the existing strength of Weill Cornell's Neuroscience Program, Steven Goldman, M.D., professor of neurology and neuroscience, is leading research into the brain's ability to regenerate and restore function. He is investigating therapeutic remyelination using human neural and white matter progenitor cells. Myelin is the substance of nerve tissue that conducts impulses from one cell to another. In multiple sclerosis and other diseases, the lack of myelin damages brain tissue. Goldman is investigating the use of progenitor cells derived from the human brain to repair this damage.

Structural biology analyzes the structure and function of biological molecules and compounds through three-dimensional visualization, with the goal of designing better therapies and treatment protocols for numerous diseases, including heart disease, AIDS, diabetes, and others.

Min Lu, assistant professor of biochemistry, has investigated the structure and fusion mechanisms of the human immunodeficiency virus (HIV) and other retroviruses. By analyzing the architecture of HIV with powerful new technologies, Lu can work to design new drugs to bind to the virus and prevent or inhibit its growth.

Other researchers hired under the strategic plan include Craig Basson, David Eliezer, Neil Harrison, Chris Lima, and Hao Wu. They are among the new tenured faculty members, out of a goal of thirty, recruited by the college. The Strategic Plan calls for twelve new recruits in genetic medicine, seven in neuroscience, and eleven in structural biology.

Meanwhile, building is well under way. In spring 2000, the medical college dedicated a $39-million renovation of seven floors (plus one mechanical floor) of the Whitney Pavilion for new research labs.

"The choice to recruit mostly junior scientists conducting pioneering research, incorporating their uniqueness and expertise into our current faculty, will invigorate the intellectual atmosphere here and complement the strengths found at such neighboring institutions as Sloan-Kettering and The Rockefeller University, with whom we are collaborating in our recruitment," Gotto says.

In summer 2000 the three institutions, with Cornell's Ithaca campus, announced a $160-million Tri-Institutional Collaboration in basic biological research, inspired by a private donor who is providing half the total cost. <<

Nature is a constant inspiration for much of this interdisciplinary research.

Molecule Makers Aid, Abet, and Even Outwit Nature

by Roger Segelken

What do you make of molecules these days?

"Well, they're still the place where life gets really interesting, where nature encrypts the plans for all the processes that matter, and we're still learning how much we have to learn."

And how about your lab—what do you make of molecules?

"Almost anything you want!"

This might be a typical conversation between scientists at Cornell these days as researchers with different approaches but complementary goals increasingly are working across campus, across the hall, or across the lab bench from one another. The details they are discovering about how the basic bits of nature come together are enabling a remaking of the molecules of life. All the basic studies of life at the most fundamental level are helping molecule-makers aid and abet nature, and even to outwit nature by attacking diseases.

An intriguing place to begin a cross-campus molecular mystery tour is the Riley-Robb Hall laboratory of Carlo Montemagno, associate professor of agricultural and biological engineering—a workshop for the biologically inspired that contains elements of the fantastic. "Like microscale robots powered with muscle and fueled by light, by photons," he hints. "Or smart dust—devices smaller than bacteria with a well-directed intelligent function to perform."

Smart dust, says Montemagno, is based on bacteriorhodopsin, the protein in heliobacter and certain other bacteria that allows them to be photosynthetic. NASA wants to use smart dust on Mars to look for likely sites where life—albeit equally tiny life—might exist. Dust that's even smarter could have a diagnostic and therapeutic function, seeking out and treating pathogens in plants. Or people.

>> Thinking small

If you want to deal with living things on the molecular level, you want devices in a size and form that life's molecules can understand, Montemagno says, stating the nanobiotechnologist's creed that will be heard again and again across campus. "Our goal is to integrate micro- and nano-scale engineered devices with human cells, and we would like components to self-assemble on devices and become part of the devices. In molecular motors, we have a propeller that spins and makes the motor move and we're now testing integrated chemical switches to turn the motors on and off," Montemagno says.

NASA isn't the only group funding such schemes. The Defense Advanced Research Projects Administration and Office of Naval Research are both very interested in Cornell work on developing myosin, the motor protein in muscles, to move a light shutter or an actuator in robotic sensors. Then there's the Department of Energy, the funder that keeps some of the more than two dozen researchers and students in Montemagno's group busy, developing light-fueled molecular-motor-powered machines. Also, the National Science Foundation is funding a project to use molecular motors to sort other molecules, as well as a bigger, macro-scale effort to make insect-sized smart sensors.

>> Hot-rodding molecular motors

All of this research is aimed at moving simple objects with molecular motors, those tiny but elegant ways that nature has developed to move other molecules around cells. It is easy to forget that until recently graduates knew more about General Motors' motors than molecular biologists did about the self-propelled miniatures.

Then Cornell graduate student Hongwei Yin started work with Anthony Bretscher, a professor of molecular biology and genetics, and she solved a long-standing mystery of cell division. She showed how tiny molecular motors, carrying target proteins, help orient the mitotic spindle to transfer genetic material from the nucleus of the "mother" cell to the "daughter."

While the mitotic mechanics labored in the Biotechnology Building, biophysicist Michelle Wang was in Clark Hall, elucidating an even earlier role of molecular motors. The assistant professor of physics' molecular motors run along the DNA template each time an RNA copy is synthesized. Without RNA molecular motors there would be no replication of DNA and nothing for the mitotic spindle to deliver.

>> Modular games

Next door in S. T. Olin Laboratory, molecule-maker Dotsevi Sogah is thinking about Lego®. The professor of chemistry and chemical biology is careful to write the name with a little trademark symbol, out of respect for the intriguing children's game of modules that inspired him to assemble diversely shaped molecules into forms that nature never knew.

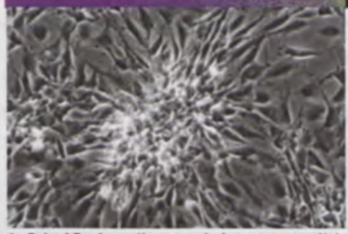
The key to the Lego method is catenation—the formation of chains of atoms—Sogah explains, "and we're not limited to naturally occurring protein sequences. We can handle a variety of synthetic polymers. We build a functional material on a scaffold with catenation—A plus B, A plus B, repeated as many times as necessary. That's catenation. That's the biomolecular Lego-set modular method, and that's what is letting us achieve the ultimate goal of the synthetic polymer chemist: to precisely control polymer architecture and obtain materials with well-defined properties."

Sogah describes one bioinspired material he's

continued on page 12

Molecular Medicine

The path from cancer cells to a plan to stop cancer.



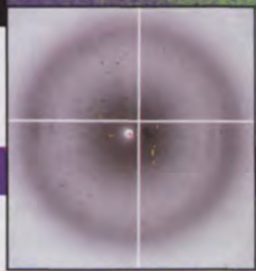
Credit: Wen Jin Wu

1. Cdc42 signaling protein, responsible for malignant transformation of cancer cells, is cloned and purified.

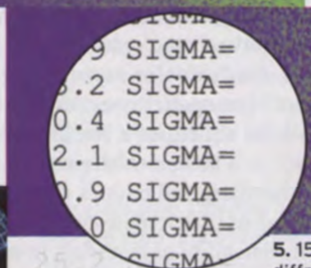
Credit: Wen Jin Wu

2. Cdc42 and GDI, another signaling protein, are converted to crystalline form for X-ray diffraction study.

3. Complex of Cdc42 with GDI is examined at CHESS.

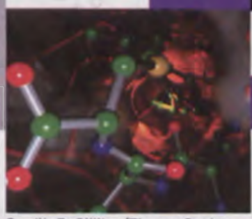


4. Diffraction pattern gives the first clue to Cdc42/GDI molecular structure.



5. 15,000 reflections from X-ray diffraction allow calculation of 3-D models of proteins.

6. Electron density map of Cdc42/GDI structure.



7. Ball-and-stick model of Cdc42/GDI complex.

Credit: R. Gillilan/Theory Center

Credit: R. Gillilan/Theory Center

8. Ribbon diagram of Cdc42/GDI.

Credit: Copyright 2000 Dede Hatch

9. Virtual reality "cave" at the Cornell Theory Center allows 3-D exploration of the molecules' structure, perhaps inspiring the design of a drug to inhibit malignant transformation.

Illustration by Clive Howard Office of Publications Services

Before structure-based drug design begins, Cornell researchers must determine the molecular structure of the protein they hope to modify.

>> Dotsevi Sogah, left, professor of chemistry and chemical biology, and College of Arts and Sciences senior Adam Braunschweig review the structure of newly developed, bioinspired molecules in S. T. Olin Laboratory. A children's game of modules, Lego®, inspires parts of their research.

continued from page 10

working on—artificial silk. "Natural spider silk has some excellent properties. Pound for pound, it's stronger than the strongest manmade material, Kevlar, and spider silk has properties of elasticity and resilience that Kevlar does not. First, we examine the natural materials to see what makes them work as well as they do. Then we try to reproduce the natural material as closely as possible, and look for ways to put the parts together on our Lego scaffold." Sogah also likes to merge the "soft" (or organic) materials with the "hard" (inorganic) ones, especially on the nanoscale (in structures a few billionths of a meter in size), in a domain where many of the old rules of chemistry and physics don't apply. Nanocomposites of plastic-plus-clay could reduce the flammability of materials in aircraft seats, or make a better timing belt for automobile engines. Operating on the nano level lets Sogah and Emmanuel Giannelis, a professor of materials science and engineering, independently make microspheres with improved porosity to deliver drugs to sensitive parts of the body, such as the brain.

Nature is a constant inspiration for much of this interdisciplinary research. Take, for instance, the super-small directionally sensitive hearing aid that is based on the auditory organ of a tiny parasitic fly that homes in on the mating calls of crickets. Ron Hoy, professor of neurobiology and behavior and a specialist in bioacoustics, had been listening to bug noises for years when he discovered how a minuscule creature—one that theoretically shouldn't know the direction that sounds come from—manages to cheat physics.

The fly's directional hearing organ was little more than a footnote in neurobiology until Norman Tien, assistant professor of electrical engineering, had an idea. Now the Cornell collaboration of biologists and engineers is on the way to producing a better hearing aid.

>> The art of inhibition

Attacking disease is a major goal of nanobiotechnologists, who dream of drugs being delivered straight to needy cells by smart micropharmacies. Where will this next generation of pharmaceuticals come from? Perhaps from Cornell's Baker Laboratory where Jon Clardy, professor of chemistry and chemical biology, practices the science and extremely fine art of structure-based drug design—atom by atom, molecule by molecule. Clardy recently was appointed to the National Cancer Institute's advisory unit, the NCI Board of Scientific Counselors.

Clardy explains how knowing the exact, three-dimensional structure of an enzyme called DHODH (for dihydroorotate dehydrogenase) could lead to a treatment for malaria and possibly other parasitic diseases, and even cancer.

"DHODH catalyzes important reactions, including synthesis of nucleotides, the basic units of nucleic acid in DNA and RNA," Clardy says. "Nucleotides are difficult and energetically expensive to synthesize in the body, so we tend to recycle them through salvage pathways, but sometimes recycling is not sufficient and we need to make new nucleotides. T-cells in the immune system need to make new nucleotides—and so do cancer cells—and this tells us that DHODH could be the Achilles' heel of nucleotide synthesis. If we could find the right inhibitor to block nucleotide synthesis, cancer cells couldn't grow."

Another organism that uses a form of DHODH to make its own nucleotides is the blood-borne malaria parasite *Plasmodium falciparum*. "It turns out that the malaria parasite is very dependent on the DHODH pathway—it lives inside red blood cells, it feeds on them, they burst and that harms the capillaries—and *Plasmodium* needs to synthesize its own nucleotides, in order to reproduce, because it can't get nucleotides from red blood cells," he says.

One of the most exciting places on campus for molecular research, says Clardy, gesturing southward across campus, is the X-ray crystallography labs of CHESS, the Cornell High Energy Synchrotron Source. There, intense X-rays, a by-product from the electron-positron beam ring of the Wilson Synchrotron Laboratory, are used to illuminate the atomic structure of almost any material, from flu viruses to geological samples.

