VOL. 7, No. 2

BIOFEEDBACK

THE FISCHELL DEPARTMENT of BIOENGINEERING
A. JAMES CLARK SCHOOL of ENGINEERING

www.bioe.umd.edu

A NEWSLETTER FOR ALUMNI AND FRIENDS OF THE FISCHELL DEPARTMENT OF BIOENGINEERING AT THE A. JAMES CLARK SCHOOL OF ENGINEERING, UNIVERSITY OF MARYLAND, COLLEGE PARK.

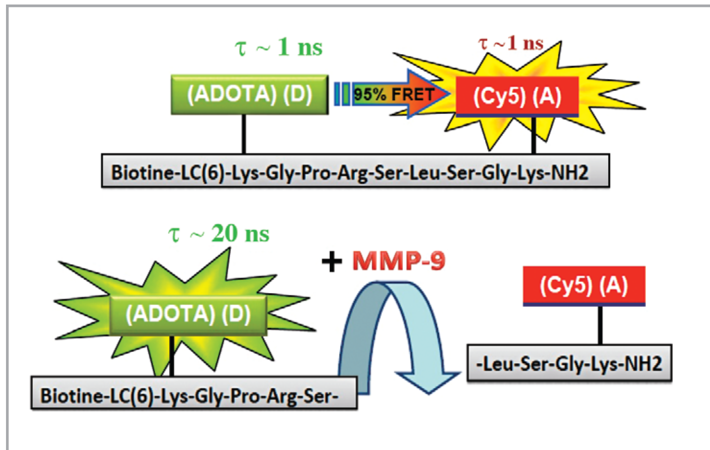
IN THIS ISSUE:

Yu: $1.8M for Noninvasive Bioimaging Project

FLUORESCENT DYE STUDY WILL IMPROVE OBSERVATION OF DISEASE PROCESSES AND DRUG EFFICACY

Dyes that create a better picture of the progression or retreat of disease and report on how well therapeutics are being delivered may soon be available to doctors and technicians thanks to a new biomedical imaging project underway at the Clark School.

The National Institute of Biomedical Imaging and Bioengineering (NIBIB), part of the National Institutes of Health (NIH), has awarded a four year, $1.8 million Research Project Grant (R01) to Associate Professor **Bruce Yu** (joint, School of Pharmacy) and Professor **Zygmunt Karol Gryczynski** (Department of Molecular Biology and Immunology, University of North Texas) for their proposal, "Novel Fluorophores for Molecular and Cellular Imaging." Gryczynski and Yu are the principal investigators on the joint project.



NEW DYES FOR BIOIMAGING: A BIOACTIVE PEPTIDE IS LABLED WITH A FLUORESCENT DONOR (ADOTA) AND A FLUORESCENCE ACCEPTOR (CY5). IN THIS CONSTRUCT, FLUORESCENCE EMITTED BY THE DONOR IS UNQUENCHED BY THE ACCEPTOR, LEADING TO VERY WEAK SIGNAL INTENSITY. HOWEVER, IF THE TISSUES OR CELLS CONTAIN METALLOPROTEINASE MMP-9, THE BIOACTIVE PEPTIDE WILL BE CLEAVED, LEADING TO THE SEPARATION OF THE DONOR AND THE ACCEPTOR. CONSEQUENTLY, THE DONOR DYE IS NO LONGER QUENCHED AND WILL EMIT MUCH STRONGER FLUORESCENT SIGNAL THAN THE QUENCHED VERSION. THIS ALLOWS THE DETECTION OF MMP-9 ACTIVITY IN TISSUES OR CELLS.

When doctors want to observe the status of living tissue inside the body, they may use fluorescence imaging, a technique in which the patient is injected with a special dye that can emit fluorescent light when excited by a laser called an excitation beam. The dye, which penetrates the tissue and can be tailored to attach to specific types of cells, drugs, or proteins, "lights up," capturing a brief period of activity which may reveal processes that indicate health or disease, or

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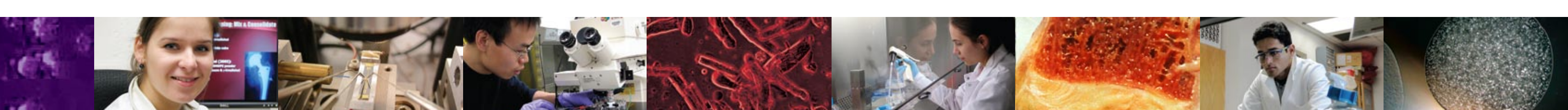

chair's MESSAGE

WILLIAM BENTLEY

I'D LIKE TO START OFF WITH SOME LATE-BREAKING NEWS:

We are very pleased to announce the launch of a new collaboration between the Fischell Department of Bioengineering and Canon U.S. Life Sciences, Inc., to develop a highly automated system providing rapid infectious disease diagnosis. Utilizing Canon U.S. Life Sciences' proprietary genetic analysis system, the project aims to expedite the delivery of infectious disease test results while also simplifying the test processes to allow a variety of clinical staff to perform them on-site. I'll be working on the project with Canon U.S. Life Sciences senior fellow and newly-appointed BioE Professor of the Practice Hiroshi Inoue, and my colleagues, BioE professors Keith Herold and Ian White. Together, we'll develop the microfluidic chip technology to be used in disposable testing cartridges containing human blood samples.

Our department continues to grow in so many ways, including student enrollment, new collaborations (both with Canon and our counterparts in Trento, Italy—see p. 3), the planned addition of ten professors in the next five years, new fellowships and scholarships for our students (see pp. 8-9), new grants and awards for our faculty (see our cover story and p. 2), the development of award-winning startup companies and inventions (see pp. 14-15), and as always, new ideas and advances in our research. We hope you'll continue to follow us on our way to becoming one of the top departments in the nation.

With Best Regards,

William E. Bentley
Robert E. Fischell Distinguished Professor and Chair
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GRANT, continued from page 1

the successful delivery of drugs to a targeted location. When molecules labeled by the dye fluoresce, they become visible to a device called a fluorometer, which produces images that reflect the distribution of the dye and by extension the molecules' presence, number, and what they are doing.

"Two fundamental problems in biomedical imaging, from single molecule studies to whole body imaging, are background noise that makes the image harder to interpret, and the lack of very bright dyes that fluoresce long enough to get a good image," Yu explains.

Gryczynski and Yu will be developing a new group of dyes made with small organic compounds called triangulenium that fluoresce when exposed to red and near-infrared light, the wavelength of choice for deep tissue penetration. The dyes have enhanced spectral properties, including high photostability, increased sensitivity, and extra-long fluorescence lifetimes.

Long, however, is relative. "At present we lack dyes that fluoresce in the red spectral range for longer than ten nanoseconds," says Yu. "This isn't long enough to accurately image large membrane and cellular proteins that may take tens or hundreds of nanoseconds to go through important changes or complete activities we need to see.

"The dye molecules we're working on now," he continues, "are interesting because they fluoresce for 20 nanoseconds, which makes it possible to collect background-free fluorescence images of these large molecules."

Gryczynski and Yu's research groups will collaborate with that of Associate Professor **Bo Laursen** (Department of Chemistry, University of Copenhagen), the inventor of the triangulinium dyes. Laursen's group will manufacture the dye, Yu's group will attach it to a rigid peptide scaffold to create a brighter macromolecule with a higher signal intensity, and Gryczynski's group will conduct fluorescent spectroscopy studies.

The R01 grant program, the NIH's oldest and one of its most prestigious, funds investigator-initiated, health-oriented research that supports the Institutes' mission.

Yu and Gryczynski, who have collaborated since 2003, previously received a R01 grant from NIBIB for an ongoing study on the engineering of peptide-based biomaterials, a project that earned Yu a Presidential Early Career Award for Scientists and Engineers in 2005.

SEOG WINS NSF CAREER AWARD

Fischell Department of Bioengineering Assistant Professor **Joonil Seog** (joint, Materials Science and Engineering) has received a $500,000 National Science Foundation (NSF) Faculty Early Career Development (CAREER) Award for a proposal titled "Direct Observation of Dynamic Self-Assembly at the Single Molecule and Nanoscale Level." The research will be conducted in Seog's Molecular Mechanics and Self-Assembly Laboratory.

The project outlined in the Seog's proposal will use a novel technique to study the self-assembly behavior of peptides at the single-molecule and nanoscale levels. Peptides, polymers made out of amino acids that are found in every cell, perform some of the most crucial biochemical and physiological functions required to sustain life.

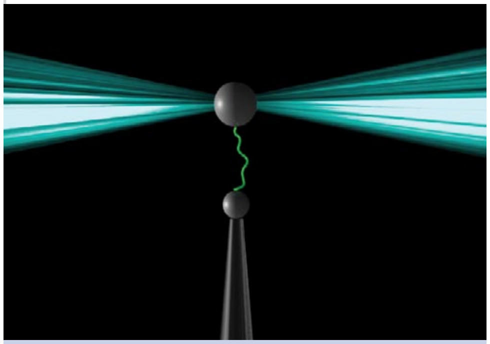
"Current methods of examining peptides have provided detailed information on their molecular structures, but they are largely limited to a static, averaged view rather than a dynamic one that expresses the rich variations in their behaviors," says Seog.

At the molecular level Seog expects that his methods, which will use a combination of optical mini-tweezers and a novel single molecule construct, will provide fundamental information about the dynamic behaviors of two particular peptides, amyloid beta and tau. These peptides self-assemble into a nanofiber that can be used as a platform to create bioinspired materials. At the nanoscale level, his group will use atomic force microscopy to examine the growth of the nanofibers, the optimal conditions to control their growth, and the effects of nanomechanical forces on their assembly.

The implications of the work extend beyond Seog's lab. "The experimental approaches we've developed are general and can be readily extended to answer questions about other self-assembling molecular systems," he says.

Seog's award will also support several educational objectives inspired by his research, including the development of new and existing biomaterials and nanomechanics courses at the undergraduate and graduate levels, as well as undergraduate research opportunities in his lab. He also plans to continue developing nanotechnology and microscopy lab models for visually impaired high school students.

