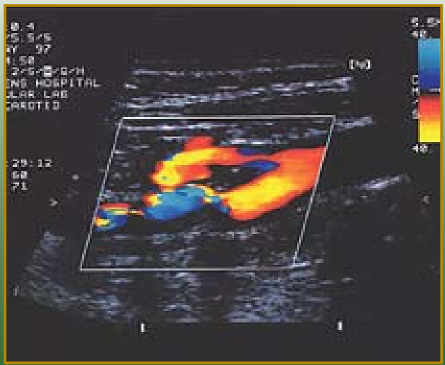
Biomedical Engineering

Biomechanics and Biomaterials

Molecular, Cellular, and Tissue Engineering

Medical Diagnostics, Devices, and Imaging



SCHOOL OF BIOMEDICAL ENGINEERING

Colorado State University

We are pleased to announce Colorado State University's new School of Biomedical Engineering (SBME). The SBME is supported by four CSU colleges and has over 50 faculty members in 14 departments, providing a unique interdisciplinary focus on bioengineering research and education. The School's structure offers many advantages over the traditional academic department structure because it enables horizontal integration of faculty and their research programs across multiple departments. SBME faculty and students work in interdisciplinary teams to fight cancer, develop new orthopedic implants, or design new biosensors to treat neurological disorders. Some of CSU's strongest faculty and researchers are among the SBME faculty. The new School structure facilitates their ability to work together, to attract the brightest graduate students to their laboratories, and to partner with industry in solving today's bioengineering problems. The biomedical industry also will benefit from hiring SBME's uniquely trained graduates who have mastered the balance of in-depth engineering skills and broad interdisciplinary clinical, science, and engineering topics to work in today's challenging bioindustry.

We look forward to building partnerships with you in the future and will keep in touch as the School grows, new research programs develop, and new faculty come on board. We always welcome input on our curriculum. Please keep an eye on our website at www.engr.colostate.edu/sbme for the most timely developments.

This publication showcases SBME's interdisciplinary research themes on the following pages:

Dr. Susan James, Director and Professor
School of Biomedical Engineering
sjames@engr.colostate.edu

Mission Statement

The Colorado State University School of Biomedical Engineering combines Colorado State University's strengths in veterinary medicine, engineering, and the sciences to provide an interdisciplinary focus on improving health, fighting disease, and aiding persons with disabilities.

Degree Offerings

Doctor of Philosophy (Ph.D.)
Master of Science (thesis based)
Master of Engineering (coursework only)
B.S./M.S. (combined degree program)
Interdisciplinary Studies Certificates for undergraduate students

First-year rotations with funding (tuition and stipend) are provided for the top incoming doctoral students.

Multi-College Effort

The Colleges of Applied Human Sciences, Engineering, Natural Sciences, and Veterinary Medicine & Biomedical Sciences form the School of Biomedical Engineering. The SBME faculty are drawn from fourteen different departments within these four colleges.

SBME Connections

Our website at www.engr.colostate.edu/sbme/ features faculty research. Faculty work closely with biomedical companies along the Front Range as well as companies all over the world, and they are actively involved in the State of Colorado's new Bioscience Discovery Evaluation Grant Program administered by the Colorado Office of Economic Development and International Trade.

Translational Research

In addition to industrial funding, our faculty's research programs are also funded by federal agencies such as the National Science Foundation and the National Institutes of Health. CSU's world-class Veterinary Medical Center offers specialized resources for biomedical researchers planning *in vivo* animal models as a transition to clinical studies.

Biomedical engineering offers a particularly rich theme for industry-funded research and transfer of university-owned technology to the private sector, which is key to the success of SBME faculty and the University and also leads to economic and workforce development in the Colorado community. For these reasons, strong higher education programs like SBME have been linked to the growth of the bio-industry in other parts of the country.

Bioengineering Academic Programs

Bioengineering is one of the largest and fastest growing industries in Colorado and the U.S. Through an innovative curriculum and interdisciplinary projects, Colorado State University is preparing biomedical and bioengineering students at both the graduate and undergraduate levels to address society's current and emerging needs in the health fields.

Building on the strength of the College of Engineering's Biomedical Engineering Program established in 2000, the new School of Biomedical Engineering (SBME) is now offering Ph.D. and M.S. degrees in bioengineering, in addition to the existing Master's of Engineering and Interdisciplinary Studies Certificate programs in biomedical engineering.

