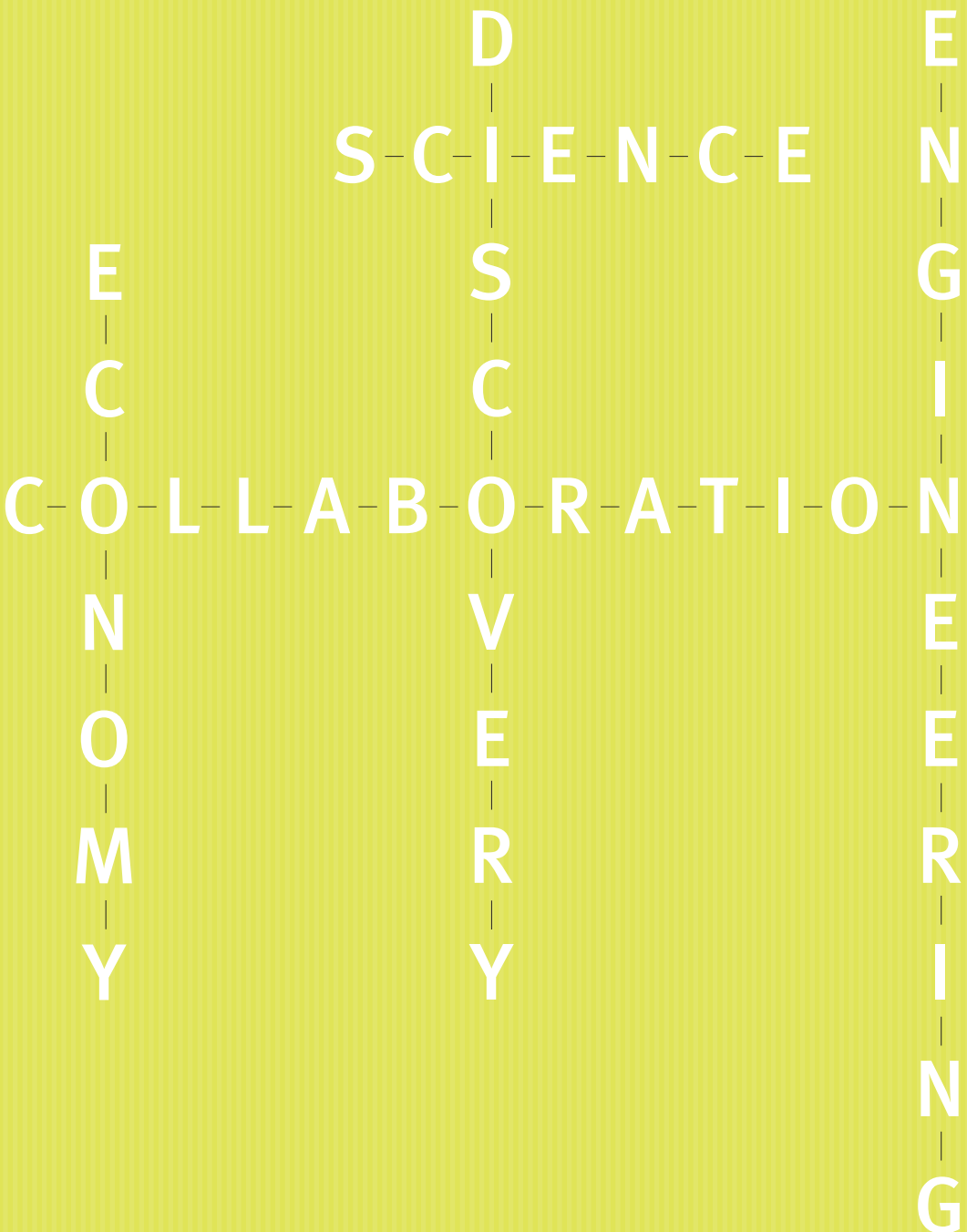
BUILDING STRATEGIC PARTNERSHIPS

California NANOSystems Institute

2005 Annual Research Report



For more information about the
California NanoSystems Institute please visit:
www.cnsi.ucla.edu

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California NANOSystems Institute
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HIGHLIGHTS

118 U.S. patent filings and 5 patents issued

Invited Conferences and Seminars Invited to 16 countries

Over 100 Guest Lectures by world-renowned scientific leaders

Web presence expanded to include resource links and faculty accomplishments

Construction of new facility underway with expected move in date of 2006

91 Invention Disclosures

CNSI membership increased from 32 to 52 within 2005

UCLA

CNSI

THE CNSI MISSION

- Establish a world-renowned center for nanosystems research & development
- Develop commercial applications of CNSI's technology
- Educate the next generation of scholars in nanosystems R&D
- Promote regional development through commercial use of nanotechnology
- Generate public appreciation and undertanding of nanotechnology

FOREWORD

Just as the four letter word NANO has taken on a magic of its very own when it comes to bringing together interdisciplinary teams of the very best researchers and innovators to tackle fundamental issues in academia, with possible technological bents to them, the four letters CNSI, that make of the acronym for the California NanoSystems Institute, are being accepted as being synonymous with one of the world's leading centers in NANO today.

Poised as it is today on the brink of entering its sixth year, the CNSI has made some significant strides towards achieving its goals: it is assisting here in California to nurture the next generation of scientists, engineers and entrepreneurs: it is operating like a magnet in attracting the very best and brightest young researchers by supporting, through industrial collaborations, project-based learning and a systems-oriented approach to the acquisition of new knowledge and practices.

During the past 12 months the CNSI has had the great good fortune to have been served by two far-seeing and hard-grafting associate directors in Carlo Montemagno and Lenny Rome. While Lenny has been focusing his mind on some key strategies for the provision of the essential core facilities to carry out nanosystems-related research that is cutting edge, Carlo has acted as a catalyst to provoke discussion about the future of the CNSI amongst its membership. The outcome of this brainstorming during many weeks and months has been the identification of thrust groups, with their separate advocates, in three topical areas where the institute's expertise is world-class. These three areas are (1) Nanobiotechnology and Biomaterials, (2) Nanoelectronics, Photonics and Architectonics, and (3) Nanomechanical and Nanofluidic Systems. The leaders of these three thrust groups are now intimately involved in vetting the equipment and staffing needs of the CNSI as its permanent home comes ever closer to becoming a reality. The step from virtual to real is one that simply has to involve the entire membership of the CNSI in the decision making process. Like much of NANO, the CNSI must evolve just as much from the bottom-up as it does from the top-down.

The needs and aspirations of the CNSI members are being met now by a highly professional administrative staff led by Susan Rubin in a thoughtful yet caring manner.

What follows in these pages demonstrates the remarkable research that has been accomplished at UCLA by the members of the CNSI working in collaboration with students – both graduate and undergraduate as well as postdoctoral – other universities, and technical organizations in both the private and public sectors.

The CNSI is an enormous asset for the State of California in today's knowledge-based economy where, in the words of Thomas Friedman, "The World is Flat." With the appropriate investment, it can help create jobs, foster economic growth, and promote technological advancements that will improve the quality of life for the people in California and beyond.

J. FRASER STODDART | DIRECTOR OF THE CALIFORNIA NANOSYSTEMS INSTITUTE

LOOKING EXTERNALLY

EXTERNAL AFFAIRS

It's an exciting time at the CNSI. Ongoing faculty collaborations and the construction of the new state-of-the-art facility have considerably increased the CNSI's visibility both nationally and internationally. The CNSI Office of External Relations is actively coordinating strategic partnerships with industry, foundations, and other universities. The next year will be focused on raising funds to help operate and fully outfit the new building.

We have established a number of relationships with major industry corporations and other scientific institutions. These collaborations will serve as the foundation to bring together the brightest researchers from around the world to work with CNSI faculty, graduate students, and postdoctoral scholars. Our weekly NanoSystems Seminar Series and annual International Conference continue to be consistent vehicles for sharing ideas and establishing collaborations. Additionally, as an institute we have been invited to participate in site visits and university conferences in the U.S., Asia, and Europe.

We acknowledge the investments of the federal and state governments in our infrastructure and research. The Office of External Relations will continue to apprise elected officials, agency representatives, and legislative staff of the Institute's achievements. Together with all of our partners, we look forward to working on a long term strategy to ensure that California is the hub for nanoscience research, which will help foster economic growth for the State.

WENDY NISHIKAWA | DIRECTOR OF EXTERNAL AFFAIRS

INTERNATIONAL STRATEGIC ALLIANCES

Many initiatives are in progress to enhance awareness of CNSI worldwide, raising its visibility as an important resource in the pursuit of developments in nanotechnology and nanoscience. Alliances are being cultivated with overseas educational and research institutions, governmental agencies, corporations, entrepreneurs, and investment firms in an effort to increase awareness of CNSI's unique resources.

Utilizing the extensive network of UCLA alumni in Asia and Europe, we are working to build strong relationships with our counterparts at academic and research institutions in those areas. Given UCLA's Pacific Rim location, the growth of Asian-American communities, and California's growing involvement with the economies in Asia, we are developing strong relationships with academic and research institutions in that region. Over the past year CNSI members have given presentations at major universities and research centers in China and Japan. Similar meetings are planned for 2006 and will include institutions in Korea, Taiwan, and Singapore. These contacts will provide invaluable opportunities for collaborative research, student and faculty exchanges, and other related activities.

Our next step involves increasing CNSI contacts with Asian corporations engaged in nano related R&D to discuss opportunities for technology licensing and for sponsored or collaborative research. This reflects the strong commitment of the Institute to the technology transfer process as mandated by the State of California. These contacts will increase in 2006 and will be expanded to include companies in Korea, Taiwan, and Singapore. In the coming year, attention will be extended to building relationships with corporations and academic and research institutions throughout Europe, Canada, and Latin America.

DAVID LUNDBERG | DIRECTOR OF INTERNATIONAL STRATEGIC ALLIANCES

UCLA OFFICE OF INTELLECTUAL PROPERTY ADMINISTRATION

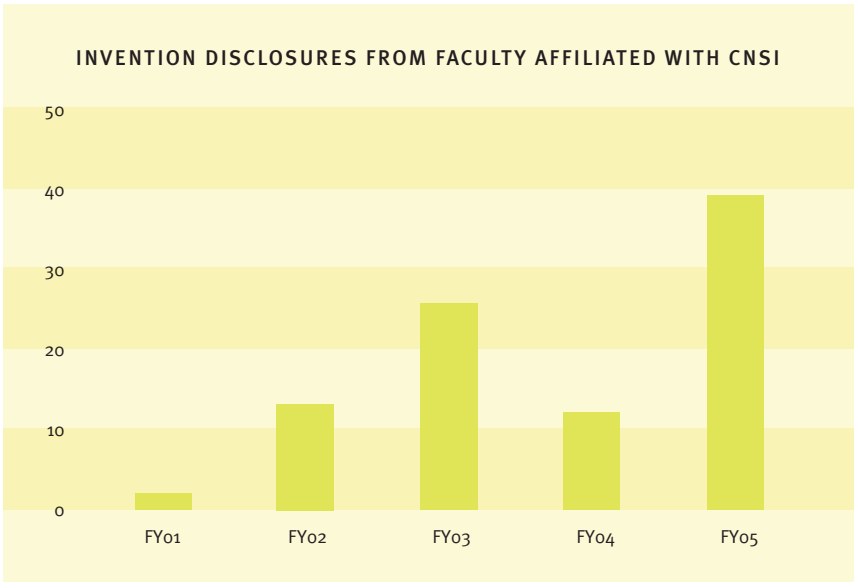
UCLA's Office of Intellectual Property Administration (OIPA) is working with the California NanoSystems Institute (CNSI) faculty to accelerate technology development and new business opportunities developed through the multidisciplinary science integration of physical, materials, information, biomedical, and manufacturing sciences at the nano scale. Intellectual property protection is a key element for the establishment of new business opportunities. OIPA manages the far-ranging intellectual property needs for the campus, including patent applications, incoming and outgoing material transfer agreements and a variety of agreements needed to facilitate the sharing of confidential information such as confidential disclosure agreements, secrecy agreements, and visiting scientist agreements. As commercial partners are identified, we assist with technology transfer through license agreements and sponsored research agreements to allow further development of the research and development. In fiscal year 05 OIPA managed 310 inventions disclosures, filed 215 patent applications, and generated over $19 million in royalty and fee income resulting from the commercialization of faculty IP. This revenue is divided, as spelled out in UC Patent Policy, to faculty inventors, campus departments and the university in general.

OIPA has seen acceleration in the number of invention disclosures from CNSI faculty confirming the vibrancy of the faculty research mission (see accompanying figure). In fiscal year 05 thirty-eight CNSI invention disclosures were received. This represents over a 2X increase versus invention disclosure activity in 2004. Since its inception CNSI inventors have disclosed over 90 inventions. The multidisciplinary science conducted at CNSI is reflected in the nature of the 2005 invention disclosures which range from a revolutionary new Si Raman laser technology to table-top nuclear fusion to stem cell differentiation technology to biochemical synthesis within bubbles!

The interaction between diverse faculty is also reflected in the collaborating inventors data: examples include a new catheter developed by Neurosurgery and Electrical Engineering faculty, a new DNA sequencing tool developed by Pathology and Chemical and Biochemical faculty, and a new fusion technology developed by Physics and Chemical and Biochemical faculty. During Fy05 there were no single inventor disclosures, again confirming the multidisciplinary nature of CNSI science.

OIPA looks forward to continuing to serve the research and technology transfer needs for the faculty of the CNSI through educational programs, office hours and assistance with industry relations. Best of luck for FY 06!

KATHRYN ATCHISON | INTERIM VICE PROVOST OF INTELLECTUAL PROPERTY & INDUSTRIAL RELATIONS



EDUCATION/COMMUNITY OUTREACH

Reaching out to aspiring scientists

SEEING NANO

The challenge of properly educating our future science and technology leaders is in providing a broad-based, thorough educational experience. Since its inception, the California NanoSystems Institute has counted community outreach as a fundamental part of its mission. With a goal toward enriching science education in the Los Angeles public school system through the use of hands-on experiments, the CNSI has developed an outreach program to bring nanoscience and nanotechnology to high school students. Currently, over 35 high school science teachers have been trained by graduate students and postdoctoral researchers on different experiments that can be taught in the classroom, such as the assembly of scanning-tunneling microscopes.

The field of scanning-probe microscopy has revolutionized the way in which we see and interact with nanoscale objects. In probe microscopy, a fine tip is rastered across a surface, and either the movement of the tip, as in atomic force microscopy, or current passing through from the tip to the surface, as in a scanning-tunneling microscope (STM), is used to map out the topography of a surface. The resolution of probe microscopy far exceeds anything possible by light microscopy and is even able to image single atoms.

The goal was to design a STM that is affordable and robust, while, at the same time, simple enough for high-school students to operate and learn topics in the California Science Standards. Such an instrument incorporated into high-school curriculum serves as both a teaching tool and an opportunity for students to engage directly with the tools of nanotechnology. The challenge is both to build a working, affordable device (commercial instruments sell for >$100,000) and develop a curriculum suitable for high-school students.

The CNSI Outreach Program, coordinated by Professor Sarah Tolbert, designed and constructed 14 robust, functioning STMs at a cost of less than $1500 each. In collaboration with Center X in the UCLA Graduate School of Education and Information Sciences, a curriculum was developed to incorporate the objectives of the California Science Standards into the hands-on STM lab for high-school students. In April 2005, 10 of these microscopes were distributed to some of the poorest-performing schools in the Los Angeles Unified School District (Chemical & Engineering News, 2005, 83(28), 36-37), and, with help from volunteers in the CNSI Outreach, high-school students imaged a variety of samples with nanoscale features. Two other microscopes were distributed to UCLA undergraduate teaching laboratories.

The microscopes were capable of resolving features smaller than 100 nm with a resolution limit of 5 nm or less. The samples imaged by high-school students and undergraduates include polyaniline nanofibers, polystyrene nanoparticles and a galena surface. In the case of the polyaniline nanofibers, students were able to determine a mean height of the fibers to be 53 ± 24 nm whereas literature values for the same fibers were 30 – 60 nm demonstrating that the microscopes were analytically accurate. The microscope consists of a mechanical body (Fig.), an electronic feedback controller and a computer controller run on software generously donated by the National Instruments Corporation.

For more information about the Nanoscience Community Outreach Program please visit http://www.cnsi.ucla.edu/education-nano-edu.adp

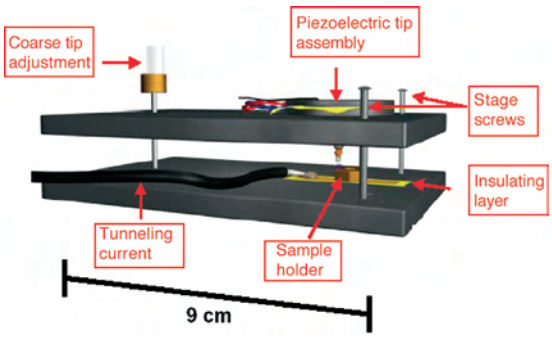


Fig. The imaging stage of the CNSI Outreach scanning-tunneling microscope is shown above. A fine tip is rastered across a small sample. Changes in current between the sample and tip are used to make a topographical map of the sample surface.

VENTURING BEYOND THE CLASSROOM

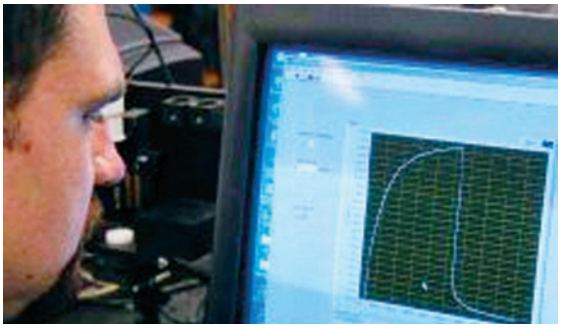
It is the aim of the CNSI to educate an elite cadre of broadly-educated engineers and scientists in nanosystems-related research by fostering an environment in which student-driven collaborative research projects flourish.

An important educational wing of the CNSI is the Materials Creation Training Program (MCTP), a National Science Foundation supported Integrative Graduate Education and Research Traineeships (IGERT) supported by the Exotic Materials Institute at UCLA. Under the direction of Fred Wudl, the MCTP is training the next generation of scientists and engineers in the synthesis and characterization of new materials, including nanoscale ones, and in the design, fabrication and characterization of electronic and photonic devices based on these materials. In addition to completing a normal PhD program in their discipline, MCTP students also participate in activities that (1) provide a cross-disciplinary foundation in language, methods, intellectual problems and technical challenges in materials science and engineering, (2) offer an integrated laboratory experience in materials synthesis, characterization and fabrication, (3) provide experience in team-building, (4) establish student-driven collaborations, and (5) train students in issues that reach out beyond the laboratory, such as intellectual property, ethics, patenting, entrepreneurship, and start-up companies.

The MCTP program involves a variety of information forums designed to foster a basic goal of discovery, design, synthesis, and characterization of a new material, device fabrication, and even planning aspects of commercialization including interdisciplinary lectures from scientists, engineers, business people and outside experts such as a patent attorney.

The MCTP-IGERT and the California NanoSystems Institute have proven exceptionally effective in recruiting top students.

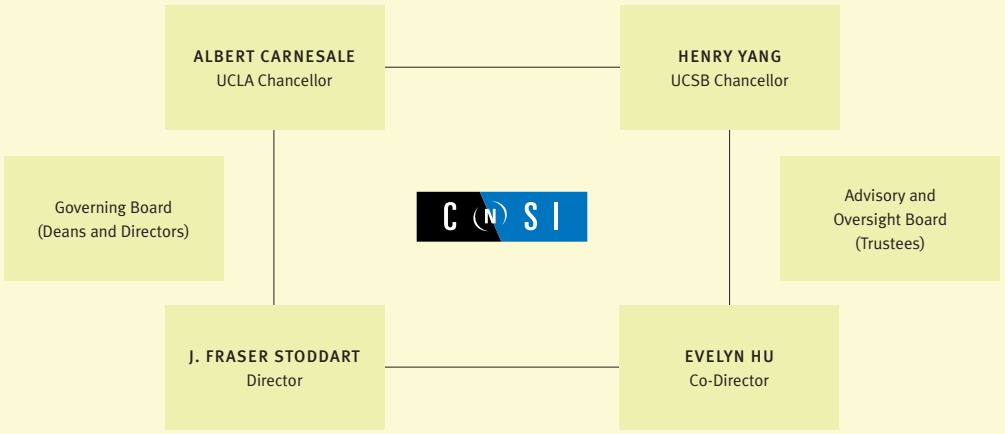
For more information about the specific experiments being taught please visit http://voh.chem.ucla.edu/outreach.php3.



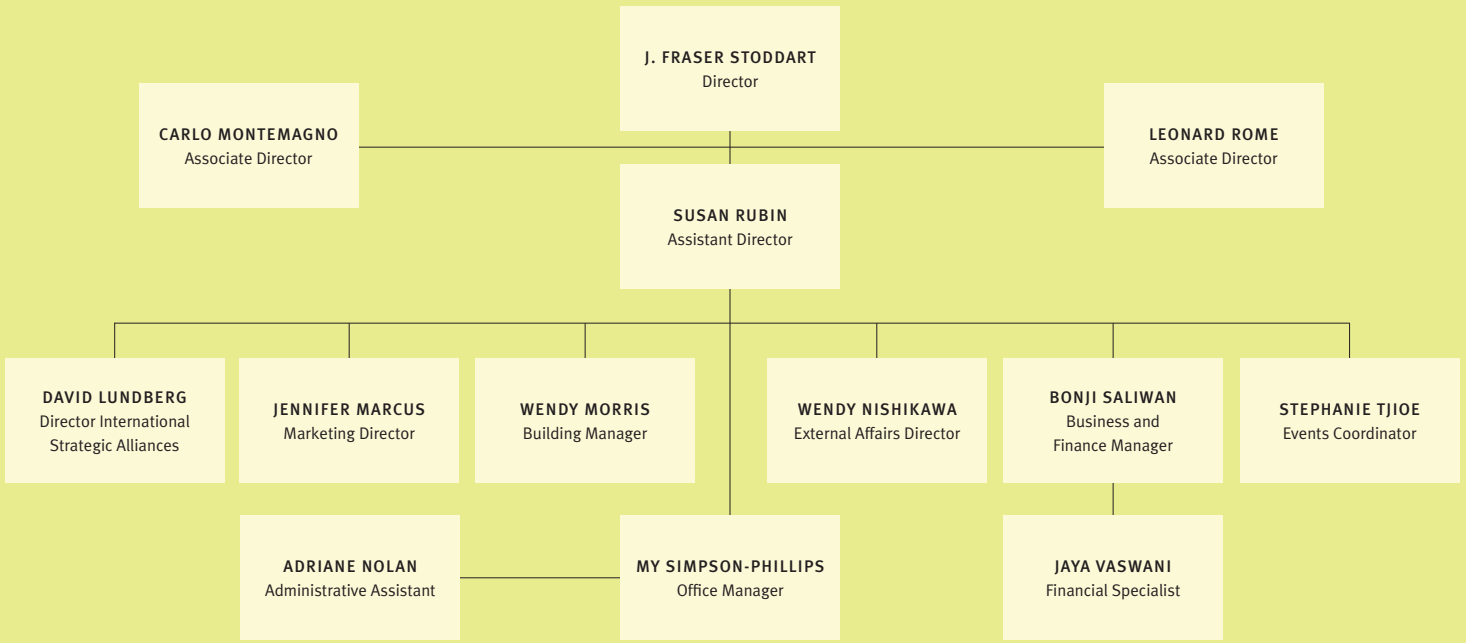
"This is not the stuff you would ordinarily do as a regular organic chemistry student. Internships offer students the chance to leave the academic world to see what national labs or R&D firms can do."

— BRIAN NORTHROP, MCTP TRAINEE

ORGANIZATIONAL CHARTS



CNSI/UCLA ADMINISTRATION



CNSI BOARD MEMBERS

ADVISORY AND OVERSIGHT BOARD

Derek Cheung	Rockwell Scientific Company (Thousand Oaks) President & CEO
Roy Doumani	Entrepreneur (Los Angeles)
Paolo Gargini	Intel Corporation (Santa Clara) Director, Technology Strategy
Jim Heath	California Institute of Technology (Pasadena) Professor of Chemistry
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Peter Preuss	Preuss Foundation (La Jolla) President UC Regent
Ralph Shapiro	Avondale Investment Company (Los Angeles) Chairman
Stan Williams	Hewlett-Packard (Palo Alto) Director, Quantum Research

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Michael Witherell	Vice Chair for Research UCSB)
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Emil Reisler	Dean, Life Sciences (UCLA)
Lenny Rome	Senior Associate Dean for Research, School of Medicine (UCLA)
Matt Tirrell	Dean, College of Engineering (UCSB)

THRUST GROUPS

NanoBiotechnology & Biomaterials

GROUP LEADERS

Kenneth Bradley
Fuyu Tamanoi

Linda Baum
Yong Chen
Bruce Dunn
David Eisenberg
Robin Garrell
Jim Gimzewski
Chih-Ming Ho
Jack Judy
C.J. Kim
James Liao
Heather Maynard
John Miao
Jeff Miller
Carlo Montemagno
Andre Nel
Mike Phelps
Leonard Rome
Jacob Schmidt
Fraser Stoddart
Ren Sun
Mike Teitell
Kang Wang
Shimon Weiss
Owen Witte
Fred Wudl
Todd Yeates

NanoElectronics, Photonics, Architectonics

GROUP LEADERS

Hong-Wen Jiang
Kang Wang

Russ Caflisch
Yong Chen
Jim Gimzewski
George Gruner
Richard Kaner
Vidvuds Ozolins
Benjamin Schwartz
Fraser Stoddart
Sarah Tolbert
Fred Wudl
Eli Yablonovitch

NanoMechanical & Nanofluidic Systems

GROUP LEADER

Jack Judy

Russ Caflisch
Linda Demer
Miguel Garcia-Garibay
Jim Gimzewski
C.J. Kim
Carlo Montemagno
Vidvuds Ozolins
Seth Putterman
Fraser Stoddart
Mike Teitell
Sarah Tolbert
Fred Wudl
Jeffrey Zink

L-E-A-D-E-R-S-H-I-P

V-I-S-I-O-N

"If I have seen further it is by standing on the shoulders of giants."

— ISAAC NEWTON

Linda G. Baum

Professor of Pathology and Laboratory Medicine
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RESEARCH

Many biologic and disease processes are governed by carbohydrate-protein mediated cell-cell interactions. We examine these processes in the immune system, investigating the interaction of lymphoid cells with stromal cells, antigen presenting cells and tumor cells. Our goal is to understand mechanisms controlling cellular glycosylation and the roles of cellular glycans in lymphocyte development, defense against microbes and tumor cells, and cellular transformation. We focus on a family of lectins, the galectins, that participate in all these cellular processes.

The outcome of galectin binding to lymphocytes depends on expression of specific glycan ligands on specific cell surface glycoproteins and the organization of the glycoproteins into discreet domains or lattices on the cell surface. The components of the lattice, the spacing of glycoproteins in the lattice and the separation of different glycoproteins into distinct lattices on the cell membrane all contribute to the outcome of galectin binding. We collaborate with CNSI members to use novel tools to examine the architecture of the lectin-glycoprotein lattices, by manipulating cellular glycosylation, examining binding to artificial ligands, and creating synthetic galectins that vary in ligand specificity and binding domain spacing and flexibility, to understand structural features of galectins that deliver specific cellular signals.

SELECTED PUBLICATIONS

Hahn, H.P., Pang, M., He, J., Hernandez, J.D., Yang, R-Y, Li, L.Y., Wang, X., Liu, F-T, Baum, L.G. (2004) Nuclear translocation of Endonuclease G in caspase- and cytochrome c-independent galectin-1 induced T cell death. *Cell Death and Differentiation* 11:1277-86.

Nelson, A., Belitsky, J.M., Vidal, S., Joiner, C.S., Baum, L.G.*, Stoddart, J.F.* (2004) A self-assembled multivalent pseudopolyrotaxane for binding galectin-1. *Journal of the American Chemical Society* 126:11914-22 (*contributing authors).

He, J. and Baum, L.G. (2004) Presentation of galectin-1 by extracellular matrix triggers T cell death. *Journal of Biological Chemistry* 279:4705-4712.

HONORS AND AWARDS

2004, President-Elect (2006), Society for Glycobiology

PROFESSIONAL AFFILIATIONS

American Association of Immunologists, American Society for Biochemistry and Molecular Biology, Society for Glycobiology

KEYWORDS

cellular glycosylation, glycoprotein-lectin interactions, glycoimmunology, cell death

Ken Bradley

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Microbiology, Immunology & Molecular Genetics
Director, Molecular Screening Shared Resource
Ph.D., Microbiology and Molecular Genetics, 2002,
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RESEARCH INTERESTS

The Bradley lab is interested in i) identifying host proteins that are usurped by bacterial pathogens and ii) understanding how these interactions promote virulence. Specifically, we are studying protein exotoxins produced by *Bacillus anthracis* (the causative agent of anthrax), *Campylobacter jejuni* (the most common cause of bacterial diarrhea in the U.S.), *Vibrio cholera* (the causative agent of cholera), and *Clostridium deficile* (responsible for most hospital-acquired diarrhea). To better understand these interactions, our lab utilizes a number approaches including i) proteomics, ii) chemical genetics and iii) somatic cell genetics. We are also interested in developing therapeutics and detection systems for bacterial pathogens based on nanotechnology. To this end, we collaborate with a number of labs at UCLA and nationwide.

SELECTED PUBLICATIONS

Scobie, H.M., Rainey, G.J.A., Bradley, K.A., Young, J.A.T. (2003) Human capillary morphogenesis protein 2 functions as an anthrax toxin receptor. *PNAS,* 100(9); 5170-5174.

Bradley, K.A., Mogridge, J., Rainey, G.J.A., Batty, S., Young, J.A.T. (2003) Binding of anthrax toxin to its receptor is similar to alpha integrin-ligand interactions. *J. Biol. Chem.* 278(49) 49342-7.

Banks, D.J., Barnajian, M., Maldonado-Arocho, F.J., Sanchez, A.M., and Bradley, K.A. (2005) Anthrax toxin receptor 2 mediates Bacillus anthracis killing of macrophages following spore challenge. *Cellular Microbiol* 7(8): 1173-85.

PROFESSIONAL AFFILIATIONS

American Society of Microbiology

RESEARCH KEYWORDS

anthrax, toxin, receptor, somatic cell genetic

Russel E. Caflisch

Professor
Mathematics Department
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AREAS OF INTEREST

Modeling, analysis and simulation for epitaxial growth of thin films and for strain in epitaxial systems. Simulation, design and optimization of quantum structures for quantum devices.

RESEARCH

Professor Caflisch and his research group work on modeling, analysis and simulation for applications in nanotechnology, materials science, fluid mechanics and other fields. Specific projects include (1) Stranski-Krastonov growth of self-assembly and directed self-assembly of quantum dots, (2) design and optimization of material structures for quantum computing devices, (3) stability and structure of strained nanoscale crystals and wires, (4) singularity formation in incompressible flow, (5) hybrid numerical methods for plasma dynamics, and (6) simulation and optimal design of plasmon waveguides and electrodeposition shapes. This work often requires development of new numerical methods and analysis of the mathematical properties of models from materials physics, including multiscale and stochastic methods. Numerical methods developed by this group include a level set method for epitaxial growth, a multiscale method for atomistic strain, and accelerated Monte Carlo methods for integration and optimization. The research group is multidisciplinary, including mathematics, physics and material science. The group collaborates with researchers in industry, government labs and academia from many different disciplines.

SELECTED PUBLICATIONS

R. E. Caflisch, C. Anderson, M. Gyure, H. Robinson and E. Yablonovitch. "Modeling, Design and Optimization of a Solid State Qubit" SIAM *J. Appl. Math.* 65 (2005) 1285-1304.

R. Vardavas, C. Ratsch and R.E. Caflisch. "Submonolayer growth in the presence of defect sites" *Surface Science* 569 (2004) 185-192.

HONORS AND AWARDS

2006: Invited speaker, International Congress of Math., Madrid. Plenary speaker. European Consortium for Math. in Industry, Madrid.

PROFESSIONAL AFFILIATIONS

American Mathematical Society, Society for Industrial and Applied Mathematics, American Physical Society, Materials Research Society.

RESEARCH KEYWORDS

epitaxy, simulation, kinetic Monte Carlo, level set methods, island dynamics

Yong Chen

Professor
Departments of Mechanical and Aerospace Engineering; Materials Science and Engineering
Ph.D., Materials Sci. & Eng., 1996, University of California, Berkeley
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RESEARCH INTERESTS

Dr. Yong Chen is a joint Professor of California NanoSystems Institute, Mechanical and Aerospace Engineering, and Materials Science and Engineering at UCLA. His current research focuses on nanofabrication technologies, integrated nano device and circuit, and nanoscale biological and medical sensors. Before he joined UCLA, he worked as a Scientist, a Senior Scientist, and a Master Scientist in Quantum Science Research, in Hewlett-Packard Laboratories from 1996 to 2003. The research group led by him in HP demonstrated the world's highest density (40Gbits/inch2) electronic memory circuits in 2003 and the first nanoscale de/multiplexer for electric circuits. His thesis research focused on optoelectronic materials, especially on self-organized semiconductor quantum dots.

SELECTED PUBLICATIONS

D. Ho and Y. Chen, Interfacing cellular systems with abiotic materials using composite collagen-block copolymer thin films, The first international conf. on bio-nano-information fusion, Marina del Ray, CA, July, 2005.

Z. Li, Y. Chen, X. Li, T. I. Kamins, K. Nauka, and R. S. Williams, "Sequence-specific label-free DNA sensors based on silicon nanowires", *Nano Lett.*, 4, 245 (2004).

G. Y. Jung, S. Ganapathiappan, Douglas A. A. Ohlberg, Deirdre L. Olynick, Y. Chen, William M. Tong, and R. Stanley Williams, Fabrication of a 34x34 crossbar structure at 50 nm half-pitch by UV-based nanoimprint lithography, *Nano Lett.* 1225 (2004).

Y. Chen, G. Jung, D. A. A. Ohlberg, X. Li, D. Stewart, J. O. Jeppesen, K. A. Nielsen, J. F. Stoddart, and R. S. Williams, "Nanoscale molecular-switch crossbar circuits", *Nanotechnology,* 14, 462 (2003).

Y. Chen, D. A. A. Ohlberg, X. Li, D. Stewart, and R. S. Williams, "Nanoscale molecular-switch devices fabricated by imprint lithography", *Appl. Phys. Lett.* 82, 1610 (2003).

PROFESSIONAL AFFILIATIONS

Member of MRS, IEEE, APS, ACS

RESEARCH KEYWORDS

nanofabrication, nanoelectronics, nanolithography, nanosensor, nanocircuits

Linda L. Demer

Vice Chair, Department of Medicine, UCLA School of Medicine
Professor of Medicine, Physiology, and Bioengineering, UCLA
Co-Director, UCLA Specialty Training and Advanced Research (STAR) Program
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RESEARCH INTERESTS

In embryogenesis, immature mesenchymal cells aggregate and organize into patterned tissues. Later in life, a pathological recapitulation of this process takes place in atherosclerotic lesions, when vascular mesenchymal cells organize into trabecular bone, cartilage and fat tissue within the artery wall. In our laboratory, we developed a tissue culture model for this process, and demonstrated that the ectopic tissue is formed by mesenchymal stem cells present in the artery wall that undergo abnormal lineage acquisition. We further showed that these cells self-organize in vitro into patterns that are predicted by a mathematical model based on molecular morphogens interacting in a reaction-diffusion process governed by partial differential equations. We identified the activator and inhibitor morphogens as bone morphogenetic protein and its inhibitor, matrix GLA protein (MGP). We confirmed the mathematical model predictions in culture, showing that addition of MGP alters the pattern from stripes to spots and showing that addition of warfarin, which inhibits MGP, creates a doubling of stripe density. Thus, reaction-diffusion principles may play a significant role in pathological morphogenetic processes in the adult. We are now growing these stem cells on carbon nanotubes to attempt to modulate and refine the pattern formation for future potential use in tissue reconstruction.

SELECTED PUBLICATIONS

Radcliff, K., *et al.,* Insulin-like growth factor-I regulates proliferation and osteoblastic differentiation of calcifying vascular cells via extracellular signal-regulated protein kinase and phosphatidylinositol 3-kinase pathways. *Circ Res* 2005;96:398-400.

Garfinkel, A., Tintut, Y., Demer, L.L., Pattern formation by vascular mesenchymal cells. *Proc Natl Acad Sci USA* 2004;101:9247-50.

Hsiai, TK, *et al.,* Micro sensors: Linking real-time oscillatory shear stress with vascular inflammatory responses. *Ann Biomed Eng* 2004;32:189-201.

Tintut Y, *et al.,* Multilineage potential of cells from the artery wall. Circulation 2003:108:2505-10.

HONORS AND AWARDS

AHA Jeffrey M. Hoeg Award for Basic Science and Clinical Research; Franklin D. Murphy, M.D., Prize for Research; Davidson Memorial Endowed Lectureship, Royal College of Physicians of Edinburgh; Stein / Oppenheimer Award for Biomedical Research.

AREAS OF INTEREST

vascular biology, biomineralization, adult stem cells

Bruce Dunn

Professor and Nippon Sheet Glass Company Chair in Materials Science and Engineering
Department of Materials Science and Engineering
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bdunn@ucla.edu

RESEARCH

Our research involves the synthesis of inorganic and hybrid organic-inorganic materials and characterization of their electrical, electrochemical and optical properties. One of our principal themes is the use of sol-gel methods to synthesize a number of the materials studied in the group. This synthetic approach enables us to prepare materials which incorporate a wide variety of organic and biological dopants and are capable of developing unique microstructures and properties.

