McCormick

Northwestern Engineering

# Biomedical Engineering

Robert R. McCormick School of
Engineering and Applied Science
Northwestern University

SUMMER 2009

## McCormick Pioneers Low-cost HIV test

In developing countries, where 1.5 million HIV-positive women become pregnant each year, residents face a unique problem: babies born to HIV-infected mothers carry the virus's antibodies — the usual indicator of the virus in the body and what most HIV tests look for — whether they are infected or not.

Early detection in infants is important. While adults can manage the disease for decades, an infant who isn't treated will likely die within a year or two. But tests available today that search for other indicators of the virus, such as DNA or proteins, use complex instrumentation, require specimens to be transported long distances, and can be cost prohibitive.

David Kelso, professor of biomedical engineering and director of the Center for Innovation in Global Health Technologies, and his research group now offer an answer: two new low-cost, portable HIV tests that use DNA or proteins to test for HIV.

McCormick researchers began working on the problem in 2006 after receiving a grant from the Bill & Melinda Gates Foundation. To jumpstart the process, Abbott provided Kelso's lab with a working HIV test that uses polymerase chain reaction (PCR) technology that extracts RNA from blood to detect the virus. "Our job was to replace the existing large, expensive instrument with something that was small, cheap, and battery operated," Kelso said.

Inverness gave Kelso's lab an HIV test that works similar to a home pregnancy test. This strip test is portable, simple, and extremely low cost — but it tests for antibodies, which, in the case of infants with HIV-positive mothers, is not reliable. So Kelso's goal was to create a test that used the same strip but detected the presence of the p24 protein of HIV.

In addition to the two infant tests, Kelso's lab also worked on a similar low-cost, quick test that could measure the viral load of HIV in a patient. The test shows how much of the virus is still active in a patient's body, which in turn indicates whether a drug is working or whether the patient has a strain of HIV that doesn't respond to that medication.

In 2006 Kelso and his lab — which includes a dozen research professors, postdoctoral researchers, and graduate students — went to work trying to find novel ways to perform these tests. For the strip test that detects the p24 protein, researchers made two breakthroughs: they developed a way to separate the protein from the infant's antibodies, and they changed the indicator line from pink to black, making it easier to see. What resulted was an HIV test that is just a tiny strip of paper and may cost as little as 50¢ to manufacture.

*Abhishek Agarwal, Kunal Sur, and David Kelso examine a prototype for an HIV test.*

While the test is inexpensive, it sacrifices a measure of accuracy. At stake in these tests are two performance indicators: sensitivity and specificity. Sensitivity is the percentage of the results that will be positive when HIV is present, and specificity is the percentage of the results that will be negative when HIV is not present. In other words, if a test's specificity is 90 percent, 10 percent of people who take the test will be incorrectly told they have HIV. The strip test has a sensitivity of 90 and a specificity of 98 percent.

The PCR test, which amplifies DNA, required researchers to find a way to extract nucleic acids in order to replicate them to detect the disease. The result was a battery-operated machine that is about the size of a toaster. This test costs more — $1 to $2 — and requires more power than the strip test, but initial results show the test to be 100 percent sensitive and specific.

For the viral load test — which uses some of the same technology as the PCR test — researchers took a test that used a device the size of a table and found a way to use a microfluidic platform that would simplify the process.

Researchers plan to take the two infant tests to Africa for testing soon.

"This is real-world product development," Kelso says. "The end goal is not a paper in Science. It's a humanitarian product on the market."

