



ILLINOIS INSTITUTE OF TECHNOLOGY

CHEMISTRY ELEMENTS

A publication of the Chemistry Division at IIT



Kilpatrick Lecture, 2014. Speaker Roald Hoffmann [front center]

Fall 2014

Letter from the Chair



We are pleased to present our second issue of *Chemistry Elements*, the newsletter of IIT Chemistry. This issue celebrates our recent developments as we prepare for our formal transition to an independent department, anticipated for academic year 2015-16.

We began the start of the current academic year with another Kilpatrick Lecture, "All the Ways to Have a Bond," given by Nobel Laureate Roald Hoffmann on September 15. Hoffmann was the Kilpatrick lecturer back in 1973 and returned to IIT after 41 years as a chemistry Nobel Laureate. After the lecture, students, faculty, and guests enjoyed a reception and poster session exhibiting the research of chemistry faculty and students.

Since our last newsletter, we successfully completed an external program review. We continue to build our research portfolio and strengthen our teaching efforts. Chemistry faculty members have won major grants from The National Institutes of Health (NIH) as well as The U.S. Department of Energy (Advanced Research Projects Agency-Energy grant) that help further invigorate the research environment in the department. To meet our growing research and teaching needs, we have launched an initiative to create a future Chemistry Research Resource Center. We wish to thank adjunct faculty member Jim Kaduk for his generosity in

providing a gift for instrumentation, and Emeritus Professor Robert Filler for another gift. Finally, we are pleased to welcome our new lecturer, Nosheen Gothard, who received her Ph.D. in organic chemistry at Northwestern University and completed her postdoc research at the University of Chicago.

This past year, 35 students graduated from our program with a bachelor's, master's or Ph.D. degree. Our graduates continue to attract top institutions and employers; for example, one of our recent undergraduate students, Chris Kalnmals, is now a graduate student at Stanford, Ph.D. graduate Ravi Putrevu is a Process Engineer with Intel Corporation, and Ph.D. graduate Kadir Aydemir is at the Scientific and Technological Research Council of Turkey (TUBITAK).

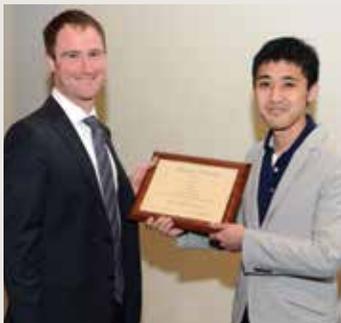
This issue's research article focuses on "Chemistry in Healthcare" and features the work of Assistant Professor David Minh, and Associate Professors Rong Wang and Richard Guan. We are also featuring news of our alumna Susan Solomon (CHEM '77) and alumni reflection from Vince Rotello (CHEM '85).

As always, we want to thank you for your support to keep the tradition of chemistry strong at IIT. Please feel free to contact us with your news or memories from your days at IIT, and we look forward to meeting you in person if you happen to be in the area!

Ishaque Khan

*Executive Associate Chair, Chemistry Division
Co-Chair, Department of Biological and Chemical Sciences*

2014–15 KILPATRICK STUDENT AWARDS



2014-15 Kilpatrick Fellow, Bo Hu, receives his award with advisor Assistant Professor Adam Hock at the 2014 Kilpatrick Lecture.



Last year's 2013-14 Kilpatrick Fellow, Bofan Zhu, poses with advisor Associate Professor Rong Wang.



2014-15 Undergraduate Kilpatrick Scholar, John Clark, receives his award from Chairman Khan.



2014-15 Undergraduate Kilpatrick Scholar, Matthew Seludo, receives his award.

IIT Chemistry in Healthcare

The contemporary problems of the world include developing affordable healthcare and finding sustainable solutions to the staggering energy needs of society. At IIT Chemistry, we are interested in both of these areas. In our last issue, we explored some of the energy research conducted in the department. Here, we present the work of several faculty members who are carrying out research work in the area of biological chemistry in the context of healthcare. This includes interdisciplinary research projects aimed at developing safe, effective, and targeted drugs for cancer and neurodegenerative diseases. Additionally, efforts are under way to discern how the microenvironment impacts stem cells for potential application in regenerative medicine. Chemistry faculty are also employing state-of-the-art computational chemistry methods for drug discovery. Following is an overview of some of the department research in this field.

