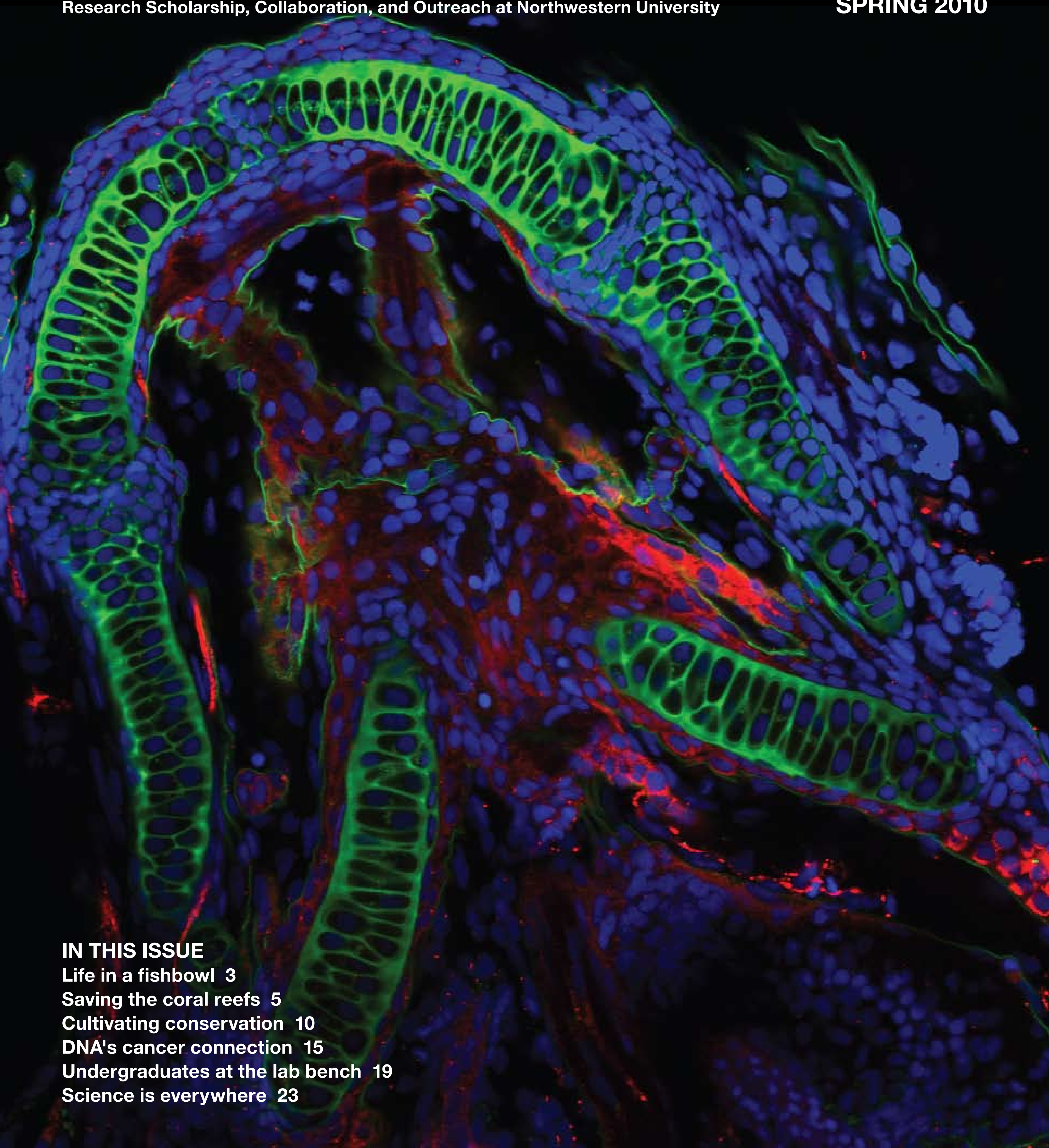
CenterPiece

Research Scholarship, Collaboration, and Outreach at Northwestern University

SPRING 2010



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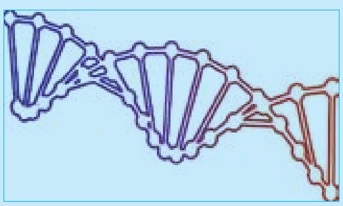
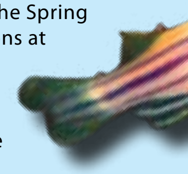


The United Nations has declared 2010 to be the International Year of Biodiversity, a celebration of life on earth and the value of biodiversity for our lives. The Spring 2010 issue of *CenterPiece* celebrates the diversity of research collaborations at Northwestern: research with affiliates such as Children's Memorial Research Center, the Field Museum, Shedd Aquarium, and Chicago Botanic Garden; research with federal agencies such as the National Science Foundation and National Cancer Institute; and research with one another at the undergraduate level.



NORTHWESTERN UNIVERSITY

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Jay Walsh, Vice President for Research

Office for Research Planning, Finance, and Communication
Meg A. McDonald, Executive Director
Joan T. Naper, Director of Research Communications
Kathleen P. Mandell, Senior Editor
Amanda B. Morris, Publications Editor

Address all correspondence to:
Joan T. Naper
Director of Research Communications
Northwestern University
Office for Research, 633 Clark Street
Evanston, Illinois 60208

Editors
Joan T. Naper, Kathleen P. Mandell, Amanda B. Morris
Tom Fredrickson, University Relations

Design, Art Direction & Production
Kathleen P. Mandell

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COVER – Confocal microscopy image of a head of four-day-old zebrafish embryo. Cartilage elements that make up the zebrafish jaw are stained in green, while red marks primary cilia, nerves, and muscle, and blue, the cells' nuclei. Image courtesy of Jacek Topczewski, pediatrics.

FISHING FOR ANSWERS

What could a human possibly have in common with a fish?

Scaly and cold-blooded with unblinking eyes and a tail, these creatures seem so different from humans that it's difficult to believe they have much to teach us about ourselves. But within the last two decades, zebrafish — those blue-striped little minnows that are typically seen in home aquariums and pet stores — have emerged as a popular new research model, bringing insights into human behavior, development, and disease.

Acting Fishy

"Fish actually have a lot of behavior," says Jill Morris, pediatrics. "They dart to the front of the tank when you enter the room. They demonstrate schooling behavior and have a very distinct predator response."

It's this startle response that interests Morris the most. She was the first researcher to use zebrafish to study the Disrupted-in-Schizophrenia-1 (or DISC-1) gene — the susceptibility gene for behavioral disorders, such as schizophrenia, autism, and Asperger syndrome, which emerge during development.

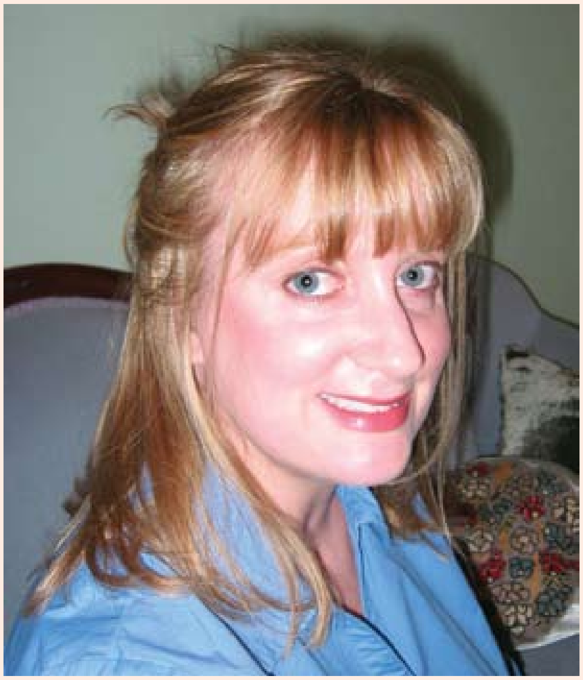
"These mental illnesses are characterized by hallucinations and delusions," she says. "But how can you tell if a fish is hallucinating? A main way to determine schizophrenia is prepulse inhibition, which is the startle response."

If a person unexpectedly opens your office door, then it's inevitable that you would jump. If a person knocks first and then opens the door, then you most likely wouldn't startle. However, schizophrenic humans would startle regardless of whether or not a person knocks first; this may also be true for zebrafish that contain the DISC-1 gene.

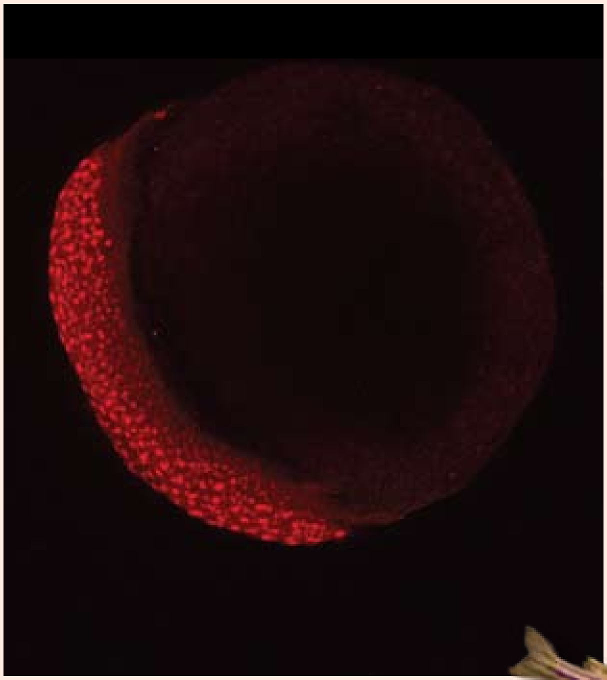
"The startle response is a distinctive S wave of the tail," Morris says. "We can actually see this in the embryos, so we don't have to wait for them to reach adulthood. We can externally watch all the little development stages as they occur."

