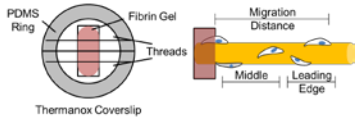
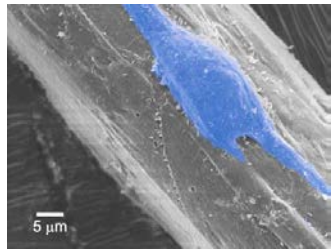
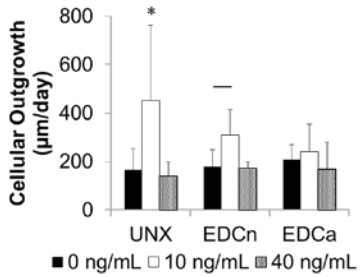
Multiscale Fabrication of Complex 3D Tissues with Biopolymer Microthreads

3D Models of Cell-Biomaterial Interactions for Tissue Regeneration

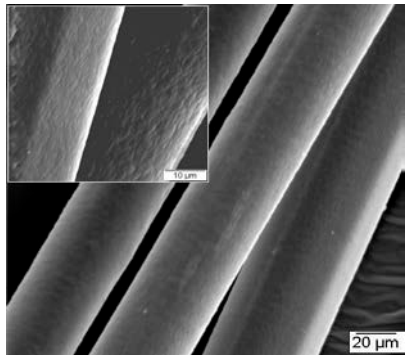






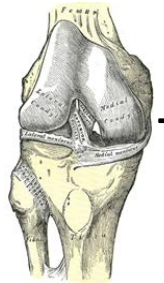
Human skeletal myoblasts seeded on HGF doped fibrin microthread

Cornwell, **Tissue Eng.**, 16: 3669, 2010,
Grasman, **Acta Biomater.,** 10: 4367, 2014
Grasman, **Tissue Eng.,** epub 27 Mar 2017



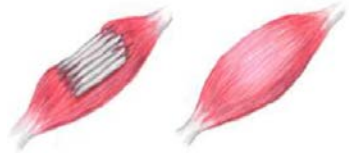
Biopolymer Microthreads (collagen/fibrin/composite)

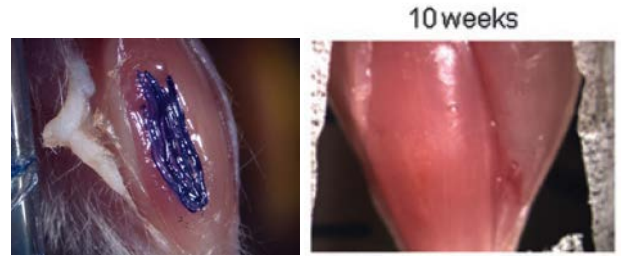
O'Brien, **Curr Stem Cell Rep** (2016) 2:147–157
US Patent: 9,662, 415



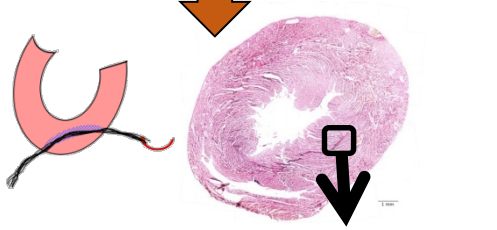
Tendon/ligament Regeneration

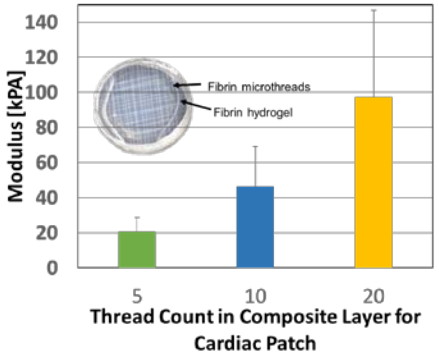
Skeletal Muscle Regeneration



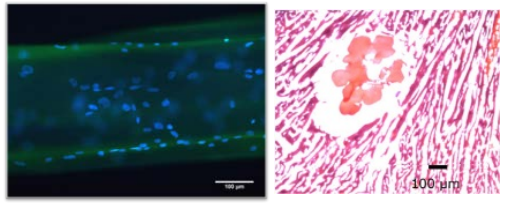


Page, **Tissue Eng.**, 17, 2629, 2011,
Grasman**, Biomater.**, 72: 49, 2015
Grasman, **Acta Biomater.,** 10: 2, 2015

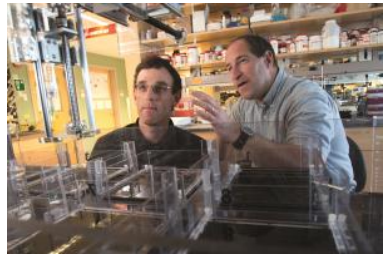




Chrobak, **ACS Biomaterials** epub 1 Dec 2016



Stem Cell Delivery and Cardiac Regeneration



Biomanufacturing Microthreads

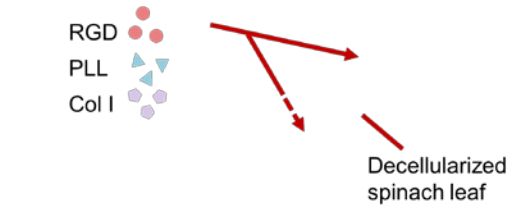
Proulx, **JBMR**, 96A: 301, 2011
Guyette, **J Biomed Mater Res A**. 101:809, 2013
Tao, J **Tissue Eng Regen Med.** 2017

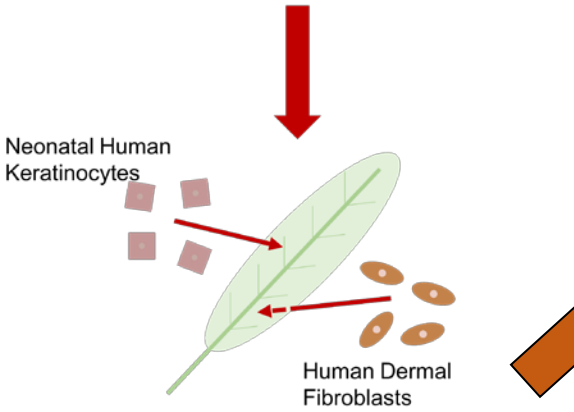
Pins Lab

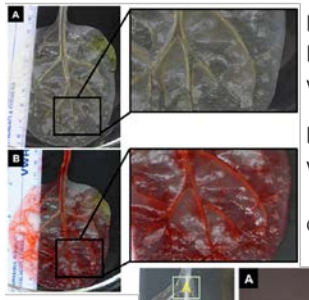
VITAthread

NSF TATRC The Whitaker Foundation American Heart Association. Learn and Live. National Institutes of Health

Integrating Plant Structures and Systems (iPASS) for Wound Healing: Decellularized Spinach Leaves as a Multifunctional Platform for Tissue Engineered Skin