The graduate programs in bioengineering integrate physical, chemical and mathematical sciences with engineering principles and clinical studies. There are boundless opportunities for research, ranging from new therapies and imaging modalities for fighting cancer, to improving the design of vital medical equipment used in open heart surgery or developing the next generation of gene therapies and engineered tissues. These new graduate programs will produce well-trained researchers who will dedicate their careers to creating advances in the treatment of acute and chronic health conditions that directly affect the citizens of Colorado, the nation and the world.

Colorado State University is uniquely positioned to offer these advanced degree programs. CSU's highly ranked College of Veterinary Medicine and Biomedical Sciences are co-located with engineering and sciences on the CSU campus, providing a rich environment for interdisciplinary research and day-to-day collaborations.

For information about Colorado State's biomedical engineering program or questions about your application for admission, contact Lori Dwyer at 970-491-7157 or Lori.Dwyer@colostate.edu

In Fall 2007, Colorado State University began accepting applications for the Doctor of Philosophy degree in bioengineering, the first of its kind in the state. Preparing students to play a leadership role in the biomedical community, the Ph.D. program allows students more involvement in directing research projects and laboratories.

The thesis-based Master of Science degree is another enhancement to the bioengineering program at Colorado State. In addition, the new SBME offers a Master of Engineering degree, a coursework-only professional degree that provides a time-effective way for students and professionals to update skills and obtain advanced training in the field of biomedical engineering.

At the undergraduate level, the Interdisciplinary Studies Certificate in Biomedical Engineering offers academic opportunities to students from diverse backgrounds interested in the field. Similar to a minor, the certificate may be added to any undergraduate degree program. The SBME also offers a combined BS/MS degree program in bioengineering.

Course Offers Cutting-Edge Interdisciplinary Tools

Addressing the increasingly interdisciplinary nature of engineering, Dr. Amy Pruden, assistant professor of civil and environmental engineering, *(pictured above with master's student Matt Hewitt)* has designed a new laboratory-based course intended to introduce engineering students who lack a background in biology to concepts and skills in biotechnology and molecular biology. CIVE/BIOM-535, Biomolecular Tools for Engineers, is a core requirement of the new biomedical engineering curriculum, and is also cross-listed as an elective for students of other engineering backgrounds.

The new course will provide students with the opportunity to learn cutting-edge skills via hands-on methods. Throughout the duration of the semester, students will become familiar with qualitative and quantitative aspects of biomolecular analysis including Polymerase Chain Reaction (PCR), cloning and microbial community profiling, DNA extraction and DNA sequence analysis. The potential for application of biomolecular tools to engineered systems will also be a major theme.

Teaching and research are integrated by having students present current journal articles to the class, and by carrying out a semester-long project in which the students analyze the microbial communities present in a sample of their choice and write up a draft manuscript presenting and discussing their results.

Support for this course was received through the National Science Foundation Course Curriculum and Laboratory Improvement program. As part of the program, course content and delivery was developed in collaboration with environmental engineering faculty at four other universities: the University of Cincinnati, Pennsylvania State University in Harrisburg, the University of Wisconsin in Milwaukee, and the University of Southern Florida.

Investigating Osteoarthritis

Recognized as a premier center for equine and human joint disease, the Equine Orthopaedic Research Center (EORC), part of the College of Veterinary Medicine and Biomedical Sciences, is a leader in innovative treatments for arthritis and cartilage healing. Examining new treatment methods for osteoarthritis, Dr. David Frisbie, associate professor and Doctor of Veterinary Medicine, in collaboration with researchers nationwide, is engineering cutting-edge technology to address joint injuries in the athletic horse.

Stem cells as treatment for osteoarthritis

Heading up a multi-center clinical trial, Dr. David Frisbie and Dr. John Kisiday, assistant professor in clinical sciences at the EORC, working in collaboration with Oakridge Equine Hospital in Oklahoma, Washington State University, and Texas A&M, are having great success utilizing stem cell therapy in addressing equine orthopaedic disease. Well suited for use in damaged joints, adult bone marrow-derived stem cells have the potential to regenerate tissues without the production of scar tissue during the healing process.

