CONTENTS

Greetings . . . . . . . . . . 1
Research Highlights . . . . 2
Departmental Accomplishments . . . . 14
Graduate Student Highlights . . . . . . . . 18
Undergraduate Student Highlights . . . . . . . . 20
Colloquium Speakers . . . . 21
Warm greetings from Nashville

In recent years, the Chemistry Department has sustained an aggressive expansion in teaching and scientific research across the spectrum of disciplines in chemistry. This season of growth has included major research initiatives focusing on problems at the chemical biology interface, nanotechnology and materials science, and in structural biology. I hope you will enjoy reading about some of the exciting aspects of the wide spectrum of science in Vanderbilt chemistry labs.

We are particularly proud of our outstanding students who come from across the U.S. and around the world. In May, we graduated 24 students with ACS-certified Bachelor degrees in Chemistry, most of whom will continue with graduate or professional education this fall. We also graduated 9 students with the Masters degree and 16 students with the Ph.D. degree in Chemistry.

As you read this, the class of 2017 will have arrived and have matriculated into the Vanderbilt community. About one half of them, roughly 850 students, will be enrolling in a chemistry course. We will also welcome sixteen new students to our graduate program in Chemistry.

We always love to hear from you. The Department of Chemistry has experienced a period of unprecedented growth and expansion, so please visit us the next time you find yourself in Nashville.

Michael P. Stone
Professor and Chair
An interdisciplinary research team at Vanderbilt University have developed a biohybrid, photoelectrochemical energy conversion device with multilayer films of Photosystem I (PSI) deposited on silicon electrodes, which yielded an average photocurrent density of 875 μA/cm², one of the highest reported photocurrent densities for a film of PSI deposited onto an electrode of any material.

The research provides a way to combine the photosynthetic protein that converts light into electrochemical energy in spinach with silicon, the material used in solar cells, in a fashion that produces substantially more electrical current than has been reported by previous “biohybrid” solar cells.

The research was reported in Journal of Advanced Materials and Vanderbilt has applied for a patent on the combination.

“This combination produces current levels almost 1,000 times higher than we were able to achieve by depositing the protein on various types of metals. It also produces a modest increase in voltage,” said David Cliffl, associate professor of chemistry, who collaborated on the project with Kane Jennings, professor of chemical and biomolecular engineering. “If we can continue on our current trajectory of increasing voltage and current levels, we could reach the range of mature solar conversion technologies in three years.”

The researchers’ next step is to build a functioning PS1-silicon solar cell using this new design. Jennings has an Environmental Protection Agency award that will allow a group of undergraduate engineering students to build the prototype. The students won the award at the National Sustainable Design Expo in April, 2012, based on a solar panel that they had created using a two-year old design. With the new design, Jennings estimates that a two-foot panel could put out at least 100 milliamps at one volt – enough to power a number of different types of small electrical devices.

**Harnessing the Power of Spinach**

More than 40 years ago, scientists discovered that one of the proteins involved in photosynthesis, called Photosystem 1 (PS1), continued to function when it was extracted from plants like spinach. Then they determined PS1 converts sunlight...
into electrical energy with nearly 100 percent efficiency, compared to conversion efficiencies of less than 40 percent achieved by manmade devices. This prompted various research groups around the world to begin trying to use PS1 to create more efficient solar cells.

Another potential advantage of these biohybrid cells is that they can be made from cheap and readily available materials, unlike many microelectronic devices that require rare and expensive materials like platinum or indium. Most plants use the same photosynthetic proteins as spinach. In fact, in another research project Jennings is working on a method for extracting PS1 from kudzu.

Since the initial discovery, progress has been slow but steady. Researchers have developed ways to extract PS1 efficiently from leaves. They have demonstrated that it can be made into cells that produce electrical current when exposed to sunlight. However, the amount of power that these biohybrid cells can produce per square inch has been substantially below that of commercial photovoltaic cells.

Another problem has been longevity. The performance of some early test cells deteriorated after only a few weeks. In 2010, however, the Vanderbilt team kept a PS1 cell working for nine months with no deterioration in performance. “Nature knows how to do this extremely well. In evergreen trees, for example, PS1 lasts for years,” said Cliffel. “We just have to figure out how to do it ourselves.”

SECRET IS “DOPING” SILICON

The Vanderbilt researchers report that their PS1/silicon combination produces nearly a milliamp (850 microamps) of current per square centimeter at 0.3 volts. That is nearly two and a half times more current than the best level reported previously from a biohybrid cell. The reason this combo works so well is because the electrical properties of the silicon substrate have been tailored to fit those of the PS1 molecule. This is done by implanting electrically charged atoms in the silicon to alter its electrical properties: a process called “doping.” In this case, the protein worked extremely well with silicon doped with positive charges and worked poorly with negatively doped silicon.

To make the device, the researchers extracted PS1 from spinach into an aqueous solution and poured the mixture on the surface of a p-doped silicon wafer. Then they put the wafer in a vacuum chamber in order to evaporate the water away, leaving a film of protein. They found that the optimum thickness was about one micron, about 100 PS1 molecules thick.

PROTEIN ALIGNMENT

When a PS1 protein is exposed to light, it absorbs the energy in the photons and uses it to free electrons and transport them to one side of the protein. That creates regions of positive charge, called holes, which move to the opposite side of the protein.

In a leaf, all the PS1 proteins are aligned. But in the protein layer on the device, individual proteins are oriented randomly. Previous modeling work indicated that this was a major problem. When the proteins are deposited on a metallic substrate, those that are oriented in one direction provide electrons that the metal collects while those that are oriented in the opposite direction pull electrons out of the metal in order to fill the holes that they produce. As a result, they produce both positive and negative currents that cancel each other out to leave a very small net current flow.

The p-doped silicon eliminates this problem because it allows electrons to flow into PS1 but will not accept them from proteins. In this manner, electrons flow through the circuit in a common direction.

“This isn’t as good as protein alignment, but it is much better than what we had before,” said Jennings.

If we can continue on our current trajectory of increasing voltage and current levels, we could reach the range of mature solar conversion technologies in three years.