The Advantages are Clear

These transparent embryos are a main reason why zebrafish are also used as models for physical development. They develop from a fertilized egg to a free-swimming larva in just five days, so researchers are able to complete experiments during this timeframe. This rapid development and transparency along with low cost and potential for genetic manipulation have heightened the popularity of zebrafish with researchers. »



Jill Morris

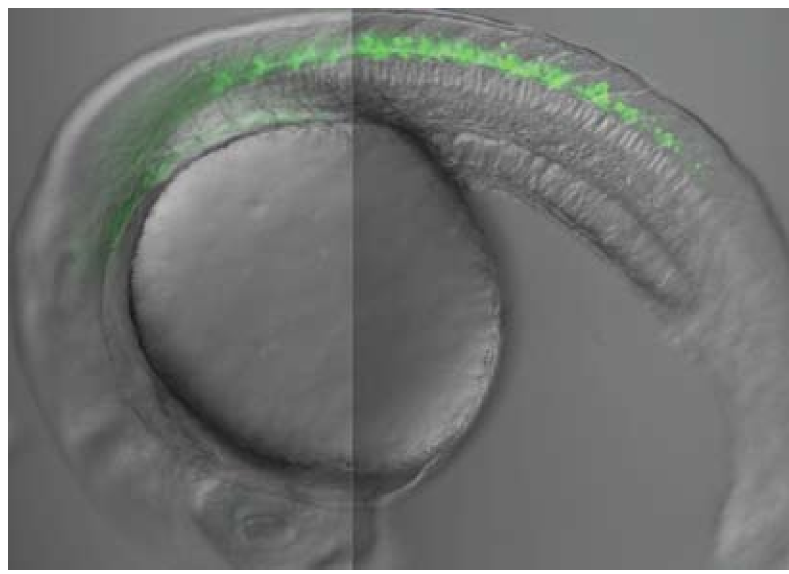


A zebrafish embryo expresses a red fluorescent protein. Image courtesy of Morris laboratory.

Jacek Topczewski

An image of a transgenic zebrafish embryo is easily distinguished by its fluorescent green heart. This is a ventral view of a one-day-old embryo, with clearly visible eyes, brain, and blood flowing over the yolk. Image courtesy of Topczewski laboratory.


David McLean


Cells in the spinal cord of a one-day-old zebrafish embryo glow green due to the expression of fluorescent proteins. Photo and image courtesy of McLean laboratory.

"We can observe and easily manipulate the transparent embryo," says Jacek Topczewski, pediatrics, who oversees the sprawling, 2,000-tank zebrafish facility at Children's Memorial Research Center. "We have access to the embryos from the moment the egg is fertilized. Then we can follow the cells through the development stages or even the whole life, really."

Topczewski's research group studies craniofacial development. Craniofacial abnormalities, such as cleft lips and cleft palates, are the most common congenital defects in humans. Topczewski points out that because zebrafish are vertebrates, they share the same genes and signaling pathways that are engaged in the development of higher vertebrates, including humans. "What we're trying to understand is the biological basis of human development," he says. "And if something goes wrong during development, that of course can lead to a defect."

Growing and Glowing

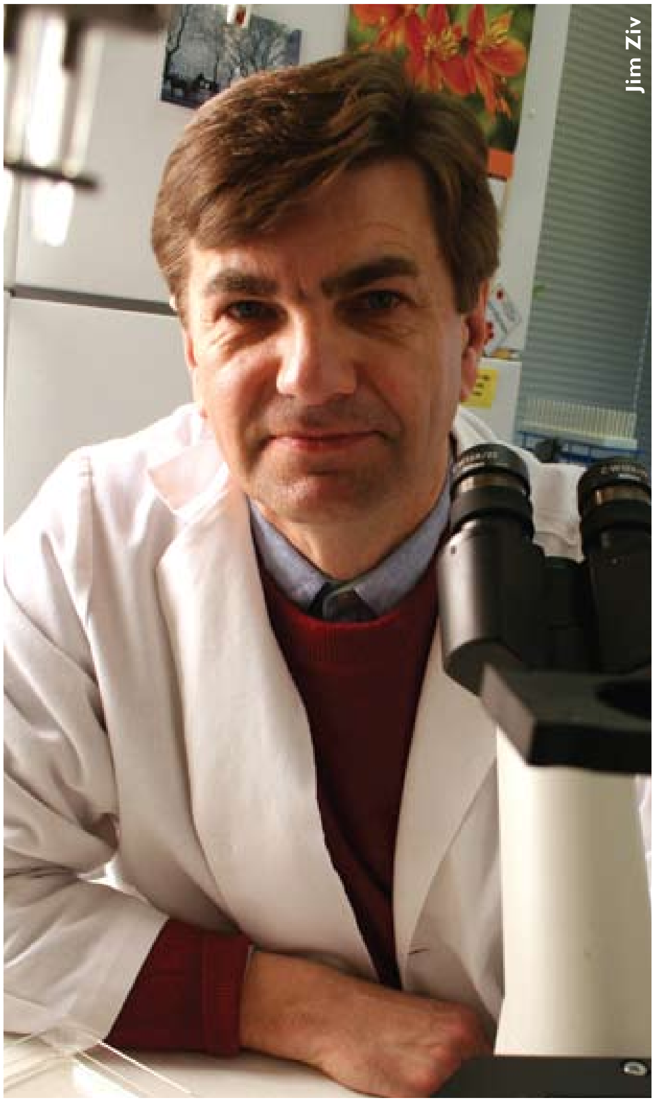
One way to follow development and highlight different tissues is by making genetically modified "transgenic" fish with fluorescent protein trackers. This popular technique is used in Topczewski's lab as well as the lab of David McLean, neurobiology and physiology. McLean says the transparency of the embryos allows usage of glow-in-the-dark mechanisms to help visualize the cells and circuitry of the nervous system and see how those correspond to the cells in humans.

"We use molecular biology tools to selectively label subsets of cells and monitor the changes in their interactions during development and during different movements," says McLean, who studies spinal cord injury. "The beauty of using molecular markers is that spinal cords are constructed in a very similar way, whether you are a human or a fish. We can apply our findings to more complex animals where these types of experiments are not yet possible."

McLean's research shows that multiple classifications of important cells are involved in both slow and fast body movements. He says this insight will help guide stem-cell therapies as more than one cell class will be needed to recover a full range of movements in paralyzed patients. "We're addressing how cells plug into one another and how their activity is responsible for different intensities of movement," he explains. "It's difficult to address these issues in mice and rats because they aren't exactly see-through."

Of course, the embryos eventually become full-grown fish and the fascinating period of development is over. Most researchers keep the fish to breed them in the lab. With 100 or 200 eggs laid as frequently as two days after spawning, McLean says, "once you get a few adults to breed, you never really have to buy another fish for the rest of your career." »

LIKE A FISH IN WATER Jacek Topczewski discovered a passion for zebrafish research when he began studying them more than 13 years ago. In addition to his own research, he manages the Fish Facility at Children's Memorial Research Center (CMRC). As the biggest fish facility affiliated with Northwestern, it comprises three rooms that accommodate nearly 2,000 tanks and approximately 25,000 fish. Topczewski says one of the best assets to working with fish is the ease of maintenance. All of the tanks at CMRC are equipped with automatic filtration systems. Inlet valves exchange the water three times per hour, keeping the conditions at optimal quality with little manual maintenance required. "We have to get the same ACUC approval as with other animals," Topczewski says. "That applies to keeping the facility clean, not overcrowding the tanks, and closely following all the regulations." Photos by Amanda Morris.



Sergei Revskoy

A 40-day-old adult zebrafish has red fluorescent proteins that express the liver and green fluorescence in the exocrine pancreas. Photos courtesy of Revskoy laboratory.

Living in a Fishbowl

Adulthood is exactly when zebrafish become interesting for Sergei Revskoy, hepatology, who studies liver tumors. He transplants tumor cells from adult fish into younger fish or embryos and then watches the tumor development through bioimaging. This is done by first labeling tumors with fluorescent markers, so every single cell or group of cells can be monitored as they disseminate throughout the body. "These fluorescent protein markers can be detected under just a regular fluorescent microscope, which is very simple," Revskoy says. "If you were to do this in mice, then you'd need to do an MRI to detect the tumor and even then the resolution is lower."

To make the tumors even more visible, Revskoy recently started developing transparent adult zebrafish. The liver and the heart are visible as the fish freely swims about its tank. "It's the ease of monitoring," he says. Their tiny bodies literally become a fish bowl as their internal organs are watched constantly.

Revskoy, who is one of fewer than 50 researchers from approximately a dozen labs exploring cancer in zebrafish internationally, is no stranger to engineering his own fish. In addition to creating this transparent variety of zebrafish, he also makes his own clonal lines. "To transplant tissue from one animal to another, the animals have to be completely identical genetically, which is why clones are needed," he explains. "The advantage of transplantable models is that you know exactly when the tumor emerges and can specifically monitor it from the initial stage to full-blown."

Like behavioral symptoms, structural development, and spinal-cord signaling, cancer is another area of study that links humans and zebrafish. "Although we recognize that fish are very different from us," Revskoy says, "the molecular and genetic make-up of the tumors are exactly same."

Although zebrafish were not identified as an emerging model until 1996, their popularity has expanded exponentially since then. According to Topczewski, there are as many as 300 laboratories in the United States working with zebrafish and more than 12,000 papers have been published on the topic. One could say that this field of research is going quite swimmingly. — *by Amanda Morris*

REVIVING THE "RAINFORESTS OF THE SEA"

Imagine diving deep beneath the surface of the ocean, rubber flippers on your feet, a scuba tank on your back, your breath rising in bubbles from your mouthpiece. Your mask magnifies the magnificence of the underwater scenery: nubby palaces of colorful coral, inhabited by brightly colored fish and otherworldly creatures. You thread through green forests of seaweed and algae. Darting shadows flit by: are they predators or prey?

Now imagine visiting the scene again once the coral has been bleached white and left for dead by the fish and the greenery, a cemetery of the sea. The second scenario has already happened in many once-fertile undersea coral reefs. Some of the same factors that have endangered their terrestrial cousins, the rain forests, are threatening the underwater communities known as coral reefs.

"Coral turns white or is 'bleached' when large numbers of algae that live in the tissues of the coral and provide it with food are lost," says Luisa Marcelino, civil and environmental engineering. "This causes a loss of equilibrium in the underwater ecosystem." Marcelino's research group is using optical and genomic methods to understand how coral bleaches and why some corals bleach and die while others close by in the reef hardly bleach or recover quickly once the bleaching event subsides.