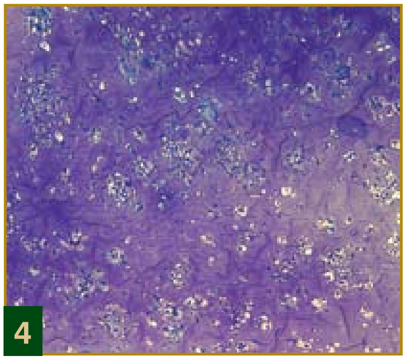
Of the 15 horses chosen for clinical trial – all of which researchers felt had little hope of recovery with conventional therapy – 10 (67%) became sound and returned to their previous level of work. To date the group has treated 40 joint-related cases. The next step is to acquire funding to compare fat-derived cells, a commercially available source, to those derived from bone.

Investigation of gene regulation cell-by-cell in equine osteoarthritis

Another project involving Dr. Frisbie and Dr. Katja Düsterdieck, a recent Ph.D. graduate, involves investigation of gene expression patterns between two different layers of osteoarthritic and normal articular cartilage. By studying the differences in gene expression patterns, researchers hope to yield genes that may play a role in the pathophysiology of osteoarthritis and the identification of new possible targets for the treatment of the disease.

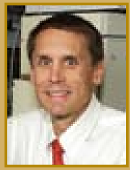
Düsterdieck first isolated RNA from individual cells of various cartilage layers, a feat not accomplished before in articular cartilage, to obtain enough material to be analyzed on an equine gene chip. The research team then determined what genes are differentially expressed in osteoarthritic versus normal articular cartilage from different depths within the cartilage. Over 150 genes, from adult horses with carpal osteoarthritis, were found to be differentially expressed based on depth of the chondrocytes in the articular cartilage. Similarly, different expression patterns were found for osteoarthritic and control cartilage.

Osteoarthritis remains a common and debilitating disease. Research at Colorado State provides the basis for future investigation into the pathophysiology of osteoarthritis and the identification of new therapeutic targets for the treatment of this debilitating disease in humans, horses, and other mammalian species.

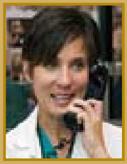


A toluidine blue stain for proteoglycans in a marrow cell-seeded gel.

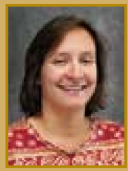
Faculty: Biomechanics and Biomaterials



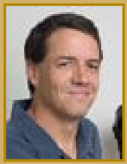
William Dernell, associate professor, clinical sciences; *Research interest:* Preclinical evaluation of therapeutics and devices for the treatment of cancer and severe infection



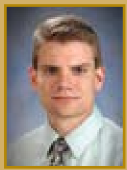
Nichole Ehrhart, associate professor, clinical sciences; *Research interest:* Osteoneogenesis, limb salvage, allograft science, cytokine therapy



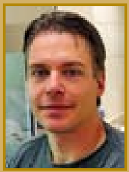
Susan P. James, director and professor, mechanical engineering; *Research interest:* Polymeric materials, biomechanics



Chris Kawcak, assistant professor, clinical sciences; *Research interest:* Osteoarthritis, fracture repair

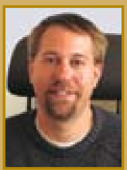


Matt J. Kipper, assistant professor, chemical and biological engineering; *Research interest:* Polymeric biomaterials, polysaccharides



John Kisiday, assistant professor, clinical sciences; *Research interests:* Tissue engineering, mechanobiology

Wayne McIlwraith, professor, clinical sciences; *Research interest:* Diagnosis and treatment of joint disease including cartilage healing



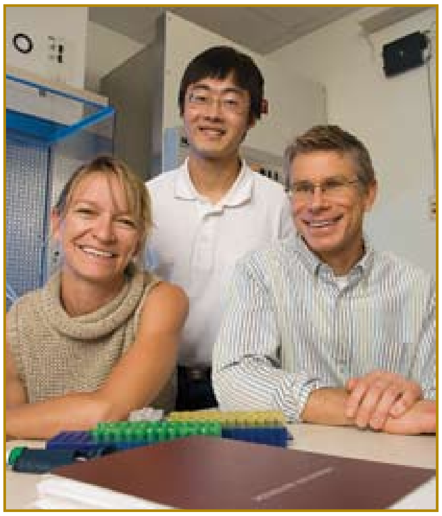
Christian Puttlitz, assistant director and associate professor, mechanical engineering; *Research interest:* Orthopaedic biomechanics