>> Discovering the switch

It was at CHESS that a team, based both in the Department of Molecular Medicine at Cornell's College of Veterinary Medicine and in the Department of Chemistry and Chemical Biology, demonstrated for the first time the atom-by-atom structure of a molecular "switch" called Cdc42, and a regulator of the switch, a protein called GDI. These control an essential chemical pathway for both normal and cancerous cells. The achievement was deemed so significant that their diagram of molecules merited the cover of the journal *Cell* in February 2000.

Richard Cerione, leader of Cornell's Cdc42 team and professor of molecular medicine, notes that more options are being found for therapeutic intervention because "the more molecules we learn about, the more we can interfere with." It was Cerione who "discovered" the human Cdc42 protein at Cornell in 1990. He and his collaborators—postdoctoral researchers, graduate students, even undergraduates—cloned and purified the protein, then tried to turn it crystalline for the X-ray diffraction studies. "Making a crystal that will diffract X-rays properly is not a trivial task," Cerione says. The prettiest crystals are not necessarily the best at defracting. It can often take years."

The Cdc42 team was impelled by the knowledge that the cell-growth-regulating protein was "conserved" throughout evolution, appearing in organisms as primitive as yeast and continuing to function in human cells. Then they "went fishing," as Cerione modestly puts it, for another link in the cell-signaling reaction, the regulator of the Cdc42 regulator, and finally found GDI, which stands for guanine nucleotide-dissociation inhibitor. And they figured out how to make a crystal form of the two proteins together in complex, to discover exactly how they interact in normal and cancerous cell growth.

Sometimes as Cerione makes the Tower Road "commute" between his labs in veterinary medicine and in chemistry, he reflects on why Cornell is the perfect place to do his brand of biomedical research.

"We have the biologists, the physicists, the engineers, the computer programmers, and the chemists who really know how to make molecules," Cerione says, "people in all areas who might not have thought they could make an impact on cancer and our understanding of how cells work." <<

>> An artist's conception of an array of molecular motors coupled to nanofabricated structures.

Drawn by Francis Peters ©Montemagno Research Group

Harold Craighead

"Setting Minds on Fire All Over the World"

NANOBIOTECHNOLOGY

>> Harold Craighead

Harold Craighead, director of the Nanobiotechnology Center, joined the Cornell faculty in 1989 as a professor in the School of Applied and Engineering Physics. Until 1995 he was director of the National Nanofabrication Facility (predecessor of the Cornell Nanofabrication Facility), where he initiated new efforts in biochemical surface patterning, biological sensors, and molecular motion in nanofluidic systems. In this article Craighead discussed the birth and future of nanobiotechnology, a word that was coined at Cornell.

Nanobiotechnology is one of the most promising fields to emerge from the collaboration of life scientists with engineers and physicists. Researchers in this exciting new field use the tools and processes of microfabrication on the "nano" scale (increments of a billionth of a meter, approximately the diameter of three silicon atoms) to build devices that examine biological systems. The researchers also apply their discoveries to create new types of useful devices based on nanofabrication.

It's astounding how rapidly this is catching on at so many institutions. The idea is setting minds on fire all over the world. A lot of small companies clearly want to take advantage of this, although I don't see industry as being a long-term funder of nanobiotechnology at universities. Long-term federal and state funding probably is the only stable source.

When the National Science Foundation granted Cornell $20 million to establish the first Nanobiotechnology Center (NBTC) for research and education in January 2000, the agency cited the university's multi-institutional program—in which the term nanobiotechnology was coined.

>> A new focus on life processes

Nanobiotechnology can be viewed as the union of nanofabrication—the method of crafting small-scale structures and devices—with biology to create new experimental possibilities and new types of devices. This will give scientists new ways of exploring life processes at the subcellular and molecular levels.

The idea of bringing physical science and engineering-based activities closer to biology is a fundamental change in the way people are looking at science. Physics, at one time, had its main intellectual thrust in looking at subatomic activities, high-energy physics, and interstellar activities, and I think some of the orientation now is turning more toward life processes.

Life processes are as complex as any of the subatomic structures. Leading U.S. research universities, like Cornell, are uniting more of physics, technology, engineering, and biology. That gives new tools for the biologists to use, it gives theorists an opportunity to turn their attention to processes that go on in cells and even above the cellular level, at the level of organisms and ecosystems.

These are very complex systems. The idea is to develop more quantitative mathematical descriptions and find different ways of testing hypotheses. I think we are seeing biology becoming more quantitative and physical sciences becoming more influential in biological problem solving.

>> Research horizons

The academic and industrial researchers and technical practitioners of the future will be students we are training today. They will be well grounded in traditional disciplines, but they will have knowledge of a broader sort of problem-solving skills and techniques.

Recently I spoke with a student who wants to do a master's degree in engineering physics with biological uses. We are seeing more and more students with these kinds of interests. They are following their interests where they perceive the new, interesting jobs to be.

Frankly, I believe a lot of upcoming students no longer want to go into big semiconductor industries, because those industries are too mature and it would be like plugging into a big machine. But the idea of entering a field that is wide open—and might lead to a whole new way to cure disease, for example—is a possibility that excites students greatly. <<

>> Novel fabrication techniques are used to construct nanoscale and atomic-scale features, such as these tips, that are used to produce engineered substrates for attachment of biological motors.

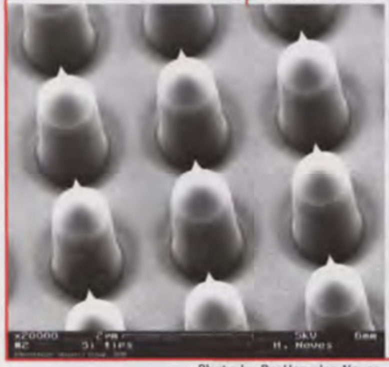


Photo by Dr. Hercules Neves

>> One method of characterizing a molecular motor's properties is by using a laser-generated optical gap to monitor the movement of a microscale bead attached to the motor.

Drawn by Francis Peters ©Montemagno Research Group

Solving Scientific Problems

by Blaine P. Friedlander Jr.

The dry-erase marker board has seen better days. Differential equations go one way, arrows connecting proteins go another, and the mind-challenging process of understanding a cadre of kinases continues.

Cornell physics graduate student Colin Hill marks up his latest findings on PI3 kinase. The diagrams on the board become ever more complex as the group tries to understand how the nerve growth-factor-treated cells differentiate and become neurons. He tells faculty members sitting around the conference table that experiments verified predictions from the mathematical model.

The Cornell Computational Cancer Group is a serendipitous ensemble of biologists, physicists, engineers, and chemists devoted to a better understanding of the pathways of cancer.

The group's existence illustrates how walls between departments at Cornell are coming down. Interdisciplinary approaches to solving scientific problems are sprouting so quickly that now there are dozens of groups on the campus collaborating to resolve a variety of life-science issues.

"We have some unique strengths at Cornell that other places don't have," says Richard Cerione, professor of molecular medicine at the College of Veterinary Medicine as well as a faculty member of the Department of Chemistry and Chemical Biology. "We have the physics and chemical sciences and engineering and informatics and nanofabrication. We have resources that are not available at a med school. It's truly a marriage of disciplines."

This marriage probably could not take place anywhere other than at a major research university. Gregory Baxter, senior research associate at the Cornell Nanofabrication Facility (CNF), recalls his experience in the private sector, where engineers and biologists rarely talked to each other. "As a result, projects took years to complete. But at Cornell we act as a team, and what once took years can now take months. It's a different way of thinking."

Collaborative research makes better use of university resources, according to Michael Shuler, professor of chemical engineering. "Since I've been at Cornell," he adds, "every project I've been involved with has been a collaboration with someone from the life sciences."

>> "Biology isn't as simple as it used to be"

The gene group started in 1999 when Cerione began looking for new ways to tackle the increasing complexity of biological problems.

Guillermo Calero, an M.D. conducting postgraduate research in Cerione's laboratory, along with Hill, had been taking a class on chaos taught by Steven Strogatz, Cornell professor of theoretical and applied mechanics, and suggested a mathematical approach.

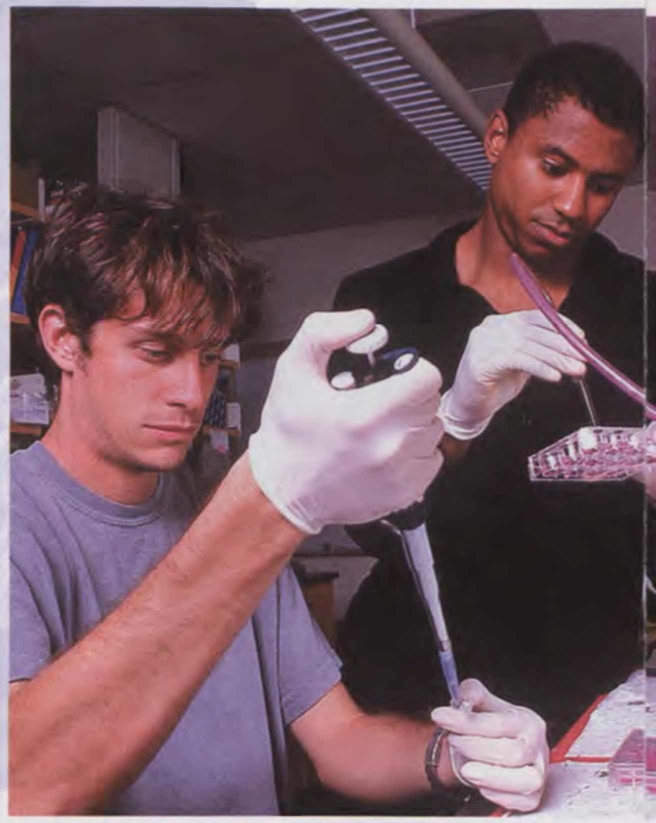
Calero and Hill started attending a weekly informal meeting organized by Strogatz. Cerione and physics professor James Sethna joined the group. They also met engineering professor Kelvin Lee and Bruce Ganem, professor of chemistry and chemical biology. Graduate student Kevin Brown later joined the group. While the physicists and engineers learned biology nomenclature, the biologists learned physics.

From only a vague goal at first, the researchers now are concentrating on computer simulation of biochemical networks involving extracellular regulated kinase protein, known as ERK. Knowing this information will provide basic research information on whether a cell divides and grows, or whether it becomes a differentiated cell.

"We once thought of the pathways to cells as simple, but we are finding out that they are more complex than once believed," says Cerione. "It turns out that there are extensive networks, and there is lots of cross talk going on through these networks. Biology isn't as simple as it used to be."

>> "The amazing thing is this works"

Trying to test new pharmaceuticals for toxicity in humans is laborious, time-consuming, and expensive. But now, pharmaceutical companies could have a new way to test the toxicity of drugs



without having to depend on laboratory animals. Introducing: the "animal on a chip."

Baxter and his colleagues, including co-inventor Shuler, have reproduced the major systemic organs like the liver, the lungs, and other organs and tissues of a rat on a microchip. Other collaborators are William Olbricht, professor of chemical engineering; Brad Anton, associate professor of chemical engineering; and research physiologist Raymond Glahn of the U.S. Department of Agriculture's Plant, Soil and Nutrition Laboratory on campus. The project is sponsored in part by a Nanobiotechnology Center grant to Shuler. According to Baxter, the development is typical of the way research collaborations are making possible micro solutions for macro problems.

"The physiology is reproduced right on this chip, making it perfect for testing new drugs or confirming old ones," explains Baxter, who is CNF's biological research associate. "I would say that more and more biologists, chemists, and

Antje Baeumner, assistant professor of agricultural and biological engineering, demonstrates how microchips detect pathogens in food and water. She works in collaboration with the Cornell Food and Water Safety Group.

with a "Marriage of Disciplines"

Theoretical physics graduate students Kevin Brown, left, and Colin Hill carry out a test for the Cornell Computational Cancer Group in professor Richard Cerione's laboratory in the College of Veterinary Medicine.

materials scientists are looking toward microchips for solutions to their problems."