THE DAMAGED ECOSYSTEM

The world's coral reefs were probably the first ecosystem to show major damage from climate change. Mass coral bleaching was unknown in the long oral history of many countries such as the Maldives and Palau before their reefs were devastated in 1998, according to the Global Coral Reef Monitoring Network. About 16 percent of the world's corals bleached and died in 1998, following one of the hottest years on record in the tropical oceans. Already 19 percent of the world's coral reefs have been lost and 35 percent are seriously threatened with destruction. Further climate change will cause even more dramatic loss.

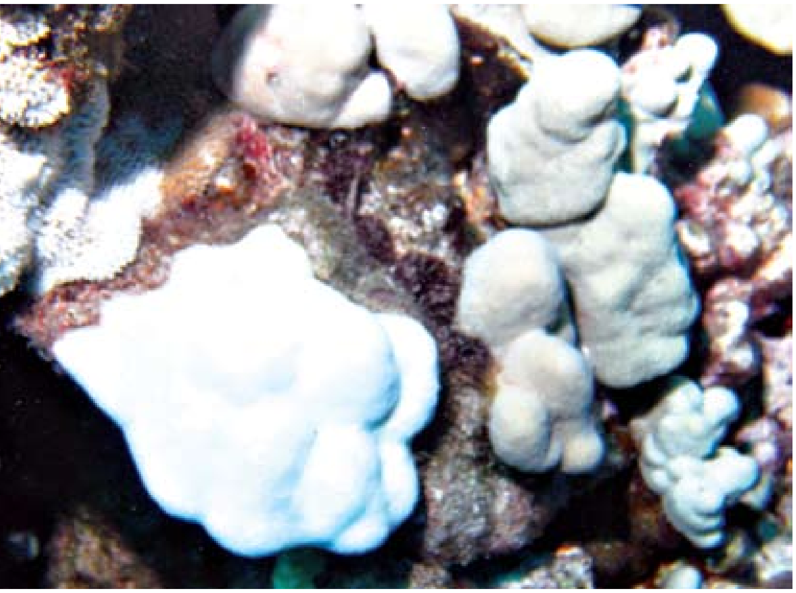
"Coral reefs evolved some 240 million years ago and today's reefs might be as old as 5,000 to 10,000 years," Marcelino says. "They can serve as reservoirs of recording sea temperatures, like ice cores in the Arctic. When the reefs die, we lose not just their structures, we lose their history as well."

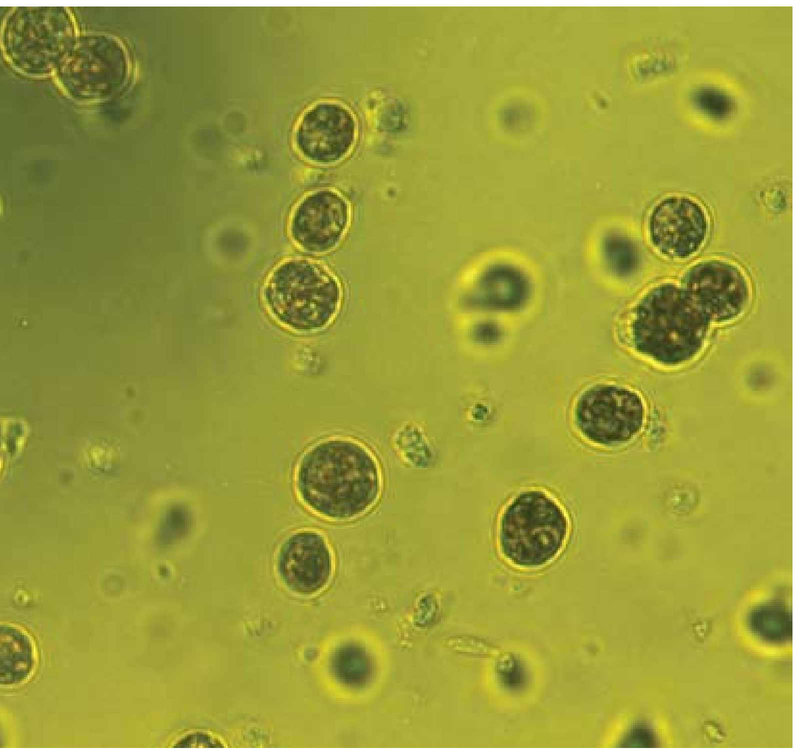
What leads to the death of this coral? Marcelino credits chronic stressors like water pollution and sedimentation resulting from deforestation of surrounding land, overfishing, and global climate change. A rise in temperature of just 1 to 2 degrees Celsius above the monthly maximum can trigger bleaching, she says. Furthermore, global warming also is causing ocean acidification because more carbon dioxide emitted from anthropogenic or man-made sources is entering the ocean and reacting with water to produce carbonic acid. This compromises skeleton calcification, which results in weaker reef structures and loss in biodiversity of entire reef communities.

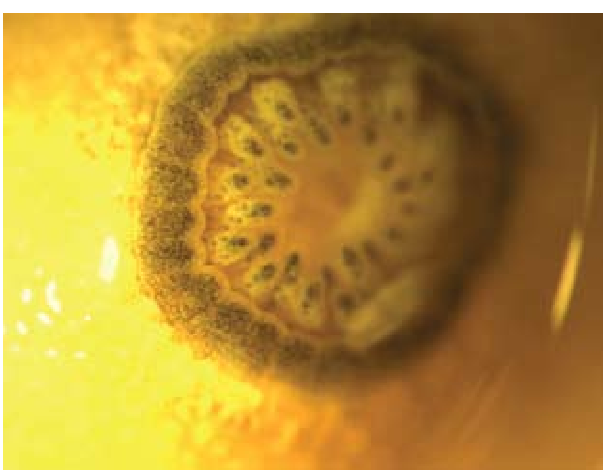
Loss of coral reefs unbalance not just the underwater ecosystem, but also contributes to economic distress in the countries surrounding them from loss of tourism, the potential for inundation, erosion and loss of agriculture, and the displacement of people and cultures, reports the Global Coral Reef Monitoring Network. The network estimates that global climate change damage to coral reefs will threaten the livelihoods of 500 million people around the world and seriously reduce the $100 billion that reefs provide the global economy. »

PHOTOS Opposite page: A hawkfish forages amid coral and algae in a Hawaiian coral reef (Crystal Cove, Big Island). Photo by Luisa Marcelino.

This page: Luisa Marcelino diving at Dome Reef, Big Island, Hawaii. Courtesy of L. Marcelino.







WHAT MAKES A CORAL REEF WORK?

Marcelino started her academic life as a molecular scientist studying gene mutations in cancer cells. But once she started diving on Caribbean coral reefs during graduate school, she changed her focus to the biodiversity of coral reefs. She and her lab have been teasing apart the potential mechanisms by which the coral and algae might influence the response to bleaching for solutions to conserve coral reefs. Her research concentrates on two areas: the type of algae or zooxanthellae that inhabit the coral and the characteristics of the corals themselves and how they reflect and scatter light.

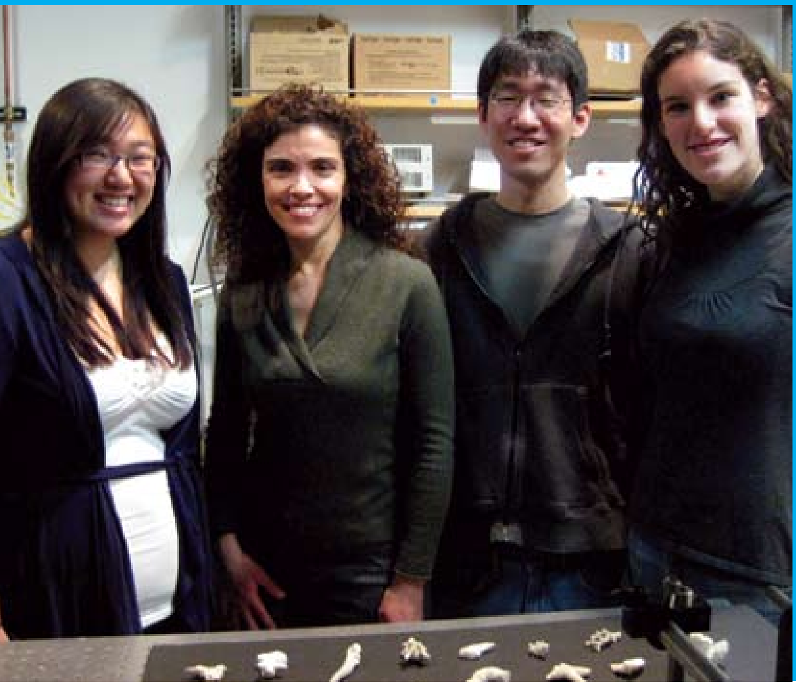
Coral is made up of polyps, living creatures that secrete calcium carbonate to provide the structure that supports them. Coral polyps do not photosynthesize but have a symbiotic relationship with single-celled organisms called zooxanthellae. These algae, which provide color to the coral, carry out photosynthesis within the tissues of the coral polyps and produce nutrients that are then used by their hosts. Some of these algae confer to the coral more resistance to bleaching than others. Marcelino is conducting genetic analysis to discover the differences in the DNA of these zooxanthellae species.

Marcelino and her students also are studying the physical characteristics of the coral skeletons themselves, which can scatter light in different ways. They measure how much of the light that hits the skeleton gets scattered back to the tissues and how that light impacts the bleaching and mortality of the coral. Some coral skeletons are more porous at the nanoscale because they grow faster linearly than calcify or cross-link, which allows light to travel longer distances inside the skeleton. This results in better light redistribution to the whole coral and higher availability of light to the zooxanthellae. It appears that these corals evolved a strategy to give more light to their algae and in return receive more food to grow faster. The tradeoff, however, is that in the presence of water that is warmer due to global warming, this excess light further magnifies the stress already experienced by the algae and accelerates bleaching. The evolutionary adaptation that has worked for corals for hundreds to thousands of years may now

PHOTOS Top: Bleached thick finger coral (*Porites sp.*) colony surrounded by healthy (light gray) colonies. Bleached corals lose most of their algae and may die if they are not repopulated soon after the bleaching. Photo by Luisa Marcelino.

Middle: Algae that live in symbiosis with the coral (zooxanthellae) were isolated from coral tissue and observed under light microscope for density counts. Image courtesy of Marcelino research group.