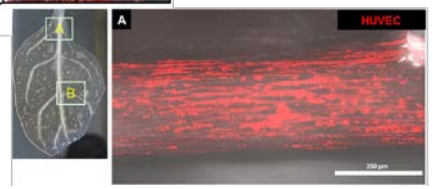


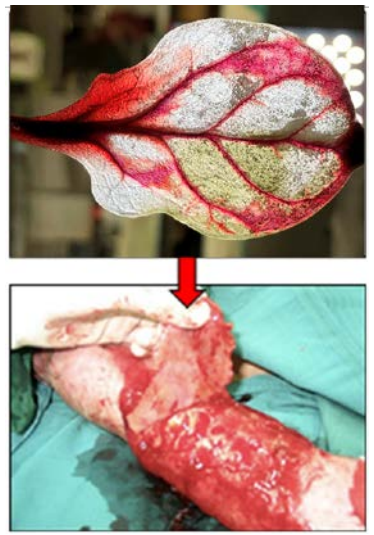


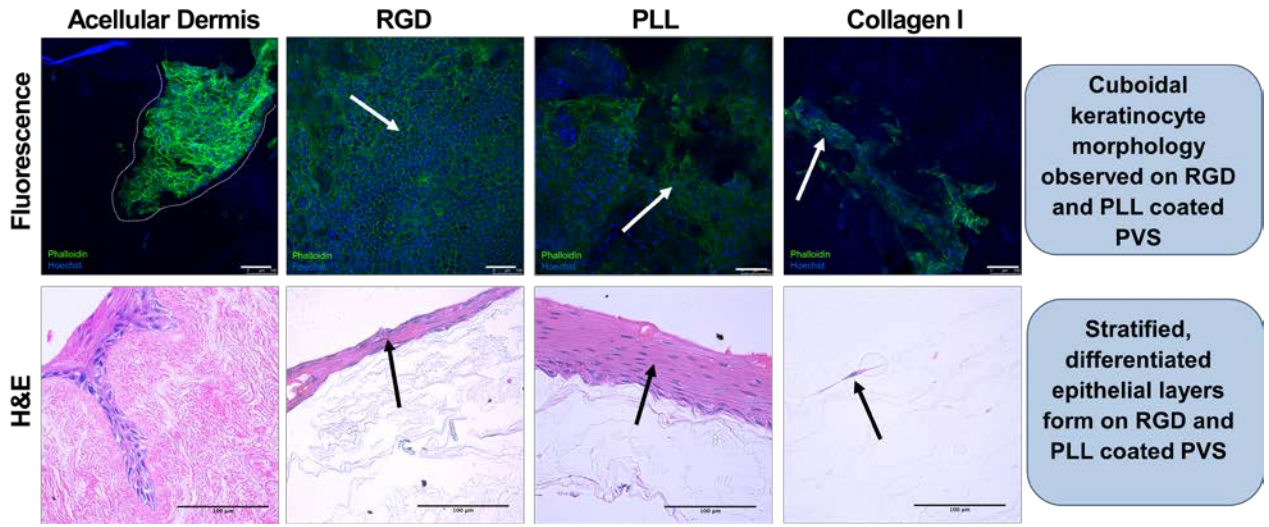
Left: The profusion of Ponceau Red for visualization of intact leaf vasculature.

Below: Endothelialization of leaf vasculature.

Gershlak, *et al. Biomaterials.* 2017.







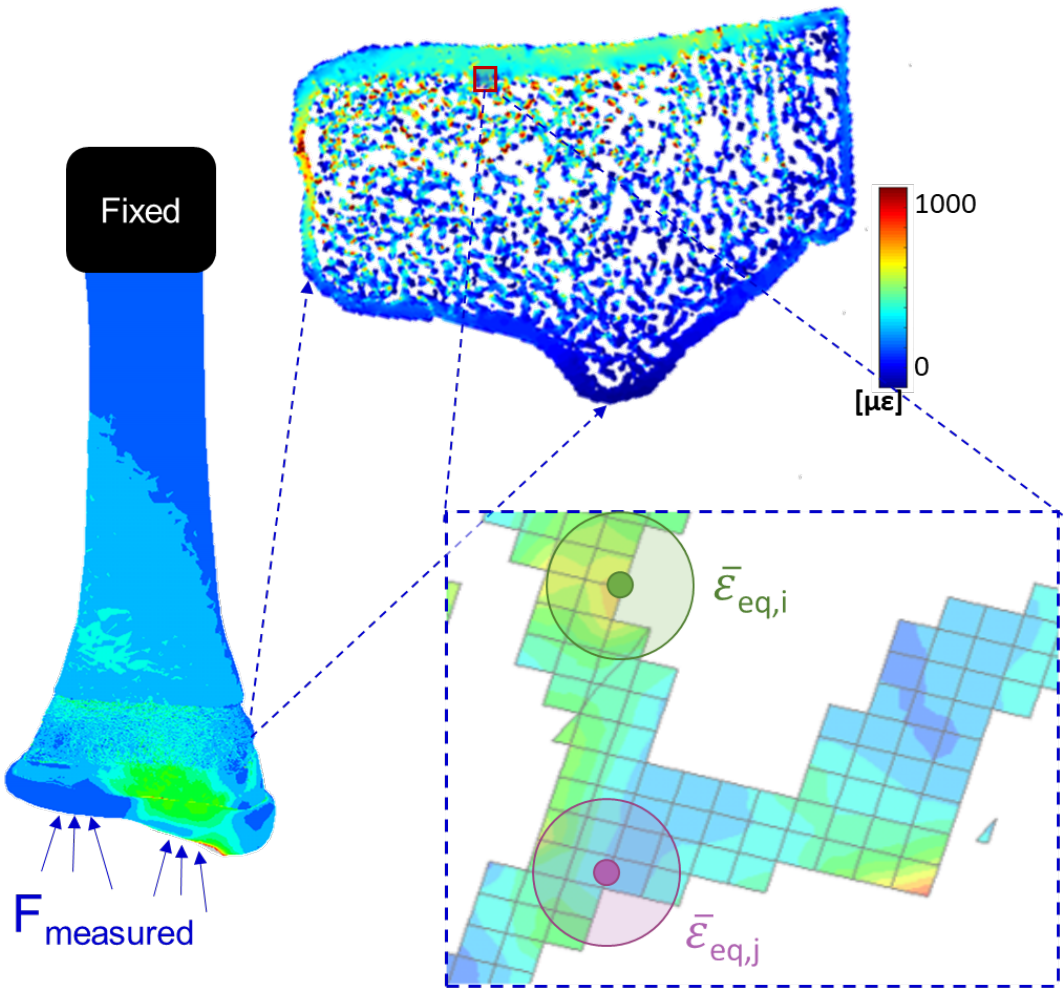
Karen Troy – Musculoskeletal Biomechanics Laboratory

How does bone adapt its structure in response to functional activities?

We work on REAL people in REAL clinical and research settings!

