

# The Evolving Multidisciplinary Biosciences: Bio-X

“Even when we know the function of every gene in the genome, we will still not understand how the body or the brain work, nor how they adapt and change with age, training, or disease. Now is the time to move beyond reductionism and construct a new biology of complex life systems. To do this we need every tool in the toolkit, and we need to invent new technologies and disciplines.”

**Carla J. Shatz**

Sapp Family Provostial Professor of Biological Sciences and Neurobiology  
Director of the Bio-X Program



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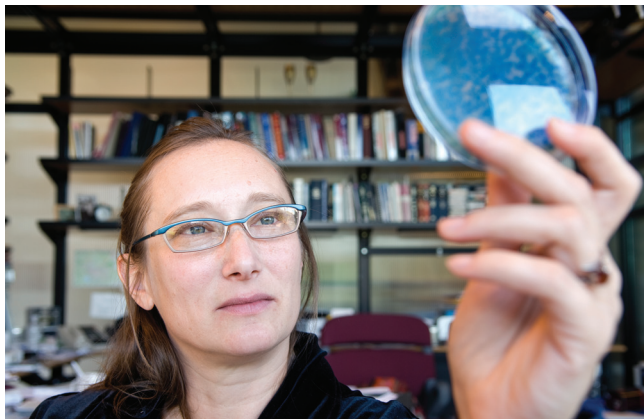
**WE HAVE MADE EXTRAORDINARY ADVANCES IN THE** biosciences in recent years. We have deciphered the human genetic code; we have developed technology to watch cells work in the human body; and we have begun to learn how to repair or replace whole organs.

Having discovered the building blocks of life, researchers now face the even greater challenge of grasping how these building blocks all fit together to make protein machines, nerves, muscle, skin, and whole organs—and then using that knowledge to transform human health.

This is the mission of Bio-X, Stanford’s pioneering interdisciplinary biosciences program. Bio-X brings together biomedical and life science researchers, clinicians, engineers, physicists, and computational

scientists to unlock the secrets of the human body. Rather than study cells and tissues in isolation, Bio-X investigators work to understand entire organ systems in all their complexity.

Such an ambitious undertaking requires teams of experts from any number of disciplines working together, using every tool at their disposal, and inventing new ones when needed. It is an undertaking perfectly suited for Stanford, a place with some of the top scientists, engineers, and clinicians in the world and a long history of iconoclastic, entrepreneurial thinking. The university is proving to be the ideal place, and Bio-X the ideal program, to lead the biosciences into the future.



LEE ABEL

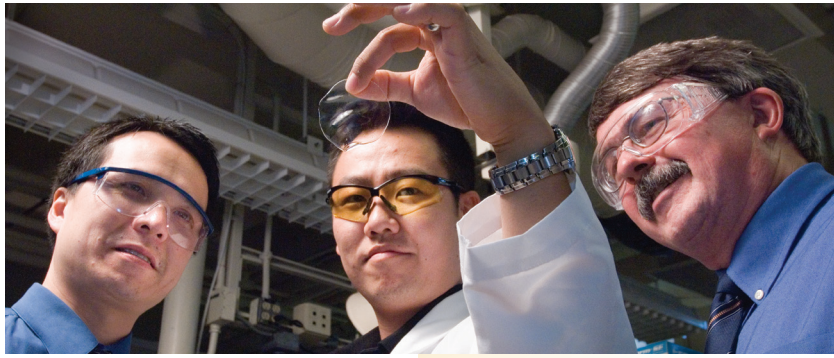
Proteins are natural nanomachines that perform vital functions in the bodies of all living organisms. Before they can do their work, however, they must fold into specific three-dimensional shapes. Failure to fold proteins correctly can lead to serious diseases. But how proteins fold is not well understood. Investigators have recently discovered that molecular “chaperones” play key roles in this complex process, helping to fold and assemble proteins and performing quality-control checks to remove misfolded ones.

Judith Frydman, a professor of biological sciences at Stanford, is at the forefront of protein-folding research, which draws on cell biology, computer science, biochemistry, genetics, and mechanical engineering, among other fields.

Discovering how chaperones perform what she calls their “molecular origami” may lead to new therapies for Alzheimer’s, diabetes, heart disease, cancer, Huntington’s disease, and other disorders. Conversely, learning how to block chaperones that assemble proteins into viruses could lead to therapies that prevent viral infection with no risk of the virus developing drug resistance.

