P.C. ROSSIN COLLEGE OF ENGINEERING AND APPLIED SCIENCE

Welcome to the 11th issue of *Resolve*, a magazine dedicated to research and educational innovation in the P.C. Rossin College of Engineering and Applied Science at Lehigh University.

Two years have passed since Congress adopted the Patient Protection and Affordable Care Act, and Americans are still conducting a vigorous debate over the best way to provide healthcare and health insurance.

Meanwhile, a consensus is forming that systems engineers will play a central role in the effort to reform healthcare, improve its quality and deliver it more efficiently. READ MORE >

—S. DAVID WU
Dean & Iacocca Professor

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HEALING EFFICIENCIES

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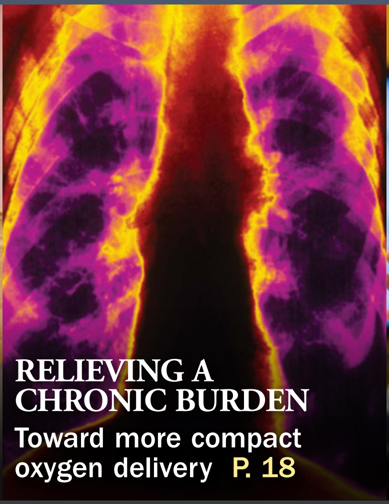

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A FOCUS ON LEHIGH ENGINEERING

VOLUME 1, 2012

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CHALLENGING GREAT MINDS...INSPIRING GREAT IMAGINATIONS

Engineering lasting reform

Welcome to the 11th issue of* Resolve*, a magazine dedicated to research and educational innovation in the P.C. Rossin College of Engineering and Applied Science at Lehigh University.

Two years have passed since Congress adopted the Patient Protection and Affordable Care Act, and Americans are still conducting a vigorous debate over the best way to provide healthcare and health insurance.

Meanwhile, a consensus is forming that systems engineers will play a central role in the effort to reform healthcare, improve its quality and deliver it more efficiently. In the past decade, studies by NAE, NSF, NAS, the Institute of Medicine and half a dozen other agencies have argued persuasively that systems engineers are ideally suited to help healthcare become more patient-centered, more responsive and more flexible.

The findings of these reports should come as no surprise. In their effort to optimize processes, systems engineers constantly seek complementarities. They measure, analyze and model every aspect of a process to assess its strengths and weaknesses and to learn how its components can be adjusted or altered to work toward a greater goal or objective.

This holistic approach is nowhere more needed than in healthcare delivery. A multitude of players interact in this arena – from patients, doctors and nurses, to insurers, administrators and financiers, to technicians, pharmacists and researchers. Systems engineers provide the tools to analyze huge quantities of patient, treatment and operational data, to improve communication and performance tracking, and to optimize resource usage. The ultimate goal is for the system to provide informative and high-quality care while utilizing resources in the most efficient manner.

This issue of *Resolve* examines Lehigh's new initiative in Healthcare Systems Engineering. The initiative consists of two main components (see page 12): first, a new professional master's degree program in Healthcare Systems Engineering (page 22), and, second, broad partnerships we have forged with all sectors of the healthcare industry. These partners include major hospital and home-healthcare networks, insurance and pharmaceutical companies, government agencies and consulting firms. They are helping to inform the education and research directions that our new initiative will take. We have a particularly close collaboration with the Mayo Clinic, whose dean of research and academic affairs, Gary Sieck, is featured in the Q&A on page 8.

Many more articles in this issue are devoted to healthcare-related research. Chemical engineers (page 18) are developing a lightweight medical oxygen concentrator for patients with chronic obstructive pulmonary disease. Computer scientists (page 10) have designed and tested an anti-obesity smartphone application that enables kids to get physical exercise while they interact with digital technology and with each other. Materials scientists (page 24) study how adult stem cells can be reimplanted to help regenerate nerves.

"The ultimate goal is for the healthcare system to provide informative and high-quality care while utilizing resources in the most efficient manner." —S. David Wu

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

S. David Wu, *Dean and Iacocca Professor*
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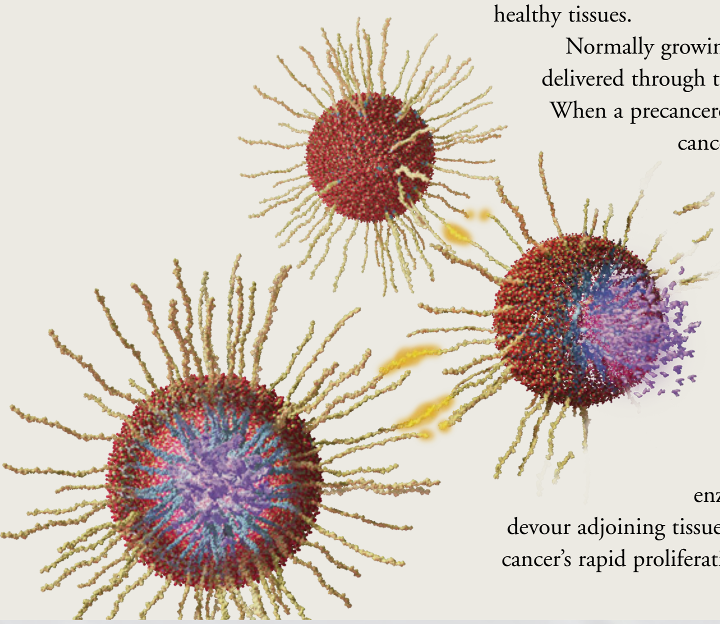
Turning a tumor's weapon against itself



A sensitive peptide triggers a nanoscale package to release drugs at cancer sites.
View larger ▸

Understanding the building blocks of biochemistry and structural biology, says Bryan Berger, can lead to creative solutions to medical mysteries.

Berger studies protein structure and molecular recognition and is particularly interested in how cell receptors switch on and off in relation to disease and how engineered peptides function in the body to combat disease.

He and Mark Snyder, both assistant professors chemical engineering, are developing nanoscale packages that, like smart bombs, release chemotherapy drugs at the site of a rapidly growing tumor while limiting the drugs' toxic effects on healthy tissues.

Normally growing cells feed off oxygen delivered through tiny blood vessels in tissue. When a precancerous cell morphs into a cancerous state, it grows at a rate faster than the oxygen supply can support. It then adjusts its metabolism to consume sugars stored in the cells and grow anaerobically.

This anaerobic metabolism causes the tumor cells to secrete enzymes called proteases that devour adjoining tissue to make room for the cancer's rapid proliferation. The process produces lactic acid, which lowers the pH around the tumor site.

Berger synthesizes peptides (sequences of amino acids) and programs them to use the tumor's protease weapons against itself.

"My lab designs peptides that the protease secreted by a specific cancer act upon," he says. Utilizing knowledge about the types of amino acid bonds that a specific protease will attack, and the size and shape of molecules that can penetrate the diseased tissue, Berger develops a peptide that will fold or change shape when it senses the tumor's enzymes and lowered pH.

Snyder incorporates the peptide into a silica-based nanoparticle package that encapsulates a small amount of an effective anti-cancer drug. The package is designed so that in the low-pH tumor environment, the peptide unfolds and is cleaved by protease, which causes the nanopackage to release the drug where it is needed.

"Most cancer drugs are effective but toxic," Berger says. "We want to keep them stable, shield them and release them at the right time."

Other organic, polymer-based approaches to packaging chemotherapy drugs exist, he says, "but the polymers are much more susceptible to degradation and have shorter half-lives than silica, which is inorganic and much more resilient."

Berger and Snyder have a grant from the Pennsylvania Department of Health's Commonwealth Universal Research Enhancement (CURE) program. They collaborate with Ellen Puré, professor of molecular and cellular oncogenesis at the Wistar Institute, a cancer research center in Philadelphia.

New adsorbent combats both arsenic and fluoride

Two of the world's most harmful groundwater contaminants are arsenic and fluoride.

Chronic consumption of water with excessive levels of fluoride can cause pain and damage to bones and joints and other symptoms. The consequences of arsenic are more severe and include skin lesions, cancer and even death.

Scientists estimate that as many as 500 million people in Africa and Asia consume groundwater that is naturally contaminated by one of the two toxins, says Arup K. SenGupta, professor of civil and environmental engineering and also of chemical engineering.

SenGupta and Surapol Padungthon, a Ph.D. student, have developed an adsorbent that can remove both arsenic and fluoride. The adsorbent is reusable and takes advantage of the unique surface properties of metal oxide nanoparticles.

SenGupta has a Fulbright Environmental Leadership Award to spend six months in the Center for Sustainable Technologies at the Indian Institute of Science in Bangalore, India.

The project is titled "Mitigating Fluoride and Arsenic Crisis." The award SenGupta received is called the Fulbright-Nehru Grant and is named for Jawharlal Nehru, the first prime minister of independent India.

The grant will enable SenGupta to collaborate with scientists and engineers in India to streamline the development of the adsorbent through lab and field work in areas whose groundwater is contaminated with fluoride or arsenic. The two contaminants, he says, rarely occur together.

Arup SenGupta's first Sustainable Arsenic Removal System was installed in India in 2004.

The award will also enable SenGupta to build on the success of an inexpensive filtration system that removes arsenic from groundwater at the wellhead. The system has been installed in more than 200 villages in eastern India and is also in use in the U.S., Hungary, Ecuador and Brazil. A patent for the system was awarded to SenGupta and Luis Cumbal '05 Ph.D., who is now director of graduate studies at the Army Engineering Polytechnic School in Quito, Ecuador.

Sending a rocket to the site of a cancer

Biomimetic microfluidic chips help researchers visualize the performance of nanomedicine.

Yaling Liu envisions the day when physicians can detect cancers before they are visible to modern diagnostic tools and then rocket drugs to cancerous cells in doses that treat the disease but don't kill surrounding tissues.

It's a big dream, and to realize it, Liu, assistant professor of mechanical engineering and mechanics, is thinking small – in nanometers. Liu is one of a growing number of researchers drawn to nanomedicine, the use of chemical particles that are an order of magnitude smaller than conventional drugs and are engineered to unleash their power directly at the site of a tumor rather than on the body as a whole. The global nanomedicine market was $73 billion in 2011 and is predicted to increase to $131 billion this year.

Nanoparticles can be designed with special coatings, or ligands, that lock into the unique chemical receptors on the surface of cancer cells. They can also be crafted to bond to tiny early-stage cancers and reveal them to diagnostic equipment. Using conventional methods, many cancers cannot be "seen" by medical scanners until they become larger and more difficult to treat.

Liu wants to engineer a "nanorocket" with drug and diagnostic components that seek out hidden cancer cells and deliver treatment at the same time. He is attempting to determine how much medication should be injected into a patient's bloodstream so that the proper dosage is delivered to the affected region of the body.

It is not a simple relationship. The size and shape of the drug particle, the geometry of the patient's vascular system, and the rate of blood flow at the site of the disease all influence how much of the drug will attack diseased tissue and how much of it will pass uselessly through the bloodstream.

For current nanomedicines, says Liu, as little as 3 percent of the drug injected into the bloodstream of a patient actually bonds to and attacks tumors.

Liu aims to improve those odds. In a project for the National Institutes of Health, he found that spherical nanoparticles, the easiest ones for drug makers to fabricate, bond less efficiently to diseased cells than rod- or disc-shaped particles.

Now, two years into a five-year NSF grant, Liu and his team have developed mathematical and computational models of blood flow in blood vessels of different sizes. These models can be used to predict what size and shape of particles most effectively "stick" to diseased cells and deliver a drug to various organs and tissues invaded by cancer.

Liu has developed an inexpensive way to turn his models into experiments that can be conducted on microfluidic chips using microscopic pathways to mimic the vascular system so that flow and nanoparticles can be visualized.

Compared to *in vivo* animal or human studies, Liu's *in vitro* biomimetic microfluidic chip is "much cheaper and faster, and has a higher throughput, because we can perform a variety of experiments at the same time."

