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The Seventh Annual
BEACON Symposium and Technology Fair
Bionanotechnology: The World of Small in Medicine

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PROGRAM OF EVENTS

- 7:30 am Registration and Continental Breakfast
• Breakfast Sponsored by Regional Technology Corporation
- 8:15 am WELCOME
• Dr. Joseph Bronzino, Ph.D., P.E., President, BEACON
- 8:30 am SPEAKER PANEL 1
• Dr. Gregory Tew, Ph.D., UMASS- Amherst, Polymer Science Center
• Dr. Kambiz Pourrezaei, Ph.D., Drexel University, Nanotechnology Institute
• Dr. Jun Li, Ph.D., NASA Ames Research Center, Nanotechnology Center
• Dr. Mark Saltzman, Ph.D., Yale University
- 10:00 am BREAK
- 10:15 am SPEAKER PANEL 2
• Dr. David Reisner, Ph.D., President, CEO, Inframat Corporation
• John Lanzafame, President, Nanolution Division, Biophan Technologies
• Dr. Gualberto Ruaño, M.D., Ph.D., President, GENOMAS
• JoAnne Feeney, Ph.D., Punk, Ziegel & Company
- 11:45 am BREAK
- 11:55 am Introduction to Keynote Speaker
• Stephen Waite, author of *Quantum Investing* and Co-founder and CIO, Hedge Capital Partners, LLC
- 12:00 pm KEYNOTE ADDRESS
• Dr. Michael Connolly, Ph.D., President & CEO Integrated Nano-Technologies
- 1:00 pm LUNCH AND TECHNOLOGY FAIR
• Lunch: Sponsored by eR Portal Software Group and CT Nanobusiness Alliance
• Exhibits and Poster Session
• Poster Awards: Sponsored by Robinson and Cole, LLP and UBS Financial Services
- 3:00 pm RECEPTION AND AWARDS CEREMONY
• Cash Awards for 1st, 2nd and 3rd Best Posters
• Presentation of Awards by Oz Griebel, President & CEO, Metro Hartford Alliance
- 4:00 pm Reception with Members of CVG
• Co-sponsored with Connecticut Venture Group
- 5:00 pm CVG Panel Discussion
• *Future Trends of Nanotech Investment: Are We Passing Through the Inflection Point?*

Saint Francis Hospital & Medical Center is accredited by the Connecticut State Medical Society to sponsor continuing medical education for physicians. This Symposium has been approved by Saint Francis Hospital & Medical Center for a maximum number of 4 hours of Category 1 credit towards the AMA Physician's Recognition Award.

The Seventh Annual
BEACON Symposium and Technology Fair
Bionanotechnology: The World of Small in Medicine

SPEAKER ABSTRACTS

**“Merging Chemistry, Materials Science and Biology
to Create New Materials for Biomedical Applications”**

Gregory Tew, Ph.D
UMASS- Amherst, Polymer Science Center

Research in my group uses the tools of synthetic chemistry to build new macromolecules and materials. Our primary aim is to create new materials using a combination of principles many of which are inspired by biology. Primarily, we target supramolecular chemistry to organize molecules into novel materials. In addition, the design of simple molecules that mimic the complex structures and functions of biology is at the heart of our work. In this presentation, we will illustrate several examples of these principles including facially amphiphilic polymers based on conformationally flexible backbones, helical folded molecules, and biodegradable hydrogels with increased storage modulus.

Gregory Tew, Ph.D

Education:

B. S. Chemistry, North Carolina State University, May 1995

Ph. D. Materials Chemistry, University of Illinois at Urbana-Champaign, May 2000

Post-Doctoral Fellow, University of Pennsylvania Medical School, August 2001

Assistant Professor of Polymer Science and Engineering, University of Massachusetts,
Amherst, September 2001

Research Interest:

Supramolecular polymer science, bioinspired and biomimetic structures, polymers for biomedical science, self organization, well defined macromolecular architectures, functional materials, novel biomaterials, hydrogels.

Awards:

Presidential Early Career Award for Scientists and Engineers (PECASE)

2002 Army Research Office Young Investigator

2003 Office of Naval Research Young Investigator

3M Nontenured Faculty Award

DuPont Young Faculty Grant

American Chemical Society-Division of Organic Chemistry Graduate Fellowship

Beckman Institute for Advanced Science and Technology Research Assistantship

R. C. Fuson Award for Outstanding Graduate Research

“Applications of Nano Optical Probe to Single Cell Imaging”

**Kambiz Pourrezaei, Ph.D.
Drexel University, Nanotechnology Institute**

We have developed a real-time live single-cell imaging technology platform capable of sensing/mapping biological macromolecules with nanometer spatial resolution. In this platform we can simultaneously examine expression of proteins through use of novel enhanced Raman spectroscopy and metallic nanoparticle-enhanced fluorescence resonance energy transfer (FRET) imaging. This unique capability is the result of our ability to fabricate metallic nanoparticle coated tapered optical-fiber probes with tip diameters of several tens of nanometers. Excitation of these nano-features by light transmitted through the coated optical fiber gives rise to; (a) enhanced Raman scattering and, (b) highly selective FRET excitation of acceptor molecules. These nano-features act as size-tunable donor molecules.

Kambiz Pourrezaei, Ph.D.

Dr Pourrezaei is a professor in the School of Biomedical Engineering, Science and Health Systems at Drexel University, Philadelphia, PA. He is a co-founder and co-director of Nanotechnology Institute (NTI) in Philadelphia, Pennsylvania. NTI was initiated with a \$10.5 million dollars grant from the State of Pennsylvania. Dr Pourrezaei has been involved with research in the area of nanotechnology since 1982. In particular Dr Pourrezaei has focused on Bio application of nanotechnology.

“Nanodevices for Biomedical Applications”

**Prepared by Dr. Jie Han, Ph.D.
NASA Ames Center for Nanotechnology**

**Presented by Dr. Jun Li, Ph.D.
NASA Ames Center for Nanotechnology**

Biomedical nanodevices in the NIH's Nanomedicine Initiative (NMI) are envisioned to search out and destroy the very first cancer cells of a tumor developing in the body, the biological nanomachines to remove and replace the cell's broken part, and the molecule-sized pumps to deliver life-saving medicines precisely where they are needed in the human body. These scenarios are becoming realistic due to the rapid, tremendous progress in nanobiotechnology. For example, nanostructures such as functional nanoparticles, dendrimers, fullerenes, carbon nanotubes, and semiconductor nanocrystal including quantum dots have been exploited for drug delivery, diagnostics and treatment at molecular level; the assemble nanostructured fibrous scaffolds reminiscent of extracellular matrix has been used for mimic properties of bone; and protein nanotubes based on self-assembly of unique cyclic peptides for novel antibiotics. While the most work is still in the laboratory research, some has found applications.

The presentation will review and discuss these advances mainly based on the research work on the biomedical nanodevices carried out in the NASA Ames Center for Nanotechnology and its collaborators.

Jun Li, Ph.D.

Dr. Jun Li is a physical scientist with NASA at Ames Research Center's Nanotechnology Center. His current research interests focus on the development of new methods to integrate the nanostructured materials to micro- and macro- sized devices in which the unique properties of individual nanoelements are utilized to improve the performance. The approach is to combine the lithographic/nonlithographic patterning, self-assembly, catalytic growth, semiconductor processing techniques, and chemical functionalization to build individual nanoelements such as carbon nanotubes (CNTs) and semiconducting nanowires (SNWs) into large-scale integrated devices. Currently he is working on CNT nanoelectrode arrays for ultrasensitive DNA chips and electrical biomedical devices.

Dr. Li received BS degree in chemistry from Wuhan University (P.R. China) in 1987, MS and PhD degree in chemistry from Princeton University in 1991 and 1995, respectively. From 1994 to 1997, he held a postdoctoral research associate position in Chemistry Department of Cornell University. He worked for Molecular Imaging Co. from 1997 to 1998 and the Institute of Materials Research and Engineering in Singapore from 1998 to 2000. He joined NASA Ames Research Center in 2000. Dr. Li has published over 50 technical papers and filed over 8 patents.

“Biomaterials and Nanotechnology in Drug Delivery”

**W. Mark Saltzman, Ph.D.
Yale University**

The potential intersection between nanotechnology and the biological sciences is vast. Biological function depends heavily on units that have nanoscale dimensions, such as viruses, ribosomes, and molecular motors. In addition, engineered devices at the nanoscale are small enough to interact directly with subcellular compartments and to probe intracellular events. The ability to assemble and study materials with nanoscale precision leads to opportunities in both the basic biology (e.g. testing of biological hypotheses that require nanoscale manipulations) and development of new biological technologies (e.g. drug delivery systems, imaging probes, or nanodevices). This presentation will focus on the potential applications of nanotechnology in controlled release and drug delivery.

Millimeter-scale and micrometer-scale controlled release systems have been well studied and some systems have been approved for clinical use, such as Gliadel® wafers for treatment of brain tumors and Lupron® depot for treatment of endometriosis. One of the major advances in recent years has been further reduction in the size of these systems: it is now possible to make polymer delivery systems that are nanometer-scale, can be injected or inhaled, and are much smaller than—and capable of being internalized by—many types of human cells. While there are a variety of ways of achieving nanoscale delivery systems, including self-assembling systems based on liposomes or micelles, the most stable and versatile systems are miniaturized versions of the synthetic materials that have already been used in drug delivery applications. This is usually accomplished with degradable polymers such as poly(lactide, glycolide), which will degrade over the course of several months once it is exposed to water. The rate of drug release from this material can be controlled by changing composition of the copolymer. These particles can be injected for circulation or used to release drugs locally. The encapsulated drugs can be complex. For example, it is now possible to make 300 nm particles that have functional DNA within the solid matrix.