The animal on a chip consists of a network of micro-fluidic channels, segregated into discrete compartments containing living cells, selected to mimic animal organ systems.

To make a test, chemical compounds are introduced into the microchip. The cells are then stained to indicate if they are alive or dead. The latter means the compound is toxic and should be rejected for pharmaceutical purposes.

"It's simple—and the amazing thing is this works," Baxter exclaims.

"A dynamic coalition"

If all goes as planned, in late 2001 a tumor antigen vaccine will emerge from the Cornell-Ludwig Partnership laboratory and will be ready for clinical testing.

"This kind of facility is not common in an academic setting," says Carl Batt, Liberty Hyde Bailey Professor in the Department of Food Science.

The Cornell-Ludwig Partnership originated with Carl Nathan, M.D., director of the Seaver Laboratory of Cancer Immunology at Cornell's Weill Medical College in New York City. About two years ago, Nathan introduced Cornell president Hunter Rawlings to Lloyd Old, the chief executive officer of the Ludwig Institute, which funds cancer research around the globe. And thus was born a collaboration.

Rawlings involved Shuler, who in turn called on Batt and David Wilson, Cornell professor of molecular engineering. The group relies on the expertise of Alan Woods from the Boyce Thompson Institute for Plant Research at Cornell and Yao-Tseng Chen, M.D., a professor of pathology at Cornell's Weill Medical College in New York City.

In July 1999, these collaborators and the Ludwig Institute created the Bioprocess Research Laboratory, and plans have been laid out for a bioproduction facility. "The Cornell-Ludwig Partnership is a vital link in the process from the discovery of tumor antigens in the laboratory to the assessing of their therapeutic potential in the clinic," says Batt. "The partnership represents a dynamic coalition of two world-class institutions."

"Everyone in the group brings a much-needed specialty"

To find pathogens in food or water, microbiologists traditionally have detected antigens on viable cell surfaces, which is a laborious, costly investigative process. Now, through a cooperative research program in food science and agricultural engineering, the testing might soon be handled by biosensors that detect specific genetic sequences optically or electrochemically.

The biosensors were developed by Antje Baeumner, assistant professor of agricultural engineering, and Richard Durst, professor of chemistry and chair of the Department of Food Science and Technology at the New York State Agricultural Experiment Station in Geneva, New York.

"Food and water safety is a complex area," says Baeumner, who joined the Cornell faculty in 1999 after completing postdoctoral research in Durst's lab. "You have to have different specialties, otherwise you can't solve the problems. I know about pathogens, for example, and everyone in the group brings a much-needed specialty."

The biosensor research is an outgrowth of the interdisciplinary Food and Water Safety Group, assembled by Kathryn Boor, associate professor of food science, and Martin Wiedmann, assistant professor of food science, who also joined the faculty in 1999. The members, faculty from the College of Agriculture and Life Sciences, the College of Veterinary Medicine, and the College of Human Ecology, meet monthly to discuss research problems.

"Working in a collaboration means we can improve the safety of our food and water," says Baeumner. "That's a good reason to be part of it."

Research Dreamhouse

>> Renderings of Duffield Hall as envisioned by the architecture firm Zimmer Gunsul Frasca Partnership.

A model of Duffield Hall, the new interdisciplinary research building planned for the Engineering Quad, is described by project manager Bob Stundtner, right, to Clifford Pollock, left, the Ilda and Charles Lee Professor of Electrical and Computer Engineering. Pollock is the academic program leader on the Duffield management team. In the middle is Al Clark, associate director of the Cornell Nanofabrication Facility.

Will Be a Cornell "National Resource"

by David Brand

One of the most intricate and carefully planned moves in the history of Cornell will begin in 2003. Piece by piece, over about four months, forty major instruments, such as optical lithography steppers and ion-beam etching systems, will be moved through a specially constructed clean corridor into a new facility. Amazingly, while this is going on, researchers from around the country will continue their work without interruption.

The move will cap the relocation of Knight Laboratory, the home of the Cornell Nanofabrication Facility (CNF), into its new quarters in Duffield Hall, Cornell's $58.5-million, high-tech research center, whose three stories will begin rising on the Engineering Quad, adjacent to Phillips Hall, in spring 2001.

Gregory Baxter, a biological research associate who helps physicists and engineers with biological processes at the Cornell Nanofabrication Facility, assists applied physics graduate research assistant Andrea M. Perez Turner with pipetting central nervous system cells onto a silicon wafer.

In a project that will require fine-print planning, the new multidisciplinary research building will be constructed around the present Knight Lab, which adjoins Phillips Hall. Once CNF is safely ensconced in its new home, the old Knight Lab will be torn down to make way for a commanding atrium, one of three that will make Duffield the "winter palace" of the Cornell campus.

"I think Duffield is going to become a national resource," says Christopher Ober, director of the Department of Materials Science and Engineering and a member of the faculty since 1986. "What we are dreaming of right now is so advanced that it will take industry time to digest. Initially Duffield will focus on highly competitive academic research."

The "dream" of Duffield is to manipulate molecular structures to synthesize new materials for biology, optics, and electronics, and to advance this research by encouraging daily interaction among engineers, physicists, chemists, and biologists. This mix will be commanded by Duffield's three main occupants: CNF, the Nanobiotechnology Center (NBTC), and components of the Cornell Center for Materials Research (CCMR). In addition, a first-floor characterization lab, directed by John Silcox, vice provost for physical sciences, will provide a wide array of analytical tools, such as scanning tunneling electron microscopes.

"It will be for people who really need to work at the nanotechnology scale," says Clifford Pollock, the Ilda and Charles Lee Professor of Electrical and Computer Engineering, who is the academic program leader on the Duffield management team. "It will be an interactive space and a project space."

Like all future occupants of Duffield—and aware that the research center will vault Cornell into new prominence in the field of nanotechnology—Pollock talks about the art of the possible in terms that sound like science fiction. One of the major research areas will be into tiny mechanical devices known as MEMS (for micro-electromechanical systems) that manipulate matter at nearly atomic dimensions.

"The next big jump will be making thousands of MEMS devices work in concert as a system on a single chip," says Pollock. And after MEMS might come moletronics, or a new generation of electronic devices at the molecular level.

Increasingly, this research is using the tools of biology to create new materials, devices, and systems, such as cell-sized devices with their own self-contained memory programmed to analyze, probe, and synthesize. In Duffield, says Harold Craighead, director of NBTC, "we will have everything we need to do high-resolution analysis of biosystems." NBTC researchers will be working side-by-side, culturing cells on devices in one room, for example, and doing optical and electrical measurements in another.

"My guess is that users are going to become more biological. Already I am seeing engineers moving more toward biosystems. So I suspect that with time there will be increasing demand for new types of fabrication processes," Craighead says.

Initially, NBTC scientists will have use of about one-fourth of the 12,000 square feet of clean rooms on Duffield's first floor. CNF associate director Al Clark explains that it is essential to dedicate clean room space for NBTC, "so that biologists can do a lot of stuff with saline solutions and other things that could grossly contaminate normal CNF operations."

CNF, which is a national user facility, needs about forty percent more clean-room space than it has at present to alleviate crowding and to allow for growth. Over the past three years, in particular, growth at the facility has accelerated to about fourteen percent a year.

The reason, says CNF laboratory manager Lynn Rathbun, is the huge growth in nanotechnology research. Most of the researchers who use the facility are physicists, biophysicists, and bioengineers, and perhaps only twenty percent have some biology relation. But, says Rathbun, the number is growing.

The user committee, chaired by Pollock, is still considering how much space the three major occupants of Duffield finally will get. This involves many difficult decisions about who and what projects will occupy the 20,000 square feet of lab space on the second and third floors. But Pollock emphasizes that space will be allocated only for three to six years at a time, and once a project is concluded, the space will be allocated to others.

Already, says Ober, the promise of Duffield is attracting new researchers to Cornell, and prospective students want to know when it will be finished. "In two years," he predicts, "we will see an explosion of students coming to Cornell just because of Duffield."

Christopher Ober

"The potential for synergy is enormous"

>> Christopher Ober, department director and professor of materials science and engineering, demonstrates research using a silicon wafer in his laboratory in Bard Hall. "We already have essentially a blurring between the lines of physics, engineering, and chemistry," he says.

With thirteen faculty members and roughly a hundred graduate students and visiting researchers, the Department of Materials Science and Engineering is a major player in interdisciplinary research on campus. It also will be one of the groups occupying Duffield Hall, the new multidisciplinary research building that will open for business on the Engineering Quad in 2003. The department pursues a broad range of materials research in physics, chemistry, engineering, and increasingly, biology. Christopher Ober, director of the department, serves on the executive committee of the Nanobiotechnology Center (NBTC) and is on the users committee of the Cornell Nanofabrication Facility (CNF) and Duffield Hall.

Recently Ober discussed the future of interdisciplinary research with David Brand, Cornell News Service's senior science editor.

What is the future of the new interdisciplinary research?

I think we are going to see new ways of carrying out research. Although the sets of disciplines we have now are going to be carried forward for a decade, I see a broader range of research interests across the Cornell campus. If you look at our department as a microcosm of what's going on, we already have essentially a blurring between the lines of physics, engineering, and chemistry. We are starting a search for one or two people to join our new efforts in biomaterials. Perhaps they will even come out of one of Cornell's existing programs.

Will the department's interdisciplinary nature be a microcosm of what is going on across campus?

The focus of research in each department is a little bit different. However, chemical engineering, for example, has features of chemistry and biology. Chemists have added chemical biology. We've seen the hiring of people in the biological sciences who have engineering and physics backgrounds. Materials science is also undergoing a similar evolution. Of course, we cross research boundaries every day in our department. We are pioneers in interdisciplinary research and people in materials science are quite comfortable with this crossover.

Has your association with NBTC and its director, Harold Craighead, changed your research focus?

This is a marvelously dynamic process. When Duffield was first imagined my major focus was in photolithography, and my students and I imagined we would be doing synthesis of photoresists and dashing over to CNF for testing. Then NBTC was created. As a result of this new interaction, we are interested in surface patterning, surface function and control. So now I imagine that a lot of our photopatterning work will be associated with NBTC. I get to turn today's science fiction into fact. I'm convinced we can do it.

Are there other interdisciplinary projects that are especially notable?

Yes. For example, during my last sabbatical I sat in on Harold Craighead's weekly group meeting. At the time my interest in biotechnology was in carefully modifying surfaces so that biomolecules could be bound to semiconductors, metals, and other types of structures. But while sitting in on discussions with Harold's students, I realized that my group also knew how to make very small-scale porous structures from block copolymers. As a result of these discussions, we are now trying to integrate these porous block copolymers into devices for separating protein fragments. That's a project that's under way that just wouldn't have happened before. His students are largely in applied physics, while mine are in materials science, so the potential for synergy is enormous. Several of my colleagues in materials science have also caught the biotechnology bug and have obtained a large industrial grant for research in biosensors. This involves work by Steve Sass in materials science and Melissa Hines in chemistry and chemical biology on patterning surfaces, Barbara Baird in chemistry and myself on binding biomolecules to surfaces, and Uli Wiesner and Yuri Suzuki, both in materials science, on nanoparticle tags for molecular detection.

What effect is this new level of cooperation going to have on education?

One of the more interesting things for me has been to participate in teaching the nanobiotechnology course (MSE 563). My estimation is that the students taking such courses are going to come out skilled in all the areas needed for advances in nanobiotechnology, and even the professors are going to learn a lot; students will see the full measure of this new direction in research. More unpredictable is what the benefit will be of having all these students from different disciplines running into each other and talking. I think it's going to be rather large. Another development is that students want to know a lot about Duffield Hall, and it's my guess that in two years or so, as Duffield nears completion, we will see an explosion of students coming here because of Duffield. <<

Training the First Generation of "New Scientists"

>> Learning by doing at the Cornell Nanofabrication Facility, Randall Goldsmith, left, a junior in agricultural and biological engineering, and Avery Degloyer, a sophomore with the same major, research nanobiotechnology devices in the laboratory of associate professor Carlo D. Montemagno.

by Roger Segelken

Cornell is making it clear that it aims to become the very best place to learn sciences that don't fit the old academic labels.