Nanopore Sensing

Associate Professor Xiyun “Richard” Guan’s group is working on the development of biosensors for detecting environmental toxins and biomolecules using nanopore sensing. A nanopore is a nanoscale cavity or channel, sometimes created by a pore-forming protein. When a nanopore resides in a membrane, only single molecules can pass through the pore, and as a result the pore acts as a single-molecule detector. Over the last 15 years, these nanoscale pores have been used not only to analyze the sequence of DNA, but also to study various types of chemical interactions. They have been used to investigate biomolecular structure, for example the folding and unfolding of proteins, and for other applications.

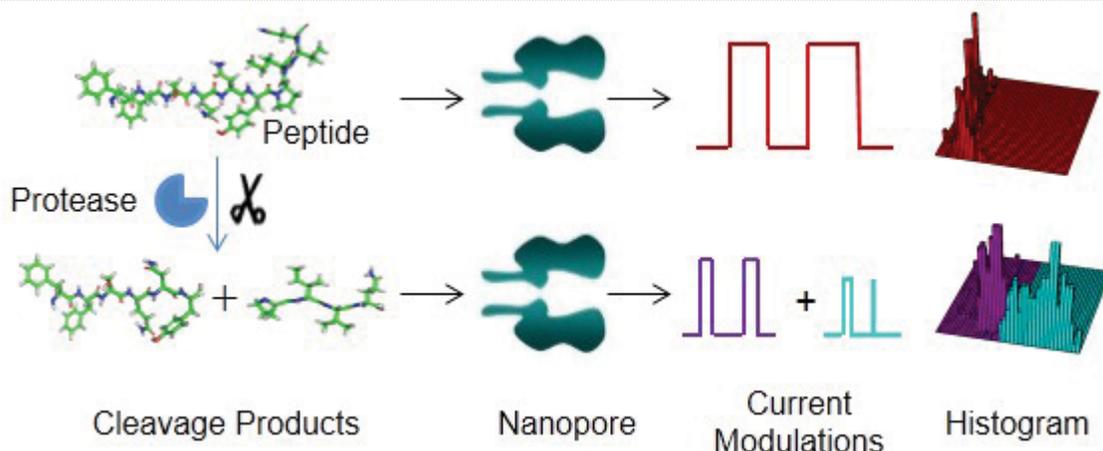
As an emerging technique, nanopore sensing has many advantages over existing techniques, including real-time detection. It also does not require the use of fluorescent dyes or radioactive materials; therefore, it is known as a label-free technique. Nanopore sensing has the ability to detect ultra-low concentrations of analytes (targeted species), for example trace amounts of biomolecules as found in human blood samples. Nanopore sensors can detect the concentration and identity of an analyte based on the ionic current modulations in a salt solution. When the molecules of interest, such as peptides, proteins, or DNA (with diameters smaller than the nanopore) pass through a single nanopore, they will produce current modulations for analysis.

One aspect of Guan’s nanopore research is centered on pioneering a new, highly selective and sensitive technique to measure the activities of proteases, which are enzymes that break down proteins and peptides (short amino acid chains). Proteases occur naturally in all living organisms and play key roles in diverse biological processes, from cell regeneration and metastasis to cell deterioration and immune defense. Accordingly, alterations in the structure and expression patterns of proteases underlie many human pathological processes including cancer, arthritis, osteoporosis, inflammatory disorders, and neurodegenerative, cardiovascular and autoimmune diseases. Thus, proteases may serve as valuable diagnostic or prognostic markers for disease states, and are becoming increasingly important targets for drug discovery.

Nanopore measurement of protease activity is achieved by real-time monitoring of the cleavage of a peptide. As shown at the top of Figure 1, when there is no presence of a target protease, peptide molecules pass through the nanopore giving one signal reading. By contrast, at the bottom of the figure, if a protease is present in a solution and, acting like a scissors, cuts the peptide molecules, the cleavage products produce entirely different current modulations. A comparison of the readings quantifies protease enzymatic activity.

