

A New Course on Robotics and Combinatorial Experimentation (CHE 562 Spring 2002)

IME Associate Director Scott L. Diamond, Ph.D. has developed a new course on Robotics and Combinatorial Experimentation (CHE 562) in the Spring Semester of 2002. Twenty-four students enrolled in this course, which provided an introduction to high throughput experimentation. Topics included robotic liquid handling, combinatorial chemistry, fluorescence spectroscopy, DNA and protein microarrays, microfluidics, and lab-on-a-chip. Guest speakers from Glaxo SmithKline and two plant trips complemented the lectures. A description of this course will be presented at the Bioinformatics Session at American Institute of Chemical Engineers (AIChE) in November 2002.

Fall 2002

IME

IME-Pathology Interdisciplinary Seed Grant in Alzheimer's Research

A one-year grant to support a Pilot project on interdisciplinary research related to Alzheimer's Disease at a level of up to \$20,000/year was awarded to Ari Borthakur, PhD of the Radiology department for studies of innovative MRI imaging modalities for Alzheimers Disease. The intent of this grant program is for pilot interdisciplinary research on the etiology, pathogenesis, diagnosis or management of dementia of the Alzheimer's type or related conditions. The purpose is to assist faculty in the Engineering, Imaging,

Physical, and Computational sciences to obtain preliminary data to serve as the basis of a grant application to the NIH or other public or private agencies concerned with this important medical and social problem. The Pilot grant, jointly funded by the IME and the department of Pathology and Laboratory Medicine, is administered through the Alzheimer's Disease Center at Penn (Dr. Virginia Lee) and is complementary to 2 additional Pilot grant opportunities through that Center directed to biomedical investigators.



News from the
IME

Institute for Medicine and Engineering

From the Director's Desk Dr. Peter F. Davies

The contents of this newsletter indicate another excellent year of research and training in the IME. Important scholarly publications in multiple fields have been accompanied by more than 20 patent filings since 1999 demonstrating the utility of the intellectual contributions. Some changes have also occurred this year, most happily the appointment of Drs Paul Janmey and Scott Diamond as IME Associate Directors (see box this page), the appointment of a permanent Dean of the Medical School, Arthur Rubenstein formerly Dean of Medicine at Mt Sinai and a 'giant' in Internal Medicine (see page), and the move of the Center for Bioinformatics, previously administratively parked in the IME, to the new Genomics Institute. Some trainees have moved on to begin great careers and new ones have arrived (see Comings and Goings). We bid bon voyage to Dr Michal Bental Roof, the IME Scientific Development Administrator, who will greatly be missed (see page 2). As the seventh year of the Institute begins, we are planning a series of minisymposia to be held on campus that will enhance the cross fertilization of clinical and research departments in the Medical School and

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A gourmet feast of membrane biophysics one Disch-er at a time

Since arriving at Penn in 1996, IME Member Dennis Discher PhD, Associate Professor of Chemical and Biomolecular Engineering has pushed the frontiers of biophysical research using a variety of proven and innovative approaches to membrane physics, mechanics and molecular biology. A unifying theme in his studies is 'membranes'. Primary systems under investigation include: 'marker of self' proteins on natural membranes, membrane skeletons and their component mechanics, membrane adhesion (muscle adhesion & adhesion molecule extensibility), copolymer-based mimics of biomembranes such as "Polymersomes", physicochemical properties of the nucleus, and liquid crystal elastomers.

The cell biophysical questions of great interest in his lab are in the areas of cell membrane micromechanics and adhesion and relations to molecular structures and assemblies. One of the target systems is the muscle cell membrane where his group is focused on understanding in some detail the molecular basis of the devastating disease, muscular dystrophy. Dystrophin is a peripheral membrane cytoskeletal protein that anchors to adhesion receptors known as dystroglycans; these, in turn, associate with extracellular matrix laminin. Defects and deficiencies in any of these components are disastrous to muscle cells, and an understanding of the how and why of these mechanisms is of great importance. Discher's group has developed single cell manipulation approaches to address these issues.

A second system under intensive study is the erythrocyte, which consists most simply of a plasma membrane. This cell's membrane is highly elastic — for

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To add your name to the IME mailing list, please contact us by telephone, 215-573-6813, or send an email to ime@pobox.upenn.edu

Questions, comments about the Newsletter?
Contact Marvin Jackson

Upcoming IME Seminars

Unless indicated otherwise, IME Seminars are held Tuesdays, 12:00 noon (coffee at 11:45)
2nd floor conference room, Vagelos Research Labs, 3340 Smith Walk
For more information, please contact Marvin Jackson, 215-573-6813

Oct 22nd

Dawn Bonnell
Penn Center for Nanotechnology
"Multicomponent Nanostructures: Local Properties of Complex Systems"

Oct. 29th

Anna Huttenlocher
University of Minnesota
"Adhesive Regulation during Cell Migration".

