Department of Chemistry

Chemistry is the Central Science because it is a clear conduit between the physical and life sciences. Considering that most innovations occur at the interface of scientific disciplines, chemistry additionally plays a critical role in translational research. The UMass Chemistry Department is highly collaborative and exemplifies this definition of chemistry.

Chemistry is the understanding, control, and multiscale design of natural and synthetic matter

The discipline of Chemistry has been focused on understanding molecular transformations and interactions at all levels. The last century saw unprecedented advances in the former, *i.e.* our ability to manipulate covalent bonds and synthesize new molecules. Our understanding of the latter, *i.e.* non-covalent interactions, has improved over the last century, but is far from complete. The challenges of the 21st century involve understanding and controlling noncovalent molecular interactions. These studies could range from understanding how metal surfaces catalyze chemical reactions of adsorbed molecules, to predicting the properties of polymer assemblies or band gaps in semiconductor materials, to understanding protein folding and its effect on enzyme active site function. Developments in each of these cases will arm us with the capability to address the myriad challenges confronting society, from health to sustainability to information technology.

Continuing Technologies

- Targeted Drug Design
- Photovoltaics & Energy Harvesting
- Cancer & Neurodegeneration
- Protein Structure & Allostery

Next Generation Frontiers

- Targeted drug delivery
- Optoelectronics
- Computation in Materials & Biology
- Smart & Adaptive Materials
- The "RNA World"
- Mesoscale Molecular Assemblies

The inherently interdisciplinary and highly collaborative mind-set of the UMass Chemistry faculty place the department at a unique position to grow as a campus and a national leader in confronting tomorrow's scientific challenges. Collaborations are already spread widely across campus, from leadership in the NIH Chemistry Biology Interface Training Program and in the Institute for Applied Life Sciences, to leadership in large impact materials research and alternative energy research centers and initiatives, in addition to synergies with engineering. Our faculty collaborate and publish in peer-reviewed journals with faculty in Biochemistry and Molecular Biology, Biology, Food Science, Microbiology, Physics, Polymer Science and Engineering, and Veterinary and Animal Sciences within the college, and with the Chemical Engineering and Mechanical Engineering faculty in the College of Engineering.

Our primary research mission is to enhance the fundamental understanding of the phenomena that underlie molecular level interactions. Also, our faculty have had a consistent eye towards translational opportunities. As a result, our faculty have been granted multiple patents, starting with our rich tradition in peptide chemistry a couple of decades ago. Our successes in translation include two recent start-ups, one of which was acquired by a large biotechnology company and the other one in its very beginning. We aim to further strengthen translational initiatives, especially related to our strengths in biomedicine and smart materials. We target emerging areas of high societal impact, such as cancer and neurodegeneration in biomedicine, and designer, high value materials for strategic purposes, such as drug delivery, sensing, catalysis, and optoelectronics.

Opportunity for (Re-)Investment. Investments in Chemistry have brought excellent returns to the University. Chemistry faculty secured $303K in external funding per FTE in 2014; this is substantially higher than the CNS average ($223K/FTE), despite the fact that the Chemistry department bears one of the highest teaching loads in the College of Natural Sciences. This excellence in funding reflects our faculty's ability to address challenges critical to the nation, as the funding comes primarily from NSF, NIH, DOD and DOE. Also, our industrial funding is on the rise, which is a clear indicator of the evolving translational mind set of our faculty. The department recognizes that with proper investment, we could do even better, especially in our industrial contracts and sponsorships.

The department's excellence in research has not come at the expense of its teaching mission, the core service that UMass provides to the Commonwealth. Our faculty have been consistently at the top of teaching innovations — our faculty play leadership roles in innovative interdisciplinary teaching approaches (*e.g.* iCONS), technology in teaching and learning (*e.g.* OWL and eExams), and classroom delivery (*e.g.* University and College teaching awards). However, sustaining this balance requires further investment in the department. Chemistry at UMass lost a substantial number of tenure system faculty with the early retirement incentives of 2003 and it has never regained its numbers. In 1998, there were 33 tenure system faculty; that number is down to 24 today. We anticipate one retirement in 2015, with 2-3 more in the next 5 years. Hiring must begin immediately at a rate higher than simple replacement.