The NSF CAREER program supports the career development of outstanding junior faculty who most effectively integrate research and education within the goals and missions of their programs, departments, and schools. Seog is the third assistant professor since the department's launch in July 2006 to receive a CAREER Award, preceded by **Adam Hsieh** in 2009 and **Helim Aranda-Espinoza** in 2007.



SEOG RESEARCH: STRETCHING AND RELAXING A SINGLE BIOLOGICAL MOLECULE USING OPTICAL TWEEZERS. THE TOP BEAD IS "TWEEZED" BY A LASER LIGHT AND THE BOTTOM BEAD IS FIXED ONTO A PIPETTE TIP. A BIOLOGICAL MOLECULE (E.G. DNA) IS TETHERED BETWEEN THE TWO BEADS AND CAN BE REPEATEDLY PULLED AND RELAXED, REVEALING ITS MECHANICAL PROPERTIES AT THE SINGLE MOLECULE LEVEL. THIS METHOD CAN ALSO PROVIDE INFORMATION ABOUT THE DYNAMIC PROPERTIES OF BIOMOLECULES, WHICH CAN SHED LIGHT ON PROTEIN FOLDING, SELF-ASSEMBLY, AND PROTEIN-PROTEIN INTERACTIONS. *ILLUSTRATION BY POSTDOCTORAL RESEARCH ASSOCIATE **CHENYANG TIE.***

BENTLEY, KOFINAS PART OF RESEARCH PARTNERSHIP WITH TRENTO, ITALY

BioE professors **William E. Bentley** and **Peter Kofinas** are part of group of Clark School faculty specializing in systems research that will strengthen ongoing and engage in new collaborations with their counterparts in the Autonomous Province of Trento, Italy. The Institute for Systems Research (ISR) and the University of Maryland's long-standing and successful relationship with researchers from Trento led to a formal cementing of the partnership in May 2011.

A series of overseas exchange visits fostered the development of two key agreements. Most recently, Kofinas was part of a delegation of Maryland researchers and staff that attended a technical workshop and extensive laboratory tours in Trento. The delegation also included ISR director and BioE affiliate faculty member Professor **Reza Ghodssi** (Department of Electrical and Computer Engineering).

The research and education role of the University of Trento is particularly significant, and a memorandum of understanding between the University of Maryland and the University of Trento is being signed. A second memorandum of understanding between the State of Maryland and the Autonomous Province of Trento is in the works. The partnership is beginning with research, and an education component will be added in the near future.

Specific, strategic research topic areas are being defined to build significant collaborations, while work in three existing topic areas will continue. New projects will be added as the partnership develops.

Bentley, Kofinas and their colleague Professor **Alessandro Quattrone** (University of Trento) will lead ongoing efforts in the bioengineering, biomedical devices, and biomicrosystems group.

Participants are committed to future four- to six-month bi-directional student exchanges, two- to three-month researcher and professor exchanges, and seed-funded collaborations with matching funds from the Autonomous Province of Trento, the European Union, the State of Maryland, and the United States federal government.

UMD/AUTONOMOUS PROVINCE OF TRENTO PARTNERSHIP: LEFT TO RIGHT: **ALBERTO LUI** (TRENTO, INTERNATIONAL RELATIONS DEPARTMENT); **MARIANO ANDERLE** (TRENTO, DIRECTOR OF INTERNATIONAL RELATIONS); PROFESSOR **REZA GHODSSI** (ISR); ASSOCIATE PROFESSOR **PAMELA ABSHIRE** (ELECTRICAL AND COMPUTER ENGINEERING); **PETER KOFINAS** (BIOE); AND **JEFF CORIALE** (DIRECTOR OF EXTERNAL RELATIONS, ISR).

ISR is leading the U.S. effort on behalf of the University of Maryland and the University System of Maryland, while the Autonomous Province of Trento coordinates efforts overseas. The leading research and education collaborators in Trento are the University of Trento, the Consiglio Nazionale delle Ricerche, and Fondazione Bruno Kessler.

"BACTERIAL DIRIGIBLES": NEXT-GENERATION DISEASE FIGHTERS

"Bacterial dirigibles" that serve as mobile pharmaceutical factories, both producing disease-fighting substances and delivering the potentially life-saving cargo exactly where it's needed, are the newest candidates for treating illnesses ranging from food poisoning to cancer.

BioE professor and chair **William E. Bentley**, who developed the bacteria with graduate student **Hsuan-Chen Wu** and other members of his research group at the Biomolecular and Metabolic Engineering Laboratories, reported on the novel biodevices at the 241st National Meeting & Exposition of the American Chemical Society (ACS), held in Anaheim, Ca. in March 2011.

"We're building a platform that could allow bacterial dirigibles to be the next-

continues pg. 5

"POCKET CHANGE SPECTROSCOPY" IMPROVES DETECTION OF TOXINS, EXPLOSIVES

New research from the Clark School showing how surface-enhanced Raman spectroscopy (SERS), a highly-sensitive technique used to detect the merest traces of targeted materials, can be made more affordable and more portable by replacing one of its components with a chemical reaction applied to pocket change, was highlighted in *Chemical & Engineering News*.

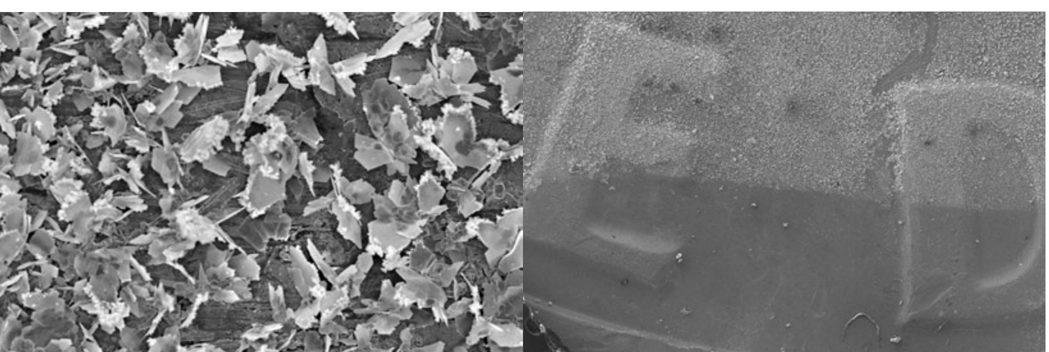
The article covered a contributed talk given at the 241st National Meeting of the ACS by BioE graduate student **Jordan Betz**, titled "SERS on a dime: Galvanic displacement as a rapid, robust, and simple method for SERS substrate fabrication." Betz is advised by Professor **Gary Rubloff** (Department of Materials Science and Engineering and Director, Maryland NanoCenter).

Raman spectroscopy is used to detect and identify substances which may only be present in minute quantities measured in molecules. When light from a laser floods a sample in a sensor, it scatters when it hits the molecules present. Since every kind of molecule scatters the light in its own unique way, scientists can tell what is present, and in what quantity, by analyzing the resulting spectrum. Surface-enhanced Raman spectroscopy takes the process a step further by placing the samples on specially-designed substrates (metal surfaces) capable of greatly intensifying the scattered light, allowing the detection of even tinier traces of a target substance.

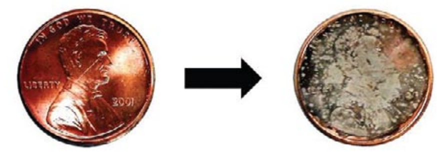
While this makes SERS a powerful sensor, its use has been limited by the difficulty of making the substrates, and the cost and short shelf-life of prefabricated ones. Designing an affordable, easy-to-use system for use in the field has been a challenge. Betz and Rubloff think they've found one way around the problem by developing a technique that can use ordinary metal objects like coins as substrates.

In his presentation, Betz described how ordinary coins interact with a solution of silver nitrate in a spontaneous electrochemical process called galvanic displacement. The silver ions in the solution diffuse into the surface of a coin, where they steal electrons from the atoms of copper or nickel. This causes the silver ions to lose their charge and become solid silver atoms, creating a starting point from which micro- and nanoscale crystal structures begin to blossom. The properties of the crystals can be controlled by changing the reaction conditions. The copper and nickel atoms, which convert to ions as they lose their electrons to the silver, diffuse outward into the solution.

Betz, Rubloff and their colleagues found that when exposed to the Raman spectrometer's laser, the combination of silver crystals and the roughness of the coins' surfaces created a very high, localized electromagnetic field that intensified the scattering signal returned by a factor of 109, allowing them to detect lower amounts of a



"BUDDY, CAN YOU SPARE MY RAMAN SPECTROMETER A DIME?" LEFT: MICRO- AND NANOSCALE SILVER PLATES GROW OUTWARD FROM THE SURFACE OF A DIME. MANY OF THE EDGES OF THESE PLATES TERMINATE IN SMALLER, SHARP FEATURES THAT GREATLY ENHANCE THE RAMAN SCATTERING SIGNAL FROM MOLECULES THAT ADSORB TO THEIR SURFACES. RIGHT: THE EDGE OF A DROPLET OF SILVER NITRATE ON A DIME. THE LIGHTER AREA IS WHERE A GALVANIC DISPLACEMENT HAS OCCURRED AND SILVER CRYSTALS HAVE GROWN.



target molecule than they could with normal Raman spectroscopy alone. The coins even outperformed high-tech substrates made with state-of-art equipment in the lab.

"Interestingly, the low-tech approach worked best," says Betz. "We hypothesized that the roughness and oxidation on the surface of circulated coins might create more sites at which the silver crystals could grow. To test this, we evaporated very thin films of smooth, unoxidized copper and nickel onto glass slides, then subjected them to the galvanic displacement reaction. In every case, the coins and their crystals were more effective at increasing the scattering."

The process does not deface the currency. "The silver crystals that grow on the coins are so weakly attached you can use scotch tape, a tissue, or even water to remove them," Betz explains. "After cleaning up the coins, they don't look or behave any differently. The amount of copper or nickel displaced by the silver is miniscule. Kicking a coin down the street would probably have more of an effect on its mass and cosmetic appearance."