The research was supported by National Science Foundation grant DMR 0907619, NSF EPSCoR grant EPS 1004083 and by the Scialog Program of the Research Corporation for Science Advancement.
Extractionator could bring high-tech medical diagnostics to rural areas

By David Salisbury

They call it “The Extractionator.” The prototype looks like nothing more than a length of clear plastic tubing until you inspect it closely. But it could be the basis of an easy-to-use and low-cost sample collection and preparation system that will help bring the benefits of medical diagnostic testing to the people who live in the poorest areas of the world.
The device is the idea of an interdisciplinary team of Vanderbilt scientists, and the Bill & Melinda Gates Foundation has given them $3 million for it to be developed. The grant is part of the Grand Challenges in Global Health initiative that seeks to engage creative minds across scientific disciplines to work on solutions that could lead to breakthrough advances for resource-poor settings.

The Grand Challenges point-of-care diagnostics program provides funding to scientists and researchers worldwide to create technologies and components to assess conditions and pathogens at the point-of-care in the developing world. Performing a wide variety of diagnostic tests is the first step in treating most patients in a modern hospital, but they are difficult if not impossible to administer in rural clinics without highly trained technicians, sophisticated medical equipment, electricity or water.

Collecting and preparing the patient samples required for these tests is the goal of the Vanderbilt research, which is being performed by David Wright, professor of chemistry, Rick Haselton, professor of biomedical engineering, and Ray Mernaugh, associate professor of biochemistry.

The device is deceptively simple. It consists of a length of clear plastic tubing. The tubing is filled with a series of liquid chambers separated by short lengths of air or oil. At one end, the tube also contains tiny magnetic beads. The surface of the beads is covered with molecular hooks to catch the biomarker of interest.

It works something like a miniature car wash. When a patient sample is introduced into the end of the tube, the operator uses an external magnet first to coat the beads with the target material. The beads have special coatings that bind with the specific biological molecules needed for a given diagnostic test. The operator then drags the beads through the air spaces, which the engineers call surface tension valves, into the subsequent chambers. Each of the sequential chambers contains special chemicals that remove molecules that interfere with the accuracy of the test. As a result, when the beads reach the other end of the tube, they carry a purified and concentrated sample of the sort required for testing.

The ultimate goal is to make sample collection and preparation so simple that it can be operated properly by people with little training and can be easily integrated with the other detection methods under development by other grantees.

The researchers have explored how the system works with a number of potential applications – biomarkers for the RSV respiratory virus, HIV, tuberculosis, and for malaria – and found that their system is effective. They evaluated the extraction and concentration of the RSV biomarker and found that the Extractionator worked as well as commercial lab-based kits. In the case of malaria, they observed that sample processing through the cassette improved the performance of even the least effective commercial rapid diagnostic test strip.

“It's low-tech, high-science,” said Wright. The surface tension valves that keep the different liquid baths apart are formed by a specific balance between the surface tension of the liquid, the internal diameter of the tubing and the surface properties of the plastic. One of the team’s research goals is to identify the various physical features that affect valve formation. The chemical makeup of the plastic is also critical because biological molecules stick to the surface of many plastics, so the researchers need to identify types of plastic that are chemically inert relative to biological molecules. In addition, there is the issue of the coating on the magnetic beads. So far, they are customizing the coating so that it picks up a single biomarker that can be used for a specific diagnostic test. “In the future we want to develop a coating that will target 20 different targets in a single sample,” Mernaugh said.

Students who worked on this project were graduate students Keersten Davis, Nick Adams, Josh Swartz, and Lauren Gibson.

Support for this work was provided by the Bill and Melinda Gates Foundation Grand Challenges in Global Health: Develop Technologies that Allow Assessment of Multiple Conditions and Pathogens at Point-of-Care (Grant # OPP1028749)
New tool for mining bacterial discovery

By David Salisbury

Vanderbilt chemists Brian Bachmann and John McLean have discovered that the process bacteria undergo when they become drug resistant can act as a powerful tool for drug discovery.

Their findings were reported in the Proceedings of the National Academy of Sciences. This advancement should give a major boost to natural products drug discovery (the process of finding new drugs from compounds isolated from living organisms) by substantially increasing the number of novel compounds that scientists can extract from individual microorganisms.

Bacteria have traditionally been the source of important drugs such as antibiotics and anticancer agents. Researchers looking for new bacterially synthesized drugs have long known that bacterial genomes contain a large number of “silent genes” that contain the instructions for making drug-like compounds. But, until now, scientists have found it is very difficult to find ways to turn on the production of these compounds, known as secondary metabolites.

While investigating how bacteria develop drug resistance, Bachmann and McLean discovered that strains of antibiotic-resistant bacteria express hundreds of compounds not produced by their progenitors, many of which are potential secondary metabolites.

“It’s as if the bacteria respond to the assault by the antibiotic with a ‘save-all-ships’ strategy of turning on hundreds of silent genes,” said Bachmann, Associate Professor of Chemistry.

“This technique is something like fracking in the natural gas industry. We’ve known for a long time that there were large amounts of underground natural gas that we couldn’t extract using conventional methods but now we can, using hydraulic fracturing technology. In a similar fashion we think we can use bacteria’s antibiotic resistance to intensively mine the bacterial genome for new drug leads,” he said.

The original purpose of the study was to take the most detailed look yet at what happens when microbes develop drug resistance. Bachmann is an expert in natural products drug discovery and McLean, an associate professor of chemistry, is a pioneer in the development of analytical instrumentation and chemical techniques that can identify thousands of different biological compounds simultaneously, such as ion mobility-mass spectrometry.

“One of the daunting challenges is to rapidly inventory the tens to hundreds of thousands of molecules the bacteria construct to live, and then to read this inventory to understand how the bacteria compensate for their changing circumstances. To complicate matters further, we are looking for new drug-like molecules, so by definition we are looking for something that has not been seen before,” said McLean.

Working with research assistant Dagmara Derewacz, postdoc, Cody Goodwin, and graduate student, Ruth McNees, Bachmann and McLean started with the well-characterized soil bacterium Nocardiopsis. They exposed the bacterium to the antibiotics streptomycin and rifampicin and observed the results.