Bottom: Polyp of *Turbinaria sp.* showing zooxanthellae around the polyp and inside each tentacle. The polyp can contract during the day to protect the algae from excessive irradiance. Photo by Marcelino research group.



Marcelino and students. Left to right: Jenny Fung, Luisa Marcelino, Andrew Fang, Hannah Wolfman.

Andrew Fang and Jenny Fung using optical instruments to view a coral specimen to see how light transports through it structure.

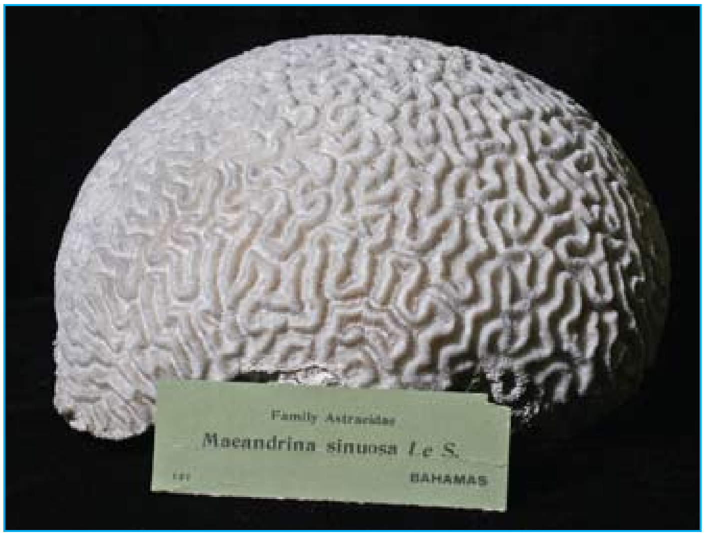
in the face of extreme thermal anomalies work against them. Marcelino and her students collaborate with the research group headed by Vadim Backman, biomedical engineering, to understand how light is transported through coral structures.

COLLABORATING WITH CHICAGO INSTITUTIONS

Marcelino also holds an appointment with the Field Museum in Chicago. She is collaborating with Mark Westneat, director of the Biodiversity Synthesis Center at the Field Museum to examine whether light transport has an evolutionary context and which genes in the zooxanthellae may be a risk factor for bleaching resistance. Her technicians there have been invaluable in sequencing zooxanthellae genes at the museum's Pritzker Laboratory for Molecular Systematics and Evolution. She also works with live corals from the John G. Shedd Aquarium in collaboration with George Parsons, director of Fishes.

Marcelino receives research funding from the National Science Foundation and through the board of Northwestern's Chemistry for Life Processes Institute to help support her work on the optical properties of corals. "The more diverse an ecosystem, the more resilient it is in its ability to bounce back from its stressors," she says. "Understanding the structures and functions of coral reefs will ultimately help us conserve them, preserving what exists and managing them to protect from future adverse impacts." — *by Joan Naper*

Photos of Luisa Marcelino and students by Amanda Morris.



Coral skeletons from the Field Museum of Natural History, Chicago, Illinois. Photos by Gary Parr.

Boots on the Ground: Plant Biology and Conservation

Plant biologists have a term for it: plant blindness. It's the lack of awareness many people experience when confronted with a landscape. They might notice the animals or people in the picture, but never really see, much less are able to identify, the plants.

"Those plants growing in the scenery are the foundation of most of life," says Nyree Zerega, director of Northwestern's graduate program in plant biology and conservation and lecturer in the program in biological sciences. "They supply oxygen, food, building materials, and medicines, and play a large part in our economies. Without plants, we wouldn't be able to sustain most forms of life."

Zerega's own research into the origins and genetic diversity of the jackfruit supports this premise. Jackfruit, the largest tree-borne fruit, is an important crop in Southeast Asia including in Bangladesh, where it is the national fruit. Jackfruit can weigh up to eighty pounds and are so large that one falling from a tree could kill a person unfortunate to be standing below. Zerega was awarded a National Science Foundation grant to study jackfruit and its relatives. Her research will inform the conservation and management of the germplasm, or genetic material, of the jackfruit. She will travel to Bangladesh this summer, along with one of her students, Colby Witherup, a first-year graduate student in the Plant Biology

Jackfruit. Photo taken in Hawaii by Nyree Zerega.

Nyree Zerega examines a preserved specimen of breadfruit from Hawaii.

and Conservation Program. They will conduct work in villages throughout the country in collaboration with Bangladeshi scientists from the University of Rajshahi.

Collaborating with the Chicago Botanic Garden

Zerega came to Northwestern in 2005 to head up the University's collaboration with the Chicago Botanic Garden in Glencoe, Illinois, to provide a master's degree-level program in plant biology and conservation. The program expanded to include PhD-level students in 2009. Seven to eight new students enter the master's program each year; there are currently two PhD students. Classes in this program are also open to upper level undergraduates, including those in the plant biology concentration within the biology major.

"More and more, Northwestern students are interested in plant conservation and environmental concerns," Zerega says. "Conservation is a complex issue that requires an interdisciplinary approach. Through the collaboration with the Chicago Botanic Garden, there are more than a dozen research scientists who teach and mentor student research. Students can take advantage of classes in ecology, evolution and conservation as well as Northwestern's expertise in other areas such as political science and economics. Students are clamoring for more curricula and research opportunities in environment-related fields." »

Looking down into the interior of the Rice Plant Conservation Science Center showing the public space. Large windows provide views into the laboratories. Interactive exhibits on botanic garden research projects line the walls. The main goal of the public space with the windows and exhibits is to communicate science to the public and to show children that science is cool, and that real scientists look just like their parents.

The collaboration brings the Chicago Botanic Garden's facilities and resources to Northwestern students. The Garden's new Daniel F. and Ada L. Rice Plant Conservation Science Center, which opened in September 2009, offers nine labs where scientists work on solving plant conservation problems caused by climate change, habitat loss and fragmentation, invasive species, and pollution. The labs house state-of-the-art equipment such as growth chambers that control light and CO_2 levels, a seed quarantine chamber and seed bank facility, microscopes outfitted with digital cameras and analysis equipment. One lab contains GIS (geographic information systems) equipment which is used to understand plant species distributions and has applications for predicting locations where a species might occur under climate change scenarios and determine appropriate sites for plant restoration.

The Gold LEED-designated (Leadership in Energy and Environmental Design) building has two green roofs where scientists and students can carry out research in the factors that contribute to creating successful green roofs such as varieties of soil depth, mix of plants, and measurements of energy savings. Photovoltaic panels on the roof provide power directly to the building. Even the building's floor is made of rubber from recycled automobile tires laid over pipes for radiant heat. The Rice building is open to the public with interactive exhibits on plant biology, diversity, climate change, invasive species management, soil ecology, seed gathering and storage, and plant usage.

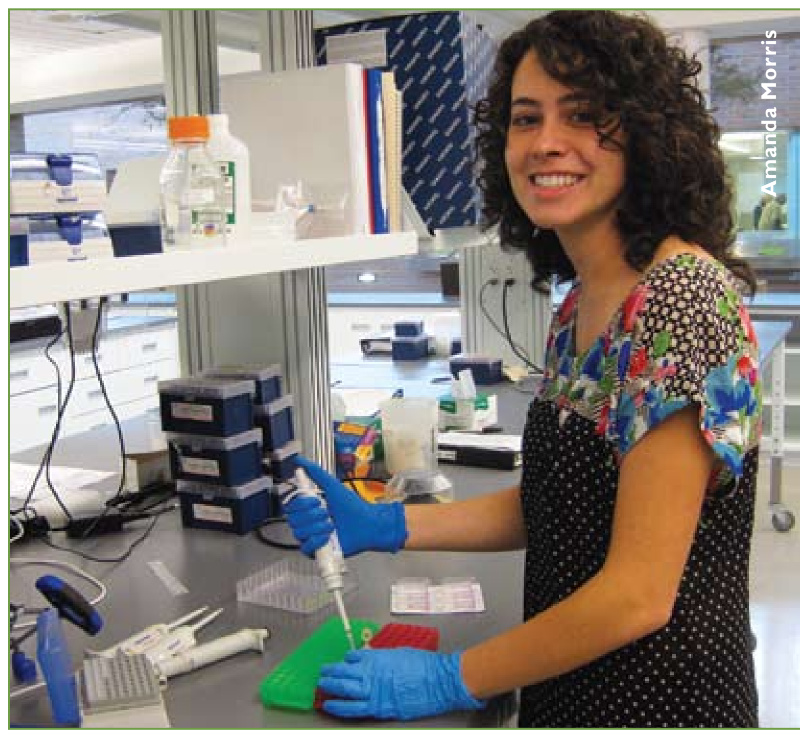
Exterior of the Rice Plant Conservation Science Center. The building is on piers because it is in a floodplain. A rainwater garden with native plants has been planted around the building.

On the roof at Rice Plant Conservation Science Center. Unlike most green roofs, this one is open to the public to see and study. It's another interesting place for the public to view plant conservation and evaluation in action. Photos by Patrick Herendeen.

"The Northwestern-Chicago Botanic Garden program is unique," says Patrick Herendeen, director of academic partnerships and co-director, division of plant science and conservation at the Chicago Botanic Garden. "We focus on biology as it relates to the environment. We look closely at plant diversity, endangered plant species, and the implications of climate change."

Outside the building are natural, restored, and created habitats that include native woodlands, prairies, and river wetlands. "Our habitats give students opportunities for 'boots on the ground' research studies," says Herendeen. "Our masters students are finding that there's great demand for them in jobs in conservation at state and local agencies, restoring nature preserves, and as conservation biologists." »

Patrick Herendeen checks out an herbarium specimen from one of the many cabinets that house a myriad of plant specimens from around the world.



Masters student Colby Witherup works in one of the labs. She's studying the genetic diversity and ethnobotany of jackfruit in Bangladesh with Nyree Zerega.

Students who go on to the PhD program generally are more interested in an academic track, teaching and doing research at the college and university level. "One advantage of our collaboration with the Chicago Botanic Garden is the opportunities students have to teach and interact with the general public," says Zerega. "The Garden offers outreach programs for 2-year-olds to 102-year-olds. Our students are able to present their research findings and get feedback not just from their teachers, but from the public as well."

