BOSTON UNIVERSITY

Office of the Provost
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From the Provost

Welcome to *Research at Boston University*. With literally hundreds of laboratories, research centers, and libraries spread across the seventeen Schools and Colleges on our two campuses, Boston University research covers an enormous intellectual range, contributing to our understanding of issues from philosophy, sociology, and archaeology through the natural sciences and engineering to medicine, health, and technology. We address questions that are vital for the well-being of people and the environment and that nurture our inherent curiosity about our future and our past.

In this publication, which covers only a very small fraction of the ongoing research here at Boston University, we have highlighted some of the investigations of the timely topics of climate change and of biological adaptations in response to the dynamic environment. Time and again, observations have shown that small environmental changes can have an enormous impact on the survival of a vulnerable species, while at the same time some species have demonstrated a remarkable ability to adapt to changing conditions. An interesting case in point is illustrated on this year's cover, which features Professor Karen Warkentin, a member of our biology department, and an instrumented clutch of frog eggs. Professor Warkentin's research has revealed that these frog eggs have the ability to respond to perceived danger by hatching earlier than normal. In the section "Learning to Adapt," we report on her work and on that of a number of other researchers who are examining the adaptive strategies of different species—all point to an encouraging robustness in the ability of organisms to survive change.

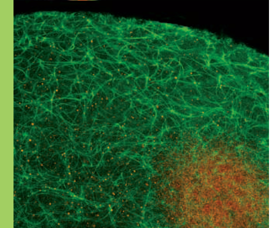
We humans are also proficient in adaptability, particularly in developing technologies to support our biological systems. The article "Moving Research into Action" highlights some of the innovative medical technologies being developed in collaborative projects involving faculty in our College of Engineering and School of Medicine. Several projects, funded with a $2.9 million, five-year grant from the Coulter Foundation, are described in this section. Among them is an automated glucose regulation system being developed by a team led by biomedical engineer Edward Damiano that will assume the work of damaged insulin-producing cells, thus transforming the lives of people living with diabetes.

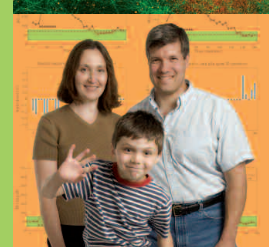
Our current success in adaptability is a direct by-product of our past, and in the section "Bringing the Past to Life," we chronicle archaeologist Kathryn Bard's fascinating probe into the 4,000-year-old timbers that have been unearthed on the Red Sea coast in Egypt, remains from the pharaohs' journeys to an ancient kingdom. Just as these relics provide insight into the distant past on another continent, archaeological finds in New England, investigated by BU archaeologist Mary Beaudry, provide insight into the nature of family life in the seventeenth century, from medicinal practices to food preferences.

As always, Boston University faculty are mentors and nurturers to the next generation of researchers. In "Students: Bringing a Fresh Eye to Research," we highlight the "Rhythmic Rehab" research of Amir Lahav, whose study of the effect of music on brain function facilitated a clinical tool to promote movement in stroke patients. Junior Beth Ann Cimini, the recipient of a two-year Beckmann Grant for undergraduate research, is working with her neurobiology advisor, Professor Bill Eldred, to investigate how acetylcholine activates a neurotransmitter in the retina, ultimately unraveling the complexity of a simple visual image.

This past year at BU was one of enormous energy and excitement, highlighted by the inauguration of our tenth president, Dr. Robert A. Brown, Professor of Engineering and a member of the National Academy of Sciences, the National Academy of Engineering, and the American Academy of Arts and Sciences. Under his leadership, the Schools and Colleges of Boston University have sharpened their focus, strategically planned for the future, and collaborated on interdisciplinary projects that share the core mission of educating the best and the brightest to lead in the research of the future. We hope that this magazine challenges, inspires, and motivates you to learn more about the research endeavors described here as well as the thousands of other research projects under way on our campuses. Please visit our website, *www.bu.edu/research*, to learn the latest in research news at Boston University.

David K. Campbell
Provost





2006

RESEARCH
AT BOSTON UNIVERSITY

Geographer Curtis Woodcock and his daughter Cleo are standing in front of a satellite photo of the region surrounding the Black Sea, an area that Woodcock studies to reveal how land use and the carbon cycle are related. He hopes that by better understanding these interrelationships, catastrophic climate changes can be avoided and the health of our planet can be preserved for future generations.

MANAGING A CHANGING CLIMATE

The consequences of global climate change are mind-boggling. The future may see huge sections of the Earth's polar ice caps melting away; major coastal cities flooding under rising ocean levels; large portions of tropical rainforests transformed to wasteland; and massive hurricanes and violent tornadoes on a scale never before seen.

According to a 2003 Zogby opinion poll, nearly four of every five Americans have accepted that global warming is real and that something must be done about it. With initiatives such as the Kyoto Protocol and the Intergovernmental Panel on Climate Change, most governments have also moved from a wait-and-see posture to one of action.

Such shifts in public perception have resulted from careful scientific work—and Boston University researchers have been at the fore, engaging the issue on many levels. From examining the effects of climate change on natural ecosystems, to understanding its impact on human economies, to engineering ways to reduce human impact on the environment—researchers at BU have developed tools, information, and understanding essential to deal with this ever-growing challenge.

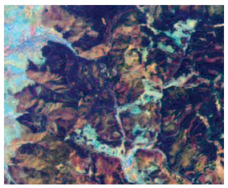
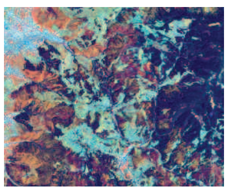
Visualizing Climate Change

One of the difficulties in understanding the large-scale consequences associated with climate change is, quite simply, seeing what is happening. Curtis Woodcock, a geographer associated with the Center for Energy and Environmental Studies and the Center for Remote Sensing, has approached the problem by using satellite imagery and GIS (Geographic Information Systems) data to examine and forecast the impacts of land-use changes on the carbon cycle.

After more than 25 years in the field, Woodcock says that improved satellite imagery and more powerful computer technology have allowed researchers to study larger areas more efficiently and accurately. He credits the designers of the original Landsat imaging technology for building a system that has provided scientists with an invaluable record of images, documenting changes on the Earth's surface for more than 30 years.

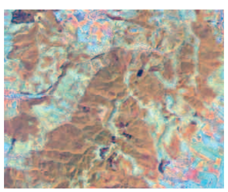
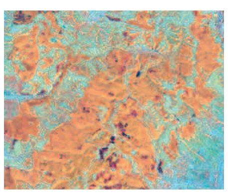
Woodcock focuses on understanding how changes in a particular piece of land alter the way carbon "flows" through that ecosystem. "If you watch the way the world is changing, reforestation is occurring in some places, like New England," says Woodcock, "while at the

With each change made by man—the planting of a field of corn or construction of a parking lot—comes a change in the carbon dynamics of that piece of land.

These pairs of Landsat images show two locations in Romania at two time periods (1990 and 2000). The images are false color composites, with vegetated areas appearing in brown or reddish tones and barren areas in light blue.

In the first set of images, the forests are primarily composed of conifers (dark in tone) and show dramatic change—a significant reduction in conifer forests in 2000 as compared with 1990. This is an example of a carbon "source," or an area releasing more CO_2 into the atmosphere than it is absorbing.

In the second set of images, the forests are primarily hardwood species that cover most of the area. The images show very little change between 1990 and 2000, indicating stable land-use patterns and a location that is a carbon "sink."

Satellite images such as these provide an important record of human actions on the surface of the Earth that helps us understand the ways we are modifying the landscape.

same time deforestation is happening in the tropics." With each change made by man—the planting of a field of corn or construction of a parking lot—comes a change in the carbon dynamics of that piece of land. Individually, these alterations may or may not be significant. But when such changes are looked at cumulatively, on a regional or global scale, they may have a pronounced impact on ecosystems and climate patterns.

His current work is focused on the area surrounding the Black Sea in Georgia, Ukraine, Bulgaria, Romania, and Turkey. His work is made more challenging by the influence of human development in the area. In the former Soviet-bloc state of Romania, for example, Woodcock has observed the impact of social upheaval on the landscape. Using a series of NASA's Landsat satellite images that begin before the collapse of the Soviet Union, Woodcock has observed large, single-crop communes carved up into smaller individually controlled plots. The change in land utilization means a change in the way that carbon flows in and out of the ecosystem. "The fall of communism marked a drastic change in the land use and carbon dynamics of the region," says Woodcock.

Even as research is moving ahead, there are uncertainties about the global carbon cycle, a complex series of processes in which carbon circulates between the Earth and its atmosphere. Plants, both terrestrial and aquatic, absorb carbon dioxide (CO_2) from the atmosphere and through photosynthesis incorporate, or sequester, carbon atoms into their biomass. Fossil fuels, produced millennia ago by natural processes that put organic material under enormous pressure, contain large quantities of sequestered carbon. As they breathe, or respire, both plants and animals release CO_2, returning a small portion of their carbon to the atmosphere, but most of the carbon stored as biomass is released only when it decomposes or burns. The different places where carbon is accumulating—the soil, vegetation, and fossil fuels—are called carbon sinks.

Current models of atmospheric concentrations of CO_2, for instance, cannot balance the incoming and outgoing CO_2, as input exceeds output. According to Woodcock, finding this "missing sink" is a common goal among carbon cycle researchers. Of the approximately 7.5 gigatons of CO_2 added to the atmosphere each year through tropical deforestation and the burning of fossil fuels, the fate of nearly 2 gigatons remains uncertain. There are competing theories as to where the carbon is going. Some say it is dissolved in the rivers of the Amazon; some say it is absorbed in the boreal forests and tundra of the northern latitudes.

One thing that carbon cycle scientists do agree on is that the continued unchecked burning of fossil fuels, and the freeing of the carbon in the estimated 4,000 gigatons of fossil fuel remaining, have the potential to cause even more catastrophic shifts in global climate.

Like much climate research today, Woodcock's work has major policy implications. However, he dismisses the idea that climate science has been politicized. "Anyone who works in the field is serious about their work. Politics does not influence our research or our conclusions," he says. Woodcock also says that his work has ramifications beyond the sphere of climate change. "The study of land use tells us much about the overall health of our planet, about human impact on biodiversity and on natural systems across the planet." To these ends, he works with Global Observation of Forest and Land Cover Dynamics, or GOFC-GOLD, an international organization working to improve the land-use data available to land managers and researchers.

For more information, see *www.bu.edu/geography/people/faculty/woodcock.*


Left: An aerial view of the experimental forest near Chapel Hill, North Carolina, where biologist Adrien Finzi conducts carbon enrichment experiments. *Right:* A view of a free-air CO_2 enrichment plot containing the towers that release controlled amounts of CO_2 into the atmosphere.

Focus on Forests

At a forest plot in North Carolina, fitted with a special array of sensors and PVC tubes, biology professor Adrien Finzi observes as increased loads of carbon dioxide are piped into the air. He is interested in learning how forests—with their photosynthetic cellular machinery that converts carbon dioxide into wood and sugars—may be able to compensate for increased levels of atmospheric carbon dioxide. According to Finzi's projections, by 2050 carbon dioxide levels will be more than 50% higher than they are now. His research at this experimental forest, owned by Duke University, employs a state-of-the-art system known as free-air CO_2 enrichment, or FACE, to help researchers better simulate future high CO_2 conditions.

Finzi's data shows that conifers and hardwoods on this plot speed up their rate of photosynthesis in response to increased CO_2 levels. The more CO_2 put into the system, the more efficient these trees become at converting atmospheric carbon to sugars and woody cellulose and giving off oxygen. The findings, on the surface, seem to suggest that the Earth's forests naturally compensate for increased atmospheric carbon levels; however, Finzi cautions against an oversimplified view. "As you can imagine, much support for our research has come from pro-emissions people," says Finzi. "But they focus on only a fraction of our findings." One group, the Greening Earth Society, actually went so far as to create a campaign that opposed "global warming alarmists," stating that increased CO_2 levels actually increased forest productivity.

The problem, says Finzi, is that pro-emissions proponents selectively overlook many important factors. First, he says, the rate at which carbon is currently being introduced into the atmosphere is far greater than the rate at which the forests can absorb it. Second, the makeup of the soil is as important as CO_2 concentration in determining the rate at which forests are able to take up, or sequester, atmospheric carbon. "In general, the more nitrogen in the soil the higher the rate of carbon sequestration. But not all forests grow in nitrogen-rich areas and are therefore less able to respond to increases in carbon levels," says Finzi. Finally, increased CO_2 levels in the atmosphere trigger warming that causes forests to reach maturity faster—and mature trees metabolize more slowly and do not take up carbon as quickly. "The ways that people are changing the Earth's atmosphere are also causing an overall decline in the capability of the Earth to sequester carbon," he says.

For further information, see *http://people.bu.edu/afinzi.*

Calculating the Costs

Center for Energy and Environmental Studies (CEES) geographer Robert Kaufmann has taken a different approach to visualizing the problems associated with climate change. His studies connect the natural productivity of the land, a measurement called net primary production, or NPP, to economics. "NPP can be viewed as the 'currency' of nature," says Kaufmann. Using satellite imagery and a unit called the normalized difference vegetation index, or NDVI, he has mapped the "value" of NPP in terms of dollars and cents. He uses his model to estimate the impact of climate change and environmental degradation on economic output. Only by assigning a proper economic value to NPP, says Kaufmann, can the true value of a healthy environment and the real costs of environmental damage be measured.

The economics of energy is a complex, interdisciplinary field. It requires fluency in disparate studies—from geophysics and geography to the economics of oil markets and the political maneuverings of organizations like OPEC (Organization of the Petroleum Exporting Countries).

With degrees in biology, economics, and energy policy, Kaufmann has the right mix of tools. A basic premise of economics, says Kaufmann, is that in order to understand how much something is worth, you must first know how much there is; in the case of energy, this means calculating a reliable figure of remaining oil supplies. However, Kaufmann says, the prevailing model to calculate supply, known as the Hubbert model—and named after famed geophysicist Marion King Hubbert—is flawed. Kaufmann says that the problem with the Hubbert model is that it assumes as long as there is oil in the ground, supply will increase steadily. By looking at historical data, Kaufmann has found something different is going on. His analysis of oil production data shows that demand, itself, can impact oil production. For instance, in the early 1970s, immediately after OPEC tripled the price for a barrel of oil, the drop in demand caused a subsequent drop in production. Kaufmann has incorporated his ideas about the effect of demand on oil supply into a forecasting model he built for the European Central Bank and one he is currently working on for the World Bank.

With its social and political implications, Kaufmann's work has inevitably found its way into the policy realm. In a 2002 white paper called *Oil Supply and Oil Politics: Déjà vu all over again*, Kaufmann and CEES director and colleague Cutler Cleveland evaluated the economic impact of the Bush administration's push to open the Arctic National Wildlife Refuge (ANWR) to oil exploration. Their paper provides a detailed analysis and concludes that the relatively small amount of oil available at ANWR would not increase the U.S.'s domestic oil supply in any significant way.

They also challenge a view held by many energy economists that oil price shocks, and the recessions that follow, result from our dependency on foreign oil. To reduce the possibility of price spikes, these economists have lobbied to reduce U.S. dependence on foreign oil—and, by extension, OPEC's price controls. However, Kaufmann and Cleveland have observed that price shocks have little to do with where oil is coming from and more to do with the intrinsic volatility of the oil market. For example, the jump in oil prices that preceded the recessions of the 1950s and '60s happened while the U.S. produced more than 80% of its own oil. Today, the U.S. imports much more, over half of the oil it consumes.

Kaufmann and Cleveland's conclusion is a sobering one. Skyrocketing demand and flagging production leave little doubt about the future: "It's not dependence on foreign oil per se that makes the economy vulnerable to price swings, it is the dependence on oil itself," they conclude. Kaufmann says that time is running dangerously short to make the transition to alternative energy sources without major economic and social disruptions. "Even if we happen to make one of the largest oil discoveries we've ever made, with demand increasing the way it has, the peak comes in the 2030s."

For more information about the Center for Energy and Environmental Studies, see *www.bu.edu/cees/*.

