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Exploring the intersection between engineering and health
Global health, in all its complexity

We asked several alumni to talk with us about the future challenges and opportunities in global health, and their answers — excerpted on page 13 — offer striking insights. From equity of access to the prevention and management of chronic diseases, the issues are complex. As dean, I am proud to be part of a school with alumni engaged in this caliber of work, thinking and service.

The answers also remind me of the essential relationship between engineering and the liberal arts, and why it is vital that we build on our success in fostering teaching and research that is at once deeply grounded in fundamental scientific knowledge and highly nimble in making connections across the humanities and sciences. On these pages you will find just a sampling of research projects that bring a very broad range of perspectives to bear on improving health, from pushing the boundaries of biological knowledge to innovative ways to treat and monitor disease.

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The elimination of health disparities in the United States, especially those based upon race and ethnicity, is a major challenge. I applaud the fact that the National Institutes of Health has launched a new initiative dedicated to minority health and health disparities. For example, a cholera outbreak in a developing country following a natural disaster will require a vastly different response than a disease that spreads widely and rapidly through such means as airplane travel.

What do you see as the major challenges for health?

Patrick Beattie ’04 is in charge of global health operations for Diagnostics For All, a Massachusetts-based non-profit that creates low-cost, easy-to-use point-of-care diagnostic devices for the developing world.

Infectious disease is a major problem and causes significant morbidity and mortality, but chronic disease issues are rapidly growing, and in some areas, have already overtaken infectious disease as the number one health problem. Chronic health issues typically require monitoring and extended treatments as opposed to one-time interventions. How to provide this level of health care to large populations with low incomes is a very big challenge.

Christopher Loose ’02 is chief technology officer and co-founder of Sempurus BioSciences, a venture-funded biomedical company based in Massachusetts:

A major challenge for global health will be to support innovation in an increasingly cost-constrained environment. New therapeutics to improve health continue to require substantial investment. The appropriate incentives are necessary to drive these breakthroughs to the patients who need them.
Princeton engineers have found a surprising link between battery life and the day-to-day physical forces acting on an overlooked battery component that could make batteries last as long as the gadgets, laptop computers and cars they power.

“People think of batteries as chemical devices,” said Craig Arnold, an associate professor of mechanical and aerospace engineering. “We’re looking at how mechanics or physical forces affect the electrochemical performance of the system.”

Efforts by others to study the mechanics of a lithium-ion battery have focused on the battery’s electrodes, the “plus” and “minus” connectors. Arnold and his graduate student Christina Peabody Ph.D. ’11, were the first to correlate battery performance with the mechanics of a part called the separator, which divides the positive and negative components, but allows electrically charged particles to pass through. They found that typical forces acting on a battery compress the separator, thereby limiting the flow of lithium ions and dramatically diminishing charge capacity.

“That’s an interesting and surprising result,” said Arnold, who is affiliated with the Andlinger Center for Energy and the Environment, and the Princeton Institute for the Science and Technology of Materials. “The role of the separator in this sense hadn’t really been appreciated before.”

Taking their work one step further, Arnold and Peabody recommend ways to mitigate this effect: modify the surface of the electrodes or change the separator’s properties. A separator made of a less compressible material could result in longer battery life. The researchers published their findings in the *Journal of Power Sources*. –Prachi Patel

Graduate student Christina Peabody (left) and Associate Professor Craig Arnold investigated a previously unexplored cause of shortened lifetimes in batteries and are developing technology to extend battery performance. Scan the QR code to watch Arnold explain his work in a video (www.bitly.com/uRZb4f).
A cell phone networking project led by Princeton engineers could reduce fuel consumption by letting drivers know how to adjust their speed to avoid having to brake heavily or stop at traffic lights.

The system, called SignalGuru, involves a network of cell phones mounted on car dashboards, with each device using its camera to detect traffic lights and then reporting the status of the lights to a central computer system.

Drivers using the system receive tips about when to slow down or make a detour to avoid stop-and-go situations that consume fuel. Emmanouil Koukoumidis, a graduate student in electrical engineering, and Professor of Computer Science Margaret Martonosi are developing the system in collaboration with Li-Shiuan Peh, a former Princeton professor of electrical engineering, now at the Massachusetts Institute of Technology.

