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IUPUI

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THE BME NETWORK

IUPUI - Purdue School of Engineering & Technology

Newsletter of the Department of Biomedical Engineering

Mechanical Principles of Bone Adaptation: Powerful Alternative to Pharmacological Treatments?

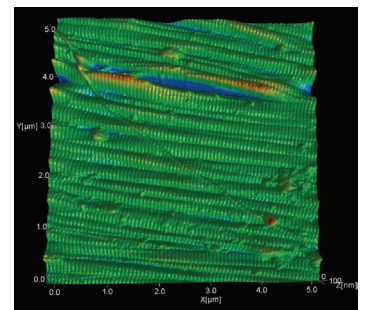
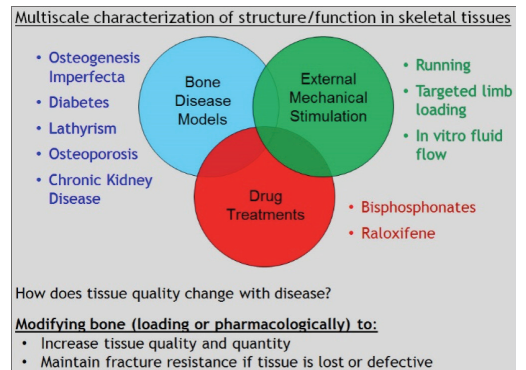
Bone is an elegant material that serves important structural and metabolic roles in the body. Despite the importance of a healthy skeleton to overall health and well-being, it is unclear how bone's fundamental constituents (Type I collagen and mineral) produce a material that is capable of handling the daily structural and metabolic demands that are placed on it. There is also limited understanding of how perturbations to these constituents alter bone's fracture resistance. Basic and clinical research focuses heavily on bone's mineral phase, but collagen's role is often overlooked or considered secondary. The Bone Biology and Mechanics Laboratory (BBML) is intensely focused on collagen and the roles it plays in bone health. Collagen provides ductility and toughness, properties essential to fracture resistance, and is responsible for tensile strength. The various studies in the lab focus on conditions which alter specific aspects of collagen in an attempt to understand their impacts from mechanical engineering and materials science perspectives. By investigating approaches that can make bone stronger through alterations in collagen rather than mineral or architecture, a paradigm shift may be possible in the way that we approach bone disease prevention and treatment.



Our research falls into three independent yet interconnected arenas: bone disease, adaptation to external mechanical stimulation and pharmacological treatments for disease (Figure 1).

Multiscale effects on musculoskeletal

mechanics: The fundamental constituents of bone exist at the nanoscale (i.e. an individual collagen molecule is about 1.5 nm x 300 nm; mineral platelets are ~ 50 nm x 25 nm x 3 nm). Nanoscale features of tissues are inherently difficult to study given their small size. The major focuses of the lab are to interrogate collagen morphology and mechanics using atomic force microscopy (AFM) and to validate what these characteristics mean to larger scale properties in bone and other connective tissues. As opposed to microscopes which focus light or electrons on a sample to produce an image, AFM works by dragging a sharpened probe over the sample's surface and using electrostatic interactions to build a map of sample topography. The most prominent feature of collagen is an oscillating surface pattern known as the D-spacing (appears as a striped pattern perpendicular to the fibrils' axis in Figure 2), and it is present on fibrils in all Type I collagen-based tissues. Over the past 5 years, our data indicate that D-spacing is a window into a tissue's nanoscale status. We have demonstrated clear and quantifiable changes in collagen nanoscale structure in bones and tendons from several disease models including Osteogenesis Imperfecta (OI), Type II Diabetes, Osteoporosis, Lathyrism, and Chronic Kidney Disease. Relating nanoscale findings to chemical, architectural and functional changes at larger length scales is the real focus of this work (Figure 3). AFM has been used to extract mechanical information from collagen in tendon and



Message from the Chair



Edward J. Berbari

Chancellor's Professor
and Chair of Biomedical
Engineering

BME Word Jumble

hknquoxdiyelh

model of action potential initiation,
named for the Nobel Prize-winning
scientists who developed it

einageiiimlbrnedgcoen

best major ever

ndotuhusg

best treat ever

vauacrdsciraol

best organ system ever

Each fall provides me with an opportunity to reflect on the successes of our graduating class and share with you the exciting careers some of our alumni have chosen. The Indiana Zeta Chapter of Tau Beta Pi was installed at IUPUI on March 28, 2015. The 2014 Convention granted a chapter to Tau Beta Zeta, represented in Spokane, WA by Leandro Moretti, president; Jeremy Mihajlovich, vice-president; and Ken Yoshida, PhD and chief advisor. Dean David J. Russomanno, PhD, congratulated the new members and expressed his pride in this milestone event for the school and university. Eight of our BSBME students received various awards as members of the 16th Annual IUPUI Top 100 Outstanding Students, recognizing them for scholastic achievement, extracurricular activities on campus, to civic and community service. They are Megan Bryant, Caleb Comoglio, Wiaam Elkhatib, Timothy Emmel, Ellen Maue, Javed Syed, Katie Wight, and Rachael Bridegroom. Our fall 2015 newsletter highlights the careers of two of our alumni, Sara McGowan (Smith) and Paul Curtis. Sara is currently at The Scripps Research Institute in Florida, working in the Aging and Metabolism Department. Paul Curtis is currently employed part-time at IU Health as a Simulation Specialist and is also founder of Curtis Life Research (CLR), where he has developed a medical simulator for ECMO. I am proud to note that since the inaugural 2008 graduating class, 139 students have received their BSBME degree from our program. "IUPUI Biomedical Engineering Department Alumni" on LinkedIn is a great way to drop a note from time to time and stay in touch with other alums. Please consider joining the group.

