

# Biomedical Engineering Research Projects 2007-08

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## **SGER: Fabrication of Nanoporous Membranes for Enhanced Treatment of End-Stage Renal Disease**

*Narayan, Roger*  
UNC - UNC Chapel Hill  
\$25,000  
8/1/08 - 7/31/09

We hypothesize that novel reactive oxygen species scavenging agents may be used to protect end-stage renal disease patients from these conditions. We will use high resolution transmission electron microscopy and X-ray diffraction to examine the structure of reactive oxygen species scavenger-functionalized nanoporous alumina membranes. We will also examine cell proliferation on these novel membranes using lung cells, neuronal cells, keratinocyte cells, and other cancer-relevant cell types. We will assess the genotoxicity of reactive oxygen species scavenger-functionalized nanoporous alumina membranes using both mammalian and bacterial cell models. Finally, we will examine the ability of reactive oxygen species scavenger-functionalized nanoporous alumina membranes to reduce reactive oxygen species levels, quench hydrogen peroxide solutions, and inhibit hydrogen peroxide-mediated DNA damage.

## **The Rational Design of Textiles for Surface Hemostasis**

*McCord, Marian*  
UNC - UNC Chapel Hill  
\$30,000  
9/1/08 - 8/31/10

The goal of this research program is to combine recent advances in polymer and fiber science with new knowledge about processes for surface (topical) hemostasis to produce an advanced generation of textiles for control of hemorrhage. Research will proceed in three stages. First, the surfaces of natural and synthetic fibers will be modified with respect to charge, hydrophobicity, and geometrical arrangement of chemical moieties to maximize the activation of hemostatic processes. Secondly, the ability of the modified fibers to turn over the humoral coagulation cascade, activate platelets, and render red blood cells hemostatic, will be quantified. Finally, candidate fibers will be used to produce textiles that will be tested in animal models for the ability to control hemorrhage.

## **MR-Derived Cerebral Oxygen Metabolism as a Predictor of Infarction**

*Lin, Weili*  
UNC - UNC Chapel Hill  
\$16,808  
1/1/09 - 6/30/09

Magnetic resonance derived cerebral oxygen metabolism will be investigated as a predictor of cardiac infarction.

## **Use of Yttrium Oxide Nanoparticles as Reactive Oxygen Species Scavengers For Space Flight Applications**

*Narayan, Roger*  
UNC - UNC Chapel Hill  
\$19,000  
7/1/08 - 6/30/09

Reactive oxygen species, including hydrogen peroxide, hydroxyl radicals, and superoxide anions, have been recently implicated in several neurodegenerative processes. We hypothesize that the unique valence structure and oxygen defect structure of yttrium oxide nanoparticles can be optimized to promote scavenging of reactive oxygen species. This proposed program involves synthesizing yttrium oxide nanoparticle solutions, determining defects in yttrium oxide nanoparticles, and assessing cell interactions with yttrium oxide nanoparticle solutions.

## **The Development of a Plan-to-the-Patient Adaptive Radiation Therapy Package**

*Lalush, David*  
UNC - UNC Chapel Hill  
\$8,620  
3/1/08 - 2/28/10

This project involves the development and testing of a unique X-ray imaging device for attachment to a radiotherapy system. The imaging device makes use of multiple discrete X-ray sources to obtain images from multiple views without the gantry rotation of a CT system. The images obtained will be used to position the patient for accurate radiotherapy. Dr. Lalush's group will develop and evaluate algorithms for the reconstruction of images from the proposed system, and simulate data to determine likely image contrast and effectiveness of images for computer-driven patient positioning.

## **Laser Rapid Prototyping of Patient-Specific Ossicular Replacement Prostheses**

*Narayan, Roger*  
UNC - UNC Chapel Hill  
\$199,582  
7/1/08 - 6/30/11

Our preliminary results suggest that two photon polymerization is able to create medical microdevices with a larger range of shapes and material properties than conventional polymer, metal, or silicon microfabrication techniques. The specific aims of this research and development program will be executed in three overlapping phases. Phase I will involve biological and chemical characterization of Ormocer® materials created using two photon polymerization. Phase II will involve process-oriented computational geometric analysis and process control techniques for two photon polymerization of ossicular replacement prostheses. Phase III will involve mechanical and functional characterization of ossicular replacement prostheses that were fabricated using two photon polymerization.