Biocompatible and degradable polymeric biomaterials have been available for some time and much is known about assembling them together with different classes of drug molecules. But one usually obtains a complex mixture of particles of different sizes and shapes; the methods of fabrication are imperfect. Matching methods of particle formation with drugs has been one of the major challenges in this area. There are now in the literature many different ways, especially with nanotechnology, to make small particles. Unfortunately few of these methods are compatible with most drugs. Finding better ways to make controlled particles, which are compatible with drug incorporation, is a challenge for the future.

There are some applications of drug delivery in which non-polymeric materials will be preferable. With this general concept in mind, we have developed methods, which use controlled surface conditions to induce uniform DNA-doped nanomineral particulates. These nanominerals are formed under mild biological conditions. The mineral composition of these particles, as well as the loading of DNA, can be controlled. Both of these features (composition and loading) influence the activity of the particles for gene transfection. In previous work we have shown that particles of

controlled size and density can be used to facilitate uptake and expression by concentrating DNA at the cell surface.

Some cells will internalize nanoscale particles. Cultured cancer cells, for example, can be loaded with fluorescently labeled nanoparticles. Polymeric nanoparticles can also be conjugated with cell ligands for targeting specific cell populations. While the factors that control internalization of polymeric and mineral particles are not fully understood, this phenomenon may be exploitable for drug delivery. For example, there are many potential applications for the controlled intracellular localization and release of drugs.

Nanotechnology is providing new methods for the encapsulation of biological compounds. Because of their combination of properties—including subcellular size and controlled release capability—these new materials should enable new applications in biological and medical science.

W. Mark Saltzman, Ph.D.

W. Mark Saltzman graduated with distinction from Iowa State University, earning a B.S. in Chemical Engineering in May of 1981. He obtained his graduate training at the Massachusetts Institute of Technology, earning a M.S. in Chemical Engineering in 1984 and a Ph.D. in Medical Engineering in 1987. Dr. Saltzman accepted a position as Assistant Professor of Chemical Engineering at The Johns Hopkins University in 1987 and a joint appointment in the Department of Biomedical Engineering at The Johns Hopkins School of Medicine in 1990. He was promoted to Associate Professor of Chemical Engineering in 1992 and Professor in 1995. In 1996, Dr. Saltzman accepted a position as Professor of Chemical Engineering at Cornell University. His research interests include controlled drug delivery to the brain, polymers for supplementing or stimulating the immune system, cell interactions with polymers, and tissue engineering. In 1990, Dr. Saltzman received the Camille and Henry Dreyfus Foundation Teacher-Scholar Award. He also received the Allan C. Davis Medal as Maryland's Outstanding Young Engineer in 1995, the Controlled Release Society Young Investigator Award in 1996, and was elected a fellow of the American Institute of Biological and Medical Engineers in 1997. Dr. Saltzman has received awards for teaching from Johns Hopkins and Cornell. In 2000, he was honored by receiving the Professional Progress in Engineering Award from Iowa State University and being named the Britton Chance Distinguished Lecturer in Engineering and Medicine at the University of Pennsylvania. In 2001, he was selected to be the first holder of the BP Amoco/H. Laurance Fuller Chair in Chemical Engineering at Cornell. He joined the faculty of engineering at Yale University, as the Goizueta Foundation Professor of Chemical and Biomedical Engineering, in July of 2002 and became the first chair of Yale's Department of Biomedical Engineering in 2003.

“Bioengineered Nanocoatings for Prosthetic Devices”

**David E. Reisner, Ph.D.
CEO & President, Inframat**

The earliest commercial applications coming out of pure-play emerging nanotechnology companies are in the field of nanocoatings, whether they be (i) thin film coatings with thickness in the nanoscale range or (ii) industrial coatings that are thick (on the order of 20 mils) but exhibit unique and enhanced properties attributable to nanoscale grain structure. Antifogging coatings as applied to eyeglasses or hydrophobic coatings applied to clothing for stainproofing are excellent examples of rapidly growing consumer acceptance of nanocoatings. Likewise, industrial nanocoatings customers include the U.S. Navy, which is exploiting robust wear-resistant ceramic nanocoatings, which exhibit extraordinarily long service life, in part attributable to the discovery that they are strain tolerant and impact resistant, properties not typically associated with ceramics.

Inframat® has been developing the industrial nanocoatings, which are gaining acceptance in the Navy, using conventional thermal spray processes based on both traditional powder feedstocks as well as a novel solution feedstock approach in which an atomized aqueous solution containing salts of the desired coating materials is injected directly into the hot zone of a plasma spray gun. Thermal spray has also been the traditional means to manufacture coatings for implantable devices including hip and knee joint stems, typically using hydroxyapatite (“HAp”) as the coating material. However, these thermal spray coatings are less than satisfactory, due to poor adhesion to the substrate and high solubility of the coating in human body fluid, primarily attributable to the amorphous nature of the thermal spray coating.

Inframat has addressed the shortcomings of conventional coatings in both prosthetic device stems and wear couples. First, we have departed from the traditional thermal spray process and have exploited an electrophoretic approach to the fabrication of nanostructured HAp coatings, that has significantly improved bond strength as well as dramatically reduced solubility attributable to their nanocrystalline structure. Second, we have taken advantage of the enhanced properties of nanostructured thermal spray coatings to apply ceramic nanocoatings to implantable device substrates for joint wear couples. These ceramic nanocoatings exhibit an attractive combination of properties, which reside in a “sweet spot” between coatings that are too hard and hence brittle and coatings that are too soft and hence fail to prevent wear. Selected details follow.

Electrophoretic Hydroxyapatite Nanocoatings for Prosthesis Stems

Hydroxyapatite coatings applied to prostheses, particularly femoral stems for artificial hips, are used for non-cemented applications. Bonding between tissue and the HAp coating requires a longer period than that with cemented prostheses. However, the non-cemented design provides for longer life, as the methylmethacrylate cement tends to pull away over time and loosen the prosthesis-to-tissue bond.

Inframat is presently evaluating a nano-HAp coating, which is applied by electrophoresis, where suspended HAp particles, with a surface charge, are attracted to and deposited on the prosthesis, in an electric field. Biomedical (inert) glass is deposited in tandem with the nano-HAp, in such proportion that the coefficient of thermal expansion of the combination closely matches that of the metal prosthesis. This facilitates a subsequent heat treatment, (without any concern for cleaving of

the coating at the substrate interface), wherein the glass is fused, and the nano-HAp crystallizes and densifies. Corrosion studies in simulated human body fluid have shown dissolution rates three orders of magnitude less than those of conventional (micron)-sized thermal-sprayed or chemically-deposited HAp.

An additional feature that is under study relates to enhanced osseointegration. Nano-HAp grains are of the same size (40–60 nm) as those of bone cells or femoral cortical bone osteoblasts. We anticipate that with this size similarity, the nano-HAp in immediate proximity to an active surface of bone cells will result in enhanced osseointegration, resulting in a more rapid healing rate, and a stronger bond.

Thermal Spray Ceramic Nanocoatings for Joint Wear Couples

Hip and knee prosthesis wear couples rely on metal against ultra high molecular weight cross linked polyethylene (UHMWPE), metal-on-metal, or in more recent designs, monolithic (thick) dense-ceramic-on-dense-ceramic, as well as a thin indigenous grown metal oxide on the femoral head (*e.g.*, Smith & Nephew's Oxinium™) against UHMWPE. Each wear combination exhibits strengths and weaknesses. Most important is the wear rate.

Inframat is developing a novel air plasma-sprayed thick ceramic nanocoating coupled against itself, *i.e.* the same ceramic coating on the (i) femoral head as that on the acetabular cup in hips or (ii) paired in knee prostheses. Two such ceramic nanocoatings are under evaluation. Pin-on-disk and pin-on-ring wear data have revealed wear rates dramatically less than those for metal-on-metal, or metal-on-UHMWPE.

The authors gratefully acknowledge funding through NSF Grant No. DMI-0319325 and NIH Grant No. 2 R44 AR047278-02A1.

David E. Reisner, Ph.D.

President & CEO – The Nano Group™, Inc

President & CEO - Inframat® Corp.

President & CEO – US Nanocorp®, Inc.

Dr. David Reisner, a 1978 University Honors graduate from Wesleyan Univ, received his Ph.D. at MIT in 1983 in the field of chemical physics. In 1996, Reisner co-founded both Inframat® and US Nanocorp® as a vehicle to develop nanostructured materials technology. Since founding, Inframat and US Nanocorp have been funded nearly \$20 MM in Government Contract R&D. Both companies received the Deloitte & Touche Connecticut Technology Fast50 Award in both 2002 and 2003. He is a member of the Connecticut Academy of Science and Engineering. Reisner is serving a 3-year term as a Technology Pioneer for the World Economic Forum.

“Development of a Novel Field of Nanotechnology”

**Prepared by Michael Weiner
CEO, Biophan Technologies, Inc.**

**Presented by John Lanzafame
President, Nanolution Division Biophan Technologies**

As each day passes, the awareness and excitement for the potential of nanotechnology grows in both the popular press and the scientific literature. The potential for this technology to affect every facet of medical science is compelling, and reminds us of the advances and impact the transistor had in the early nineteen-fifties as it progressed to the integrated circuit and improvements in miniaturization, reliability, and capability eventually enabled its use in many facets of device design, diagnostics, drug discovery, and therapeutics. Nanotechnology has the capability to cause a paradigm shift just as exciting.

Biophan Technologies, Inc. has seen the development of a nanotechnology capability within our company that was born in a surprising and highly beneficial way; making us realize how lucky we were to tap into a center of competence in nanotechnology and incorporate it into our macro-sized technology challenges. The initial promising opportunity and the resulting iterations have produced results that, in retrospect, are somewhat stunning and unexpected. This led us to realize that taking a view of technology development that runs a “nano-possibility” track, in parallel, is what paid off for us and can pay off for many others.