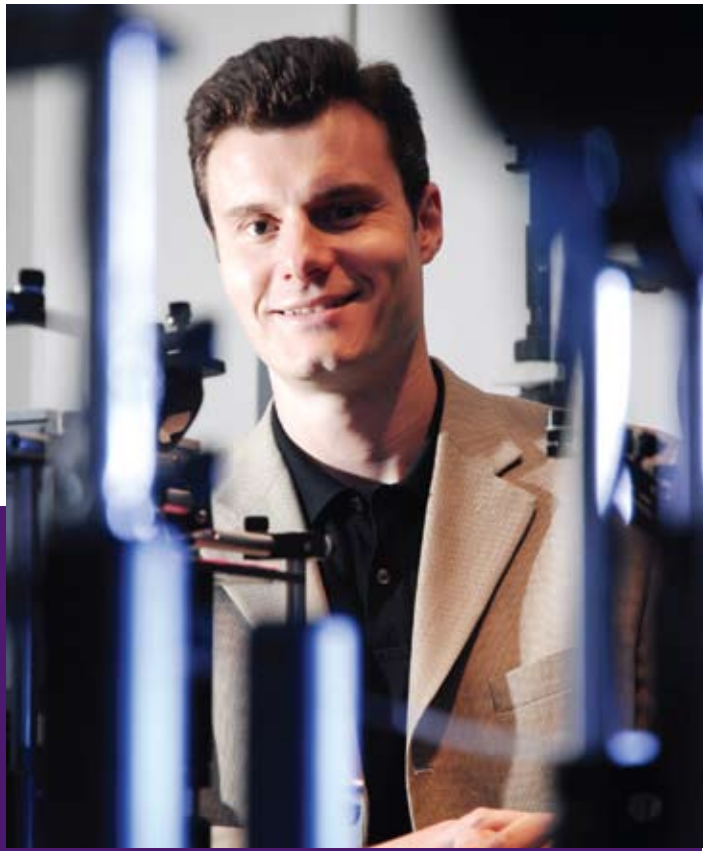
# Optical Techniques Show Continued Promise in Detecting Pancreatic Cancer

Optical technology developed by Vadim Backman has been shown to be effective in detecting the presence of pancreatic cancer through analysis of neighboring tissue in the duodenum, according to clinical trial results published in the journal *Disease Markers*.

The promising new technology — which researchers hope could help raise the extremely low survival rate of pancreatic cancer patients by aiding early detection — uses novel light-scattering techniques to analyze extremely subtle changes in the cells of the duodenum, part of the small intestine neighboring the pancreas. The cells are obtained through a minimally invasive endoscopy.

The study shows that cells that appear normal using traditional microscopy techniques do show signs of abnormality when examined using the Northwestern technique, which provides cell analysis on the much smaller nanoscale.

The technology was developed by Backman, professor of biomedical engineering at the McCormick School of Engineering and Applied Science, and Vladimir Turzhitsky, a graduate student in Backman's lab.



*Vadim Backman has developed technology that makes use of a biological phenomenon known as the "field effect," a hypothesis that suggests the genetic and environmental milieu that results in a neoplastic lesion in one area of an organ should be detectable throughout the organ and even in neighboring tissue.*

In the study of 203 patients, the technique accurately discriminated with 95 percent sensitivity between healthy patients and those with differing stages of the disease. (Only 5 percent of patients were found to have been diagnosed with false negatives after testing.) The specificity of the testing group was 71 percent. These results confirm those of an earlier study of 51 patients published in August 2007 in the journal *Clinical Cancer Research*.

The larger number of patients in the more recent study allowed researchers to calculate the "area under the receiver operator characteristic" (AUROC), which is an analysis of the accuracy of the test in distinguishing healthy samples from diseased samples. While the sensitivity and specificity of tests may vary based on the threshold set by researchers for diagnosis, the AUROC measures the overall efficacy of the diagnostic technique. The analysis showed an 85 percent AUROC for the Northwestern method. (Clinically sound tests typically have an AUROC greater than 70 percent.)

The study in Disease Markers also reports promising results in detecting mucinous cyst lesions, which are a precursor to cancer. If confirmed in further clinical trials, this approach may lead to a method for early diagnosis.

Pancreatic cancer is among the most deadly forms of cancer, with a five-year survival rate of just 5 percent. It is so deadly, in part, because early detection is difficult.

"Typically, by the time a patient is diagnosed with pancreatic cancer, it is too late for the most successful treatments," says Backman. "Our hope is that this technology will provide a better method for early diagnosis of the disease, which could greatly improve the survival rate."

The technology combines two complementary optical techniques, four-dimensional elastic light-scattering fingerprinting (4D-ELF) and low-coherence enhanced backscattering spectroscopy (LEBS). The researchers found that the two combined work better than one alone in pancreatic cancer screening.

During the test, a xenon lamp shines intense, white light through a series of lenses and filters onto the specimen — cells from the duodenum. The light refracts through the outermost layer of tissues and scatters into a spectrograph, a device that separates a beam of white light into its component wavelengths and measures them. An image sensor captures the result, then a computer analyzes the pattern of light scattering, looking for the "fingerprint" of carcinogenesis in the nanoarchitecture of the cells.