Liu wants next to perform specific studies of lung and prostate cancer cells. Applying his modeling tools to real-world diseases will be a boon to drug makers, he says, "because every disease changes your design, and every region of the body is different."

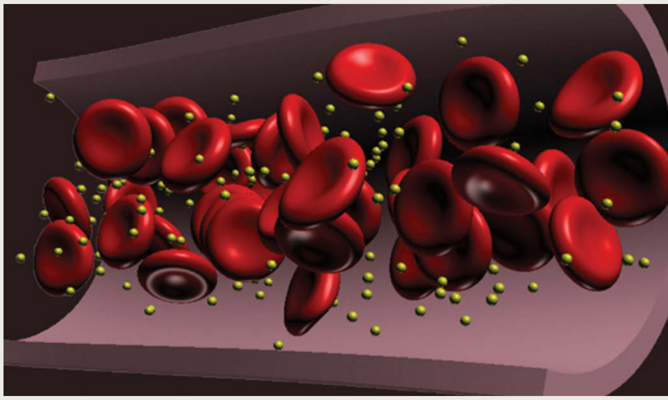
The ability to combine the fluid mechanics of blood flow and the biological properties of particle design with a better understanding of various cancers will allow physicians to more accurately administer effective doses of anti-cancer agents while reducing side effects.

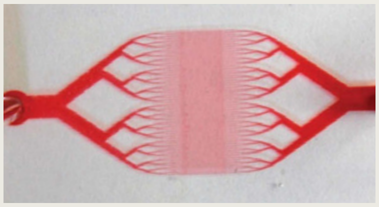
And understanding the complex interactions between particle design and the vascular system may help pharmaceutical companies customize a line of drugs matched to patients' age, cardiovascular health and the stage of their cancer, Liu says.

"Cancer is the number one killer of Americans," Liu says.

Will his group's work help give patients a better chance at recovery?

"I tell my students to dream big," Liu says. "Dream big – and you'll always achieve something."



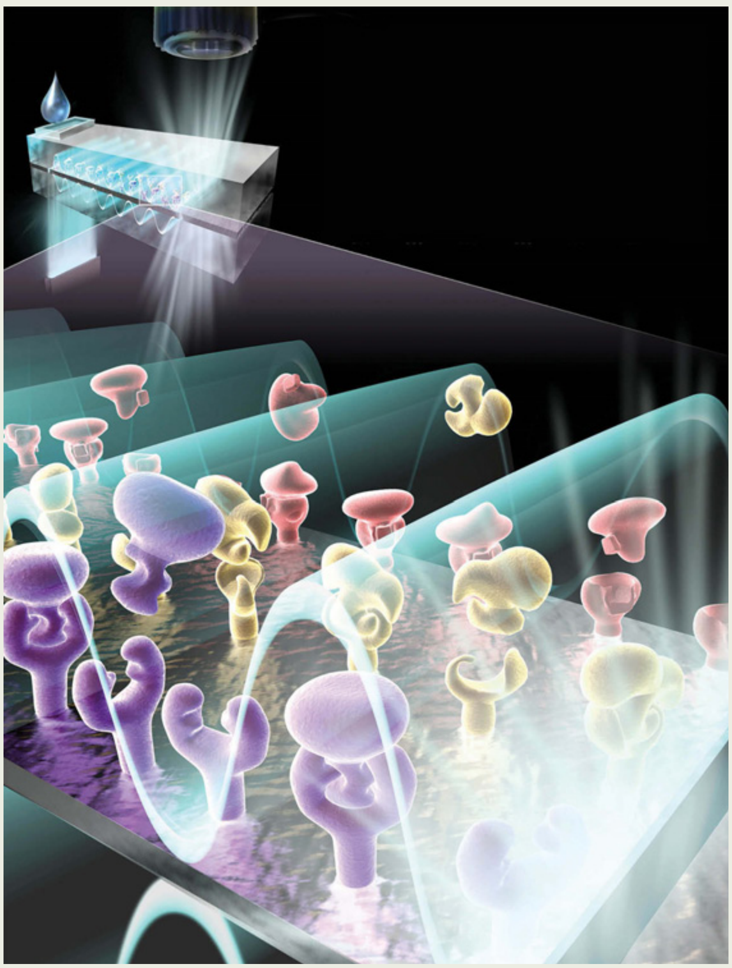


Yaling Liu and graduate students Jifu Tan and Antony Thomas (above left) design "nanorockets" (yellow particles, above) that navigate through red blood cells before binding to the vascular wall (gray) and penetrating the wall to attack cancer cell sites (not shown).
View larger ▶

Moving toward "real-time" detection of proteins

Researchers focus on the interference pattern created by the coupling of light with electrons.

The healthcare industry has a huge need for fast-acting, ultrasensitive, compact biosensors that allow biological processes to be monitored in real time. The ability to detect the different types of proteins being secreted in cell lines would open doors for researchers working on tissue regeneration.



Bartoli's biosensor couples light waves and electrons to detect biomolecules, opening the door to multi-receptor chips and sensor arrays. *View larger ▸*

The most promising devices capable of achieving this are based on a surface plasmon polariton (SPP), a type of electromagnetic wave generated when an incident beam of light couples with an oscillating wave of electrons in the surface of a metal.

Writing in *ACS Nano*, a research team led by Filbert Bartoli, professor of electrical and computer engineering and member of Lehigh's bioengineering program, has reported a new type of microfluidic chip-based plasmonic biosensor that outperforms current nanoplasmonic devices by an order of magnitude.

"Most commercial plasmonic-based sensing devices employ a prism to couple incident light with the surface plasmon," says Bartoli. "While this approach has an advantage in terms of sensitivity, the intrinsic size and alignment requirements are a significant limitation.

"To overcome these problems, scientists have designed nanoplasmonic sensors based on nanoparticles, nanoslit arrays and nanohole arrays. However, a significant improvement in sensitivity for detecting proteins has to be made before they can compete with prism-based systems."

Bartoli's simple device contains two parallel nanoslits etched a few microns apart into a thin film of silver deposited on a glass slide. When an incident light beam is focused onto one of these slits, the electrons at the outermost surface of the metal film oscillate, causing an SPP to propagate along the surface of the metal.

"Two SPPs are generated," says graduate student Yongkang Gao. "One travels along the metal-air interface on the film's top surface and the other along the metal-glass interface on its bottom surface."

On reaching the second slit, these two waves interact to form an interference pattern whose fringes are highly dependent on the difference in the effective refractive index of the interfaces along which they have traveled. The light emanating from the second slit is collected by a modified optical microscope that ensures only SPP-mediated radiation is collected. It is then passed through an optical fiber-based compact spectrometer to obtain information on the interference pattern.

"As the optical field of an SPP is strongly confined to a very thin region along the metal surface," says Bartoli, "it is extremely sensitive to changes in the local refractive index, such as those induced by proteins and other biomolecules binding to the metal surface."

Working with Xuanhong Cheng, assistant professor of materials science and engineering, Bartoli's group tested the device on the affinity that biotin has for the protein streptavidin. They coated the top metal surface with a monolayer of biotinylated bovine serum albumen. A buffer solution was then introduced to define a base line.

"We then focused on the interference peak around 690nm and recorded its spectral position," says Gao. "The injection of a very dilute solution of streptavidin caused a peak shift of 15.7nm, which was much larger than that previously reported for devices based on nanoparticles or nanohole arrays."

A control experiment was carried out using a monolayer coating of bovine serum albumen without the biotin linkage. A peak shift of only 0.7nm was observed. "This proved that the large shift of 15nm was due solely to the specific binding of the streptavidin to biotin," says Gao.

"The next step is to modify the device to detect molecules secreted by stem cells during neuronal differentiation," says Sabrina Jedlicka, assistant professor of materials science and engineering. "This will allow us to monitor real-time neuronal differentiation and ultimately neuronal response to certain stimuli, including novel drug compounds."

The team is also designing a multiplex device comprising a 2-D array of sensors to allow simultaneous detection of a mixture of proteins or spatial distribution of a protein.

The project is funded by NSF and is part of the engineering college's Healthcare Research Cluster.

Exploring tiny structures with big consequences

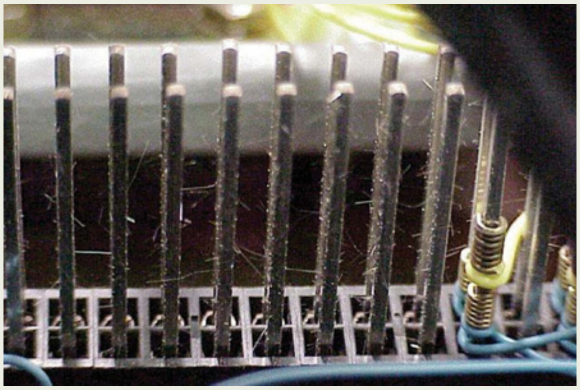
Probing the rapid mass transport mechanisms of tin whiskers.

Even when not shaving, Edmund B. Webb III and Yibo Wang worry about whiskers – tin whiskers, to be specific, that cause significant material destruction.

Webb, associate professor of mechanical engineering and mechanics, and Wang, a graduate student, study tin thin films, which are used in electronic circuits as coatings on contacts and solders for joining components. The films are found in everything from cell phones to satellites.

It's widely known that the films grow "whiskers," or thin crystalline structures, about 1/100th the thickness of human hair and long enough, sometimes, to form circuits between contacts and cause damage and loss.

NASA reports tin whiskers have caused system failures on Earth and in space. In a handful of incidents, whiskers have caused complete loss of satellite functionality. Typically, says Webb, whiskers are not a problem for products like cell phones or computers, which most people upgrade every few years. But they can become a concern in components and systems that sit idle for years and then must be restarted.



Whiskers growing from tin-plated wire wrap terminals have sufficient length to form short circuits between adjacent contacts.

Lead had been used to solve this problem for more than 50 years, but its use today is precluded by health concerns. Webb and Wang are collaborating with Sandia National Laboratories to understand the rapid mass transport mechanisms of whisker growth.

"Most metal films are composed of microscopic crystallites, or grains, that grow together and merge during the formation process," says Webb. "Regions where grains merge are called grain boundaries, and we suspect these regions control the formation of whiskers. We are studying the influence of atomic transport along grain boundaries to determine where on a surface a whisker will form. We also want to understand how stress in a thin film – known to play a role in driving whisker formation – influences grain boundary transport."

Their models are revealing for the first time that anomalously rapid atomic transport for some boundaries directly determines where a whisker forms. If this is true, then preventing whiskers requires preventing the formation of the anomalous boundaries.

This phenomenon may explain why adding lead mitigates whisker formation since lead atoms are expected to reside in grain boundaries. The next step will be to use models to suggest non-lead-based processing strategies for achieving this same effect.

Lessons from a bowl of Cheerios

James Gilchrist, associate professor of chemical engineering, watches Cheerios converge in a bowl of milk. The oats attract each other to reduce the milk's surface energy, a phenomenon called the "Cheerios effect" that explains other examples of self-assembly. Something similar — "the coffee ring effect" — occurs when a drop of coffee dries into a ring instead of a spot.

Gilchrist observes these effects at the nanoscale where arrays of nanoparticles self-assemble. He and Prof. Nelson Tansu of electrical and computer engineering are trying to learn how minute particles deposit themselves into optical coatings. Their work has led to development of LEDs that are three times brighter.

Gilchrist also collaborates with Profs. Xuanhong Cheng of materials science and engineering and Mark Snyder of chemical engineering to fabricate membranes for improving separation devices that monitor HIV infection as well as molecular separations of high-value chemicals produced by biorefineries.