The research areas currently being investigated include (1) Electrochemical materials where we are investigating the electrochemical properties of materials with designed chemistry and microstructure; (2) Mesostructured materials based on the self-assembly processes which occur upon addition of surfactants to sol-gel materials; (3) Bio-hybrid materials in which biomolecules are encapsulated within sol-gel derived inorganic matrices; (4) Biomolecular materials where we try to exploit biological structures for engineering applications. We also demonstrate the utility of these materials in various device applications. Among the topics being investigated are three-dimensional batteries, biological fuel cells, bio-sensors, nanodimensional biochemical reactors and nanowire arrays.

SELECTED PUBLICATIONS

V.A. Kickhoefer, Y. Garcia, Y. Mikyas, E. Johansson, J.C. Zhou, S. Raval-Fernandes, P. Minoofar, J.I. Zink, B. Dunn, P.L. Stewart and L.H. Rome, "Engineering of Vault Nanocapsules with Enzymatic and Fluorescent Properties", *Proc. Nat. Acad. Sci.* 102, 4348 (2005).

T-J. M. Luo, *et al.,* "Photo-Induced Proton Gradients and ATP Biosynthesis Produced by Vesicles Encapsulated in a Silica Matrix", *Nature Materials* 4, 220 (2005).

D. Sun, *et al.,* "The Relationship Between Nanoscale Structure and Electrochemical Properties of Vanadium Oxide Nanorolls", *Advanced Functional Materials* 14, 1197 (2004).

J.W. Long, *et al.,* "Three-Dimensional Battery Architectures", *Chem. Rev.* 104, 4463 (2004).

P.E. Tang, *et al.,* "V2O5 Aerogel as a Versatile Host for Metal Ions", *J. Non-Cryst. Solids,* 350, 67 (2004).

PROFESSIONAL AFFILIATIONS

American Ceramic Society (Fellow), Materials Research Society, Electrochemical Society

RESEARCH KEYWORDS

sol-gel materials, biomolecule encapsulation, electrochemical properties, aerogels, mesoporous materials.

David Eisenberg

Director, UCLA-DOE, Institute for Genomics and Proteomics
Professor of Chemistry & Biochemistry
Professor of Biological Chemistry
Ph.D., Theoretical Chemistry, 1964, Oxford University
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RESEARCH INTERESTS

Our long term goal is to understand and manipulate the metabolism of cells through the interactions of their constituent proteins. One goal is to be able to infer functional linkages of proteins, on the basis of genome sequences and protein expression data. Computational methods have been developed for establishing these relationships, including the phylogenetic profile and Rosetta Stone methods. To benchmark these computational methods, a large Database of Interacting Proteins has been built up. X-ray crystallography remains a powerful tool for exploring protein structure and interactions. Our X-ray projects are of two types. The first are on amyloids and prions, pathologically interacting proteins. The goal is to understand the structures that underlie the pathologies. The other projects are on the structural biology of Mycobacterium tuberculosis, as part of the TB Structural Genomics Consortium.

SELECTED PUBLICATIONS

"Cross-beta Order and Diversity in Nanocrystals of an Amyloid-forming Peptide", Ruben Diaz Avalos, Chris Long, Eric Fontano, Melinda Balbirnie, Robert Grothe, David Eisenberg, and Donald L. D. Caspar, *J. Mol. Biol.,* 330, 1165-1175, (2003).

"*In Silico* simulation of biological network dynamics" Lukasz Salwinski and David Eisenberg, *Nature Biotechnology,* 22, 1017-1019, (2004).

"Use of Logic Relationships to Decipher Protein Network Organization" Peter Bowers, Shawn Cokus, David Eisenberg, Todd Yeates, *Science,* 306, 2246-2249, (2004).

"Structure of the cross- β spine of amyloid-like fibrils" Rebecca Nelson, Michael Sawaya, Melinda Balbirnie, Robert Grothe, Anders Madsen, Christian Riekel, David Eisenberg, *Nature,* 435, 773-338, (2005).

"Amyloid-like Fibrils of Ribonuclease A with a 3D Domain-Swapped, Native-like Structure", Shilpa Sambashivan, Yanshun Liu, Michael Sawaya, Mari Gingery, David Eisenberg, *Nature,* in press.

HONORS AND AWARDS

Howard Hughes Medical Institute, Investigator, 2001 - present
National Academy of Sciences, 1989

RESEARCH KEYWORDS

protein design, amyloids & prions, protein interactions

Miguel Garcia-Garibay

Professor
Department of Chemistry and Biochemistry
Ph.D., Chemistry, 1988, University of British Columbia
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AREAS OF INTEREST

Solid-state organic chemistry and molecular nanocrystals, photochemistry and spectroscopy, solid-state reaction mechanisms, dipolar lattices and molecular machines.

RESEARCH

The Garcia-Garibay research group is dedicated to the study of solids and crystalline materials spanning a wide range of properties and length scales. There are four main research thrusts in the group" (I) The design of reactions in crystals for both synthetic and materials applications; (II) The design of solid state materials with functions that rely on controlled mechanical changes at the molecular level, including electrooptics, ferroelectrics, etc. (III) The use of nanoparticles to control photochemical processes, and (IV) the study of structure-reactivity correlations based on solid state reaction rates and X-Ray structural analyses, including the control of reactive intermediates and a better understanding of quantum mechanical tunneling.

SELECTED PUBLICATIONS

Garcia-Garibay, Miguel A. "Crystalline molecular machines: Encoding supramolecular dynamics into molecular structure" *Proc. Natl. Acad. of Sci.* 2005, 102,10771-10776 (feature article).

Warrier, Manoj; Lo, Michael K.F.; Monbouquette, Harold; Garcia-Garibay, Miguel A. "Photocatalytic Reduction of Aromatic Azides to Amines using CdS and CdSe Nanoparticles" Photochem. *Photobiol. Sci.,* 2004, 3, 859-863.

Horansky, R. D.; Clarke, L. I.; Price, J. C.; Khuong, T.-A.V.; Jarowski, P D.; Garcia-Garibay, M.A. "Dielectric Response of a Dipolar Molecular Rotor Crystal" *Phys. Rev. B.,* 2005, 72_ 014302.

AWARDS

Faculty Development Award, University of California, Los Angeles, 1995; NSF Career Award 1996; Dean's Marshal Award for the Division of Physical Sciences, UCLA, 1997; Herbert Newby McCoy Award, UCLA, 1999.

PROFESSIONAL AFFILIATIONS

The American Chemical Society,
The American Association for the Advancement of Science,
The Inter American Photochemical Society.

Robin L. Garrell

Professor of Chemistry and Biochemistry and
Member of the Biomedical Engineering Interdepartmental Program Faculty
Ph.D., Macromolecular Science & Engineering, 1984, University of Michigan
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RESEARCH INTERESTS

Professor Garrell's team develops new methods for characterizing and utilizing molecules and molecular assemblies at liquid-solid interfaces. Techniques they have pioneered include surface-enhanced Raman spectroscopy (SERS) for determining molecular orientations and conformations at metal surfaces, the quartz crystal microbalance to detect phase transitions and viscosity in thin films, and g-factor spectroscopy as a rapid probe of protein secondary structure. Quantum mechanical calculations provide further insights into the surface and intermolecular interactions of molecules in self-assembled monolayers. Garrell's team correlates the molecular structures of self-assembled monolayers and thin films with the resulting macroscopic adhesion and wetting behaviors. These interfacial phenomena are being exploited in the design and fabrication of droplet-based "digital" microfluidic devices for biosensors, proteomics and drug discovery. Digital microfluidic devices are reconfigurable, can be used to perform many identical or unique (bio)chemical manipulations simultaneously, and may incorporate optical, electrochemical and/or impedance detection.

SELECTED PUBLICATIONS

Yoon, J.-Y.; Kim, C.-J.; Garrell, R. L. "Preventing Biomolecular Adsorption in Electrowetting-Based Biofluidic Chips," *Anal. Chem.,* 75 (2003) 5097-5102.

Huang, J., *et al.,* "Enantioselective Discrimination of d- and l-Phenylalanine by Chiral Polyaniline Films," *Adv. Mater.,* 15 (2003) 1158-1161.

Wheeler, A.R., *et al.,* "Electrowetting-Based Microfluidics for Analysis of Peptides and Proteins by Matrix Assisted Laser Desorption/Ionization Mass Spectrometry (MALDI-MS)," *Anal. Chem.,* 76 (2004) 4833-4838.

Wheeler, A.R., *et al.,* "Digital Microfluidics with In-line Sample Purification for Proteomics Analyses with MALDI-MS," *Anal. Chem.,* 77 (2005) 534-540.

Yoon, J.-Y., *et al.,* "Using a Stirred Cell to Evaluate Conformational Changes in Proteins Adsorbed on Particles," *AIChE Journal,* 51 (2005) 1048-1052.

PROFESSIONAL AFFILIATIONS

American Association for the Advancement of Science (AAAS), elected fellow, American Chemical Society, Coblentz Society, International Society of Quantum Biology & Pharmacology, Iota Sigma Pi, Society for Applied Spectroscopy (President, 1999)

RESEARCH KEYWORDS

surface and interface chemistry, microfluidics, proteomics, vibrational spectroscopy, adhesion.

Jim Gimzewski

Professor
Department of Chemistry & Biochemistry, Institute for Cell Mimetic Space Exploration (CMISE)
Ph.D., Physical Chemistry, 1977, University of Strathclyde, Glasgow, Scotland
gim@chem.ucla.edu

RESEARCH

Professor Gimzewski's Pico Lab is concerned with developing a nanosystems approach to radical shifts in technology. The projects themselves stem from the ability to image and manipulate matter all the way up from the atomic scale. Pico Lab is equipped with state of the art techniques that enable atoms and molecules to be studied and manipulated in environments that vary for extreme vacuum at cryogenic temperatures. Nanomechanics is a new area of science that has evolved in the last ten years. It is concerned with the mechanics of systems with components or motions on the scale of the nanometer. Mechanical processes appear in most living systems and much of the research work has expanded from molecular systems to cell based or whole animal investigations. These latest studies are aimed at medical diagnostics, stem cell research and biosensor related applications. Biological systems also form the focus of bio-inspired materials and devices in which cellular systems are being used as models for the design of new paradigms in engineering.

Gimzewski embraces the convergence of all disciplines to develop a new form of thinking necessary for Nanotechnology to have a global societal and economic benefit within the next 10 years. This convergence goes beyond Science, Medicine and Engineering, and embraces the Arts as an essential part of the process.

SELECTED PUBLICATIONS

"Observation of nuclear fusion driven by a pyroelectric crystal," B. Naranjo, J. K. Gimzewski and S. Putterman. *Nature,* 434, 1115-1117 (2005).

"Nanoscale visualization and characterization of Myxococcus xanthus cells with atomic force microscopy," A. E. Pelling, Y. Li, W. Shi, and J. K. Gimzewski. Proceedings of the National Academy of Sciences, 102, 6484-6489 (2005).

"Local Nanomechanical Motion of the Cell Wall of Saccharomyces cerevisiae," A. E. Pelling, S.Sehati, E. B. Gralla, J. S. Valentine, and J. K. Gimzewski. *Science,* 305, 1147-1150 (2004).

PROFESSIONAL AFFILIATIONS

International Society for Nanoscale Science, Computation and Engineering; Elected Fellow of the World Innovation Foundation; Elected Fellow Royal Academy of Engineering, London, United Kingdom (FREng); Elected Fellow of the Institute of Physics (FinstP), London, UK

RESEARCH KEYWORDS

nanotechnology, nanomechanics, nanomedicine, nuclear fusion, cell sonics

George Gruner

Distinguished Professor
Department of Physics
Ph.D., Eotvos Lorand University, Budapest, Hungary
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AREAS OF INTEREST

Professor Gruner's primary interests include the fabrication, investigation and application of nanoscale electronic materials and devices. The materials architectures include a network of nanoscale wires such as carbon nanotubes and polymeric nanofibers. Active electronic devices such as nano-scale transistors can also be fabricated using such networks. The research involves the exploration of the fundamental electronic properties of the material architectures involved, and of device oriented physical measurements. Large-scale fabrication avenues are also explored by the group. Merging electronics with biology is also part of the program pursued by the Gruner group. Size compatibility between devices and biological species, together with the charged nature of biomolecules lie behind such bio-electronics approach. The devices can be combined with a variety of species, thus giving the structures specific chemical or bio-functionality. Fabrication of elements of an artificial sensory system – converting a chem/bio presence into an electronic signal, together with the design and investigation of cell-device interfaces is currently also pursued.

RESEARCH INTERESTS

Nano-bio-electronics. Fabrication, and exploration of nanoscale material architectures. Integration of biological systems and electronic devices. Applications in emerging technology areas, such as plastic electronics, printed photo-voltaics, and disposable biosensors.

SELECTED PUBLICATIONS

Bradley, Gabriel, J.-C. P., Briman, M., Star, A., Grüner, G., "Charge Transfer from Ammonia Physisorbed on Nanotubes", *Phys. Rev. Lett.* 91, 218301 (2003).

N.P. Armitage, M. Briman, G. Gruner, "Charge Transfer and Charge Transport on the Double Helix", *Phys. Stat. Sol.* 241, 69-75 (2004).

A. Star, V. Joshi, T.-R. Han, M. V. P. Altoé, G. Grüner, J. F. Stoddart, "The electronic detection of the enzymatic degradation of starch", *Org. Lett.* 6, 2089 – 2092.

Keith Bradley, Alona Davis, Jean-Christophe P. Gabriel, and G. Grüner, "Integration of Cell Membranes and Nanotube Transistors", *Nano Lett.* 5, 841-845 (2005).

E. Artukovic, M. Kaempgen, D. S. Hecht, S. Roth, G. Grüner, "Transparent and Flexible Carbon Nanotube Transistors", *Nano Lett.* 5. 757-760 (2005).

Chih-Ming Ho

Ben Rich-Lockheed Martin Professor
Mechanical & Aerospace Engineering
Ph.D., 1976, The Johns Hopkins University
chihming@seas.ucla.edu

RESEARCH INTERESTS

Our interests lie in controlling the position of macromolecules, DNA/RNA, proteins and supermolecules for facilitating function processes such as molecular recognition, biochemical reactions and self assembly. As these processes always take place in fluid flows, a key goal is the creation of nano-fluidic technologies to handle nanoscale molecules in microscale reactors. We recognize that a fundamental understanding of the interactions between intermolecular force fields and global forces provides the path for developing efficient nano-fluidic technologies. Ultimately, nano-fluidics forms the backbone for a wide spectrum of bio-nano application such as genosensing, drug discovery and health maintenance.

HONORS AND AWARDS

K.T. Lee Honorary Professor
Kuo-Nien Honorary Chair Professor of National Tsinghua University
Honorary Professor of Institute of Mechanics, Chinese Academy of Sciences
Science Advisor for LNM of Institute of Mechanics, China
Honorary Professor of Nanjing University of Aeronautics and Astronautics, China

PROFESSIONAL AFFILIATIONS

Member	(1997)	National Academy of Engineering
Member	(1998)	Academia Sinica
Fellow	(1994)	American Institute of Aeronautics and Astronautics
Fellow	(1989)	American Physical Society

Eric M.V. Hoek

Assistant Professor and HSSEAS Fellow
Civil & Environmental Engineering Department
Henry Samueli School of Engineering and Applied Science
Ph.D., Environmental/Chemical Engineering, 2002,
Yale University
hoek@seas.ucla.edu
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AREAS OF INTEREST

Dr. Hoek's "Nanotechnology & Water Research Group" conducts research in three main areas: environmental nanotechnology, physicochemical processes, and surface fouling phenomena.

RESEARCH

Environmental nanotechnology presently encompasses two major areas of research: synthesis and characterization of nanomaterials for use in environmental systems, and understanding of the colloidal properties (stability, transport, and adhesion) of nanomaterials in the natural environment. We have filed a patent and founded NanoH2O, LLC in an effort to commercialize a new class of inorganic-organic thin film nanocomposite membranes made from standard membrane polymers and antimicrobial nanoparticles.

Physicochemical processes are at the heart of nearly all water production processes, desalination, and wastewater reclamation. Our current research comprises three areas: pressure driven membrane processes, electrochemical processes, and hybrid membrane processes. We recently have initiated research on a new hybrid membrane process for water purification capable of simultaneous oxidation, clarification, disinfection, and hydrogen production in a single unit operation.

Surface fouling phenomena plague many biological, environmental, and chemical engineering systems such as medical implants, environmental sensors, and membrane processes. Understanding and controlling surface fouling in aquatic systems requires knowledge of colloid and surface chemistry, interfacial phenomena, and fluid mechanics. We currently are using direct microscopic observation to understand and control microbial cell adhesion to membranes.

SELECTED PUBLICATIONS

"Thin Film Nanocomposite Membranes: The Next Generation of Reverse Osmosis Membranes," *J. Membrane Sci.* 2005, in preparation "Predicting Flux Decline due to Interacting Nanoparticles in Crossflow Membrane Filtration," *J. Colloid Interf. Sci.* 2005, submitted "Direct Observation of Biofouling in Cross-flow Microfiltration," *J. Membrane Sci.* 2004, 244, 151-165 "Effect of Surface Roughness on Colloid-Membrane DLVO Interactions," *Langmuir* 2003, 19, 4836-4847.

HONORS AND AWARDS

2005/2004/2003: North American Membrane Society Outstanding Student Paper Award (as co-author with students)
2002: CH2M Hill/AEESP Doctoral Dissertation Award.

Bahram Jalali

Professor
Department of Electrical Engineering, UCLA
Ph.D., Applied Physics, 1989, Columbia University
Jalali@ee.ucla.edu
www.ee.ucla.edu/~oecs/

RESEARCH INTERESTS

The Optoelectronic Circuits and Systems Laboratory at UCLA performs multi-disciplinary research and development in the fields of communication and sensing. The Lab has two complementary missions. The first is to solve critical problems faced by Defense and Commercial industries through innovative approaches that enable revolutionary advances in devices or systems. The second and equally important mission is to produce creative and highly skilled engineers who will be the driving force for technological innovation in the 21st century. The Lab enjoys the strong support of the US Defense Department and private companies. Prof. Jalali has published over 200 scientific papers and holds six U.S. patents with four applications pending.

SELECTED PUBLICATIONS

O. Boyraz and B. Jalali, "Demonstration of a silicon Raman laser," *Optics Express,* Vol. 12 (no.21), pp. 5269-73, October 2004.

O. Boyraz, D. Dimitropoulos, and B. Jalali, "Observation of simultaneous Stokes and anti-Stokes emission in a silicon Raman laser", *IEICE Electronics Express,* Vol. 1 (no.14), pp. 435-41, October 2004.

O. Boyraz and B. Jalali, "Demonstration of 11 dB fiber-to-fiber gain in a silicon Raman amplifier," *IEICE Electronics Express,* Vol. 1 (no.14), pp. 429-34, October 2004.

HONORS AND AWARDS

Recipient of The BridgeGate 20 Award for his contribution to the Southern California economy;
Senior Consultant to the Communication Group at Intel Corporation; a Fellow of IEEE and OSA; and Chair of the LEOS-Los Angeles Chapter.

PROFESSIONAL AFFILIATIONS

Director of the UCLA Optoelectronic Circuits and Systems Laboratory at UCLA
Director of COAST (Consortium for Optical A/D System Technology)

Hong-Wen Jiang

Professor
Department of Physics and Astronomy
Ph.D., 1989, Case Western Reserve University
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RESEARCH INTERESTS

Jiang's group is actively working on the solid-state implementations of quantum information processing using electron spins in semiconductor nanostructures. The group is currently developing a fundamental building block for quantum computation and quantum communications with advanced semiconductor nanostructures, called spin-resonance-transistors. The ongoing effort includes the electrically controlled manipulation of electron and nuclear spins, detection of the quantum states of a single electron spin, nanofabrication of solid state traps (i.e., quantum bits) and read-out channels. The group has recently made the first measurement of the magnetic spin resonance of a single electron. Another area of research of the group is in experimental condensed matter physics: quantum phase transition and localization phenomena in highly correlated low-dimensional electronic systems. The group's recent focus is on high-sensitivity thermodynamic measurements of interacting disordered semiconductor heterostructures. The thermodynamic measurements provide means to probe the many-body ground state properties of the interacting charge carriers. Jiang's group has made several path-breaking discoveries on the studies of quantum Hall systems over the years.

SELECTED PUBLICATIONS

M. Xiao, I. Martin, E. Yablonovitch, and H. W. Jiang, "Electrical Detection of the Spin Resonance of a Single Electron in a Silicon Field-Effect Transistor", *Nature* 430, 435 (2004).

M. Xiao, I. Martin, and H. W. Jiang, " Probing Spin State of a Single Electron Trap by Random Telegraph Signal", *Phys. Rev. Lett.* 93, 078301 (2003).

I. Martin, D. Mozyrsky, and H. W. Jiang, "A scheme for Electrical Detection of Spin Resonance Signal from a Single-Electron Trap", *Phys. Rev. Lett.* 90, 18301 (2003).

PROFESSIONAL AFFILIATIONS

Fellow of American Physical Society

RESEARCH KEYWORDS

quantum information processing; spintronics; nano-electronics; condensed matter physics; quantum hall effect

Jack Judy

Associate Professor
Electrical Engineering and Biomedical Engineering
Ph.D., Electrical Engineering, 1996, University of California, Berkeley
IEEE and Society for Neuroscience, Electrochemical Society
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RESEARCH INTERESTS

Prof. Judy and his research group work in two fields: (1) novel nano- and micro-electro-mechanical systems (NEMS/MEMS) and (2) application of state-of-the-art engineering technologies to brain research, a field now called *neuroengineering*. Specific NEMS/MEMS research activities include ferromagnetic NEMS/MEMS for physical actuation and sensing at many levels of scale and miniaturized chemical-sensing systems. Examples include ferromagnetic actuators for optical, RF, and biomedical applications and micromachined electrochemical nitrate sensors with integrated microfluidics. His lab is also actively investigating the scaling limits of ferromagnetic actuators through a study of nanomagnetomechanical devices. Specific neuroengineering research interests include technologies for improving brain-computer interfaces, such as multi-electrode neural microprobes for neural recording and stimulation and miniature wireless neural transceivers. The neural-probe technologies are being used for deep-brain-stimulation applications, such as Parkinson's disease research. The wireless neural transceivers are being developed for a wide range of behavioral and neurophysiological research projects. In addition, some research projects bridge his lab's two broad research fields NEMS/MEMS and neuroengineering. Examples include nanomachined single-cell patch-clamp instruments with integrated microfluidics and clog-resistant MEMS-enabled hydrocephalus shunts.

SELECTED PUBLICATIONS

Brian Matthews and Jack W. Judy, "A Micromachined Planar Patch-Clamp Chip with Integrated Microfluidics", Solid-State Sensor and Actuator Workshop, Hilton Head Island, SC (June 6-10, 2004), pp. 111-116.

Dohyun Kim, Ira B. Goldberg, and Jack W. Judy, "Micromachined Amperometric Nitrate Sensor with an Anion Permeable Membrane", Proceedings of the Sixth International Symposium on Chemical and Biological Sensors and Analytical Systems, 206th Meeting of the Electrochemical Society, Honolulu, Hawaii (October 3-8, 2004).

Shahin Farshchi, Paul H. Nuyujukian, Aleksey Pesterev, Istvan Mody, and Jack W. Judy, "A TinyOS-Based Wireless Neural Sensing, Archiving, and Hosting System", 2nd International IEEE EMBS Conference on Neural Engineering, Washington, DC (March 16-19, 2005).

RESEARCH KEYWORDS

nanomachining, nanomechanics, nanomagnetics, nanoactuators, nanoneuroengineering

Richard B. Kaner

Professor of Chemistry
Professor of Materials Science and Engineering
Ph.D., Chemistry, 1984, University of Pennsylvania
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AREAS OF INTEREST

Nanostructured Conducting Polymers with Applications for Sensors, Actuators, Molecular Memory and Flash Welding; Rapid Synthetic Routes to Refractory Materials; Ultra-incompressible, Hard Materials; New Routes to Carbon-based Materials and Composites.

SELECTED PUBLICATIONS

"Designing Superhard Materials", *Science* 2005 308, 1268.

"Osmium Diboride, An Ultra-Incompressible, Hard Material" *J. Am. Chem. Soc.* 2005 127, 7264.

"Nanostructured Polyaniline Sensors", *Chem.-Eur. J.*, 2004 10, 1314.

"Polyaniline Nanofiber Gas Sensors: Examination of Response Mechanisms" *Nanoletters* 2004, 4, 491.

"Polyaniline Nanofibers: Facile Synthesis and Chemical Sensors" *J. Am. Chem. Soc.* 2003 125, 314.

HONORS AND AWARDS

2005: Australian-American Fulbright Fellow; Visiting Professor University of Wollongong; Eka-Granules Lecturer University of Tasmania;
2002-04: UCLA Gold Shield Faculty Prize;
1997: American Chemical Society Buck-Whitney Research Award;
1996: Guggenheim Fellow; 1993: Sloan Fellow;
1991-93: Dreyfus Teacher-Scholar;
1989-94: Packard Fellow;
1989: American Chemical Society Exxon Fellowship in Solid State Chemistry;
1987: National Science Foundation Presidential Young Investigator.

Chang-Jin (CJ) Kim

Professor
Mechanical and Aerospace Engineering
Ph.D., Mechanical Engineering, 1991, University of California, Berkeley
cjkim@ucla.edu

RESEARCH INTERESTS

Professor Kim's research encompasses: 1) advancing the understanding of physical phenomena in micro/nano scale; 2)broadening and advancing micro/nano fabrication techniques; and 3) developing new micro/nano mechanical devices for applications. A typical research project has all three of the above aspects intertwined, starting with a daring new design concept based on scale effect and ending with demonstration devices for real-world applications. Good examples are the projects using surface tension as a key mechanical element in the design. Surface tension is merely an interesting force in normal scale but a dominant force in the world below a millimeter. A series of demonstration devices span from those using surface tension to passively impede movement, such as bubble check valves, to those controlling surface tension to actively generate motion, such as electrowetting-on-dielectric (EWOD) devices; the latter spawned the new field of digital microfluidics. For nanotechnology, the main interest is formed around mechanical issues. An example is development of novel macro properties by creating intricate 3-D nanostructures. Although all the research projects are based on miniaturization, their application areas are anywhere from biomedical (handheld lab-on-a-chip system, micromachined pins and particles for microarrays), electronics (liquid-metal microswitches), energy (micro fuel cell, 3-D microbatteries), to aerospace (micro cryogenic coolers).

SELECTED PUBLICATIONS

J.-A. Paik, *et al.,* "Development of Spin Coated Mesoporous Oxide Films for MEMS Structures", *J. Electroceramics,* Vol. 13, 2004, pp. 423-428.

U.-C. Yi and C.-J. Kim, "Soft Printing of Droplets Pre-Metered by Electrowetting", *Sensors and Actuators A,* Vol. 114, No. 2-3, 2004, pp. 347-354.

A. R. Wheeler, *et al.,* "Digital Microfluidics with In-line Sample Purification for Proteomics Analyses with MALDI-MS", *Analytical Chemistry,* Vol. 77, No. 2, Jan. 2005, pp. 534-540.

W. Shen, R. T. Edwards, and C.-J Kim, "Electrostatically-Actuated Metal-Droplet Microswitches Integrated on CMOS Chip", *J. MEMS* (Accepted).

RESEARCH KEYWORDS

microelectromechanical systems (MEMS); design and fabrication of microdevices; digital microfluidics; microdevices with droplets and bubbles; nanostructures for new physical effects

James C. Liao

Professor, Chemical Engineering
Ph.D., Chemical Engineering, 1987, University of Wisconsin, Madison
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AREAS OF INTEREST

Systems Biology, Synthetic Gene-Metabolic Circuits, Regulation Networks, Network Evolution and Design

RESEARCH INTERESTS

Professor Liao and his research group are focusing on elucidating and reconstructing biological regulatory networks at the systems level. Experimental and computational methods are being developed to understand, predict, and redesign cellular behavior. An integrative technique called Network Component Analysis (NCA) have been developed which utilizes mRNA expression and transcriptional network connectivity to determine network component dynamics, functions, and interactions. This approach has been applied to elucidate transcription factor dynamics in *Saccharomyces cerevisiae* cell-cycle regulation, detect cross-talks in *Escherichia coli* two component signaling pathways, and characterize *E. coli* carbon source transition. In addition, novel synthetic gene-metabolic circuits have been designed and constructed to demonstrate system-wide understanding of cellular regulation. To this end, artificial feedback regulation, cell-cell communication, and oscillatory circuits have been constructed, which demonstrate the design principles of gene-metabolic regulation in the cell.

SELECTED PUBLICATIONS

Fung, E.; Wong, W.W.; Suen, J.K.; Bulter, T.; Lee, S.G.; and Liao, J.C., (2005) A synthetic gene-metabolic oscillator, *Nature,* 435, 118-122.

Bulter, T;. Lee, S.-G.; Wong, W.W.; Fung, E.; Connor, M.R. and Liao, J.C. (2004) "Design of artificial cell-cell communication using gene and metabolic networks" *Proc. Natl. Acad. Sci. USA*, 101:2299–2304.

Kao, K.C.; Yang, Y.; Boscolo, R.; Sabatti, C.;Roychowdhury, V. and Liao, J.C. (2004) Transcriptome-based determination of multiple transcription regulator activities in *Escherichia coli* using network component analysis, *Proc. Natl. Acad. Sci. USA*, 101:641-646.

Liao, J.C.; Boscolo, R; Yang, Y.L.; Tran,L.M.; Sabatti, C.; and Roychowdhury, V. (2003) Network component analysis: Reconstruction of regulatory signals in biological systems" *Proc. Natl. Acad. Sci. USA,* 100: 15522–15527.

Zhou, B.; D. Beckwith; L. R. Jarboe, and J.C. Liao (2005) Markov Chain Modeling of Pyelonephritis-Associated Pili Expression in Uropathogenic *Escherichia coli, Biophysical J.* 88, 2541–2553.

Thomas G. Mason

Assistant Professor of Chemistry & Biochemistry
and John McTague Chair
Assistant Professor of Physics & Astronomy
Ph.D., Physics, 1995, Princeton University
mason@chem.ucla.edu
www.chem.ucla.edu/dept/Faculty/Mason

RESEARCH INTERESTS

The research interests of the Mason Group include: (1) nanoemulsions: forming nanoscale dispersions of droplets of one liquid in another immiscible liquid through extreme shear, (2) microrheology: the study of the microscale deformation and flow of nanostructured synthetic and biological materials, (3) LithoParticles: structure of lithographically designed colloidal particles dispersed in a liquid solution, and (4) small angle neutron scattering as a probe of the structure of nanoscale hydrocarbon materials and dispersions. Our group thrives on interdisciplinary interactions, and we seek research areas that combine aspects of traditionally different fields.

SELECTED PUBLICATIONS

Formation of Concentrated Nanoemulsions by Extreme Shear, K. Meleson, S. Graves, T.G. Mason, *Soft Materials* 2 109-123 (2004).

Structure of Concentrated Nanoemulsions, S. Graves, K. Meleson, J. Wilking, M.Y. Lin, and T.G. Mason, *J. Chem. Phys.* 122 134703/1-6 (2005).

Density Profiles of Temperature Sensitive Microgel Particles, T.G. Mason and M.Y. Lin, *Phys. Rev. E Rapid Comm.* 71 040801(R)/1-4 (2005).

PROFESSIONAL AFFILIATIONS

American Chemical Society
American Physical Society
Society of Rheology

RESEARCH KEYWORDS

nanoemulsions, microrheology, particulate dispersions, neutron scattering

Heather Maynard

Howard Reiss Career Development Chair,
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Chemistry & Biochemistry
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RESEARCH INTERESTS

Maynard and her research group integrate synthetic polymers with biologically-derived molecules, such as peptides, proteins, and sugars, to prepare materials for applications in human medicine and nanotechnology. Specifically, polymer functionality and architecture are manipulated using controlled radical polymerization to prepare universal polymer scaffolds. Reaction of these scaffolds with amino acids and peptides to produce ligands that function as specific antagonists of cell-surface receptors are being pursued. Potential applications of the polymeric drugs include cancer treatment. Controlled radical polymerization is also used to synthesize peptide- and protein-polymer conjugates. Polymer bioconjugates are important commercial therapeutics and arguably will become valuable building blocks of nanostructured materials. It is known that having well-defined conjugates with a specific number of monodisperse polymer chains is critical for resultant conjugate properties including bioactivity and self assembly. Maynard's group explores several new strategies to synthesize materials of this description. In addition, protein mico- and nanoarrays are prepared using reactive polymer surfaces. These surfaces allow for the conjugation of active biomolecules in specific conformations. These materials may be useful in sensors for cancer and also as biomaterial coatings to enhance cell adhesion.

SELECTED PUBLICATIONS

Bontempo, D.; Maynard, H. D.; "Streptavidin as a Macroinitiator for Polymerization: In Situ Protein-Polymer Conjugate Formation" *J. Am. Chem. Soc.,* 2005, 127, 6508-6509.

Christman, K. L.; Maynard, H. D.; "Protein Micropatterns Using a pH-Responsive Polymer and Light," *Langmuir*, 2005, accepted for publication.

Heredia, K. L.; Maynard, H. D. "Aminooxy-Functionalized Semitelechelic Polymers Synthesized by Atom Transfer Radical Polymerization" *Polym. Prep.,* 2005, 46, 593-594.

Bontempo, D; Maynard, H. D. "Protein Macroinitiators for Atom Transfer Radical Polymerization," *Polym. Prep.,* 2005, 46, 78-79.

HONORS AND AWARDS

Amgen New Faculty Award

PROFESSIONAL AFFILIATIONS

The American Chemical Society; Society for Biomaterials; Materials Research Society

RESEARCH KEYWORDS

polymer bioconjugates; functional polymers; smart polymers; materials for protein detection; protein micro- and nanoarrays

Jianwei (John) Miao

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RESEARCH

My research interests lie in the interplay of physics, nanoscience and biology. I am particularly interested in developing new physical methods for quantitative imaging of nanoscale materials and biological systems in three dimensions. I have pioneered 3D coherent diffraction microscopy based upon coherent scattering in combination with a method of direct phase recovery called oversampling. I, together with my students, postdocs and collaborators, will continue to improve the spatial resolution of this imaging technique and pursue its applications in nanoscience and biology by using optical lasers, coherent X-rays and electrons. With the prospects of X-ray free electron lasers that are under rapid development worldwide, coherent diffraction microscopy can in principle be used to image non-crystalline specimens at the atomic resolution in three dimensions.

SELECTED PUBLICATIONS

J. Miao, Y. Nishino, Y. Kohmura, B. Johnson, S.H. Risbud and T. Ishikawa, "Quantitative Image Reconstruction of GaN Quantum Dots from Oversampled Diffraction Intensities Alone", *Phys. Rev. Lett.* in press (2005).

J. Miao, H. N. Chapman, J. Kirz, D. Sayre and K. O. Hodgson, "Taking X-ray Diffraction to the Limit: Macromolecular Structures from Femtosecond X-ray Pulses and Diffraction Microscopy of Cells with Synchrotron Radiation", *Annu. Rev. Biophys. Biomol. Struct.* 33, 157-176 (2004).

I. K. Robinson and J. Miao, "Three Dimensional X-ray Diffraction Microscopy", *MRS Bulletin* 29, 177-181 (2004).

J. Miao, J. Amonette, Y. Nishino, T. Ishikawa and K. O. Hodgson, "Direct Determination of the Absolute Electron Density of Nanostructured and Disordered Materials at Sub-10 nm Resolution", *Phys. Rev. B* 68, 012201 (2003).

J. Miao, K. O. Hodgson, T. Ishikawa, C. A. Larabell, M. A. LeGros and Y. Nishino, "Imaging Whole *Escherichia Coli* Bacteria by Using Single Particle X-ray Diffraction", *Proc. Natl. Acad. Sci. USA* 100, 110-112 (2003).

Jeff Miller

Professor and Chair
Microbiology, Immunology and Molecular Genetics
M. Philip Davis Chair in Microbiology and Immunology
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RESEARCH INTERESTS

Our laboratory studies the roles of sensory transduction in bacterial-host interactions. Genes and operons that encode virulence factors are often subject to coordinate regulation in response to environmental signals, and bacterial virulence factors frequently target host cell signaling pathways. Specific areas of interest include: a) biochemical analysis of signal transduction pathways in pathogenic bacteria, b) genetic organization of bacterial virulence regulons, and c) in vivo and in vitro studies of mechanisms of pathogenesis.

We are also investigating mechanisms involved in the induction of cytotoxic T cell responses by Listeria monocytogenes (LM). Infection induces LM specific CD8+ cytotoxic T cells which contribute to long lasting cell mediated immunity. We are using recombinant Listeria as probes to ask fundamental questions regarding immune recognition with a focus on autoimmunity. In the course of these studies, we have developed a new class of live Listeria-based vaccines with activity against heterologous pathogens and tumors.

Host-parasite interactions are often driven by mechanisms that promote genetic variability. In a third project, we have discovered a new class of retroelements, called "diversity-generating retroelements," which are capable of generating vast amounts diversity in proteins involved in ligand-receptor interactions. The diversification process involves a unique template-driven, reverse transcriptase-dependent mechanism which is conserved among diverse bacterial species.

SELECTED PUBLICATIONS

Doulatov, S., *et al.,* (2004) Tropism switching in Bordetella bacteriophage defines a family of diversity-generating retroelements. *Nature* 431:476-481.