Nov 5th

Steve Albelda
Penn Pulmonary Medicine Division
"Mechanisms of Action of PECAM-1 (CD-31)".

Nov 19th

Peter Lloyd Jones
University of Colorado
"The Multi-talented Nature of PAired-related Homeobox Genes in Vascular Development and Disease"

Dec 3rd

Skip Brass
Penn School of Medicine
"Signaling during the Late Events of Platelet Activation"

Dec 17th

David Butler
University of Cincinnati
"Functional Tissue Engineering for Soft Tissue Repair: A Cellular-Based Approach"

November 7th Minisymposium

with the Molecular Center for Liver and Digestive Diseases. A 4 hour Minisymposium sponsored by the IME and the Department of Medicine to explore imaging and tissue engineering opportunities related to liver and digestive diseases.

NBIB Deputy-Director Dean at IME January 7th

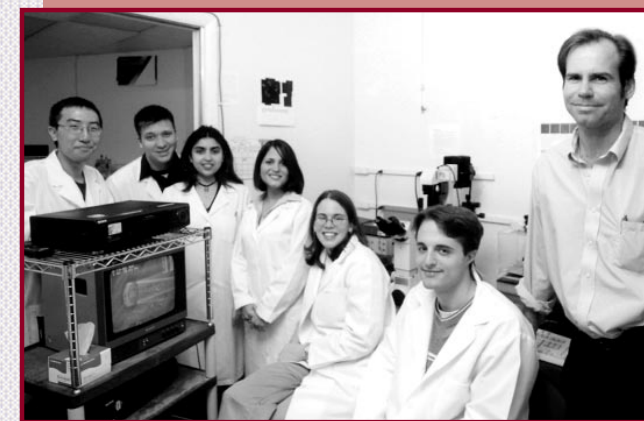
Dr Donna Dean, Deputy Director of the new National Institute of Biomedical Imaging and Bioengineering (NBIB) at the NIH will visit Penn to outline the institutes current status and future plans.

Cosponsored by the IME, and the Departments of Bioengineering and Radiology

IME Seminar Room Vagelos 2000 12:00 noon

Drs Diamond and Janmey appointed IME Associate Directors

It is a pleasure to announce the appointment of Paul A. Janmey PhD and Scott L. Diamond PhD as Associate Directors of the IME. Scott joined Penn from SUNY Buffalo in 1997 and is Professor of Chemical and Biomolecular Engineering at Penn. Paul joined the IME from Harvard Medical School in 1999; he is Professor of Physiology at Penn. Both are well known for their excellent science, great intellects, and constructive, collegial personalities. They will assume more formal administrative and advisory roles in the IME.



Dr Dennis Discher (extreme right) with several members of his research team. From left to right: Ansel Hsaio, Peter Photos, Fariyal Ahmed, Cindy Newman, Maureen Sheehan, and Adam Engler.



Educational Initiatives

New trainees appointed to the IME Cardiovascular Bioengineering training grant

The IME NIH training grant supports 8 trainees in interdisciplinary research for a 2 year period after which a new cohort of trainees are appointed. In September 2002, 4 new predocs and 2 postdocs became new trainees as part of the normal turnover of positions. They began their research in various labs of the IME, and the departments of Bioengineering, Pulmonary Medicine, Radiology, Neuroscience, and Chemical and Biomolecular Engineering. They are:

Continuing Postdocs: Tony Passerini PhD (Cardiovascular Genomics in Peter Davies' Lab) and Clinical Fellow David Kaufman MD (Molecular mechanisms of Pecam-1 and junctional proteins in stressed cells in the IME jointly with Steve Albelda's lab in Pulmonary Medicine).

New Postdocs: Shinghua Ding PhD (Ion channel investigations in brain vasculature, in Phil Haydon's lab in the department of Neuroscience), and Jocelyn Clark (Site-directed therapy, in Bob Levy's Lab at Childrens Hospital).

New Graduate Students: Nas Zahir (in Val Weaver's Lab, Pathology/IME), Julie Ji (in Scott Diamond's Lab, Chemical and Biomolecular Engineering/IME), Brian Avants (in Jim Gee's Lab, Radiology), and Penelope Georges (in Dr Janney's Lab, Physiology/IME)

New Medical School Dean and Executive VP of HUP appointed

Arthur H. Rubenstein, MBBCh, an accomplished physician, diabetes researcher and academic leader, was named Dean of the School of Medicine and Executive Vice President of the University of Pennsylvania for the Health System. Dr Rubenstein, who assumed the positions in September 2001 has already implemented a major Strategic Planning initiative for the Medical School.