SEPARATING THE SEEDS FROM THE CHAFF Jim Traxler is a retired chemical research scientist who volunteers in the Plant Reproductive Biology Laboratory. He spends and enjoys long hours assisting masters degree student Kate Gallagher in preparing her last year's grass seeds for her 2010 summer research experiments. Photo by Amanda Morris.

INTERNATIONAL CONNECTIONS

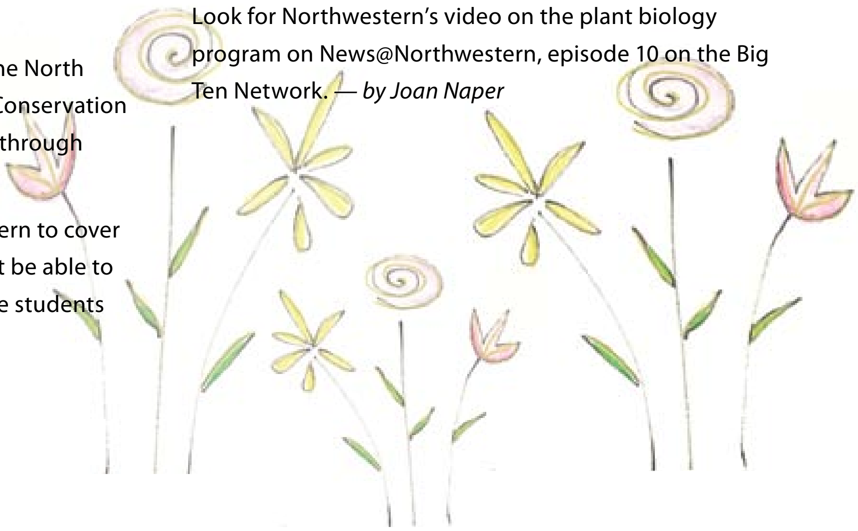
The Chicago Botanic Garden connection links students to international plant biology and conservation networks, including the Millennium Seed Bank Partnership that was started at Kew Gardens in England. The Millennium Seed Bank Partnership prevents plant extinction by collecting and storing seeds from throughout the world. The Chicago Botanic Garden is the leading repository of seeds from tallgrass prairies, like those found in Illinois, and collects and preserves these seeds in its seed bank along with associated preserved plant material in its herbarium. The goal for the Millennium Seed Bank Partnership is to conserve 25 percent of the world's plant species by 2020.

"We have armies of volunteers who help us with our seed bank project," says Herendeen. "Once the seeds are collected they have to be cleaned and counted, dried, and sealed into envelopes for long-term storage." Seeds are stored at the Garden as well as sent to seed banks throughout the world.

The Chicago Botanic Garden also serves as the North American headquarters for Botanic Garden Conservation International, which promotes conservation through botanic gardens.

"Teaming with the Garden allows Northwestern to cover aspects of environmental biology it wouldn't be able to on its own," says Herendeen. "And having the students here makes the Garden a more interesting place. The students come in and ask questions that make you think. And that's a good thing for research scientists to do."

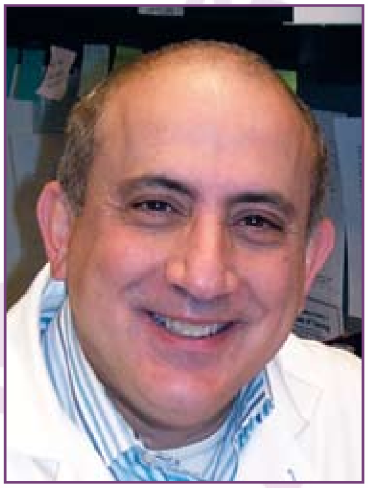
For more information about Northwestern's program in plant biology and conservation, see www.plantbiology.northwestern.edu. For more information about the Chicago Botanic Garden, visit www.chicagobotanic.org. Look for Northwestern's video on the plant biology program on News@Northwestern, episode 10 on the Big Ten Network. — *by Joan Naper*



Line and watercolor art © 2009 Kathy Mandell.

Shedding New Light on the Fundamental Nature of Cancer


Jonathan Widom


Jonathan Licht

Within every one of the estimated 50 trillion to 100 trillion cells of the human body are 6 meters (6.6 yards) of DNA. These cells are not 6 meters long, as we all know; one cell, for example, might be 6 microns long (one millionth of 6 meters). The underlying mechanical and biological mechanisms of both normal healthy cells and potentially cancerous cells that make it possible for the human body to stuff that much DNA into such a tiny space are subjects for the basic research now being done at Northwestern's Physical Sciences and Oncology Center (PS-OC).

"What's missing from the current understanding of the cancer problem isn't just specific bits of medically relevant information, but absolutely fundamental concepts about how cells work and evolve and how the molecules that underlie those processes work," says Jonathan Widom, biochemistry, molecular biology and cell biology (BMBCB), and principal investigator of the PS-OC. "These are processes where the physical sciences can shed a lot of light."

Last fall the National Cancer Institute (NCI) awarded cooperative agreements to 12 leading institutions to build a collaborative network of physical science-oncology centers. The NCI funded these centers to develop new fields of study based on the application of physical science approaches to major questions and barriers in cancer research. Northwestern's PS-OC was established last October, with Widom as principal investigator, and Jonathan Licht, chief, medicine: division of hematology-oncology, serving as senior scientific investigator.

Northwestern's PS-OC comprises five research projects, two core facilities, pilot projects, additional projects across the NCI network, education, training, and outreach programs. The Chemistry of Life Processes Institute and the Robert H. Lurie Comprehensive Cancer Center of Northwestern University jointly administer the PS-OC. Sheila Judge, operations and outreach director for CLP Institute serves as the program manager. The PS-OC team includes members from Children's Memorial Hospital, California Institute of Technology (Caltech), the University of Chicago, and the Weizmann Institute of Israel. Northwestern faculty from BMBCB, biomedical engineering, chemistry, materials science, applied mathematics, chemical and biological engineering, physics and astronomy on the Evanston campus and from medicine in the Feinberg School of Medicine are members of the center.

"Tumor biologists and oncologists typically seek to identify genetic and molecular changes that distinguish normal cells and tumor cells and to develop therapeutic agents that can

Photos on this page: Widom: by Rick Gaber; Licht: by Deidre Weber exploit these differences," says Benette Phillips, co-director of education and outreach at PS-OC and scientific program director of the Robert H. Lurie Comprehensive Cancer Center. "NCI is hoping that physical scientists and engineers will ask different kinds of questions, investigate different parameters such as energetics, entropy, and mechanical forces, and employ a more quantitative and theoretical approach to trying to understand cancer."

How will this research lead to better treatments for cancer? "There are now certain cancers that can be treated very effectively," says Widom. "Yet an enormous diversity of diseases that are completely distinct at the molecular level looked the same to pathologists and got called this type of cancer or that. Because there are so many diseases, will all of them be cured in our lifetime? Probably not. But the efforts of these 12 centers are surely going to lead to discoveries that will motivate whole new kinds of therapies."

Five Central Projects

The overarching theme of Northwestern's PS-OC is the coding, decoding, transfer, and translation of information in cancer. Its five central projects all explore newly discovered types of information encoded in the human genome as well as in proteins.

Project one, Information Encoded in the Sequence-Dependent Mechanics of DNA, is headed by Robert B. Phillips, of Caltech. He has developed techniques to measure the flexibility of DNA and is studying how the ability of DNA to bend and loop affects how sequence information is used by the cell. Widom, who has demonstrated that the flexibility of a region of DNA is in turn influenced by the sequence, is collaborating with Phillips in this project.

Widom heads project two, DNA Sequence-Encoded Nucleosome Positioning and Gene Regulation, which seeks to understand and predict where nucleosomes are located along DNA strands. Nucleosomes are spool-like subunits of chromosomes in which DNA is wrapped around a complex of proteins called histones. The location of the spools has a large influence on which genes are expressed, or activated. "One way of thinking about what distinguishes a cancer cell is that it represents a particular genetic state," says Widom. "That state is a set of genes that are expressed in certain amounts. What we are seeking is a quantitative, predictive understanding of that."

John Marko, BMBCB and physics and astronomy, heads project three, DNA Information and Organization at

Sheila Judge

Benette Phillips

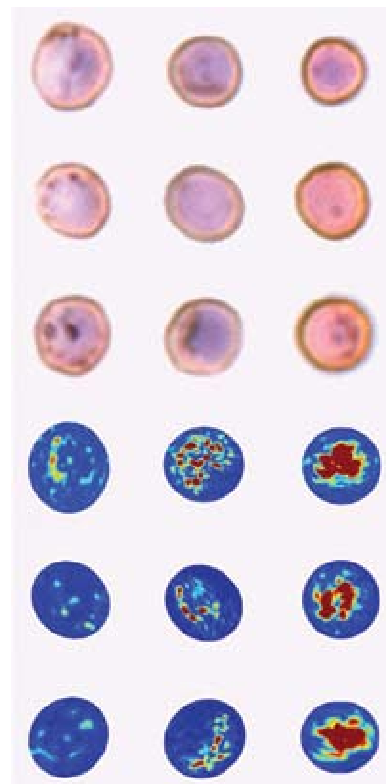
John Marko

Photos on this page: Phillips: courtesy of Benette Phillips; Judge and Marko: by Rick Gaber.

Supranucleosomal Scales: Chromatin Folding and Higher Order Structure, Heterochromatin, and Domain-Wide Repression. Marko's laboratory conducts micromechanical studies of chromosomal structure and protein-DNA interactions in the chromosome. In this project, PS-OC researchers are exploring the higher levels of chromosome architecture in both normal cells and in certain malignant-cell lines. They are seeking to understand the basic nature of this chromosomal architecture and how it influences a phenomenon in which the expression of multiple genes in a long stretch of DNA is completely suppressed.

Vadim Backman

Vadim Backman, biomedical engineering, is a key team member on project three. He has developed novel, minimally invasive methodologies for detecting tumors. The cellular changes that these techniques report are due to alterations in the statistics of nanoscale cell architecture. The light-scattering technique used is detecting changes in the chromosomal architecture in these seemingly normal cells. One of the main objectives of the project is to elucidate the genomic consequences of this reorganization of the nanoscale nuclear structure.