The high research productivity combined with the high teaching productivity in Chemistry makes it a prime investment opportunity, with the demonstrated potential for high return to the University. Such investment benefits will spread across the College and University, as new hires will almost certainly involve themselves in inter-departmental initiatives and collaborations, as do our current faculty. Renewed investment will also allow us to return more research active faculty to our service courses, providing tangible benefits to students in a wide variety of majors.

Interdisciplinary strengths and opportunities. The core focus of investigating the fundamental properties that underlie covalent and non-covalent molecular interactions will continue in the department. Within these basic science investigations, we envision investing in faculty who will connect these basic investigations to translational research. These connections could be either through publications that change the way people think about molecular interactions, facilitating translation elsewhere, or through faculty taking the translational next step themselves, independently or through collaborations. In the context of this document, we specifically focus on the following interdisciplinary strengths and thus the places for investments in Chemistry.

Materials genomics. Following an announcement from the White House, a multi-agency Materials Genomics Initiative was launched in 2011. This initiative aims to enhance the competitiveness of the US in global innovations and the economic marketplace by supporting US institutions "in the effort to discover, manufacture, and deploy materials twice as fast, at a fraction of the cost," noting that "advanced materials are essential to economic security and human well being." Since 2011, the federal government has invested over $250 million in R&D and infrastructure. Within this umbrella, the Chemistry Department focuses on two sub-topics: materials for sustainability and materials for biomedicine.

Within the area of materials for sustainability, we envision chemistry contributing in three different ways, *viz.* (*i)* energy harvesting, (*ii*) energy storage; and (*iii*) catalysis (energy use).

The Chemistry Department faculty are very strong in the first and the third topics and we would like to enhance these capabilities by hiring new complementary faculty in these two areas and also by hiring in the energy storage area (all will complement faculty in other departments within UMass). Our faculty's leadership in several materials and energy initiatives and centers across the campus exemplifies our existing strengths.

Our department boasts world-class leadership in designer materials for interfacing with biology. Molecular designs for materials that involve sensing, diagnostics or drug delivery have been rather heuristic. Members of our faculty lead rational design of materials for biomedical applications, which is exemplified by our faculty playing leading roles in the Institute for Applied Life Sciences and spinning off start up companies based on novel materials for biological applications. This is another area that is ripe for investment, because it is critical that we maintain and hopefully further our leadership in this research area.

Interface with Biology and Medicine. Molecular level understanding of structure and function of biological molecules has been the key for developing drug targets and for drug development. In this context, our department has focused on two key areas: (*i*) understanding the structure and function of biological macromolecules and (*ii*) optimizing the biological interface with abiological molecules to generate next generation biomaterials.

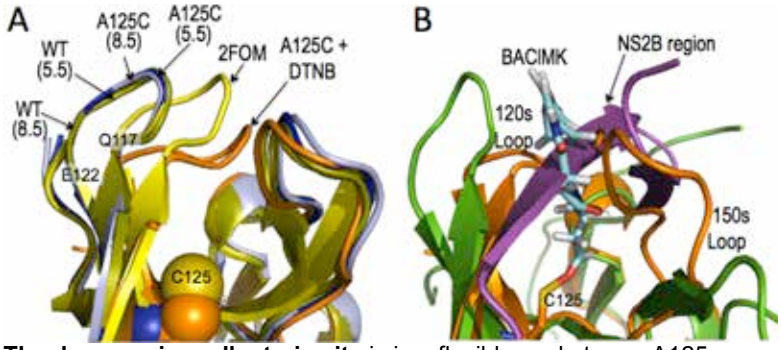
Understanding active site structure and function will continue to be essential to controlling (or correcting) key systems in biology and human health. Consistent with our strengths, faculty in Chemistry are also interested in understanding the broader envelope, from protein folding and misfolding, to protein-protein or inter-domain structural rearrangements, to allosteric control of active site function. A deep mechanistic understanding of targets is essential to the design of new drugs that are specific and effective. Finally, an emerging area of biology, large noncoding structured RNAs, promises fertile new territory