The technology makes use of a biological phenomenon known as the "field effect," a hypothesis that suggests the genetic and environmental milieu that results in a neoplastic lesion in one area of an organ should be detectable throughout the organ and even in neighboring tissue.

If similar results are found when the technique is applied to other organs, the method could have broad impact on the timely treatment of breast cancer, lung cancer and other forms of cancer.

"We are developing a suite of optical technologies that we hope will transform our ability to detect cancer at its earliest stages," says Backman.

# Nanodiamond Drug Device Could Transform Cancer Treatment

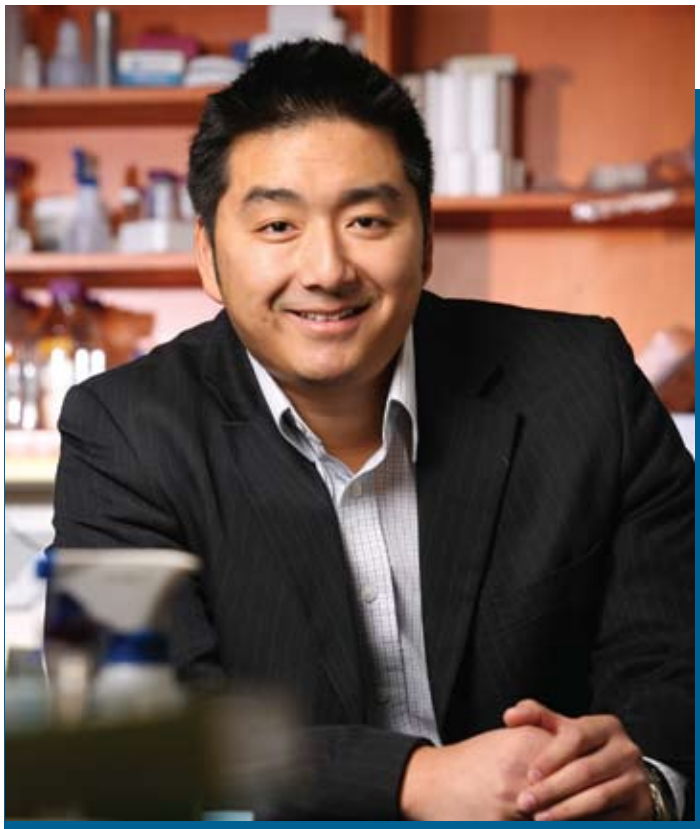
A Northwestern University research team has developed a promising nanomaterial-based biomedical device that could be used to deliver chemotherapy drugs locally to sites where cancerous tumors have been surgically removed.

The flexible microfilm device, which resembles a piece of plastic wrap and can be customized easily into different shapes, has the potential to transform conventional treatment strategies and reduce patients' unnecessary exposure to toxic drugs. The device takes advantage of nanodiamonds, an emergent technology, for sustained drug release.

The researchers demonstrated that the device releases the chemotherapy agent Doxorubicin in a sustained and consistent manner — a requirement of any implanted device for localized chemotherapy. The results were published by the journal *ACS Nano*.

"The thin device — a sort of blanket or patch — could be used to treat a localized region where residual cancer cells might remain after a tumor is removed," said Dean Ho, assistant professor of biomedical engineering and mechanical engineering at the McCormick School of Engineering and Applied Science, who led the research.

If a surgical oncologist, for example, was removing a tumor from the breast or brain, the device could be implanted in the affected area as part of the same surgery. This approach, which confines drug release to a specific location, could mitigate side effects and complications from other chemotherapy treatments.



*Dean Ho has developed a promising nanomaterial-based biomedical device that could be used to deliver chemotherapy drugs locally.*

> *The thin device — a sort of blanket or patch — could be used to treat a localized region where residual cancer cells might remain after a tumor is removed.*

In their study, Ho and his colleagues embedded millions of tiny drug-carrying nanodiamonds in the FDA-approved polymer parylene. Currently used as a coating for implants, the biostable parylene is a flexible and versatile material resembling plastic wrap. A substantial amount of drug can be loaded onto clusters of nanodiamonds, which have a high surface area. The nanodiamonds then are put between extremely thin films of parylene, resulting in a device that is minimally invasive.