## **A MEMS-Based Adjustable Stiffness Catheter**

*Walker, Glenn*  
Wallace H. Coulter Foundation  
\$240,000  
8/1/08 - 7/31/10

The goal of this project is to develop a catheter for stent delivery that possesses adjustable stiffness. The project addresses

a crucial clinical need for a catheter that is compliant enough to navigate tortuous blood vessels yet stiff enough to remain fixed during stent delivery. We will use microfabrication and micro-electro-mechanical systems (MEMS) technology to create a catheter containing microscale quantities of magnetorheological (MR) fluids. The actuated MR fluid, via micropatterned electromagnets, will serve to modulate the stiffness of the catheter. We envision the catheter eventually being used in all carotid and intracranial stenting operations. The proposed catheter may even have applications in other surgical procedures not yet realized.

### **Nano-DSC (Differential Scanning Calorimeter): An Absolute Temperature Sensor**

*Walker, Glenn*

*Defense Advanced Research Projects Agency (DARPA)*

*\$40,000*

*10/1/08 - 9/30/09*

The purpose of this project is to develop a second-generation microfabricated differential scanning calorimeter (DSC). The effectiveness of the various materials at insulating the DSC chamber will be modeled and experimentally verified, with a goal of further optimizing DSC design. The amount of time and energy required to bring the chamber to temperature, and how long the chamber takes to cool will also be quantified.

### **Mouse Mucociliary Clearance Imaging Project**

*Lalush, David*

*UNC - UNC Chapel Hill*

*\$13,889*

*BERM Memo*

*1/1/08 - 12/31/09*

To investigate the physiological role of mechanical stresses on mucociliary clearance regulation, we have designed and utilized a number of devices to subject oscillatory shear and compressive stress, mimicking the cyclical forces associated with breathing, to cultured airway epithelial cells derived from normal and diseased human lungs at the time of transplantation. Using these devices, we provide data that is not only important for understanding the role of mechanical forces in the regulation of mucus clearance, but also provides insight into understanding how to modulate this system to maintain/accelerate mucus clearance in patients with chronic obstructive pulmonary diseases, such as cystic fibrosis.

### **Immune-Shielded, Ultrasound-Stimulated Contrast Agents for Molecular Imaging**

*Dayton, Paul*

*Columbia University / NIH*

*\$125,953*

*9/30/08 - 6/30/09*

We propose research studies to examine in detail the physicochemical mechanisms of immune response to ultrasound contrast agents, and we will use this data to design contrast agents which are shielded from this immune response. Simultaneously, we will study the ultrasound interaction with stealth agents that have been shown in preliminary data to be selectively activated by ultrasound radiation force. Collaboration with an ultrasound device manufacturer will allow the modification of a small-animal imaging system for specific optimization to work with the new stealth contrast agents for enhanced pre-clinical imaging. The end goal will be to develop safer ultrasound contrast agents which

will also exhibit increased specificity and circulation time in-vivo, and to improve ultrasound scanner technology to take advantage of new stealth-contrast agents.

### **High-Sensitivity Molecular Imaging With Ultrasound**

*Dayton, Paul*

*National Institutes of Health*

*\$816,048*

*12/1/07 - 8/31/09*

In this proposal, we present a plan to increase the sensitivity of ultrasound to targeted contrast agents over an order of magnitude. This proposal describes a three-part method to achieve the desired substantial increase in sensitivity by combining a completely new contrast agent with a novel contrast agent delivery technique, and we package these improvements with the substantially improved detection strategies only possible due to the improvements in the agent and the delivery. The combined tools and experience of the Joint Department of Biomedical Engineering, North Carolina State College of Engineering, and the University of North Carolina at Chapel Hill School of Medicine, provide a unique and qualified research group for implementing this new system for molecular imaging with ultrasound.