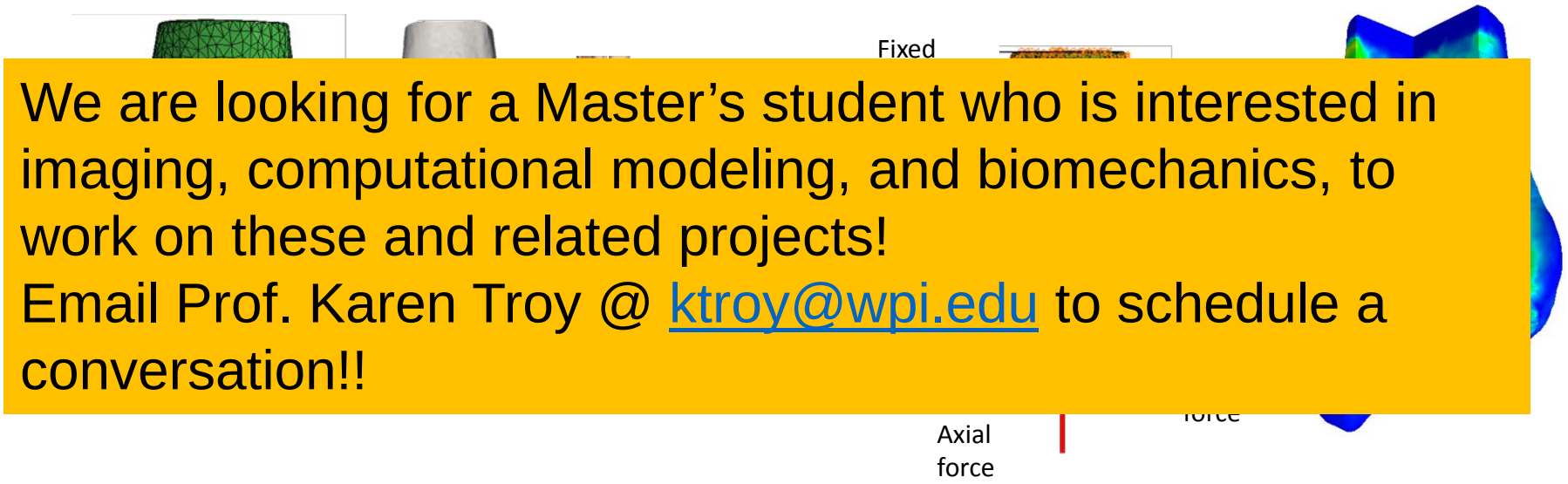
- What mechanical signals are the most important predictors of bone adaptation?
- How can we measure these signals noninvasively?
- How does bone structure respond to changes in mechanical environment?
- Do the same rules apply in disease or aging?

Musculoskeletal Biomechanics Laboratory



Approach to estimating *in vivo* bone loading conditions

Identify structures interacting with the bone(s) of interest	Measure kinematics and kinetics	Calculate joint contact forces	Apply forces and constraints to model

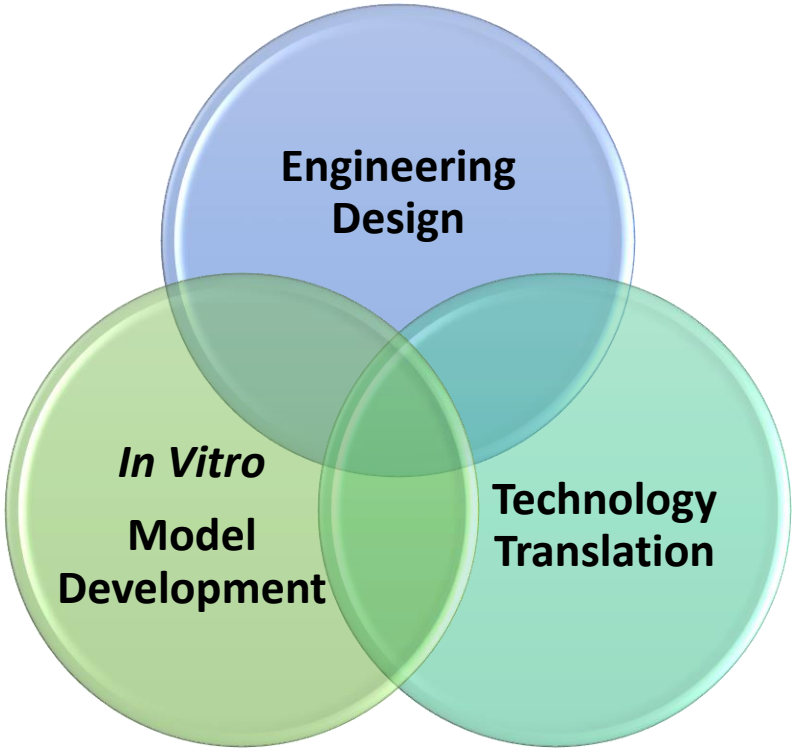


We are looking for a Master's student who is interested in imaging, computational modeling, and biomechanics, to work on these and related projects!
Email Prof. Karen Troy @ ktroy@wpi.edu to schedule a conversation!!

Project Examples

- Exoskeleton-assisted walking therapy for bone health in people with spinal cord injury (DOD-funded clinical trial)
- How do bone structure and exercise performance biomechanics interact to create bone strain and elicit bone adaptation?
- Identifying biomechanical risk factors for metatarsal stress fracture in runners.

Whittington Laboratory



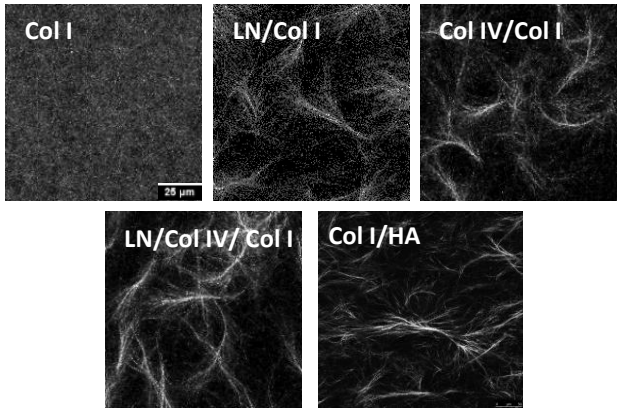
- **Bio-instructive biomaterials**
- **Precision control over hydrogel properties (tunable)**
- **Control of dynamic cell environments**
- **Phenotypic-based assessment**
- **High throughput integration**

INCREASE understanding of disease, regenerative medicine, and drug discovery

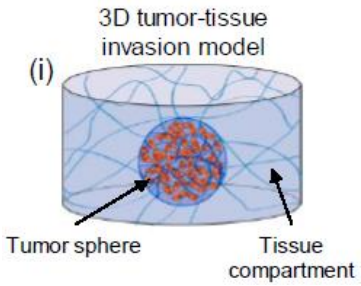
IMPROVE predictive power of preclinical models