The real-time, label-free nanopore sensing technique discovered in this project should find useful application in the detection of proteases of medical or biological importance.

Figure 1. Schematic representation of the principle for nanopore detection of protease activity.



How do you design a drug? Drugs work by throwing a wrench into biological machinery. Some drugs shut down enzymes that catalyze essential chemical reactions. Others interfere with communication between and within cells. Disrupting these critical functions can sabotage a pathogen or correct a chemical imbalance in the body.

If a molecule binds tightly and specifically to a biological target, it is more likely to be a safe and effective drug. Drugs should bind tightly so that a small dose works well. They should bind specifically so they don't interact with unintended targets and cause side effects.

Finding a molecule that fulfills these requirements is difficult. It may not even be clear how to start. The number of possible small organic molecules is astronomical, estimated to be around 10^{60} ! How do we choose which molecules to focus on?

Computers can help us find these starting points, known as drug leads. Scientists have solved three-dimensional structures for thousands of possible drug targets. You can think of these structures as jigsaw puzzles and drug design as trying to create a missing piece. Computers can virtually screen millions of possible molecules, fitting them into a target and scoring how well they fit. We can then follow up on the best-ranked molecules in the laboratory.

Computational Chemistry in Drug Discovery

Assistant Professor David Minh develops and applies methods for computer-aided drug design. Computational chemistry has already played a large part in discovering a number of drugs, but existing techniques are not perfect. Although the jigsaw puzzle is a helpful analogy, in real life everything is moving, and moving a lot. Unfortunately, a computer simulation that accounts for all this motion can consume a large amount of processor time.

Minh has recently derived a new and formally exact theory for calculating binding affinities. It is especially promising for predicting binding affinities between proteins and small organic molecules. In his theory, flexibility of the target is accounted for by using multiple rigid structures of the target. Other groups use multiple rigid structures in their methods, but their approaches are not based on the fundamentals of statistical physics; they do not "dot their i's" and "cross their t's" to calculate formally exact binding affinities. Minh's theory explains how to do so. His approach has the potential to combine the speed of fast methods that use rigid structures with the accuracy of slower methods that allow full receptor flexibility. The primary goal of his group is to turn this promise into a reality.

Minh's group also uses computer methods to study interactions between small organic molecules and proteins. These efforts are not limited to drug discovery projects. For example, Minh is working with the IIT Institute for Food Safety and Health to predict possible biological targets for anthocyanins, a class of antioxidants common in strawberries and blueberries that have been found to naturally counteract some symptoms of diabetes.

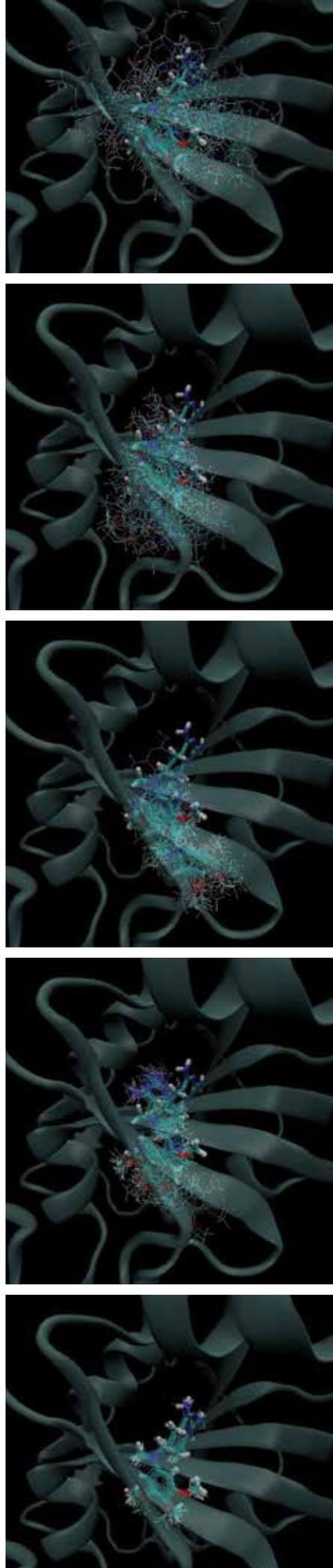


Figure 1. A set of ligand conformations from states in which the small organic molecule is non-interacting, partially interacting, and fully interacting with the protein. The simulated conformations are shown as lines, one experimental conformation as a thicker line, and the protein as a large ribbon. In the fully interacting state, the predicted conformations match the experimental structure. The colors signify different elements: carbon (cyan), hydrogen (white), oxygen (red), and nitrogen (blue).

