COUNTERING AIDS IN AFRICA

A hand-held, point-of-care diagnostic tool offers new hope.

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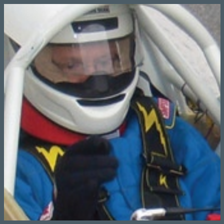

A RECORD FALLS AT BONNEVILLE

Light and composite, a sleek streamliner sets a speed mark on Utah's desert.

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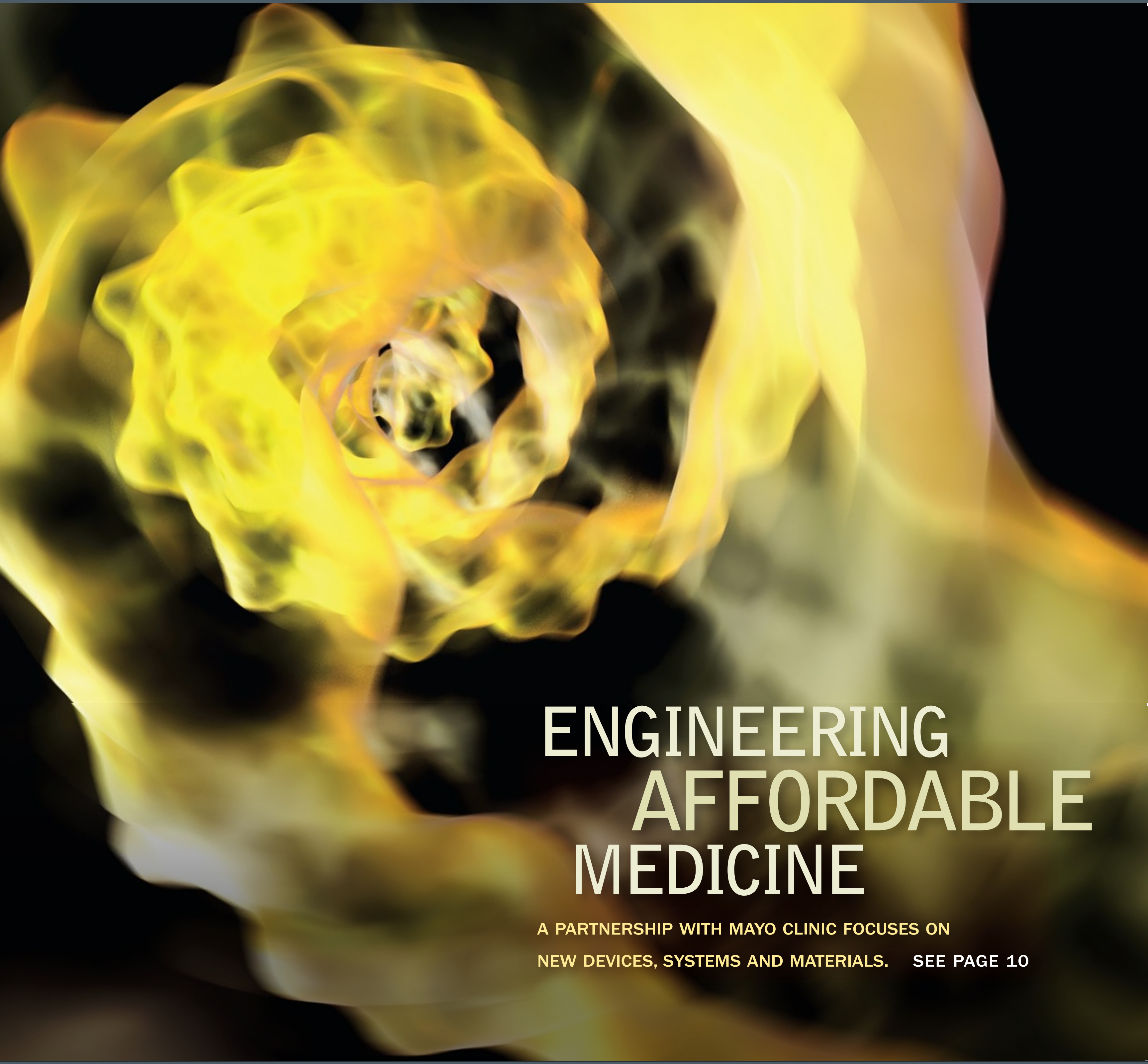

ENGINEERING AFFORDABLE MEDICINE

A PARTNERSHIP WITH MAYO CLINIC FOCUSES ON NEW DEVICES, SYSTEMS AND MATERIALS. SEE PAGE 10

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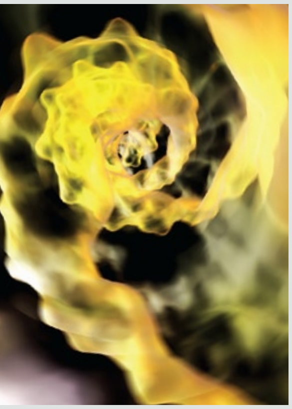

ON THE COVER

A computer model of DNA viewed along its central axis. Lehigh-Mayo teams are investigating new biomaterials and developing new medical devices and systems.

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VOLUME 1, 2010

EDITOR
Kurt Pfitzer

CREATIVE DIRECTION
Kurt Hansen

ART DIRECTION
Michelle Boehm

RCEAS ADVISORY BOARD
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DESIGNER
Linda Gipson

CONTRIBUTING WRITERS
William Johnson
Carol Kiely
Chris Larkin
William Tavani

PHOTOGRAPHERS
Douglas Benedict
Kate Holt
Ryan Hulvat
Jan and Agneta Isidorsson
John Kish

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www.lehigh.edu/resolve

P.C. ROSSIN COLLEGE OF ENGINEERING AND APPLIED SCIENCE
Lehigh University
19 Memorial Drive West
Bethlehem, PA 18015
610-758-4025
www.lehigh.edu/engineering

OFFICE OF UNIVERSITY COMMUNICATIONS AND PUBLIC AFFAIRS
Lehigh University
125 Goodman Drive
Bethlehem, PA 18015-3754
610-758-4487

SUBSCRIBE OR SEND COMMENTS:
engineering@lehigh.edu

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CHALLENGING GREAT MINDS…INSPIRING GREAT IMAGINATIONS

Medical care at our fingertips

Welcome to the seventh issue and fifth year of **Resolve*****, a magazine dedicated to research and educational innovation in the P.C. Rossin College of Engineering and Applied Science at Lehigh University.***

It wasn't that long ago that the capabilities of smart phones and other digital gadgets seemed dizzying. Now, we hardly think twice about the comprehensive technical infrastructure that supports them, or about the wireless, portable world of personalized information and entertainment that is forever at our fingertips.

What if we were to apply a similar model to rethink today's diagnostic, therapeutic and drug-delivery technologies? The potential for dramatic improvement in the accessibility and cost of medical care cannot be overstated – nor can the urgency of that need.

Think of advances in biocompatible materials, optics, nanotechnologies, and biosensors and electronics, and imagine integrating these with state-of-the-art communication devices and imaging and data-management systems. This could make it possible to complement or even replace massive, stationary, hospital-bound equipment with small, portable and even self-administered devices. Currently, however, no major U.S. biomedical research program offers this integrated biomedical and systems engineering approach to research in affordable and accessible medical technologies.

Meanwhile, a major demographic shift – some have called it an "agequake" – looms as the baby boomer generation begins to retire. Over the next two decades, this phenomenon will overwhelm our hospitals and clinics. From an engineer's perspective, it's not a matter of politics; it's a matter of capacity and efficiency. Such growing demand makes a medical-technology framework that provides accessibility and affordability not only desirable, but altogether necessary.

Engineers do not deliver medicine, but working with our colleagues in the medical sciences, we can make medicine more accessible and affordable. This is the focus of Lehigh's Biotech Cluster and its emerging partnership with the Mayo Clinic, as described in our cover story on page 10. The multidisciplinary initiative draws upon distinctive and complementary research expertise at Lehigh and Mayo. It combines strengths in materials science, nanotechnology, optical technologies and systems engineering with world-class biomedical research and clinical expertise to create a unique blend of research competence that neither institution could deliver on its own. Its goal is to develop systems architecture, integrated devices and new materials that will have a translational impact on therapies, diagnostics and drug-delivery technologies.

> *"A systems engineering approach to medicine can have a translational impact on therapies, diagnostics and drug-delivery technologies."* – S. David Wu

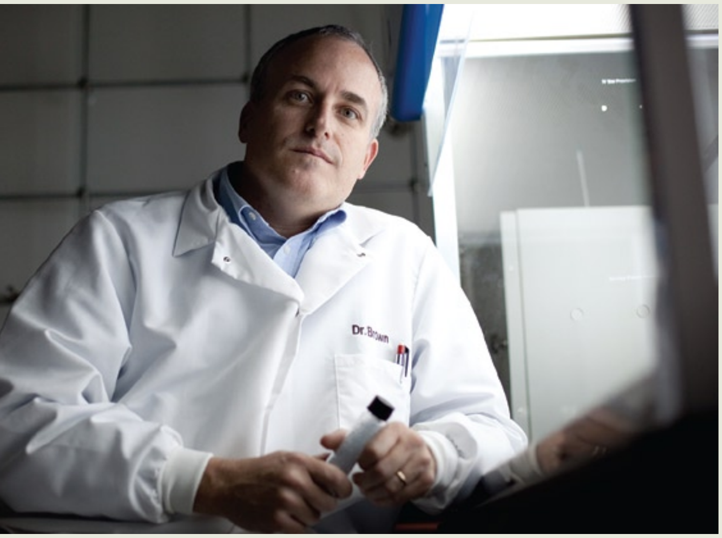
This issue of *Resolve* focuses on Lehigh's research and innovation in biotechnology and our commitment to an area where engineering, life science, medical science and healthcare intersect. The Lehigh Valley is emerging as a hotbed of biomedical device development, located at the geographical center of five major biotechnology hubs in the U.S. (Boston, Baltimore/D.C., Philadelphia, New York and New Jersey). Our goal is to leverage our core strengths in engineering through partnerships, innovative programs and unique facilities that will propel us into this field's intellectual center.

I hope you enjoy this issue of *Resolve.* Please drop me a note to share your thoughts and comments.

David Wu

S. David Wu, *Dean and Iacocca Professor*
P.C. Rossin College of Engineering and Applied Science
david.wu@lehigh.edu

A microbiologist's curiosity, an engineer's perspective



Tailoring the properties of surfaces, says Brown, can affect a bacteria's behavior.

As an aerospace engineer with McDonnell Douglas two decades ago, Derick Brown decided to take a few classes in environmental engineering at the University of California-Irvine. He fell for the field and the way it brought together chemistry, biology, hydrology and other disciplines.

Brown earned a Ph.D. at Princeton and joined Lehigh's department of civil and environmental engineering, where he is now Class of 1961 Associate Professor. He received a CAREER Award from NSF and is studying, among other things, the increase in metabolic activity that a bacteria cell undergoes when it adheres to a solid surface.

"Wherever bacteria interact with solid surfaces, metabolic activity can vary," says Brown, "even on clean surfaces like the glass we use in our lab. We have found that when bacteria adhere to a surface, the cell's adenosine triphosphate (ATP) level can change dramatically. ATP is the main energy carrier for living organisms, and we want to know how its concentration is affected by the process of adhesion."

Brown hypothesizes that there is a link between ATP formation and the variation in a cell's surface charge and pH as it approaches another surface. He believes the adhesion process itself, rather than the presence of nutrients or growth substrate at the solid surface, is what affects ATP formation.

Even clean surfaces like glass can alter ATP.

"Bacteria don't have eyes or fingertips, so how do they know when they hit a surface?" Brown asks. "I want to understand what triggers that change in ATP. What tells the cells they've hit something? Then perhaps we can utilize ATP to either encourage or inhibit cells from colonizing certain surfaces."

This complex link between physiochemical and bio-energetic processes fascinates Brown. If engineers can tailor the properties of a solid surface, perhaps they can control ATP formation. The right surface coating could deplete cellular ATP and kill bacteria adhering to a water pipeline. Or it could increase cellular ATP and stimulate bacteria to degrade toxic chemicals in polluted water.

Brown also studies the movement of bacteria through soils, which is of interest to scientists tracking the spread of pathogens in groundwater or home-builders seeking a safe distance from a septic system to a water well.

"People often think of me as a microbiologist, but I'm not. I am an engineer who happens to be studying microbiology," he says, "and I love using math to describe microbiological processes." Ⓡ

Wireless networks for better healthcare

Wireless communication may soon be at the heart of a secure and reliable patient healthcare network. The challenge, however, is to prevent signals from mobile phones and laptops from interfering with more sensitive medical equipment and patient monitoring devices. Healthcare organizations are also under tremendous financial constraints so cost must be considered.

Shalinee Kishore, an associate professor in electrical and computer engineering, studies the design, analysis and performance of different types of wireless networks. Her group is currently working to optimize these networks, an endeavor that includes signal verification, anomaly detection, algorithms for information gathering and retrieval from sensors, sensor networking, and secure and low-power wireless communications.

Kishore now plans to focus on the needs of the healthcare industry.

"The optimization of wireless communications within a healthcare facility could lead to a healthcare information network constructed around an individual patient," says Kishore. "This would ultimately bring about an improvement in that patient's treatment."