“The first thing that happens is almost all of the bacteria die. Less than one cell in a million survives,” said Bachmann. The chemists then cultured the survivors (six streptomycin-resistant strains and five rifampicin-resistant strains) without further treatment.
The antibiotic and used McLean’s instrumental methods to profile the drug-like compounds that they produced. They discovered that the differences were much greater than they expected. The survivors had undergone extensive mutations, not only in the genes that produce secondary metabolites but also in the housekeeping genes that alter the way they make RNA and proteins. As a result, they determined that the resistant strains produced more than 300 compounds that were not expressed by the original organism.

“The cells appear to be ‘de-repressing’ as many of their silent genes as possible. This seems like a very drastic way to become drug resistant,” Bachmann said.

McLean’s team has developed strategies that allow them to automatically identify and compare the relative uniqueness and the relative abundance of tens of thousands of molecules from which the hundreds of novel compounds were found.

“What we are looking for are new species of molecules in the mutants that are the most unique and the most abundant,” said Bachmann.

In the antibiotic-resistant Nocardiopsis strains, the researchers found a total of five compounds that were both unique enough and abundant enough to isolate, determine their molecular structures and test for biological activity.

“Normally, we only find one compound per organism, so this is a significant improvement in yield, allowing us to get many new compounds from previously mined microorganisms,” Bachmann said.

The research was supported by National Institutes of Health grants 1R01GM09221B and RC2DA028981 and the Defense Threat Reduction Agency grant HDTRA-09-1-0013.
Sandra Rosenthal, the Jack and Pamela Egan Chair in Chemistry, and Randy Blakely, the Allan D. Bass Professor of Pharmacology and Psychiatry, have managed to tag a protein that regulates the neurotransmitter serotonin with tiny fluorescent beads, allowing them to track the movements of single molecules for the first time.

The capability makes it possible to study the dynamics of serotonin regulation at a new level of detail, which is important because of the key role that serotonin plays in the regulation of mood, appetite and sleep. The achievement was reported in the *Journal of Neuroscience*.

The regulatory protein that the Rosenthal and Blakely successfully tagged is known as the serotonin transporter, which helps regulate the concentration of serotonin in the area around the cell.

Serotonin transporters are an important research subject because they are the target for common drugs used to treat depression, such as Prozac, Paxil and Lexapro. Problems with serotonin transporter regulation have also been implicated in autism. The brain’s other key neurotransmitters have their own transporter proteins, so scientists can use the capability to track the motion of individual transporter molecules to determine how they are regulated as well.

Attempts to understand how these transporters work have been limited by the difficulty of studying their dynamic behavior. “In the past, we have been limited to snapshots that show the location of transporter molecules at a specific time,” said chemistry graduate student Jerry Chang, who developed the tagging technique. “Now we can follow their motion on the surface of cells in real time and see how their movements relate to serotonin uptake activity.”

The fluorescent tags that the researchers used are nanoscale beads called quantum dots, made from a mixture of cadmium and selenium. Quantum dots emit colored light when illuminated; small changes in their size cause them to glow in different colors. Team member, Ian D. Tomlinson, research assistant professor of chemistry, developed a special molecular string that attaches to the quantum dot at one end and, on the other end, attaches to a drug derivative that binds exclusively with the serotonin transporter. When a mixture that contains these quantum dots is incubated with cultured nerve cells, the drug attaches to the transporter. As the protein moves around,
it drags the quantum dot behind it. When the area is illuminated, the quantum dots show up in a microscope as colored points of light.

Using their new procedure, the researchers looked at extensions of the nerve cell that are involved in secreting serotonin, presuming that transporters would be localized there as well. The investigators suspected that the transporters would be concentrated in cholesterol-rich parts of these extensions called rafts.

The quantum dot studies showed two distinct populations of transporters in these areas: Those that can travel freely around the membrane and those that seem immobile. They found that the immobile transporters were located in the rafts.

When they stimulated the cell to increase transporter activity, they were surprised at what happened. “We found that the transporters in the rafts began to move much faster, whereas the motion of the other population didn’t change at all,” Rosenthal reported.

Since the mobilized transporters do not leave the rafts, they appear to whizz around inside a confined compartment. These observations suggest it is likely that the two populations are controlled by different regulatory pathways.

“By understanding the basic mechanisms that naturally turn serotonin transporter activity up and down, maybe we can develop medications that produce milder side effects and have even greater efficacy,” said Blakely.

Graduate students who worked on this project are Jerry Chang, Oleg Kovtun, Emily Jones-Ross, Teresa Rosson, and Sarah Claiborne; and undergraduates Zach Glaser, Nick Weaver and Nate Levinson.

The research was supported by grants from the National Institutes of Health, the Vanderbilt Institute of Nanoscale Science and Engineering and the NIMH Silvio O. Conte Center for Basic Neuroscience Research.
Drug companies are struggling to fill the "pipeline" with new compounds that potentially can solve important problems in human health. At the same time, many firms are downsizing their research operations, laying off scientists and tightening their belts, as patent protection ends for some of their best-selling brand name products.

Increasingly drug discovery is being outsourced to academia. Vanderbilt's drug discovery program is flourishing in part because of growing interdisciplinary collaborations involving chemists, biochemists, and pharmacologists working in concert with the Vanderbilt University Institute of Chemical Biology (VICB) led by Lawrence J. Marnett, University Professor and Mary Geddes Stahlman Professor of Cancer Research, Professor of Biochemistry, and Professor of Chemistry. Bold ideas are being pursued thanks to a unique recipe for drug discovery that blends bench science in the Department of Chemistry and other basic science departments with clinical medicine, and academia with industry. Vanderbilt scientists and their physician colleagues believe they are on the threshold of a new era of innovation.

"I think we're right on the cusp of real breakthroughs because our scientific understanding has increased dramatically," said Jeffrey Conn, Professor of Pharmacology and Director of the Vanderbilt Program in Drug Discovery (VPDD), which explores new treatments for neurological and psychiatric diseases.