Using substrates made on common metal objects, he says, will provide new opportunities to develop remote and portable SERS-based sensors that could be used to detect toxins, explosives, and contaminants in groundwater and food, as well as identify specific viruses and bacteria.

"The portability of the coins coupled with the simplicity of the reaction make the possibility of remote, field use of SERS a distinct possibility," says Betz. "For example, other researchers have shown that SERS can be performed using a laser pointer as the excitation source. Hand-held Raman spectrometers are available on the market, and we believe it's only a matter of time before someone develops a Raman spectrometer attachment for a smartphone. Using our method of substrate fabrication, you could have your spectrometer in one pocket, and your SERS substrate in the other."

DIRIGIBLES, continued from page 3

generation disease fighters," he said. "The concept is unique."

Bentley explained that in the pharmaceutical industry, traditional genetic engineering is used to reprogram bacteria so that they produce antibiotics, insulin, and other medicines and materials. The bacteria grow in nutrient solutions in enormous stainless steel vats in factories. They release antibiotics or insulin into the vats, and technicians harvest the medicine for processing and eventual use in people.

Bacterial dirigibles take the process a step further by doing all of the work "on location." Scientists genetically modify bacteria to produce a medicine or another therapeutic substance, then give the bacteria a biochemical delivery address, the location of the disease. Swallowed or injected into the body, the bacteria travel to their target, where they start producing substances to fight the disease.

Bentley chose the term "bacterial dirigibles" because the modified bacteria are shaped like blimps or zeppelins, and seem to float like them as they make deliveries. The prototype bacterial dirigible is a strain of *E. coli* that Bentley and his colleagues modified in the lab.

"We have created a genetic circuit that endows *E. coli* with targeting, sensing and switching capabilities," he explained. "The resultant cell...autonomously navigates and carries or deploys important 'cargo.'"

The "targeting" molecule is attached to the outer surface of the bacteria. It gives them the ability to "hone in" on specific cells and attach to them—in this instance, the intestinal cells where other strains of *E. coli* cause food poisoning. Inside the bacteria is a gene segment that acts as a "nanofactory." It uses the bacteria's natural cellular machinery to make drugs, such as those that can fight infections, viruses, and cancer.

The nanofactory can also produce signaling molecules that enable the dirigible to communicate with natural bacteria at the site of an illness. Some bacteria engage in a biochemical chit-chat, called "quorum sensing," in which they coordinate the activities needed to establish an infection. The dirigibles could produce their own signaling molecules that disrupt quorum sensing, preventing bacteria from starting an infection, before it ever requires antibiotics to stop it.

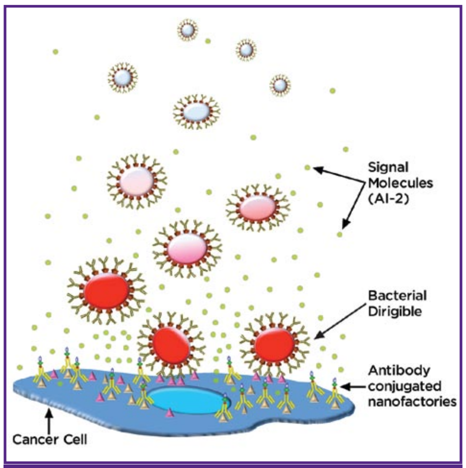
Bentley's group showed that the prototype re-engineered strain of *E. coli* could both seek out and attach to intestinal cells growing in laboratory cultures, as well as produce chemical signals that triggered neighboring bacteria to make certain proteins that they don't normally produce.

The latter finding means the dirigibles can become enablers that prompt the body to help itself by causing cells to synthesize natural disease-fighting substances, such as immunoglobulins. Immunoglobulins are proteins used by the immune system to identify and destroy foreign invaders, including viruses and the bacteria that cause food poisoning.

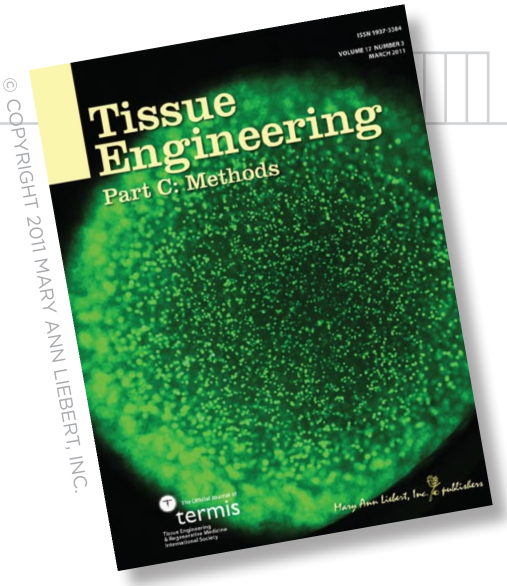
Bacterial dirigibles could be given to patients in the form of probiotics, live, beneficial microorganisms like those found in certain kinds of yogurt, Bentley said. Doctors could also inject dirigibles into the bloodstream or directly into a diseased area, such as a tumor.

The bacterial dirigibles research is funded by the Defense Threat Reduction Agency (part of the U.S. Department of Defense), the National Science Foundation, and the Robert W. Deutsch Foundation.

Story adapted from the original press release by and courtesy of the American Chemical Society.



ANTIBODY TAGGED NANOFACTORIES TARGET TO CANCER CELL SURFACES AND THEN ACTIVELY PRODUCE BACTERIA CHEMOATTRACTANT (AI-2), WHICH SERVES AS THE HOMING SIGNAL FOR ATTRACTING BACTERIA DIRIGIBLES. IN RESPONSE TO AI-2, THE DIRIGIBLES PRODUCE RECOMBINANT PROTEINS FOR POTENTIAL THERAPEUTIC PURPOSES. FOR MORE ABOUT BENTLEY GROUP RESEARCH ON AI-2, SEE P. 8. *ILLUSTRATION BY HSUAN-CHEN WU.*



PROFESSOR **JOHN FISHER** AND GRADUATE STUDENT **ANDREW YEATTS'** RESEARCH ON THE COVER OF *TISSUE ENGINEERING PART C: METHODS.* THE IMAGE SHOWS A FLUORESCING LIVE/DEAD IMAGE OF HUMAN MESENCHYMAL STEM CELLS CULTURED IN AN ALGINATE BEAD THAT FORMS PART OF A NEW BIOREACTOR USED TO GROW REPLACEMENT BONE AND TISSUE.

A BETTER WAY TO HEAL BROKEN BONES

Your own stem cells could one day be quickly and efficiently cultured into new bone and tissue used to heal a serious injury, thanks to advances in the development of a device designed in the Fischell Department of Bioengineering.

A paper about the device, "Tubular Perfusion System for the Long Term Dynamic Culture of Human Mesenchymal Stem Cells," by BioE graduate student **Andrew Yeatts** and his advisor, Associate Professor **John Fisher**, was recently featured on the cover *Tissue Engineering Part C: Methods.*

In 2009, Fisher and Yeatts were part of a team that won the Best Inventor Pitch at the university's annual Professor Venture Fair for its design of a patent-pending tissue engineering bioreactor system that grows bone and other types of tissue for implantation. Their bioreactor makes tissue engineering more efficient by reducing cost and complexity while increasing the amount of nutrients the cells inside receive, resulting in a more prolific culture. The system is easy to set up and customize, and can be assembled from off-the-shelf components.

continues pg. 6

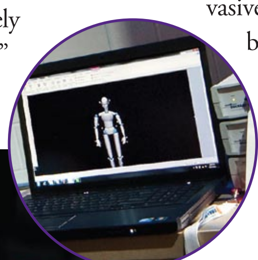
Although many tissue and bone injuries heal naturally, large or catastrophic injuries, or those in delicate areas such as the face, often require surgery, bone grafts, or artificial implants in order to reconstruct what has been lost. The results are often less than ideal, both physically and cosmetically.

Fisher's group is designing tissue engineering solutions that quickly grow the patient's own stem cells in the lab in a special biocompatible material, an alginate hydrogel called a scaffold. The cells are then transplanted back into the body at the injury site, where they literally fill in the gaps and repair the damage. The bioreactor provides a protective environment for the cell-filled scaffolds that encourages growth.

The recent publication, Yeatts explains, covers the next stage in the device's development. "Previously, we developed a bioreactor, the tubular perfusion system (TPS), that utilizes a unique design in which nutrient-rich media is pumped through tightly packed beads of alginate scaffolds," he says. "The new study evaluates how cells respond to it."

Fisher and Yeatts loaded the TPS with scaffold beads containing human mesenchymal stem cells, which are found in bone marrow and are capable of differentiating into many kinds of tissues, including bone and cartilage. The pair then observed their growth and noted whether they became bone cells called osteoblasts.

"We were excited to discover that not only did the stem cells grow faster in the bioreactor, they more effectively differentiated into osteoblasts," says Yeatts. "We were able to show this by analyzing typical genetic markers of osteoblastic differentiation as well as observing the amount of calcium, a key extracellular matrix component in bone, that was deposited by the cells."



STEVE GRAFF IS PART OF A TEAM TRANSLATING THE BRAIN'S ELECTRICAL ACTIVITY INTO ACTION TAKEN BY A COMPUTER OR PROSTHETIC LIMB. *(PHOTOS BY JOHN CONSOLI)*

Yeatts says he and Fisher are currently working toward making their bioreactor available in clinical settings. "We hope to complete an *in vivo* study to demonstrate the system's effectiveness," he says, "and then work on gaining FDA approval. We really want to provide doctors with a better way to treat devastating bone injuries."

