



Virginia Tech
Wake Forest University

School of Biomedical Engineering and Sciences

newsletter
Fall 2013

Crusade

Against

CANCER

**CANCER IS ONE OF SEVEN
RESEARCH CATEGORIES**

**TISSUE ENGINEERING
BIOMEDICAL IMAGING**

**NANOMEDICINE
BIOMECHANICS**

NEUROENGINEERING

CARDIOVASCULAR ENGINEERING

OUR BIOMEDICAL ENGINEERING PROGRAM BY THE NUMBERS:

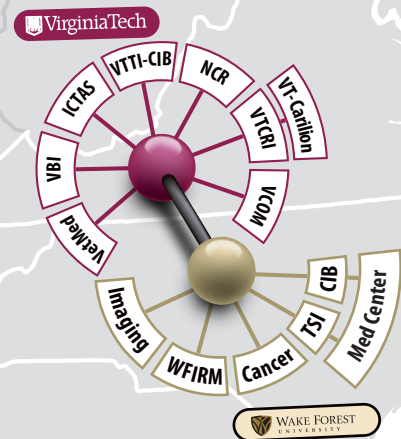
- 78 Total Faculty
 - 25 Primary Faculty
 - 53 Core/Joint Faculty
- \$55,000,000 Research Expenditures
- 14 Partner Centers & Institutes

At Virginia Tech

VetMed	College of Veterinary Medicine
VBI	Virginia Bioinformatics Institute
ICTAS	Institute for Critical Technologies and Applied Sciences
VTI-CIB	Virginia Tech Transportation Institute - Center for Injury Biomechanics
NCR	National Capital Region
VT-Carilion	Virginia Tech – Carilion Medical School
VTCRI	Virginia Tech – Carilion Research Institute
VCOM	Via College of Osteopathic Medicine

At Wake Forest University

Imaging	Center for Biomolecular Imaging, Biomedical Imaging Division
WFIRM	Wake Forest Institute for Regenerative Medicine
Cancer	Comprehensive Cancer Center
TSI	Translational Sciences Institute
CIB	Center for Injury Biomechanics
Med Center	Wake Forest University Baptist Medical Center



FIGHTING

CANCER

- Targeted Drug Delivery
- Microfluidic Tumor Mimics
- Microenvironmental Targeting
- Thermal & Photo-Activated Therapy
- Nano Therapy
- Image-Guided Surgery
- Microdevices for Cellular Analysis
- Tumor Engineering
- Membrane Targeting Electrotherapeutics
- Focused, Image-Guided Radiation Therapy
- Clinical & Molecular Imaging
- Imaging of BRCA1 Processes
- Surrogate & Translational Cancer Models
- Presymptomatic Detection



COMPLETING OUR FIVE-YEAR GROWTH PLAN

sound more reasonable within the context of the size of the Virginia Tech College of Engineering, which has over 330 tenure track faculty and over 8,000 undergraduate and graduate students. When our growth plan is complete next year, biomedical engineering faculty will comprise approximately 25% of all engineering faculty and be on par with many of the larger programs across the country.

Dr. Stefan Duma is the Department Head of the Virginia Tech - Wake Forest University School of Biomedical Engineering and Sciences.

We are entering the fifth year of our five year growth plan that called for the addition of 50 new tenure track faculty in our biomedical engineering program. We will be searching for three more positions in the fall that will complete this plan. Starting from 31 faculty in 2008, we will have 81 faculty by the end of this year, with 26 full time primary appointments and the others joint appointments. As I noted last year, these faculty numbers are indeed quite large. However, they

I am excited to announce that our program will be recognized again at BMES this year in Seattle. For the third year in a row, our student chapter will receive the Fleetest Feet Award for the chapter with the most students who traveled the farthest to attend the national conference. Last year we had 106 papers and posters presented in Atlanta.

Our focus continues to shift to recruiting more graduate students and post-docs as our new faculty research programs begin to develop. To this end, we continue to organize our research topics into the following seven theme areas: Biomedical Imaging, Tissue Engineering, Biomechanics, Cardiovascular Engineering, Nanomedicine and

Nanobioengineering, Neuroengineering, and Translational Cancer Research. These areas are further discussed in this newsletter.

Finally, please stop by our booth at BMES where we will have interactive displays that feature our current research projects. We are bringing over 70 faculty and graduate students that are presenting 77 technical papers and posters. I hope you will have the opportunity to see one of these presentations. I look forward to seeing you all in Seattle!

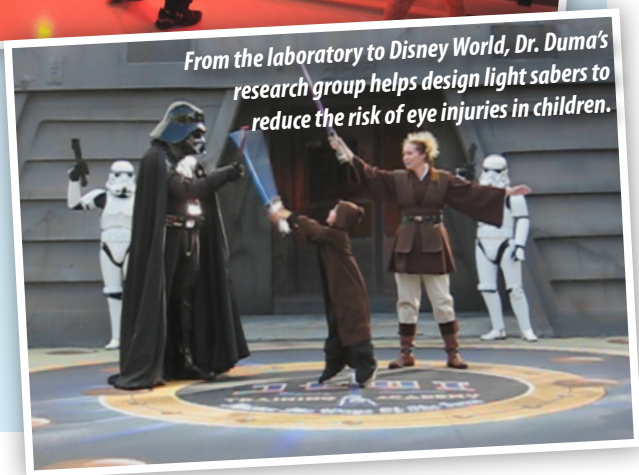
Sincerely,

Stefan Duma, PhD
Harry C. Wyatt Professor and Department Head

LIGHT SABER DESIGN

While Darth Vader would have little use for the light sabers we help design, children around the world can enjoy the toys with minimal risk of injury. The popular expanding light sabers have a mechanical spring deployment mechanism. The design of this spring, weight of the moving parts, and stiffness of the saber can all be optimized to allow for optimum performance while reducing the risk of injuries. Dr. Duma's team helped develop these devices by starting with experimental research that included extensive volunteer testing with motion capture cameras. This allowed for the determination of swing velocity as a function of age and gender. Next, these parameters were used to create experimental prototypes of the deploying light sabers. The prototypes were evaluated for injury risk using the FOCUS head form and previously developed injury risk functions. The final products have been on the shelf for years and a trip to Disney World will see them in action with children fighting Darth Vader.

For nearly two decades, Dr. Duma's research group has developed injury risk functions for military applications. In a different twist on translational research, these injury risk functions are used to help design a wide range of consumer products. Beyond light sabers, the research has helped develop water park toys, dart guns, remote control helicopters, and a range of sporting equipment.



From the laboratory to Disney World, Dr. Duma's research group helps design light sabers to reduce the risk of eye injuries in children.

JOEL STITZEL APPOINTED ASSOCIATE HEAD OF SBES

We are pleased to announce the appointment of Joel Stitzel, Ph.D., as Chair of Biomedical Engineering at Wake Forest University, and Associate Head of the Virginia Tech – Wake Forest School of Biomedical Engineering and Sciences, effective March 1, 2013.

Dr. Stitzel is presently a Professor of Biomedical Engineering at Wake Forest and Program Leader of the Virginia Tech-Wake Forest University Center for Injury Biomechanics.

