the chemists club

Spring 2018

THE UNIVERSITY OF CHICAGO

IRRATIONAL DESIGN

BRYAN DICKINSON HARNESSES DIRECTED EVOLUTION TO CREATE MOLECULES WITH BIOLOGICAL FUNCTIONS

An Interview with

BRYAN DICKINSON

By Irene Hsiao

Dickinson with graduate student Saara-Anne Azizi

As a graduate student, assistant professor Bryan Dickinson spent much of his time absorbed in the typical undertakings of a synthetic organic chemist: drawing molecules, devising ways to create them, and hoping they would have the function he anticipated. "That's a powerful approach," he says, "but our intuition for how to create structure with function is limited to a couple of different types of activities." Instead, he and others are finding that human insight and design can be supplemented and even surpassed by processes that have been honed for billions of years. "I've always been interested in the idea of using evolution—nature's design—to search for molecules that do different things in an unbiased way," he says. Though evolution in nature can take time, Dickinson's lab harnesses the principles of natural selection to discover and produce molecules for biological use in just days using an accelerated process known as directed evolution.

The particular method Dickinson's lab uses for directed evolution, phage-assisted continuous evolution (PACE), was developed during his postdoctoral studies with David Liu at Harvard. Genetically encoded material—a protein or a sequence of amino acids—is inserted into viruses that replicate every ten minutes, producing hundreds of generations in a single day under a controlled selection pressure. Generations of viruses modify the material until they can pass through a designed barrier, while growing in a fixed volume vessel in which their media are constantly being diluted. Dickinson compares the viruses to salmon swimming upstream to reproduce: "if they don't swim fast enough, they'll get washed away." Those that develop successful modifications are able to replicate quickly enough to maintain the system.

Producing the right selection pressure is the main challenge in the process. "If you want to force an organism to evolve an interesting functional property, you have to be able to link the property you want in that molecule to some sort of fitness advantage," he explains. "How do we put a selection pressure that forces them not only to evolve to replicate quicker but also to do exactly what we want them to do? How do we give them a molecule and put them under a pressure that forces them to change that molecule into something new? If you try to force an ant to turn into a giraffe, it's probably going to go extinct. You can't go from A to Z—you have to go from A to B to C."

To improve their ability to construct an accurate selection pressure, Dickinson and his lab have developed biosensors that are able to make measurements about their environment and trigger a biological response. For example, their biosensors can indicate whether a molecule interacts with a particular target by producing a fitness advantage that allows the host system to live or replicate. Dickinson's biosensors are made of split RNA polymerases fused to engineered sensing domains. When the sensing domains bind to their targets, a split polymerase becomes a functional enzyme, driving an RNA—and thus a protein—output. "RNA is the most versatile output you can have in a cell," Dickinson says. "You can make a protein that gives a cell a fitness advantage, you can make a virus replicate. And we can fuse any sensing domain we want to our RNA polymerase." The Dickinson lab used directed evolution to develop such a proximity-dependent split enzyme.[1] "We broke an unwritten rule," he says. "If you want to solve a problem using evolution, you should never have the first step in solving that problem be evolving the materials you need to evolve the solution. But that's actually what we did—we used our evolution tools to evolve the RNA polymerase to be a biosensor."

Because Dickinson mainly focuses on biomedical problems, he uses directed evolution for targets that have stymied more traditional approaches—for instance, protein-protein interactions, often considered "undruggable" because their large interfaces and weak interac-

Evolution is totally indifferent to structure. It only cares if the molecule does the thing that it needs to do. It doesn't care how it does it.

tions can be difficult to disrupt with a small molecule. To address such a problem, Dickinson and his team can link a virus life cycle to its ability to transform its starting material into a molecule that can break up a disease-causing interaction. Dickinson estimates his lab can test 10 million to 100 million molecules in a single day using this method. "The amount of space we can sample is astronomical, so we can pick targets that are more challenging. A random sample of a couple million molecules may not contain a solution—you need to sample many more. One of our hopes is to democratize the drug discovery process by making it inexpensive to make functional molecules for new targets." His lab is currently developing evolution systems in search of functional molecules that interact with critical cancer targets that have eluded traditional methods for drug discovery.