Biological molecules are perhaps the most promising therapeutics, as they can directly address a functional deficiency. Similarly, functional biomolecules can also be harnessed for applications outside their native environment for everyday applications, *e.g.* catalysis. In both these applications, it is critical that these molecules are efficiently interfaced with abiological materials as they are produced and used in very specific environments. For example, protein-based therapy is the simplest and most direct solution for protein deficiency. However, artificially incorporating the therapeutic protein into a specific tissue or sub-cellular compartment is an enormous challenge. Similar challenges exist for RNA-based therapies. Faculty in our department focus on developing agents that effectively interact with these biological molecules, encapsulate them, and unload them in appropriate locations. Although our materials based strengths are excellent in this area, there is a critical need to hire complementary faculty with a chemical biology focus, to further enhance those strengths.

In the following sections, we provide vignettes of several Chemistry faculty. Note that these are by no means comprehensive and are intended to merely highlight research in Chemistry.

Small molecule inhibitors for the treatment of dengue fever

Dengue fever is an emerging mosquito-borne disease that has been reported in 125 countries worldwide and is endemic in parts of Hawaii, Texas and Florida. Infection causes significant morbidity, particularly in children, yet neither vaccine nor drug is available. Dengue virus is a flavivirus made up of only a handful of proteins. One of these, the dengue virus protease, is essential for viral replication and propagation of the viral infection. Inhibition of the protease stops the viral life cycle, and is therefore a promising drug target for treating dengue fever and dengue hemorrhagic fever. Unfortunately, up to this point, all of the active site inhibitors developed for dengue virus protease have failed in clinical trials. Prof. Hardy believes this failure is due to the slow activity of the protease, which makes active site inhibitors highly susceptibility to off-target effects. To combat this deficiency, her group is working to identify new inhibitory (and allosteric) sites on other parts of the protease, developing a new method to probe the surface of the protease. They have found a new site on the protease that is susceptible to allosteric inhibition. Their crystal structures suggest that changes in the conformation of the 120's loop will allow them to control the function of the protein. Current work focuses on identifying additional allosteric sites and developing inhibitors that can be used for the treatment of dengue fever.

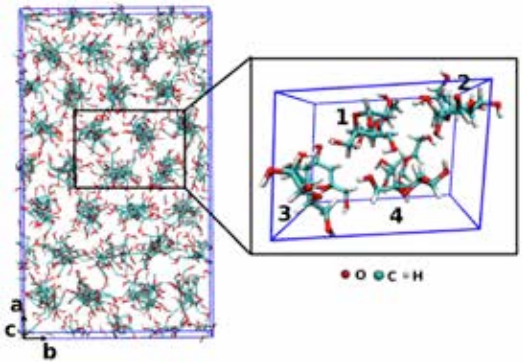


The dengue virus allosteric site is in a flexible pocket near A125, A. Conformational flexibility is evident in the 120's loop. B. Modeling of the allosteric inhibitor, BACIMK bound to A125C showing steric clash between BACIMK and the NS2B region of the protease.

M. Yildiz, S. Ghosh, J. A. Bell, W. Sherman and ***J. A. Hardy***, *ACS Chemical Biology* 8, 2744–2752 (2013)

Understanding thermal decomposition of cellulose

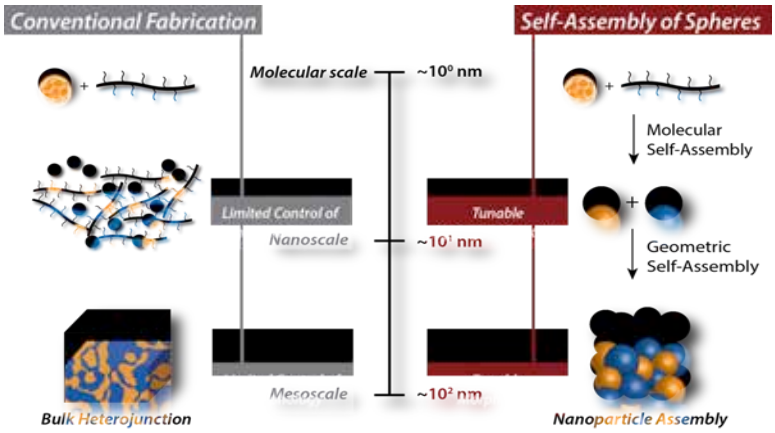
Determining how cellulose breaks down upon heating is critical for efficiently converting cellulose to biofuels. Computational studies by Prof. Auerbach have recently revealed the previously unknown decomposition mechanism – how cellulose decomposes at the atomic level, and how these pathways depend on temperature. Prof. Auerbach combined quantum calculations of energies with classical molecular dynamics to discover that the hydrogen bonds that keep cellulose solid at lower temperatures actually catalyze its decomposition upon further heating, eventually forming major products useful for biofuels and biochemicals. Complementary experiments by Prof. Dauenhauer (Chem. Eng.) confirm the accuracy of the predictions. Insights from these simulations are being used to find more efficient ways to produce biofuels.



