



3rd Annual GREAT* Training Retreat



Laguna Beach, California
November 5 & 6, 2006

**UC Systemwide Biotechnology
Research and Education Program**

*Graduate Research and Education in Adaptive bio-Technology Training Program

3rd Annual GREAT Training Retreat
Aliso Creek Inn
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**UC Systemwide Biotechnology Research
and Education Program**

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**Graduate Research and Education in Adaptive bio-Technology
GREAT Training Program**

The University of California Biotechnology Research and Education Program, Graduate Research in Adaptive bio-Technology Training (GREAT) Program

Our Program supports the training of the brightest young graduate students within the University of California system for research at the interface between the life sciences and any of the disciplines within the physical, chemical, material, engineering, mathematical and computational sciences. The result—the Graduate Research and Education in Adaptive bio-Technology (GREAT) Training Program awards individual fellowships up to \$50,000 each per year.

By providing funding directly at the trainee level, our Program has more direct control of where the funds are allocated, has the potential to greatly increase distribution across campuses, has a greater impact in evolving cutting edge cross-disciplinary fields, and provides a means of tracking results.

The response to our first three calls for GREAT pre-proposals was overwhelming! We received 109 pre-proposals in 2003, over 140 in 2004 rising to almost 200 (195) in 2005, all of outstanding quality and tremendous diversity. The final proposals were all of exceptional quality and the competition was extraordinarily rigorous since the excellence of the proposals and the caliber of students were uniformly outstanding. From the finalists of each year, eleven proposals that best reflected the mission of the UC Biotechnology Research and Education Program and the GREAT Program were selected.

In 2006, we introduced a new review step in the selection of GREAT trainees from 20 finalists. Pairs of preceptor-candidate made formal presentations to the UC BREP Executive Committee (EC). For the Director and EC, it was an important lesson in realizing the extra value incurred from individual engagement that allowed applicants to clearly project candidates' knowledge of subject matter and their ability to think on their feet as well as field questions outside of their comfort zones. Most faculty participants commented on the value of this exercise in preparing their students for careers beyond graduate school.

All projects provided an environment for non-traditional cutting-edge cross-disciplinary training from investigators who displayed the greatest expertise and creativity working at the interface of complementary disciplines in:

- **nanotechnology as it applies to the life sciences**
- **novel biosensors**
- **medical microdevices/delivery systems, bio-materials**
- **bio-devices/instrumentation/bio-MEMS**
- **microarrays**
- **bioinformatics and molecular modeling**
- **chemical proteomics,**
- **genomics**
- **bio-imaging**
- **computation in the cognitive sciences**

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PROGRAM OVERVIEW

Sunday, November 5, 2006

- 11:30 – 12:00 PM **Registration and check-in;** lunch and poster set up
Terrace Room and Terrace Room Foyer
- 12:00 – 12:30 PM **Lunch, poster set up and presentation preparations** continued
Terrace Room
- 12:30 – 12:45 PM **Welcome by Fred Fox, Chair**
- Overview of program Martina Newell-McGloughlin Director,
UC Biotechnology Research & Education Program
- 12:45 – 5:30 PM **Presentations by the 2005 and 2006 GREAT trainees**
- 5:30 - 6:00 PM **BREAK** for poster session/networking/Aliso Creek Room check in
- 6:00 PM **Dinner**, Main Dining Room (No-Host Bar)
- 7:00 PM **Industry presentations**, Terrace Room

Monday, November 6, 2006

- 7:30 – 8:00 AM **Continental breakfast**, Terrace Room
- 8:00 – 12:00 noon **Presentations by the 2005 and 2006 GREAT trainees, continued**
- 12:00 noon **Lunch** (Soup & Salad Buffet), Green Room
- 1:00 – 3:00 PM **Presentations**, continued, Terrace Room
- 3:30 PM Summary, conclusion, adjournment

GREAT trainees will make presentations of their research and cross-disciplinary training environment according to topic area. **2005-07 GREAT Trainees are allotted 20 minutes** for his/her presentation. **2006-2008 GREAT trainees will have 15 minutes.** There will be five minutes Q&A after each presentation. Total time includes sponsor introduction and speaker transition.

Themes: **Systems Analysis**
 Nanotechnology/Tools
 Tools
 Biomaterials

Sunday, November 5, 2006

Theme: Systems Analysis

12:45 Engineering Cellular Signal Processing: Introducing Synthetic Feedback Loops into Kinase Pathways

Caleb Bashor, UCSF; introduced by sponsor Wendell Lim

1:15 A Pooling-Deconvolution Strategy for Biological Network Elucidation

Fulai Jin, UCLA; introduced by sponsor Jing Huang

1:45 Pulling Apart RNA Folding with Optical Tweezers

Jeffrey Viereggs, UCB; introduced by sponsor Ignacio Tinoco

2:15 A System Level Analysis of the Mitotic Machinery

Roy Wollman, UC Davis, introduced by sponsor Jonathan Scholey

2:45 BREAK

3:00 A Model System to Study the Translocation of Single Biopolymers through Pores and Cavities in Biological Molecular Machines

Eliane H. Trepagnier, UCB, introduced by sponsor Jan Liphardt

3:30 Systems Analysis of Cellular Energy Metabolism Elucidates Mitochondrial Roles in Health and Disease

Thuy Vo, UCSD; introduced by sponsor Bernhard Palsson

4:00 A Novel System to Quantitatively Analyze Cause-Effect Relationships in Cellular Pathogenesis

Siddhartha Mitra, UCSF; introduced by sponsor Steven Finkbeiner

Theme: Nanotechnology/Tools

4:30 Nanobiosensor Based on One-Dimensional Nanostructures

Mangesh Bangar UCR, introduced by co-sponsor Ashok Mulchandani

5:00 Trehalose Preservation of Model Cell Membranes Investigated at the Nanometer Scale

Sandra Bennun Serrano, UCD; introduced by co-sponsor Margie Longo

5:30 Break, Poster session/networking/Aliso Creek Room check-in

6:00 Dinner, Aliso Creek Inn Restaurant

7:00 Industry Presentations

Discovery of Functional Antibodies of Therapeutic Applications

David Light, Berlex

Invitrogen

Paul Predki, Invitrogen

Agilent Technologies

Brian Peter of Agilent Technologies

Pioneering Projects at Applied Biosystems: Next Generation Sequencing as an Example

Ken Livak, Distinguished Scientific Fellow, Exploratory Research, ABI

Intelligent Optical Systems, Inc. (IOS)