### **Noninvasive Monitoring Glutathione Metabolism in Tumors**

*Gamcsik, Michael*

*National Institutes of Health*

*\$526,875*

*2/27/08 - 1/31/10*

This proposal builds upon the feasibility established in the pilot project and plans to use these methods to monitor glutathione metabolism non-invasively in R3230 mammary, 9L glioma and FSA fibrosarcoma tumors and drug-resistant variants in rats. Glutathione metabolism will be assessed in relation to tumor growth rate, vascularization and expression of key enzymes involved in redox metabolism. Since a drop in intracellular glutathione levels is one of the earliest events in apoptosis, therapy-induced changes in glutathione metabolism detected by magnetic resonance will be an early indicator of tumor response. Since altered redox balance appears to be a universal characteristic of proliferating cells in general and cancer in particular, methods to non-invasively monitor redox metabolism offers new insight into a process critical to planning and evaluating cancer therapy.

### **Human Enterohepatic Cell Model for Predictive Toxicology**

*Gamcsik, Michael*

*UNC - UNC Chapel Hill*

*\$53,461*

*7/1/07 - 6/30/09*

An in vitro system that is a much better model of a human liver is needed. Over the past dozen years this research team has been developing a state-of-the-art multicoaxial bioreactor (MCB) for creating the first human bioartificial liver. Over the past four years the team has focused on identifying the optimum human liver cell population for seeding the three-dimensional (3-D) bioreactor cultures. It has been determined that an unfractionated mixture of human liver cells shown to contain hepatic stem/progenitors provides favorable bioreactor results. In addition to this work the team has developed versatile NMR-compatible bioreactors that can obtain in situ metabolomics and fluxomics data.

### **Precision Engineering of Ultrasonically-targeted Drug Delivery Vehicles**

*Dayton, Paul*  
*National Institutes of Health*  
 \$324,469  
 4/1/09 - 2/28/10

This proposal describes a three step process for the development, improvement, and exploration of acoustically-active drug delivery vehicles for site-specific drug delivery. The first step in this proposal is the precision engineering of acoustically active drug delivery vehicles through the application of novel microfluidic technology. The second component consists of testing and optimizing the stability, acoustic properties, and drug release characteristics of these new vehicles. Finally, the delivery potential and biodistribution of the new vehicles in-vivo will be examined with optical imaging and ultrasound. This collaboration provides the unique and qualified research group with expertise in ultrasound, microbubbles, drug delivery vehicles, and microfluidics required to achieve these goals.

### **Spectroscopic Imaging of Antioxidant Metabolism in the Brain**

*Gamcsik, Michael*  
*National Institutes of Health*  
 \$364,478  
 9/1/07 - 8/31/09

This proposal delineates novel experiments to evaluate the use of noninvasive magnetic resonance (MR) spectroscopic imaging techniques to follow the uptake, distribution and metabolism of these antioxidant prodrugs in rat brain. Since these innovative methods are noninvasive, this will allow us to study alterations in antioxidant metabolism during disease progression in individual rats. In addition, proper substrate selection will allow us to probe defects in cellular metabolism that may hinder prodrug efficacy. The use of both MR and stable isotope methodology is amenable to translation into the clinic.

### **Implementing Nanogap Sensors in Neuroscience Research**

*McCarty, Gregory*  
*National Institutes of Health*  
 \$280,874  
 9/15/07 - 6/30/10

The expected result of this effort will be new analytical tools that will enable ultra-sensitive detection of neurologically related molecules of interest in extremely small volumes of ionic solution. The measurement of these molecules will enable the acquisition of neuro-physiological data that was not practically available previously. The analysis of this now available data will lead to new treatment methods for neurological and neurodegenerative disorders. While these techniques are applicable to a variety of problems in the sciences, initial applications will be focused on neuronal function due to the importance of neuroscience research and its impact on human health.

### **Carolina Center for Cancer Nanotechnology Excellence: Project #3 and Small Animal Imaging Core #3**

*Lalush, David*  
*UNC - UNC Chapel Hill*  
 \$62,817  
 10/1/05 - 8/31/09

The C-CCNE will bring together researchers and clinicians not only at UNC but nationally and internationally to meet the Challenge Goal of eliminating the suffering and death from cancer by 2015. This will be accomplished by establishing a national NCI asset we refer to as the PARTICLE FOUNDRY. The PARTICLE FOUNDRY will be one of the outcomes of this project within the Center of Cancer Nanotechnology Excellence at UNC. The PARTICLE FOUNDRY will be the portal for researchers around the world to gain access to UNC's breakthrough PRINT technology for the fabrication of "smart" functional particles for their studies and evaluations.