Dr. Stitzel has developed an internationally renowned research program focused on crash injury research and engineering biomechanics of trauma, automotive safety, and sports and military biomechanics. Major projects with which he has been involved include the Crash Injury Research and Engineering Network supported by the National Highway Traffic Safety Administration (NHTSA), a collaboration with Critical Care Surgery, Orthopedic Surgery, Radiologic Sciences and Virginia Tech. His group is also performing Advanced Automatic Crash Notification research for Toyota's Collaborative Safety Research Center (CSRC), with Public Health Sciences and Critical Care Surgery.



Dr. Stitzel and collaborating faculty, staff and students at WFU are creating a new generation of human body computational models to represent live humans with the Global Human Body Models Consortium, a consortium of automotive manufacturers and NHTSA. Their group is working with the Total Human Model for Safety (THUMS) human body model to computationally model real world crashes for Toyota's CSRC. In addition, his group is studying concussions and head impact exposure in youth football, a collaboration with Virginia Tech, Neurosurgery, Neuroradiology, Neurology, and Neurobiology and Anatomy supported by the Childress Institute for Pediatric Trauma. These research areas span the range of automotive, sports, military and orthopedic biomechanics for human protection, and are expected to provide crucial knowledge to better predict and understand the biomechanics of trauma.



Compression induced spinal fracture from a motor vehicle crash. Injuries like this are the type that the CIREN team is working to understand and prevent.

An award presented to Dr. Scott Gayzik for successful development of the GHBMC 50th male. This model is the culmination of multiple person-years of work devoted to creating the world's most biofidelic human body model for use by vehicle manufacturers around the world.

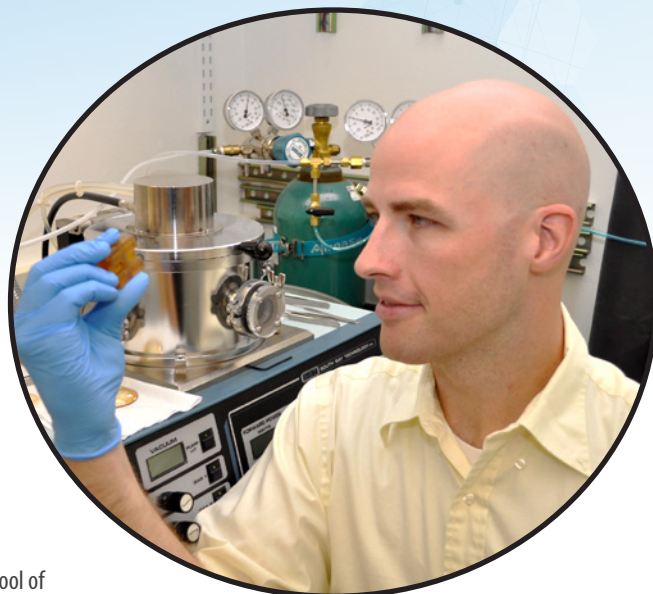
ADAM HALL

Dr. Adam Hall is joining the VT-WFU SBES as an Assistant Professor on the Wake Forest Campus. Dr. Hall received his training at the University of North Carolina at Chapel Hill, where he performed research on nanoelectromechanical systems incorporating individual nanomaterials. Among the accomplishments in his dissertation work were the first direct measurements of torsional mechanical properties of single-wall carbon nanotubes and demonstration of a self-sensing nanomechanical oscillator.

He then trained as a postdoctoral researcher at Technische Universitat Delft in the Netherlands, where he performed experiments on solid-state nanopores. His projects included measurements of nucleoprotein complexes at the single-molecule level and development of hybrid biological-artificial nanopores.

Over the past three years, he has been an Assistant Professor of Nanoscience at the Joint School of Nanoscience and Nanoengineering in Greensboro, NC, where he has earned awards for both his research and educational activities. There, he pioneered new methods of fabricating devices to interface with biological molecules.

His work has been published in several high-impact journals, including *Nature Nanotechnology*, *Nano Letters*, and *Physical Review Letters*, and he has been awarded funding from North Carolina Biotechnology Center and NASA. In his new role as Assistant Professor of Biomedical Engineering, he will focus on developing clinically-relevant applications of nanotechnology. He looks forward to integrating closely with several institutes, centers and departments at Wake Forest- including the Wake Forest Institute for Regenerative Medicine, the Center for Nanotechnology and Molecular Materials, the Comprehensive Cancer Center, and Physics- as well as partners at Virginia Tech.



WFU ANNOUNCES DR. EMMANUEL OPARA AS THE NEW GRADUATE PROGRAM DIRECTOR

We are very pleased to announce Dr. Manny Opara, Professor in the Wake Forest Institute for Regenerative Medicine, has accepted the position of graduate track/program director for Biomedical Engineering at Wake Forest Baptist Health, effective Monday, July 22, 2013.

In this capacity, Dr. Opara will work closely with Dr. Stitzel and Virginia Tech to administer our joint School of Biomedical Engineering and Sciences graduate program activities including recruitment, managing student support in conjunction with research support, increasing diversity in BME, and developing new models of scholarship and curriculum delivery to serve faculty and student interests and further improve employment prospects for our graduate students. Dr. Opara will serve on the biomedical sciences graduate Dean's committee in his role as well.

A bio for Dr. Opara is available at the WFIRM website. Dr. Opara is a member of the Musculoskeletal Tissue Engineering (MTE) study section of the NIH. He was the designer and founding co-director of a program linking the BME program at Illinois Institute of Technology with the University of Chicago Medical school. He is also actively developing a T32 grant proposal to the NIH for Bioengineering Interdisciplinary Training for Diabetes Research. We are therefore very excited to have Manny's involvement to achieve the vision of improving integration of our program with the Medical School and with Virginia Tech.

The position of graduate track director is a 2-year appointment. Please join us in welcoming Dr. Opara to his new role!

Cardiovascular Engineering



Drs. Robert Gourdie and Steve Poelzing

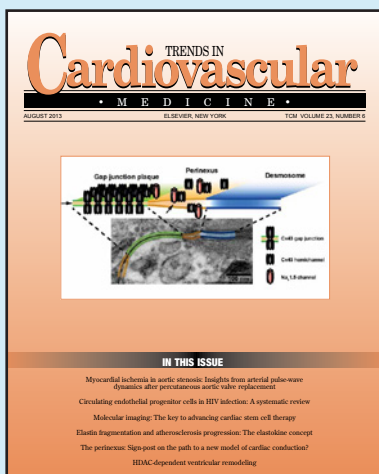
Big Effects from Little Spaces in the Heart

At the Virginia Tech Carilion Research Institute, Drs. Rob Gourdie and Steve Poelzing are discovering how the amount of water in your heart affects your risk for sudden cardiac death. Their group, called the Center for Heart and Regenerative Medicine, recently discovered that electrical activity can occur between cells by a new mechanism called ephaptic coupling. Ephaptic coupling means that direct signaling between cells in our body does not occur either by synapse or gap junction. In the body, synapses can couple neurons in the brain and gap junctions can couple heart cells. Instead, using super-high resolution microscopy which can image down to 20 nm, Drs. Gourdie and Poelzing discovered that at the very edges of the cardiac cells, the gap junctions that normally electrically connect the cells are surrounded by a pocket of water. This pocket called the perinexus is full of sodium channels that depolarize cells by allowing sodium to flood into the cell. The location of the sodium channels in the perinexus has another important function

particularly when water increases in the heart. In short, when the perinexus is small, sodium channels from one cell depletes the number of sodium ions in this very small space. The loss of charge in the perinexus creates a voltage that the downstream cell senses, and the downstream cell responds by also opening sodium channels. By this ephaptic mechanism, electrical activity rapidly by-passes a gap junction. But under many cardiac disease conditions, water accumulates in the heart. When this happens, the perinexus becomes larger, and the ability to electrically signal down-stream cells is lost.