Nanobiological Materials and Methods

Associate Professor Rong Wang's research group works on developing new tools, methods and materials to study the concerted and dynamic changes of cells, tissues, and their environments. The studies provide the molecular basis for developing new strategies in correcting cell behaviors and tissue functions, in order to achieve effective disease treatments and drug discovery.

One effort in Wang's group is to clarify the structure-function relation of collagen in clinical tissues and to develop collagen-based composite materials as potential biological scaffolds for tissue engineering and cell therapeutics. Collagen is a natural, one-dimensional nanomaterial. It confers robustness and resilience to connective tissues, and is one of the most abundant proteins in the human body. In collaboration with surgeons at the University of Illinois at Chicago Hospital and Rush University Medical Center, Wang examined collagen's structure and elasticity in pelvic floor connective tissues on the nanoscopic to macroscopic scales to correlate with the stage of pelvic organ prolapse (POP), a debilitating condition that affects millions of women. More research is under way to establish a quantitative POP prediction profile for accurately assessing risk factors, allowing clinicians to employ preventative therapies reducing the need for invasive surgical procedures.

Along with collagen, Wang has incorporated other one-dimensional materials, such as CNT (carbon nanotubes), TiO₂ (Titanium dioxide) nanotubes, and silk proteins producing desired materials for biomedical research. This effort of in vitro (cells in a culture) study is aimed at modulating the nanostructure and elasticity of collagen. Stem cells are capable of self-renewal and differentiation, and therefore are a beneficial source for creating all cell types forming the human body. The enhanced mechanical and structural properties of collagen-CNT have been found to allow for rapid and high-yield neural differentiation (a less specialized cell becomes a specialized cell type) from both embryonic and adult placenta stem cells.

A highly ordered collagen fibril material was also developed. The aligned collagen fibrils were found to induce unidirectional cell polarization and development, and to support neural differentiation of stem cells. The aligned collagen fibrils offer potential scaffolds for transplantation in cellular replacement therapies for neuro-degenerative disorders such as Alzheimer's and Parkinson's. Finally, the development of unidirectionally aligned neural cells has laid the groundwork with a neural tissue engineering approach to create bio-circuits for neuron network repair.