In a collaboration with a team of scientists led by Dr. Barry Gilbert and Dr. Erik Daniel at the Mayo Clinic, Kishore is planning to develop an optimized wireless communication network that can handle data transfer from patient monitoring devices. These wearable devices will be used to track a person's physiological data or physical activity. They will be designed to carry out an initial analysis and to send relevant data to an upstream network for detailed interpretation by a trained professional. Such data transfer systems could be used to support a broad range of medical studies in areas ranging from endocrinology, orthopedics, obesity and neurology.

"Our aim is to develop a more efficient, secure and reliable method for collecting and correlating patient information," she says. Ⓡ

Predicting the onset of blood clot formation

A chemical engineer seeks to predict the likelihood of platelet adhesion in damaged blood tissues.

When a blood vessel becomes damaged, platelets come to the rescue. These disc-shaped cells, which are formed in the bone marrow, are the first element in the blood to adhere to damaged endothelial tissue. A subsequent series of biochemical reactions then leads to the production of a fibrin mesh that traps red blood cells and more platelets to form a blood clot.

Being able to predict the likelihood of platelet adhesion is the focus of a fundamental computational study conducted by a research group led by Ian Laurenzi, assistant professor of chemical engineering.

A blood platelet measures approximately 2 to 3 microns in diameter. A pint of blood in a healthy adult contains between 70 and 190 billion platelets. The surface of a platelet contains a glycoprotein, which acts as a receptor that can grab onto, react with and form a "tether bond" with a certain type of ligand, or chain of atoms. This is known as the von Willebrand Factor.

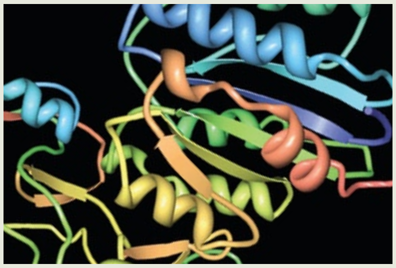
As a platelet flows past damaged tissue, the likelihood that it will form a tether bond depends on many factors, including the number of platelets that are passing through the damaged zone, how fast they are traveling (the blood flow rate), and how quickly a bond can form between the platelet receptor and ligand (the chemical reaction rate).

Because most chemical reactions are reversible to some extent, the rate at which the tether bond can be broken must also be considered when determining the likelihood that the bond will form. The number of platelets passing through a damaged area at any one time can also fluctuate significantly; thus, even when a platelet comes into contact with the wound site, formation of a chemical reaction is not guaranteed.

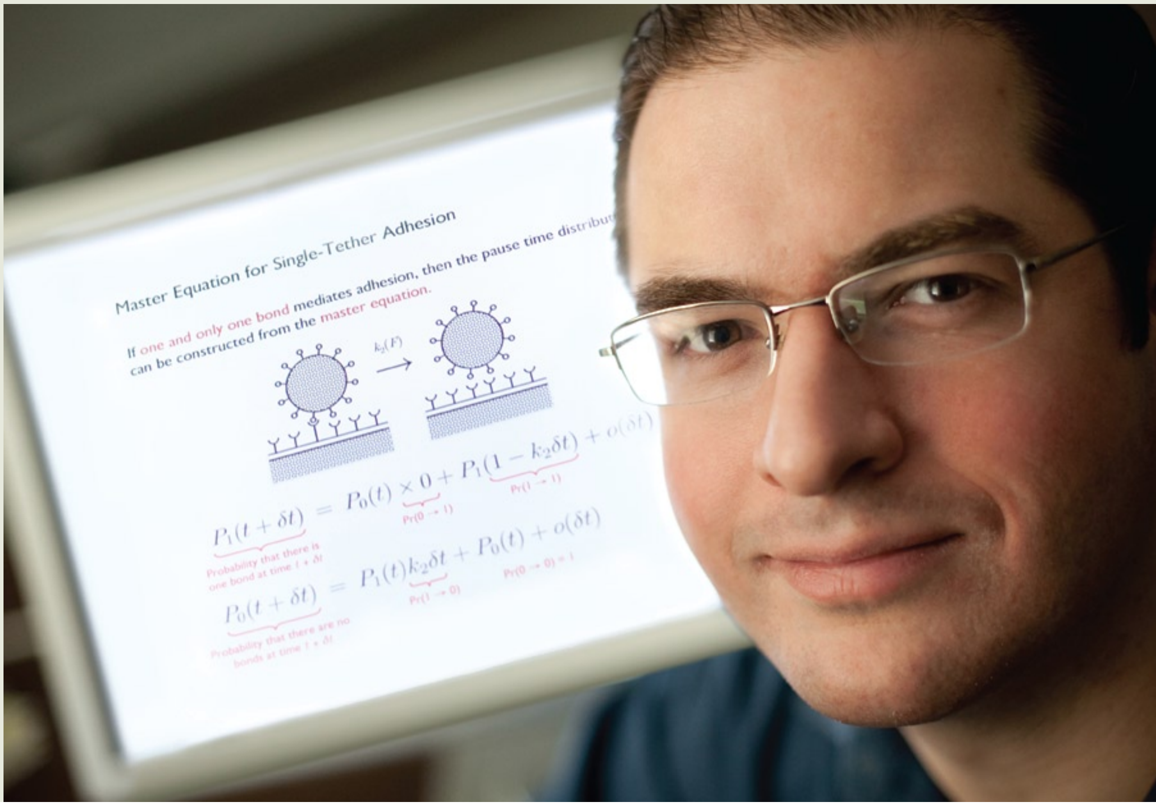
Numerical values for many of these parameters have been gleaned from experiments. For example, the lifetime of tether bond strength under different flow conditions was obtained by using a microscope and a high-speed camera to observe the interaction of platelets with microspheres coated with von Willebrand Factor. This experiment was carried out in a specially designed flow chamber in a collaboration involving Laurenzi and Thomas Diacovo, assistant professor of pediatrics and pathology at Columbia University.

Ian Laurenzi's computational model accounts for a wide variety of factors related to platelet adhesion and incorporates a "statistical approach" to biochemical kinetics.

"Most studies so far have looked at only one piece of the puzzle," says Laurenzi. "Our model takes into account all these factors and incorporates a statistical approach to biochemical kinetics." The model can account for many variables, such as a change in blood flow rate, alterations to the platelet receptors, and differing platelet concentrations. Its application extends beyond predicting the probability of platelet adhesion and may play a key role in the future development of new clot-controlling drugs.



Laurenzi's research could play a role in the development of clot-controlling drugs. Above, the von Willebrand Factor (vWF) A1-botrocetin complex.



Nanoparticles toughen wind turbine blades

Pearson and Robert Oldak (above) are seeking to optimize the performance of self-assembling diblock polymers.

Wind turbine blades, like those atop the Pocono Mountains in northeast Pennsylvania, can cost upwards of $100,000 a blade, says Raymond Pearson, director of the Center for Polymer Science and Engineering.

So it's no surprise that manufacturers and power generation companies are interested in making blades that produce electricity for as many years as possible. To prolong the lifespan of these futuristic "windmills," Pearson's group is investigating rubber nanoparticles that could toughen the glass-reinforced, epoxy-matrix composites out of which the massive blades are made.

"If wind turbines are guaranteed to last five years, and we can lengthen that by a factor of 2, it would go a long way toward making wind energy cheaper," says Pearson. "We haven't gotten to the point of testing actual blades, but we're seeing some promising results on laboratory test specimens."

"If we can double the lifespan of wind turbines, that would go a long way toward making wind energy cheaper." – Raymond Pearson

Pearson's experience with triblock polymers, which self-assemble on a nanoscale, has led to a partnership with Arkema Inc., a French company with research facilities in King of Prussia, Pa. The researchers are studying the use of diblock polymers in turbine blades. Diblock polymers are preferable to commercial triblock copolymers because the resulting rubber-toughened epoxies flow better during turbine blade manufacturing.

Arkema has supplied Pearson's group with diblock polymers that self-assemble in epoxy resins, enabling the researchers to control and potentially optimize the performance of the composite material. The group is assessing the type of microstructures that provide the best properties for making blades that would last longer than the current generation of turbines.

Pearson's group also is experimenting with diblock polymers to increase the fracture toughness of printed circuit boards, which are now subjected to higher solder reflow temperatures. Such high temperatures are necessary because the use of environmentally unfriendly lead tin solder is now banned in many countries. The challenge is to determine the optimum structure of the diblock copolymer additives that will reduce cracking.

Electron microscopy and fatigue fracture testing are conducted in Lehigh's Center for Advanced Materials and Nanotechnology. The work is funded by the Pennsylvania NanoMaterials Commercialization Center.

Imaging advances greener catalysts

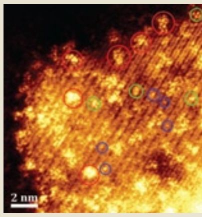
The catalytic processes used to produce chemicals and fuels could become much more environmentally friendly thanks to a discovery by researchers at Lehigh and Rice Universities.

In an article published Nov. 8 in *Nature Chemistry*, the researchers reported a novel imaging study of tungstated zirconia that enabled them to design a preparation procedure that increased the activity of the solid acid catalyst by more than 100 times.

Liquid acid catalysts are used to produce chemicals but pose concerns due to evaporation, spilling and corrosion. Solid acid catalysts, a potential replacement, can be more cleanly used and disposed.

The Lehigh-Rice team used aberration-corrected scanning transmission electron microscopy and advanced optical microscopy and spectroscopy techniques to illuminate the nanostructure and nanoscale behavior of a tungstated zirconia solid acid catalyst.

The team was able to directly image a variety of tungsten-oxide species that were supported on a nanocrystalline zirconia substrate. Studies revealed that the most active catalytic species were tungsten-oxide clusters that measured 0.8 to 1 nm in diameter and were mixed with a few zirconium atoms emanating from the support.



Mono-tungstate (blue), poly-tungstate (green) and highly active Zr-WO_x clusters (red).

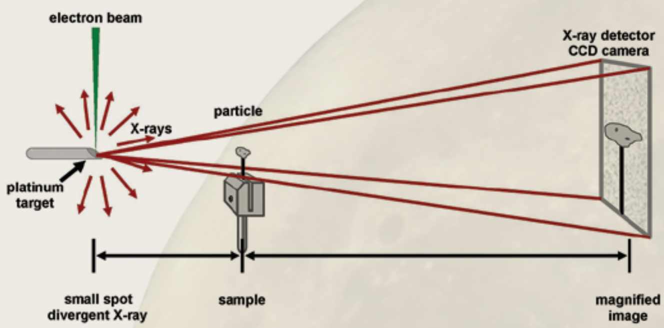
When the team deposited these clusters onto a tungstated zirconia catalyst with low catalytic activity, the activity of the poor catalyst improved by two orders of magnitude, confirming the team's hypothesis about the identity and structure of the active species within the tungstated zirconia material.

The *Nature Chemistry* article's authors include Wu Zhou, a Ph.D. candidate at Lehigh; Israel Wachs, professor of chemical engineering (Lehigh); Christopher Kiely, professor of materials science and engineering (Lehigh); and Michael Wong, associate professor of chemical and biomolecular engineering (Rice).

A noninvasive probe of lunar soil, with X-ray vision

Using a new imaging technique, materials scientists open a window on the moon's geological history.

Ever since July 20, 1969, when Neil Armstrong left the first human footprint on the surface of the moon, scientists have been fascinated by the fine powdery soil in which that impression was made. Today, more than 40 years later, Carol and Christopher Kiely are using a new imaging technique called X-ray ultramicroscopy (XuM) to examine the internal structure of the lunar soil particles that were collected from the Sea of Tranquility during the Apollo 11 mission.



"These particles are like tiny time capsules," says Carol Kiely, an adjunct professor in the department of materials science and engineering. "They provide us with clues to all the geological processes that have occurred on the lunar surface for the past 3.5 billion years."

To the naked eye, lunar soil is a fine charcoal gray powder. Under a microscope it becomes a collection of tiny rock, mineral and glass fragments of all shapes and sizes. This assortment, Kiely says, owes its origin to the fact that the moon, unlike the earth, has no atmosphere to protect it from solar wind or from micrometeors that smash into its surface at velocities of up to 25 km per second. This continuous bombardment, over billions of years, has led to the formation of lunar soil, or regolith.

The huge amount of energy behind a micrometeor impact, says Kiely, can fracture the underlying rock and cause localized melting. Splashes of molten regolith can then form droplets, which cool and solidify to form glassy spheres, ellipsoids, teardrops and dumbbells before returning to the lunar surface.

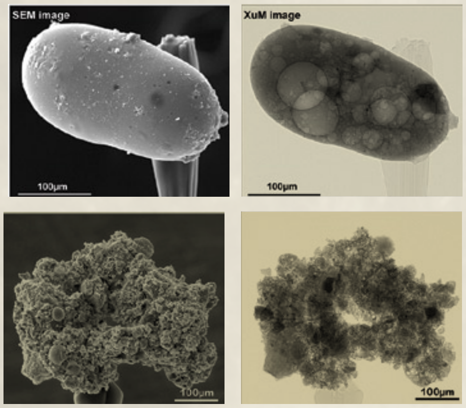
Some of this molten regolith returns to the surface before cooling and seeps down in between the underlying soil. As it cools, it encases the tiny mineral and other fragments in a glassy matrix, forming a type of particle called an agglutinate that is not found anywhere on Earth. The rise in temperature also releases trapped gases implanted by the solar wind, causing bubbles to form in the molten regolith. As a result, much of the glass found on the lunar surface is vesicular.