"It's not dependence on foreign oil per se that makes the economy vulnerable to price swings, it is the dependence on oil itself."

Climate-Friendly Solutions

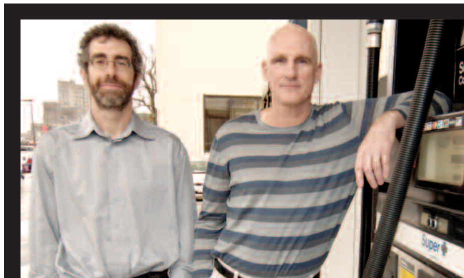
Boston University engineering professors Uday Pal and Srikanth Gopalan have taken up Kaufmann's challenge and are designing hydrogen fuel cells—a technology that may someday replace fossil-fuel-burning engines. Pal, who worked as a steel manufacturing researcher, an engineer at Westinghouse, and an MIT faculty member before coming to Boston University, also has an interest in reducing the costs associated with the manufacturing industry, which accounts for an estimated 25% of the world's energy use.

Gopalan, who began his career as an engineer at Siemens-Westinghouse before coming to Boston University, says that the promises of hydrogen cell technology are significant; yet, so are the challenges. One obstacle in using hydrogen as a replacement for fossil fuels is building the infrastructure to produce large quantities of pure hydrogen gas. The current methods—electrolysis and steam methane reformation—are both costly and energy intensive. The other challenge, he says, is manufacturing alternative fuel technology inexpensively enough to warrant investment from the private sector.

Pal and Gopalan have worked together since 2001 designing solid oxide fuel cells (SOFCs) that may someday overcome these barriers. These are essentially like batteries that generate electricity from a reaction between air and fossil fuels. SOFCs, say Pal and Gopalan, are highly efficient and emit negligible levels of the pollutants emitted by gasoline engines.

Though the chemistry involved in SOFCs is relatively simple, the manufacturing methods currently used to produce them are not. The different parts of the battery—cathode, anode, and electrolyte— must be produced at different temperatures and, therefore, require three separate manufacturing phases. Parts must be reheated, then cooled, requiring large energy inputs; these "extra steps," say Pal and Gopalan, result in high production costs.

Pal and Gopalan are looking to cut these manufacturing costs by more than half by developing a process that will allow the components to be fired at a single temperature, reducing the manufacturing process to a single step. "Our process would allow a huge reduction in the manufacturing complexity and cost," says Gopalan. Small prototypes produced by the team have been promising and



Above: Engineers Uday Pal *(right)* and Srikanth Gopalan are developing the technologies needed for fuel cells to become a viable source of energy for transportation, heating, and electricity.

Left: Geographers Robert Kaufmann and Cutler Cleveland, colleagues at the Center for Energy and Environmental Studies, analyze how social, political, and economic factors interact to determine available supplies of energy.

"The hydrogen produced with oxide membranes could be available at 'hydrogen filling stations' for fuel-cell-powered vehicles."

perform comparably to cells produced by traditional means. "The important thing is that it's simplification without a sacrifice in performance." Pal and Gopalan envision a wide range of applications for their SOFCs—from car engines and residential furnaces, all the way up to megawatt-generating power plants.

Pal and Gopalan say their other project, to produce hydrogen using a composite material known as an oxide membrane, also holds great promise. Oxide membranes are designed to generate large quantities of pure hydrogen from steam. They work when one side of the oxygen-permeable membrane is exposed to steam and the other side to hydrocarbon gasses. The oxygen from the steam passes through the membrane and reacts with the hydrocarbon gasses on the other side of the membrane—leaving ultra pure hydrogen on the "steam side" of the membrane. "The hydrogen produced with oxide membranes could be available at 'hydrogen filling stations' for fuel-cell-powered vehicles," says Pal. Their novel design is being produced in partnership with private-sector companies.

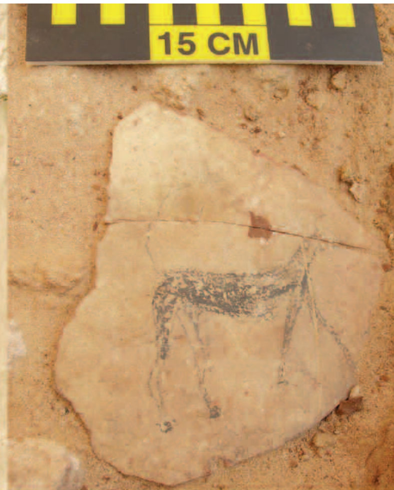
Most importantly, perhaps, is the reduction in greenhouse emissions that these cells represent. According to Pal, fuel cells are more than twice as efficient as the typical gas turbine engine—meaning that for the same amount of energy, less than half the amount of carbon dioxide is emitted. And, since the energy-generating reactions occur in sealed spaces away from air, production of nitrogen and sulfur oxides—major components of smog—is negligible.

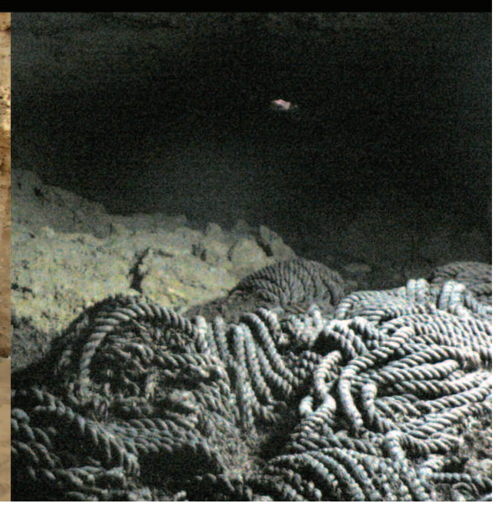
The two researchers are also looking to overcome another major drawback of hydrogen: the difficulty of transport and storage. Currently hydrogen gas must be compressed into heavy containers that are difficult to transport and susceptible to rupture. A possible solution, according to Pal, is contained in the bottles of grey sludge lined up on the shelves of his laboratory. He explains that they hold magnesium hydride slurry, a liquid in which hydrogen gas can be temporarily "locked up." The advantage, says Pal, is that hydrogen gas can be stored in a slurry at standard temperature and atmospheric conditions, then released merely by adding water.

Yet, the method has one major hurdle: it produces huge amounts of magnesium hydroxide—or milk of magnesia—as a by-product. The solution, says Pal, lies in devising a cost-effective method to convert the waste back to the initial compounds. Faced with the prospect of lakes of milk of magnesia, Pal smiles, "This problem will keep us busy for the next ten years at least."

For more information about Uday Pal's research, see *http://people.bu.edu/upal/*. For information about Srikanth Gopalan's research, see *www.bu.edu/mfg/research/researchlabs/green.shtml*.

—by Jeremy Miller





BRINGING THE PAST TO LIFE

Archaeologists like finding firsts—the first tool, the first domesticated plant, the first fire pit—but Boston University's Department of Archaeology is a first in its own right. When it was created in 1982, it was the first independent department of archaeology in the United States.

As the Department of Archaeology nears its quarter-century mark, members of the department focus on a wide range of geographic areas and time periods, bringing to bear expertise in classics, art history, anthropology, earth sciences, geography, and biology. For archaeologists, excavating the past is not about finding objects to take our breath away, it is about breathing life back into ancient cultures by understanding their history, politics, economy, and religion.

Finding Pharaohs' Ships

Mention archaeology and people imagine pith-helmeted scholars unearthing artifacts from the sands of time in faraway deserts. Minus the pith helmet, this more or less describes archaeologist Kathryn Bard. At the site of Wadi Gawasis on the Red Sea coast in Egypt, Bard and Rodolfo Fattovich, her co-director from the Oriental Institute in Naples, have uncovered timbers from the world's oldest-known seagoing ships. These are all that remain of epic journeys that Egyptian pharaohs organized to the ancient kingdom of Punt (modern Eritrea and Sudan) almost 4,000 years ago.

Punt was the luxury department store of ancient Egypt, the source of high-status items such as gold, frankincense, and the giraffe tails that adorned the belts of the pharaohs. But procuring these items was no easy trip to the mall. It was a complex and minutely orchestrated journey. A lack of fresh water prevented the shipbuilders from living along the shore during the months it took to construct the ships, so they built them inland in the town of Qina. Traders obtained cedar from the mountains of Lebanon and shipped it to the Nile delta, then upriver to Qina. After the ships were built they were dismantled and

Kathryn Bard's discoveries on the Red Sea coast of Egypt include: *Top row:* Ship timbers and cargo boxes from the world's oldest-known seagoing ships; a pottery fragment with an image of a dog; the interior of Cave 3, used for storage and housing while ships were being reassembled. *Middle row:* Clay seal. *Bottom row:* Entrance to Cave 2; ship ropes.

carried, along with all necessary supplies, on a 10-day trek across the Eastern Desert to the Red Sea. According to a stone stele found at Wadi Gawasis, one of these expeditions involved 3,000 workers and 500 sailors. On the coast they reassembled the ships and the sailors set sail for Punt.

Over the last two years Bard and her team have uncovered more than 40 ship timbers, some longer than 12 feet, as well as dozens of stone anchors. They also discovered a series of six caves used for storage, and where the work crews may have slept as well. One cave still contained more than 20 bundles of rope used on the ships.

Although inscriptions in the Nile Valley tombs of several pharaohs mention these sea voyages, until Bard's discoveries, archaeologists knew little about how these expeditions were organized, where they sailed from, or how the Egyptians, not known as accomplished sailors, managed such a long, dangerous voyage.

For more information, see *www.bu.edu/archaeology/faculty/bard.htm.*

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Top: Archaeologist Kathryn Bard. Middle: Entrance to Cave 4 showing a timber from a ship. *Bottom:* A stone slab, or stele, engraved with the names of Amenemhat III (Pharaoh of the 12th Dynasty/Middle Kingdom), a ship's anchor, and pottery shards.

Digging Up Dirt on New England Families

"I'm not a scientist," says BU archaeologist Mary Beaudry, "but I use what scientists can tell me." Much of Beaudry's research focuses on the lives of New England families, from the first European settlers to the early 20th century. By combining information from historical documents and artifacts with data provided by biologists who study pollen, plant remains, and even insects, she is filling out the picture of how people in New England lived. "There are a lot of hidden histories," she says, "and by doing the background research you can meet new people."

Beaudry has excavated for over a decade at the Spencer-Peirce-Little Farm in Newbury, Massachusetts, originally built circa 1690. Her research has provided insights into the changing nature of family medicine in early New England. She found pollen and plant remains from local herbs in deposits from the 18th century, but she unearthed patent medicine bottles in 19th-century deposits, indicating that families had abandoned home-grown medicine in favor of store-bought preparations. "Apparently someone was very concerned about their hair, because we found a lot of hair restorers," Beaudry says.

Combining historical records and scientific analysis also helps Beaudry understand how families used the resources of the farm and surrounding countryside. When she and her crew found bones and plant remains at the base of a cellar stairwell that had been blocked by renovations, they conjectured that the finds might be the remains of a dinner given by one of the home's owners. Because they knew from historical records when the cellar was rebuilt, they could date the remains to 1788. Since some of the bones were from young suckling pigs, which can only be butchered in the spring, they were able to identify the season. Finds of pigeons and wild plants told them that the homeowners gathered food from the surrounding countryside in addition to what they grew on the farm.

The Spencer-Peirce-Little excavations explored farm life, but Beaudry also studies urban archaeology. She's excavated boarding houses in Lowell where textile factory workers lived and is currently writing a book on the archaeology of Boston, much of it based on discoveries made by the city archaeologist (one of Beaudry's former students) during the "Big Dig," Boston's two-decade-long highway/tunnel project. In one instance historical records indicate that a brothel madam married a homeopathic doctor, a fact supported by finds of huge hypodermic needles found at the site. "Cities," she notes, "are places where people always find interesting ways to get by."

For more information, see *www.bu.edu/archaeology/faculty/beaudry.htm.*

Tracing the Chocolate Road

To the ancient Maya living in Belize, Guatemala, and the Yucatan state of Mexico, cacao, the basic ingredient of cocoa and chocolate, was not just an indulgence—it was the food of the gods and a form of currency. Elite Maya living in major cities, like Chichen Itza in Mexico and Tikal in Guatemala, used cacao in both religious and political ceremonies. But those areas were not environmentally suitable for cacao cultivation according to BU archaeologist Patricia McAnany, who is trying to determine who controlled the cacao trade—local villagers or members of the elite classes living in important Maya cities. McAnany, who focuses on questions of economic and political control in ancient societies, says "We can't fully understand ancient societies until we understand the basis of their food and luxury crop production."

During the course of McAnany's Xibun (pronounced shee-boon) Archaeological Project (XARP), "wild" cacao trees were found in the Xibun River Valley of Belize. There is also ethnohistoric evidence of cacao cultivation in the region during the 17th century. McAnany's team is now searching for direct evidence of cacao and trying to determine whether production in the valley was regulated by outsiders, much as Europe used the Caribbean for sugar production, or whether local villages controlled production and made alliances with major cities to secure their markets.

Evidence from throughout the Xibun Valley indicates that around 825 CE, political power shifted from the old heartland in the west to cities in the drier north. Inscriptions found at one site in the valley, known as the Hershey site, link it to Naranjo, a Maya city to the west. Downriver, on the other hand, three round shrine structures have been discovered. They are similar to a type used at Chichen Itza and provide evidence of northern influence.

McAnany's team found scattered human bones in a buried passageway at the Hershey site that date to just before the city was abandoned during the 9th century. The remains, males and females of various ages, indicate that they may have belonged to a family, and teeth that were filed and inlaid with jade indicate wealth and power.

Mary Beaudry's studies at the Spencer-Peirce-Little Farm in Newbury, Massachusetts, built in the late 17th century, have yielded insights about the changing nature of family life in early New England.

McAnany thinks that the crypt of an important family may have been desecrated, or that they were possibly murdered—either case pointing to a shift in power.

While the north was clearly becoming more important, it is not clear whether it was actively controlling cacao production in the Xibun Valley. Graduate students working with McAnany are currently analyzing pottery found throughout the valley to determine if it was made locally or imported. The bones of an elite male burial are undergoing isotopic analysis to determine his place of birth. His excellent physical condition (his bones indicate the well-developed musculature of a warrior or a ball player) and a carved trophy skull found in his grave are proof of his high status. Since bones preserve chemical traces from the region where people grew up, McAnany is trying to determine if this man's chemistry is similar to that of other skeletons found in the Xibun Valley. If his bone chemistry is not a match, it will indicate that outsiders had important roles in the political and economic life of the valley.

Although McAnany focuses on smaller sites rather than major cities, her goal is to understand the interplay of politics, economics, and religion in the broader Maya society. "I come at it from an economic angle, but I am studying it in context with the rest of society," she explains.

For more information, see *www.bu.edu/tricia/reports/xarp2004/*.

"We can't fully understand ancient societies until we understand the basis of their food and luxury crop production."

Patricia McAnany and her team on-site at excavations in Xibun, Belize, where they are learning about the cultivation of cacao and the changing power relationships of ancient Mayan societies.

Reading Human History in the Earth

Geoarchaeologist Paul Goldberg studies the geology of archaeological sites. He compares analyzing layers of earth found at sites to reading "a crazy language where the translation code isn't ready yet." Unlike most archaeologists, who excavate while sweating under a hot sun, Goldberg mainly works in caves throughout Europe, Africa, and Asia that were home to early hominids, including *Homo erectus*, Neanderthals, and the earliest *Homo sapiens*.

Goldberg's method of choice is micromorphology, the microscopic study of undisturbed sediments and soils. He collects blocks of sediment from archaeological sites, carefully packages them to keep them from falling apart, and ships them back to his lab at BU. There he soaks them in polyester resin, essentially turning the once loose sediment into a rock. He cuts the blocks into sections thinner than a sheet of notebook paper and studies them under a microscope, much as other geologists study rock samples. Under the microscope the sections reveal what is in the sediment and what mineralogical and physical changes have occurred. And because this technique preserves the original internal integrity of the soil/sediment sample and its individual components, Goldberg can also determine how the sediment was deposited, whether grains of sediment washed in or whether they fell from the roof of the cave.