Glenn Bastiaans of Intelligent Optical Systems, Inc

MediaCybernetics

Will Casavan of MediaCybernetics

Genzymes

Michael A DiMicco of Genzyme Preclinical Orthopaedics

9:00 PM Adjourn

Monday, November 6, 2006

7:30 AM Continental Breakfast, Terrace Room

Theme: Systems Analysis, revisited

8:00 Single-Molecule Studies of Protein Folding Dynamics

Jesse W. Dill, UCB, introduced by sponsor Susan Marqusee

Theme: Tools

8:30 Mechanisms of Lipid Spreading at Hydrophilic and Hydrophobic Surfaces

Babak Sanii, UC Davis, introduced by sponsor Atul Parikh

- 9:00** **Light Microscope for Sub-Diffraction Nano-scale Bio-imaging**
Margaret Chiang, UCLA, introduced by sponsor Jia-Ming Liu
- 9:30** **Optimized Molecular Imaging with the Xenon Biosensor**
Tom Lowery, UCB; introduced by sponsor David Wemmer
- 10:00 BREAK**
- 10:15** **Integrated Bio-Photonic Waveguide Devices for Optical Studies of Single Biomolecules**
Dongliang Yin, UCSC; introduced by sponsor Holger Schmidt
- 10:45** **Development of an Integrated Laser Microbeam/Microscope Platform for Time-Critical Single Cell Analytics**
Amy Hellman, UCI, introduced by sponsor Vasana Venugopalan
- 11:15** **High-Throughput Screening for Compounds that Regulate β -cell Proliferation and Differentiated Function**
Alice Kiselyuk, UCSD, introduced by sponsor Fred Levine
- 11:45** **Locus-specific CHIP-MS: An Innovative New Technology for Studying Epigenetic Gene Regulation during Stem Cell Differentiation**
Ryan Jason Schmidt, UCLA, introduced by sponsor Yi Eve Sun
- 12:15** **Lunch (Soup & Salad Buffet, Green Room)**

Theme: Bio/Materials

- 1:00** **Controlling Neural Stem Cell Behavior with Synthetic Hydrogels**
Krishanu Saha, UC Berkeley; introduced by mentor Kevin Healy
- 1:30** **Linear Dendritic Block Copolymers for Nerve Tissue Engineering**
Jennifer Cash, UC Davis, introduced by sponsor Timothy Patten
- 2:00** **An Interdisciplinary Approach: Zinc and Halogens in the Jaws of a Marine Worm**
Rashda Khan, UCSB, introduced by sponsor Galen Stucky
- 2:30** **Designing a 3D Tissue Culture Platform: Cardiac Regeneration**
Karen Wei, UCSD, introduced by sponsor Andrew McCulloch and co-sponsor Mark Mercola
- 3:00** **Therapies Bioengineering Synovial Fluid and Diarthroidal Joints: A Platform for Biotechnology and Biomaterial Therapies**
Megan Blewis, UCSD, introduced by sponsor Robert Sah
- 3:30 PM** **Summary, conclusion, adjourn**

GREAT Trainee Abstracts

Engineering Cellular Signal Processing: Introducing Synthetic Feedback Loops into Kinase Pathways

Trainee Caleb Bashor
Sponsor Wendell Lim
Co-sponsor Adam Arkin
Campus UC San Francisco

Caleb Bashor*, Shude Yan, Noah Helman, and Wendell Lim
Department of Cellular and Molecular Pharmacology, University of California, San
Francisco

Living cells are remarkably sophisticated information processing units that respond in complex ways to environmental signals. Thus a frontier in biotechnology is the engineering of cells as biosensor devices for diverse applications areas including medicine and bioremediation. However, the engineering of useful cell-based devices would demand precise control over the biochemical circuits that underlie cellular input/output (I/O) behavior. Our understanding of how to manipulate these circuits is poor. In natural signaling systems, feedback loops are a principle means by which cells transform environmental inputs into diverse, non-linear output behaviors. Thus, to probe the engineerability of cellular signaling systems, we are attempting to reprogram the I/O behavior of a natural kinase signaling cascade in yeast by introducing synthetic feedback control circuits. In order to achieve feedback, we are engineering synthetic linkages between kinase activity and a number of output properties, including modulation of protein transcription, protein degradation, and modulation of protein-protein interactions. We outline progress toward realizing these mechanisms, and demonstrate how each mechanism could be used to generate feedback circuits within the kinase pathway. Additionally, as evidence of progress toward sophisticated control over the I/O behavior of the pathway, we describe several simple circuits which we have generated that exhibit feedback modulation of the pathway.

A Pooling-Deconvolution Strategy for Biological Network Elucidation

Trainee Fulai Jin
Sponsor Jing Huang
Co-sponsor
Campus UCLA

*Fulai Jin¹, Tony Hazbun^{2,3}, Larisa Avramova³, Gregory A. Michaud⁴, Michael Salcius⁴, Paul F. Predki⁴, Stanley Fields⁵, Jing Huang¹

¹ Department of Molecular and Medical Pharmacology, David Geffen School of Medicine, and the Molecular Biology Institute, University of California, Los Angeles, CA 90095

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⁴ Protein Microarray Center, Invitrogen Life Technologies

⁵ Howard Hughes Medical Institute, Departments of Genome Sciences and Medicine, University of Washington

The generation of large-scale data sets is a fundamental requirement of systems biology. But despite recent advances, generation of such high-coverage data remains a major challenge. We developed a pooling-deconvolution strategy that can dramatically decrease the effort required. This strategy, pooling with imaginary tags followed by deconvolution (PI-deconvolution), allows the screening of $2(n)$ probe proteins (baits) in $2 \times n$ pools, with n replicates for each bait. Deconvolution of baits with their binding partners (preys) can be achieved by reading the prey's profile from the $2 \times n$ experiments. We validated this strategy for protein-protein interaction mapping using both proteome microarrays and a yeast two-hybrid array, demonstrating that PI-deconvolution can be used to identify interactions accurately with fewer experiments and better coverage. We also show that PI-deconvolution can be used to identify protein-small molecule interactions inferred from profiling the yeast deletion collection. Recently, using this pooling strategy, we developed a two-hybrid smart pool array (SPA) system where, instead of individual AD strains, well-designed AD pools are screened in an array format that enables built-in replication and prey-bait deconvolution. Using this method, a *Saccharomyces cerevisiae* genome SPA increases Y2H screening efficiency by an order of magnitude.

Pulling Apart RNA Folding with Optical Tweezers

Trainee	Jeffrey Vieregg,
Primary Sponsor	Ignacio Tinoco, Jr.
Co-sponsor	Carlos Bustamante
Mentor	
Campus	UC Berkeley

RNA plays many roles in the cell, including not only information transfer (mRNA) but also structural, regulatory (RNAi, riboswitches), and catalytic (ribozymes, ribosomes) functions, many of which were previously thought to be only performed by proteins. The process by which linear RNA molecules fold into their three-dimensional active structures is important for all these functions. Traditional bulk biochemical studies have revealed many important properties of the RNA folding problem, including its hierarchical organization and the important role of divalent cations. Recently, single-molecule techniques have made it possible to access more and different aspects of the folding process. With so-called “optical tweezers”, we can apply controlled mechanical force to an individual molecule and watch it unfold and refold repeatedly in real time. We can identify intermediates in the folding process and directly measure thermodynamics and kinetic properties without the averaging associated with bulk studies. In addition to applying mechanical force, we can control environmental properties such as temperature and ionic strength. The new information provided by single-molecule studies offers the possibility of making big strides toward understanding how RNA and other biomolecules fold.