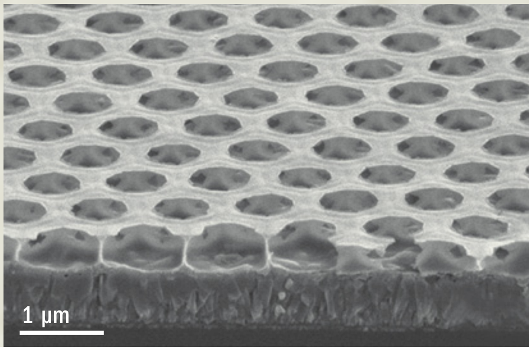
Snyder and Gilchrist have formed a company to develop nanoscale coatings and dye-support anodes to enhance dye-sensitized solar cells (DSSCs). Reversing the engineering of the LED project (engineers want to get light *out of* LEDs but *into* solar cells), they are flipping the microlens array inside the solar cell device and using dye molecules instead of silicon to absorb light. Solar cells with internal microlenses have proven to be 30 percent more efficient.

A $1.1 million NSF grant is helping Gilchrist and his colleagues develop two processes that enable commercial scale-up of these products. Both utilize roll-to-roll technology, similar to high-speed newspaper printing, to produce monolayer particle coatings that self-assemble into well-ordered arrays as they are being deposited.

With Snyder and Prof. Jeetain Mittal of chemical engineering, Gilchrist is studying fundamental deposition and developing numerical models, respectively. Process development is done with Versatilis, a Vermont company that manufactures advanced electronics for solar, lighting, display and related markets.

"In the 1980s," says Gilchrist, "scientists began to understand the underlying physics of particle interaction and deposition. "Today, we are learning to manipulate fluid properties to control the process more efficiently, which can lead to high-rate precision commercial processes. We hope these processes become the benchmark for others."

Gilchrist studies applications in LEDs and solar cells for particle self-assembly at the nanoscale.



When a dare becomes a direct query

Helping AI make the leap from transcribing a document to interpreting it.

Dan Lopresti has spent years teaching computers to extract text and meaning from handwritten documents. His latest dare could change the paradigm by which certain difficult artificial intelligence (AI) problems are solved.

"Researchers want to build algorithms that approach human levels of performance," says Lopresti, professor of computer science and engineering. But the model for doing this hasn't changed in nearly half a century.

To tackle pattern recognition problems, a researcher identifies a promising algorithm, "trains" it by analyzing text and writing samples that are already recognized by human experts and then turns it loose on new documents.

The media may have evolved from punch cards to CD-ROMs to websites, and data sets have grown much larger, he says, "but nothing else has changed about the way we do this research."

Experiments in machine perception require lots of data, mostly in the form of scanned images of printed and handwritten pages. Some well-known data sets favored by researchers date back to 1972 and are "getting a little stale," he says.

A platform for exploring pattern recognition problems turns elements as small as a single character on a page into individual queries in a database.

Even if new computer code has never "seen" well-known data, often the human author has, which subtly influences how algorithms are built. Experiments are usually run on a subset of a larger data collection, and researchers rarely cite exactly which documents were used.

Lopresti's solution, the DARE paradigm, for Document Analysis Research Engine, is a collaboration with Bart Lamiroy of Nancy Université in France. It uses a powerful server computer at Lehigh that supports the development of algorithms and the running of experiments while serving data to researchers, providing an integrated platform for exploring pattern recognition problems. The idea emerged while Lamiroy was a visiting research scientist at Lehigh in 2010-11.

The 2008 Minnesota Senate race

One data set on the server consists of scanned ballots from the contested 2008 U.S. Senate race in Minnesota between Al Franken and Norm Coleman. The recount and six-month court battle, in which Franken was declared the winner by 312 votes out of 3 million cast, hinged on how humans interpreted ballots that had not been marked according to specified guidelines, Lopresti says.

"I can show you ballots where you can reasonably disagree with me as to a voter's intent," he says. The algorithms that processed these ballots thus had to explore the possibilities of multiple interpretations, rather than try to distill a single truth. "That is a leap from simply transcribing a document to extracting intelligence from it."

The DARE server lets researchers tackle complex questions by breaking apart data collections and turning elements as small as a single character on a page into individual queries in a database. The database is huge – but the ability to query elements directly has the potential to change the game for researchers.

Assessing a reputation

Querying a database can produce a truly random selection of documents from multiple data sets, so researchers don't have to keep working with the same samples. A query is in the form of an Internet URL address, so other researchers can see which documents were used and test their own algorithms against the identical data to verify the results. Because the data is random, the content of the samples doesn't influence a researcher's design. The server also tracks the documents an algorithm has "seen," allowing objective tests of the code's ability to interpret previously unseen data.

"Normally," says Lopresti, "algorithms can be pushed to the point where they do well on training data. The proof of the pudding is in how it does with unseen data."

Lopresti is also investigating ways of having the system evaluate the reputation of data sources, algorithms and even individual researchers.

"When you move from transcribing a document to interpreting it, the question becomes, who is interpreting it?" he says. "Nobody knows how to quantify this yet. I have an opinion of the reputation of my colleagues, of algorithms, of data, but it's in my head. The question is how to get it out in a way that can be used."

By combining specificity, objectivity and reproducibility, DARE can quickly identify algorithms that are tweaked for specific data but not generally useful, thus helping researchers make faster progress. A paper given by Lopresti and Lamiroy at the 2011 International Conference on Document Analysis and Recognition in Beijing was cited for its potential to change research in the field.

Fuel cells that any fuel would love

Imagine a power plant in your home. The idea is not so far-fetched – if fuel cells can be scaled up to produce that amount of power.

Solid oxide fuel cells (SOFCs), which convert a fuel's chemical energy to electrical energy, are one of the most promising technologies for generating and distributing electricity more efficiently. Companies like Google, Walmart and FedEx are piloting their use in stores on a limited basis.

Steve McIntosh, assistant professor of chemical engineering, wants to make SOFCs even more commercially viable. He is seeking to maximize the flow of electrical current through fuel cells by minimizing the voltage needed to drive reactions, and move ions, within the cell.

To produce energy as efficiently as possible, McIntosh and his group are studying advanced functional materials. Their goal is to design a cell that can run on any fuel – something no one has yet achieved.

"Fuel cells operate by transporting oxygen anions from the air side of the cell to the fuel side," says McIntosh. "Catalysts facilitate the key reactions at both sides of the cell. If you can reduce the cell's resistance to this process, you can drive more current, and thus generate more power, from a single cell.

"We want to understand the fundamental barriers to these reactions in order to develop more active materials and structures."

In one NSF project, McIntosh is trying to run fuel cells with natural gas instead of hydrogen. Currently fuel cells must break down hydrocarbons such as natural gas into carbon monoxide and hydrogen before they can be utilized to generate electrical power. The key to further commercialization, McIntosh says, is designing a cell that will react with any fuel.

In addition to the catalytic components, McIntosh is also seeking to transport ions easily across fuel cells, batteries and other solid-state ion conductors. In pursuit of this goal, McIntosh is working with Oak Ridge National Laboratory and its accelerator-based neutron source. He and his colleagues are studying the structure and properties of crystals under fuel cell operating conditions to find the optimal design for ion transport.

Understanding catalysis, says McIntosh, is key to generating more power from fuel cells.

"We've had success in operating these fuel-flexible cells at the laboratory scale," he says. "What we want to do is scale up the performance to a level that would allow commercial manufacture.

"If that can be achieved, fuel cells could revolutionize the generation and distribution of electrical power."

Optimization on steroids

One of the fastest-growing optimization fields is derivative-free optimization, or DFO, and Katya Scheinberg is among its pioneers. She has patented DFO software and is coauthor of a textbook published in 2008.

Scheinberg, associate professor of industrial and systems engineering, uses a comparison to explain DFO. As you walk in the dark down a slope into a valley, your feet detect the incline of the slope. When you reach the bottom, your feet detect level space.

"The typical derivative-based algorithm tells you which way is down," says Scheinberg. "But in DFO, you have to find the bottom of the valley when it is filled with water. You can't feel the slope, but you can drop an anchor at different points to measure depth.

"Intuitively, DFO requires much more effort. Our research helps minimize simulation costs by designing intelligent approaches that do not use too many measurements and [that] progress to solutions."

At IBM, Scheinberg patented software that has been used to fine-tune decisions about wire width, transistor properties, power consumption and other concerns related to circuit design.

At Lehigh, she is working with Prof. Brian Chen of computer science and engineering to detect the binding properties of a class of proteins used in drugs. Chen uses Scheinberg's algorithm to discover similar patterns in proteins important in drug development.

Optimization has become a hotter field, Scheinberg says, since the web opened up the possibility of building algorithms with large-scale data derived from Internet searches.

"When optimization originated in 1947, algorithms handled 10 variables. Now we have billions. We kept pace before because computer speed increased. But as soon as we thought we could solve anything, along came the web, creating new problems and opportunities. More data allows for new models, and so we've seen a boom in interest in optimization in general and in DFO in particular."

Q&A INTERVIEW BY WILLIAM TAVANI • PHOTOGRAPHY BY CHRISTA NEU

A MEDICAL NEED

THE DEMAND FOR SYSTEMS ENGINEERS IS GROWING.

Gary Sieck is dean of research and academic affairs and Vernon T. and Earline D. Dale professor and chair of the department of physiology and biomedical engineering at Mayo Clinic's College of Medicine. He also directs the Biomedical Engineering program in the Mayo Graduate School. Sieck received the Mayo Research Educator Award from 2001 to 2004 and was named Mayo Distinguished Investigator in 2007. He is a past president of the American Physiological Society and a fellow of the American Institute of Medical and Biological Engineering. Before joining Mayo in 1990, Sieck served on the biomedical engineering faculty at the University of Southern California. In January, he was elected chair of the industry leadership board of Lehigh's Healthcare Systems Engineering program.

Q: ***Your research specialties include cell behavior, protein expression and the effects of anesthesiology. What notable research have you led?***

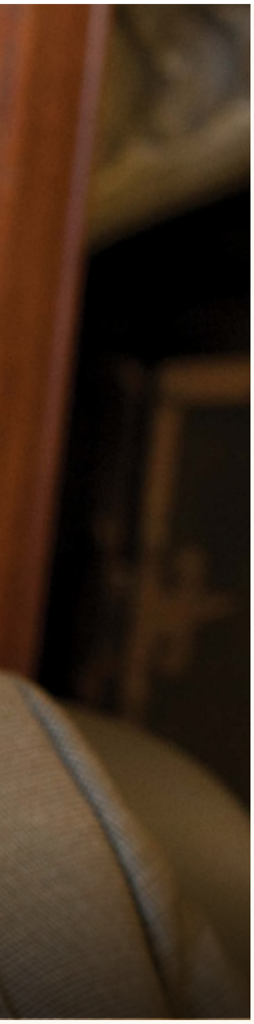
A: My research interests for the past 35 years have focused on neural control of respiratory muscles, particularly the diaphragm muscle and airway smooth muscle. Patients with weak breathing muscles might be placed on mechanical ventilators or run the risk of pneumonia and respiratory complications.

Our research has given us a much clearer understanding of how the nervous system controls these muscles. We're able to target therapies either to motor neurons or to muscle fibers. A current project is looking at spinal cord injury and how it affects the diaphragm muscle. We're developing therapies that could potentially restore the ability to breathe in patients with upper cervical spinal cord injury.

Q: ***Mayo Clinic is widely praised for offering quality care while controlling costs, and it is ranked third in*** **U.S. News & World Report's** ***2011-12 issue of America's Best Hospitals. Tell us about the evolution of team medicine at Mayo.***

A: Founder William Worrall Mayo established a practice in Rochester, Minn., at the end of the Civil War. His two sons, William and Charles, both physicians, later joined him. They introduced the idea of medical group practice and specialization in medicine. They understood the importance of academic training and partnered with the University of Minnesota. This was the start of the Mayo Clinic team medicine approach, which continues today and is essential to our success.

Research has been an integral part of the Mayo Clinic since 1914, when Mayo founded the Institute of Experimental Medicine. Today we have a wide range of research activities.