In addition to the clinical applications for his work, Dickinson notes that his biosensors can offer information about evolution on a more fundamental level. "Can we recapitulate an evolution that took 100 million years in nature in ten days in the lab?" For a given problem, "is there one best answer? Are there many? If you do the same evolution multiple times, do you get the same answer every time? Those are questions that are very much unanswered, partly because the evolution tools that have existed previously haven't allowed us to answer such questions in a controlled environment, and they haven't allowed us to answer those questions for many kinds of activities. Now, because we can detect a much more diverse array of target activities with the biosensors our group has made, we can ask those kinds of questions for a similarly diverse array of target functional molecules." In pursuit of answers to some of these questions, Dickinson's lab is designing experiments that attempt to replicate the evolution of divergent functional molecules, focusing on families of human proteins that function in protein-protein interaction networks.

Ultimately, Dickinson is fascinated by the possibilities directed evolution offers as a design tool. "Evolution, given enough time, given the right system, can in principle solve any challenge. Most chemists are interested in reactivity—in creating and breaking bonds—or they're interested in coming up with ways to synthesize complex molecules. My main interest is in neither of those. It's just in function. I care very little about structure, though structure is integrally related to function. One nice thing about evolution is that it's totally indifferent to structure. Evolution only cares if the molecule does the thing that it needs to do. It doesn't care how it does it."

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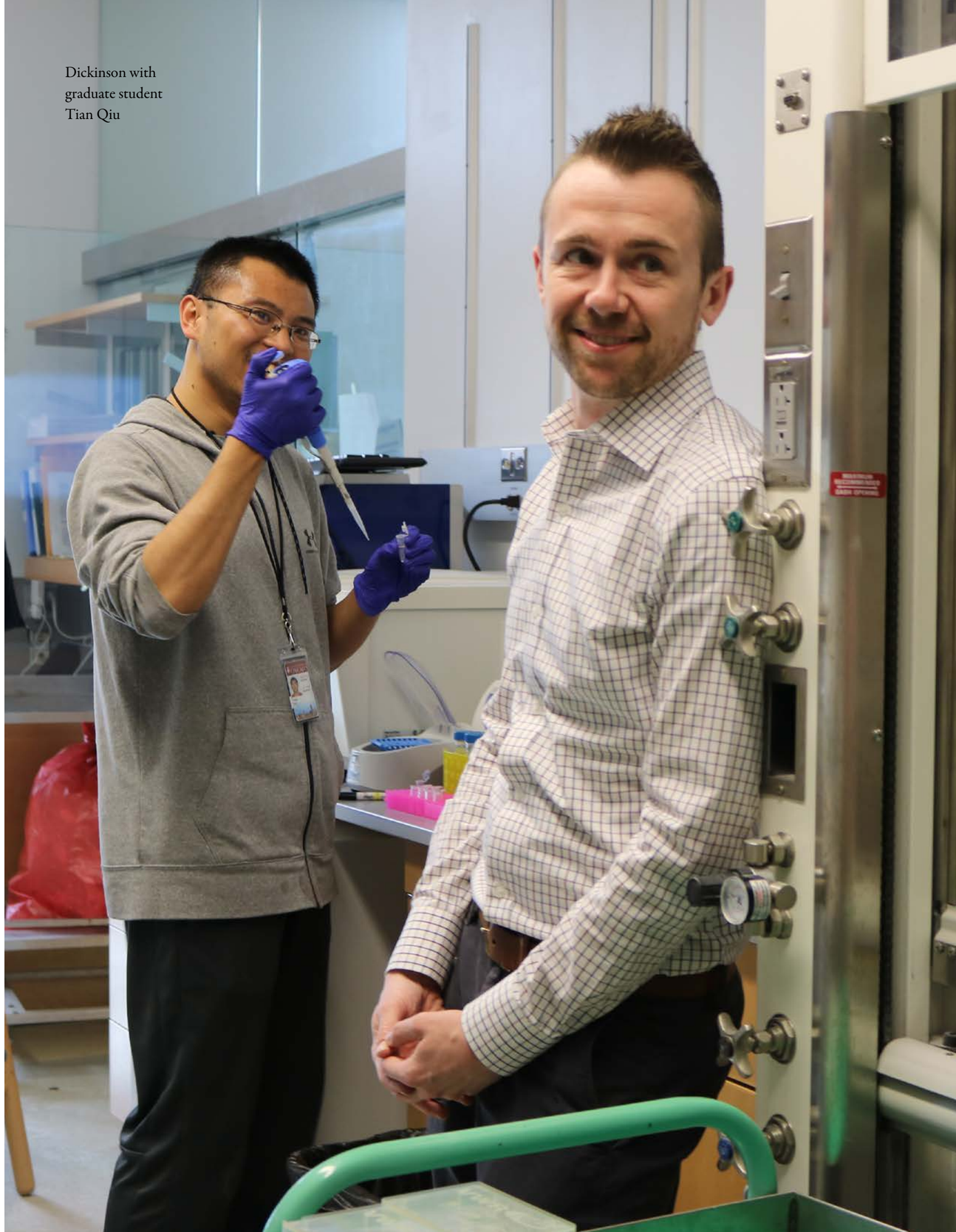
[1] J. Pu, J. Zinkus-Boltz, B. C. Dickinson, "Evolution of a split RNA polymerase as a versatile biosensor platform," *Nat. Chem. Biol.* 13 (2017) : 432-38.



