2023 Project Descriptions
Summer Research Experience for Undergraduates & Master’s Level Graduate Students

35+ Projects in Biomedical Engineering and Biomedical Informatics
## 2023 Project Descriptions

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Osteoporosis is a significant public health problem among older adults and is exacerbated with weight loss. Identification of intervention strategies to minimize weight loss associated bone loss is needed. This NIH funded randomized controlled trial is designed to test whether weighted vest use during a 12 month weight loss intervention attenuates bone loss compared to weight loss alone, and similarly to weight loss plus resistance training (a bone-sparing strategy which is effective, but present barriers to large scale implementation) in 192 older adults with obesity.

The student will: 1) review the literature on weight loss associated bone loss and techniques for measuring bone health using computed tomography (CT), 2) form a hypothesis to test the effect of skeletal loading interventions on CT-derived bone outcome such as bone mineral density (BMD), cortical thickness, bone strength, or fracture risk measured from the hip and spine of study participants (Figure 1), and 3) experimentally test the hypothesis by applying learned CT analysis and finite element (FE) modeling techniques to collect, analyze, and draw conclusions from the resulting bone outcome data.
Additive Manufacturing for Clinical Research

There are several opportunities within Biomedical Engineering and through collaborations with orthopedics, neurosurgery, plastic surgery, and others for the experimental validation and exploration of surgical techniques. These procedures are intended to preserve and/or restore physiological function. Our lab conducts surgical biomechanical experiments on new and standard surgical techniques of repairs to bones, ligaments, tendons, and joints. Students selected for this research area will be heavily engaged in experimental design, fixture design, tissue handling and dissection, instrumentation, material testing, data analysis, as well as maintaining professional partnerships with clinical faculty.

This research effort will be in the Center for Injury Biomechanics (CIB) and you will have the opportunity to work on a range of projects in the field of automobile safety, military restraints, and sports biomechanics. The CIB has two primary research facilities. The first is in the WFU School of Medicine in Winston-Salem, NC and the second is at Virginia Tech. The research at the CIB combines experimental testing, computational modeling, and case analysis to investigate human injury biomechanics.

Location: Wake Forest University School of Medicine

Philip Brown, PhD

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http://www.wakehealth.edu/CIB/CIB-People.htm
Project 3 - Summer 2023

Novel Research and Medical Device Development

There are several opportunities within Biomedical Engineering and through collaborations with orthopedics, neurosurgery, the center for biomedical imaging, plastic surgery, and others for the development of novel medical and research devices. These include experimental fixtures, exercise/rehabilitation machines and instruments, as well as surgical tools and hardware. Students selected for this project will be heavily engaged in the design process, conceptualization, prototyping, quality assurance, and experimental evaluation of multiple concurrent device development projects.

The student will aid in research and development of novel medical devices and operation of 3D printing support. This will involve review of literature on current and future medical procedures and techniques. The student will receive training in operation of professional software and hardware tools for industry quality CAD and FEA software as well as 3D printing systems. Mechanical material testing and analysis may also be conducted.

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Surgical Robotics and Biomechanics

Advancements in robotics, computing power, medical imaging and processing, augmented reality, artificial intelligence, motion tracking, and topology scanning are combining to increase the performance and applications of robotic surgery. The trend is driving down system cost and improving effectiveness, and prevalence in care pathways. Biomedical Engineering is fostering opportunities for collaborative research and technology development with physicians and industry partners. We have interest to investigate the following areas of surgical robotics: surgeon to robot interface, force feedback control, autonomous operations, robot tool and tissue interaction, laparoscopic tissue mechanics, surgical instrument design, visualization aids, augmented reality interfaces, training tissue surrogate development, analysis of training and surgical operation, artificial intelligence surgical aids, patient safety, operating room safety & efficiency.

The student will research one or more of these areas by reviewing current understanding and technology development through literature review. This will be followed up by a proposal of novel technology development or pilot research and experimentation. This may include hypothesis formation, experimental design, cadaveric testing, and data analysis. The student will receive training in robot control and any other relevant technical skills. Outcomes from their summer research experience will contribute to proposals for grant funding.

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Characterization of Subcutaneous Pelvic Adipose Tissue for Enhancement of Human Surrogate Models

Occupant submarining occurs mainly in frontal motor vehicle crashes when the lap belt slides over the ASIS of the pelvis. The issue of submarining has become more urgent given the potential of highly autonomous vehicle occupants to recline more frequently or for longer durations when compared to traditional seating postures. Human body models present the unique opportunity to study the risks associated with reclined seating and would greatly benefit from studies characterizing the morphology and quality of adipose tissue in the ASIS region. This study involves analysis of subcutaneous adipose tissue (SAT) in medical imaging scans in supine and seated postures. Linear regression will be used to develop relationships between subject characteristics (BMI, sex, and age) and four quantitative measures of SAT: cross sectional area (CSA$_{SAT}$), adipose tissue depth to boney prominences like the ASIS, posterior superior iliac spine (PSIS), or others (D$_{SAT,1,2,...,N}$), fat quality (Q$_{SAT}$ by grayscale unit), and seat belt sign location distance to ASIS (SBL).