"If we are able to overcome the technical hurdles and if we can find small molecules that inhibit targets that we're pursuing," added Stephen Fesik, who holds the Orrin H. Ingram II, Chair in Cancer Research and is Professor of Biochemistry, Professor of Pharmacology, and Professor of Chemistry and a leader of Vanderbilt's cancer drug discovery effort, "we could have a dramatic effect on cancer therapy, effects that won't just give you a slight increase in lifespan … but would actually lead to cures."

"One thing that's unique about Vanderbilt now is we've built the infrastructure to look just like a pharmaceutical company," said Craig Lindsley, Professor of Pharmacology and Professor of Chemistry and Director of Medicinal Chemistry in the VCNDD, who, like Conn, came to Vanderbilt from Merck. "We have all of the instrumentation and technology that you'd find at a Merck or a Pfizer or a GlaxoSmithKline."

Consider these examples:

**DIMMER SWITCHES IN THE BRAIN**

Conn, Lindsley and their colleagues have pioneered a novel approach to treating neurological and psychiatric disorders using compounds called "allosteric modulators." Rather than turning a receptor "on" or "off" (which is what traditional drugs usually do), allosteric modulators "tune" the receptor function up or down, like a dimmer switch in an electrical circuit. The researchers have discovered promising candidates for treating a wide range of disorders including Parkinson's disease, schizophrenia and Fragile X syndrome.

An estimated 1.5 million Americans have Parkinson's disease, a progressive brain disorder characterized by uncontrollable muscle tremors and rigidity. It is caused by the death of nerve cells in a specific brain region that produce the neurotransmitter dopamine. Dopamine replacement therapy can relieve symptoms, but it also causes side effects and eventually becomes less effective as the disease progresses.

With support from the NIH and the Michael J. Fox Foundation for Parkinson's Research, the Vanderbilt researchers have identified drug-like molecules that may avoid the limitations of current therapy by acting on a brain receptor that binds a different neurotransmitter, glutamate.

Schizophrenia affects more than 2 million Americans. Current therapy can reduce hallucinations and delusions but is less effective in relieving cognitive symptoms and social withdrawal.

With funding from the NIH and Janssen Pharmaceutica, a Johnson & Johnson company, Conn's team is testing ways to "tune" a specific glutamate receptor in order to alleviate all symptoms of schizophrenia.

Fragile X syndrome is the most common inherited form of intellectual and developmental disabilities, and the most common genetic cause of autism. In collaboration with Seaside Therapeutics in Cambridge, Mass., the researchers are trying to "tune down" signaling through two different brain receptors – one involved in learning and memory, and the other associated with autistic and other behavioral symptoms of Fragile X syndrome.
‘HIT MOLECULES’ FOR CANCER

Vanderbilt’s cancer drug discovery program, led by Professor Fesik, was established by a NIH “Grand Opportunities” grant. Fesik also became the first Vanderbilt scientist to receive a prestigious NIH Director’s Pioneer Award to support his work. Professor Fesik is developing new approaches to target proteins that currently are considered to be “undruggable.”

Protein-protein interactions play a central role in nearly all signaling processes in cells, including cancer cells, but targeting these proteins will require a new set of tools beyond those used in traditional drug discovery.

Fesik is using fragment-based methods – and screening small chemical fragments with NMR spectroscopy, to probe their ability to bind to small pockets on a protein target. He and his colleagues then obtain and examine crystal structures of the “hit molecules” bound to their targets. This information can show them how to link the fragments into drug-like compounds with the “right pharmaceutical properties to move forward,” he said.

Gary Sulikowski, Stevenson Professor of Chemistry and associate director of the VICB Chemical Synthesis Core, is leading another cancer drug discovery effort. His group has synthesized several anti-tumor antibiotics isolated from various soil microorganisms.

Sulikowski also is co-principal investigator with Alex Waterson, of the Vanderbilt Chemical Diversity Center, and Research Assistant Professor of Pharmacology, and Research Assistant Professor of Chemistry, as part of a National Cancer Institute effort to spur the discovery and development of new cancer drugs. The partnership between the School of Medicine and Department of Chemistry “really opens up new approaches,” Sulikowski said.

BREAKING THE DOSE ‘CEILING’

Acetaminophen, the ingredient in Tylenol and similar drugs, is the most commonly used fever and pain reliever in the world. In high doses, however, it is toxic to the liver.

Every year in the United States, acetaminophen overdose causes more than 50,000 cases of liver toxicity – and more than 400 deaths, said John Oates, M.D., the Thomas F. Frist Sr. Professor of Medicine and professor of Pharmacology.

Were it not for the 4-gram-a-day dose ‘ceiling’ imposed by toxicity, acetaminophen could do more than ease pain and lower fever. Recent animal studies conducted by Oates and his colleagues suggest that in higher doses the drug could prevent kidney failure following traumatic injuries, and neurological damage following bleeding in the brain.

Myoglobin is a protein that transports oxygen to the muscle, just as hemoglobin does in the blood. When muscle is crushed, it releases myoglobin, which travels to the kidneys and, through a reaction called lipid peroxidation, generates free radicals and other kidney-killing products.

“In a situation like the recent earthquake in Haiti … they had to go to the medieval extreme of amputating limbs that were crushed in order to prevent kidney failure,” Oates noted. Similarly, bleeding in the brain can, via lipid peroxidation, cause stroke-like damage.

Oates, who founded Vanderbilt’s Division of Clinical Pharmacology, and longtime colleague L. Jackson Roberts II, M.D., the T. Edwin Rogers Professor of Pharmacology, wondered if they could design a replacement for acetaminophen – a drug that blocks lipid peroxidation without damaging the liver. They joined forces with Ned Porter, Stevenson Professor of Chemistry, to do just that.

“I have a high level of confidence … that we will have some successful compounds because we’re working on a mechanism we understand for both the effectiveness and the toxicity,” said Oates. “We know enough about those to know that we can pull them apart.”
Leipzig collaboration yields valuable relationships

By David Salisbury

In 2007, while Jens Meiler was visiting his parents in Germany, the associate professor of chemistry was invited to give a lecture at his alma mater, the University of Leipzig.

