

Controlling Molecular Motion with Photonic Reagents



Rabitz laboratory for controlling molecular motion with photonic reagents. The laser is in the background with the means to shape the laser pulses in the foreground, along with several operational experiments.

It has been a long-standing dream since the invention of lasers in the 1960s to use them for precise manipulation of dynamical events at the atomic and molecular scale. Professor Herschel Rabitz has been pursuing the fundamental principles behind this concept and in recent years has opened a laboratory for this purpose. Controlling molecular motion calls for applying intense shaped laser pulses acting as “photonic reagents,” which last for approximately a femtosecond (10^{-15} sec) in keeping with the timescales of natural atomic and molecular scale dynamics phenomena. The Rabitz laboratory now has two fully operating laser systems with a third expected later this spring.

The theoretical and experimental programs are tightly linked with the goal

of revealing the basic principles of controlling quantum molecular dynamics. Several graduate students, undergraduates, and postdoctoral associates are involved with the research. A special focus is on establishing the ultimate capabilities of photonic reagents and the scientific information that may be extracted from control at this scale. Applications being pursued include the control of chemical reactivity and the creation of novel means to detect the presence of chemical agents, possibly in a background of other very similar but benign materials. In all applications, molecular control is a matter of achieving discrimination to steer the molecule to one final state versus that of another less desirable state. In recent experiments, this concept was extended to detecting

New Chemistry Approach Promises Less Expensive Drugs

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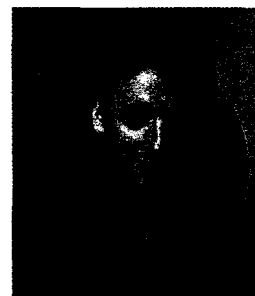
With a newly discovered method of assembling organic molecules, a team of Princeton chemists may have found a way to sidestep many of the expensive and hazardous barriers that stand in the way of drug development.

The new approach allows scientists to synthesize molecules without employing toxic catalysts, and it also does not generate alternate versions of drug molecules that can damage the body, two perennial issues that plague the manufacturing process. David MacMillan, a researcher on

the team, said the discovery is important for its industrial applications—and the new research possibilities it creates.

“This is a new type of chemistry that could expand the way people think about making biologically active molecules,” said MacMillan, the A. Barton Hepburn Professor of Organic Chemistry and director of the chemistry department’s Merck Center for Catalysis. Broadly stated, the discovery will open up new possibilities for two chemical groups, ketones and aldehydes.

The paper, which MacMillan cowrote with first author Teresa Beeson and Anthony Mastracchio, Jun-Bae Hong, and Kate Ashton, all members of his research group, appeared in the March 29 issue of *Science*.



Celera Licenses Chemical PCR Patents

Celera Genomics/Diagnostics obtained a nonexclusive license last month for commercialization of the "chemical PCR" technology invented by Raj Chakrabarti and Clarence Schutt in the Princeton chemistry department in 2002.

PCR, the central technique for DNA amplification used in essentially all biotechnology research carried out throughout the world, was invented by Kary Mullis and awarded the 1988 Nobel Prize in Chemistry. Its most notable application was arguably the sequencing of the human genome by Celera Genomics in 2001 and the publicly funded Human Genome Project announced at the same time.

In the "post-genomic era," since the recent expiration of original patents on PCR, Celera has been seeking new PCR-based technology platforms for genetic diagnostics in an effort to breathe new economic life into the technique. Although it has evolved over time, PCR still has many shortcomings, the most prominent being the difficulty of replicating high-GC content DNA sequences, which are very common in genomic DNA. Another drawback is the requirement to cycle between relatively high temperatures that can make faithful DNA replication difficult. Chemical PCR (reviewed in *PCR Technology: Current Innovations*, CRC Press, 2003) aims to overcome these problems by using small molecules instead of high temperatures as chaotropic agents to separate the two strands of the DNA double helix. Lower cycling temperatures also minimize damage to the enzymes used in PCR. Chakrabarti and Schutt show that the addition to the PCR reaction mix of molecules selected from four broad classes of small organic additives not only improves the fidelity of DNA polymerization catalyzed by these enzymes, an important consideration for quantitative PCR, but renders PCR possible where previously intractable.

The major focus of Schutt's research over the years has been the elucidation of structures of actin and actin-binding proteins by X-ray crystallography, a technique that requires large amounts of purified protein. The discovery of PCR, coupled with bacterial expression systems, provided a means to obtain such amounts. In his thesis research, Chakrabarti proposed to determine the role of an actin-binding protein involved in modulating synaptic strength in neurons, but was stymied by the failure of PCR to yield requisite amounts of DNA for protein expression. Undeterred, he studied the physical chemistry of the PCR reaction and realized that very few chaotropic agents, molecules that help separate DNA strands in the double helix, had been tested. In a sense, these molecules play the same role as raising temperature to denature the DNA and open the possibility of isothermal PCR. Remarkably, Chakrabarti's chemical compounds enabled amplification of several famously difficult genes. This work was published in *Gene and Nucleic Acids Research*.

Celera carried out extensive internally funded research assessing the potential of chemical PCR technology before approaching Princeton for licensing rights (US Patents 6,949,368 and 7,276,357). ■

Souza Honored with Glassblowers Award

Michael Souza has been named recipient of the American Scientific Glassblowers Society's Andrews Glass Award. The award is for Best Technical Paper, presented at an ASGS symposium, titled "In Search of Dark Matter; An Argon Separator for Deeply Mined CO₂." The award will be presented to Souza at the 53rd AGS Symposium this June in Atlantic City. ■

Special Issue Dedicated to Edward I. Stiefel

A special issue of the November 2007 *Journal of Inorganic Biochemistry* was dedicated to the memory of Edward I. Stiefel, formerly the Ralph W. Dornte visiting professor in the chemistry department. The issue, a celebration of the science that Ed helped so much to pioneer, was produced with the assistance of former colleagues who served as guest editors for the issue, including John T. Groves and Thomas G. Spiro of Princeton, Stephen J. Lippard of the Massachusetts Institute of Technology, and Harry B. Gray, of the California Institute of Technology. All four editors began their association with Ed during the mid-1960s at Columbia University during a period that spawned the origins of both bioorganic and bioinorganic chemistry at Columbia. For a more complete account of Ed's accomplishments, see *JIB* 101 (2007) vii-viii and *Science* 314 (2006) 1406. ■