The focus of the research is to understand how early hominids used fire. Archaeologists consider the ability to start and maintain a fire an important indication of a hominid's cognitive development. Not only could fire-using hominids move into and exploit colder territories, they could also cook food, making it easier to digest and perhaps giving them an adaptive advantage.

But because these sites are so old, identifying fires can be difficult. Archaeologists working at the site of Zhoukoudian, in China, had claimed for decades that the site contained fires dating back almost 700,000 years. Although previous studies showed that they did contain burned bone and possibly organic matter, Goldberg's examination of thin sections of the putative hearth layers revealed that sediment had been deposited by flowing water. He argues that any possibly burned material was in fact washed into the cave and was not evidence of fires as the original excavators had thought.

In his latest research project, funded by the National Science Foundation, Goldberg is studying fire sites from Neanderthal settlements in Europe and the Middle East with an international team of specialists from Spain, Germany, and Italy. These fire sites range from 50,000 to 200,000 years old. Goldberg calls the sites "mini-Pompeiis."

By studying the fire sites microscopically and identifying the types of fuel used, how hot the fire was, and how long it was used, Goldberg and his associates hope to create a clearer picture of Neanderthal behavior. He hopes that by comparing Neanderthals' use of fire with that of early modern humans, he can translate the traces of charcoal and ash into an understanding of what constitutes "modern behavior" and what might be some of the differences that helped humans survive while their Neanderthal cousins went extinct.

For more information, see *http://people.bu.edu/paulberg.*

Investigating Ancient People and Plants

Archaeologist Ksenija Borojevic began her research at an early age. When she was ten she constructed a museum of "old things" for her mother's 40th birthday—complete with an exhibition guide, a guest book, and an entrance fee. Her mother may have appreciated the gift, but her parents, both plant geneticists, were not thrilled with her ultimate career choice. They wondered why she wanted to look at the past instead of the future, and of course they worried that she would never find a job. But Borojevic persevered and in 2005 she joined the archaeology faculty at Boston University. She did follow in her parents' footsteps in one regard—her research focuses on paleoethnobotany, the study of how ancient people used plants.

"Archaeologists often look at the pots and forget to think about what's inside of them," she says. "But by studying plant remains we can learn about the local environment, what season of the year people lived at a site, what they ate, how they farmed, and what kind of medicinal plants they used." Borojevic collects plant remains by pouring samples collected during excavation into specially designed "flotation tanks" that allow sediment to sink to the bottom while the lighter seeds rise to the top. Once collected, she identifies each seed under a microscope.

Much of her research focuses on the village of Opovo, Serbia, that was occupied during the Late Neolithic period, from 4700 to 4500 BCE, when Europeans first learned to farm domesticated plants. While paleoethnobotanists often focus on major food sources, principally wheat and other grains, Borojevic looks at all of the remains from a site. While she found domestic wheat and barley at Opovo, she also found that the villagers used many wild plants, including water chestnuts. Archaeologists had thought that once people began to farm, domesticated grains became their major food, but Borojevic's research demonstrates that early farmers at Opovo continued to eat a wide variety of foods gathered from the wild.

As the principal archaeobotanist at another site, Tel Megiddo in Israel, Borojevic studies plant remains from a city that was an important crossroads of the ancient world. She is also involved in studying plant remains at Tel Kedesh, a Hellenistic period site (ca. 2nd century BCE) in the Upper Galilee of modern Israel, and at other archaeological sites in southeastern Europe.

For more information, see *www.bu.edu/archaeology/faculty/Borojevic.htm.*

—by Trina Arpin

Biologist Karen Warkentin *(insert)* studies the adaptive behaviors of the eggs of the red-eyed treefrog.

LEARNING TO ADAPT

All animals, from fruit flies to human beings, need to adapt to changing environments. Biologists at Boston University study a multitude of creatures—escape-artist treefrogs, pugnacious lobsters, busy beavers, indigobird mimics, and multitasking ants. These researchers are shifting our understanding of the evolution, physiology, and behavior of these creatures, and revealing the complexity and adaptability of life on Earth.

Escape Artists

As a graduate student in the early 1990s, biologist Karen Warkentin set out to "be paid to look at cool frogs in cool places." Now, she regularly travels with students to the rainforests of Panama to study the adaptability of red-eyed treefrogs. These frogs live in trees and lay their eggs in a gelatinous clump, or clutch, stuck to leaves overhanging water. The eggs face many risks, including predatory wasps, a pathogenic fungus, drowning, and the four snake species that consider them dinner.

In her graduate research, Warkentin showed that treefrog eggs can hatch up to 30% early if necessary by wriggling within the egg and dropping into the pond below to become a tadpole. "Before that, people didn't think that eggs responded behaviorally until they hatched," says Warkentin. A new interest in the behavioral ecology of eggs was triggered by her discovery that these embryos are not merely passively awaiting birth, but actively responding to their environment.

The time of hatching is a crucial switch point between the frogs' egg and water stages. An early hatch, even two days, is a very risky decision, Warkentin explains: it's like a human being born three months premature. Choosing between getting eaten by a snake or facing predators in the pond is not taken lightly by vulnerable embryos. "A snake could stare at the clutch all day and the embryos wouldn't budge," she says; however, early hatching can be induced by vibrations made by an attacking snake. And, according to Warkentin, red-eyed treefrog embryos can distinguish between recordings of vibrations from a snake attack and those produced by harmless rain.

To learn how the eggs use vibrational cues to distinguish between signs of danger and a benign disturbance, Warkentin teamed up with Michael Caldwell, a graduate student in

Above: A snake attack on a clutch of treefrog eggs may induce early hatching. *Below:* Treefrogs producing a clutch of eggs on a hanging leaf.

Right: According to biologist Peter Busher, beavers such as this one are beneficial to the environment, creating wetlands that filter groundwater and provide habitat for other wildlife.

Red-eyed treefrog embryos can distinguish between recordings of vibrations from a snake attack and those produced by harmless rain.

biology, and mechanical engineer Gregory McDaniel, an expert in acoustics. Working with synthetic white noise, they varied both the duration of the vibrations and the spacing between them. They found that the embryos responded only to vibration patterns similar to those produced by snake attacks.

But snake attacks are only one of the risks that treefrogs face. If they make it into the water and survive a vast array of predators under the surface, they face another risk when attempting to leave the pond as juveniles. Fishing spiders patrol the surface of the pond, just waiting for the froglets to "run the gauntlet to the forest," Warkentin says. Working with post-doctoral researcher James Vonesh, she recently demonstrated that tadpoles can delay metamorphosis in response to a perceived risk in the next stage of life: in this case, fishing spiders. She hopes that learning more about risk-sensitive hatching and metamorphosis will lead to an understanding of how such plasticity affects the overall ecology of treefrog populations.

This research was published in the April 15, 2006 issue of *The Journal of Experimental Biology* and the March 2006 issue of *Ecology*.

To see a video of early hatching, visit *http://people.bu.edu/kwarken/*.

Beavers, Beavers Everywhere

A century ago, there were virtually no beavers in Massachusetts. Farmers in the state had cleared beaver habitat for pasture and cropland, and the population of the North American beaver dwindled. Restoration campaigns during the last half of the 1900s and a decline in the fur market returned them to a near-original range, and today the beaver population seems to be growing exponentially. Between 1996 and 2001, the beaver population grew from 24,000 to nearly 70,000 animals. Beavers are beneficial for the environment because they dam streams, expanding the wetlands which in turn filter groundwater and provide habitat for other wildlife. But beavers can also be a nuisance to humans, damaging property, contaminating water supplies, and flooding roads and buildings.

Many people want to harvest beavers to control these threats, but biologist Peter Busher suggests a more passive approach. "My old advisor puts it this way," he says. "Either you love beavers or you hate them, and that depends on whether they're doing positive or negative things for you." Busher says that the high numbers may not represent the true population across the state because beavers tend to live in small groups, making their population difficult to estimate. Also, the beaver population is dynamic; beaver families may try out one area but move on the next year if it turns out not to be suitable habitat. Dispersal of young adults also affects mating and rearing behavior. Two-year-old beavers leave the parent territory to find mates, so an extended period of migration can delay reproduction.

Busher adds that the high rate of increase seen in beaver populations, while alarming to residents whose trees have been cut or basements flooded, may not be a permanent trend. For years, Busher has been monitoring beaver populations on Prescott Peninsula, the strip of land between the east and west sections of Quabbin Reservoir that is off limits to visitors. After plotting the number of beavers on the peninsula over the past half-century, he noticed that the population grew exponentially at first, reached a brief plateau, and then fell to stabilize at 25% of its peak.

Many regions in the state are in the expansion phase, Busher explains, because they haven't had beavers as long as the reservoir has. He says that although it seems like a big problem now, some of those areas are not suitable habitats for beavers and the animals will eventually move on. "The state is just lagging behind the peninsula," Busher says. "We have studied how the natural population [in the absence of human impact] has grown and then decreased on the peninsula. This understanding can be applied to populations that are butting up against humans where conditions are less favorable for the beavers. If you give an area 25 years, it will stabilize at some lower level."

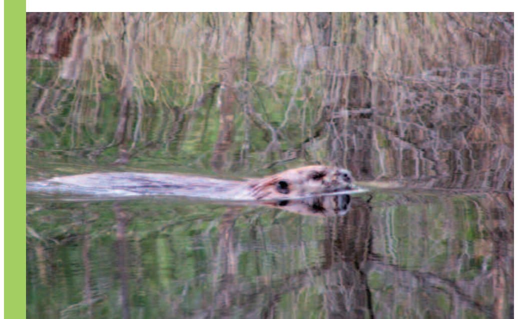
The issue at hand, he explains, may be one of human tolerance. "It's what wildlife people would call the 'cultural carrying capacity'. How much will humans put up with?" There are so many benefits to tolerating the beavers, he says.

"We need to be more aware of our place in the whole ecosystem and learn to live with wildlife," Busher says. If people can learn to live with beavers now, they will reap environmental benefits and the beaver problem will most likely take care of itself.

To read more about Busher's research, visit *www.bu.edu/cgs/faculty/inserts/busher.html*.

For information on Quabbin Reservoir Fishery, visit *www.mass.gov/dfwele/dfw/dfw_quabbin.htm*.

For information on beavers in Massachusetts, visit *www.mass.gov/dfwele/dfw/dfw_beaver_law.htm*.



A Fine Sense of Smell

Marine biologist Jelle Atema has a discriminating palate—and a connoisseur's nose for fine food and wine. Each spring he collects a new crop of lobsters from the waters near his laboratory in Woods Hole, Massachusetts—for his observation tank, not for his dinner table—where he investigates this crustacean's curiously fine sense of smell.

After arriving on Cape Cod in the 1970s from his native home in the Netherlands, Atema searched for a model animal to reveal the secrets of chemical messaging between aquatic species. Lobsters, it turned out, proved to be a very good model for learning about social communication. He has studied them for decades, producing a wealth of knowledge about chemical communication in this species.

Atema's recent work reveals even more complexity in what he calls the "underwater odor world." The whole social structure of lobsters is held together by chemical recognition of dominance, sex differences, and molting state, he explains. "It's remarkable that what humans consider a higher-animal behavior is found in what's known as a lower animal." Male lobsters fight to establish dominance, and the losing male, in subsequent encounters, will back down to avoid another fight with a previous victor. The animals identify each other *individually* by "smelling" odors in urine released during the fight.

Lobsters have five major chemoreceptive organs on a variety of antennae and hairs projecting from their heads and legs. One hair type, known as aesthetasc sensilla, leads directly to the olfactory (odor-receptive) area of the brain. You can see them flick in a quick downstroke, a sniffing-like action, says Atema. He hypothesized that receptors in these hairs might allow lobsters to recognize an individual's unique scent.

To test the theory, Atema pitted male lobsters, either with or without the hairs, against one another in a fight for dominance. In round two, he measured how long the weaker lobster challenged the dominant one. Male lobsters that had their aesthetasc sensilla removed spent longer challenging the dominant males, seeming not to remember their vanquishers from round one. "Without any doubt," Atema says, "this experiment shows that for individual recognition lobsters need aesthetasc sensilla."

Atema's newest collection of lobsters will help him search for the specific urine chemicals to which the hairs react. The immune system of humans and other vertebrate animals is based on gene families called the major histocompatibility complex (MHC). These genes generate chemicals that protect the body from foreign invaders *and* provide individual odors. "Now comes the kicker," says Atema. "In

invertebrates like lobsters, no MHC system is known. So how do they do it?"

His next step is to painstakingly hone down the list of urine chemicals to the ones essential for individual recognition. He expects that it might be a protein of similar structure and size to the MHC, but because this is "totally novel research," Atema says, his mind is open to all possibilities. "As soon as you know the chemistry, a whole new world opens up because you can talk about the evolution of these substances, their sources, their function besides recognition, and their role in neurobiology." He compares the yet-unknown recognition chemicals to unexplored territory: "The exciting part is that we just don't know what we'll find when we get there."

This research was published in the August 1, 2005, issue of *The Journal of Experimental Biology*. To find out more about the Boston University Marine Program, visit *www.bu.edu/bump/*.

"Indigobirds are just a unique and fascinating example of things working a little bit differently than the usual."

Top: Jelle Atema's research has identified specialized hairs on the heads of male lobsters that allow them to recognize each other individually by odor.

Right: The indigobird *Vidua chalybeata (top)* lays its eggs in the nests of the red-billed firefinch *Lagonosticta senegala (bottom)*. These species are found in and around Lochinvar National Park in Zambia.

Evolution of a Con Artist

Evolutionary biologists traditionally thought that for new species to evolve, groups of animals had to be geographically separated long enough that they became unable to interbreed. This classic view is known as allopatric speciation. The possibility that new species might develop in the same geographical area, known as sympatric speciation, is less accepted among biologists, but may be possible if groups become reproductively isolated by physiology, genetics, or behavioral quirks.

The case for sympatric speciation is made stronger by the findings of biologist Michael Sorenson, who sees evidence in the fascinating behavior of indigobirds. Sorenson and his graduate students travel to Tibati, Cameroon, to study indigobirds that display brood parasitism, a phenomenon that he says floored him the first time he learned of it. The birds lay their eggs in the nests of other bird species. The young indigobirds look and act like the hosts' chicks, so the hosts are tricked into raising the imitators as their own. As the birds become adults, they learn to sing the hosts' song and use both it and their native indigobird songs to attract mates.

About ten species of indigobirds display brood parasitism, Sorenson explains, and each species lays its eggs in the nests of a specific host. Because the birds will only mate with other indigobirds that were raised in nests of their own hosts, they become reproductively isolated from indigobirds with different hosts.

For the theory of sympatric speciation to hold weight, behaviors, like song preferences, must lead to reproductive isolation, and ultimately an inability for the birds from two different groups to interbreed at all. Along with his collaborator and former advisor Robert Payne, a University of Michigan biologist, Sorenson has been studying two "races" of the Cameroon indigobird that differ only in their hosts. One parasitizes the African firefinch, the other the black-bellied firefinch. He explains, "We think they may represent two reproductively isolated populations in the very beginning stages of speciation."

To test the overall model of sympatric speciation in this group, Sorenson and former student Chris Balakrishnan designed an experiment to play back the mimicked host songs to the males of each group. As expected, the indigobirds that grew up in the nests of African firefinches were agitated by hearing mimicked African firefinch songs, responding as if to a competitor for female interest. More importantly, if the mimicked black-bellied firefinch song was played, the males showed no interest, perceiving no threat. "In indigobirds sympatric speciation is definitely plausible," Sorenson says, "and we have just about all the pieces of the puzzle."

Such behavioral reproductive isolation may eventually lead to enough genetic changes over time to turn the races into recognizably different species, but the evolution of a new species is not immediate. "You might have to come back in 20,000 years or so," Sorenson says. "But we know it has happened in the past, because we have ten species of indigobirds today, each with different hosts." Sorenson is now expanding his observations to indigobird populations in East Africa. The driving force of this research, he says, is to understand how evolution has produced the diversity of life on this planet. "Indigobirds are just a unique and fascinating example of things working a little bit differently than the usual."