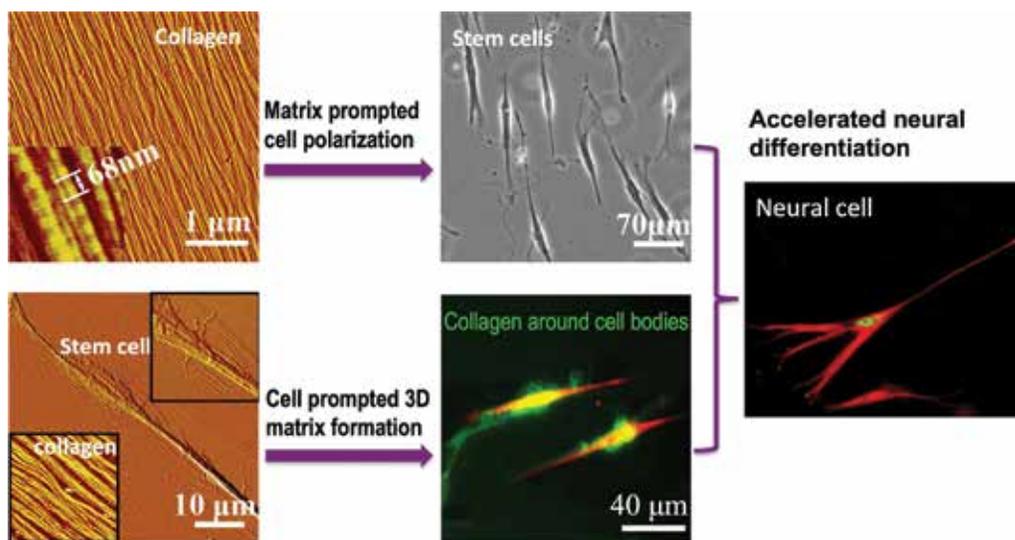


Figure 1. Two-way regulation (result of communication) between cells and aligned collagen fibrils (matrix). At the top of the figure, the collagen matrix prompts cell polarization. At the bottom of the figure, the stem cell prompts 3D matrix formation. The combined effect (far right) leads to accelerated neural differentiation of adult stem cells.

New Certificate Program in Chemistry

The Chemistry Division has a new certificate program in regulatory science. Kim Huynh-Ba is instructor for the two required courses: Understanding ICH Quality Guidelines (ICH refers to The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) and Good Manufacturing Practices. Many life science industries, both in the United States and abroad, are subject to U.S. regulations, especially in the fields of big pharma, food manufacturing, and biotechnology.

Student News

Bofan Zhu, our 2013-14

Kilpatrick Fellow, received a Microscopy and Microanalysis Student Award to present a paper at the M&M 2014 meeting in Hartford, Conn., in August. His presentation was entitled "A Study of Unidirectionally Aligned Collagen-silk Composite Fibers and the Application in hdpPSC Neural Differentiation."

Graduate student

Matt Weimer is one of two students at IIT who was awarded the ARCS (Achievement Rewards for College Scientists) Foundation Scholarship for 2014-15. In the Hock research group, Weimer is working on new precursor development for understanding reaction mechanisms at the gas/solid interface of thin films growth by atomic layer deposition (ALD).

Alumni News



Alumna Susan Solomon (CHEM '77), the Ellen Swallow Richards Professor of Atmospheric Chemistry and Climate Science at Massachusetts Institute of Technology, has recently been named as founding director of a new environment initiative at MIT. This multidisciplinary program will encourage collaborations among researchers in different fields, working in teams to generate ideas in hopes of bringing about significant advances and understanding for critical real-world problems.

David Chandler in the MIT news office writes that a major component of the initiative will be the Abdul Latif Jameel World Water and Food Security Lab (J-WAFS). The lab is “intended to help humankind adapt to a rapidly rising population, a changing climate, and increasing urbanization and development.” The teams “will work toward environmentally benign, scalable solutions for water and food supply across a range of regional, social, and economic contexts.”

Alumni Reflection by Vince Rotello



Vince Rotello is the Charles A. Goessmann Professor of Chemistry at the University of Massachusetts, Amherst. He is also editor-in-chief of *Bioconjugate Chemistry*.

I was at IIT quite a while ago, 1981-1985. I remember fondly running cross-country, popping across the Dan Ryan and having Italian ice, and hanging out at the Bog. More profoundly, I still feel the impact that my time at IIT had on my career. IIT then and now is the sort of program that has top-notch researchers that are interactive and accessible to undergraduate and graduate students. I took advantage of the opportunities this community provided, doing undergraduate research all four years.

During this time I learned what I liked (organic synthesis) and what I was less fond of (changing pump oil). My ability to get into the lab let me see both the science and the people behind the science—experience that has followed me throughout my career. The journey really started in Organic with Pete Johnson—he introduced me to a simple and beautiful vision of organic chemistry that I use both in teaching and in research. Vision only gets one so far, though. Phil Garner was the one who introduced me to the messy and exciting real world of research. Phil was a demanding taskmaster and a fiery personality, making for an exciting ride. And the ride was a very productive one. Besides getting my first publication, I had the skill and knowledge to walk into my graduate life at Yale and hit the ground running. Looking back, the teaching was excellent at IIT, but other schools have great teachers. What made (and makes!) IIT Chemistry unique is the quality of the research coupled with an interactive and accessible environment—an opportunity not to be missed.