Colon cancer cell lines genetically modified to reflect different stages of malignancy (Columns 1- 3) look similar under conventional microscopy (Rows 1-3). When observing these cells under the light-scattering technique developed by Backman's group (Rows 4-6), a clear difference in the nanoscale molecular density of the cells can be observed (Subramanian et al., *PNAS*, 105(51), 20124-20129, 2008).

William Kath

The leader of project four, Dynamic Nucleosome Signatures in Epigenetic Memory and Cancer Development, is William Kath, engineering sciences and applied mathematics. Changes in gene expression that occur without changes in DNA sequence and which are potentially reversible are termed "epigenetic changes." Kath and his colleagues are using sophisticated mathematical analyses and computational modeling to analyze the stability of these changes in both normal cells and cancer cells. »

Andreas Matouschek

Photos on this page: Backman: by Sam Levitan; Kath by Jasper Chen; Matouschek: by Rick Gaber.

Project five, Encoding and Interpreting Information at the Protein Level, is headed by Andreas Matouschek, BMBCB. This project also investigates sequence information, but in this case, the focus is on the sequence of the amino acids in proteins. Once made in a cell, proteins persist for varying amounts of time before being degraded. How much of a particular protein is in a cell at a given time depends both on how fast it is made, by stringing the amino acids together, and how fast it is degraded. Matouschek will be examining cancer cells for partial degradation products that play a role in maintaining the cell's malignant characteristics.

Cancer researchers and clinicians from the Robert Lurie Cancer Center are involved in all projects, in part to make sure that the model systems being analyzed are meaningful in cancer biology. "Jon Licht, a clinician who also runs a big cancer biology research group, and others from the cancer center are involved and help keep a clear cancer focus on all five projects," says Widom. "They even are involved in project one, which had only an indirect—although essential—cancer link to begin with."

Core Facilities

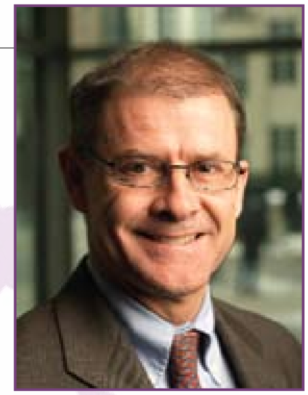
Two research cores directly support PS-OC investigators. The bioinformatics core, headed by Ji-Ping Wang, statistics, provides a platform for interaction between computational scientists and biologists or cancer researchers and creates training opportunities for postdoctoral fellows and graduate students. Peter Kopp, medicine: endocrinology, directs the deep-sequencing core, which provides the instrumentation and support to conduct high-throughput DNA sequencing.

Center investigators also have access to an extensive network of other core facilities housed on both Northwestern campuses.

Outreach and Education

Critical features of the PS-OC include extensive interactions among the 12 centers of the NCI network, mandated pilot projects, data sharing, and educational and training programs designed to produce a new generation of scientists who understand both the physical sciences and cancer biology. "For example, we will be holding summer workshops to introduce basic principles of tumor biology to trainees in the physical sciences and principles in the physical sciences to tumor biologists," says Phillips. "The center also is sponsoring summer research experiences for undergraduates and

Ji-Ping Wang



Peter Kopp

medical students that will provide cross-disciplinary training and education."

To further inform the Northwestern community and the general public about its activities, the PS-OC will sponsor seminars, an annual open house, and an annual symposium.

Encouraging extensive dialogue among physical scientists and engineers and tumor biologists, the PS-OC holds quarterly all-day "science jams" where the five projects are discussed. An annual investigators' meeting and regular conference calls among leaders of the 12 network centers are also planned.

One of the mandates of the NCI grant is that Northwestern collaborate with the other physical science-oncology centers throughout the country. "NCI is really driving us toward team science," says Sheila Judge, program manager and co-director of education and outreach at PS-OC. "They want to see synergy between the centers."

"We've had less than a year and are on track by all the milestones," says Widom. "NCI is supporting this with large amounts of money and wants real discoveries in return. And we want that too. Everybody is really motivated. It's a huge challenge and a huge opportunity."

For more information, visit the PS-OC web site at www.psoc.northwestern.edu. — *by Joan Naper*

Photos on this page courtesy of Chemistry of Life Processes Institute.

Cathy Gao, Monisha Banerjee, and John Froberg are undergraduates participating in research in addition to taking regular courses in the biological sciences program. Gao is a junior currently spending her third year in the laboratory of Richard Carthew, biochemistry, molecular biology, cell biology, where she researches virus-host interactions in fruit flies. Banerjee participates in the lab of Melina Kibbe, surgery, at Feinberg. Froberg has spent the past two years in the lab of Jonathan Widom, biochemistry, molecular biology, cell biology; he is attempting to understand how the genomes of both the malaria parasite and higher eukaryotes like mice and humans are organized in the nucleus.

The Gift of Discovery: Undergraduate Research in Biological Sciences

Questions are asked. Possible answers are explored. Something clicks. A previously unsolved problem is explained.

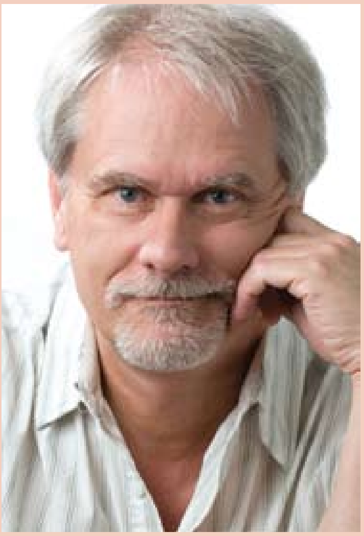
Being the first person to learn something new is what makes the process of discovery special. Whether it's a small revelation or a radical breakthrough in knowledge, the joy of searching for new scientific phenomena is what researchers live for. It is also one thing that faculty members in Northwestern's Program in Biological Sciences most enjoy imparting to their young undergraduate students.

"We get to discover amazing things here, like the basis of life," says Richard I. Morimoto, biochemistry, molecular biology, and cell biology. "Making a discovery is bigger than anything, and it's what we're trying to make available to students. We want to extend the joy of discovery."

With anywhere between 5 and 16 undergraduates in his laboratory at a time, Morimoto has a reputation for involving a diverse array of students in research. Unlike many faculty members whose typical lab is full of upper classmen specializing in their own subjects, Morimoto accepts freshmen and sophomores as well as students in engineering and even communications. His only requirement is that the student sees discovery as a part of his or her life.

"We're students of knowledge; we're always learning," he says. "So it's perfectly reasonable to take freshmen and give them an opportunity. If we were required to know everything already, then it wouldn't be science." »

Richard I. Morimoto



Richard Gaber

Learning How to Think

Even after working in a lab through an entire undergraduate career, sometimes that special "click" never happens. The discovery never comes. This, too, is a part of the discovery process and just as important as the discovery itself.

"Research can be disappointing," says John Mordacq, director of the undergraduate biology labs. "The reality is that not everything goes well. It's a lot of trial and error."

Mordacq's students currently are learning about a progressive neurodegenerative disorder called Huntington's disease, which affects muscle coordination and cognitive function. His students study the mutant protein responsible for the disease by examining nematodes with green fluorescent protein markers. "It's scary because I don't know how well this experiment will work," he laughs.

But perhaps that doesn't matter. Discovery or not, working in a lab gives students something they wouldn't necessarily get in a classroom: how to think like a scientist.

"In the classroom, we always have a manual to follow," says Kelsie Eichel, a senior in Morimoto's lab who serves as director of the student-led Morimoto Undergraduate Research Seminars. "Class doesn't give us that same element of uncertainty. Here, you don't just carry out an experiment, but you design one."

The skills learned in a lab cycle back into the classroom, improving student work all around. "The problem solving I've done in the lab has made me a better critical thinker," says Anil Wadhwani, a junior in the Integrated Sciences Program and researcher in the lab of William Klein, neurobiology and physiology. "I better understand how to approach a problem from all angles."

Extending the Opportunity

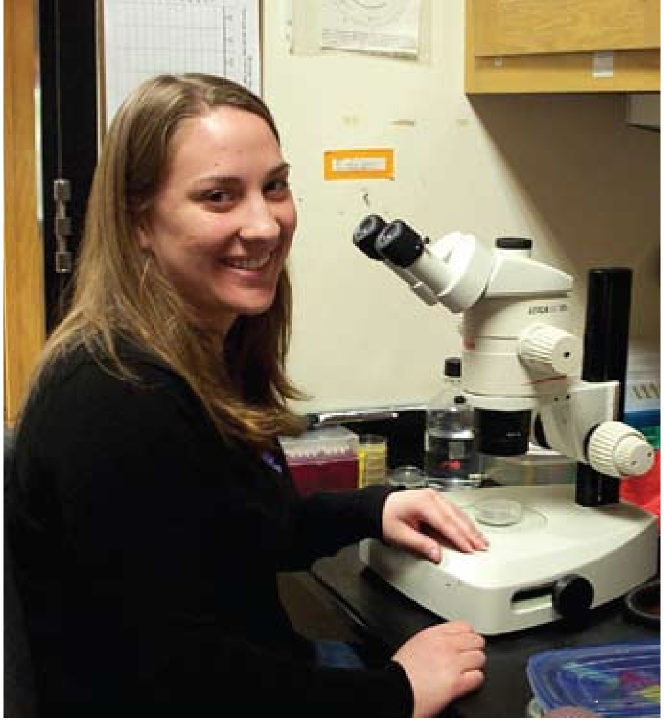
Wadhwani spent the past two summers completing lab work on campus. With a summer research grant, students can work full-time in a lab without needing a second job to allow them to live in Evanston for three months.

"During the year, I have to balance my research with my classes," explains Wadhwani who received a summer research grant from Weinberg College of Arts and Sciences in 2008 and a Research Experience for Undergraduates (REU) summer grant from the International Institute of Nanotechnology in 2009. "In the summer I can immerse myself in the lab."

Unfortunately, undergraduate research grants are limited in number. While many students vie for them, not all applications are granted. Richard Gaber, director of the Program in Biological Sciences, worked with Northwestern's Searle Center for Teaching Excellence to develop the Science Research Workshop (SRW), a program funded by the National Science Foundation that teaches undergraduates in chemistry and biology how to write proposals, enhance portfolios, and effectively interact with faculty members.