This research appears in the May/June 2006 issue of *Behavioral Ecology*. For more information, visit *http://people.bu.edu/msoren.*

Nurses, Foragers, and Soldiers

In many ant species, age correlates with an individual's role in the colony. Young ants of the worker caste toil within the nest, while older ants leave the nest for riskier tasks. Biologists have assumed that such behavior is programmed: that age-related changes are caused by neural and physiological development, and as ants age, they shift among non-overlapping tasks. But, according to biologist James Traniello, this might not be the whole story.

Traniello studies the behavior and neurobiology of the ant *Pheidole dentata* for clues to how social insects divide labor among colony members. *P. dentata* is a completely dimorphic species, meaning that workers are either minors who perform most labor within a colony, or majors who, with their large heads and strong mandibles, are primarily defenders and food processors. In the paradigm, young minors specialize in brood care. "They're basically nurses," says Traniello. At about twenty days old, they start foraging. Task sets are thought to be segregated, he explains. "Nurses are only nurses and foragers are only foragers. But we've found that the traditional model might not be correct."

Traniello observed that the minors start as nurses but retain the ability to perform nursing tasks as they age. "In a large number of colonies we saw that older workers did more than their normal foraging tasks. They added tasks as they matured," he says, "undergoing up to a six-fold increase in tasks from day one to day twenty." His research showed that young ants with weak mandible muscles are ill-suited for riskier tasks. "They're simply not ready to work efficiently, so as they mature they add more work as they are able." Traniello has also experimentally removed members of a colony and shown that ants take over the roles of the missing castes. "They switch tasks almost immediately," he says, suggesting that they are readily able to perform a variety of jobs.

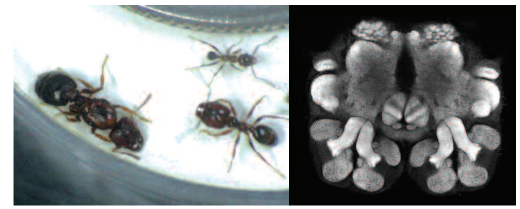
Together with graduate student Mario Muscedere and undergraduates Tara Willey and Jennifer Berglund, Traniello is studying *P. dentata* and other ants to determine if age- and size-related behaviors are correlated with neurology. In recent work, graduate student Marc Seid found that levels of the neurotransmitters dopamine and serotonin increased as minor workers matured. He also found age-correlated changes in the connectivity and strength of synapses, the message-trafficking connections between neurons. "This is the pattern in many organisms; they start with synapses, then prune them. We found that ants were doing the same thing, supporting our hypothesis that they gain abilities as they grow by refining neural connections." As he continues to correlate ant behavior with neurobiology, Traniello hopes to better understand the remarkable adaptability of insect behavior and the source of their complex social structure.

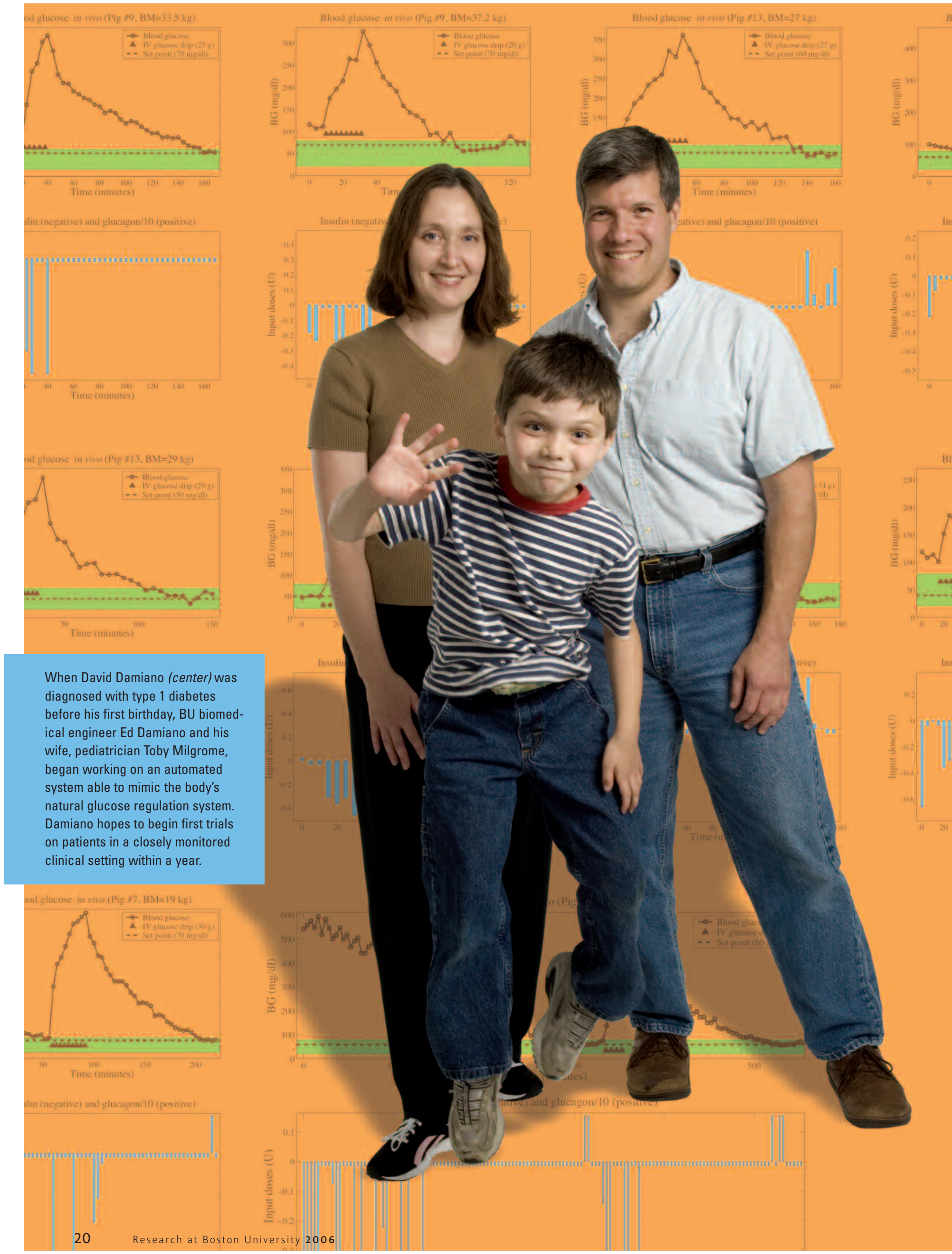
This research will appear in an upcoming issue of *Behavioral Ecology and Sociobiology*. For more information, visit *www.bu.edu/biology/Faculty_Staff/jft.html.*

—by Leah Eisenstadt

"In a large number of colonies we saw that older workers did more than their normal foraging tasks. They added tasks as they matured."

Left: Pheidole dentata individuals can be easily identified by size. The queen *(at left)* is the largest, a major worker *(seen bottom right)* is smaller and has a big head, and a minor worker *(right top)* is much smaller. *Right:* Confocal micrograph taken through the center of a *Pheidole dentata* minor worker brain. The front of the head is at the top of the image showing antennal lobes (grainy clumps of tiny balls).





When David Damiano *(center)* was diagnosed with type 1 diabetes before his first birthday, BU biomedical engineer Ed Damiano and his wife, pediatrician Toby Milgrome, began working on an automated system able to mimic the body's natural glucose regulation system. Damiano hopes to begin first trials on patients in a closely monitored clinical setting within a year.

MOVING RESEARCH INTO ACTION

Universities are often portrayed as ivory towers separated from the real world. A researcher in a biology department might study how heart cells react during a myocardial infarction, while a physician at a medical school attempts to treat a patient having a heart attack. But a new idea in medical research, called translational medicine, breaks through the tower walls, bringing research from the lab bench to the bedside. At Boston University, translational research has long been a reality, a fact that has recently been recognized with a $2.9 million grant from the Coulter Foundation that will fund four to five projects a year for five years to connect biomedical engineers and medical clinicians.

A Personal Research Agenda

One recipient of a Coulter grant is biomedical engineer Ed Damiano. For many years he did what he calls "basic science stuff," investigating the biomechanics of the circulation system. But six years ago he was drawn to an entirely new field of research. His son, then not yet a year old, was diagnosed with type 1 diabetes, historically referred to as insulin-dependent or juvenile diabetes. The disease requires constant vigilance, including frequent monitoring of blood glucose levels, close attention to diet and exercise, and either multiple daily insulin injections or continuous insulin infusion with an insulin pump.

Spurred by the experience of living with a child with type 1 diabetes, Damiano began to work on an automated system that would continually measure glucose levels and provide insulin as needed—a system that would mimic the natural function of the insulin-producing cells of the pancreas. He recruited his wife, pediatrician Toby Milgrome, in this effort.

Almost two million Americans have type 1 diabetes, an autoimmune disease in which the body attacks the insulin-producing beta cells in the pancreas. The trigger for the attack is unknown. Without insulin, most of the body's cells are unable to absorb and use the glucose that fuels cell processes. The glucose remains in the bloodstream where high glucose levels can lead to a range of problems including kidney disease, blindness, nerve damage, high blood pressure, heart attack, and stroke. "There is no cure for type 1 diabetes, but if people can maintain their blood glucose within the normal range, they can reduce and possibly eliminate the deleterious consequences of type 1 diabetes," says Damiano. "But," he continues, "because glucose levels fluctuate constantly (especially after meals), even intensive therapy fails to adjust insulin levels to their every rise and fall."

Insulin pumps, devices the size of a cell phone that administer insulin through a small catheter implanted in the skin, are an increasingly common treatment alternative. These devices provide a baseline dosage of insulin throughout the day and the patient administers a bolus (or additional dose) when glucose levels increase (most commonly after meals). But to know how much additional insulin is needed, glucose levels must be checked several times a day using a small meter that tests a tiny drop of blood. Damiano and his wife check their son twelve times a day, more than most.

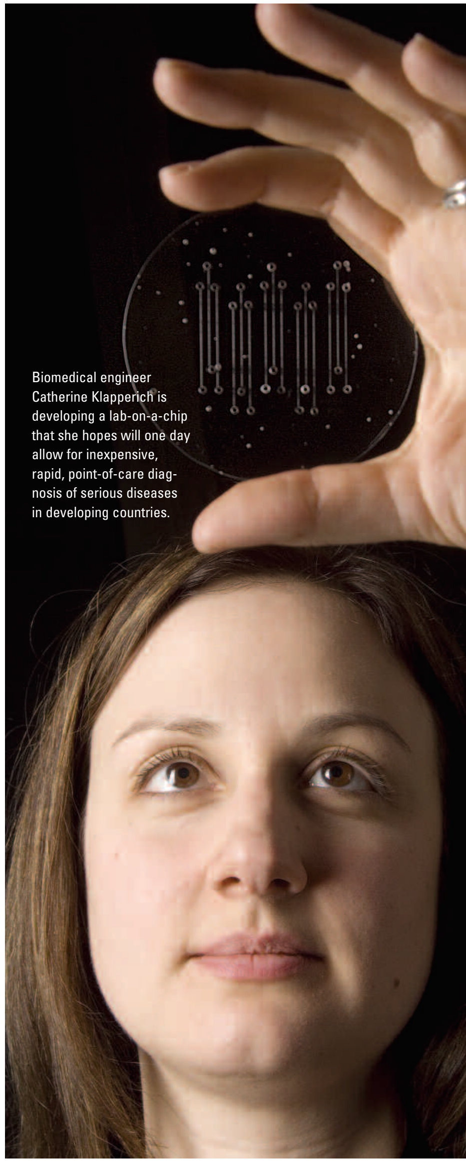
Damiano, his research team, and Milgrome are designing a more automated system that combines an insulin pump with a device to automatically measure glucose levels every few minutes via an electrochemical wire embedded in the skin. A small computer chip will use this data to instruct the device to deliver more insulin if needed.

Although the system uses technology already approved by the FDA, some technical hurdles remain. The meter they are using tests interstitial fluids, not blood. Glucose levels in these fluids lag behind and are less concentrated relative to blood glucose. Since it is the blood glucose levels that must be treated, this poses a problem. One of Damiano's former graduate students, Firas El-Khatib (now a post-doc in his lab), is working on extending his original glucose-control algorithm by developing a scheme that translates the glucose measurements from the interstitial fluid into estimates of blood glucose.

Also, the individual pieces of technology must communicate with each other. Damiano and El-Khatib have already tested the system on pigs, by combining wirelessly actuated insulin pumps, a glucose meter, and their control algorithm running on a laptop computer. They had to sedate the pigs to keep them from running around and upsetting the system. They plan to use the Coulter grant to build a system that can be mounted on a pig's back and tested while the pigs are awake and active.

Damiano is also looking ahead to introducing their system to people with diabetes. He hopes to begin his first trials on patients in a closely monitored clinical setting, using a non-portable system, within a year—and thinks a fully portable system could be ready to test in two to three years. "I have a deadline," says Damiano. "I have to have this ready before my son goes to college."

For more information, see *www.bu.edu/dbin/bme/faculty/?prof=edamiano.*



Biomedical engineer Catherine Klapperich is developing a lab-on-a-chip that she hopes will one day allow for inexpensive, rapid, point-of-care diagnosis of serious diseases in developing countries.

"I'm really interested in making a difference by enabling point-of-care diagnosis of emerging diseases in poor countries."

High-tech Disposables

For some life-threatening diseases, treatments exist but the route to diagnosis is costly, slow, and cumbersome. Often health-care workers must wait hours or even days for laboratory test results before they can diagnose and treat patients. Workers in the field or in developing countries, without access to expensive equipment or even a power supply, can face a daunting task in reaching even the most straightforward diagnosis.

Biomedical engineer Catherine Klapperich, another Coulter award winner, is developing a small, disposable diagnostic device, sometimes referred to as a "lab-on-a-chip" that may eliminate this problem and allow point-of-care testing and field-based analysis even in remote areas. She and her students are conducting the initial work to develop a range of labs-on-chips to diagnose dangerous bacterial infections or signal the presence of biomarkers that may predict life-threatening events.

One chemical that Klapperich is targeting is C-reactive protein (CRP). This biomarker of heart disease can predict a second event for someone who's had a previous heart attack or even a first event for seemingly healthy patients. Traditionally, physicians determine levels of CRP by taking a vial of blood, spinning it down in a centrifuge, removing the serum layer, and performing a lengthy test called an enzyme-linked immunosorbent assay (ELISA). "With a traditional ELISA you are washing the thing half the day," Klapperich says, referring to the many steps involved in the test. "We want something that is quick, disposable, and simple to use, and that has an easy-to-read output."

Her solution is a plastic chip a few inches long, imprinted with microfluidic channels each roughly the size of a human hair. These channels have a very high surface to volume ratio, speeding the ELISA reaction and reducing the length of the test to less than 30 minutes. A chemiluminescent substrate reacts with antibodies that bind CRP to produce an image on instant film that can be easily read by a health worker.

The chip's disposability, speed of analysis, and small sample requirement, says Klapperich, might make it ideal for a wide range of biomarkers. She is also working on a version of the chip to detect influenza viruses and help control the spread of a flu pandemic. The classic way to diagnose influenza infection is with a hemagglutination assay, which indicates a flu virus is present but not which strain. To diagnose a specific flu, a PCR (polymerase chain reaction) must be run to amplify the DNA. By replacing the ELISA step with a PCR step, the researchers hope to detect the specific flu virus quickly so that steps can be taken to combat its spread.

Another worrisome invader is *C. difficile*, a bacterium that causes debilitating diarrhea, often in patients who are already sick and taking antibiotics for other illnesses. Experts also worry that antibiotic resistance may make *C. difficile* more virulent over time. The current test to diagnose *C. difficile* infection involves a 2–4 day wait to see if the patient's fecal sample kills cultured fibroblasts, but it provides no information about the strain of bacteria infecting the patient. Klapperich's PCR device could enable a quick and precise analysis of the infection by purifying and extracting its nucleic acids, and prevent inappropriate usage of antibiotics.