“When I gave that talk on my research in structural and chemical biology, I found a tremendous amount of interest in what we are doing at Vanderbilt and learned that there is a great deal of complementary research going on in Leipzig,” Meiler said. In fact, Meiler stirred up so much interest that two years later Annette Beck-Sickinger, professor of biochemistry and bioorganic chemistry at Leipzig, spent her sabbatical at Vanderbilt. During her visit she helped establish a number of collaborations, leading the administrations of the two universities to sign a five-year memorandum of understanding that allows and encourages academic exchanges, facilitates joint research programs, student programs and a cultural exchange program. Over the last few years, the size of the collaboration has grown to embrace 20 faculty members at the two universities. More than 20 graduate students have spent time studying at the other campus, and groups of five undergraduates have been exchanged for the last few summers. Last October, Leipzig Professor Daniel Huster spent 10 days on campus to teach a mini-course on the use of NMR spectroscopy in biology.

“Leipzig has become one of our half-dozen strategic international partners,” said Tim McNamara, vice provost for faculty and international affairs. “It is a very productive relationship and we certainly want it to prosper.”

Leipzig University was founded in 1409 and has enjoyed 600 years of uninterrupted teaching and research, making it the second oldest university in Germany. It is also one of Germany’s top 20 research organizations. The university has made it a tradition to cross academic boundaries and promote interdisciplinary research.

Meiler and his colleagues have received a grant from the National Science Foundation that has enabled the group to hold research symposia at both Leipzig and Vanderbilt involving faculty from both schools, pay for research trips for graduate students, allow faculty to teach short courses at each other’s campuses and provide postdoctoral and undergraduate students with summer internships. In addition, several Vanderbilt undergraduates have been awarded scholarships from a German Research Internships in Science and Engineering program that has allowed them to carry out research in chemical biology in Leipzig.

The Leipzig connection is one of many cases where grassroots from Vanderbilt researchers have led to formal relationships. Other such international partnerships include Queen’s University Belfast, which was established by faculty members in the Robert Penn Warren Center; the University of Sao Paulo, which has productive collaborations in art, education policy and history; and the University of Melbourne, one of Vanderbilt’s strongest relationships, which extends across many academic fields.
Recently, Vanderbilt and the University of Melbourne in Australia jointly provided funding to support partnership grants for faculty. One of those projects has Terry Lybrand, professor of chemistry, joining forces with colleagues at the University of Melbourne to analyze data from studies of small peptides and proteins that produce antimicrobial effects. Lybrand provides the in-depth computational work to analyze the data and his Melbourne counterparts provide solid-state NMR spectroscopy support.

These types of associations yield surprising benefits. For example, Melbourne has poured money into a gorgeous new eye institute, says Associate Professor of Chemistry Eva Harth. Professor Harth develops targeted drug delivery for cancer treatment and researches nanoparticles to treat glaucoma. Melbourne’s eye institute is eager to work with world experts to enhance their productivity and global standing. Already Harth was part of a plenary lecture in nanomedicine at Melbourne and is considering more possible collaborations. The improved access to talent, resources and funding benefits both institutions, Harth says, adding, “You can accelerate only so much without good collaborators.”

Jens Meiler creates world’s largest human-designed protein

Vanderbilt researcher, Jens Meiler, Associate Professor of Chemistry, and his team have created the largest human-designed protein containing 242 amino acids, more than doubling the previous record. The super-sized protein, FLR, is a computer model of a protein that creates the amino acid histidine. They used algorithms and 400 processors of the supercomputer at Vanderbilt’s Advanced Computing Center for Research and Education to engineer large proteins with shapes unseen in nature. “This gives us the tools we need to create new, more effective antibodies and other beneficial proteins,” Meiler says.
Ned Porter Receives James Flack Norris Award
Ned Porter, Stevenson Professor of Chemistry, has received the 2013 James Flack Norris Award from the American Chemical Society. Dr. Porter’s pioneering work has helped chemists recognize that free radicals can act as highly useful intermediates in organic reactions, a lesson that is now included in undergraduate organic chemistry courses. Much of his research has focused on the interaction of free radicals with lipids. Dr. Porter’s recent research has focused on the role of free radical species in a broad range of diseases including cancer, stroke, diabetes, atherosclerosis, Parkinson’s and Alzheimer’s.

Craig Lindsley receives Philip S. Portoghese Lectureship
Craig Lindsley, is the 2013 recipient of the Philip S. Portoghese Lectureship, awarded jointly by the Journal of Medicinal Chemistry and the American Chemical Society. Lindsley, the William K. Warren Jr. Chair in Medicine and professor of Chemistry and Pharmacology, is widely recognized as a pioneer who brought technology-enabled synthesis to the forefront of drug discovery chemistry. Using the technology platform he developed, Lindsley has discovered and developed high quality novel compounds in multiple therapeutic areas, from cancer to neuroscience, and pioneered the medicinal chemistry of allosteric modulation.

Richard Caprioli Elected AAAS Fellow
Richard Caprioli, Professor of Chemistry, Stanford Moor Chair in Biochemistry, and Director of the Mass Spectrometry Research Center, is among the newest American Association for the Advancement of Science (AAAS) Fellows. Caprioli was elected for his distinguished research in the fields of Chemistry and Biochemistry, for seminal advances in mass spectrometry, and innovation imaging/profiling mass spectrometry (IMS). Fellows are selected by their peers because of their scientifically or socially distinguished efforts to advance science or its applications.

Richard Armstrong Named American Chemical Society Fellow in 2012
Richard Armstrong, Professor of Biochemistry and Chemistry has been named American Chemical Society (ACS) Fellow in recognition of his “outstanding achievements in and contributions to science, the profession and the society.” He was cited by the ACS as “a leader in the application of multiple disciplines ... to understand the chemistry of biological processes” and for his service to the society.
Ned Porter Named American Chemistry Society Fellow in 2013
Ned Porter, Stevenson Professor of Chemistry has been named American Chemical Society (ACS) Fellow in 2013. Dr. Porter is being honored for his contributions in the study of organic free radical mechanistic chemistry, particularly in the study of the reaction of lipids and molecular oxygen. His contribution to the ACS community was also noted.