Stanford gains IME's Michal Bental Roof PhD

In July we bid goodbye to Dr Roof who has served as IME Scientific Development Administrator since 1996 (and editor of this newsletter). Michal will join her husband, David Roof, who has relocated from Penn to the San Francisco area. Michal will join Stanford's Medical School administrative staff. We wish Michal and David well in their new positions and will be sure to visit (in the winter of course!)

CONTINUED FROM COVER....

From the Director's Desk

Engineering (and Physics) faculty. The first of these, jointly sponsored by the IME and the Center for Molecular Studies in Liver and Digestive Diseases (directed by Anil Rustgi MD), will be an exploration of imaging modalities and tissue engineering approaches applicable to research into these important clinical problems. The minisymposia are particularly aimed at new faculty with the intention of fostering interschool collaborations that will lead to new grants.

Which brings me to an issue that concerns all universities and Bioengineering departments in particular. The new NIH Institute of Biomedical Imaging and Bioengineering (acronym NIBIB) is growing steadily principally through the transfer of existing grants residing in other NIH institutes with approx one third of its allocated funding as 'new' money. While such growth is good, it is highly unlikely that the NIH budget will increase significantly in FY 2004; indeed all predictions are for zero growth above inflation. This is occurring after a 5-year period of spectacular bipartisan-approved appropriations that produced a doubling of the NIH budget. The looming slow-down will reduce the available funds for all applicants for NIH grants and comes at an awkward time for NBIB and particularly for Bioengineering. Why? Through the efforts of the Whitaker Foundation, there has been (and continues to be) a large increase in the number and size of Bioengineering programs in the US. Many new programs and departments have sprung up leading to fierce competition among new and old departments alike for young newly-trained faculty. Thus the expansion of BE is coincident with greatly increased competition for NIH funds. While this itself is a major challenge, it is further compounded by the Whitaker Foundation which will disperse its assets by 2006 including the ending of the Whitaker Investigator grants (last competition this year). These 3-4 year grants have served for many years as an excellent 'bridge' grant to launch the careers of new BE researchers who quickly become competitive for NIH funding. That role will need to be replaced by other mechanisms such as increased intramural support and industry contributions. Fortunately Penn remains highly attractive to the top echelon of students, trainees and faculty recruits interested in interdisciplinary careers; in this respect Institutes like the IME are critical.

(See box on back page about the Minisymposium on Liver and Digestive Diseases)

Peter and Geri Skirkanich Donate \$10 Million for Penn Bioengineering

University of Pennsylvania alumnus J. Peter Skirkanich and his wife Geri have pledged \$10 million to help finance a 58,400-square-foot bioengineering laboratory facility in the engineering school complex. The facility, to be located near the Penn School of Medicine, will house faculty, staff, students and researchers as part of the school's \$57 million bioengineering initiative. The gift accompanies a \$14 million five-year grant from the Whitaker Foundation to support programs and faculty in bioengineering. Seven new faculty will be added in the next five years in the core areas of injury bioengineering, neuroengineering, orthopedic bioengineering and cardiovascular bioengineering. At the same time, the number of bioengineering graduate students will nearly double from 18 to a target level of 35 a year.

Penn president Judith Rodin said the Skirkaniches' gift "is a vote of confidence in Penn's groundbreaking bio-engineering efforts. Close collaboration between the engineering and medical school faculty at the University of Pennsylvania provides a huge basis for these efforts. We are grateful to Pete and Geri for their generosity and their vision."

Penn Undergraduate Symposium on Simple Behavior in Complex Neural Systems, April 2002

The IME co-sponsored the "Penn Undergraduate Symposium on Simple Behavior in Complex Neural Systems" in April 18-19, 2002. The symposium, organized by IME member Dr. Philip Nelson and Dr. Vijay Balasubramanian, explored whether there are simple principles underlying the design of the brain. Speakers were Drs. Dmitri Chklovskii, from Cold Spring Harbor Laboratory ("How evolution engineered a brain"), Simon Laughlin from Cambridge University in the UK ("Looking at brain design"), and Didier Chatenay, from the Universite de Strassburg, France ("How the architecture of neural networks gets built"). Penn was represented by IME Member Dr. Kwabena Boahen, who talked on "Morphing brains into microchips". Over 75 people attended the two-day event, including some from Drexel, Swarthmore, Princeton, and Lehigh Carbon Community College. Other sponsors included Penn's College of Arts and Sciences and Institute for Research in Cognitive Science, and the Santa Fe Institute.