A system level analysis of the mitotic machinery

Trainee	Roy Wollman
Primary Sponsor	Jonathan Scholey
Co-sponsor	Tim Patten
Mentor	
Campus	UC Davis

Mitosis is the process by which the duplicated genetic material is segregated, thereby ensuring that each cell gets a full set of genetic instructions. This process is important since mitotic dysfunction can lead to cancer and birth defects. We want to know how multiple mitotic force generators and regulatory molecules comprising the mitotic machinery coordinate the transitions between sequential stages of mitosis. To accomplish this we will first identify the key genes involved in mitosis in the fruit fly genome. We will combine molecular biology techniques of gene function silencing with high-throughput automated microscopy. To deal with the very large amount of data produced in this phase of the project, we will develop and utilize computer vision techniques to automatically identify dividing cells. To complement this large scale screen we will perform a more focused analysis that will characterize in detail all the genes that are found to be important for mitosis. To understand how these genes and their products interact to coordinate the events of mitosis, we will use computational tools to systematically test literally millions of mathematical models of mitosis and we will thereby determine which properties and components of the mitotic network play key roles.

A model system to study the translocation of single biopolymers through pores and cavities in biological molecular machines

Trainee	Eliane H. Trepagnier
Primary Sponsor	Jan Liphardt
Co-sponsor	Lydia Sohn
Mentor	
Campus	UC Berkeley

Cells are organized in a modular fashion. Each central function (e.g. division, motility, intracellular signaling) is performed by complex assemblies of interacting components that behave as self-contained molecular machines. In many of these machines, charged polymers such as DNA, RNA, and proteins, are translocated through pores during the machine's operating cycle. Polymer translocation takes place in the vast majority of cellular processes, including protein synthesis, DNA transcription, and protein degradation. The proteasome, a molecular complex which degrades proteins, rips folded proteins apart and passes the unstructured amino acid chain through a 1.3 nm diameter aperture [1] for proteolysis. The ring-shaped translocase FtsK passes 2nm-diameter DNA through its 3nm channel, stripping off DNA binding proteins as it goes.

By combining single molecule biophysics with microfabrication and technology we will develop a model system to mechanically pull individual biopolymers through artificial nanopores. This system applies the same local shearing forces applied by molecular machines. We will answer questions such as: how do biopolymers respond to local application of mechanical forces? What forces are required to shear bound proteins from DNA? What are the kinetics of mechanical shearing by small apertures? These are fundamental biological questions inaccessible to any other experimental technique.

Systems Analysis of Cellular Energy Metabolism Elucidates Mitochondrial Roles In Health And Disease

Trainee Thuy Vo
Primary Sponsor Bernhard Palsson
Co-sponsor W. N. Paul Lee
Mentor
Campus UC San Diego

BACKGROUND: In 1951, Leigh syndrome (LS) was first described as subacute necrotizing encephalomyelopathy in an infant. LS is now often characterized with inborn errors affecting mitochondrial energy metabolism and mutations have been identified in respiratory chain complexes and the pyruvate dehydrogenase complex (PDHC). The disease shows considerable variability in onset time, clinical signs, symptoms, and course, and therefore no single assay has proved to be a reliable method of diagnosis. The considerable variations in results of present clinical tests suggest that the present methods of diagnosis and analysis are insufficient in distinguishing the different causes of LS.

MOTIVATION: Techniques for characterizing cellular defects at higher resolution and details are necessary before appropriate treatments can be developed. A more comprehensive metabolic profile of Leigh affected cells is likely to provide a better understanding on the cellular responses to the mutations, thereby elucidating the affected enzymes or energetic processes in LS patients. **METHODS:** Control and LS affected fibroblasts (obtained from patient) were grown in DMEM media containing ¹³C labeled glucose. Amino acids from media and proteins as well as lactate were analyzed with GC-MS to identify their label distributions.

A computational model of human fibroblast with emphasis on mitochondrial energy metabolism was developed to compute intracellular reaction fluxes based on measured substrate uptake and secretion rates as well as label data. **RESULTS:** /i/) LS-affected cells have slower metabolism than control fibroblasts evidenced by their overall slower substrate utilization and lower secretion of end products; /ii)/ Intracellular fluxes predicted by the models, some of which validated with biochemical assays published in the literature, showed that the respiratory chain in LS-affected cells can produce ATP at a similar rate as the controls, but at a much more restricted flux range; and /iii) /Mutations leading to the defects observed in the Leigh's cells are likely to be in complexes I-IV, particularly complex II. **CONCLUSIONS:** Tracer analysis using a modeling framework can elucidate substrate utilization, energy production, and deficiency in enzymes associated with a metabolic disease. The identification of affected complex(es) has implications not only in disease diagnosis and characterization but also in treatment consideration as options for treating deficiency in PDHC and ATP synthase are different from that for complexes I-IV.

A Novel System to Quantitatively Analyze Cause-Effect Relationships in Cellular Pathogenesis

Trainee	Siddhartha Mitra,
Primary Sponsor	Steven Finkbeiner
Co-sponsor	Mark Segal
Mentor	
Campus	UC San Francisco

S Mitra^{1,2*}; M Arrasate¹; S Finkbeiner^{1,3,4}

1. Gladstone Inst of Neurological Dis, San Francisco, CA, USA
2. Medical Scientist Training Program,
3. Dept of Neurol.,
4. Dept of Physiology, UCSF, San Francisco, CA, USA

Determining cause-and-effect relationships between biological events is critical for understanding the molecular basis of cellular homeostasis and in elucidating mechanisms of cellular pathogenesis. Unfortunately, many biological processes may begin stochastically, progress slowly, and affect only a subpopulation of cells that may be hard to isolate and measure. For example, Huntington's disease is initiated by a widely-expressed mutant protein that elicits time-dependent, cell-selective neurodegeneration. To increase the spatial and temporal resolution in the measurement of cellular pathogenesis, we developed a high-throughput robotic imaging and analysis system that enables us to follow the fates of individual cells and intracellular proteins over time. Previously, we have used this system to elucidate the relationship between the formation of intracellular deposits of mutant protein, called inclusion bodies, and neurodegeneration in a neuronal model of Huntington's disease. Here, we apply our system to determine if impairment of cellular protein degradation through the ubiquitin-proteasome pathway contributes to the pathogenesis of Huntington's disease. We repeatedly measure mutant protein expression, inclusion body formation, proteasome function, and survival of individual neurons over time. By applying survival analysis to these measurements, we quantify the beneficial or detrimental effects of early cellular changes in the context of Huntington's disease and employ our novel system to identify critical steps in disease pathogenesis.

Nanobiosensor Based on One-Dimensional Nanostructures

Trainee	Mangesh Bangar
Primary Sponsor	Nosang Myung
Co-sponsor	Ashok Mulchandani
Mentor	Wilfred Chen
Campus	UC Riverside

M. A. Bangar^{*}, B.-Y., Yoo, W. Chen, A. Mulchandani, and N.V. Myung

Department of Chemical and Environmental Engineering and
Center for Nanoscale Science and Engineering
University of California, Riverside

Abstract:

The sensor technology is moving towards simultaneous detection of multiple analytes. Due to their high sensitivity and selectivity, biosensors are very attractive for such sensing applications. Many of the available biosensors are based on ligand-receptor protein binding reactions that require arduous and time consuming labeling of either the sensor or the analyte. On the other hand, sensors based on electrical detection offer direct, real-time, rapid and label-free sensing. The signal and the sensitivity of these sensors can be further improved by the use of one-dimensional nano-structures like nanowires. Unlike conventional two-dimensional thin films, charge depletion/addition area covers almost the entire cross-section of the one-dimensional nano-structure leading to improved sensitivity.