The student working on this project will be trained in collecting measurements from abdominal-pelvic CT and/or MRI medical images, and statistical analysis of data collected from human subjects.

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Development and Validation of a Brain Phantom for Therapeutic Cooling Devices

An emerging area of interest is the study of bio-heat transfer for modeling brain therapeutics and pathology such as epilepsy. This project will focus on the study of heat transfer as it pertains to human body modeling, specifically quantifying thermal dose in the human body based on well-known bio-heat transfer experiments in the literature. The student will conduct experiments on a previously-developed brain phantom which simulates cooling therapy.

Next, using an established finite difference model, the student will calculate the predicted transient temperature response of both the phantom and of a brain, and compare those mathematical results to those from the lab experiment. In conjunction with this effort, the phantom will be improved upon in a laboratory setting in order to ensure repeatability of experiments as well as the ability to match the expected physiological response.

Lastly, the student will be tasked with developing prototypes of novel cooling devices within relevant design criteria. Understanding the context and application of such a device will be key to development.

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Human Body Model Development for Trauma Research

Computational modeling is a growing component of injury biomechanics and trauma research. This project is a multi-center effort developing a next generation set of human body finite element (FE) models for enhanced injury prediction and prevention systems. The student will learn specific skills that are highly translatable to future graduate research experience including finite element volume meshing, high performance computing and morphometric operations such as scaling and medical image analysis. There will be a specific emphasis on applying the scientific process to these efforts. Students will review the literature in the subfield of modeling in which they are working. Computational efforts will focus on hypothesis driven activities, with simulations designed and conducted by the student to verify or refute their inquiries. These activities will be focused around model validation, studies related to injury risk predication in a given environment, or how best to scale results to match literature data from different body habitus.

This research effort will be in the Center for Injury Biomechanics (CIB) and you will have the opportunity to work on a range of projects in the field of automobile safety, military restraints, and sports biomechanics. The CIB has two primary research facilities. The first is in the WFU School of Medicine in Winston-Salem, NC and the second is at Virginia Tech. The research at the CIB combines experimental testing, computational modeling, and case analysis to investigate human injury biomechanics.

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Underbody Blast Biomechanics

Underbody blast loading creates vertical accelerative loading and is a significant threat to the modern warfighter. The goal of this project is to develop a biomechanically based strategies for mitigating injury in these environments. This includes team-oriented work on the development of anthropomorphic testing devices (ATD, aka dummy) with biofidelic capabilities specific to the underbody blast environment. Additionally, human body finite element modeling in this environment will be a component of the project. Human modeling work is focused on the hypothesis that computational human body models can be used this environment to predict injury and thus be used as a novel surrogate to establish preliminary guidelines on human tolerance to severe vertical loading. Component level tests will be evaluated for statistically significant agreement with experimental trials and we will explore the suitability of a modeling approach for foundational biomechanical work in vertical loading. The student will assist in the development and execution of code to generate human injury probability curves and use of finite element models in matched trials of dummy and laboratory tests.

This research effort will be in the Center for Injury Biomechanics (CIB) and you will have the opportunity to work on a range of projects in the field of automobile safety, military restraints, and sports biomechanics. The research at the CIB combines experimental testing, computational modeling, and case analysis to investigate human injury biomechanics.

Location:

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Molecular Detection and Analysis of Trauma Bioindicators

Hyaluronan (or hyaluronic acid, HA) is a key linear sugar that is found in all physiological fluids and tissues, where variation in its composition can either result from or be a direct cause of disease emergence. While changes in net HA abundance in biofluids can be probed conventionally, this metric ignores a critical size-function relationship in which high- and low-molecular weight (MW) HA exhibit contrasting effects on inflammation, angiogenesis, cell motility, and more. Consequently, determination of both HA abundance and size distribution is essential. However, many important physiological systems contain small total amounts of HA and technologies for comprehensive assessment have critical limitations in sensitivity as well as challenges in dynamic range, cost, ease of implementation, and/or delivery of quantitative results.

In response, our laboratory has applied a molecular detection strategy using the solid-state nanopore platform, which is able to detect and size HA electrically and with tremendous sensitivity. Here, we will apply our assay to probe the HA content of plasma derived from trauma patients. As a central goal of this project, we aim to investigate HA MW as a bioindicator of outcomes for patients presenting with similar trauma severities.

The student who joins our team will learn and/or perform one or more of the following activities:

- Biochemical extraction of hyaluronan from physiological samples
- Molecular detection with the solid-state nanopore platform
- Data analysis & reporting

Location: Wake Forest University School of Medicine

Adam Hall, PhD

Assistant Professor, Biomedical Engineering
VT-WFU School of Biomedical Engineering and Sciences
Wake Forest University School of Medicine
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Winston-Salem, NC 27101
https://thehallab.org
Impact of Kinematics and Ball Weight on Shoulder and Elbow Stress During Weighted Ball Drills

The safety and efficacy of weighted ball drills for the baseball pitcher are highly debated. While some research has shown that throwing weighted balls improves pitching velocity, it is unknown how the kinematics and ball weight of specific weighted ball drills directly impact stress at the shoulder and elbow. This project involves collecting 3D motion capture data of weighted ball drills to investigate the impact of player specific kinematics and ball weight on the player’s arm health.