The inclusion of an educational component in interdisciplinary research is viewed as essential training for what will be the first generation of researchers in the new science of life. These invaluable opportunities for education and research in novel scientific areas will enable more Cornell students to take up president Hunter Rawlings on his offer—to "study at the best research university for undergraduate education."

As just one example, the loosely defined "computational biology group" at Cornell is gaining a wide reputation not only for its researchers but also because it is making education an essential part of this frontier discipline. The group, working in collaboration with the office of undergraduate biological sciences, has created a program of study in computational biology for undergraduates majoring in the biological sciences. An interdisciplinary program has also been created to allow Ph.D. candidates to bridge the biological sciences and computational sciences.

The freshman year, some educators say, is not too soon to start. Some freshmen find themselves quickly enlisted by Carlo Montemagno, the associate professor of biological engineering whose nanobiotechnology research tries to create biomechanical devices even smaller than bacteria. "Freshmen are doing some extraordinary things," Montemagno says.

A senior research associate in his group agrees. Hercules Neves, who oversees undergraduates working in the Cornell Nanofabrication Facility, reports that the young scientists-in-training work side-by-side with graduate students, postdocs, and staff researchers. The undergraduates, notes Neves, are accorded the same research privileges and the same expectations of success.

Undergraduate research fellowships from corporations, including General Electric, provide work-study salaries and laboratory supplies. The professor's job, says Montemagno, is to "keep the students focused on what they are doing and raise the challenges incrementally so they are not swamped but not bored, either."

Ron Elber, professor of computer science and a leading figure in the computational biology group, co-teaches a graduate course in plant breeding and computer science, "Problems and Perspectives in Computational Molecular Biology," that also is open to undergraduates. The best way to conduct such a course, says co-instructor Susan McCouch, associate professor of plant breeding, is to pair up students from biology backgrounds with students from math, computer science, and statistics backgrounds.

McCouch is particularly proud of the undergraduates she works with in the Presidential Research Scholars program. And she cites student Chris Maher as an outstanding example: He excels in plant research while creating instructional materials for high school students. Among Maher's science-outreach projects is a computer game to teach younger students about transposable genetic elements in rice and maize.

"My undergraduate research at Cornell has been an enriching experience, allowing me to interact with remarkable faculty members in multiple disciplines," Maher says. "It has been very rewarding working for faculty who have given me many opportunities and responsibilities."

One new curriculum grew from an interdisciplinary field that hardly existed until a Cornell professor coined a name for it: nanobiotechnology. Now the W. M. Keck Program in Nanobiotechnology enrolls doctoral students who work at the "nano" scale (a nanometer is a billionth of a meter) on medically oriented devices that combine properties of the organic and the inorganic. Although based in the College of Engineering, Keck Fellows are free to range across the university, learning their skills wherever they are taught.

"We knew that tomorrow's nanobiotechnologists would need the best education from several different disciplines," says Michael Isaacson, Cornell physicist and founding director of the Keck Program.

A new class for Keck Fellows—and anyone else who is interested and qualified—has mathematician Richard Durrett teaching a course that is a good example of the interdisciplinary nature of the Keck program: "Using Probability Models to Understand DNA Sequence Evolution." Another course, taught by Elber, is called "Numerical Methods in Comparative Molecular Biology." <<

"The beauty of inbreds is that they keep the seeds in the hands of the farmers at no additional cost."

Susan McCouch, associate professor of plant breeding

A Race to Feed the World

by Susan Lang

In Cornell's Biotechnology Building, molecular biologist Ray Wu and his colleagues are making use of insect-resistant genes from potato plants and salt- and drought-hardy genes from barley plants. By transferring them to rice plants they hope to improve the tolerance of the rice plants to insects, salt, and drought stresses.

Two floors down in the Biotechnology Building, Stephen Kresovich of the Institute for Genomic Diversity is working with international researchers to understand genetic diversity to improve yields and hardiness of two of the developing world's most vital crops, cassava and millet.

And across campus, plant breeders Steven Tanksley and Susan McCouch are working to unlock the genetic treasures in the germplasm of wild, often inedible species to enhance the nutritional value, yields, and disease resistance of edible crops in the developing world.

>> Feeding the developing world

This flurry of research depends on the latest tools of genetics in an effort to feed the world's hungry people—and to do so before population pressure threatens widespread starvation. It is research in which Cornell has a large and growing stake.

"Future productivity increases will require raising the genetic yield potential of crops, and the only way to do that is with sophisticated genetic engineering and biotechnology techniques," says Tanksley, Cornell's Liberty Hyde Bailey Professor of Plant Breeding and Biometry.

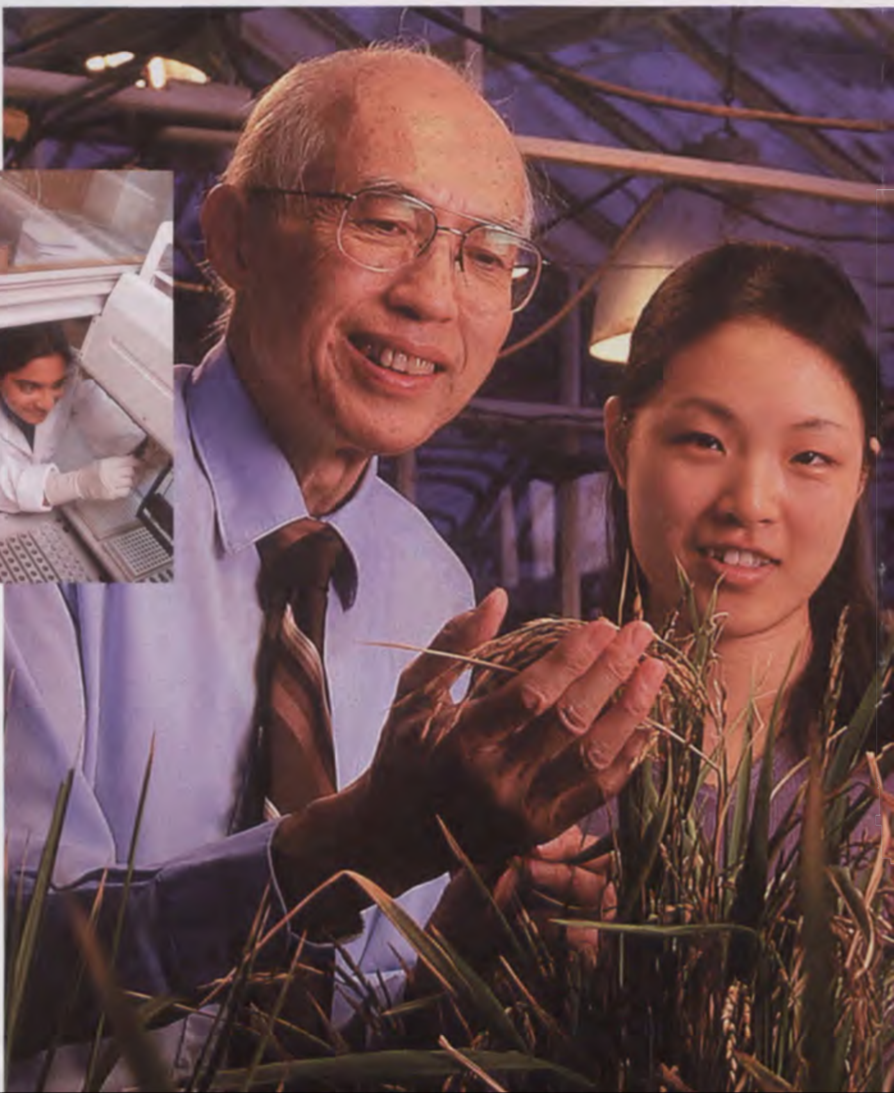
But Cornell researchers like Tanksley, McCouch, and Wu can't do this alone, and increasingly they are turning to the opportunities for interdisciplinary research that Cornell offers. Because genomics sits at the intersection of biology and genetics, and computational science and bioinformatics, it offers a wide range of opportunities for cooperative research on Cornell's campus.

The plant geneticists are able, for example, to work with colleagues in the Center for Bioinformatics and Comparative Genomics, established at Cornell by the U.S. Department of Agriculture, where they can explore and compare information about the genome structure and function of agricultural plants. Or researchers can consult the center's databases, Demeter's Genomes—named for the Greek goddess of the harvest—to look for specific information on such areas as DNA maps and markers and beneficial traits in crops, contributed by plant scientists worldwide.

Further emphasizing the depth of information and technology resources in plant genetics available at Cornell are the powerful computers at the Cornell Theory Center (CTC), known informally as the Velocity Complex. These systems support genome and related databases, as well as advanced research in computational molecular biology and genomics.

Much essential information is provided through CTC's Parallel Processing Resource for Biomedical Scientists, funded by the National Center for Research Resources, where the focus is on developing interdisciplinary approaches to molecular structure focused on revealing the relationship between the structure and function of proteins, which are the products of genes.

New faculty members frankly admit that these resources are among the research outlets that attracted them to Cornell. "The expertise and information available in bioinformatics and the gene databases will be particularly helpful to me," says Walter De Jong, who recently came to Cornell as an assistant professor of plant breeding. De Jong, who is genetically characterizing resistance to a highly destructive cyst nematode of potatoes, adds, "I hope to begin conducting microarray analyses soon, looking at the expression of thousands of genes simultaneously in potatoes."



>> Stephen Kresovich, above, director of the Institute for Biotechnology and Life Sciences Technologies, works with, from left, lab technician Amber Carmon, a senior majoring in biological sciences in the College of Agriculture and Life Sciences, and Ramya Rajagopalan, a junior biology major in the College of Arts and Sciences. They are setting up DNA amplifications on the liquid-handling workstation in the institute's lab in the Biotechnology Building.

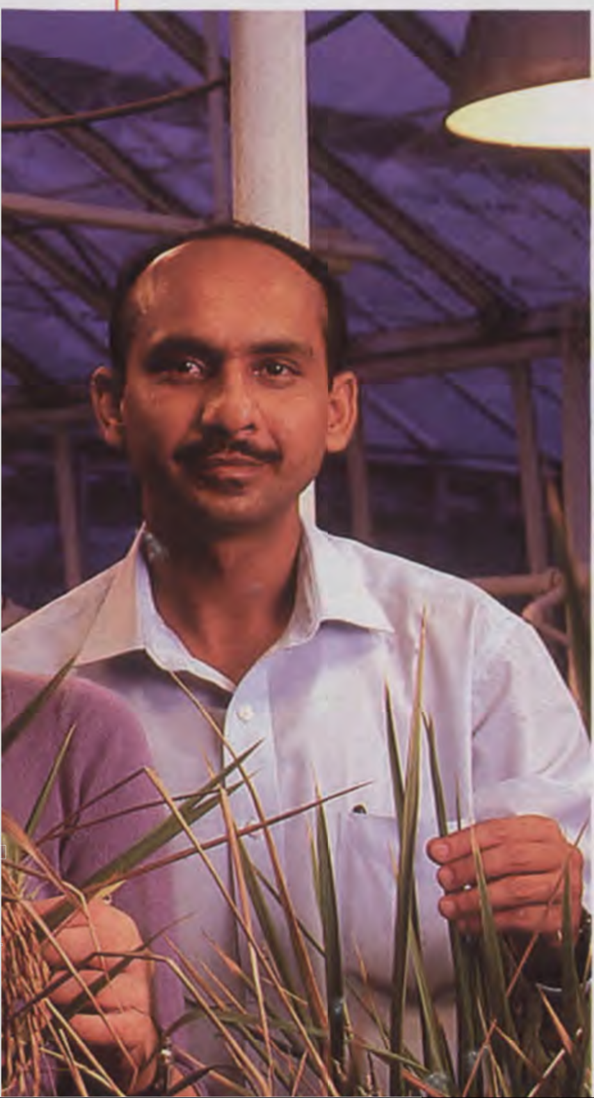
The need for this interdisciplinary cooperation is critical.