Snapshot of cellulose as it decomposes, catalyzed by its own hydrogen bonds

V. Agarwal, P. J. Dauenhauer, G. W. Huber and ***S. M. Auerbach***, *J. Am. Chem. Soc.* 134, 14958-14972 (2012). http://bit.ly/1yHLw7R

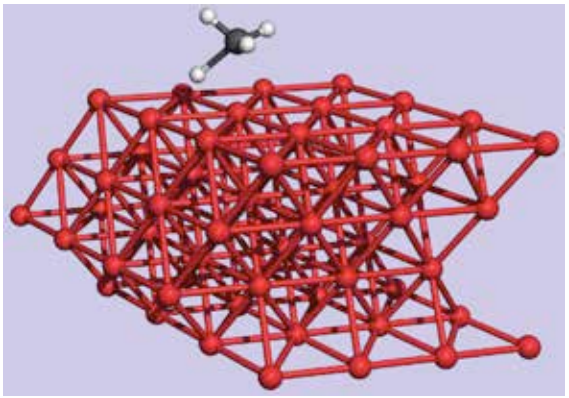
Self-assembled organic materials for photovoltaics



Organic photovoltaic cells have several potential advantages over conventional, silicon based cells – they are flexible and can be made in any shape, or even as a coating, and are easier to fabricate. However, current organic photovoltaics are less efficient than silicon cells, and require halogenated solvents to produce. The key to efficient organic solar cells is to control the assembly of the component molecules over length scales from a few to hundreds of nanometers. Profs. Venkataraman and Lahti, in collaboration with Prof. Russell (PSE) have designed and synthesized polymers which self-assemble into nanospheres. The nanospheres, in turn, pack into assemblies with predictable, *controllable* structures. Using this powerful method, they have fabricated organic photovoltaic cells using environmentally friendly water as the solvent. These cells have power conversion efficiencies similar to cells prepared by conventional methods. The ability to control the structures means that it will be much easier to further improve the cell efficiency.

T. S. Gehan, M. Bag, L. A. Renna, X. Shen, D. D. Algaier, ***P. M. Lahti***, T. P. Russell and ***D. Venkataraman***, *Nanoletters*, 2014,14, 5238-5243 http://bit.ly/1pbUGZW

The mechanism for methane activation by metal catalysts



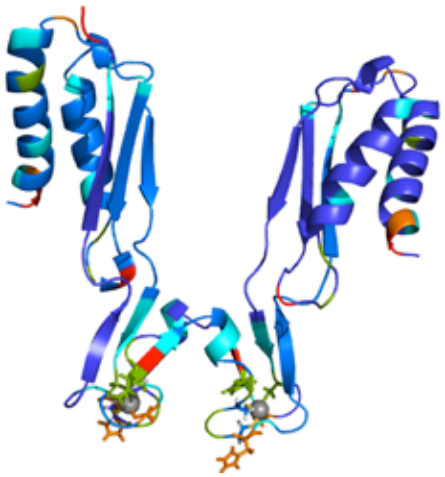
Transition state for methane dissociation on the nickel (111) surface

The hydrogen gas used to produce fertilizers and for fuel cells is primarily produced from steam reforming of natural gas. The rate-limiting step for this reaction is chemisorption of methane on the surface of the metal catalyst (usually nickel), in which a C-H bond is broken, and metal-H and metal-methyl bonds are formed. Prof. Jackson uses electronic structure theory to determine the potential energy surface that governs this process and then uses quantum mechanics to calculate the dynamics for the reaction. Prof. Jackson has developed new, highly efficient methods that include all of the methane stretches and bends, and some metal motions, so the effect of temperature and methane vibrations on the reaction probability can be accurately modeled. This project, supported by the DOE, will help to improve catalysts for this industrially important reaction.