While 40 years of research has revealed much about the physical and chemical properties of lunar regolith, it has been impossible to view the internal structure of a particle without fracturing it or slicing it open. The X-ray ultramicroscope now enables scientists to do this. Originally developed at the Commonwealth Scientific and Industrial Research Organization (CSIRO) in Australia, XuM utilizes the divergent beams of X-rays generated in a scanning electron microscope (SEM) when the electron beam is focused onto a piece of platinum. These X-rays then pass through a lunar dust particle and onto an X-ray detector. Unlike many other microscopy techniques, this method of imaging does not require any focusing optics – the entire XuM image is always in focus – and the resolution, which can be better than 300 nanometers, depends on the size of the X-ray source. This means that for the first time, the entire internal structure of a lunar particle can be imaged with the particle still intact.

"Combining these new X-ray images with the corresponding secondary electron micrographs has allowed us, for the first time, to view the internal and external structure of the same particle," says Christopher Kiely, a professor of materials science and engineering and director of Lehigh's Nanocharacterization Laboratory. "This gives us a much fuller understanding of a particle's morphology. For example, glassy particles that often appeared smooth on the outside were found to contain a myriad of pores, far more than we expected."

The XuM's ability to take a sequential series of images while rotating the sample through 360 degrees yields a more global view of the internal structure of a particle and can help prevent erroneous conclusions being drawn from a single flat 2-D projection image. For example, a platelike inclusion could be mistakenly identified as a needlelike feature when viewed 'edge-on' in a single 2-D projection image.

Sequential imaging also enables rotational movies to be made, which provides a fascinating 3-D view of a particle's internal structure.



SEM and XuM images of a rodlike particle of lunar soil (top) and of a lunar agglutinate particle (bottom).

As part of Apollo 11's 40th-anniversary celebrations in July 2009, a collection of XuM and SEM micrographs, together with SEM stereoimages, was displayed in the Smithsonian Air and Space Museum in Washington, D.C. Carol Kiely presented the latest XuM/SEM results at the 41st Lunar and Planetary Science Conference in March.

The greening of multihop sensors

Wireless sensor networks (WSNs) are indispensable to modern life. They monitor the temperature and depth of permafrost in the Swiss Alps, regulate traffic on highways and make it possible to track a person’s pulse rate and other vital signals remotely.

In a WSN, battery-powered nodes containing radio transceivers and CPUs are embedded in the environment to sense and process data and transmit it to a base station, where data is interpreted and a response determined. Data can be transmitted from each node directly to the base station or along a chain of nodes to the base station, in what is called a “multihop” topology.

A multihop WSN, says Cheng, should use as little energy to transmit as much data as possible.

The batteries that power WSN nodes, says Liang Cheng, consume a growing amount of energy, much of which could be saved by optimizing a network’s configuration.

Cheng, an associate professor of computer science and engineering, is principal investigator in an NSF-funded project to develop smarter, more energy-efficient topologies for multihop wireless networks, including WSNs.

“Topology control,” says Cheng, “involves placing and connecting WSN nodes in strategic locations with optimal powers so that total energy consumption – the energy required to do the computation and to transmit data – is minimized without affecting performance.”

> *“We want to see if we can reduce the amount of data transmitted to the base station by determining which data is vital.”*
>
> – Liang Cheng

About 80 percent of the energy consumed by a WSN, says Cheng, is used for data transmission. The remainder is used for data processing by nodes in the network.

“We want to see if we can reduce the amount of data transmitted to the base station by determining which data is vital and needs to be transmitted, and which is not. If you are trying to transmit too much data, you consume too much energy.

“To make this determination, more data processing has to be done by the nodes. The overall goal is to transmit as much data using as little energy as possible in a multihop network with reduced interference and higher capacity in the presence of multipath fading, link failures, high error rates and many other radio irregularities.”

In another NSF project, Cheng is collaborating with Sibel Pamukcu, professor of civil and environmental engineering, to develop WSNs that identify the properties of soil and other subsurface media while monitoring landslides, chemical spills and other geo-events, and the direction and flow rate of spills.

A wired sensor network can sense only those events occurring in the areas local to the fibers connecting the network, says Cheng, but a WSN is not similarly constrained.

“One of the questions we’re hoping to answer is how far apart the sensors can be and still yield useful data.”

The efficient capture of CO_2 from power plants

Lehigh’s Energy Research Center (ERC) has developed a variety of technologies that improve the operating efficiency of power plants while reducing emissions of toxic substances and greenhouse gases.

Recently, the ERC received a DOE grant to develop methods of recovering and reusing heat generated by the carbon-dioxide (CO_2) compression process in a carbon capture and sequestration (CCS) system.

A CCS system makes it possible to generate electric power from coal without emitting significant amounts of CO_2 to the atmosphere. The system separates CO_2 from power-plant flue gas and compresses the CO_2 to high pressure. The compressed CO_2 can be transported by pipeline and is now used to help extract oil from underground reservoirs in a process known as enhanced oil recovery. Scientists are also evaluating the feasibility of injecting compressed CO_2 below the earth’s surface into saline aquifers whose geological features would sequester, or store, the CO_2.

The goal of the current project, says ERC director Edward Levy, is to recover heat that is generated when CO_2 is compressed and to use that heat to improve the efficiency of the power plant’s operation. The ERC is developing computational models of the methods used to capture and compress CO_2 and estimating the increases in efficiency that will result from each.

“It requires a tremendous amount of pressure, about 2,200 pounds per square inch or close to 150 atmospheres, to compress CO_2 to a supercritical state,” says Levy. “In the compression process, CO_2 heats up, creating the potential for heat to be recovered and used beneficially within the power plant.

“All carbon capture schemes reduce power plant efficiency and increase the cost of generating electricity. We’re trying to mitigate this. We’re looking at different types of compressors to see how much heat can be recovered and what we can do with this heat to improve power plant efficiency.”

The ERC has conducted other research projects that promoted the reduction of carbon emissions. One involved the recovery of water from flue gas and another removed water from high-moisture coals. Both resulted in improvements in power plant efficiency and reduction in the rates of CO_2 formation.

The project is funded through DOE’s National Energy Technology Laboratory.

A smart wheelchair with laser vision

Disability, John Spletzer believes, should pose no obstacle to mobility.

A blind person may not be able to see or a paraplegic to walk, but each can access technology that restores their ability to interact with their environment.

Spletzer, an associate professor of computer science and engineering, recently received a five-year CAREER Award from NSF to develop a robotic wheelchair that navigates on its own, with no human guidance, through a city.

Armed with high-fidelity LIDAR (light detection and ranging) lasers and detailed maps, the "smart" wheelchair avoids stationary objects like parking meters and light poles as well as "random events" like pedestrians and bicyclists. It transports users who may not be able to see or walk to doctors' appointments, the pharmacy and the grocery store.

Spletzer and his students have taken a cue from Google Street View, which allows users to take virtual tours of cities by looking at thousands of stored images.

"We're making similar maps that are useful for robots, not people," he says. "Robots respond to different cues than humans do. People see the real world and all its details. Robots using lasers recognize objects that reduce to an exact point and are easy to track."

Spletzer's students drive through sections of a city taking laser photos to make a hi-fi 3-D map of the environment. The map is downloaded to the robotic wheelchair, which can then navigate that environment, halfway in the real world, halfway in the virtual world.

"The robot identifies landmarks – trees, poles, building faces and corners – in the real world and looks for them in the laser map," says Spletzer. "Once it finds them, it will be able to accurately estimate its position in the real world. It doesn't need GPS, because of the accuracy of the server vehicle maps and because of the LIDARs."

The robotic wheelchair has traversed a 1-km route and arrived at its destination to within an accuracy of 20 cm. Meanwhile, says Spletzer, the robot learns from experience by comparing new objects it sees in the environment with images in its database.

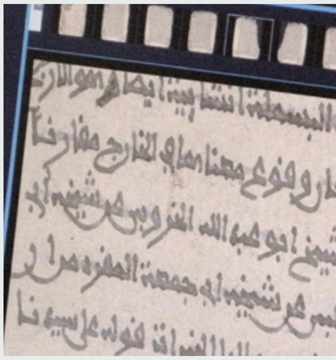
Robots, says Spletzer, respond to different cues than do humans.

An automated boost for military intelligence

What happens when soldiers capture documents written in a language they don't speak and a script they can't read? Are the materials exploited for intelligence value or stored unread?

Too often, it is a case of too many documents and too few translators. The American military has captured several million documents in Iraq and Afghanistan, but fewer than 3 percent have been evaluated, all by humans with little help from computers.

Henry Baird and Daniel Lopresti, professors of computer science and engineering, urged DARPA several years ago to fund research to develop faster, more computerized document-analysis techniques to help intelligence agencies.



The result was the MADCAT (Multilingual Automatic Document Classification, Analysis and Translation) project, in which Baird and Lopresti participated. Its purpose was to use computers to convert foreign-language text images into English transcripts, and it has made impressive progress in recognizing Arabic handwriting.

The Lehigh team made the case for a second DARPA undertaking, the Document Analysis and Exploitation (DAE) project, recently approved by Congress. In this project, Baird, Lopresti and Prof. Hank Korth of computer science and engineering are collaborating with BBN Technologies to improve the automation of document analysis and build a national resource for shared research and access.

Optical character recognition (OCR) can identify fonts in printed documents and enable searching and editing, says Baird, but is limited mostly to Western languages on clean documents.

"You can buy OCR machines for printed text, but not for handwriting. But no technology covers, for example, Arabic or the Ethiopian languages.

"Intelligence officers might get papers in handwritten Arabic that also contain maps, tables, drawings and photographs," says Baird. "We'd like to automate the analysis of these as well."

"We want to go beyond written text to meta-data," Lopresti says. "For example, if we can tell that documents appear to be written by the same author, that's incredibly valuable information."

Automating the analysis of documents involves scanning a document, converting images to computer-readable characters, and translating and evaluating content. Lehigh's researchers are focusing on the second step. They will exploit synergies of document layout analysis, character recognition, language modeling and parsing, link analysis, and semantic modeling. The result will be script- and language-independent, making it easily transferable to new applications.

INTERVIEW BY WILLIAM TAVANI • PHOTOGRAPHY BY JOHN KISH

MUTUAL REINFORCEMENT

WHY ENGINEERING IS DRIVING BIOMEDICAL RESEARCH

Vincent Forlenza is president of Becton, Dickinson and Co., a leading global medical technology company that manufactures and sells medical devices and diagnostics. Headquartered in New Jersey, BD employs 28,000 people in 50 countries and serves healthcare institutions, life science researchers, clinical laboratories and pharmaceutical companies. Forlenza oversees BD's three business segments (BD Medical, BD Diagnostics and BD Biosciences), as well as its International and Quality functions. A member of the advisory board of the P.C. Rossin College of Engineering and Applied Science, Forlenza earned a B.S. in chemical engineering from Lehigh in 1975 and an MBA from the University of Pennsylvania's Wharton School in 1980.

Q: ***Do you think research in biomedicine will spur a revolution in science and engineering as information technology (IT) has?***

A: IT and biomedicine have actually been reinforcing each other for several decades. Advances in life sciences depend on the ability to generate and sort through vast amounts of data. Progress in understanding genes, proteins and cells, for example, has been driven by advances in biology and enabled by IT. At BD, we make a cell sorter that can analyze 40,000 cells per second and generate 14 different data points on each. That kind of capability will continue to drive progress in biotechnology and biomedical engineering.

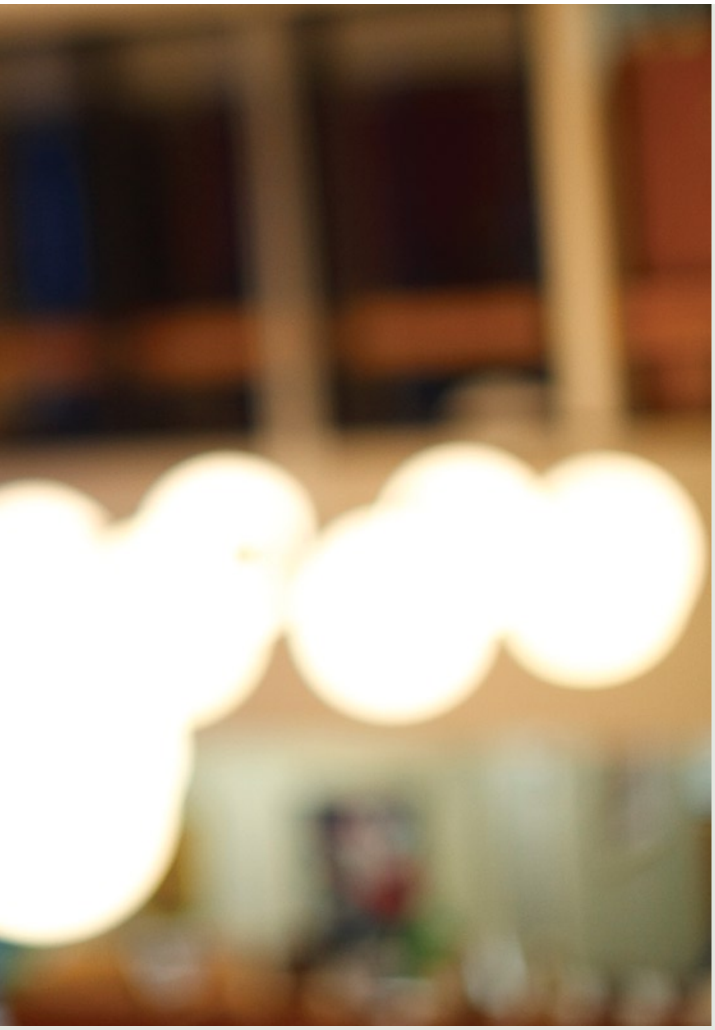
Q: ***The U.S. healthcare system has given rise to spectacular advances in medicine. How can health-related research support breakthrough progress and be affordable?***

A: You start by building cost-effectiveness into your goals. For example, new biological drugs are very expensive. Industry is working to personalize medicine by targeting drugs to patients who respond to them. Pharmaceutical companies have invested in new diagnostics that segment patients into responders and nonresponders. You test the patient before you administer the drug to see if he or she will respond.