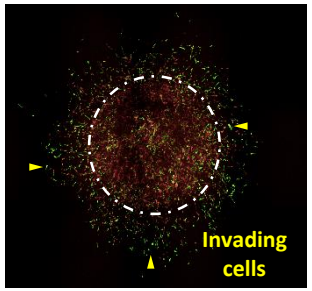
Projects

1. Engineering Dynamic ECMs to Model Progressive Desmoplasia and Early-stage Invasion in Pancreatic Cancer

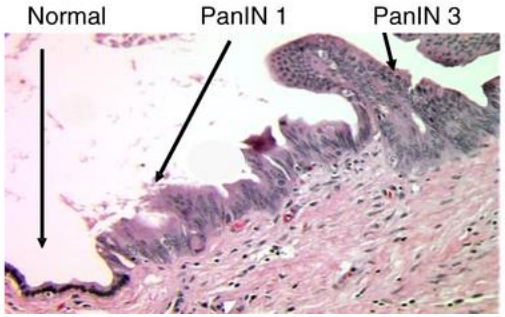


Defined ECM composition that reflects in vivo tissues

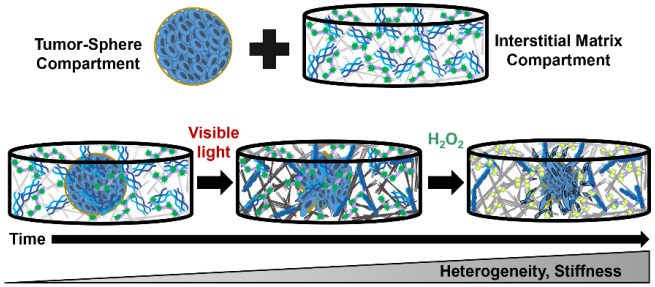




Model early-stage invasion into the interstitial space (including signaling)

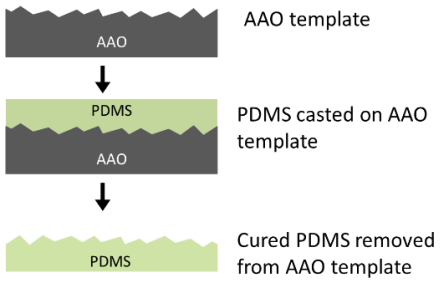


https://commons.wikimedia.org/wiki/File:Pancreas_neoplasia_carcinoma_sequence.png

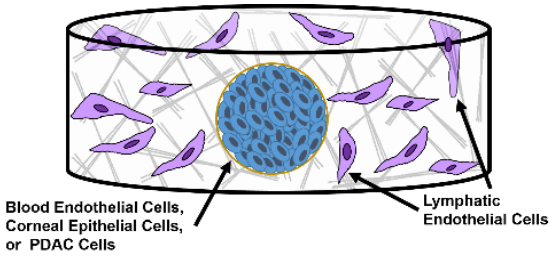


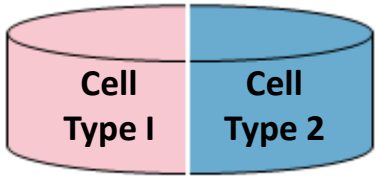
- *Spatiotemporal control over ECM heterogeneity*
- *Dynamic control over ECM biophysical properties*

2. Defining the Role of the ECM in Regulating Tissue-Specific Lymphangiogenesis in Fibrotic Conditions



Controlled ECM topography (microstructure) and stiffness





Controlled cell interactions for wound healing, inflammation, and metastasis

Raymond Page (rpage@wpi.edu)
August 20, 2018

Title: Development of optimized cancer cell and cancer stem cell isolation and culture procedures for chemo-sensitivity assays.

Although valuable insight can be gained into the detailed molecular and genetic mechanisms of cell processes leading to the development of disease can be gained from animal studies, species differences in gene/protein function, development, anatomical size, and rate of metabolism exist. In addition, subtle and difficult to predict species differences in these mechanisms may contribute to the failure of animal tested therapies applied to humans. The effect of these differences may be realized only when the cells being analyzed reside within the native tissue architecture due to the dependence of interaction with other cells on function.

The focus of this research addresses the need for better and more efficient culture systems for a variety of cancer types evolving from a variety of different tissue types. Moreover, current methods tend to have a "one size fits all" when it comes to cells culture. Every tissue in the body has a unique microenvironment where cell signaling and function is a complex interplay between the cells and the cellular, biochemical, and mechanical environment. Using a combination of cell culture methods development, microfuidics and biofabrication techniques, we aim to address these challenges.

1. Development of advanced cell separation and culture techniques that can enable rapid and reliable amplification of cells derived from human tumors and circulating tumor cells. Having suitable numbers of cells isolated from small biopsies or from the peripheral blood circulation would enable accurately matching the efficacy of cytotoxic agents to a patient specific cancer cell population. In addition, the mechanisms of cancer cell acquisition of drug resistance could also be identified and used to develop better drug treatments.

2. Development of advanced tissue mimetic systems *in vitro* to be used for the study of disease progression or to be used as tools more accurately predict the potential success of pharmaceutical and biopharmaceutical treatments. This would essentially create an engineered model of each patient's cancer in the context of their own cells which would not only represent their unique genetics, but also includes their unique epigenetics.

Medical FUSION Lab
PI: Haichong (Kai) Zhang
Contact: hzhang10@wpi.edu

Medical FUSION Laboratory

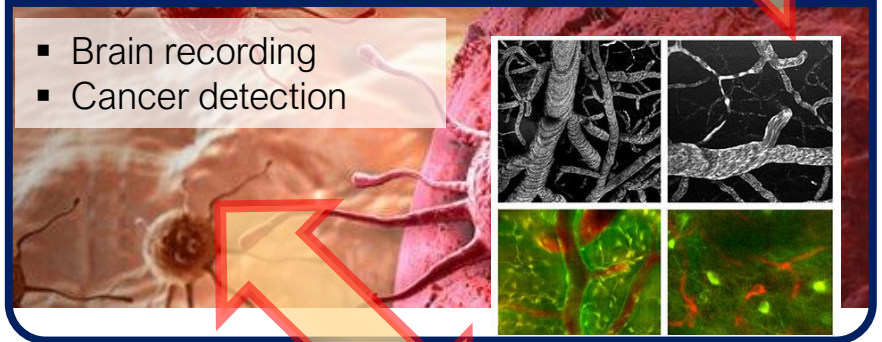
Medical FUSION (Frontier Ultrasound Imaging and Robotic Instrumentation) Lab focuses on:

- Interface of medical robotics, sensing, and imaging.
- Develop robotic assisted imaging systems and Image-guided robotic interventional platforms
- Ultrasound and photoacoustic imaging are two key modalities to be investigated and integrated with robotics.