Research News



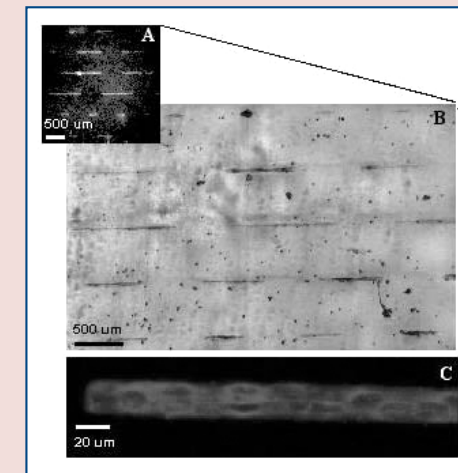
CONTINUED FROM COVER....

A gourmet feast of membrane biophysics one Disch-er at a time

reasons having to do with blood flow — and it is now clear that the dystrophin homolog spectrin has a primary role in red cell elasticity. Additional proteins are also crucial, however, since severe anemias can result when they are defective or deficient. The group is studying the assembly and molecular characteristics of this system, as well as its genesis. Single cell and molecular-level manipulations are performed using microscopy methods that range from fluorescence polarization to fluorescence photobleaching to atomic force microscopy.

A third area of research is in engineering artificial cells where they are using, making, or isolating synthetic polymers as well as purified biological components such as actin filaments and myosin motors. These are variously used to make membranes that encapsulate active micro-machinery responsive to its environment.

Dr Discher's work is widely recognised and resulted in his award of a prestigious Presidential Early Career Award for Scientists and Engineers in 2000. An attractive environment for trainees, his lab now hosts 15 graduate students and postdocs.



Lithographically patterned substrates for long term cell growth. The patterns are being used to control the morphology of differentiating skeletal muscle cells. By imposing well-defined boundary conditions on the cells, the proteins involved in cell attachment - relevant to muscular dystrophies - can be more systematically studied through novel micro-peeling techniques. Similar patterns will also be employed for "cells-on-a-chip" drug discovery.



Research News

Recent Honors and Awards to IME Members:

Daniel Hammer PhD, Professor and Chair of Bioengineering, was named the Alfred G. and Meta A. Ennis Professor of Bioengineering. ♦ **Scott L. Diamond, Ph.D.** was promoted to Professor of Chemical and Biomolecular Engineering ♦ **Dawn M. Elliott, Ph.D.** was appointed Assistant Professor of Orthopaedic Surgery ♦ **Irena Levitan, Ph.D.**, was co-chairperson of the platform session "Protein-Lipid Interactions" at the 2002 Annual Meeting of the Biophysical Society. Dr. Levitan was an invited speaker at the 2001 International Meeting on Physiology and Molecular Biology of Chloride Ion Channels in Leuven, Belgium ♦ **Vladimir Muzykantov, M.D., Ph.D.**, was honored by the National American Heart Association "in recognition of outstanding efforts in research fighting the heart disease and stroke in 2001". He was an invited speaker at the Gordon Research Conference on Drug Delivery in Ventura, CA ♦ **Susan Davidson PhD**, was awarded the Leonore Row Williams Award by the Association of Women Faculty and Administrators (AWFA) for her work in informatics and database research and for her contributions to SEAS through teaching and service. She was also cited for her role in "raising the visibility of successful women scholars, providing a venue for women students and faculty to network and support each other." ♦ **Dr. Eric Boder** and **Dennis E. Discher** were invited to the National Academy of Engineering 2002 Frontiers of Engineering Symposium of the in Irvine, California. These symposia promote cross-disciplinary innovation and allow 50 young engineers who are performing leading-edge research to meet colleagues in other areas ♦ **Dennis Discher PhD** has been invited by an editor at Science to co-author a review on "Polymer Vesicles". ♦ **Peter F. Davies, Ph.D** was the Keynote Speaker at the NorthEast Regional Bioengineering Conference at Drexel University, and delivered Plenary lectures in London and Edinburgh, and Invited Lectures in Sweden, Germany, MIT, Utah, California, Calgary, and New Orleans ♦ **Kwabena Boahen PhD** received a Young Investigator Award from the Office of Naval Research for "Neuromorphic Episodic Memories" in March 2002 ♦ **Dawn Elliott PhD, Edward Vresilovic MD PhD, and Curtis Slipman MD** have received a 1 year grant from Arthrocare to begin March 2002 for the project titled "Nucleus pulposus coblation: in vitro effects on disc mechanics" ♦ **Randall Kamien, Ph.D.** was elected a Fellow of the American Physical Society. Dr. kamien authored a Feature Article in the Journal of Physical Chemistry, "Maximizing Entropy by Minimizing Area: Towards a New Principle of Self Organization" ♦ **Louis J. Soslowsky, Ph.D.** was appointed 2003 Summer Bioengineering Conference Chair, and appointed to the Executive