Frydman’s preliminary research to study chaperones by single molecule approaches was supported by a seed grant from Bio-X’s Interdisciplinary Initiatives Program (with W. E. Moerner in the Stanford chemistry department). The National Institutes of Health subsequently awarded her funding to co-direct a new Center for Protein Folding Machinery.





David Myung, PhD '08, MD '11 (center), holds a sample of a transparent hydrogel with many of the attributes of natural bodily tissues. In a project funded by the Bio-X Interdisciplinary Initiatives Program, Myung has created an artificial cornea along with a team led by Christopher Ta (left), an associate professor of ophthalmology, and Curtis W. Frank (right), the W. M. Keck Senior Professor and a professor, by courtesy, of chemistry and of materials science and engineering. More than 10 million people worldwide are blind due to damaged

or diseased corneas, but cornea transplants are limited by a shortage of donors, tissue rejection, and a prolonged recovery period. The artificial cornea may one day restore sight to millions, and improve the vision of millions more who are farsighted or presbyopic.

## Fostering New Approaches

**BEGUN AS A BOLD EXPERIMENT, BIO-X HAS GAINED AN INTERNATIONAL REPUTATION AS THE** most exciting and productive program in the interdisciplinary biosciences. Working at the frontiers of knowledge, Bio-X investigators are making breakthroughs in biomedical technology and our understanding of how the body works. These breakthroughs promise to revolutionize health care.

Bio-X research focuses on efforts to understand organ systems in all their complexity. Scientists still do not understand how individual proteins assemble into molecular machines, how sets of muscle cells work together to make a heart beat, or how neural cells generate complex behaviors. These are questions that can never be answered by the prevailing paradigm of studying the body cell by cell, molecule by molecule. Consider the brain: Even the most detailed understanding of its genes and molecules will never reveal how it works.

In place of this reductionistic model, Bio-X investigators use approaches that are “synthetic” in many senses—studying how individual organs work together as a system, bringing multiple disciplinary perspectives to bear on problems, and in some cases using models to understand complex systems. These approaches are leading to a more integrated understanding of human biology in health and disease.

Bio-X builds on the strengths of Stanford’s outstanding schools and departments by providing faculty and students with the resources and facilities needed to build new bridges between disciplines that have traditionally been separate. Bio-X researchers conduct their work across the entire university. To date, more than 500 faculty members from more than 60 departments have participated in Bio-X teams to tackle important research problems in the life sciences or biotechnology.

The James H. Clark Center, completed in 2003, serves as the hub for Bio-X. Situated both symbolically and physically at the crossroads leading to the School of Medicine, Stanford Hospital & Clinics, the Lucile Packard Children’s Hospital, the School of Engineering, and the School of Humanities and Sciences, the Clark Center features flexible laboratory spaces and shared equipment that encourage unprecedented levels of collaboration among researchers from an extraordinary array of disciplines. The center was explicitly designed to encourage serendipitous encounters among faculty and graduate students that can lead to unusual but fruitful collaborations in the biosciences.

## How Bio-X Generates Results

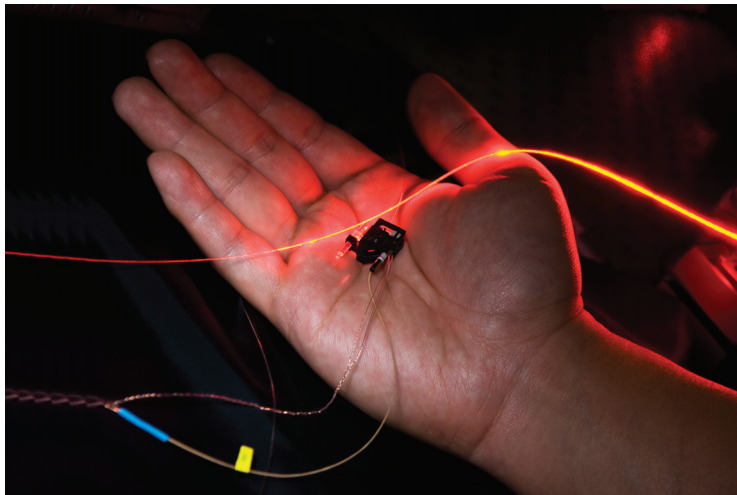
**BIO-X RESEARCHERS PRODUCE ASTONISHING RESULTS. INVESTIGATORS HAVE CREATED** artificial corneas with the potential to restore sight to more than 10 million blind people around the world. Other faculty collaborations have combined laser, microscope, and endoscope technology to invent a device that fits into the palm of one's hand but is powerful enough to produce sharp images of cells and tissues in living organisms.