Mattoo, S., *et al.,* (2004) A partner switching complex regulates type III secretion in Bordetella species. *Molecular Microbiology* 52: 1201-1214.

Joseph, S.B., *et al.,* (2004) LXR-dependent gene expression is important for macrophage survival and the innate immune response. *Cell* 119: 299-309.

Craft N., *et al.,* (2005) The TLR 7 agonist imiquimod enhances the anti-melanoma effects of a recombinant Listeria monocytogenes vaccine. *J. Immunology*: 175: 1983-1990.

McMahon, S.A., *et al.,* (2005) The C-type lectin fold as an evolutionary solution for massive sequence variation. *Nature Structural and Molecular Biology*: In Press.

Hal Monbouquette

Professor
Chemical & Biomolecular Engineering Department, UCLA
Ph.D., 1987, North Carolina State University
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RESEARCH INTEREST

The Monbouquette group conducts research on biosensors, the biotechnological applications of extremely thermophilic microorganisms, protein nanocapsule technology, and on the molecular engineering of surfaces. The group is collaborating with a UCLA neuroscientist on the micromachining of biosensors for in vivo monitoring of neurotransmitter release and uptake. In other work, a reporter enzyme has been engineered to behave as a molecular switch for several sensing applications under exploration including the detection of environmental toxins and the high-throughput screening of drug candidates. Extremely thermophilic microbes are being investigated as a source of enzymes and metabolic pathways useful in specialty chemical synthesis and of highly stable lipids for potential applications in drug delivery and in biosensor design. The Monbouquette laboratory also is discovering conditions for the controlled opening and closing of naturally occurring protein nanocapsules, in collaboration with Prof. Rome's group, such that they may be useful in drug delivery or in the synthesis of nanomaterials. Finally, the group is pursuing development of a process for the creation of complex, user-defined surface patterns with ~2-3 nm feature size. This new nanopatterning concept is based on the use of electrophoretically mobile, photocatalytic nanoparticles as "pens" to draw nanopatterns on a photocatalytically reactive surface.

SELECTED PUBLICATIONS

S. Lim, I. Schröder, H.G. Monbouquette, "A Thermostable Shikimate 5-Dehydrogenase from the *Archaeon Archaeoglobus fulgidus*", *FEMS Microbiol. Lett.,* 238, 101-106 (2004).

M.Warrier, M.K.F. Lo, H.G. Monbouquette, M.A. Garcia-Garibay, "Photocatalytic Redtuction of Aromatic Azides to Amines using CdS and CdSe Nanoparticles", *Photochem. Photobiol. Sci.,* 3, 859-863 (2004).

PROFESSIONAL AFFILIATIONS

American Institute of Chemical Engineers,
American Chemical Society

RESEARCH KEYWORDS

biosensors; molecular engineering of surfaces for materials and nanoelectronics applications; biotechnology of extremely thermophilic microorganisms; protein nanocapsule technology

Carlo Montemagno

Chair of Academic Affairs, Biomedical Engineering
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Professor, Mechanical and Aerospace Engineering
School of Engineering and Applied Science
Associate Director of the California NanoSystems Institute
Ph.D., University of Notre Dame
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RESEARCH INTERESTS

Professor Montemagno's research is focused on the application of nanotechnology to biological systems. He is well known for having engineered and fabricated the first nanobiomechanical motor system. His current research projects are directed at the development of biomolecular motor powered nanoelectromechanical devices, muscle powered MEMS devices, micro-robotics, and the engineering of on-chip detectors for pathogens.

SELECTED PUBLICATIONS

Luo, T.J., Soong, R., Lan, E., Dunn, B., Montemagno, C., Photo-Induced Proton Gradients and ATP Biosynthesis Produced by Vesicles Encapsulated in a Silica Matrix, *Nature Materials,* Vol. 4, March 2005.

Xi, J., Schmidt, J., Montemagno, C., Self-Assembled Microdevices Driven by Muscle, *Nature Materials,* Vol. 4, February 2005.

Choi, H.J., Brooke, E., Montemagno, C., Synthesis and Characterization of Nanoscale Biomimetic Polymer Vesicles and Polymer Membranes for Bioelectronic Applications, Nanotechnology, 16 (2005) S143-S149.

St. John, M., Li, Y., Zhou, X., Denny, P., Ho, C.M., Montemagno, C., Shi, W., Qi, F., Wu, B., Sinha, U., Jordan, R., Wolinsky, L., Paaark, N.H., Liu, H., Abemayor, E., Wong, D., Interleukin 6 and Interleukin 8 as Potential Biomarkers for Oral Cavity and Oropharyngeal Squamos Cell Carcinoma, *Arch Otolaryngol Head Neck Surg*/Vol 130, August 2004.

Roco, M., Montemagno, C., (eds) The Coevolution of Human Potential and Converging Technologies, *Annals of the New York Academy of Sciences,* Volume 1013, NY, New York, 2004.

RESEARCH KEYWORDS

hybrid nano-devices, F1-ATPase, sol-gel, ATP generation, biomolecular motors

André E. Nel

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Department of Medicine, UCLA
M.B., 1975, University of Stellenbosch, Capetown, R.S.A.
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RESEARCH INTERESTS

Dr. Nel's laboratory is engaged in three different but complementary types of research, namely: (i) the role of air pollutants in asthma, (ii) the decline of the immune system with aging, and (iii) nanotoxicology. The basis of all three types of research centers around the concept that oxygen can become toxic if the molecule is catalytically converted to oxygen radicals by particulate pollutants, mitochondrial dysfunction and possibly by nanoparticles. Mitochondria are cellular fuel generators and are also targeted by aging. Nanoparticles in ambient air as well as some engineered nanoparticles target and lodge in mitochondria. Oxygen radicals can lead to airway inflammation, manifesting as asthma and increased allergic responses in the lung. Clarification of the air components which are most toxic, allows regulation of those substances and development of rational treatment for adverse health effects caused by pollutants. Similar consideration have to be given to the potential toxicity of some engineered nanoparticles, which dependent on whether their chemical composition, surface size and surface reactivity may catalyze the production of oxygen radicals as the basis for their toxicity.

SELECTED PUBLICATIONS

Nel, A. Air pollution-related illness: Biomolecular effects of particles. *Science.* 308: 804. (2005).

Li, N., Alam, J., Venkatesan, M.I., Eiguren- Fernandez, A., Schmitz, D., Di Stefano, E. M., Slaughter, N., Killeen E., Wang, X., Huang, A., Wang, M., Miguel, A.H., Cho, A., Sioutas, C., Nel, A.E. Nrf2 is a Key Transcription Factor that Regulates Antioxidant Defense in Macrophages and Epithelial Cells: Protecting Against the Pro-inflammatory and Oxidizing Effects of Diesel Exhaust Chemicals. *J. Immunol.* 173: 3467-3481. (2004).

Wang, M., Xiao, G.C., Li, N., Xie, Y., Loo, J.A., and Nel, A.E. Phosphorproteome and cytokine array analysis show MAP kinases mediate inflammation by pro-oxidative diesel exhaust particle chemicals. *Electrophoresis.* 26: 2092-2108 (2005).

Kim, H-J., and Nel, A.E. The Role of Phase II Antioxidant Enzymes in protecting Memory T-cells from Spontaneous Apoptosis in Young and Old Mice. *J. Immunol.* In Press (2005).

HONORS AND AWARDS

Chair NIH Study Section: Allergy, Immunology, and Transplantation Research Committee, NIAID 2004-2005. Keynote speaker, International Nanoparticle Symposium, National Institute for Environmental Studies, Tsukuba, Japan, June 2005, Title: "The role of Oxidative Stress and Mitochondrial damage in mediating the effects of DEP and Ultrafine particles".

Stanley Osher

Professor
Mathematics Department
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RESEARCH

Professor Osher and his research group work on level set methods in inverse problems and optimal design. These problems involve optimizing geometry and other quantities to achieve physically desirable results (such as maximizing band gaps in photonic crystals). The group has developed the level set method, originated by Osher and Sethian in 1987 and connected it to shape sensitivity analysis, new numerical methods and regularization of ill-posed inverse problems. The level set method has had an enormous impact on science and technology (25,000 references on Google) and this includes inverse problems and optimal design problems involving geometric objects as unknowns. The application of level set methods to such kinds of problems has not only increased the computational efficiency, but also opened completely new possibilities due to its flexibility in handling topological changes. This has led to a change of paradigm in inverse obstacle problems: instead of reconstructing geometric objects with strongly restricted topology under a variety of a priori assumptions, the aim has changed to reconstruction of rather general objects with minimal a priori knowledge. The applications include: structural optimization, e,g., the design of a dam, band structure design and photonic crystals, inclusion of detections, e. g., semiconductor contact regions, scattering and tomography problems, e.g., impedance tomography, image processing and segmentation, medical imaging and state-constrained optimal control. New, emerging areas include crack detection and nucleation.

SELECTED PUBLICATIONS

C.-Y. Kao, S. Osher and E. Yablonovitch, "Maximizing Band Gaps In Two-Dimensional Photonic Crystals by Using Level Set Methods" *Applied Physics B: Lasers and Optics,* v81, pp235-244, (2005).

M. Burger and S. Osher, "A Survey on Level Set Methods for Inverse Problems and Optimal Design", *European J. of Appl. Math,* v16, pp263-301, (2005).

HONORS AND AWARDS

2005: Elected to US National Academy of Sciences
2005: Ralph E. Kleinman prize of the Society of Industrial and Applied Mathematics
2005: Concurrent Professor, Nanjing University

PROFESSIONAL AFFILIATIONS

American Mathematical Society, Society for Industrial and Applied Mathematics

RESEARCH KEY WORDS

level set methods, inverse problems, band gaps, photonic crystals, optimization

Vidvuds Ozolins

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Department of Materials Science & Engineering
Ph.D., Theoretical Physics, 1998, Royal Institute of Technology, Sweden
Principle Member of Technical Staff, Sandia National Laboratories
Postdoctoral Fellow, National Renewable Energy Laboratory
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RESEARCH INTERESTS

Prof. Ozolin's research deals with theoretical understanding and design of advanced materials using computational modeling. Using a parameter-free first-principles approach, he uses quantum mechanics and statistical mechanics to study electronic structures, interatomic bonding and microscopic kinetic processes in modern high-performance materials. Current research directions include: (i) study of nanoscale self-assembly and ordered pattern formation on metal and semiconductor surfaces, (ii) modeling of alloy film growth and structure, (iii) new nanostructured materials for reversible hydrogen storage. His research group also develops new computational algorithms for predicting crystal structures and physical properties of complex materials.

SELECTED PUBLICATIONS

A. J. Ardell and V. Ozolins, "Trans-interface diffusion-controlled coarsening," *Nature Materials* 4, 309-316 (2005).

C. Wolverton, V. Ozolins, and M. Asta, "Hydrogen in Aluminum: First-Principles Calculations of Structure and Thermodynamics," *Physical Review B* 69, Art. No. 144109 (2004).

G. E. Thayer, N. C. Bartelt, V. Ozolins, A. K. Schmid, S. Chiang, and R. Q. Hwang, "Linking surface stress to surface structure: Measurement of atomic strain in a surface alloy using STM." *Physical Review Letters* 89, 036101 (2002).

B. Krack, V. Ozolins, M. Asta, and I. Daruka, "'Devil's Staircases' in bulk-immiscible ultrathin alloy films." *Physical Review Letters* 88, 186101 (2002).

V. Ozolins, M. Asta, J. J. Hoyt, "Elastic relaxations in ultrathin epitaxial alloy films." *Physical Review Letters* 88, 096101 (2002).

RESEARCH KEYWORDS

self-assembly, pattern formation, directed self-assembly, metal and semiconductor heteroepitaxy, nanostructured materials, first-principles calculations, phase diagrams and phase stability, dynamical properties of solids.

Matteo Pellegrini

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Department of Molecular, Cell and Developmental Biology
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RESEARCH INTERESTS

Our lab is interested in the development of computational approaches to model and interpret genomic data. These models allow us to elucidate the mechanisms of signal transduction, transcription and other biological processes. Our approach is to build models that integrate varied data that sheds light on these phenomena. This data includes expression microarrays, high throughput protein binding and phosphorylation data as well as genome sequences. Our research focuses on the development of predictive models that we will test in collaboration with experimental labs. Our goal is to develop models that quantitatively predict the outcome of perturbations in cells.

SELECTED PUBLICATIONS

Li, H., Pellegrini, M., Eisenberg, D., (2005) Detection of parallel functional modules by comparative analysis of genome *Nat Biotechnology* 23 (2): 253-260.

Bowers, P.M., Pellegrini, M., Thompson, M.J., Fierro, J., Yeates, T.O., Eisenberg, D., (2004) Prolinks: a database of protein functional linkages derived from coevolution *Genome Biology* 5 (5): R35.

Strong, M., Graeber, T.G., Beeby, M., Pellegrini, M., Thompson, M.J., Yeates, T.O., Eisenberg, D., (2003) Visualization and interpretation of protein networks in Mycobacterium *Nucleic Acids Research* 31 (24): 7099-7109.

Gertz, J., Elfond, G., Shustrova, A., Weisinger, M., Pellegrini, M., Cokus, S., Rothschild, B., (2003) Inferring protein interactions from phylogenetic distance matrices *Bioinformatics* 19 (16): 2039-2045.

Strong, M., Mallick, P., Pellegrini, M., Thompson, M.J., Eisenberg, D., (2003) Inference of protein function and protein linkages in Mycobacterium *Genome Biology* 4 (9): R59.

RESEARCH KEYWORDS

computational biology, systems biology, protein networks comparative genomics, functional genomics

Michael E. Phelps

Norton Simon Professor
Chair, Department of Molecular and Medical Pharmacology
Director, Crump Institute for Molecular Imaging
Director, Institute for Molecular Medicine
Ph.D., Chemistry, 1970, Washington University
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AREAS OF INTEREST

Science and technology in molecular imaging, systems biology and nanotechnologies; development of in vitro and in vivo molecular diagnostics of disease from basic science to patients.

RESEARCH

The areas of research are in: (1) development of integrated microfluidics devices that can tolerate a wide range of organic solvents for accelerating, diversifying, simplifying and lowering the cost for producing positron labeled molecular imaging probes, biomarkers and drugs for molecular diagnostics and to guide development of molecular therapeutics; (2) development of integrated microfluidics and nanotechnologies for examining the molecular mechanisms of systems biology transformations of normal cells and intercellular networks to those of disease, particularly cancer and a number of neurological disorders; (3) development of molecular imaging technologies for performing in vivo assays of rates metabolic reactions, concentrations and activity of signal transduction pathways and various biological processes of disease (e.g., DNA replication, cell proliferation, apotosis, etc). This research involves faculty and students from basic and clinical science departments and institutes at UCLA, as well as those at Caltech and the Institute for Systems Biology in Seattle. Tech transfer to commercialization of discoveries and inventions to the public's benefit is important.

SELECTED PUBLICATIONS

Heath, J.R., Phelps, M.E., Hood, L., NanoSystems Biology. *Molec Imag Biol* 5:312-25, 2003.

Hood, L., Heath, J.R., Phelps, M.E., Lin B. Systems Biology and New Technologies Enable Predictive and Preventative Medicine. *Science* 306: 640-643, 2004.

HONORS AND AWARDS

Enrico Fermi Presidential Award awarded by President Clinton, 1998; Kettering Prize, 2001, General Motors Cancer Research Foundation; Elected to the Institute of Medicine in 1985; Elected to the National Academy of Sciences in 1999.

Seth Putterman

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RESEARCH INTERESTS

Recent research has explored energy focusing phenomena in off equilibrium continuous systems. Fluids and solids which are driven off equilibrium do not return smoothly to the equilibrium state. Instead they can display a wide range of energy focusing phenomena. The limits of focusing are often determined by processes at the nanoscale. An example is sonoluminescence where pulsating bubbles concentrate diffuse acoustic energy by 12 orders of magnitude to make picosecond flashes of light. In a one megahertz sound field the temperature inside the collapsed bubble reaches one million degrees (*Physical Review Letters* 92, 124301, 2004). A compelling issue is whether the energy density becomes large enough to trigger nuclear fusion in a hydrogenated bubble. Our first attempt to observe bubble fusion was reported in a one- hour documentary filmed in our lab, October 2004, by the BBC: "An experiment to Save the World". Although these results were negative, our project is ongoing and we predict that someone will achieve success with some region of cavitation parameter space. In another system-pyroelectric crystals we actually achieved nuclear fusion in a very simple compact arrangement. By heating and cooling a walnut sized sealed object which contained lithium tantalate and deuterium inside, we generated fusion by products such as 2.45MeV neutrons (Naranjo, Gimzewski, Putterman, *Nature* April 28, 2005).

SELECTED PUBLICATIONS

Sonoluminescence: How Bubbles Turn Sound into Light. S. Putterman & K. Weninger, *Annual Reviews Fluid Mechanics,* (32), p445 (2000).

Quantum Fokker-Planck Equation for Interacting Waves. Seth Putterman, R. Sinclair, Robert Roberts. *Phil.Trans. Roy Soc.* A354,951 (1996).

Correlation Between Charge Transfer and Stick-Slip Friction at a Metal Insulator Interface; *Phys. Rev. Lett.* 85,1000 (2000), R. Budakian, S. J. Putterman.

Sonoluminescence: Nature's Smallest Blackbody; *Optics Letters;* 26, 575 (2001), G. Vazquez, C. Camara, K. Weninger, S. Putterman.

Sonoluminescence from a Single Bubble Driven at 1MHz; *Phys. Rev. Lett.* 92, 124301 (2004), C. Camara, S. Putterman, E. Kirilov.

Observation of Nuclear Fusion Driven by a Pyroelectric Crystal; *Nature* 434, 1115 (2005), B. Naranjo, J. Gimzewski, S. Putterman.

RESEARCH KEYWORDS

friction, sonoluminescence, fusion, pyroelectric, cavitation

Leonard H. Rome

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RESEARCH INTERESTS

We are interested in the biogenesis and function of subcellular organelles. We have been concentrating on novel cytosolic ribonucleoprotein particles (RNPs) called vaults. Vaults were discovered in our laboratory and found to exist in most eukaryotic cells. They have an intricate shape composed of multiple arches reminiscent of cathedral vaults, hence their name. Vault size (~74 x 42 x42 nm), shape and localization suggests that they may be involved in nucleo-cytoplasmic transport.

We are interested in elucidating the function of these unique structures and in manipulating their structure to give them new functions. We are using the baculovirus expression system to produce recombinant vaults in order to test the concept that vaults can have a broad nanosystems application as malleable nanocapsules. Toward this aim we are currently designing particles with encapsulated fluorescent probes and enzymatically active protein domains. In addition, a number of strategies are currently being considered to encapsulate chemically active small molecules into the vault particle. If successful, these vault nanocapsules can be bioengineered to allow their use in a wide variety of biological applications including drug delivery, biological sensors, enzyme delivery, controlled release, and nano-electrical machine (NEMS) application.

SELECTED PUBLICATIONS

N. Emre S. Raval-Fernandes, V.A., Kickhoefer, and L.H. Rome: Analysis of MVP and VPARP promoters indicates a role for chromatin remodeling in the regulation of MVP. *Biochim Biophys Acta.* 1678: 33-46 (2004).

Y. Mikyas, M. Makabi, S. Raval-Fernandes, L. Harrington, V. A. Kickhoefer, L. H. Rome and P. L. Stewart : Cryoelectron Microscopy Imaging of Recombinant and Tissue Derived Vaults: Localization of the MVP N Termini and VPARP. *J. Mol. Biol.* 344: 91-105 (2004).

V. A. Kickhoefer, Y. Garcia, Y. Mikyas, E. Johansson, J. C. Zhou, S. Raval-Fernandes, P. Minoofar, J. I. Zink, B. Dunn, P. L. Stewart, and L. H. Rome: Engineering of Vault Nanocapsules with Enzymatic and Fluorescent Properties. *Proc. Natl. Acad. Sci. USA* 102: 4348-52 (2005).

RESEARCH KEYWORDS

vaults, nano-capsules, drug delivery, DNA delivery, biosensors

Jacob Schmidt

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AREAS OF INTEREST

Nanobiotechnology; Single molecule sensing using membrane proteins; Biomimetic membranes; microfluidics; manipulation and creation of biologically-functionalized devices

RESEARCH

Professor Schmidt and his group have strong interests in single molecule biophysics and bioengineering, with a focus on biological membranes and membrane proteins: 1) creation of long-lived and robust biomimetic membranes; 2) single-molecule transport measurements of membrane proteins; 3) construction of devices and apparatus for the manipulation and study of biomimetic membranes and membrane proteins. The techniques used to pursue these interests are highly multi-disciplinary, drawing on methods of genetic cloning and manipulation, biochemistry, micromachining, low-noise electronics, and microfluidics. The group aims to advance the science and technology of membrane proteins through the development of tools and techniques enabling other researchers to perform experiments previously impossible due to limitations in technology or expertise. The group also maintains a strong interest in technology development enabling more efficient drug discovery targeted toward membrane transport and channel proteins.

SELECTED PUBLICATIONS

"Stochastic Sensors", Jacob J. Schmidt, *Journal of Materials Chemistry* 15, 831-840 (2005).

"Bionanomechanical Systems", Jacob J. Schmidt and Carlo D. Montemagno, *Annual Review of Materials Research,* 34, 315-337 2004.

PROFESSIONAL AFFILIATIONS

American Physical Society, Materials Research Society, Biophysical Society

Benjamin Schwartz

Professor of Physical Chemistry
Department of Chemistry and Biochemistry
Ph.D., Physical Chemistry, 1992, University of California, Berkeley
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RESEARCH INTERESTS

Research in the Schwartz group is focused on the study of electronic dynamics in disordered media. Our efforts fall into two principle areas. First, we study how the motions of solvent molecules control the dynamics of electron transfer reactions in liquids. Since the relevant solvent motions take place on pico-second time scales, we use femtosecond laser spectroscopy and mixed quantum/classical molecular dynamics simulations to study these processes. The experiments allow us to "watch" the relevant motions in real time, and the simulations provide molecular detail that is unavailable from the experiments; the combination of theory and experiment on the same chemical systems is synergistic. Second, we study the electronic properties of conjugated polymers. Conjugated polymers are remarkable materials that have the electrical properties of semiconductors but the mechanical properties and processing advantages of plastics; thus, these materials have enormous potential for use in displays that have large areas and/or are flexible. We use femtosecond laser and other spectroscopies to understand how the polymer chain conformation and packing controls electronic properties such as how easily charges move between the polymer chains. We also build and characterize optoelectronic devices such as LED's and photovoltaic cells from these novel plastic semiconductors.

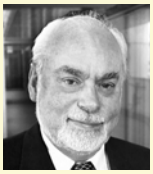
SELECTED PUBLICATIONS

M. J. Bedard-Hearn, R. E. Larsen and B. J. Schwartz, "The Role of Solvent Structure in the Absorption Spectrum of Solvated Electrons: Mixed Quantum/Classical Simulations in Tetrahydrofuran (THF)," *J. Chem. Phys.* 122, 134506, 1-11 (2005).

I. B. Martini, E. R. Barthel and B. J. Schwartz, "Building a Molecular-Level Picture of the Ultrafast Dynamics of the Charge-Transfer-to-Solvent Reaction of Sodide (Na^-)," *Pure Appl. Chem.* 76, 1809-25 (2004).

I. B. Martini, *et al.,* "Evidence for the Direct Production of Interchain Species in Conjugated Polymer Films: The Ultrafast Stimulated Emission and Fluorescence Dynamics of MEH-PPV," *Phys. Rev. B*, 69(3) 035204, 1-12 (2004).

R. E. Larsen and B. J. Schwartz, "An Efficient Real-Space Configuration-Interaction Method for Simulation of Multi-Electron Mixed Quantum/Classical Non-Adiabatic Dynamics in the Condensed Phase," *J. Chem. Phys.* 119(15), 7672-84 (2003).



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AREAS OF INTEREST

Self-Assembly Processes and Molecular Nanotechnology; Templated-Directed Synthesis; Catenanes and Rotaxanes; Artificial Nanoscale Machines; Molecular Shuttles and Switches; Energy Transduction

RESEARCH

Professor Stoddart and his research group work primarily in four areas. They are (1) template-directed synthesis, that is either kinetically or thermodynamically controlled, (2) physical organic chemistry, principally as it relates to chemical topology and supramolecular phenomena, (3) design and construction of artificial molecular machinery, with special reference to actuators and switches, and (4) the application of nanoscale chemistry conducted on surfaces and at interfaces to fundamental problems in materials science and the life sciences. A wide range of knowledge and skill sets are required in order to pursue research effectively and efficiently in such a multidisciplinary environment. Collaboration is encouraged within the Stoddart Group and beyond. Presently, it involves both graduate and undergraduate students, as well as postdoctoral scholars, and extends nationally and internationally, as well as departmentally and campus-wide. Much emphasis is put on the development of presentational skills. Communication is central to the culture of a group which recognizes that the world is flat!

SELECTED PUBLICATIONS

"A Molecular Elevator", *Science* 2004, 303, 1845-1849.

"Molecular Borromean Rings", *Science* 2004, 304, 1308-1312.

"Whence Molecular Electronics?", *Science* 2004, 306, 2055-2056.

"Single-Walled Carbon Nanotubes Under the Influence of Dynamic Coordination and Supramolecular Chemistry", *Small* 2005, 1, 452-461.

"A Reversible Molecular Valve", *Proc. Natl. Acad. Sci. USA* 2005, 102, 10029-10034.

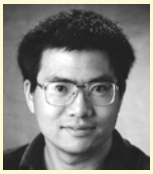
"From a Meccano Set to Nano Meccano" *Pure Appl. Chem.* 2005, 77, 1089-1106.

HONORS AND AWARDS

2004: Nagoya Gold Medal in Organic Chemistry. 2005: Honorary Doctor of Science Degree (University of Birmingham); Alumnus of the Year Award 2005 (University of Edinburgh); Carnegie Centenary Professorship at the Universities of Scotland; First Novartis Lectureship (ETH Zurich); Paul Gassman Lectureship (University of Minnesota).

PROFESSIONAL AFFILIATIONS

The Royal Society of London; The German Academy of Natural Sciences (The Leopoldina), The American Chemical Society; The Royal Society of Chemistry



Ren Sun

Associate Professor
Department of Molecular and Medical Pharmacology
Ph.D., Molecular Biophysics & Biochemistry, 1993,
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RESEARCH INTERESTS

Viral infections are associated not only with acute illnesses, but also chronic diseases. In contrast to the rapidly manifesting SARS, Epstein-Barr virus (EBV) and Kaposi's Sarcoma-associated Herpesvirus (KSHV) are associated with several malignancies. To understand the molecular mechanism of viral replication and its role in pathogenesis, we are pursuing our research in the following directions. 1) We have identified a viral gene, which can initiate the complete lytic replication cascade of KSHV. We are addressing the questions of how it controls the expression of downstream genes and how cellular signal pathways control the viral switch. 2) We will determine the optimal combination of these cellular factors/pathways to most efficiently reactive the herpesviruses, using a microfluidic system consisting of nano transducers, which will be capable of sensing, making logical decisions, and providing real-time feedback control. 3) Murine herpesvirus-68 (MHV-68) is utilized as an in vivo model to dissect the roles of virus-encoded cytokines in viral replication and tumorpathogenesis. 4) We take genomic, proteomic, and structural biology approaches to define the structure and function of viral proteins encoded by MHV-68 and SARS coronavirus. 5) We are initiating clinical trials by intentionally activating viral lytic gene expression in tumor cells to destroy tumor lesions.

SELECTED PUBLICATIONS

Hongyu Deng, Julia T. Chu, No-Hee Park, and Ren Sun. "Functional Identification of an original lytic replication and the cleavage/packaging signal of murine gammaherpesvirus-68." *Journal of Virology,* 2004 Sep;78(17):9123-31.

Moon Jung Song, *et al.,* "The DNA architectural protein HMGB1 facilitates RTA-mediated viral gene expression in gamma2 herpesviruses." *Journal of Virology.* 78:12940-50, 2004.

Qingmei Jia, *et al.,* "Murine Gammaherpesvirus 68 Open Reading Frame 45 Plays an Essential Role During the Immediate Early Phase of Viral Replication." *Journal of Virology,* 2005 Apr;79(8):5129-41.

Moon Jung Song, *et al.,* "Identification of Viral Genes Essential for Replication of Murine Gammaherpesvirus 68 Using Signature Tagged Mutagenesis." *Proc Natl Acad Sci USA.* 2005, 102, 3805-3810.

RESEARCH KEYWORDS

carcinogenesis, herpes, SARS virus, biological detection, systems biology

Fuyuhiko Tamanoi

Professor
Microbiology, Immunology & Molecular Genetics
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RESEARCH INTERESTS

Professor Tamanoi's group is interested in molecular switches and cellular signaling networks. The research focuses on the Ras family proteins that act as a nanoscale switch by shuttling between a GTP bound active form and a GDP-bound inactive form. The switch can be turned on by growth, nutrient and energy signals. Current research is aimed at characterizing two members of the Ras family proteins called Ras and Rheb. While Ras activates signaling pathways such as Raf/MAP kinase signaling, Rheb activates mTOR signaling that regulates protein synthesis. Overactivation of these molecular switches forms the basis of human diseases such as cancer, neurofibromatosis and tuberous sclerosis. The following approaches are taken to characterize these molecular switches. First, regulation of these switches by proteins such as GAP (GTPase activitating protein) and GEF (GDP/GTP exchange factor) is studied. Second, lipid modification and their membrane association are being investigated. Third, we have identified small organic molecule compounds that can regulate the activity of molecular switches. One type of compound blocks their membrane association. The other type of compounds inhibits protein-protein interaction between Ras and its downstream effector Raf.

SELECTED PUBLICATIONS

Clarke, S. and Tamanoi, F. (2004) Fighting cancer by disrupting C-terminal methylation of signaling proteins. *J. Clin. Invest.* 113, 513-515.

Aspuria, P-J. and Tamanoi, F. (2004) The Rheb family of GTP-binding proteins. *Cellular Signaling* 16, 1105-1112.

Kato-Stankiewicz, J. , *et al.,* (2002) Inhibitors of Ras/Raf-1 interaction identified by two-hybrid screening revert Ras-dependent transformation phenotypes in human cancer cells. *Proc. Natl. Acad. Sci. USA* 99, 14398-14403.

Gau, C.L., Kato-Stankiewicz, J., Jiang, C., Miyamoto, S., Guo, L. and Tamanoi, F. (2005) Farnesyltransferase inhibitors reverse altered growth and distribution of actin filaments in Tsc-deficient cells via inhibition of both rapamycin-sensitive and insensitive pathways. *Molec. Cancer Therap.* 4, 918-926.

PROFESSIONAL AFFILIATIONS

American Association for Cancer Research, American Society for Biochemistry & Molecular Biology

RESEARCH KEYWORDS

molecular switch, signaling network, cancer, small molecule compounds, virus reactivation

Michael Teitell

Associate Professor
Chief, Division of Pediatric and Developmental Pathology
Department of Pathology & Laboratory Medicine
Pediatrics (joint appointment)
Ph.D., Molecular Immunology, 1991, UCLA
M.D., Medicine, 1993, UCLA
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RESEARCH INTERESTS

The Teitell lab is interested in the etiology, mechanism, and therapy of immune system cancers, normal immune system development, and the generation of novel investigative nanotools. One project area focuses on epigenetic silencing of gene expression. A second project area is in the biology of the TCL1 oncogene. A third area of work involves studies on a novel type of RNA degradation that regulates cell metabolism and survival leading to cancerous transformation. A fourth project area is to design new methods for interrogating cell motion and functions in real-time. These distinct areas of study all converge on the common goal of increased understanding, diagnosis and treatment of human malignancies.

SELECTED PUBLICATIONS

Teitell, M.A. TCL1 Family Oncoproteins: Co-activators of Transformation. *Nature Reviews Cancer,* 5, 640-648, 2005.

Teitell, M.A. and Pandolfi, P.P. Lymphoid Malignancies. In Holland, E.C.: Mouse Models of Cancer, 1st Ed., New York, J. Wiley & Sons, pp. 237-259, 2004.

Hoyer, K.K., *et al.,* Dysregulated TCL1 Promotes Multiple Classes of Mature B-Cell Lymphoma. Proceedings of the National Academy of Sciences, USA, 99:14392-14397, 2002.

HONORS AND AWARDS

2001 Millenium Pharmaceuticals Award for Genomics Research
2003 Scholar Award, Leukemia and Lymphoma Society
2004 American Society of Clinical Investigators (ASCI)

PROFESSIONAL AFFILIATIONS

National/International:
American Association of Immunologists (AAI), American Soc. for Biochem. and Molecular Biology (ASBMB), American Association for Cancer Research (AACR), American Society of Clinical Investigators (ASCI)
Intramural:
UCLA Association of Chemists and Biochemists Molecular Biology Institute, Jonsson Comprehensive Cancer Center, UCLA AIDS Research Institute, Institute for Cell Mimetic Space Exploration (CMISE), Institute for Stem Cell Biology and Medicine (ISCBM)

RESEARCH KEYWORDS

cancer, immunology, stem cells, epigenetics, nanotechnology

Sarah Tolbert

Associate Professor of Chemistry
Chemistry and Biochemistry
Ph.D., Chemistry, 1995, University of California, Berkeley
tolbert@chem.ucla.edu

RESEARCH INTERESTS

Research in the Tolbert group is focused on using self-organization to create nanostructured composites with applications as optical, electronic, magnetic, and structural materials. Specific research areas include the following: (1)Assembly and self-organization of semiconducting polymers with other nanoscale inorganic species for applications in controlled polymer emission and photovoltaics. (2)Formation of periodic nanoporous semiconductors using Zintl clusters as soluble inorganic building blocks. (3)Control of magnetic coupling and thus magnetic properties in ordered nanocrystal arrays using host guest chemistry in periodic nanoporous inorganic materials. (4)Tuning mechanical properties (e.g. stiffness, toughness, or elasticity) in periodic nanostructured inorganic/organic composites through control of nanometer scale architecture. (5)The design and testing of new ultra-hard materials. (6) Formation of micro- and nano-scale batteries using solution phase processing. (7)Optically active bio-composites based on well defined protein cages such as virus capsids or vaults. For the majority of these projects, the goal is to use control of nanometer scale architecture to produce new physical properties and new combinations of properties by the intimate mixing of disparate and complex components.

SELECTED PUBLICATIONS

B.L. Kirsch, X. Chen, E.K. Richman, V. Gupta, and S.H. Tolbert, "Probing the Effects of Nanoscale Architecture on the Mechanical Properties of Hexagonal Silica/Polymer Composite Thin Films." *Adv. Func. Mater.,* 15, 1319- 1327, (2005).

R.W. Cumberland, M.B. Weinberger, J.J. Gilman, S.M. Clark, S.H. Tolbert, R.B. Kaner, "Osmium Diboride, An Ultra-Incompressible, Hard Material." *J. Am. Chem. Soc.,* 127, 7264-7265 (2005).

A. Rugge, J.-S. Park, R.G. Gordon, and S.H. Tolbert, "Tantalum(V) Nitride Inverse Opals as Photonic Structures for Visible Wavelengths." *J. Phys. Chem. B.,* 109, 3764-3771 (2005).

D. Sun, C.W. Kwon, G. Baure, E.K. Richman, J. MacLean, B. Dunn, and S.H. Tolbert, "The Relationship between Nanoscale Structure and Electrochemical Properties of Vanadium Oxide Nanorolls." *Adv. Func. Mater.,* 14, 1197-1204 (2004).

PROFESSIONAL AFFILIATIONS

American Chemical Society, Materials Research Society

RESEARCH KEYWORDS

nanostructured materials; self-organized materials, particularly polymer and surfactant templated inorganic phases; host-guest composite materials; semiconducting polymer based materials and devices; novel structure materials through control of nanometer-scale architecture; nanoscale power sources such as photovoltaics and batteries.

Kang L. Wang

Professor
Department of Electrical Engineering
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RESEARCH

Dr. Wang's interests in nanoscience technology include self-assembly of quantum dots, nano-fabrication technology for nanoelectronics, photonics and sensors applications. He is a leader in Nanotechnology. In nanoelectronics, he studies the power dissipation of electronic and spintronic devices and the use of these devices for information processing. His prior work leads to the use of strained SiGe in CMSO and in opto-electronics such as integrated Ge and infrared detectors. He was the founding director of Nanoelectronics Research Facility at UCLA (established in 1989) with the infrastructure to further research in nanotechnology, which led to the recent establishment of California NanoSystems Institute, funded by the State of California, the first of its kind in the nation. He leads the MARCO Center on FENA to address the issues and opportunities for nanoelectronics devices and their implementation in information processing from the fundamental atomic and molecular level. The Center currently has over 30 investigators from 12 leading universities in the nation.

SELECTED PUBLICATIONS

K.L. Wang, S. Tong, H.J. Kim, "Properties and applications of SiGe nanodots," *Materials Science in Semiconductor Processing,* Vol 8. pp 289-399, 2005.

S. Tong, J.Y. Lee, H.J. Kim, F. Liu, K.L. Wang, Ge dot mid-infrared photodetectors," *Optical Materials,* Vol 27, pp 1097-1100, 2005.

M. Bao, F. Liu, and F. Baron and K.L. Wang, "Tunneling spectroscopy of metal-oxide-semiconductor field-effect transistor at low temperature", *Applied Physics Letters* 86, 242104-1. June 2005.