Preceptorship course in Clinical Bioengineering expands

Following its third successful experimental years, the innovative Clinical Preceptorship course (BE300) for Junior year undergraduates in Bioengineering will expand to the entire class by 2006

At the University of Pennsylvania, as at most other institutions, the degree of exposure of undergraduate Bioengineering (BE) students to real-life problems that are amenable to Bioengineering solutions is highly variable. Experience is often limited to a visit to an operating room or to an industrial or biotech setting and significant exposure to a clinical setting is usually delayed to graduate level work or later. We propose that BE students who will graduate to become employed in the private sector as well as those who will pursue medical school or graduate engineering studies should receive exposure as undergraduates to a wide spectrum of clinical practice and research problems through an in-depth experience in the hospital and in hospital laboratories. A formal course to accomplish this aim was therefore conceived, approved, and first offered on an experimental basis in academic year 1999-2000.

The opportunity was both timely and appropriate at the University of Pennsylvania where interdisciplinary education has been a prominent objective of the University's strategic plan, and where IME's purpose is to bridge engineering to all aspects of medicine and biomedical research and training through innovative, interdisciplinary initiatives.

The course has two major objectives. The first is to expose BE undergraduate students to a range of clinical areas that either employ Bioengineers or in which BE techniques and approaches are critical for the effective implementation of clinical procedures or clinical research. This is accomplished through 18 hours of interactive lectures given by selected clinical and biomedical faculty. The second major objective is immersion in a single clinical speciality. This is accomplished through a Preceptorship in a clinical division of the Medical School/University Hospital for ten weeks. Pairs of students are assigned to a Preceptor (or designated surrogate of their choice) in a clinical division, department, or center for in-depth exposure to a single specialized clinical environment. Thus the course introduces selective aspects of clinical medicine to upper junior year students who have completed two and one-half years of a rigorous BE curriculum but have limited hands-on clinical knowledge or experience. A course in Human Physiology is taught earlier in the same academic year. Additional objectives are to impress upon the students the importance of engineering in the execution of hospital practice and lead them to appreciate the value of engineering knowledge, research, and design in contributing to the success of clinical research and device development. The latter objective is an

important element in extending the use of engineering skills to design-driven research that is complementary to hypothesis-driven research, a more common element of their experience. The course is taught concurrently with the last term of a required four course laboratory sequence involving experiments and projects in all aspects of BE science, problem solving, and design (3). A final course objective is to provide the students with a personal level of knowledge and comfort with clinical medicine and the role of engineering methods in a hospital setting prior to entering their final year of study. We expect, and have already found, that the preceptorship experience will provide the background for selecting a clinical problem as the subject of the required senior year design project, with a clinician as a major mentor or co-advisor to the project.

The course, run by IME Director Peter Davies and BE Professor Mitch Litt, has been well received by students and medical school faculty alike and is an important educational component of the Whitaker Initiative of the Bioengineering department.

Lecture Topics in 2002 included:

Anaesthesiology, Rehabilitation Medicine, Epilepsy Neurology, Neurotrauma, Cardiac Surgery, Pediatric injuries, Cancer Pharmacology Mass Spectroscopy, Pulmonary Imaging, Cardiac Intervention, Orthopaedic Surgery, Medical Informatics, Radiological Imaging

Preceptorship Topics in 2002 included:

- Pressure ulcer therapy
- EEG prediction of epileptic seizures (experimental surgery)
- Optimization of intervertebral disk design (replacement)
- Electrical therapy in healing
- Spatial monitoring of heart function (crystal sensors on heart)
- Finite element analysis for cardiac valve design (replacement)
- Micro-gas bubbles in anesthesiology circuits
- Mass spectrometry: decomposition of lipid hydroperoxides in cancer research
- Cerebrospinal fluid shunts in pediatric patients
- Intracranial electrodes in management of seizure prediction
- 3-D point to point cardiac deformation
- Neurosurgical operating procedures
- Radiological image analyses of pulmonary dysfunction
- Spinal cord injury
- Pediatric trauma and post-traumatic shock syndrome
- Acupuncture and nerve networks in wound healing
- Anesthesiology: operating room procedures and instrumentation
- Design of mechanical devices for joint rehabilitation
- Automated Twitch-Obtaining Intramuscular Stimulation (ATOIMS)