Q: ***What are the next big research frontiers in medical technology? What role will engineers play?***

A: One trend is toward more biological medicines. Plants to produce these drugs can cost $500 million and will pose many process engineering challenges. I see an enormous need for engineers to solve these challenges and move therapeutic cells from research to practice.

In the area of diabetes management, there's a big effort to create an artificial pancreas. This



will require mechanical engineers to develop small pumps and chemical and materials engineers to make sensors.

Q: *How can research institutions and corporations collaborate in the field of medical technology?*

A: By understanding what each other does well, by grasping the realities of shared risk and shared rewards, and by aligning goals, practical relationships, leveraged opportunities and access between patients and technologies. Universities do the early research. They communicate how their areas of expertise can be leveraged. Companies communicate their needs. This provides the basis for collaboration.

For example, Lehigh and the Mayo Clinic are seeking to marry Lehigh's engineering know-how with Mayo's clinical expertise. (See story on page 10.) BD is supporting this; its role would be to provide internships for the Ph.D. program. Our goal is to train clinical entrepreneurs by building engineering requirements and an understanding of cost into the program right from the start.

Industry and academia, says Vincent Forlenza, must "grasp the realities of shared risk and shared rewards."

Q: *How can a university have the most impact on biomedical research?*

A: By leveraging its core competences, building centers of excellence and partnering with industry. For example, Lehigh does not have a medical school, but it has capabilities in engineering and it has a biomedical engineering program. Many life science problems involve materials science and engineering. Understanding the environment in which cells grow is a materials problem. Also, a tremendous amount of value for customers and for society is driven by continuous improvement. Engineering skills in manufacturing and process development are critical here. Industry needs people from schools like Lehigh who have the mentality that something can always be made better.

Q: *How does BD come up with new ideas for products and services?*

A: We look for large unmet healthcare needs that relate to one of our three core businesses—medical devices, diagnostics and biosciences. All of these businesses are generating new opportunities. We create business cases around these opportunities and we interact with our customers to discuss their needs. Then we make a judgment as to the areas where we think we can have the biggest impact.

Q: *Firms like yours rely on a pipeline of science and engineering talent. What are we not doing in K-12 and in universities that we ought to be doing to support this?*

A: We haven't done a good job in the early grades of linking challenges of the day, such as energy, to science. Going into science and engineering isn't viewed as being cool. We also need to attract more people into science teaching.

The people we hire at BD come from schools that prepare them well in the fundamentals. But more needs to be done in cross-functional areas. Students have to learn better communication and management skills and acquire an ability to work on cross-functional teams.

Q: *As an engineer and corporate leader, how does engineering thinking influence the decisions you make?*

A: Engineering teaches you to take complex problems, define them, identify their key variables, understand their relationships, and build models to quantify them. That's what you do in business all the time. Also, engineering teaches you to make a decision with the best approximation you can come up with. That's the real world. We do the best analysis we can, but at the end of the day we have to make a call.

Q: *What is your most memorable accomplishment at BD?*

A: Working with the Clinton Foundation to provide low-cost diagnostic testing for AIDS patients in poor countries. We started doing HIV testing in five countries. Now we're working in more than 35 countries and we've added TB testing. We give these countries special pricing, about 60 to 70 percent less than in the developed world. We teach people good laboratory practices, how to do testing and how to service their instruments. This is a common theme in the developing world. You can't just sell a product. You have to back it up with medical infrastructure.

Q: *Talk about BD's work in Africa and other regions of the developing world.*

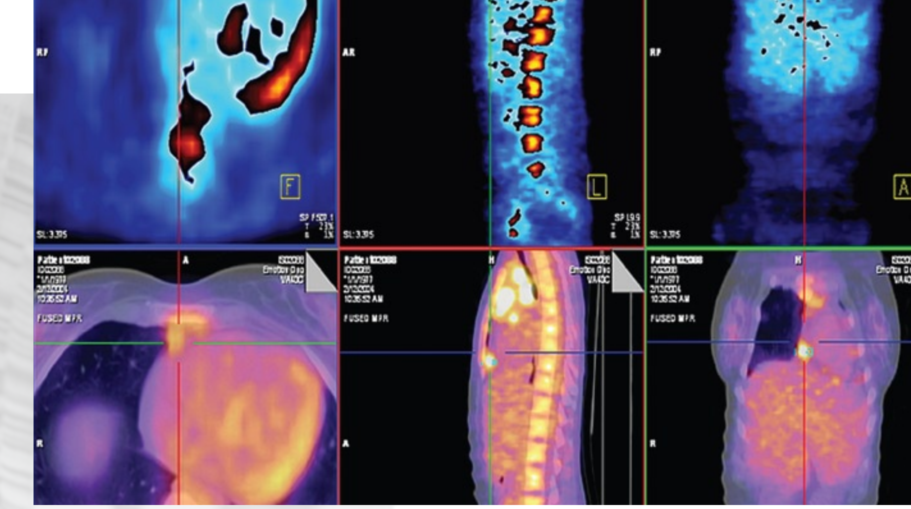
A: We saw that some people were reusing vaccination syringes, which causes HIV to spread. We worked with them to create very low-cost, auto-disabled syringes that you could use only once. In China, people were infusing drugs with a wing needle set. This is not a good device; the developed world uses IV catheters. We knew the Chinese market couldn't afford a regular catheter, so we developed a less-expensive hybrid device that has been incredibly successful.

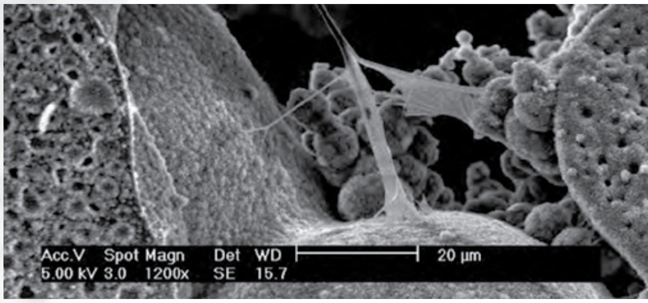
Q: *What attracted you to chemical engineering?*

A: In Engineering 1 at Lehigh, a professor from each engineering department taught a class to illustrate the kinds of problems each field solves. Prof. Fred Stein in chemical engineering demonstrated an analog computer model of a brewery. It was fascinating.

Q: *What is the most striking difference between the Lehigh you attended and Lehigh today?*

A: The integrated cross-college degree programs represent the single biggest difference. Departments were much more siloed when I was at Lehigh. You didn't have the collaboration across colleges. Lehigh has carved out a leadership position in this area and is attracting great students.





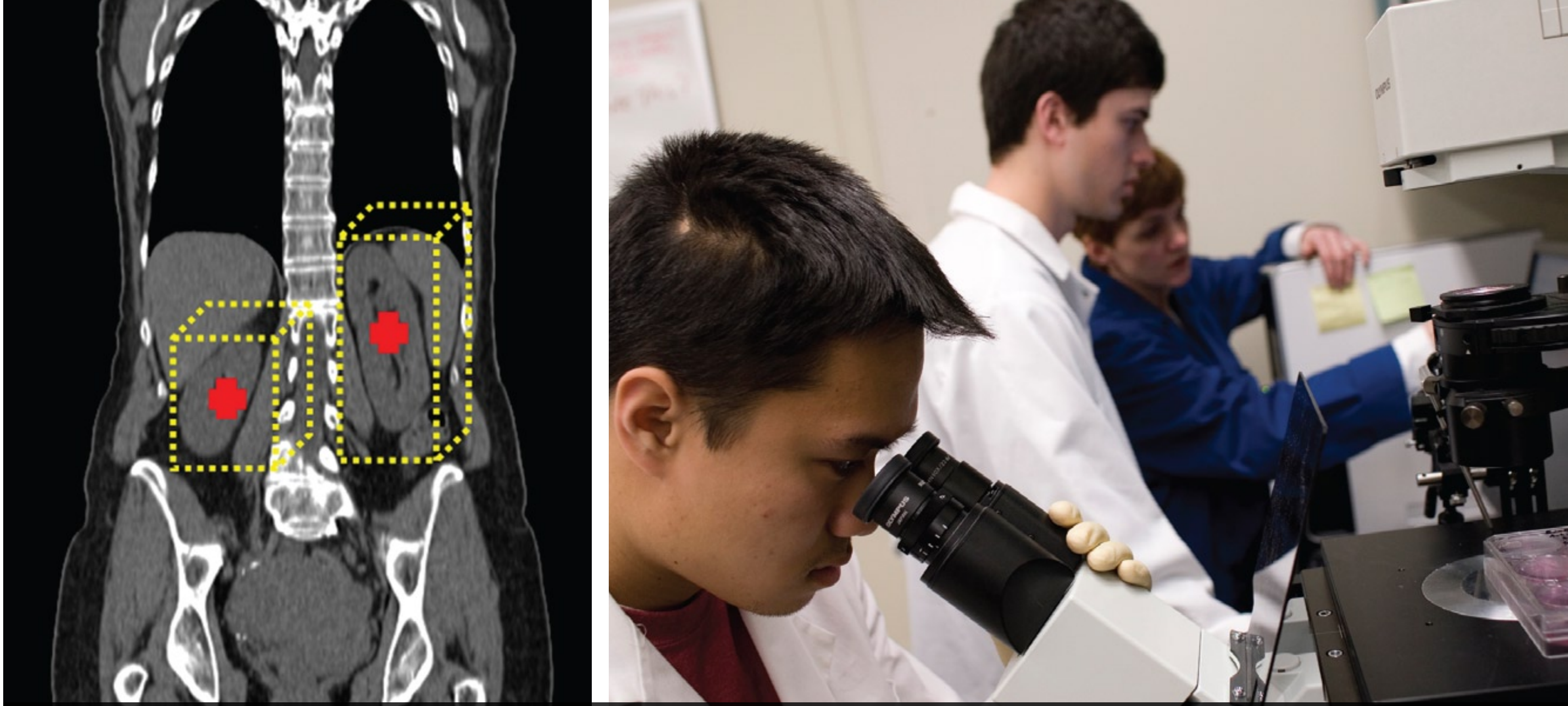
ENGINEERING AFFORDABLE MEDICINE

Lehigh and the Mayo Clinic are collaborating to make medical care more affordable and accessible. Researchers are focusing their attention on medical systems engineering, integrated devices and monitoring, and emerging biomedical materials.

The politics of healthcare may be impossible to predict, but one trend in medicine seems certain to gain momentum in the 21st century: Engineers working with biologists and physicians will develop new therapies, new devices and new diagnostic tools that improve the quality of life while giving people more control over their medical choices.

Indeed, says Anand Jagota, considering the potential benefits, engineers are compelled to expand the role they play in medicine.

"The huge expense of healthcare in the United States is unsustainable and is a drag on the economy," says Jagota, a professor of chemical engineering who directs Lehigh's



Glass bone (left) and other new materials, combined with computer-generated image analysis (top left, above) and wireless technology, exemplify how engineering influences medicine.

bioengineering program. "This is due partly to the system and partly to tremendous inefficiencies in healthcare delivery itself.

"Engineers cannot necessarily reform the system, but we can help make the delivery of healthcare cheaper, simpler and much more efficient, and we have an obligation to try to do so."

Jagota is taking the lead in a collaboration between Lehigh and the Mayo Clinic in Rochester, Minn., whose goal is bold if not breathtaking: To help bring about a revolution in medical care that parallels the metamorphosis of agriculture and manufacturing in the 20th century.

The research and educational partnership counts more than three dozen participants. Key players at Mayo include Gary Sieck, vice dean for research and chair of the physiology and biomedical engineering department, and Michael Yaszemski, chair of the division of spine surgery in the orthopedic surgery department. The team at Lehigh includes Mayuresh Kothare, professor of chemical engineering, and Filbert Bartoli, department chair of electrical and computer engineering.

During the last century, say the researchers, agriculture and manufacturing evolved from "diverse, small-scale and independent entities to coordinated and efficient integrated systems" producing many times more goods and services with a small fraction of the previous work force. Medical care today is ripe for a similar transformation in accessibility, affordability and efficiency – if engineering principles and technological advances are applied systematically across modern medicine's broad and diverse landscape.