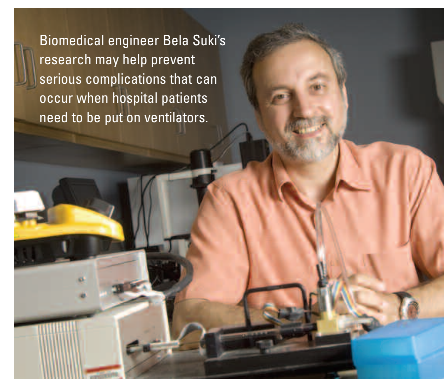
"I'm really interested in making a difference by enabling point-of-care diagnosis of emerging diseases in poor countries," she says. "What we're facing is primarily an engineering problem—bringing the test down to a tiny scale and making something that can be manufactured in quantity." The main hurdle is sample preparation, either filtering blood to remove proteins or lysing tough bacterial cells to isolate the nucleic acids. Klapperich adds that if they can succeed in developing a field-based tool, without the need for external power or a refrigerator to store reagents, then they can start thinking about the device's utility in developing countries. "You could actually change the spread of some nasty diseases with this device."

For more information, see *www.klapperichlab.org.*

Preventing Damaged Lungs

The hum and hiss of ventilators pushing air into the lungs of patients who cannot breathe on their own are common sounds in intensive care units and operating rooms. For most, these ventilators are life saving, but some patients develop a serious complication called Ventilator-Induced Lung Injury (VILI), a condition with a mortality rate of 30–40%.

Biomedical engineer Bela Suki's research focuses primarily on understanding the biomechanical properties of lungs that contribute to cell damage, but with the support of a Coulter grant he is also



Biomedical engineer Bela Suki's research may help prevent serious complications that can occur when hospital patients need to be put on ventilators.

developing a novel system that he hopes will prevent VILI and help thousands of patients every year.

Suki looks at lungs as basic biomechanical devices that stretch and contract ten times every minute. While many researchers focus on the biology of lungs and the presence of enzymes or other chemicals that affect how lungs work, Suki argues that mechanical factors have a huge impact as well.

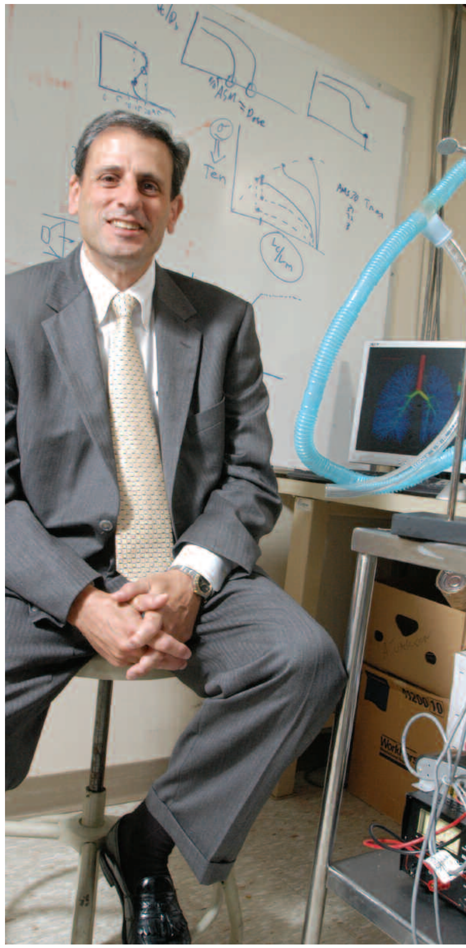
When hospital patients are put on a ventilator, it pushes air into their lungs then lets them exhale. Doctors calculate the volume and rate of the air to be forced in with a standard chart that considers a person's height, weight, and age. But a small number of patients develop complications. "Even if there were no problems with your lungs initially, the machine can cause problems," Suki says. He suspects that if a patient's lungs are being over-inflated cell damage may result, leading to fluid accumulation in the lungs and further complications. If part of a lung collapses, but the ventilator continues to push the same amount of air into the reduced space, overstretching and damage may also occur.

Suki notes that while ventilators use a constant volume and rate of air, our breathing normally varies: sometimes we breathe deeply, other times not. He has developed a method of variable ventilation that uses an algorithm to adjust the flow of air from ventilator to patient. In tests on guinea pigs, rats, and sheep he found that the method not only prevents injury but also allows more air to get from the lungs into the bloodstream. He is awaiting FDA approval to test the system in humans.

During the 15 years that he has been at Boston University, Suki has collaborated with researchers in a number of departments from Physics to the School of Medicine. "You can find almost everything here," he says.

For more information, see *www.bu.edu/dbin/bme/faculty/?prof=bsuki.*

If doctors knew the pattern of airway constriction in a particular patient, they could tailor medications to respond to that pattern.



Ken Lutchen, the new Dean of Boston University's College of Engineering, is also actively engaged in the laboratory where he is using three-dimensional imaging to better understand how airways shut down during asthma attacks.

A New View of Asthma

Another researcher helping people breathe easier is biomedical engineer Ken Lutchen. Recently appointed Dean of the College of Engineering, Lutchen has chaired the Department of Biomedical Engineering for the past eight years and spearheaded both the $14 million Whitaker Leadership Award and the Coulter Foundation translational research grant. At the same time he has been actively engaged in teaching and mentoring students as well as working in the lab where he is developing a new understanding of how airways constrict during asthma attacks.

Asthma is a rapidly growing disease. It currently affects 300 million people worldwide and is increasing at a rate of 50% every decade according to the Canadian Lung Association. Lutchen is developing an image-driven modeling system to give doctors a real-time picture of what happens in the lungs during an attack so that they will be able to design more personalized and effective treatments.

When people suffer an asthma attack, the inflamed airways constrict, reducing their size and making it more difficult for air to flow freely. In some patients asthma attacks occur when the immune system overreacts to allergens like pollen or dander. In other patients inflammation is provoked by a wide variety of factors, including stress and exercise. When attacks occur, most patients take medications to minimize inflammation and relax the muscles of the lungs.

Just as the causes of asthma can vary, the reaction of the lungs can differ as well. The airways in the lungs are like intricately branching trees. In some patients, asthma may constrict many of the smallest branches farthest away from the main trunk. In other patients, fewer but larger branches may constrict.

If doctors knew the pattern of airway constriction in a particular patient, they could tailor medications to respond to that pattern. Lutchen's image-based modeling system may be able to give doctors this information. His system feeds information from a three-dimensional MRI image of the lungs and data about how much air is moving in and out of the lungs into a computer model. The model calculates which size airways must be closing down to produce this pattern of response.

Tests so far have shown that in most patients, very small airways contribute to asthma attacks in very big ways. Armed with this information about each patient's response, doctors can choose those drug therapies that best target the affected airways—and help asthma patients breathe a little easier.

For more information, see *www.bu.edu/dbin/bme/faculty/?prof=klutch.*

Protecting the Heart

Many of us think of fat as the lard-like stuff that expands our waistlines. But according to Ken Walsh, a biochemist at the BU Medical Center's Whitaker Cardiovascular Institute, fat is also an organ that pumps out a variety of chemical messengers. Walsh has spent the last few years trying to understand how these chemicals affect our bodies, and his current work focuses on a particular chemical, called adiponectin, that may protect the heart and blood vessels.

While fat stores energy, it also produces a wide variety of hormones. Some stimulate the immune system, protecting against infection, but excess fat may produce inflammation, giving rise to a state in which the immune system is constantly revving its engine.

Adiponectin is one hormone produced by fat cells that helps prevent inflammation. Curiously, levels of adiponectin for unknown reasons are inversely proportional to fat levels—that is, obese people have low levels of the hormone and lean people have high levels. Studies in mice have shown that low adiponectin levels are not simply associated with heart disease but actually help cause it.

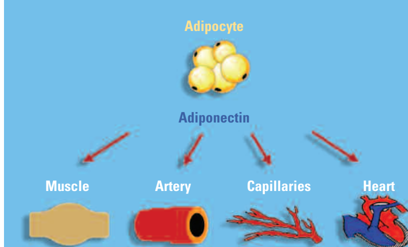
With his Coulter award Walsh is investigating possible clinical uses for adiponectin. One promising possibility is as a treatment to reduce the injury to heart tissue associated with heart attacks, also known as myocardial infarctions. Studies have shown that a one-time administration of adiponectin immediately following a myocardial infarction will significantly minimize damage and improve heart function in experimental models. Walsh is currently working with colleagues at Boston University to search for other molecules that function in a similar way.

Walsh credits much of the success of his research to the interdisciplinary and stimulating environment at the Whitaker Cardiovascular Institute. "Here," he says, "walls practically don't exist."

For more information about the Whitaker Cardiovascular Institute, see *www.bumc.bu.edu/bumc/wci.*

—by Trina Arpin
"High-tech Disposables" by Leah Eisenstadt

Biochemist Ken Walsh studies adiponectin, a hormone produced in fat cells that may protect the heart, blood vessels, and muscle tissue.

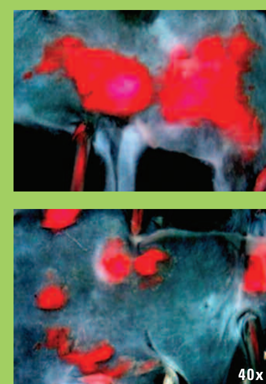


MAPPING MOLECULAR PATHWAYS

Boston University researchers bring together innovations in technology with discoveries in molecular biology to study the fundamentals of disease and physiology and to decipher the latest genomic information. Combining expertise in genetics, physics, biochemistry, nanotechnology, engineering, and bioinformatics, these scientists envision new ways of diagnosing and treating disease, and of studying the genetic building blocks that make us human.

> "People will take better care of their teeth if they know it can prevent heart disease."

Left: Oral biologist Salomon Amar has shown that severe gum disease may trigger atherosclerosis and heart disease. *Below:* These images show the buildup of atherosclerotic plaques *(in red)* in the aortic trees of mice infected with *Porphyromonas gingivalis,* a major pathogen in periodontal disease.



Linking Inflammation to Systemic Disease

Millions of Americans are afflicted by cardiovascular disease which can lead to life-threatening events like stroke and heart attack. Most people agree that exercising and eating right can reduce the risk of developing heart disease, but what about tooth brushing, flossing, or treating gum infections? Oral biologist Salomon Amar says that treating an infection, whether it's herpes, pneumonia, or gum disease, may be one route to lower the risk of systemic diseases like heart or pulmonary disease.

Epidemiological studies have suggested a link between atherosclerosis (hardening of the arteries) and severe periodontal disease (a chronic bacterial infection of the gums). Evidence from Amar's lab supports this hypothesis, indicating that infection causes an inflammatory response in the body which may trigger systemic diseases such as atherosclerosis. This line of research has enormous implications for dental health care. "People will take better care of their teeth if they know it can prevent heart disease," says Amar.

In earlier research, Amar had shown that people with severe gum disease often have dysfunction of the endothelium lining blood vessels, a sign of cardiovascular trouble. He also found higher levels of disease markers in their blood plasma, including the bacteria themselves, their by-products, or inflammatory mediators produced in response to the bacteria entering the bloodstream. "But," says Amar, "if you treat the infection you drastically reduce the chance of developing systemic disease."

To test whether treating gum infection might reduce evidence of heart disease, Amar gathered a group of eight people with periodontal disease and treated them with scaling, root planing, and surgery. He found drastic improvement in the function of endothelial cells lining blood vessels and less inflammation in all the subjects who received intensive periodontal treatment. Amar is currently conducting a phase II/III clinical trial to confirm these findings in a larger group of subjects.

Aware that the progress from infection to inflammation and systemic disease is not an isolated one, Amar is now studying obesity, a condition that may complicate the pathway. In new study results, he found that obese animals were incapable of mounting an adequate immune response to infection, produced lower levels of immune chemicals to fight infection, and had infections that lasted longer, potentially harming healthy cells. In addition, he found that the activity of enzymes, such as kinases, known to be critical to the molecular pathways that respond to inflammation, were dysfunctional in obese animals. These results suggest that obesity may be a factor in reducing an organism's ability to fight infection and potentially play a role in chronic infection, systemic disease, and lower quality of life.

Amar is planning a clinical trial that will compare immune responses in patients with a normal body mass index (BMI under 25) and obese subjects (BMI over 35). He hopes that by further elucidating obesity's role in the pathway that leads from infection to systemic disease he may also help explain why obesity poses such a danger to overall health.

For more information, visit *http://dentalschool.bu.edu/Research/perio/amar.htm.*

Genetic GPS

Biologist James Deshler says that after the genomes of humans and other primates were sequenced, he was surprised at the high degree of their overall similarity. The chimpanzee genome, for example, differs from the human genome by only a few percent. "The big question I wanted to ask was, 'What genetic sequences make us so different from other primates?' If our genes are so similar, then what is it that makes us human?" Deshler says he now thinks that the answer, at least concerning cognitive abilities, may lie in part where messenger RNA (mRNA) is located within cells.

Around the time that Deshler finished his post-doctoral research in the mid-1990s, the prevailing idea was that mRNA is randomly distributed within the cytoplasm to relay messages from genes encoded by DNA in the nucleus. “Everyone thought mRNA just floated around the cytoplasm and directed the assembly of proteins without much organization,” he says. Experiments on embryonic development in frogs and other species, however, revealed that some mRNAs prefer one side of the egg over the other, indicating that mRNA can sort itself in the cytoplasm.

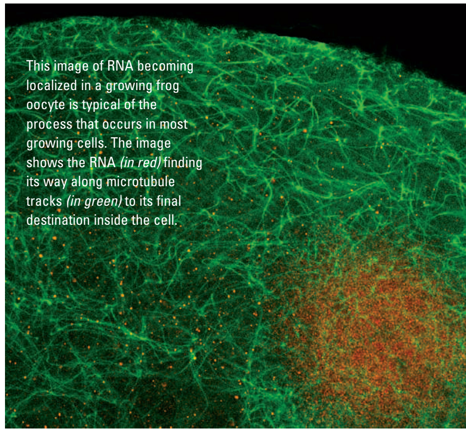
Further work revealed that the location of mRNA determines how proteins are positioned in the cell, a process critical to embryonic development and for the growth of polarized cells, like neurons. “A highly evolved mechanism of RNA localization allows neurons to grow appropriately during development and learning,” says Deshler. Proteins (and their respective mRNAs) control the growth of neuronal axons during embryonic development and the reinforcement of connections necessary for learning in adults. The distinction between humans and chimps, therefore, might lie in the relative amounts of proteins and RNA that gather at synapses, the connections between neurons. Higher-order cognitive functions might be genetically hardwired in the unique way synapses are regulated in humans.

In earlier work with mRNAs known to localize within cells, Deshler had noticed short repeating sections in the non-coding portion of the RNA, corresponding to so-called “junk” sequences. Experiments showed that those “words,” which repeated in the sequence more often than expected, were necessary for mRNAs to recruit the accessory proteins needed to move themselves around the cell. Without these words, the mRNAs floated around, lacking any apparent ability to sense direction. Deshler refers to these repeating words as the GPS (global positioning system) of the cell, while others in the field prefer to call them zip codes.

He originally discovered repeated GPS codes with his own eyes, visually scanning a sequence for repeating words, but now he harnesses computer power. Researchers in his lab designed a program called REPFIND which scans one gene for words that repeat more than twice and produces a list of those potential GPS codes. He uses REPFIND to search neuronal genes for repeated words, and then tests whether those words are actually GPS codes by conducting cellular lab experiments. He also wanted the ability to search the genomes of other organisms to see if certain codes are repeated in them as well, reasoning that if a word shows up frequently in many genomes, it may represent a fundamental language for mRNA localization. Because each gene takes about 30 seconds to scan in REPFIND, however, it would take several days to look for a single repeating word among the thousands of genes in each organism.

To speed up the process, Deshler recruited Ben Kennedy and In Lim, bioinformatics graduate students taking Gary Benson’s Biological Databases course. They created an online database of all repeating words and their probabilities, called GeneFinder. Researchers can use the database to see how many genes contain repeats of a particular word and then test in the lab whether those words are GPS codes. Deshler plans to use GeneFinder to crack the genetic code for mRNA localization, and potentially discover what sets us apart from our fellow primates.

For further information, see *www.bu.edu/biology/Faculty_Staff/jdeshler.html*. To try REPFIND for yourself, visit *http://zlab.bu.edu/repfind/*.