To test the device's drug release performance, the researchers used Doxorubicin, a chemotherapeutic used to treat many types of cancer. They found the drug slowly and consistently released from the embedded nanodiamond clusters for one month, with more Doxorubicin in reserve, indicating a more prolonged release (several months and longer) was possible. The device also avoided the "burst" or massive initial release of the drug, a common disadvantage with conventional therapy.

In control experiments, where the drug was present but without the nanodiamonds, virtually all of the drug was released within one day. By adding the drug-laden nanodiamonds to the device, drug release was instantly lengthened to the months-long timescale.

In addition to their large surface area, nanodiamonds have many other advantages that can be utilized in drug delivery. They can be functionalized with nearly any type of therapeutic. They can be suspended easily in water, which is important for biomedical applications. The nanodiamonds, each being four to six nanometers in diameter, are minimally invasive to cells, biocompatible and do not cause inflammation, a serious complication. And they are very scalable and can be produced in large quantities.

Ho and his research group previously pioneered the application of nanodiamonds for systemic drug-carrying applications. This new work successfully transitions the nanodiamonds from basic materials to serving as a foundation for device manufacturing.

"One of the most significant aspects of this work is that the fabrication procedures are highly scalable, meaning hundreds, or even thousands, of devices potentially could be manufactured in parallel and at low cost," said Ho.

# Professor Guillermo Ameer's Start-Up Wins Business Plan Competition

*Guillermo Ameer started* VesselTek Biomedical *after he realized that the biocompatible coating that promotes the safety and success of vascular repairs that he developed in his lab would need outside funding and support if it were ever to make it to market.*

A McCormick startup recently won the Chicago Biomedical Consortium business plan competition.

VesselTek Biomedical, an innovative vascular products company started by Guillermo Ameer, associate professor of biomedical engineering at the McCormick School of Engineering and Applied Science at Northwestern University, his former student Antonio Webb, and Melina Kibbe, assistant professor of surgery at the Feinberg School of Medicine, received a $10,000 prize for winning the annual competition, which invites graduate student teams from its three participant schools — Northwestern, University of Chicago, and University of Illinois at Chicago — to submit biomedically relevant business plans in order to compete for the grand prize. This year, six teams competed.

VesselTek Biomedical started a year ago after Ameer realized that the biocompatible coating that promotes the safety and success of vascular repairs that he developed in his lab would need outside funding and support if it were ever to make it to market.

Webb, VesselTek's senior scientist/development engineer, became the company's first employee, and last fall the company entered into the State of Illinois's entrepreneurial innovation competition called Innovate Illinois. Though it was selected as one of the 12 finalists, the company ultimately didn't win. When Webb presented at the CBC business plan competition, it was another chance to show investors what the company was made of.

"Tony Webb did an excellent job presenting," Ameer says, "and winning this competition validates the company's goals. When it comes to raising funds, we hope it will open doors."

Ameer says a synthetic graft with biocompatible coating that would reduce thrombosis could be on the market within three years. A drug-eluting version, making artificial graft procedures as successful as those using natural vessels, will follow within the next five years.

The Chicago Biomedical Consortium (CBC), launched in 2002, aims to stimulate collaboration among scientists at Northwestern University, the University of Chicago, and the University of Illinois at Chicago that will transform research at the frontiers of biomedicine. The Chicago Biomedical Consortium is supported by The Searle Funds at The Chicago Community Trust.

# Professor Heads to Los Angeles, Gets Science in Movies

Malcolm MacIver: teacher, researcher, and now — Hollywood consultant?

MacIver, assistant professor of biomedical and mechanical engineering at the McCormick School of Engineering and Applied Science at Northwestern University, left his lab for Los Angeles this past winter in hopes of bringing good science to the silver screen.

MacIver met with the writers and developers of Tron 2 — a sequel to the 1980s cult classic Tron, in which computer programmers are transported inside a computer to battle a dictator-like Master Control program — to help develop a storyline that incorporates accurate science and revolutionary research.

MacIver's expertise was provided through a new program called the Science and Entertainment Exchange, which aims to connect top scientists and engineers with writers, producers and directors in the entertainment industry to "help bring the reality of cutting-edge science to creative and engaging storylines."