As an undergraduate, Gaber remembers being confused about how to get involved in research. "I was invited to join a laboratory, and my truthful response was 'How much do I have to pay?' I really thought I had to pay extra to be in a lab," he

John Mordacq



Kelsie Eichel, senior in Weinberg College of Arts and Sciences, sits at her bench in the Morimoto lab where she studies protein-folding diseases. Eichel serves as director of the student-led Morimoto Undergraduate Research Seminars, an undergraduate group that encourages research-focused discussions and presentations. After graduation, she plans to pursue a PhD that will lead to a full-time career in research. Photo courtesy of Sue Fox, Morimoto lab.

Anil Wadhwani is a junior in Weinberg College of Arts and Sciences and in the Integrated Sciences Program. He participates in William Klein's laboratory in neurobiology and physiology where they research the toxic effects of a protein that mediates learning and memory and may be linked to Alzheimer's disease.

says. "I was surprised to learn that there are often grants available to support undergraduate research."

The purpose of SRW is to erase such misconceptions as well as help students decide if research is right for them and prepare them to embark successfully upon their undergraduate research careers.

"If students want to get involved with research, then the workshop is a good starting point," Gaber says. "The course explains what is required and expected in a laboratory. Students learn how to approach professors, conduct themselves during the interview process, and simply how to behave in a lab."

SRW, which is now in its third year on campus, is organized around peer-led workshops and science cafés in which faculty members share how they entered the research field and address a theme for the week, such as how to approach research labs or how to navigate the proposal process. At the end of SRW, participants construct and submit a research proposal to the Undergraduate Research Grants Committee for summer funding.

"Younger students are typically denied by the committee, but they are evaluated and encouraged to submit their proposals to the Weinberg offices for a second round of consideration," Gaber says. "In the last two years, every worthy proposal received funding to stay during the summer."

Beyond the Lab

Most undergraduate researchers in biological sciences continue their work as graduate students or medical students. Whatever path they choose, many say their experiences in undergraduate research helped form their interests and set their goals.

"Laboratory research played a big role in shaping my career and has confirmed my desire to become a doctor while continuing research during my residency," says Monisha Banerjee, senior in biology, president of the Biology Students Association, and undergraduate researcher in the lab of Melina Kibbe, surgery. "It also helped me learn to manage my time and give me some real-world experience to put my studies to action."

It might not be the type of knowledge that directly cures illness or solves an international problem, but the most important discovery that occurs in the lab is the opportunity that undergraduates have to discover themselves. — *by Amanda Morris*

Photos in this article courtesy of Richard Gaber unless otherwise noted.

Unearthing Gems with Synthetic Biology

Would you mind the smell of bacteria if it were banana-scented? Would *E. coli* bacteria seem as scary if it could be used safely and inexpensively to detect toxins in water? These are two of the many interesting questions that undergraduates have explored using synthetic biology through the International Genetically Engineered Machine (iGEM) competition.

Started in 2004 with only five teams in the United States, iGEM had more than 120 teams from 20 countries in 2009. That number is expected to grow by at least one more team this year as Northwestern throws its hat into the ring.

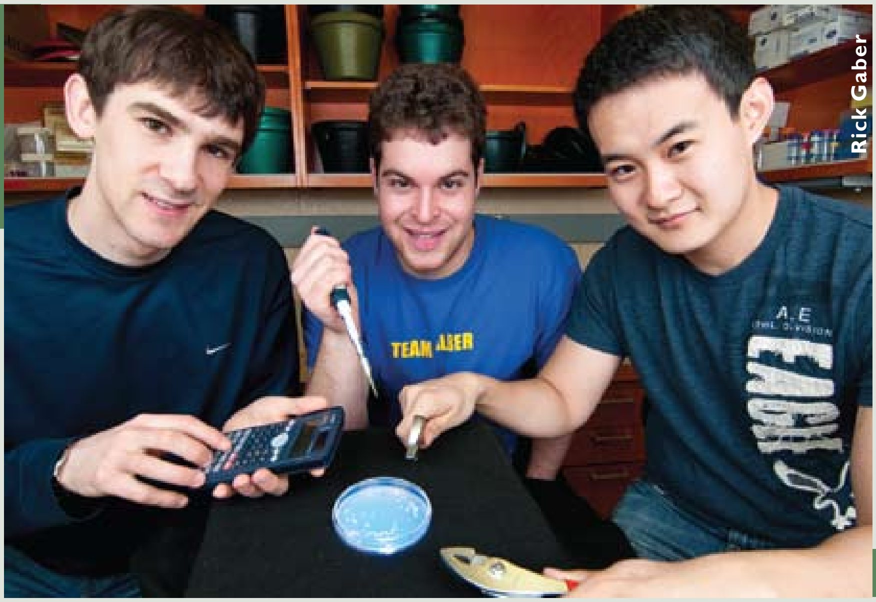
Teams are given a kit of biological ingredients from the Registry of Standard Biological Parts, a constantly growing collection of genetic parts that can be mixed and matched to build synthetic biology devices and systems. Interdisciplinary teams design and develop a device to perform a novel function and then present their biological machines at Massachusetts Institute of Technology during the summer. Last year's winning team used organic dyes produced by *E. coli* to become sensitive to specific heavy metals in water.

Avi Samelson, senior in biology and undergraduate researcher in the lab of Alfonso Mondragon, biochemistry, molecular biology, cell biology, is responsible for bringing iGEM to Northwestern after hearing about the competition from a friend at Harvard University. Along with Jeremy Schifberg, senior in the Integrated Sciences Program, and Ben Zheng, junior in biomedical engineering, Samelson applied for and received funding from Weinberg and the Provost's Office to create a Northwestern team.

"This spring we'll finalize members of our team, narrow down what our project will be, and get started," Samelson says. "I'm really excited about it."

In addition to the funding that Samelson secured, Josh Leonard, chemical and biological engineering, received a 2009 Murphy Society Faculty-Funded Projects grant from McCormick to launch the team and help ensure a successful first year in the competition. Leonard mentors the team along with Michael Jewett, chemical and biological engineering, and Andreas Matouschek, biochemistry, molecular biology, and cell biology (BMBCB).

"iGEM is exciting because these student-driven projects are both advancing science and addressing real societal needs," Leonard says. "This whole competition is an experiment aimed at learning how to design and engineer biological systems to solve real problems and help people."



Rick Gaber

Right now prospective team members gather weekly for informal meetings to read papers about synthetic biology and share ideas. John Mordacq, director of the undergraduate biology labs, will oversee the team's project. "Synthetic biology is a new field; it's where science is moving," he says. "It's fun to see students who are curious about it."

"The students aren't even earning credit for this," adds Richard Gaber, BMBCB and director of the Program in Biological Sciences. "They are just doing this for the joy of getting together and accomplishing something new." —**A.M.**

TAKING A STAB AT IT After securing funds to bring the iGEM synthetic biology competition to Northwestern, Jeremy Schifberg (left to right), Avi Samelson, and Ben Zheng flex their scientific muscles with the hopes of bringing home a win.

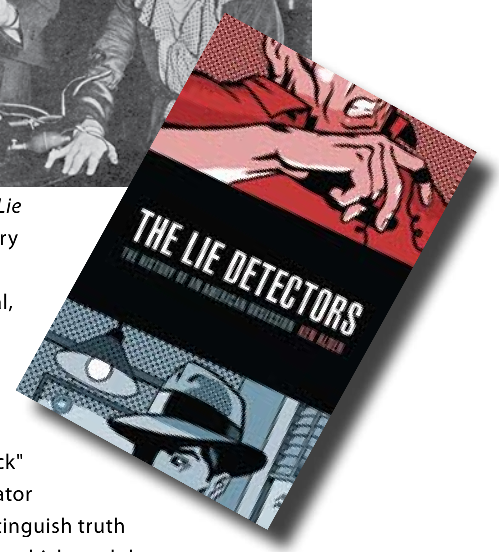
CONNECTING THE DOTS WITH SCIENCE

In the 1920s a bishop in the Church of England recommended that science take a ten-year holiday. He claimed that science was developing too swiftly for ordinary people to cope, and society needed time to "catch up." The British Association for the Advancement of Science disagreed and the holiday never occurred.

Ken Alder, history, loves sharing this story with undergraduates in his history of science course. "This idea of a gap doesn't make sense," he says, "because science is as much a product of the social world and the culture we live in as its morals and values. Of course, around the same period of time, some scientists were saying that physics was 'ahead' of biology, and they encouraged grants officers to pour money into a new field they dubbed 'molecular biology.' So even though such gaps exist only in the eye of the beholder, the idea of a gap can shape how science evolves."

Ken Alder

Northwestern's Science in Human Culture Program, which Alder has directed since 1994 with the exception of a yearlong break in 2008, examines how science and society are consistently intertwined. By exploring the development of the sciences through the lens of the humanities and social sciences, researchers and students in the program better understand how science has shaped the world and, in turn, how we have shaped science.



Ken Alder's latest book *The Lie Detectors* explores the history of America's obsession with using science as an impartial, truth-making operation. The above photo shows Leonard Keeler, inventor of the lie detector, demonstrating the "card trick" with his wife, Kay. The operator proves the machine can distinguish truth from lies by using it to guess which card the subject has secretly selected. Leonard and Kay Keeler were both Northwestern faculty members in the 1930s.

"Science has produced amazing technological breakthroughs that have radically transformed our world," says Alder who is an expert in the history of science. "But there's a reciprocal relationship involved here. What kind of science gets funded? What types of scientific problems get solved? We need to understand both."

With nearly 30 faculty affiliates in the Science in Human Culture Program, participants in the program approach these questions from various disciplinary angles. Together they show that science is implicated in many of our social and political debates, from medical care to art history. »

Photos and images in this article courtesy of Ken Alder, Steven Epstein, and Claudia Swan.

Steven Epstein

Another Kind of Gap

The question of what type of research is funded or not funded is particularly important when it comes to medicine. Steven Epstein, sociology, finds that many illnesses are not just health issues but political and sociological issues as well. Epstein has spent his career exploring what treatments are studied in biomedical research and which people are included in clinical trials.

