

**Caltech/MIT Enterprise Forum
Venturing in Proteomics and Bioinformatics: Decoding the Opportunities
Saturday, March 23, 2002**

Speakers

Keynote

William A. Goddard III
**Charles and Mary Ferkel Professor of Chemistry, Materials
Science, and Applied Physics; Director of Materials and Process
Simulation Center, Ph.D.**
Caltech, Pasadena, CA

626/395-2731
wag@wag.caltech.edu

The long-term objective of Professor Goddard's research has been to describe the properties of chemical, biological, and materials systems directly from first principles (without the necessity of empirical data). To accomplish this his research group has been developing new theory, new methods, and new software. The group's approach builds from Quantum Mechanics (QM) through a hierarchy of more approximate methods suitable for longer length and time scales, including Molecular Dynamics (MD), mesoscale dynamics, and macroscopic dynamics.

These methods are applied to critical problems in chemical, biological, and materials systems. Usually in such problems, there is a dearth of reliable experimental data, and hence they validate their new methods by application to problems well characterized experimentally. Areas of current research interest include:

- ◆ BIOTECHNOLOGY (Protein Folding, Structure and function of G-Protein Coupled Receptors, design of non-natural Amino Acids to be incorporated in biopolymers, Pharma)
- ◆ POLYMERS (prediction of structures and properties of Dendrimers, Gas diffusion through polymers, Surface Tension of polymers)
- ◆ CATALYSIS (Methane Activation, Metathesis, Selective Oxidation and Ammoxidation of alkanes)
- ◆ SEMICONDUCTORS (Reconstruction and Epitaxial Growth of GaN, structure and properties of the Si/SiO₂ interface, diffusion of dopants in Si nanoscale devices)
- ◆ CERAMICS (structures and phase diagrams, structural and catalytic properties)
- ◆ METAL ALLOYS [Plasticity (dislocations, crack propagation, spall), Glass Formation]
- ◆ NANOSCALESYSTEMS (Carbon Nanotubes, Self-Assembly, NanoStructured diamond, bionanotechnology)
- ◆ ENVIRONMENTAL (Dendrimers for Selective Encapsulation, phase equilibria in particulates)

Most of these projects involve collaborations with experimentalists at Caltech, other universities, national laboratories, or industry.

Professor Goddard has had a long and distinguished career in science and technology, and has been a professor at Caltech since the 1960's. Professor Goddard has founded four companies over the last twenty years, including his latest company, Bionomix.

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Panelists

Richmond Wolf, Ph.D.
Office of Technology Transfer
Caltech, Pasadena, CA

626/395-2322
wolf@caltech.edu

Richmond Wolf, Ph.D., is the Associate Director of the Office of Technology Transfer at the California Institute of Technology (Caltech), a nonprofit university that also manages the Jet Propulsion Laboratory (JPL) for NASA. He assesses the commercial and technical merit of technologies developed at Caltech and JPL, and manages the operations of the intellectual property portfolio, which includes over 1500 issued and pending patents. He directs outside counsel in patent prosecution and negotiates agreements to license intellectual property from JPL and Caltech to outside companies. Dr. Wolf has experience working with start-up companies from Caltech and JPL in areas of business and product development, and he was a co-founder of two companies. He has been or is a member of the advisory board of ITU Ventures, Oak Grove Systems, and the Egg Factory. He is a graduate of Princeton University, received a Ph.D. from Caltech, and he is a registered patent agent.

Alfred N. Fonteh, Ph.D.
Lipid Biochemist
Huntington Medical Research Institute (HMRI),
Molecular Neurology Program
Pasadena, CA

626/795-4343
afonteh@hmri.org

At HMRI since October 1, 2001, Dr. Fonteh is an expert in receptor-mediated signaling pathways. The overall objective of Dr. Fonteh's research is to discover important therapeutic targets for neurological disorders and inflammation. The ultimate goal of his research is to provide biochemical basis for clinical observations from the Molecular Neurology Program and thus a rationale for diagnosis and/or treatment of diseases of the brain.

Dr. Fonteh received his B.Sc. in Biochemistry with Chemistry from University of London and M.Sc. in Medicinal Chemistry from Loughborough University of Technology. Dr. Fonteh is a graduate of the Faculty of Medicine (Ph.D. in Biochemistry, 1989) of the University of London.

Research interest

-The Brain Lipid Project- Although the bulk of the human brain is made up of lipids, very little is known about the molecular composition and functions of the various classes of lipids found in the brain and their potential impact on health or diseases. Dr. Fonteh is using state-of-the-art technology (High Performance Liquid Chromatography and electrospray tandem mass spectroscopy) to completely map out the composition of cerebrospinal fluids (CSF) and major regions of the brain. Currently, he is looking at changes in lipids in the CSF of study participants in our Proteome Project. These studies have the potential of uncovering new therapeutic targets that will be the basis for the rational design of effective strategies for the management of neurological processes (migraine and neurodegenerative disorders).

-Allergy and inflammation at Forest University School of Medicine (Research Associate, 1991-3; Instructor of Medicine, 1993-7; and Assistant Professor, 1997-01).