Through the exchange, scientists act as more than just fact checkers who tell writers and producers when they misplace stars in the sky or overstate the possibility of getting dinosaur DNA from mosquitoes trapped in amber.

"We get in on the scriptwriting phase, in the development phase," MacIver says.

So MacIver, along with four other scientists from California Institute of Technology, spent time brainstorming ideas with the Tron 2 team. Though the actual storyline is under wraps, MacIver did say that they offered advice on how to make certain aspects of the story convincing.

"I think we as scientists and researchers can contribute a lot to storytelling," he says. "They say that truth is stranger than fiction, and a lot of us, the research we work on, would be great grist in the narrative mill. Plus we know the laws of science, so when there are irregularities in movies, we can make sure they're there not because of a mistake but because of dramatic effect."

Now that President Barack Obama stated in his inaugural address that he will "restore science to its rightful place," MacIver hopes that scientists can shed their nerdy images and show people the wonder behind science and research.

"It would do us good, as a society, to have science celebrated more," he said.

MacIver says he's already been in talks to help consult on another project — though until the deal is done, he's not saying a word. That's Hollywood for you.


*Malcolm MacIver with Michael Rymer, executive producer of Battlestar Galactica and son of Zev Rymer, MacIver's colleague in the Department of Biomedical Engineering, during another interaction with the entertainment industry in 2008.*

# Grouping Muscles To Make Controlling Limbs Easier

With more than 30 muscles in your arm, controlling movement — whether it's grasping a glass or throwing a baseball — is a complex task that potentially takes into account thousands of variables.

But researchers at Northwestern University have shown that it could be possible to control a limb by stimulating groups of muscles rather than individual muscles — a finding that could make it easier to restore muscle movements in people who have become paralyzed.

Matthew Tresch, assistant professor of biomedical engineering at the McCormick School of Engineering and Applied Science and of physical medicine and rehabilitation at the Feinberg School of Medicine, and colleagues from the Rehabilitation Institute of Chicago used a model of the muscles in a frog's hind leg to perform a computational analysis that, when run as a simulation, shows that researchers can control the limb using muscles groups just about as well as by controlling individual muscles. Their research was published by the journal *Proceedings of the National Academy of Sciences*.

"By controlling muscle groups instead of individual muscles, we're reducing the variables, but we're not losing efficiency," Tresch says.

The idea that the body's nervous system controls a limb using muscle groups, or "synergies," has been a controversial hypothesis in the research community for the last decade. If this were the case, it would reduce the number of variables that the nervous system needs to control.

"We still don't know if that's how the central nervous system works, but what has been missing from the rhetoric is the question of whether this is a viable way to produce behavior," Tresch says. "That's what our experiment tried to do."

Using both analytical approaches and techniques from control theory, the researchers chose the muscle combinations that let the frog's hind leg do what it wants to do most effectively. The simulation showed that by choosing the most effective balance of muscle synergies, the researchers could control movement without degrading performance.

"Having all these muscle variables complicates control of behavior, but it also makes certain behavior easier," Tresch says. "The complexity might be there to make certain kinds of movements more efficient than others."

By having this framework, researchers might be able to predict how muscle activation changes when a person loses a muscle or becomes paralyzed.

"Whether or not the nervous system uses this, it does seem like an approach that can simplify control for a complicated mechanical system, like a limb," Tresch says. "For people with spinal cord injuries, you can put electrodes into their muscles and stimulate them. We can use this synergies approach to make controlling a limb simpler."

Next Tresch will perform similar research using a rat model, and he is currently working with other professors at Northwestern to bring the research to patients.

"The end goal is to restore movement in people who are paralyzed," he says.

# World Health Imaging Alliance Partners For X-Rays in Developing World

The World Health Imaging Alliance (WHIA), a nonprofit, diagnostic medical imaging solutions provider of which Northwestern is a partner, has cemented key partnerships that will enable it to significantly ramp up its efforts to bring digital imaging technology to sites in need around the world.

Basic diagnostic x-ray services are a key component of primary health care delivery. However, two-thirds of the world's population is without access to it, according to World Health Organization estimates.