The student will: 1) review literature on weighted ball drills and pitching biomechanics, 2) collect 3D motion capture data of players performing weighted ball drills, and 3) analyze the kinematics and ball weight influence on shoulder distraction force and elbow varus torque. The student will apply skills they learn in human subjects’ research, experimental design, data collection and processing, biomechanics and human movement, and statistical analysis to better understand the impact of weighted ball drills on the health of the pitchers’ arm.

Location:

Kristen Nicholson, PhD
Assistant Professor, Orthopedic Surgery
Wake Forest Baptist Health
Medical Center Boulevard
Winston-Salem, NC 27157
Computational Fluid Dynamic (CFD) Modeling of Hemorrhagic Shock

The student will: 1) review literature on hemorrhagic shock, 2) design a hypothesis-driven project to evaluate the efficacy of EHC devices, and 3) apply learned CFD and FE skills to quantify key fluid mechanics properties (e.g., shear stress, blood pressure) in the aortofemoral region. This data will help inform improved designs of EHC devices, ensuring the restoration of blood pressure and fluid flow, while delivering sufficient oxygen to mitigate ischemic injury.

Non-compressible hemorrhage, referring to regions of the body that cannot be tourniquet pose a serious threat to one’s survival. To address this problem, Endovascular Hemorrhage Control (EHC) devices such as REBOA have been implemented to create a partial or full occlusion of the aortofemoral artery via inflation of a balloon catheter. However, these methods are of high risk, often resulting in significant ischemic injury and vascular damage. This project exploits CFD modeling to better understand the hemodynamics during hemorrhage and EHC device usage.
Crash Injury Research and Engineering Network (CIREN)

CIREN is a research catalyst that can be used to conduct a wide range of motor vehicle trauma studies. It has been an ongoing project at WFUBMC since 2005.

The student will: 1) conduct detailed investigations of real-world motor vehicle crashes and determine mechanism and causation of occupant injuries to improve prevention, mitigation, and treatment of motor vehicle crashes, 2) collaborate and work closely with a broad range of medical specialties, including biomedical engineers, crash investigators, radiologists, orthopedic surgeons, and trauma surgeons, and 3) conduct finite element (FE) modeling reconstructions of CIREN crashes using the simplified GHBMC human body model of a simplified vehicle model providing kinematic visualizations and injury analyses to supplement our investigations.

Location: Wake Forest University School of Medicine

Joel Stitzel, PhD
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Head Impact Exposure Quantification and Mitigation in Motorsports

The Pilot testing of individualized mouthpiece deployment in motorsports involving injury risk assessment for the optimization of safety measures

The student will: 1) conduct analysis to quantify environmental and crash head kinematics, 2) utilize finite element (FE) modeling for injury risk assessment for drivers in crash scenarios, and, 3) FE simulation to optimize safety measures and driver comfort.

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Sensor technology offers researchers and consumers the ability to collect head impact data in the real-world; however, the accuracy of such sensors has been limited. This project involves development, testing, and field deployment of a novel instrumented mouthpiece in contact sports (e.g. football, gymnastics, soccer, hockey) and everyday activities (e.g. sitting, running).

The student will: 1) review literature on head kinematics in athletic and everyday activities, and 2) work on a project to evaluate kinematic data collected from the mouthpiece. The student will apply skills they learn in human subjects' research, experimental testing, data collection and processing, statistical analysis, and FE modeling with a brain model to derive conclusions and a better understanding of head kinematics and TBI risk in sports and everyday activities.

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Due to rising concern of head impact exposure and concussion in the 21 million children involved in team sports, this project aims to examine the biomechanical basis of sub-concussive and concussive head impact exposure in adolescent athletes instrumented with helmet-mounted and mouthpiece sensors.

The student will: 1) review literature focused on cumulative exposure of sub-concussive and concussive head impacts and factors influencing exposure (e.g. coaching techniques; practice and game guidelines/rules; community-based interventions; athlete age, size, experience, and position), and 2) design a hypothesis-driven experiment to examine analytically and computationally-based metrics of head impact exposure using FE modeling, on-field video analysis, biomechanical data processing, and statistical approaches learned from mentored training. The student will directly contribute to the broader research goal of reducing sub-concussive and concussive head impact exposure to improve sport safety in adolescents.

Location: Wake Forest University
School of Medicine

Jillian Urban, PhD, MPH
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Weight loss is controversial in older adults due to its association with bone loss and increased fracture risk. We are conducting several randomized controlled trials (RCTs) to test the effects of dietary (higher protein), exercise (resistance training), loading (weighted vest), and medication (bisphosphonates) interventions in preserving bone health in older adults as they lose weight.

We analyze computed tomography (CT) scans and create subject-specific finite element (FE) models to assess changes in bone mineral density, bone thickness, bone marrow adiposity, and bone strength and fracture risk over the course of various interventions. These computational analyses produce data on the effectiveness of these interventions in protecting against bone loss and fracture in an aging population at high risk for fracture.