The Mayo Clinic, says Gary Sieck, has been applying engineering principles to healthcare for more than a century.

In particular, we're taking advantage of our extensive patient clinical records, which are very relevant to the Healthcare Systems Engineering concept for improving clinical practice. The patient-focused nature of our medical research has been vital to our success.

Q: ***Mayo has for four years hosted an international Conference on Systems Engineering (SE) and Operations Research (OR) in Healthcare. When did Mayo begin implementing SE practices?***

A: Mayo has been involved in innovation and in the application of engineering principles to medical practices since 1901, when Henry Plummer joined Mayo as a physician. Plummer is widely regarded as the architect of modern medicine. He implemented a wide range of innovations to clinical practice that improved efficiency in patient care. In 1907, he introduced standardized, individualized medical records for patients so that physicians would know what medical tests and treatments patients had received.

Plummer brought systemized approaches to medicine using engineering principles. A Systems and Procedures group was established in 1947 at Mayo. Industrial engineers were among those they hired. The people in this group are the type of people being trained at Lehigh today in the HSE program.

Q: ***How large a staff has Mayo committed to the implementation of SE practices? How is this staff deployed?***

A: The Systems and Procedures group now has approximately 100 people. Systems engineers also work in other areas, such as the Department of Laboratory Medicine Pathology. The sheer volume of samples tested requires tremendous organization: keeping track of samples, doing and reporting the analyses. We also have one of largest esoteric clinical testing facilities for rare, complicated diseases. All this work requires SE skills. Mayo has also initiated a research focus in the science of healthcare delivery, which involves healthcare systems engineering and operations research in clinical practice to improve outcomes and efficiencies.

Q: ***In what areas of operation has Mayo seen the most dramatic benefit from the implementation of SE practices?***

A: Every area really. One example: We have more than 120 surgical starts every morning. The staff and equipment, induction of anesthesia, and post-op care all have to be organized and coordinated. We treat more than 600,000 patients per year. We have to keep track of who they are, what their problems are, who should see them. All this information should be organized so that patients get as much as possible out of a single visit to the clinic. I call this one-stop shopping for clinical care. That's where systems engineers come in.

Q: ***In general, what areas of healthcare do you think could most benefit from the application of SE principles?***

A: Communication among specialists treating complex diseases is one area that must be improved and where SE skills are needed. Information should follow patients around so that every specialist knows the tests and treatments a patient has received.

Q: ***According to a UCLA study, the U.S. spends about one-third of its healthcare resources for care given in the last year of patients' lives. How can SE practices reduce this percentage?***

A: SE can play a role in improving health and wellness. Many patients don't see a physician until a disease is well progressed. We need increased attention on sustaining wellness and avoiding disease. Recognizing the growing incidence of obesity, diabetes and heart disease, we need better management of these chronic diseases. Diabetes, for example, if left untreated, can lead to complications requiring intensive care, which is where most of the expense occurs. The earlier a patient is seen, the better the outcome. SE practices can also make a contribution in health-monitoring systems.

Q: ***What has attracted the Mayo Clinic to collaborate with Lehigh University on its new HSE program?***

A: We're not a university. We have no school of engineering. Lehigh has an outstanding school of engineering but no medical school. We started a partnership five or six years ago. We saw advantages for both institutions, first in biomedical engineering but also Healthcare Systems Engineering. Mayo provides outstanding clinical care, but we have to rely on other institutions to provide necessary academic training. So we decided to collaborate with Lehigh. But Mayo is only one of many places where Lehigh's HSE students could get practical experience.

Q: ***What kind of "niche" can the new program carve out?***

A: There's a great need for engineers trained in healthcare. Look at the national focus on things like electronic medical records, improving the efficiency of healthcare and the political discussion on the direction of healthcare. HSEs will be needed no matter which direction the field takes. Certainly, when the industry moves to electronic medical records — which only a small fraction of medical practices have — HSEs will play an important role.

Q: ***What kind of value will the graduates of Lehigh's new HSE program offer to an institution like Mayo?***

A: Finding people trained for the kind of work done by our Systems and Procedures group is a challenge. By introducing a systematic approach to healthcare management, Lehigh is doing a great service. Its HSE grads will bring immediate value to our SE efforts.

An act of liberation

AN ANTI-OBESITY SMARTPHONE APP COAXES KIDS AWAY FROM THEIR VIDEO AND TV SCREENS.

From the Nintendo Wii to Sony's EyeToy, the home entertainment industry is seeking to motivate kids to get out of their chairs and move around when they play video games.

Stung by charges that video games are contributing to what some call an epidemic of obesity in America, the industry is hoping virtual reality can transform a passive activity into a physical one like shadow boxing with virtual targets or playing ball with remote teammates.

Mooi Choo Chuah also worries that a diet of video games, computers and movies is converting America's kids into couch potatoes and "small muscle athletes."

But Chuah, associate professor of computer science and engineering, wants to go a step or two further than Nintendo and Sony.

She wants to push physical fitness by liberating kids from their consoles and reconnecting them with the real world – and with each other.

Chuah and her undergraduate students have designed a mobile smartphone application that mounts a two-pronged attack on America's sedentary lifestyle.

"If you want to entice kids to run around and engage in physical activity," says Chuah, "you have to do it in a fun and social way.

"You need two things – competitiveness and an element of surprise."

A virtual treasure hunt – played in the great outdoors

Chuah's new mobile app, called WiFiTreasureHunt, combines treasure hunting with social networking and sensors.

When you click on the WiFiTreasureHunt app, your smartphone generates a map with, say, 10 locations chosen randomly from your immediate vicinity. Three sites might have a treasure – a coupon for a healthy snack or points that can be used to buy a ticket to a batting cage or skating rink.

The app prompts you to press your thumb against your phone's camera. A pulse-reading program calculates your heartbeat and displays it on the phone screen. To begin a game, you send your heartbeat and starting time to a remote server where your personal data – age, weight, gender – are stored.

The remote server will tell you if there are other online users you may want to invite to your game. You and your friends can devise your own strategy for visiting the sites and looking for the treasures.

Each time one player visits a location, the map on everyone's screen will be updated to reveal if that location contains a treasure or not. The game ends when all the treasures have been discovered. You and the other players are then prompted to measure your heartbeats again.

The starting and ending heartbeat readings, the time it takes to complete the game, and the locations visited by each user will be sent to the remote server for tallying. Your group can invite other groups to play the game for a week or a month; in this case, the remote server will tally the data for all the groups and identify the winning group at the end of the competition duration.

"WiFiTreasureHunt is like playing a video game in real life,"says Chuah. "You interact not just with the computer, but with the environment and potentially your friends as well."

Chuah has consulted with Judy Lasker, professor of sociology, on Fitness Tour. Several undergraduate students, including Steve Sample '11 and Gregory Jakes, have helped with software programming.

Chuah's next step is to test the app with human subjects, starting with college students. She also plans to add a barcode scanner program that will tell users the calorie content of the snack food they eat and suggest more healthful alternatives.

Further down the road, Chuah and her group will conduct a large-scale test to compare the exercise benefits between a control group using WiFiTreasureHunt and a group playing Wii games.

"Our goal is to design games with educational value and to do this in a way that is exciting and can help people," she says.

An assist for special-ed teachers

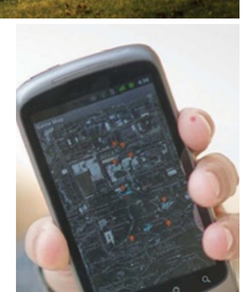
In a related project, Chuah is developing a mobile-health smartphone app for autistic children and their teachers. Her collaborators include Linda Bambara, professor of special education, and Michael George, director of the Centennial School, a special-ed facility run by Lehigh.

"Autistic children have short attention spans," says Chuah. "They might not react well to strangers or to other unexpected stimuli. If we can correlate these events with misbehaviors, we can play an audio clip on a child's earplugs. This could be the child's mother or someone else with a soothing voice who can give guidance for proper behaviors."

The autism application contains a feature that automates the data that teachers are required to record, potentially reducing their workload and freeing them to spend more time with students.

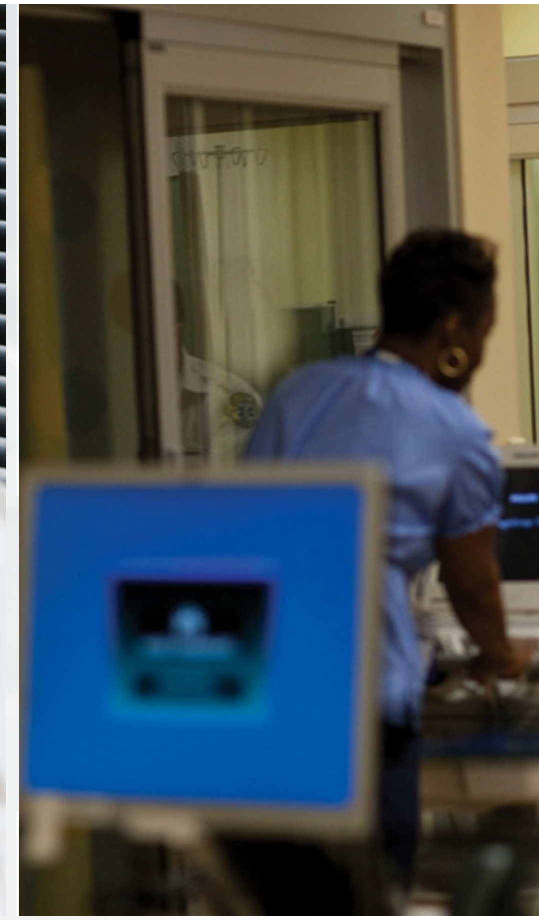
Chuah's past research has been supported by NSF, the Pennsylvania Infrastructure Technology Alliance, the Army Research Laboratory and DARPA. She recently submitted an NSF proposal to conduct research into the system and security design of a mobile healthcare system.

"To entice kids to run around and engage in physical activity, you need two things – competitiveness and the element of surprise." —Mooi Choo Chuah



In a computer science senior design project Chuah recently supervised, Michael DiBlasio '11 designed an autism social alert system that correlates environmental stress factors with typical autistic behaviors. The system collects and analyzes accelerometer readings from a child's phone to identify behaviors such as leg shaking or hand clenching that can occur in response to loud noises or other sudden changes in a child's environment.

Michael DiBlasio and Greg Jakes (above) and graduate student Ziyuan Qin (above left) click on the WiFiTreasureHunt app to generate a map with random locations.



HEALING EFFICIENCIES

Systems engineers help healthcare refine its processes and achieve a more compassionate bottom line.

The weary looks on the faces of the people in the crowded emergency room lobby make it plain that you are in for a long wait.

Your injury is painful but not life-threatening – a fractured metacarpal, sustained in a game of pick-up basketball.

As you take a seat near the TV and begin marking time – 30 minutes, one hour, two hours – you also begin experiencing what Hisham Nabaa calls America's contradictory health-care picture.

The information you print onto your five-page patient history form is the same that you provided on your last three or four visits to the doctor – but you need to give it again because the ER doesn't have access to your doctor's records. And as you struggle to tune out the blaring sit-com, three or four ER waiting rooms might actually be sitting empty due to a staffing mix-up that assigned too many nurses to other hospital departments.

When finally you are treated, however, your doctor, and later your physical therapist, will have at his disposal an impressive array of world-class diagnostic equipment, surgical tools and medical devices.

The scenario, says Nabaa, director of Lehigh's new Healthcare Systems Engineering (HSE) program, underscores the dilemma of 21st-century American healthcare: The U.S. offers perhaps the world's best medical care but at an unsustainable cost and with an efficiency that is barely mediocre.

According to the U.S. Centers for Medicare and Medicaid Services, health expenditures in the U.S. totaled $2.5 trillion in 2009 – more, per capita, than in any other country – and consumed 17.6 percent of gross domestic product. According to the World Health Organization, the U.S. healthcare system ranked 37th globally in overall performance in 2000.