The Faculty Highlight showcases Dr. Joseph Wallace and his research lab, summarizing the current research he and his lab members are focused on. Our congratulations to Dr. Wallace, as he recently received his first federal grant from the National Institutes of Health as Principal Investigator. He began his career with the Biomedical Engineering Department at IUPUI in 2010, and continues to teach at both the undergraduate and graduate levels, in addition to publishing over 40 papers, a book chapter, numerous poster sessions and podium presentations, along with several awards and distinctions, most recently the "Featured investigator in the 2014 IUPUI Research Report-February 2015".

New Hire: Join me in welcoming our new part-time office assistant to the department, Anita Adams Sale.

New Appointments: Dr. Steven Higbee has been promoted to Clinical Assistant Professor and will continue in his teaching and undergraduate research duties. Dr. Karen Alfrey continues in our department under the new title of Clinical Associate Professor, along with her duties as Director of Undergraduate Admissions and Associate Chair of Biomedical Engineering, and Dr. Sungsoo Na has been promoted to Associate Professor. Congratulations to all!

Sara McGowan, BS BME 2011



I work as a Research Assistant for Laura J. Niedernhofer, M.D., Ph.D., in the Aging and Metabolism department at The Scripps Research Institute Florida. In Dr. Niedernhofer's lab, we investigate the role DNA damage has on DNA structure, cell function and organism's health-span. I manage a mouse colony of over 30 genetic mutations, write and execute experiments, collect data and perform statistical analysis. I have used my degree in the statistical analysis of data and in creating an animal database that stores information for animals, breedings, in vivo data, necropsy collections and specimen tracking. I particularly appreciate the programing skills we learned in the BME program. My programming skills have significantly improved efficiency and streamlined workflow in our lab. It also allows me to easily learn other programming languages when needed.

Paul Curtis, BS BME 2010 & MS BME 2012



I was in the first graduating class of BME BS, but I graduated in 2010 when I completed my second undergrad degree ECE. I am currently employed part time at IU Health as a Simulation Specialist. My other part time job is the founder of Curtis Life Research (CLR) where I have developed a medical simulator for ECMO. At IU Health, my job is to provide technical skills to support the use of simulation in multidisciplinary healthcare settings. I am trained to operate patient simulators (computerized manikins) during simulation for students and assist in training faculty in the use of simulation equipment. At CLR, I'm currently producing and selling an ECMO simulator titled EigenFlow. My work consists of research and design, demonstrating the product as a vendor at medical conferences, and working with physicians to develop new solutions. The skills that I have gained from my BME degree have been a thorough understanding of biology, physiology, basic electronics, and numerical computation. My education also helped me develop critical problem solving and leadership skills.

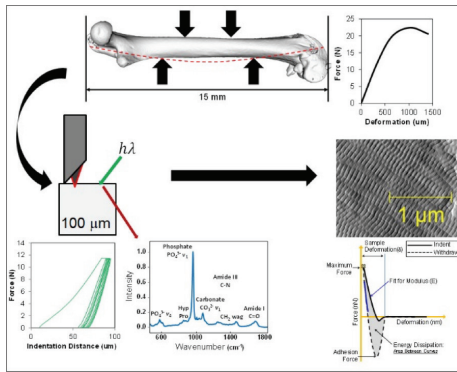
[Mechanical Principles] Continued from page 1

showed that phenotypic changes in morphology are accompanied by altered mechanical properties at the nanoscale and in larger-scale collagen fibers. Studies in OI bone revealed connections between nanoscale changes in collagen and whole bone functional deficiencies. These studies demonstrate that changes in collagen morphology and mechanics are present in diseased tissues, and may be related to structural mechanical alterations. Continuing these multiscale characterizations is an ongoing goal of the lab and has expanded into new disease and drug treatment models through collaborative efforts with researchers in the Departments of Anatomy and Nephrology in the IU School of Medicine.

Mechanical adaptation in bone: The second major thrust of the lab is to study the multiscale impacts of mechanical stimulation in bone. As opposed to the static view many have of our skeletons, bone is constantly adapting to its ever-changing mechanical environment. Our long-term goal is to determine if fracture resistance can be improved using mechanical loading to directly alter collagen and mineral. Our methods of mechanical stimulation include whole body exercise (e.g. treadmill running) as well as more targeted loading of individual limbs (axial compression of the tibia). In vitro studies are also being carried out to understand the direct impact mechanical cues have on matrix production and quality from bone cells. In combination with the various disease models discussed above, we are also using mechanical stimulation to prevent and/or treat disease-induced changes in bone quality and fracture resistance. Specifically, a recently funded grant from the NIH is focused on molecular mechanisms underlying collagen defects in disease models, and the ability of mechanical loading to prevent or compensate for these defects and protect collagen quality.