Most of the current nano-sensors require tedious and time consuming post synthesis processing, alignment and positioning of the nanostructures. To address these issues, two different techniques (i.e. in-situ fabrication¹⁻³ and magnetic alignment of template-fabricated nanowires⁴) have been developed by our group.

Previously, using in-situ fabrication we showed electrochemical growth and confinement of conducting polymer nanowire within a lithographically written nanochannel between gold electrodes in individual and array configurations.^{1,2} By simple addition of biomolecules in the monomer solution, biomolecule entrapment in the conducting polymer nanowire was also achieved.³ Thus, ready to use sensor was fabricated in one single step of electropolymerization avoiding any post synthesis processing or alignment of nanowires.

Alternatively, prefabricated segmented nanowires with conducting polymer and ferromagnetic metal (Nickel) segments were electrochemically fabricated using highly porous anodized alumina templates. Length of each nanowire segment was controlled by controlling the electrodeposition parameters. Followed by, magnetic alignment and positioning of nanowires on prefabricated contact electrodes in the presence of external magnetic field. Due to the magnetic interactions between ferromagnetic nanowire segment and the ferromagnetic contact electrodes, direction and positioning of nanowire alignment can be precisely controlled. By controlling the number of nanowires during the alignment step, single nanowires could be assembled on contact electrodes for individual addressability.⁴ This simple and cost effective method allows high-density nanowire array assembly. Using this technique we could characterize the electrical properties of these novel multi-segmented nanowires.

In short, electrochemical pathway is very simple and cost effective way of fabricating and bio-functionalizing one-dimensional conducting polymer structures. Using carefully designed contact electrodes and electrochemically driven or magnetic assembly techniques, these nanostructures can be assembled into an active device for sensing.

Trehalose Preservation of Model Cell Membranes Investigated At the Nanometer-Scale

Trainee	Sandra Bennum Serrano
Primary Sponsor	Roland Faller
Co-sponsor	Margie Longo
Mentors	Fern Tablin
Campus	UC Davis

Biological membranes depend on the presence of water to maintain their structure and functionality. However dried state preservation is a natural process for which many organisms survive complete dehydration conditions, this capability of reassuming life is mainly related to the production of disaccharides in response to the stress resulting for the lost of water.

Interest in this area has grown and mostly focuses in understanding the role of the sugar trehalose in dried preservation of food, pharmaceuticals and cells. For instance, experimental evidence suggests that trehalose can extend the shelf-life of blood platelets for long-term storage, avoiding their destruction after 3-5 days due to bacterial contamination. Moreover, it was suggested that the fundamental mechanism involves changes in the phase behavior of lipids in membranes. A complete understanding of the effect of trehalose on lipid membrane systems at the nano-scale length is lacking. The goal of this project is to understand the mechanism of action of trehalose by determining if and how trehalose acts to preserve the sub-micron structure in dry and rehydrated model membranes. We are applying a concerted effort of molecular simulations of lipid bilayers and experiments on synthetic lipid membranes and real blood cells.

In order to accomplish the goal of this project, a two component lipid mixture of DLPC and DSPC lipids is studied as model system for understanding the influence of trehalose on phase separation and microdomain structure of dry membranes.

Experimentally preliminary results using fluorescent techniques shed light on lipid mobility and the microstructure of hydrated, dried and dehydrated DLPC/DSPC model membranes in the presence and absence of trehalose. These experiments allowed to study the ability of trehalose to preserve the integrity of dried supported bilayers, but more importantly they provided insight into the effects of trehalose on DSPC domain microstructure under “equilibrium “ (slow thermal cooling) domain conditions.

Initial simulations using a coarse-grained model at different DLPC-DSPC concentrations and temperatures were performed to study domain formation and structure in mixed bilayers. A phase diagram of DLPC-DSPC is being reproduced by obtaining lipid transition temperatures, determined by the area per lipid head group and the deuterium order parameter, these transition temperatures show a semiquantitative agreement with experimental values. In phase separated systems the dynamic heterogeneity is characterized and will be correlated with the static heterogeneity.

Single-molecule studies of protein folding dynamics

Trainee	Jesse W. Dill
Primary Sponsor	Susan Marqusee
Co-sponsor	Carlos Bustamante
Mentors	
Campus	UC Berkeley

We are interested in using a new tool for direct manipulation of single molecules, optical tweezers, to explore the protein folding process. Proteins are the main working agents within a cell: synthesized as a single strand of amino acids, which folds into a much more compact structure, their function is determined by both their shape and composition. Traditional measurements in solution use high temperature or harsh chemicals to destabilize proteins and probe their folding behavior. These experiments, though powerful, suffer from the limitation that the molecules observed number in the quadrillions, obscuring many intriguing but infrequent variations.

With optical tweezers, we can directly apply force to a single protein molecule and monitor its behavior. The applied force destabilizes the protein, which eventually unfolds into an extended, structure-free strand. Relaxing the force allows the protein to refold; repeating this process yields several interesting parameters. For example, comparing the forces required to unfold a protein's different sub-domains will demonstrate their various contributions to its overall stability. Novel statistical mechanical techniques can also be used to extract the net energy required to unfold the protein; with these tools in hand, we plan to illustrate the role of mechanical stability in protein folding.

Mechanisms of Lipid Spreading at Hydrophilic and Hydrophobic Surfaces

Trainee	Babak Sanii
Primary Sponsor	Atul Parikh
Co-sponsor	John Rutledge
Mentors	Thomas R. Huser
Campus	UC Davis

The hydration of phospholipids on hydrophobically patterned substrates induces the spreading of fluid mono- and bilayers on high- and low-energy surfaces respectively. Both films grow with time as the square-root of time although the monolayer grows ~ 2.7 x faster than the bilayer. We account for this kinetic disparity in terms of differences in the energetics of spreading and the pervasive role of inter-leaflet drag in bilayer spreading. A novel application of a fluorescence photobleaching technique furnishes experimental evidence indicating that concomitant sliding and rolling motions occur during bilayer spreading. Spontaneous phospholipid spreading plays a roll in biological membrane fusion and cell mobility, and furnishes a powerful experimental platform to investigate two dimensional compositional mixing and interaction

Light Microscope for Sub-Diffraction Nanoscale Bio-Imaging

Trainee	Margaret Chiang
Primary Sponsor	Jia-Ming Liu
Co-sponsor	Enrico Stefani
Mentors	
Campus	UC Los Angeles

In the post-genomic era, the next challenge is nanoscale imaging. Technological advances are setting the stage as more molecular tools are becoming available. However, the main obstacle is the resolution of the light microscope, which is limited by diffraction to ~ 200 nm lateral and ~ 500 nm axial. Breaking the diffraction limit will usher in a new wave of important scientific investigations on subcellular biological complexes. We propose to create a microscope (4Pi-Stimulated Emission Depletion, 4Pi-STED) with a 3-D resolution (x, y and z directions) of 10-20 nm to determine the nature of biological complexes. Because this type of microscope is nonexistent in the U.S., the success of this project will mark a major breakthrough in nanoscale bio-imaging and its medical applications. The nominated student, Margaret C. Chiang, will carry out this project as her Ph.D. thesis research under Professor Jia-Ming Liu from UCLA's Electrical Engineering Department with the joint mentorship of Professor Enrico Stefani from the Division of Molecular Medicine in UCLA's Department of Anesthesiology. This project is feasible due to the non-overlapping, but complementary, expertise of Professor Stefani in molecular studies and confocal microscopy and of Professor Liu in nonlinear optics and ultrafast laser technology.