For more information, see: AB Yeatts and JP Fisher. "Tubular Perfusion System for the Long Term Dynamic Culture of Human Mesenchymal Stem Cells." Tissue Engineering Part C, Methods. 17: 337-348 (2011)

THOUGHT-TO-MOTION RESEARCH FEATURED ON COVER OF *TERP*

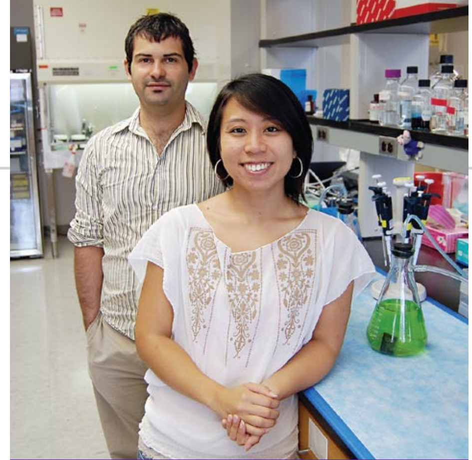
Groundbreaking research that decodes the brain signals behind physical activity and uses them to control devices such as computers and prosthetics is featured on the cover of the latest issue of *Terp,* the University of Maryland's alumni magazine.

The work, spearheaded by BioE affiliate professor **José Contreras-Vidal** (Department of Kinesiology), also involves past and present BioE graduate students, including **Trent Bradberry** (Ph.D. '10), **Steven Graff** (B.S. '10, bioengineering), and **Kimberly Kontson**.

In 2010, Contreras-Vidal and Bradberry were the first to publish research demonstrating that brain activity recorded using noninvasive electroencephalography (EEG) could be used to reconstruct hand movements. Their findings were significant because they could pave the way for safe, thought-controlled devices that do not require the user to have a surgical implant.

The brain-computer interface could also be used to rehabilitate or assist people who have lost motor control due to an injury, following a stroke, or, as in Graff's case, live with a disorder such as muscular dystrophy.

The Terp feature story, "Think. Move. Live" (available online at **www.terp.umd.edu/4.8/think/**) describes the group's latest efforts, which include matching EEG data to specific movements and motor-sensory control



DANIEL SERRANO (BACK) AND JANET HSU (FRONT) ARE STUDYING A NEW WAY TO TREAT FABRY DISEASE.

points in realtime, and a collaboration with a team at the Johns Hopkins Applied Physics Laboratory developing the next generation of robotic arms.

TAKING AIM AT A RARE LYSOSOMAL STORAGE DISEASE

Recently published work from the research group of Assistant Professor **Silvia Muro** (joint; Institute for Bioscience and Biotechnology Research) shows how a new nanocarrier can more effectively deliver therapeutic enzymes used to treat Fabry disease, a rare, life-threatening condition that damages blood vessels, organs and the nervous system.

BioE graduate student **Janet Hsu** and Biological Sciences Graduate Program student **Daniel Serrano** are the first authors of the paper, which was featured on the cover of the *Journal of Controlled Release,* one of the top publications focusing on drug and gene delivery.

Fabry disease is a hereditary disorder that affects lysosomes, hollow, organ-like structures within cells that contain enzymes that accelerate or enable chemical reactions. The lysosomes' job is to break down the lipids, carbohydrates, and other proteins cells require for food, making them easier to digest. Lysosomal storage disorders are those in which a genetic defect results in a shortage or absence of a particular enzyme the lysosomes need in order to function. As unprocessed material accumulates in the cells, they swell and rupture.

In the case of Fabry disease, the body fails to produce enough α-galactosidase (α-Gal), an enzyme that breaks down certain sugar residues attached to fat molecules. Fabry disease damages the cardiovascular and renal systems, leading to kidney and liver failure, heart disease, skin and vision problems, pain, and premature death.

Currently, enzyme replacement therapy (ERT) is used to treat patients with the condition. Large doses of medication are required because only a small percentage of the α-Gal administered is successfully delivered to the lysosomes of the cells. Hsu, Serrano and their colleagues devised a new, more effective kind of ERT that uses a targeted delivery system to bring α-Gal to the affected cells and make it easier for the cells to ingest it.

Hsu attached α-Gal to a nanocarrier coated with anti-ICAM, a molecule designed to fit perfectly, like a neighboring puzzle piece, into a protein called intercellular adhesion molecule 1 (ICAM-1), which is produced by the endothelial cells that line the interior surfaces of blood vessels throughout the body. As the nanocarriers move through the cardiovascular system, the anti-ICAM and ICAM-1 molecules lock together, pulling the α-Gal to the cells and depositing the enzyme into their lysosomes so normal cellular function can resume. Hsu found that the use of the anti-ICAM-coated nanocarriers improved amount of α-Gal successfully delivered to and taken up (ingested) by endothelial cells, rendering them capable of breaking down the aberrant lysosomal storage. The results suggest that the targeting system could improve the efficacy and reduce the cost of ERT treatments.

In a commentary on the article, *Journal of Controlled Release* editor-in-chief **Kinam Park** noted the novelty of the system and emphasized the relevance of the multiple parameters measured in the work, describing it as an example to follow in future studies of targeted drug delivery systems.

Hsu and Serrano's work has been funded by the Maryland Department of Business and Economic Development's Nanobiotechnology Program, the Minta Martin Foundation, the American Heart Association, and the National Institutes of Health.

For more information, see: Janet Hsu, Daniel Serrano, Tridib Bhowmick, Kishan Kumard, Yang Shene, Yuan Chia Kuoa, Carmen Garnachoc, and Silvia Muro, "Enhanced endothelial delivery and biochemical effects of α-galactosidase by ICAM-1-targeted nanocarriers for Fabry disease." Journal of Controlled Release 149 (2011) 323–331.

UNDERGRADS NOMINATE KOFINAS FOR NSF HONOR

Peter Kofinas was one of six professors elected to the A. James Clark School of Engineering's first class of ENGAGED Faculty. The Clark school bestowed the honor on Kofinas and his colleagues based on nominations from undergraduate engineering students.

The ENGAGED Faculty project is a component of a National Science Foundation-funded program called ENGAGE: Engaging Students in Engineering. The University of Maryland was one of ten schools selected to participate in the first year of the program, which seeks to increase the undergraduate student retention rate in engineering programs by implementing three educational strategies: integrating everyday examples of engineering concepts into coursework, improving spatial visualization skills, and improving and increasing faculty-student interaction.

The ENGAGED Faculty were nominated by Clark School undergraduates on the basis of being approachable and accessible, having high expectations of their students, providing advice and support on academic and extracurricular activities, and having a genuine interest in and concern for their students, especially outside of the classroom. Each ENGAGED faculty member has also been described as dedicated and patient, and has been identified as a positive mentor and role model.

"For me, the greatest honor is to be nominated by undergraduate students for an award," says Kofinas, who is also a Keystone Professor, one of a select group of Clark School faculty members specializing in the education and retention of freshmen engineering students. "The best personal satisfaction for an educator is when his or her own students recognize that one has indeed put a lot of effort into trying to teach them, even when sometimes the required material is boring. I am really happy and grateful to the students who nominated me. Because of this recognition I am now motivated to become an even better teacher."

For more information about ENGAGE, visit **www.engageengineering.org**.

BENTLEY, PAYNE RECEIVE USM REGENTS' AWARDS FOR NANO-, BIODEVICE WORK

BioE professors **William E. Bentley** and **Gregory Payne** have received two of the University System of Maryland's 2011 Board of Regents' Faculty Awards for Scholarship, Research, or Creative Activity. The awards represent the highest honors given to faculty members throughout the university system in five categories: excellence in teaching; scholarship, research, or creative activities; public service; mentoring; and collaboration. Bentley and Payne each received $1000 and a plaque commemorating the honor.

Bentley, the Robert E. Fischell Distinguished Professor and Chair of the Fischell Department of Bioengineering and the director of the Biomolecular and Metabolic Engineering Laboratories, holds a joint appointment with the Institute for Bioscience and Biotechnology Research (IBBR). His research interests include the modeling of genetic circuits, cellular stress responses, bioreactor design and optimization, and protein expression. His group's work on nanofactories, biological devices engineered to locate specific bacteria and synthesize molecules capable of triggering communication between them, has been widely featured in academia and the news media. *(See related story, p. 5.)*

Payne, who also holds a joint appointment with IBBR, studies and applies biofabrication approaches in the construction of devices at the nanoscale, with a specific focus on stimuli-responsive biological polymers and enzymes. His research group is creating the means to integrate biological sensing elements into electronic devices that can diagnose disease at the point of care, detect pathogens on site, and aid in drug discovery. The group also explores biocompatible approaches for personalized therapy, regenerative medicine, and less-invasive surgery. Payne is an internationally recognized expert on chitosan.

Bentley and Payne are currently two of the five co-PIs of the Biochip Collaborative, an interdisciplinary effort to "translate" the communication between biological and microfabricated systems to create biofunctionalized devices.

JOSHUA THOMPSON

THOMPSON WINS OUTSTANDING ASPIRE STUDENT RESEARCH AWARD

BioE junior **Joshua Thompson**, advised by Associate Professor **John Fisher**, won the 2011 Outstanding ASPIRE Student Research Award for his work on skeletal muscle regeneration. ASPIRE, A Scholars Program for Industry-Oriented Research in Engineering, run by the A. James Clark School of Engineering, offers students the opportunity to move beyond the classroom by working with faculty or staff on real-world engineering projects.

Thompson has worked for Fisher in the Tissue Engineering and Biomaterials Laboratory since the summer of 2010. He pursued the opportunity to conduct undergraduate research because he felt it would be a "unique and exciting opportunity" to prepare for a career in medicine. He describes Fisher's lab as "a perfect fit" with his interests.

Thompson joined BioE graduate student **Martha Wang** on a study of the efficacy of gene delivery for skeletal muscle regeneration. The goal of the project was to study the characteristics of porous polymer scaffolds—special biocompatible materials that provide an environment that supports the growth of new cells—as gene delivery devices. The project required the use of approaches from several areas of biology and chemistry.

"I was interested in this project because, since it built off of previous work, it seemed like an excellent way to hit the ground running," says Thompson. "The idea of speeding growth through gene delivery was new and exciting to me, and it was amazing to see how the ideas I was exposed to in my biology and bioengineering classes are put into practice. This [was] a great way to learn about...the practical applications of biomaterials."