"Millions of people in the Third World are facing food insecurity and malnutrition," says McCouch, an associate professor of plant breeding. "Is it ethical for the well-fed people of the West to use biotechnology to prolong their own lives through bio-engineered pharmaceuticals and ignore the potential of biotechnology to better feed the undernourished world?"

According to McCouch, today's population of 6 billion is expected to reach 8 billion by 2030 and the demand for food is expected to double over that same period. Yet, as the world population grows by 250,000 a day, land, fresh water, and other natural resources needed to produce staple crops are declining.

McCouch, Wu, and Tanksley and other Cornell researchers are acutely aware that the most effective strategy for feeding the world is to enable people to grow their own food—but to grow crops that have better nutritional value, higher yields, greater disease resistance, and higher tolerance to drought and saline soils than in the past.

>> **In a Cornell greenhouse, Ray Wu, left, professor of molecular biology and genetics, sophomore biology major Joan Lee, and molecular biology and genetics postdoctoral student Ajay Garg study an example of genetically modified rice that is insect-, salt-, and drought-tolerant.**



"Hundreds of millions of hungry people need these crops now because the crop losses to insects, drought, and increasing salinization of soils are devastating," says Wu, professor of biochemistry, molecular and cell biology, and leader of an international team that splices genes from other plant species into rice.

>> Mining wild rice

Tanksley sees the best hope for meeting the developing world's food needs through mapping wild varieties in order to pick out the best characteristics of each.

"Owing to the advent of molecular mapping and our ability to scan the genomes of wild species for new and useful genes, we can now mine wild inedible species for previously undiscovered genes and harness them for human food production," he explains.

For example, Tanksley, McCouch, and their colleagues have systematically used molecular markers to map rice and tomato genes, and have identified specific genes, or loci—known as the quantitative trait loci—that can boost production. Before the use of molecular markers, breeders had no way of identifying specific genes that controlled complex (or quantitative) traits in any species.

"Rice will be the first crop plant in the world to be completely sequenced, and this provides us with an opportunity to look at the entire genetic repertoire of this important species," says McCouch. "As rice geneticists, we try to understand how the genome is structured, how it evolved, and how it functions. In other words, we want to understand how genetics contributes to the biology of the rice plant in its natural environment and how specific genes contribute to agriculture by driving higher grain yields, pest resistance, etcetera. We also study the repetitive, non-coding portion of the genome to understand how the whole organism works."

This work is aimed at tapping the potential of genetic maps, which allow McCouch and others to identify and move genes for high yield, for example, from wild rices into widely eaten cultivated varieties. New lines are being tested in China that are expected to produce fifteen to twenty percent more than any existing Chinese rice hybrids.

McCouch also is working on developing high-yield inbred rice varieties, because they "breed true." That means their seeds serve both as food and as the source of new plants for the next generation. Varieties now being developed in collaboration with researchers from throughout the rice-growing world are expected to generate increased yields of three percent to five percent a year for the next twenty years. The beauty of inbreds, McCouch says, is that they keep the seeds in the hands of the farmers at no additional cost.

McCouch not only gets this information out to researchers around the world but also trains undergraduate students as future plant scientists. Presidential Research Scholar Vincent Lee, a sophomore in the College of Agriculture and Life Sciences (CALS) whose major is biology, with a focus on molecular biology and bioinformatics, works on computational approaches to genome analysis to try to better understand how sequence information can be used to predict biological function.

McCouch also looks ahead to recruiting junior and high school students. For example, Presidential Research Scholar Chris Maher, a junior in CALS, works with McCouch and Margaret Corbit at the Cornell Theory Center on developing multi-user virtual worlds on the Internet. These virtual worlds involve high school and junior high school students in learning about transposable elements in rice and maize. The science outreach program is supported by the Cornell Theory Center, the USDA, and the National Science Foundation.

>> Improving cassava and millet

Cornell researchers are now applying to cassava and millet what McCouch and Tanksley have learned about tomatoes and rice. Cassava and millet are staple foods in some developing countries. Much of this work is being carried out at the Institute for Genomic Diversity at CALS, where researchers apply state-of-the-art genomics and bioinformatics to solve problems affecting global food security and the conservation of biodiversity. Researchers such as institute director Kresovich and his colleagues work closely with scientists from around the world to improve vital crops, among them cassava and millet.

One of the regular visitors to the institute is Nigerian scientist Martin Fregene of the International Center for Tropical Agriculture (CIAT) in Cali, Colombia, a research organization dedicated to alleviating hunger and preserving natural resources in developing countries. Fregene is working to improve cassava, a crop that more than 500 million people in the developing world depend on for their food and livelihood. (The crop is also known as manioc; in the United States it is more familiar processed as tapioca). Cassava provides more than half the daily calories for 200 million people in sub-Saharan Africa and provides significant amounts of starch and protein.

"Pests and poor agronomic practices can cut production in half," says Fregene, noting that in 1998 Africa lost sixty percent of its cassava crop, the region's largest source of calories, to the mosaic virus.

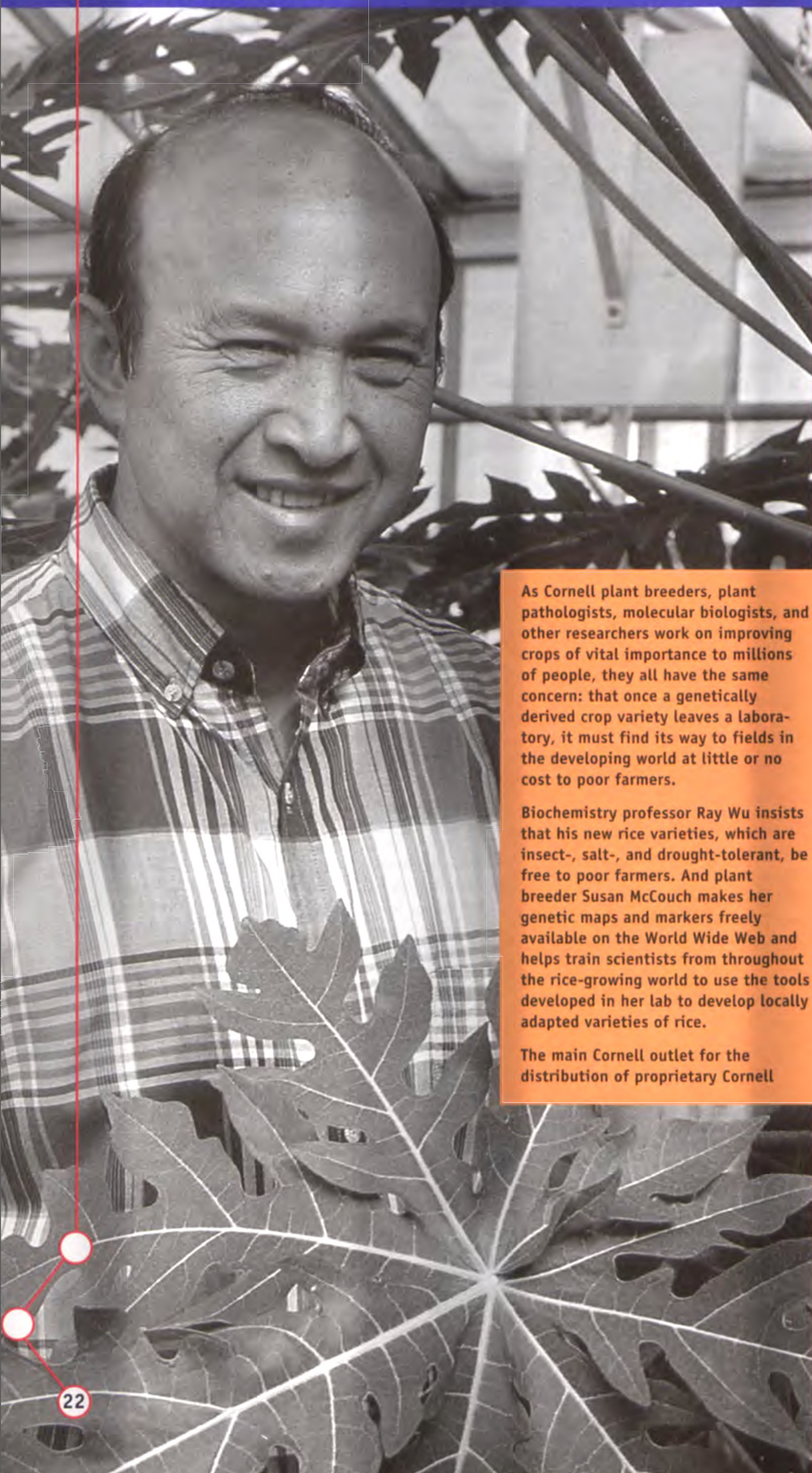
Now, with Kresovich's help, Fregene is trying to develop cassava with higher yields, nutritional content, and disease resistance.

"We help him through understanding genetic diversity of the crop so that he can genetically modify cassava to resist pests and diseases that can wipe crops out in Latin America and Africa," says Kresovich. "We've also been involved with Fregene's work to boost the carotene, iron, and zinc content of the roots, improving dry foliage yield."

Cornell also is helping improve millet, a staple grain for millions in Asia and Africa. <<

From Papaya to Rice, Foundation Gets Research to World's Poorest

by Susan Lang



>> Cornell plant pathologist Dennis Gonsalves of the New York State Agricultural Experiment Station in Geneva helped genetically engineer resistance for papaya ringspot virus into papaya plants. Here, he shows one of the resistant plants he has grown in a greenhouse at the Experiment Station.

As Cornell plant breeders, plant pathologists, molecular biologists, and other researchers work on improving crops of vital importance to millions of people, they all have the same concern: that once a genetically derived crop variety leaves a laboratory, it must find its way to fields in the developing world at little or no cost to poor farmers.

Biochemistry professor Ray Wu insists that his new rice varieties, which are insect-, salt-, and drought-tolerant, be free to poor farmers. And plant breeder Susan McCouch makes her genetic maps and markers freely available on the World Wide Web and helps train scientists from throughout the rice-growing world to use the tools developed in her lab to develop locally adapted varieties of rice.

The main Cornell outlet for the distribution of proprietary Cornell technology is the Cornell Research Foundation (CRF). The foundation spends much of its energies on protecting and commercializing Cornell research products by negotiating and managing licenses. When it comes to technologies for improved crops, CRF seeks to use its intellectual property to balance legitimate commercialization with philanthropic concerns.

"We want to ensure these crops are widely available, often for free, so that poor farmers anywhere in the world might benefit from Cornell technology," says Richard Cahoon, associate director of CRF. "We have mechanisms in place, however, so that if the technology is used for commercial enterprises, we have the ability to negotiate for licenses and some sharing of returns."

Cornell plant breeders typically aim to genetically modify staple crops of the developing world, such as rice and papaya, to improve yields, resist destruction by disease and insects, and to withstand environmental stresses such as aridity and climate. To ensure that the world's poor farmers will benefit from this research they enlist the help of CRF and Cahoon.

Papaya is one of Cornell's technology-transfer success stories of a genetically altered crop now benefiting small-scale farmers. It is Hawaii's second most important fruit crop, with farm revenues of more than $45 million annually. Papaya also is an important crop in Latin and Central America and Southeast Asia. Between 1993 and 1997, the papaya ringspot virus wiped out farm after farm in Hawaii, cutting fresh-market production to 36 million pounds, from 58 million pounds. As the papaya industry fell away, small farmers experienced great financial losses and several packing companies were forced to close. The virus is causing similar destruction in other parts of the world, where the production of papaya is much greater than in Hawaii. For example, Brazil produced 1.8 million metric tons of papaya in 1997, about a hundred times more than Hawaii's production. The virus has affected Brazil so severely that its industry has had to keep moving to different regions to escape the virus.