The student on this project will be trained in image segmentation, image registration, pipelines for quantifying bone quality (i.e. cortical thickness, bone mineral density), and finite element modeling and simulation. The student will form a hypothesis to test the effects of the intervention on bone. To test the hypothesis, CT of participants will be analyzed to measure the changes that occur from baseline and follow-up CT scans.
Vertebral Strength and Injury Risk Following Long-Duration Spaceflight

Prolonged spaceflight can degrade the vertebrae and spinal muscles, leading to astronaut injury. This study is collecting pre- and post-flight CT and magnetic resonance imaging (MRI) scans of astronauts to quantify vertebral BMD, cortex thickness, geometry, and spinal muscle volume changes in 6-month space missions. Vertebral strength and injury risk will be quantified from simulations with a human body model altered to represent each astronaut’s pre- and post-flight vertebrae and spinal muscles.

The student will: 1) review literature on astronaut musculoskeletal deconditioning and form a hypothesis to test the effect of spaceflight on a bone or muscle outcome, and 2) learn image segmentation and registration, BMD and cortical thickness algorithms, and FE modeling to analyze pre-to post-flight changes in the astronauts to improve our understanding of injury risks associated with spaceflight deconditioning.

Location: Wake Forest University School of Medicine

Ashley Weaver, PhD
Associate Professor, Biomedical Engineering
VT-WFU Center for Injury Biomechanics
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http://www.wakeforestinnovations.com/experts/ashley-weaver-phd/
High-Resolution Peripheral Quantitative Computed Tomography (HR-pQCT) Scanning in Clinical Trial Interventions

The XtremeCT II HR-pQCT scanner provides highly specialized CT scans at the distal radius and tibia. These images can be used to quantify changes in volumetric bone mineral density (BMD) as well as structural changes by providing detailed resolution of the bone microarchitecture.

These data are being used by our group in the clinical setting as part of interventional trials designed to evaluate the outcome of varying weight loss modalities (dietary, exercise, surgical) on metrics of bone health. The ability to see microarchitecture remodeling may lead to an increased understanding of how bones are affected by weight loss, particularly among older adults.

The student will: develop HR-pQCT scanning and analysis protocols, assist with HR-pQCT scanning of participants, and analyze HR-pQCT scan to extract bone microstructure properties (e.g., trabecular spacing, cortical porosity, trabecular and cortical BMD, finite element estimated failure load and bone stiffness) to explore how clinical trial interventions alter the skeleton.

Location: Wake Forest University School of Medicine

Ashley Weaver, PhD

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http://www.wakeforestinnovations.com/experts/ashley-weaver-phd/
Loss of muscle mass and strength can lead to mobility disability and increase risk of osteoporosis and fracture as muscle acts both mechanically and biochemically on bone. We are conducting studies utilizing computed tomography (CT) and magnetic resonance (MR) imaging to assess muscle changes with weight loss (diet/exercise-based or bariatric surgery), disease (e.g., myotonic dystrophy; heart failure), or normal aging. We apply automated machine-learning and semi-automated methods to assess changes in muscle area, volume, quality, and intermuscular fat in CT and MR scans.

We also use automated radiomics analysis to extract high-dimensional muscle quality measures, such as uniformity, heterogeneity, randomness, and repetitive patterns from CT. These muscle properties can be correlated to bone mineral density and bone strength, which we derive from imaging. These analyses assess effectiveness of interventions, characterize mechanisms of disease, identify therapeutic targets, and will help establish imaging biomarkers to predict musculoskeletal decline.

The student on this project will be trained in image segmentation and pipelines for quantifying muscle properties from radiology. The student will examine muscle quality/radiomics features in a human subject population and explore how these features are affected by a clinical trial intervention or disease such as myotonic dystrophy.
VICIS is a study focused on reviewing and analyzing vulnerable pedestrian crash data for injury causation and crash causation factors.

The study conducts detailed investigations of real-world pedestrian crashes and determines the mechanism and causation of pedestrian injuries to improve prevention, mitigation, and treatment of motor vehicle crash injuries.

The project involves collaboration and working closely with a broad range of medical specialties, including biomedical engineers, crash investigators, radiologists, orthopedic surgeons, and trauma surgeons.

We also use finite element (FE) modeling reconstructions of pedestrian crashes using the simplified GHBMC human body model and a simplified vehicle model. These reconstructions provide kinematic visualizations and injury analyses to supplement our investigations.

The student on this project will be trained in: Abbreviated Injury Scale (AIS) based coding of injuries sustained by pedestrians struck by a motor vehicle, gathering medical record data, radiology, and crash investigation evidence for pedestrian crashes, engineering analysis of the evidence data to determine the cause and biomechanical mechanism of each pedestrian injury.