S. Nave, A. K. Tiwari and ***B. Jackson***, *J. Phys. Chem*. A 118, 9615 (2014)

Ulcers and Nickel Trafficking

The human pathogen *H. pylori* requires nickel to infect the stomach, where it causes ulcers and stomach cancer. The nickel is used by two key enzymes, hydrogenase and urease. The protein HypA binds nickel and transports it to the enzymes. Prof. Maroney's group is studying the structure of this protein, and how structural changes affect the protein-protein recognition necessary to its function. Working with Prof. Ciurli (U. Bologna), they have used NMR to determine the structure of HypA, particularly the nickel binding site, and how it is affected by pH. They have also shown that point mutations in a structural zinc site far from the nickel-binding site greatly reduce the function of HypA. This in turn eliminates the ability of *H. pylori* to survive stomach pH levels.



NMR structure of HypA colored by changes in chemical shift at pH 6.3

K. A. Higgins, C. E.,Carr and ***M. J. Maroney*** *Biochemistry* **51**, 7816–7832 (2012)

Developing on-target therapeutic delivery systems for biomedical applications

Delivering a therapeutic molecule precisely to a disease location is critical for many human diseases. Nowhere is this need more evident than cancer chemotherapy; patients undergoing chemotherapy treatment experience debilitating side effects, which have negative effects both physically and socially. The rather indiscriminant cell-killing nature of chemotherapeutic drugs is the primary reason for these undesirable side effects. Therefore, it is critical that practical approaches are created for directing these molecules precisely to the desired locations. One of the most promising approaches is to generate "smart" molecular assemblies that are capable of not only selectively localizing on the targeted diseased tissues, but also releasing therapeutic molecules in response to the micro-environment specific to those tissues. The molecular design criteria for such drug delivery vehicles requires consideration of several major factors such as biocompatibility, good drug loading capacity, convenient synthetic methods and stability. Beyond this there are an array of other factors that can enhance a delivery vehicle such as size tunability, surface modification, targeting capabilities, and bio-relevant stimuli-sensitive drug release. The Thayumanavan group has developed a self-assembling polymeric nanogel platform that satisfies the above criteria for applications in drug delivery. Using guiding principles developed in these nanogels, we are able to finely tune the chemical and or physical characteristics to tailor the carrier properties for desired therapeutic applications. The versatility of these nanogels lends itself for use in other related applications such as diagnostics and sensing.

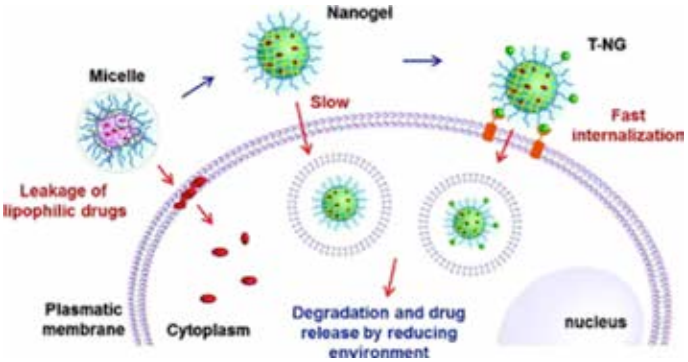
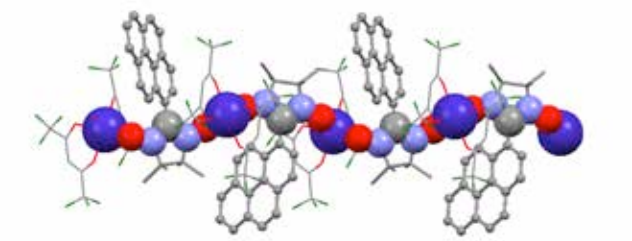