To develop a disease-resistant papaya, Dennis Gonsalves, a Liberty Hyde Bailey Professor of Plant Pathology at Cornell's New York State Agricultural Experiment Station in Geneva, New York, identified and cloned a gene from the virus. Using a gene gun developed at the Geneva Experiment Station, he "shot" the viral gene into cells of the papaya plant to stimulate resistance to disease without causing the disease itself—much like immunization. The resulting transgenic papaya has no harmful effects on humans, because the virus already infects fruit that consumers eat.

"The only way we have affected papaya quality is to make it resistant to the virus with a sort of molecular immunization, which improves its survivability," says Gonsalves.

CRF worked with the U.S. Department of Agriculture and the University of Hawaii, which, in turn, worked with papaya farmers. "We came up with a sharing scheme to commercialize the technology," explains Cahoon.

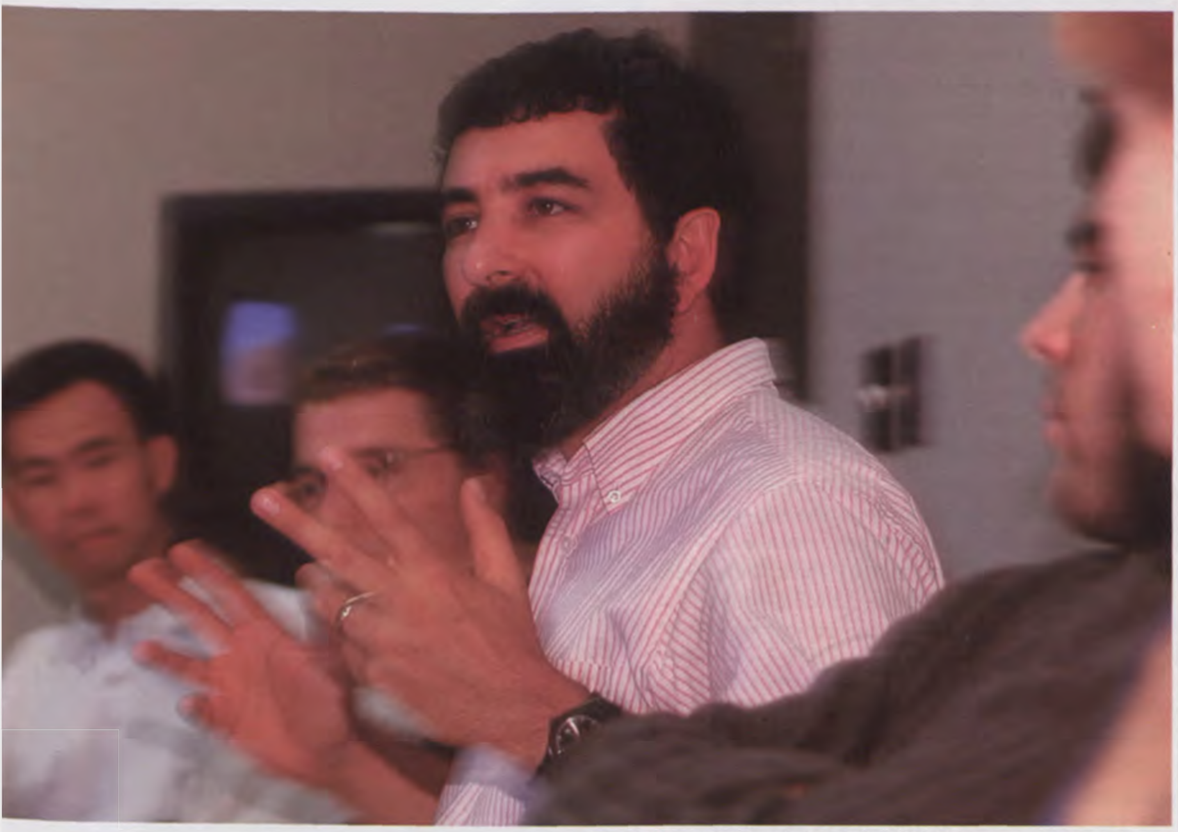
"In Hawaii, the Papaya Administrative Committee distributes the papaya seeds free to small and large farmers after they have signed a license agreement," Cahoon adds. Those farmers are now growing the world's first commercialized, virus-resistant transgenic fruit crop, and the new Rainbow and SunUp papaya varieties are among the few genetically modified crops that have not been produced and distributed by a commercial seed company.

Different strains of the same disease are also hurting farmers in nearly every tropical country, including Brazil, Jamaica, Taiwan, Thailand, Mexico, India, Venezuela, and Colombia. Cahoon is working with collaborating institutions that are testing the virus-disease strains in those countries. He hopes that in Thailand, where papaya is a staple food, the transgenic variety will be available within a few years at basically no cost.

But in Hawaii, farmers are rebounding since the transgenic papaya was released for commercial use in May 1998. As a result, the industry had an increase in papaya production in 1999, the first increase since 1993 when the virus started to severely affect yields.

"Currently, these farmers are marketing their fruit throughout the United States. Current deregulation discussions regarding exports to Japan and Canada hopefully will soon lead to acceptance of Hawaii's transgenic papayas in those countries," says Gonsalves' wife, Carol, who surveyed papaya farmers as part of her master's thesis. <<

Burgeoning Technology Makes Study of Ethics a Priority



>> From left, graduate students Mark Chong and Matt Nisbet take part in the Public Communications Science and Technology class taught by Bruce Lewenstein, associate professor of science communication, in Kennedy Hall. The course is one of two Lewenstein teaches in which ethical issues are addressed.

by Franklin Crawford

It's easier to picture an apple falling on Isaac Newton's head than it is to visualize an ethical dilemma. But you can find solid evidence of Cornell's commitment to the study of the societal, moral, and legal problems bred by burgeoning scientific technology. That engagement long predates the development of the area now known as genomics, the advent of silicon technology, or such agricultural advancements as bovine growth hormone.

The study of ethics is a priority at Cornell and the robust nature of that concern can be found within the interdisciplinary Program on Ethics and Public Life (EPL), founded in 1987 by Professor Henry Shue and dedicated to the exploration of concrete ethical and public issues in the humanities, social sciences, and hard sciences.

Under the direction of Michele Moody-Adams, the Wyn and William Y. Hutchinson Professor of Ethics and Public Life, the program is engaged in an active educational role in ethical issues within the new biology, in connection with a new project called the Ethical, Legal and Social Issues initiative, or ELSI. Part of the Cornell Genomics Initiative, ELSI is an educational work-in-progress developed recently by Stephen Hilgartner, assistant professor of science and technology studies.

This highly imaginative effort forms the leading edge of a campuswide initiative to teach ethics throughout the disciplines and reinvigorate the undergraduate experience at Cornell. These ethics-related activities are funded by $1.68 million from the Pew Charitable Trusts.

Hilgartner estimates that more than sixty courses at Cornell include discussions of the social, ethical, or legal aspects of biology. These courses range from environmental management to ethics and animal science; from the fundamentals of food law to ethical issues in engineering, information technology, and health and medicine. In addition, Weill Medical College of Cornell has its own Bioethics Center in New York City with affiliations to the Ithaca campus through EPL and the Law School, among other programs and departments.

ELSI has the goal of fostering an intellectually vibrant community that engages people from many disciplines in research, education, and outreach activities on ethical aspects of the new biology. The program holds public events on campus, including a major workshop recently that was titled "Genomic Futures: Ethical Challenges, Social Choices and the University."

In addition to leading a seminar on the politics of genetic engineering and teaching a course on research ethics, Hilgartner is conducting a long-term study of the field of genome research. He is one of a handful of historians and sociologists studying the Human Genome Project, the mapping and sequencing of the human body's genes (see the interview with Stephen Hilgartner on the facing page). Indeed, ELSI takes its name from a similar initiative launched by the National Institutes of Health in 1988 as the Human Genome Project was taking shape.

"The rapid expansion of genomics raises many significant issues that call for interdisciplinary studies involving the humanities, social sciences, and natural sciences," Hilgartner says. "Understanding these issues, and addressing the problems of governance that they pose, will require sustained and critical inquiry, and Cornell has an important role to play in this area."

The appointment recently of Moody-Adams has strengthened EPL in its traditional role of providing guidance to faculty members in the humanities as well as in the social sciences and "hard" sciences. Although its academic home is in the College of Arts and Sciences, EPL offers consultation and advice to departments in the colleges of Veterinary Medicine, Agriculture and Life Sciences, and Engineering. Moody-Adams, a moral philosopher who works on contemporary ethical issues in law, politics, class, race, and gender, among other areas, also is a key member of the multidisciplinary committee that oversees ELSI.

Such projects as EPL and the ELSI initiative demonstrate that attention to ethical problems is being more tightly integrated with scientific research and training—as moral philosophers, legal and political analysts, and social scientists increasingly interact with researchers in addressing social problems. This development is partly driven by the rapidity—and societal implications—of discoveries in the new biology. The debate about GMOs, genetically modified organisms (see the related articles on pages 20–22 and 26), is just one manifestation of public anxiety about the direction of scientific research.

"The faculty members who are gathering together as part of the ELSI initiative are working in a domain that is constantly changing, because the research is taking us into some hitherto uncharted territory," says Moody-Adams. "This poses difficult challenges as we seek to puzzle through the ethical implications of genome research. But they are challenges we cannot afford to ignore."

Cornell has been in the vanguard of research on the ethics of science since 1969, when the late Franklin Long helped establish a Science, Technology and Society program. Long became the program's first director and, with the late Max Black and Stuart Brown, guided the field toward the development of its first undergraduate major, Biology & Society, in 1976. The first report on Biology & Society, issued 1977–78, describes a course of study that is "designed to equip students with an understanding of the interactions between biology, society, and ethics."

In the mid-1980s, a separate program, The History and Philosophy of Science and Technology, was developed in the College of Arts and Sciences. In 1991, the two programs merged to create a new department, now known as Science and Technology Studies, within the college. The department offers two undergraduate majors: science and technology studies, and biology and society. Both are aimed at furthering understanding of the historical, social, political, and ethical aspects of science and technology.

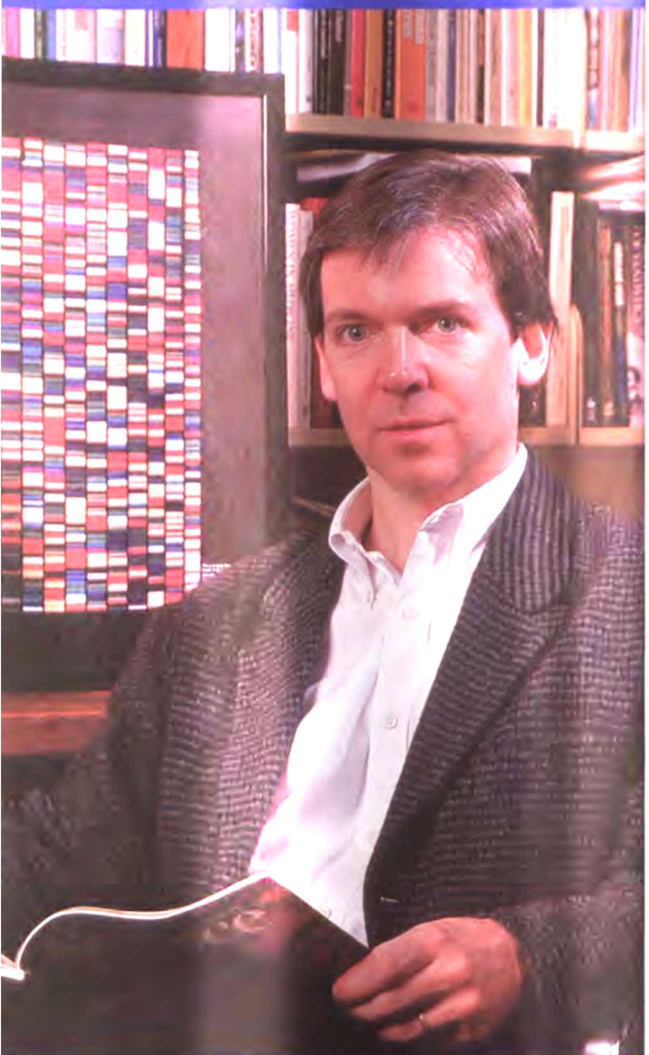
Since its beginnings, ethical issues have been very much a part of the department's mission. The university sharpened its focus on ethical issues in the new biology through Hilgartner's appointment in 1995. The advent of the Cornell Genomics Initiative in 1998 brought these ethical concerns to new levels of complexity.