Location: Wake Forest School of Medicine

Ashley Weaver, PhD

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Image-based Biophysical Modeling to Differentiate Radiation-induced Injury from Tumor Recurrence Following Stereotactic Radiosurgery

Patients with intracranial metastasis treated with stereotactic radiosurgery (SRS) are evaluated for local control using serial MR imaging. Lesions can often be seen during these follow-up imaging sessions with expanding areas of contrast enhancement and surrounding tissue abnormality. Determining the underlying pathology of the lesion presents enormous clinical challenges as tumor recurrence and radiation-induced injury appear radiographically similar. Lesions are often classified as indeterminate and monitored with additional and costly serial follow-up imaging, at the risk of letting a potential recurrent tumor progress. New methods are desperately needed to guide therapeutic intervention decision-making in this important patient group. This project investigates the development of computational modeling methods that are driven by clinical imaging data. As the underlying physiology of the two conditions is fundamentally different, biophysical models may allow parameterization of lesion properties as a model-based biomarker to determine post-SRS enhancing lesion etiology, reducing costs due to unnecessary imaging or missed diagnosis.

The student will gain experience with medical image processing (segmentation, registration) and biophysical finite element modeling based on MRI data. The student will develop and deploy computational analysis pipelines and contribute to the development of computational model-based image analysis methodologies to guide interventional therapy for cancer patients.

Location: Wake Forest University School of Medicine

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Project 22 - Summer 2023

Neuroimaging and Cognitive Changes in Youth Football Players

Sports-related head impacts are common and involve significant forces that can result in mild to severe traumatic brain injury (TBI). Football has the highest incidence of sports-related TBI and limited data is available for the effects of repetitive head impact exposure for the millions of participants in youth and adolescent football leagues (8-18 years old) during this time of rapid brain development. We obtain functional/structural magnetic resonance imaging (MRI), magnetoencephalography (MEG), and cognitive measures, as well as detailed biomechanical head impact data from sensors embedded within the helmets of youth and adolescent athletes to determine the effects of repetitive subconcussive head impact exposure, and the true incidence of cognitive and objective imaging changes. The student selected will perform literature review focused on changes in the brain measureable from imaging and cognitive testing that are associated with cumulative head impact exposure and subconcussive head impacts.

The student will: 1) review literature on impact-induced changes in the brain that are measurable with neuroimaging and cognitive testing, and 2) develop a hypothesis-driven project to correlate neuroimaging measures, cognitive testing, and biomechanical head impact data in youth football players. The student will be trained in multimodal imaging acquisition and analysis (diffusion tensor imaging, functional MRI, arterial spin label imaging, susceptibility weighted imaging, magnetoencephalography), cognitive testing, biomechanical instrumentation (helmet-mounted accelerometers), and statistical analysis. They will apply these skills in their project to analyze youth football data to identify neuroimaging and cognitive biomarkers that are sensitive to cumulative subconcussive head impact exposure in youth football.

Location:

Christopher T. Whitlow, MD, PhD, MHA

Chief of Neuroradiology and Vice Chair for Informatics
Director, Radiology Informatics and Image Processing Laboratory (RIIPL)
Director, CTSI Translational Imaging Program
Director, Combined MD/PhD Program
Departments of Radiology and Biomedical Engineering
Clinical and Translational Sciences Institute (CTSI)
Wake Forest School of Medicine
The Rodent Research-18 Mission to the International Space Station: Prevention of Skeletal Complications

Loss of bone, cartilage, and muscle during periods of microgravity in space serves as a challenge to astronaut health during and after the mission. Our previous spaceflight data (from the International Space Station and Space Shuttle) identified damage to soft (cartilage, menisci) and hard (bone) joint tissues. Our group is again part of a team of investigators examining spaceflight affects on musculoskeletal health. Our team is examining will characterize the role of mitochondria in regulating oxidative stress-induced musculoskeletal damage, and will also determine the extent to which an antioxidant metalloporphyrin (MnTnBuOE-2-PyP5+), and a return to weight-bearing, protects against spaceflight environment-induced damage to bone and joint tissues.

Our upcoming mission will send mice to the International Space Station in December, 2021. While a group of mice will return in January to examine damage/protection of skeletal tissues, another group will return and be permitted to reload joints normally until June-July, 2021. The REU student will perform microCT analysis to measure degraded/preserved hindlimb bone architecture as strength changes/preservation via finite element modeling. The student will also perform contrast-enhanced microCT analysis to measure cartilage and meniscal degradation in the knee, and then assist with histology for biomarkers of joint damage. Outcome of these data will identify if a novel, well-tolerated antioxidant can serve to protect musculoskeletal health in astronauts during long-duration missions.

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Biomedical imaging of the brain tumor microenvironment

Malignant brain tumors that are characterized by profound angiogenesis and intratumoral hypoxia and necrosis are highly resistant to conventional multimodal therapies. Delivery of therapeutic agents to the brain tumor remains a major challenge partially due to the blood brain barrier (BBB). The BBB in brain tumor is known to be heterogeneously disrupted with tumor growth. Non-invasive MRI provides not only anatomic images, but also information about vascular function in brain tumors.