In effect, Drs. Gourdie and Poelzing have discovered that certain cells have two systems for coordinating the spread of electrical activity, gap-junctions and ephaptic coupling. During disease, when one system fails to operate properly, the other system functions as a backup. When both systems fail, then the risk that electrical activity cannot pass from cell-to-cell increases dramatically, and without the spread of electrical activity across the heart, the heart will not contract.

Center for Heart and Regenerative Medicine

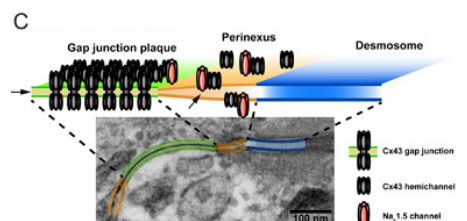
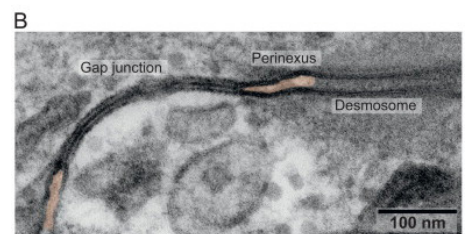
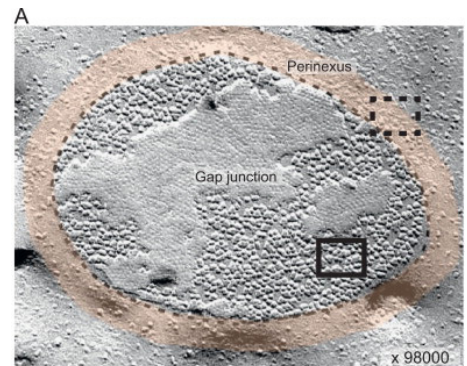


www.journals.elsevier.com/trends-in-cardiovascular-medicine
www.elsevier.com

The focus of the Center will be to translate benchtop discoveries to the bedside.

Focus includes:

- Sudden death during chronic inflammation and Diabetes
- Cardiac Regeneration post infarction (post heart attack)
- Therapies for reducing scarring
- The role of cardiac edema on sudden death - **Featured on the Aug. 2013 cover of "Trends in Cardiovascular"**



CRUSADE AGAINST CANCER

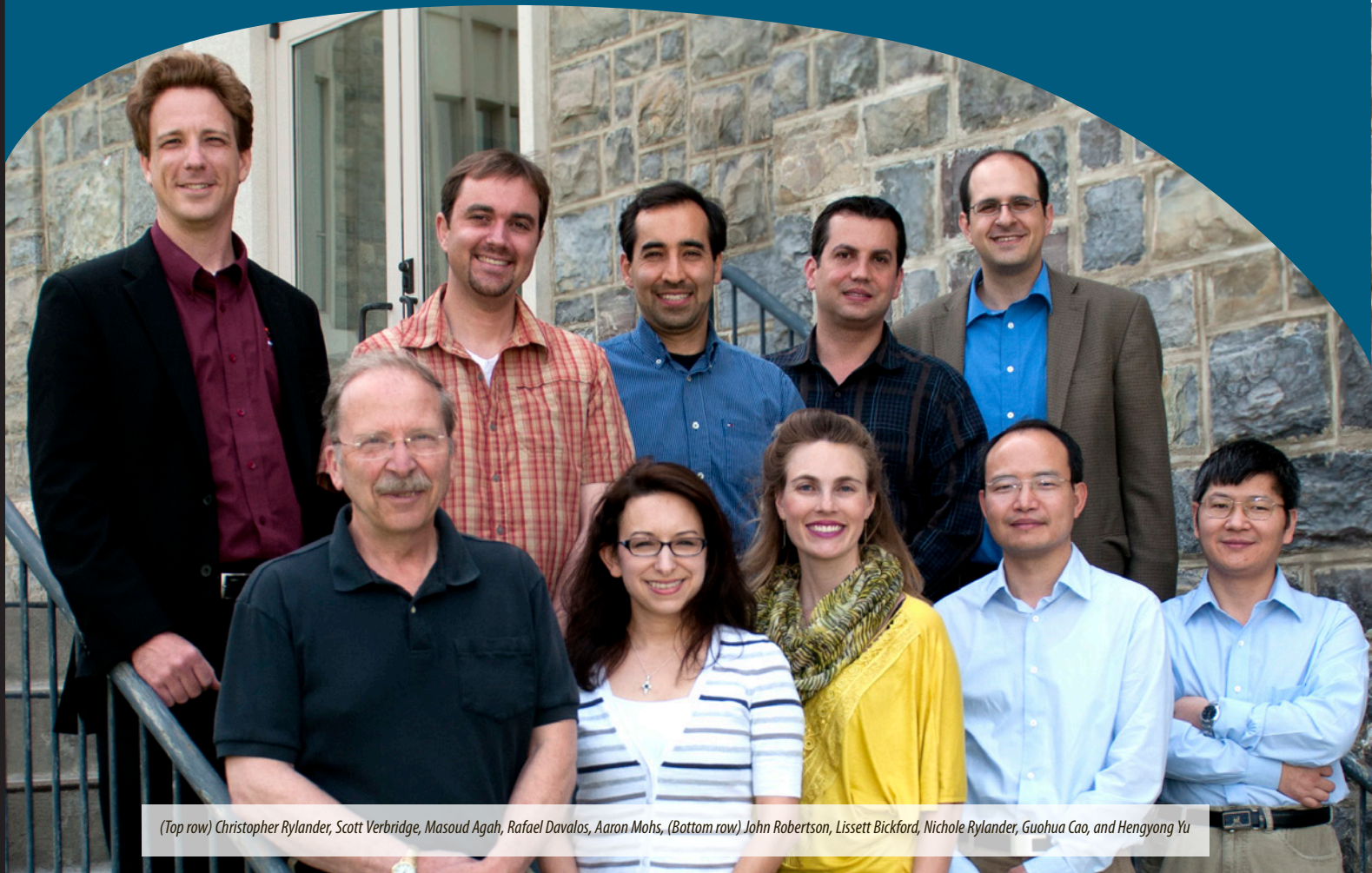
It is rare to hear the words “cancer” and “engineering” in the same sentence, but this is now common parlance and daily conversation within the Translational Cancer Engineering Group in the School of Biomedical Engineering and Science. Over the past five years, a team of engineers, biomedical scientists, physicians, veterinarians, and physicists has collaborated to detect, control, and cure cancer. This Group, formed through active collaborations between Virginia Tech and Wake Forest University, is highly focused on defeating the most aggressive types of cancer. They are achieving success. The Group works in several areas, including:

Cancer detection

- Rafael Davalos has invented a method (contactless dielectrophoresis) that can isolate cancer stem cells from normal cancer cells based on their electrical fingerprint, which is supported by an R21. This technology also has applications for drug screening and was featured on the June 2013 cover of *Integrative Biology*.
- Engineers/scientists in the Biomedical Imaging Group (led by Guohua Cao and Aaron Mohs, and including Dan Bourland, Mike Munley, Lissett Bickford, and John Robertson) have developed novel agents and high-resolution imaging systems and procedures for targeting small tumor cell clusters. This is funded by the National Cancer Institute.
- Dr. Hengyong Yu (Wake Forest) is currently focused on lung cancer. In the United States, lung cancer is the leading cause of cancer death, with a five-year relative survival rate of only 15.8% (for smokers and non-smokers combined). Recently, two medical groups have given new lung screening advice for heavy smokers. The American College of Chest Physicians and the American Society of Clinical Oncology recommend that patients at greatest risk of developing lung cancer be screened with low-dose CT. We expect that screening for lung cancer with low-dose CT will become the standard of care. The CT screening and the follow-up scans expose the patient to ionizing radiation which carries an increased risk of malignancy. To maximize the benefit of CT lung cancer screening, we need to minimize the radiation dose. In collaboration with Dr. Caroline Chiles in the Department of Radiology, one of Dr. Yu’s current research interests is to develop an compressive sensing based ultra-low-dose method for lung cancer screening via dictionary learning based approach.

Tumor modeling

- An effort led by Scott Verbridge and Nichole Rylander, and in collaboration with Rafael Davalos, Guohua Cao and John Robertson, is devoted to building three-dimensional, living, fully-(dys)functional tumors by integrating tumor cell culture, biomaterials and high resolution patterning techniques. These experimental



(Top row) Christopher Rylander, Scott Verbridge, Masoud Agah, Rafael Davalos, Aaron Mohs, (Bottom row) John Robertson, Lissett Bickford, Nichole Rylander, Guohua Cao, and Hengyong Yu

engineered tumors, in combination with mathematical modeling, have enabled quantitative study of the role of tumor-stromal interactions in cancer, leading to recent publications. Nichole Rylander is funded by the National Institute of Health and the National Science Foundation. Ongoing work in collaboration with the Wake Forest Brain Tumor Center of Excellence, led by Dr. Waldemar Debinski, promises to provide new insights into tumor progression and treatment response, leveraging these pre-clinical quantitative tools to complement more traditional 2D cell cultures and animal models of cancer.

Diagnosis & Treatment Devices

- A team led by Chris Rylander (including co-PIs John Rossmeis, David Grant, Nichole Rylander, and John Robertson) has developed a “fiberoptic microneedle device (FMD)” that penetrates tumors and allows simultaneous delivery of optical energy (light) and drugs (nanoparticles for local hyperthermia or photo-activated chemicals). A portion of the work involves active collaboration with Dr. Karen Brewer’s Oncology Therapeutics Team in the Dept. of Chemistry. FMD prototypes are being developed and tested for use against cancer of the urinary bladder and malignant gliomas (the most devastating form of brain cancer). Funding sources are NSF, NIH, and Coulter Foundation.
- Lissett Bickford is working with clinicians at Wake Forest (Girish Mishra and Perry Shen) to develop minimally-invasive devices for pancreatic cancer detection. This team, further including Rafael Davalos, Chris Rylander, and Chris Williams (Mechanical Engineering), is also designing innovative medical devices for performing localized pancreatic cancer theranostics.
- A multidisciplinary team, led by Rafael Davalos, Paulo Garcia, and John Rossmeis (Vet Med), and including Michael Sano and Christopher Arena, has demonstrated that the administration of high-pulsed electric fields to tumors (“irreversible electroporation”) can control and cure some malignant gliomas and soft tissue sarcomas. Another study of the efficacy of electroporation is being conducted in horses, a species with a very high incidence of spontaneous malignant melanoma and infiltrative squamous cell carcinoma. This work is being led by Mike Cissell (Vet Med), in collaboration with members of the Davalos Group with support from the NSF I-Corps program and previous funding by the Coulter Foundation.

Therapeutics

- A novel nanoparticle-based chemotherapeutic, incorporating doxorubicin and targeting cell surface receptors highly-expressed in cancer cells, is being developed by YongWoo Lee and Maren Roman (Dept. of Forestry), with collaboration of Nichole Rylander, Rafael Davalos, and John Robertson. This novel therapeutic approach is being tested by Katelyn Colacino against several types of breast cancer cells and sarcomas.
- Lissett Bickford is focused on developing engineered nanomaterials that incorporate complex compounds for treating malignant glioma and other hard to treat cancers.

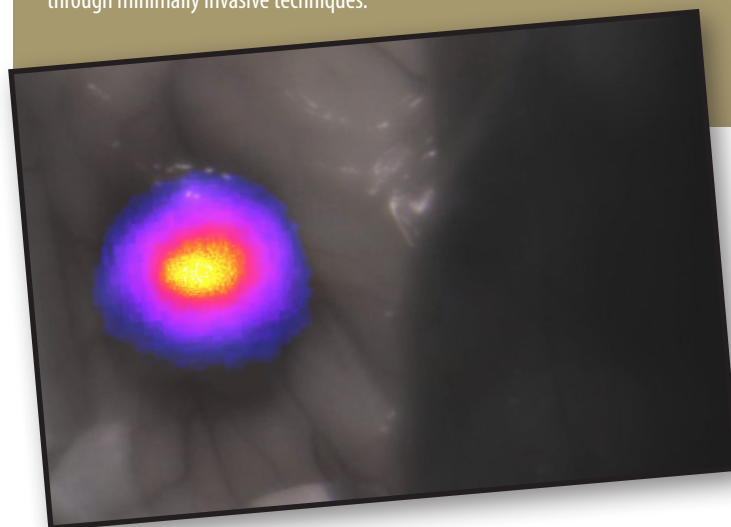
The predictable success of this Group is determined by their shared focus on conquering cancer, the many positive interactions that happen every day, the dedicated graduate students who work tirelessly to sustain and extend the shared vision, and the support and leadership provided to every member by WFU & VT. Together, these biomedical engineers, physicians, and scientists can and will make a difference.

Dr. Aaron Mohs Awarded Nanotechnology Grant from the National Cancer Institute

Complete resection of tumors is one of the most important predictors for cancer patient survival. However, a significant number of patients have recurrent disease, due to undetectable differences between malignant and benign hyperplastic or normal tissue at the time of surgery. In addition, patients that undergo surgery often suffer a decreased quality of life due to injury associated with the surgery.