Research News



Recent Honors and Awards to IME Members:

Committee of the Bioengineering Division of the American Society of Mechanical Engineers (ASME). Dr. Soslowsky will be a keynote speaker at the German Society of Shoulder and Elbow and German Society of Biomechanics Symposium in Frankfurt, Germany, in October 2002 ♦ **Dr. Lou Soslowsky** and **Dave Glaser** have received a 1 year grant from Selective Genetics to begin March 2002 for the project titled "Feasibility of gene activated matrices (GAM) for tendon repair" ♦ **Dr. Pedro Beredjikian, Lou Soslowsky, and Tim Crombleholme** have received a 2 year grant from the OREF to begin July 2002 for the project titled "Subcutaneous Implantation of Adult and Fetal Tendons: Effect of Adult Environment on Wound Healing" ♦ **Kenneth Ryan, Ph.D.**, was awarded an American Heart Association Scientist Development Grant. He was an invited speaker at the American Heart Association Scientific Sessions 2001 Meeting in Anaheim, CA ♦ **Victor Romanenko, Ph.D.**, Postdoctoral fellow in Irena Levitan's lab, was awarded an AHA Postdoctoral Fellowship ♦ **Makoto Fumaki, M.D.**, from Paul Janmey's Lab received a one-year Research Fellowship from the Uehara Memorial Foundation of Japan ♦ **Wujing Xian, Ph.D.**, post doc in Paul Janmey's lab, won the Best Poster Award in the post-doctoral category at the 2001 annual IME Symposium ♦ Several students in IME Members' labs won awards and fellowships this year. ♦ In Dennis Discher's lab, **Peter Photos** (Chemical Engineering) was awarded an AHA pre-doctoral fellowship. **Richard Law**, (Chemical Engineering) was awarded an IGERT training slot in Nanotechnology. Richard won the Best Poster Award for the pre-doctoral category for his poster presentation of his work at the 2001 annual IME Symposium ♦ As a result of her work on cytoskeletal 4-dimensional imaging in the Davies Lab, **Amy Rosen** (Bioengineering class of 2002) received a Rose Award (\$1,000) from the University of Pennsylvania Center for Undergraduate Research and Fellowships in university-wide competition ♦ Graduate student **Tony Lin** (Louis Soslowsky's lab) has been accepted into the Penn Towne Fellows program as of January 2002 ♦ In Dawn Elliott's lab, Mechanical Engineering graduate student **Heather Anne Lynch** won the award for best graduate student paper/podium presentation at the 28th Annual Northeast Bioengineering Conference; Bioengineering senior Greg Miller won the best poster presentation at the annual Spruce College House Research Symposium ♦ **Jason W. Nichol** (Bioengineering graduate student in Keith Gooch's lab) was selected by the ASME Bioengineering Division as one of the six Ph.D.-level finalists for the Student Paper Competition at this year's International Mechanical Engineering Congress and Exposition (IMECE), at the Winter Annual Meeting of the American Society of Mechanical Engineers



New Faces at PENN and the IME

Comings and Goings...

LEAVINGS: **Michal Bentel Roof Ph.D.**, Scientific Development Administrator (See page 1) ♦ **Valerie Clerin, Ph.D.**, post doc in Keith Gooch's lab is now at the Genetics Institute in Boston. ♦ **Pierre Hardy M.D. Ph.D.**, Postdoc in the Davies Lab is appointed Assistant Professor of Pediatrics and Pharmacology at the University of Montreal. ♦ **Brian Brunk, Ph.D.** is leaving CBIL to direct the new Penn Genomics Institute bioinformatics core facility. Also leaving CBIL is **Shannon McWeeney, Ph.D.**, who is taking a faculty position at the Oregon Health & Science University, **Vladimir Babenko, Ph.D.**, who has left to join Eugene Koonin's group at NCBI, and **Yuri Kondrakhin, Ph.D.** who is returning to Russia. ♦ **Sam Young, M.D.** is leaving Louis Soslowsky's group to resume his orthopaedic residency program at Penn ♦ **Danielle Dominic** from Valerie Weaver's lab graduated with a Masters Degree from the CAMB program ♦ **Anji Wall**, Summer Undergraduate intern in Peter Davies lab returned to the Catholic University, DC, and **Amy Rosen**, Undergraduate Researcher in the Davies Lab entered the MD PhD program at SUNY Stony Brook NY. ♦