Looking at how medical science fits into society, Epstein sees it as a discipline that is strongly shaped by human culture. He cites AIDS activism in the late 1980s and early 1990s as an example. It is the focus of his book *Impure Science: AIDS, Activism, and the Politics of Knowledge*. During that period social groups openly challenged the Food and Drug Administration and National Institutes of Health with regard to which treatments should be studied, how clinical trials should be conducted, and when new drugs should be licensed for sale. As AIDS activists learned the science, they became a new kind of expert and found a seat at the table with AIDS researchers and government officials.

“Biomedicine is one domain where lay people in organized groups increasingly stake out claims that they should have a voice,” he says. “The tension between expertise and democracy or participation is framed in a particularly sharp way.”

Epstein is now examining how the politics around sexuality affects the production of knowledge and federal regulation as they relate to Gardasil, the vaccine to prevent certain types of human papillomavirus. “Ordinary people and everyday issues really influence biomedicine,” he says. “In some ways that might be deemed problematic by researchers, but sometimes it has advanced knowledge.”

Science as Decoration

In the 17th century — long before the era of the AIDS epidemic, modern treatments, and vaccinations — science exerted a strong influence on human culture, including art.

Claudia Swan, art history, studies Dutch art that is also pronouncedly scientific. The early modern artist Jacques de Gheyn (1565-1629), who lived in Holland, worked in close collaboration around the year 1600 with members of the

Claudia Swan

Jacques de Gheyn, *Tulipa Gesneriana*, 1603, "Lugt album" fol. 20v, watercolor and gouache on vellum, 22.7 x 17.5 cm, Collection Frits Lugt, Institut Néerlandais, Paris.

medical faculty at Leiden University in the Netherlands. Many of his artistic works feature representations of the natural world, from insects and flowers to anatomical specimens.

"What fascinates me is what it means to call an image 'scientific,'" Swan says. "In order to answer that for the early modern period, you have to look at the history of science."

Many of De Gheyn's botanical works depict interior and exterior views of flowers. Swan says that images such as these were often used to identify plants for pharmaceutical use. She points to a painting of a tulip by De Gheyn, which shows the pistils and stamen in cross-section and explains that this image does not qualify as scientifically useful because it excludes the roots or the bulb of the plant.

"This is a fancy watercolor on vellum," she says, "that was probably owned by the Holy Roman Emperor Rudolf II."

While science was the inspiration for De Gheyn's work, the painting ultimately served as a fine work of art; it was kept in the Emperor's collection of marvels. Swan says her research brings together science and art history because she would not be able to analyze the function or meaning of art without a historical understanding of science.

Four-Star Science

Science as art doesn't just live on our walls; it also has a place in our movie theaters. Scott Curtis, radio/television/film, says from about 1910 to 1930, motion pictures of microscopic life were an especially popular part of the film program. "During that time period, people were thrilled to see cell life on the big screen," says Curtis, who studies how moving images are used for scientific evidence.

Curtis has spent time examining films created by Yale University psychologist Arnold Gesell from the 1920s through the 1940s. Gesell took thousands of feet of film of children and then meticulously examined the footage. What resulted were ideas about developmental stages of child behavior that are still accepted today. "Our understanding of childhood is rooted in the study of motion pictures," Curtis says. "The moving image itself has actually shaped our thinking."

Connected by Science

Although these views of science come from researchers in different departments, all the faculty members mentioned here say the multidisciplinary nature of the Science in Human Culture Program helps their work immensely.

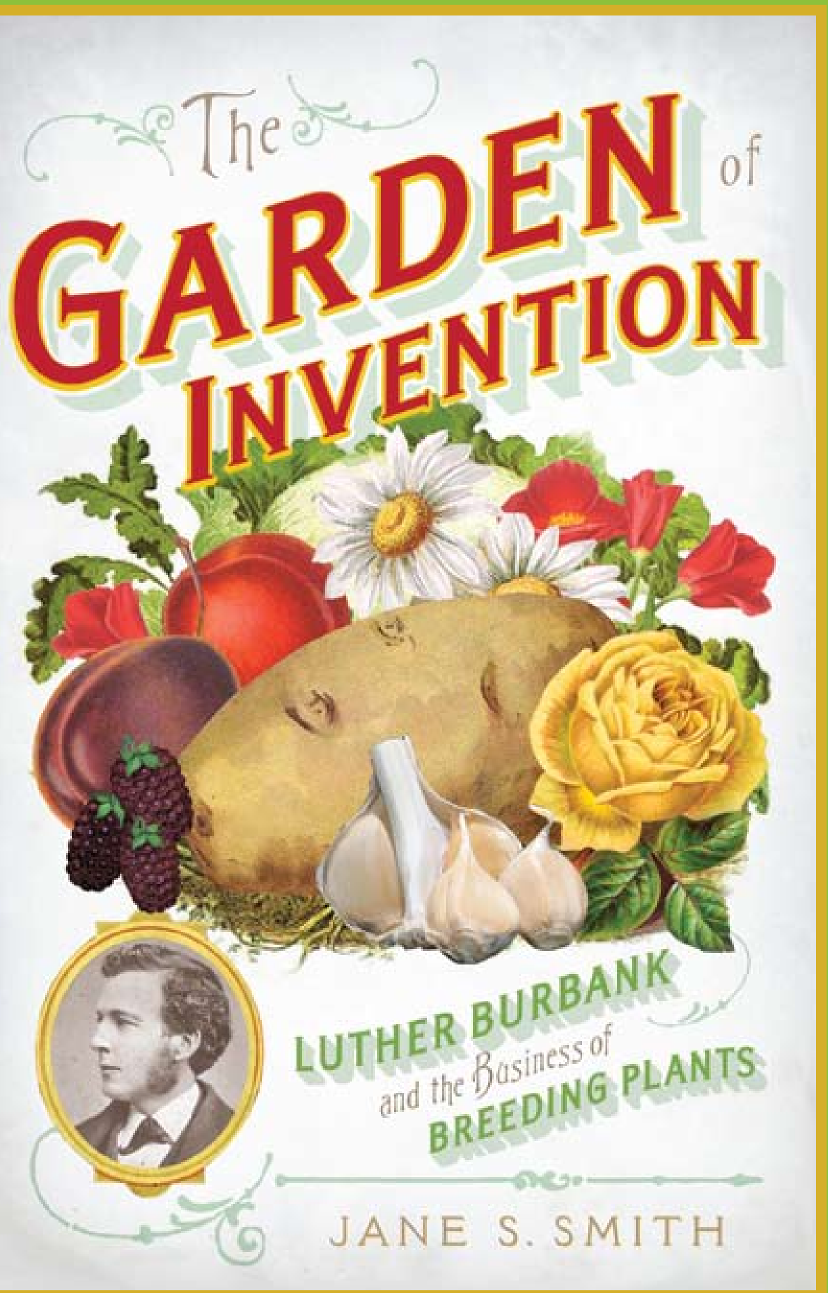
"I'm not trained in science; I'm trained in film studies," Curtis says. "So the challenge of my research is to catch up to this other discipline. Being a part of a science studies community helps with that."

The program offers training for undergraduate, graduate, and postdoctoral students, all of whom learn this same multidisciplinary approach. Graduate students participate in a Science Studies Cluster Initiative through which they explore science in its historical, social, and representational contexts. The initiative does not lead to a degree but is seen as a supplement to the disciplinary study in a department that grants a PhD.

"I like this approach to knowledge because it enables us to bring together people with different intellectual tools to solve complicated problems," Alder says. "We then address the question of how and why science is implicated in so many other social and political questions."

For undergraduates, the program offers an adjunct major and minor. Alder says these degrees are particularly popular among pre-med students. "These future doctors are fascinated by the way that medicine operates in a social and economic context, especially given our current debate about the delivery of medical care," he says. "Students are drawn to medicine not just because it is a skill to practice but because it is a practice that changes how people live. The Science in Human Culture Program helps them think about the kind of contribution doctors can make."

Alder says that when the science holiday was proposed in the 1920s, a prominent physicist named Oliver Lodge argued that calling a halt to scientific progress — even a temporary one — would cause the world to fall to pieces. Research in the Science in Human Culture Program proves that science is so interwoven with all disciplines that it could hardly take a holiday without taking the rest of the world with it. — *by Amanda Morris*



Famed American gardener Luther Burbank posed between Henry Ford and Thomas Edison when they came to Burbank's home in Santa Rosa, California. That photograph grabbed the attention of Jane Smith, history, when she, too, visited what is now a museum dedicated to Burbank's life.

With Ford's name still adorning modern automobiles and Edison's name gracing the pages of monthly power bills, these two inventors are impossible to forget. Though Burbank was once equally famous for breeding new and improved plants, his name is now far less remembered.

"In a sense, we've lost our ties to agricultural knowledge," says Smith, who is affiliated with Northwestern's Science in Human Culture program (see article on page 23). "Our culture has moved away from the backyard garden and family farm to the factory farm."

Smith's visit to Burbank's home in California led her down a path of research and discovery back to a time when the science of genetics was still an unexplored frontier — a time when Burbank's breeding and crossbreeding of ordinary plants for tastiness and hardiness turned him into a popular hero.

"Burbank introduced new fruits and flowers during California's second Gold Rush when agriculture began to bring great wealth," Smith says. "He improved plums for prunes, fostering the 'prune boom' of the 1880s, and created the Burbank potato, the Shasta daisy, the plumcot, and many more."

Smith turned her research into her latest book, *The Garden of Invention: Luther Burbank and the Business of Breeding Plants*. By revisiting the early years of bioengineering and agribusiness, Smith hopes America can learn more about its current relationship to nature and food.

Burbank, who lacked a formal background in science, learned about evolution and biodiversity by reading books by Charles Darwin in the public library. His approach to the subject was different from that of other scientists at the time. "Most people read Darwin to learn about the distant past," Smith says. "But Burbank read Darwin to learn how to help evolution — how to help speed up the future."

As the world celebrates 2010 as the International Year of Biodiversity, people are encouraged to reflect upon the variety of life on Earth. What more appropriate time to remember Burbank, who was a self-proclaimed "evoluter" of fruits, vegetables, and flowers, developing more than 800 new varieties of plants during his career. ■

— by Amanda Morris

NORTHWESTERN
UNIVERSITY

CenterPiece

Office for Research
633 Clark Street
Evanston, IL 60208-1108