Recently, Dr. Aaron Mohs initiated the R00 phase of his K99/R00 grant. His R00 from the NCI Alliance for Nanotechnology in Cancer (<http://nano.cancer.gov>) totals \$731,594 over three years, with a primary objective of integrating the unique capabilities of nanotechnology with minimally invasive instrumentation, to improve detection and removal of malignancies. Mohs, and members of his research team, are actively developing biodegradable and nontoxic activatable fluorescence nanoparticle contrast agents based on the chemistry of near-infrared dyes. In addition to looking at specific fluorescence activation, Dr. Mohs is interested in tumor targeting using well-established protein ligands, such as epidermal growth factor and novel peptides for seeking and destroying tumor cells at invasive margins. Initially, fluorescence enhancement will be validated in orthotopic (implanted) tumors in mice. Based on the success of the fluorescent nanoparticles to highlight tumor margins (see Figure above), Dr. Mohs hopes to examine the combined uses of specific tumor enhancement and minimally invasive optical techniques for treating canine patients suffering from cancer. Treating these canine patients should provide useful and immediate feedback regarding the efficacy of the nanoparticles and instrumentation in tumors that occur naturally in an animal with relevant clinical size. Successfully accomplishing these ambitious goals could have the potential to decrease the rate of tumor recurrence by more accurately detecting surgical margins and residual cancer and reduce surgery-associated morbidity, such as decreasing patient pain, discomfort, and disability through minimally invasive techniques.



Detection of a breast tumor grown in a mouse. The strong enhancement is due to fluorescent nanoparticles in the tumor. Intraoperative detection is provided by a near infrared (NIR) imaging system that detects both visible and NIR light in real time.

Nanomedicine & Nanobioengineering

Nano Electrotherapy & Targeted Cancer Treatment

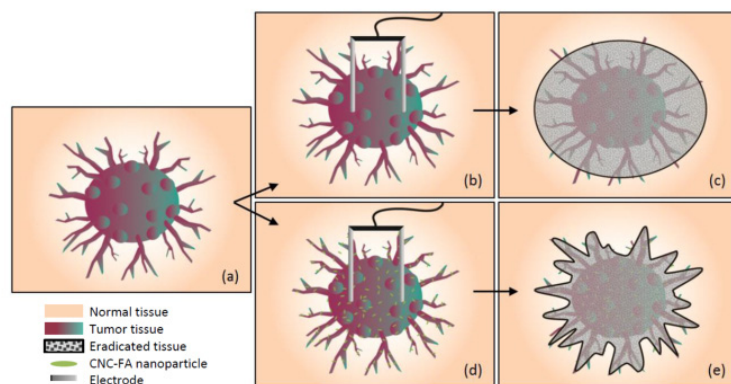
Recent progress in nanotechnology enables creation of useful, functional materials, devices, and systems of nanometer scale in dimension. In particular, the application of nanotechnology to medicine and nanomedicine, is becoming an emerging and rapidly developing research area for diagnosis, prevention, and treatment of various human diseases, including cancer.

Cellulose nanocrystals (CNCs), rod-like polysaccharide-based nanoparticles, are produced by acid hydrolysis of natural cellulose fibers. Owing to their favorable chemical, physicochemical and mechanical properties, CNCs have been evaluated for a wide range of potential applications. The non-toxic nature and high biocompatibility of cellulose render CNCs particularly suitable for applications in the pharmaceutical and medical field.

Irreversible electroporation (IRE), a non-thermal focal ablation technique, exposes cells to pulsed electric fields to increase the permeability of the cell membrane past the point of recovery. This enables the treatment of tumors that are normally considered surgically inoperable due to their close proximity to sensitive structures. One challenge associated with IRE as an electrotherapeutic approach for cancer treatment is that all type of cells, healthy or cancerous, are subject to structural changes if their transmembrane potential is raised above a critical threshold. Therefore, we hypothesize that the selectivity of IRE can be potentiated through the use of cellulose nanocrystals (CNCs) functionalized to selectively target cancer cells.

Our recent studies demonstrated that CNCs conjugated with cancer targeting molecule (CNC-FA) significantly potentiated the cytotoxicity of irreversible electroporation (IRE) on cancer cells. As illustrated in the figure, tumors (A), treated with IRE alone (B), have a uniform distribution of IRE regions including both cancerous and normal tissues (C). However, when bioconjugated CNCs are introduced to the tumor before IRE (D), tumors have a less uniform region of IRE with a higher tumor to normal tissue ratio (E). This

technique will provide great possibilities in developing novel nanocarrier systems that can deliver pulsed electric fields selectively to targeted cancer cells and minimize clinical side effects.



This project fosters the continued collaborations of an innovative, multi-disciplinary research program by integrating the cancer biology and IRE expertise of Virginia Tech-Wake Forest University School of Biomedical Engineering and Sciences (Dr. Yong Woo Lee and Dr. Rafael Davalos), and nanomaterials/polymer chemistry strength of the Department of Sustainable Biomaterials at Virginia Tech (Dr. Maren Roman).

Studies in this area are anticipated to advance the understanding of how nanotechnology can contribute to improvements in human health as well as to provide new opportunities for therapeutic explorations in combination with current treatment methods. It will also have the potential to translate basic laboratory discoveries into clinically effective treatments that eventually make great contributions to the development of new therapeutic approaches.



Drs. Rafael Davalos and Yong Woo Lee

Cancer Facts:

Cancer accounts for nearly 1 of every 4 deaths and is the second leading cause of death in the United States. The American Cancer Society estimates that about 1.7 million new cancer cases are expected to be diagnosed and approximately 580,000 Americans are expected to die of cancer in 2013. Although there have been great improvements in early detection and treatment, cancer remains a significant public health problem due to the limitations of currently available therapy.

Biomechanics

Shock and Awe - The Real Story

The area of injury biomechanics in SBES is expanding faster than the speed of sound. REALLY! Shock waves, which are generated from blast exposures, travel faster than the speed of sound. Blasts are by far the most common cause of wounded-in-action injuries and death of military personnel. Increasing numbers of US Veterans are returning from military ventures suffering from blast exposure and injuries, such as amputations, complex bone fractures and traumatic brain injury. Greater than 50% of all wounds sustained by combatants in action have been reported to be blast injuries. The most commonly injured organ systems include musculoskeletal, pulmonary, vestibular, and neurological including the brain, spinal cord, and peripheral nerves. SBES researchers in the Center for Injury Biomechanics (CIB) are conducting pioneering studies which will help understand how the body responds to these high-rate insults. Experimental models remain the foremost means to investigate injury biomechanics as well as validate computational simulations, therapies, countermeasures, or protection technologies. While the tissue response to low-rate impacts has been investigated by many, only a few researchers have the capability of testing tissues at rates which align with blast. With the addition of our newest facility (fourth lab in addition to sled, helmet, and tissue labs), we have the resources to simulate a blast. State-of-the-art advanced blast simulators generate calibrated shock waves which most accurately represent the blast environment. Several new studies are currently underway which focus on how the human body is injured as a result from blast exposure. Drs. Danelson, Duma, Gayzik, Hardy, Kemper, Stitzel, and VandeVord are at the forefront of understanding blast injuries. This research is vital in order to lay the long-term groundwork for the prevention, diagnosis and treatment of our nation's Veterans returning from Iraq and Afghanistan with injuries due to exposure to blasts.

Dr. Pam VandeVord, Adam Little and Sujith Sajja



Dr. Pam VandeVord, Anthony DeGregorio and Brad Hubbard



The VandeVord Lab group conducting tests.

Neuroengineering

fMRI Elucidating Decision Making and For Neurofeedback

Functional magnetic resonance imaging (fMRI) was developed in the 1990s and very rapidly became the premiere method for neuroscientific discovery because of its capacity for noninvasive, whole-brain recordings. Two SBES faculty members (Brooks King-Casas, Ph.D. and Stephen LaConte, Ph.D.) have active research programs aimed at harnessing the experimental flexibility of fMRI and improving this technology.