The student will: 1) review literature on cancer imaging and brain tumor pathophysiology, 2) learn post imaging processing skills with MatLab. The student will apply skills they learn in imaging segmentation of brain tumors in small animals and mathematic models-based quantitative imaging analysis of vascular perfusion and permeability parameters.

Location: Wake Forest University School of Medicine

Dawen Zhao, MD, PhD

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Substance Use Disorder and the Influence of Pain on COVID-19

The erosion of connection is a devastating consequence of substance use disorder (SUD) impacting millions of American individuals, families, and communities. This loss is compounded by the complex barriers of stigma and social isolation, which is worsening SUD even more during the social distancing of COVID-19. Despite the attention the opioid crisis and other substance use disorders are receiving, a lack of understanding about risk and predictive factors undermines the development of novel effective solutions. We are studying SUD on existing data and by focusing on a real-world approach that incorporates the complexities to move toward more precise, individualized predictors of risk.

Goal: The student will work on National COVID Cohort Collaborative (N3C) platform, which includes close to 17M patients and develop and test models.

Expectation: The student in this project will is expected to have Python programming skills and work on building ML models.

Meredith C. B. Adams, M.D., M.S., FASA, FAMIA

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Propensity Score Matching using Self Organizing Maps

**Background:** In epidemiology, propensity score matching is frequently used to find controls (individuals with no disease/condition) with a similar profile to cases (individuals with disease/condition). However, very simple methods, such as logistic regression, are typically used for this purpose ignoring the possible non-linear nature of the data.

**Goal:** The goal of this project is to assess the utility of Self-Organizing Maps (SOM) to match controls for cases. SOM is a type of artificial neural networks designed to cluster data in an unsupervised way. Its weights are adjusted in a way similar data entries would be placed in close proximity within an outcome layer. This project will also expand existing SOM architecture to be able to cluster signal type of data such as ECG.

**Expectation:** The student in this project will be expected to have Python programming skill and work on 1) building the SOM architecture for propensity score matching and 2) apply them to real-world problems, 3) compare results to traditional propensity score matching.

Oguz Akbilgic, PhD

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Deep Survival Learning for Signal Type Data

**Background:** Survival analysis, e.g. Cox Proportional Hazard’s Regression is frequently used to model the relationship between a set of input (continuous, binary, or categorical) to a future event taking time-to-event information into account. However, there has been a lack in deep learning methodology to take time-to-event information into account. Despite there is a recent literature on integrating survival analysis with deep learning for image analysis, there a lack in literature to associate physiologic signals into future events.

**Goal:** The goal of this project is to create a new deep learning model that can process signal type of data to predict risk for a future event a desired time point.

**Expectation:** The student in this project will is expected to have Python programming skills and work on 1) building the deep survival model for signal type data 2) apply them to real world problems such as heart failure risk prediction.

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Remote Artificial Intelligence Applications on ECG Data

**Background**: Electrocardiogram (ECG) is a frequently used tool to assess cardiovascular health. Recent advances in wearable technologies allow remote collection of ECG data. There are now opportunities to screen large patient populations remotely by integrating such technologies with artificial intelligence. For this purpose, our Lab has developed an IOS application (ECG-Air) to stream ECG from Apple Watch and run AI models. Yet, there is a need for a vendor-agnostic app.

**Goal**: The goal of this project is to expand ECG-Air application to receive data from other smartwatches or ECG devices as well as to develop an Android version. The project also include execution of deep learning on smartwatch via Tensorflow-Lite.

**Expectation**: The student in this project will is expected to have mobile application development skills (e.g. swift) and work on 1) developing Android apps and 2) creating sensor-app data transmitting pipelines.

Oguz Akbilgic, PhD

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Diseases of the ear, particularly acute otitis media (AOM) and middle ear effusions, are the most commonly treated childhood pathologies. The financial burden of ear disease is estimated at more than $3.2 billion per year. Because ear diseases are common, a significant problem is over-diagnosis and over-treatment.

Our group is a worldwide leader in this area. We have access to one of the largest databases in the world and several expert clinical collaborators. The student will: 1) develop, test, and validate state-of-the-art machine learning methodology, 2) collaborate and work closely with ear, nose, throat (ENT) specialties 3) analyze the impact of the developed algorithm’s impact on more accurate diagnosis.
Machine Learning Methods for Maternal Health

African-American women across the US experience alarmingly higher rates of maternal mortality than their white counterparts. Factors associated with social determinants of health (SDoH), including education, housing, transportation, and nutrition, are recognized as potentially contributing to this disparity in maternal health outcomes, along with clinical risk factors including hypertension and heart disease. However, the complex associations among these factors, along with the causal role they play in increased risk for maternal mortality, are not well understood, nor are there comprehensive health care interventions that take these combined factors into account to provide decision and communication support for patients, providers, and community support workers.

The student will: 1) clarify and track contributions of biological, clinical, and SDoH factors toward specific maternal morbidities associated with eventual mortality, 2) conduct efficient and accurate risk predictions to determine whether patients fall into defined target risk groups.

Location:

Metin Gurcan, Ph.D.