HONORS AND AWARDS

2003 Director of FENA Focus Center
TSMC Honor Lectureship (2004)

PROFESSIONAL AFFILIATIONS

IEEE Member, American Physical Society American Vacuum Society, Eta Kappa Nu Member, International Symposium on Silicon Molecular Beam Epitaxy. Editorial board of the Encyclopedia of Nanoscience and Nanotechnology (American Scientific publishers). Editor, Handbook of Semiconductor Nanostructures and Nanodevices

Shimon Weiss

Professor
Department of Chemistry and Biochemistry
Department of Physiology, UCLA
D.Sc., Electrical Engineering, 1989, Technion, Israel Institute of Technology
sweiss@chem.ucla.edu

RESEARCH INTERESTS

Biophysics, Biophysical Chemistry, Nano-Spectroscopy, Bio-Nano-Technology. Single molecule detection and spectroscopy, application of single molecule detection to biology, dynamic structural/molecular biology, protein folding, protein-protein and protein-DNA interactions, single molecule enzymology, novel Bio-Nano-Technology probes, semiconductor nanocrystals, quantum dots, fluorescence microscopy/spectroscopy, physics/chemistry of mesoscopic systems, scanning probe microscopies, near-field microscopy, ultrafast processes in mesoscopic systems, ultrafast processes on surfaces.

SELECTED PUBLICATIONS

Michalet, X.; Pinaud, F.; Bentolila, L. A.; Tsay, J.; Doose, S; Li, J.; Sundaresan, G.; Wu, A. M.; Gambhir, S.S.; Weiss, S., Quantum Dots for Live Cells and in vivo Imaging, Diagnostics and Beyond, *Science* 2005, 307 (5709), 538-544.

Pinaud, F.; King, D.; Moore, H. P.; Weiss, S., Bioactivation and Cell Targeting of Semiconductor CdSe/ZnS Nanocrystals with Phytochelatin-related Peptides. *J. Am. Chem. Soc.* 2004, 126, 6115-6123.

Kapanidis, A.N.; Lee, N.K.; Laurence, T.A.; Doose, S.; Margeat, E.; Weiss, S., Fluorescence-aided molecule sorting: Analysis of structure and interactions by alternating-laser excitation of single molecules, *Proc Natl Acad Sci,* 2004, 101 (24), 8936-8941.

Doose, S.; Tsay, J. M.; Pinaud, F.; Weiss, S., Comparison of Photophysical and Colloidal Properties of Biocompatible Semiconductor Nanocrystals Using Fluorescence Semiconductor Nanocrystals Using Fluorescence Correlation Spectroscopy, *Anal. Chem.* 2005 , 77(7):2235-42.

Kapanidis, A.N.; Laurence, T.A.; Lee, N.K.; Margeat, E.; Kong, X.; Weiss, S., Alternating-laser excitation of single molecules, *Accounts of Chemical Research* (Special Issue on Single-Molecule Spectroscopy), 2005.

HONORS AND AWARDS

The 2005 Rank Prize, Royal College of Physicians, London.
The 2001 Michael and Kate Barany Biophysical Society Award
Fellow of the Optical Society of America, 1999.

PROFESSIONAL AFFILIATIONS

APS, ACS, OSA, AAAS, Biophysical Society.

RESEARCH KEYWORDS

single molecule biophysics, nanobiotechnology, conformational dynamics of biomolecules, fluorescence spectroscopy, molecular imaging

Owen Witte

Distinguished Professor
Department of Microbio., Immuno. and Molecular Genetics
Investigator, Howard Hughes Medical Institute
Director, Institute for Stem Cell Biology and Medicine
President's Chair in Developmental Immunology
Professor of Molecular and Medical Pharmacology
David Geffen School of Medicine
M.D., 1976, Stanford University School of Medicine
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RESEARCH INTERESTS

Research involves the interrelated problems of cell growth regulation, differentiation and understanding function of oncogenes found in human leukemias and epithelial cancers. This includes the Bcr-Abl tyrosine kinase important in human chronic myelogenous leukemia and understanding regulation of lymphocyte growth in disease states during immune responses. We discovered gene defects in primary immunodeficiency X-linked agammaglobulinemia are a single gene called Bruton's tyrosine kinase and now study its mode of action.

We identified a G protein-coupled receptor family which regulates inflammatory responses and autoimmunity and study mechanisms of action. We use PET and other imaging modalities to study lymphocyte movement during the immune response as regulated by these receptors.

Prostate cancer is unique in its highly regularized pattern of metastasis to the bone marrow. We use surface markers to fractionate normal murine prostate cell populations in an attempt to define active stem cell populations and recently developed dissociated cell reconstitution systems in which prostate epithelial stem and progenitor cells can be induced to form glandular tissue structures.

SELECTED PUBLICATIONS

Dubey, P., Su, H., Adonai, N., Du, Shouying, Rosatao, A., Braun, J., Gambhir, S.S., Witte, O.N. 2003. Quantitative imaging of the T cell anti tumor response by positron emission tomography. *Proc. Nat. Acad. Sci.* 100:1232-1237.

Radu, C.G., Nijagal, A., Mclaughlin, J., Wang, L., Witte, O.N. 2005. Differential proton sensitivity of related G protein-coupled receptors T cell death-associated gene 8 and G2A expressed in immune cells. *Proc Natl Acad Sci U S A.* Feb 1:102(5):1632-37.

Xin, L., Lawson, D.A., Witte, O.N. 2005. The Sca-1 cell surface marker enriches for a prostate-regenerating cell subpopulation that can initiate prostate tumorigenesis. *Proc Natl Acad Sci U S A.* 102(19):6942-7. Epub 2005 Apr 28.

PROFESSIONAL AFFILIATIONS

Fellow (1996) American Academy of Arts and Sciences
Member (1997) National Academy of Sciences
Member (2003) Institute of Medicine

RESEARCH KEYWORDS

positron emission tomography (PET), imaging, tumor, immune

Fred Wudl

Dean M. Willard Professor of Chemistry and Materials
Chemistry and Biochemistry; Materials Science and Engineering, UCLA
Director of the UCLA Materials Creation Testing Program (MCTP) IGERT
Director of the UCLA Exotic Materials Institute
Ph.D., 1967, UCLA
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www.chem.ucla.edu/dept/Organic/wudl.html

RESEARCH INTERESTS

Professor Wudl's research group works in five different areas: (1) organic Electronics including OLEDs, OPVs and PLEDs, (2) high energy density devices including lithium passivation, three-dimensional batteries and supercapacitors, (3) Synthesis of "unnatural" products such as paracyclophanes, electron donors and electron acceptors, (4) novel engineering plastics such as Self-mending polymers and (5) fullerene chemistry. His group is most widely known for their interdisciplinary interactions with physicists and engineers.

SELECTED PUBLICATIONS

A Processable Green Polymeric Electrochromic. Sonmez, G.; Sonmez, H.B.; Shen, C.K.F.; Jost, R.W.; Rubin, Y.; Wudl, F. *Macromolecules,* 2005, 28(3) 669-675.

Completion of the Three Primary Colours: The Final Step Toward Plastic Displays. Sonmez, G.; Wudl, F.; *J. Mat. Chem.,* 2005, 15(1), 20-22.

A Robust Electroactive n-Dopable Aromatic Polyketone, Chiechi, R.C.; Sonmez, G.; Wudl, F., *Adv. Funct. Mater.,* 2005, 15(3), 427-432.

PROFESSIONAL AFFILIATIONS

The American Chemical Society; The Chemical Society, London, Sigma Xi, Phi Lambda Upsilon; American Association for the Advancement of Science

Reviewer of research proposals for NSF, DOE, PRF, Swiss National Scientific Foundation, National Research Programme, The Israel Foundation, The National University of Singapore
External Examiner, Universidad Complutense, Madrid; Eindhoven University of Technology

Eli Yablonovitch

The Northrop Grumman Opto-Electronics Chair
Professor of Electrical Engineering
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RESEARCH INTERESTS

The Optoelectronics Group is dedicated to finding the technology that will define the culmination of the electronics roadmap. That will emerge a few years down the road, when individual electronic components will be as small as molecules, and when they consume the minimal possible energy per function. One of the important technologies that will dominate the future is plasmonics, whereby electromagnetic energy can be focused and concentrated down to the 1nm scale. Plasmonics refers to the collective motion of electrons in metallic wires. Metal wires will evolve from simple interconnects to become active components, and nonlinearities will become routinely large allowing fast switching. Short distance communication consumes too much energy, and that problem will also have to be solved. After classical electronics will be as good as it could possibly be, then quantum information processing will emerge as the next big challenge. Electrons in semiconductors will store quantum states, which can be manipulated to harness astronomical volumes of information. These technologies, plasmonics, qubits in semiconductors, and new communications nano-devices, will emerge from current high technology, but they will represent a more revolutionary change than we have been accustomed to in past generations of electronics.

SELECTED PUBLICATIONS

Xiao, M., Martin, I., Yablonovitch, E., Jiang, HW. Electrical detection of the spin resonance of a single electron in a silicon field-effect transistor. *Nature*, vol.430, no.6998, 22 July 2004, pp.435-9. Publisher: Nature Publishing Group, UK.

Burger, M., Osher, S., Yablonovitch, E. Inverse Problem Techniques for the Design of Photonic Crystals. *IEICE Transactions on Electronics*, vol E87-C, no. 3, March 2004, pp. 258-265.

Baron, F.A., Kiselev, A.A., Robinson, H.D., Kim, K.W., Wang, K.L., Yablonovitch, E. Manipulating the L-valley electron g factor in Si-Ge heterostructures. *Physical Review B-Condensed Matter*, vol.68, no.19, 15 Nov. 2003, pp.195306-1-10. Publisher: APS through AIP, USA.

HONORS AND AWARDS

Morris Loeb Lecturer, Harvard University 2005
Anson L. Clark Memorial Lecturer at the University of Texas, Dallas 2004
Honorary Doctorate 2004, Royal Institute of Technology, Stockholm Sweden

RESEARCH KEYWORDS

photonic crystals, plasmonics, quantum information, electron spin, nano-electronics

Yang Yang

Professor
Materials Science and Engineering
Ph.D., Physics, 1992, University of Massachusetts, Lowell
yangy@ucla.edu

RESEARCH INTERESTS

Professor Yang's primary research interests include: nano-organic hybrid electronics materials and devices with emphasis on light-emitting, energy harvesting, charge storage memory devices, charge injection, transport, and photon-electron interaction.

SELECTED PUBLICATIONS

Ryan C. Chiechi, Ricky J. Tseng, Filippo Marchioni, Yang Yang, and Fred Wudl, Efficient Blue Electroluminescent Devices with a Robust Fluorophore: 7,8,10-Triphenylfluoranthene, *Adv. Mat.* (in press).

Jiahung Tseng, Jianyong Ouyang, Jiaxing Huang, Richard Kaner, and Yang Yang, "Polyaniline nano-fiber nonvolatile digital memory", *Nano Letters,* 5, 1077 (2005).

Colin Stuart, Qianfei Xu, Ricky J. Tseng, Yang Yang, H. Thomas Hahn, and Yong Chen, Nanofabrication module integrated with optical aligner (APL, submitted).

Tony Jun Huang, Amar Hugh Flood, Branden Brough, Yi Liu, Paul A. Bonvallet, Seogshin Kang, Chih-Wei Chu, Tzung-Fang Guo, Weixing Lu, Yang Yang, J. Fraser Stoddart, and Chih-Ming Ho, "Understanding and Harnessing Biomimetic Molecular Machines for NEMS Actuation Materials", *IEEE,* Submitted.

Qianfei Xu, Yang Yang, Hieu M. Duong, Fred Wudl, "Efficient Single-Layer "Twistacene"-Doped Polymer White Light-Emitting Diodes", *Appl. Phys. Lett.* 85, 3357, (2004).

PROFESSIONAL AFFILIATIONS

MRS, APS, ACS

RESEARCH KEYWORDS

organic electronics, nano-organic electronics, nano-particle induced memory effect

Todd O. Yeates

Professor of Biochemistry
Department of Chemistry and Biochemistry
Ph.D., Biochemistry, 1988, UCLA
yeates@mbi.ucla.edu

AREAS OF INTEREST

Protein Structure; Supramolecular Protein Assemblies: Filaments, Cages, and Layers; Protein Design; Protein Interaction Networks; Bioinformatics and Comparative Genomics; Computational Biology; Protein Crystallography; Symmetry.

RESEARCH

Professor Yeates and his research group work in the areas of molecular, structural and computational biology. In structural biology, the emphasis is on supramolecular protein assemblies, such as self-assembling protein filaments, layers, and cages. Supramolecular assemblies of interest include both natural and designed structures. Natural assemblies of particular interest include the actin filament and the bacterial microcompartment, a shell-like structure that appears to serve as a primitive organelle inside bacterial cells. The Yeates group has recently determined the structures of the proteins that make up a bacterial microcompartment, providing the first detailed clues about how they operate. Strategies are also being developed for designing novel proteins to assemble into ordered structures on the mid-nanometer scale. In the area of computational biology, the emphasis is on bioinformatics and comparative genomics. Current work in comparative genomics has led to the discovery of unusual microbes that are able to stabilize their proteins at extreme temperatures through the use of widespread disulfide bonding. Finally, in the area of bioinformatics, new methods for deciphering protein function and protein interactions have been developed by applying ideas in symbolic logic to genomic data.

SELECTED PUBLICATIONS

"Protein structures forming the shell of primitive bacterial organelles", *Science* 2005, 309, 936-8.

"Use of logic relationships to decipher protein network organization", *Science* 2004, 306, 2246-9.

HONORS AND AWARDS

2004: Hansen-Dow Award for Excellence in Teaching – UCLA Chemistry

PROFESSIONAL AFFILIATIONS

American Crystallographic Association; American Chemical Society

Z. Hong Zhou

Professor
Microbiology, Immunology and Molecular Genetics
Ph.D., Biochemistry, 1995, Baylor College of Medicine
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RESEARCH INTERESTS

Recent advances have given electron cryomicroscopy and single-particle reconstruction ("cryoEM") an increasingly important role in determining subnanometer-resolution structures of macromolecular complexes or biological nano-particles (>150 kDa and 10 nm in dimension). At this resolution, secondary structural elements such as α-helices and β-sheets are readily recognizable either by eye or by computational means. The emerging method of cryo-electron tomography (cryoET) allows the determination of three-dimensional architectures of objects ranging in size from a nanometer to micrometers. These structural methods provide exciting opportunities to determine the structures of subcellular assemblies that are either too large or too heterogeneous to be investigated by conventional crystallographic or NMR methods. Research in my laboratory aims to understand the mechanisms governing macromolecular functions by pushing the resolution limit of cryoEM to near-atomic resolution and by describing large, pleomorphic, dynamic structures or conformations using the integrative approach of cryoEM and cryoET. The long-term goal of my research is to study the structures of supramolecular assemblies to high resolution by an integrative approach using cryoEM/cryoET, high performance computing, and atomic modeling.

SELECTED PUBLICATIONS

Chen, S., Chen, L., Zhang, Q., Deng, Y., Lin, W., Lu, X., Brannan, J., Zhou, Z.H., Zhang, J., (2004) Genetic, biochemical and structural characterization of a new densovirus. *Virology,* 318, 122-133.

Wan, Y., Chiu, W., Zhou, Z.H., (2004) Full contrast transfer function correction in 3D cryo-EM reconstruction. IEEE Proceedings of ICCCAS 2004, pp 960-964.

Liu, F., & Zhou, Z.H. (2005) Comparative virion structures of human herpesviruses. In *Human Herpesviruses: Biology, Therapy and Immunoprophylaxis.* Arvin, A., Campadelli-Fiume, G., Moore, P., Mocarski, E., Roizman, B., Whitley, R. & Yamanishi, K., eds., Cambridge University Press. In Press.

Yu, X., Shah, S., Atanasov, I., Lo, P., Liu, F., Britt, W.J., and Zhou, Z.H. (2005) Three-dimensional localization of the smallest capsid protein in the human cytomegalovirus capsid, *J. Virol.* 79, 1327-1332.

Yu, X., Trang, P., Shah, S., Atanasov, I., Kim, Y.H., Bai, Y., Zhou, Z.H. and Liu, F. (2005) Dissecting human cytomegalovirus gene function and capsid maturation by ribozyme targeting and electron cryomicroscopy , 102, 7103-7108.

HONORS AND AWARDS

2004 Burton Award, American Microscopy Society; 2002 Established Investigator Award, American Heart Association; 2000 Basil O'Connor Scholar Award, March of Dimes Foundation; 1999 Pew Scholar in the Biomedical Sciences

Jeffrey I. Zink

Professor of Chemistry
Department of Chemistry and Biochemistry
Ph.D., Chemistry, 1970, University of Illinois
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RESEARCH

Professor Zink and his research group work primarily in four different areas: excited state properties of large molecules; laser assisted chemical vapor deposition of nano-particles and structures; functional (optical and electrical) nano-structured materials; and nano-machines. Research on excited states is currently focused on coupled potential energy surfaces with special emphasis on photo-induced electron transfer. The research on deposition makes use of excited state properties to design molecules and direct bond-breaking to lead to desired products such as pure metals or semiconductors. Photolysis in confined spaces is used to produce nanoparticles. Studies of functional nano-materials are currently focused on energy transfer and electron transfer at the nanoscale. Active molecular components designed to produce the desired function are placed in spatially-separated regions in a one-step self-assembly process. Research on nano-machines is focused on rotating machines, oscillating "molecular impellers" and nano-valves. Unifying themes that run through all of these areas include theoretical understanding of molecular properties, materials synthesis and characterization, and spectroscopy (for measuring the excited state properties, monitoring photo-driven reactions, and observing the action of the molecular machines).

SELECTED PUBLICATIONS

"Electrical or Photocontrol of the Rotary Motion of a Metallacarborane," *Science,* 42, 4308-4315 (2004).

"An Operational Supramolecule Nanovalve," *J. Am. Chem. Soc.,* 126, 3370-3371, (2004).

"Formation of Titanium Nitride Nanoparticles within Mesoporous Silica SBA-15," *J. Phys. Chem. B.* 109, 4404-4409, (2005).

"Multiple Doped Nanostructured Silicate Sol-Gel Thin Films: Spatial Segregation of Dopants, Energy Transfer, and Distance Measurements," *J. Am. Chem. Soc.*, 127, 2656-2665, (2005).

"Engineering of Vault Nanocapsules with Enzymatic and Fluorescent Properties", *Proc. Natl. Acad. Sci. USA,* 102, 4348-4352 (2005).

HONORS AND AWARDS

John Simon Guggenheim Fellow; Invited Visiting Professor, University of Paris; Invited Visiting Professor, University of Amsterdam; Dow-Hanson Distinguished Teacher Award; U.S. Department of Energy Materials Sciences Award for Outstanding Scientific Accomplishment in Metals and Ceramic Sciences; J. Clarence Karcher Lecturer, University of Oklahoma; Foster Chemistry Colloquium Lecturer, SUNY Buffalo.

CORE LABORATORIES

The research conducted at the CNSI is organized around seven core laboratories. In addition to the established core laboratories described below, the CNSI is also developing core facilities in the areas of AFM/STM; Diffraction Analysis; and Quantum Information Resource.

ADVANCED LIGHT MICROSCOPY / SPECTROSCOPY

The accelerating field of molecular imaging has witnessed major technical advances that are now introducing the cell biologist and the physician alike to a new, dynamic, subcellular world where genes and gene products can be visualized to interact in space and time and in health and disease. The mission of the Advanced Light Microscopy/Spectroscopy Shared Facility is to provide consultation, services and support for the application of novel spectroscopic methods and advanced image analysis techniques for the study of macromolecules, cellular dynamics and nano-scale characterization of bio-materials.

ELECTRON IMAGING CENTER FOR NANOMACHINES (EICN)

Viewing molecules, materials and molecular machines at high magnification is important for research at the molecular scale and critical to nanoscience. Electron microscopy (EICN) is now able to cover these and larger size ranges delivering valuable structural information for cell biological, biomolecular, molecular and materials sciences. EICN is no longer merely a confirming technology, but has risen to become a unique tool for data collection. The CNSI cannot be a comprehensive center for nanoscience without state-of-the-art EICN capability including the appropriate equipment, skilled technical expertise and academic leadership. We are currently designing a state of the art EICN facility for the CNSI building. This facility will offer all major EICN modalities. It will be operated by highly skilled technical staff that will be able to assist CNSI faculty address their complex imaging needs.

INMOS

We will be working in a clean room because of the very small devices we will be making. We will be using tried-and-true semiconductor equipment as well as novel and untested "Nanofabrication" tools to make, measure and test very small structures and systems.

What is unique about the CNSI approach is that we hope to integrate semiconductor tools and processes with biological, chemical and medical applications. Traditionally, semiconductor processing excludes these types of applications because of the possibility of cross-contamination. High speed Intel processors would not function correctly if exposed to cellular material, for example.

INMOS can be thought of as a high-tech machine shop for making substrates for cell growth or manipulation, mixing and controlling chemicals (on a molecular scale), making electrical connections to very small things such as cells or molecules etc. We are opening up to chemists, biologists and doctors, as well as engineers, tools which have traditionally been dedicated to integrated circuit manufacturing. As these tools have evolved and become capable of working with features 100 to 1000 times smaller than before (i.e., nanometer scale), they can now interact with DNA, single molecules, and a host of other, very small entities.

MOLECULAR SCREENING SHARED RESOURCE (MSSR)

High-throughput screening (HTS) involves assaying a large number of unique molecules in order to identify those that have a specific biological or chemical function. Pharmaceutical and biotech companies have traditionally performed the lion's share of HTS. However, having so much of our screening capacity outside the academic and public research community, and having that capacity narrowly focused on drug discovery, restricts both the pace of basic science as well as its translation into improved health. Thus, the establishment of academic HTS centers will serve the long-term goals of basic science and health research by providing a much broader range of screens than commercial firms typically undertake. Toward this end, UCLA has established the Molecular Screening Shared Resource (MSSR) to provide HTS capabilities to the academic community. Through close collaborations between physicians, biologists, and chemists, it is our goal to identify molecules with novel functions in basic cellular and molecular biology, and to develop probes and research tools whose uses include but are not limited to direct drug discovery. In addition, these efforts will gain leverage from the California NanoSystems Institute (CNSI), as we incorporate new nanotechnologies into the screening process in order to advance miniaturization, improve throughput and reduce costs.

"Judge a tree from its fruit; not from its leaves."

— EURIPIDES

R-E-S-E-A-R-C-H

C-O-L-L-A-B-O-R-A-T-I-O-N

For more information about the California NanoSystems Institute please visit: www.cnsi.ucla.edu

Collaboration between CNSI and The University of Cambridge

The Next Generation of Switchable Rotaxanes for Nanoelectronics

In recent years, developments in the area of mechanically interlocked molecules designed to act as artificial molecular switches and machines have proceeded apace. The potential applications of these molecules varies widely and includes nanoelectronics and nanoelectromechanical devices. Many different control stimuli have also been demonstrated, including light, electricity and chemicals.

One of the most prolific mechanically-interlocked systems to be incorporated into nano-devices is based on the donor-acceptor interaction between an electron-poor tetracationic cyclophane ($CBPQT^{4+}$) and two electron-rich aromatic units—tetrathiafulvalene (TTF) and a dioxynaphthalene (DNP). Bistable [2]catenanes—two mechanically interlocked rings—and bistable [2]rotaxanes—a ring mechanically trapped on a dumbbell shaped component—constructed using this recognition motif have been incorporated into molecular switch tunnel junctions (MSTJs) and shown to switch reversibly between high and low conductivity states by application of a bias across the junction. A working 64-bit memory was assembled (*ChemPhysChem,* 2002, 3, 519-525) using this technology and at least 56 bits shown to operate.

One of the consequences of the four positive charges carried by the electron-poor cyclophane component of this recognition motif is the presence of four anions to counterbalance the charge. In condensed phases, such as in a MSTJ device, these counterions may induce drag on the cyclophane component and limit the accessible switching speeds. In addition, these counterions can exchange with other anions present in the processing steps for device assembly, leading to a degree of uncertainty regarding the final composition of the molecular monolayer. Thus, it was desired to design and synthesize neutral equivalents.

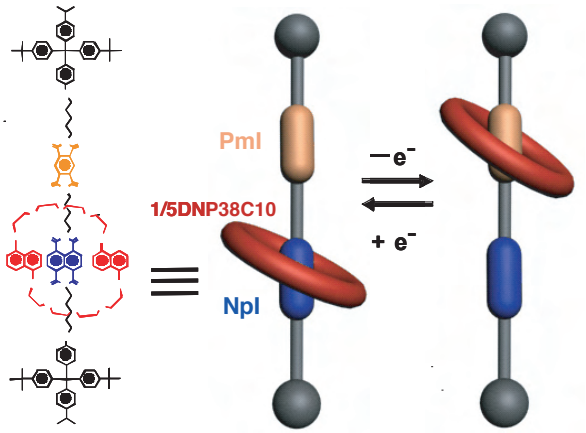


Fig. Redox-switching in a bistable neutral [2]rotaxane.

Neutral [2]rotaxanes have been conceived that can fulfil the role of switches in a future generation of molecular electronic devices.

In a collaboration between the CNSI and scientists at the University of Cambridge in the UK, the feasibility of incorporating uncharged recognition motif into bistable [2]rotaxanes was investigated. The Cambridge group has worked for many years on a neutral recognition motif, where a electron-rich crown ether ring (1/5DNP38C10) is paired with two electron-poor aromatic units—pyromellitic diimide (PmI) and naphtho-diimide (NpI).

Several [2]rotaxanes (Fig.) have since been synthesized (*J. Am. Chem. Soc.* 2004, 126, 9884-9885), including model compounds and bistable ones, and their properties investigated. Kinetic and thermodynamic parameters for the relevant mechanical motions were determined in order to facilitate optimization of the molecular design. In addition, both the chemical and electrochemical control mechanisms have been shown (*Chem. Eur. J.* 2004, 10, 6375-6392) to operate effectively in the bistable neutral [2]rotaxanes.

The speed with which this new system has been developed simply could not have been achieved without the knowledge of all those involved. The importance of this type of collaboration is expected to become even more important as the various components used to assemble nano-devices become ever more complex. ■

This research received federal funding from NSF, DARPA, MARCO, FENA and CNID

Collaboration between CNSI, M&T Technologies and Unilever

Water Purification by Reverse Osmosis using an Aquaporin Z-embedded Polymer Vesicle Network

Aquaporin proteins represent a family of membrane bound orthodox water channels that exclusively permit water molecules to pass through their pores in single file. In fact, Aquaporins are so selective, they will exclude the passage of all contaminants including bacteria, viruses, proteins, DNA, salts, detergents, dissolved gases, and even protons from an aqueous solution. These channels are employed in many places by the human body, including red blood cells, the lens of the eye, brain tissue, and the collection ducts of the kidney. Aquaporin Z (AqpZ) is a bacterial Aquaporin from E.coli that shows high homology to its mammalian counterparts. This particular Aquaporin was chosen because of its ease of production in an overexpression cell line and because of its extreme ruggedness. It is a highly stable protein that resists denaturing due to voltage, heat, detergent, or extremes of pH. This makes AqpZ suitable for use in a commercial or industrial setting.

In nature, Aquaporins move water across membranes from areas of low dissolved solids to an area of higher dissolved solids by osmosis. However, if pressure is applied to the side of the membrane containing higher concentrations of dissolved material, pure water can flow through the aquaporins back into the low concentration side of the system. In this sense, pressure can be used to induce reverse osmosis across a membrane embedded with aquaporins and effectively purify contaminated or salty water.

Normally, channel proteins are housed in the cell's lipid bilayer or membrane. Unfortunately, such membranes are not strong enough to maintain their structure under the pressures required to perform reverse osmosis. Therefore a synthetic membrane to house these proteins has been created that is composed of polymerized ABA triblock copolymer monomers. This polymer, PMOXZ-PDMS-PMOXZ, consists of a hydrophobic core set between two hydrophilic groups that mimic the electrostatic conditions and thickness (about 5nm) of a natural lipid bilayer. Thus, AqpZ has no difficulty inserting itself into such a membrane. Of course, the synthetic membrane is much more durable than lipid and can hold its shape under pressure once the special methacrylate end groups on the hydrophilic blocks have been crosslinked to one another by irradiation with 254 nm UV light. The morphology of the polymer chosen for UV preservation is that of a vesicle.

AqpZ channels are inserted in 5 nm thick, 200 nm diameter polymer vesicles. Concentrated protein vesicles are deposited on inexpensive nitrocellulose filters and crosslinked to one another using UV light. Contaminated water is purified as it passes through these devices under pressure.

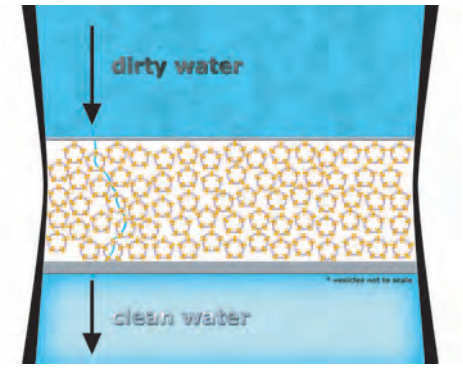


Fig. 1. Pure water is forced through the AqpZ network under pressure.

Much like lipids, the ABA copolymer will spontaneously assemble into a more stable hollow-sphere structure (or vesicle) when it is exposed to an aqueous environment. Protein is added, and vesicle size is standardized at 200 nm by repeated extrusion through 0.2 μm pore-sized polycarbonate filters. The vesicles are crosslinked with UV to preserve their shape and then super concentrated to obtain a solution of extremely high vesicle density. This solution is pipetted onto an inexpensive 25 nm pore-sized nitrocellulose support filter and exposed to UV light once again so that adjacent vesicles are directly crosslinked to one another (via remaining methacrylate groups) to form a water tight vesicle network. Thus, contaminated water cannot move around the spheres, and every vesicle acts as a functional unit, with fresh water passing into and then out of each hollow sphere under pressure.

Coated UV-cured disks are paired with a 3 μm top filter for packaging and inserted in a stainless steel filter holder. Nitrogen gas pressurizes a connected vessel containing contaminated source liquid and pure water is then forced through the AqpZ device into a collection tube. Device performance is assessed by processed water clarity and change in conductivity due to removal of dissolved salts. ■

Collaboration within CNSI

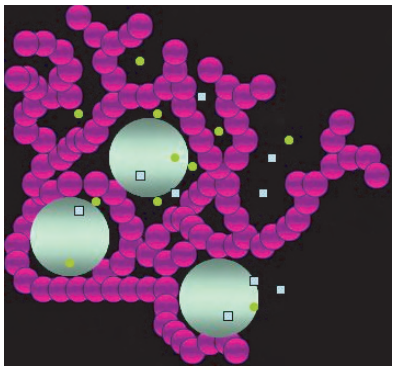
Photo-Induced Proton Gradients and ATP Biosynthesis produced by Vesicles Encapsulated in a Silica Matrix

A new material has been created which exploits the properties of transmembrane proteins. Using sol-gel immobilization methods, we prepared a nanocomposite that uses light to drive the biosynthesis of ATP.

There are a variety of methods for immobilizing biomolecules including entrapment, microencapsulation, covalent attachment and adsorption. Sol-gel approaches, pioneered at UCLA, have emerged as highly versatile methods for immobilization which contain features common to both entrapment and microencapsulation. The process is largely based on the use of liquid silane precursors, such as tetraalkoxysilanes. Hydrolysis and condensation of the silanes in the presence of proteins in buffered solution lead to the formation of a nanostructured material with interpenetrating mesoporosity that is filled with a solvent phase. The dopant biomolecules reside in the mesoporous network and become part of the nanostructured architecture of the entire material. The list of proteins that have been immobilized in sol-gel derived materials is extensive and includes globular and membrane-bound proteins, enzymes and other biosystems. In almost all cases, sol-gel encapsulation preserves the intrinsic protein functionalities. This method has proven to be extremely successful at enhancing the stability of proteins and the demonstration of protein activity over many months has been accomplished routinely.

While sol-gel immobilization of soluble proteins has been widely investigated, the immobilization of membrane-bound proteins has proven to be more difficult. The generation of alcohol from the alkoxysilane hydrolysis is the principal reason for this limitation because the alcohol can disrupt the membrane structure. This problem has now been circumvented by the development of a low alcohol sol-gel synthesis method in which polyethylene glycol becomes part of the solvent phase and protects the biomolecule. With this synthesis, unique materials can be designed which harness the properties of transmembrane proteins and potentially lead to a wide variety of applications, from power generation and energy storage to powering biomolecular motor-powered systems.

This research has involved the creation of a liposome/sol-gel architecture in which lipid vesicles provide membrane structure and protein orientation to two transmembrane proteins, bacteriorhodopsin (bR) and F_oF_1-ATP synthase. The purpose of sol-gel encapsulation is to provide chemical stability and mechanical integrity so that the resulting material can be handled and integrated into a biochemical system. Incorporating bR proteoliposomes in the sol-gel matrix can achieve photo-induced proton gradients across a membrane, a property that represents a central element for biologically based power generation for such devices as biosolar cells and solar-based biofuel cells. By incorporating F_oF_1-ATP synthase in the proteoliposome, the photo-induced proton gradient generated by the bR is used in the biosynthesis of ATP. In this way, the liposome/sol-gel architecture uses biochemical reactions to store solar energy. Moreover, because the energy is stored as ATP, there is an opportunity to use this material to directly power motor proteins. ■



The liposome/sol-gel architecture. A photo-induced proton gradient is used to drive the biosynthesis of ATP.

This research received federal funding from NSF

Collaboration between CNSI and UCLA

Nanomachined Patch-Clamp System with Integrated Microfluidics

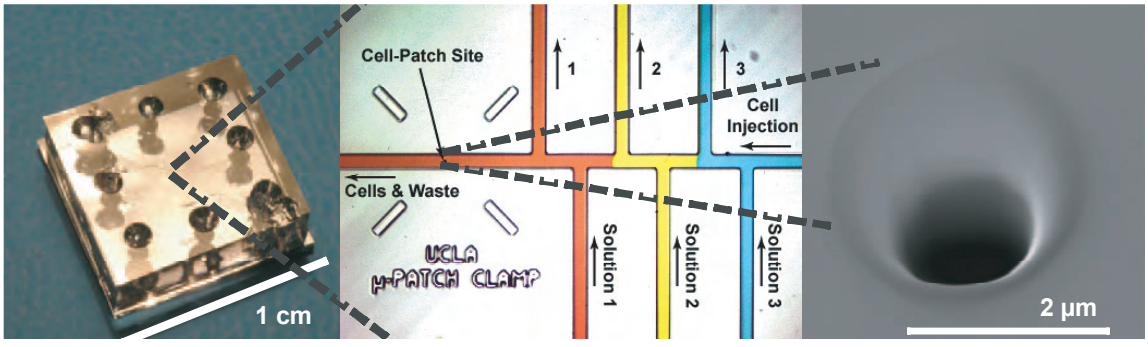
ION-CHANNEL proteins embedded in the lipid bilayer of cell membranes, control the flow of ions across the membrane and consequently control many cellular processes. The patch-clamp technique is a powerful tool for the investigation of these trans-membrane ionic currents. Specifically, the patch-clamp technique has been used extensively to study many electrophysiological cell properties, such as the characterization of the kinetics and steady-state effects of toxins, chemical agonists, antagonists, and drugs in ion channels, transporters, and pumps.

Although the traditional equipment used to perform the patch-clamp technique has been very successful, conventional pipettes are not easily adapted to all the applications for which the patch-clamp technique would be useful. Examples of electrophysiological applications that would benefit from uniquely tailored patch-clamp systems include measuring dose-response curves for single cells, high-throughput screening, applications needing optical access to the cell (e.g., confocal and florescence microscopy), and applications needing rapid intracellular perfusion.

A Collaboration between the CNSI, NASA, and NSF is working to develop a micromachined planar patch-clamp system with integrated microfluidics that will create a new paradigm in patch-clamping. The technology will make possible new patch-clamp configurations that extend the range and versatility of the technique. The possible new configurations that this technology can address are; rapid intracellular perfusion, improved optical access for concurrent optical measurements, rapid measurement of single-cell dose-response curves, and a large improvement in experimental throughput.

The approach being developed is to modify the configuration of traditional patch-clamp systems, which use micro-pipettes to interface with the cell membrane. In this new approach, micromachining technology is used to create planar substrates with an orifice that interfaces with the cell membrane, replacing the traditional micro-pipette. The planar configuration of these substrates allows for the integration of complex micro-fluidic systems, multiple orifices on one chip, and an optical path in line with the optical path of a microscope. ■

Nano- and micro-machined patch-clamp instruments with integrated microfluidics can dynamically monitor the physiology of single cells and can provide great insight into their fundamental biology.



Photograph of a micromachined planar patch-clamp chip integrated with a PDMS microfluidic system. Optical micrograph of the microfluidic dose-response measurement system and cell-patch site. Scanning-electron micrograph of the cell patch site.