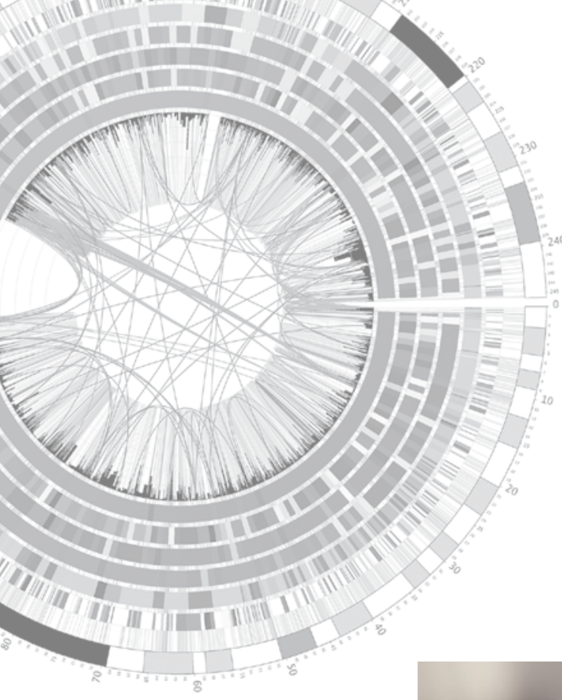
A THREE-PRONGED APPROACH

Researchers from Lehigh and Mayo are working on projects in three categories: medical systems engineering, integrated devices and monitoring, and emerging medical materials. Advances in these areas, the researchers say, promise to have a significant impact on several aspects of future medical care.

> ***"Engineers can help make the delivery of healthcare much more efficient, and we have an obligation to try to do so."***
>
> – Anand Jagota

Imagine, for example, taking cell phones and other wireless mobile gadgets and fitting them with biocompatible sensors and optical attachments that monitor the body's vital signals as people work, play and sleep. These new devices will alert users, and the healthcare providers in a user's network, when a trip to the hospital or clinic is in order. They will also house medical histories and records. In the process, they will decentralize medical care, says the Lehigh-Mayo team, by extending diagnosis and treatment beyond hospitals and clinics into aspects of a patient's daily life.

On another front, new devices and software will enable patients to "self-administer" many of the monitoring, therapeutic and drug-delivery functions that specialists now do, again cutting costs. Advances in understanding the human genome will allow doctors to personalize treatment. Microfluidic devices will enable "point-of-care" diagnoses that eliminate the need for samples to be sent to labs. Intuition born of professional



A circular genome map (above) shows genetic material shared between humans and other species. Glass bone developed by Lehigh researchers (right) is porous at both the nano and macro scales. A light micrograph (facing page) shows invasive cervical carcinoma.

experience will still be critical, but more and more medical decisions will be assisted by precise measurements interpreted by computers that learn from vast medical information databases.

Simplification, automation and miniaturization, say the researchers, will result in devices that cut costs by allowing expensive medical procedures to be moved away from specialized facilities requiring highly trained operators to doctors' offices and eventually to home care.

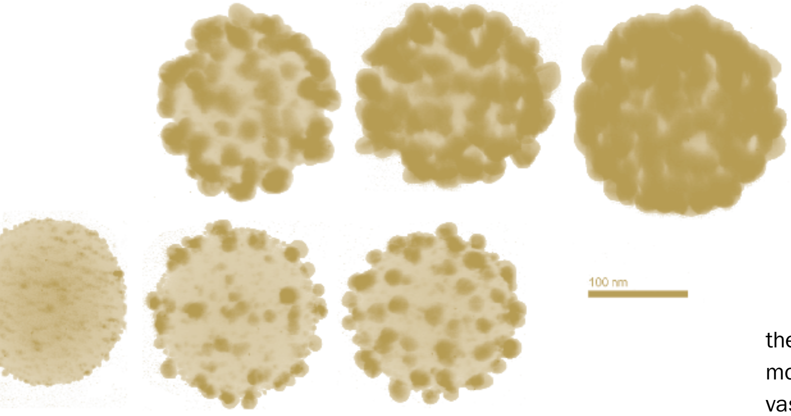
Meanwhile, new materials will lend greater biocompatibility to artificial organs and synthetic tissue. Coupled with advances in bioelectronics and biophotonics, for example, a new generation of microchips could be developed that, when implanted in the brain or spinal column, will rewire nerve cells, rejoin synapses and reconnect nerve signals to muscles. Similarly, implanted microdevices will achieve "as-needed drug delivery" by, for example, triggering a surge of insulin when glucose levels rise.

Critical to all three of these areas, say the Lehigh-Mayo researchers, and critical to the overall drive to make medical care more affordable with technology, is systems engineering.

"In the future healthcare system," the researchers believe, "constant monitoring of patients will produce vast data sets for new clinical research studies. It will enable early identification of the onset of disease and greater quality and duration of life outside managed-care facilities.

"Many innovations will be required, such as novel, unobtrusive sensors; power-efficient, small-form-factor data-acquisition, storage, and analysis units; and power-efficient, high-reliability, high-availability, secure communications and networking solutions. This wealth of challenges opens exciting new opportunities for students in engineering and students in medicine."

The new partnership thus has an important educational component: Mayo students seeking the Ph.D. or M.D. in biomedical engineering will study at Lehigh to master engineering fundamentals and quantitative systems skills, while students in Lehigh's new bioengineering Ph.D. program (see page 23) will complete laboratory rotations or clinical internships at Mayo. These exchanges will give students an integrated biomedical and systems engineering perspective and enable them to develop the "essential technology framework for affordable medical care."



Latex particles (above) encapsulated with gold nanoparticles are being studied for their ability to perform diagnostic tests and to bind to and target cancer cells.

Making it harder for cancer cells to hide

Cervical cancer was once one of the most common causes of cancer death for American women. But death rates fell by 74 percent from 1955 to 1992 and, says the American Cancer Society, continue to drop about 4 percent a year, chiefly because of increased use of the Pap smear.

Nonetheless, it is estimated that over 4,000 American women will die of cervical cancer this year. And the disease is one of the leading causes of death in middle-aged women in the developing world.

Now, a new computer-assisted visual interactive recognition system developed by a research team led by Xiaolei Huang may lead to a more cost-effective method of detecting cervical cancer in its early stages.

The Lehigh-Mayo collaboration is a key element of the emerging Lehigh Biotech Cluster, a comprehensive initiative designed to support the efforts of biomedical researchers and leverage capabilities in advanced materials, optical technologies and systems engineering.

A LOGICAL MERGING OF INTERESTS

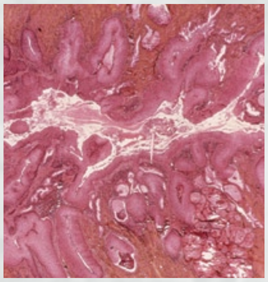
The Mayo Clinic enjoys renown not only for the quality of medical care it delivers but also for its efforts to reduce the cost of its services. President Barack Obama has praised Mayo for offering “the best quality and lowest cost of just about any healthcare system in the country” and has urged other providers to “learn from what Mayo is doing.” Journalists and bloggers have joined the National Academy of Engineering in lauding Mayo’s commitments to “patient-first medicine” and “team medicine.”

Lehigh in recent years has forged research partnerships with hospitals, medical schools, and medical technology and drug companies. These include the Johns Hopkins University School of Medicine, the Lehigh Valley Hospital, Merck and Co. Inc., Olympus, B. Braun, and Becton, Dickinson and Co. (BD). In 2002, with support from NSF, Lehigh launched an undergraduate bioengineering program (see page 22) with concentrations in cell and tissue engineering, biopharmaceuticals, and bioelectronics/photonics.

In 2007, to coordinate research efforts in diagnostic and therapeutic technologies for affordable medicine, Lehigh’s board of trustees approved the Biotech Cluster. The endeavor is part of the university’s Healthcare Initiative, which is a centerpiece of Lehigh’s 10-year strategic plan. A specific plan has been developed to establish a state-of-the-art facility to house the Biotech Cluster and

A complementary test to the Pap smear is the cervigram, a digital photo of the cervix. To highlight abnormal tissue, a weak solution of acetic acid is applied. Upon contact with the acid, all forms of precancerous tissue exhibit some degree of opacity, or aceto-whiteness. Various patterns signaling cervical lesion, such as vasculature, mosaicism and punctations, can appear inside the aceto-whitened region. The whitening starts to wear off after about five minutes.

A cervigram enables a medical professional to identify areas containing aceto-whitened tissue. This negates having to send out samples for analysis, which is important when access to wet lab facilities is limited or nonexistent. A cervigram can also be transmitted via the Internet to a professional at a remote site for interpretation.



“Recognizing aceto-whitened areas and other abnormal visual patterns, however, is not as easy as you might think,” says Huang, the P.C. Rossin Assistant Professor of computer science and engineering. “Every patient is different, and the conditions under which images are taken may vary. Our aim is to develop a software system that will facilitate the recognition process and reduce the number of false-positive and false-negative results.”

Such a system, says Huang, must be robust. A simplistic approach might identify pixels of a certain color or intensity and highlight these as affected areas. This would be error-prone as pixels in unrelated parts of the image might have similar characteristics due to glare or other imaging anomalies. Color and contrast ranges will not be the same in every image.

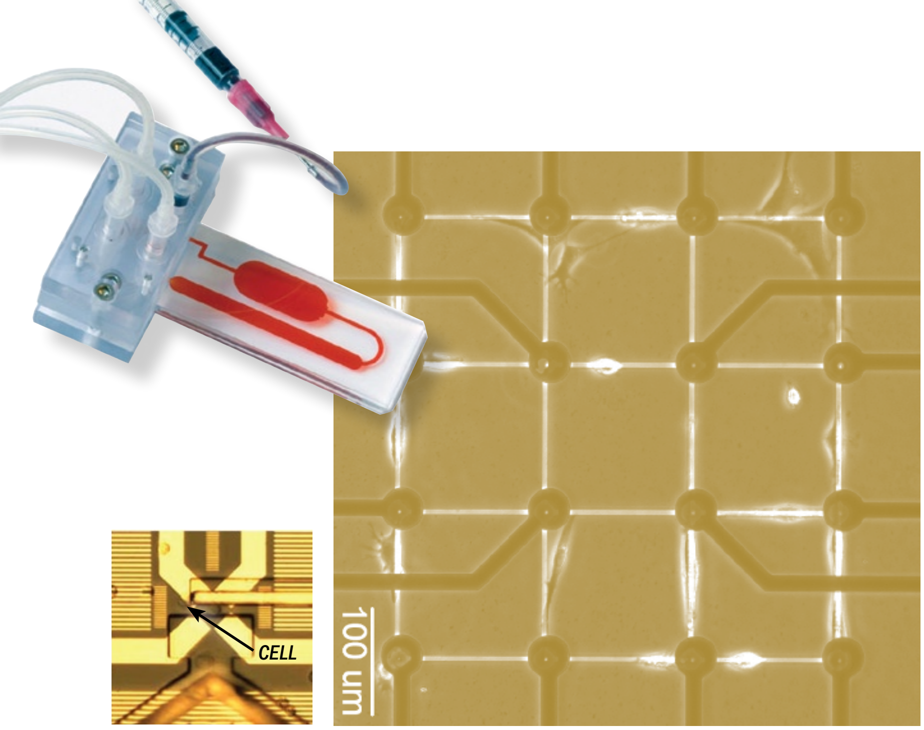
“In order to develop a reliable cervigram analysis system,” says Huang, “the texture, size and relative geometry of regions must also be considered.”

Huang’s system combines data derived from images annotated and analyzed by trained medical professionals with computer learning software to reduce false-positive readings. The reliability of the system depends on the number of annotated images used. To help Huang achieve her goal, the National Library of Medicine (NLM) and the National Cancer Institute have given her team access to more than 100,000 anonymous cervigrams and their corresponding diagnostic notes.

Although she is only in the second year of her project, Huang’s software can already reliably identify aceto-whitened areas. Another goal of the project is to enable users to retrieve similar cervigrams, along with diagnostic comments from the NLM archive, via a Web connection. This may help medical personnel who must grade cervical lesions and decide what treatment to take.

“We hope to be able to extend this methodology to other fields of imaging diagnostics such as the analysis of mammograms,” says Huang.

Huang is working with Profs. Daniel Lopresti and Gang Tan in Lehigh’s department of computer science and engineering; George Nagy of Rensselaer Polytechnic Institute; and Dr. Joseph Patruno of the department of obstetrics and gynecology at Lehigh Valley Hospital in Allentown. The work is funded by NSF.



A hand-held HIV diagnostic device (top left; see page 18). A microelectrode array chip (above) cultures hypothalamic neurons from mice, while dielectrophoretic quadrupole electrodes (above left) trap and compress a cell.

Lehigh materials scientist Sabrina Jedlicka (above) and mechanical engineer John Coulter modify nanoscale substrates with protein-derived peptides to promote the adhesion and differentiation of adult stem cells. Vibro-acoustography (facing page, left column) produces speckle-free images of tissues and improves the characterization of the tissues' material properties.

create space for Lehigh's biomedical researchers and for collaborative projects with Mayo. The initiative also calls for a major expansion of the bioengineering faculty, the appointment of endowed chairs in health and the construction of user facilities devoted to cell-tissue cultures, imaging and characterization, device microfabrication, and genomics and proteomics.