This image of RNA becoming localized in a growing frog oocyte is typical of the process that occurs in most growing cells. The image shows the RNA *(in red)* finding its way along microtubule tracks *(in green)* to its final destination inside the cell.

Shape Matters

DNA microarrays can monitor expression of thousands of genes simultaneously, making them powerful tools for biological research. These devices rely on hybridization, or the binding of sample DNA to oligonucleotide probes, short strands of DNA with a known sequence that are tethered to a glass slide. The pattern of where a sample has bound to the probes provides information about how genes are expressed in the DNA sample.

As powerful as microarrays are for researchers, they have not yet been approved by the Food and Drug Administration for diagnostic use. One reason is that the percentage of sample DNA strands that are able to hybridize fluctuates, making the process too imprecise for clinical purposes.

“To improve the hybridization efficiency of microarrays, researchers must understand the factors that influence how DNA binds to the array surface,” says physicist Bennett Goldberg. He is part of a team that has devised a new way to precisely measure the conformation, or shape, of DNA molecules tethered to a surface. “There are physical barriers that make it difficult to predict conformation,” explains Goldberg, “as well as differing densities of DNA on the array that complicate matters.” In addition, he says, a single strand of nucleic acids is floppy, like a soft rope, and can wiggle freely.

Goldberg’s collaboration with electrical engineers Anna Swan and Selim Ünlü, and former graduate student Lev Moiseev, has resulted in a new method called spectral self-interference fluorescence microscopy (SSFM). SSFM, Goldberg explains, is able to provide precise information about the size and shape of individual DNA molecules for the first time.

In SSFM, fluorescent labels are attached to one end of DNA tethered to a glass surface. Light is bounced off the top surface of the DNA layer, but it also travels through and bounces off a reflective bottom surface. The interaction of the two wavelengths—one reflected from the fluorescent label, the other from the bottom layer—produces oscillations in the spectrum of the returning light. The pattern of oscillations, or interference spectrum, describes the location and shape of the DNA molecule with sub-nanometer accuracy.

The team’s experiments showed that unhybridized single-stranded probes moved somewhat randomly, wriggling like worms at an average height of 2 to 2.5 nanometers above the surface. After hybridization, double-stranded DNA formed a rigid rod shape that was, on average, 5.5 to 10.5 nanometers from the surface and tilted at an angle of between 40 and 50 degrees relative to the surface.

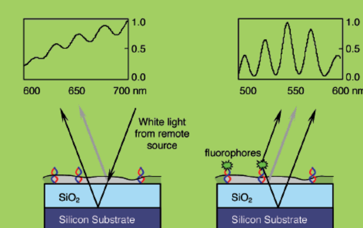
Microarray manufacturers will soon be able to use SSFM to measure hybridization efficiency and optimize their product. According to Goldberg, SSFM can also be used to predict the virulence of viruses by measuring the conformation of sugars on their surface, and to study the shape of molecules on the surface of live cells. “One reason we care about DNA conformation is that it tells us about how molecules organize and act near surfaces,” he says. “Such information is crucial to design biosensors and biomimetic materials. It provides a template for measuring and controlling biomaterials at nanometer-length scales.”

This research was published in the February 2006 issue of the *Proceedings of the National Academy of Sciences*. For more information, visit *http://nanoscience.bu.edu* and *http://ultra.bu.edu/projects.asp?project=fluorescence*.

Predicting the Roles of Proteins

The recent completion of the mapping of the human genome has uncovered the genetic sequence for the approximately 30,000 human genes, but scientists are largely in the dark concerning the role of those genes and the proteins they encode in development, physiology, and disease. One way to decipher the biologically relevant meaning of the human genome’s code of letters is to change, or mutate, each sequence in the laboratory and examine the physical or physiological changes in a model organism. Bioinformaticist Boris Shakhnovich has developed an easier way: exploiting the power of computer modeling to narrow the potential roles of a protein before beginning lab experiments on the genes themselves.

This schematic contrasts traditional white light reflection spectroscopy (WL) with spectral self-interference fluorescence microscopy (SSFM). In WL the oscillations created by the interference of the light reflected from the top surface and that reflected from a silicon substrate produce periodic oscillations. In SSFM the spectral oscillations created by the self-interference of the light from fluorophores attached to the tops of DNA and the light reflected by the silicon substrate yield the vertical position of the fluorophore and describe the position and shape of the DNA molecule with sub-nanometer accuracy.



“If someone sequences a new genome or finds a pet new gene, they are, of course, interested in what it does,” explains Shakhnovich. “The easiest thing to do is compare the new sequence to other genes. But there’s inherent ambiguity because even the function of a protein’s closest relative is not exactly a match.” The sequence of a gene can be used to predict the secondary structure, or building blocks, of the protein it encodes. But protein function is tied to how those blocks are put together—its three-dimensional shape, or tertiary structure, which is quite hard to predict from sequence alone. Predicting a protein’s function is further complicated by the fact that structure and function have a many-to-many relationship, meaning that there are many functions that can result from one structure and many structures that can give rise to the same function.

According to Charles DeLisi, Arthur G. B. Metcalf Professor of Science and Engineering, one of the “founding fathers” of the Human Genome Project and Shakhnovich’s mentor, “Although researchers had previously developed ways to approximate relationships between structure and function, Shakhnovich significantly improved on previous work by creating a mathematical method that is able to correlate protein structure and function with a high degree of accuracy.”

Shakhnovich began with a previously established ontology, a structured, controlled vocabulary that maps gene products in terms of their molecular function, such as DNA-binding or ATP-producing. By measuring the “distance” between two proteins on the ontology, he could then assign a score of functional similarity between protein structures.

“This was the first instance of distance in functional space,” says Shakhnovich, “but we wondered if it corresponded to known relationships between structure and function.” After comparing his measure with the structural distance, he saw a tight correlation that let him know he was on the right track. Shakhnovich then compared his functional distances to a measure of phylogenetic distance, a gauge of similar distributions on an evolutionary tree, and again observed a correlation. By mapping structural, phylogenetic, and functional distances on one functional landscape, he realized that function could best be predicted by considering structural distance in a genomic context.

The goal of the work is to narrow down the range of possible functions of a particular protein to a few possibilities, thus making it easier to design experiments that predict the protein’s function exactly. “Given the new definition of functional distance, we can say that the protein function is a certain distance away from known functions, with one of those nearby functions being a perfect match.” Shakhnovich gives an analogous example: “If the only thing you know is that a structure has four legs, it could be a chair or a table or an elephant.” You then can test to see which of the four-legged possibilities is accurate. “My hope is to redefine the notion of how we predict functions,” he adds. The goal is not to hit it exactly on the mark, but to predict the range of options accurately so that researchers can quickly test a gene’s function in the laboratory and more quickly understand how it functions in the organism.

This research was featured in the June 2005 issue of the journal *Public Library of Science Computational Biology*. For more information, visit *http://romi.bu.edu/research/bioinfo_thr.htm* and *http://cagt.bu.edu/*.

—by Leah Eisenstadt

Resident Health Advocates *(from left)* Yanick Francois, Rosa Maldonado, Gayisha Barrow, Cheryl Fielding, and Corinne Brun and SPH graduate and team manager Alex Muenze *(center rear)*, work with the Partners in Health and Housing Prevention Research Center to bring health education and wellness initiatives to people in their own communities.

REACHING OUT TO THE COMMUNITY AND TO THE WORLD

From poverty and endemic disease in developing nations to domestic violence in the inner cities of the United States, researchers at the Boston University School of Public Health are exploring ways in which education can help overcome the complex health issues that face the world today.

Creating Healthy Partnerships

The Partners in Health and Housing Prevention Research Center (PHH-PRC) brings a community perspective to the health issues of residents of public housing in Boston. Funded by the United States Centers for Disease Control (CDC), the PHH-PRC is an equitable partnership among four groups—Boston University School of Public Health, the Boston Housing Authority (BHA), the Boston Public Health Commission, and the Community Committee for Health Promotion—that is addressing the health needs of residents of public housing.

"By and large, the population living in public housing is in poorer health than most people in Boston," says BU epidemiologist and program director Robert Horsburgh. "The data suggest that health problems go hand-in-hand with poverty. In addition, public housing residents have less access to information about disease prevention and health promotion programs."

The program's main objectives are to identify health issues affecting people in public housing, to design research plans to collect data on these issues, and to implement strategies to address them. One of the strategies implemented by the partnership is to find leaders among the residents of the housing developments and to train them to become health advocates within their own communities.

The program, now in its fourth year, is fully funded by the CDC, which has apportioned nearly $30 million to 33 centers across the country. "The CDC has been very supportive and patient . . . Community-wide public health initiatives like these take time," says Horsburgh.

Horsburgh has worked on public health issues since the early 1990s, first focusing on infectious diseases like tuberculosis and HIV/AIDS, then moving on to address other disparities in health care among ethnic groups. "The methods have changed a lot since this kind of research began. Now we do research with community members, not on them," he says.

Specific initiatives of the PHH-PRC have targeted health issues from smoking cessation and dental health to domestic violence and motivating younger teenage girls to become more physically active. The group has found that community participation is critical. "We have swung away from the SWAT team approach where we came in like an army and never came back," says Horsburgh.

"Today we work with community members to develop objectives for their communities."

Alex Muenze, a graduate of the School of Public Health, co-manages the recruiting and training of each year's group of resident health advocates, or RHAs. RHAs are selected from applicants living in housing developments across the city. This is done in collaboration with Rachel Goodman, BHA's Community Services Director and Greg Davis, BHA's Family Services Program Manager. Each year 12 RHAs participate in a 10-week training course. Once certified, they receive stipends and are supervised by Davis and work on various community initiatives—from door-to-door outreach to manning tables at health fairs.

While Muenze says that much of the collaborative work has been fruitful, tracking the effectiveness of the program has, in some cases, been a challenge. "Long-term data is hard to gather because after our initial year of contact with the RHAs it can be hard to maintain contact. We may find that phone numbers are out of service or people have changed their address for a variety of personal and economic reasons," she says.

Yet the work RHAs perform in their year appointments is the essence of grassroots community activism. Soamy Rodriguez, an RHA from Dorchester, said she was able to distribute bags filled with health materials to residents at a recent morning event. "We got a good response, probably a dozen people came out," said Rodriguez.

Another RHA, Crystal Zollarcoffer of the Gallivan Boulevard Development, said that she has had success in her neighborhood with a car seat safety program called "Buckle Up Boston!"—an alliance of hospitals, health centers, and public and private institutions led by the Boston Public Health Commission. Working as an intermediary with the program, Zollarcoffer says that she has helped many people in her community learn to properly install car seats and exchange smaller seats for larger ones.

Mirlande Joseph, an RHA from the Archdale Development in Roslindale, has carried her duties to the physical rejuvenation of the community. Last year, she renovated and reopened the Archdale Community Center that had been closed for some time. According to Joseph, who lobbied the City Council and BHA for assistance, the plan came to fruition after she became an RHA. "I know that I have a great support system here and can call on any of the other RHAs for help," she says.

The climate of some housing developments can make grassroots work difficult. For example, Rosa Maldonado of South Boston said that some residents of her community view her work with skepticism and see her as an agent of BHA management or law enforcement. "Some people think that because I'm getting paid by BHA that I'm there to spy on people," says Maldonado. "They don't realize that I'm not there to judge, I'm there to provide information." As a group, the RHAs agree that the best way to overcome such misperceptions is through consistency and pursuing their goals even after their RHA appointments are finished. "We've got to stay connected. Our work has to be maintained after we're gone," says Zollarcoffer.

Muenze says the effect of each initiative is small but cumulative. "We work within a realistic set of parameters… We do not expect miracles, but we believe that over time, the program will have a significant impact on the health of these communities."

For more information about the Partners in Health and Housing Prevention Research Center, see *www.bu.edu/dbin/sph/research_centers/prevention.php.*

> "The goal is to provide students… with the background needed to work in an international, humanitarian setting."

The mock refugee camp organized by students in the School of Public Health provided hands-on experience in managing and coordinating the services needed to cope with disasters and humanitarian emergencies such as those in New Orleans, Pakistan, and Darfur.

Managing Disasters

The world's great humanitarian crises are a tangle of social, political, and economic factors. The genocide in Darfur, Sudan, for example, is a scenario fueled by massive poverty and state-sponsored ethnic cleansing. The aftermath of Hurricane Katrina was a blend of short-sighted planning, racial division, and the lack of an efficient, coordinated response. Yet, though the causes may vary, all humanitarian emergencies have certain common elements, says Monica Onyango, an instructor in Boston University's International Health Program. "Whether it is war or famine, when large numbers of people are displaced there are basic needs—food, water, shelter, medicine."

Onyango, who served as a relief worker in Africa before completing a master's degree in Public Health at BU in 2000, has used her firsthand experience to design and teach a 12-week intensive course called Managing Disasters and Complex Humanitarian Emergencies. The course provides a broad look at the management of relief efforts in the wake of natural and man-made disasters. From understanding human rights law and learning to write grants, to gaining a solid grasp of epidemiology and acquiring techniques for land-mine removal—the program gives students an opportunity to learn from leading experts in the field. The course also examines the complex coordination required between large, bureaucratic relief organizations. "Most of our instructors are professionals who have worked in conflict situations worldwide, including the Balkans, Afghanistan, the Congo, Sudan, and Liberia," Onyango said.

Other schools such as Harvard, Columbia, and Tulane offer courses in international public health, but few, if any, take the intensive, hands-on approach that her course does, she continues. Students work for six hours a day on assignments ranging from case studies to role-playing. Experts in the field teach specific portions of the course. CDC researchers, for example, teach the epidemiology sections of the course; FEMA (Federal Emergency Management Agency) representatives discuss emergency response coordination. News reports, white papers, and policy analyses are incorporated to keep coursework current. "The goal is to provide students, many of whom have no international experience, with the background needed to work in an international, humanitarian setting," said Onyango. Graduates have gone on to serve as aid workers in the aftermath of Hurricane Katrina and in the refugee camps of Darfur.

The hands-on focus of the course is perhaps best illustrated in an exercise held this past April in collaboration with the American Red Cross to organize a mock refugee camp. Onyango says she approached the Red Cross after attending a mock emergency event in Boston's Back Bay last year. Complete with medical and resettlement tents, feeding center, field latrines, and visitors playing the roles of displaced civilians, the mock camp immersed the participants in the experience of an unfolding humanitarian crisis. Students played the roles of representatives from various NGOs and were

"We encourage doctors to think about different culturally and religiously defined approaches to healing."

The Boston Healing Landscape Project helps to educate medical practitioners about culturally and religiously defined approaches to healing, such as the Santeria ritual pictured here. It is a celebration of the birthday of the Orisha Elegua, one of the guardian spirits. Santeria is one of many syncretic religions created in the New World. It is based on the West African religions brought by slaves imported to the Caribbean to work the sugar plantations.

responsible for setting up the camp, coordinating services, and processing refugees.

The objective of this first camp was to re-create a camp similar to the ones found in Darfur, says Jirair Ratevosian, an International Public Health student. "No matter how much you learn in the classroom, you are never prepared for the complexity of these situations," said Ratevosian, who plans to attend medical school after graduating this year. "This hands-on, immersive experience will definitely help me with my future work in medicine."

Despite minor logistical issues, such as whether the camp should be held indoors or outdoors next year, Onyango agreed with Ratevosian. "The goal of the mock camp is to give students as genuine an experience as possible. Learning like this cannot be accomplished by books alone," she said.

A Healing Landscape

A group of about twenty men and women sat in rapt attention as a tall, well-dressed young man spoke of how as a youth in Haiti he learned to listen to his dreams and to allow them to guide his path. The man was Niete Decimus, a Vaudau (Voodoo) priest and anthropologist, and the listeners were medical residents at Boston University Medical Center. They were brought together as part of a new training program instituted by BUMC's Department of Internal Medicine. This session, led by medical resident Cynthia Garner, drew upon the resources of the Boston Healing Landscape Project (BHLP), a partnership of researchers, health workers, anthropologists, and scholars of religion, that is charting a course to integrate alternative medical practices into Western medicine.