Dickinson with graduate student Tian Qiu

In Memoriam: Jack Halpern (1925-2018)

By Alan Goldman, Clark Landis, and Ayusman Sen

Jack Halpern was a virtuoso mechanistic chemist and an energetic scholar, editor, mentor, and consultant. He innovated strategies for rigorous mechanistic and thermodynamic evaluation of fundamental inorganic transformations that laid the groundwork for organometallic and bioinorganic chemistry. Halpern led the development of catalysis by transition metal complexes, a field now interwoven throughout modern chemistry and chemical engineering. He developed the first molecular catalyst for the hydrogenation of olefins, which ultimately led to his elucidation of the key principles underlying the field of asymmetric catalysis. More so than any other chemist, Halpern helped to build the intellectual framework of modern catalytic science.

Jack Halpern, emeritus Louis Block Professor of Chemistry at the University of Chicago, died on January 31, 2018 at the age of 93. He was born in Poland and moved to Montreal at the age of four. After completing BS and PhD studies (Carl Winkler) at McGill, Halpern took an NRC Overseas Postdoctoral Fellowship to study with A. G. Evans at Manchester University. Although trained in physical organic methods, Halpern's first academic position was in the Department of Metallurgy and Mining at the University of British Columbia. Accordingly, he turned his attention to the chemistry of metal complexes. Beginning in 1954, Halpern published a series of papers that demonstrated heterolytic (bimolecular) and homolytic (termolecular) pathways for dihydrogen activation by aquated transition metal ions such as Cu^{2+}, Hg^{2+}, Rh^{3+}, Pd^{2+}, and Ag^{+}. This work set the stage for the first catalytic hydrogenation of alkenes by homogeneous metal complexes as reported by Halpern, Harrod, and James in 1961—and thus, modern homogeneous catalysis science was born.

In 1962, Halpern moved to the University of Chicago, and the scope of his mechanistic studies broadened to include many of the elementary steps—oxidative addition, reductive elimination, insertion, ligand substitution, and radical processes—that form the basis of modern organometallic chemistry. However, some of Halpern's greatest lessons in catalytic science came from mechanistic investigations following the discovery that phosphine complexes of rhodium in neutral (by Wilkinson and coworkers) and cationic forms (by Osborn and Schrock) catalyze alkene hydrogenation with high rates under mild conditions.

Few scientists exhibit Halpern's uncanny ability to identify the heart of a mechanistic problem and resolve it with elegant experimentation and clear logic. The elucidation of the details of multistep mechanisms involved in catalysis by metal complexes is complicated by the appearance of intermediates in several forms due to ligand and substrate lability. Halpern's elegant kinetic studies of both the overall catalytic reaction and many of the constituent elementary steps for alkene hydrogenation catalysts revealed insights, sometimes referred to as "Halpern's rules," that continue to guide modern studies of catalysts. His kinetic studies are essential because catalysis is wholly a kinetic phenomenon: many of the true intermediates along the cycle exist only fleetingly, and those species with sufficient stability for direct observation commonly lie off-cycle ("if you can isolate it, it is probably not the catalyst").

Such themes recurred especially in Halpern's seminal mechanistic studies of asymmetric hydrogenation systems. Here, mechanistic studies revealed that the more stable diastereomeric adduct of the alkene substrate with the catalyst was relatively inert toward hydrogenation; the majority of catalytic flux funneled through the spectroscopically invisible minor diastereomer. With implications well beyond asymmetric hydrogenation, this work undercut the then widely accepted "lock-and-key" paradigm of catalysis.

Halpern's deep appreciation for physical organic methods and principles guided much of his research. His investigations of metal-promoted rearrangements of strained rings, establishment of analogies between metal and organic reactivities (later generalized as isolobal analogies by Roald Hoffmann), and determinations of metal-carbon bond thermodynamics reflected his training and his drive to establish principles of transition metal reactivity that extended beyond simple electron transfer. His studies strongly impacted the then nascent field of bioinorganic chemistry by establishing a deeper understanding of the reactivities of vitamin B12 (a result of studies of organocobalt complexes) and hydrogenase (resulting from studies of catalytic reduction of one-electron oxidants by dihydrogen).