Northwestern, the University of Cape Town, Rotary International, and other organizations created the World Health Imaging Alliance (WHIA) in 2007 with the vision of facilitating the deployment of 20,000 digital x-ray systems worldwide, providing one billion people with access to diagnostic imaging.

Now WHIA has developed partner relationships with key vendors. Sedecal, a global OEM manufacturer of x-ray systems, has partnered with WHIA to provide the WHO-approved x-ray machine. Digital medical imaging is provided through a relationship with Carestream Health, a global company providing medical and dental imaging systems and information technology solutions. The software systems that manage the digital images have been provided through a partnership with Merge Healthcare, a leading medical imaging software solutions company.

WHIA is also working to significantly enhance the benefits of digital imaging by adding next generation functionality and services to its solution. It is concentrating on developing future capabilities that will make it possible for clinics and hospitals to access telemedicine for improved health service delivery; provide a platform that will be used to develop improved tools for computer aided detection and diagnosis; and provide clinics and hospitals with the ability to utilize electronic medical records and offer every patient direct access to their own personal health records.

Another key facet to WHIA's ability to provide a sustainable solution is its close ties to the local universities in the communities with WHIA sites. WHIA currently has a site established in South Africa and another under implementation in Guatemala. Close relationships with the Rotary International and local organizations have provided WHIA with a lineup of candidate sites interested in receiving its solution. In addition, WHIA has established relationships with many of the global not-for-profit organizations involved in providing imaging services.

"WHIA has a great model for delivering leading edge diagnostic tools to developing markets," says Ivy Walker, WHIA's CEO, "but that is just the beginning. Our efforts in data compilation can create a platform that can be used to develop improved tools for computer assisted diagnosis and public health data analysis. Ongoing partner and solution development under this model will continue to move WHIA toward this vision."

# News and Notes

## FACULTY

**Guillermo Ameer** and **David Kelso** were elected to the American Institute for Medical and Biological Engineering College of Fellows.

**Jeffrey Burgdorf**, **Roger Kroes**, and **Joseph Moskal** received the Frank A. Beach Comparative Psychology Award from the American Psychological Association.

**Robert Linsenmeier** was named a fellow of the Association for Research in Vision and Ophthalmology. He was also appointed co-editor for *Current Eye Research*.

**John Troy** was appointed to the editorial board of *Nanoengineering and Nanosystems*.

**Mitra Hartmann**, **Dean Ho**, and **Malcolm MacIver** have received Faculty Early Career Development (CAREER) awards from the National Science Foundation.

**Mitra Hartmann** was selected for the Associated Student Government Honor Roll for 2008-2009.

**Phil Messersmith** has been selected to receive the Langmuir Lecture Award from the American Chemical Society and to give the Stevenson Biomaterials Lecture at Syracuse University.

**Chad A. Mirkin** was selected to the National Academy of Engineering. He has also been named to the President's Council of Advisors on Science and Technology and was awarded the prestigious 2009 Lemelson-MIT Prize.

**Eric Perreault** was named McCormick Adviser of the Year.

**W. Zev Rymer** has been appointed vice president for research at the Rehabilitation Institute of Chicago (RIC).

**Malcolm MacIver** is co-PI on an Integrative Graduate Education and Research Traineeship (IGERT) for Integrative Training in Motor Control spanning Northwestern University, University of Chicago, the Field Museum, and IIT. Other participating faculty at Northwestern include **Wendy Murray**, **Mitra Hartmann**, and Neelesh Patankar (mechanical engingeering). This training program is designed to expose students to cross-disciplinary training in biology and engineering through classes and seminars that will be held at the Field Museum.

*Members of NSBE at the regional conference*

## UNDERGRADUATE STUDENTS

### NSBE Wins Award

Members of Northwestern's chapter of the National Society of Black Engineers traveled to their fall regional conference and took home several awards. The chapter's Academic Technical Bowl team took first place in the regional competition. Team members included Okechukwu Chika (electrical engineering '09), **Reginald Sandy** (biomedical engineering '11), Evan Dickerson-Rusan (electrical engineering '11), and **Taju Sanusi** (biomedical engineering '12). Other winners included **Zuri Hemphill** (biomedical engineering '11), who placed third for her research in memory alloy stents, and **Uchenna Moka** (biomedical engineering '09), who took first place for her research on the formation of pancreatic islets in the developing mouse.