"Although people are interested in the technical achievements of scientists, it's clear that often they are really concerned with social or ethical implications of science," says Bruce Lewenstein, associate professor of science communication, who has a dual appointment in agriculture and life sciences and in science and technology studies. Lewenstein teaches two courses in which ethical issues are addressed.

"Once adults leave school, they get most of their information about science and technology from the media," Lewenstein adds. "The people looking at social issues must have deep understanding of the technical issues. Similarly, the people looking at technical issues can find their work enriched by understanding the social issues." <<

>> **Michele Moody-Adams, The Wyn and William Y. Hutchinson Professor of Ethics and Public Life.**

Stephen Hilgartner



"Cornell is and should be an important contributor to ongoing societal debates"

The Ethical, Legal and Social Issues initiative (ELSI) at Cornell offers a fresh and exciting window on the university's Genomics Initiative. A marriage of the humanities and the sciences, as reflected by the interdisciplinary makeup of its committee members, ELSI is chaired by Stephen Hilgartner, assistant professor of science and technology studies at Cornell, who proposed the program.

Here, Hilgartner discusses the goals and prospects of ELSI with Cornell News Service writer Franklin Crawford.

What is the purpose of the ELSI committee and its program?

The goal of the ELSI committee is to foster an intellectually vibrant community at Cornell that engages people from many disciplines in research, education, and outreach activities on social and ethical aspects of the new biology. Cornell has a long-standing tradition of addressing issues regarding science and society and has one of the world's leading departments [Science and Technology Studies] studying these issues. What's more, the breadth of expertise represented in Cornell's diverse colleges leaves us well prepared to contribute to the study of issues that will ultimately touch many aspects of contemporary societies.

What are the ELSI committee's other duties?

The committee is charged with building research capacity, which means engaging faculty, generating excitement, and beginning some collaborative projects. Curriculum development is also important. We are currently identifying gaps in the curriculum and studying the need for new course offerings that address ELSI issues at the undergraduate and graduate levels. To succeed, ELSI needs visibility, and we are working to inform the entire Cornell community of this program. A speaker fund is established, we are planning workshops and awarding grants to graduate students to support research on social and ethical aspects of biology. In addition, we have a fund for undergraduate research projects in this area. Regarding curriculum development, we have completed a preliminary survey of existing courses that may be relevant to ELSI issues. In response to student requests, we have discussed with law professor Larry Palmer the possibility of reviving a course called "Biotechnology and the Law." Our plans include the development of an undergraduate lecture course titled "The Biological Revolution: Science and Society."

What about the outreach component of ELSI?

In conjunction with the New York State Bar Association, we are co-sponsoring a forum for policymakers, called "The New Genetics: Science, Policy, Ethics." We also are holding a workshop on genome issues for journalists, in New York City. Since 1994 Cornell has organized annual workshops for journalists with the sponsorship of the Josephine L. Hopkins Foundation, and these have attracted national media. We hope to do the same.

In discussing these controversial issues, does ELSI risk becoming entangled in highly charged debates?

This field is emerging, and the creative tension of scholarly debate can be productive. It's important to understand that ELSI is not a propaganda apparatus for people who have strong views about particular issues, such as GMOs [genetically modified organisms]. Our goal is to contribute to society's capacity to address the challenges posed by the new biology. It's important that ELSI be multidisciplinary and represent divergent perspectives. Cornell is and should be an important contributor to ongoing societal debates. The new biology is going to have impact over decades, and ELSI fits in with the university's mission of working over a scale of decades—building research capacity, conducting studies of critical issues, and training young people. These are the kinds of activities that will have a significant impact on society and our ability to address these issues in an intelligent way. ELSI is not about this week's debate or a new product on the shelf tomorrow.

Do you think this program will grow?

I'm optimistic. The prospects for building ELSI research and teaching at Cornell are very good. Not only does Cornell possess strength in the relevant genome sciences, but it has a long-standing commitment to the study of social and ethical aspects of science and technology. <<

Monarchs, Corn, and Cornell:

by Blaine P. Friedlander Jr.

There was a deluge of news coverage when on May 19, 1999, the science journal *Nature* released news of a Cornell laboratory study that had found that pollen from genetically modified Bt corn killed monarch butterflies when it was dusted on milkweed, the insects' main food source.

"The magnitude was surprising," says John E. Losey, assistant professor of entomology, who conducted the study with Linda S. Rayor, entomology instructor, and Maureen E. Carter, a researcher in entomology.

Within days, the food and agricultural industries and some scientists denounced the study, criticizing the work for being done in the laboratory and not in the field. And in the months since, the monarch-Bt corn study has become one of the university's most visible pieces of scientific research.

As a result, it has brought to the forefront, particularly in the United States, a public anxiety about the role that genetically modified organisms (GMOs) are playing in modern life. To answer these public concerns, Cornell has stepped forward to make certain the facts accurately reach a concerned public.

Cornell Cooperative Extension (CCE) has hired a full-time educator, T. Clint Nesbitt, to develop literature and distribute information on issues related to genetically engineered food and new agricultural technologies. The information is distributed to Cooperative Extension offices throughout the state.

"We're not trying to be advocates, but a source of balanced information," says Nesbitt, whose job is supported by a grant from the Smith-Lever Act of 1914 and the U.S. Department of Agriculture.

A problem for dissemination of accurate information is that the issues are so complex. "The scientists doing the research have a different perspective than the public. There is not a lot of information flowing back and forth between the scientists and the public, so the scientists don't understand why someone is upset about genetically engineered food," Nesbitt says.

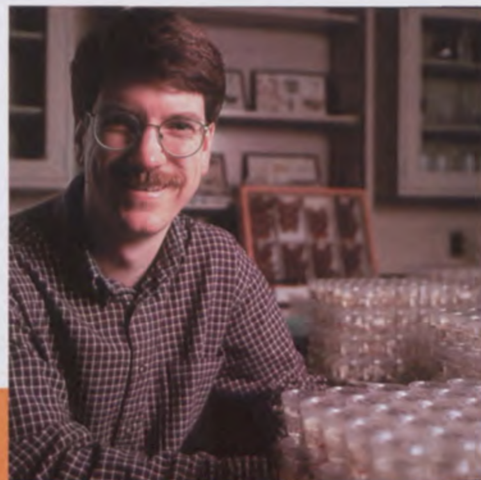
To correct this notion, Susan Henry, the Ronald P. Lynch Dean of Cornell's College of Agriculture and Life Sciences (CALS), and Anthony M. Shelton, professor of entomology and the associate director of research for CALS, have assembled a GMO advisory group that meets regularly to discuss the issues and the role CALS should play.

The dean is determined to have a balanced public dialogue. "Within the college, we have numerous researchers, educators, and communicators who can facilitate enlightened public discussion," Henry says. "We aren't choosing sides."

Group members from the Cornell experiment station in Geneva and from the Ithaca campus have held workshops, participated in field days, set up displays at community events, and organized conferences on GMOs and agricultural biotechnology.

"The general public climate in many areas is that there isn't much trust across the landscape. Whether you are talking about politicians, physicians, scientists, or teachers, I think this lack of trust has to be corrected," Shelton says. The best thing for scientists to do, he adds, is to listen more closely to the public interest and to develop a dialogue. <<

In the Eye of an Issue

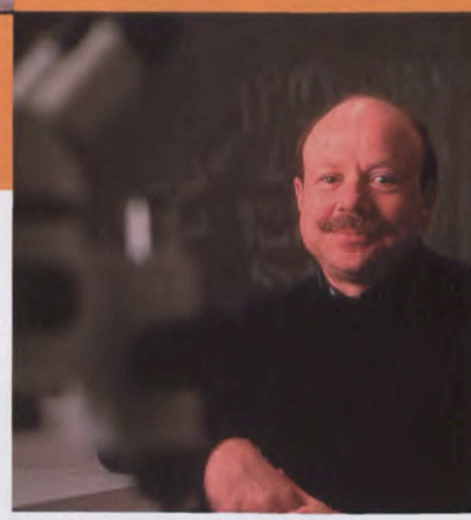


"I haven't changed my position on GMOs. We need to determine the extent of those risks as we do for any other pest management tactic. Then we can determine which tactic is the most environmentally sound and the most economically viable. . . . I'm neither a detractor nor a proponent. I am completely open to being convinced by the data."

John Losey, assistant professor of entomology

Susan Henry, Ronald P. Lynch Dean of Agriculture and Life Sciences

"The Cornell community reflects a variety of opinions about GMOs. Our goal is to provide the most reliable and objective information about the science behind agricultural biotechnology and GMOs and the potential impacts—both positive and negative—of this new technology."



Anthony M. Shelton, professor of entomology

"The best thing for scientists to do is to listen more closely to the public interest and to develop a dialogue about such issues as agricultural biotechnology. In today's world, it's even more imperative scientists be very careful about how they present their results to the public."

"These days any biologist who doesn't have a 'wet lab' could be called a computational biologist."

From Vast

Steven Tanksley, left, the Liberty Hyde Bailey Professor of Plant Breeding, and David Shmoys, professor of operations research and industrial engineering, examine hybrid tomatoes in one of Tanksley's experimental fields. Shmoys has used computer analysis to help Tanksley choose groups of plants in which the location of important genes is most likely to be found.

by Bill Steele

The first phase of the human genome project is done: We know the order of the three billion or so DNA "base pairs" of the human genetic code. The code includes some 80,000 to 100,000 or more genes, depending on who's counting.

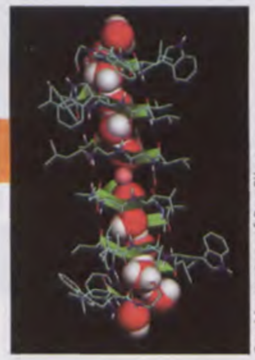
But what we have is like a city map that shows all the street names and numbers but doesn't tell us who lives or works in the buildings. Each gene codes for a protein that does some specific job in the body, from holding the skeleton together to fending off disease. But which gene is which, and what do all those proteins look like and do? We only have answers here and there along the human genome, and we're asking the same questions about the genomes of dogs, cats, cows, horses, wheat, corn, rice, and other plants and animals.

It's from these questions that the new field of computational biology has emerged, using computers to crunch through the vast genomic database for meaning and to simulate the biological processes these genes control.

"Everybody wants to understand what life is all about and to understand this at a molecular level, where the most dense information is," says Ron Elber, professor of computer science. Elber was recruited by Cornell in 1999 as part of an effort to build a major program in computational biology.

The loosely defined "computational molecular biology group" now includes Elber; Jon Kleinberg, assistant professor of computer science; David Shalloway, the Greater Philadelphia Professor in Biological Sciences and chair of the Department of Molecular Biology and Genetics; Harold Scheraga, professor emeritus of chemistry and chemical biology; David Shmoys, a professor with a joint appointment in operations research and industrial engineering and computer science; Benoit Roux, professor of biochemistry and structural biology at the Weill Cornell Medical College; Rasmus Nielsen, assistant professor of biometrics; and Golan Yona, assistant professor of computer science.

According to Shalloway, who chairs the subcommittee on computational biology of the Faculty of Computing and Information, at least forty-six faculty members in a wide range of disciplines on



Graphic courtesy of Ron Elber

>> Computer simulation shows how a sodium ion (the small ball near the center) is transported through an ion channel in the wall of a cell. This is one frame from an animated sequence.

Genomic Database, New Field of Computational Biology Emerges

>> Jon Kleinberg, left, assistant professor of computer science; Ron Elber, right, professor of computer science; and postdoctoral research associate Koneshan Siva discuss Siva's work on the simulation of ion channels in cell membranes during a recent session in Elber's office in Upson Hall.