Lehigh's areas of expertise are well-suited to the needs of advanced biomedical research. The university's spectroscopy and microscopy facilities are world-renowned for their ability to characterize the properties and behaviors of materials at the nanoscale. The newly restructured Emulsion Polymers Institute has first-class labs for synthesizing and characterizing polymers and colloids. The Center for Optical Technologies and Sherman Fairchild Center for Solid-State Studies contain labs that are ideal for the fabrication of microelectronic devices capable of sensing and manipulating cells, molecules and nanoparticles.

Biomedical research efforts now underway at Lehigh and at Mayo are highly complementary. At Lehigh, computer scientists are automating the analysis of MRIs and other medical images with novel computational and data-processing tools. Chemical engineers are developing nanomaterial hybrids of DNA with carbon nanotubes, while chemists are sequencing single DNA molecules with magnetic "tweezers" using massively parallel dynamic force spectroscopy. Electrical engineers are applying bioMEMS (microelectromechanical systems) to study lung cells and, separately, developing arrays of microelectrodes to monitor electrical activity in neuronal networks. Physicists use laser "tweezers" to manipulate and study cells, and materials scientists and mechanical engineers are learning to control the differentiation of adult stem cells.

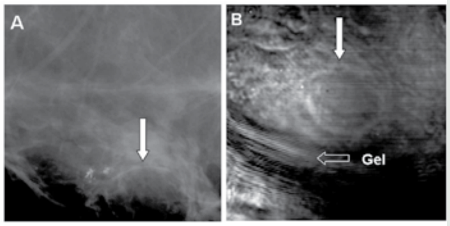
At Mayo, a team of biomedical engineers is developing wearable monitors to gather patient data for studies in endocrinology and obesity, as well as orthopedics and neurology. Wireless devices communicating with the monitors will process data and transfer it to an upstream network. The project requires solving, and integrating, issues related to the flow and analysis of information, the reliability of data, the detection of anomalies, and the privacy and security of data traversing through a network. The Mayo group is collaborating with an electrical engineer at Lehigh (see page 2) who has expertise in wireless communications networks.

UBIQUITOUS, 24/7 CARE

Solving challenges like these, say the Lehigh-Mayo researchers, will enable healthcare networks to reach patients in any location at any time, thus cutting costs by reducing patient travel times and hospital visits.

In one proposed collaboration, Mayo's Sieck and Lehigh's Kothare will investigate the implantation of chips and microdevices that could restore function to patients with Parkinson's disease, epilepsy, cerebral palsy and other neurodegenerative conditions. The issues involved are deep-brain stimulation, brain-computer interfaces, computational modeling and control theory. Under the educational component of the Lehigh-Mayo partnership, a Mayo student would study control theory at Lehigh while a Lehigh student would learn at Mayo how to apply control theory to patients undergoing neuro-rehabilitation therapy.

In another proposed joint project, Mayo researchers are exploring vibro-acoustography, an imaging method used in radiology that produces speckle-free images of tissues while offering a low-cost alternative to magnetic resonance imaging (MRI). Mechanical engineers at Lehigh will contribute expertise in large-scale numerical analysis, including finite element analysis, which clarifies the results of lab experiments by improving the characterization of the material properties of biological tissues. Finite element analysis, say the researchers, "can provide valuable insights into the mechanical response of tissues that are unobtainable by any other technique."



The overall goal of all the Lehigh-Mayo partnership goes beyond developing new devices, systems and therapies to propose a fundamentally new approach to medical care.

"The discoveries in biology in the last half-century," says Jagota, "have changed the way we look at the world. Now it's incumbent on us to develop systems that can handle the complexity of biological processes and generate efficiencies."

Software illuminates the inner workings of the human genome

The Human Genome Project, says Stefan Maas, provided an unprecedented understanding of the body's genes while raising questions about how complexity and diversity arise in humans.

The approximately 30,000 genes discovered in the human genome, says Maas, a biological sciences professor in Lehigh's College of Arts and Sciences, are far fewer than the 50,000 to 140,000 scientists had expected. Some simpler organisms have more genes than do humans. The rice genome, for example, contains 50,000 genes.

This lack of correlation between genome size and complexity suggests other phenomena contribute to complexity and diversity in humans. Maas and Daniel Lopresti, a professor of computer science and engineering, have studied one of these phenomena, RNA editing, for four years.

RNA editing, says Maas, includes a variety of mechanisms by which gene sequences are altered after DNA is transcribed into RNA and before RNA is translated to the proteins that determine an organism's structural, enzymatic and regulatory functions. The most important of these mechanisms involves the modification of single nucleotides, the molecules that connect to form the structural units of RNA and DNA.

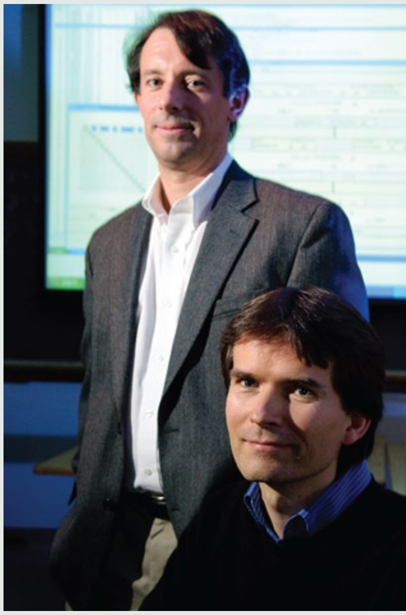
The human genome contains 3.4 billion nucleotides. Modifications in them can cause changes to the amino acids in the proteins that are synthesized, which can lead in turn to an alteration of protein function. Thus, says Maas, RNA editing yields a potentially exponential increase in the number of gene products that can be generated from a single gene — and a staggering volume of information to analyze.

"Only by examining all RNA sequences," says Maas, "can you determine how much RNA editing occurs in the human genome, how much diversity it generates and how many genes are subject to RNA editing."

"Searching for RNA editing sites," says Lopresti, "is like looking for a needle in a gigantic haystack. You cannot do this manually, and you cannot guess where editing sites are going to be."

Lopresti has developed RNA Editing Dataflow System (REDS), a software program that identifies discrepancies that arise when DNA is transcribed into RNA, and eliminates those that occur for reasons other than RNA editing. Maas and his students examine suspected editing sites, isolating DNA and RNA from brain and other tissues and amplifying the sequences of both to determine whether editing has occurred.

"We then take the data we obtain from the lab and feed it to our software to improve on our predictions," says Maas. "The more data we obtain, the more our predictions can be based on machine learning."


Lopresti and Maas study RNA editing.

Maas and Lopresti are most interested in a type of editing known as A-to-I editing, which can cause amino acid changes in protein products. These changes have been implicated in epilepsy, depression and other illnesses.

The researchers also examine RNA folding and the correlation between folding structures and the incidence of RNA editing. RNA's structure is in constant flux, like strands of spaghetti that fold and loop over each other. It is at these double-stranded regions where editing is most likely to occur.

Lopresti has written an algorithm that attempts to deduce RNA's structure from its sequence and to determine, based on that structure, the location of likely editing sites.

"We've developed fast computational techniques that simulate folding in order to confirm the structures that are right for editing," he says. "Our algorithm ranks all potential editing sites based on predicted folding because of structure."

"Each gene we find in which RNA editing occurs," says Maas, "opens a new chapter about the significance of editing, the pathways that are involved and potential diseases that result from RNA editing deficiency or overactivity."

The product of five years of design and testing, Grenestedt's streamliner set a new U.S. land speed record for 125-cc-engine vehicles in Utah last September.

JAN AND AGNETA ISIDORSSON

A LAND-SPEED RECORD

SMALL ENGINES AND COMPOSITE MATERIALS REACH A NEW LEVEL AT BONNEVILLE.

Joachim Grenestedt's enclosed streamlined motorcycle seemed ill-suited to the rigors of racing.

The streamliner looked like a miniature airplane with no wings. To fit inside its tiny cockpit, Grenestedt, who is 6 feet 4 inches tall, had to lie almost flat on his back. After strapping safety restraints against his body, arms, ankles, knees and thighs, he could barely move his left foot to change gears. The vehicle's low center of gravity made it wobbly at low speeds, and steering was counterintuitive: to go left, one had to first steer right, causing the streamliner to lean, and then steer left.

Last September, on the snow-white, level surface of the Bonneville Salt Flats in Utah, Grenestedt raced his streamliner to a speed of 133.165 miles per hour, shattering the previous U.S. land speed record of 125.594 mph for 125-cc engines running on gasoline.

"I felt many impressions," Grenestedt says of his dash across the desert. "New sounds, new smells, new feelings, new sights. There were too many impressions to sort out, because there was no blood running through my veins, just adrenaline."

Speed is Grenestedt's first engineering love. Composite materials run a close second. As a teenager, he built and raced remote-control boats. As director of Lehigh's Composites Laboratory, he has fashioned ships, airplanes and even the deck of his house out of carbon and glass fiber composites, often in the form of sandwich structures with honeycomb or foam cores.

Composite materials, says Grenestedt, a professor of mechanical engineering and mechanics, are strong, easy to shape, resistant to corrosion and efficient. Being lightweight, they boost speed.

The Bonneville Salt Flats is home to the Bonneville Speedway and many of the world's land speed records. Grenestedt traveled there in 2004, watched some runs and talked with drivers and engineers. After he read the rule book for land speed racing, he resolved to challenge the U.S. land speed record.

"I was looking for a new project," he says. "I had checked into drag racing, but its rules discouraged innovation. The rules for land speed racing have stringent requirements for safety, but impose few other restrictions. I did some calculations for aerodynamic drag, power and acceleration, and I saw that it should be possible to beat a number of records without spending a fortune on engines."

Grenestedt worked on the streamliner more than five years. Bill Maroun, a technician at Lehigh, helped with welding and accompanied him to Bonneville.

He had only a handful of opportunities to test-drive the racer.

"My first run with the bike was a few years before the race," he says. "I had mounted the wheels, but I hadn't yet installed the engine, brake or any other systems. I took the machine out on the street in front of our house and rolled it down a slope. My seven- and 10-year-old sons pulled on a long rope to stop me. I used training wheels to avoid falling over and damaging the fuselage.

"For my second test, I installed the engine and kept the training wheels. I really started to learn to drive the thing."

The next run, and the last before Bonneville, came in 2008 at the Maple Grove Raceway in Mohnton, Pa. There, Grenestedt revved the engine higher and completed a quarter-mile.

Contending with salt and wind

At Bonneville, Grenestedt completed shake-down runs of 75 mph and 100 mph, and tried out the parachute brake deployment to stop the streamliner. Just before stopping, he electrically deployed two skids, one on each side of the streamliner, for the vehicle to lean on.

"This was the first time I had pulled the brake 'chute. It felt like a gentle tug, with no hint of pulling to the side. The skids came out nicely and I was able to stop."

On his third and final shake-down run, Grenestedt reached 122 mph while contending with two new phenomena – the slippery salt surface and a light but steady crosswind.

"The streamliner was not nearly as stable as it had been on the asphalt at Maple Grove. I had new tires for Bonneville – high-speed slicks with a round cross section – whereas I had more square tires at Maple Grove. But I think the real difference was that the salt was more slippery than the asphalt.

"I also think the slight crosswind made it feel less stable. I had to lean into the wind but steer straight, which fights natural steering."

13,000 rpm and a new speed record

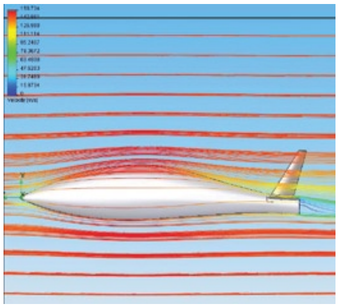
The 11-mile-long raceway at Bonneville contains a "timed mile" at its midway point. Drivers use the first five miles of the track to accelerate and the final five to slow to a stop. They repeat the process in the opposite direction, and their official time is determined by averaging the two speeds achieved over the timed mile.

"After my third trial run," Grenestedt says, "I mounted a smaller rear sprocket to get more speed for the same engine rpm. My first run on the 11-mile course went fine. The launch was good, the acceleration good, the engine temperature was high but not dangerously so.

"It was quite exciting seeing the speed creep up to 120, 123, 125, to the record of 126 and finally to 133. By this time, the engine was revving at 13,000 rpm, well past its peak power at about 11,800 rpm. I should have been able to go quite a bit faster if I had used an even smaller rear sprocket."

His pursuit of the land speed record, says Grenestedt, allowed him to tie together his favorite engineering themes.

"I enjoy carbon and glass fiber work, and I have a soft spot for two-stroke engines. And I love cramming myself into small, fast vehicles. I wouldn't feel comfortable driving a supersonic streamliner, but I felt great driving at the speeds I designed my streamliner for."