Stephen Fesik Honored for Outstanding Achievement in Chemistry in Cancer Research
The American Association for Cancer Research recently recognized Stephen W. Fesik, with the 2012 AACR Award for Outstanding Achievement in Chemistry in Cancer Research. Fesik won for his use of nuclear magnetic resonance (NMR) to discover novel, potent small molecules that can be used as cancer therapeutics. He was one of the first researchers to utilize NMR spectroscopy for cancer drug discovery. He developed many NMR methods and determined the three-dimensional structures of several proteins, especially those involved in apoptosis. In addition, through his “SAR (structure-activity relationships) by NMR” method, several inhibitors of protein-protein interactions were discovered.

Libin Xu Receives Pathway to Independence Award
Research Assistant Professor Libin Xu has been awarded an National Institutes of Health K99 Pathway to Independence Award. The research grant is related to a human metabolic disorder known as Smith-Lemli-Opitz Syndrome (SLOS) that results from a mutation in the enzyme that promotes the last step in cholesterol biosynthesis. The consequence of this defect is a buildup of a sterol precursor to cholesterol that is highly susceptible to reaction with molecular oxygen. Dr. Xu’s hypothesis for his studies is that sterol oxidation products are key causal agents in the underlying molecular and pathophysiological mechanisms of SLOS.

Janet Macdonald Receives NSF CAREER Award
Janet E. Macdonald, Assistant Professor of Chemistry, has been awarded a National Science Foundation Career Award. Her proposal was entitled “SusChEM: Hybrid Nanoparticles of the Copper Sulfides.” Prof. Macdonald’s proposal to develop new hybrid nanoparticles of copper sulfides with applications in solar energy conversion positions her at the cutting edge of chemistry, nanoscience, and materials science and engineering.

At Vanderbilt University, she has recruited a team of students to work in her lab, and has leveraged resources associated with the Vanderbilt Institute of Nanoscale Science and Engineering (VINSE). With Prof. Sokrates Pantelides of the Department of Physics and Astronomy, Prof. Macdonald has already produced important results characterizing the wurtzite-type phase of copper sulfide nanomaterials.

The Faculty Early Career Development (CAREER) Program represents the National Science Foundation’s most prestigious awards in support of junior faculty who exemplify the role of teacher-scholars through outstanding research, excellent education and the integration of education and research within the context of the mission of their organizations. The goal of the CAREER program is to build a firm foundation for a lifetime of leadership in integrating education and research. This award provides early career funding for five years.

Professor Jeffrey Johnston Appointed to ACS National Committee on Professional Training
The American Chemical Society’s (ACS) President and Board of Directors have appointed Professor Jeffrey N. Johnston to the ACS Committee on Professional Training beginning in 2013. This committee is charged with establishing the guidelines for undergraduate chemistry education through the ACS-approved degree program, reviewing and accrediting 669 of these programs at universities and colleges throughout the country, and formulating policy for the role of chemistry education in allied disciplines.
The challenge of David Wright’s research is to develop an easy-to-use, low-cost method to collect patient samples from people who live in the poorest areas of the world and systems to process those samples to diagnose diseases such as malaria and the RSV respiratory virus.

Wright and his collaborators, Rick Haselton, a biomedical engineer, and Ray Mernaugh, a biochemist, developed the “Extractionator” (see the article on page 4). The extractionator had its genesis in an idea underwritten by a one million dollar grant from the Bill and Melinda Gates Foundation.

“VU Chemistry is in its ascendancy. These students arrive ready for the kinds of challenges we present in the classroom and in the laboratory. They want to probe the important questions that challenge chemists and they recognize that finding the answers means working across disciplines and looking at research from many different angles.”

David Wright came to Vanderbilt in 2002. He earned his Ph.D. at Massachusetts Institute of Technology.

The ultimate goal for Macdonald’s lab is to capitalize on new, efficient technology that captures sunlight in ways that maximize energy transfer and facilitate storage without energy loss.

The need for reduced dependence on fossil fuels and increased demand for alternative energy sources drives our work,” says Macdonald. “We are exploring semiconductor hybrid nanoparticles which, when illuminated, undergo charge separation. This separation is the requirement for light-harvesting technologies such as photovoltaics and photocatalysis.”

Macdonald, joined VU Chemistry in summer 2011, after completing her doctorate at the University of Alberta and a post-doc at Hebrew University in Jerusalem. In Israel, she was part of a team that discovered a copper-based nanoparticle that may lead to new ways to sense glucose when diagnosing diabetes as well as a new way of generating clean energy.

Macdonald is particularly pleased with the graduate, undergraduate, and other students who work in her lab and share her passion. “Great science is more than how hard you work or how smart you are; it’s about being a visionary, about seeing the possibilities that lie in the questions.”
Aegis Sciences Corporation, a forensic sciences company providing toxicology and consulting services to sports organizations, medical examiner systems, crime laboratories, physicians, corporations and other organizations, has awarded a grant to provide graduate fellowships in analytical chemistry at Vanderbilt.

Chad W. Chumbley, a fourth year student in the research lab of Dr. Richard Caprioli, was the 2012 recipient of the Aegis Fellowship. Chumbley used the award to further his work on the development and validation of methods for quantitative matrix-assisted laser desorption/ionization imaging mass spectrometry (MALDI IMS) of pharmaceuticals from tissue sections using an isotopically labeled internal standard.

MALDI IMS has become an important tool for demonstrating the distribution of compounds, including potential therapeutics, directly from tissue sections, a vital step in the drug discovery process.

MALDI IMS eliminates the requirement for the homogenization of tissue and for a radioactive label while providing spatial information within the sample. This is particularly useful when analyzing tissues containing heterogeneous microenvironments such as granulomas in tuberculosis-infected lungs. Current projects include determining the most accurate and precise method for applying the internal and calibration standards and examining the interactions between pharmaceuticals with varying chemical properties and different tissue types.