Halpern contributed to the chemistry community in many ways, including his twenty-five years as associate editor of the *Journal of the American Chemical Society* and editorial work for the *Proceedings of the National Academy of Sciences*, his service as vice president of the National Academy of Sciences, and his participation on many advisory boards, including those of the National Science Foundation and Caltech. He was a highly valued consultant at Monsanto and Argonne National Laboratory. Commensurate with his towering intellectual stature, he was the recipient of many lectureships, fellowships, honorary doctorates, and awards. He received three awards from the Inorganic Chemistry Division of the American Chemical Society and shared the Welch Award with Albert Cotton.

Halpern was a man of passions and deeply ingrained habits. He had deep love for and knowledge of art, music, and theater. He was a regu-

FURTHER WORDS ON JACK HALPERN

Jack Halpern and I were colleagues for 56 years, following his arrival in Chicago in 1962. More than that we were friends, and for many years we socialized frequently. In his professional life, it is well known but bears emphasizing that he was an outstandingly original chemist with an intense interest in mechanistic organometallic chemistry, especially homogeneous catalysis. He made many important contributions to the subject, which include the first demonstration of the activation of hydrogen by soluble complexes, elucidation of the mechanism of the hydrogenation of alkenes, determination of the key step in asymmetric hydrogenation processes, understanding the reactivity of metal-carbon bond, and more. Jack practiced and promoted the highest possible intellectual standards in his scientific work, in the sustenance of the university and in the larger scientific enterprise. He was engaging in conversation—often aggressively argumentative, but always open to logical reasoning—and he strongly believed in the pursuit of excellence in all endeavors. As to his life outside the university, he and his wife, Helen, had an abiding love of contemporary art and accumulated a substantial collection, and they were long-time supporters and patrons of Court Theatre. His emphasis on intellectual quality as the guiding theme for human activity therefore also found expression in his selection of art and his support of theater. He is sorely missed by his many friends.

Stuart Rice, Frank P. Hixon Distinguished Service Professor Emeritus

Jack Halpern epitomized the Chicago scientist for me. I first met him when he came to give a seminar at Yale, where I was an assistant professor. That was in spring of 1964, and I had accepted a faculty position at the University of Chicago, where Jack had come two years earlier. Hence much of our conversation was about my moving, about living in Hyde Park, and being on the Chicago Chemistry faculty. He made it sound even more lively and exciting than I'd conceived when I accepted the job.

My wife Carla and I quickly became very good friends of Jack and Helen Halpern. We shared many common interests: theater, music, art. The Halperns were serious and committed art collectors. They shared a strong liking for fine art and were also interested in the less-established works of the annual 57th Street Art Festival. We encountered them at concert after concert. Jack was also a gourmet who enjoyed Helen's cooking, as well as the many meals he had at restaurants.

Often Jack would exhibit deep insights through his criticism. Jack was a very sharp, perceptive critic, very much in the tradition of the University of Chicago. No sloppy or ill-formed concept ever got past his judgment and his frequent, devastating comments. He had high intellectual standards and expected the same of his peers. It seemed as if visiting speakers were rather in fear of his challenging questions and comments—but invariably, those questions and comments added real substance to the formal presentations.

R. Stephen Berry, James Franck Distinguished Service Professor Emeritus

FURTHER WORDS
(Continued)

Jack Halpern was arguably the preeminent mechanistic inorganic chemist of the 20th century—a real pioneer. He was an exceptionally rigorous scientist, known for studying his systems in great detail and providing strong evidence for his conclusions. He made seminal contributions to many areas of inorganic chemistry and catalysis, including the synthesis of novel metal complexes, the measurement of metal-carbon bond energies, and the determination of the mechanisms of fundamental inorganic reactions such as electron transfer, ligand exchange, oxidative addition, reductive elimination, insertion, and activation of dihydrogen to produce metal hydride species. His most influential work may have been his studies of the mechanisms of metal-catalyzed alkene hydrogen reactions. In particular, through a series of ingeniously designed and carefully executed experiments, he and his students discovered the surprisingly subtle ways in which chiral metal catalysts control enantioselectivity in asymmetric hydrogenation reactions. These processes are widely used in synthetic organic chemistry.

Jack had an incredible command of seemingly all areas of chemistry. After I moved to Chicago, I would occasionally visit him in his office to seek advice about my own research. Only rarely was I was able to surprise him with something new! In most cases, my novel result would be something that he had already anticipated or that was related to something he had done earlier in his career. Needless to say, these discussions went a long way in broadening my own perspectives on chemistry. Jack was legendary for asking penetrating and incisive questions at seminars and pointing out the faulty logic and unsubstantiated conclusions of speakers who ran loose with the facts or tried to sweep complications under the rug. He set the bar for high quality rigorous research in mechanistic inorganic chemistry. He will be sorely missed.