"This [project] involved a steep learning curve that Josh was able to overcome with ease," says Fisher. "Despite several unforeseen setbacks that nearly compromised the project, Josh remained dedicated and optimistic. Due to his initiative and creative solutions when dealing with challenges, he was able to complete the necessary work to demonstrate the ability of our scaffolds for use a gene delivery vehicle."

Thomspon's perseverance paid off, and not only in the success of his experiments: a paper on the research that that he co-authored with with Fisher Group was published in *Pharmaceutical Research,* one of the top pharmacology journals.

"The thing that I enjoyed most about the experience was learning new procedures and techniques that I had never done before," Thompson adds. "It was great to be part of the enormous amount of work that goes into a long term project and eventually witness the results of that project as a publication...it has definitely given me a unique knowledge and understanding of the long process that takes an idea to a result that can help patients."

Thompson is the third BioE undergraduate to win the ASPIRE award since the department's launch in July 2006, and the fourth whose project was based in a BioE laboratory or research group. He is preceded by **Omar Ayyub** (2010, B.S. '10), **Adam Behrens** (2009, B.S. '10, chemical and biomolecular engineering, advised by BioE professor **Peter Kofinas**), and **Gunja Dave** (2007, B.S. '09), all of whom are now students in the Graduate Program in Bioengineering.

ROY WINS ACS'S PETERSON AWARD

Graduate Program in Molecular and Cell Biology (MOCB) student **Varnika Roy**, advised by BioE Professor and Chair **William E. Bentley**, was presented with the American Chemical Society's (ACS) W.H. Peterson Award at the organization's national meeting in March.

Each year, two Peterson Awards are presented to the students who delivered the best oral and best poster presentations in sessions sponsored by the ACS's Division of Biochemical Technology at the previous year's meeting. Roy received the 2010 Best Poster Presentation Award for her work, "Analogs of the Bacterial Signaling Molecule AI-2 as Quorum Quenchers."

Roy, a member of the Maryland Biochip Collaborative, works in Bentley's Biomolecular and Metabolic Engineering Laboratories, where she is involved in developing methods that can be used to interrupt cross species bacterial communication, also known as quorum sensing. This form of cell-to-cell communication relies on the production and detection of signaling molecules. When enough bacteria produce enough signaling molecules, they will respond as an organized group with a predetermined action. While sometimes the action is beneficial, it more often leads to infection or disease. Stopping the communication could shut down an infection in progress, while "tricking" bacteria into action before an actual quorum has been reached—that is, before they're organized enough to do harm—could provoke a natural immune system response capable of stopping them without the use of drugs. As an increasing number of bacteria species become resistant to antibiotics, controlling quorum sensing could prove an effective way to treat disease or lead to the next generation of antimicrobial drugs.

Much of Roy's work centers on a "universal" signaling molecule known as autoinducer 2 (AI-2), which is used by over 70 species of bacteria. In various experiments, she has been able to interrupt or encourage communications by controlling the production or suppression of AI-2. At the 2011

VARNIKA ROY

national meeting of the ACS, Roy reported on advances in her work in an invited presentation titled "Altering Communication Networks of Multispecies Microbial Systems by Engineering Signal Transduction."

Roy's fellow Bentley Group member, **Rohan Fernandes** (Ph.D. '08), won a 2007 W.H. Peterson Best Oral Presentation Award for his work on nanofactories.

RECORD YEAR FOR NSF FELLOWSHIPS

Five BioE graduate students have been awarded 2011 Graduate Research Fellowships from the National Science Foundation (NSF), and a sixth has received an Honorable Mention. Two BioE alumni have won a fellowship and an honorable mention, respectively.

Current graduate students **Gunja Dave** and **Rasa Ghafarrian**, and incoming graduate students **Rachel Manthe**, **Tony Melchiorri** and **Michael Wiederoder**, have each received a Graduate Research Fellowship, while current graduate student **Omar Ayyub** has received an Honorable Mention. Alumnus **Anthony Awojoodu** (B.S. '08), who attends the University of Virginia, received a Graduate Research Fellowship; and alumna **Jennifer Lei** (B.S. '10), who attends Georgia Tech, received an Honorable Mention.

"This is a record for our program," says BioE graduate program director and Keystone Professor **Peter Kofinas**. "The fact that eight former and current bioengineering students have been recognized by this very prestigious NSF fellowship program is proof of the high-caliber bioengineering graduate and undergraduate programs at the University of Maryland. Although our graduate program is the newest in the Clark School, we are already competing for the same applicants with the top bioengineering and biomedical engineering graduate programs such as Johns Hopkins, MIT, and the University of Washington at Seattle, and we are able to win them over."

Dave, advised by Assistant Professor **Sameer Shah**, studies the mechanics of diffuse axonal injury, a severe type of traumatic brain injury that leads to cognitive dysfunction. Her research focuses on understanding the transport of mRNA, molecules that encode the proteins required for cell function, in both maturing and injured neurons (nerve cells). Increasing our understanding of the process could ultimately lead to enhanced therapeutic strategies for neurodegenerative diseases. "I not only feel blessed but above all more inspired to deliver results," she says of her award.

Ghafarrian, advised by Assistant Professor **Silvia Muro**, is developing a novel drug delivery system that uses targeted carriers capable of crossing the gastrointestinal epithelium. Perfection of the technique could pave the way for more drugs to be delivered orally. The carriers could also be used to orally deliver imaging agents, genetic material, and other molecules used in the diagnosis, monitoring, and treatment of disease. The system tied for first place in the University of Maryland's Office of Technology and Commercialization's Invention of the Year competition in the Life Sciences category. *(See related story, p. 15.)*

Ayyub, advised by Professor Peter Kofinas, studies color changing polymer films as a biosensing platform. The sensor has been specifically fabricated to sense glucose, but further work could lead to pathogenic sensing. Reaching such goals can result in easy to use sensors for applications ranging from food safety to bioterrorism defense.

Each Graduate Research Fellowship consists of three years of support which may be used over a five-year period. For each year of support, the NSF provides a stipend of $30,000 to the fellow and a cost-of-education allowance of $10,500 to the degree-granting institution.

Honorable Mentions are granted to meritorious applicants who do not receive fellowship awards as an acknowledgement of significant national academic achievement. Recipients of Honorable Mentions are granted access to TeraGrid, the NSF's open scientific discovery supercomputing infrastructure.

BIOE SENIOR WINS PRESTIGIOUS DOD FELLOWSHIP

BioE senior (now alumnus) **Zachary Russ** (double major, mathematics) received a 2011 National Defense Science and Engineering Graduate (NDSEG) Fellowship from the U.S. Department of Defense. The highly selective and prestigious award includes full tuition and required fees for three years at any accredited U.S. college or university that grants advanced degrees in science and engineering, as well as an annual stipend.

Russ, who is interested in developing molecular toolboxes for synthetic biology and biological nanomachines to solve medical and environmental problems, plans to pursue his Ph.D. in bioengineering at the University of California, Berkeley.

"I'm very thankful for the numerous research opportunities and excellent mentorship that being a bioengineering student at Maryland has afforded me," he says. "It really is one of the best places to be."

During his time at the University of Maryland, Russ received a 2009-2010 Goldwater Scholarship, BioE's Outstanding Junior Award, and second place in the Clark School's 2010 Sustainability Video Contest. He has also received praise for his writing on ethics in bio-oriented research. His back-to-back wins in the Institute of Biological Engineering's annual bioethics essay contest and subsequent publication in the *Journal of Biological Engineering* led to an invitation to pen a guest column on preserving the integrity of statistics in *Genetic Engineering & Biotechnology News.*

ZACHARY RUSS
PHOTO BY AL SANTOS

studentAWARDS

Congratulations to the following students, who were recognized at the Clark School's 2010-2011 Honors and Awards Ceremony held this spring. They have all demonstrated outstanding academic and research performance, and have made contributions to the Department and field. Complete award citations are available on our web site at: **www.bioe.umd.edu/news/news_story.php?id=5641**

PROFESSIONAL SOCIETY AWARDS

- The ASABE, American Society of Agricultural and Biological Engineers' Student Honor Award: **Victoria Stefanelli**
- The Washington, D.C.–Maryland Section of ASABE, American Society of Agricultural and Biological Engineers' Scholarship: **Laith Abu-Taleb** and **Alison Clark**
- The Institute of Biological Engineering's annual National Bioethics Essay Contest *(See story, p. 11)*:

  Spencer Sokoloski: Third Place
  Yasmin Kadry: Honorable Mention
  Mian Khalid: Honorable Mention

DEPARTMENT AWARDS

- The Fischell department of Bioengineering's Outstanding Junior Award: **Kelley Heffner** and **Mariya Sitnova**
- The Fischell Department of Bioengineering's Outstanding Senior Award: **Kathleen Jee** and **Thomas Metzger**
- The Fischell Department of Bioengineering's Outstanding Research Award: **Bao-Ngoc Nguyen**
- The Fischell Department of Bioengineering's Outstanding Volunteer Award: **Edward Vogel**
- The Fischell Department of Bioengineering's Outstanding Citizen Award: **Jessica Stewart**
- The Capstone Design Awards, Sponsored by Mrs. **Susan Fischell**: See our coverage of our seniors' final projects on pp. 12-13 to find out who won!

CLARK SCHOOL AWARDS

- Outstanding ASPIRE Research Award: **Joshua Thompson** *(See story, p. 8.)*
- The Dinah Berman Memorial Award: **Esmaael Paryavi**
- The Keystone Design Challenge Award: **Richard Baik** and **Addison Goodley** were members of Team Legend, which won the Spring 2010 competition.
- The Outstanding Engineering Co-op/Intern Award: **Charles Chiang**

OTHER AWARDS

- Honorable Mention, Goldwater Scholarship: **Esmaael Paryavi**
- The ACS W.H. Peterson Award: **Varnika Roy** *(See story, p. 8.)*
- Best Posters, Graduate Research Interaction Day: **Janet Hsu** and **Wei Yu** *(See story, right.)*
- U.S. Department of Defense National Defense Science and Engineering Graduate Fellowship: **Zachary Russ** *(See story, p. 9.)*

HSU, YU WIN GRID DIVISIONS

Presentations by BioE graduate students **Janet Hsu** and **Wei W. Yu** won their respective divisions at the University of Maryland's 2011 Graduate Research and Interaction Day (GRID).