Since HSE was launched last summer, Nabaa has recited these and similar statistics to a variety of audiences. No one knows what direction the national debate over health-care reform will take, he says. But systems engineers, by applying the same optimization tools that have already streamlined the airline, manufacturing, transport and other industries, are positioned to transform the provision of healthcare as well.

"Healthcare is a very fragmented world and, therefore, a good environment for systems engineering skills."

—Tom Cassidy, director for operational quality assurance, BAYADA Home Health Care

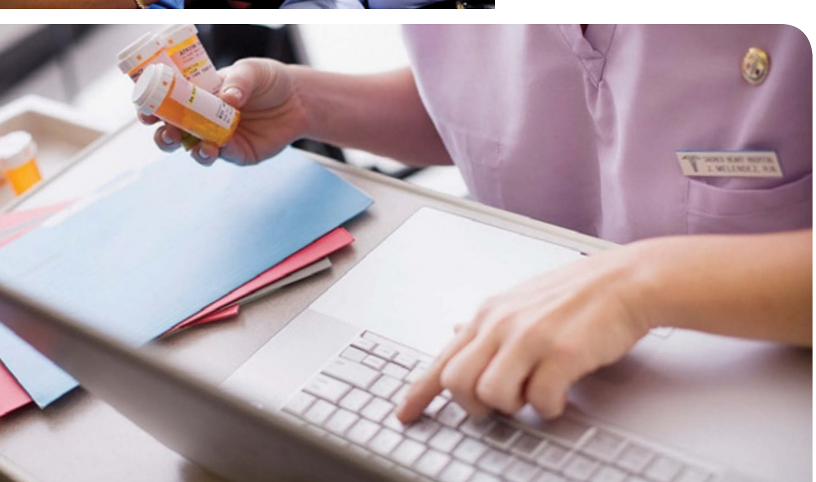
By applying the optimization tools that have streamlined the airline and other industries, systems engineers are transforming the provision of healthcare.

The HSE program is an outgrowth of the Lehigh University Strategic Plan, which identifies three areas – globalization; health; and energy, environment and infrastructure – where Lehigh is seeking to be a leader in learning, innovation and creativity. Together with programs in energy systems, structural engineering and technical entrepreneurship, the HSE program is among a new breed of innovative professional master's-degree programs in the P.C. Rossin College of Engineering and Applied Science. Each of these programs was created to address a pressing societal need, each has received extensive industry and community input, and each is partnering with national leaders in the field.

HSE's goal is twofold: to prepare graduate students in a new one-year master of engineering degree (see p. 22) for leadership positions in healthcare and related organizations, and to bring together representatives from all sectors of the economy related to healthcare. A close collaboration with the Mayo Clinic is helping to shape HSE's systems engineering focus and give the program a unique identity. HSE's industry leadership board (ILB) has attracted the leaders of health insurance companies, hospital networks, home-healthcare agencies, pharmaceutical companies and government agencies. (ILB chairman Gary Sieck, dean of research and academic affairs at the Mayo Clinic, is featured in the Q and A section on pp. 8-9.)

This mix of viewpoints and backgrounds, says Nabaa, will improve communication among healthcare's varied players, help HSE students gain hands-on experience while completing their degrees, and enable Lehigh to develop an innovative database of best practices in healthcare and its related fields.

The new HSE master's program provides students with the tools to model, optimize and improve the hundreds of processes that make up healthcare.



A case to be made

HSE is one of the few graduate-level healthcare programs in the U.S. with a systems engineering and analytical focus. Its diverse population of students includes physicians, nurses and engineers. Many programs in healthcare policy and healthcare management are offered by the nation's universities, says Nabaa, but HSE meets an unfilled need. It offers tangible tools to model, optimize and improve the hundreds of processes that make up healthcare, and to intelligently analyze the enormous amounts of real-time data that are generated by these processes.

But can the tools of systems engineering – algorithms, statistical modeling, information management, data mining, simulation – optimize something as subject as healthcare is to the vagaries of human nature and the whims of Mother Nature?

Several decades ago, says Nabaa, leaders of the airline industry raised similar doubts.

"When systems engineering was introduced to the airlines, they said, 'Our industry is very complex. You can't implement your methods here.'"

Today, says Nabaa, from the moment you first search online flight options to the moment you collect your luggage in the baggage terminal, air travel is a model of optimized seamlessness. Advanced software lets you choose your flight time and seat assignment and issues you an electronic ticket that you pay for through a secure online, automated system. This involves streamlining millions of processes in minutes.

"By contrast," he says, "you can have two healthcare facilities in the same town, both run by the same company, and they'll have two completely different information systems."

With the ability to refine large amounts of data into ever-smaller subsets and draw meaningful inferences from that data, says Nabaa, modeling and optimization tools are well-suited to streamline the delivery of healthcare. Sophisticated modeling tools already in use, for example, generate nursing schedules that account not only for shift preference, but also for individual tendencies to arrive early or late, for experience levels and for areas of expertise.

The technology also exists for patients to electronically authorize a healthcare provider to access their entire medical histories with the swipe of a card, much as a supermarket verifies your credit history in a split second.

Systems engineers can also identify and eliminate redundancies, says Nabaa, by enabling healthcare facilities to examine their entire operations in a "holistic" way.

"Studies have shown that through the use of systems engineering principles, modeling techniques and analytical thinking, healthcare industries can improve efficiency, cut costs and treat more patients with a smaller staff."

Improving the flow – and utilization – of data

The HSE program's industry leadership board reads like a roster of Who's Who in Medical Care. Members represent the region's largest hospital networks – Lehigh Valley Health Network, St. Luke's Hospital and Health Network and Easton Hospital – as well as the Mayo Clinic, Geisinger and Susquehanna Health; BAYADA Home Health Care, one of the largest providers of its kind; the Hospital and Healthsystem Association of Pennsylvania; the pharmaceutical risk management company ParagonRx; insurers such as Capital Blue Cross and Highmark; and the global consulting firm Towers Watson.

"We are an accurate reflection of the healthcare industry," ILB member Anne Baum said at an HSE panel discussion last fall. Baum is vice president of the Lehigh Valley region of Capital Blue Cross. "We are an unusual group of individuals with a set of common goals – to improve healthcare while cutting costs and making delivery more efficient.

Getting a grasp on infinity

A company needs to deliver a day's worth of parcels to their destinations while minimizing the number of miles its drivers log.

An oncologist sets out to destroy a tumor with microwave radiation while restricting damage to healthy tissue.

The first of these two optimization problems contains a finite number of variables, says Frank Curtis. The second is continuous. How will heat from the microwave radiation disperse across millions of cells? How will the individual temperatures of the various cells influence each other? How will these temperatures be affected by the amplitude and frequency the oncologist chooses?

Curtis, assistant professor of industrial and systems engineering, develops algorithms, or mathematical methods, that aim to solve optimization problems with thousands or millions of variables and to do so as quickly and reliably as the existing methods that solve smaller problems.

Software programs based on robust algorithms can solve the kind of continuous, large-scale, nonlinear optimization problem facing the radiologist, says Curtis, but they do not have the luxury of time when patients' lives are at stake.

"Computers will never be fast enough to solve continuous problems. We need better algorithms."
—Frank Curtis

Curtis, who has a three-year, single-investigator grant from NSF, has developed an algorithm capable of solving large-scale continuous optimization problems in less than a quarter of the time required by contemporary methods. In one such problem, the challenge is to optimize the cost-effectiveness of computing server rooms by minimizing the air flow required for cooling.

In modeling the bio-heat transfer involved in the oncologist's radiation problem, Curtis represents each point of interest — cell temperatures in this case — with a partial differential equation.

Curtis's algorithm solves large-scale continuous problems in a fraction of the time required by other methods.

"Our goal is to hit a target temperature for the tumor while keeping the temperature below the threshold for the noncancerous area and also monitoring the heat transfer.

"Because the body is a continuous entity with many overlapping regions, we have to model for space and time. We do that by turning one large-scale problem into a series of finite-dimensional ones."

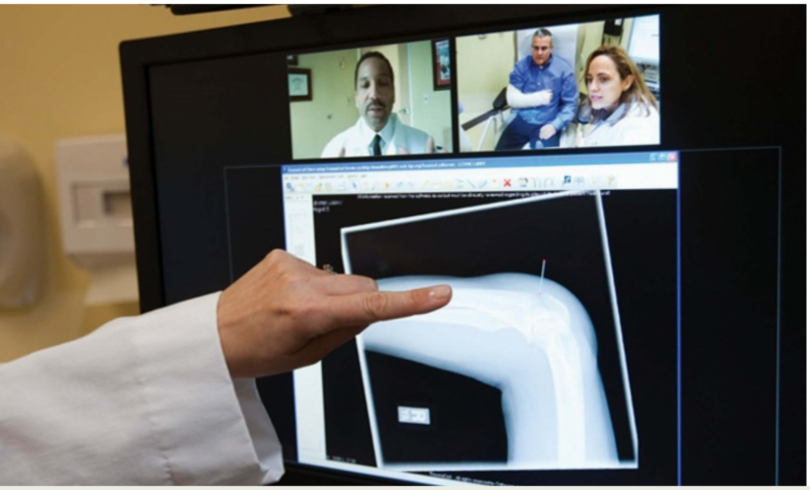
Like an image that gains resolution in proportion to its quantity of pixels, says Curtis, a mathematical model achieves greater discreteness, and a more accurate rendition of reality, in proportion to the number of equations it generates. If an algorithm is too complicated, however, it can require more computer time to generate a solution.

"Because of the complexity of the real world, you have to make sacrifices," says Curtis, who tests his algorithms on software and then on applications. "You have to make your model simple enough for the computer to generate an answer."

Curtis's goal is to develop algorithms that overcome computers' limitations.

"Continuous problems are infinite-dimensional," says Curtis. "Computers will never be fast enough to solve them. To stay ahead of these problems, we need better algorithms."

"One role of systems engineers is to be good stewards of resources, including people, materials, equipment and time." —Deborah Halkins



"But the organizations we represent often operate in silos. A lot of the data we generate is not transported between healthcare providers and patients, between different providers, or between insurance companies and providers.

"The HSE program gives us a rare opportunity to sit down together, share data across the entire gamut of healthcare, and integrate our individual goals into a common initiative."

The need for smoother flow of data is perhaps the most frequent topic of conversation at ILB meetings. Better communication, members say, would improve healthcare quality and accountability and enable the industry to shift from a volume- to value-based reimbursement structure – a change being pushed by the 2010 Patient Protection and Affordable Care Act.

"Insurance companies, as the ultimate payer of healthcare services, generate a huge amount of data," says Tom Huntzinger, account manager for Emerson, Reid & Co., the largest group health insurance general agency in the northeastern U.S. Huntzinger also chairs the Healthcare Legislative Committee of the Greater Lehigh Valley Chamber of Commerce.

"The ability to share data with providers is crucial to making improvements over time. Students in the HSE program can analyze data from multiple perspectives and help us evaluate insurance plans in terms of their outcomes. For example, if an insurance carrier introduces a wellness incentive into a plan, students can help us quantify corresponding changes in policy holders' behavior and improvements to their health. This will help carriers provide information to providers about the cost-effectiveness of plans.

"Students could also do comparative studies of different health insurance companies to find out which are doing well in a particular area, and which are not. This could help us write policies that help improve individual behaviors."

Another area of healthcare where

From impersonal data to more personal care

A graduate student uses analytics to predict the likelihood of rehospitalization.

In the arena of healthcare, says Ana Alexandrescu, numbers are cold, hard and devoid of personality. But data, intelligently interpreted and efficiently shared, can help America's healthcare industry cut costs, improve efficiency and give more individualized care to patients.

Alexandrescu recently developed a predictive analytical model to help BAYADA Home Health Care draw more meaningful conclusions from the data it keeps on 25,000 patients in 25 states.