Optimized Protein Detection and Molecular Imaging with the Xenon Biosensor

Trainee Tom Lowery
Primary Sponsor David Wemmer
Co-sponsor Fanqing Chen
Mentors
Campus UC Berkeley

T. J. Lowery*, L. Schröder, C. Hilty, J. L. Mynar, J. M. J. Fréchet, A. Pines, and D. E. Wemmer

Department of Chemistry, University of California, Berkeley, and Lawrence Berkeley National Laboratory

We are developing a new type of magnetic resonance (MR) contrast agent for detecting and imaging biomolecular analytes in opaque samples using hyperpolarized xenon biosensors. Xenon biosensors consist of a xenon-binding cryptophane-A cage that has been functionalized with a targeting moiety. We have generated the first images of the xenon biosensor using an agarose-immobilized xenon biosensor phantom.¹ Because higher sensitivity is required for *in vivo* molecular imaging, we have worked on two means of amplifying xenon biosensor signal. The first consists of increasing the number of xenon biosensor cages per target via non-covalent supramolecular assembly using dendrimers. This method leads to a 8x gain in sensitivity.² The second means of signal amplification we have developed, called HYPER-CEST, involves detecting the xenon biosensor signal indirectly via the reservoir of solution-dissolved xenon. HYPER-CEST works by taking two images of the solution-dissolved xenon, one with and one without selectively depolarizing xenon atoms that cycle through biosensor cages. The difference between these two is an image with signal specific for the distribution of xenon biosensor molecules within the sample. This method improves sensitivity by over 1000x and makes possible xenon biosensor detection at levels practical for *in vivo* molecular imaging.³

References

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2. Mynar, JL; Lowery, TJ; Wemmer, DE; Pines, A; Fréchet, JMJ. Xenon Biosensor Amplification via Dendrimer-Cage Supramolecular Constructs. *J. Amer. Chem. Soc.* 2006, 128: 6334-6335.
3. Schröder, L; Lowery, TJ; Hilty, C; Wemmer, DE; Pines, A. Molecular Imaging using a Targeted Magnetic Resonance Hyperpolarized Biosensor. *Science* 2006 in press.

Integrated Bio-photonic Waveguide Devices for Optical Studies of Single Biomolecules

Trainee	Dongliang Yin
Primary Sponsor	Holger Schmidt
Co-sponsor	David Deamer
Mentor	
Campus	UC Santa Cruz

Dongliang Yin^{1*}, John Barber², Aaron Hawkins² and Holger Schmidt¹

¹Department of Electrical Engineering, University of California Santa Cruz

²ECE Department, Brigham Young University

Single molecule fluorescence spectroscopy provides a powerful tool to investigate structure and conformational dynamics¹ of biological systems down to the molecular level. It can be applied to numerous problems and applications, including flow cytometry, protein folding, ribosome dynamics, and DNA sequencing. So far, many single molecule studies of using fluorescence technique are based on confocal and sensitive CCD microscopy². An alternative to bulk microscopy is using an integrated optical platform based on ARROW waveguides that we recently proposed³. Instead of capturing the signal in free space, the fluorescence was efficiently collected and optically guided in a specially designed waveguide channel over a couple centimeters. Additional integrated optical components can be added to provide further manipulation of the collected signal. Together with the other inherent advantages of integrated optics such as compact size, robustness, inexpensive fabrication, this low cost and small device is very attractive for fluorescence detection from single biomolecules.

Here, we present an integrated intersecting ARROW waveguide structure, in which ARROWs with liquid and solid core are interconnected with each other at 90 degrees. To perform the fluorescent experiment, analyte solution is pipeted into one of the two reservoirs on the surface and the excitation beam propagates in the solid core. Once the excitation beam hits the analyte at the intersection, the fluorescence signal will be generated and guided in the liquid core to the detector. This geometry results in excitation volumes on the order of femtoliters that is required for single molecule detection². The confinement of the light in the low-index core results from the surrounding dielectric multilayer structure. We demonstrate fluorescence detection from Alexa 647 dye molecules versus concentration in the liquid core excited by the pump beam propagating in the solid core. Single molecule sensitivity was achieved at the minimum concentration. Reducing the excitation volume and applying time resolved technique can further improve the signal to noise ratio. We will further apply this device to real biochemistry applications such as DNA sequencing and ribosome dynamics in the future.

Development of an Integrated Laser Microbeam/Microscope Platform for Time-critical Single Cell Analytics

Trainee Amy Hellman
Primary Sponsor Vasan Venugopalan
Co-sponsor
Mentor
Campus UC Irvine/UC San Diego

Amy N. Hellman^{1,3*}, Nancy Allbritton², Vasan Venugopalan¹

1. Department of Chemical Engineering & Materials Science, UC Irvine
2. Department of Physiology & Biophysics, UC Irvine
3. Department of Bioengineering, UC San Diego

Pulsed laser microbeams offer significant advantages for non-contact manipulation of cells, ranging from subtle perturbations such as transient cell membrane permeabilization (optoporation) to more disruptive processes such as cell lysis. Optoporation can be used to load cells with a wide variety of biomolecules on very short timescales (ms-sec), such as reporter molecules for enzyme activity. After loading, a short laser pulse can achieve cell lysis to analyze cellular reaction kinetics. To accomplish this most effectively, we must first study of the critical laser parameters (pulse duration and energy) governing the mechanisms of laser-cell interactions.

We have used time-resolved imaging to visualize the cell lysis and optoporation process generated by pulsed laser microbeams. The process dynamics of lysis of adherent cells were examined using 532 nm laser pulses with durations ranging from 180 ps to 6 ns and pulse energies corresponding to 1x, 2x, 3x, and 5x the threshold for plasma formation. The cell lysis process was imaged at times of 0.5 ns to 50 μ s after laser pulse delivery and revealed the processes of plasma formation, pressure wave propagation, and cavitation bubble dynamics. Cavitation bubble expansion was the primary agent of cell lysis and the spatial extent of cell lysis increased with pulse duration and pulse energy. Hydrodynamic analysis indicated that cells subject to transient shear stresses in excess of a critical value were lysed while cells exposed to lower shear stresses remained adherent and viable. Fluorescence assays were used to correlate the physical effects with the subsequent biological response, and cell viability and transient membrane permeabilization are assessed.