While working on the problems of MRI safety that plague pacemakers and pacemaker leads, Biophan discovered a novel solution space that has led to our entry into a new and exciting area of nanotechnology applied to medical device development. While working on solving the problem of MRI safety of pacemakers by traditional means, we developed a parallel path technology using thin film nanomagnetic particle coatings for which we budgeted up to a year of time and several hundred thousand dollars to develop.

Ultimately, we were able to solve the problem of pacemaker leads using traditional radio frequency technology, employing a low pass filter and an induction loop, which enabled a 90% reduction in heating and an 80% reduction in induced voltages in pacemaker leads. This approach provided a significant margin of safety and a marketable solution. The thin film nanomagnetic particle coatings averaged a 20% to 50% reduction in heating and had not yielded significant reductions in induced voltages. Based upon traditional project management criteria, we would have considered the parallel effort less effective and it would have been abandoned. In fact, this almost happened.

A debate about the exact nature of the problem and the way in which the solutions were tested had resulted in a detailed review of the parallel nanomagnetic technology program. In this review, we noted an anomaly that had occurred during the year of testing. The anomaly that was observed was that test fixtures on which we applied and tested our nanomagnetic coatings sometimes appeared much brighter in the MRI scanner, sometimes disappeared, and sometimes barely appeared with a ghostlike presence as the coatings were varied.

Understanding of the cause of this anomaly led to the development of a new technological capability that dwarfs pacemaker safety in its economic potential, and has the capability to touch many fields of medicine, including interventional diagnostics and therapeutics for cardiovascular disease, oncology, orthopedics, and many others.

Biophan planted the seed for a new technology with that investment in nanomagnetic particle coatings – a new technology that we are now aggressively developing for multiple applications. Tiny nanomagnetic particles, whether in thin films or in colloidal suspensions, can be “tuned” to specific frequencies of RF and/or magnetic field response and to have different responses in magnetic fields. The coatings can also vary impedance, conductance, capacitance, inductance and, in combination, can even reduce magnetic susceptibility which is responsible for much of the MRI image artifact seen in images that include implants of materials such as stainless steel. The ability to reduce image artifacts has the capability to be applied to devices ranging from cardiovascular stents to interventional guidewires to orthopedic implants.

As a suspension, the nanoparticles have the capability to provide contrast agents that are brighter than gadolinium and which can be tuned to allow the particles to have preset and predictable variations of signature in an MRI image. This capability would allow the physician to identify different species of particles from each other, similar to how airplanes can be differentiated from one another by radar by having different transponder frequencies. Applied to the field of MRI contrast agents, this capability would result in multiple markers tagged to multiple binding agents available in a single contrast agent. This agent, combined with appropriate software tuning, would enable a single procedure to be performed with a contrast agent that highlighted a tumor in one color, the vasculature feeding the tumor in a different color and any blood clots formed in a third color.

Combining the nanomagnetic particles with appropriate coatings to enable them to bind to appropriate targets can provide a contrast agent with better visibility, more specific imaging information and improved imaging windows as compared to current MRI contrast agents such as those containing gadolinium.

Biophan has recently announced the newest application of this technology which we currently have under development. The addition of drugs bound to the tuned nanomagnetic particles results in a drug delivery technology with exciting implications. The magnetic properties combined with the ability to tune particles to specific frequencies provides the capability to deliver particles to specific locations with magnetic guidance, verify their position with MRI and activate the particles selectively to provide drug delivery on demand. This would allow the physician to activate the drug release where and when it is needed. Incorporating these drug-loaded nanomagnetic particles into device coatings have equally exciting applications. This broadens the potential applications for this technology to include several large medical device markets as well as a large number of potential application in pharmaceutical drug delivery, including exciting oncology applications.

By pursuing multiple research approaches to a single problem and looking upon scientific discoveries with an opportunistic business view, Biophan has been able to enter new markets that we expect to be far more lucrative than the area we originally targeted.

More importantly, by taking a risk in pursuing a parallel path, in this case using nanotechnology, where the initial evidence was limited, we have realized a significant payoff. Even though the primary goal of reduction in heating was not achieved, by staying attuned to the potential capabilities that emerged from the fundamental research, we identified some important new applications in reducing image artifacts, and in controlling the release of drugs, that have opened up a new area of technology, and business opportunity, for us.

John Lanzafame

Mr. Lanzafame has fifteen years experience in the medical device industry. With a background that includes education in chemical and industrial engineering, Mr. Lanzafame combines a strong technical background with extensive experience in business development and executive level management. Until early 2004, Mr. Lanzafame was employed by STS Biopolymers, Inc., a privately held medical device company that marketed high performance polymer-based coatings for the medical device industry, including drug eluting surfaces for devices such as coronary stents and indwelling catheters. Mr. Lanzafame held a variety of positions with STS Biopolymers, including positions in research, product development, and sales and marketing, ultimately leading to his assuming the position of President of STS Biopolymers beginning in 2003.

In 2004, Mr. Lanzafame left STS Biopolymers following sale of the company to Angiotech Pharmaceuticals, and is currently President of Nanolution, the drug delivery division of Biophan Technologies, Inc. This newly formed division was created to leverage new discoveries in the field of nanotechnology for the purposes of targeted drug delivery and highly controlled drug elution from medical devices.

“Physiogenomics and Nanotechnology: A Systems Engineering Approach to Personalized Healthcare”

**Gualberto Ruaño, M.D., Ph.D.,
President, GENOMAS**

Physiogenomics is an integrated approach composed of genotypes and phenotypes and a population approach deriving signals from functional variability among individuals. Allelic (SNPs, haplotypes) and phenotypic (gene and protein expression) genomic markers are analyzed to discover statistical associations to physiological characteristics in populations of individuals after they have been similarly exposed to an environmental trigger. Variability in a genomic marker among individuals that tracks with the variability in physiological characteristics establishes associations and mechanistic links with specific genes.

Genomas has developed unique capabilities in parallel processing of gene arrays through the Illumina BeadArray technology. This cutting edge platform merges the parallel processing capability of fiber optic technology with nanoscale high resolution scanning. Recent advances in physiogenomics at Genomas allow us to couple human phenotypic information (e.g., lipid, glycemic and inflammation profiles) with genotypic information from hundreds of genes (e.g., derived from endocrine, energy and immunology pathways) to advance personalized health. Genomas is developing PhysioType* products to personalize healthcare.

Gualberto Ruaño, M.D., Ph.D.

Gualberto Ruaño, M.D., Ph.D., President of Genomas, a biotechnology firm specializing in personalized healthcare using genomics, and Director of Cardiovascular Genetics Research at Hartford Hospital has been elected a member of the Connecticut Academy of Science and Engineering (CASE).

CASE was chartered by the General Assembly in 1976 to provide expert guidance on science and technology to the people and to the state of Connecticut, and to promote the application of science and technology to human welfare and economic well-being.

CASE Chairman John Cagnetta, Ph.D., said, “Dr. Ruaño is a national leader in the science of applying genetic variation to human disease and a pioneer in personalized medicine who has successfully bridged academia and commerce.”

Membership in the Academy, which is limited by state statute to 200, is determined by peer nomination and considered among scientists and engineers to be very prestigious. Members are elected on the basis of significant original contributions in theory or application as demonstrated by original published books and papers, patents, the pioneering of new and developing fields and innovative industrial products, outstanding leadership of nationally recognized technical teams, and external professional awards in recognition of scientific and engineering excellence.

Hartford Hospital CEO John Meehan commented, “On behalf of the entire Hartford Hospital community, I wish to congratulate Dr. Ruaño on this esteemed appointment. His work is leading the way in this important new field of personalized medicine and as a result of his pioneering

efforts, patients will soon experience the benefits of powerful new diagnostic and preventive medicine tools. We are proud to have him as a member of our Hartford Hospital team.”

Dr. Rúaño is a pioneer in several molecular technologies for profiling genome diversity stemming from population and evolutionary genetics. He has been instrumental in advancing gene haplotypes as the gold standard for pharmacogenetic associations and as one of the fundamental technologies for personalized medicine. He is considered one of the industry's leaders in the impact of gene variation on clinical medicine and drug development.

In addition to being president of Genomas and his position at Hartford Hospital, Dr. Rúaño is also Adjunct Professor of Biochemistry and Molecular Biology at the George Washington University School of Medicine in Washington, D.C. In Washington, he has worked with the FDA and pharmaceutical industry representatives in formulating the regulatory issues and scenarios for the use of pharmacogenetic data in drug applications.

Dr. Rúaño, a native of Puerto Rico, is Ad Honorem Professor of Medical Sciences at the University of Puerto Rico. He came to Connecticut in 1982 from Johns Hopkins University, where he was an undergraduate, to begin his medical studies and research at Yale University School of Medicine. At Yale, he completed both M.D. and Ph.D. degrees, and was a fellow of the Medical Scientist Training Program and of the Ford Foundation. He trained with Professors Dr. Kenneth K. Kidd and Dr. Frank H. Ruddle on population genetics and evolutionary biology. Work he performed at Yale led to breakthrough publications and patents in genomics, which later became the basis of the technology of his two previous companies, BIOS Laboratories and Genaissance Pharmaceuticals, which as its CEO and founder he took public in 2000. One of his inventions is used worldwide for therapeutic management of AIDS and hepatitis.

Jon Soderstrom, Director of the Office of Cooperative Research at Yale said, “Dr. Rúaño has effectively translated his Yale training and ideas in genetics into valuable applications that have had a significant impact on biotechnology and its development in New Haven and Connecticut. This is a well-deserved award.”

“Economic Drivers for Nanotechnology in Health Care”

**JoAnne Feeney, Ph.D.
Punk, Ziegel & Co.**

The development of applications from the growing discipline of nanoscale science and technology is promising to introduce new platforms for pharmaceutical and health care industries. This overview will examine the economic drivers that will differentiate among the extensive scientific possibilities to highlight those with the strongest near term potential. Emerging technologies provide novel approaches to drug discovery, drug delivery and medical therapeutics and are being developed by start-ups and established players. With their high costs, an integrated approach to new products is being pursued and this approach will shape future business opportunities.