Rich Jordan, Paul Snowden Russell Distinguished Service Professor

Jack was a real giant and icon in inorganic chemistry. Jack was extremely critical; he set the standard for the rest of us in the department. This is a huge loss for the University of Chicago and the entire chemistry community.

Chuan He, John T. Wilson Distinguished Service Professor

While many professors become a little less aggressive and intense with their questioning with age, Jack was notoriously sharp even after becoming emeritus. As an undergraduate from 2004-2008, when Jack was over 80, I first witnessed his approach to questions at a departmental seminar. Afterwards I leaned over to a graduate student and asked, "Who is that?" In my time here, Jack was a regular and vigorous contributor to our seminar series. Even at that early stage in my career, I learned a lot from his approach to scientific debate.

John Anderson, Assistant Professor

lar at the Lyric Opera of Chicago and celebrated Beethoven's birthday with his group. Coming through his ante office, one encountered the fragrance of Constant Comment tea, light strains of classical music from WFMT, and the chuckle of his long-time secretary, Lorene. Through the door sat Halpern, a small man at a big desk wearing his customary blue shirt and gray pants.

Halpern's quick mind, skill at debate, and love of scientific argument led to many lively exchanges at seminars and conferences. Seated in the front row, Halpern's hand would shoot up at a lecture's end, and he would announce, "I have a question and a comment." Punctuating his remarks with jabbing motions of his pen, Halpern would distill a talk to its essence, place the work in context, and identify weak arguments. This was hugely appreciated by those who knew him well—perhaps less so by those unfamiliar with his style—but it was always a teaching moment that challenged and enriched all who were present.

Alan Goldman received his PhD from Columbia University in 1985 and then worked as an IBM Postdoctoral Fellow in the laboratory of Prof. Jack Halpern at the University of Chicago (1985-1987). He then joined the faculty at Rutgers University where he is currently Distinguished Professor of Chemistry.

Clark Landis received his PhD from the University of Chicago in 1983 under the direction of Prof. Jack Halpern. His independent career includes faculty positions at the University of Colorado-Boulder (1986-90) and the University of Wisconsin-Madison (1990-), where he is the Helfaer Professor of Chemistry.

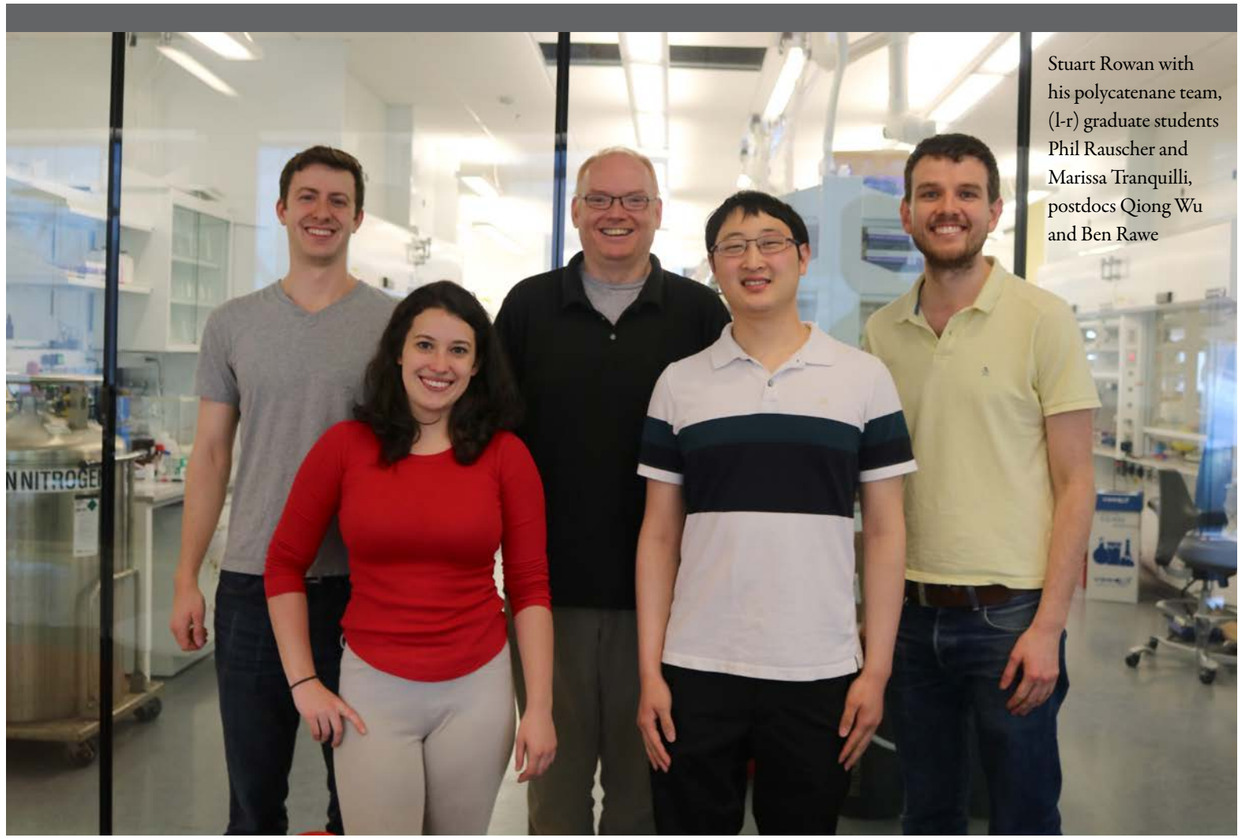
Ayusman Sen received his PhD from the University of Chicago in 1978 under the direction of Prof. Jack Halpern. Following a year of postdoctoral research with Prof. John Bercaw, who also worked previously with Jack, Ayusman joined the faculty at the Pennsylvania State University where he is currently a Distinguished Professor of Chemistry.