High-Throughput Screening for Compounds that Regulate β -cell Proliferation and Differentiated Function

Trainee	Alice Kiselyuk
Primary Sponsor	Fred Levine
Co-sponsor	Shankar Subramaniam
Mentor	Mark Mercola
Campus	UC San Diego

Knowledge from diverse fields, including cell biology and chemical genomics, will be applied to the problem of beta-cell replacement therapy for diabetes. Beta-cells, which secrete insulin in response to blood sugar level, are absent or functionally deficient in diabetics. Increasing the number of beta-cells by promoting them to divide, either in the patient or in culture, could remedy this problem. We will investigate the mechanisms that control beta-cell replication using high-throughput screening technology to discover small molecules that induce beta-cells to proliferate. This technology, the same as that used by pharmaceutical companies to find new drugs, is available in the Burnham Institute Screening Center, led by Dr. Mercola. Thousands of compounds will be tested for their ability to affect beta-cell replication in a human beta-cell line developed in Dr. Levine's laboratory. Positive compounds will be selected using a sophisticated image analysis process developed by Dr. Jeff Price. A large dataset of the effect of the compounds on the proteins and genes in the cell line will be inputted into algorithms developed by Dr. Subramaniam to create a model of the signaling pathways controlling pancreatic beta-cell replication. Compounds discovered from this research may serve as the basis for new diabetes treatments.

Locus-specific CHIP-MS: An Innovative New Technology for Studying Epigenetic Gene Regulation During Stem Cell Differentiation

Trainee	Ryan Jason Schmidt
Primary Sponsor	Yi Eve Sun
Co-sponsor	Joseph Loo
Mentor	Michael Carey
Campus	UC Los Angeles

The action of turning genes on and off is performed by the interaction of a large number of proteins at regulatory sequences contained in our DNA. In order to fully understand how these molecular switches control our genes, we must identify the components of the protein machineries that bind them. Current techniques for doing so are limited because they ask the question from the perspective of the individual proteins (where do I bind?) rather than from the perspective of the regulatory sequence (what binds to me?). Thus, we propose to reverse this paradigm by developing a new technology that will allow us to take a molecular snapshot of the proteins present at a regulatory sequence at a given time. In this way, we can identify all of the proteins that cooperate to control a gene, including those that have not been previously identified. In conclusion, our new technology will greatly advance our understanding of one of the most fundamental processes in biology by focusing on the forest rather than a single tree at gene regulatory sequences.

Controlling Neural Stem Cell Behavior with Synthetic Hydrogels

Trainee Krishanu Saha
Primary Sponsor David Schaffer
Co-sponsor John Ngai
Mentor Kevin Healy
Campus UC Los Angeles

Krishanu Saha^{*1}, David V. Schaffer^{1,4}, and Kevin E. Healy^{2,3}

¹Departments of Chemical Engineering, ²Bioengineering, and ³Materials Science and
⁴The Helen Wills Neuroscience Institute
University of California at Berkeley

Highly-regulated signals surrounding stem cells, such as growth factor concentrations and matrix mechanical stiffness, have been implicated in modulating stem cell proliferation and maturation¹. However, tight control of proliferation and lineage commitment signals is rarely achieved during growth outside the body, since the spectrum of biochemical and mechanical signals that govern stem cell renewal and maturation are not fully understood^{2,3}. Therefore, stem cell control can potentially be enhanced through the development of material platforms that more precisely orchestrate the presentation of the aforementioned signals to stem cells. Using a biomimetic interfacial polymer hydrogel, we define a robust synthetic and fully mechanically and chemically defined platform to regulate stem cell number and differentiation for the culture of adult neural stem cells. This platform is highly tunable in manipulating cell-matrix molecular interactions and could potentially be used to translate *in vitro* control of stem cells to an *in vivo* implantable biomaterial that can be harnessed for tissue regeneration.

1. Fuchs, E., Tumber, T. & Guasch, G. Socializing with the Neighbors: Stem Cells and Their Niche. *Cell* 116, 769-778 (2004).
2. O'Neill, A. & Schaffer, D. V. The biology and engineering of stem cell control. *Biotechnol Appl Biochem* (2004).
3. Svendsen, C. N. & Langston, J. W. Stem cells for Parkinson disease and ALS: replacement or protection? *Nat Med* 10, 224-5 (2004).

Linear Dendritic Block Copolymers for Nerve Tissue Engineering

Trainee	Jennifer Cash
Primary Sponsor	Timothy Patten
Co-sponsor	Kristi Anseth
Mentor	
Campus	UC Davis

Cell based therapies offer much promise for the treatment of nervous system diseases and conditions that require tissue regeneration, such as Parkinson's disease or spinal chord injuries. The direct delivery of cells to the target site is less than optimal, because few cells survive over the long term. Typically, delivering the cells in a polymer gel material offers better results, because the gel can be decorated with important biochemical molecules that signal the cells to attach, proliferate and develop into mature tissue. For nerve tissue culture the gel material must be porous to provide sufficient room for the nerve cells to extend processes and make contacts with other cells. In this work, we will prepare polymeric molecules that can self-assemble into the desired porous gel structures. Biochemical molecules will be attached to the polymers, so that the cells will receive biochemical cues to grow and differentiate. When completed, the project will generate a new approach to tissue engineering and potentially a therapy for treating nervous system diseases and conditions that require tissue regeneration. The student working on this project will work between groups that have expertise in synthesizing polymers and gel materials and in biological engineering and tissue culture.

An Interdisciplinary Approach: Zinc and Halogens in the Jaws of a Marine Worm

Trainee	Rashda Khan
Primary Sponsor	Galen Stucky
Co-sponsor	J. Herbert Waite
Mentor	
Campus	UC Santa Barbara

**Rashda K. Khan^{1*}, Peter K. Stoimenov¹, Henrik Birkedal⁴, Chris C. Broomell²,
J. Herbert Waite^{1,2} and Galen D. Stucky^{1,3}**

*Presenting Author, ¹Department of Chemistry and Biochemistry, ²Department of Molecular, Cellular and Developmental Biology, ³Materials Department, University of California, Santa Barbara; ⁴Department of Chemistry, University of Aarhus, Denmark

The polychaete worm, *Nereis virens* (commonly known as a clamworm), is omnivorous and hunts for prey in sediment, algal mats and macrofouling ensembles such as mussel beds. The jaws are exposed as the proboscis is everted which happens whenever the worm attacks or burrows by crack propagation. Given the novelty of their chemistry, their hard, lightweight and wear-resistant properties, *Nereis* jaws merit a serious multidisciplinary investigation. We have used a wide range of experimental techniques in various disciplines (surface chemistry, biochemistry and materials science) to elucidate, structure, composition and function. The jaw bulk is observed to be fibrous in nature with SEM (Scanning Electron Microscopy). Compositionally the jaws are primarily organic polymers: proteins reinforced by metal ions (Zn^{+2}) and halogens (Cl, Br and I). XPS (X-ray Photoelectron Spectroscopy) has confirmed that Zn, I, and Br in the jaws have single chemical valence states and chlorine is present in two chemical bonding environments. Halogens are observed to vary in surface depth according to location in the jaw with SIMS (Secondary Ion Mass Spectrometry) and the halogens modify aromatic protein functionalities. Acid hydrolysates of the whole jaw have revealed a variety of post-translationally modified amino acids including halogenated histidine, tyrosine and cross-linked tyrosines. Several of these have been characterized for the first time, including dibromohistidine, bromiodohistidine, bromiodotyrosine, mono-chlorodityrosine, mono-chlorotryrosine and dibromotryrosine. Furthermore, nanoindentation of the biological material shows a correlation between hardness and Zn. Research into structure-function relationships of polychaete jaws enables biomimetics in revealing novel designs for robust lightweight materials.