This is only a sampling of the innovative research Bio-X investigators have undertaken. Bio-X research is guided by four overarching goals:

- To image and simulate life from molecules to mind
- To restore the health of cells and tissues
- To decode the genetics of health and disease
- To design therapeutic devices and molecular machines

In its first decade of existence, Bio-X has shown how powerful its interdisciplinary approach to the life sciences can be. Investigators have made scientific advances and technological innovations that would not have been possible without the unusual cross-disciplinary collaborations Bio-X inspires among faculty and graduate students.

In fact, Bio-X has become a model for other multidisciplinary programs. At life science programs at universities around the world, Bio-X has become a respected “brand.” The creative ferment and entrepreneurial spirit of Bio-X have also inspired other programs here at Stanford.



This incredibly small instrument—a miniature fluorescence microscope, or “microendoscope”—uses fiber optics and micro-optics to image blood cells and neurons within deep tissues that are inaccessible to conventional microscopy in living subjects. The microscope was developed by a team led by Mark Schnitzer, associate professor of biological sciences and applied physics, whose lab uses these tiny imaging devices to study the nervous system. In collaboration with Nikolas Blevins, associate professor of otology and neurotology and the director of the Stanford Cochlear Implant Center, the Schnitzer lab is developing a microendoscope to capture the first images of the human cochlea in live subjects. The researchers hope to gain insight into the causes of inner-ear hearing loss, which remains extremely difficult to diagnose and treat. The Schnitzer lab

is also combining the use of microendoscopy with electrophysiological, behavioral, and computational approaches to the study of learning and memory. Schnitzer’s innovative work on this and other projects has been honored with a prestigious National Institutes of Health Director’s Pioneer Award, which recognizes bold and creative research.



What happens in the brain as it learns, and what goes wrong when it is affected by disease? Scientists are just beginning to find out. One central question is how neural circuits perform the calculations needed to deliver instructions to the body about how to move. A team of Stanford biologists, neurobiologists, and geneticists hopes to answer this question through an experimental project supported by a Bio-X Interdisciplinary Initiatives Program grant.

Associate Professor of Neurobiology Jennifer Raymond and her colleagues are focusing on the neural circuits of the cerebellum, which plays a key role in motor learning, the process by which movements become smooth and precise through practice. By inactivating parts of

neural circuits, the team hopes to learn what happens to circuits as a movement is perfected or impaired by disease. It is among the first empirical studies of its kind.

The research ultimately should point the way to a better understanding of how the brain lets us think, move, and perceive. Practical applications include building computers and robots that better mimic the brain's abilities.

## The Bio-X Interdisciplinary Initiatives Program: Shaping the Cutting-Edge of the Life Sciences

**THE INTERDISCIPLINARY INITIATIVES PROGRAM (IIP) IS AT THE HEART OF BIO-X. THE PROGRAM** funds collaborative research in bioengineering, biomedicine, and the biosciences, led by scientists and educators throughout the university.

IIP provides seed funding—an average of \$150,000 per project to be used over two or three years—for research that might not get funding otherwise. Major federal institutions such as the National Institutes of Health and the National Science Foundation generally reserve their funding for work that has already demonstrated feasibility. And it's difficult in any case to secure funding for research that does not fit neatly within the confines of a traditional discipline.

IIP grants support research that is so forward-looking it may not even work, but could have tremendous benefits if it does. Research work that succeeds, having demonstrated proof of principle, can then go on to secure funding through federal and other sources. This strategy has already had impressive payoffs in generating significant outside funding.

Competition is stiff. IIP grants go to fewer than one in four research proposals. Awards so far have supported an astonishing variety of multidisciplinary projects from around the university. Hundreds of faculty teams have been formed, including faculty from the schools of medicine, humanities and sciences, engineering, earth sciences, law, and education.