Faculty News



Nosheen Gothard, lecturer in chemistry, joined us for the 2014-15 academic year. Gothard received her Ph.D. in chemistry from Northwestern University in 2013, where her research was focused on computer-assisted design, prediction, and the development of novel tandem chemical pathways to medicinally important quinoline scaffolds and inhibitors used in anti-asthma treatment. Prior to Northwestern, she worked at the University of California, Irvine, as a research assistant, where she pursued projects involving solid-phase synthesis of unnatural peptides and the development of unique intramolecular fluorescent energy transfer assays. Gothard's postdoctoral research was at the University of Chicago, where she worked to develop biocompatible surfactant polymers to seal cell membranes and refold denatured proteins. Her interests include chemical education, scientific management, medicinal chemistry, and organic syntheses.

Professor Hyun-Soon “Joy” Chong has been promoted to full professor beginning in the 2014-15 academic year. She has been very successful in receiving continued funding from the National Institutes of Health and has active research programs related to the development of cancer therapeutic and diagnostic drugs.

Associate Professor Xiyun “Richard” Guan received a grant award from the National Institutes of Health for his project entitled “Label-Free Nanopore Biosensor for Rapid, Ultrasensitive, and Multiplex Detection of Protease Activities.”

Hock Develops New Catalyst



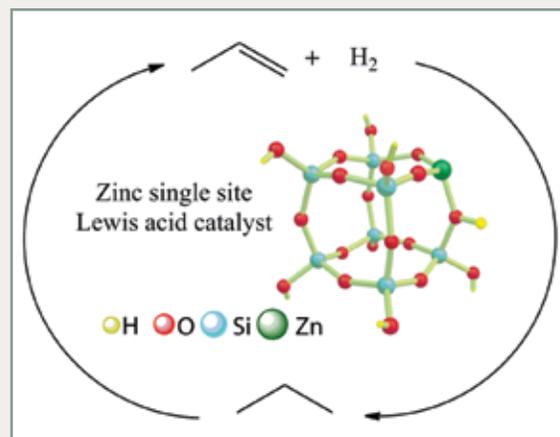
Adam Hock, assistant professor of chemistry and assistant scientist at Argonne National Laboratory (ANL), and colleagues at ANL and Northwestern University have developed a new catalyst to transform propane into propene (propylene).

Propene, with worldwide sales of \$90 billion in 2008, is a crucial

product for the petrochemical industry, used in the manufacture of plastics, packaging and other applications. Current catalysts, while very active for the production of propene, also produce methane and ethylene (smaller hydrocarbon fragments) through unwanted side reactions. Separating the desired products adds to the energy demand and cost of the process. The new catalyst, a silica supported single-site Zn(II) catalyst, is more selective for the desired propane to propene transformation, reducing waste, increasing efficiency, and potentially lowering production costs. Propane dehydrogenation for propene production is used in the United States and globally, particularly in the Middle East, and many plants are currently being built.

The Hock research team's new catalyst is described in an article published in *ACS Catalysis* and is the subject of a patent application by IIT and ANL. The *ACS Catalysis* article is the first in a series that will explore these types of catalysts.

Hock and his team used isolated zinc atoms rather than the particles of metal typically used as the catalyst. Because the zinc atoms are isolated, they have a small number of available reaction pathways to follow and thus they are very selective for the removal of hydrogen from the short-chain alkane propane to yield propene and hydrogen.



"Chemists have long sought to transform one substance into another; however, chemical transformations often result in mixtures of products," said Hock. "This is especially true for difficult reactions that require the input of large amounts of energy because excess energy can cause side or subsequent reactions. Therefore, very selective catalysts for difficult reactions are highly sought-after."

Added Russell Betts, Dean of the College of Science, "This is an example of how profound understanding of basic science can lead directly to innovation in industry and in the marketplace."

Chemistry Executive Associate Chair and Professor Ishaque Khan gave a keynote lecture entitled "Functional Nanomaterials: Potential and Promise for Addressing Current Technological Challenges" at the International Conference on Nanoscience and Nanotechnology, in Aligarh, India, March 8-10.

Assistant Professor David Minh gave invited talks at the following meetings in May: The International Symposium at the Vasundhara Sarovar Premiere in Vayalar, Kerala, India; Biological Physics Seminar at Northeastern University in Boston, Mass.; The Harvard-MIT Universities Allied for Essential Medicines student organization, at Harvard Medical School in Boston, Mass; and a workshop at Vertex Pharmaceuticals in Boston. Minh also gave a talk at the Molecular Recognition Workshop at the Telluride Science Research Center in Telluride, Colo.,

on August 11-15, and at the Midwest Enzyme Chemistry Conference at Northwestern University on Sept. 27.