This research received federal funding from NASA and NSF

Collaboration within CNSI

Dramatic Slip Effect of Liquids Flowing on Nano-Engineered Surfaces

The slip of liquid flow over a solid surface is important for many practical problems such as tribology, lubrication, flows through porous media, liquid coating, particle aggregation, and microfluidic devices, etc. While many studies have confirmed the existence of liquid slip over certain solid surfaces, there has not been a deliberate effort to design and fabricate a surface that will maximize the slip in practical conditions. Here, a nano-structured super-hydrophobic surface has been engineered that would minimize the liquid-solid contact area so that the liquid flows predominantly over an air layer (Fig. 1). The surface is made full of non-wetting sharp and tall post structures by black silicon method (Fig. 2). The main engineering significance is that the posts are populated with nano-scale pitch and remain dry even under pressurized liquid, which represents most real flow conditions. Measured through a cone-and-plate rheometer system, the nano-engineered super-hydrophobic surface has demonstrated a dramatic slip effect useful for drag reduction in practice: a slip length of ~20 μm for water flow and ~50 μm for 30 wt% glycerin, which also shows the dependence of slip on the liquid viscosity (Fig. 3). It can reduce the friction in liquid flow by a significant amount not only for droplets but also in continuous flows in various micro-scale fluidic problems (Fig. 4). It could also be applied to reduce the viscous skin friction in macro-scale applications, if the boundary layer thickness of the body in the flow is comparable to the slip length. Furthermore, the nano-engineered surface can open many new possibilities in various application areas including biomedical. ■

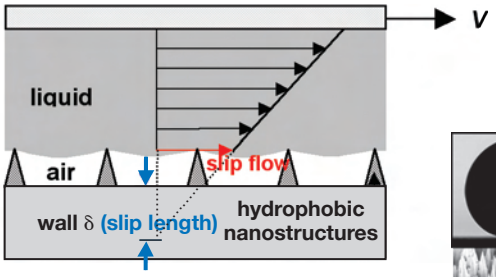


Fig. 1. Concept of large slip flow by a nano-engineered surface in Couette flow. Liquid sits on hydrophobic structures by surface tension. Majority of liquid boundary is with air where shear stress is much smaller.

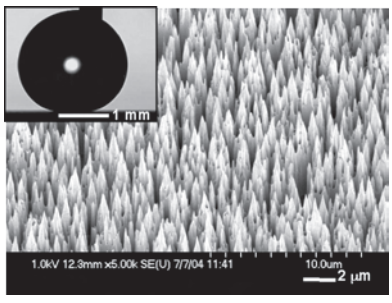


Fig. 2. SEM image of a NanoTurf surface made by the black silicon method. The inset shows the contact angle of water droplet on the hydrophobic NanoTurf surface.

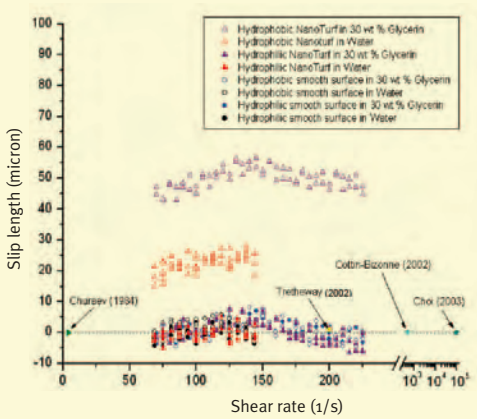


Fig. 3. Experiment results for effective slip length. Hydrophobic NanoTurf shows dramatic effective slip lengths for both water (Δ,~20 μm) and glycerin (Δ, ~50 μm), where all others show slips not much different from the measurement uncertainties. Some data in the literature are included for comparison.

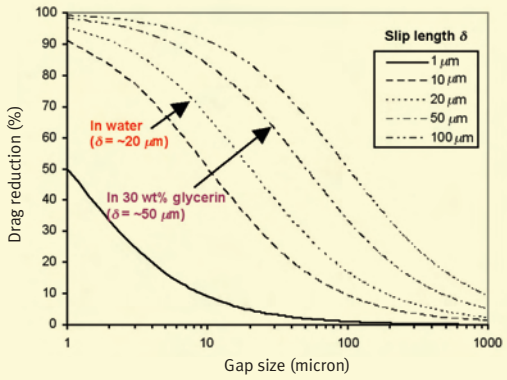


Fig. 4. Projected drag reduction by the hydrophobic NanoTurf as function of gap size between two plates in Couette flow, where only a stationary plate surface allows a slip with a slip length δ.

This research received federal funding from NSF

Collaboration between CNSI and University of Bologna

Operating Nanoelevators

Natural molecular machines, such as ATP-synthase, myosin, kinesin, or dynein are complex and inspiring biological assemblies whose structures and working mechanisms have been elucidated in a few cases. These intriguing systems have prompted scientists to design and build artificial molecular machines by mimicking their biological counterparts. In this sense, phenomena that control the form and function of living systems, such as self-assembly, molecular recognition, and multivalency have been employed in supramolecular chemistry and template-directed synthesis in order to construct functional molecular devices. Attempts to extend the concept of a machine to the molecular level, by taking advantage of biomimicry, have yielded a plethora of switches, tweezers, shuttles, and even molecular muscles, walkers and rotary motors. Each of these molecular machines has been designed specifically to perform particular functions upon application of an external energy input.

The development of synthetic molecular machines has been greatly enhanced by pooling intellectual resources of appropriate groups. In this regard, the collaboration between CNSI and the University of Bologna has resulted in an important contribution to the field of Supramolecular Chemistry and Molecular Nanotechnology. CNSI has focused activities on designing and building molecular-level devices and machines in the frame of bottom-up approach to nanotechnology. The University of Bologna has investigated such devices and machines powered by chemical energy, electrochemical energy, or light in order to understand the properties and operational mechanisms of these kinds of artificial machines as a prelude to optimizing their performance.

Multivalency can be harnessed in the construction of mechanically interlocked molecular components beyond the realm of a relatively simple bistable [2]rotaxane.

Inspired by the concept of multivalency and using template-directed synthesis, two trivalent mechanically interlocked molecular machines were conceived (*Science* 2004, 303, 1845-1849 and *J. Am. Chem. Soc.*, In press) with two orthogonal recognition sites for dibenzo[24]crown-8 (DB24C8), and 2,3-dinaphtho[24]crown-8 (DN24C8) – one a dialkylammonium ion ($CH_2NH_2^+CH_2$) and the other a bipyridinium dication ($BIPY^{2+}$). Whereas at low pH, the $CH_2NH_2^+CH_2$ sites bind the DB24C8/DN24C8 macrocycles preferentially, at high pH, deprotonation occurs with loss of hydrogen bonding, allowing the macrocycles to move to the $BIPY^{2+}$ sites where they can acquire some stabilizing π–π stacking interactions. ^{1}H NMR spectroscopy and cyclic voltammetry, aided and abetted by absorption spectroscopy, have been employed to unravel the details of the mechanism by which the rig and platform components move on the alternate addition of base and acid. For each molecular elevator, the platform operates by taking three distinct steps associated with each of the three deprotonation/reprotonation processes. Thus, molecular elevators are more reminiscent of a legged animal than they are of passenger on freight elevators. ■

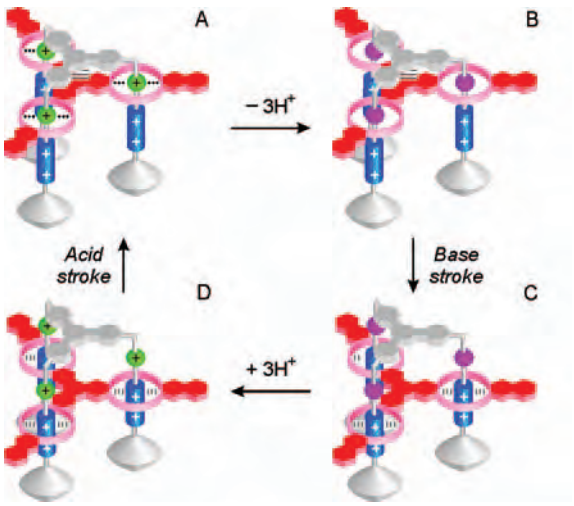


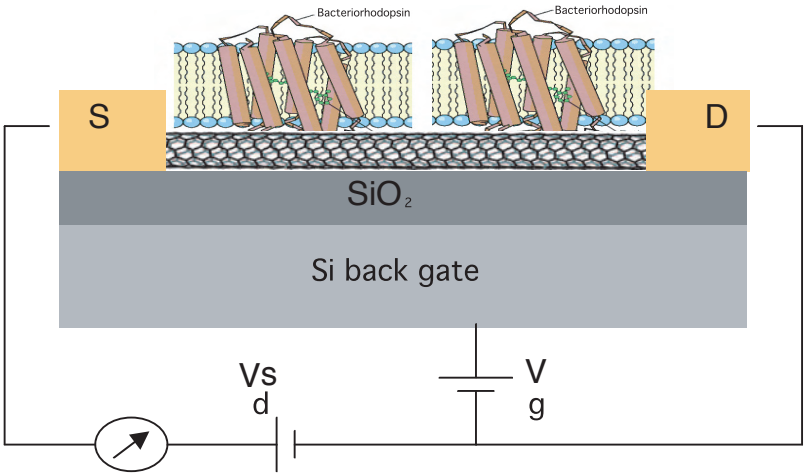
Fig. The base-acid controlled mechanical switching in the molecular elevators.

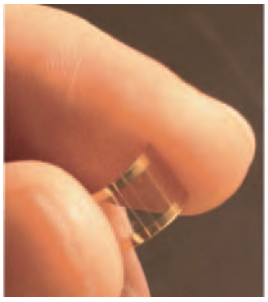
This research received federal funding from NSF and CAPES, Brazil

Collaboration among CNSI, Max Planck Institut fur Festkorperforschung and Nanomix, Inc.

Nanoscale Materials for Novel Electronics

Transparent and flexible transistors have been fabricated using random networks of nano-scale materials such as carbon nanotubes, the word's smallest electronic wires. The performance of the devices exceeds that of all other transistor devices, and the work opens up the avenue for applications in the area of what is called flexible or macro-electronics. Using such transistors, the first integration of a nanoelectronic device with a biological system, a cell membrane containing the bacterium *Halobacterium salinarum* has been demonstrated. Both components remained intact during integration, and the characteristics of the transistor could be used to gain information on some important aspects of the biological system, such as the charge distribution of the bacterium. The work represents the first step towards "cellectronics" the integration of cells with active electronic devices. ■





Electronic devices built of nanoscale wires will have major impact in emerging technologies such as flexible/transparent macroelectronics, bio-inspired detection and cellectronics.

This research received federal funding from NSF

Collaboration within CNSI

Bio-Signature Detection of Oral Fluid

Saliva in its native state is a complex diagnostic medium that contains biomarkers in both the cell and serum phase. The high specificity NEMS processor will separate cells from the serum and examine the analytes in both phases of a patient's saliva sample, to facilitate the detection and to form a complete diagnostic profile. The analytes include antigens for antibody molecules, and target DNA or RNA for complementary DNA fragments.

An electrochemical DNA sensor is being developed to detect strep-mutans bacteria since detection of DNA inside the cell provides for highly specific and sensitive identification. Electrochemical DNA detection is based upon hybridization of the target ssDNA to a capture probe immobilized on an electrode surface (Fig. 1). A detector probe labels the target ssDNA and produces a measurable amperometric signal. An ultra-sensitive sensor with atto mole sensitivity has been developed. The current output of the electrochemical DNA sensor is shown in Fig. 2. The presence of ssDNA can be identified as well as decreasing current values coupled with decreasing DNA concentrations. This technique is currently being applied for detecting strep-mutans. The preliminary experiments verify the ability of the electrochemical method to detect DNA strep-mutans. Improvements in the signal to noise ratio are being made to increase sensitivity. Furthermore, results from noise analysis experiments reveal that non-specific binding of the enzyme to the electrode surface is the main contributor to the background noise. The surface will be modified to discourage non-specific binding in the electrode design. ■

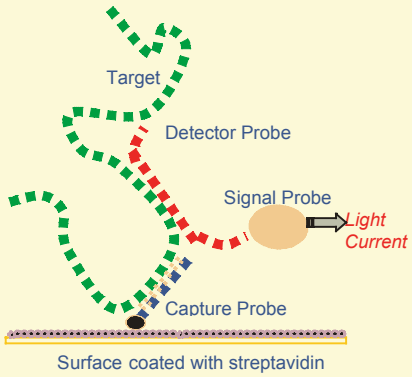


Fig. 1. DNA Detection Scheme

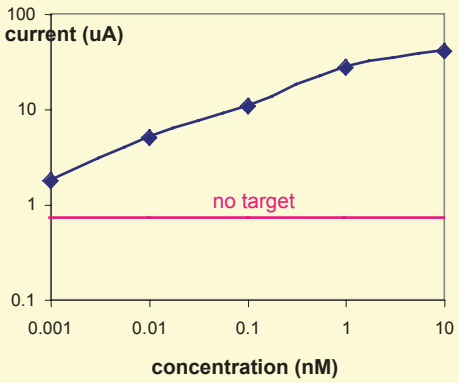


Fig. 2. DNA measurement: current vs. concentration

This research received federal funding from NIH and a CNSI scholarship

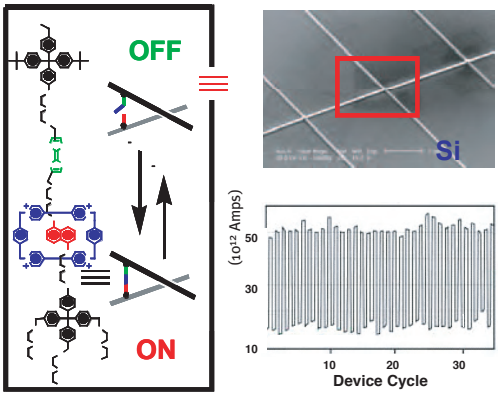
Collaboration between CNSI and Caltech

Nanoelectronics: From Solution to Devices

The field of molecular electronics is teeming with results, rationalizations and speculations from many research laboratories. At the heart of this field is the drive to construct molecular electronic devices that exhibit and take advantage of the rich set of molecular properties which are under modular chemical control through contemporary synthesis. This challenge is being met with increasing frequency, ranging from the simplest molecular electronic devices that include resistive tunnel junctions and rectifiers to active devices, including two- and three-terminal electronic switches. In a long-standing collaboration, since 1999, CNSI and Caltech have developed molecular memory devices that have withstood extensive scientific scrutiny.

In 2000, the UCLA and Caltech groups reported (*Science* 2000, 289, 1172–1175) that a two-terminal molecular switch tunnel junction (MSTJ) device containing a bistable catenane sandwiched between silicon and metallic electrodes exhibits a memory effect. When biased at +2 V the device is switched ON. Whereas, following a –2 V bias, the device is returned to its OFF state. The ON state has a finite, temperature-dependent lifetime of about 10 minutes, i.e., it is metastable. Subsequently, amphiphilic bistable rotaxanes were reported (*ChemPhysChem,* 2002, 3, 519-525) to switch by a related mechanism.

Bistable mechanically interlocked molecules have been demonstrated to work as molecular switches, that can be turned ON and OFF, regardless of the physical environment they find themselves inhabiting.



MSTJ device (Top right) that contain a monolayer of the [2]rotaxane (Left) sandwiched between silicon and metallic electrodes. The device can be switched reconfigurably and cycled repeatedly between ON and OFF states (Bottom right).

The explanation advanced to account for these observations is based on a cycle of voltage-controlled, mechanical movements between two isomers that occur within the bistable molecules in the device. This mechanism agrees qualitatively with that derived from solution-phase measurements but with significant quantitative differences. For example, the relaxation of the ON to OFF state within the MSTJ is much slower than that observed in solution. Subsequently, similar results for bistable rotaxane-based MSTJs were reported. The hypothesis was that, although the confined environment of the MSTJ impacts the molecular switching cycle, the overall mechanism is the same. Thus, variable temperature measurements were performed on the cycle of switching bistable molecules in solution, in self-assembled monolayers, in a polymer matrix, and in MSTJs (*Appl. Phys. A* 2005, 80, 1197-1209). Within these environments, we recorded the lifetime of the metastable state increases from ~0.1 second to several minutes as the molecules are confined to smaller spaces.

The UCLA and Caltech groups reported recently (*Science* 2004, 306, 2055–2056) their findings in support of the role the molecules play in their memory devices. As practitioners of molecular electronics, they believe the field will be best able to provide practical support to the traditional electronics industry when its development is based on sound scientific conclusions that have been tried and tested at every step. The most important early applications will emerge when molecules are integrated in hybrid fashion with existing technologies. When this development happens, the opportunities for bringing the science to maturity will be obvious. ■

This research received federal funding from NSF, DARPA, MARCO, FENA and CNID

Collaboration between CNSI and FENA

Devices and Structures beyond CMOS

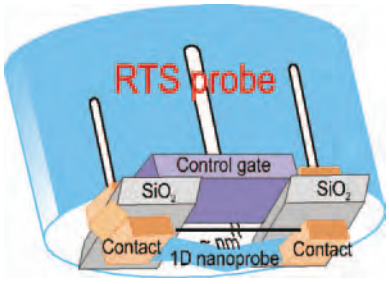
Integrated circuits based on Complementary Metal Oxide Semiconductors (CMOS) have been one of the main forces for economic growth during the past half-century. These circuits have enabled the creation of many important products such as personal computers, cellular phones, global positioning systems, medical instruments and others. The International Technology Roadmap for Semiconductors highlights uncertainties in scaling beyond the 10nm CMOS node size.

Next generation post-CMOS devices such as the Spin Wave Bus will gain considerable attention as scaling of CMOS continues to face increasing power and cost challenges.

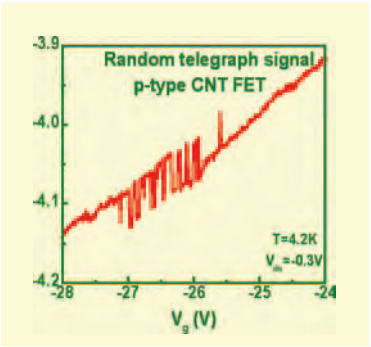
To address this situation, in a joint industry-government partnership, the Center on Functional Engineered Nano Architectonics (FENA) has been established through the Focus Center Research Program (FCRP) managed by the Microelectronics Advanced Research Corporation (MARCO). FENA is a multi-institutional distributed research center consisting of 12 US universities and 30 distinguished principal investigators. FENA examines novel nanoscale materials and structures, focusing on fundamental atomic and molecular level understanding, to enable new properties to be more rapidly incorporated in devices and architectures. FENA research endeavors are in close collaboration with CNSI.

One of the many research achievements of FENA in collaboration with CNSI has been the development of a novel Telegraph signal microscope (TSM) as a nano-metrology probe based on random telegraph signal (RTS) principle. TSM uses telegraph signals due to single charge in one-dimensional nanodevices such as carbon nanotubes (CNTs) / nanowires as a sensitive nanoscale probe for single defect/impurity, single molecular characterization. The TSM can combine with atomic force microscopy to both acquire morphology and characterize material with ultra-high sensitivity. Information such as the defect/impurity/molecular 3-dimensional position, energy and even the small bandgap of nanowires, are critical for nanodevices, novel material, and their reliability test can be characterized by using the TSM. Another achievement has been the conceptualization of a spin-based computational device utilizing spin waves as a physical mechanism for information transmission and processing. The novelty of this approach is that information transmission is accomplished without charge transfer. A bit of information is encoded into the phase of spin wave propagating in a ferromagnetic film - *Spin Wave Bus*. The communication between the Spin Wave Bus and outer devices is performed in a wireless manner via a magnetic field.

The realization of the Telegraph Signal Microscope and the Spin Wave Bus are just some of the ways FENA is looking to go beyond the limits of conventional CMOS. Collaborations with CNSI and multidisciplinary faculty are key to FENA's ambitious research endeavors. ■



Single atom CNT/nanowire RTS nanoMOS probe.



The graph shows RTS single charge fluctuation.

This research received federal funding from SIA, DARPA and MARCO

Collaboration between CNSI and The Aerospace Corporation

Polyaniline Nanofibers for Chemical Sensing

Polyaniline nanofibers on a simple gap electrode sensor provide a rapid means to detect hazardous vapors. The use of nanofibers reduces the response time while a variety of additives allow specific detection of harmful chemicals.

The ability to sense toxic chemicals have become a national priority. There is a current lack of inexpensive gas sensors that can be used to prevent harm from many industrial hazards and chemical attacks. A potential solution is a diverse polyaniline nanofiber based sensor under development in a collaboration between CNSI and the Aerospace Corporation for the Department of Homeland Security. The low cost and versatile chemistry of polyaniline has allowed the development of gas sensors with ultra-low detection levels for a variety of substances that are toxic or industrially relevant.

Polyaniline is a conducting polymer which has a uniquely simple doping/dedoping chemistry based on acid/base reactions. When blue non-conducting emeraldine base comes into contact with acidic vapor it rapidly dopes to form the green conducting emeraldine salt. This change is seen as a dramatic decrease in the resistance (Fig. 1b). Conventional polyaniline is synthesized at low temperature and requires organic solvents such as N-methylpyrrolidinone for processing into a chemical sensor. A facile room-temperature rapid polymerization method for water dispersible polyaniline nanofibers has now been developed. When polyaniline has a nanofibrillar morphology the resistance change is more than 10 times faster than that of a conventional thin film of polyaniline.

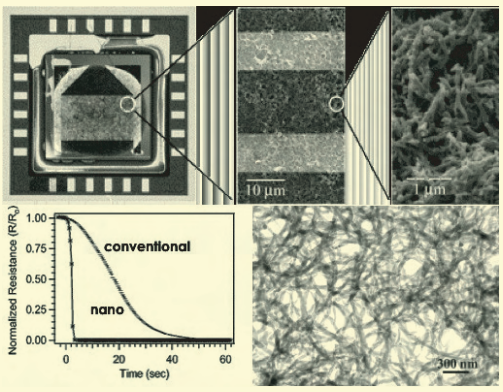


Fig. 1 a) The polyaniline nanofiber sensor, gap electrodes and nanofibers are shown from left to right. b) Polyaniline nanofiber thin films respond much faster to strong acid vapor (100 ppm HCl) than conventional polyaniline. c) A closeup TEM image of polyaniline nanofibers.

The chemistry developed for conventional polyaniline can be exploited for specific sensing with polyaniline nanofibers through the generation of doping or dedoping agents. The collaboration with the Aerospace Corporation supported by Homeland Security has led to the discovery of several chemical additives that provide a resistivity change when a specific analyte comes in contact with the polyaniline film. One particularly hazardous chemical, hydrogen sulfide (H_2S), desensitizes the olfactory senses preventing detection of its distinctive rotten egg smell. It can cause respiratory failure at 200 ppm and has a permissible exposure limit of 20 ppm. Polyaniline nanofibers decorated with metal halides can easily detect the presence of H_2S at less than 10 ppm through the generation of HCl, which rapidly lowers the resistivity of polyaniline emeraldine base. Another toxic chemical, hydrazine, which is a chemical reducing agent and a hazardous component in rocket fuels, can be detected at ultra-low levels with a suitable additive, hexafluoroisopropanol, to the polyaniline nanofibers. Exploration of other additives such as metal nanoparticles and organic catalysts are leading to developments for chemical detection of specific chemical agents. By incorporating different elements into a sensor array, accurate and inexpensive analyte detection will become a reality. ■

This research received federal funding from the Department of Homeland Security

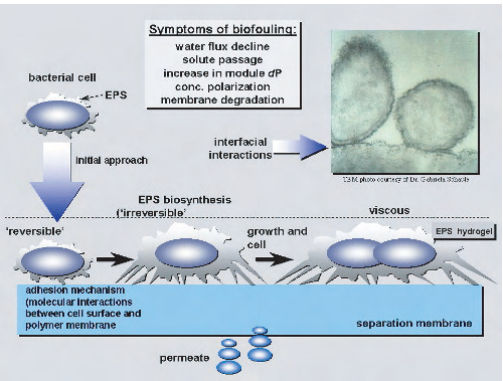
Collaboration between CNSI, UCLA and NanoH2O, LLC

Low-Fouling Thin Film Nanocomposite Membranes for Water Production

Biofouling has been called the 'Achilles heel' of membrane processes. Nanocomposite materials are enabling rapid advancements in structural and functional materials. Thin film nanocomposite membranes could revolutionize water production processes due to their low energy consumption and resistance to fouling.

Surface fouling phenomena plague many biological, environmental, and chemical engineering systems such as medical implants, environmental sensors, and membrane processes. Understanding and controlling surface fouling in aquatic systems requires knowledge of colloid and surface chemistry, chemical equilibria and kinetics, momentum and mass transfer, and interfacial engineering. Biofouling has been called the 'Achilles heel' of water treatment membrane processes because it can not be eliminated by feed water pretreatment, membrane surface modification, module hydrodynamic improvements, process optimization, or chemical cleaning. Hence, a breakthrough in membrane technology is required to overcome this recalcitrant and costly problem.

The first viable reverse osmosis membrane was made from cellulose acetate as an integrally skinned asymmetric semi-permeable membrane. This membrane was made by Loeb and Sourirajan at UCLA in 1959 and patented in 1960. The current generation of reverse osmosis (RO) membrane materials are based on a composite material patented by FilmTec Corporation in 1970. FilmTec's FT30 membrane is known as a polyamide thin film composite membrane. However, these membranes are highly susceptible to biofouling and are easily degraded by common oxidizing disinfectants.



A new method of synthesizing super-hydrophilic nanoparticles and incorporating the synthesized nanoparticles into a polyamide thin film has been developed. This new type of membrane is called a "thin film nanocomposite (TFN)" membrane. This approach represents the next generation of RO membrane materials because, unlike all other membrane surface modification approaches, it can be immediately incorporated into existing commercial manufacturing facilities. In addition, nanoparticle properties can be selected or modified to impart a wide array of advantageous membrane surface properties such as chemical reactivity, antimicrobial activity, and vibratory motion.

Characterization of the first generation of low fouling TFN membranes suggests they can produce as good or better product water quality using significantly less pressure (energy) requirements and they are more resistant to microbial adhesion and easier to clean. A nanocomposite formed from super-hydrophilic and antimicrobial nanoparticles has also been synthesized and tested. In these membranes, adhered cells are rapidly inactivated due to the intrinsic and regenerative biocidal properties of the synthesized nanoparticles. UCLA has filed a provisional patent application for the process of making thin film nanocomposite membranes and in collaboration with NanoH$_2$O, LLC, UCLA and CNSI researchers will develop this new class of hydrophilic and antimicrobial membranes into a viable commercial technology for desalination and water purification. In the future, this nanocomposite approach may be used to form low-fouling coating layers on other objects such as electrodes, sensors, and implants. ■

Collaboration between CNSI and UCLA

Multivalent Carbohydrate-Protein Interactions Through Self-Assembly

Two of the central building blocks of life are proteins and carbohydrates. The interactions between these two disparate types of biomolecules play a role in numerous biological processes and are critical to the onset, detection, and, potentially, prevention, of human diseases such as cancer. Despite the importance of these interactions, the binding between an individual protein and an individual carbohydrate is typically quite weak and not very specific. Nature obtains strong and specific responses through multiple protein-carbohydrate interactions, a phenomenon known as *multivalency*.

Previously, the UCLA department of Pathology has focused on understanding natural multivalent carbohydrate-protein interactions and their biological consequences, particularly in the human immune system, and the departments of Chemistry and Biochemistry have focused on developing novel architectures for displaying carbohydrates and multivalency in unnatural systems. Under the aegis of the CNSI, an interdisciplinary collaboration has been initiated to study multivalent protein-carbohydrate interactions using self-assembly and nanotechnology. A potential clue to the understanding of multivalent carbohydrate-protein interactions is that they typically take place at cell surfaces, where one or both of the components are attached to cellular membranes. These are fluid and dynamic interfaces, which suggests that properties such as flexibility and adaptability may play important roles in these multivalent interactions.

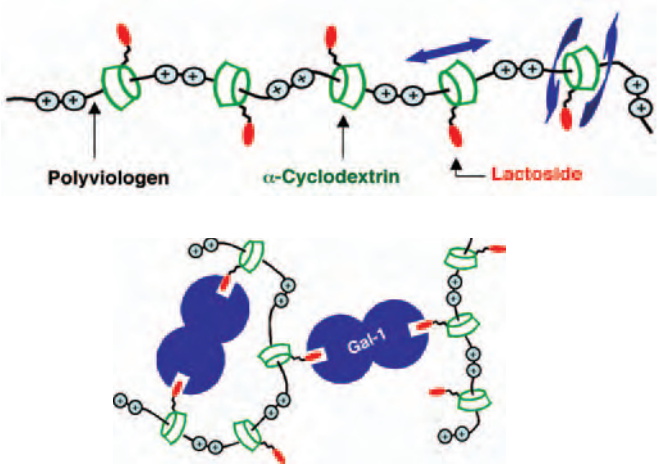


Fig. Self-assembled pseudopolyrotaxane and its potential multivalent interactions with galectin-1 (Gal-1).

The interactions between proteins and carbohydrates affect numerous biological processes, including cancer. Using self-assembly, nanoscale systems to probe and potentially exploit these interactions have been developed.

Using self-assembly, highly flexible and adaptable systems (Fig.) for displaying carbohydrates (lactosides) have been developed. In the so-called *pseudopolyrotaxanes* comprised of lactoside-displaying cyclodextrin (CD) "beads" threaded onto linear polyviologen "strings", the CDs are able to spin around the axis of the polymer chain as well as to move back and forth along its backbone to alter the presentation of lactosides (*J. Am. Chem. Soc.* 2004, 126, 11914–11922).

The interactions of these self-assembled, multivalent, nanometer-scale assemblies have been tested with galectin-1, a dimeric lactoside-binding protein with two binding sites. Galectin-1 plays a prominent role in the immune system and in certain human cancers. Synthetic multivalent ligands for galectin-1 have potential as cancer diagnostics and therapeutics. The self-assembled pseudopolyrotaxanes outperformed a more traditional polymer with covalently attached lactosides in T-cell agglutination assays, with valency-corrected enhancements of up to 10-fold over native lactose. The flexible and dynamic ligand presentation by pseudopolyrotaxanes adds a new dimension to the study of protein-carbohydrate interactions and the exploitation of multivalency for targeting therapeutically relevant lectins. ■

This research received federal funding from NSF and NIH

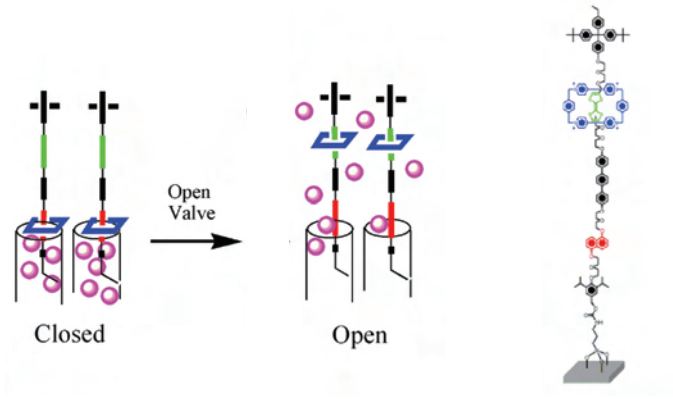
Collaboration among CNSI, University of Amsterdam, and University of Bonn

Powered Artificial Nano-Machines: Molecular Valves and Impellers

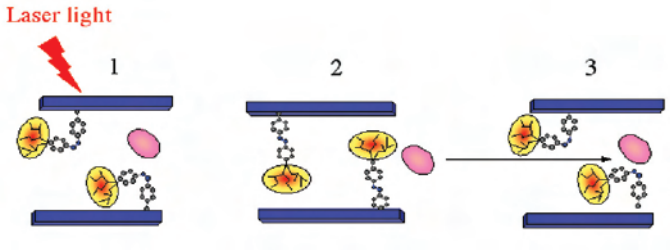
A machine is defined as a device that contains moving parts attached to a solid support that accomplishes a desired objective. In order to function, a machine also needs a source of power. The nano-machines that have reached the highest stage of development in current work are a reversible molecular valve and a molecular impeller. Both are the result of collaborative projects between CNSI and colleagues in the chemistry department (valve) and CNSI and European colleagues (impeller).

The molecular valve uses as its moving part a rotaxane consisting of a ring that is mechanically trapped on a dumbbell shaped component. The motion is of ring is powered by chemical energy or light energy. This system is attached to the pore openings in a solid silica support (consisting of 100 nm thin films or 500 nm spherical particles) each of which contains ordered arrays of 2 nm diameter tubular pores. In the closed configuration the movable ring blocks the openings of the pores and traps molecules inside of the pore. In the open configuration the ring moves away from the pore opening and allows trapped molecules to escape. This fully reversible trapping and releasing of molecules from pores is an example of a molecular valve.

The operation of the valve is powered by chemical or light energy. In the simplest operation, oxidation of the moving part causes the ring to block the pore and reduction of the moving part reverses the action and opens the pore. The operation of the valve is monitored by spectroscopy. The location of the trapped and released molecules is observed by its luminescence and the function of the valve itself is followed by measuring the quenching and recovery of its intrinsic luminescence.



The molecular valve traps (left) and releases molecules (right) from nano-pores.



Wagging motion impels molecules through the pores.

The impeller uses light-powered derivatized azobenzene molecules as its moving parts. The molecules are attached to the interiors of 2-nm pores in silica. When irradiated with appropriate wavelengths of light, the molecules “wag” back and forth. Molecules that are not attached to the pore walls are free to move through the pores and are impelled by the moving azobenzenes. In this light-driven machine, the action is monitored by fluorescence spectroscopy.

These collaborative projects combine the skills of synthetic, materials and physical research groups. In order to achieve success, theoretical, synthetic, spectroscopic and materials concepts had to be integrated to design, synthesize, self-assemble, power and monitor the complex nano-components comprising the valve and impeller. ■

Nano-machines consisting of moving parts attached to solid supports are powered by chemical or light energy to trap and release molecules in pores (nano-valves) or impel molecules through the pores (impellers).

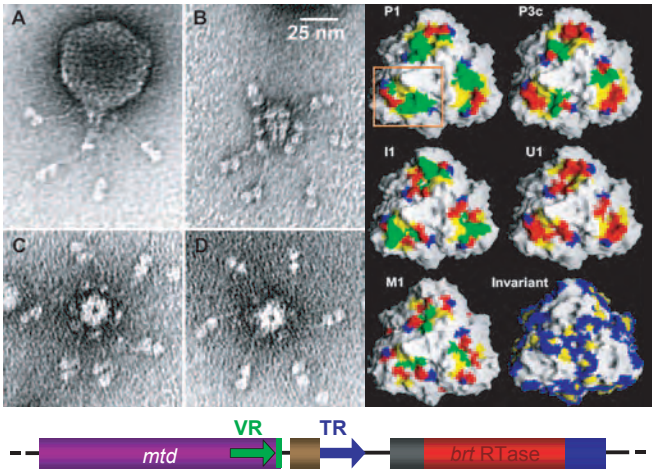
This research received federal funding from NSF

Collaboration among CNSI, UCLA, UCSD and AvidBiotics Corp

Diversity-Generating Retroelements

Viruses that infect bacteria (a.k.a. bacteriophage) are the most abundant replicating biological entities on the planet. These remarkable nanomachines have evolved myriad ways to subvert their bacterial hosts and multiply. A family of "diversity-generating retroelements" (DGRs) that function to diversify DNA sequences and the proteins they encode has recently been identified. The prototype DGR was found in a bacteriophage on the basis of its ability to generate variability in a viral receptor protein that specifies tropism for ligand molecules on host cells. This microevolutionary adaptation is produced by a novel genetic element that combines the basic retroelement life cycle of transcription, reverse transcription and integration with site-directed, nucleotide-specific mutagenesis. Central to this process is a reverse transcriptase-mediated exchange between two repeats, one serving as an donor template (TR) and the other as a recipient of variable sequence information (VR). Based on patterns of marker transfer in response to variant selective pressures, a TR reverse transcript is proposed to have integrated into VR as a single non-coding strand and then be partially converted to the parental VR sequence. This allows the diversity-generating system to minimize variability to the subset of bases under selection, and provides an opportunity to maximize receptor affinity through iterative rounds of optimization. Using the *Bordetella* phage cassette as a signature, numerous related elements in diverse bacteria have been identified. These comprise a new family of retroelements with the potential to confer selective advantages to their host genomes.

Diversity-generating retroelements may provide unique tools for protein engineering and for the development of "smart" antimicrobial agents able to overcome bacterial resistance.



A DGR-containing bacteriophage is shown (top left) along with the structure of the diversity-generating genetic cassette. On the right is a space filling model of trimeric, variable binding sites found in an array of phage receptor proteins. At bottom is the structure of the phage DGR. The electron micrograph was provided by Mari Gingery and Fred Eiserling (UCLA) and the phage receptor protein crystal structures were determined by Partho Ghosh and co-workers (UCSD).

DGRs encode polypeptides that are designed to tolerate massive sequence variation. This collaboration has recently discovered that a conserved C-type lectin fold is used to display amino acid sequence variability, with variable residues occupying a discrete, solvent exposed receptor binding site. The C-type lectin fold provides a strikingly static scaffold for combinatorial display of variable residues and it represents a unique solution for balancing diversity with protein stability.

In addition to their fundamental importance as naturally occurring agents of evolution, DGRs are of considerable interest as a result of their applications for generating vast amounts of targeted diversity for protein engineering. In the context of bacteriophage genomes, they may also allow the development of a new class of "dynamic" antibacterial agents able to keep pace with the development of antimicrobial resistance. A current collaborative effort is underway involving industry and academic-based scientists with expertise in bacterial genetics, bacterial pathogenesis, bacteriophage biology and structural biology to exploit DGRs for directed protein evolution. ■

This research received funding from The University of California Discovery Grant

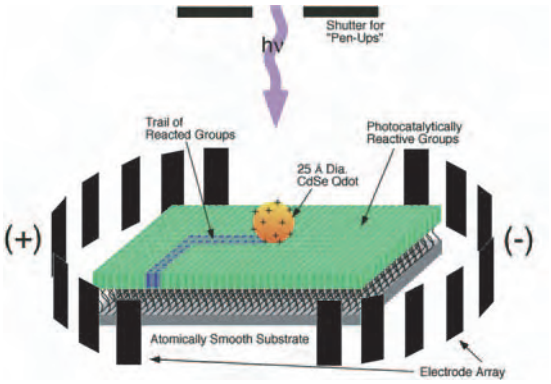
Collaboration between CNSI and FENA

Surface Nanopatterning by Electrophoresis of Photocatalytic Nanoparticles

A new concept is under development for drawing complex surface patterns at the molecular scale. This technology may provide a useful tool for creating nanoelectronic circuitry.