JoAnne Feeney, Ph.D.

Dr. Feeney covers Nanotechnology/Nanoelectronics in the Equity Research group at Punk, Ziegel & Company. Prior to joining the firm, Dr. Feeney served as Senior Business Strategist for Albany NanoTech, a \$1.0 billion facility for nanoelectronics innovation at the University at Albany (State University of New York). Using insights from over ten years' experience in the economics of technology and financial markets, Dr. Feeney facilitated partnerships for technology and product development with both established and emerging nanoelectronics firms. She provided expertise on commercialization strategy, paying particular attention to market opportunities, IP valuation, pricing and product development, trade and financial markets, and technology and market risk. She also served as program chair for the 2003 Albany Symposium on the Global Business of Semiconductors and Nanotechnology, where she brought together leaders from the semiconductor industry, equipment suppliers, and nanomaterial innovators to present emerging business strategies for nanoelectronics to an international audience. She holds an M.A and Ph.D. in Economics from the University of Rochester and held previous faculty positions at the University at Albany, the Stern School of Business at New York University, and the University of Colorado at Boulder.

**“A Developing Story:
Metallization of DNA...the Effects, Possibilities and Implications”**

**Michael Connolly, Ph.D.
President & CEO, Integrated Nano-Technologies**

As the limits of conventional circuitry are approached, new technology is needed to continue advancement, while providing additional functionality. Since its inception nanotechnology has been mostly theoretical science. Nature however, has been doing nanotechnology for millennia, using a powerful mechanism called DNA. DNA stores information, performs computations, and builds structures; however manipulating DNA for a specific purpose is what lies between theory and practical application. DNA metallization techniques discovered by the Israel Institute of Technology (Technion) and further developed by Integrated Nano-Technologies are closing the gap between the natural world and the existing world of conventional electronics.

The characteristics of DNA allow it to be 'programmed' to assemble a nearly infinite number of structures. By themselves, these structures are of little use outside the laboratory; however INT's DNA metallization technology will transform such structures into useful components.

Metallization is achieved through a simple and stable process, making DNA both conductive, and rigid. DNA's specificity makes it an ideal mechanism for the creation of electronic components, and for their post-creation manipulation. Technion has published a process for creating DNA-based electronics. This technology is under further development at INT.

Using DNA metallization, INT has developed a sensor to detect biological organisms. This technology is a rapid, PCR-free, low cost, easy to use, and highly accurate genetic assay. The sensor combines a biological and chemical event with microelectronics, to produce a signal indicating the presence of an organism. This sensor has been called “disruptive” technology and will currently in beta testing.

Products using DNA based nano-electronics will appear in the foreseeable future. From materials that can communicate with the devices that they comprise to nano-scale machines performing medical tasks currently dependent on high-risk surgery, this technology will revolutionize every industry it touches.

Michael Connolly, Ph.D.

Dr. Connolly is the CEO and Chairman of the Board of Integrated Nano-Technologies. He is also the inventor of the company's technology and company founder. After receiving a BA from the Integrated Sciences program at Northwestern University, Dr. Connolly went on to be awarded a PhD in molecular biology and biochemistry also from Northwestern. He then completed a post-doctoral fellowship in the Department of Microbiology at the University of Illinois Medical Center in Chicago. Dr. Connolly then went on to studies at Cornell Law School, during which time he worked as a patent agent for a prominent law firm. After receiving his JD from Cornell, he practiced as a patent attorney at Nixon Peabody, LLP, playing a significant role in the licensing strategy for a major genomics company, as well as patenting, protecting and licensing technologies for several major companies and universities. Dr. Connolly's background in multiple sciences enables him to

work well with personnel in a variety of disciplines necessary to round out INT's successful nano-scale bioelectronics development team. In addition, his experience in law and intellectual property ensured that INT was founded and operated on a solid patent and business foundation. Dr. Connolly has patented numerous inventions and is a frequent speaker in diverse fields such as microfluidics and defense industry contracting.

The Seventh Annual
BEACON Symposium and Technology Fair
Bionanotechnology: The World of Small in Medicine

POSTER ABSTRACTS

Name: Becket Greten-Harrison, Susmita Bhandari, Abigail Garrity, J.Harry Blaise
Trinity College, Depts. of Engineering and Neuroscience

Title: *Hippocampal Plasticity is Dependent on Stimulus Frequency in 30-day old Rats*

There has long been speculation on what exactly is the key to learning. Recently, Long-term depression (LTD) and Long-term potentiation (LTP), mechanisms of activity-dependent synaptic plasticity, have been implicated with learning and memory. It has been shown that there is a frequency dependent transition from LTD to LTP in the perforant pathway/dentate gyrus synapse of rats, which varies as a function of age. Previous research has shown that in adult (90 days) and immature (15 days) rats, sustained low frequency stimulation (LFS) results in the depression of synaptic activity and sustained high frequency stimulation (HFS) in the excitation of activity. This transition frequency is found to be significantly lower in immature rats than in mature ones. In the present study, we carried this investigation of age-dependent synaptic plasticity further by examining responses in 30 day-old rats to determine how this intermediate age group compares with 15 and 90 day old animals. This also permits us to assess any changes occurring in synaptic plasticity during the critical period between 15 and 90 days of age. Changes in Field EPSP (Excitatory Post-Synaptic Potential) slope and Population Spike Amplitudes (PSA) from the original baseline readings were used as vectors for measuring changes in the direction and strength of synaptic plasticity in 30 day-old rats in the vigilance state of quiet waking after sustained stimulation at varying frequencies (900 pulses). Tetanization of the perforant pathway occurred at frequencies ranging from 1 to 30 Hz. Our findings indicate that the transition from LTD to LTP occurs between 7 and 20 Hz, thus lying intermediate to those of 15 and 90 day old rats. These results suggest a rapid development of brain systems involved in the establishment and maintenance of bi-directional synaptic plasticity in rats 30 days of age. We are now in the process of obtaining data in animals as young as 10 days of age in order to more completely characterize age-related alterations in hippocampal plasticity.

*This study was made possible through funding from NSF Grant 0342594

Name: Douglas J. Adams, Vilmaris Diaz-Doran, and Stephen A. Santangelo
MicroCT Facility, Department of Orthopaedic Surgery University of Connecticut Health Center

Title: *Trabecular Bone Micro-Architecture at the Tibial Site of ACL Graft Incorporation*

Reconstruction of a ruptured anterior cruciate ligament (ACL) of the knee involves fixing graft tissue within tunnels cored in the distal femur and proximal tibia. The integrity of trabecular bone is critical in achieving strong initial fixation and subsequent incorporation of graft tissue, and is more problematic in the tibia due to relatively less dense and weaker trabecular bone. This study quantified the micro-architecture of 24 trabecular cores removed from a 14 to 57 year-old age spectrum of patients undergoing ACL reconstruction. Bone mineral content and area-projected density were measured using micro-DXA, revealing a 3.8-fold range in density (80-304 mg/cm²). Volumetric bone density (147-366 mg/cm³) and volume fraction (26-64%) were measured using high-resolution quantitative CT imaging, each reflecting a 2.5-fold range. Three-dimensional micro-architecture was imaged at 20 μ m resolution using micro-CT, providing accurate measures of trabecular volume fraction varying from 9.4-33.9% (3.6-fold range), with concomitant profound differences in trabecular thickness and organization. No correlation with patient age or gender was evident, but a long interval between ACL injury and surgical repair was associated with lower density. Collectively, these results suggest that patient-specific measures of bone quality should be considered in order to maximize initial graft fixation strength and subsequent incorporation.

Acknowledgments: NIH AR46026. The authors thank Dr. Carl Nissen and Dr. Robert Arciero for providing tissue samples.

Name: Thomas Barry and Aaron Beal, College of Engineering, Technology and Architecture, University of Hartford

Title: *Safety Enhancement of Wheel Chairs*

Even with today's crosswalk ramp standards an individual in a wheelchair will often be faced with the challenge of descending off a curb. For younger and athletic individuals this is less of a problem since they will simply wheelie off the curb. The problem here is that not everyone has the strength, agility, or balance to accomplish this. Studies have shown that approaching a curb without performing this sometimes impossible feat can have bad results^{1'2'3}. It is therefore necessary to market a design that not only handles this situation but is affordable, simple, robust, and efficient.

Quality function deployment (QFD) tools were utilized to arrive at the engineering needs described in this paper. Conceptual and detail designs were generated; the best chosen based on the merits most important to the QFD. A design was completed. Manufacture of a prototype has begun. This poster will offer a description of that design, how that design was developed, and also why it is superior to existing wheelchairs on the market today.

Name: Sarvesh Kumar Agrawal, University of Massachusetts, Amherst

Title: *Polymer Hydrogels for use in Drug delivery and Tissue Engineering*

Biodegradable and biocompatible polymers made from Poly(lactide)-poly(ethylene glycol)-poly(lactide) have attracted a lot of attention recently because of their property to form hydrogels, which has potential applications in drug delivery and tissue engineering applications. We have investigated here the microstructure of these gels through light and neutron scattering and its mechanical properties using rheology. We have also performed comparative study of PLA-PEO-PLA copolymers where the PLA block has been made from crystalline L-lactic acid (LLA) versus those made from a mixture of D and L lactic acid (DLA), which is amorphous. A significant difference in microstructure and mechanical strength of the two series of polymers was seen. This difference in microstructure has important implications for use of these polymers in drug delivery applications. The mechanical properties were also found to be strongly dependent upon the molecular weight of hydrophobic PLA block. Thus we can tune the mechanical strength of these gels depending upon the specific application we need it for. The value of elastic moduli of these gels is in the same range as several soft tissues, making these materials excellent candidates for a variety of tissue engineering applications. The profiles for release of drugs (e.g. sulindac, tetracaine) from dilute solutions of these polymers show an almost zero order release behavior that continues slowly and steadily over several days and is found to be strongly dependent on the chemistry of the PLA block and the hydrophobicity of the drugs.