In the United States, where new immigrants often arrive with native traditions intact, the relationship among certified medical workers, traditional practitioners, and non-native patients is often fraught with shadows of skepticism and misunderstanding. The Boston Healing Landscape Project has assumed the task of helping Boston's medical practitioners—who work in a city of tremendous diversity—understand the complex and varied landscape of healing and medicine.

"We encourage doctors to think about different culturally and religiously defined approaches to healing," says Linda Barnes, director of BHLP. "We also work with doctors on anthropological issues that are part of their everyday practice."

While the tools and health-care goals of BHLP are unique, Barnes says she owes much of her initial thinking on the subject to Harvard professor Diane Eck and her Pluralism Project. "Diane Eck's work on growing religious pluralism in the United States got me thinking about the comparable trend happening in health care."

A thrust of the group is developing information resources for Western practitioners. One, an online database of herbs used by various ethnic groups in Boston, provides information about substances' physiological effects, chemical makeup, possible drug interactions, and toxicities. Another project in development is a country index that links to online resources that can help doctors and medical students better understand the cultural, religious, and political backgrounds of

Vaudau priest Niete Decimus *(left)* was brought to Boston University by Cynthia Garner *(right)* to talk with medical residents about Haitian beliefs on health and medicine.

non-native patients. An interactive world map allows the user to select a country of interest. By clicking on, say, Africa, then on the country of Ghana, the user is taken into a series of menus that provide information on immigration, health-care issues, spirituality, religion, and economics. "The Country Index provides a Web resource that contains the best information available on a range of issues affecting our foreign-born patients," said Barnes. "It is designed to be easy to use in a clinical setting when taking the medical history of patients from other cultures."

When doctors are sensitive to different religious and cultural outlooks on health, says Barnes, they can make better recommendations to their patients. For example, BHLP researcher and General Pediatrics Fellow Lance Laird is working to understand how Muslims are represented in medical literature and how Muslim patients perceive the Western health-care system.

Medical interpreters are an important—yet relatively new—resource in helping doctors bridge these cultural gaps. Justine de Marrais, a project manager and researcher with BHLP, has looked at the role and effectiveness of medical interpreters as cultural brokers in medical settings. One example de Marrais gave—which, coincidentally, she said, inspired her current research—was when doctors in the pediatric ward noticed a small red ribbon tied around a baby's waist. De Marrais and doctors in the ward learned later from an interpreter that the tying of protective ribbons is a common practice among some Southeast Asian peoples. "The ribbon served as an amulet or talisman to ward off harmful spirits. The removal of that ribbon could have been very offensive to the parents," said de Marrais.

Although there are potential benefits, according to de Marrais, there is disagreement about the overall value of interpreters as cultural liaisons. "Right now there is not a lot of consensus on whether medical interpreters play a legitimate role in communicating cultural practices," said de Marrais. The group's findings suggest that the lack of consensus may be the result of inconsistent relationships between doctor, patient, and interpreter. According to de Marrais, these relationships depend on a number of key variables including the "cultural fluency" of an interpreter and whether or not an interpreter has previously worked with a particular doctor or nurse. "In spite of these variables, recognition is growing that interpreters are positioned to provide an important service to patients and doctors," she said.

As Boston's population continues to diversify, the medical field grows more complex—and the value of cross-cultural knowledge and understanding increases. "It hasn't been a tough sell to doctors," says Barnes. "We are giving them useful information that applies to their everyday reality."

In 21st-century Boston, it seems, there is no single road to wellness—but the BHLP is creating an invaluable map of the terrain.

For more information about the Boston Healing Landscape Project, see *www.bmc.org/pediatrics/special/bhlp/*.

—by Jeremy Miller

Undergraduate Roxanne Chess *(right)* collaborated with recent ScD Amir Lahav *(left)* on a study directed toward understanding the effect of music on brain function and developing new therapeutic modalities based on music.

STUDENTS: BRINGING A FRESH EYE TO RESEARCH

Rhythmic Rehab

With a ScD from Sargent College and a $40,000 award from the Grammy Foundation, Amir Lahav has come a long way since coaching women's volleyball in his home country of Israel. Lahav, whose father was a famous volleyball coach, says he "grew up under the net," but at the same time took his first steps on the piano. After majoring in physical education and serving as a combat fitness officer in the Israeli army, Lahav turned to music. As a professional musician he composed, performed, and gave piano lessons to beginners and experts alike.

With a desire to combine his passions for music and movement into "something more scientific," Lahav entered the graduate program in Rehabilitation Sciences at Sargent College in 2003 to study the effect of music on brain function and to explore possible therapeutic modalities. Lahav explains his hypothesis: Blinking lights in a crowded room do not motivate people to move in synchrony, but music or a steady beat starts people tapping their feet and moving to the music. He speculated that this special communication between auditory and motor pathways in the brain could be harnessed to create a useful clinical tool for patients with movement problems, such as those recovering from a stroke.

Working with his advisor, Elliot Saltzman, and his collaborator, neurologist Gottfried Schlaug at Beth Israel Deaconess Medical Center and Harvard Medical School, Lahav designed the Music, Mind, and Motion Laboratory and created software to teach non-musicians to play by ear. "We used the piano keyboard as a model task," he says, "in which learned movements produce sound."

He recruited Roxanne Chess, a Sargent College undergraduate majoring in occupational therapy, as a research assistant through the Undergraduate Research Opportunities Program (UROP). Chess, whose aunt is an occupational therapist and who has a disabled cousin, chose her field because, she says, it takes a holistic, personal approach to therapy, changing and adapting the environment so that individuals with disabilities can participate fully in life.

Last summer Lahav and Chess designed a behavioral study to see if music could improve motor skills. “We wondered,” Chess says, “if a musician knows a piece of music well, then aside from mentally rehearsing it, can hearing it be a form of practice?”

They taught subjects to play a piece of music and used brain imaging to see what areas were activated while the subjects listened to the music they had learned. They found that listening to a previously learned song activated motor-related regions in the brain, and even improved the subject’s performance of the song. “Even listeners distracted by doing puzzles while listening to the music showed a performance improvement somewhere between that of active listeners and those listening to nature sounds,” Chess explains. “Our study suggests that a patient who produces segments of a song through a particular sequence of movements may be able to listen to that song at home and, effectively, without moving, continue to practice the movements.”

Even though he didn’t win a Grammy for his own music, the award will support Lahav’s postdoctoral research at Harvard Medical School, where he hopes to further develop his Virtual Music Maker (VMM), the human-computer interface he designed that translates a patient’s therapeutic exercises into music. “For patients, listening to the VMM-produced music is like interest on a bank account—you gain a couple of cents. But for a stroke patient those couple of cents could add up to a big benefit, especially where conventional therapy has failed,” says Lahav.

Lahav’s neuroimaging research won the Sargent College Dean’s Award at BU’s 2006 Science and Engineering Research Symposium.

To learn more about the Music, Mind, and Motion Lab, visit *www.mmmlab.com.*

—by Leah Eisenstadt

“Alzheimer’s patients, who are already confused, are seeing a confusing picture.”

Healthy Contrast

After watching her great-grandmother struggle with Alzheimer’s disease, Karen Sullivan wanted to do something to help others. After high school she worked for a time as a live-in home health aid for people with the disease. Now she is a PhD candidate studying how vision problems caused by Alzheimer’s may interfere with a patient’s ability to function in daily life. Sullivan received a national research service award from the National Institute of Neurological Disorders and Stroke for her research in the Psychology Department’s Vision and Cognition Laboratory.

Alzheimer’s disease damages nerve cells in the brain that control memory and language, but the disease also harms the optic nerve, reducing the ability to see contrasts. (A similar problem occurs in Parkinson’s patients.) Sullivan explains, “Alzheimer’s patients, who are already confused, are seeing a confusing picture.” For example, patients with a reduced ability to perceive contrasts may have difficulty seeing blue buttons on a blue shirt and find it hard to dress themselves.

Sullivan’s advisor, Alice Cronin-Golomb, previously showed that Alzheimer’s patients, who often must eat soft foods like mashed potatoes or pasta, ate significantly more when food was served on a red rather than a white plate, probably because they could see their food more clearly.

Sullivan also notes that perceiving contrasts is a critical part of recognizing people’s faces. For her dissertation project, Sullivan has designed experiments involving everyday activities like finding the right pill, getting dressed, and writing checks. She is testing to see if simple changes, like using buttons in a contrasting color on a sweater, can help patients in the beginning and middle stages of Alzheimer’s. Her goal is to find solutions that will make visual information more comprehensible to Alzheimer’s patients. “If their brain gets better quality input they are less confused,” she says. By implementing adaptations to enhance their vision, she hopes that some patients will be able to function as well as their peers without the disease.

—by Trina Arpin

Visual Coordination

Singing with an *a cappella* group, with its harmonies and multiple voices meshing into one song, parallels in some ways the coordination of the body’s nervous system, where multiple stimuli must be integrated into a singular experience. Perhaps, then, it’s no surprise that one of Boston University’s most gifted young neurobiology students is also an *a cappella* singer.

Junior Beth Ann Cimini, the first in her family to study science, is the recipient of a coveted two-year Beckmann Grant for undergraduate research. She has taken up the challenge of understanding how the retina processes visual stimuli. Specifically, she is looking at the role of the neurotransmitter acetylcholine, a chemical relay that operates in the synapses, or junctions, between nerve cells.

While the eye may seem a marvelous piece of stand-alone biological architecture, Cimini says much of it is derived from the same tissue as the nervous system. This means that parts of the eye that

These black-and-white images illustrate how people with Alzheimer’s disease may see the world as confusing, low-contrast images, further exacerbating any confusion associated with other brain damage resulting from the disease.

connect directly to the brain—the retina and the optic nerve—use similar means to produce the visual messages generated there.

Under the guidance of her advisor, neurobiology professor Bill Eldred, and in partnership with researchers at the University of Alabama, Cimini is studying how acetylcholine activates nitric oxide, another key neurotransmitter in the retina. In muscle cells, for example, acetylcholine is released into the synapse and triggers the opening of ion channels that cause muscle contraction. In the retina, however, it appears that acetylcholine not only acts directly to generate nerve impulses but also works indirectly through a series of other chemicals.

Using a special staining technique called immunocytochemistry, in which a fluorescent protein is attached to a particular target cell, Cimini is looking at how acetylcholine initiates a “chain” or “cascade” of chemicals that generate nerve impulses in the retina. Her work suggests that acetylcholine may “turn on” nitric oxide, which, in turn, activates another set of chemicals known as cyclic GMPs, or cGMPs. “The cGMPs appear to determine which cells are being turned on and off,” she says.

Cimini’s work contributes to a clearer view of how the eye itself may process visual information before it is sent to the brain. “The more complex the system, the more complete a picture that can be generated in the eye itself, before the brain even becomes involved.”

—by Jeremy Miller

Modeling Molecules

What do accounting and computer modeling of RNA molecules have to do with one another?

Not much, says Poornima Chalasani, a master’s candidate in bioinformatics who began her college career as an accounting student. She became interested in computer engineering after a few undergraduate computing courses at Andhra University in India and completed a master’s program in computer applications in 2001.

Her initial foray into biology came after she moved to Boston University in 2002 to pursue a second master’s in computer systems engineering. “In India, biology was mostly geared toward medicine, which I was not interested in,” said Chalasani. “But in the U.S. there are many directions in biology, even for computer people.” After working as a molecular biology lab technician, she thought about how she could apply her computer expertise to the world of biological molecules.

Chalasani and a team led by Nikolay Dokholyan, her former advisor at Boston University who is now a professor at the University of North Carolina, have developed a computer simulation to compute the folding properties of RNA molecules. Their work is moving in a promising direction; in March, Chalasani won the coveted Provost’s Award at BU’s Science and Engineering Research Symposium for her part of this work.

RNA is a vital molecule, which functions as a “messenger” in the production of proteins and as a catalyst in various reactions in the cell. Like all biological molecules, RNA’s function depends on the way it’s made. “In order to understand what’s going on, we’ve got to understand the shape and composition of the tiny particles that make up our cells," says Chalasani.

"On the surface, the RNA molecule seems simple. But under the surface, there is a lot of complexity." This complexity is overcome today with computers. Using powerful processors and 3-D modeling programs, the shape of RNAs can be inferred from their "sequence." The "sequence" is a veritable alphabet, which scientists abbreviate using the first letters—A, C, U and G—of the chemicals, or nucleotides, that make up this alphabet. The programs currently used to generate 3-D models of RNA molecules are, according to Chalasani, "computationally heavy," meaning that the algorithms in the software take a lot of computer processing power to carry out. "Some of these models take weeks to generate . . . our technique cuts processing time to a matter of hours," she says.

The complexity arises from the multiple interactions between atoms within the RNA itself. Each nucleotide is made up of 16 or 17 atoms, and an individual RNA strand may comprise hundreds of thousands of nucleotides.

Adopting principles used in protein computer simulations, Chalasani's model overcomes this intrinsic complexity by consolidating sets of atoms into groups. "Instead of looking at an RNA nucleotide as a set of a few dozen atoms, we look at it as a set of three distinct groups, or 'beads,'" Chalasani said.

The "beads" correspond to the sugar, phosphate, and base that are common structural elements in all nucleotide molecules. Looking at the atoms of RNA in terms of these groups drastically reduces the number of molecular interactions—and, thus, the computational complexity.

Once the structure is computed, the program generates a movie file. Like a digital flipbook, these movies depict how an RNA strand folds itself up into its distinct 3-dimensional shape. The group's results have been promising.

"Of course, when you take away some of the complexity you sacrifice a bit of accuracy," says Chalasani. "But these models do a good job of generating an accurate pathway by which an RNA molecule arrives at its unique 3-D structure."

Chalasani says her team's work holds promise for cell biologists and disease researchers trying to understand how mutations can lead to misshapen macromolecules that contribute to disease.

—by Jeremy Miller

Fishing in the Frog Pond

Two 4-foot-high bronze frog sculptures watch over the winter skaters and summer waders at the Frog Pond on Boston Common. From their perch on the eastern end of the pond they look across Charles Street to the trees in the Boston Public Garden. According to Joseph Bagley, if you were standing on the same spot 8,000 years earlier, the pond would still be there, inhabited by real, not bronze frogs. In place of the skaters and waders, you'd find indigenous peoples living around the pond, and thousands of clamshells would be visible, scattered along a shoreline reaching as far as Charles Street. Bagley, a recent archaeology graduate, easily paints this picture—the fruit of senior work for distinction, funded by UROP, in which he studied artifacts excavated from the area around the Frog Pond.

When Bagley arrived at Boston University, he knew he wanted to major in archaeology. "I liked science, I liked history, and I didn't want a desk job," he says. He had also honed his skills and interest in high school by attending an archaeological field school in his home state of Maine. Originally interested in classical archaeology, a second summer excavating in Maine refocused his interests to the history of New England before the arrival of Europeans.

Working with his mentor, archaeologist Curtis Runnels, Bagley learned that a prehistoric site on the Common had been excavated but the artifacts had never been studied. He saw in this both a subject for his senior work for distinction and an opportunity to explore the earliest history of Boston. With the permission of the City of Boston archaeologist, Bagley analyzed and photographed the finds. From them, he created a portrait of Native Americans who lived around the pond from 8,000 years ago until European settlers arrived. Among Bagley's most important discoveries was a Neville spear point, the oldest artifact ever found in Boston. Bagley also found pottery fragments bearing the impressions of woven textiles, the oldest examples of weaving in Boston. Another tool in the collection, called a scraper because it could be used to scrape fat and muscle from animal hides, was made from Pennsylvania jasper, showing that villagers traded well beyond the local area.

Based on the artifacts from the Frog Pond excavation, Bagley wrote a brief story describing the village and the villagers—children chase each other brandishing toy spears made from reeds, while grown-ups make pottery, tend fires, or butcher deer. The Frog Pond artifacts are typical of those from villages of this time period along New England's coast, says Bagley, but given the tremendous amount of construction in Boston, the Common is one of the few areas where evidence of this early history is still preserved. He adds that part of the site's importance is in reminding people that "the history of Boston began long before 1630 when the colonists arrived."