Outcomes of IIP supported research include:

- Discovering a way to increase the resolution of MRI scans a hundredfold, giving researchers and clinicians a noninvasive way to see individual cells in the body.
- Developing an artificial retinal nerve connection, which may lead to a cure for macular degeneration, the most common form of irreversible blindness in the United States.
- Launching an effort that draws on synthetic chemistry, protein engineering, and biophysics to engineer a new kind of molecular tag that holds the potential to detect cancer at its earliest stages.



“So many things happen at one time to create movement,” explains mechanical engineering doctoral student Melinda Cromie. “Every time you move, all the tiny elements of the muscle, called sarcomeres, are working in unison, creating force and motion.” Thanks to a new microscope system that Cromie and other Bio-X researchers developed, scientists can now observe sarcomeres in motion in the human body. As the recipient of a Bio-X Stanford Interdisciplinary Graduate Fellowship (SIGF), Cromie has been able to work between labs in engineering, physics, and biology, collaborating with orthopedic surgeons and laser microscopy experts. “For the first time, we are able to directly study the microscopic basis

of whole muscle force and motion,” she says. Cromie and her fellow researchers believe this research will lead to a better understanding of motor control diseases such as stroke and cerebral palsy.

## The Bio-X Stanford Interdisciplinary Graduate Fellowships: Nurturing the Next Generation of Problem Solvers

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**THE FUTURE OF BIOMEDICAL RESEARCH LIES IN THE HANDS OF CREATIVE AND MOTIVATED** graduate students. Armed with state-of-the-art training and unconstrained by traditional, discipline-bound thinking, these students will offer bold new approaches to age-old problems. Bio-X has created unique fellowships to encourage this barrier-breaking training: the Bio-X Stanford Interdisciplinary Graduate Fellowships (SIGF).

Students often have a hard time funding their graduate education if they want to work across disciplines, precisely because their research is so innovative. And because they are at the beginning of their academic careers, these students may not yet be prominent enough to attract support beyond their main academic fields.

The Bio-X SIGF program rewards novel, risk-taking thinking by providing tuition and a stipend to promising graduate students for up to three years while they pursue interdisciplinary research projects. At any one time, Bio-X supports at least 30 fellows. Applications are welcome from students around the university working to bridge gaps between biology and other disciplines, such as physics, engineering, computer science, and chemistry. Each year, about 10 fellows are selected from a pool of close to 100 applicants representing more than 25 departments and three schools.

Cutting-edge work being supported through Bio-X SIGFs include finding ways to engineer proteins that can speed wound healing; developing neural prosthetics to treat Parkinson’s disease sufferers by allowing them to control a “virtual keyboard” through mental effort alone; improving the control systems used in robotic surgery; and developing a new technique to pinpoint and image exactly what happens in a brain suffering from depression, which may lead to promising new treatments.



# Bio-X NeuroVentures: Building the Future

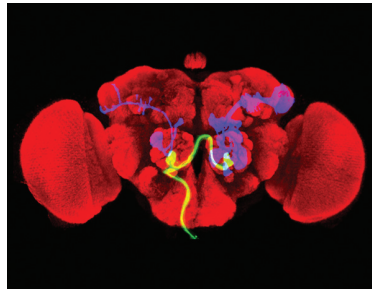
## WHILE OTHER UNIVERSITIES ARE JUST BEGINNING TO DISCUSS HOW TO IMPLEMENT

interdisciplinary life science programs, Bio-X has already stimulated more than 200 scientific collaborations and awarded several rounds of research grants and fellowships.

The results so far have included numerous biomedical inventions and life science discoveries that have expanded our understanding of the human body and how to treat disease. But this is only the beginning: Bio-X is an experiment in progress. The achievements to date are in some sense a “proof of principle” of even greater things to come.

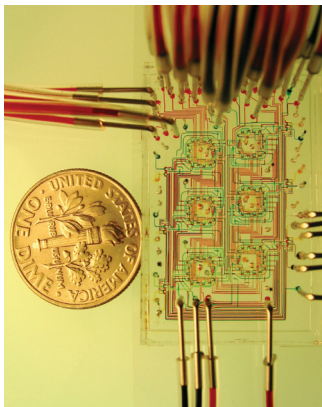
As Bio-X matures, its leaders expect its endeavors to grow in scope and ambition, necessitating a deeper commitment of seed funding. Bold new undertakings—called Bio-X Ventures—will rely on large-scale, team-based collaborations that are more typical of engineering and biotechnology work.