Of particular interest to Alexandrescu, who earned an M.S. in industrial and systems engineering from Lehigh earlier this year, was helping BAYADA more accurately predict the likelihood that its patients will be admitted to hospitals.

Hospitalization rates have become a critical issue since Congress passed the Patient Protection and Affordable Care Act of 2010. In hopes of promoting accountability and shifting healthcare from a volume-based to value-based endeavor, the law authorizes penalties for providers who fail to meet new standards. One metric being closely watched by the federal Centers for Medicare and Medicaid Services (CMS) is the rate at which patients discharged from hospitals are readmitted within 30 days.

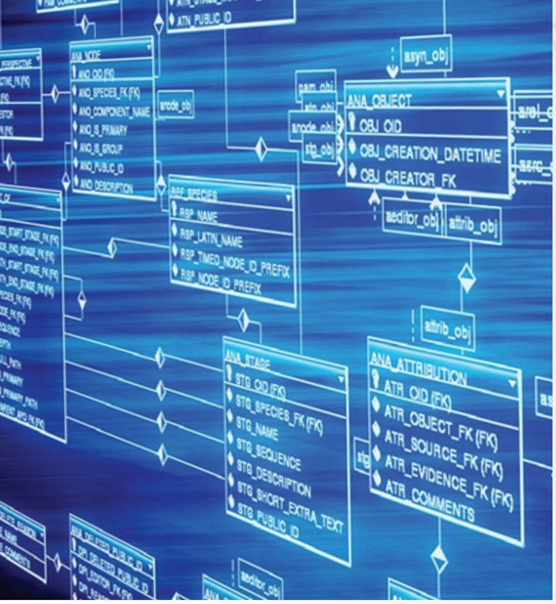
To limit rehospitalizations — and avoid possible reductions in CMS reimbursements — hospitals and home-healthcare agencies are turning to analytics, says Alexandrescu.

"Analytics means harnessing the power of large amounts of data. With the revolution in information technology, we have the ability to look at huge amounts of data. The challenge is to develop models that can analyze this data, spot trends and patterns, and help predict a likely outcome."

During her project with BAYADA, Alexandrescu analyzed data from 71,000 patient records. Testing several different statistical models, she developed a "decision tree," breaking data into progressively smaller subsets, for example, the portion of the sample group who are admitted with more than two diagnoses, the percentages of these patients who do and do not require oxygen, the percentages of oxygen users who live alone or with someone, etc.

She's confident that she has set up a good analytical foundation for BAYADA. But much remains to be done.

"I tested several different statistical models and tried to refine them to get the best prediction from the data set. The next challenge is to refine



systems engineers can contribute, says ILB member Tom Cassidy, is in enabling patients to avoid hospitalization and recuperate at home.

"Healthcare is a very fragmented world," says Cassidy, who earned a B.S. in industrial engineering from Lehigh in 1987 and is an area director responsible for operational quality assurance for BAYADA Home Health Care. "It's an oddly shaped sandbox we have to play in – and, therefore, a good environment for systems engineering skills.

"In particular, systems engineers can figure out the optimum discharge time and follow-up plans for hospital patients. This will help us minimize the possibility of rehospitalization."

A systems engineer's potential impact

Deborah Halkins uses a variety of methods to analyze healthcare processes at Lehigh Valley Health Network (LVHN), where she has served 11 years as director of management engineering.

Halkins and her staff combine systems engineering tools such as productivity analysis, statistical modeling, simulation and data mining with the traditional skills of observation, interviewing and time studies. They pay special attention to dynamic events where errors, delays and bottlenecks are most likely to happen. These include the "hand-offs" that occur when patients pass from one provider to the next in their journey through the continuum of care.

"As systems engineers, we work with everyone involved in a process, from the people who make meals and prepare operating rooms to nurses and doctors, in order to improve that process," says Halkins, who earned an M.S. in industrial engineering from Lehigh in 1983 and a Lehigh MBA in 1997.

"Our main focus is to heal, comfort and care for people by providing compassionate, quality healthcare."

In the last few years, says Halkins, LVHN has incorporated Toyota's Lean Thinking and A3 problem-solving techniques into its continuous improvement efforts.

"One role of systems engineers is to be good stewards of resources, including people, materials, equipment and time. Everything falls into place when creating systems that provide the best patient care possible.

"We are looking forward to working with the HSE program and engaging its students in solving systems problems in healthcare."

and test these models on much larger sets of data."

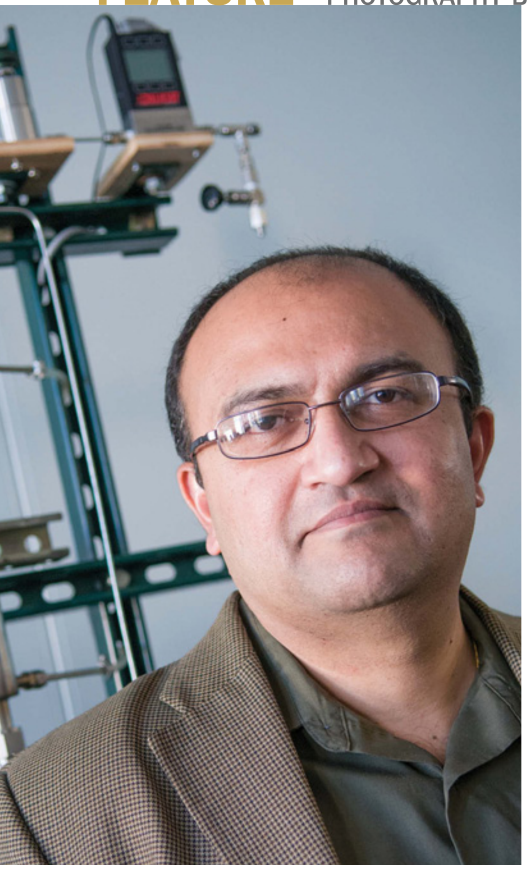
The ultimate goal, Alexandrescu says, is to extract meaningful information, share it efficiently among providers and optimize the quality of patient-care decisions.

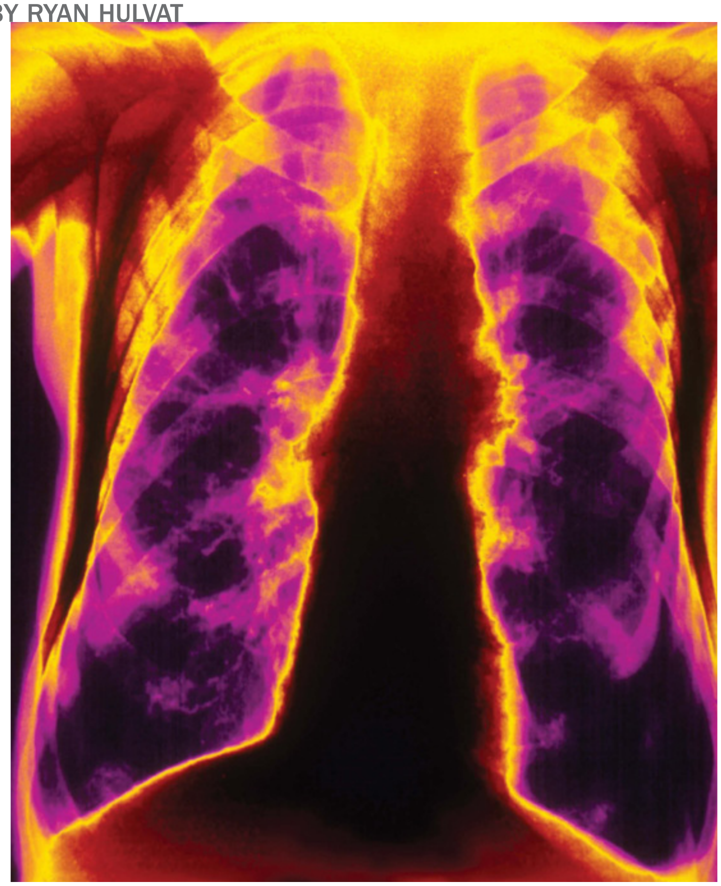
"The trends and patterns revealed by data-analysis tools can provide additional insights to physicians and complement or confirm their assessments," she says.

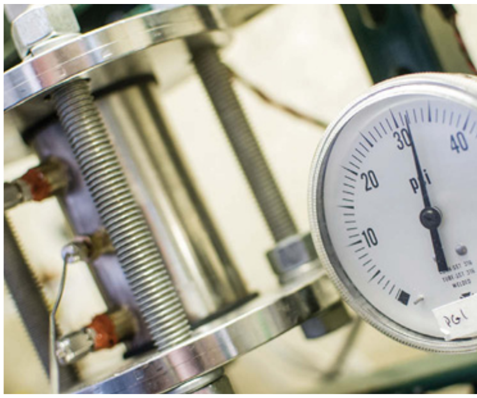
While systems engineers are not concerned with people, at least not officially, Alexandrescu notes, the tools they develop to analyze data have the potential to make healthcare more personal.

"Systems engineering doesn't look at the person, but at numbers and what they say about trends, patterns, cues. Our goal is to build a more integrated healthcare system that more effectively links providers and cares for the whole patient. Accountable care means that everyone works together to keep people out of hospitals."

As he conducts a teleconference with a patient and a physician, a radiologist examines a remote image that has been transmitted electronically immediately after being taken.



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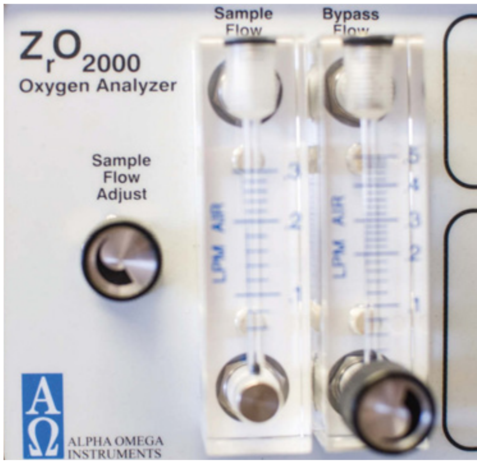
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Bypass Flow
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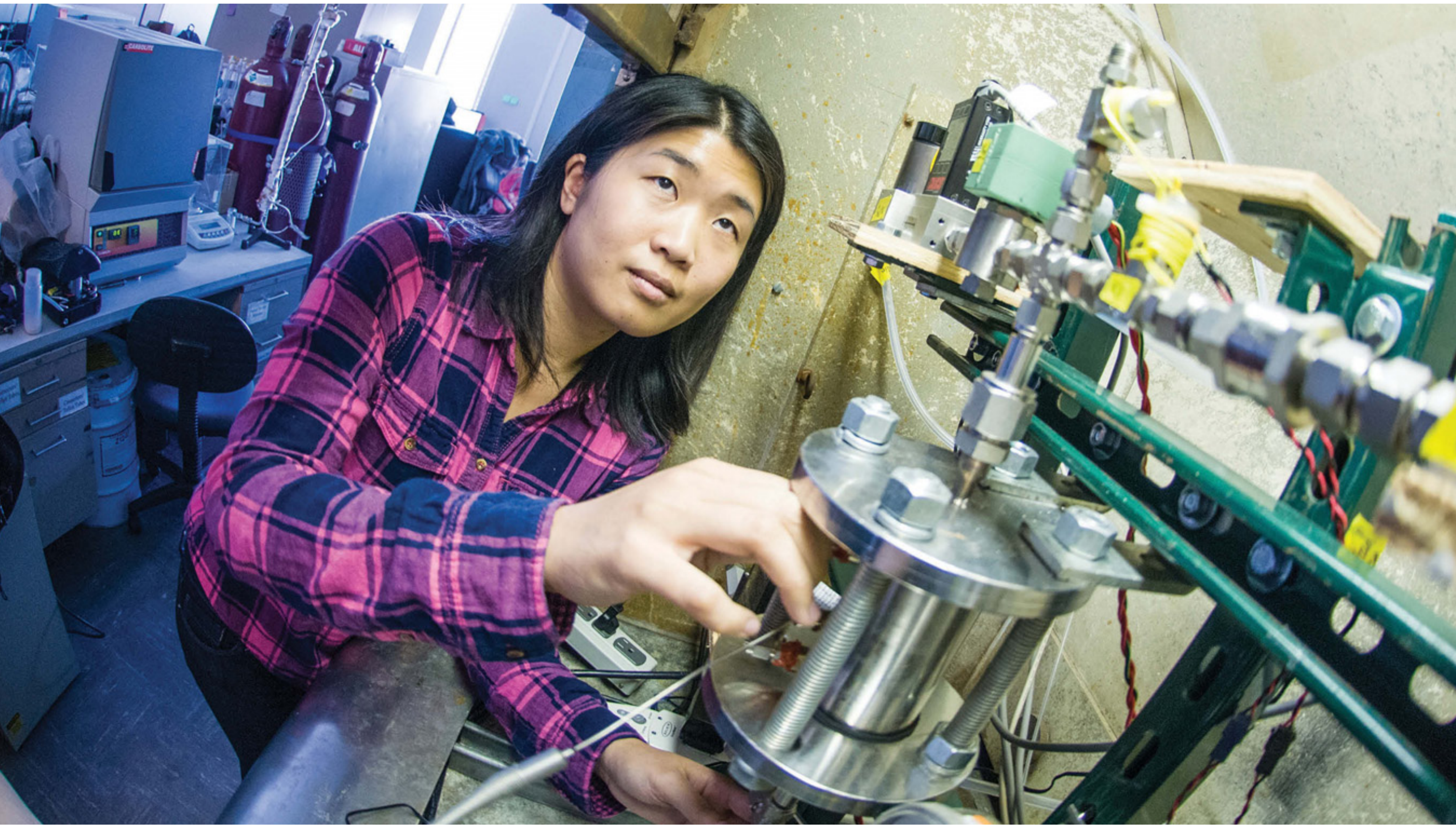
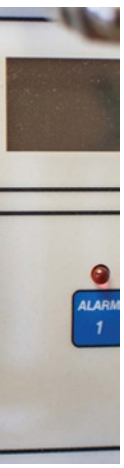