-Interactions of drugs with membrane lipids, receptors and enzymes. Lipid signaling pathways and asthma at the University of London and Johns Hopkins University Asthma and Allergy Center, Baltimore, USA from 1990-91.

Key Discoveries

-Enzyme pathways in homeostatic control of arachidonic acid in normal and diseased conditions.

-Novel Receptors in mediator release from inflammatory cells.

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- Dietary strategy for controlling lipid mediator formation.
- Cytokine like properties of enzymes.
- Anti-apoptotic properties of enzymes and potential therapeutic significance of signaling pathways in breast cancer and leukemia.

Dr Fonteh's has collaborated with four major pharmaceutical companies and his peer-reviewed studies have been funded by the National Institute of Health and the Environmental Protection Agency.

Sydney G. Edwards, Ph.D.
TL Ventures
Santa Monica, CA

310/664-7449
sedwards@tlventures.com

Sydney Edwards joined TL Ventures in March 2001 as a Principal in the Biotechnology Practice. In his role, Sydney evaluates investment opportunities in biomedical technology companies that develop therapeutic drugs and/or drug discovery tools.

Previously, Sydney was a Senior Manager in Corporate Finance for Amgen, Inc., where his work included providing financial and strategic analyses for Amgen's Executive Committee as well as numerous teams, including those focused on R&D Portfolio Management, M&A and Drug Development. Prior to Amgen, Sydney was a Management consultant in Andersen Consulting's Pharmaceutical Practice, where he worked closely with major pharmaceutical companies in the areas of R&D portfolio management, clinical development, and business process reengineering. Prior to Andersen, Sydney also worked in business development in Monsanto Corporation's Ag-biotech business and was a Biochemical scientist at Lawrence Berkeley Labs.

Sydney earned a Ph.D. in Biochemistry from Pennsylvania State University, an M.B.A. in Strategy & Finance from the MIT Sloan School of Management and a B.A. in Biochemistry from UC Berkeley.

Case Presenters

Dr. Bassil Dahiyat, CEO
Xencor, Inc.
Pasadena, CA

626/305-5900
*****@xencor.com**

Dr. Dahiyat is co-founder of Xencor and co-inventor of the Protein Design Automation technology. He has been CEO since incorporation of Company's research activities and directs an aggressive patent strategy for Xencor's technology platform and proprietary proteins. Dr. Dahiyat has co-authored numerous scientific papers in the fields of protein design and drug delivery and has received scientific awards from the American Chemical Society, the Controlled Release Society, the Protein Society and Caltech. Dr. Dahiyat holds a Ph.D. in Chemistry from Caltech and BS and M.S.E. degrees in Biomedical Engineering from the Johns Hopkins University.

Xencor is a privately held proteomics company founded in 1997 to apply advanced technologies to speed the high-throughput analysis and optimization of proteins. Xencor's proprietary tools, ProCode™ and Protein Design Automation, were designed to handle proteins' enormous biochemical diversity, the central challenge faced in the large scale study of proteins.

ProCode™ allows the simultaneous analysis of the entire proteome of a cell by creating protein expression libraries where each protein is covalently linked to its corresponding cDNA. The key advantage of ProCode™ proteome display libraries is their ease of expression in a wide range of cell types, including human cells. Protein expression in

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native cells, critical for accurately assessing protein function, is combined with the incredible sensitivity of DNA detection, a billion-fold improvement over standard proteomics tools such as mass spectrometry. Xencor is applying ProCode™ to create safer, more potent drugs by profiling proteome-small molecule interactions, and to assign gene functions and identify new targets by profiling proteome-wide protein expression and protein-protein interactions. ProCode™ is enabling the field of chemical genomics by linking drug molecules to the genes that they act upon.

Xencor's PDA technology combines supercomputing with experimental screening to search the entire range of potential protein sequences for improved proteins, overcoming the limitations of natural and directed evolution. PDA's ultra-high throughput in silico prescreening reduces the number of candidate proteins that require experimental testing, saving significant time and cost compared to solely experimental techniques. Xencor is using PDA to create a new generation of biotechnology products tuned for their specific applications, such as more effective and robust proteins for chemical processing, new agricultural products and more potent and specific biopharmaceuticals.

Bill Boyle, Vice President of Biology
Protein Pathways, Inc.

818/340-2004
bboyle@proteinpathways.com

Bill Boyle is Vice President of Biology at Protein Pathways, and heads its experimental research platforms. He was formerly Director of Discovery Research and the Biosystems technology platforms at Amgen, Inc., and led a basic research effort as part of the preclinical and clinical development of OPG and OPGL antibody. Bill received his Bachelors degree in Biology from UCLA in 1980, and his Masters in Biology from UCLA in 1982. He went on to obtain his Doctoral degree in Experimental Pathology from the UCLA School of Medicine. From 1986-1990 he pursued postdoctoral studies at the Salk Institute for Biological Studies as a Howard Hughes Medical Institute Fellow of the Life Sciences Research Foundation. His current research interests include elucidating the molecular and cellular biology of key signaling and metabolic pathways linked to disease. His long-term career interests are in using genome-enabled informatic technologies to facilitate therapeutic drug development.