Director, Center for Biomedical Informatics
Professor, Department of Internal Medicine, Pathology, BME
Wake Forest School of Medicine

https://school.wakehealth.edu/research/labs/clinical-image-analysis-lab
Novel Deep learning Algorithms and Explainable AI on ECG

**Background:** In Deep Learning (DL), there are various types of layers that are specialized for specific tasks. For example, the convolutional layers slides over the input (image or its representation) spatially to extract features. However, there is still a gap in the literature to design a DL layer for ECG specific. And the black-box side of the DL is still an open-research area, specifically for ECG based models.

**Goal:** The goal of this project is to build ECG inputted novel DL algorithms (layers, activation functions, or architecture based) for prediction/classification of cardiovascular diseases. And the other goal is to uncover the black-box side of ECG fed DL models by spatial perspectives of the input data (ECG).

**Expectation:** The student in this project will is expected to have Python programming skill and work on 1) building novel DL algorithms fed by ECG 2) design infrastructure to uncover the black-box of ECG fed DL models, 3) compare results with state-of-the art algorithms

Ibrahim Karabayir, PhD
Assistant Professor, Wake Forest University Health Sciences, Wake Forest University School of Medicine, Internal Medicine, Section on Cardiovascular Medicine
Remote Device Data Collection Platform

Remotely gathering health data from patients is increasing in demand for health care providers. This enables doctors and nurses to have a broader understanding of health outside of a clinical setting for their patients. Collecting this data requires creating endpoints to transmit the data and then visualizing the information for the clinicians.

Each device and company have different protocols for sending the data, which requires building out models to accept and normalizing the information. Building a centralized platform enables consolidation of these various data transmissions and allows for a “one-stop-shop” for the clinicians to view the data.

The student working on this project will be trained in web application programming and API design. The student will get familiarity with various cloud technologies and device transmission protocols. Additionally, there will be opportunities to learn about user interface/user experience design and implementation.

Required skills: Programming. Prior experience with APIs and web-based technologies is helpful.

Eric Kirkendall, MD, MBI

Deputy Director Center for Healthcare Innovation
Director of Digital Health Innovation
Professor – Pediatric Hospital Medicine
Wake Forest School of Medicine
Project 33 - Summer 2023

Deep learning for neuroimaging-based cortical surface analysis

**Background:** Cerebral cortex of the brain is a crucial structure for our cognitive functions and is affected by neurodegeneration. However, the cortex is a highly convoluted structure, and conventional deep learning methods such as convolutional neural networks cannot be directly applied. The recent graph neural network enables the application of deep learning for cortical shape analysis. However, there are limited studies exploring the application of cortical-shape-based deep learning models to achieve precision and clinically explainable prediction.

**Goal:** The goal of this project is to develop novel deep learning models that can process cortical shape analysis to predict the risk and progression of brain diseases such as Alzheimer’s Disease, and identify clinically-relevant disease-related local cortical features.

**Expectation:** The student in this project will be expected to have Python programming skills and work on 1) building cortical-shape-based deep graph neural network models for early brain disease prediction. 2) use explainable AI methods on graph neural networks to identify local disease-related cortical features. Prior experience in Matlab is also beneficial.

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Project 34 - Summer 2023

Longitudinal Deep Learning Model to predict disease progression

**Background:** Longitudinal changes in localized regions of the neuroimage data holds strong potential to infer individualized future disease trajectory. However, most current neuroimage-based deep learning models are only applied for single timepoint data, and predict disease risk at specific time windows. The combination of deep learning based longitudinal analyses such as image registration and survival analysis provide a powerful tool to achieve precision medicine.

**Goal:** The goal of this project is to develop novel deep learning models that can extract longitudinal information from multi-timepoint neuroimage data through 1) data-driven image registration; 2) models of the risk of developing the neurodegenerative disease as a function of time through deep survival analysis.

**Expectation:** The student in this project will be expected to have Python programming skills and work on 1) deep-learning-based longitudinal image registration 2) deep survival analysis. Prior experience in Matlab is also beneficial.

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Project 35 - Summer 2023

Language-based AI Model on genomic data to predict multimorbidity

**Background:** Our Genomes such as DNA encode molecular-level information about disease risk. Traditional methods using polygenic risk scores only explore the risk of a single disease for every single gene, omitting the high-level genetic interaction of genomic sequences that are associated with multiple diseases. The recent development of the Natural Language Processing (NLP) model has shown success in the comprehension of high-level context in sequence data such as sentences. Similarly, NLP models can also be applied to genomic sequences to extract high-level genotype information for multiple related diseases. However, studies in this field are still limited despite the huge potential.

**Goal:** The goal of this project is to 1) develop novel NLP-based deep learning models on genomic data to predict the composite risk for multiple diseases.

**Expectation:** The student in this project will be expected to have Python programming skills and work on 1) developing representation learning models to extract high-level genomic features 2) predicting multi-disease risk factors and identifying high-level genomic associations.