“Individual SignalGuru cellphones collect data,” she said. “But by collaboratively sharing their observations with other nearby SignalGuru users, the prediction error is reduced by four-fold and the usefulness of the system is greatly increased.” — Teresa Riond

Top graduate students in the Department of Computer Science will receive a prestigious award and lifelong membership in a network of leading scholars under the newly established Siebel Scholars program. The program is funded by a $2 million gift from the Thomas and Stacey Siebel Foundation.

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Gazing up at a projected map displaying the changing dietary habits of people from countries around the world, students in Professor Eric Wood and research scholar Justin Sheffied’s freshman seminar faced a difficult question: “Why do you think we’re seeing a global transition to a meat-based diet?”

Sheffield asked the 1.4 freshman gathered for the session of “Global Environmental Change: Science, Technology and Policy.” The seminar, offered for the first time this fall, addresses the issue of climate and sustainability through the lens of many disciplines.

One student postulated that the shift in diet may indicate that consumption of meat connotes high social status in some cultures. Another student suggested that the increasingly globalized economy could be a factor in the transition — or, perhaps, that more and more people simply like the taste of meat.

With each question posed during the three hour session, Wood and Sheffield extend the initial query into a further exploration of complex issues.

“OK, well, this creates an interesting dilemma,” said Wood, the Susan Dod Brown Professor of Civil and Environmental Engineering at Princeton University and director of the Program in Environmental Engineering and Water Resources. “If the world switches to a U.S.-style, meat-based diet, is that going to be sustainable?”

It had been less than 30 minutes since class began and already the room hummed with discussion that would continue until everyone was dismissed. Focusing primarily on global food crises that afternoon, Wood and his students — along with co-instructor Sheffield, a research scholar and lecturer in civil and environmental engineering — touched on a range of topics including the impact of modern technology on global agriculture, the importance of food security, the causes of recent spikes in food prices, and the pros and cons of U.S. foreign aid policies.

The previous week, their students focused on the environmental causes and socioeconomic effects of natural disasters around the world. Before that, the class focused on water scarcity and its impact on economic development. And earlier sessions covered the impact of rapid population growth on communities and the environment. The aim of the seminar, said Wood, is to explore the threads linking each of these issues and to challenge students to consider possible solutions.

“One of the things the students are starting to understand is the interconnectedness of all these issues,” said Wood, whose research focuses on climate, terrestrial hydrology, remote sensing and water resources. “We want students to realize that these aren’t one-dimensional problems. You can’t think of energy, food security and land degradation in isolation.”

Students are required to compose biweekly essays addressing environmental and policy quandaries. While he admitted they are very challenging, freshman Ray Chao likes these essays. “We’re encouraged to create our own solutions and ideas,” Chao said. “It requires a lot of creativity, and it’s exciting to take what we’re learning to come up with something new.”
Two Princeton engineering groups hope to use technologies based on inexpensive, easily available materials to give villagers in developing countries access to safe drinking water and help create local jobs. One group led by Wolé Soboyejo, a professor of mechanical and aerospace engineering, has developed a ceramic filter made from a clay-and-sawdust mixture to remove pathogenic bacteria from water. Baking the mixture burns off the sawdust, leaving behind tiny pores that block microbes. Currently available filters and treatment methods based on heat, the sun or chlorine are costly, inaccessible or ineffective. The clay filter developed in Soboyejo’s lab eliminated water-borne diseases within weeks in a Nigerian village near Abeokuta, where the researchers have helped set up a factory. They are now transferring the technology to Burkina Faso and Kenya.

The clay filter developed in Soboyejo’s lab of Professor Peter Jaffe, a graduate student in the Princeton’s Grand Challenges program on global health, are now collaborating to develop filters made from both clay andapatite that could remove pathogens and fluoride from drinking water at once. Lab tests show thatapatite composed of lime and phosphoric acid works as well as today’s more expensive activated alumina filters. Once the engineers optimize the filter’s operation, they hope to test it in a village in India where excess fluoride is endemic and study the spentapatite’s potential as a fertilizer, Jaffe said. “It would be irresponsible if we don’t figure out what to do with the used material,” he said.