New view of DNA processing ‘hub’

By Leigh McMillen

Propagation of our genome requires molecular machines assembled from proteins that process the DNA. At the center of these various machines lies replication protein A (RPA), the central “hub” that serves as the anchor to the DNA. Walter Chazin, Professor of Chemistry and Chancellor’s Chair in Medicine, and colleagues have now combined small-angle X-ray and neutron scattering with dynamic molecular modeling to determine how the structure of RPA responds as it engages DNA. They report in *Nucleic Acids Research* that RPA becomes more compact and less dynamic as it interacts with ssDNA. They also demonstrated that RPA undergoes two transitions as it binds ssDNA, not three as previously believed.

*This research supported by grants from the National Institutes of Health (GM065484, GM046312, CA092584).*

Carcinogenic chemicals cramp DNA

By Melissa Stamm

Cancer-causing chemicals can bind to the nucleotide bases of DNA and form lesions called adducts, causing errors in DNA copying and transcription. One such adduct, N2,3-ethenoguanine, or N2,3-εG, can result from exposure to industrial chemicals like vinyl chloride. Carmelo Rizzo, F. Peter Guengerich, Martin Egli, and colleagues were able to stabilize this adduct and investigate its miscoding potential. The researchers found that, in the presence of all human Y-family DNA polymerases (enzymes that catalyze replication and DNA repair), this adduct incorrectly forms bonds with thymine instead of its normal binding partner cytosine. The findings, featured on the cover of the *Journal of Biological Chemistry*, provide clues to how this adduct may cause DNA errors that spark cancer formation.
Andrew Harris' research, improving fuel cell functionality while decreasing cost by synthesizing nanoparticle alloy catalysts supported on novel carbon supports for application in proton exchange membrane fuel cells (PEMFC), landed him at the Arctic Circle this past winter. Harris, a fourth year graduate student in Chuck Lukehart’s lab, spent 9 months working with Henrik Grönbeck in the Chalmers Institute for Technology Competence Center for Catalysis (KCK), a research lab in Goteborg, Sweden.

Harris was awarded a National Science Foundation Graduate Research Fellowship in 2011, his first year of graduate school at Vanderbilt. He then took advantage of the international research opportunity offered as a supplemental award for NSF GRFs, the Nordic Research Opportunity (NRO), which enables fellows to gain international research experience and establish collaborations with counterparts at Nordic research institutions (Sweden, Norway, Denmark and Finland). This international research opportunity is intended to enrich the GRF experience by exposing fellows to leading Nordic scientists and institutions, thus enabling them to develop early-career collaborations with European research partners. Results are expected to expand opportunities for innovation and add an international dimension to GRF research projects.

In Sweden, Harris worked on computational research on the binding energies and configurations for metal alloy catalyst particles on carbon supports for use in fuel cells. In addition to working in the lab with only 5 hours of daylight at times, Harris visited the Arctic Circle and experienced dog sledding as well as the Aurora Borealis.
AMANDA DURAN AND ALEXIS WONG
AWARDED NSF GRADUATE RESEARCH FELLOWSHIPS
The National Science Foundation’s Graduate Research Fellowship Program (GRFP) supports outstanding graduate students in NSF-supported science, technology, engineering and mathematics disciplines.
This year, two graduate students in the Department of Chemistry were awarded NSF Graduate Research Fellowships. Amanda Duran is a third-year graduate student in computational chemistry in Jens Meiler’s lab. Alexis Wong is a second-year graduate student in David Wright’s lab.
The Graduate Program in Chemistry is home to four earlier NSF GRF award winners: Brittany Allison (Jens Meiler lab), Keersten Davis (David Wright Lab), Andrew Harris (Chuck Lukehart lab), and Nicholas Wright (David Wright Lab).

GABRIEL LEBLANC AWARDED ACS ANALYTICAL CHEMISTRY GRADUATE FELLOWSHIP
Gabriel LeBlanc, a fourth-year graduate student in the Cliffel research group, was recently awarded the American Chemical Society (ACS) Division of Analytical Chemistry (DAC) Graduate Fellowship Program (GFP). This honor supports and recognizes future leaders in the field of analytical chemistry. LeBlanc’s research focuses on studying the interface between a photoactive protein, Photosystem I, and electrode materials. The global abundance and exceptional properties of Photosystem I make this biomaterial an ideal candidate for use in solar energy conversion devices. His research has demonstrated how we can incorporate these biohybrid electrodes into photovoltaic devices, photoelectrochemical cells, and hydrogen generation systems.

TIM SENTER AWARDED ACS DIVISION OF MEDICINAL CHEMISTRY PREDOCTORAL FELLOWSHIP
Tim Senter is a fourth-year graduate student working in the lab of Professor Craig Lindsley. His research involves Chromosomal rearrangements of the Mixed Lineage Leukemia (MLL) gene leading to fusion proteins that interact with the protein menin to upregulate HOX gene expression, enhancing cell proliferation and blocking hematopoietic differentiation, ultimately leading to acute leukemia.
The development of small molecule inhibitors of the menin-MLL fusion protein interaction could provide a new strategy to reverse the oncogenic activity of MLL fusion proteins in acute leukemias.
Chemistry majors with honors thesis

Patrick Donahue
Thermodynamic Characterization and Structural Determination of DNA with 5-Hydroxy-2’-deoxycytidine in Multiple Base Pairing Contexts

Tyler Gilcrest
Computational Docking of Chromone-Based Inhibitors Into Signal Transducer and Activator of Transcription (STAT) Proteins

Amanda Hirsch
Uncovering Mechanisms of Staphylococcus Aureus Resistance to Small Molecule Inhibitors That Impair Metabolic Flexibility

Joseph Laakman
Visualization and Characterization of Methylglyoxal Induced DNA-Protein Cross-Links

Melinda Shearer
Photosystems I and II for the Production of Biohybrid Solar Cells

Pieter Valk
An Investigation of Substrate-Selective Inhibitors of Cyclooxygenase-2

Undergraduate awards in chemistry

Melinda Shearer
Donald E. Pearson Award for Outstanding Graduating Senior Majoring in Chemistry

Amanda Hirsch
Outstanding Undergraduate Research in Chemistry Award

Ajan Sivaramamoorthy
D. Stanley and Ann T. Tarbell Prize in Organic Chemistry

Tyler Gilcrest
Thomas W. Martin Prize in Physical Chemistry

Patrick Donahue
Robert V. Dilts award in Analytical Chemistry

Miranda So
Mark M. Jones award for Undergraduate Achievement in Inorganic Chemistry

Vanderbilt outreach initiative puts chemistry in hands of Tennessee students

By Kara Furlong

Middle school students in Robertson and Dickson counties in Tennessee are getting hands-on chemistry instruction thanks to a Vanderbilt outreach initiative. It’s called VSVS Rural, a new collaboration between Vanderbilt Student Volunteers for Science and the Vanderbilt Institute of Nanoscale Science and Engineering, directed by Sandra Rosenthal, the Jack and Pamela Egan professor of chemistry at Vanderbilt.