Dr. King-Casas studies social behavior and decision making. By adapting experimental methods from decision neuroscience and behavioral economics, he is able to quantitatively study the human computations that underlie decisions made with and about other people. Understanding these social computations is extremely important because of the ever-pervasive influence that our family, friends, colleagues, and competitors have on our ongoing actions and priorities. In fact, how we value the consequences of our actions for ourselves and for others likely plays a major role in our quality of life and our susceptibility to substance abuse, depression, and even post-traumatic stress.

Dr. LaConte is an innovator in “real-time” fMRI. He developed an experimental technology that he calls “temporally adaptive brain state” (TABS) fMRI. The inception of TABS arose from two major recent advances in neuroimaging, namely 1) the recognition that multi-voxel patterns of fMRI data can be used to decode brain states (determine what the volunteer was “doing,” such as receiving sensory input, effecting motor output, or otherwise internally focusing on a prescribed task or thought) and 2) continued advances in MR imaging systems and experimental sophistication with fMRI that have led to the emergence of real-time fMRI as a viable tool for biofeedback.

TABS provides neuroimagers with a new level of experimental flexibility to adapt stimulus presentation “on-the-fly,” as the brain is responding. Beyond providing advance basic science applications, Dr. LaConte’s lab is also exploring the use of TABS for neurorehabilitation and therapy for psychiatry and neurological disorders. Current ongoing projects include the study of fMRI signatures of motor learning and how this affects multivoxel pattern analysis, classification of fMRI signatures of craving to cigarette cues in smokers, and potential links between functional and structural MRI data in mild traumatic brain injury.

Both the King-Casas lab and the LaConte lab are highly collaborative and have ongoing projects with other groups at VT as well as nationally and internationally. One project that the two teams have been working on together has been the study of concussions in the VT football team and throughout the VT athletics program. Capitalizing on the years of accelerometer recording research performed at SBES (led by department head Stefan Duman, Ph.D., associate head Joel Stitzel, Ph.D., and assistant professor Steve Rowson, Ph.D.) these two imaging groups have been examining the neural mechanisms of concussions and recovery from head injuries in VT Football players pre-season, post-concussion, and post-season and have recently expanded the study to include any VT athlete who suffers a concussion.



Dr. Brooks King-Casas



Dr. Stephen LaConte

Tissue Engineering

Spotlight on Wake Forest Institute for Regenerative Medicine

From engineering replacement livers and muscle to developing a cell therapy for diabetes, SBES students assigned to the Wake Forest Institute for Regenerative Medicine (WFIRM) in Winston-Salem, N.C., collaborate on projects that could dramatically affect health care. Regenerative medicine – the science of replacing or repairing damaged tissues – has been called the next evolution of medicine and offers the promise of curing, rather than merely treating, many diseases.

Students in the SBES Cell and Tissue Engineering Track work with SBES/WFIRM faculty members and make contributions in areas such as biomechanics, fluid flow, and material science. Some current projects, and the faculty members and students involved, include:

- Lab-engineered replacement muscle has the potential to help patients with muscle defects due to cleft lip and palate and traumatic injuries or surgery. In animal studies, engineered muscle constructs that were “exercised” on a computer-controlled device before implantation resulted in significant functional recovery. (George Christ, Ph.D.; Hannah Baker, B.S.)
- For large segments of lab-grown muscle tissue to function after implantation, it must be stimulated by the body’s nerves. But, it takes time for existing nerves to grow to meet the new tissue and form the neuro-muscular junction. To keep the tissue functioning in the meantime, scientists are exploring a pharmacologic agent to “trick” the muscle into thinking it is innervated before it actually is. (George Christ, Ph.D.; John Scott, B.S.)
- Functional mini-livers have been engineered in the lab – a promising milestone in the quest to grow replacement livers for patients. The team is currently exploring various ways to optimize the bioengineering process to support self-organization of the liver tissue. (Shay Soker, Ph.D.; Emma Moran, B.S.)
- Institute researchers built the first anal sphincters that function in a lab setting, suggesting a potential future treatment for both fecal and urinary incontinence. Bioengineered with both muscle and nerve cells, the structure is “pre-wired” for placement in the body. Studies in animals are under way. (Khalil N Bitar, Ph.D., AGAF, and Shreya Raghavan, M.S.)
- Encapsulating insulin-producing cells inside a thin membrane may one day offer a new treatment for diabetes. With this strategy, donor cells could be used to provide insulin control for patients. The membrane allows oxygen and nutrients to enter the capsule, but would prevent a rejection response. (Emmanuel Opara, Ph.D.; J.P. McQuilling, B.S.)
- The ability to visualize the regenerative process in real time would allow scientist to optimize their techniques and build better tissues. A fiber-optic based imaging system developed at Virginia Tech is being applied to such bioengineered tissues as blood vessels. (Shay Soker, Ph.D., and Yong Xu, Ph.D.; Etai Sapoznik, B.S.)



Dr. Emmanuel Opara

Bioprinting Wins Edison Award

A WFIRM team has won a gold Edison Award for innovations in bioprinting. The Edison Awards™, which recognize and honor innovative new products, services, and business leaders, are named after renowned inventor Thomas E. Edison.

The institute received the “Game Changer Award” in the science and medical category for two unique printers designed by institute scientists to print living cells and biomaterials rather than ink. The goal of the bioprinting projects is to print replacement tissues and organs for human patients.

Institute scientists were the first in the world to engineer an organ in the lab that was successfully implanted in patients. These original structures were built by hand using biomaterials and cells. In an effort to scale up this process, institute scientists designed a 3-D bioprinter that allows for the precise placement of cells and for multiple cell types to be printed. The 3-D printer is unique because it can print both gels and synthetic materials, which helps ensure structural integrity of tissues and organs.

The second printer designed by institute scientists is a bioprinter to print skin cells onto burn wounds. The impetus for the project is the need for improved care for patients with severe wounds, who often don’t have enough healthy skin to harvest for skin grafts. With this system, a scanner will determine the surface dimensions and depth of the wound, and the data guides the printer to precisely place the appropriate type and number of cells.

Both printers are still in the research stage and not yet ready for use in patients. Institute scientists who are part of the bioprinter team are Anthony Atala, M.D., director, James Yoo, M.D., Ph.D., professor, Sang Jin Lee, Ph.D., assistant professor, John Jackson, Ph.D., associate professor, Hyun-Wook Kang, Ph.D., fellow, Aleksander Skardal, Ph.D., fellow, Carlos Kengla, Ph.D., student, and Mohammad Z. Albanna, Ph.D.