“Local people need to generate income from making these filters,” Soboyejo says. “That’s the key to making this sustainable.”

Other than filter-maintenance, the biggest challenge is educating villagers about sanitation and the filter’s benefits, he said. “You’d think it’s as easy as telling people ‘You should use these because it’s good for you,’” Soboyejo said, “but that’s like telling me to eat salad because it’s good for me.”

Another group led by Peter Jaffe, a professor of civil and environmental engineering, is usingapatite, a phosphate compound, to make filters for well water that remove fluoride, which can deform teeth and bones if ingested in high amounts. Lab tests show thatapatite composed of lime and phosphoric acid works as well as today’s more expensive activated alumina filters.

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The following pages offer a snapshot of health-related research at Princeton Engineering. The research often extends well beyond the work described here — sometimes into entirely different fields such as energy, environment and security — because the research grows out of fundamental approaches to broadly relevant problems.

For more details visit

www.princeton.edu/engineering.
**PAINLESS: LASERS ALLOW NON-INVASIVE TESTS**

Princeton engineers are collaborating with Maryland-based Vorbeck Materials to develop printable sensors that greatly improve the performance of many basic medical tests.

The researchers in the laboratory of Ilhan Assay, professor of chemical and biological engineering, are using “functionalized graphite”—a single-atom thick sheet of carbon with certain structural and chemical modifications—that could form the basis for inexpensive, highly reliable tests for chemicals such as glucose and dopamine.

A very low-power infrared laser could measure blood sugar without the conventional pinprick, a plot of the light reflected from the skin is one of many tests to demonstrate that the laser penetrates deeply enough to monitor glucose. At right, the white dot on the finger of the lower image shows the infrared beam hitting the skin. The power of the laser is on par with the heat generated at the palm of the hand, which also appears white in the infrared image.

What is the potential for moving breath sensing forward,” he said. The increasing understanding of quantum cascade lasers also is leading to their possible use in laser surgery, because they could provide more controlled, less damaging incisions than conventional lasers. Princeton engineers are helping develop surgical lasers that are currently being tested in experimental corneal surgeries at Johns Hopkins University.

**PRINTABLE SENSORS FORM BASIS FOR MANY TESTS**

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**SEEKING GLOBAL ACCESS TO CERVICAL CANCER PREVENTION**

Women in the developing world have a far greater chance of dying of cervical cancer than American women largely because of the lack of screening programs that could detect precursors of the cancer when it’s more treatable. Princeton senior Shivani Sud, a molecular biology major working toward an engineering biology certificate, has a plan to change that. Working with Wele Soboyejo, a professor of mechanical and aerospace engineering, Sud is developing a system that uses an off-the-shelf digital camera and freely available software produced by the National Institutes of Health to help clinic workers who have modest training identify women who should receive further care.

With the Princeton system, a clinic worker takes a picture of a woman’s cervix during a gynecological exam then swabs the cervix with vinegar or a similar solution and takes another picture. The software performs a pixel-by-pixel comparison of the two pictures to identify cancerous or precancerous tissue, which changes color when exposed to vinegar. “Sometimes it’s not invention,” Sud said, “but innovation that’s needed, taking things that we take for granted and putting them together in a novel way that is a practical solution for another community.”

Sud tested the system in India last summer and planned to return during winter break to continue refining it.

**Christian Punkt (left), a scientist with Vorbeck Materials and a visiting research collaborator at Princeton, works with post-doctoral researcher Sibel Koruk Ph.D. “OB, on testing the properties of ‘function- alized graphene,’” which holds promise for sensing important biological molecules.**
OUTSMARTING BACTERIA

Bacteria are survival experts, but Mark Brynildsen, an assistant professor of chemical and biological engineering, is working to keep them at bay. In one project, Brynildsen studies bacteria’s ability to enter and exit a quiescent state that makes them impervious to antibiotics. “You’re basically nuking them and they’re OK,” he said. “If we could figure out how they do that we could learn how to kill them and avoid relapses of infections.”