GRID, run by the Graduate Student Government, is a campus-wide event in which graduate students from all parts of the university present and discuss their work with faculty and fellow students, enabling them to receive feedback from a broader audience and perfect their conference presentation skills. Participants are judged in a variety of categories by faculty, postdoctoral fellows, administrators, and other specialists from around campus.

Hsu, advised by Assistant Professor **Silvia Muro**, won the "Pushing the Boundaries of Science" division for her presentation "Enhanced Delivery of Therapeutic Enzymes into the Brain," about her work on an enhanced drug delivery method specifically designed to address the challenges of crossing the body's blood/brain barrier. The award came with a grant that helped fund Hsu's travel to the 38th Annual Meeting and Exposition of the Controlled Release Society in July 2011, where she delivered a talk on her work. *(For more about Hsu's research on the treatment of rare disorders, see related story, p. 6.)*

Yu, advised by Assistant Professor **Ian White**, won the "Technology in the 21st Century" division for his presentation "Inkjet Printed Paper Sensors for Chemical and Biomolecular Analysis," which described a technique that employs an ordinary inkjet printer to make a sensitive, portable and inexpensive biosensor component for use in surface-enhanced Raman spectroscopy. *(See related story, Biofeedback, Vol. 7, No. 1.)* The technology has applications in the detection of food contamination, infections, cancer, pesticides, DNA, or even explosives. "We have [also] leveraged the ability to modify paper to allow for microfluidic techniques such as small sample requirements and analyte concentration," says Yu.

◀ BIOE CLASS OF 2011 WITH FACULTY

BIOE@UMD: STRONG PERFORMANCE IN BIOETHICS CONTEST

BioE freshmen **Yasmin Kadry**, **Mian Khalid**, and **Spencer Sokoloski** were three of the five finalists in the Institute of Biological Engineering's (IBE) annual bioethics essay contest. Sokoloski took third prize for his essay "The Ethics of Biological Engineering: Community Versus the Individual," while Kadry and Khalid received Honorable Mentions. The students presented their essays at the IBE's annual conference in Atlanta, Ga. in March, where the winners were decided.

Over the four years the IBE has run the contest, Clark School bioengineering majors from the University of Maryland have dominated it, representing fourteen of the twenty total finalists and scoring two first place, a second place, and three third place wins.

In his essay, Sokoloski argued that it was crucial to invest first and foremost in addressing preventable health issues that affect entire communities or developing nations, such as epidemics and starvation. He compared the situation to plugging the leak in the sinking ship before pausing to bail out individual buckets of water. A strong, healthy community would ultimately be better equipped to address the problems of its individual members, he wrote.

"One of the things I enjoyed most about the conference was being able to meet a lot of grad students and being able to ask them some in-depth questions about their research," says Sokoloski. "They gave us some really good advice...it was really fun and exciting to get this kind of exposure to the bioengineering field as a freshman."

Kadry's essay, "The Application of the 'Reductionist Approach' to Solve Societal Health Problems and Develop New Health Technologies," advised a different approach to community health, stating that we can "[improve] the health of society by focusing on developing technologies for the betterment of individual health, rather than for the broader, less defined needs of whole communities, in order to bring about broader societal changes."

Kadry says attending the conference was "a memorable and rewarding experience," and adds that she particularly enjoyed networking with other bioengineers at all levels. "There were many seminars on topics from all aspects of bioengineering...allowing me to discover current trends and research...and helping me to gauge my interests and narrow my career goals. After hearing all of the essays read at the competition, I came to truly appreciate the complexity of the ethical dilemmas that face the field of bioengineering, and the plethora of possible solutions."

Like Sokoloski's essay, Khalid's essay, "Biological Engineering: Looking Beyond the Boundaries," discussed how a community-based approach for bioengineering technologies is more likely to impact a larger population. It argued for enhancing the effectiveness of existing technologies over the exploration of novel, more individualized solutions, and emphasized that bioengineers must begin by looking—and traveling—beyond their national borders in order to develop contextually relevant solutions to health problems that are being faced by impoverished communities around the world.

Khalid enjoyed meeting fellow bioengineering undergraduates from across the U.S. and Canada, as well as bioengineers from industry, and particularly enjoyed attending the conference's biosensor symposium. "The IBE conference was fantastic in terms of exposing me to cutting-edge research," he says. "I was very excited to see...people researching topics ranging from biofuels to biosensors [to] biomolecular computing."

recent DISSERTATIONS

DECEMBER 2010

Michael Armani: "Nucleic Acid Extraction and Detection Across Two-Dimensional Tissue Samples." Co-Advisors: Benjamin Shapiro and Elisabeth Smela (Mechanical Engineering)

Brendan Casey: "Blood Coagulation Inducing Synthetic Polymer Hydrogel." Advisor: Peter Kofinas

Marina Chumakov: "The Novel Use of Nitroxide Antioxidants as Free Radical Scavengers in Ultra-High Molecular Weight Polyethylene (UHMWPE) for Total Joint Replacements." Advisor: Mohamad Al-Sheikhly (Materials Science and Engineering)

Deborah Sweet Goldberg: "Poly (amido amine) Dendrimers: Transepithelial Transport Mechanisms and Applications in Oral Drug Delivery." Co-advisors: Hamid Ghandehari (University of Utah) and Peter Swaan (School of Pharmacy)

MAY 2011

Christopher Byrd: "Local and Global Gene Regulation Analysis of the Autoinducer-2 Mediated Quorum Sensing Mechanism in *Escherichia Coli*." Advisor: William E. Bentley.

Melanie Freed: "A Dual Modality, DCE-MRI and X-ray, Physical Phantom for Quantitative Evaluation of Breast Imaging Protocols." Advisor: Aldo Badano (FDA Center for Devices and Radiological Health).

Ling Ma: "Auditory Streaming: Behavior, Physiology, and Modeling." Advisor: Shihab Shamma (Department of Electrical and Computer Engineering).

Anshu Rastogi: "Regulation of Intervertebral Disc Cell Interactions with Their Surrounding Microenvironment." Advisor: Adam Hsieh.

Peter Thomas: "Oxygen Measurements: From Multiwell Plates to Microfluidic Devices." Advisor: Srinivasa Raghavan (Chemical and Biomolecular Engineering).

2011 Capstone Projects

Smartphone-based solutions, diagnostics, wound care and new surgical techniques were on display as bioengineering seniors presented their final projects at the Capstone II finale, held in May 2011. Teams discussed the results of two semesters of research and testing, outlined challenges and successes, and demonstrated their prototypes.

Capstone, a two-part course taken in the fall and spring semesters of senior year, challenges teams of seniors to utilize what they have learned throughout their undergraduate studies to create their own engineering designs from concept to product.

Mrs. **Susan Fischell** is the creator and sponsor of our annual Capstone Design Awards. In this competition, launched in 2009, the top three project teams as selected by a panel of judges win monetary prizes donated by Mrs. Fischell and are invited to present their work to the public at the Fischell Festival. The teams may also have the opportunity to have their inventions put on track for development at the Robert E. Fischell Institute for Biomedical Devices.

This year, Capstone Design judge **Brian Lipford**, Partner and VP of Strategic Initiatives for medical device developer Key Technologies Inc., was the keynote speaker at the awards ceremony. In his talk, Lipford discussed the development process from concept to production and current trends in device types, approval procedures, and markets. Successful new biomedical product development, he told the audience, centered around three simple rules: understanding that "It's not about you"—it's about the needs of the stakeholders, whether patients, doctors or technicians; focusing on the human interface to prevent user error; and remembering that "It's all about risk," both for patients and developers.

1ST: TEAM 1 WITH PROFESSOR BENTLEY (LEFT) AND MRS. FISCHELL (CENTER)

2011 CAPSTONE II DESIGN AWARDS: AND THE WINNERS ARE...

FIRST PLACE

BACHomeSafe: Smart-Phone Alcohol Breath Detector to Reduce Drinking and Driving

Ariel Ash-Shakoor, Tahnee Hasan, Stevephen Hung, Synthia Mariadhas, and Mai Tran

Faculty Advisor: Assistant Professor Ian White

Mentor: Officer William Morrison, Traffic Division—Chemical Testing for Alcohol Unit, Montgomery Co. Police

Alcohol plays a role in one third of all traffic deaths, costing thousands of lives and billions of dollars in damage and medical expenses every year. Team 1 designed BACHomeSafe to help people determine their blood alcohol content (BAC) before they head for the car. The two-part system uses an inexpensive, portable breath alcohol analyzer to send its results wirelessly to any Android-based smartphone running the BACHomSafe app, which is also capable of tracking results over time. Team 1 says their system will help people avoid excess drinking, make responsible decisions about when to stop and whether to drive, understand BAC and impairment levels, and automatically call friends, a taxi, or even an ambulance if necessary.

SECOND PLACE

Development of a Personal Wireless ECG System with Remote Monitoring Capability

Joshua Hoffman, Tyler Keay, Natan Simhai, and Andrew Zayac.

Faculty Advisor: Associate Professor Keith Herold

Mentor: Dr. John Arnold, M.D.

Heart-monitoring implants and wearable devices used by high-risk patients are capable of sending warnings and data to doctors and patients. Their ability to continuously monitor the heart's electrical activity (electrocardiogram, or ECG) and log abnormalities has allowed them save lives by warning of heart attacks before they occur, and by drastically shortening the time between the detection of a problem and medical intervention. Existing devices for monitoring a patient's ECG, however, either do not have a user interface, or can display but not transfer data.