Developing a 3D Tissue Culture Platform: Cardiac Regeneration

Trainee	Karen Wei
Primary Sponsor	Andrew McCulloch
Co-sponsor	Mark Mercola
Mentor	Wayne Giles and Randall Johnson
Campus	UC San Diego

Adult heart cells are too fragile to transplant, but immature, fetal cardiomyocytes grafted into injured animal heart muscle improves heart function and minimizes long-term disease. To extend these studies to humans will require a renewable source of human heart muscle cells and improvement in the technology to ensure the incorporation of cardiomyocytes into the damaged heart. Specifically, we propose to create a three-dimensional (3D), in-vitro model of cardiac tissue, using human embryonic stem cells, to identify the physical factors that regulate myocyte maturation and the phenotype of cardiac muscle. To study the integration and function of replacement heart muscle cells in as natural an in-vitro environment as possible, we will culture the engineered tissue under mechanical strain using a novel culture platform. We will use this system to characterize cellular interactions and metabolic conditions that are needed for cardiomyocyte maturation and the creation of a robust muscle tissue. Exploring these inputs will lay the foundation for new therapies and drug discovery techniques. This work will be conducted under the guidance of Drs. McCulloch and Mercola, leaders in their respective fields of cardiac biomechanics and tissue engineering and cardiac stem cell biology.

Bioengineering Synovial Fluid and Diarthroidal Joints: A Platform for Biotechnology and Biomaterial Therapies

Trainee Megan Blewis
Primary Sponsor Robert Sah
Co-sponsor William D. Bugbee, M.D.
Campus UC San Diego

*Megan E Blewis, MS¹, Brian J Lao¹, Gayle E Nugent-Derfus, PhD¹, Tannin A Schmidt, PhD¹, Jennifer M Antonacci, BS¹, Barbara L Schumacher, BS¹, William D Bugbee, MD², Gary S Firestein, MD³, Robert L Sah, MD, ScD¹

Departments of Bioengineering¹, Orthopedic Surgery², and Medicine³
University of California, San Diego

The synovial fluid (SF) of diarthroidal human joints normally functions as a biomechanical lubricant. SF provides articulating cartilage with low-friction and low-wear properties through the combined contributions of putative lubricant molecules proteoglycan 4 (PRG4), hyaluronan (HA), and surface active phospholipids (SAPL). These lubricants are secreted by cells in tissues lining joints, including chondrocytes in articular cartilage and synoviocytes in synovium. Lubrication failure may contribute to erosion of cartilage in arthritis after acute injury and to graft failure in biomaterial and tissue engineering treatments of cartilage defects. However, the environment of the living joint is complex, with a variety of chemical and mechanical regulatory mechanisms modulating chondrocyte and synoviocyte secretion of lubricants into SF. Thus, there is a need for a technology platform to analyze lubricant regulation and function in whole joints. The overall aim of this proposal is to develop a joint scale bioreactor for knee joints, and to establish this as a new biotechnology platform. The specific aims are to: (1) establish an integrative model of how chemical and mechanical factors coordinately regulate joint components to generate SF that is effective in lubrication, (2) bioengineer the SF component of the joint, relating its composition and SF-like lubrication function, and (3) test the consequences of altered lubrication on selected rehabilitation, biomaterial, and tissue engineering therapies for restoration of lubricated joint function.

Aim 1. A framework was established for bioengineering SF through development of an integrative theoretical model to describe essential features of steady-state and kinetic SF lubricant composition in normal and injured whole joints. A quantitative inter-compartmental model was developed to predict *in vivo* SF lubricant concentration in normal and injured joints. Applied to human knee joints, the model predicted steady-state lubricant concentrations that were within physiologically observed ranges, and that were markedly altered with chemical regulation. The model also predicted that PRG4 and HA have distinct kinetics associated with perturbations due to disease or therapeutic injections.

Aim 2. Next, biomimetic methods were developed to bioengineer a SF-like liquid lubricant. Chondrocyte conditioned culture medium was concentrated to achieve a PRG4 concentration equivalent to that of normal SF. This solution was spiked with HA, normally contributed by synoviocytes, to achieve a physiological concentration. This bioengineered liquid lubricant was assessed for lubrication functionality with a cartilage-on-cartilage friction test. It exhibited a boundary-mode friction coefficient markedly lower than that of the PBS control, approaching that of normal SF. Considering the model features and predictions, these methods should be translatable to a bioreactor, to generate within it a SF-like liquid lubricant.

A novel bioreactor platform for whole-joints, capable of developing a functional SF and providing physiological motion and manipulation of the fluid environment, will allow studies on therapies that attempt to restore joint lubrication after acute injury or treat cartilage defects. The bioreactor system may also be applied to create whole biological joints for functional joint restoration.

Company Affiliates

Agilent Technologies. Agilent technologies strives to be the world's premier measurement company. The company operates two primary businesses—electronic measurement, and life sciences and chemical analysis—supported by Agilent Labs, a central research group. Agilent Labs focuses on longer-range, multidisciplinary, high-risk research to ensure leadership in Agilent's existing businesses and to provide technology foundations for new measurement tools. Areas of bio-analytical research include chemical and environmental measurements; separations, such as chromatography and capillary electrophoresis; microfluidics; inorganic and organic spectroscopy; proteomics and genomics reagents, systems biology and software tools, and molecular diagnostics for personalized medicine. As an example of Agilent's engineering expertise applied to biological problems, I will discuss Agilent's microarray printing technology and the application of microarrays to a new research area: microRNA measurement. miRNA research is growing in importance, but accurately measuring miRNAs presents a number of unique challenges.

Brian Peter of Agilent Technologies

Applied Biosystem's Advanced Research Group. Applied Biosystems has demonstrated its position as a technology leader and driving force in the changing dynamics of the life science marketplace. The Applied Biosystems business is focused on the following markets: basic research, commercial research (pharmaceutical and biotechnology) and standardized testing, including forensic human identification, paternity testing and food testing. The company has an installed base of approximately 180,000 instrument systems in nearly 100 countries.

Basic research includes work at university, government and other non-profit institutions that focus on uncovering the basic laws of nature and understanding human disease. Pharmaceutical and biotechnology companies use Applied Biosystems' products to discover and develop new drugs more effectively. Standardized testing customers require systems that produce precise results from a high volume of automated tests.

Ken Livak, Divisional VP of ABI

Pioneering Projects at Applied Biosystems: Next Generation Sequencing as an Example

Berlex. A specialty pharmaceutical company whose history reaches back more than 130 years. Berlex's singular approach to developing and making specialized medicines already has yielded innovations in treating multiple sclerosis, female health concerns, cancer and in the creation of new diagnostic imaging techniques. Berlex's research mission is to be a world leader in innovative drug discovery and development with centers of excellence in cardiovascular, cancer and immuno-based diseases by combining the best of biotechnology and pharmaceutical technologies.

David Light of Berlex

Discovery of Functional Antibodies of Therapeutic Applications

Intelligent Optical Systems, Inc. (IOS) An R&D company developing cutting-edge technologies in optical sensing and instrumentation. IOS drives innovative technologies through the development cycle all the way to fully-functioning, independent spin-off companies that focus on physical, chemical, remote sensing, and biological sensing instrumentation, in key markets segments such as homeland security, biotechnology, medical, aerospace, environmental, and industrial control.