VSVS Rural distributes kits containing chemistry projects as well as instructions to Middle Tennessee schoolteachers. Each kit serves up to 30 students and includes a PowerPoint lesson, hands-on experiments and worksheets that supplement the Tennessee curriculum. Topics include chemical energy conversion, convection chimneys, chemical reactions, electromagnetism, and the elements of compounds and mixtures.
2013 Colloquium Speakers

The Chemistry Colloquium Series is a mainstay of VU Chemistry, broadening knowledge of emerging science and deepening connections between researchers at all levels. Following are 2012-2013 speakers.

Mitchum E. Warren Jr. Lecture
Professor George M. Whitesides, Harvard University, “Simplicity as a Component of Invention”

Arthur William Ingersoll Memorial Lecture
Professor Stephen Buchwald, Massachusetts Institute of Technology, “Palladium-Catalyzed Carbon-Nitrogen and Carbon-Carbon Bond-Forming Reactions: Progress, Applications and Mechanistic Studies”

Frederic LeRoy Conover Lecture
Professor Jonathan Swedler, University of Illinois at Urbana-Champaign, “Mass Spectrometry-based Metabolomics and Chemical Imaging for Probing the Cellular Heterogeneity in the Brain.”

Sigma-Aldrich Lectures
Professor Melanie Sanford, The University of Michigan, “Recent Developments in Metal Catalyzed C-H Bond Functionalization”
Professor Michael Krische, The University of Texas at Austin, “Hydrogenation for C-C Bond Formation”

Howard Smith Lecture
Professor Peter Wipf, University of Pittsburgh, “Computational Solutions for Stereochemical Problems in Organic Synthesis”

Professor Brandon Ashfield, University of Notre Dame: “Tailoring Chemoselective Nucleophilic Acyl Substitutions for Natural Products and Designed Materials Synthesis”

Professor Jochen Autschbach, University of Buffalo: “Spectroscopic parameters obtained ‘in silico’”

Professor Brian Baker, University of Notre Dame: “Biophysics of Molecular Recognition by Alpha/Beta T Cell Receptors”

Professor Babek Borhan, Michigan State University: “Stereoelectronic Determinants of Color Vision: Engineering Protein Mimics of Pigmented Rhodopsins and Designing New Protein Fusion Tags”

Professor Abhishek Chatterjee, Boston College, “Discovery and Engineering of Novel Biochemical Systems: I. Understanding the Biosynthesis of Vitamin B1 and II. Expanding the Scope of Unnatural Amino Acid Mutagenesis in vivo”

Professor Emily Derbyshire, Harvard University: “A Chemical Genetics Study of Liver Stage Malaria”

Professor Eric Ferreira, Colorado State University: “Accessing and Harnessing Metalated Intermediates toward Synthetic Utility”


Professor Kenneth Henderson, University of Notre Dame: “Control of network assembly and stabilization of geminal dianions using alkali metal aggregates”

Professor Seth Herzon, Yale University, “Target-Driven Total Synthesis”

Professor Piotr Kaszynski, Vanderbilt University, “Pushing the Boundaries of Liquid Crystal Research”

Professor Rebecca Lai, University of Nebraska-Lincoln: “Folding-based Electrochemical Biosensors”

Professor Scott Laughlin, Stonybrook University, “Chemical tools for the biological frontier: (I) Imaging the glycome and (II) controlling instinctive fear neural circuitry”

Professor Juliette Lecomte, Johns Hopkins University: “Hemoglobin in fold only: Novel chemistry in an ancient protein”

Dr. Paul Lobben, Bristol-Myers-Squibb: “Process Development of Brivanib Alaninate, a VEGFR/FGFR Inhibitor”

Professor John McLean, Vanderbilt University: “Structural mass spectrometry strategies for systems biology”

Professor Nicholas Reiter, Vanderbilt University, “Structural mechanisms of the ribonuclease P enzyme and the emerging themes of RNA-based shape recognition.”

Professor Adam Renslo, University of California, San Francisco: “Applications of Chemical Biology in Lead Discovery for Infectious Disease”


Professor Eric Skaar, Vanderbilt University: “Using small molecule probes to study the bacterial heme paradox”

Professor Guido Verbeck, University of North Texas: “New Development in Mass Spectrometry: From Single Cell Analysis to Preparative Devices”

Professor Larry Walker, The University of Mississippi, “Approaches to the discovery of better 8-aminoquinoline antimalarial drugs with improved hematological safety profile in G-6-PD deficiency”

Professor Brian Weiner, Vanderbilt University, “BCL::MP-Fold: Folding Membrane Proteins through Assembly of Trans-Membrane Helices”

Professor Emily Weiss, Northwestern University, “A Molecule to Detect and Perturb the Confinement of Charge Carriers in Colloidal Quantum Dots”

Professor David Wright, Vanderbilt University, “Diagnosing Disease without a Net”

Professor Bo Zhang, University of Washington, “Fluorescence-enabled Electrochemistry and Single-Cell Imaging”

Professor Xuan Zhao, The University of Memphis: “Design of photocatalytic systems for H2 production”
In 1879, Vanderbilt University's first doctoral degree was awarded, in chemistry, to James Thomas Anderson. The study of chemistry was a cornerstone of the institution's early curriculum and laid the groundwork for graduates' success in emerging fields.