2ND: TEAM 9 WITH DR. FISCHELL (LEFT)

To address these shortcomings, Team 9 combined a noninvasive ECG monitor with a smartphone app and a web site that can be used to display and analyze data in realtime. Their prototype processes and transmits ECG information from the patient using existing Bluetooth wireless technology to any Android-based smartphone. Their custom app both displays the ECG and sends the data to the web site, allowing doctors, patients, caregivers and EMTs to access the information immediately from almost anywhere, or to review logged data. The phone running the ECG app detects the wearable device's Bluetooth hardware automatically within a range of ten meters. Team 9 believes their combination of a wearable device and near-ubiquitous use of cell phones and web sites can now make this life-saving technology available to an entire at-risk population.

THIRD PLACE (TIE)

CoagCapture: An Anticoagulant Monitoring Device

Charles Chiang, Kathy Jee, Christine Lim, Ka To, and Kathy Wann

Faculty Advisor: Professor Yang Tao

Mentor: Dr. James Lightfoot, M.D., Washington Adventist Hospital

Blood clotting, a natural part of wound healing, sometimes results in complications after surgery. Excessive clotting can lead to blockages in blood vessels that cause embolisms, deep vein thrombosis, or strokes. Each year, hundreds of thousands of patients using the drug Warfarin, an anti-coagulant, must be closely monitored due to its small therapeu-

SEE DESCRIPTIONS OF ALL OF THE PROJECTS ONLINE:
www.bioe.umd.edu/news/news_story.php?id=5768

tic range and its potential to cause its own dangerous side effects. Patients visit their doctors for special blood tests two or three times week while using Warfarin, and may wait up to a week for the results of each test. Team 7 created CoagCapture, a portable, at-home testing device for patients using Warfarin. CoagCapture almost immediately displays blood test results and transmits them from the patient's smartphone to the doctor's, reducing the time, effort, delays and cost associated with monitoring the drug's effects. The device uses a combination of a heated test strip, a signal circuit, and the phone's audio output and input to measure the electrical impedance of the blood and report the results to an app on the phone. The team estimates the device will cost $900-$1100 less than existing comparable portable systems.

THIRD PLACE (TIE)
PulseLife: A Portable Pulse-Oximeter Monitor with Direct Audiojack Connection to Smartphone

Thomas Metzger, David Minor, Corinne Riggin, Jessica Stewart, and Edward Vogel III

Faculty Advisor: Professor Yang Tao

Mentor: Dr. Ron Samet, University of Maryland School of Medicine

A pulse oximeter is a device that indirectly measures the oxygen saturation of hemoglobin based on the color of the blood it "sees" when a light is shined through an area of skin. It is used to monitor a patient's condition during and after surgery, or in cases of cardiac distress. Team 2 discovered that this essential piece of medical equipment is present in only five percent of operating rooms in third world countries. Existing portable units require external power sources (which may not exist in facilities off the grid), cannot store patient data, and typically retail for more than hospitals in impoverished nations can afford. To solve the problem and meet a global need, Team 2 designed an inexpensive pulse oximeter that connects to a smartphone using its standard audio jack. The device amplifies and modulates the oximeter's DC signal, converts the voltage to an analog frequency signal, and sends it to the phone. An app running on the phone interprets the changes in dynamic frequency, calculates the patient's pulse and oxygen levels, and displays the information. The data can be saved for future review.

3ND (TIE): TEAM 2

THANK YOU!

Our seniors would like to thank their professors and mentors; **Melvin Hill** for guidance, time, and labor in the lab; administrative staff members for help with financial support and purchasing; Professor and Chair **William E. Bentley**; and friends in outside academia and industry for the advice and supplies they donated that helped these projects succeed.

The Fischell Department of Bioengineering and its students would like to thank Mrs. **Susan Fischell** for her sponsorship of the Capstone Awards, and our panel of judges: Professor **Leigh Abts** (College of Education/BioE), **Brian Lipford** (Key Technologies Inc.), and Dr. **Jafar Vossoughi** (President, Biomed Research Foundation and adjunct faculty, BioE).

3ND (TIE): TEAM 7 WITH PROFESSOR TAO (RIGHT) AND THEIR PROTOTYPE

OUR OTHER INNOVATIVE SENIOR PROJECTS INCLUDED:

LifeBeats: Wireless Portable EKG Machine on Android Platform

Avinash Hiriyanna, Tony Kallracakal, Timothy Mahoney, Krishan Patel, and Mark Saxman

Faculty Advisor: Professor Yang Tao

Mentor: Dr. Ramesh Patel, M.D.

A Surgical Tool for Minimally Invasive Mitral Valve Repair

Kelsey Nadig, Adam Pampori, Zachary Russ, and Dominick Valenzano

Faculty Advisor: Assistant Professor Ian White

Mentor: Dr. James S. Gammie, M.D., Associate Professor of Cardiac Surgery, University of Maryland Medical Center

MarrowScope: A Fiber Optic Bone Marrow Biopsy Needle

Jeff Misiewicz, Bao-Ngoc Nguyen, Ashutosh Poudyal, and Kelliann Wachrathit

Faculty Advisor: Assistant Professor Yu Chen

Mentor: Dr. Peter Ledakis, Mercy Hospital, Baltimore

E.A.R.: Electronic Auditory Receiver

Anike Freeman, Kelly Grob, Christina Hitz, and Helen Ji

Faculty Advisor: Associate Professor Benjamin Shapiro

Mentor: Cynthia Compton Conley, Professor of Hearing, Speech, and Language Sciences, Gallaudet University

A Novel Delivery Mechanism for Bioprobes Monitoring Renal Health in Real-Time

Amin Asemani, David Gaddes, Mostafa Lotfi, Sindhu Raghunandan, and Martin Vilarino

Faculty Advisor: Assistant Professor Ian White

Mentors: Professor Elias Balaras, Associate Professor, Department of Mechanical and Aerospace Engineering, George Washington University; Dr. Bartley Griffith, M.D., Professor, Department of Surgery, University of Maryland School of Medicine; and Dr. Thomas Pallone, Professor of Medicine and Physiology, Division of Nephrology, University of Maryland School of Medicine

A Muscle Cramp Alleviating Sleeve

Patrick Fernandes, Peter Hoang, Ayedee Manneh, A.J. Mensh, and Tom Zhu

Faculty Advisor: Associate Professor Hubert Montas

Advanced Suture Device: Needleless Design for Scar-Less and Infection Free Wound Healing

Martin Enos, Prashant Rao, and Jin Xiao

Advisor: Dr. Martha Connolly, Director, Mtech Partnerships

(See related story, p. 14)

BioE@UMD: Big Wins at $75K Business Plan Competition

POLYVEC SYSTEMS DOMINATES BUSINESS PLAN COMPETITION

In a surprise sweep reminiscent of a night at the Academy Awards, **PolyVec Systems**, a startup company co-founded by Fischell Department of Bioengineering (BioE) professor **Peter Kofinas** and graduate student **Irene Bacalocostantis**, won $45,000 in three categories at the University of Maryland's 11th annual $75K Business Plan Competition, organized by the Maryland Technology Enterprise Institute (Mtech).

PolyVec Systems won $25,000 and the Lockheed Martin Grand Prize in the High Technology & Biotechnology division for its development of a synthetic polymer carrier that delivers therapeutic genes directly to breast cancer cells. The company also won the $10,000 Maryland Biotechnology Center Best Biotechnology Company prize, and a second place, $10,000 Warren Citrin Social Impact Award.

PolyVec Systems' carrier is designed to improve the safety, efficiency and efficacy of breast cancer treatments. By improving the successful delivery of gene therapy options developed by pharmaceutical companies, it will reduce the cost of treatment, the need for more radical procedures such as mastectomies, and the side effects of chemotherapy and radiation. The carrier's strength is its ability to sense when it has been taken up by a breast cancer cell's vacuole (a compartment that assists in cellular digestion). Only then will it activate, swelling until it ruptures the vacuole, then degrading and releasing its genetic cargo into the cell. The technology can ultimately be adapted to treat other types of cancer as well.

This was the fourth year in a row that one of Kofinas' companies reached the final round of the competition, and his third and fourth wins. In 2009 and 2008, Trauma Solutions (co-founded by **Brendan Casey**, Ph.D. '10) and Intelligent Packaging Systems (co-founded by 2007 Fischell Fellow **Dan Janiak**, Ph.D. '09) won their divisions, and in 2010 PoLiion was in the running.

"I had a great time putting together the business plan and I learned a lot," says Bacalocostantis. "My mentors **Craig Dye** from Mtech and Foundercorps member **Donna Harris** are wonderful, as is the entire Mtech staff. I'd recommend anyone who is even slightly interested in industry try out for the competition."

"I am very proud of Irene," says Kofinas. "She worked really hard. We hope our technologies will translate into future products that will improve the quality of life of millions living with cancer."

IRENE BACALOCOSTANTIS

WHAT'S IT ALL ABOUT?

The Maryland Technology Enterprise Institute's annual UM $75K Business Plan Competition promotes the commercialization of innovative ideas and University of Maryland-created technologies by offering faculty, students, and alumni prizes for the best new venture plans.

The competition emphasizes learning by offering one-on-one coaching for finalists, as well as the experience of presenting ideas to an experienced panel of judges. Companies active in the competition have generated millions in revenues, grants and awards.

In addition to the prize money, $75K Business Plan Competition Winners like ASD and PolyVec are eligible for one free year in Mtech's TERP Startup Laboratory, a program designed for entrepreneurs who need a place to quickly develop technology prototypes and obtain help in launching their companies.

To learn more, visit **bpc.umd.edu**.