Future directions: As the lab has matured and new collaborations have begun, there are several exciting new projects that are getting underway. This includes on campus work with the IU Department of Anatomy and Cell Biology, Nephrology, and Biology in addition to the Wells Center for Pediatric Research. In addition, active collaborations off campus with researchers and clinicians from IU health, the Washington University Department of Pediatric Nephrology and Columbia University are expanding the overall scope of our work. One study of particular interest is an effort to understand the impacts that muscle has on bone (and vice versa). We are in the process of developing exciting new techniques to characterize the muscle-tendon-bone functional unit and will begin applying these methods in many of our other ongoing studies. The potential impact of this work is far reaching, especially given the recent push by both the National Institutes of Health and the American Society for Bone and Mineral Research in this area.

Special Thanks: We would like to recognize the following groups for their financial support of our work. Without funding, the research we do would not be possible: National Institutes of Health (NIAMS and NHLBI), Indiana Clinical and Translational Sciences Institute (CTSI), IUPUI Office of the Vice Chancellor for Research (OVC), IUPUI Biomechanics and Biomaterials Research Center (BBRC), and the IUPUI Department of Biomedical Engineering.



The Class of 2015

Congratulations to our undergrad class of 2015!



8 Top 100 Awards:

Megan Bryant, Caleb Comoglio, Wiaam Elkhatab, Timothy Emmel, Ellen Maue, Javed Syed, Katie Wight, Rachael Bridegroom

BME award recipients for 2014-15

Charles H. Turner Award for Outstanding Achievement in the Senior Year:

Alycia Berman

Bepko Award for Outstanding Achievement in the Junior Year:

Matthew Arkenberg

Bepko Award for Outstanding Achievement in the Sophomore Year:

Brian Frondorf and Jackson O'Brien

Biomedical Engineering Outstanding Service Award:

Megan Bryant

Exemplary Internship or Research Award:

Katie Wight

Medtronic Outstanding Senior Design Team:

Emily Ragozzino, Camron Dawes, Demicca Rice, Katie Wight, Harrison Holmes

Outstanding Engineering Dual Degree BME Student Award:

Krista Hakola



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BME Graduate Seminar

The BME Graduate Student Seminar series schedule for Fall 2015 will consist of a series of ~15 weekly seminars co-sponsored by the Department of Biomedical Engineering and the BME Graduate Student Association (BMEGSA). The seminars will run weekly on Friday between 12 noon and 1pm. The first Friday of the month, called "Faculty News and Views", will showcase research by regular faculty in the BME Dept. The third Friday of the month will be informal seminars that features the research of adjunct faculty.

The second and fourth Fridays of the month will be student run seminars planned and run by the BMEGSA. They will coincide with the BMEGSA meeting and will be reserved for Graduate Students to practice presentations for upcoming conferences.

These seminars aim to introduce faculty and student research to BME students. Furthermore, they aim to facilitate the development of critical thinking and effective presentation skills in the student participants. These will be held jointly with the undergraduate seminar series.

2015 Fall Series Time:
Fridays at Noon - 1pm

Place: SL 148

Faculty Seminar

Organizer:

Dr. Yoshida

Adjunct Seminar

Organizer:

Dr. Higbee

Student Seminar

Organizer: BMEGSA:

Jay Kadakia (Pres),
Armando Diaz-Gonzales (VP),
Yucan "Mia" Zhao (Sec),
Michael Bertram (Treas),
Hao Chen (Prog Coord)

Upcoming Seminars

Nov. 6	Faculty seminar Dr Chien-Chi Lin	Nov. 13	Adj Faculty seminar Dr Jason Organ	Nov. 20	Student seminar BMEGSA Meeting/Seminar	Dec. 4	Faculty seminar Dr. Edward Berbari	Dec. 11	BME696/697 Presentations
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Research Areas of BME Faculty

BIOMATERIALS

Steven Higbee, Ph.D., *Clinical Assist. Professor*

Chien-Chi Lin, Ph.D., *Assistant Professor*

Dong Xie, Ph.D., *Associate Professor*

BIOMEDICAL INSTRUMENTATION

Edward Berbari, Ph.D., *Professor and Chairman*

CARDIOVASCULAR ENGINEERING

Bill Combs, MSEE, *Clinical Assoc. Professor*

Julie Ji, Ph.D., *Associate Professor*

MECHANOBIOLOGY

Sungsoo Na, Ph.D., *Associate Professor*

Joseph Wallace, Ph.D., *Assistant Professor*

Hiroki Yokota, Ph.D., *Professor*

NEUROENGINEERING

Karen Alfrey, Ph.D., *Associate Chair of Biomedical Engineering/Clinical Associate Professor*

John Schild, Ph.D., *Associate Professor*

Ken Yoshida, Ph.D., *Associate Professor*

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