A shorter version of this Obituary was originally published in *Angewandte Chemie* (A. S. Goldman, C. R. Landis, A. Sen, *Angew. Chem. Int. Ed.* **2018**, *57*, 4460; *Angew. Chem.* **2018**, *130*, 4548). It can be accessed online at https://doi.org/10.1002/anie.201802390

Unconventional Touch:

Stuart Rowan's lab makes molecules into miniature chains

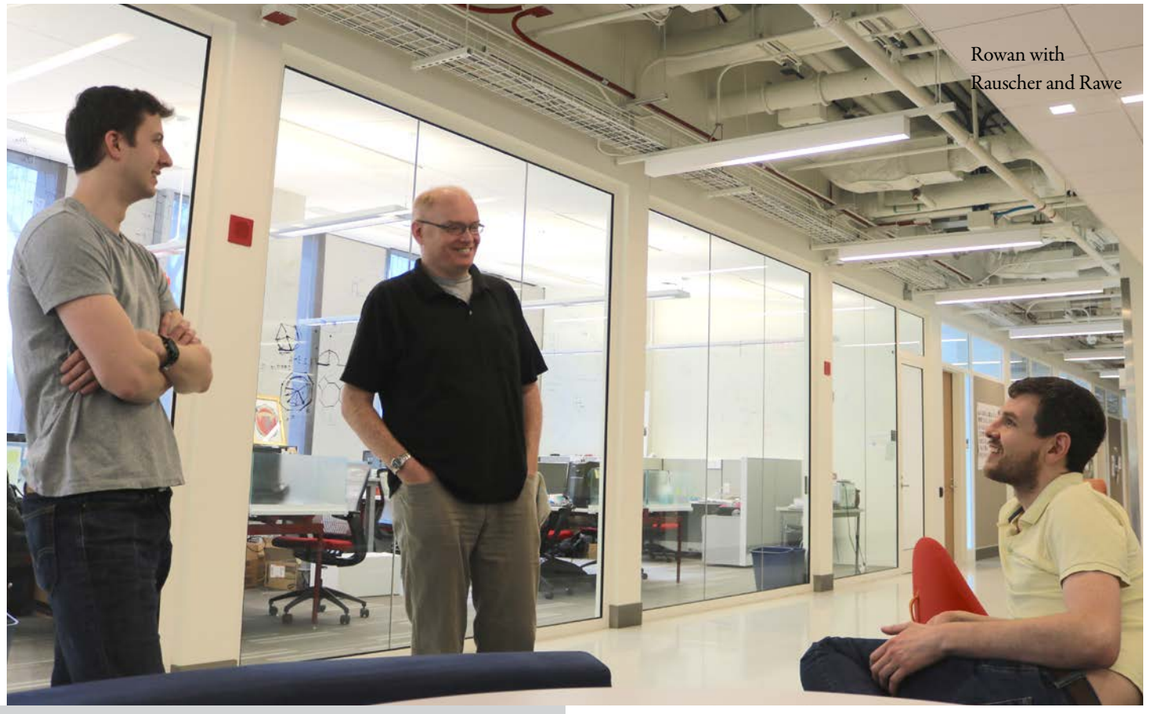
By Irene Hsiao



Stuart Rowan with his polycatenane team, (l-r) graduate students Phil Rauscher and Marissa Tranquilli, postdocs Qiong Wu and Ben Rawe