Research Scopes

Biological Sensing / Imaging

- Brain recording
- Cancer detection



Medical Robotics

- Co-robotic imaging system
- Robot-assisted intervention
- Point-of-care system

Enabling Technologies

- Image reconstruction
- Advanced signal processing
- Machine learning
- Hand-eye calibration
- Enabling low-cost system

WPI
Medical FUSION Lab
PI: Haichong (Kai) Zhang
Contact: hzhang10@wpi.edu

Medical FUSION Laboratory

Human-Robot Cooperative Ultrasound Imaging System

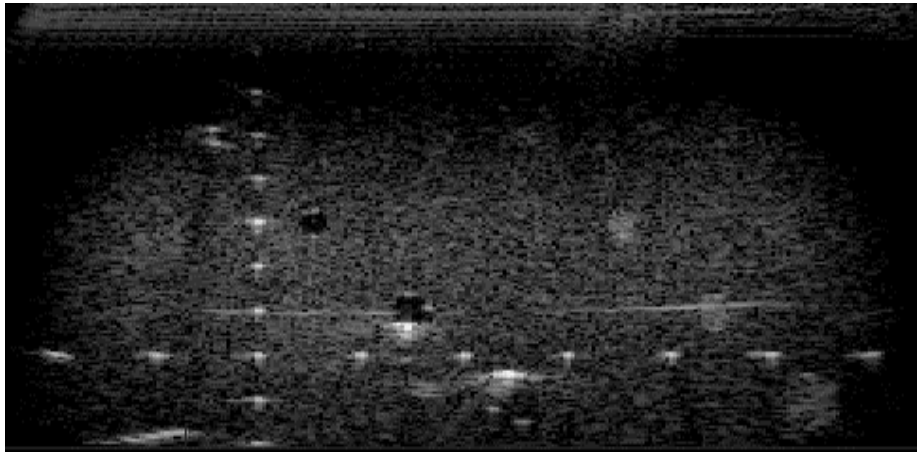
Cooperative Controlled Robotic Ultrasound Scanning

- A cooperatively controlled robotic (co-robotic) ultrasound system reduces the force sonographers apply.

Synthetic Tracked Aperture Ultrasound Imaging

- Ultrasound image quality is constrained by the physical design of ultrasound array. Synthetic tracked aperture ultrasound (STRATUS) imaging is a method to extend the available aperture size in reconstruction by sweeping an ultrasound transducer while tracking its orientation and location.

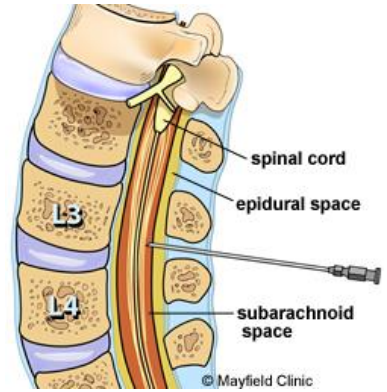
High resolution ultrasound imaging
enabled by human-robot cooperative control

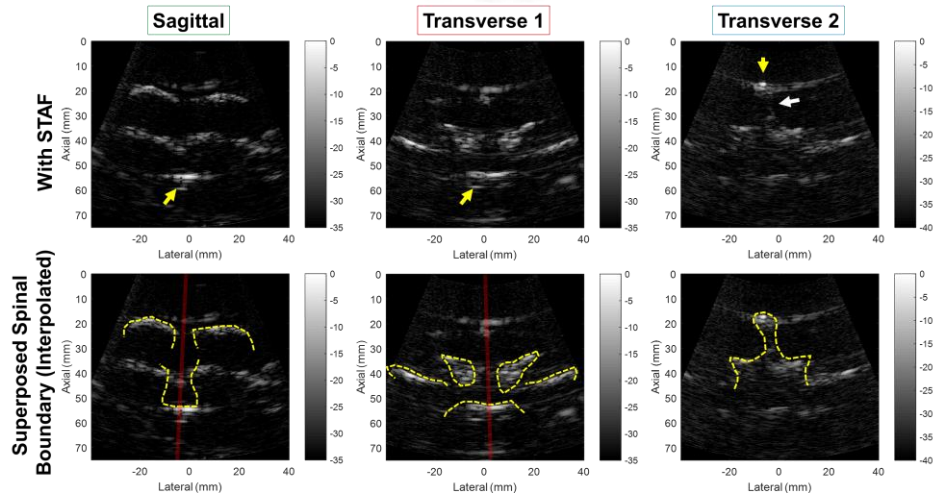


Ultrasound-Embeded Needle for Point-of-Care Application

- A single-element needle-based ultrasound system is composed of a needle-shaped ultrasound transducer that reconstructs B-mode ultrasound images by combining robotic tracking and ultrasound reconstruction.

Single element ultrasound
provides lumbar puncture guidance





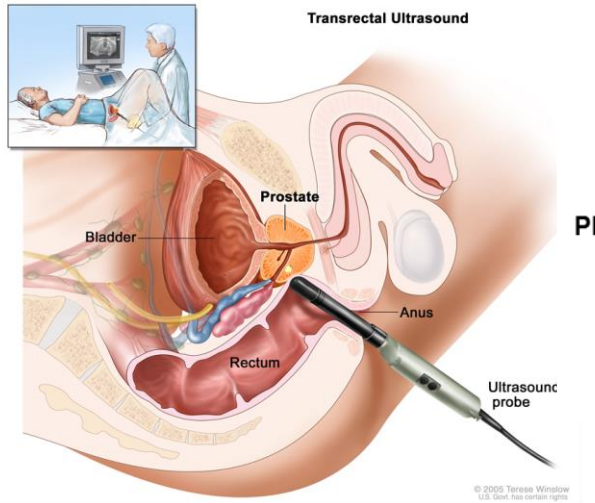
WPI
Medical FUSION Lab
PI: Haichong (Kai) Zhang
Contact: hzhang10@wpi.edu

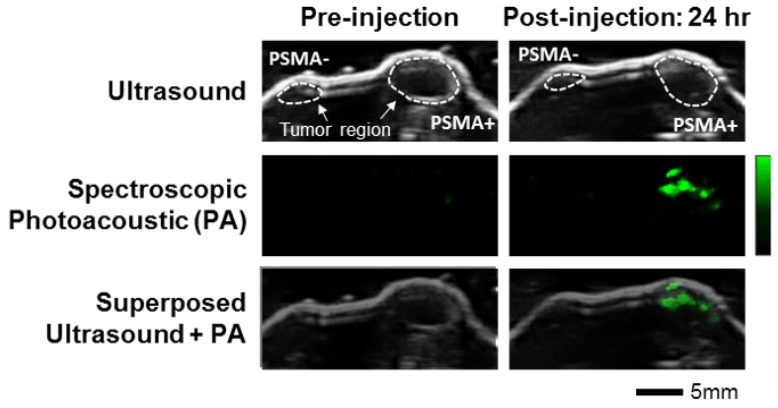
Medical FUSION Laboratory

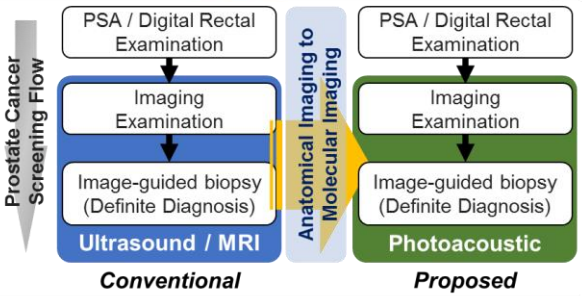
Advanced Functional Ultrasound/Photoacoustic Imaging