Xianghong Qian, assistant professor, mechanical engineering; *Research interest:* Computational biomaterials science

Raoul Reiser, assistant professor, health and exercise science; *Research interest:* Musculoskeletal kinematics

David (Qiang) Wang, assistant professor, chemical and biological engineering; *Research interest:* Polymeric biomaterials

Soy Products and Heart Health: Using Proteomics to Understand the Connection



Cardiovascular disease (CVD) continues to plague the United States and other industrial countries. As researchers continue to look for explanations and treatments, soy has been receiving considerable attention for its potential role in decreasing CVD risk. Part of the reason for this is the observation of a lower incidence of CVD in Asian populations, who consume high phytoestrogen diets, primarily in the form of soy products. Soy contains a host of potentially bioactive phytochemicals including phytoestrogens such as sterols, saponins, and isoflavones.

The FDA approved labeling foods containing soy as protective against heart disease in 1999. Initially, it was thought that soy promoted a favorable blood lipid profile, thus decreasing CVD risk. However, the effects of soy on cholesterol levels are now known to be minimal except in the most severe cases. Clearly, much remains to be discovered about the cardiac health promoting effects of phytochemicals in soy.

Dr. Karyn Hamilton, assistant professor in the Department of Health and Exercise Science, and Dr. Ken Reardon, professor of chemical and biological engineering, are using proteomics to learn more about the cardiac effects of soy phytochemicals. Proteomics refers to the system-wide analysis and identification of proteins in cells and tissues. Using current methods, it is possible to obtain information on more than 1,000 proteins in each sample.

Since proteins are central to all biological functions, a comparison of the differences in the proteins of cardiac cells treated with soy phytochemicals compared to untreated cells will provide important insights into the "heart healthy" potential of soy. Together with Ph.D. student Zeyu Sun, Hamilton, and Reardon *(shown above)* are focusing their efforts on genistein and daidzein, the predominant phytoestrogens in soy. (One cup of soy milk contains about 6 milligrams of genistein and 5 milligrams of daidzein.) Their initial experiments involve exposing cultured heart muscle cells (cardiomyocytes) to different levels of these soy phytoestrogens and comparing the resulting protein profiles. In other experiments, they will mimic the effects of diseased hearts by stressing the cells with low oxygen levels or high concentrations of fatty acids. Proteins that are present at higher or lower levels after the soy treatment will be identified and used to form hypotheses about the potential effects of soy on cardiac health.

The research of this multidisciplinary CSU team will shed light on the connection between soy protein and heart health, and may also lead to some novel approaches to the treatment of cardiovascular disease .

Faculty: Molecular, Cellular, and Tissue Engineering

Jim Bamburg, professor, biochemistry and molecular biology; *Research interest:* Regulation of cell behavior through cytoskeletal dynamics

Norman Curthoys, professor, biochemistry and molecular biology; *Research interest:* Control of mRNA turnover, proteomics

David Dandy, professor, chemical and biological engineering; *Research interest:* Biosensors, microfluidics

Frank Dinenno, assistant professor, health and exercise science; *Research Interest:* Integrative cardiovascular physiology, vascular dynamics and regulation

David Frisbee, associate professor, clinical sciences; *Research interest:* Gene therapy, intra-articular therapeutics, new methods of cartilage repair.

Charles Henry, assistant professor, chemistry; *Research interest:* Lab-on-a-chip, bioanalytical chemistry

Amy Pruden, assistant professor, civil and environmental engineering; *Research interest:* Biomolecular methods

Ken Reardon, professor, chemical and biological engineering; *Research interest:* Environmental biotechnology, biosensor design, bioreactor strategies, proteomics

Stuart Tobet, professor, biomedical sciences; *Research interest:* Determination of cell positions in the developing neuroendocrine

Ranil Wickramasinghe, associate professor, chemical and biological engineering; *Research interest:* Biomedical devices, blood separations, bioseparations

Other faculty working in this area:
Matt J. Kipper
Wayne McIlwraith
Xianghong Qian
David (Qiang) Wang

Mathematician Develops Solutions for Heart and Lung Patients

Each day at the Electrical Impedance Tomography Laboratory in the Department of Mechanical Engineering at the University of São Paulo (USP), Brazil, physicians and engineers, graduates and undergraduates are working together to advance a technique for heart and lung imaging from electric fields. In spring 2007, USP was also the sabbatical home to CSU mathematics professor Jennifer Mueller.