### **Cartilage Matrix Damage and Chondrocyte Response to Normal and Shear Injury**

*Mente, Peter*  
*National Institutes of Health*  
 \$140,680  
 9/1/07 - 8/31/09

We propose to use an in vitro porcine patellae impact injury model to document changes in chondrocyte gene expression and tissue damage that may initiate the degenerative processes. We will examine different types of injury (normal and shear) and the physical extent of over which damage occurs. We will examine three different loading cases; a normal impaction, a shear impaction, and a non impacted control.

### **Nanofluidics Devices for Rapid Single Cell Analysis of Protein Expression**

*Walker, Glenn*  
*UNC - UNC Chapel Hill*  
 \$191,626  
 10/1/05 - 8/31/09

The C-CCNE will bring together researchers and clinicians not only at UNC but nationally and internationally to meet the Challenge Goal of eliminating the suffering and death from cancer by 2015. This will be accomplished by establishing a national NCI asset we refer to as the PARTICLE FOUNDRY. The PARTICLE FOUNDRY will be one of the outcomes of this project within the Center of Cancer Nanotechnology Excellence at UNC. The PARTICLE FOUNDRY will be the portal for researchers around the world to gain access to UNC's breakthrough PRINT technology for the fabrication of "smart" functional particles for their studies and evaluations.

### **Dynamic Micro-CT Using a Field Emission x-ray Source**

*Lalush, David*  
*UNC - UNC Chapel Hill*  
 \$86,583  
 9/1/05 - 8/31/09

The aim of this proposal is to develop a dynamic micro-computed tomography (micro-CT) system with enhanced spatial and temporal resolution and more versatile imaging

capabilities compared to the current commercial micro-CT scanners, and to explore its applications for biomedical research. The goal is to provide a scanner that will maximize image resolution for in vivo scanning of mice and with the target organ systems being the cardiopulmonary system.

### **The Role of Palladin in the Mechanobiology of Human Mesenchymal Stem Cells**

*Lobo, Elizabeth*  
*NC Biotechnology Center*  
 \$250,000  
 6/1/07 - 5/31/10

The proposed approach is to investigate if cell morphology and cytoskeletal tension affect hMSC differentiation and to determine if changes in palladin expression play a role in these processes and or mechanotransduction due to its association with actin. We have shown that hMSCs express palladin and that palladin is associated with the actin cytoskeleton. It is hypothesized that palladin will be upregulated in hMSCs exposed to mechanical load and that palladin expression will affect the contractility of hMSCs.

*Ultrasound for reversible male contraception*  
*Dayton, Paul*  
*UNC - UNC Chapel Hill*  
 \$2,125  
 5/12/08 - 8/31/08

The overall aim of this project is to assess whether subjecting the testis to ultrasound waves can result in reversible infertility. If reversible infertility can be so induced, this may provide a drug-free method for male contraception. These questions will be addressed by analyzing the histopathological effects of ultrasound treatment on the rat testis, surveying changes in gene-expression induced by ultrasound to help formulate a hypothesis about the mechanisms involved in the loss of fertility, assessing the integrity of the blood-testis barrier, and analyzing rat immune response after ultrasound treatment. Studies will also be done on in vitro ultrasound treatment of human sperm.

### **Chondrocyte Protein Expression in a Porcine Osteoarthritis Model--Early Detection of Tissue Degenerative Factors**

*Ashwell, Melissa, Mente, Peter*  
*NCSU Faculty Research & Professional Development Fund*  
 \$20,000  
 7/1/08 - 6/30/09

We propose to use 2-D gel electrophoresis and mass spectroscopy to examine how porcine chondrocytes respond following an impact injury as a model for a degenerative joint disease, osteoarthritis (OA). We propose to use an in vitro porcine injury model to determine changes in protein expression that initiate the degenerative processes leading to diseases such as osteoarthritis. We hypothesize that proteins involved in matrix degeneration and chondrocyte apoptosis will be up-regulated immediately following an injury.