WHEN FASTER IS NOT NECESSARILY BETTER

Tuning the parameters of adsorption science to make a lighter, more efficient medical oxygen concentrator.

If you find yourself a bit winded after running up a flight of stairs, chances are you needn't worry – you've probably been spending too much time at your desk or in front of the TV. Once you resume exercising or walking, you'll be fine.

The feeling of being short of breath, however, can be a steady and unwanted companion for the estimated 16 million Americans who suffer from chronic obstructive pulmonary disease (COPD).

COPD doesn't receive nearly as much attention as cancer, heart disease or diabetes. But it can be just as serious. Globally, the World Health Organization estimates that COPD afflicts more than 64 million people, causing 3 million deaths a year. By 2030, WHO predicts COPD will be the third leading cause of death in the world.

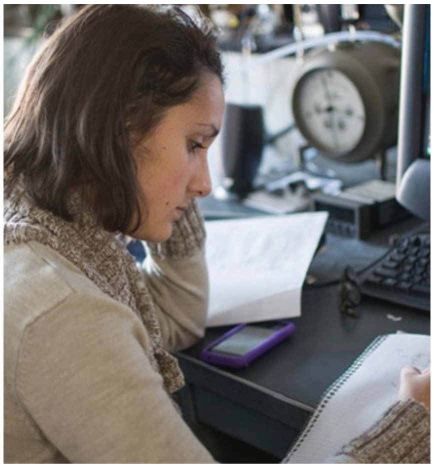
COPD is a family of diseases, ranging from chronic bronchitis, emphysema and pulmonary fibrosis to less common illnesses like lymphangioleiomyomatosis (LAM). All are characterized by a gradual loss of lung capacity and a progressive reduction in the amount of air that flows to and from the lungs. Many COPD patients eventually require concentrated oxygen in order to survive.

Those patients were once confined mostly to their beds, connected by breathing tubes to bulky cylinders or machines filled with compressed oxygen. Besides needing frequent refilling, the pressurized containers posed a hazard if they were dropped or if they came into contact with a spark or flame. And users could not leave home without carrying a cylinder or hauling a tank on a dolly.

In recent years, battery-operated medical oxygen concentrators (MOCs) weighing as little as six to eight pounds have made life easier for COPD patients. MOCs draw in compressed ambient air containing about 21-percent oxygen, enrich it to a concentration of 90- to 93-percent oxygen and supply it to a user. This is usually accomplished with rapid pressure swing adsorption (RPSA), an air-separation technology employing a zeolite adsorbent, which selectively retains the nitrogen from the air and produces the oxygen-enriched gas.

Shivaji Sircar and Mayuresh Kothare, both professors of chemical engineering, are seeking to substantially improve the performance of RPSA and the quality of life for COPD sufferers. They have developed

Mayuresh Kothare (above left) and post-doctoral researcher Chin-Wen Wu are fine-tuning a prototype device that selectively removes nitrogen from the air.



a new technology that could significantly reduce the weight of a portable MOC device while improving oxygen recovery, which lowers the power requirement for air separation and, thus, the compressor size.

The two researchers collaborate with and receive support from one of the half-dozen U.S. companies currently marketing MOCs. In December 2011, they were one of three research teams to win $200,000 in funding from the Science Center in Philadelphia. Fifty groups, many affiliated with research and teaching hospitals, competed for prizes. The Lehigh team was chosen from among 10 groups that had been invited to make business and technical presentations to the Science Center.

"Our experiments show that faster is not always better. We've demonstrated that beyond a certain cycle speed, you see diminishing returns." —Shivaji Sircar

Looking beyond cycle speed

Sircar, a member of the National Academy of Engineering, has more than 40 years of R & D experience in adsorption and separation, including 30 years with Air Products and Chemicals Inc., where he served as chief scientist before retiring and joining Lehigh in 2002. He is the author of numerous publications and patents.

Kothare studies microchemical systems, feedback control and neuroengineering and has also published extensively. He is also a visiting professor of biomedical engineering at Johns Hopkins University, where he works with neurologists to improve brain-computer interface technology and help patients regain control of functions lost to brain damage.

Kothare and Sircar (below, with graduate student Alexandra Simons and Wu) have a patent pending on a device that could reduce MOC weight by 30 percent and boost oxygen recovery by 20 percent.

The two researchers began their current collaboration about three years ago when Kothare, who was pursuing new applications for microreactors, asked a graduate student to investigate the feasibility of building an adsorption-driven separations system on a silicon wafer. The researchers later determined that reducing the size of a conventional MOC was a more realistic goal.

The new project was conducted by Siew Wah Chai, who earned her Ph.D. in 2011 and now works for Praxair. Chai demonstrated in a lab-scale unit that, by modifying the design of the RPSA cycle and the adsorbent material, it would be possible to make a more compact, lightweight and energy-efficient MOC. Chai, Kothare and Sircar published their findings in a key paper in *Industrial and Engineering Chemistry Research*, a notable journal of the American Chemical Society, and filed a patent application.

The Lehigh team is now seeking to optimize the typical MOC unit, which contains two columns packed with a preferred zeolite for air separation. As compressed air flows through the columns, the zeolite adsorbs nitrogen while oxygen passes through. The flow is then reversed in order to desorb the adsorbed nitrogen by backpurging with a part of the oxygen product gas at a lower pressure. The cyclic adsorption-desorption steps are employed in conjunction with other complementary process steps to obtain the best performance from the MOC.

Researchers have traditionally sought to reduce the total cycle time of the pressure-swing adsorption process in order to decrease bed size factor (BSF, or pounds of adsorbent used by the MOC per ton of oxygen produced per day), to increase cycle frequency and to boost oxygen recovery.

The Lehigh team, after testing different adsorbent particle sizes, adsorption pressures and cycle times, reported in *Industrial and Engineering Chemistry Research* that, contrary to established

belief, BSF cannot be "indefinitely reduced" by lowering total cycle time.

"The conventional wisdom about pressure-swing adsorption technology says that the faster the cycle time, the better," says Sircar. Consequently, other researchers have sought mechanical solutions, such as devices that switch air flow in subseconds or use complex rotary valves, to speed up the frequency of RPSA cycling.

"Our experiments show that faster is not always better. We've demonstrated that beyond a certain cycle speed, you see diminishing returns. We've looked at other factors – operating condition, cycle time, material, cycle design. We believe we've achieved the appropriate combination of all the parameters involved in order to improve BSF as well as oxygen recovery."

Greater mobility for COPD patients

The Lehigh team has a patent pending on technology that promises to reduce the MOC device's weight by 30 percent, while boosting oxygen recovery by 20 percent. The resulting higher energy efficiency and lower power requirement will extend the operating time of a typical MOC, which currently runs for two to three hours before batteries must be recharged, and provide patients with longer periods of mobility.

The team plans next to build and test a prototype RPSA device, demonstrate its performance under realistic conditions, and fine-tune its operating conditions, including pressure, flow, temperature and switch times.

Two designs are envisioned – a more conventional two-column RPSA with an external oxygen storage tank and a novel "snap-on" MOC that has no compressor but can be plugged into one of the existing compressed air lines that are commonly provided in hospitals, ships, airplanes and other facilities.

Smaller, lighter, more energy-efficient MOCs, say Sircar and Kothare, are the wave of the future. As the world's population ages and more cases of COPD are diagnosed, the global market for MOCs is expected to grow from less than $400 million in 2011 to about $1.8 billion by 2017. Evidence suggests that oxygen therapy might also slow the decline in mental cognitive abilities in people with dementia. And new applications in aeronautics, the automotive industry and even scuba-diving equipment are possible.

Just as importantly, lighter, smaller MOCs will grant greater mobility to COPD patients, enabling them to spend more time on their feet and engage in the cardiovascular exercise that physicians believe promotes pulmonary rehabilitation and could increase life span.

"A project like this makes you feel that your work is very tangible and helpful to society," says Kothare. "Will we be the group that succeeds in developing the next-generation MOC? We don't know. But we believe that our approach of producing a better MOC using the fundamental science and technology of adsorptive gas separation will get us there."

FIG. 1 • TWO-COLUMN RPSA

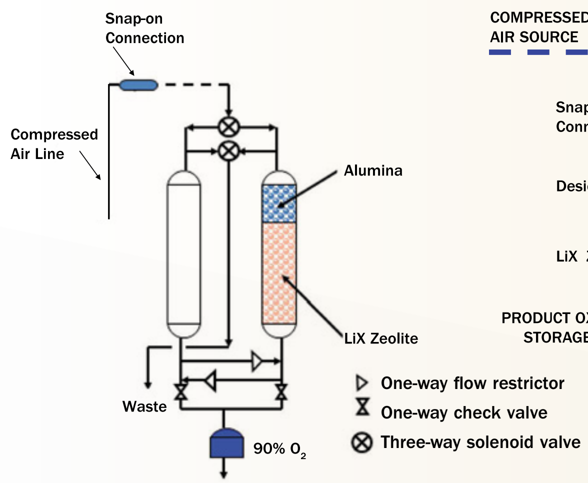
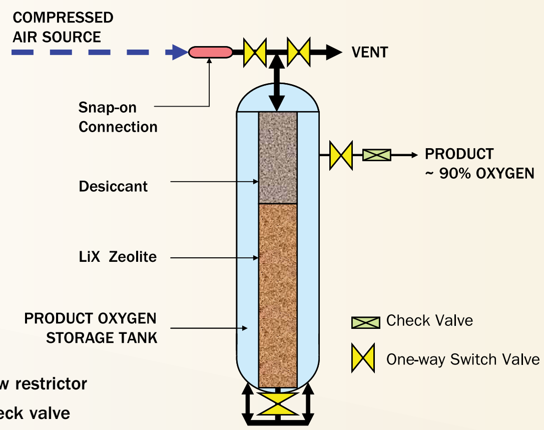


FIG. 2 • ONE-COLUMN RPSA



The team is developing a conventional two-column MOC with an external oxygen storage tank as well as a novel "snap-on" device without a compressor that plugs into an existing line of compressed air.