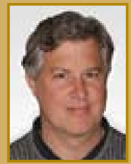
Electrical impedance tomography (EIT) is a relatively new imaging technique in which electrodes are placed on the surface of the body, a low-amplitude current is applied on the electrodes, and the resulting voltages are measured. An inverse problem is solved to determine the conductivity distribution in the body, and the results are plotted to form an image. The resolution of the image is very poor compared to that of an MRI or CT scan. However, the usefulness of EIT in heart and lung imaging is that "while other technologies are focused on and therefore represent anatomy, EIS serves as a visualization of regional organ function and has very good resolution in time," says Stephan Böhm, a member of the research team in São Paulo.

Patients with ARDS (acute respiratory distress syndrome) have collapsed alveoli, or airways, in the lungs. The treatment for this condition is mechanical ventilation, which reinflates the airways (recruitment) over time. Eventually, the patient recovers and can be weaned from the ventilator. However, alveolar collapse, cyclic closing and reopening of the airways, and lung overdistention are dangerous side effects of mechanical ventilation that can be prevented by choosing the proper settings for the ventilator.

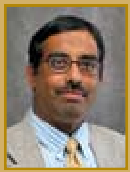
Physician Marcelo Amato founded the research team in 1997 when he became convinced that EIT technology would provide the best solution for the problem of monitoring patients undergoing mechanical ventilation. The protective ventilation technique employs a low inspiratory driving pressure, which should result in slower recruitment, and high end-expiratory pressure to avoid reclosing of alveoli. These settings are currently determined from the pressure-volume (PV) curve. Prior to EIT, a method did not exist for determining regional ventilation data or monitoring for ventilator-induced problems such as cyclic lung collapse or over-inflation. Methods used to monitor patients undergoing mechanical ventilation include monitoring blood gases and pressure-volume curves, but these quantities do not provide regional information about lung aeration. EIT can also effectively diagnose lung pathologies such as pulmonary embolus, pulmonary edema and pneumothorax.

Mueller has been working in EIT for the past 10 years. She is co-advising the Ph.D. theses of two USP students in EIT who plan to spend the 2008-2009 academic year in residence at CSU.

Faculty: Medical Diagnostics, Devices, and Imaging

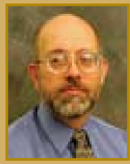


Chuck Anderson, associate professor, computer science; *Research interest:* Biomedical image and signal processing



V. Chandrasekar, professor, electrical and computer engineering; *Research interest:* Bio signal processing

Tom Chen, professor, electrical and computer engineering; *Research interest:* Intracellular communicative sensor development



Kevin Lear, associate professor, electrical and computer engineering; *Research interest:* photonic biosensors

Jennifer Mueller, associate professor, mathematics; *Research interest:* mathematical biology and imaging

Brad Reisfeld, assistant professor, chemical and biological engineering. *Research interest:* Metabolomics, computation toxicology, systems biology

Other faculty working in this area:
Jim Bamburg
Norman Curthoys
David Dandy
William Dernell
Frank Dinenno
Charles Henry
Susan P. James
Stuart Tobet
Ranil Wickramasinghe

Dr. Raul Gonzalez-Lima and Dr. Julio Aya in the electrical impedance imaging lab at USP.

Beyond the Classroom

Innovative Modeling: Examining Facet Joints of the Cervical Spine

Daniel Woldtvedt, mechanical engineering and biomedical science double major, and Ph.D. student Wesley Womack *(shown at right)* recently collaborated to develop a novel three-dimensional model showcasing the physiological distribution of cartilage thickness in cervical spine facet joints. Recognized for his outstanding biomedical engineering research and paper titled "Three-dimensional Cartilage Thickness Mapping of Cervical Facet Joints," Woldtvedt was recently honored with the 2007 Biomedical Engineering Society (BMES) Undergraduate Research and Design Award.