Assistant Professor Andrey Rogachev chaired the section on Molecular Design at the International Conference on Chemical Bonding, July 24-28, in Kauai, Hawaii, and gave a talk entitled "Sandwich-like Aggregates of Highly Reduced Corannulene: Theoretical Study of Their Formation and Electronic Structure." Rogachev also gave a talk at a conference near Casablanca in Morocco, Sept. 22-25, on theory and prediction of sandwich-like aggregates of buckybowls.

Associate Professor Rong Wang gave a talk entitled "Collagen-based Nanocomposite Materials and Their Roles in Stem Cell Differentiation" at the International Conference on Composites/Nano Engineering (ICCE-22) in Saint Julien, Malta, July 13-19.

Hock Receives Award for Hybrid Fuel Cell Research

Adam Hock, assistant professor of chemistry and assistant scientist at Argonne, received a grant from the Department of Energy's Advanced Research Projects Agency – Energy (ARPA-E) with Physics Professor Carlo Segre and Argonne National Laboratory. This \$2 million project seeks to develop a fuel cell that can turn methane into usable liquid fuel. ARPA-E is an agency within the U.S. Department of Energy. The fuel cell would both produce electricity and convert methane gas to ethane or ethylene that could then be converted to a liquid fuel or valuable chemicals. These cells could use natural gas—which is mostly made up of methane—directly.

"Increasing the selectivity of catalytic transformations, making more of what you want and less unwanted byproducts, is a critical part of transforming our energy infrastructure," said Hock.

2014 Kilpatrick Lecture

Roald Hoffmann, who received the Nobel Prize in chemistry in 1981, delivered the 2014 Kilpatrick Lecture on Monday, September 15, in the McCormick Tribune Campus Center (MTCC) Auditorium. A poster session followed the lecture, exhibiting some of the ongoing research in chemical sciences at IIT, along with a reception. This was the second time that Hoffmann was selected; he also gave the lecture in 1973 and is one of seven Nobel Laureates to deliver the prestigious Kilpatrick Lecture.

The event was attended by students, faculty, alumni, and guests from various universities, Argonne National Laboratory, and industry. After welcome remarks from Chairman Khan, President Anderson spoke, and Assistant Professor Andrey Rogachev, former post doc in Hoffmann's research group, introduced the speaker.

In his lecture, "All the Ways To Have a Bond," Hoffmann gave an overview of how people look at chemical bonds, from both the theoretical and experiential



Speaker Roald Hoffmann

perspective. Earlier in the day, students and faculty enjoyed a breakfast with Hoffmann in the department, hearing stories about his past, about the Nobel Prize, and interesting perspectives on the history of chemistry, the impact of modern technology on the discipline, and what the future holds.

Hoffmann was awarded the Nobel Prize, jointly with Kenichi Fukui, for "their theories, developed independently, concerning the course of chemical reactions." A pioneer computational chemist, Hoffmann developed the Extended Hückel method in 1963 and applied it for investigation of the electronic

structure of boron hydrides and polyhedral molecules. He also developed, together with R. B. Woodward, rules for elucidating reaction mechanisms, later known as the Woodward-Hoffmann rules, and introduced the isolobal principle to predict and explain bonding properties in organometallic compounds.

Hoffmann is the Frank H.T. Rhodes Professor Emeritus of Humane Letters at Cornell University. His research group at Cornell studies bonding in chemical systems to provide a conceptual framework for experimentalists who are synthesizing new compounds with unusual structures and properties. Hoffmann has received numerous honors including the Linus Pauling Award and the Priestley Medal. He has written poetry, books and plays, and was featured on the "World of Chemistry" series on PBS.

The Kilpatrick Lecture honors Martin and Mary Kilpatrick, who were a longtime chair and faculty member, respectively, in the chemistry department.



Ishaque Khan [left] and President John Anderson [right] with Roald Hoffmann.