Biomedical Imaging

The iTAKL Study: Imaging Football Head Impacts

There are over 5 million athletes playing organized football in the United States, with the vast majority in the youth and high school leagues. Researchers at Wake Forest are working with Virginia Tech and combining biomechanical head impact exposure data for the Kinematics of Impact Data Set (KIDS) study, the largest and only study yet conducted of youth football head impacts from ages 6-18. The effects of head impacts on these vulnerable younger players, especially in some of the youth leagues (ages 8-12), have never been effectively studied. Researchers at Wake Forest are specifically looking at these youth and high school players using the most sophisticated imaging, biomechanical, and cognitive testing currently available, at a scale never before attempted. The study is appropriately called iTAKL (Imaging, Telemetry And Kinematic modelIng in football). The investigators have already acquired a rich pilot data set of ~50 youth (8-12 yo) and high school (14-18 yo) football players followed over the course of the 2012 football season. All players were instrumented with the Head Impact Telemetry System (HITS) for collection of real-time head impact data. Baseline, post-season and post-concussion multimodal magnetic resonance imaging (MRI), including structural T1-weighted, diffusion tensor and kurtosis imaging (DTI/DKI), susceptibility weighted imaging (SWI), arterial spin labeling (ASL), and resting-state functional MRI (fMRI), as well as magnetoencephalography (MEG) were performed in all subjects. This experience represents the largest for any research group in the realm of imaging/biomechanics in youth football and has not been duplicated at any concussion research center. What sets this study apart is the ability to acquire all the critical data elements in the same population, including the detailed biomechanical measures from sensors in the helmets during all practices and games, cognitive testing across multiple domains, and sophisticated imaging, not only with MRI, but also with MEG, including pre and post-season measures. The study is focused on determining if there are brain changes detectable in youth and high school football for subconcussive impacts, which go undetected during play.



Youth in MRI Scanner

This project provides a new, unique computational challenge – the problem of modeling, processing, analyzing and visualizing trauma-induced changes in the brain. While all the imaging is important, the imaging group has been particularly focused on the diffusion data and the MEG data as biomarkers of pediatric neural injury. The analyses are already indicating a compelling relationship between impacts and a variety of imaging brain changes associated with mTBI. As an example, the analysis of resting state MEG data is extremely innovative, as the vast majority of MEG studies and software are task-based, with a relative paucity of work on resting state MEG analysis, and expertise in resting

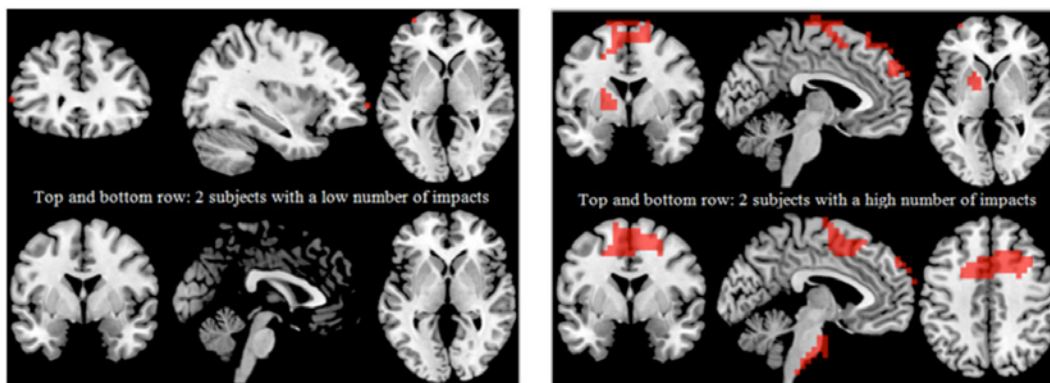


Figure 1. MEG delta wave z-maps for low impact (left) and high impact (right) players.

(0-4 Hz) that are typically not present in normal awake adults, but these have never been effectively studied in children and adolescents. Using the ANSIR lab MEG analysis pipeline, the researchers looked at the change in delta wave activity in 18 of the high school players over the 2012 season. The players were separated into a group of high hitters (>600 impacts) and low hitters (< 250 impacts) based on the biomechanical HITS data. The low-impact players demonstrated few, or no, areas of delta wave difference over the season (Figure 1 - left). The high-impact players demonstrated large areas of significant increases in delta waves, particularly parasagittally around the falx, in areas known to be preferentially affected in TBI (Figure 1 - right). Data of this type provided by the study will be critical in establishing the effect on the brain of repeated head impacts in youth and high school football. The long term benefit of the research will be to allow equipment designers, researchers, and clinicians to better prevent, mitigate, identify and treat injuries to help make youth league football a safer activity for millions of children.

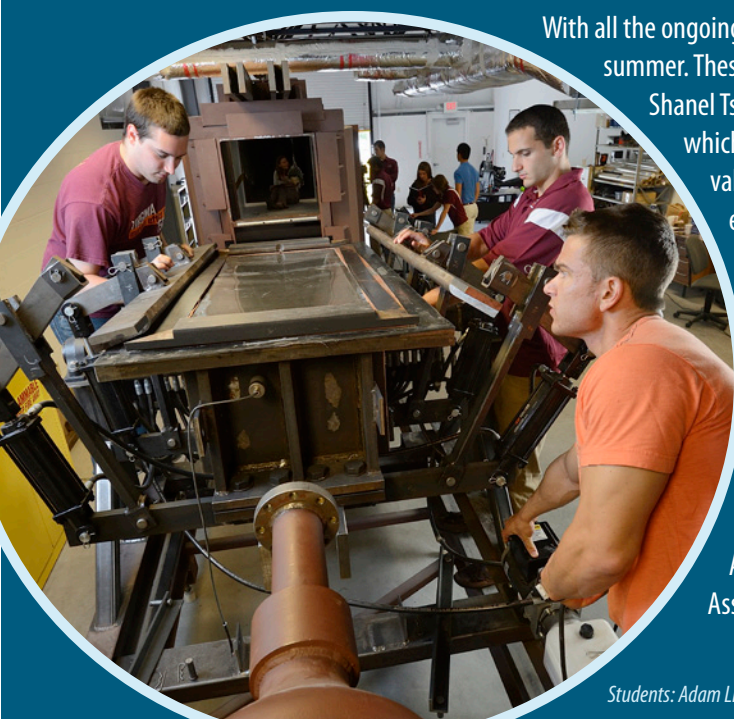
The iTAKL project involves a highly talented and multidisciplinary group of investigators and staff with a strong history of collaboration, leveraging institutional investments in facilities and resources. These include Dr. Joel Stitzel, an expert in biomechanical modeling of trauma, Dr. Alex Powers, a pediatric neurosurgeon experienced in the evaluation and management of pediatric mTBI, Dr. Daryl Rosenbaum, a sports medicine physician with experience in concussion evaluation and management, Dr. Gerry Gioia, director of Pediatric Neuropsychology at Children's National Medical Center and an expert in pediatric mTBI and neurocognitive assessment, and Dr. Mark Espeland, a biostatistician experienced in large multi-institutional longitudinal studies and analyses of cognitive and neuropsychologic data. The imaging group includes Dr. Maldjian, a neuroradiologist with expertise in advanced image analyses and software development and director of the ANSIR lab, Dr. Chris Whitlow, a neuroradiologist with expertise in study design and imaging statistical analyses of pediatric developmental data, Dr. Youngkyoo Jung, an MRI physicist with expertise in ASL and diffusion imaging, and Ben Wagner, an experienced programmer in the group. Technical support for MEG data acquisition was provided by Dr. Dwayne Godwin and his students through the Department of Neurology MEG Center. Technical support for MRI data acquisition was provided by Sandra Kaminsky and Debra Fuller through the Center for Biomolecular Imaging. BME PhD students critical to the success of the study include Jillian Urban and Elizabeth Davenport. Funding for the study has been provided by the Childress Institute for Pediatric Trauma.