### BME undergraduate student John Sheppard receives the 2009 Barry M. Goldwater Scholarship

The Barry M. Goldwater Scholarship and Excellence in Education Program was established by the United States Congress in 1986 to honor Senator Barry M. Goldwater, who served his country for 56 years as a soldier and statesman, including 30 years of service in the U.S. Senate. The creation of this program pays tribute to the leadership, courage, and vision of Senator Goldwater and establishes in his name an endowed recognition program to foster and encourage excellence in science and mathematics. With the support of this scholarship, John Sheppard will study the network hub behavior in the brain via graph theoretical analysis.

### KMC ApneAlert Team Wins Another Award For Design

A team of undergraduate students from Northwestern University's McCormick School of Engineering recently won a $10,000 prize for creating a device designed to keep more babies alive in the developing world. Called the KMC ApneAlert, the small device can be attached to a baby to monitor its breathing. The device then alerts the mother if the baby stops breathing. Such a device is needed in the developing world, where incubators and heart rate monitors to monitor premature babies are few.

The device, designed by McCormick biomedical engineering undergraduate students — **Lauren Hart Smith**, **Kurt Qing**, **Alec Zopf**, **James Yang**, and **Shonali Midha** — for their senior capstone design project, was named one of the top ten finalists in the Center for Integration of Medicine and Innovation Technology Prize for Primary Healthcare competition — a selection that comes with a $10,000 award to support continuing efforts of the project.

Senior **James Rein** won first place at the 2009 MIT Enterprise Forum White board Challenge. He won the award for TiltAlign, a feedback system that gives cerebral palsy patients an incentive to stand up straight.

## GRADUATE STUDENTS

**Robert Van Lith** received the AHA (American Heart Association) Predoctoral Fellowship Award.

Graduate student **Carrie Brubaker** was named to the 2009 "50 for the Future" list sponsored by the Illinois Technology Foundation (ITF).

**Kvar Black** and **Dominic Fullenkamp** have received Ruth M. Kirschstein NRSA Predoctoral Fellowships to support their PhD research.

# McCormick Announces the Winners of the 2009 Frey Prize

The winners of the 2009 Margaret and Muir Frey Memorial Prize were announced at the 2009 McCormick Convocation. The prize is awarded each year for innovation and creativity in senior capstone work, as judged by a jury of recognized leaders from the fields of engineering. It was established by Donald Frey, professor of industrial engineering and management science, in honor of his late parents.

**First Place**
$12,000 to the student(s) and $5,000 to the faculty adviser(s)

Female Pelvic Exam Simulator for the Developing World

Students: Tadas Sileika, Rebecca Etrenne, John Leuthner, and Lee Lamers

Advisers: Matthew Glucksberg and Alan Sahakian

**Second Place**
$8,000 to the student(s) and $3,000 to the faculty adviser(s)

Robotic End-Effector for Automation of Sliced Meat Packaging

Students: Jennifer Breger, Nathan Henry, Mark Straccia, and Matt Turpin

Adviser: Wei Chen

**Third Place**
$5,000 to the student(s) and $2,000 to the faculty adviser(s)

The TiltAlign — Alignment for Patients with Postural Difficulties

Students: Annie Baltes, Dan Choi, Blerta Mandro, James Rein

Adviser: Matthew Glucksberg and Michael Peshkin

**Honorable Mention**
Rewet Detection Device — in absorbent products used for urinary incontinence

Students: Ankur Bakshi, Lizhou Huang, Alexander Sheu, Scott Tuttle

Adviser: Matthew Glucksberg

# Homecoming Weekend Alumni Reception

Mark your calendar for the 3rd Annual BME Homecoming Reception. It will be held on Friday, Oct. 23 from 7 to 8:30 p.m. at Tommy Nevin's Irish Pub (1454 Sherman Avenue, Evanston). Come for food, drinks, and great conversation with former colleagues, professors, and friends!

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Photographers: Sam Levitan, Andrew Campbell
Design: Amy Charlson Design

NORTHWESTERN UNIVERSITY

**McCormick**
**Department of Biomedical Engineering**
**Robert R. McCormick School**
**of Engineering and Applied Science**
Northwestern University
Technological Institute
2145 Sheridan Road
Evanston, Illinois 60208-3100

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