Working under Dr. Christian Puttlitz, assistant professor of mechanical engineering and co-director of the new School of Biomedical Engineering, Womack and Woldtvedt have been conducting research in state-of-the-art facilities at the Colorado State Orthopaedic Bioengineering Research Laboratory (OBRL). The laboratory, part of the Musculoskeletal Program——an interdisciplinary program between Colorado State's College of Veterinary Medicine and Biomedical Sciences and the College of Engineering—is one of 16 Programs of Research and Scholarly Excellence at CSU.

Facet joints, those linking vertebrae together, preserve flexibility in the spine and provide needed limits to motion, especially rotation. Together, both researchers successfully generated the first three-dimensional map of cartilage between cervical facet joints, relying heavily on custom-written computer algorithms.

Creating the three-dimensional map involved dissecting cervical vertebrae from seven human cadavers, sectioning the vertebrae into 1 millimeter slices and photographing each slice alongside a scale. Womack was then able to write mathematical code used to define the cartilaginous regions on each slice in three-dimensional coordinates. Subsequently, a series of MathCad algorithms generated maps of the cartilage distribution.

Mechanical models provide numerous applications for biomedical advancements. These maps have already been implemented into Womack's computational (finite element) model of the cervical spine, with a significant effect on its accuracy. The model is intended to simulate spine biomechanics, with the end result of understanding the effects of intervertebral disc replacements on load distribution at the facet joints, and can be used as a tool to model and engineer biomedical treatments for the future.

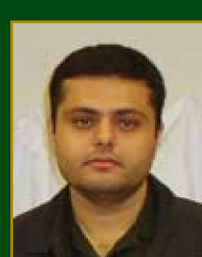
In addition to developing an innovative model, Womack and Woldtvedt have benefited from their research in many ways. Their student-mentor relationship provided Womack an opportunity to gain invaluable mentoring experience critical to a career in academia, in addition to a hands-on research opportunity for Woldtvedt.

"Working at the OBRL has been an incredible experience," said Woldtvedt. "Dr. Puttlitz, Wes, and the other graduate students have served as excellent mentors and really enriched my entire undergraduate experience."

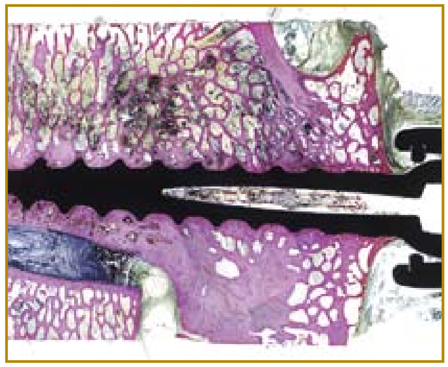
Other key research conducted by Dr. Puttlitz and his research team includes modeling of the lumbar spine and engineering scaffolds to treat cartilage damage in the human knee. In collaboration with Dr. Sue James, researchers are teaming to develop scaffolds for tissue repair with information derived from the knee model.

Recent Hires with Biomedical Engineering Research Interests:

Diego Krapf, assistant professor, electrical and computer engineering; *Research interest:* use of nanoscale devices to unravel the dynamic behavior of protein-DNA complexes, crucial in understanding human diseases, including many types of cancers and neurological disorders



Dr. Ketul Popat, assistant professor, mechanical engineering; *Research interest:* Bio-nanotechnology and application in tissue engineering, nanostructured interfaces for orthopedic applications, drug eluting coatings for implantable devices, biomaterial surface modification and characterization



School of Biomedical Engineering
Leadership Team

Dr. Susan James, Director and Professor
School of Biomedical Engineering
Campus Delivery 1376
E-mail: sjames@engr.colostate.edu

Dr. Christian Puttlitz
SBME Associate Director and Assistant Professor
E-mail: puttlitz@engr.colostate.edu

Dr. Ranil Wickramasinghe
SBME Associate Director and Associate Professor
E-mail: wickram@engr.colostate.edu

For additional information or an application for admission:
970-491-7157
www.engr.colostate.edu/sbme

Colorado State University

COLLEGE OF ENGINEERING

1301 Campus Delivery
Fort Collins, Colorado 80523-1301