The first of these, Bio-X NeuroVentures, is an incubator for exceptionally creative ideas that have great potential for illuminating the brain, the mind, and intelligence. Bio-X NeuroVentures convenes faculty from multiple fields to open new research avenues by developing novel brain-imaging technologies. In addition, researchers are working to rapidly advance groundbreaking techniques for turning brain cells on and off using light. This promises to be a powerful tool for understanding and mapping the neural circuits underlying behavior, and may lead to new treatments for brain disorders ranging from Parkinson’s disease to autism and depression.



LIQUN LUO

**TOP:** At left is a compound image of a fly’s brain. A Bio-X team of experts in biology, engineering, applied physics, genetics, and neurobiology is developing laser technology that will allow scientists to image 96 fruit fly brains simultaneously at high speed. The technology, known as massively parallel brain imaging, is expected to greatly increase our understanding of neural circuits in humans. How neural circuits, or groups of interconnected nerve cells, work is one of the great mysteries of the brain. This revolutionary brain-imaging project will allow researchers to see for the first time the structure and function of entire neural circuits in living organisms. By using fly models of human diseases, researchers hope to gain greater understanding of and new treatments for human brain disorders ranging from addiction to Parkinson’s disease. The project drew on the expertise of prominent scientists around the university, including Tom Baer, executive director of the Stanford Photonics Research Center; Thomas Clandinin, associate professor of neurobiology; Mark Horowitz, the Yahoo! Founders Professor of Electrical Engineering and Computer Science; Liqun Luo, professor of biological sciences and, by courtesy, of neurobiology; Mark Schnitzer, associate professor of biological sciences and applied physics; and Matthew Scott, professor of developmental biology, genetics, and bioengineering.



FREDERICK BALAGADDE

**LEFT:** Stephen Quake, the Lee Otterson Professor in the School of Engineering, professor of bioengineering and, by courtesy, of applied physics, was convinced that biology research that traditionally had been slow, labor-intensive, and conducted in large laboratories could be done differently. Quake, who is co-chair of the Department of Bioengineering, worked with a research group drawn from the schools of medicine, engineering, and the humanities and sciences to find a way of fabricating thousands of valves on a single tiny chip, allowing scientists to create “labs on a chip” that may do for biology what the computer chip has done for information processing.

Researchers are investigating applications that range from synthesizing pharmaceuticals to screening for rare genetic diseases cheaply and quickly. Quake’s lab recently used the technology to develop a prenatal test for Down syndrome and other conditions that produces results in a few hours rather than weeks.

# Giving Opportunities

Many gift opportunities are available to support Bio-X. Key funding needs are outlined below.

## ENDOWED DIRECTORSHIP OF BIO-X

\$5 MILLION

A gift at this level will ensure that Bio-X continues to flourish under the strengths of its leadership, providing resources that enable the director to foster interdisciplinary collaborations, encourage novel uses of technology, and fund research opportunities that arise serendipitously. The directorship may be named for the donor or someone the donor wishes to honor.

## BIO-X STANFORD INTERDISCIPLINARY GRADUATE FELLOWSHIPS

\$600,000 (MATCHED 1:1)

To attract the most talented and promising applicants, Bio-X aims to support at least 30 graduate fellows at any given time. Gifts of at least \$600,000 will be matched one-to-one, creating endowed funds of at least \$1.2 million. Endowed fellowships exist in perpetuity and may be named for the donor or someone the donor wishes to honor.

## BIO-X PROGRAM SUPPORT FUNDS

GIFTS OF VARIOUS SIZES

Support funds are critical and may be provided in the form of expendable gifts, term endowment, or endowment. Stanford seeks a total of \$25 million in support funds for Bio-X in the areas highlighted below. Gifts of all sizes from \$25,000 to \$1 million or more will make a significant difference in accelerating research and advancing discoveries.

- The Interdisciplinary Initiatives Program (IIP), which awards competitive grants to innovative, collaborative projects led by scientists and educators in bioengineering, biomedicine, and the biosciences.
- Bio-X NeuroVentures, a bold venture to develop new technologies and approaches with the potential to unlock the secrets of the brain.
- Funds to support Bio-X's educational mission, such as symposia and teaching on topics in the interdisciplinary biosciences.
- Funds to develop new technology cores for Bio-X faculty, including imaging, computation, and fabrication.



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