Protein Pathways is a privately held biotechnology company, founded in 1999, that is a leader in the development of algorithms that can be applied to the functional interpretation of sequenced genomes. Its proprietary system of pathway elucidation is called the ProMaps™ discovery system. While most comparative genomics analyses are based almost exclusively on similarity searches that infer only limited aspects of biological function, the ProMaps™ discovery system can predict gene function, place newly discovered genes in existing pathways and elucidate interactions between pathways. In other words, by using the ProMaps™ discovery system it is possible not only to predict the biological classification of a gene product, but to also gain insight into interacting proteins, the nature and identification of probable substrates, and the biological context of the associated pathway. The company has established the discovery of molecular interactions as its core competency because of the firm belief that placing genes in existing pathways and understanding the network interactions between pathways will inevitably lead to improved methods that facilitate the small molecule drug discovery process.

Protein Pathway's early efforts focused exclusively on applying computational approaches to completely sequenced bacterial genomes. From this work emerged the microbial version of the ProMaps™ discovery system that can be used as a powerful tool to identify protein-protein relationships or functional links. The prediction of functional links, that are associated with confidence values, allows the development of new hypotheses that can be used to guide research dedicated to the development of new anti-microbials, the identification of novel enzymatic functions, and the optimization of foreign proteins expressed in bacterial hosts.

Protein Pathways is now engaged in applying its technologies and philosophies to devising and applying new methods of discovery science that will be used to guide the costly downstream steps in the drug discovery process. To accomplish these goals Protein Pathways is adding groups with expertise in experimental genomics, computation

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chemistry, and structural biology. A central assumption is that many databases covering the fields of chemistry and biology now exist and that pattern recognition algorithms can be applied to develop hypotheses about how small molecules impact biological processes. Furthermore, expression profiling (e.g. microarrays) can be used to test and refine these hypotheses. Together, these computational and experimental platforms that bridge chemistry and biology, will allow us to discover the detailed molecular pathways that underlie the pharmacological and toxicological impacts of small molecule drugs and drug candidates. Of critical importance is the notion that the tools developed in the course of this work will lead to improved predictive computational and experimental approaches to develop proprietary drugs for existing and newly discovered targets.

Moderator

Stephanie Yanchinski
Executive Director, Pasadena Entretec
Pasadena, CA

626/356-9933
yanchinski@earthlink.net
www.pasadenaentretec.com

Stephanie C. Yanchinski is the Executive Director of Pasadena Entretec, which is non-profit organization dedicated to bringing high tech jobs and investments to companies in Pasadena and the San Gabriel Valley. Pasadena Entretec does this by providing leads on financing, real estate, professional services and other contacts, as well as offering consulting to its members.

Stephanie is an award-winning writer and marketing and communications specialist who has successfully built and managed a business consulting company serving a diverse clientele in the high tech arena. Her past clients included innovators in the molecular diagnostics field, investment companies, government agencies and academic centers. First established in London UK, the company operated successfully in Europe, Singapore and Toronto, Canada. As a past research scientists in biotechnology, she brings in-depth industry knowledge and an extensive international network of professional contacts in science, technology, business and finance. In Toronto, she successfully drove the foundation stages of a \$20 million medical science incubator located in the downtown core. She also created the Mastermind™ mentoring program, budgeted at over \$1.5 million dollars, for the international biotechnology industry. An experienced and skilled multi-faceted communications professional with strengths in strategic planning, she adds an exceptional marketing and technical support. Stephanie authored two books on biotechnology and currently writes as a columnist for *Genetic Engineering News*.

Producers

Renee Rottner
Consultant, O'Melveny Consulting
Los Angeles, CA

310/712-8993
rottner@consultOMC.com
www.consultomc.com

Renee has co-founded three technology companies. She was president and chief executive officer of Numedeon, Inc., an affiliate of California Institute of Technology, which develops Web-based tools for education and science and on the launch team of two other technology ventures. She is a member of the Caltech-MIT Enterprise Forum, on the Marketing Committee and chair of the Web Committee.

She was a founder of Michigan Development Corporation, an incubator for technology transfer, and co-founded EOtech, a high-tech manufacturer that commercialized the Bushnell holo-sight. Both are wholly-owned affiliates of Environmental Research Institute of Michigan, a 50-year old non-profit government research and development institute. Renee holds three B.S. degrees from Eastern Michigan University in written communication, philosophy

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and literature. She also studied engineering for two years as an officer candidate at the United States Air Force Academy.

Daniel R. Kimbell, Esq.
IP attorney, Christie, Parker & Hale, LLP
Pasadena, CA

626/795-9900
drk@cph.com
www.cph.com

Dan is an attorney with the Pasadena office of Christie, Parker & Hale. His practice emphasis is in domestic and foreign patent and trademark counseling, licensing and prosecution in a wide variety of technology areas including the chemical, pharmaceutical, and mechanical arts.

Dan was a co-founder of United Voicemail, a voicemail company that provides web access to voicemail. www.reachme.com. Dan holds a B.S. in Chemistry from UCLA, a J.D. from Loyola Law School, and is a California attorney and a registered patent attorney.