Glenn Bastiaans of Intelligent Optical Systems, Inc.

MediaCybernetics. Media Cybernetics helps individuals and organizations extract and mine knowledge from images through world-renowned software for image capture, processing, analysis, display, and management. Their products simplify and enhance image-based data collection and analysis for those who wish to increase accuracy and automate research, development, and quality processes.

Will Casavan of MediaCybernetics

Genzymes. Genzyme's leadership in surgical biomaterials traces its roots back almost to the company's founding. Since 1984, Genzyme has been a leader in the high-quality production of sodium hyaluronate, or HA, a naturally occurring biopolymer that is used in many medical indications. Over the years, Genzyme has pioneered the development and commercialization of HA-based medical products. Genzyme Biosurgery now brings a suite of HA-based products to the market, including Synvisc® (hylan G-F 20), for pain due to osteoarthritis of the knee, and the Septra™ family of products, for improving the outcome of surgery by reducing the incidence of adhesions. Genzyme Biosurgery product development efforts are focused on developing new applications and next-generation versions of Synvisc.

Michael A DiMicco of Genzyme Preclinical Orthopaedics

GREAT Participants

Campus Year	Trainee	email address	Primary and CoSponsor or Mentor	email address	GREAT Project Title
UC Berkeley					
2005	Jeffrey Vieregg	jvieregg@berkeley.edu	Ignacio Tinoco Carlos Bustamante	INTinoco@lbl.gov carlos@alice.berkeley.edu	Measuring Thermodynamics and Kinetics of RNA Folding. One Molecule at a Time
2005	Krishanu Saha	saha@berkeley.edu	David Schaffer John Ngai Kevin Healy	schaffer@berkeley.edu jngai@socrates.berkeley.edu kehealy@berkeley.edu	Engineering Synthetic, Injectable Scaffolds For Stem Cell Control
2005	Thomas Lowery	tjlowery@lbl.gov	David E. Wemmer Fangqing Chen	dewemmer@lbl.gov f_chen@lbl.gov	Developing the Magnetic Resonance Xenon Biosensor for in situ Biomolecular Assays and Imaging
2006	Jesse Dill	jessedill@berkeley.edu	Susan Marqusee Carlos Bustamante	marqusee@berkeley.edu carlos@alice.berkeley.edu	Single-molecule studies of protein folding dynamics
2006	Eliane Trepangier	eht@berkeley.edu	Jan Liphardt Lydia Sohn	liphardt@physics.berkeley.edu sohn@me.berkeley.edu	A model system to study the translocation of single biopolymers through pores and cavities in biological molecular machines
UC Davis					
2005	Sandra Bennun Serrano	sbennun@ucdavis.edu	Roland Faller Margie Longo	rfaller@ucdavis.edu mllongo@ucdavis.edu	Trehalose Preservation of Model Cell Membranes Investigated at the Nanometer-Scale: Experiment and Simulation
2006	Roy Wollman	rwollman@ucdavis.edu	Jonathan Scholey Alex Mogilner	jmscholey@ucdavis.edu mogilner@math.ucdavis.edu	A system level analysis of the mitotic machinery
2006	Jennifer Cash	incash@ucdavis.edu	Tim Patten Kristi Anseth	patten@chem.ucdavis.edu kristi.anseth@colorado.edu	Linear-Dendritic Polymers as Scaffolds for Nerve Tissue Engineering
2006	Babak Sanii	bsanii@ucdavis.edu	Atul Parikh John Rutledge	anparikh@ucdavis.edu jcrutledge@ucdavis.edu	Using Mechanical Curvature to Promote

Campus	Year	Trainee	email address	Primary and CoSponsor or Mentor	email address	GREAT Project Title
UC Irvine						
2006	Amy Hellman	ahellman@uci.edu	Vasan Venugopalan Nancy Allbritton	wvenugop@uci.edu niallbri@uci.edu	Development of a Laser Microbeam/Microscope Platform for Rapid Single Cell Bioanalysis	
UCLA						
2005	Fulai Jin	fjin@mednet.ucla.edu	Jing Huang James Liao Paul Predki (Invitrogen)	jinghuang@mednet.ucla.edu liao@ucla.edu Paul.Predki@invitrogen.com	A Novel Strategy for Efficient Protein Interactome Mapping	
2006	Margaret Chiang	marge@ucla.edu	Jia-Ming Liu Enrico Stefani	liu@ee.ucla.edu estefani@ucla.edu	Light Microscope for Sub-Diffraction Nanoscale Bio-imaging	
2006	Ryan Schmidt	schmidtr@ucla.edu	Yi Eve Sun Joseph Loo	ysun@mednet.ucla.edu jloo@chem.ucla.edu	Locus-specific ChIP-MS: An Innovative New Technology for Studying Epigenetic Gene Regulation during Stem Cell Differentiation	
UC Riverside						
2005	Mangesh Bangar	mbangar@engr.ucr.edu	Nosang V. Myung Ashok Mulchandani	myung@engr.ucr.edu adani@engr.ucr.edu	Bio-Affinity Label-Free Sensing Using Bioreceptors Embedded Conducting Polymer Nanowires	

Campus Year	Trainee	email address	Primary and CoSponsor or Mentor	email address	GREAT Project Title
UC San Diego	2005	tvo@bioeng.ucsd.edu	Bernhard O. Palsson W.N. Paul Lee	bpalsson@bioeng.ucsd.edu lee@gcrc.rei.edu	Towards an in silico mitochondrion
	2006	akiselyu@ucsd.edu	Fred Levine Shankar Subramaniam	flevine@ucsd.edu shsubramaniam@ucsd.edu	High-Throughput Screening for Compounds that Regulate Beta-Cell Proliferation
	2006	kwei@ucsd.edu	Andrew McCulloch Mark Mercola	amcculloch@ucsd.edu mmercola@burnham.org	Designing a 3D Tissue Culture Platform
2006	Megan Blewis	mblewis@ucsd.edu	Robert Sah William Bugbee	rsah@ucsd.edu wbugbee@ucsd.edu	Bioengineering Joints: A Platform for Biotechnology and Biomaterial Therapies
UC San Francisco					
2005	Caleb Bashor	cbashor@gmail.com	Wendell A. Lim Adam Arkin	wlim@itsa.ucsf.edu aparkin@lbl.gov	Engineering Cellular Signal Processing: Introducing Synthetic Feedback Loops into Kinase Pathways
2005	Siddhartha Mitra	smitra@gladstone.ucsf.edu	Steven Finkbeiner Mark Segal	sfinkbeiner@gladstone.ucsf.edu mark@biostat.ucsf.edu	A novel system to quantitatively analyze cause-effect relationships in molecular and cellular pathogenesis
UC Santa Barbara					
2005	Rashda Khan	rkhan@chem.ucsb.edu	Galen D. Stucky J. Herbert Waite	stucky@chem.ucsb.edu waite@lifesci.ucsb.edu	The chemical and mechanical properties of the bio-halogenated coating of the Nereis jaws
UC Santa Cruz					
2005	Dongliang Yin	yindl@soe.ucsc.edu	Holger Schmidt David Deamer	hschmidt@soe.ucsc.edu deamer@soe.ucsc.edu	Integrated biophotonic waveguide devices for optical studies of single biomolecules