Name: Mauricio Barrero and Douglas J. Adams, Skeletal Micromechanics Laboratory, Department of Orthopaedic Surgery, University of Connecticut Health Center

Title: *A Fracture Toughness Test for Rat Cortical Bone*

Assessment of skeletal strength in small rodents relies on structural tests of whole bones. Strength tests at the tissue level have not been prevalent due to the size difficulty involved in machining standard test specimens. In this study a standard arc-shape fracture mechanics test specimen was adapted for rat cortical bone by machining open-ring specimens from serial femoral cross-sections. Applying ASTM standard E-399 for the arc-shaped configuration, the critical stress intensity factor (K_{IC}) for propagating a crack averaged 0.795 ± 0.170 MPa.m^{1/2} (21% variation). Sensitivity of the test was assessed by denaturing calcified collagen via heat exposure to 150°C, reflecting a 40% decrease in K_{IC} values and acute sensitivity of the test. This study demonstrates that reproducible measurements of fracture toughness (K_{IC}) can be achieved for rodent cortical bone, providing sensitive measurements of tissue strength at the microstructural level. By taking advantage of the circular shape of long bone cross-sections, machining time and cutting artifacts are minimal. Moreover, multiple samples can be obtained from a single long bone, further improving statistical power in hypothesis testing related to bone physiology research.

Acknowledgments: This work was completed with the aid of Major Research Instrumentation grant DBI-0079707 from the National Science Foundation.

Name: Levent Gosterisili, Ronald Adrezin, University of Hartford

Title: *The Quality Function Deployment for a Hospital Bed*

The very first item that a patient needs is as simple as a bed, and most beds that are being used in hospitals use the same technology and the components for many years. Market research for a future hospital bed was conducted and incorporated into a Quality Function Deployment (QFD). This is the first step in the design process and is a powerful and widely used method to define your customers, determine their needs, benchmark the competition, and define engineering parameters and targets, that when met, will lead to a successful product. The QFD diagram, referred to as the House of Quality because of its shape, provides an important view of the customers' needs. Understanding your customer and the environment in which you must compete, is crucial to your problem definition. As part of this research, patients as well as professionals including nurses, physicians and clinical engineers were interviewed. Survey instruments were also used. After completion of the QFD, a functional decomposition was performed followed by employment of Pugh's Selection Criteria.

Name: Hilde Bakke, Amos Howard, Tefo Bubi, Bokani Mtengi, Mpho Musengua, Elifho Obopilwe, Sara Zajac, Ron Adrezin, Juan Garbalosa, University of Hartford

Title: *Development of a Portable Device to Measure Skin Properties*

Persons with diabetes may develop a mild to severe form of nervous system damage, which may lead to sores. As a step towards prevention, an understanding of the skin properties of both diabetic and non-diabetic patients must be gained. For this reason, a portable device to measure the material properties of plantar tissue was designed and built. The input devices used were a stepper motor, a load cell, a displacement sensor, and a dead man switch. Software written in LabView was used for controlling the execution data, data acquisition, calculations, and preparing the final results in the form of a text file. The design was a modification to an earlier design, with three important functions: to determine the physical characteristics of the plantar tissue, to be user friendly and accurate, and to meet FDA specifications for human and machine interaction. The device was tested using foam to collect the load-deformation properties. This data was compared to the load-deformation properties collected with an Instron electromechanical testing device. The data collected using the foam provided the accuracy and precision of our skin property device that was necessary to confirm before research application. Clinical studies will begin shortly.

Name: Ronald Adrezin, Michael Nowak, Thomas Filburn, University of Hartford

Title: *Biomedical Engineering Senior Design at the University of Hartford*

The Biomedical Engineering program at the University of Hartford has required students to conduct an external senior project in a hospital-based biomedical engineering laboratory since inception. This has regularly led to employment and offers to graduate assistantships for our seniors. To ensure that our students implement proper design methodology, our one semester internal senior project was expanded to a full year. The objective of this course is to present the student an opportunity to perform capstone level engineering design in the realm of Biomedical Engineering. The student, with the assistance of a Biomedical Engineering faculty advisor, develops a project utilizing the techniques and principles learned in the Biomedical Engineering curriculum. This project, which culminates in either a physical system or computer model, must have a strong design component. In addition the project must address issues such as safety, manufacturability and cost. Devices developed in past projects have been used in clinical studies. This year's project is a device to aid a person with disability.

Name: Daniel Shepard, Jessica Koranda, Emily Dorward, Emily Reisner, Joshua Griffis, J.H. Blaise, J.D. Bronzino Trinity College, Departments of Engineering and Neuroscience

Title: *Effects of Varying Basolateral Amygdala Prestimulation Protocols on Synaptic Plasticity in the Dentate Gyrus of the Hippocampus in Freely Moving Adult Rats.*

Prior studies have shown that the amygdala, the “gateway to emotion,” has direct connections to the hippocampal formation, one area implicated in learning and memory. It has also been shown that stimulating areas of the amygdala, specifically the basolateral amygdala (BLA) causes glucocorticoid release. Due to the direct connections to the hippocampus, when the BLA is stimulated glucocorticoids released act as neuromodulators helping to shape learning and memory and thus giving memories an “emotional tag.” Learning and memory are often associated with increased synaptic efficacy commonly referred to as long-term potentiation (LTP), and can be measured by quantifying the potentiation of evoked signals recorded at the level of the neuronal population. In the present study, the effect of different BLA prestimulation protocols on the plasticity of the perforant pathway/dentate granule cell synapse was studied. Microelectrodes were chronically implanted into the brain of adult male rats and the animals were allowed to recover. Before LTP induction, the animals were tetanized with one of three protocols: no prestimulation of the BLA, 30 second prestimulation of the BLA, and 1 hour prestimulation of the BLA. Following LTP induction, the population spike amplitude (PSA) and EPSP slope of evoked field potentials were obtained over time. Data analysis showed a correlation between prestimulation protocol and plasticity, where the 30 sec prestimulation animals exhibited enhanced potentiation, while the 1 hr prestimulation resulted in diminished potentiation, or depotentiation. This difference results from a biphasic effect in which the fast excitatory phase serves to “mark” and help in the retention of important events while the slower inhibitory phase acts to weed out unnecessary details. Thus, it appears that under normal conditions BLA activation works to strengthen memory by working via two mechanisms.*This study was made possible through funding from NSF Grant 0342594

Name: Odelia Mualem Burstein, Drexel University

Title: *Methods for Producing Drug Loaded Ultrasound Contrast Agents*

The objectives of this research are to develop methods to produce polymeric ultrasound (US) contrast agents (CA) with the added capability of serving as drug carriers, and study the resulting changes in the process factors that could affect their echogenicity in the medical imaging range. Although about 30 million US diagnostic scans are performed yearly, discrimination between diseased and normal tissue is not possible without the use of CA. Combining imaging and drug delivery functions would enable targeting a drug into a specific disease site, triggering its release at the right time and enabling delivery of relatively high local doses of the drug, thus greatly reducing undesired effects as in the case of systemic administration. This is crucial in cancer treatment where the drugs are highly toxic. This work describes methods to produce and load hollow Poly-lactic acid microcapsules with drugs of different chemical characteristics, by absorption or incorporation. In vitro and In vivo dose response and time response echogenicity of the microcapsules are presented, showing US enhancement of 12-23 dB, a half life of 12-15 min and US triggered drug released for a period of 5 minutes. These results indicate the potential for producing polymeric microcapsules with therapeutic capabilities.

Name: Laura Cimino, University of Connecticut Health Center

Title: *The Effect of the Biochemical Nature of Two Novel Adjuvants on Immune Response*

To evaluate if the biochemical nature of two novel biomimetic crystalline adjuvants influence the innate immune system. C57BL/6 mice were injected intraperitoneally at different time points with 500µg of either monosodium urate monohydrate (MSUM) crystal particles (sieved < 125µm) or calcium phosphate (CaP) crystal particles (sieved < 45µm) in 100µl of phosphate buffer solution (PBS). Additional mice were injected with 100µl of PBS as negative controls. Crystal characterization was performed through x-ray diffraction, Fourier transform infrared spectrophotometry, and particle size analysis. Surface activation markers MHC-class II, CD206, CD11b, CD11c and their respective isotype controls were used to determine the activation status of cells extracted from the peritoneal cavity. Following staining, the peritoneal exudate cells (PECs) were analyzed using a fluorescence-activated cell scanner. MSUM induced significantly greater up-regulation of MHC-class II on the surface of the CD11b positive PECs than CaP, as compared to the PBS control, with the greatest activation occurring at the 24 hour time point. Neither MSUM nor CaP significantly influenced expression of CD206 on the PEC surface. The biochemical nature of crystals influences the up-regulation of innate immunity. This assay can be used to select the most immunologically active crystals for vaccine adjuvants.

Name: Ashley Deliso, University of Connecticut Health Center

Title: *Efficacy of a Novel Chemotherapeutic Drug Delivery System*

In this study, the in vivo and in vitro safety and efficacy of a nanocrystalline calcium phosphate/cisplatin (CaP/CDDP) particulate drug delivery system for intratumoral chemotherapy treatment of solid tumors was investigated. The CaP/CDDP conjugates were prepared through electrostatic binding of an aquated species of cisplatin to the CaP crystals in a chloride-free phosphate buffer. A loading rate of 49-51 mg CDDP/mg CaP was achieved. An in vitro release profile of the CaP/CDDP conjugate was determined over a period of 15 days. The conjugates' performance was evaluated both in vivo and in vitro against a stage IV mammary carcinoma cell line (4T1) and compared to a control dose of cisplatin equivalent to that used clinically. In vitro cytotoxicity tests were performed utilizing the CellTiter96 proliferation assay to determine IC50 values at days 1, 3, 8 and 15. Female BALB/c mice, 6-8 weeks old, received intradermal tumor cell inoculations to initiate tumor growth. Tumors were injected directly with the CaP/CDDP conjugate. Results: Significant tumor growth inhibition was observed after intratumoral injections of the CaP/CDDP conjugate despite the small loss of drug activity observed in the in vitro assays.