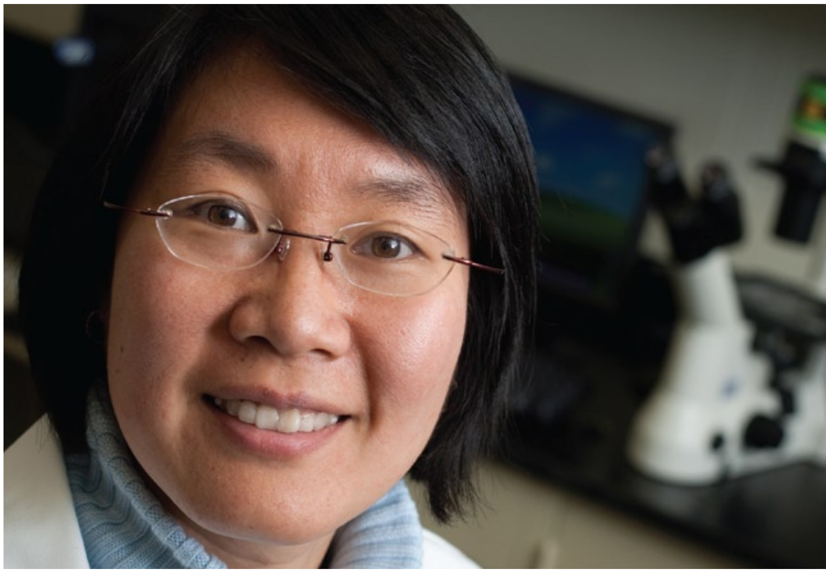
A computational fluid dynamic (CFD) analysis of the streamliner (above). Grenestedt's design (top) did not account for driver comfort.

Grenestedt has retired from land speed racing. He is now the adviser to Lehigh's Land Yacht Club. Several of his students have traveled to Lake Ivanpah, a dry lake in the California desert. There, last year, they watched a land yacht set a new world record – 126 mph – for wind-powered land speed racing.

Grenestedt won't disclose his plans. But his students have built a tire-testing rig and tried it out at Lake Ivanpah. And the club is converting an airplane glider into a high-speed land yacht.

"If I were a student today," he says, "nothing could keep me from getting involved in a project like this."

PHOTOGRAPHY BY KATE HOLT



Kenya's healthcare workers are dedicated, says Cheng, but subpar facilities may require her to reconfigure her diagnostic device.

In Africa, a point-of-care battle against AIDS

MORE THAN 400,000 CHILDREN A YEAR CONTRACT HIV IN SUB-SAHARAN AFRICA. XUANHONG CHENG CREATES HAND-HELD DEVICES THAT HELP TRACK THE VIRUS'S PROGRESS.

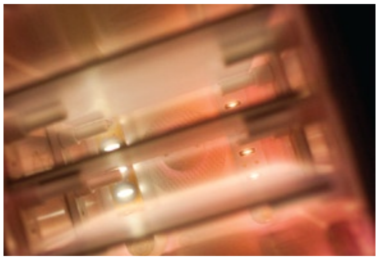
Medical science has not yet developed a cure or vaccination for AIDS or for the HIV virus that causes it, but efforts to combat the global AIDS epidemic appear to be having some effect.

According to UNAIDS (the Joint United Nations Program on HIV and AIDS) and the World Health Organization (WHO), the estimated number of new HIV infections reported annually has dropped 30 percent worldwide since it peaked at 3.5 million in 1996.

The number of people dying from AIDS-related diseases is also declining, the two organizations say. And new treatments are enabling persons with HIV to lead productive and, in many cases, long lives.

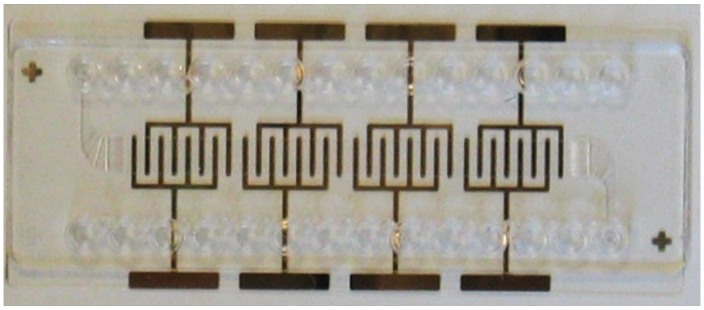
This encouraging news, says Xuanhong Cheng, is tempered by the tragedy of sub-Saharan Africa. Of the 33.4 million people in the world now coping with HIV, two-thirds live in sub-Saharan Africa. And more than 14 million children in the region, according to UNAIDS, have lost one or both parents to AIDS.

For Cheng, an assistant professor of materials science and engineering, one statistic stands out. More than 400,000 children each year are infected with HIV. The vast majority contract the virus through mother-to-child transmission, a phenomenon that occurs during pregnancy, labor, childbirth or breastfeeding. Preventing or decreasing the likelihood of mother-to-child transmission is a top priority of global health organizations.



Cheng's first device contains a chip (below) that uses microfluidic chromatography to separate cells from blood. An electrical current counts the cells.

HIV testing and diagnosis are critical to this effort. But in Kenya, to cite one example, an estimated 83 percent of the people with HIV remain undiagnosed because of the lack of resources in hospitals and clinics. To help overcome the shortage of facilities and staff in outlying areas, as well as difficulties in transportation, health officials are seeking to develop point-of-care diagnostics that eliminate the need to send blood samples and other specimens to laboratories for analysis. The goal is twofold: to determine if a child is infected with HIV and to monitor the progress of the disease, thus helping a doctor decide what level or type of treatment is necessary.



TRACKING THE PROGRESS OF HIV

Cheng is part of a research team that has developed a hand-held point-of-care diagnostic device that monitors the progression of HIV by measuring the concentration of lymphocytes – a type of white blood cell – that possess a CD4 receptor on their surface in a droplet of blood.

In an infected patient, the HIV virus attaches itself to a CD4 receptor and uses the cell to make copies of itself, completely damaging the cell in the process. Because CD4 cells help initiate the body's response to invading microorganisms, they are a vital component of the immune system. If they are destroyed, the immune system is compromised. A CD4 count in a healthy individual is around 1,000 cells per cubic millimeter of blood. Values below this level may indicate the early stages of the disease even though the patient might not show any symptoms. Counts below 200 are a sign that the immune system has been severely weakened and the patient is then classified as having AIDS.

This CD4-counting device that Cheng helped develop is now being made commercially by Daktari Diagnostics Inc., a company based in Cambridge, Mass., that was founded by Bill Rodriguez, a former professor at Harvard Medical School. The device uses microfluidic cell chromatography to isolate cells from a blood sample without having to add chemical reagents. A droplet of the patient's blood enters a tiny channel into an assay chamber whose walls contain antibodies that act like Velcro, capturing only the CD4+ lymphocytes. Everything else in the blood passes through. The chamber contains a simple electrical contact that is used to detect the number of captured cells.

A MISSION TO KENYA

Cheng's group is hoping to carry out a field test of the hand-held CD4-counting device later this year in Africa. In December 2009, to gain a better understanding of the conditions faced by African healthcare professionals, Cheng went on a weeklong fact-finding mission to Kenya. The trip was organized and funded by PATH, an international nonprofit organization dedicated to finding solutions to world health problems.

"To me, the use of this technology is straightforward, but there was no way of identifying potential problems without talking to Kenyan healthcare workers and seeing for myself the conditions in which they have to work," says Cheng.

In Kenya, there are several different grades of health facility ranging from major National Referral Hospitals to local healthcare centers and dispensaries. The larger and better-equipped hospitals are situated near urban centers such as Nairobi, Mombasa, Nakuru and Kisumu. In rural areas, patients have access only to small healthcare centers, dispensaries and mobile clinics, many of which do not have a full-time resident doctor.

During the first three days of her trip, Cheng visited the Mbagathi and Kiambu District hospitals, the Karuri Health Centre, the National Public Health Laboratory and the Kenya

Medical Research Institute (KEMRI) in Nairobi. On the fourth day she flew to Kisumu, a town in eastern Kenya.

"With the exception of KEMRI, laboratory facilities in Kenya are minimal, even in the large hospitals," says Cheng. "A lab is considered to be well-equipped if it has a microscope and a centrifuge. A major problem is that all the samples obtained from patients throughout the hospital, irrespective of the disease, are analyzed in the same room. Ventilation is often inadequate. This can lead to cross-contamination and to the spread of disease to the people who work there."

In addition, a stable electricity supply cannot be guaranteed and power, in many cases, is available only during the day. And the lack of air conditioning means that temperatures inside hospitals vary considerably from day to night. "This has serious implications for the use of our device as we use electrical measurements to obtain a CD4 cell count," says Cheng. "We may now have to introduce a self-calibrating system into our device so that it can be operated at different temperatures."

Funding for healthcare systems in Kenya has not increased for several years and hospitals are lucky if they have 60 percent of the required staff. Money for even the most basic of diagnostic testing is limited. All funding for point-of-care diagnostics would have to be obtained from outside charitable agencies.

AN AFFORDABLE BLOOD TEST FOR HIV

Despite these challenges, says Cheng, the healthcare workers she met were dedicated, often working long hours.

"One thing you notice is that the Kenyan people in general are always smiling," she says. "They seemed very pleased to see us and waved to us as our cars went by. The visit has made me even more determined to play a part in improving their level of health care."

Back at Lehigh, Cheng is working on a second hand-held point-of-care diagnostic device that will measure the concentration of HIV virus particles present in a blood sample.

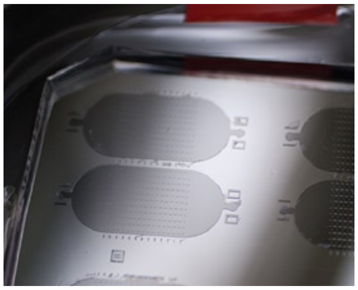
"HIV diagnosis in adults is simple," says Cheng. "You take a sample of blood or saliva and put it on a strip. If the blood contains HIV antibodies, the strip changes color and you know the patient is infected with the virus. Diagnosis in infants, however, is not as straightforward. A baby receives a lot of antibodies from its mother so the only way to confirm whether or not a baby has HIV is to detect the number of virus particles in the blood."

Currently, HIV viral loadings are measured using one of three proprietary commercial methods. All are based on nucleic acid amplification and all require state-of-the-art laboratory facilities that are prohibitively expensive and not available in developing countries.

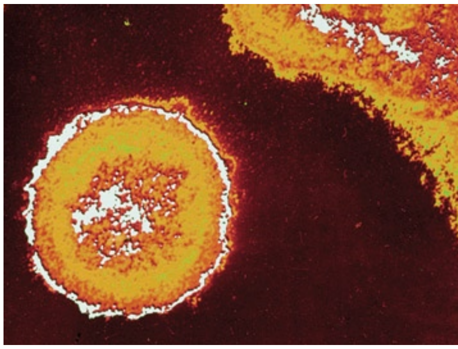
Cheng's second hand-held device, also based on microfluidic technology, will be more complicated than the CD4-counting device because HIV viruses are much smaller than CD4 cells and therefore more difficult to detect.

The new device will contain a prefiltration chamber designed to separate out viral particles, which are only 120 nm in diameter, from much larger particles such as red and white blood cells. The amount of blood required for this test is approximately 1 milliliter – considerably more than the single droplet required for the CD4-counting device. By passing this larger quantity of blood through the chamber, the concentration of viral particles is increased 1,000 times, which makes them easier to detect and leads to a more accurate measurement of concentration. The separated viral particles will then be impregnated into a nanoporous membrane that contains specific antibodies to which the viral particles will selectively adhere. The number of particles will be determined from the pressure differential across the membrane.

The hand-held CD4 counter Cheng helped develop would eliminate the need to test blood samples in labs. It could be field-tested later this year.



Designing this type of device requires expertise in several fields of materials engineering and biomedical science. Cheng is collaborating with Profs. Wojciech Misiolek and William Van Geertruyden of Lehigh's materials science and engineering department and with Dr. Timothy Friel, an infectious disease specialist at Lehigh Valley Hospital in Allentown, Pa. Daniel Ou-Yang, a professor of physics, is helping Cheng determine the feasibility of using optical techniques to measure viral concentrations.



"While both of these devices are designed for point-of-care diagnostics in developing countries, there is no reason why they can't be used in the U.S.," says Cheng. HIV patients are advised to check their viral loading every four months to monitor the effectiveness of their treatment regime. Cheng's devices could lead to a more cost-effective and accessible method of monitoring the disease.

PHOTOGRAPHY BY DOUGLAS BENEDICT

Matthew Havener '06 has helped Orthovita develop a bioactive composite material that facilitates human bone growth, along with a delivery system (below) that injects the material into the bone.

BIOENGINEERS TAKE

STUDENTS ARE MAKING THEIR MARK IN INDUSTRY AND GRADUATE SCHOOL.

Lehigh's undergraduate bioengineering program is one of the university's newest engineering majors and is quickly becoming one of its most popular.

Established in 2002 and accredited in 2008, the bioengineering program today enrolls more than 100 students. Alumni are enrolling in graduate school and taking jobs in the healthcare, biomedical, pharmaceutical, biomaterials and biotechnology industries.

The program seeks to prepare students for a field that is constantly changing, says its director, Anand Jagota.

"We are in the midst of a second wave of bioengineering, spurred by the maturation of the underlying cell and molecular biological sciences," says Jagota. "Cells and biochemical pathways are well understood, which gives engineers and physical scientists the basic knowledge and building blocks to develop new technologies, therapies, diagnostics and materials."