One of the first two faculty members to hold a joint appointment in the Institute for Molecular Engineering and the Department of Chemistry, Stuart Rowan joined the University of Chicago in 2016, after 17 years in the Department of Macromolecular Science and Engineering at Case Western Reserve University. Now Barry L. Maclean Professor of Molecular Engineering and Professor of Chemistry, Rowan laughs when he remarks, "I've never had an engineering course in my life, but I've been a professor of engineering for 18 years now." Trained as a small molecule organic chemist from his undergraduate and graduate degrees at the University of Glasgow through two postdoctoral fellowships at Cambridge and UCLA, Rowan translated his interests in supramolecular interactions and noncovalent bonding into his current work in soft materials. "I had never deliberately made a polymer in my life until I started as a professor," he says. "But I like being in environments where I have a steep learning curve. Sometimes you make naive mistakes—that's the nature of interdisciplinary science—but if you come into a new field and you haven't gone through the traditional education for that field, you tend to think about it a little bit differently."

Rowan's unconventional approach recently brought an unusual task to fruition: the synthesis of mechanically interlocked polymeric chains, or polycatenanes.[1] The smallest molecular ring through which one can string a thread of atoms can be as short as 22 atoms. To form chains—that is, each ring enclosing two or more others—Rowan's links range from 42 to 68



Rowan with
Rauscher and Rawe

We made this molecule about five years ago, and we spent the last five years proving to ourselves that we made it.

atoms in length. The polycatenanes are made by starting with a macrocycle that has two metal-binding ligand sites. Addition of metal ions with C-shaped molecules that also contain two ligands results in the formation of a polymeric template, driven by the coordination of the metal ions to the ligands in both the C-shaped and macrocyclic molecules. A ring-closing reaction of this template produces a polymer comprised of interlocked rings, the molecular equivalent of a macroscopic chain.

Published in *Science* in November 2017, the project has its roots in Rowan's postdoctoral work on rotaxanes, another interlocked molecular architecture, in Fraser Stoddart's lab at UCLA. Stoddart's work with Jean-Pierre Sauvage and Bernard L. Feringa on how interlocked and other structures can work as molecular machines received a Nobel Prize in 2016. "I started thinking, 'How can we develop new synthetic methods to make these catenanes or rotaxanes polymeric, so you actually have a material?'" says Rowan. "Polycatenanes had been a goal of the supramolecular chemistry community since people started making catenanes in the late '80s, but no one had ever made them before."

Rowan began the polycatenane project seventeen years ago. "One of my first graduate students started some tentative steps. It wasn't quite working out the way we wanted, so I switched him to another project. Every time I'd get a new student, I'd put them on this project for a year or two. It became the death project for this group, but we never stopped trying," Rowan explains. "About eight years ago, we'd gotten far enough down the road that I felt confident to put one student full time on this project. His name was Rudy Wojtecki, and he was a very smart graduate student. I thought, 'Ok, I'm going to let him go the full five years on this project, and if he doesn't do it, I'm not putting anyone else on it.' He was able to produce the first paper on a small molecule version of these systems in 2013 that pointed the way to polycatenanes."[2] It was the first paper to support the project in thirteen years.

"The whole process we went through with this project could be considered a master class in how you can keep funding a project and keep students' interest while having no papers come out of it," notes Rowan. "It's a credit to the US funding system, NSF in particular, as well as to the students themselves." When postdoc Qiong Wu joined Rowan's lab as a graduate student, the project caught his imagination, and he forged the material that stars in the *Science* paper. Phil Rauscher, a joint graduate student with Juan de Pablo, built atomistic molecular models that supported Wu's experimental work. "Coming to Chicago moved the project along much faster," says Rowan. "We made this molecule about five years ago, and we spent the last five years proving to ourselves that we made it."

Rowan's work on polycatenanes is far from complete. He expresses enthusiasm for investigating their material properties, particularly their viscoelastic properties—how they flow and bend. "You can think about polymers like cooked spaghetti," he suggests. "They're tangled—that's what gives polymers their properties. If you pull on one piece of cooked spaghetti, it brings all the rest of them with it. Their ability to entangle allows you to form films with polymers." Furthermore, interlocked chains are more flexible than the material with which they are made. "If you had a solid piece of metal, it doesn't have the flexibility of a metal chain. The flexibility there is a product of the chain's topology. The same can be argued at a molecular level. What if I have a polymer strand comprised only of interlocking rings? These strands should be able to collapse and expand at low energy costs. This suggests that polycatenanes may well have very interesting properties—for example, the ability to absorb energy through the rotation of the rings."