Name: Susan Gibbons, PT, PhD, Geraldine Pellechia, PT, PhD, Michelle Fox, SPT, Nicole Leveille, SPT, Carmine Masi, SPT, Thomas Psitos, SPT, Margaret Zabohonski, SPT, University of Hartford

Title: *The Relationships Among Gait Variables, Balance, Fear of Falling, Quality of Life, and Tendency to Fall Among Older Adults*

Purpose: This study investigated the relationships among gait, balance, falling, fear of falling, and quality of life in a sample of older adults. **Subjects:** Twenty-two older adults (age 75—96) from a convenience sample of individuals living in two congregate housing centers participated.

Methods: Measurement tools included the GAITRite®, Berg Balance Scale, Survey of Activities and Fear of Falling in the Elderly (SAFE), Short Form 36 (SF-36), and a health history questionnaire.

Data Analyses: Multiple regression analyses were used to explore relationships among the variables, and to predict tendency to fall and health related quality of life. **Results:** Multiple regressions revealed that the best predictor for tendency to fall was a combination of decreased fast gait speed and subjects' fear of falling (adjusted R² = 0.30). The best predictors of social functioning on the SF-36 were the participants' fear of falling and their scores on the Berg Balance Scale (adjusted R² = 0.227).

Conclusion/Clinical Relevance: Gait speed and fear were important predictors of tendency to fall in this sample, while Berg scores and fear were important predictors of components of health related quality of life. Results suggest a multi-dimensional approach to predicting an older adult's tendency to fall and quality of life.

Name: Seunglee Kwon, Drexel University

Title: *The Development of PLA Nano-dispersion System for Cancer Site Imaging*

In this study, a PLA nano-dispersion system was designed for targeting and imaging of cancer sites. PLA is a FDA-approved polymer, which is biocompatible and biodegradable. Nanoparticles between 100 nm and 300 nm would allow delivery into the cancer site specifically via the EPR (Enhanced Permeability and Retention) effect. Also, by reducing RES uptake and renal excretion, the nanoparticles would have longer circulation time under physiological conditions with minimal side effects. This advantageous system was prepared by a single emulsion solvent diffusion method and optimized. Camphor, which makes the nanoparticles hollow enabling gas introduction, was added to offer echogenicity to the particles. Dynamic light scattering (DLS) results demonstrated that these nanoparticles have approximately a 200 nm unimodal distribution. AFM results showed that the nanoparticles have an elliptic shape and supported DLS results. And under the physiological pH and ionic strength, the nanoparticles stable enough to maintain their size and distribution. Thus, we can conclude that this PLA nano-dispersion system has the potential for creating amultifunctional particle acting as a cancer targeting molecule, a contrast agent, and further a drug carrier.

Name: L. Priest, L. Stadmeyer, V. Deregowski, E. Gazzo, and E. Canalis
Saint Francis Hospital and Medical Center

Title: *Notch Overexpression Impairs Osteoblastogenesis Exclusively by Downregulating Wnt Signaling*

Notch is a family of transmembrane receptors that mediate signaling mechanisms controlling cell fate decisions. Notch activation requires a regulated intramembranous proteolytic cascade leading to the release of Notch intracellular domain (NotchIC) and its nuclear translocation. Overexpression of NotchIC in ST-2 stromal cells results in depresses osteoblastogenesis and the response to bone morphogenetic protein 2 (BMP) and enhanced adipogenesis. The mechanisms involved are not known, but interactions between Notch1 and Wnt/ β -catenin may explain the effects observed, since they have opposite effects on cell differentiation and fate. NotchIC overexpression in stromal cells opposes Wnt/ β -catenin signaling, decreasing the activity of the Wnt/ β -catenin responsive construct, pTOPFLASH, containing Tcf4/Lef1 binding sequences upstream of the luciferase gene, by 50%. NotchIC overexpression induced low density lipoprotein receptor (LRP) 1 mRNA, providing a mechanism for Wnt downregulation since LRP-1 interacts with the Wnt receptor Frizzled to repress Wnt binding and signaling. Moreover, NotchIC overexpressing cells expressed lower β -catenin levels by Western blot analysis. In accordance, transfection of a stable mutant β -catenin expression construct rescued the inhibitory effect of NotchIC on transfected pTOPFLASH constructs. To exclude additional mechanisms involved in the inhibition of osteoblastogenesis by NotchIC, we explored whether Notch1 modified the BMP dependent Smad or mitogen activated protein (MAP) kinase signaling pathways. BMP-2 induced phosphorylation of Smad 1/5/8 and enhanced the transactivation of a transiently transfected BMP-responsive 12xSBE-Oc-pGL3 construct, containing 12 repeats of a Smad binding site directing luciferase expression, but NotchIC overexpression did not modify the level of phosphorylated Smad 1/5/8 or the transactivation of the 12xSBE construct in control or BMP-2 treated cells. BMPs had no significant effect on the phosphorylation of the MAP kinases ERK, p38 or JNK, or on the transactivation of a transfected construct containing seven AP-1 binding site repeats directing luciferase expression, in either control or NotchIC overexpressing cultures. These results indicate that whereas NotchIC overexpression prevents BMP-2 induced osteoblastogenesis, it does not inhibit Smad or MAP kinase signaling pathways, but it impairs Wnt/ β -catenin signaling, possibly by inducing LRP-1. This also suggests that maintaining Smad/MAP kinase signaling is not sufficient for BMP-2 dependent osteoblastogenesis.

Name: Larry Deutsch, M.D., Assistant Clinical Professor of Pediatrics, UCONN Health Center;
Children's Health Network

Title: *The Children's Health Network*

The Children's Health Network has been a unique software-development project originally funded by the U.S. Public Health Service, Maternal and Child Health Bureau. It created a basic remotely accessible computer-based medical record for infants and children, migrant workers, and others for whom health care is improved by better accessibility to personal health data. The system will also yield tracking information for public health and research areas. Proceeding from software which is currently in the public domain, technical innovations available now provide opportunities for further development and distribution of an enhanced product. Features (handheld, wireless, voice recognition, Web-based) will make such a program of great interest and modest expense to health providers in a wide range of office and clinic settings. Support from investment and grant-based sources will allow contracting for revision, training, publicity, and distribution. At the BEACON Tech Fair, the system will be detailed and demonstrated, with discussion of options for production and expansion.

Name: Roman Pichardo, Joseph Adam, Eric Rosow, Joseph Bronzino, Leonard Eisenfeld

Title: *Vibrotactile Stimulation System to Treat Apnea of Prematurity*

We modified a system that uses vibrotactile stimulation (VTS) to treat apnea (a cessation of respiration) in neonates in order to make the system more portable and easier to use by clinicians and nurses. The biomedical engineering department at Hartford Hospital (Hartford, CT) together with the Neonatology Division at the Connecticut Children's Medical Center (CCMC) (Hartford, CT), has been involved in developing the VIS system. Clinical trials were conducted in the neonatal intensive care unit of CCMS, and further preliminary data were collected. The main components of the system are a Tacaid vibrotactile stimulator (Audiological Engineering, Somerville, MA), a neonatal physiological monitor (Model 511; CAS Medical Inc., Branford, CT) a laptop computer running Windows 95 by Microsoft, National Instruments data acquisition cards DAQCard-1200 and DAQCard-5102.

Name: John Young Oh, Eric Rosow, Director Clinical Engineering, Hartford Hospital
Joseph Bronzino, Department of Engineering, Trinity College
John Enderle, Department of Engineering, University of Connecticut
Leonard Eisenfeld, Hartford Hospital

Title: *The Design and Development of a Biosensor to Measure the Concentration of Meconium in Amniotic Fluid*

Meconium aspiration syndrome occurs in 0.2% to 1% of all deliveries and has a mortality rate as high as 18%. The disease is responsible for 2% of all perinatal deaths. Meconium may be classified as being thick or thin, but this assessment is normally performed visually by clinicians. A "meconium-crit" analysis has been developed to objectively define the concentration of meconium. However, this analysis does not provide real time continuous readings. This study focused on the design and development of a sensor to provide an objective, continuous, real-time assessment of meconium thickness. Meconium has an absorption spectrum centered at 410 nm and observes Beer's law. Blue light centered at 430 nm was delivered through meconium solutions, and a photodiode translated the strength of the incoming light into a voltage. This voltage was analyzed by a microcontroller to determine the concentration of meconium.

Name: Joseph H. Mclsaac, III, MD, MS, Hartford Hospital/University of Connecticut

Title: *The Electronic Esophageal Stethoscope*

Currently to monitor a patient's heart and lung sounds during a surgical procedure, the anesthesiologist must listen through the esophageal stethoscope continuously. This is impractical considering the many tasks of the anesthesiologist throughout the operation, and as such decreases the effectiveness of this tool for monitoring purposes. Other researchers have studied the esophageal stethoscope against the standard external stethoscope using computer-assisted frequency analysis, and determined that the esophageal produced better sound quality overall. The present study aimed to completely automate the auscultation process during general anesthesia by recording the heart and lung sounds from an esophageal stethoscope onto a laptop computer, and then analyzing them through joint time-frequency representation in order to pick out pathologies and abnormalities. Five different programs and algorithms were tested to determine which produced the best graphical breakdown of the signal. Of the five, the Spectrogram algorithm yielded the most conclusive results; further experimentation will be required to find the optimal analysis set-up. The eventual goal of this research is computerized diagnosis of heart and lung sounds throughout surgery.