WELCOME NEW POSTDOCS: **Tony Passerini (Ph.D.)**, University of Akron), **David Kaufman M.D.**, (Clinical Fellow in Pulmonary Medicine, HUP), **Jenny Zilberburg (Ph.D.)**, Penn State University), and **Craig Simmons (Ph.D.)** University of Michigan) in the Davies Lab; **Jon van Kleunen, (M.D.)**, Penn), **Tung-Fu Huang, M.D.** (Taipei Veterans General Hospital) and **Samir Mehta, M.D.**, a Penn Orthopaedic Resident, in Louis Soslowsky's lab; **Drs. Xiaoliang Zhuo (Ph.D.)** in toxicology, State University of NY at Albany) and **Daljit Vudathala, (Ph.D.)** University of Alberta, Canada), a medicinal chemist previously with Agriculture Canada and Proctor and Gamble join Dr. Ian Blair's group at

Penn's Center for Cancer Pharmacology; **Hongxian He (Ph.D.)**, Boston University) with **Chris Stoeckert** at Center for Bioinformatics. New post-doctoral career conversion trainees at CBI are **Drs. Matt Mailman** and **Trish Whetzel**. ♦

WELCOME NEW STAFF:

Chandrima Chatterjee, a senior research assistant in Valerie Weaver's lab; **Steve Fischer** and **Yongchang Gan** have joined Chris Stoeckert's group at the Center for Bioinformatics from Doublet to work on genomic sequence annotation and analysis. ♦

WELCOME NEW GRADUATE STUDENTS:

Valerie Weaver's lab welcomes three new graduate students: **Nas Zahir**, a Bioengineering Graduate student, who was awarded a two year Cardiovascular Training Grant pre-doctoral fellowship; **Gabriela Rozenberg**, a non-matriculating graduate student in the BGS Cell and Developmental Biology program from University of Buenos Aires, Argentina, and **Micah Chrenek** a Ph.D. graduate student from Dr. Paul Wong's group at the University of Alberta; **Ehren Carine**, a Drexel coop student, and **Stephanie Perry**, bioengineering graduate student (University of Rochester) join Louis Soslowsky's lab; **Amanda Filanowski**, Bioengineering graduate student (Tulane University) in Dawn Elliott's lab. ♦

INTERNS:

This summer, Valerie Weaver's lab hosted **Penney Gilbert**, a summer CAMB rotation student; Bioengineering undergraduate interns **Hal Schwartzstein** and **Gary Chang** in Peter Davies' lab; High school student **Noam Feldman** and Princeton undergrad **Jonathan Jennings** will join Kenneth Ryan's lab at CHOP.

Deformation-enhanced fluctuations in the red cell skeleton with theoretical relations to elasticity, connectivity, and spectrin unfolding

In a paper that suggests that proteins can be forced to unfold in an intact cell cytoskeleton, IME member Dennis Discher and James Lee of the Wistar Institute measured local elasticity in the red cell spectrin-actin cytoskeleton by tethering nanoparticles to nodes in the network. The particle motions were then tracked as cells were controllably deformed. Motions in the axially extended cytoskeletal network were markedly increased relative to motions in the unstressed network suggesting protein dissociations that reduce network connections and/or unfolding of connected proteins. (*J.C.M. Lee and D.E. Discher. Biophysical Journal 81: 3178-3192, 2001*).

The cytoskeleton under external fluid mechanical forces

IME Director Peter Davies and colleague Brian Helmke reviewed the important role of the cytoskeleton in a decentralization model of endothelial mechanotransduction. In particular, their recent studies of 4-dimensional cytoskeletal motion in living cells under external fluid mechanical forces were summarized together with new data on the spatial distribution of cytoskeletal strain, the first measurement of strain in living cells referenced to an endogenous (cytoskeletal) reporter. The studies map strain throughout the cell and identify strain concentrations at cell junctions and adhesion sites. (*Davies P.F., Helmke, B.P. Annals Biomedical Engineering 30: 1-13, 2002*).