Other work involves understanding and predicting the formation of biofilms, structured colonies of bacteria that pose major problems for prosthetics and other implants. In a third area of work, Brynildsen is developing antibiotics called “anti-virulence therapies” that fight bacteria indirectly by disrupting their interactions with their hosts. –SS

BODY LANGUAGE: LOW-POWER DEVICES READ SIGNALS TO STAVE OFF HEALTH PROBLEMS

Naveen Verma, an assistant professor of electrical engineering, is designing wearable or implantable electronic devices that monitor brain or heart signals to prevent acute problems and perform long-term assessments in patients with neurological and hearing disorders. In one project, Prud’homme is working with Howard Stone, the Donald R. Dixon ’69 and Elizabeth W. Dixon Professor of Mechanical and Aerospace Engineering, as well as Pat Sinko, a professor of pharmacy at Rutgers University, to develop nano-size, medicine-filled particles that accumulate in the lung, where they deliver concentrated doses of cancer drugs. Prud’homme also is working with Maryland-based biotech company Sequella, Inc., and the University of Sydney in Australia to use nanoparticles to deliver anti-tuberculosis drugs to the lungs.

In a separate project, Prud’homme is collaborating with Pennsylvania-based biotech company Optimeos Life Sciences to develop a method for using nanoparticle drugs to treat bacterial infections that have become resistant to antibiotics. “This computer-generated image shows a computationally designed drug, shown in yellow and blue, binding to a cancer-related enzyme called EZH2, shown in red. Professor Christodoulos Floudas and colleagues have created mathematical methods to predict, from billions of possibilities, what combinations of amino acids would bind to naturally occurring proteins, thus leading to promising drug candidates.”

PRINCETON RESEARCHERS ARE APPLYING DARWINIAN EVOLUTION PRINCIPLES TO NATURALLY OCCURRING ANTIBACTERIAL MOLECULES TO CREATE NEW ANTIBIOTICS FOR THE FOOD AND DRUG INDUSTRIES

Princeton researchers are applying Darwinian evolution principles to naturally occurring antibacterial molecules to create new antibiotics for the food and drug industries. “The goal of these devices is to analyze large databases accumulated by researchers to create devices that patients would wear daily. The devices would use machine-learning techniques to identify the unique signals from a patient’s body and send a warning to clinicians in advance of a heart attack or seizure. The devices may also initiate treatments, such as electrical stimulation that wards off a seizure.”

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Biologists have long been fascinated by the first moments when cells divide to become complex tissues and organs. Now engineers — with an eye toward treating cancer and regenerating tissues — are increasingly joining the hunt for the quantitative principles and underlying mathematics that determine how these processes succeed or fail.

Stanislav Shvartsman Ph.D. ’99, a professor of chemical and biological engineering who also holds an appointment in Princeton’s Lewis Sigler Institute for Integrative Genomics, is developing statistical approaches to understanding the way chemicals spread signals across an embryo. Shvartsman and colleagues published a breakthrough in this work Oct. 17 in the Journal Development.

In the lab of Celeste Nelson, assistant professor of chemical and biological engineering, Cecilia Lui ‘11 recently turned her senior thesis into a peer-reviewed article on the mechanics of stem-cell differentiation in breast tissue, which could have implications for understanding breast cancer. Another former undergraduate, Jay Kwak ‘09, is co-author with Nelson of a new study revealing that normal lung-tissue development is governed by a single mathematical equation.

In one project, Stone’s group found the unexpected formation of bacterial ribbons in the middle of flowing fluids, which has implications for understanding serious infections and has led to a collaboration with Bonnie Bassler, the Squibb Professor of Molecular Biology, and Ned Wingreen, a professor of molecular biology and associate director of the Lewis-Sigler Institute for Integrative Genomics. Scan the QR code to learn about Stone’s work in a video by science photographer Volker Steger (www.bitly.com/16640s).

The development of the airways of the lungs is a focus of research in the lab of Howard Stone, which runs through November 2012. Scan the QR code at left to view the Art of Science gallery online (www.bitly.com/tM64os).
Princeton engineers are working closely with neuroscientists to understand how visual information and words are encoded in the brain.

In a five-year collaboration, a team led by Princeton’s Peter Ramadge, chair and the Gordon Y.S. Wu Professor of electrical engineering, and James Haxby, a neuroscientist at Dartmouth College, have found common patterns in data from brain scans, called fMRI, that reveal brain activity as people perform tasks. The researchers are solving a long-standing challenge of comparing one person’s brain activity to another, which until now has been difficult because both the anatomy and functional processes of each person’s brain are different.