Molecular Photoacoustic (PA) Imaging

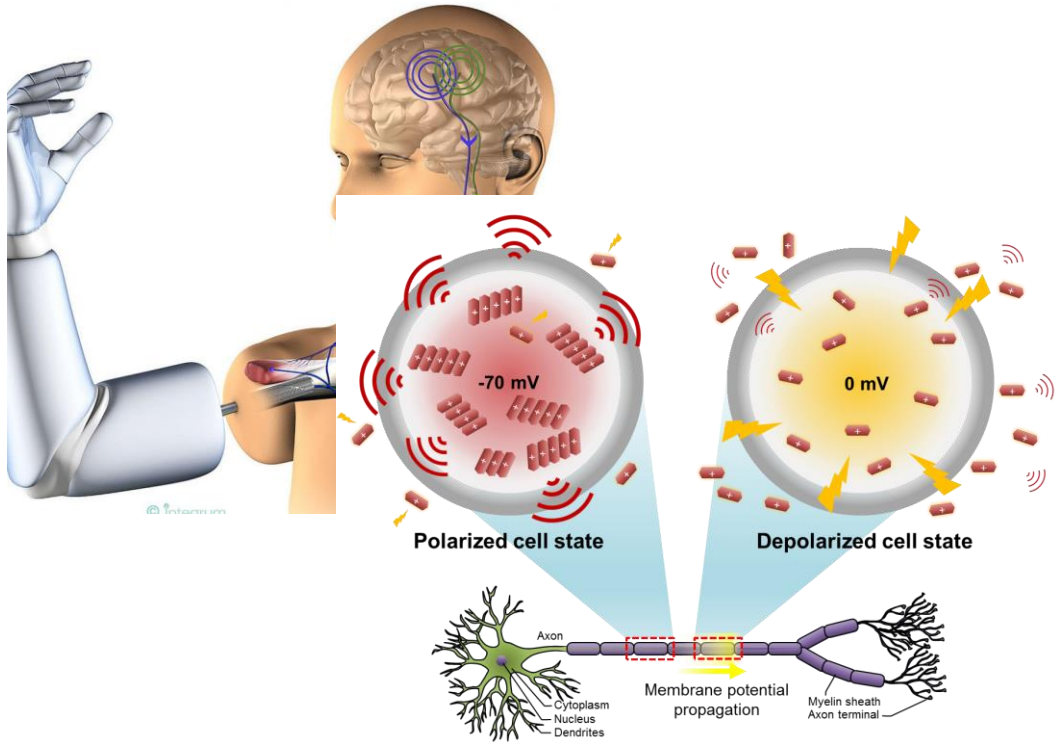
- PA imaging is capable of image targeted molecular contrast agents in vivo.
- We envision to integrate functional/metabolic information into image-guided interventional platform to achieve high sensitivity and specificity guidance.







Prostate cancer screening workflow and the proposed photoacoustic based imaging exam, and biopsy guidance.



Electrophysiological Sensing

- Photoacoustic (PA) imaging has potential to sense electrophysiological state of biological tissue as another unique functional information.
- Voltage sensitive dyes are designed to monitor membrane potential by detecting fluorescence changes in response to neuronal or muscle electrical activity.
- We developed the PA voltage sensitive dye under the theoretical concept whereby the voltage-dependent quenching of dye fluorescence leads to a reciprocal enhancement of PA intensity.
- The established system will be used to study the molecular treatment monitoring on Parkinson's disease, and has potential to be used for neurosurgical guidance.

Medical FUSION Lab
PI: Haichong (Kai) Zhang
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Medical FUSION Laboratory

Area of Interest

Biomedical imaging and sensing

- brain imaging, cancer imaging

Medical robotics with advanced sensing

- robot-assisted medical procedure, prosthetics control

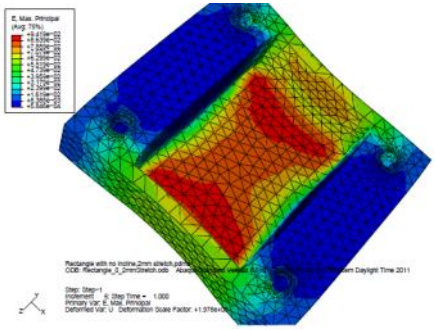
Advanced signal processing

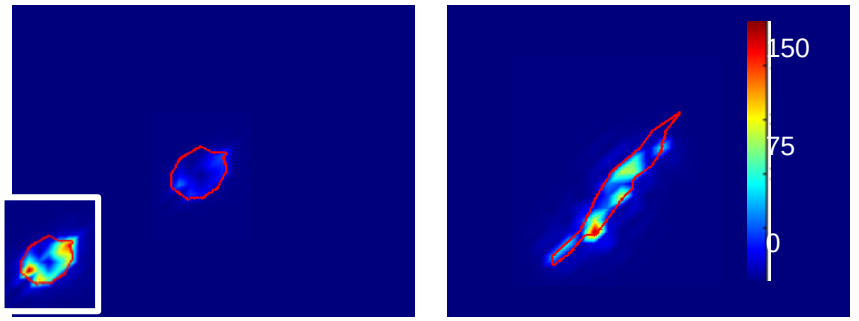
- machine learning/deep learning for bioimaging, image reconstruction

Research projects for credit and/or thesis are available for students currently enrolled in the Masters program at WPI. Email your CV and research interests to be considered.

Billiar: Biomech and Mechanobiology Lab

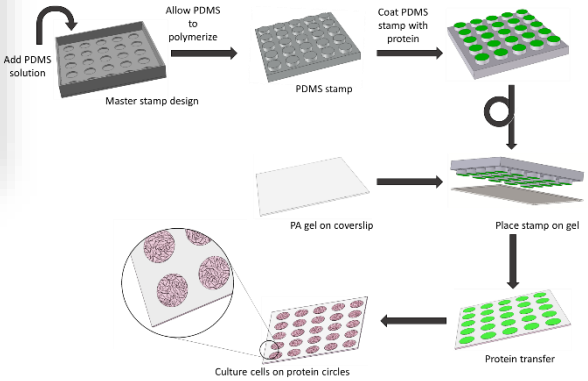
WPI Tissue Mechanics & Mechanobiology Lab