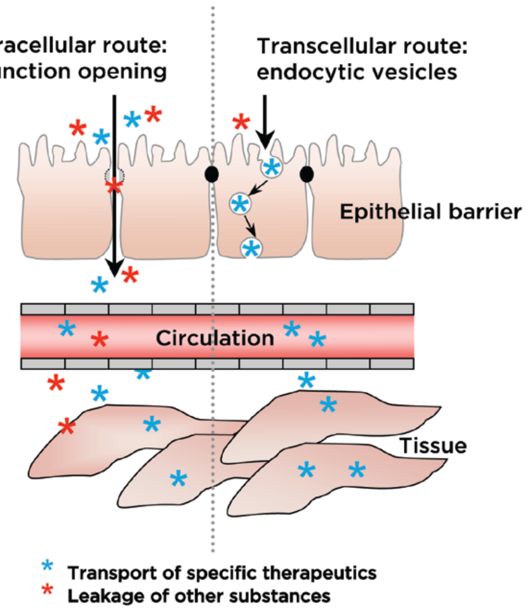
NEEDLE-FREE SUTURE DEVICE WINS UNDERGRADUATE DIVISION

Advanced Suture Device for Scarless Wound Healing (ASD), a startup company led by BioE undergraduates **Jin Xiao** (B.S. '11, double-major, mechanical engineering) and **Sharon Liu** (double-major, economics), received first place and $10,000 in the Undergraduate Division of the University of Maryland's 11th annual $75K Business Plan Competition, organized by the Maryland Technology Enterprise Institute (Mtech). ASD is advised by BioE professor **Yang Tao** and Dr. **Leigh Vinocur**, M.D. (UMD School of Medicine), and mentored by **Jonathan Aberman** (Amplifier Ventures) and **Alex Murphy** (Beyond.com Inc., and founder, Long Tail Interactive).

Xiao, who serves as ASD's CEO, has invented a wound closure product that could reduce or prevent the hypertrophy (swelling), keloid scars, and infections that are sometimes associated with the conventional stitching and stapling of surgical wounds or cuts. The system's noninvasive, needle-free technology also eliminates the needlestick injuries that healthcare workers sustain in approximately 19% of suture treatments annually, and prevents the transmission of diseases including hepatitis and HIV from patients to providers.

"It happens that the CDC [Centers for Disease Control] is calling for Prevention through Design (PtD) to reduce needlestick injuries [that]…have possibility of transmitting diseases," Xiao explains.

ILLUSTRATION BY SILVIA MURO



TRANSPORT OF THERAPEUTICS ACROSS GASTROINTESTINAL (GI) EPITHELIAL CELLS TO REACH THE CIRCULATION CAN BE ACHIEVED VIA THE PARACELLULAR ROUTE BY INDUCING OPENING OF THE CELL JUNCTIONS (LEFT SIDE OF ILLUSTRATION). HOWEVER, THIS MAY RENDER DETRIMENTAL SIDE EFFECTS DUE TO NON-INTENDED TRANSPORT OF OTHER SUBSTANCES PRESENT IN THE GI. MURO AND GHAFFARIAN'S INVENTION (RIGHT SIDE OF ILLUSTRATION) PROVIDES AN ALTERNATIVE STRATEGY: DRUGS ARE LOADED IN NANOCARRIER PARTICLES THAT ARE TARGETED TO CELL SURFACE RECEPTORS THAT CONTROL TRANSPORT ACROSS THE GI EPITHELIAL CELLS, PROVIDING A SAFE AVENUE TO REACH THE CIRCULATION WITHOUT OPENING THE CELLS' JUNCTIONS.

"Each case can cost thousands of dollars for preventative care."

The product's design uses a combination of a flexible frame and sterile medical adhesives to gently draw the edges of an open wound together. The product's design allows for the tension to be on the device and healthy areas of skin, not the wound itself.

"We are extremely excited about winning," says Xiao. "With this prize money we can finally fund our next step, getting a full patent for the ASD. In the future, we hope to gather more prize money and grants and meet with angel investors to help us with bringing our device to market."

"Joining this competition was an amazing experience," says Liu, whom Xiao invited onto the team to help her commercialize the ASD. "I've never given a presentation in such a formal way and in front of so many people. I learned a lot."

Both Liu and Xiao have a personal interest in the device: Xiao doesn't like needles, and Liu had an allergic reaction to sutures after a routine surgery that left her with a scar.

MORE INNOVATION!

Other teams with co-founders from BioE also turned in strong performances in the competition:

Ibis Microtech, whose members include 2008 Fischell Fellow **Marc Dandin** and BioE postdoctoral research associate **Roland Probst**, was a finalist in the High Technology & Biotechnology division. Ibis Microtech seeks to provide medical professionals, food quality control technicians, first responders, and national defense agencies with cost-effective diagnostic devices capable of performing fast, laboratory-grade analyses on-site.

Tikteb Solutions, whose members include undergraduates **Bernard Wong** and **Esmaeel Paryavi**, was a finalist in the Undergraduate Division. Tikteb designs web applications that can be used to improve the quality of writing through a crowd-sourced professional editing platform that helps non-professional writers commission freelance editing services.

◀ ADVANCED SUTURE SOLUTION RECEIVES TOP HONORS IN THE UNDERGRADUATE DIVISION OF THE $75K BUSINESS PLAN COMPETITION. LEFT TO RIGHT, JUDGE **SAMUEL E. FEIGIN** (NIXON PEABODY LLP), **JIN XIAO**, **MARK KASS** (NIXON PEABODY LLP), **SHARON LIU**, AND **DEAN CHANG** (TECHNOLOGY ADVANCEMENT PROGRAM AND VENTURE PROGRAMS, MTECH).

INVENTIONS & patents

NOVEL DRUG DELIVERY: LIFE SCIENCES INVENTION OF THE YEAR

A novel drug delivery strategy that uses targeted carriers capable of crossing the gastrointestinal epithelium tied for first place in the University of Maryland's Office of Technology and Commercialization's Invention of the Year competition in the Life Sciences category.

The system, created by BioE assistant professor **Silvia Muro** and BioE graduate student **Rasa Ghaffarian**, was one of four chosen for top honors out of a field of over 130 cutting-edge new products invented and patented at the university in 2010.

Oral administration of drugs is preferred over more invasive methods such as intravenous delivery because it is easier, less expensive, and more comfortable for patients. Patients are also more likely to adhere to an oral drug regimen. However, in many cases, only a fraction of the dose swallowed ever reaches its target due to the harsh environment of the digestive system and other anatomical barriers.

Muro and Ghaffarian have created a drug carrier designed to target the cells that form the gastrointestinal epithelium, which lines the digestive tract. The carriers are attracted to a specific molecule found on the surfaces of these cells, as well as other cells that may be affected by disease. Once the carrier is drawn to the outer surface of an epithelial cell, the cell is tempted to absorb it. Nutrients, drugs, or other therapeutic molecules loaded onto the carrier are absorbed as well. The delivery process, which takes advantage of the cells' natural behavior, is safe, fast, and efficient.

In addition to drug delivery, the carrier could also be used to deliver imaging agents, genetic material, biosensors, and other material used in the diagnosis, monitoring, and treatment of disease.

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ABOUT THE COVER IMAGE

THE PURPLE IMAGE USED ON THE COVERS, FROM THE MURO RESEARCH GROUP, IS A TRANSMISSION ELECTRON MICROGRAPH SHOWING ANTI-ICAM/ α-GAL NANOCARRIERS (BLUE) BOUND TO THE ENDOTHELIUM OF A BLOOD VESSEL (DARK PURPLE), AFTER BEING INTERNALIZED WITHIN VESICULAR COMPARTMENTS BY ENDOTHELIAL CELLS. THIS DELIVERY MODEL, WHICH ENHANCES TRANSPORT OF CARGO (α-GAL) TO TISSUE BY TARGETING PATHOLOGICALLY AFFECTED CELLS OVER-EXPRESSING ICAM-1, HAS BEEN PROVEN TO BE MORE EFFECTIVE THAN NON-TARGETED THERAPEUTIC METHODS CURRENTLY UTILIZED TO TREAT LYSOSOMAL STORAGE DISORDERS. TO LEARN MORE, SEE P. 6.

BIOFEEDBACK is published for alumni and friends of The Fischell Department of Bioengineering at the A. James Clark School of Engineering, University of Maryland.

Alumni news and comments are welcome! Please contact us at:
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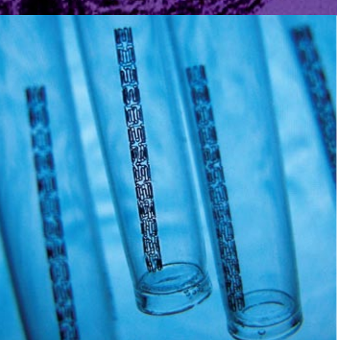
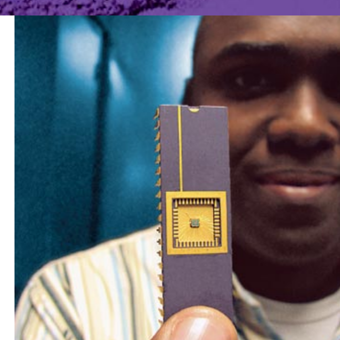




THE 2011 FISCHELL FESTIVAL

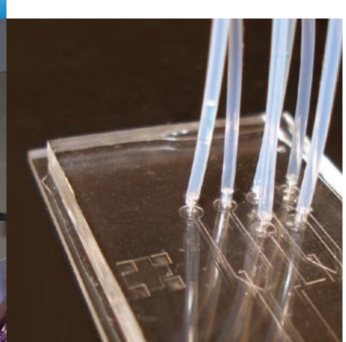
A CELEBRATION OF BIOENGINEERING'S POTENTIAL TO IMPROVE LIFE FOR MILLIONS OF PEOPLE

THURSDAY, OCT. 20 2011 • 8:30AM–6:00PM • Complimentary Registration
Jeong H. Kim Engineering Building • University of Maryland, College Park

For information, directions, and text, photos and video from previous Festivals, visit:

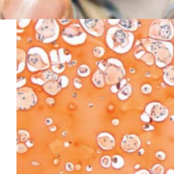
www.fischellfestival.umd.edu

Questions? E-mail us at **fischellfestival@umd.edu.**



ACTIVITIES SCHEDULED SO FAR INCLUDE:

- A Whiting-Turner Business & Entrepreneurial Lecture by Jenny Regan, CEO, President, and co-Founder of Key Tech, a product design and applied research prototyping company located in Baltimore, Md.
- Prominent speakers from academia and industry
- Presentations by faculty about current research
- The introduction of the 2011 Fischell Fellow
- A live, streamcast surgical procedure with commentary from the University of Maryland School of Medicine
- A career fair and exhibitors expo
- A poster session featuring student research



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