Name: Joseph H. Mclsaac, III, MD, MS, Hartford Hospital/University of Connecticut

Title: *The Surgical Cooling Garment*

The present system for maintaining surgeon thermal balance in the operating room requires a cold operating room (<60 deg F). This causes severe patient hypothermia requiring special warming devices which are only partially effective and cost > \$100,000 per year in direct costs and >\$2400 of complications per hypothermic patient. Cooling the surgeon and staff with non-disposable devices while keeping a warm OR changes the thermal balance in favor of both patient and surgical staff while eliminating both disposable costs and the cost of complications. This study represents a collaborative effort between Hartford Hospital, Hamilton Standard, and Mountain Laurel Biomedical. Data collected will result in development of a cooling device which will ultimately be used to prevent patient hypothermia, maintain surgeon comfort, and reduce costs.

Name: Joseph H. Mclsaac, III, MD, MS, Hartford Hospital/University of Connecticut

Title: *The Brain Temperature Tunnel: A New, Non-invasive Temperature Technique*

Maintenance of brain temperature during surgery is a crucial element in producing positive patient outcomes. However, there are no methods currently available to monitor core temperature in a non-invasive manner. Evidence has been discovered that a small area of skin between the eyes and nose may reflect the temperature of the brain, and has been called the brain temperature tunnel. The aim of the present pilot study was to perform a preliminary evaluation of the potential use of this brain temperature tunnel to continuously and non-invasively monitor brain temperature during anesthesia. The results of the present study provide encouraging evidence that the brain temperature tunnel may be able to be exploited to monitor core temperature during anesthesia.

Name: Kelleny Oum, School of Biomedical Engineering, Drexel University

Title: *Ultrasound Contrast Agents Targeted to Malignancies: Optimization of Cellular Attachment*

The objective of this study is to evaluate the influence of surface density and spacer length of Arg-Gly-Asp (RGD) peptide when conjugated to Polylactic acid (PLA) microspheres, on extent of attachment to human breast cancer cells. PLA microspheres were developed by us as diagnostic ultrasound contrast agents (CA) to enhance the ultrasound image. Surface modification promotes CA targeting to a specific address within the body which is ideal for both diagnostic imaging and/or targeted drug delivery. The RGD peptide sequence targets $\alpha_5\beta_3$ integrins, cell-surface receptors over-expressed in cancer and angiogenesis. RGD peptide was covalently bonded to the surface of our PLA microspheres. The optimal density of peptide was found to be 1:2 (RGD: PLA carboxyl). At this ratio there was a 1.7 microcapsule/cell attachment to human breast cancer cells in vitro. Studying the effect of varying length glycine spacers between the RGD peptide and microsphere surface revealed that a 3.5 angstrom spacer had the best attachment to cells. These results indicate that the amount of RGD peptide conjugated and its distance to the surface of the PLA microcapsules plays a role in targeted contrast agent performance and should be considered during the optimization of this agent.

Name: Joseph L. Palladino, Ph.D., Department of Engineering, Trinity College

Title: *Muscle and Heart Dynamics*

The mechanical complexities of contracting muscle or the pumping heart demand novel nonlinear and time-dependent equations of motion. A new, compact analytical function describes the main features of muscle contraction, with muscle acting as a force generator that is time, muscle length, and shortening velocity dependent. An analogous function describes the heart's left ventricle as a pressure generator that is time, ventricular volume, and ventricular outflow dependent. These two models may be used to study how the ventricle's complex pumping properties arise from its constituent muscle dynamics. An important feature of both models is the independence of description of the source (muscle strip or ventricle) from its load (arterial vessels or applied muscle load).

For muscle strip, one equation is able to describe isometric force, isotonic shortening and lengthening of muscle length, and force transients that arise from small, rapid changes in muscle length. For the ventricle, one equation is able to describe isovolumic pressure, normal ejecting pressures, volumes, and ventricular outflow, and pressure transients that arise from small, rapid changes in ventricular volume. This new approach also permits dynamic computation of muscle or ventricular elastance. Elastance is now independent of loading conditions and, consequently, is a measure of muscle or ventricle performance.

Name: William Dyckman, Elio Morgan, Joseph Mitchel, Charles White, Hartford Hospital

Title: *Topical Administration of Pharmacologic Agents for the Treatment of Arterial Spasm in a Porcine Model*

The porcine model has become the animal of choice for pre-clinical evaluation of interventional devices and surgical techniques, prior to human application. There are anatomic and physiologic similarities shared with humans, such as cardiac and vascular anatomy and physiology. A major limitation of the porcine model is the severe degree of arterial vascular spasm frequently encountered during surgical cut down or handling of arterial vessels. There is no standard of practice for the use of topical vasodilators used for treatment of vascular spasm in the porcine model. Due to the lack of information in the animal literature, regarding the optimal treatment of porcine arterial spasm, the goal of this study is to evaluate the anti-spasm effects of low and high dose lidocaine.

Name: Dheepak Rajasekaran, University of Connecticut

Title: *Design and development of and equipment replacement planning tool*

Replacement requests for healthcare technology and equipment in hospitals are often managed on an ad hoc basis by capital planning committees in conjunction with the department of clinical engineering. By using a systematic approach based on available data and equipment performance criteria when evaluating medical technology for replacement, a plan can be designed to identify equipment most in need of replacement, maximize the utilization of capital budget resources and increase efficiency of the healthcare process. This paper explains the development of an Equipment Replacement Planning System (ERPS), which uses a rule based expert system to the existing medical equipment management database to prioritize the equipment replacement. An expert system will be programmed with a knowledge/rule base to evaluate the imported data and produce a Relative Replacement Number for each medical device currently owned by the hospital. This number will enable prioritization of all devices in the hospital's inventory identifying the recommended order of replacement. This ERPS will be designed such that replacement criteria can be custom edited for each hospital that will use the system, according to its own requirements and restrictions.

Name: Reenajit Kaur, University of Connecticut

Title: *Design and Evaluation of an Asset Tracking System*

The proposed thesis will focus on the design and development of a Mobile Asset Tracking System to improve the current medical equipment maintenance practice at Hartford Hospital. In addition, the proposed thesis will prepare a Return on Investment (ROI) study to test the feasibility of installing a hospital-wide asset locating system.

The thesis presents the capability of a mobile device, for example a handheld, to continuously, and in real-time, determine the position of valuable medical equipment from a distance within a physical space via wireless technologies currently available. Additionally, the asset tracking module on the handheld would allow technicians to have pertinent information regarding the equipment such as account number, location code and preventive maintenance (PM) history. Ultimately, the asset tracking module would communicate directly with the Computerized Maintenance Management System (CMMS) to allow technicians to pull-up work orders from our central data repository (WOSYSTÒ) Database and have them available while carrying out repairs on medical equipment on the floors.

In this study, infusion pumps are treated as high loss items that need to be incorporated into an asset tracking system to be able to continuously and in real-time monitor the location of the pumps. The need for a tag attached to each infusion pump containing information such as control number and PM history, with the ability to communicate this information to a reader and to a handheld that the technician would carry on PM rounds.

Based on the asset tracking prototype developed, an evaluation and ROI will be carried out to determine the feasibility of installing a hospital-wide asset tracking system. The ROI will examine variables such as budgetary pressures, CMI, space constraints and wireless interference to achieve cost benefits such as savings or expense prevention and improvements in qualitative measures.

Name: Uduak Effiong, Catholic University of America

Title: *Gum Arabic Surface-modified Magnetic Nanoparticles for Cancer Therapy*

The objective of this study is to investigate the influence of Gum Arabic(GA)-modified magnetic nanoparticles(MNP) on cancer cellular uptake. The ultimate goal is to develop a technique to promote selective uptake of magnetic nanoparticles by cancer cells for cancer treatment. A novel use of magnetic fields and magnetic particles is to deliver therapeutic drugs at the desired time in the correct dosage to the correct site in the human body. In studying the physical and chemical properties of the GA-coated particles, Fourier transform Infrared(FTIR) spectroscopy was carried out which possibly showed the Absorption spectrum the Gum Arabic, iron(III) oxide magnetite, magnetite + GA as well as providing information regarding the functional groups responsible for their respective molecular binding. Transmission electron microscopy (TEM) indicated that Prostrate cancer cells sustains growth and interacts with the GA treated nanoparticles at the membrane. In this project, TEM and fluorescence (FTIC) was used to observe the surface characteristics of the molecular interactions between GA and MNP and the cancer cells as well as fundamentally understanding the influence GA-coated nanoparticles have on cellular growth.

Name: Kurt Breitenkamp, University of Massachusetts Amherst

Title: *Self-Assembly and Crosslinking of Amphiphilic Graft Copolymers-Hollow Capsules for Drug Delivery*

This poster describes the synthesis of hollow capsules produced by oil/water interfacial assembly and subsequent cross-linking of amphiphilic graft copolymers. Polycyclooctene-g-poly(ethylene glycol) (PEG) copolymers are synthesized by ring-opening metathesis polymerization (ROMP) of PEG-functionalized cyclic olefin macromonomers to afford graft copolymers with a number of tunable features, such as PEG density, length, and graft connectivity. These copolymers segregate to the interface of organic solvents and water and can be covalently crosslinked through reaction of unsaturation within the polymer backbone or through reactive grafts. This crosslinking imparts mechanical integrity to the capsules and results in an ultrathin, polymer membrane, which can be utilized to regulate drug diffusion. This strategy can be used for the preparation of encapsulants and carriers of hydrophobic molecules such as the potent chemotherapy drug Doxorubicin (DOX) and may be well suited for controlled release therapies, where the transport of drugs and drug conjugates can be tuned by variation of membrane chemistry and properties. The copolymerization of cyclic olefins containing oligopeptides and other bio-functionality offers additional opportunities for the targeted delivery of these capsules to cancerous cells and tissue.