### **Atmospheric Pressure Plasma-Electrospinning Hybrid Nanofiber Mat Production**

*Zhang, Xiangwu, McCord, Marian, Bourham, Mohamed*  
*Defense Threat Reduction Agency*  
 \$199,507  
 6/2/08 - 6/1/11

The objective of this work is to combine atmospheric pressure plasma and electrospinning to obtain a new hybrid nanofiber mat production technology. Novel nanofiber mats are promising candidates to meet the Defense Threat Reduction Agency (DTRA) requirements of protecting our nation from chemical and biological weapons because they have excellent barrier efficiency and relatively low pressure drop. Our approach is to combine electrospinning with the existing advanced atmospheric pressure plasma system, which was developed and operated by the PI's at NC State University, and obtain a novel nanofiber mat product technology, which will be used to deposit nanofiber mats with controlled structures and properties onto woven 50:50 nylon:cotton textile material.

### **ARFI Ultrasound for Noninvasive Material Characterization of Atherosclerosis in**

*Gallippi, Caterina*  
*American Heart Association - Mid Atlantic Affiliate*  
 \$66,000.00  
 7/1/07 - 6/30/09

Our preliminary ex vivo and in vivo results support ARFI ultrasound for mechanical characterization of a raised focal atherosclerotic plaque in an iliac artery extracted from a relevant pig model. Our results are correlated to matched immunohistochemistry indicating elastin and collagen composition. In regions of degraded elastin, slower recovery rates from peak ARFI-induced displacements were observed. In regions of collagen deposition, lower ARFI-induced displacements were achieved. This work demonstrates ARFI for characterizing the material nature of an atherosclerotic plaque and supports our hypothesis that ARFI ultrasound is efficacious for delineation of atherosclerosis by mechanical property.

### **Atherosclerosis and Renal Complications in Insulin Resistant, Hyperlipidemic Pig**

*Nichols, Timothy; Gallippi, Caterina*  
*NC Biotechnology Center*  
 \$250,000.00  
 7/1/08 - 6/30/10

It is unknown why patients with type 2 insulin resistant (IR) diabetes mellitus have an increased incidence of atherosclerosis compared to nondiabetics. To address this scientific question, we used selective breeding strategies to produce hyperinsulinemic pigs that develop worsening insulin resistance with high fat diet induced hypercholesterolemia (DH/IR). Our long-range goal is to provide the scientific community with a well-characterized, useful animal model of human type 2 diabetes that develops human-like coronary and aortic atherosclerosis in order to be able to address a variety of mechanisms including the pathophysiology of insulin resistant diabetes, the influence of diabetes on the development of atherosclerosis and related complications, and to identify and test new therapeutic agents.

### Agent-based modeling of virus-host cell interaction in salivary gland disease

*Giddings, Morgan; Vasa, Suzy*  
*National Institute of Dental and Craniofacial Research*  
 \$30,458.00  
 5/5/09 - 5/4/11

Caries, periodontal disease, disfigurement, mucosal pathology and occasional development of B cell lymphomas result from salivary gland disorders (SGD) such as Sjorgren's Syndrome and a related HIV SGD. These diseases are autoimmune disorders with an unknown cause and no known cure. Recently, the Webster-Cyriaque lab has shown that polyomavirus BK viral gene products are consistently found in SGD. We believe that BK virus (BKV) infection or reactivation is a factor in disrupting cellular processes leading to the development of SGD. The goal of this proposal is to aid the Webster-Cyriaque lab in determining the cause of SGD by creating a BKV-salivary gland computational model.

### Rehabilitation Engineering Design Class

*Goldberg, Richard*  
*National Science Foundation - Research*  
 \$23,991.00  
 4/1/05 - 3/31/10

This is a proposal for a Research Experiences for Teachers supplement to an NSF grant. In this program, the PI and his students will train teachers and therapists in basic electronics, so that they can develop custom switches and other simple devices for their students with disabilities. This training will take place during a 1 ½ day workshop during the summer, in which participants will do a reverse engineering project, learn basic electronic theory, and build custom switches from locally available components. Support for two undergraduate students is also requested to provide ongoing support to the participants during the school year. This program will provide the participants with important background in electronics, so that they can develop simple technologies for their students with disabilities.