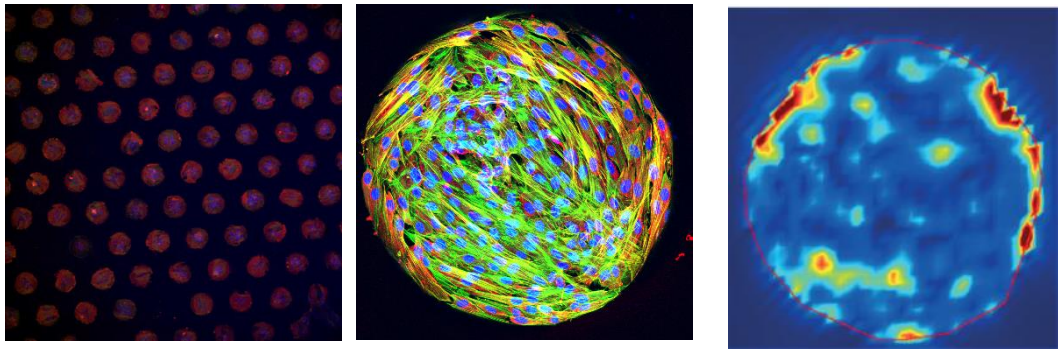




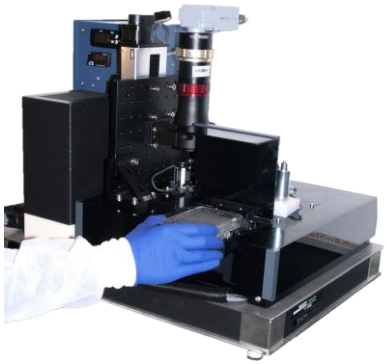
Soft (0.6 kPa) **…stretched**

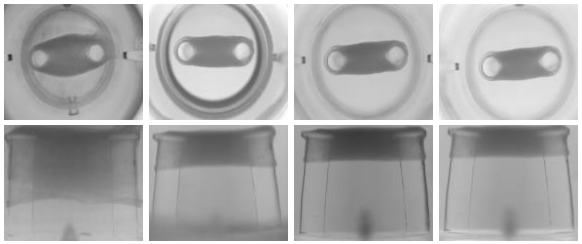
Cirka et al., *Biophys J,* 2016





Cirka et al., *Lab Chip,* 2017





QNTL
quantitative neurotechnology lab

Dirk Albrecht
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wp.wpi.edu/qntl

- **What do we do?**
  - Our lab develops and applies new methods to **record brain function** and identify **regulators of neural activity**
- **Why?**
  - Neurological disorders affect >100M people worldwide
  - Many involve **altered activity in brain circuits**
  - We don't yet know exactly how this activity is altered, for example from *trauma*, *environment*, or *genetics*
- **Our approach:**
  - We record brain activity in **living organisms**
  - We engineer **high-throughput methods** of stimulation to interrogate changes to response dynamics
- **Benefits & impact:**
  - We can record from 1000's of organisms at once for 24h
  - We examine brain changes during **learning, sleep, and aging**
  - High-throughput screens identified new neuroactive compounds
  - We created organism **models of human neuropsychiatric disorders** (via genome editing)
  - Understanding neural regulation is critical for better disease prevention, diagnosis, and treatment

QNTL
quantitative neurotechnology lab

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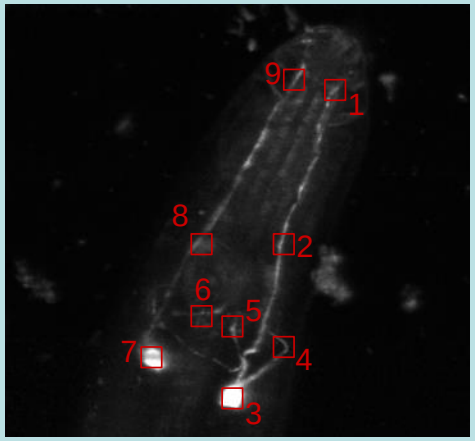
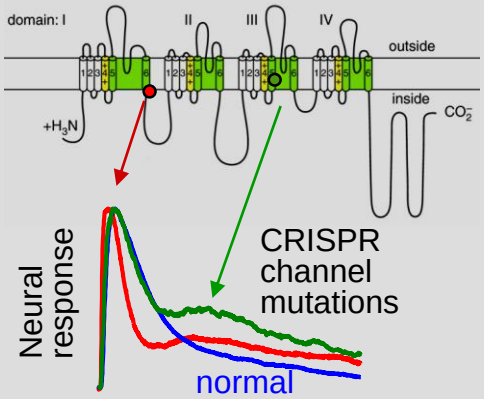
- Lab tools and topics: *what will I learn?*

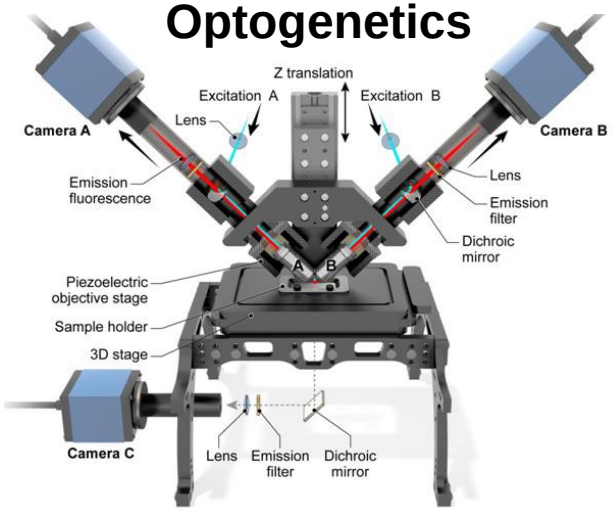
Live Neural Activity, image processing



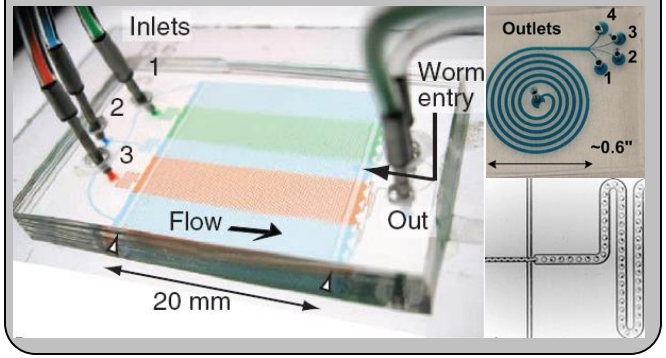
Neural Disorders, Genetics, Behavior (e.g. Sleep, Learning)



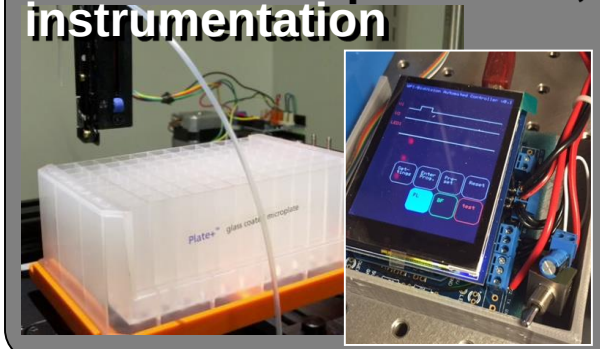
2D/3D Microscopy, Optogenetics



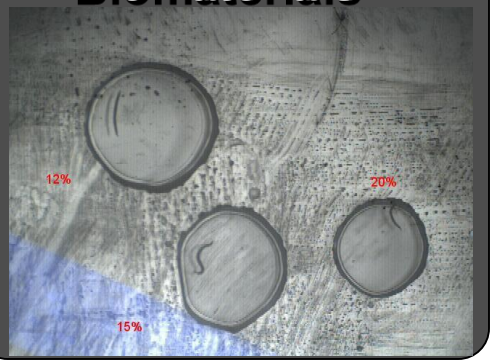
Microfabrication/fluidics



Automated experiments, instrumentation



Biomaterials



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- Available Master's / Rotation projects:

What compounds alter neural communication *in vivo*?