Drs. Joseph Maldjian and Chris Whitlow

Undergraduate Minor

The biomedical engineering campus at Virginia Tech has been humming with an abundance of undergraduate research students this summer. Students are immersed in collecting and analyzing data in order to help solve a diverse group of highly relevant biomedical engineering challenges ranging from biomechanical to tissue engineering studies. As a key component in our Biomedical Engineering undergraduate minor program, each student is required to conduct biomedical engineering research. Student projects can be independent studies which involve individual research opportunity or they can include departmental senior design projects which have a SBES faculty who mentors a group of students. With a full year of research experience, we expect that our students graduating with a biomedical engineering minor attached to their VT engineering major will be highly attractive to top ranked graduate and medical schools as well as biomedical industries!



With all the ongoing research, SBES introduced our new SBES Undergraduate Travel Award this summer. These prestigious awards sponsored two BME minor students, Nathan Roberson and Shanel Tsuda, to attend the 2013 Biomedical Engineering Society Annual Conference, which was held in Seattle, WA. During a poster presentation, the students were given a valuable opportunity to present their research study to the international biomedical engineering community. This travel experience provided the students with career development training, professional networking sessions and an overall global view of how important biomedical engineering research is to society.

For more updates on our program be sure to take a look at our undergraduate education webpage (<http://www.sbes.vt.edu/undergrad.php>). I am looking forward to another successful year!

Pamela VandeVord, Ph.D.
Associate Professor
Associate Department Head for Undergraduate Programs

Students: Adam Little, Anthony DeGregorio and Samuel Miller

Student Chapter Activities: 2012-2013

VT-WFU BMES Chapter



The VT-WFU Biomedical Engineering Society (BMES) Student Chapter was founded to bridge the gap between Virginia Tech and Wake Forest University, foster communication and collaboration among various research groups, and become more involved in National BMES events. This year, we continued to nurture this relationship both academically and socially. The year started off with a hiking trip to Hanging Rock State Park to bring together new members, and ended with over 80 student presentations at our 12th Annual SBES Graduate Student Symposium.

The Chapter was very active this year! We expanded our outreach and mentoring events immensely. Our members volunteered to judge local science fairs, donated their time through local mentoring programs, and promoted science, technology, engineering, and math to children in both the communities of Blacksburg, VA and Winston-Salem, NC. We hosted a number of social events throughout the year at both campuses. Nearly a third of our members visited BODIES The Exhibition when we travelled to Atlanta for the 2012 BMES Annual Meeting, there were two tailgates (Hokies and Demon Deacons won!) that brought out the best of school spirit, and a game night that helped raise funds for Relay for Life which showed just how competitive students can be. Our various internal and external fundraising events totaled over \$3000. We donated over \$1000 to Relay for Life, \$650 to Big Brother Big Sister, and awarded \$700 in monetary awards to the top oral and poster presentations at the 12th Annual SBES Graduate Student Symposium.

The Symposium was our largest event and required year-round planning. This year, we had 32 oral presentations and 51 poster presentations given by graduate and undergraduate students in the chapter. We would like to thank all our sponsors who help make this event such a success. This year there were four returning sponsors and one new sponsor for the 2013 Symposium: our goal is to have the Symposium fully funded by outside sponsorship. We plan to stay connected with our current sponsors throughout the year and look forward to meeting potential new sponsors at the upcoming BMES Annual Meeting in Seattle!

While we had a great year this year, we anticipate even more growth as we move forward. The addition of a biomedical engineering minor at Virginia Tech (new for the 2012-2013 academic year.) has increased undergraduate awareness of biomedical engineering. Our chapter is currently working with an undergraduate biomedical engineering interest group at Virginia Tech. This year, we plan to integrate these students into our existing BMES student chapter and encourage many of them to join BMES at the national level.

WFU EMBS Chapter

The Wake Forest University Engineering in Medicine and Biology Society (EMBS) had another successful year! The EMBS club sustains an active and vital partnership with the Winston-Salem IEEE Section, whose membership includes engineers in industry and academia. EMBS members attend monthly seminars presented by local and regional engineering leaders, with lunch generously provided by the Section. As in previous years, student members presented their research to the community at the lunch seminars. Two such seminars were held this year with presentations in the fall from Adam Golman, EMBS Social Chair JP McQuilling, and EMBS President Megan Johnston. Becky Wailes, John Scott, EMBS Secretary Jennifer Huling, and EMBS Vice President Elizabeth Davenport gave presentations in the spring. The EMBS club and IEEE section also teamed up at Forsyth Tech Community College to recruit student members to the IEEE.

The EMBS club hosted many other professional development, community outreach, and social activities. EMBS held a very successful Toys For Tots toy drive in December. A few members also had the chance to host after-school engineering activities at Hanes Middle School; one related to airplanes in February in celebration of National Engineers Week, and one in March related to the design of medical tests, especially to encourage girls to enter the field of engineering. The EMBS club joined with the BMES club to host a booth at the Atkins High School STEM night in April for their incoming freshmen to get a taste of the breadth of the fields of engineering and technology. A beginning-of-the-year cookout, Halloween luncheon, Thanksgiving potluck and several happy hour socials were also held.



Back Row: John Scott, John McQuilling, Carlos Kengla, & Tanner Hill Front Row: Hannah Baker, Tabitha Rosenbalm, Christine Kowalczewski, Elizabeth Wailes, & Elizabeth Graham

Faculty

Our Biomedical Engineering program involves:

78 tenure track biomedical engineering faculty (25 primary and 53 joint appointments)



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Crash, Auto Safety*
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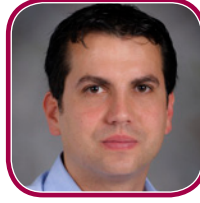
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OUR 23-YEAR HISTORY WITH BMES

1990 BMES

Virginia Tech hosted the first annual fall BMES conference in Blacksburg Virginia two decades ago. Until this time, BMES had combined with other conferences each year. The 1990 conference theme was "Biomedical Engineering: Opening New Doors."



2013 BMES

We are bringing **over 78 biomedical engineering faculty and graduate students** from Virginia Tech and Wake Forest University for the BMES conference in Seattle, Washington. These faculty and graduate student will present **over 77 papers and posters** highlighting their recent research accomplishments. Please look for these papers and stop by our booths to play a game based on our research (200/201/202/203/204/205).

The VT-WFU BMES chapter will receive the 2012 fleetest feet award at the 2013 BMES National Meeting. Our chapter brought 68 students to the BMES Annual Meeting. The Fleetest Feet award was founded in 1992 to promote and expand student participation in the BMES Annual Meeting. The award is for traveling the most miles to the BMES National Meeting.



*BMES Officers receiving
BMES Fleetest Feet Award
for the 2011 Hartford, CT
conference.*



*BMES Officers receiving both Merituous
Award and BMES Fleetest Feet Award
for the 2010 Austin, TX conference.*

Stefan Duma
editor

Pam Stiff
co-editor

Cindy Keister
designer



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SCHOOL of MEDICINE



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