Name: Anthony Shrout and Frances Antommattei, University of Massachusetts Amherst

Title: *Two-dimensional Concentrations of Receptor Fragments Modulate Signaling Activity in a Surface-Templated System*

Both eukaryotic and prokaryotic cells respond to stimuli using processes that often involve the recruitment of signaling proteins to the inner and outer membrane surfaces. Also, in the two-dimensional (2-d) space on the membrane, ligand-binding can stimulate trans-enzymatic events, e.g. transmethylation of bacterial chemoreceptor proteins and transphosphorylation of eukaryotic receptors. These phenomena reflect the importance of clustering and 2-d concentration in signaling. Previously, we used a template-directed method to assemble and restore biochemical activity to the cytoplasmic signaling proteins of the E. coli chemotaxis system (kinase CheA activation and receptor methylation), using a histidine-tagged cytoplasmic fragment of the aspartate receptor (HTCF) and Ni-NTA lipid vesicles [Shrout et al. 2003. *Biochemistry*, 42, 13379]. Here, we used this method to vary the 2-d [HTCF] (at a fixed volume concentration), which influenced CheA activation and HTCF transmethylation significantly. The HTCF methylation rate increased 10-fold when the 2-d [HTCF] was increased ~ 10-fold and the kinase activity of CheA increased 20-fold when the 2-d [HTCF] was increased ~5-fold. The increase in CheA activity depended on the level of covalent modification on the HTCF in a way that was consistent with pre-clustering of HTCF at higher levels of covalent modification. (NIGMS RO1 53210 to RMW)

Name: Anthony Shrout and Frances Antommattei, University of Massachusetts Amherst

Title: *Activation of Cellular Signaling Pathways by Template-Directed Assembly of Receptor Fragments*

Cell membranes play important organizing roles in signaling, such as facilitating specific interactions between transmembrane receptors and cytoplasmic proteins. In the *E. coli* chemotaxis pathway, the inner membrane imposes a lateral organization among chemoreceptors, which seems essential for forming the protein complexes that activate and regulate the signaling kinase, CheA. To alleviate the difficulties commonly encountered in reconstituting transmembrane receptors, we developed a method that mimics the inner surface of the cytoplasmic membrane and used it to study the properties of CheA activation. Sonicated vesicles containing Nickel-NTA lipids were used to template the assembly of a histidine-tagged cytoplasmic domain (C-domain) derived from the aspartate receptor. In the presence of the coupling protein CheW, vesicle-anchored C domains were able to bind and activate CheA, at levels similar to the signaling complexes of CheA formed with intact receptors. The activity of surface-bound CheA did not depend on covalent modification, which was determined using C domains prepared in low, medium and high modification levels. However, the combined results of vesicle binding and CheA activity measurements demonstrated that the extent of vesicle-bound (C-domain/CheW/CheA) complex assembly increased significantly with covalent modification. When the data were analyzed using simple model based on pair-wise binding equilibria, estimates for the stability of the complex increased 100-fold from the lowest to the highest level of covalent modification. This change in complex stability may plausibly serve to regulate CheA activity in the cell. Supported by NIH Grant RO1 GM53210.

Name: Anthony Shrout and Frances Antommattei, University of Massachusetts Amherst

Title: *Chemical Detection Modules Engineered From Bacterial Signaling Proteins*

Proteins in bacterial chemosensory pathways represent a diverse set of reagents from which self-assembling 'chemical detection modules' (CDMs) can be fabricated. These cellular signaling units consist of receptor proteins that are coupled to intracellular enzymes, which amplify the specific ligand binding events. Typically, the receptor proteins span the membrane to convey the information about external ligand concentrations to the cell interior. However with the advent of bacterial genomics, it has become apparent that a number of receptors sense and respond to ligands inside the cell. This arrangement has a distinct advantage for chemical sensor applications, since it provides the means to bypass challenging aspects of receptor reconstitution through the use of a template-assembled system for assembling signaling proteins (Shrout et al. 2003. *Biochemistry*, 42, 13379). When 'cis'-membrane and/or soluble receptors are used with the template-directed assembly method, the development of a CDM reduces to protein engineering efforts to (i) redirect receptor binding specificity, and (ii) improve the performance of the coupled receptor-enzyme system. Here we have focused on improving the behavior of the receptor-coupled enzyme system, with specific efforts to (i) incorporate receptor proteins with a sensing domain, (ii) increase the stability and enzymatic activity of the template-assembled system, and (iii) elucidate the underlying basis for cooperative regulation of the amplifying enzyme (CheA). CDMs are adaptable to high throughput and array detection methods, which will facilitate the generation and implementation of sensors with selectable ligand binding specificity and sensitivity.

Name: Corin Williams, Boston University

Title: *Controlling Vascular Smooth Muscle Cell Phenotype Through Substrate Topography*

In order to engineer a functional blood vessel in vitro, the in vivo characteristics of vascular smooth muscle cells (VSMCs) must be preserved. In the native artery, VSMCs maintain an elongated, contractile phenotype and are highly organized in circumferential layers. However, in culture or during vascular disease, VSMCs switch to a proliferative phenotype and become disordered. Our main objective was to test whether substrate topography that mimics in vivo structural arrangements can be used to control VSMC morphology and organization and hence slow phenotypic modulation. We also investigated whether phenotypic modulation is reversible for passaged VSMCs. Primary and passaged VSMCs were cultured on tissue culture polystyrene (TCP) in lanes of varying width separated by non cell-adhesive comb polymer barriers. Primary VSMCs maintained an elongated morphology and alignment parallel to lanes on micropatterned TCP for widths ranging 10 – 40µm. Furthermore, primary VSMCs exhibited organization and localization of proteins characteristic of contractile VSMCs. Passaged VSMCs maintained morphology and protein localization similar to primary VSMCs; however, they showed a higher tendency to bridge over the comb polymer pattern into adjacent lanes. Using this approach, we can therefore systematically investigate the relative importance of physiologically-relevant structural and organizational parameters in controlling VSMC phenotypic modulation.

Name: Shane Mulligan, Staples High School, Westport, CT

Title: *The Construction of a Self-Assembling DNA Nanohexagon Capable of Protein Storage and Release*

On-going developments in the field of nanotechnology will prove it can be effectively applied to biomedical engineering. To date, the limited control scientists have at the molecular level has constrained their ability to create nanoscale structures that have structural integrity with a high degree of precision. DNA holds massive, untapped potential to revolutionize nanotechnology given its complementary and controllable base-pairing nature. This project entails the synthesis of DNA self-assembling triangles linked together using rigid DNA sticky ends to form a hexagonal shape with a hollow center. The long-term goal of this project is to create self-assembling nanostructures in a calcium-rich environment that can selectively bind magnesium dependent enzymes. The resulting hollow cored nanohexagons represent a new structural motif in nanotechnology that could act as protein storage and release devices for biomedical applications.

Name: Anes Aref, University of Bridgeport

Title: *The New Long-Range Model for Membrane Protein Folding*

Understanding the folding process of membrane proteins is a fundamental biomedical challenge that has lagged behind that of soluble proteins due to the hydrophobic nature of the membrane proteins. The shape a protein takes after undergoing the folding process determines the function of the protein. We propose a new model for membrane protein folding that states that long-range interactions between amino acids from both loop and transmembrane helices take place during the very early stages of folding, before and during the formation of helices. To test this model, we use a computational method to predict protein folding nuclei from native state structures that is based on a constraint network model of freely rotating rods. This method uses an all-atomic analysis of the rigidity and flexibility of protein structures, which includes specific hydrophobic, polar and charged interactions. Application of this method to bacteriorhodopsin, halorhodopsin, sensory rhodopsin in the presence and absence of transducer and mammalian rhodopsin is presented. We find striking differences in the predicted folding pathway of these structurally related proteins with different functions, that suggest a relationship between folding mechanism and functional protein machinery.

Name: Jessica Koranda, Jesse Turcotte, Joshua Griffis, J.H. Blaise, Susan Masino, and J.D. Bronzino, Trinity College, Departments of Engineering and Neuroscience

Title: *LTP Induction in the Dentate Gyrus of Freely Moving Adenosine 1 Receptor Deficient Mice*

Previous studies have shown that adenosine receptors are densely located in the hippocampal formation. The hippocampus represents one of many locations in the brain where long-term potentiation (LTP), a phenomenon thought to be associated with increased synaptic efficacy and plasticity, has been observed. Furthermore, A1 receptors are coupled to the activation of potassium (K⁺) ion channels and inhibition of calcium (Ca²⁺) channels. Thus, under normal physiological conditions, A1Rs have an overall inhibitory effect in the CNS, working primarily on presynaptic glutamatergic neurons.

Glutamate, in turn works to activate NMDA receptors, which have been implicated in the process of learning and memory. Therefore, a reduction in NMDA receptor activation and an overall suppression of brain activity is often associated with extracellular adenosine. It is hypothesized that this inhibition works to produce neuroprotective measures. In order to assess the role of adenosine on synaptic plasticity in the hippocampus, LTP was induced via tetanization in freely moving A1 knockout mice, which lack the gene coding for the A1R. Microelectrodes were chronically implanted in the hippocampal I perforant path and dentate gyrus. After recovery animals, were then tetanized at an intensity of 300 uA at 100 Hz. Over time, the population spike amplitude (PSA) and the excitatory postsynaptic potential (EPSP) slope were recorded from evoked responses. Preliminary data shows a trend in which immediately following tetanization, LTP is enhanced. This correlates back to the fact that A1 receptor activation has an overall inhibitory effect in the CNS. Thus by eliminating A1Rs, neurons have an increased ability to be excited. However, elimination of the A1R also eliminates the neuroprotective properties associated with the receptor, which might imply extensive excitation can lead to neuronal death.

Name: Vishal Kamat, Drexel University

Title: *Surface Enhanced Raman Spectroscopy for Intracellular Characterization*

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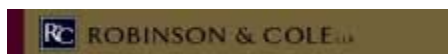
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