### Prediction of host-pathogen protein-protein interactions

*Gomez, Shawn*  
*US Army Research Office*  
 \$50,000.00  
 2/1/09 - 10/31/09

Successful prediction of host-pathogen protein-protein interactions shows great promise for contributing to significant advances in the research fields of computational modeling, proteomics, and pathogen-based disease treatment. This work will foster significant advances in biomedical modeling research and will represent an innovative development in understanding the protein function of the host-pathogen disease dynamic. Another benefit of this project is the multi-disciplinary approach envisioned to achieve the proposed goals.

### Carolina Center for Computational Toxicology

*Rusyn, Ivan; Gomez, Shawn*  
*US Environmental Protection Agency - GRANTS*  
 \$297,000.00  
 4/1/08 - 3/31/12

The objective of this proposal is to create The Carolina Center for Computational Toxicology. We present a clear plan for an effective, broad and interdisciplinary effort to devise novel tools, methods and knowledge that will utilize ToxCast and other publicly available data to assist the EPA in achieving the goals of protecting the environment and human health.

### MAP kinase regulation of cell-fate transitions in yeast

*Errede, Beverly; Gomez, Shawn*  
*National Institute of General Medicine Science*  
 \$30,634.50  
 1/1/09 - 12/31/12

The genetic program for the chemotrophic fate transition induced by low pheromone concentration is still undefined. Fus3 and Kss1 activation profiles are differentially affected at high vs. low pheromone. We hypothesize that the dose-dependent differences in their activation and their antagonistic regulatory roles control Ste12 and Tec1 activity and degradation in a manner that prepares cells for one or the other differentiation program. We propose a multidisciplinary approach to compare the regulatory networks for the two fates and the molecular basis of the developmental switch.

### Regulation of Sequential Protein Kinase Pathways

*Johnson, Gary; Gomez, Shawn;*  
*National Institute of Diabetes, Digestive and Kidney Diseases*  
 \$28,973.70  
 9/1/88 - 12/31/11

The goal of this project is to explore ways to regulate the sequential protein kinase pathways.

### Human Enterohepatic Cell Model for Predictive Toxicology

*Macdonald, Jeffrey; Favorov, Oleg; Gomez, Shawn*  
*National Institute of General Medicine Science*  
 \$331,203.00  
 7/1/06 - 6/30/10

An in vitro system that is a much better model of a human liver is needed. Over the past dozen years this research team has been developing a state-of-the-art multicoaxial bioreactor (MCB) for creating the first human bioartificial liver. Over the past four years the team has focused on identifying the optimum human liver cell population for seeding the three-dimensional (3-D) bioreactor cultures. It has been determined that an unfractionated mixture of human liver cells shown to contain hepatic stem/progenitors provides favorable bioreactor results. In addition to this work the team has developed versatile NMR-compatible bioreactors that can obtain in situ metabolomics and fluxomics data.

## Noninvasive Monitoring Glutathione Metabolism in Tumors

Macdonald, Jeffrey  
North Carolina State University  
\$35,998.00  
2/27/08 - 1/31/11

This proposal plans to use methods to monitor glutathione metabolism non-invasively in R3230 mammary, 9L glioma and FSA fibrosarcoma tumors and drug-resistant variants in rats. Glutathione metabolism will be assessed in relation to tumor growth rate, vascularization and expression of key enzymes involved in redox metabolism. Since a drop in intracellular glutathione levels is one of the earliest events in apoptosis, therapy-induced changes in glutathione metabolism detected by magnetic resonance will be an early indicator of tumor response. Since altered redox balance appears to be a universal characteristic of proliferating cells in general and cancer in particular, methods to non-invasively monitor redox metabolism offers new insight into a process critical to planning and evaluating cancer therapy.