Lithographic techniques will reach their useful limit for complex surface patterning at a feature size of >10 nm. If the predicted size, speed and power advantages of molecular electronics are to be realized completely, means must be achieved to create complex patterns with a feature size of >10 nm. At this molecular limit, logic devices with densities on the order of 10^{12} gates/cm^2 become conceivable. The UCLA approach to surface patterning has the potential to yield complex patterns with a feature size of ~2-3 nm, and perhaps smaller. The basic idea entails the use of a force field (e.g., an electric field) to direct the movement of 25 Å, photocatalytic, semiconductor nanoparticles [e.g., CdSe quantum dots (qdots)] around on a self-assembled organic monolayer (SAM) chemisorbed on an atomically smooth substrate (e.g., gold or silicon) while simultaneously illuminating the surface. If the chemisorbed organic monolayer is composed of compounds that can be photocatalytically reduced by CdSe qdots, for example, then a trail of reacted molecules will be left behind as they are directed electrophoretically about the surface. By changing the orientation of the electric field in the plane of the substrate, complicated patterns may be drawn. Large numbers of qdots (i.e., many billions) could be spread on a surface to draw the same pattern simultaneously. Further, by intermittently shielding the light source, "pen-ups" can be included in the pattern. A wide variety of chemically functionalized surfaces with characteristic dimension similar to that of the photocatalytically active qdots (~2-3 nm) could be built up from these patterned surfaces. This technology eventually could lead to a relatively inexpensive means to pattern interconnections between the logic gates of a molecular computer. Further, this approach, which involves wet chemistry and relatively unsophisticated equipment, could be carried out in inexpensive production facilities. Few technologies have been conceived for patterning surfaces of any chemistry at the scale of a few nanometers. This concept entails a shift from current lithographic methods resulting in ~100 nm-scale patterns of inorganic materials to molecular-dimension patterns composed of organic chemicals. In addition to the tremendous organic synthesis knowledge base that can be drawn upon in the design of our surfaces, organic chemistry provides for straightforward interfacing with biological molecules and systems. Besides applications in molecular electronics, nanopatterned organic surfaces may enable the organization of effective molecular devices for the mimicry of biological systems such as those for vision, sensing, and complex-molecule synthesis.

Substantial progress has been made toward an initial demonstration of this nanopatterning approach. The collaborating group of organic chemists and chemical engineers currently are nearing a successful demonstration of the basic concept. A considerable amount of scientific ground has been covered involving organic chemistry, photocatalysis, surface science, scanning probe microscopy, fluorescence microscopy, and electrophoresis. ■



A photocatalytic CdSe qdot moving under the direction of a variable electric field across a "lawn" of reactive groups leaving behind a nano-scale trail.

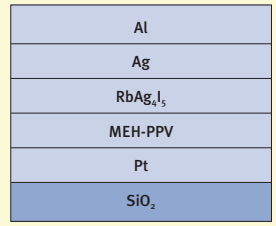
This research received funding from NSF and ONR

Collaboration between CNSI and UCLA

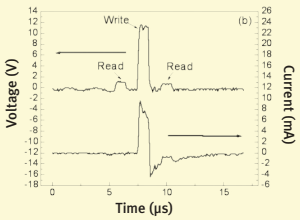
Organic Nonvolatile Memory by Configuring Ionic Dopants in Polymer

An organic nonvolatile memory device based on its conductance change induced by configuring the dopant concentration in a conjugated polymer is reported. The device consists of a poly[2-methoxy-5-(2'-ethylhexyloxy)-*p*-phenylene vinylene (MEH-PPV) polymer/inorganic ionic conductor($RbAg_4I_5$) bilayer sandwiched between two metal electrodes. When a voltage exceeding its threshold values (> +2.2 V or < -3.5V) is applied between the two metal electrodes, the conductance of the devices can be electrically switched from (to) its low-conductive "Off" and to (from) its high-conductive "On" states by injecting (expelling) iodine dopant ions to (from) the MEH-PPV layer. The devices can be switched on and off reversibly and repeatedly by pulse voltages with On/Off conductance ratios approaching four orders of magnitude and a pulse duration as small as 1 μs. The mechanism to switch a polymer device by changing its doping concentration provides a promising approach to make various electrically configurable devices in the future. ■

Organic Nonvolatile Memory



The schematic diagram of the device structure



Turn-on of a device with pulse duration of 1 μs.

Collaboration between CNSI and UCLA

Pretzelanes Go Nano

A redox-controllable bistable molecular pretzelane has been synthesized using template-directed synthetic protocol. Introduction of a stereogenic center by a stereospecific synthesis into an optically active, donor–acceptor pretzelane exhibits helicity as well as chirality.

Through its exploitation of noncovalent bonding interactions and self-assembly processes, supramolecular assistance to covalent synthesis has established itself as an efficient means of creating molecules with nanoscale dimensions. For two decades, researchers have harnessed the power of post-assembly covalent modification to produce an array of mechanically interlocked molecular compounds, some of which have been shown to behave as molecular machines and switches on surfaces and at interfaces, respectively. A template-directed protocol has been developed for the construction of [2]catenanes composed of a crown ether containing π-electron-rich aromatic ring systems and a tetracationic cyclophane comprised of two π-electron-deficient bipyridinium units. If the crown ether is covalently tethered to this second component, then the resulting cyclization(s) could occur either intramolecularly and generate a pretzelane or intermolecularly and generate cyclic or linear oligo/polycatenanes. Introduction of a stereogenic center by a stereospecific synthesis into an optically active, donor–acceptor pretzelane, that exhibits helicity as well as fixed chirality, leads to a marked preference for one conformational diastereoisomer over the other in both acetone and dimethylsulfoxide that can be understood from computational models.

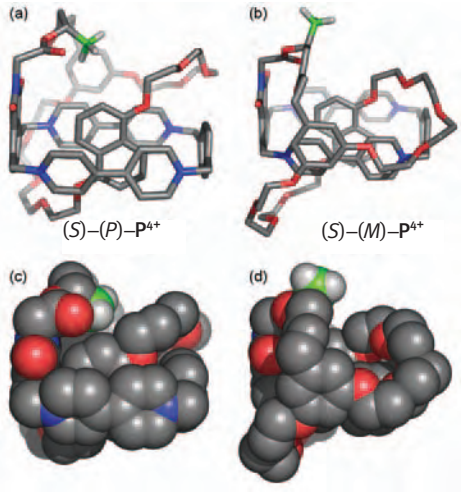


Fig. MM2-optimised structures of the (*S*)–(*P*)–$\mathbf{P}^{4+}$ and (*S*)–(*M*)–$\mathbf{P}^{4+}$ isomers as portrayed by (a and b) framework and (c and d) space-filling representations, respectively.

A group of synthetic and computational chemists have reported (*Chem. Commun* 2005, 3927–3929) the synthesis of the chiral pretzelane (*S*)–(*P/M*)–$\mathbf{P}^{4+}$ (Fig.). In the pretzelane $\mathbf{P}^{4+}$ helical chirality arises from the location of the crown ether on either one of the two bipyridinium units on the tetracationic cyclophane. Therefore, a pair of (*P*) and (*M*) enantiomers have been observed with a free energy of activation of 17.5 kcal/mol for their inversion in CD_3COCD_3 solution. Force-field modeling has been employed to provide insight into the diastereoisomeric conformational preference, namely that the (*M*)-isomer is preferred over the (*P*)-isomer in (*S*)–$\mathbf{P}^{4+}$. The calculation, based on the MM2 force field, matches closely that of the experimental ΔG° value of 1.3 kcal/mol. The energy minimized structures associated with both conformations retain the expected noncovalent bonding interactions, including the [π...π], [C–H...π] and [C–H...O] interactions that are operative when the 1,5-dioxynaphthalene unit is located inside the cavity of the tetracationic cyclophane. The methyl group on the linker in the (*S*)–(*P*)–$\mathbf{P}^{4+}$ isomer points in towards (Fig., a and c) the cavity formed by one of the tetraethylene glycol loops of the crown ether component and one of the bipyridinium units in the tetracationic cyclophane while, in the case of the (*S*)–(*M*)–$\mathbf{P}^{4+}$ isomer, the methyl group points away (Fig., b and d) from this cavity. The crowding that the methyl group experiences in the (*S*)–(*P*)–$\mathbf{P}^{4+}$ isomer is presumably the origin of the preference for the (*S*)–(*M*)–$\mathbf{P}^{4+}$ isomer. ■

This research received federal funding from NSF and DARPA

Collaboration between CNSI and UCLA

Synthesis, Control, and Assembly of Molecular Machines

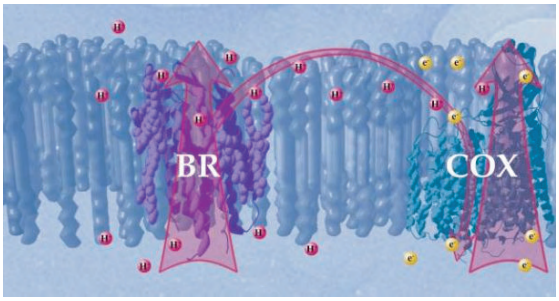
Membrane proteins have been nature's solution to perform a plethora of tasks, from transporting ions in order to maintain homeostasis to synthesizing ATP for metabolism. By utilizing the functionality of nature's molecular machines, their incredible efficiency at performing work can be harnessed.

Bacteriorhodopsin (BR) and Cytochrome C Oxidase (COX) are two proteins found in nature embedded in a lipid bilayer, the component of a natural cell membrane. Lipid bilayers, unfortunately, have a limited lifetime and can deteriorate with fluctuations with temperature or high voltages. At UCLA, the lipid bilayer is replaced with a triblock copolymer that mimics the hydrophilic-hydrophobic-hydrophilic chain of a natural cell membrane. Copolymer membranes are much more robust than lipid bilayers, resulting in longer lifetimes. Several proteins have also been successfully reconstituted, including BR and COX, into polymer membranes and protein functionality has been demonstrated in these artificial systems.

BR is a light-activated proton transporter found in the cell membrane of the bacteria *Halobacteria halobium*. Upon illumination by green light (500-650nm), BR undergoes a conformational change resulting in the translocation of a proton from the intracellular side to the extracellular side. The UCLA goal is to use BR to create a high electro-chemical proton gradient in order to drive a second protein, COX, in reverse. In nature, COX, found in mitochondria, accepts electrons from a reduced Cytochrome C, an electron mediator, to ultimately reduce O_2 into H_2O. Studies have shown, however, that given a high proton gradient and high concentration of oxidized Cytochrome C, it becomes energetically favorable for COX to function in reverse, thereby oxidizing H_2O into O_2 and donating electrons to an oxidized Cytochrome C. Using these nanoscale proteins, micro-Ampere light-dependent current production can be demonstrated in a direct current measurement. The system is currently being optimized to yield much larger currents.

By combining BR and COX, two proteins that function independently of one another in nature, into a single system, one can use the potential energy created by the proton translocation from BR to drive COX to function in reverse, essentially converting the solar energy captured by BR into electrical work performed by COX. The electrons freed in this process are then harnessed by an electrode to generate an electric current. By taking advantage of the efficiency of nature's molecular machines, this system can lead to a new generation of thin-film solar cells with exceptionally high power densities. ■

Membrane proteins possess the ability to convert energy with extremely high efficiencies. By using the membrane proteins Bacteriorhodopsin and Cytochrome C Oxidase, the ability for BR to convert solar energy into an electrochemical gradient which is then used to derive electrical energy from COX has been demonstrated.



BR and COX are reconstituted into a polymer membrane. When exposed to light, BR pumps protons, driving COX to release electrons.

This research received federal funding from U.S. DOD/Advanced Research Projects Agency

Collaboration between CNSI and The Advanced Light Source at Lawrence Berkeley National Laboratory

Rational Design of Ultra-incompressible, Superhard Materials

The quest for superhard materials for industrial applications is an important goal in the field of materials engineering. Successful collaboration has produced new ultra-incompressible, hard materials.

Interest in the mechanical properties of materials is spurred by opportunities for industrial applications. These applications require highly robust materials for use as abrasives, cutting tools and coatings where wear prevention, scratch resistance, surface durability and chemical stability are a priority. Therefore, the development of a new class of ultra-incompressible, superhard materials is of great practical interest. To address these needs, two groups at UCLA have teamed up with scientists at the Advanced Light Source at Lawrence Berkeley National Laboratory with support from the National Science Foundation to focus on the rational design, synthesis and characterization of ultra-incompressible, superhard borides.

The paradigm for rational design of these unique and impressive materials applies the specific design parameters of high valence electron density and bond covalency. Incorporation of the small main group element boron into the interstices of the hexagonally close-packed crystal structure of osmium metal yields osmium diboride, OsB_2. This compound maintains the high valence electron density of osmium that provides remarkable incompressibility while also enabling directional covalent bonds to form. These covalent bonds limit the mobility of dislocations—in other words, the degree to which the planes of osmium atoms can slide past each other, thereby increasing the hardness of the material.

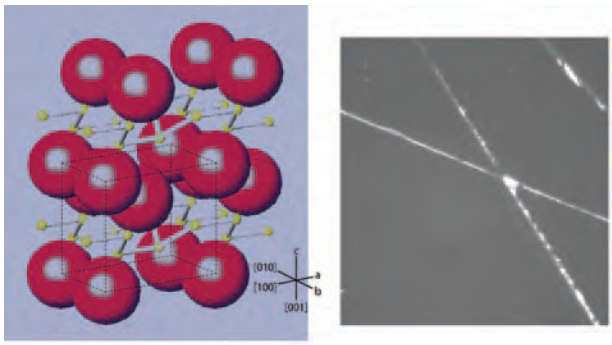


Fig. 1 a) The crystal structure of osmium diborde is pictured on the left. Osmium atoms are shown as large red spheres while boron atoms appear as small yellow spheres. b) A sapphire window scratched with osmium diborde powder under 500x magnification.

To characterize the mechanical properties of osmium diboride, several experiments have been performed. *In-situ* high pressure X-ray diffraction is accomplished using a diamond anvil cell at the Lawrence Berkeley National Laboratory. This technique allows the determination of the bulk modulus (incompressibility) of the polycrystalline material. Osmium diboride is nearly as incompressible as diamond in three dimensions and even more incompressible than diamond along one direction, the c-axis. Qualitative hardness testing of osmium diboride has been performed using a sample to scratch a sapphire window. This places osmium diboride on the Mohs hardness scale between 9 (sapphire) and 10 (diamond). Quantitative hardness testing using a nanoindentation technique is now in progress. Applying the design parameters outlined above, many other ultra-incompressible, superhard materials should be possible. For example, materials related to osmium diboride in which other dense transition metals are substituted for osmium or other small main group elements are substituted for boron, could prove to be especially interesting. ■

This research received federal funding from NSF

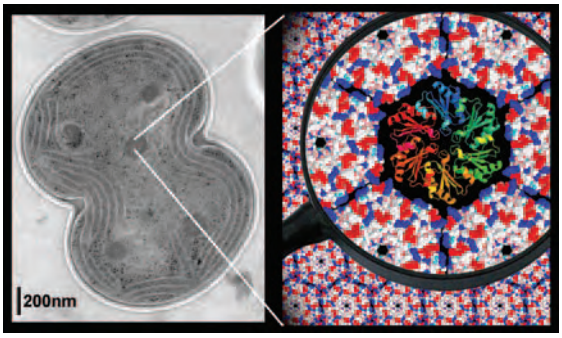
Collaboration within CNSI

Structure of Bacterial Microcompartments: Nature's Primitive Organelle

The defining distinction between the cells of bacteria and the cells of higher organisms is the presence of a high level of subcellular organization in the latter. This subcellular organization is achieved by membrane-bound organelles, which allow eukaryotic cells to carry out different metabolic processes in different regions of the cell. While true membrane bound organelles are absent from bacteria, the view that bacterial microbes lack subcellular organization is slowly changing. Bacterial microcompartments – large subcellular shells composed of protein subunits – were discovered in carbon dioxide fixing bacteria more than 40 years ago. In these microbes, the enzymes that carry out carbon dioxide fixation (e.g. RuBisCO and carbonic anhydrase) are sequestered inside the microcompartment, which in this case is called the carboxysome.

A search of genomic sequence databases reveals that proteins similar to the carboxysome shell proteins are widespread among the bacteria, including those that do not carry out carbon dioxide fixation. Bacteria appear to have evolved a variety of microcompartments inside which diverse enzymatic reactions can be sequestered.

The structural organization of bacterial microcompartments has remained a mystery until recently. Structural elucidation of the proteins that constitute the building blocks of the carboxysome provide the first high resolution clues about how these micrcompartments are organized and how they might carry out their functions.



Carboxysome microcompartments are visible in the cyanobacterial cell on the left. The three-dimensional structures of the proteins making up the carboxysome shell are shown on the right. The spacing between the centers of two hexamers is 7.0nm, with the central hexamer shown as a ribbon diagram to illustrate the protein fold. Kerfeld, et al., (2005). *Science* 309, 936-8.

Bacteria do not contain the membrane-bound organelles that are the defining characteristic of eukaryotic cells. However, it has been known for more than 40 years that certain bacteria produce protein shells or microcompartments inside their cells, which might serve as primitive organelles. Recent structural analyses of the carboxysome, the prototypical bacterial microcompartment, are providing the first detailed view of how these 100-200nm subcellular structures might operate.

When carboxysomes were first observed by electron microscopy, their apparent similarity to viruses was noted. The first high resolution structures of the bacterial microcompartment proteins reveal principles of construction highly similar to those seen in some viruses. Six identical protein subunits come together to form a hexameric unit, which constitutes the building block for the shell. These hexameric units pack tightly together to form a molecular layer that contains only tiny pores. This tight packing appears to restrict movement of molecules into and out of the microcompartment, except through the pores, where positively charged amino acid residues may promote the flow of negatively charged metabolic intermediates such as bicarbonate, a substrate for the enzymes inside the shell.

The microcompartment proteins whose structures are being elucidated might also turn out to be useful for design purposes. Assembling proteins into ordered molecular layers is a long-standing challenge, and bacterial microcompartment proteins could serve as useful building blocks for protein design research aimed at that goal. This work illustrates the rich discoveries possible at the interface between the life sciences and the physical sciences. ■

This research received federal funding from USDA

Collaboration between CNSI and UCLA

Producing Dendritic Nanostructures using Dynamic Chemistry

The high yielding formation of mechanically interlocked molecules by clipping reactions under thermodynamic control reveal the power of preparing useful exotic materials.

For over 40 years, the synthesis of exotic molecules such as catenanes, rotaxanes, knots and Borromean rings with aesthetically appealing and useful applications has been proceeding apace. During the same period of time, the synthetic protocols employed by chemists have evolved from being all statistical in the beginning, to progressively covalent, coordinative, and noncovalent templating strategies under both kinetic and thermodynamic control.

Under the aegis of the CNSI, a series of rotaxanes compounds including mechanically interlocked dendrimers have been successfully prepared in high yields through a template-directed thermodynamic synthesis. Dynamic covalent chemistry has been exploited in the template-directed syntheses of both catenanes and rotaxanes under thermodynamic control. This method can provide proof-reading and error checking for the equilibrium reaction to yield almost quantitatively the product.

Recently, employing dynamic covalent chemistry, different types of mechanically interlocked structure (Fig.) have been prepared by the thermodynamic "clipping" approach. An exotic mechanically interlocked molecular structure in which eight components cooperate to form a jumbo-sized cycle, namely a [4]rotaxane was synthesized (*Chem. Eur. J.* 2005, 11, 4655-4666) by heating the suspension containing the components. The yield of formation is over 95% determined by nuclear magnetic resonance (NMR) spectroscopy. Also, the crude product could be further purified by recrystallization to achieve a very pure sample of the branched [4]rotaxane.

In the context of constructing non-classical mechanically interlocked dendrimers by employing a convergent templation procedure, the same "clipping" thermodynamic approach have been explored to introduce steric bulky dendrons onto a trivalent ammonium ion core with seven-component self-assembly (*J. Am. Chem. Soc.* 2005, 127, 5808-5810; highlighted in *Science* 2005, 308, 326) Four generations of mechanically interlocked dendrimers from generation zero to generation three up to a molecular weight over 8,000 $gmol^{-1}$ were synthesized in a one-pot reaction by simply mixing the seven components together. As for the [4]rotaxanes, the dendrimers form in excess of 95% yield. The mechanically interlocked core of the dendrimers were able to be modified and transformed into kinetically stable dendrimers, which were characterized by mass spectrometry. ■

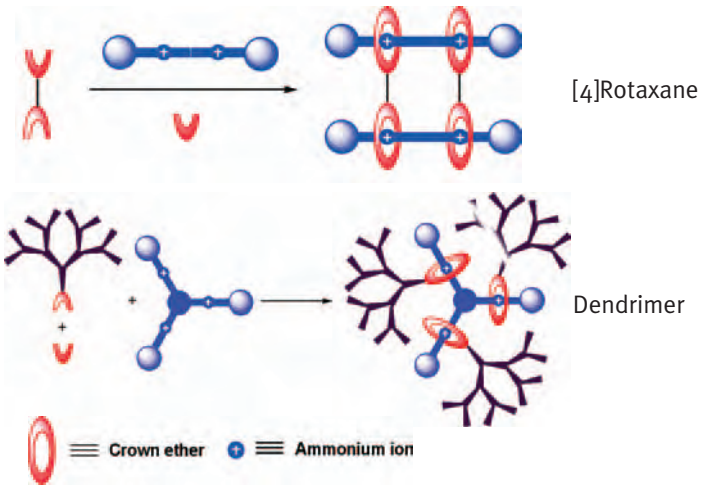


Fig. Schematic of the formation of two mechanically interlocked structures under thermodynamic "clipping" approach.

This research received funding from MARCO and FENA

Collaboration between CNSI and UCLA Center for Cell Mimetic Space Exploration (CMISE)

Self-Assembly of Cardiac Myocytes onto MEMS Devices

The diminishing dimensions of MicroElectroMechanical Systems (MEMS) challenges scientists to develop novel techniques of powering these devices. Current methods to power MEMS devices are limited in that they require the device to be attached to a substrate thru which electrical energy is delivered. Once MEMS become non-tethered devices, free to move away from the substrate they were fabricated from, the current energy delivery methods fail. In order to address this issue, a technique has been developed at UCLA which utilizes the natural self-assembling nature of muscle cells to provide a means of locomotion, and eventually powering of free floating MEMS devices.

Cells in your body break down glucose to form adenosine tri-phosphate (ATP). ATP can be considered the chemical currency of the cell, which when broken down releases energy stored in covalent bonds. This energy is then used to power many of the reactions within a cell that allows it to function.

Finding alternatives to the traditional powering schemes is not just an issue of energy, but also one of integration and miniaturization. Any substitute to conventional powering methods should be of similar scale as the device to avoid scaling issues such as surface tension. As such, cells are an interesting framework to focus on since they are of similar size to many of today's MEMS and are powered by chemical energy rather than electrical. Muscle cells convert glucose into ATP and then use the generated ATP to power reactions that allows the muscle cell to contract. Currently, the feasibility of creating microrobots powered by self-assembled muscle cells has been demonstrated.

Integration of biological entities with inorganic silicon devices presents various challenges such as biocompatibility and integration. Cells can be quite finicky in the environment they're cultured and maintained and often die due to the slightest changes in pH, temperature, or culture medium. Integrating the cells onto the MEMS devices is also problematic due to the incompatibility of the silicon material the devices are fabricated from. Through manipulating material interfaces and compatibility, we have devised a novel system for seamlessly integrating muscle cells onto silicon-based microfabricated structures. The implementation of this self-assembly strategy using cardiac muscle has allowed us to fabricate a group of muscle-powered micromachines. For example, in a two-legged microdevice, muscle cells self-assembling into legs on a silicon micro-scaffold could power the device to function for more than four hours with maximum speeds of ~40μm/s (Fig. 1).

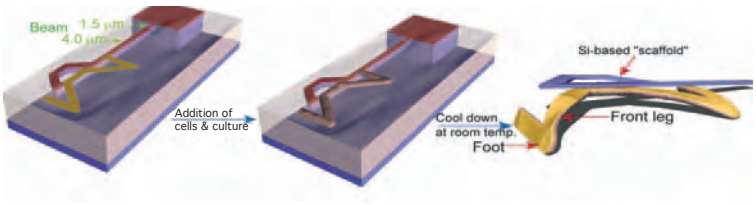


Fig. 1. Image shows a microdevice moving forward due to the contraction and relaxation of muscle. Blue, green and red bars mark the start positions of the inorganic scaffold and the motile leg, and the final position of the motile leg, respectively.

Such hybrid micromachines have the following advantages over conventional inorganic robots: autonomous functionality (non-tethered), simple fabrication, and biologically friendly operating conditions. Future work will be expanded to the fabrication of hybrid muscle-powered microgenerators by integrating this system of self-assembly with piezoelectric compounds. Successful realization of this concept will demonstrate that glucose, which is ubiquitous in physiological fluids, can be converted from its native chemical form, into mechanical and then electrical energy. Such microdevices may be utilized to power microelectronic circuitry or stimulate damaged nerves.The union of top-down MEMS fabricated structures with those synthesized, organized, and maintained by the bottom-up processes of biology could create a new class of hybrid devices with properties unattainable by either alone. The first step in engineering muscle cells onto microchips has been taken. This is an initial but critical step towards fabricating autonomous intelligent hybrid micro-machines that can be directly powered by glucose. ■

This research received federal funding from NASA

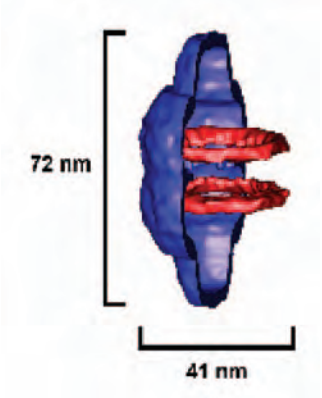
Collaboration within CNSI

Structure and Design of Vault Nanocapsules

The ideal therapeutic delivery vehicle will need to have a large internal volume, yet be small enough to avoid trapping in the kidney and liver. This vehicle will need to escape immune surveillance and be able to be modified to allow specific targeting to a tissue or cell of interest. Finally the vector will need to protect its internal cargo yet be able to release such cargo in a controlled manner. In a collaboration between the CNSI and the National Science Foundation (NSF), a Nanoscale Interdisciplinary Research Team (NIRT) has been assembled to develop a flexible, targetable nano-capsule by exploiting a naturally-occurring nanoscale structure, the vault.

With a thin (~20 Å) protein shell surrounding an internal cavity large enough to encompass two ribosomes, the vault particle is a nanocapsule with incredible potential for compound encapsulation, protection, and delivery. The vault nanocapsule has been honed by millions of years of evolution to assemble from multiple copies of a few subunits into a stable structure. The particle adheres to and is transported along cytoskeletal elements in the cell, and is likely to open and close in response to cellular signals. Understanding how such a capsule can be formed and manipulated in vivo and in vitro will allow molecular manipulations to encapsulate small molecules (drugs, sensors, enzymes, toxins etc.), lengthen and shorten capsule size, and target the engineered nanostructures to specific tissues, cells, or organelles via attachment to receptors, ligands, or fusogens.

The UCLA approach is to modify the vault using a recombinant protein production system and test the concept that vaults can have a broad nanosystems application as malleable nanocapsules. Modified vaults are being examined with molecular imaging techniques including negative-stain TEM, cryo-EM single particle reconstruction, atomic force microscopy and X-ray crystallography. Molecular manipulations, including designed encapsulated metal binding sites, enzymatically active protein domains and chemically active moieties are being engineered into the vault particle. Physical and chemical approaches are being utilized to characterize vault conformation and to determine conditions that can stimulate the interconversion of opened and closed conformers, in order to regulate the entrapment and controlled release of encapsulated materials.



This project combines the following disciplines: cell biology, molecular biology, chemistry, structural biology, chemical engineering, and engineering. The work will further our understanding of complex, self-assembling systems, a hallmark of life itself. Further, if conditions for controlled opening and closing of vaults are established, these nanocapsules may prove useful in drug delivery and in the compartmentalized synthesis of nanoscale materials such as semiconductor nanoparticles, also known as quantum dots.

A group of approximately 25-30 faculty post doctoral fellows and students who previously had no incentive to collaborate are now working together on a common problem. The highly inter-disciplinary nature of this project provides an unusually rich intellectual environment for those involved, although it is of particular benefit to the graduate students and postdoctoral scholars, who at an early stage in their careers are learning how to interact in a multi-disciplinary environment. Young researchers engaged in this project will be better prepared to attack complex problems that increasingly require input from experts in many fields. ■

Current technologies aimed at developing nano-scale delivery vehicles have been hampered by lack of biocompatibility and tissue targeting. Particle stability and flexibility is also a serious hurdle. None of the methodologies developed to date overcome the numerous technical difficulties in this area.

This research received federal funding from NSF

Collaboration among CNSI, UCLA and Novartis

Identification and Integration of Multiple Cellular Signals Controlling Viral Replication Using High Throughput Genomic and Microelectronic Mechanical Approaches

In collaboration with engineers and structural biologists, we incorporate multiple technologies to dissect mechanisms underlying viral replication and develop medical applications.

Herpesviruses can select between two distinct phases in their life cycle, latency or lytic replication, and can reactivate from latency in response to cellular signals. A viral transactivator, RTA, plays a central role in mediating the switch between these two phases in Kaposi's sarcoma-associated herpesvirus (KSHV). To systematically evaluate the cellular signals which regulate the switch between latency and lytic replication, a reporter indicative of reactivation of the latent genome was utilized to develop a high throughput cell-based screen approach. The effects of 26,000 full-length cDNA expression constructs on viral reactivation were individually assessed. One of the strongest among the list of cellular genes that were found to be able to induce KSHV reactivation is Ras. Through collaboration at UCLA, it was determined that Ras-mediated reactivation occurs via the Ras/Raf/MEK/ERK pathway. Ets-1, as one of the phosphorylation targets of this pathway, plays an essential role in this effect by activating the promoter of RTA. The commonly used viral reactivation agent TPA induces KSHV reactivation via Raf/MEK/ERK/Ets-1 pathway as well. The results suggest that different upstream signals can converge into one pathway to mediate KSHV reactivation. In addition to the discovery of a list of cellular genes that can reactivate KSHV, detailed analysis of Ras-associated pathways revealed a mechanism that mediates cellular signal transduction from the cell membrane to the viral genome in the nucleus. This study successfully utilized a high throughput genomic approach not only generated novel information for researchers in the field, but will also encourage additional applications of this technique inside and outside the virology field.

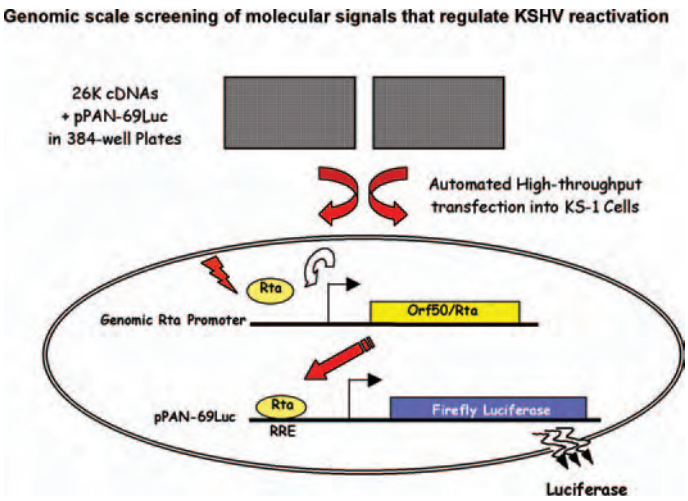


Fig. 1. Schematic representation of cDNA based functional assay. The transfected positive signals will activate RTA promoter and induce the expression of RTA protein. In response to the endogenous RTA expression, the PAN-69 promoter will become activated and drive luciferase activity to a high level.

NF-kB is one of the cellular signal pathways that regulate herpesvirus reactivation. Multiple signals can control the activities of NF-kB. Using NF-kB as a model system, a microfluidic closed-loop optimization approach was developed to cooperate multiple stimuli for controlling complex biological networks. By applying a stochastic search algorithm, a potent combination of cytokines for activating NF-kB was determined with a smaller number of tests out of a million possible combinations. The closed-loop optimization system enables a systematic approach to control, and eventually understand complex biological systems, which are generally regulated by multiple parameters.

Since viruses interact with cells via multiple points, a systematic approach integrating molecular biology and nanotechnology will give a more holistic view of what is occurring during viral infection. Viral infection can serve as leader into cellular processes. ■

Collaboration between CNSI and UCLA

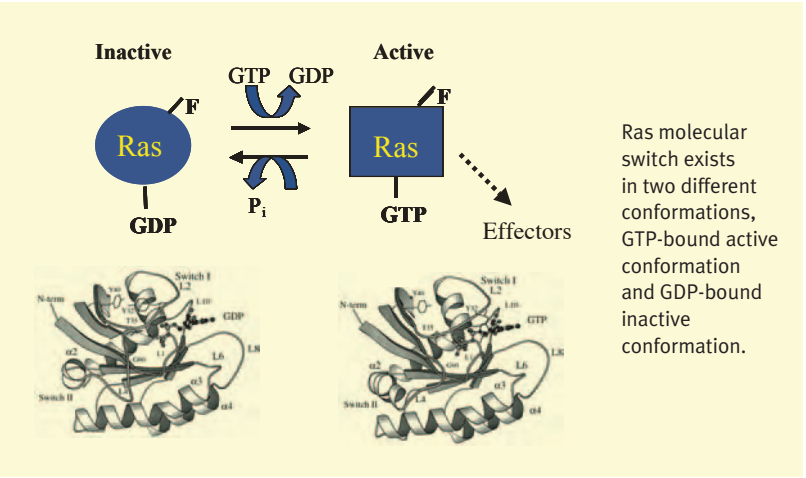
Molecular Switches and Signal Transduction Networks

Nano-scale switches play critical roles in regulating cellular signaling networks. We focus on the Ras GTPase, a monomeric protein of 21,000 dalton, that shuttles between a GTP-bound form and a GDP-bound form. In its GTP-bound conformation, Ras signals activation of downstream events that include activation of protein kinase cascades. The shuttling between the two forms is regulated by GAP (GTPase activating protein) and GEF (GDP/GTP exchange factor). This switch is located on the cytoplasmic face of the plasma membrane and this membrane association is facilitated by the help of lipid tails that include a farnesyl group and palmitic acids.

Constitutive activation of the Ras molecular switch by mutations leads to human cancer formation. Furthermore, mutations in GAP called NF1 causes genetic disorder called neurofibromatosis. A UCLA/CNSI collaboration has recently shown that the Ras signaling pathway is also important for the life cycle of human herpesvirus-8 (HHV-8). A genome-scale screening of cDNA clones whose expression leads to the activation of a key viral transactivator RTA led to the finding that the activation of the Ras/Raf/Mek/Erk signaling leads to the reactivation of the latent virus genome that is mediated by a transcription factor Ets-1.

Small organic molecule compounds provide effective tools to regulate the action of the Ras molecular switches. Farnesyltransferase inhibitors (FTIs) that act to inhibit membrane association of the Ras molecular switch are being characterized. FTIs are currently evaluated in clinical trials as anti-cancer drugs. In addition, another type of compounds called MCP that inhibit protein-protein interaction of Ras and Raf are being examined. This compound appears to interfere with the binding of Ras that relieves negative regulation of the Raf kinase by its N-terminal region.

Ultimate understanding of the signaling networks requires understanding how cellular signals lead to the activation of transcription factors that control gene expression. Deriving a mathematical model that could explain how gene expression is regulated by transcription factors should greatly facilitate the study of signaling networks. A collaboration to analyze microarray results of gene expression in yeast may provide a theoretical basis to predict consequences of interfering with signaling pathways. ■



Ras molecular switch exists in two different conformations, GTP-bound active conformation and GDP-bound inactive conformation.

Nanoscale switches play critical roles in regulating signaling networks. Perturbation of the switches causes human diseases including cancer. Small molecule compounds can be obtained that can regulate the action of molecular switches.

This research received federal funding from NIH

Collaboration between CNSI at UCLA and UCSB, University of Missouri, Nottingham-Trent University, and University of Tokyo

Nanoscale Borromean Links

The nontrivial link known as the Borromean rings has long been a source of endless fascination among artists, theologians, mathematicians, and scientists. The molecular construction of the Borromean Ring (BR) topology represents a formidable synthetic challenge as they consist of three mutually interlocked, yet noncatenated rings. The BR topology can be viewed as a three-ring system, as described in knot theory, with the sole requirement that the scission of any one of the rings destroys the unique union of the three.

On the assumption that the construction of BRs from small building blocks can be realized by appealing to constitutional dynamic chemistry protocols, the complete molecular construction of the BR topology from 18 individual components has been successfully achieved (*Science* 2004, 304, 1308-1312) under strict dynamic covalent, coordinative, and thermodynamic control (Fig.). This supramolecular assembly is fixed on the ability to control the placement of 12 organic fragments around 6 transition metals in near quantitative yields. Stabilized by combinations of 12 π– π stacking interactions and 30 dative bonds, six tridentate and six bidentate ligands are spatially preorganized around six transition metals, such that they preferentially react and form molecular Borromean Rings in a single step, on a gram scale, in yields of greater than 95%.