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Current prognostic methods in colorectal cancer (CRC) struggle to identify patients at risk of disease recurrence after surgery. With current clinicopathologic staging, around 20% of patients with stage II colon cancer will recur. Furthermore, identification of patients with stage II disease that benefit from adjuvant chemotherapy is impossible, and for patients with stage III CRC, approximately one-quarter of patients receive chemotherapy post-operatively without benefit. As part of this project, we will develop a deep learning method to directly predict not only recurrence free survival and response to therapy but also overall survival and disease free survival from histopathology images of CRC patients. Both patient care and health care resource utilization would be improved by developing deep learning derived markers that identify high- and low-risk CRC subsets.

**Learning Objectives:** The student will have the opportunity to work with cutting-edge deep learning models. Additionally, it will be a fantastic chance to work on a GPU cluster and learn how to distribute jobs among various nodes. Along the way, the student will also learn the fundamentals of computational pathology.

**Requirements:** Strong programming skills in Python and basic knowledge of machine learning.

Khalid Niazi, PhD
Assistant Professor
Center for Biomedical Informatics
Wake Forest University School of Medicine
Data Analysis Pipelines

Beyond the essential coded data elements in Electronic Medical Records (EMRs), additional metadata and free text data provide opportunities for better patient evaluation and care, if those elements can be easily incorporated into research data warehouses. In this project textual data can be mined with advanced targeted analysis as an injected step within the larger Natural Language Processing (NLP) concept extraction process and de-identification of the text to remove Protected Health Information (PHI). The use of recurrent neural networks or machine learning methods could be explored and compared with the results achieved through standard methods and tooling to gain insight on better processing of data while ensuring quality.

The student working on this project will be trained in data analytics and supporting application programming. The student will get familiarity with national medical data standards, and ontological systems. Data characterization, cleaning, NLP, and visualization will be explored.

**Required skills:** Python programming

Prior experience with databases, statistics, and machine learning is helpful.

Brian Ostasiewski

Director of Research Informatics
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Networked Data Models

Electronic Medical Records (EMRs) are aimed at supporting clinical practice at the point of care. These are often deeply customized and unique to the institutions in which they operate. Therefore, when conducting research with collaborators at other institutions it is often difficult to execute systematic analysis of these disparate observational databases. Common Data Models (CDMs) allow transformation of data contained within these databases into a common format as well as a common representation (terminologies, vocabularies, coding schemes), which then allows systematic analyses using a library of standard analytic routines that can be written based on the common format. The CTSI at Wake Forest leads and participates in several of these regional and national networks sharing data for basic science, retrospective studies, and clinical trial recruitment.

The student working on this project will be trained in data analytics and supporting application programming. The student will get familiarity with national medical data standards, ontological systems, and the full-cycle process of research from cohort identification to data extraction and analysis. Data characterization, cleaning, Natural Language Processing (NLP), and visualization may be explored.

Required skills: Programming. Prior experience with databases and statistics is helpful.
More than 20 million people will be diagnosed with cancer by 2026 in the US. 43.6% of US cancer patients are eligible for immunotherapy therapy, however the benefit from immunotherapy is tempered due to the immune-related adverse events (irAEs). Up to 65.82% of patients can develop any irAEs. As autoimmune conditions that can affect any organ in the body after ICB administration, irAEs have natural histories that are distinct from their de novo autoimmune disease counterparts. Thus, these toxicities represent a varied challenge in clinical practice and a steep learning curve to diagnose and manage.

**Goal:**
To shed predictive and mechanistic light on how patients’ tumor genetic variations and related clinical factors determine irAEs

**Expectation:** The student in this project will be expected to have Python programming skill and work on building novel Deep Learning models and compare results with state-of-the-art algorithms

**Umit Topaloglu, PhD FAMIA**

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Co-Director Bioinformatics Shared Resource
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Clinical Trials Matching with Machine Learning (ML)

Despite the proven benefits of the cancer clinical trials, only ~5% of adult cancer patients participate in a clinical trial despite 55% of patients reported to have willingness to enroll in trials. The clinical trial recruitment is a labor intensive and a time-consuming process, hence eligibility checks are not being performed for all patients timely. With the potential of ML in healthcare, we are studying natural language processing (NLP) and machine learning (ML) models in order to automate the clinical trial screening process and enhance trial enrollment.

Goal: The student will work on patient notes to have graph representations using SNOMED structure. The project also aims to use of latest developments in Geometric Deep Learning approaches.

Expectation: The student in this project will is expected to have Python programming skills and work on building novel Machine Learning models and compare results with developed algorithms.

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Preserving Federated Learning (FL) Models

Federated Learning (FL) has been introduced to alleviate some of the limitations of Machine Learning (ML), particularly the capability to train on larger datasets for improved performance, which is usually cumbersome for an inter-institutional collaboration due to existing patient protection laws and regulations. Moreover, FL may also play a crucial role in circumventing ML’s exigent bias problem by accessing underrepresented groups’ data spanning geographically distributed locations. Even for decentralized training, adversarial attacks have demonstrated that confidential and sensitive data might still be exploited and leaked.

**Goal:** The student will work on comparing accuracy degradations on several counter measures that will be implemented to protect FL models during and after the training.

**Expectation:** The student in this project will be expected to have Python programming skills and work on building ML models on FL platforms.

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