—by Trina Arpin

Facing page: These artifacts found at the Frog Pond in Boston Common include *(from top)* a stone projectile point made by Native Americans from the Archaic period of occupation at the site, 3,000–8,000 years ago; a broken Neville point, probably a spear point made with local stone by settlers during the earliest period of occupation of the site, 6,500–8,000 years ago; a stone projectile point of a type called Levanna, dating to the Late Woodland period, 400–1,000 years ago.

Given the tremendous amount of construction in Boston, the Common is one of the few areas where evidence of this early history is still preserved.

Honing in on Kidney Cancer

David Yao says he grew up asking the question "why?" Instead of reading his textbooks, the Boston University medical student says, "I wanted to be writing them." Yao's curiosity led him to study the birdsongs of European starlings as an undergraduate at Johns Hopkins University. He studied neuroscience because of his own interest; economics so that he could have something to discuss with his parents during visits home; and developmental biology, axonal guidance, and Alzheimer's disease after his grandfather developed the condition.

After entering medical school at BUMC, Yao was attracted to the field of urology and approached urologist Louis Liou. "During David's clinical rotation, he operated with me and was enthusiastic and hard-working," Liou says. Yao then suggested doing research with his mentor, and as Liou says, Yao had both the motivation and experience necessary to conduct medical research. "I gave him control over a project on kidney cancer, and he just took the ball and ran with it. He was very productive."

Yao says he knew that kidney cancer was a very bad condition and hoped to find a novel method to find and treat the cancer. "There are no good screening tools, and once the cancer spreads from the kidney there are no good treatments." The type of cancer that Yao studied, clear cell renal cell carcinoma (CCRCC), is difficult to treat because it is resistant to chemotherapy, radiation, and immunotherapy.

Liou's lab screened healthy and cancerous tissue from CCRCC patients using a DNA microarray of all human genes. Nearly a thousand genes were expressed differently in normal and cancerous cells, but a literature search narrowed the field to four probable candidates. "I was attracted to one gene in particular for the vitamin-D receptor (VDR), which is known to play a role in breast, colorectal, and parathyroid cancer," Yao says. Also, low levels of vitamin D in the body are associated with obesity, a risk factor for kidney cancer. The microarray data was confirmed using a technique called quantitative Polymerase Chain Reaction (PCR). It was found that the levels of VDR mRNA were lower in cancerous cells compared to normal ones. Yao then stained both tissue types for protein expression and observed less staining in the undifferentiated, unstructured tumor cells.

If VDR levels found in serum and urine can be correlated with a particular stage of cancer, the test may form a basis for CCRCC diagnosis and prognosis. If future work with VDR vaccines or viral transfection of cells with VDR is successful, it may lead to CCRCC therapeutics. Liou says, "David's work is a great contribution to the high-quality, groundbreaking research at Boston University."

This research was presented as an abstract at the American Association for Cancer Research meeting in April 2006.

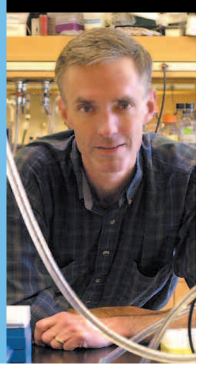
—by Leah Eisenstadt

Award-Winning Faculty

The American Society for Environmental History awarded the 2005 George Perkins March Prize (best book in environmental history) to James McCann (History) for his book *Maize and Grace: Africa's Encounter with a New World Crop, 1500–2000* (Harvard University Press). He was also named as a Patron of the Friends of the Institute of Ethiopian Studies, Addis Ababa, Ethiopia.

Courtenay M. Harding (Occupational Therapy and Rehabilitation Counseling) received the second American Psychological Foundation Alexander Gralnick Research Investigator Award for her commitment to research and education in the area of serious mental illness. The Alexander Gralnick Research Investigator Award is a biennial grant that supports exceptional research and mentoring accomplishments in this area. The award honors the late Alexander Gralnick, MD, a Life Fellow of the American Psychiatric Association.

James Collins (Biomedical Engineering, Center for BioDynamics) was named to *Scientific American*'s list of Top 50 Science and Technology Leaders for 2005.



Saralynn Allaire (Medicine) won the First Place Research Award from the American Rehabilitation Counseling Association.

Kazem Azadzoi (Urology and Pathology) was appointed to the International Continence Society Hall of Fame at the Society's 35th annual meeting.

Paul Barber (Biology) was honored with a Presidential Early Career Award for Research Endeavors (PECASE) by the National Science Foundation for his work in evolutionary and conservation biology.

Thomas Barfield (Anthropology), **Richard Primack** (Biology), **Frank J. Korom** (Religion and Anthropology), and **Julian Zelizer** (History) received Guggenheim Fellowships.

David Barlow (Psychology) was selected for the 2006 American Board of Professional Psychology Distinguished Service to the Profession Award. He was also honored as the 2005–2006 Kathryn Grover Harrington and Robert A. Harrington Distinguished Visiting Professor at Baldwin-Wallace College.

Calin Belta (Manufacturing Engineering), **Prakash Ishwar** and **Joshua Semeter** (Electrical and Computer Engineering), **Chris Passaglia** (Biomedical Engineering), **Ethan Baxter** (Earth Sciences), and **Sean Elliott** (Chemistry) were honored with Faculty Early Career Development (CAREER) Program Awards from the National Science Foundation.

Elizabeth Craig (Organizational Behavior) received the Best Paper Based on a Recent Dissertation Award from the Academy of Management, Careers Division.

Michele David (Medicine) was awarded the 2006 Physician Advocacy Fellowship by the Institute on Medicine as a Profession.

Arthur Dell Orto (Occupational Therapy and Rehabilitation Counseling) received a Distinguished Career Award in Rehabilitation Education from the National Council on Rehabilitation Education.

Carlo J. De Luca (NeuroMuscular Research Center) and **Herbert Voigt** (Biomedical Engineering) were elected founding Fellows of the Biomedical Engineering Society.

Jerome Detemple (Finance and Economics) was named co-editor of *Mathematical Finance.*

Farouk El-Baz (Center for Remote Sensing) was elected to the Moroccan Academy of Science and Technology.

Susan Fournier (Marketing) was given a Marketing Science Institute Young Scholars Award.

Thomas F. Freddo (Ophthalmology, Anatomy and Neurobiology, and Pathology and Laboratory Medicine) was elected incoming President of the International Society for Eye Research.

Donald Gair (Psychiatry/emeritus) received the 2006 Outstanding Psychiatrist Award for Lifetime Achievement from the Massachusetts Psychiatric Society. He also received the American Psychiatric Association's Agnes Purcell McGavin Award for Distinguished Career Achievement in Child and Adolescent Psychiatry.

Sheryl Grace (Aerospace and Mechanical Engineering) was elected an Associate Fellow of the American Institute of Aeronautics and Astronautics.

Michael Holick (Medicine, Physiology, and Biophysics) was awarded the Excellence in Clinical Research Award from the National Center for Research Resources.

Karen Jacobs (Occupational Therapy and Rehabilitation Counseling) was a 2005–06 Fulbright Foundation Fellow. She taught at the University of Akureyi in Iceland. **John Francis Bowley** (Restorative Sciences and Biomaterials) was a Fulbright Fellow in Taiwan, where he researched tissue regeneration in the temporomandibular joint and helped Taiwanese professors translate their work into English.

William Kannel (Medicine and Epidemiology) will receive the Stephen Smith Award for Lifetime Achievement in Public Health from the New York Academy of Medicine. Dr. Kannel, one of the founders of the Framingham Heart Study, also recently earned recognition from the University of California, Irvine, for "A Lifetime of Accomplishments in the Global Prevention of Cardiovascular Disease."

Nancy Kopell (Mathematics) received an honorary doctorate from the New Jersey Institute of Technology.

Yrjo Koskinen (Finance and Economics) won an award from the Finnish Securities Markets Foundation for an article published in the *Journal of Business.*

Thomas Kunz (Biology, Center for Ecology and Conservation Biology) was appointed to a National Research Council Committee, charged by the U.S. Congress and National Academy of Sciences to report on "The Impacts of Wind Energy Development on Wildlife."

Sharon Levine (Medicine) was awarded a 2005 Outstanding Committee Member Award by the Education Committee of the American Geriatrics Society.

Bart Lipman (Economics) was elected a Fellow of the Econometric Society.

Kenneth Lutchen (Biomedical Engineering) was elected Vice President of the American Institute of Medical and Biological Engineering (AIMBE). **Lucia Vaina, John White,** and **Joyce Wong** (Biomedical Engineering), and **Hamid Nawab** (NeuroMuscular Research Center) were elected to the College of Fellows of AIMBE.

Megan MacGarvie (Finance and Economics) was named a Research Fellow of the National Bureau of Economic Research.

J. Gregory McDaniel (Aerospace and Mechanical Engineering) was elected a Fellow of the Acoustical Society of America for his work on structural acoustics.

Anita McGahan (Strategy and Policy) was cited for Distinguished Service to the Business Policy and Strategy Division of the Academy of Management.

Michael Mendillo (Astronomy) was elected an Associate Member of the Royal Astronomical Society.

Elise Morgan (Aerospace and Mechanical Engineering) has received the 2005 International Osteoporosis Foundation-Servier Young Investigator Award.

Peter Novak (Neurology) won the 2005 Junior Award for Excellence in Clinical Research from the Movement Disorder Society and the International Congress of Parkinson's Disease and Movement Disorders.

Vini Onyemah (Marketing) was the winner of the Seventh Annual Marketing Association Sales Special Interest Group Doctoral Dissertation Award.

Michael Otto (Psychology) was elected President of the Association of Behavioral and Cognitive Therapies.

Christopher Pierce (Pharmacology and Experimental Therapeutics and Psychiatry) was awarded the Joseph Cochin Young Investigator Award by the College on Problems of Drug Abuse.

Alan Pisano (Electrical and Computer Engineering) received the 2005 GE Career Achievement Award.

Robert Pollack (Mathematics and Statistics) was chosen as a Sloan Fellow.

Paula Quatromoni (Health Sciences) was named Media Spokesperson for the American Heart Association's Childhood Obesity Initiative and "Go for Red" campaigns.

Maureen Raymo (Earth Sciences) presented the Emiliani Lecture at the American Geophysical Union.

Justin Ren (Organizational Behavior) was named to the Emerging Scholars Program by the Production and Operations Management Society.

Neil Ruderman (Medicine) was honored with the 2006 Albert Renold Award, a lifetime achievement award from the American Diabetes Association.

Miklos Sahin-Toth (Molecular and Cellular Biology) was named to the editorial board of the *Journal of Biological Chemistry* and elected an honorary member of the Hungarian Gastroenterology Society.

Michael Salinger (Finance and Economics) was named director of the Federal Trade Commission's Bureau of Economics.

Scott Stewart (Finance and Economics) shared the 2006 Distinguished Paper Award from the Academy of Finance for "Analysis of the Wealth Impact of Re-Allocation Decisions by Institutional Plan Sponsors," which he co-wrote with Jeffrey Heisler, Christopher R. Knittel, and John J. Neumann.

Matthew Wachowiak (Biology) has been given a Young Investigator Award for Research in Olfaction by the Association for Chemoreception Sciences.

Rosanna Warren (University Professors) was elected to the American Academy of Arts and Letters.

Richard West (Computer Science) won the Best Paper Award at the Institute of Electrical and Electronics Engineers' (IEEE) Real-Time and Embedded Technology and Applications Symposium (RTAS).

Boston University at a Glance

Robert A. Brown, President
David K. Campbell, Provost
Karen A. Antman, Provost, Medical Campus

Research Centers and Institutes

Center for Adaptive Systems
Center for Advanced Biotechnology
Center for Advanced Genomic Technology
African Presidential Archives and Research Center
African Studies Center
Alzheimer's Disease Center
Amyloid Treatment and Research Program
Animal Model Research Center
Center for Anxiety and Related Disorders
Aphasia Research Center
Center for Archaeological Studies
Howard Gotlieb Archival Research Center
Arthritis Center
Institute for Astrophysical Research
Center for BioDynamics
Biomedical Imaging Center
Biomolecular Engineering Research Center
Cancer Research Center
Cardiovascular Proteomics Center
Center for Chemical Methodology & Library Development
Clinical Epidemiology Research and Training Unit
Center for Computational Science
Institute on Culture, Religion and World Affairs
International Center for East Asian Archaeology and Cultural History
Center for Ecology and Conservation Biology
Institute for Economic Development
Center for Energy and Environmental Studies
Center of Excellence in Sickle Cell Disease
Fraunhofer Center for Manufacturing Innovation
Health and Disability Research Institute
Health Policy Institute
Hearing Research Center
Center for Human Genetics
Center for Information and Systems Engineering
Center for Integrated Space Weather Modeling
Center for International Health & Development
Center for Memory and Brain
Memory Disorders Research Center
Center for Nanoscience and Nanobiotechnology
NeuroMuscular Research Center
Frederick S. Pardee Center for the Study of the Longer-Range Future
Center for Philosophy and History of Science
Photonics Center
Center for Polymer Studies
Prevention Research Center
Center for Psychiatric Rehabilitation
Pulmonary Center
Center for Rehabilitation Effectiveness
Reliable Information Systems and Cyber Security Center
Center for Remote Sensing
Science and Mathematics Education Center
Center for Science & Medical Journalism
Slone Epidemiology Center
Center for Space Physics
Center for Subsurface Sensing & Imaging Systems
Systems Research Center
Center for Transportation Studies
Whitaker Cardiovascular Institute

For a complete list of centers and institutes at Boston University, with links to their websites, see *www.bu.edu/academics/centers/index.html*

Students:

16,572 undergraduate, 12,045 graduate, 3,080 non-degree

Faculty and Staff:

2,680 full-time faculty, 1,133 part-time faculty, 5,148 full-time staff, 79 part-time staff

The Campus

134 acres, 327 buildings, 478 classrooms, 2,205 laboratories, 10,815 total residence capacity

Computing Facilities

Supercomputers
IBM BlueGene/L supercomputer with 1,024 nodes
IBM pSeries 690 with 112 processors
IBM pSeries 655 with 48 processors
IBM xSeries Linux Cluster with 108 processors

Specialized High Performance Computer Laboratories
Deep Vision Display Wall
Access Grid Conference Facility
Computer Graphics Laboratory
LIVE: Laboratory for Virtual Environments

High Performance Networking
Fiber Optic Metro Ring interconnecting Boston University, Harvard, and MIT
Northern Crossroads (NoX)
Internet2 Abilene

Computing Labs
UNIX, Windows, and Macintosh labs
ResNet Computer Labs
More than 30 additional departmental computer laboratories

Libraries

23 libraries and special collections, 2.4 million volumes, 33,983 periodicals, 4.6 million microform units

Research

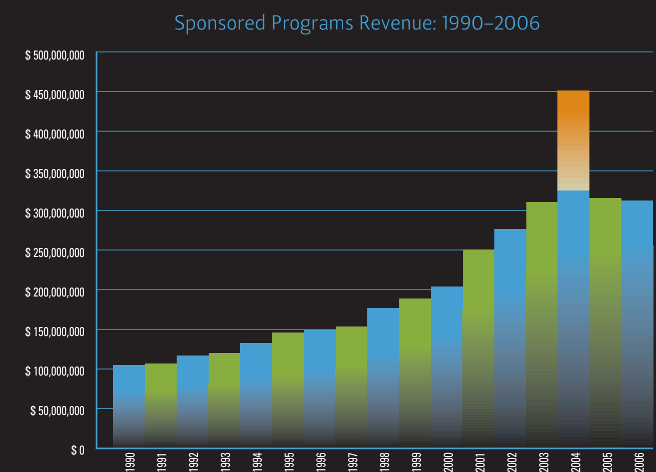
Sponsored Programs Revenue 2005/2006: $312,073,984

Financial Resources:

Endowment: $799.1 million
Total assets: $3.1 billion

Enrollment and staffing figures as of 12/20/05. All other figures as of 6/30/05 unless otherwise stated.

Research by the Numbers



* The orange area represents $128 million in funding from the National Institute of Allergy and Infectious Diseases to build a Biosafety Level 4 facility on the Boston University Medical Campus.

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