In one recent result, published in the journal Neuron, the researchers had subjects watch the entire movie “Raiders of the Lost Ark” while undergoing fMRI scans and used the data to derive a “common neural code” for how the brain recognizes complex visual images. Based on data from the first half of the movie, the researchers were able to predict, using only a person’s fMRI results, what scene he or she was watching in the second half of the movie.

Ramadge said the collaboration has not only revealed deep insights for neuroscience but has pushed the limits of the engineering techniques in ways that could be useful in many other areas. “It’s been a two-way street,” he said.

Ramadge attributed the success in part to weekly interdisciplinary meetings initiated by Jonathan Cohen, the Eugene Higgins Professor of Psychology and co-director of the Princeton Neuroscience Institute.

“It’s been a great way for my students and me to learn the language of neuroscience,” Ramadge said.

In a separate project, computer scientist David Blei and neuroscientist Ken Norman also are using fMRI data to understand how word meanings are represented in the brain and how these meanings shape memory retrieval. The researchers are showing how the meanings of words that were presented recently can linger in the brain and serve as a mental context that time-stamps memories, so that memories evoke words and vice versa. The work may aid the development of technologies for diagnosing and remediating memory problems.

Researchers in the lab of Professor of Electrical Engineering Sigurd Wagner are using their expertise in flexible electronics to give medical researchers an unprecedented view of brain damage.

Doctors would like to model brain damage in the lab by rapidly stretching nerve cells, but the electronics needed to monitor the effects typically do not stretch. Wagner’s group has developed a flexible electronic array and is testing it with biomedical engineers at Columbia University.

James Sturm ’79, the William and Edna Macaleer Professor of Engineering and Applied Science, and director of the Princeton Institute for the Science and Technology of Materials, is working with physics professor Robert Austin, of the Princeton Physical Sciences Oncology Center, on an interdisciplinary approach to understanding the evolution of cancer.

In one project, Sturm and colleagues created an array of tiny posts that hold cancer cells and allow precise control over their microenvironment. The researchers use the device to wash cancer drugs over the cells and watch how the cells develop resistance to the drugs.

Above: James Sturm (left) with graduate student Amy Wu.
Global health, in all its complexity

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What are your thoughts about the future of global health? Please view the full set of interviews and add your own comments at www.princeton.edu/engineering/futureofhealth.

What do you see as the major challenges for health?

Patricia Beattie ’04

An enormous global challenge in health care is the spread of infectious disease. It’s imperative that we think about this issue in the context of the local environment. For example, a cholera outbreak in a developing country following a natural disaster will require a vastly different response than a disease that spreads widely and rapidly through such means as airline travel.

Laura Forese ’83

As chief operating officer and chief medical officer of New York-Presbyterian/Well Cornell Medical Center, I am engaged in health care for the developing world. Infectious disease is a major challenge. I applaud the fact that the National Institutes of Health has launched a new initiative dedicated to minority health and health disparities. To improve health concerns require substantial investment. The appropriate incentives are necessary to drive these breakthroughs to the patients who need them.

Cato Laurencin ’80

The elimination of health disparities in the United States, especially those based upon race and ethnicity, is a major challenge. I applaud the fact that the National Institutes of Health has launched a new initiative dedicated to minority health and health disparities. By the year 2050, maybe sooner, ethnic minorities will be in the majority in America. The issues contributing to disparities in health care — environment, racism, genetics — need to be studied; solutions need to be proposed and tested.

Christopher Loose ‘02

A major challenge for global health will be to support innovation in an increasingly cost-constrained environment. New therapies to improve health continue to require substantial investment. The appropriate incentives are necessary to drive these breakthroughs to the patients who need them.

Laura Forese is chief operating officer and chief medical officer of New York-Presbyterian Hospital/Weill Cornell Medical Center.

Cato Laurencin is the Albert and Wilds Van Dusen Distinguished Professor of Orthopaedic Surgery at the University of Connecticut and a member of the National Academy of Engineering.'
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