- high-throughput automated screen of neural activity in living organisms!
- continuation of a successful PhD project (Dr. Ross Lagoy)
- focus on targeting gap junctions and chemical synapses

How does aging affect learning?

- develop automated microfluidics for behavior and neural imaging
- expansion of successful project from young adult to juveniles (*they don't learn?*) to aged animals (Dan Lawler)
- potential animal model for cognitive decline

Hydrogel-based microfluidics for whole-brain imaging and more!

- combine microfluidic chemical stimulation with multi-neural imaging on a cutting-edge light-sheet 3D microscope
- collaborate with optics experts (NIH, Woods Hole) and multiple user labs
- identify novel sensory neurons

How does attention work?

- selective emphasis & suppression of stimuli
- test neural/behavior responses to conflicting and unexpected stimuli, identify circuit mechanisms using genetics
- collaborate with computational neuroscientists (WashU)

BME-MicroFabrication Lab (MFL)

- Also, we run a *microfabrication cleanroom*, available for all grad students to use after training.

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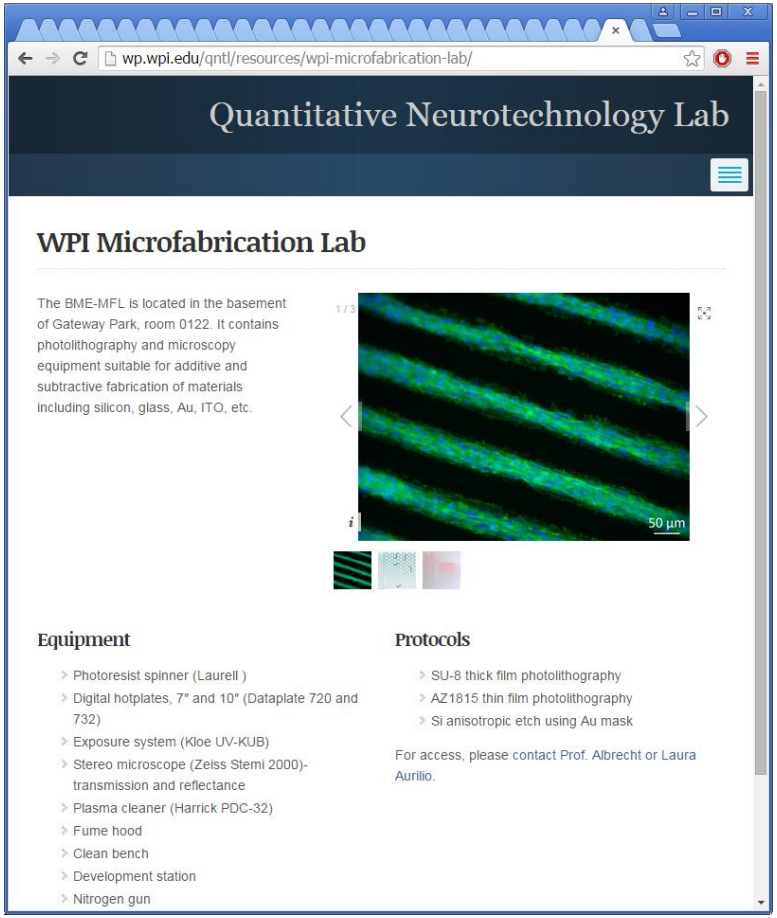
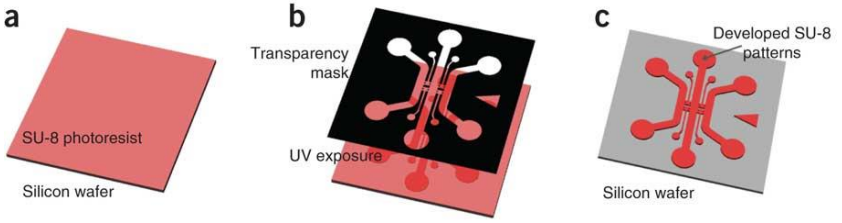
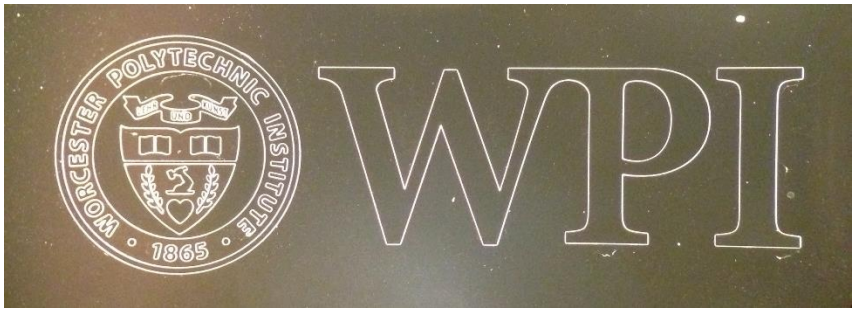
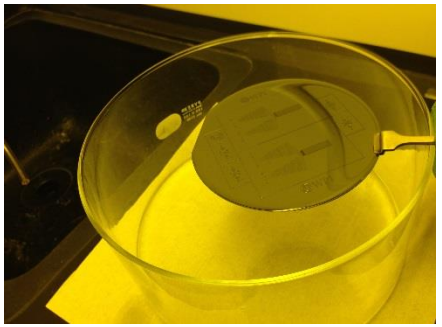


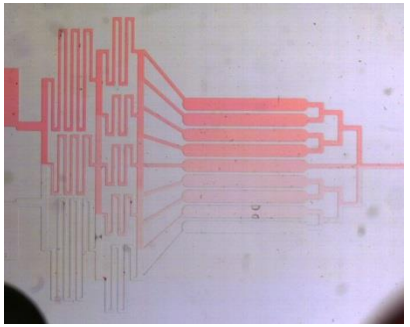
BME555: BioMEMS and Tissue Microengineering, Spring (‘21 next)

- Spin-coat, Photolithography, Etching, Stereomicroscopy, Profilometry, Plasma









- Also: 3D printing, rapid-prototyping microfluidics, etc.