## Fellow:Jeffries, Rex--Preclinical Fluxomic Model of Drug-Induced Liver Injury

Macdonald, Jeffrey; Jeffries, Rex  
National Institute of Diabetes, Digestive and Kidney Diseases  
\$28,985.00  
8/1/08 - 7/31/10

Metabolism is dynamic. Acetaminophen (APAP) overdose is a classic example of non-steady state stress that initiates a dynamic cascade of responses to toxic events occurring to varying severity depending on dose. Many metabolic pathways can protect against APAP toxicity, ranging from phase I and phase II conjugation pathways to superior bioenergetic metabolism. Therefore, the goal of this research proposal is to develop a nonsteady-state challenge test using stable-labeled nutrients that directly measures a multitude of biological functions. Four biomedical engineering technologies, tissue engineering of NMR-compatible bioartificial liver, <sup>13</sup>C NMR spectroscopy, metabolic flux modeling, and multivariate statistical analysis to acquire in vivo <sup>13</sup>C NMR spectra and determine mechanism(s) of drug injury. These are state-of-the-art in vivo methods that will make a considerable contribution to metabolomics by the added fluxomic dataset acquired from real experimental in vivo <sup>13</sup>C NMR spectral time courses.

## CAREER: Laser Processing of Microstructured Medical Devices

Narayan, Roger  
National Science Foundation - Research  
\$430,000.00  
9/1/06 - 8/31/11

A comprehensive program is needed to fully and systematically assess the structural and functional properties of Ormocer® microneedles created using two photon induced polymerization. The proposed research plan contains three overlapping phases. Phase I will involve biological, chemical, and mechanical characterization of Ormocer® materials created using two photon induced polymerization. Phase II will involve structural and functional characterization of Ormocer® microneedles. Phase III will involve integrating microneedles with pumping devices. The broader impacts of this work include development of microneedle technology as well as two photon induced polymerization technology in

particular, and medical device microfabrication technologies in general. The proposed program will also address biomaterials education and underrepresented minority outreach.

## Two Photon Induced Polymerization of Microstructured Medical Devices

Narayan, Roger  
National Science Foundation - Research  
\$15,000.00  
9/1/06 - 8/31/11

A comprehensive program is needed to fully and systematically assess the structural and functional properties of Ormocer® microneedles created using two photon induced polymerization. The proposed research plan contains three overlapping phases. Phase I will involve biological, chemical, and mechanical characterization of Ormocer® materials created using two photon induced polymerization. Phase II will involve structural and functional characterization of Ormocer® microneedles. Phase III will involve integrating microneedles with pumping devices. The broader impacts of this work include development of microneedle technology as well as two photon induced polymerization technology in particular, and medical device microfabrication technologies in general.

## Sensory based diagnostics for assessing cerebral cortical information processing

Tommerdahl, Mark; Whitsel, Barry; Favorov, Oleg; Dennis, Robert  
US Army Research Office  
\$250,000.00  
7/15/08 - 11/14/09

Multiple clinical research collaborations have been initiated in a number of areas, including: autism, chronic pain, alcoholism, and aging. The clinical research tool that we have developed, and are continuing to develop, could have a significant impact on a number of research areas which are currently being explored and could eventually be used as a diagnostic tool by not only medical researchers, but by primary health care providers for obtaining measures of central nervous system disorder and/or assessment of efficacy of therapeutic strategies. In terms of specific military applications, quantitative dosimetry of exposure to blast-related trauma is an important part of a military commander's mission, yet it is currently a very difficult, if not impossible, task. The development of a field deployable lightweight and portable diagnostic sensory testing system would allow commanders to protect personnel from excessive blast exposure by reassignment as appropriate in each individual case.

## Electrical Stimulation to Improve Proprioception in Knee Osteoarthritis

Weinhold, Paul  
Arthritis Foundation  
\$95,000.00  
9/1/08 - 8/31/10

This study's objective is to evaluate the viability of stochastic resonance electrical stimulation (SR) as a therapy for knee osteoarthritis (OA). Three conditions (no stimulation/no sleeve, no stimulation/sleeve, and stimulation/sleeve) will be compared in knee OA patients. Joint position sense will be assessed to evaluate SR's influence on knee proprioception. We hypothesize that SR will improve knee proprioception.

Additionally, knee mechanics and muscle activation will be assessed to evaluate the influence of SR on detrimental gait patterns present with knee OA. We hypothesize that SR will cause increased knee flexion and decreased muscle co-contraction, knee axial loads, and loading rates.