Illustration of the rapid cellular uptake and release of drugs using targeting polymeric nanogels

R. Chacko, J. Ventura, J. Zhuang and **S. Thayumanavan** *Adv. Drug Deliv. Rev.* **2012**, *64*, 836-851.

A new magnetic material with very high magnetic strength in temperature range that is applicable using present technology

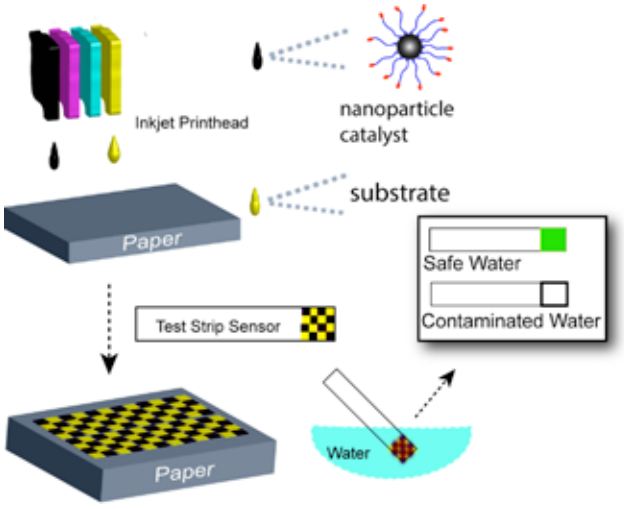


Structure of a cobalt-based single chain magnetic material (SCM)

The Lahti group has had strong ties with physicists and chemists in Brazil since the early 2000's. During a sabbatical with Professor Lahti, Brazilian faculty discovered a new structural class of single chain magnetic material (SCM). The SCM was constructed by combining inorganic and organic components, each of which has unpaired electrons. The material therefore is a hybrid - it is not a metal, and it is not a "plastic." Although none of the SCM components alone has strong magnetism, their combination in the new SCM produces a material having a 3.2T magnetic coercivity at 8K, larger than the ~1.2T of the very strong new metal alloy magnets that became recently available. This breakthrough SCM starts exhibiting desirable magnetic behavior below 17K, the highest temperature yet observed for this much-pursued class of materials. This gives prospects of new magnetic technology using materials that can be made without the high temperature fabrication used for metallic magnetic alloys, and that can run at less challenging temperatures than 4K (liquid helium) used for devices such as the magnetic field generators of MRI instruments. The early stages of the work were supported by NSF, and all stages of the work have been supported by Brazilian agencies (CNPq, CAPES, FAPRJ). As part of the project, Prof. Lahti is associated with the Brazilian Ciência sem Fronteiras scientific exchange program.

M. G. F. Vaz, R. A. A. Cassaro, H. Akpinar, J. A. Schlueter, **P. M. Lahti**, M. A. Novak, *Chem. Eur. J.,* 20, 5460–5467 (2014)

Test strips for drinking water safety in the developing world



Inkjet printing of test strips for bacteria using iron oxide nanocatalysts.

The World Health Organization estimates that 1.2 billion people worldwide are without access to safe drinking water, resulting in over 300 million illnesses and the death of an estimated 2 million children per year. Current tests for detecting pathogenic bacteria in water have required expensive equipment and the assays are not sensitive enough to assure drinking water safety. A test strip that would change color in the presence of pathogenic bacteria could give a quick answer, but no one has developed a reliably sensitive test.

Prof Rotello is working with nanoparticle researcher Irshad Hussain and molecular biologist Sohail Qureshi of the LUMS School of Science & Engineering in Lahore Pakistan to develop colorimetric test strips for detecting bacteria based on iron oxide nanoparticles. These test strips are inexpensively fabricated using inkjet printing. Prototype strips have been developed, and are being tested in Lahore and surrounding communities.

B. Creran, X. Li, B. Duncan, C. S. Kim, D. F. Moyano and **V. M. Rotello** *ACS Applied Materials & Interfaces* ***6*****,** 19525-19530 (2014)