View larger ▸

HEALTHCARE'S GAME-CHANGERS

Students in a new master's program examine the entire healthcare system.

Hisham Nabaa says queuing theory, statistical modeling and other engineering principles can improve quality and efficiency.

It's no secret that the U.S. healthcare system leaves a lot to be desired. We spend far more on healthcare than any other country, yet our patient outcomes are no better. In fact, it has been estimated that 20 to 30 percent of medical spending – roughly $700 billion a year – yields no benefit to patients.

Much of this waste is driven by defensive medicine, like redundant or unnecessary tests and procedures, and by inefficient healthcare administration. Little attention, however, has been paid to restructuring the healthcare system to reduce this inefficiency.

That's something that the graduates of the new master of engineering in Healthcare Systems Engineering (HSE) program are hoping to change. Housed in the department of industrial and systems engineering, the program aims to use these principles to improve and streamline the medical system.

"The idea of looking at the entire system is going to benefit the healthcare system tremendously," says Jeremy Benton, a student in the program who graduated from Lehigh in 2011 with a B.S. in mechanical engineering.

"For example, you might have a bottleneck in the waiting room and a $30 million CT scanning machine sitting idle. All you need to do is add another receptionist, but because the CT room never talks to the waiting room, they don't understand why they're idle. An industrial engineer can model the whole situation and find the bottleneck."

Technology is another way to improve communication, says Denise Campion, an HSE student who has a bachelor's degree in operations management from Pennsylvania State University and a certificate in project management from Lehigh.

"You can put technology behind solutions, like notifying patients on their mobile devices that the doctor is running an hour late instead of having them sit in the waiting room getting angrier and angrier," she says.

While many students in the program have backgrounds in business or engineering, like Benton and Campion, others come from the medical field. They know the frustrations of the current system firsthand.

Take Kristen Tellez, for example. She graduated from Penn State in 2010 with a degree in biobehavioral health – a combination of disciplines like psychology and biology that focuses on preventive medicine.

Tellez spent a semester as a nurse at a hospital and planned to apply to an accelerated nursing program, but she was frustrated by how inefficient the hospital was. The HSE program stood out to her because it combines basic clinical knowledge with systems engineering principles.

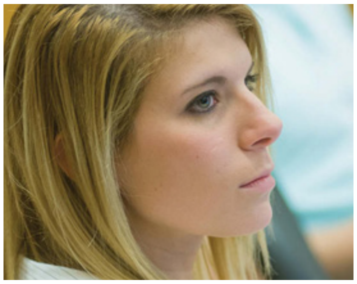
"Engineering is a totally different way of thinking, and it's really needed in healthcare," she says. "People on the clinical side think about what's best for the patient but may not think about the financial aspect, whereas people in healthcare administration mostly think about costs and saving money. With systems engineering, you can run models to get the optimal answer to the problem before you implement a solution."

Sarah Creswell, a registered nurse in the program, shares Tellez's perspective.

"It's sometimes frustrating when you work in healthcare and you keep being restricted," says Creswell. "I never liked the answer 'that's just the way it is.' I like the idea of improving the healthcare system so that healthcare professionals can do the right thing the right way for the right reason."

"I like the idea of improving the healthcare system so that healthcare professionals can do the right thing the right way for the right reason." —Sarah Creswell

Terry Theman, a retired cardiac surgeon who practiced at St. Luke's Hospital in Bethlehem for 28 years, agrees that systems engineering offers the solution.



"Engineering takes a different approach. It looks at all the components, breaks them into separate units and then starts asking the important questions," he says.

"I can see it streamlining healthcare and making it more effective. The Institute of Medicine estimated that as many as 100,000 patients die every year in America from medical errors. Some of those are preventable, and one of our missions is to reduce those to the absolute minimum."

With their new knowledge in areas like queuing theory, statistical modeling and optimization, the HSE students hope to find jobs with hospital networks, health insurers and consulting firms, and in other areas of healthcare. From there, they will play a central role in making the U.S. healthcare system more efficient and more cost-effective.

HSE AT A GLANCE

The master of engineering (M.Eng.) in healthcare systems engineering prepares students to improve the quality and efficiency of healthcare delivery.

Students in the program come from the engineering, science, business, mathematics and other disciplines. Core courses cover healthcare systems, quality and process improvement in healthcare, financial management in healthcare and information technology in healthcare.

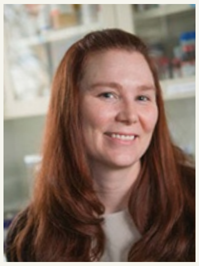
Students also take industrial and systems engineering courses in simulation, statistics, optimization modeling and probabilistic modeling. These cover project management, engineering economics, operations and process flow, and queuing.

Each student is required to complete an industry-related capstone project. The projects address issues specific to healthcare, such as optimizing the flow of patients through an emergency room, improving operating room scheduling, aiding medical decision making and modeling chronic care.

"Every student will graduate with a broad understanding of the healthcare industry along with the ability to use design thinking as a process for problem solving," says Hisham Nabaa, HSE program director and professor of practice in the industrial and systems engineering department.

"Graduates of the program will possess the technical skills necessary to analyze healthcare systems, identify inefficiencies and propose solutions or new processes to improve the overall quality and efficiency of healthcare. Having an employee with such skills is invaluable to any healthcare organization."

Nabaa has built relationships with major hospitals, home-healthcare agencies, insurance companies, pharmaceutical companies and government agencies. These partners advise the program to make sure it meets industry needs. In addition, students can work with these partners to develop capstone projects that address the healthcare problems they study.



Sabrina Jedlicka and her colleagues are seeking to determine when differentiating adult stem cells can be reimplanted to help regenerate nerves.

Probing the life of the differentiating cell

Researcher assesses a cell's behavior in its natural environment.

How do living cells interact with synthetic materials? Finding the answer is critical for understanding cell growth and development in the lab and for developing prostheses that can be successfully implanted in the body.

"Many cell-based therapeutic devices have been proposed in the last 10 years, and most of them started with isolated cells in a petri dish," says Sabrina Jedlicka, assistant professor of materials science and engineering.

Jedlicka studies adult stem cells, which can be stimulated to grow into bone, muscle and other tissues. She investigates how they are influenced during this process of differentiation by the textures of living organs and by the mechanical and chemical properties of the body.

"The better we can mimic the natural environment in the laboratory," she says, "the more we can learn about cell behavior. This will help us manipulate cells to maintain stability in a therapeutic environment."

With Filbert J. Bartoli, professor of electrical and computer engineering, to pinpoint the precise stage of differentiation at which cells can be reimplanted to help regenerate nerves.

"Most of what we know about neurons comes from taking a sample of cells, fixing them and figuring out what proteins or mRNA they are expressing," says Jedlicka. Researchers can do chemical assays to determine how many of these proteins and/or neurotransmitter molecules are secreted as a whole, she adds, but they can't determine which cells were stimulated to produce them or when.

"It's really difficult to tell what state those cells are in unless you can see what is happening in real time," she says.

Bartoli is developing a biosensor environment to determine when cells secrete chemical markers that are known to correspond to a specific stage of their development. Jedlicka engineers scaffold-like surfaces that support the cells' growth. Xuanhong Cheng, assistant professor of materials science and engineering, also collaborates.

"I build surfaces that cells adhere to and differentiate on," Jedlicka says.

> *"The better we can mimic a cell's natural environment in the laboratory, the more we can learn about cell behavior."* —Sabrina Jedlicka

Jedlicka is trying to obtain a more accurate picture of what neural stem cells do when they differentiate into neurons.

Working with mouse neural stem cells that are on the road to becoming neurons, the two researchers are seeking "Xuanhong builds surfaces that sense particular molecules, and Fil integrates these surfaces on a sensing apparatus that tells us what is happening."

Stem cells "like" surfaces based on a host of parameters – Is the surface soft or stiff? Is the topography bumpy, rough or smooth? Are there chemical molecules that are attractive to receptors on the cell surface?

In one project, Jedlicka uses solid-state, 2-D techniques to attempt to mimic the effect of extracellular matrix proteins and growth factors on developing stem cells. Using animal-derived sera or recombinant proteins to stimulate cell differentiation is well-known science, but those techniques are "astronomically expensive" on a large scale and can involve complex FDA regulations.

Jedlicka, searching for a better way, describes in a paper currently under review how she "took a 2-D surface and decorated it with mixed biochemical motifs and successfully differentiated bone cells at a rate similar to that found in natural bone repair."

The key to her approach lies in understanding the normal development of different kinds of cells.

"If I'm the stem cell in my natural environment and I'm becoming a more differentiated cell, what am I experiencing?" she asks. "What growth factors are there? What extracellular matrix proteins are there? How am I adhering (to adjacent tissue)? What are the mechanics?

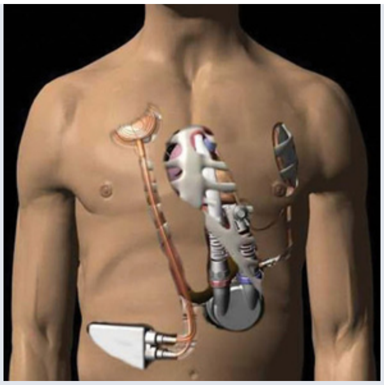
"As an engineer, I can't address all those factors in one surface, at least not yet. The experiments would be massive; I would have to test each variable individually and then in combination. So I break the problem down to 'what are the minimum requirements to stimulate a cell to do what I want it to do?'"

Four years into her Lehigh career, Jedlicka advises a growing number of undergraduate and graduate students in her lab.

"A lot of students come in without research experience," she says. "I try to help them think about research from an academic perspective and then give them room to take a project and make it their own.

"Then I have to make sure that they get the resources they need to make themselves shine in a very competitive world."

Lehigh engineering alumni hold leadership positions in healthcare organizations, research centers and medical innovation companies. Here are a few examples:



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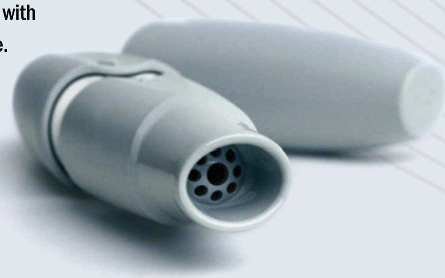
A designer of medical devices for most of his professional career, Phil Fleck '66 now brings his expertise to Norwich Ventures, assessing new technologies and assisting rising entrepreneurs in the business development process.

Julie Shimer '79G, '82PH.D. is CEO and president of Welch Allyn, a leading global provider of medical diagnostic equipment and solutions.

Jay Teich '75 is founder, president and CEO of Seahorse Bioscience, which makes analytical instruments, biomanufacturing systems and consumable labware products for biological research and drug discovery.

Glenn Batchelder '84 is president and CEO of Civitas Therapeutics. Among the firm's respiratory therapies is ARCUS™, which delivers precise dosages with a breath-activated device.



As president and CEO of global medical technology leader Becton, Dickinson and Company (BD), Vincent Forlenza '75 guides the efforts of 29,000 associates in more than 50 countries throughout the world.

Dr. Hank Dorkin '70 holds two roles at Children's Hospital of Boston — director of the Cystic Fibrosis Center and associate chief of the division of respiratory diseases.

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

www.lehigh.edu/heritage

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A MORE SYSTEMATIC APPROACH

From managing chronic disease to streamlining communication to organizing and storing information, systems engineers have the potential to play a significant role in healthcare, says Gary Sieck, the dean of research and academic affairs at Mayo Clinic's College of Medicine.

See page 8