Membrane cholesterol regulates ion channels

Modulation of inward-rectifier K⁺ current by optical isomers of cholesterol membrane potential of many cells under resting conditions is dominated by inward-rectifier K⁺ channels belonging to the Kir 2 family. Irena Levitan's group in the IME has reported the regulation of Kir by altering the cholesterol composition of the cell membrane. enriching the cells with cholesterol decreases the Kir current density, whereas depleting the cells of cholesterol increases the density of the current. The dependence of the Kir current density on the level of cellular chole-

FEATURED PUBLICATIONS: Some Ongoing IME Research

sterol fits a sigmoid curve with the highest sensitivity of the Kir current at normal physiological levels of cholesterol. To investigate the mechanism of Kir regulation by cholesterol, endogenous cholesterol was substituted by its optical isomer, epicholesterol. Substitution of about 50% of cholesterol by epicholesterol resulted in an early and significant increase in the Kir current density. Furthermore, substitution of cholesterol by epicholesterol has a stronger facilitatory effect on the current than cholesterol depletion. Neither single channel properties nor membrane capacitance were significantly affected by the changes in the membrane sterol composition. These results suggest that (1) cholesterol modulates cellular K⁺ conductance by changing the number of active channels, and (2) that specific cholesterol-protein interactions are critical for the regulation of Kir. (*Romanenko V.G., Rothblat, G.H. and I. Levitan. Biophysical Journal. In Press*).

Predicting Gene Ontology functions from ProDom and CDD protein domains

As more and more sequence information becomes available from the many national and local genome projects, how does one assign biological significance to novel sequences? Bioinformatics "Curators" are attempting to develop algorithms to address this. IME Member Chris Stoeckert in the Computational Biology and Informatics Laboratory (CBIL) has developed an algorithm for associating gene ontology-defined molecular functions to protein domains. If sufficient similarity to a known association exists, the significance of the novel sequence can be assessed. (*Schug, J., Diskin, S., Mazzarelli, J, Brunk, B.P., Stoeckert, C.J.Jr. Genome Research. 12:648-655, 2002*).

Bone formation in carotid artery plaques may be protective

Bone formation and dystrophic calcification are present in carotid endarterectomy plaques. The clinical significance of these findings is unknown. With collaborators at the University of Pittsburgh, Penn Cardiologist Emile Mohler III MD and his group in the department of Medicine evaluated 142 patients with carotid stenosis. The specimens were evaluated for bone formation, calcifications, inflammatory infiltrates, neovascularization, and histological type or grade of plaque. Patients with calcification of carotid plaques had fewer symptoms of stroke and transient ischemic attack than those without calcification. Stroke and transient ischemic attack occurred less frequently in patients with plaques with large calcific granules. They concluded that bone formation tends to occur in heavily calcified carotid lesions devoid of ulceration and hemorrhage but that patients with extensive calcification of the carotid plaques are less likely to have symptomatic disease. (*Jennifer Hunt et al and Emile Mohler III, Stroke; 33:1214-1219, 2002*)

Fastest algorithm available for solution of massive

reaction problems involving millions of reactions.

A Monte Carlo (MC) algorithm has been developed by Chemical Engineers Ian Laurenzi, John Bartels and Scott Diamond in the IME for the simulation of the time evolution of aggregation processes featuring multiple components, properties, or conservation laws. Instead of using deterministic differential population balance equations, the MC algorithm utilizes a stochastic approach to aggregation kinetics. As a result, exact simulation of spatially independent aggregation processes is possible without the need for numerical approximations. Furthermore, simulations exactly predict all moments of the size and composition distributions of aggregating particles for both nongelling and gelling kernels and extend these results to the postgelation period. The algorithm is shown to require at most O((12...)/(+1)) rate-limiting operations per time step for a -component aggregation process featuring i monomers of each component i-a substantial performance improvement over the potential of previous methods. (*I.J. Laurenzi, J.D. Bartels, S.L. Diamond. A general algorithm for exact numerical simulation of multi-component aggregation. J. Computational Physics 177, 418, 2002*).

Maximizing Entropy by Minimizing Area: Towards a New Principle of Self Organization

In a Feature Article in the Journal of Physical Chemistry, IME member Randal Kamien of the Physics and Astronomy department has proposed a heuristic explanation for the numerous non-close-packed crystal structures observed in various colloidal systems. By developing an analogy between soap froths and the soft coronas of fuzzy colloids, we provide a geometrical interpretation of the free energy of soft spheres. Within this picture, we show that the close-packing rule associated with hard-core interactions and positional entropy of particles is frustrated by a minimum-area principle associated with the soft tail and internal entropy of the soft coronas. We also discuss these ideas in terms of crystal architecture and pair distribution functions and analyze the phase diagram of a model hard-sphere-square-shoulder system within the cellular theory. We find that the A15 lattice, known to be area minimizing, is favored for a reasonable range of model parameters and so it is among the possible equilibrium states for a variety of colloidal systems. We also show that in the case of short-range convex potentials the A15 and other non-close-packed lattices coexist over a broad ranges of densities, which could make their identification difficult. (*P. Zihlerl and R.D. Kamien J. Phys. Chem. B 105 10147-10158, 2001*).