Lehigh's bioengineering students choose to specialize in one of three tracks. *Biopharmaceutical engineering* encompasses biochemistry and chemical engineering, exploring genomics, protein engineering, and drug synthesis and delivery. *Bioelectronics/biophotonics* emphasizes electrical engineering and physics with applications in biosensors, MEMs, biochips and optical technologies. *Cell and tissue engineering* straddles molecular and cell biology, materials science, mechanical engineering and electrical engineering.

Students are encouraged to take part in research projects and summer internships and are required to complete Lehigh's award-winning Integrated Product Development (IPD) program, in which interdisciplinary teams of students make and market new products for industrial sponsors.

Matthew Havener '06 was inspired by the bioengineering program to go into the field of biomaterials. Havener is now a research and development engineer for Orthovita, an orthobiologics and biosurgery company based in Malvern, Pa., that makes medical implants, synthetic bone grafts, surgical hemostats and bone cement, with a focus on orthopedics.

FLIGHT

Havener does early development work for new materials and conducts the tests that are required to obtain FDA (U.S. Food and Drug Administration) approval for new products. He recently helped develop a bone cement for vertebral compression fractures.

"The most beneficial part of Lehigh's bioengineering program for me was the research project I did with Prof. Jagota," says Havener. "It gave me something I could talk about passionately and intelligently in a job interview. It was also a lot of fun. As a result of this work, a paper I coauthored was published in *Langmuir*."

Steven Henry's research experience convinced the 2009 graduate to enroll in the University of Pennsylvania's doctoral program in bioengineering. At Penn, Henry and his adviser are trying to better understand how the human T cell, a cornerstone of the body's adaptive immune response, is able to navigate microenvironments.

At Lehigh, Henry worked with Profs. Richard Vinci and Walter Brown of the materials science and engineering department to investigate the mechanics involved in the puncture of a soft solid by a microneedle, which may one day be used to deliver drugs into patients with less pain than conventional hypodermic needles.

Bioactive glass used as a bone graft substitute.

"This experience was invaluable in shaping my thought processes as a young scientist and giving me an appreciation for what it means to be an educator both inside and outside the classroom," says Henry.

"My professors were instrumental in my decision to pursue my doctorate. I see myself working at the interface of both fields in a translational capacity, applying basic scientific principles to clinical or industrial ends or, conversely, using the needs of industry to motivate further fundamental research."

Michelle Cremeans '06 earned degrees in both bioengineering and integrated business and engineering (IBE) while participating in the IPD program and completing research projects. This variety of experiences helped her realize that, while bioengineering was a good theoretical match, dentistry would provide the greater human interaction that she desired.

Cremeans will graduate from Penn's School of Dental Medicine in May and pursue a one-year residency before going into private practice and teaching at the university level.

"The research I did at Lehigh, both in the IPD program and in my summer internships, was a very valuable and eye-opening experience," she says. "I was in the first class going through the bioengineering program and I think that the directors really let us have a say in how the classes were developed.

"The education that I received at Lehigh was amazing and I think that my critical thinking skills are far superior to those of some of my colleagues."

PH.D. PROGRAM HAS TWIN FOCUS

As interest in bioengineering has grown, so too have graduate programs at leading institutions. In the fall of 2009, Lehigh introduced M.S. and Ph.D. programs in bioengineering with emphases on cellular and biomolecular science and engineering.

Anand Jagota, who directs the program, says the growth in bioengineering programs across the nation and at Lehigh suggests that there will be more than enough applicants for the new graduate programs. And, he adds, the U.S. Department of Labor's Bureau of Labor Statistics recently reported that biomedical engineers are expected to have more rapid employment growth through 2014 than the average for job seekers in all other occupations.

"Biomedical engineers, particularly those with only a bachelor's degree, may face competition for jobs," Jagota says. "Unlike the case for many other engineering specialties, a graduate degree is recommended or required for many entry-level jobs in biomedical engineering."

Lehigh's graduate programs in bioengineering will train students to solve problems that require the application of interdisciplinary knowledge, says Jagota.

"We're looking to attract students with diverse academic backgrounds," says Jagota. "We are providing them with an integrated foundation in engineering, physical science and life science, especially at the molecular through cellular scale, with a strong appreciation of physiological context."

Jagota works with an oversight committee composed of faculty from the P.C. Rossin College of Engineering and Applied Science and the College of Arts and Sciences.

Particulate systems – “as much art as science, and fun to explore”

Gilchrist and his students study the behavior of particles in suspensions. Christopher Brunn '11 (below) tests solar cells coated with titania nanoparticles.

In a YouTube video, two barefoot young men run across a pool of white liquid and the crowd cheers. When they try to stand on the liquid, they sink. The crowd roars.

The white liquid – particles of corn starch suspended in water – is a complex fluid whose flow properties, unlike those of water or honey, are not described by a single constant value of viscosity. You can bounce a spoon off the surface of a bowl of this mixture, or allow the spoon to sink slowly, because the fluid sometimes behaves like a solid.

Flowing suspensions and their internal structures make James Gilchrist excited to come to work. Beyond tricks, he sees applications that could improve many areas of life.

“Some scientists wake up in the morning to try to cure cancer,” says Gilchrist, the P.C. Rossin Assistant Professor of chemical engineering. “I want to learn more about how particles interact in fluids.”

"Learning more about how particles interact in fluids can help us design platforms that detect HIV and cancer." – James Gilchrist

In Lehigh’s Laboratory for Particle Mixing and Self-Organization, Gilchrist and his colleagues have learned to measure the internal structure of flowing suspensions and to resolve nanoscale deviations in these suspensions by tracking the relative positions of micron-sized particles.

Predicting and controlling these deviations has enormous potential in a myriad of processes that involve suspensions. In mining, it could enable more efficient processing of waste sludge; in pharmaceuticals, it could reduce drug-production costs. In medicine, it could lead to simpler analyses of blood to detect HIV and cancer. Suspensions are also widely used in coatings. Gilchrist is working with one colleague on a coating that would improve the efficiency of solar cells.

“Particles in suspensions are usually positioned randomly when at rest,” says Gilchrist. “When suspensions flow, as blood does, they are no longer homogeneous and this results in fluids having strange properties when the concentration of solids is relatively high.”

In their experiments, Gilchrist and his students control suspensions as they transition from fluid to gel. Using confocal scanning microscopy, they observe the 3-D structure of nanoparticles. As they increase the nanoparticle concentration, the fluid turns to gel. When they electrostatically charge the suspension, it reverts to fluid.

“Other researchers have theorized as to what’s happening, but we are the first to do experiments that directly measure how particles in fluids interact to generate these unusual forces,” he says. “We want to learn more about the kinds of microstructures that give complex fluids like blood or waste products macroscopic properties.”

Gilchrist’s group analyzes suspensions flowing in microchannels that are roughly the size of a human hair. When the suspension is not flowing, they observe particles randomly dispersed everywhere. When the fluid is pushed through the channel, they watch the particles demix and migrate toward the channel center. This migration is a result of particles organizing themselves into clusters that dissipate stress in a nonuniform way. No one has measured the structures of these clusters until now. Gilchrist and his students, Changbao Gao and Bu Xu, can stop the flow, locate the position of every particle and determine their relationship to other particles.

Such information has the potential to improve blood analysis in HIV and cancer patients by controlling the blood flow so that sensors identifying AIDS and cancer cells actually come in contact with infected cells.

Gilchrist also collaborates with Prof. Nelson Tansu in the department of electrical and computer engineering on a DOE project to improve the lighting efficiency of light-emitting diodes (LEDs). Tansu creates high-efficiency LEDs; Gilchrist coats their surface with self-assembled microlens arrays to help extract light. Particles dispersed in a suspension organize when drawn into a thin film atop the LED. The resulting structure can enhance an LED’s overall performance by over 200 percent.

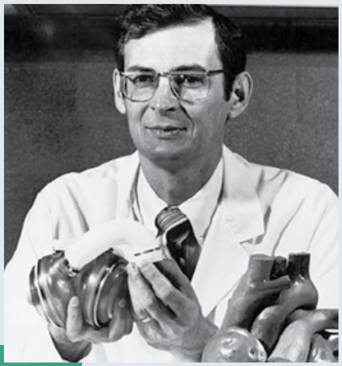
Gilchrist plans to continue studying the behavior of particulate systems.

“These systems behave in unpredictable ways. We want to develop an overarching theory that describes a broad range of suspension and granular flows. It’s as much art as science, which is part of what makes it fun to explore.”

Biotech and Biomedical Leadership

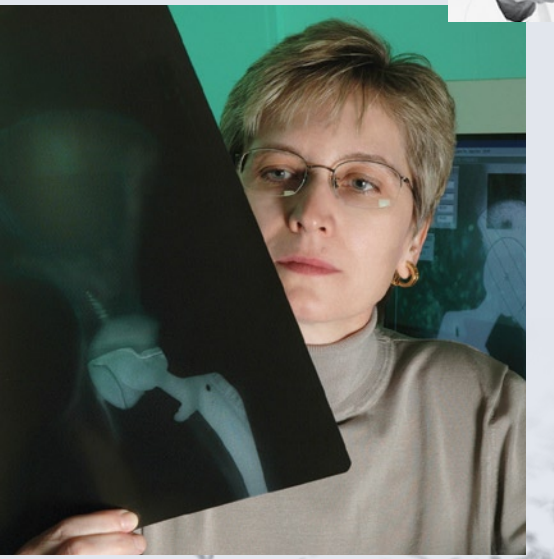
Over the years, many Lehigh engineers have led research and academic programs in biomedicine. A few examples:

In the 1970s, **William S. Pierce** '58 and his team at Penn State University's Hershey Medical Center designed and built the Pierce-Donachy Ventricular Assist Device, which was designated an International Historic Mechanical Engineering Landmark by ASME (the American Society of Mechanical Engineers) in 1990.



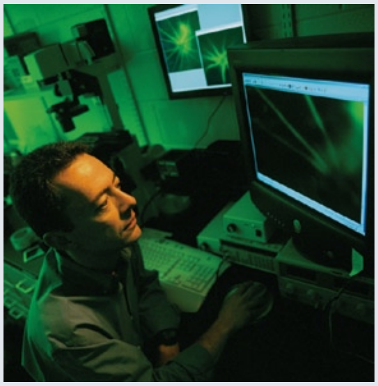
Philip Drinker '17, who helped found Harvard's School of Public Health, was the inventor of the iron lung. The "Drinker Respirator" was used in every major hospital in the U.S. during the polio epidemic of the 1930s.

Michael Yaszemski '77, '78 M.S. is chair of spine surgery and director of the Tissue Engineering and Polymeric Biomaterials Laboratory at the Mayo Clinic in Rochester, Minn. He is also principal investigator in a research consortium that is developing new techniques for treating wounded soldiers.

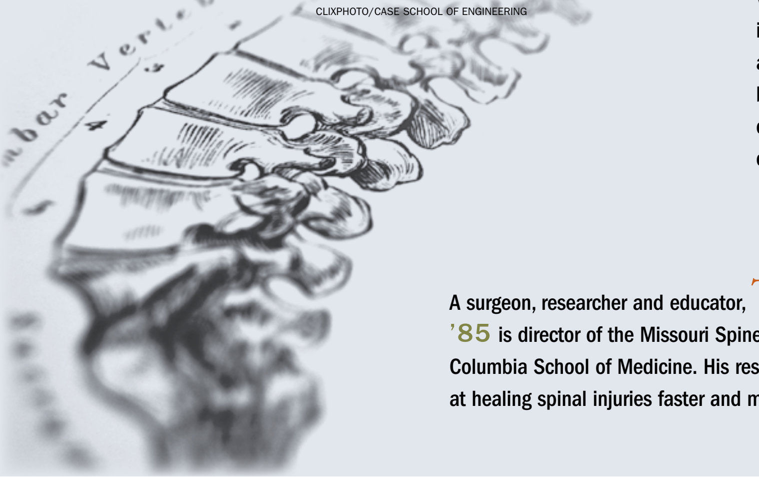


CLIXPHOTO/CASE SCHOOL OF ENGINEERING

As associate dean of research at Case Western's School of Engineering, **Clare Rimnac** '80 M.S., '83 PH.D. studies orthopedic biomechanics, seeking to improve knee and hip replacements.



Todd Giorgio '82 is chair of the biomedical engineering department at Vanderbilt University. His research into nanoscale materials quantifies and analyzes complex cellular behavior for applications in the field of biomedicine, including the detection and treatment of disease.



A surgeon, researcher and educator, **Theodore Choma** '85 is director of the Missouri Spine Center at the University of Missouri-Columbia School of Medicine. His research focuses on procedures aimed at healing spinal injuries faster and more naturally.

To learn more about the achievements of Lehigh engineers, visit the Lehigh Engineering Heritage Initiative at

www.lehigh.edu/heritage

LEHIGH UNIVERSITY
P.C. Rossin College of
Engineering and Applied Science
19 Memorial Drive West
Bethlehem, PA 18015

MUTUAL REINFORCEMENT

New biological therapies, artificial organs and other medical advances, says Vincent Forlenza ’75, president of the global medical technology company Becton, Dickinson and Co. (BD), are a natural consequence of decades of collaboration between engineers and biomedical researchers.

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