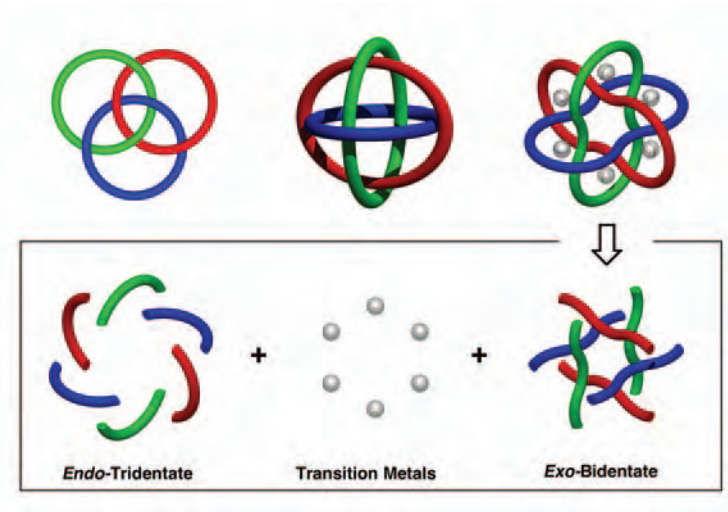


Fig. Schematic assembly of molecular Borromean Rings from a combination of endo-tridentate and exo-bidentate ligands around metal ion templates.

The successful construction of this framework opens the door to a new molecular entity with unexplored properties. Recently (*Chem. Commun.* 2005, 3391-3393), the reversible nature of at least some of the 30 dative bonds and 12 imine bonds stabilizing and constituting the three rings of the Borromean Link were assessed in scrambling experiments.

A true Borromean Link requires that the structure can exist without the presence of the template. These "real" BRs have been obtained (*Chem. Commun.* 2005, 3394-3396) by reducing the dynamic imine bonds followed by removal of the metal ions. From a design point of view, in a bottom-up sense at least, this molecular BR topology provides a unique symmetrical, nanoscale 3-dimensional scaffold into which unique features (e.g., electroactive, photoactive, and chiro-optical) can be imbedded at will. With these thoughts in mind, synthetic strategies have been developed (*J. Org. Chem.* 2005, In press) to append functional groups at the periphery of the structure to give hexasubstituted BRs.

With the intention of further exploiting the symmetry, size and topology of the BRs, the collaborators continue to alter strategically each of the components, be it the metal or the ligand, using the nearly quantitative synthetic protocol, to try and uncover functions that can emerge from such a form. ■

One problem often encountered in the field of nanoelectronics is the anisotropy of a molecule, owing to the fact that the molecule is asymmetric. Borromean Rings are remarkably symmetrical in 3-D space, and can likewise be symmetrically coated with an array of functionalities according to the desired application.

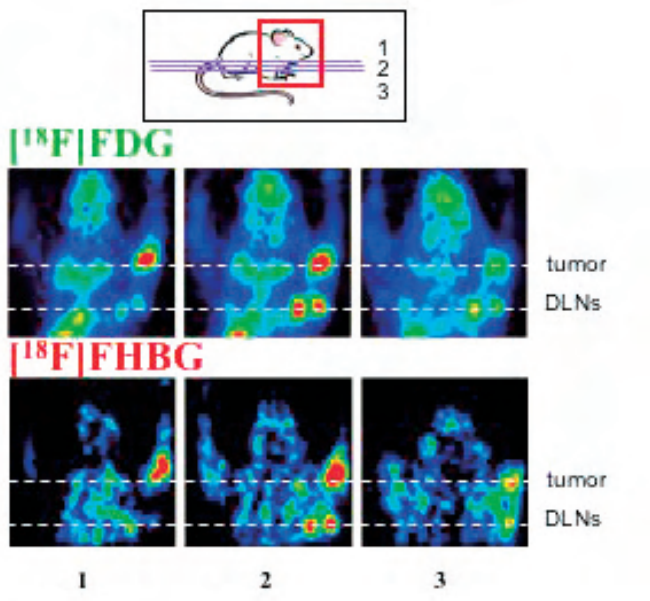
This research received federal funding from NSF

Collaboration between CNSI and UCLA Crump Institute

In Vivo Visualization of an Effective Immune Response to a Solid Tumor

During an immune response innate and adaptive immunity synergize through cellular events that create regional variations in immune cell populations in vivo. These events are dictated by a delicate balance between cell proliferation, activation-induced differentiation, migration and death. Immune response monitored by sampling blood and limited tissue sites eliminates the contextual influences of living organs and misses variation throughout the body. In the clinic, evaluation of the effectiveness of immunotherapies has often relied on surrogate and subjective endpoints, such as histologic evidence of tumor necrosis or lymphocyte infiltration, rather than objective cancer regressions. The ideal approach would be to utilize non-invasive imaging techniques to acquire serial immunological measurements to optimize dose and treatments in a patient specific manner.

PET is a sensitive, noninvasive method for repetitive imaging of cellular and molecular processes in humans on a whole body scale. Recently, advances in detector design have led to the development of micro-PET devices which allow accurate measurements in rodents. A CNSI/UCLA Crump Institute collaboration has developed a novel approach to spatio-temporally visualize primary anti-tumor immune responses using microPET imaging.



MicroPET imaging of tumor cell progression and immune cell activation and expansion using [^{18}F]FDG and [^{18}F]FHBG substates. Immune cells are activated and localized at both the tumor and its draining lymph node.

This research has received federal funding from DOE

Immune cell localization and activation at both the tumor and its draining lymph nodes were visualized with PET imaging. The goal is to obtain kinetic measurements of immune responses non-invasively in both animal models and humans to evaluate different immunotherapies.

A chimera bone marrow strategy was used to generate mice with a hematopoietic cell compartment expressing a multimodality reporter gene construct to allow visualization (fluorescence, luminescence and PET) of primary immune responses. This technique is a step forward over currently available imaging methods.

Chimeric mice were challenged with an oncogenic retrovirus which led to the induction of a strongly immunogenic non-metastasizing sarcoma. PET imaging using 2-[^{18}F]fluoro-2-deoxy-$_D$-glucose ([^{18}F]FDG) detects glucose metabolic activity. Hematopoietic cells are visualized by using 9-[4-[^{18}F]fluoro-3-(hydroxymethyl)butyl]guanine ([^{18}F]FHBG), a radioactive substrate for the PET reporter gene, sr39TK. Animals are injected with the radioactive substrate, and the cells of interest bind the substrate and retain it within the cell. The microPET scanner detects the location of the retained radioactive signal, and reconstructs a 3-dimensional tomographic image.

This method has been used to visualize immune cell localization at both the tumor and in the draining lymph nodes. Furthermore, specific changes in the pattern of immune cell localization were clearly distinguishable by microPET imaging when sarcoma-bearing mice were chronically treated with the immunosuppressive drugs. Future developments in this area should lead to the ability to obtain kinetic measurements of immune responses non-invasively in both animal models and humans, which should allow the evaluation of immunotherapies for cancer and autoimmune diseases in the preclinical and eventually the clinical setting. ■

Collaboration among CNSI, Stanford University, and Lawrence Livermore National Laboratory (LLNL)

Probing fast events in protein folding using a microfluidic laminar mixer

In protein folding, important structural events occur on a microsecond time scale. Folding experiments based on changes in chemical potential, via rapid mixing of protein solutions into and out of chaotrope solvents are versatile, as most proteins unfold reversibly in the presence of chemical denaturants such as urea and guanidinium hydrochloride and folding experiments are not limited to proteins near the folding transition range. Until recently, the main limitation of turbulent-based continuous-flow rapid mixing experiments was their inability to access very short time scales and the high sample consumption rates (typically in the order of tens of milligrams).

An ultrafast microfluidic laminar-flow mixer for studying protein folding has been developed at UCLA. This device enables access to conformational changes under conditions far from equilibrium and at previously inaccessible time scales (mixer dead-time: 7 us) with only minute sample consumption (femtomolar). The mixing device was batch-fabricated on silicon wafers (Fig. 1). The denatured protein (flowing from the top channel) is focused into a narrow stream by buffer flowing from two side channels. The performance of the mixer was tested using Acyl-CoA binding protein, a small 86-reside model protein. Using fluorescence resonance energy transfer (FRET) between a donor and an acceptor fluorophore positioned at the N- and C-terminus of ACBP, it was shown that ACBP folds according to a three-state mechanism (Fig. 2). First, the extended denatured chain collapsed into a compact coil structure on a microsecond time scale, followed by a much slower barrier-crossing event that yields the folded protein. ■

By using a microfluidic mixing device we are able to monitor the "beacon" molecules, recent discoveries begin to answer how RNA polymerase translocates along DNA templates and how it regulates transcription by abortive initiation.

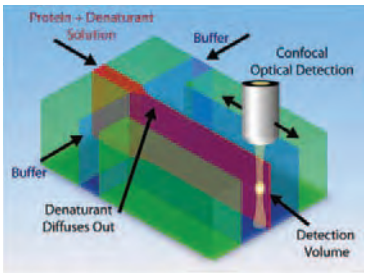


Fig. 1. Schematics of the mixing device. Protein (red) is introduced from the top channel. Buffer solutions flown from the side channels focus the protein solution into a thin stream, enabling fast mixing to occur under laminar-flow conditions. The change in FRET is detected by a confocal microscope.

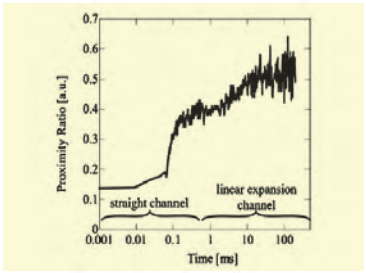


Fig. 2. Time-dependent change of the proximity ratio, obtained by scanning of the mixer region. On a fast time scale, denatured ACBP collapses into a compact coil, followed by reconfiguration into the native state on a millisecond time scale.

This research received federal funding from NSF and NIH

CNSI and UCLA Collaborative Oral Fluid Diagnostic Research Center (COFDRC)

A Spitting Image: Leveraging Micro and Nano Technology for Health and Disease Monitoring in Oral Fluid

Scientific knowledge as early as the turn of the 20th century has demonstrated saliva as an effective medium for the non-invasive measurement of biological markers. Any given saliva sample contains a complex combination of microbes, proteins, and genomic sequences indicative of conditions such as periodontal diseases, malignancy, or hereditary diseases. Researchers at the CNSI and UCLA COFDRC are exploiting the rich potential of oral fluid to open several novel windows of diagnostic opportunity for health and wellness monitoring.

Immunologists have shown that the function of antibodies arises from their attraction, or "affinity," to a particular antigen, a concept that has resulted in a wide range of clinical diagnostics. That same idea is being applied to develop an accurate and rapid detection of bacteria and oral cancer markers in saliva. The result: a low-cost, portable tool for effective risk screening and preventative health maintenance. To realize this goal, UCLA is leveraging the strengths of micro-electromechanical systems (MEMS) and nano-biotechnology to the development of affinity-based biosensors that can separate and detect bacteria and proteins in saliva (Fig. 1).

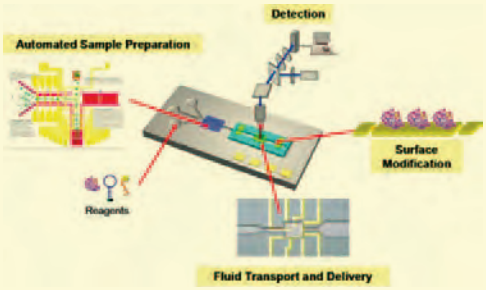
Using several methods to covalently immobilize antibody to a solid surface, a prototype that targets *Streptococcus mutans* (a cavity-causing bacterium) and interleukin-8 (a proteomic indicator of early stage oral cancer) has been built. Chips and microfluidic systems have been fabricated with the ability to capture bacteria or proteins from saliva in an upstream microseparator, and then release them for downstream detection. For example, the *S. mutans* are subsequently labeled with bioactivated semiconductor nanocrystals. These microscopic fluorescent particles attach to the cell membrane, where their color serves as an indicator of bacteria. The detected signal can thus be correlated to clinical levels for health or disease.

The capability of this research extends well beyond oral diseases. The same principles can be applied to detect a host of other disease markers relevant to overall health. Drug screening, hormone monitoring and HIV tests are only a few of the possibilities for powerful new diagnostic profiles. ■

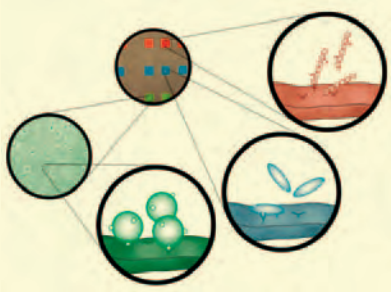
The use of oral fluid as a diagnostic medium enables non-invasive monitoring of health and disease. The goal of detecting microbial, protein and genetic biomarkers in saliva is materializing in a collaboration between the California NanoSystems Institute (CNSI) and the UCLA Collaborative Oral Fluid Diagnostic Research Center (COFDRC).

Fig. 1 **DETECTING DISEASE MARKERS IN SALIVA**

The Core Technology
A nano-functionalized fluidic MEMS separates bacteria and proteins in a saliva sample by antibody affinity. These biomarkers are then released for downstream detection.



Extensive Applications
Areas on the biosensor can be modified to capture a variety of disease markers.



Speed and Convenience
The diagnostic could be miniaturized into a palm-sized tool that delivers results in minutes, right at the dentist's office.

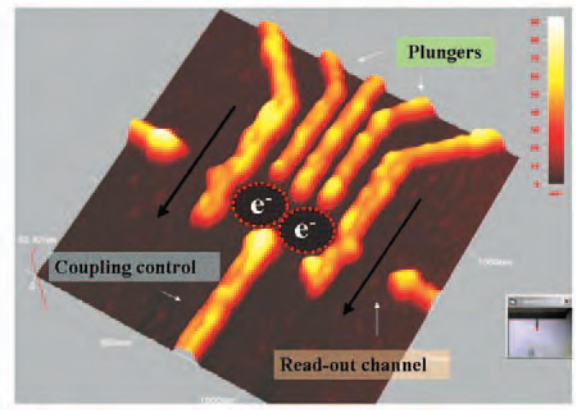
This research received federal funding from NIH

Collaboration between CNSI and Hughes Research Laboratory

Single-Spin Transistor Devices for Quantum Information Processing

Quantum information research is becoming one of the most vibrant fields due to the potential of using quantum processors to perform certain tasks no ordinary computer can do and to implement secure communications. Individual electron spins in semiconductors have many desirable properties that make the spin-based quantum bit a leading candidate for quantum information implementations. For instance, electron spins can have very long coherence times and the tunable spin-orbital coupling and the ability to control the electron wavefunctions in semiconductors allow gate operations on the spins. Furthermore, the extensive collection of chipmaking techniques, cumulated over decades, is expected to be extremely invaluable for building a scalable processor.

The quantum information research group at UCLA, in the past several years, has made several breakthroughs towards the goal of a physical implementation of a semiconductor-based processor, which includes manipulation and detection of individual electron spins in silicon-based semiconductor nanostructures.



Atomic force microscope image of a single spin transistor device, fabricated by electron beam lithography. The device contains two controllably coupled quantum bits (i.e, two electron spins).

Quantum information research will enable a computer processor to perform certain tasks much faster than any classical machine and to transmit data securely against eavesdropping.

A major goal of this interdisciplinary collaborative research is to fabricate CMOS-like single spin transistors in designed semiconductor structures that promise greater control over electron spin, the ability to entangle two spins, and to eventually build a scalable quantum processor. Recently, the team has overcome an array of technical difficulties and fabricated an electrostatic silicon quantum dot that can host a single spin, using 2D electron gas in a strained Si layer in an advanced Si/SiGe heterostructure. The quantum dot is integrated with a spin-state read-out channel. To make the devices, an unconventional approach has been developed to imbed leakage-secluded metallic side-gates in precisely etched groves. Characterization of the devices shows reproducible single-electron charging effects and stable operations for over an extended period of time of several hours. The discrete electronic occupation of the quantum dots can be effectively detected using the adjacent quantum point contact electrometer. Recent key experimental demonstrations by the UCLA group, along with several other groups around world, have considerably brightened the prospects of physical implementation of an electron-spin-based quantum information processor. ■

This research received federal funding from DARPA

Collaboration among CNSI, Stanford University, and Lawrence Livermore National Laboratory (LLNL)

Measuring Structural Heterogeneities and Fluctuations of Biopolymers

The properties of biopolymers such as proteins and nucleic acids are governed by long-range Coulomb interactions and specific, intra-chain hydrophobic interactions that strongly affect their structure and dynamics. A novel method (nanosecond alternating laser excitation, nsALEX) has been developed that combines the strengths of single-molecule and ensemble Fluorescence Resonance Energy Transfer FRET (FRET) methods, and used it to provide new information on fast fluctuations and conformational distributions of biopolymers.

Using nsALEX, multi-exponential fluorescence lifetime decays that relate to distance distributions are interpreted in terms of biopolymer contour length L and persistence length l_p(Fig. 1). Three types of biopolymers were studied using nsALEX: (i) double-stranded DNA (dsDNA), portraying a rigid rod; (ii) poly-dT single-stranded DNA (ssDNA), portraying a flexible homopolymer; and (iii) denatured proteins, portraying flexible heteropolymers that could form transient native or non-native secondary and tertiary structure. Short dsDNA molecules were found to be not as rigid as previously deduced from measurements on longer molecules. For poly-(dT), shortened base-to-base distance was found which is attributed to "residual stacking" conformers interspersed with extended, unstacked conformers (Fig. 2). In protein folding, by comparing unfolded chymotrypsin inhibitor 2 (CI2) and acyl-coenzyme A binding protein (ACBP) mutants, the observed large fluctuations (larger than the Gaussian chain limit) were proposed to be due to *transient residual structure*, and the amount of this structure increases in the presence of the folded state. Transient residual structure would cause dynamic changes in the effective contour length of the protein and widen the distributions beyond simple Gaussian chain statistics (Fig. 3). nsALEX affords the detailed study of samples where multiple subpopulations are intrinsic to the system, such as with CI2 and ACBP. ■

A novel single molecule spectroscopy was developed and used to monitor fast fluctuations and conformational distributions of single-stranded DNA, double-stranded DNA and denatured proteins.

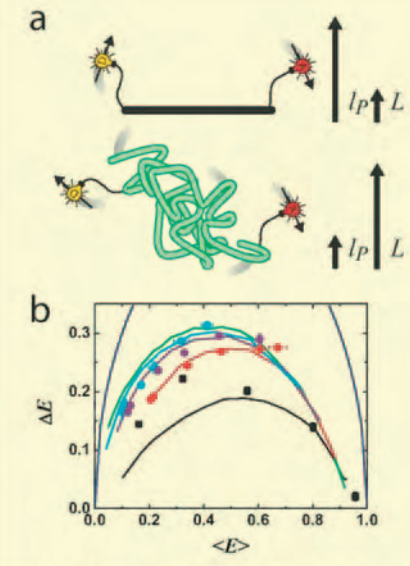


Fig. 1. Distance distributions in polymers determined from experiments and simulations, represented in standard deviation versus mean efficiency plots.

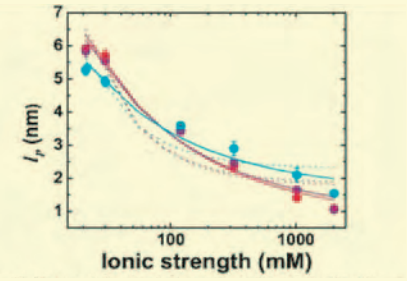


Fig. 2. Extracted persistence length versus Ionic strength for single stranded DNA with different lengths.

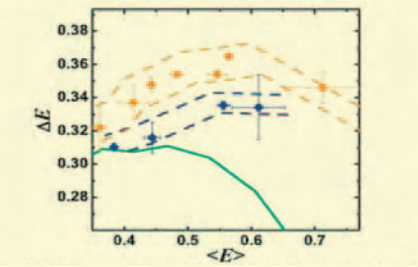


Fig. 3. Distance distribution of unfolded subpopulation of C12 (blue diamonds) and ACBP (orange hexagons) at varying denaturant concentrations.

This research received federal funding from NSF and NIH

Collaboration between CNSI and Veeco Instruments

Linear Artificial Molecular Muscles for Mechanical Nanoactuation

Two switchable, palindromically-constituted bistable [3]rotaxanes have been designed and synthesized (*Appl. Phys. Lett.* 2004, 85, 5391-5393) with a pair of mechanically-mobile rings encircling a single dumbbell. These designs are reminiscent of a "molecular muscle" for the purposes of amplifying and harnessing molecular mechanical motions. The location and switching of the two cyclobis(paraquat-p-phenylene) ($CBPQT^{4+}$) rings can be controlled to be on either tetrathiafulvalene (TTF) or naphthalene (NP) stations, either chemically (^1H NMR spectroscopy) or electrochemically (cyclic voltammetry), such that switching of inter-ring distances from 4.2 to 1.4 nm mimics the contraction and extension of skeletal muscle, albeit on a shorter length scale (*J. Am. Chem. Soc.* 2005, 127, 9745-9759).

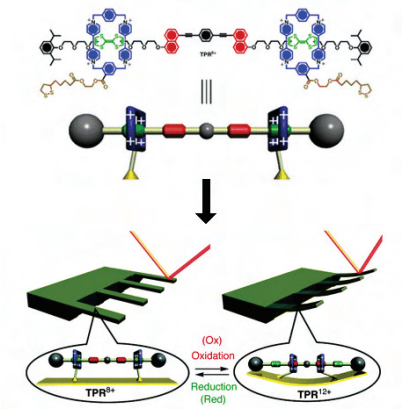


Fig. Chemical structure and schematic representation (Top) of [3]rotaxane linear motor molecules. When self-assembled onto gold coated microcantlievers (Bottom), the redox driven mechanical switching of bistable [3]rotaxane molecular motors bends and releases the cantilevers reversibly.

The active form of the bistable [3]rotaxane bears disulfide tethers attached covalently to both of the $CBPQT^{4+}$ ring components for the purpose of its self-assembly onto a gold surface. An array of flexible microcantilever beams, each 500 x 100 x 1 μm in size and coated on one side with a monolayer of 6 billion of the active bistable [3]rotaxane molecules, undergoes controllable and reversible bending up and down when it is exposed to the synchronous addition of aqueous chemical oxidants and reductants in the form of $Fe(ClO_4)_3$ and ascorbic acid, respectively. The beam bending is correlated with flexing of the surface-bound molecular muscles, whereas a monolayer of the dumbbell alone is inactive under the same conditions. Along with a simple calculation from a force balance diagram, these observations support the hypothesis that the cumulative nanoscale movements within surface-bound "molecular muscles" can be harnessed to perform microscale mechanical work.

Controllable and reversible actuation of an array of microcantilever beams has been achieved under redox conditions when a monolayer of bistable linear motor molecules were coated on the beams

The controlled actuation of cantliever beams by surface-bound nanoscale objects five orders of magnitude smaller in size demonstrates the potential of switchable, bistable interlocked molecules to function (Fig.) as nanoscale molecular machines. Numerous labs were involved in the preparation, fabrication, and investigation of these interesting functional molecules. The synthesis of the palindromic [3]rotaxane was carried out by synthetic chemists, mechanical as well as bioengineers carried out the fabrication of the nanoscale devices, and industrial partners were integral to the analysis of their function. This combination of synthesis, self-assembly, engineering, and analysis highlights the interdisciplinary nature of this work. ■

This research received federal funding from NSF, CMISE, NASA and DARPA

Collaboration between CNSI and Rutgers University

Unraveling the Molecular Machinery of Transcription Initiation

Transcription is a multi-step process. The enzyme RNA polymerase (RNAP), together with one or more initiation factor(s) (*i*) binds to promoter DNA to yield an RNAP-promoter closed complex (RP_c), (*ii*) unwinds ~14 bp of DNA surrounding the transcription start site ("transcription bubble") to yield and RNAP-promoter open complex (RP_o), (*iii*) begins RNA synthesis as an RNAP-promoter initial transcribing complex (RP_{itc}), and, ultimately, (*iv*) escapes from the promoter and enters into productive RNA synthesis as an RNAP-DNA elongation complex (RD_e).

Contrary to the traditional view of the transcription cycle, it was found that the initiation factor δ^{70} is not obligatorily released upon promoter escape in Escherichia coli using a single-molecule sorting assay that defines simultaneously the translocational position of RNAP within a single transcription complex and the δ^{70} content of a single transcription complex. The results strongly support the proposal for non-obligatory, staged disengagement of δ^{70} from the elongation complex, and raise the possibility that modification of δ^{70} region 4 can modulate δ^{70} release by weakening the δ^{70}-RNAP interactions with the elongation complex.

Typically, RNAP fails to escape from the promoter on its first attempt and, instead, engages in multiple abortive cycles of synthesis and release of short RNA products. In order to provide information on the mechanism and kinetics of abortive initiation and promoter escape, single-molecule leading-edge-FRET measurements were applied on immobilized transcription complexes, using total-internal-reflection optical microscopy with alternating-laser excitation. Small, but reproducible and abortive-product-length-dependent, decreases in distance between the RNAP leading edge and DNA downstream of RNAP were observed upon abortive initiation, and large decreases in this distance upon promoter escape. Inspection of population distribution and single-molecule time traces for abortive initiation indicates that, at a consensus promoter, at saturating NTP concentrations, abortive-product release and/or RNAP-active-center reverse translocation are rate-limiting. The results again confirm the δ^{70} retention model. ■

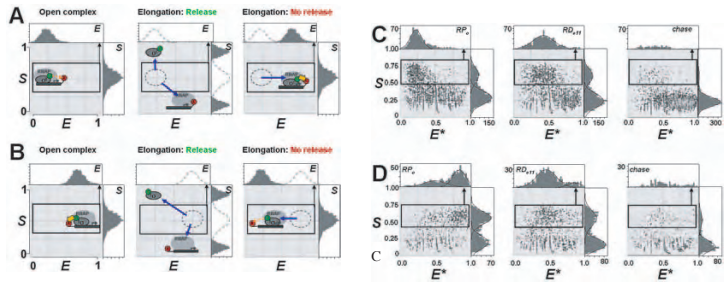


Fig. 1. Sigma release study by alternating-laser excitation and single-molecule sorting. A and B: Schematic *E-S* histograms showing sigma release and non-release models. C and D: Experimental results showing retention of δ^{70} for leading-edge (C) and trailing-edge (D).

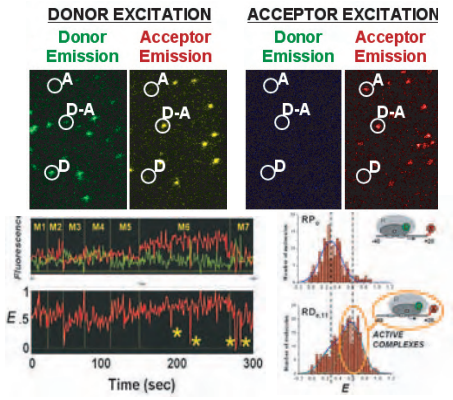


Fig. 2. Total-internal-reflection images of immobilized RNAP complexes (top), time trace of an individual complex (bottom and left) and 1-D *E* histogram showing population distribution of RP_o and $RD_{e,\,11}$ (bottom right).

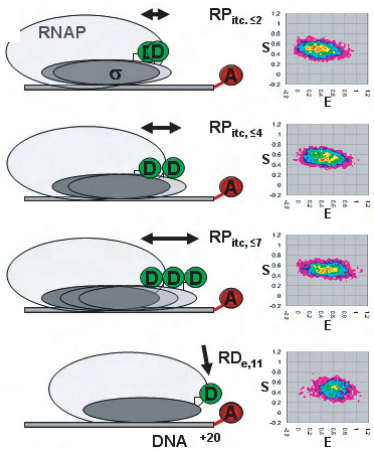


Fig. 3. 2D *E-S* histograms showing population distributions at different stages of abortive initiation.

We used single molecule spectroscopy to monitor the molecular machinery of transcription initiation, the very first step in gene expression.

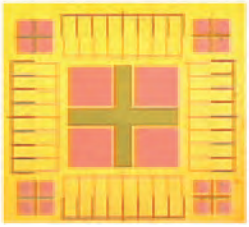
This research received federal funding from DOE

Collaboration among CNSI, UCLA, Quantum Science Research at Hewlett-Packard Labs, and University of North Carolina

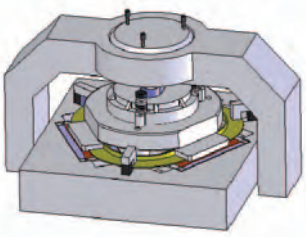
A Nanofabrication Machine with Nanoscale Alignment Accuracy

A simple module that can be integrated with a commercial optical aligner for nanoimprint lithography or optical lithography has been developed. The module provides a convenient low-cost technique to transfer an optical aligner for microfabrication to a nanofabrication machine. This combination enables the creation of nanoscale features and alignment of multiple-layer lithographic patterns with sub-micron accuracy within one instrument. Imprinting of 30-nm half-pitch lines has been demonstrated by the module, as well as sub-micron alignment. The module has also been used to fabricate micron- and nano-scale patterns simultaneously by the combination of optical and imprint lithography. A nanofabrication system with sub-5 nm accuracy is being developed by using a similar module. ■

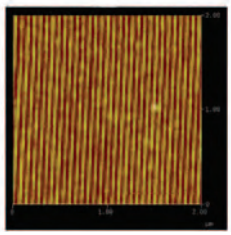
Imprint module integrated with SUSS MA-6 optical aligner.



Sub-1 μm alignment was achieved (dark layer: underlying metal patterns, pink layer: imprinted P-NIL resist).



Nanoscale fabrication systems with nanoscale alignment accuracy.



60-nm pitch lines transferred from mold to substrate.

Collaboration between CNSI and UCLA Proteomics and Mass Spectrometry Center

High-Throughput Proteomics Using Digital Microfluidics

Proteomics is the profiling of the entire constellation of proteins present in a cell or organism at a particular point in time. Each protein may be present in several forms because of post-translational modifications such as phosphorylation, glycosylation or conjugation with lipids. Proteomics promises to deliver important new insights into disease mechanisms and improved drug discovery strategies, but, like genomics, requires methods and instruments that can collect, store, catalogue and analyze vast amounts of information. Progress in proteomics would be accelerated by the availability of high-throughput methods that combine sample preparation with analysis to identify proteins in complex samples. Current standard methods in proteomics pair an analytical separation (for example, 2-D gel electrophoresis) with mass spectrometry (MS). A soft ionization method such as matrix-assisted laser desorption/ionization (MALDI) is used to desorb and ionize protein samples from a target array.

Droplet-based ("digital") microfluidics are being developed to prepare and process samples for MALDI-MS, as well as other bioanalytical assays. Samples and reagents are dispensed as droplets from reservoirs at the sides of a two-dimensional array of electrodes coated with hydrophobic, insulating layers. By applying a sequence of potentials across adjacent electrodes, droplets can be created from a reservoir and moved to locations on the device where the various sample processing steps take place (Fig. 1).

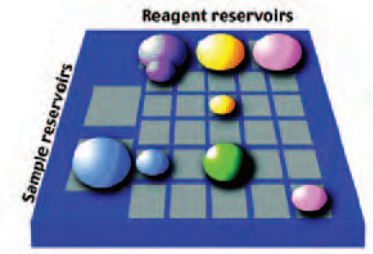


Fig. 1. Digital microfluidic array, shown without top plate.

Sample processing steps can include moving, mixing, joining, dividing, and drying of droplets, as well as dissolution, extraction, enzymatic digestion, disulfide bond cleavage, alkylation, and crystallization. The samples can be processed one at a time or simultaneously, and can be processed either uniquely or identically (in parallel). The digital microfluidics device thus provides a unique and versatile platform for method development as well as sample analysis.

The team is exploring two applications of digital microfluidics in proteomics: the identification of disease markers in saliva, and the generation of arrays for functional proteomics. ■

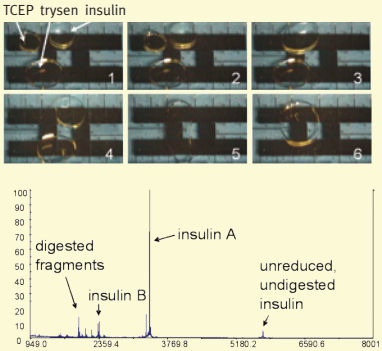


Fig. 2. Top: Sequence of frames from a movie depicting reduction and digestion of insulin on a digital microfluidics device; Bottom: MALDI mass spectrum of the spot that was formed.

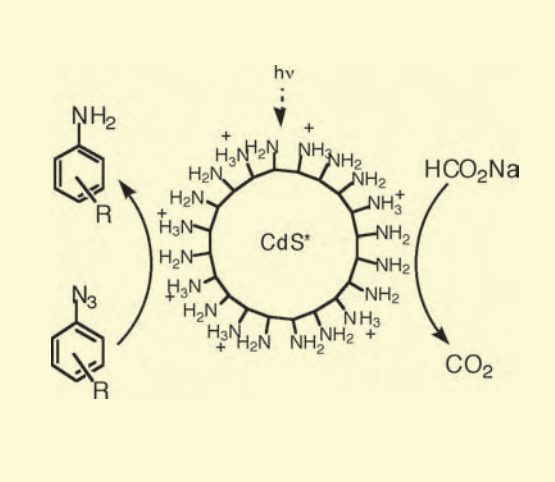
Microfluidic devices in which the liquid is transported as droplets, rather than in channels, have tremendous potential for lab-on-a-chip applications. In this UCLA collaboration, expertise in MEMS and bioanalytical chemistry are brought together to address basic challenges in proteomics and drug discovery.

This research received federal funding from NASA and NIH

Collaboration between CNSI and UCLA

Photocatalytic Reduction of Aromatic Azides to Amines using CdS and CdSe Nanoparticles

Semiconductor nanoparticles, nanocrystals, or quantum dots (Q-dots), belong in a state of matter in transition between discrete supramolecular entities and bulk solids. When particle aggregates are decreased in size to that of their characteristic exciton diameter, they exhibit properties markedly different from those of the bulk. Nanoparticles are about the same size as many proteins and may be functionalized to display different functionalities on their surface. This UCLA/CNSI collaboration has shown that semiconductor CdS and CdSe nanoparticles can act as very efficient and highly selective catalysts for the reduction of aromatic azides to aromatic amines when activated by light. In several cases, the reaction proceeds with quantum yields near 0.5, which approaches the theoretical maximum for a two-electron process. The wide scope of the reaction was confirmed with compounds containing electron withdrawing (–NO2, CO2R, COR) and electron donating groups (–OMe, –R, –Cl) at the para-, meta-, and ortho-positions. Remarkably, the reaction is relatively insensitive to the electron demands of the substituent. However, azides with meta-substituents give slightly lower yields than those with the same substituent at the ortho- or para-position. ■



Semiconductor nanoparticles prepared up of CdS and CdSe coated by layer of positively charged amines can be used as efficient photocatalysts for synthetic and materials applications when activated by UV light.

This research received federal funding from ONR and NSF

Collaboration within CNSI

Operational Nanovalves

In everyday life, macroscopic valves control the flow of fluids and gases by opening and closing passageways. These valves are essential regulatory devices that maintain the balance of fluids in living beings as well as in macroscopic machines. Construction of such a device on the nanoscale level requires (*i*) controllable switching elements, (*ii*) a method for operating them on demand, and (*iii*) appropriately sized passageways. These three conditions can be fulfilled by self-assembling addressable mechanically interlocked, linear motor-molecules on top of an inorganic chassis and then controlling them chemical, electrochemical, or photochemical stimuli.The collaborators have demonstrated (*Proc. Nat. Acad. Sci.* 2005, 102, 10029–10034) that a molecular nanovalve can be turned on and off reversibly by redox chemistry. It traps and releases molecules from a maze of nanoscopic passageways in the mesoporous silica by controlling the operation of redox-activated bistable [2]rotaxane molecules (a in the Fig.) tethered to the openings of nanopores leading out of the nanoscale reservoirs.

Redox-controllable bistable [2]rotaxane molecules have been employed as nanovalves to control the opening and closing of nanopores on the surfaces of mesoporous silica nanoparticles. These nanovalves regulate the controlled-release of guest molecules from the nanopores.

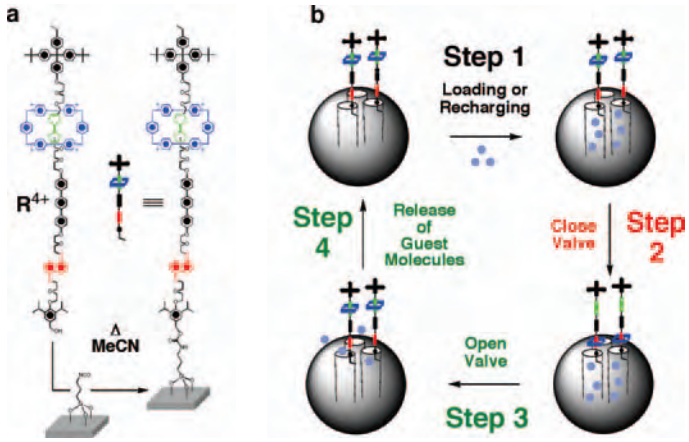


Fig. The chemical structures (a) of the redox-controllable bistable [2]rotaxane and (b) a graphical representation of their mode of operation on mesoporous silica nanoparticles.