Cornell's campus are involved in some way with computational biology.

"These days any biologist who doesn't have a 'wet lab' could be called a computational biologist," Nielsen says. Nielsen calls his work "statistical genomics." Others use the term "biometrics," and some biochemists talk about "computational chemistry."

Computational biology is one of three areas targeted for development in a $160-million collaborative program between Cornell and its Weill Medical College, Memorial Sloan-Kettering Cancer Center, and The Rockefeller University in New York City. "The expertise in computational biology on the Cornell campus is now extended to these other institutions," Elber says. Those resources include the Cornell Theory Center supercomputers and CHESS (the Cornell High Energy Synchrotron Source), which can be used to find the structure of proteins experimentally.

The genes that require so much equipment and attention are strands of DNA that tell a cell how to line up small molecules called amino acids into a chain that will become a protein. Within seconds the chain folds into a complex shape. For a protein, shape is stock in trade. Enzymes are shaped so they can lock onto other molecules and break them apart or join them together. Hemoglobin in blood is shaped to hold oxygen molecules. Proteins in skin and hair are shaped so they can lock together in firm structures.

Computational biologists are looking at the raw data of the genome, how it's transformed into proteins, and how proteins do their work.

The genome database is too big for human brains to comprehend, yet there may be some unifying principles. Computers can sift through the mountain of data, looking for repeated patterns and matching them with one another and with the patterns of known genes.

If you compare the genomes of many variants within a single species, you find that certain small areas vary widely. Paradoxically, Nielsen says, the portions that show the most variation are often those that have the most important functions. Such comparisons can help to locate genes for important traits, such as for disease resistance or yield, that can be inserted into crops. Similarly, comparison of many strains of the AIDS virus is helping to identify the parts of its genome that interact with the human immune system.

Todd Vision, a postdoctoral research associate with the USDA Center for Bioinformatics and Comparative Genomics, makes comparisons across many different species, with the number and distribution of common genes showing what the ancestral genomes might have looked like. In *arabidopsis,* the first plant to have its genome fully sequenced, he finds elements in common between plants that diverged hundreds of millions of years ago, such as tomatoes and rice.

The raw genetic data include many sequences that are quite different but nevertheless fold into the same protein shape. So Elber and Kleinberg also work with databases of protein shapes and study the number of amino acid sequences that can fit into a given fold. This study has the potential to detect remote evolutionary relationships between proteins that share folds but not sequences. Yona looks through the collection of known protein shapes for commonalities, in the same way Elber is searching for patterns in the raw genome.

Given the sequence of amino acids in a protein chain, how can we find the shape into which it will fold? The biggest challenge, perhaps the holy grail of computational biology, is getting from one to the other.

The folding results from electrostatic attractions between the negatively charged electrons and positively charged protons in the atoms and their interactions with water molecules, all spelled out by the laws of physics. But simulating the actions of those laws for something as complicated as a protein would take months or even years on today's computers. Scheraga's research group has used clever approximations like treating parts of each amino acid as single units of attraction and repulsion to find the structures of a few proteins in just a day or two of supercomputer time. Unlike others using computation, Scheraga also spends time in his "wet lab" trying to learn how proteins fold, hoping to teach computers to use similar methods to predict shapes. Elber and Kleinberg use a technique called "threading," in which the computer matches an unknown sequence with the shapes of known proteins until it finds an approximate fit, then makes refinements from there.

Computer simulations also help to visualize how proteins do their jobs. Elber and Roux have created animated simulations of the workings of ion channels, structures that move charged particles through cell membranes to send electrical signals along nerves.

Shalloway simulates molecular machinery, calculating the ways in which the parts of protein molecules move around while doing their jobs. An enzyme that joins two small molecules into a larger one, for example, must first bind to both molecules, and then move them together. Like protein folding, it's complex, but understanding it is key to developing drugs that will bind to biological molecules.

There already are payoffs to this work in plant biology, like improved varieties of rice to feed growing populations in Asia and larger, juicier tomatoes. The medical payoffs may be far greater.

"Computational biology sits at the intersection of the biological sciences and the information sciences," says Robert Constable, dean for computing and information science. "The two modern research programs are coming together to create a field of unparalleled opportunities, a field with enormous consequences for improving the human condition, deepening our knowledge of our place among living systems." <<

Spotlight on New Faculty

>>Brian Crane

Brian Crane joined the chemistry and chemical biology department as an assistant professor from the California Institute of Technology, where he was a research associate. At Cornell he focuses on the structural principles of redox- and photo-chemistry in biological catalysis and regulation. Specifically, he seeks better understanding of how metallo-enzymes stabilize transient intermediates during catalysis, how protein structure controls long-range electronic transfer and how photo and redox processes are used in biological information transfer.

First and foremost, I was impressed with the Department of Chemistry and Chemical Biology and its vision for the future of chemical biology, and I felt that my interests and experience complemented this expertise well. The proximity of CHESS and the new tri-institutional collaboration with Memorial Sloan-Kettering Cancer Center and The Rockefeller University also are very attractive aspects of conducting research at Cornell.

>>Lynden Archer

Lynden Archer, associate professor of chemical engineering, came from Texas A&M University. He studies macromolecules near surfaces to uncover the principles governing frictional drag and adhesion and lubrication properties of molecular fluids near solid substrates.

Cornell provides great possibilities for meaningful collaboration with leading researchers in materials science, engineering, chemistry, and nanotechnology, and its academic atmosphere is conducive for cross-disciplinary education and research.

>>Walter De Jong

Walter De Jong, who joined Cornell's Department of Plant Breeding as an assistant professor, was previously a potato molecular geneticist at the Scottish Crop Research Institute in Dundee, Scotland. His research focuses on the molecular characterization of genetic variation in the potato, and specifically, applying this to the development of varieties that will resist a new race of the highly destructive parasitic worm, the golden cyst nematode.

Cornell, with its outstanding reputation in the life sciences and long tradition of interdisciplinary teamwork in potato improvement, provides me with a unique opportunity to combine my interests in potato molecular genetics and potato breeding. Synergistic interactions at Cornell benefit basic science as well as solving problems of the potato industry. I look forward to the positive—and unpredictable—collaborations possible here at Cornell.

>>Rasmus Nielsen

Rasmus Nielsen came to Cornell from Harvard University, where he was a postdoctoral researcher. An assistant professor in biometrics, he is studying linkage disequilibrium mapping and the analysis of recombining DNA sequences, as well as the statistical analysis of natural selection at the DNA level. The primary goal of the research is to develop statistical methods for identifying genomic regions of functional importance.

With the Genomics Initiative, Cornell is becoming one of the leading institutions in genomics research in the country. The possibilities for collaborations with other researchers at Cornell in genomics and statistics are excellent. Also, I was attracted to the high quality of the students here.

>>Alexander Nikitin

Alexander Nikitin, who is both an M.D. and a Ph.D., became joined Cornell as an assistant professor in the Department of Biomedical Sciences in the College of Veterinary Medicine. Formerly he was an assistant professor in the Department of Molecular Medicine in the Institute of Biotechnology at the University of Texas Health Science Center, San Antonio. His area of research is experimental pathology, with a particular interest in the development and characterization of animal models for human cancer and proliferative vascular disorders.

I was attracted to Cornell because of its outstanding scientific environment for experimental pathology research in pathology and molecular medicine. Furthermore, the Department of Biomedical Sciences is committed to setting up a national program in murine experimental pathology. My expertise and interests in this area are very complementary to the development of such a program.

>> Michael Kotlikoff

Michael Kotlikoff was a professor and chair of the Department of Animal Biology in the School of Veterinary Medicine at the University of Pennsylvania until he joined the Cornell faculty in the College of Veterinary Medicine as professor and chair of the Department of Biomedical Sciences. His research involves signaling in muscle cells. He uses a variety of techniques, including gene targeting, patch-clamping, and optical methods to examine the role of individual genes in muscle excitation.

I was attracted to Cornell because of the opportunity to build a newly formed, multidisciplinary department. The collaborative and interdepartmental nature of the Cornell Genomics Initiative and the opportunity to participate in a universitywide initiative in mammalian genomics was also particularly attractive.

>> Paul McEuen

Paul McEuen, formerly at University of California-Berkeley, joined Cornell as a professor of physics. His research focuses on nanostructures—electrons in carbon nanotubes, scanned probe microscopy of nanostructures, and novel nanostructures for chemical and biological applications.

I was attracted to Cornell because it is a world leader in nanoscience and has a long tradition of doing research in a collaborative, interdisciplinary way. Equally attractive to me was the physical environment—the beautiful scenery and the small-town feel.

>> Jianhua Fu

Jianhua Fu came to Cornell as assistant professor of molecular biology and genetics from the Department of Structural Biology at Stanford University School of Medicine, where he was a postdoctoral fellow. In humans, genes in chromosomes are read by gigantic molecular machines called RNA polymerase holoenzymes, composed of dozens of different protein subunits. Fu works on understanding the three-dimensional workings of these multilayered protein machines using X-ray crystallography and other biophysical means.

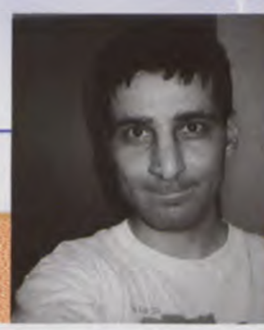
Three main strengths of Cornell attracted me here: the well-established experts in the field of gene transcription and regulation, with whom I anticipate interactions; the high-caliber students; and MacCHESS, the renowned synchrotron X-ray facility. Having MacCHESS in my backyard offers tremendous convenience by removing difficulties and uncertainties associated with shipping samples to remote sites.

>> David Lin

David Lin, formerly at University of California-Berkeley, joined Cornell as an assistant professor of neurobiology in the College of Veterinary Medicine. A molecular biologist, Lin studies how the brain is wired together during development.

I decided to move to Cornell because there is no question that this is an exciting time to be here. There is a campuswide collaborative effort to become a leader in the field of genomics, and I wanted to be a part of that effort.

>> Golan Yona



Golan Yona, formerly a Burroughs-Wellcome postdoctoral fellow in computational molecular biology at Stanford University, joined the Cornell faculty as an assistant professor in the Department of Computer Science. Yona works in computational molecular biology, searching for global principles that might chart a "road map" of the space of all possible proteins. His goal: to establish a reliable, unified framework for sequence and structure analysis.

Cornell's computer science is an excellent place to develop my research program. The university is putting a lot of attention toward genomic science, acknowledging the importance of this field. The wide interest in my research, and the collegial atmosphere in the Department of Computer Science, convinced me that Cornell would be the best place for me.

>> Lois Pollack

Lois Pollack became an assistant professor in applied and engineering physics after several years as a Cornell researcher in low-temperature physics and, more recently, in biological physics. She studies problems of self-assembly and folding of macromolecules (including proteins, nucleic acids, and polymers) as well as conformational changes associated with biological function. Her group develops and uses new experimental tools to trigger and monitor shape changes to access novel information about these processes.

Cornell is a great place to do research because of resources like the Cornell High Energy Synchrotron Source, the Cornell Nanofabrication Facility, and the Developmental Resource for Biophysical Imaging Opto-Electronics, and the outstanding support they provide for users and collaborators. I'm also interested in interdisciplinary work, combining biology with physics or engineering, that receives support through centers like the Nanobiotechnology Center.

>> David G. Russell

David G. Russell was a professor in molecular microbiology at Washington University School of Medicine, St. Louis, before joining the Cornell faculty as professor and chair of the Department of Microbiology and Immunology in the College of Veterinary Medicine. He studies the interaction between intracellular pathogens and their host cells. More specifically, he looks at the nature of the interaction between macrophages and the bacterial pathogen *Mycobacterium*, as well as the environment that surrounds the infected macrophages.

Cornell is unique in that it offers a first-rate research community in an extremely rural environment, which both I and my family find attractive. The vision that Dean [Donald F.] Smith has for the Veterinary College as an integrated community of basic researchers and clinicians is extremely appealing and one I am delighted to ascribe to.