To observe these properties, Rowan and his lab are working on improving the synthesis of polycatenanes to obtain larger quantities of the material. "If you engineer a molecule of a specific architecture, how does that architecture express itself in the macroscopic properties of the material? One thing I love about polymer science is that you can pick up the material and *feel* the chemistry," he says, citing the difference between the common plastic polyvinyl chloride and water-soluble polyvinyl alcohol. "The only difference is that one has a chlorine atom—albeit lots of them along the backbone—and the other has an hydroxyl group. You can pick up a film of these materials and feel how that one change per repeat unit changes the properties of the materials." Other aspects of the polycatenane work the Rowan group is studying includes adjusting variables such as ring size, or, as he puts it, "finding out what happens if you tighten the noose," which he expects would create higher energy penalties for ring motion, altering the mobility of the backbone.

While other projects in his lab include more pragmatic applications, such as the development of new plastics, green paints, and water purification membranes, Rowan's career in polymer science has been fundamentally driven by his curiosity. "As a chemist with no formal engineering training, joining an engineering department as an assistant professor was maybe a risky move," he says. "However, I made a strategic decision to move outside my comfort zone. I thought it would be a fun learning experience." He credits his students with a similar fearlessness and ambition. "It took courage for the students who started the project to jump on board. The project really needed students who saw the potential and believed. Rudy and Wu both did. In the end the major products of any project are the trained students and researchers who have carried out the work. To see them learn and grow as scientists and engineers—that's the best part of this job!"

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[1] Qiong Wu, Phillip M. Rauscher, Xiaolong Lang, Rudy J. Wojtecki, Juan J. de Pablo, Michael J. A. Hore, Stuart J. Rowan, "Poly[n]catenanes: Synthesis of molecular interlocked chains," *Science,* 30 Nov. 2017.

[2] R. J. Wojtecki, Q. Wu, J. C. Johnson, D. G. Ray, L. T. J. Korley, S. J. Rowan, "Optimizing the formation of 2,6-bis(N-alkyl-benzimidazolyl) pyridine-containing [3]catenates through component design," *Chem. Sci.* 2013, 4: 4440-48.

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Spring 2018

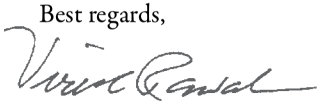
Dear friends,

The standard joke in Chicago is that if you travel for a few days in April or May, you will miss Spring. Lucky for me, I was here to enjoy all two days of it! This respite from a long, cold winter has been accompanied by many good things for the department. I am pleased to announce that Sarah King has accepted our offer to join the faculty as Assistant Professor this Fall. Sarah is currently completing a postdoc in Julia Stähler's laboratory at the Fritz Haber Institute of the Max Planck Society, having obtained her PhD with Daniel M. Neumark at UC Berkeley. We are also delighted that Professors Giulia Galli and James Skinner, both chaired professors in IME, have accepted joint appointments in Chemistry. We look forward to sharing their research and other contributions in the coming years.

In this issue, we feature the work of two other relatively new members of our faculty. Bryan Dickinson, who joined the Department in 2014 after a PhD from Berkeley and a postdoc at Harvard, describes his approach to developing functional molecules through directed evolution. His lab has created biosensors that can drive cells to respond to changes in their environment, work that has potential to fight diseases including cancer. Stuart Rowan, Barry L. Maclean Professor of Molecular Engineering, joined us in 2016 after 17 years at Case Western. Stuart describes his creative use of organic chemistry to make polycatenanes, molecules that are connected mechanically, rather than by chemical bonds. We also remember our colleague Jack Halpern, Louis Block Distinguished Service Professor Emeritus, who passed away earlier this year. A man of towering intellect, Jack made seminal contributions to our understanding of reaction mechanisms, especially of catalyzed reactions. A memorial service for him will be held later this summer.

On June 1, we will be holding our third annual Spring Reception in coordination with UC Alumni Weekend. I am proud to tell you that Reatha Clark King (PhD 1963) will deliver the inaugural Distinguished Alumna Lecture. We will also feature talks by Bryan Dickinson and Raymond Moellering, as well as an exhibition of paintings by Danute Nitecki (PhD 1961). We hope you will join us there!

Best regards,



Viresh Rawal
Professor and Chair