In the research described in this report, the movable element that has been used to control the flow of molecules in a nanovalve is the bistable, redox-controllable [2]rotaxane R^{4+}. In R^{4+}, the movable part of the molecule is the tetracationic cyclophane, cyclobis(paraquat-*p*-phenylene) ($CBPQT^{4+}$), component that can be induced to move between two different recognition sites on a dumbbell component. In its ground state, the $CBPQT^{4+}$ ring prefers to encircle the tetrathiafulvalene (TTF) unit, rather than the dioxynaphthalene (DNP) one on the dumbbell component. The DNP unit is separated from the TTF unit by an oligoethyleneglycol chain incorporating a rigid terphenylene spacer. Because the stabilization energy between $CBPQT^{4+}$ and TTF is ~2 kcal/mol more than that between $CBPQT^{4+}$ and DNP, it follows that, in ~95% of the molecules, the $CBPQT^{4+}$ ring encircles the TTF unit. Two-electron oxidation of the TTF unit with $Fe(ClO_4)_3$ to give the TTF^{2+} dication destabilizes its interaction (Coulombic repulsion) with the $CBPQT^{4+}$ ring, which moves to the DNP unit in its electro-mechanically excited state. The preference for the $CBPQT^{4+}$ ring to encircle the DNP unit instead of the TTF^{2+} dication is even greater on account of the large difference (~8 kcal mol, at least) in their stabilization energies. Reduction of the TTF^{2+} dication back to the neutral TTF unit by ascorbic acid heralds the return of the $CBPQT^{4+}$ ring to the TTF unit in a thermally activated process. This sequence of reactions is employed (b in the Fig.) to regulate the opening and closing the nanopores—a gate-keeping process that, in turn, controls the loading and releasing of guest molecules into the silica pores. ■

This research received federal funding from NASA and NSF

Collaboration among CNSI, Stanford University and University of California, Berkeley

Fluorescent Quantum Dots for Live-Cells and In-Vivo Imaging

Peptide-coated quantum dots have been developed and used for live cell and small animal imaging.

Fluorescent qdots (QDs) are small nanocrystals (1-10 nm) made of inorganic semiconductor materials in which electronic excitations (electron-hole pairs, or excitons) are confined. QDs possess several properties that make them very attractive as fluorescent probes for in vivo biological labeling and single-molecule experiments: (*i*) They have precise emission color tunability by size due to quantum confinement effects; (*ii*) QDs are very photostable and emit many more photons per particle compared to dye molecules; (*iii*) QDs have a wide absorption band and very narrow and symmetric emission band. Therefore, many color probes can be simultaneously excited by a single narrow-band excitation source, and distinguished in a single exposure. Moreover, probes can be made in the important near infrared (NIR) region of the spectrum, where auto-fluorescence is considerably reduced and no good dyes exist. (*iv*) The nanocrystal fluorescence lifetime is in the tens of nanosecond range and therefore allows for discriminating against background by time gated detection; (*v*) QDs can be detected both by fluorescence and by an electron beam and therefore can be used to image the same sample by both light and electron microscopy.

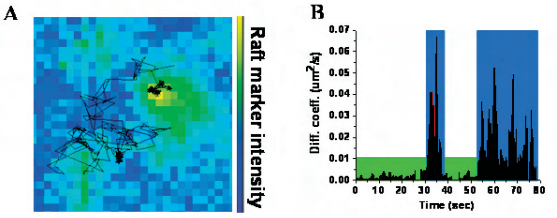


Fig. 1. Diffusion pattern of a single QD-labeled receptor in the cell membrane. (A) 80-s trajectory. (B) Variation of the diffusion coefficient reflects exit and entry in raft domains (green).

A new type of QD organic coating has been developed based on synthetic peptides that overcome the difficulties imposed by the biological milieu. These peptides prevent the quenching of QD emission in an aqueous environment and allow the elaboration of strategies for the conjugation or adsorption of molecules of interest without significantly increasing the size of the particles.

Fig. 1 shows that peptide-coated QDs can be targeted to cell-surface molecules and allow for the study of dynamic processes in live cells such as the interaction of lipid-anchored proteins with lipid rafts micro-domains or the dynamic formation of the immunological synapse in real time, down to the single molecule/single-QD detection level.

The same strategy is currently being used to facilitate QD uptakes in live cells by developing cell-permeable peptide-coated QDs, by using biological carriers such as viruses or vault capsules to target organelles or to deliver NIR QDs to specific regions of a tissue within an animal (i.e. a tumor, Fig. 2). ■

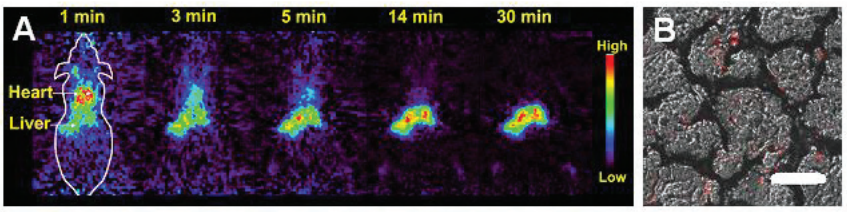


Fig. 2. MicroPET of radioactively-labeled QD in mice. (A) Accumulation of QD in the liver over time. (B) Localisation of QD in hepatic cells from a mouse biopsy.

This research received funding from NIH, DARPA and W.M. Keck Foundation

Collaboration among CNSI, RIKEN/Spring-8 and APS Technology, Inc.

3D Imaging of Nanoscale Systems by Using Coherent X-rays

Visualizing the arrangement of atoms has played a crucial role in understanding the microscopic world. There are already a few ways of imaging atomic structures, but each has its limitations. Scanning probe microscopes are limited to imaging atomic structures at surface. Transmission electron microscopes can resolve individual atoms but only for samples thinner than ~ 20 nm. Crystallography can reveal the globally averaged 3D atomic structures based on the diffraction phenomenon, but requires crystals. These limitations can in principle be overcome by coherent X-ray diffraction microscopy based upon coherent scattering in combination with a method of direct phase recovery called oversampling.

The first experimental demonstration of coherent x-ray diffraction microscopy was carried out in 1999. Since then, it has been successfully applied to imaging a variety of samples ranging from nanocrystals, biomaterials to double wall carbon nanotube in both two and three dimensions by a number of groups. Fig. 1 shows 3D imaging of a buried nanoscale material. The sample consists of two single-layered Ni patterns (each with a size of 2.5 x 2 x 0.1 μm) rotated relatively 65° to each other in-plane and separated by a distance of 1 μm. Fig. 1(a) shows a SEM image of the sample. Due to the 1 μm separation of the two layers, the SEM image shows the pattern in the top layer, and the pattern in the bottom layer is visible only as a soft blur. By using coherent X-rays with a wavelength of 2 Å, a series of thirty-one 2D diffraction patterns were recorded from the sample with the rotation angles ranging from –75° to 75° in 5° increments. A 3D image of the buried material was directly reconstructed from the diffraction patterns.

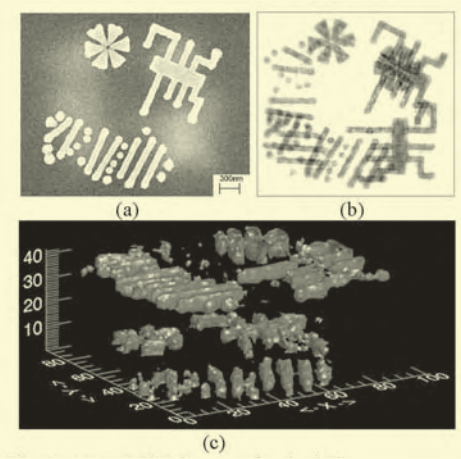


Fig. 1 (a) A SEM image of a buried nanostructure, showing the pattern in the top layer, but not the bottom layer. (b) An image from a coherent X-ray diffraction microscope with a resolution of 8 nm where both the top and bottom layered patterns are clearly seen as overlapped in this 2D image. (c) The reconstructed 3D structure displayed in iso-surface rendering.

X-ray crystallography has made revolutionary impacts in a number of fields ranging from physics, materials sciences and chemistry to biology. It, however, requires high quality and sizable crystals. It was not until recently that the key requirement in X-ray crystallography (i.e. crystallinity) was released by using coherent diffraction microscopy.

Fig. 1(b) shows an image with the same orientation as the SEM image. The top and bottom layered patterns are clearly seen as overlapped in this 2D image, and the variation of the electron density on the nanometer scale is also visible. Fig. 1(c) shows a 3D iso-surface rendering of the reconstructed image. The finest division in z-axis corresponds to 25 nm and the distance between two patterns is about 1 μm.

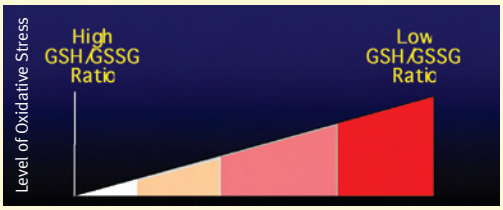
The potential of coherent X-ray diffraction microscopy is enormous. It can be applied to investigate a wide range of systems such as synthetic nanostructure, composite materials and biological systems. Furthermore, with the appearance of X-ray free electron laser facilities, it may be able to image single particles at the near atomic resolution with the sub-picosecond time resolution. ■

This research received federal funding from DOE and NSF

Collaboration among CNSI, Southern California Particle Center and Supersite, and ULA Asthma and Immunological Disease Center

Research Interest in Air Pollutants, Asthma and Heart Disease

This collaboration focuses on the adverse health effects of particulate pollutants in the lung, with specific emphasis on the effects of PM in asthma and atherosclerosis. The major hypothesis is that redox cycling organic chemicals (e.g. polycyclic aromatic hydrocarbons and quinones) and catalytic particle surfaces are responsible for inflammation in the airway and vascular wall based on their ability to generate oxidative stress. The hierachical oxidative stress hypothesis (diagram) was developed. At a lower level of oxidative stress, antioxidant enzymes are induced to restore cellular redox homeostasis. This response is regulated by the transcription factor Nrf2 and the antioxidant response element (ARE) (diagram). From a clinical perspective this response protects against asthma and heart disease. People who lack a rigorous antioxidant defense may be more susceptible to PM-induced health effects. At an intermediate level of oxidative stress, newly expressed proteins exhibit pro-inflammatory activity. This tier of oxidative stress demonstrate activation of MAP kinases and other pro-inflammatory signaling cascades (diagram). At the clinical level, this response tier is involved in airway and blood vessel inflammation. At a high level of oxidative stress, perturbation of the mitochondrial permeability transition pore and disruption of electron transfer results in cellular apoptosis or necrosis (diagram). Thiol antioxidants interfere directly in the adjuvant effects of diesel exhaust particles in a murine asthma model. This hypothesis has been expanded to the pro-inflammatory and pro-oxidative effects of "live" particulates collected with particle concentrators in the Los Angeles basin. The data indicate that the pro-inflammatory and toxic effects of fine and ultrafine (nano-size) PM are closely related to the PAH and quinone content. These principles are being applied to identification of susceptible human subsets as well as therapeutic intervention in the effects of PM on asthma. This work covers the following areas: the biology of oxidative stress, the role of oxidative stress in airway inflammation and asthma, the proteomics of oxidative stress, the role of oxidative stress in the activation of intracellular signaling pathways, inhalation exposure studies in animals and humans, the pro-oxidative effect of ambient particles of different size and different composition, and the health-related effect of redox cycling chemical compounds absorbed on particles. This work on ambient nanoparticles is also being extrapolated to the study of the possible biological effects of engineered nanoparticles, for which the possibility exists that the small size of these particles, their large surface area, surface reactivity, and chemical composition may induce toxicity based on an oxidative stress paradigm. ■



Response pathway	Normal	Antioxidant Defense	Inflammation	Cytotoxicity
Signaling pathway		Nrf-2	MAP Kinase	Mitochondria
Genetic response		ARE	AP-1	N/A
Product		Phase II enzymes	Cytokines Chemokines	Apoptosis

The hierarchical oxidative stress model in response to particulate matter (PM) involves antioxidant defense, pro-inflammatory and cytotoxic responses. Each response has its own molecular pathway of induction.

Air pollution particles as well as possibly some engineered nanomaterials may induce disease based on their ability to generate the production of reactive oxygen radicals that cause inflammation in organs such as the lung and the cardiovascular system.

Collaboration between CNSI, Caltech and the Institute for Systems Biology (Seattle)

Alliance for Nanosystems Biology

Nanotechnology devices recording proteins in cells and plasma are needed for in vitro diagnostics. Integrated microfluidics chips will accelerate, diversify, simplify and lower cost of synthesizing molecular imaging biomarkers of disease.

With the development of genomics and proteomics, there is a movement to build a new science of systems biology – genome programming of integrated circuits of cells and intercellular networks that establishes the organization and functions of organ systems and the whole organism. In systems biology, disease is viewed as a re-programming of cell circuits to gain and lose functions in the progressive transitioning of cells and cellular networks through various developmental stages of disease. This requires large-scale multiparameter measurements of the transcription of instructions (mRNA) from the genome and their translation into proteins that form the integrated circuits of cells to execute their individual and collective functions.

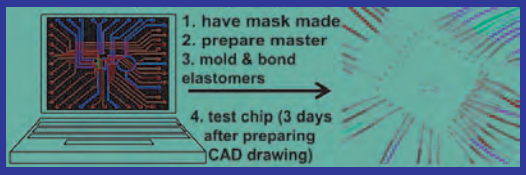
Systems biology requires the invention of new nanotechnologies and integrated microfluidics platforms on which to perform these large-scale in vitro measurements of cellular functions in general, and in disease, to identify critical proteins that consolidate the organized functions of disease. The knowledge and devices that result will be used to record protein signatures - arrays of proteins representing the transformation of cellular functions from normal to disease – and critical consolidating proteins that become drug targets to drive functions back toward normal or kill the diseased cells. These nanotechnologies will provide the new in vitro molecular diagnostics performed on a drop of blood or cells.

On the in vivo side, molecular imaging technologies are being developed to examine the expression of genes and proteins within the context of the living organism, from mouse models of disease to patients using positron emission tomography (PET) and optical imaging approaches. These in vivo molecular imaging technologies provide molecular diagnostics to search throughout the body to determine if critical proteins of disease are present, and if so, where in the body they reside. Molecular imaging with PET provides the means in patients to guide the drug discovery process and to separate patients by their disease and drug protein targets that is critically needed by the pharmaceutical industry for discovery and by medicine in selecting the right drug for the right patient on an individual basis.

Labeled molecular imaging probes, biomarkers and drugs must be synthesized for PET labeled with positron emitting radionuclides. Integrated microfluidics chips are being developed to accelerate, simplify, diversify and lower the cost of producing PET molecular imaging probes. CNSI, the Crump Institute for Molecular Imaging and Caltech are working with a number of companies (Molecular Technologies, Inc., Fluidigm, Liquidia and Materia to produce organic solvent resistant integrated microfluidics chips, chemical synthesis reactions, input/out put systems (electronic and fluid) and overall system design. In addition, new approaches such as "In Situ Click Chemistry" in which the protein target builds a molecular imaging probe for itself are being employed and migrated to the microfluidics chip.

All of these projects involve and require the integration of engineering, physical, biological and medical sciences to be successful and important. ■

Integrated Microfluidics Chips for PET Biomarkers



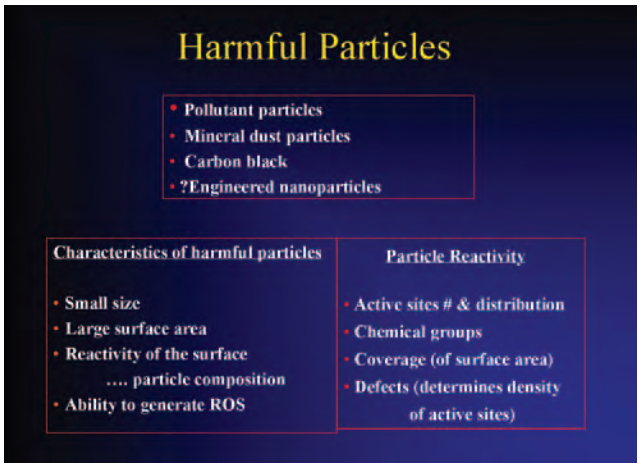
Chip design, manufacturing, testing of application specific chips

Collaboration between CNSI and Manufacturers of Nanomaterials

Biological Effects and Toxicology of Engineered Nanoparticles

There is big interest in the safety assessment of engineered nanomaterials. To study the toxicity of these products, a predictive paradigm is required. Study of air pollution and mineral dust particles indicate that specific particle characteristics predict their ability to generate harmful oxygen species as a predictive paradigm.

Nanomaterials are increasingly being used for commercial purposes such as catalysts, semiconductors, cosmetics, microelectronics, and drug carriers. Materials in the 1 to 100 nm size range behave according to the laws of quantum physics, which allows them to perform almost magical feats of conductivity, reactivity, and optical sensitivity. A potential downside of these capabilities is adverse interactions with biological systems and the environment. The high expectations and promise of nanotechnology is dependent on the safety evaluation of these new products. This collaboration aims to develop a rational approach to nanotoxicology, which is defined as the safety evaluation of engineered nanomaterials. Currently there are no comprehensive or predictive paradigms by which to study the possible adverse biological effects of nanomaterials. However, in studies on ambient nanoparticles, also known as ultrafine particles, a predictive test paradigm has been developed which is centered around the ability of these particles to generate reactive oxygen species (ROS) and oxidative stress. This disease mechanism also applies to the study of mineral dust particles which give rise to occupational lung disease. Particle Toxicology from the perspective of effects of air pollution and mineral dust particles is a mature science, which have shown that small particle size, large surface area, and reactivity are important predictors for particle toxicity. Moreover, these properties are related to the abilities of the particles to generate ROS. While for air pollutant particles, generation of ROS is dependent on coating of the particle surface with the redox cycling chemicals, particle reactivity may also dependent on other surface groups that form active sites on the surface. These sites serve a depots for electron storage. Binding of molecular oxygen to defect areas on the surface places the molecule in a position to capture electrons, leading to the formation of oxygen radicals. The material makeup determines the coverage of the surface by active and defect sites. This could explain why carbon black and titanium dioxide nanoparticles can participate in ROS production and generation airway inflammation in experimental animals. The same principle may also apply to certain engineered nanoparticles that come into contact with biological tissue. A series of assays has been developed which can assess the toxicity of ambient and engineered nanoparticles based on ROS generation. These assays can be used as a predictive toxicity model for nanomaterials testing. Sound scientific principles can be developed to allow the safe production and adoption of engineered nanomaterials. ■



Priniciples of particle toxicity and the relationship to particle properties.

This research received federal funding from NIH

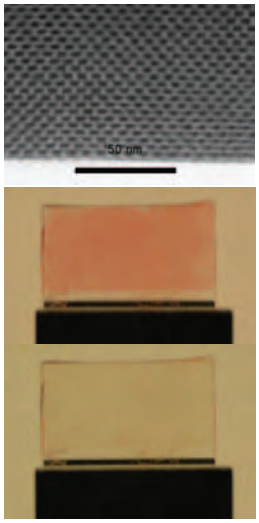
Collaboration between CNSI and Canon Corporation

Optical Materials from Semiconducting Polymer Encapsulated in Porous Silicas

Conjugated polymers are novel materials that have the electronic properties of semiconductors but the mechanical properties and processing advantages of plastic. As a result, conjugated polymers have the potential for use in many novel applications, including large-area, flexible displays or photovoltaic cells

One feature of conjugated polymers is that their electronic properties depend on both the physical conformation of the individual polymer chains and chain-chain interactions. Since typical polymer processing conditions do not provide precise control over the polymer morphology, it is challenging to optimize the performance of a polymer-based device for a particular application. The goal of this collaborative work is to provide for precise control over the nanoscale conformation of the conjugated polymer chains by encapsulation in periodic porous silicas.

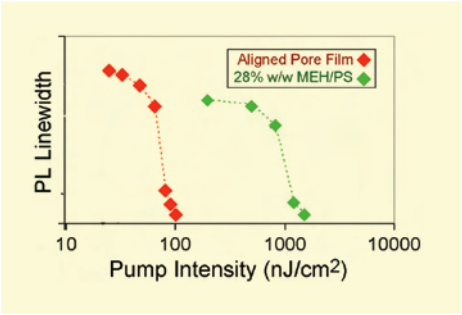
Mesoporous silicas are formed by the cooperative self-organization of surfactant molecules and reactive silicate oligomers to form ordered composite materials. Condensation of the oligomers leads to robust silica frameworks, which can then be made porous by removing the surfactant template. One structure of particular interest is a silica thin film containing a hexagonal array of ~4-nm diameter straight pores, as shown in the cross-sectional STEM figure at right (top). These pores are uniaxially aligned in the plane of the film. By passivating the insides of the channels, conjugated polymers can be incorporated into the pores from solution using osmotic pressure. The alignment of the channels results in a high degree of alignment of the polymer chains. For example, the figure at right shows photos taken through a polarizer oriented either along the pore direction (middle) or perpendicular to it (bottom). The orange color visible when the polarizer is along the pore direction comes from the aligned semiconducting polymer chains. This alignment allows many experiments that build a detailed knowledge of the electronic properties of these materials, including: the orientation of the absorption and emission dipoles; the nature of the production of charge carriers



and how it depends on chain packing; and the way in which electronic excitations on the polymer chains interact with each other.

One particularly exciting recent development is the fact that conjugated polymers encapsulated in mesoporous silica films can be made into lasers. The lasing threshold for the aligned chains in the mesoporous silica is more than 20x lower than that of randomly ordered chains in a comparable spin-cast conjugated polymer film, as shown by the energy at which the emission line narrows in the figure below. ■

Conjugated polymers are plastic semiconductors with the potential for applications in optoelectronic devices such as large-area, flexible displays or solar cells. One route to improving such devices is to control the nanoscale conformation of the polymer chains.



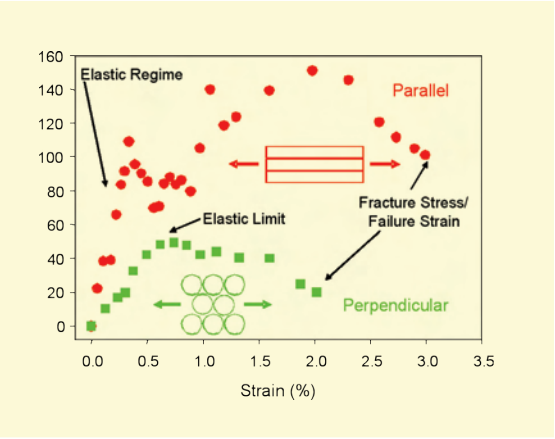
This research received federal funding from NSF

Collaboration between CNSI and UCLA

Using Nanometer Scale Architecture to Control the Mechanical Properties of Periodic Composite Materials

As the miniaturization of electronic circuits continues, the need for high performance low dielectric layers increases. One way to fill this need is by producing thin films with significant porosity. However, porous films are usually structurally weak compared to nonporous materials, and are often damaged by standard polishing treatments. In an effort to combine porosity and structural integrity into a single material, this collaboration has focused on periodic inorganic/organic composites with characteristic length scales on the order of nanometers. These materials consist of inorganic frameworks surrounding organic domains that are periodically arranged into hexagonal or cubic structures. These composites can be treated to remove the organic domains, yielding periodic porous materials. Importantly, periodic composite films can be constructed with continuous inorganic domains, leading to solids that have the potential to be less brittle than macroscopic cellular structures.

In recent work in this area, the tensile properties of periodic silica/polymer composites with a hexagonal honeycomb structure have been examined. Oriented films are produced so that tension can be applied either parallel or perpendicular to the unique hexagonal axis. The results, shown in the figure to the right, demonstrate how nanoscale architecture can be used to tune the properties of composite material. When tension is applied perpendicular to the nanoscale cylinders (green), a large elastic region is observed, although the young's modulus is fairly low. This elastic region is followed by a plastic region and then failure at ~2% strain. The large elastic region likely results from deformation of the hexagonal honeycomb architecture under strain. By contrast, when tension is applied parallel to cylinder axes (red), a much higher modulus is observed, equal to the highest value theoretically predicted for a composite of this composition. Since the cylinders can not easily deform when loaded in this manner, however, the elastic region is somewhat smaller. Moreover, the films do not fail until 3% strain. For comparison, bulk silica shows a failure strain of just 0.1%. The dramatic increase in failure strain likely results because cracks can not propagate through the nanoscale structure of the composite films. The unique combination of stiffness and elasticity in a single material, combined with the ability to produce structural anisotropy suggests that control of nanometer scale architecture may be an exciting new route for controlling the mechanical properties of materials.



Macroscale architecture has long been used to control the mechanical properties of composite materials. Recent results now indicate that nanometer scale architecture can also produce a high level of control, combined with the ability to produce improved mechanical behavior.

This work is a collaboration between UCLA materials chemistry and mechanical engineering groups. The expertise of both groups is vital, as only by combining cutting edge nanomaterials fabrication and characterization with state of the art mechanical measurement and modeling can a project such as this succeed. Work in this area is continuing and current experiments utilize *in-situ* structural measurements to directly visualize deformations on both the atomic and nanometer length scales. ■

This research received federal funding from NSF

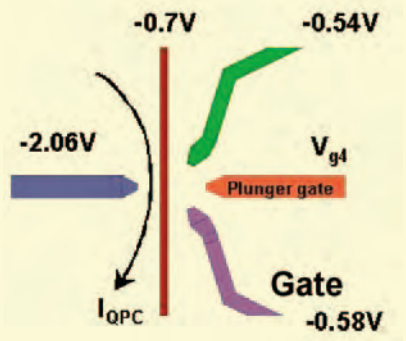
Collaboration within CNSI

Nano-Electronics, Quantum Information Processing and Plasmonics

With collaborators in physics, the devices that will dominate the future of quantum information processing are being developed. Collaborators are trying mathematically to optimize the design of plasmonic nano-electronic devices that might replace the transistor.

Through collaborative research between UCLA physicists and mathematicians, devices that will dominate the future of quantum information processing are being developed. These new nano-electronic spin-based devices will store information in a quantum format. In this way, astronomical volumes of information can be processed with only about 100 nano-spin transistors. New Si-Ge materials will make this possible.

At the same time we are witnessing the shrinkage of classical electronics down to its last vestiges, a transistor as small as one molecule. The question is what will that ultimately consist of? Many believe that the key will lie in the concentration of electromagnetic energy into the nanoscale, where a tiny amount of energy can have a huge impact due to its large concentration ratio. These types of devices will supplant the transistor as we have known it. The problem is how to optimize these nanoscopic devices. Trial and error design is hopeless since the nanoscopic devices are so hard to make, when we do not know exactly what we are looking for. The solution is to apply powerful mathematical design techniques that will tell us ahead of time what device design would perform most optimally. These designs are being solved using mathematical algorithms, so that we end up making the right nano-device, right from the first time. ■



An example of a transistor-like device that has been shown to capture and hold a single electron, for quantum information processing.

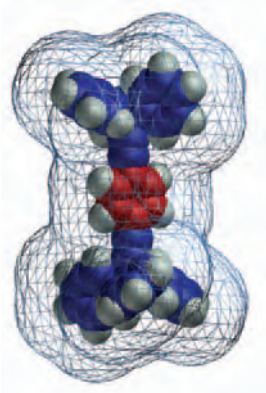
This research received federal funding from ARO, ONR, DARPA and NSF

Collaboration among CNSI, UCLA and University of Colorado, Boulder

Dielectric Response of a Dipolar Molecular Rotor Crystal

Molecules that emulate the structure and properties of compasses and gyroscopes have interesting materials properties and offer entries into the realm of artificial molecular machines. In this collaboration the molecules interface with the macroscopic world by use of electric fields.

The possibility of observing interesting and technically important dielectric and phonon phenomena in ordered arrays of molecular dipolar rotors has been recognized for some time. Ferroelectric and anti-ferroelectric phases are expected, and polar rotary phonons could propagate at velocities much less than typical sound velocities. Also, Goldstone modes are predicted in 2-D, square and triangular lattices. Although rotating groups are common in solid polymers6 and several other solid systems, almost no realizations of ordered dipolar rotor systems are known. However, the rapidly developing field of crystal design is opening new paths to realizing novel solid-state properties, while at the same time synthesized molecular rotors have received new attention as a fundamental element of nanotechnology. Combining these avenues, this collaboration describes polar phenylene rotor crystals and characterizes the rotor's rotational potential by both NMR and dielectric spectroscopy. The approach to the creation of ordered polar rotor arrays allows control over the rigid super structure, the axle of rotation, the size and dipole moment of the rotating group, and the spacing of the dipoles, thus providing a tunable solid state system. By using a combination of NMR and dielectric spectroscopy, the rotor's environment and interactions can be characterized in detail over a wide range of time scales. ■



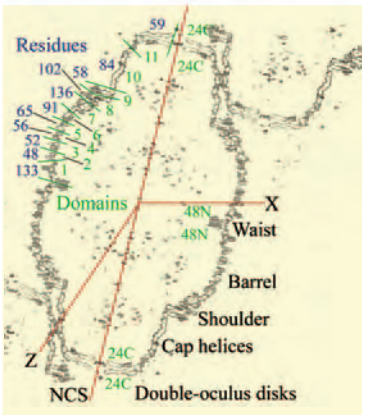
This research received federal funding from NSF

Collaboration between CNSI and UCLA-DOE Laboratory of Structural Biology and Molecular Medicine

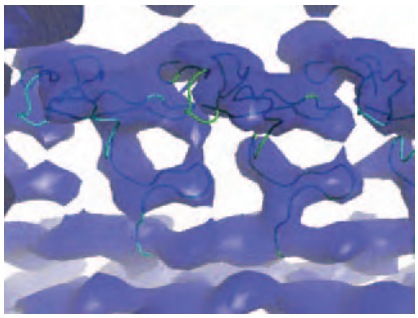
Atomic Structure of Vaults

Vaults are ribonucleoprotein particles that have been conserved throughout evolution. Cryo-electron microscopy and single particle reconstruction have revealed the vault to be a hollow, barrel-like structure with two protruding caps and an invaginated waist. The volume of the internal cavity of the vault is 50 million cubic angstroms. The goal is to solve the crystal structure of recombinant vault particles expressed in baculovirus. Atomic resolution information from crystallography will be essential for identifying internal and external peptide targets for molecular and chemical modification. Initial vault crystals diffracted only to ~ 100 Å resolution, but as methods for crystallization and crystal handling have improved, the resolution gradually extended. Adding a small amount of cyclohexane made a major improvement. At present, the best crystals are of empty vaults built from a cysteine-tag construct of rat MVP, diffracting anisotropically to 8-9Å resolution, for which the structure, and a partial atomic model have been determined.

From these crystals, 142,203 unique diffraction intensities were measured at ALS Beamline 8.2.2 focused on the detector, and a helium chamber to reduce air absorption and scatter over the 700 mm crystal-to-detector distance. Though not uniform, the map patterns at this point showed that most of the MVP monomer is built from autonomously folded domains. Dot models" were used in a manual ARP/wARP protocol to improve the phases and to escape the initial cryo-EM mask. In this procedure, the density representing each domain of the MVP monomer was filled with unidentified atoms ("dots"). Gross errors could then be detected by difference-Fourier maps. The dot models allowed easy editing of the averaging and solvent mask envelopes, and gradually improved the envelope shapes. The 24- and 48-fold NCS axes are coaxial, with 48-fold symmetry breaking down to 24-fold near the C-terminal caps. The chain is not traceable at this resolution, but the density envelopes around many domains are shapes suggestive of beta-propellers, and one domain (10) is certainly a coiled-coil. From fold assignment methods, tertiary structures for some of the domains have been predicted and morphed into the structure. ■



The MVP Vault structure at 9 Å resolution. a. (above) Electron density section containing the off-vertical 48-fold axis (marked NCS) through a vault particle, packed against two other vaults. The electron density forms a thin shell, partitioned into Domains 1-11, labeled in green with the approximate number of residues contained in each, given in blue.



b. (above) Domain 1, with a conjectural chain fitting, starting with residue 26, which is near the waist. There are 96 such chains, 48 in the upper half vault. The vault has 48-fold symmetry until the chain approaches it C-terminus in Domain 11, at the double-oculus disks, where the symmetry drops to 24-fold.

c. (above) A representation of the entire MVP vault at 9Å resolution.

This research received federal funding from NSF and DOE

Collaboration within CNSI

Powering a Supramolecular Machine with a Nanoscale Power Supply

Machines need power supplies to generate mechanical movement. Just as macroscopic machines require macroscopic energy sources, natural and artificial molecular machinery require nanoscale power supplies to effect precise molecular movement. While macroscopic machines do not move or work until energy is supplied to them for a specific function, nanoscale machines down at the molecular level are in perpetual Brownian motion at ambient temperature. For machine-like functions to be performed by molecular systems, they should be able to execute stimuli-induced specific and directional mechanical movements that are otherwise restricted, except for Brownian motion. Chemists and material scientists have developed donor–chromophore–acceptor-based molecular triads that can transduce light into electrical energy by mimicking the photosynthetic pathway. In a collaborative effort between two research groups, a nanoscale power supply (Fig.) in the form of a light-harvesting molecular Triad has been developed.

The ultimate goal of this project is to develop a solar cell. Donor–chromophore–acceptor-based molecular triads that can convert light to electrical energy are some of the most effective molecules that can serve the purpose of energy transduction. Furthermore, it has been demonstrated (*Small* 2005, 1, 87–90, *Chem. Eur. J.* 2005, 11, ASAP) that the photocurrent generated by the Triad can be utilized (Fig.) to drive a supramolecular machine in the form of a pseudorotaxane.

A tetrathiafulvalene–porphyrin–fullerene (TTF–P–C_{60}) molecular triad, which generates electrical current by harnessing light energy when self-assembled onto gold electrodes, has been developed. The Triad, comprised of three unique electroactive components, namely, i) an electron-donating TTF unit, ii) a chromophoric porphyrin unit, and iii) an electron-accepting C_{60} unit, has been synthesized in a modular fashion. A disulfide-based anchoring group was tagged to the TTF end of the molecule in order to allow its self-assembly onto gold surfaces. In a closed electrical circuit, the Triad-functionalized working-electrode generates a switchable photocurrent of ~1.5 μA/cm^2, when irradiated with a 413 nm Kr-ion laser. The electrical energy generated by the Triad at the expense of the light energy is ultimately exploited to drive (Fig.) a supramolecular machine in the form of a [2]pseudorotaxane comprised of a π-electron-deficient tetracationic cyclobis(paraquat-*p*-phenylene) ($CBPQT^{4+}$) cyclophane and a π-electron-rich 1,5-bis[(2-hydroxy-ethoxy)-ethoxy]naphthalene (BHEEN) thread. The dethreading of $CBPQT^{4+}$ cyclophane from the BHEEN thread has been monitored by measuring the increase in the fluorescence intensity of the BHEEN unit. A gradual increase in the fluorescence intensity of the BHEEN unit concomitant with the photocurrent generation, even at a potential (o V) much lower than that required (–300 mV) for the direct reduction of the $CBPQT^{4+}$ unit, confirmed that the dethreading process is driven by the photocurrent generated by the Triad. ■

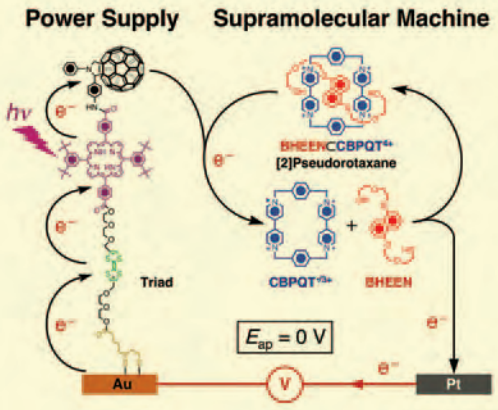


Fig. The mechanism by which a photoactive molecular triad generates the electrical power to drive a supramolecular machine.

A photoactive molecular triad has been demonstrated to transduce light to electrical energy. The photocurrent generated by the triad has been utilized to drive the dethreading of a pseudorotaxane. In essence, light produces electrons that drive a supramolecular machine.

This research received funding from NSF, CMISE, NASA and ONR

"Form is the expression of inner content."

—WASSILY KANDINSKY

M-O-D-U-L-A-R-I-T-Y

E-Q-U-I-P-M-E-N-T

CNSI FACILITY

Opening in mid 2006, the CNSI building is currently under construction on the Court of Science, strategically located amid the disciplines that comprise the membership, Life and Physical Sciences, Engineering and Medicine. Approximately 50% of the 188,000 square foot world-class research facility will be devoted to lab space designed to facilitate interactivity between researchers. The state of the art equipment will be available to corporate and academic partners.

The vision for use of the building space is to further collaborative research for CNSI members, UCLA faculty, other universities and industry partners. To support such collaboration, the building offers:

- CORE research labs
  - Advanced Light Microscopy/Spectroscopy
  - AFM/STM
  - Diffraction Analysis
  - Electron Imaging Center for Nanomachines
  - INMOS
  - Molecular Screening Shared Resource
  - Quantum Information Research
- Lab suites constructed with special attention to vibration, acoustical and electromagnetic noise
- Open labs conducive to collaborative research, allowing wet and dry lab members to work in close proximity
- A 260-seat auditorium with over 4,000 sf of adjacent exhibition space
- 10 conference rooms

The building will also be home to the UCLA Institute for Digital Research and Education, the UCLA Art|Sci Center, and the Crump Institute for Molecular Imaging which includes the Crump Imaging Technology Center.

WENDY MORRIS | BUILDING MANAGER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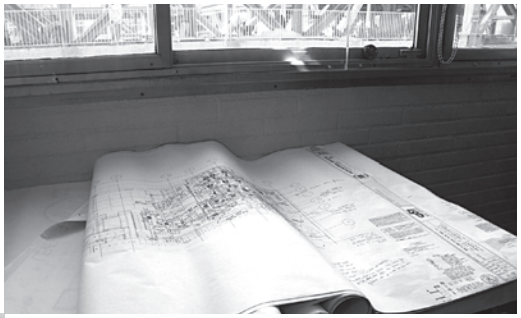

YEE-PING CHO DESIGN