Developing New Strategies for Musculoskeletal Tissue Repair and Regeneration using Biomedical Engineering Approaches

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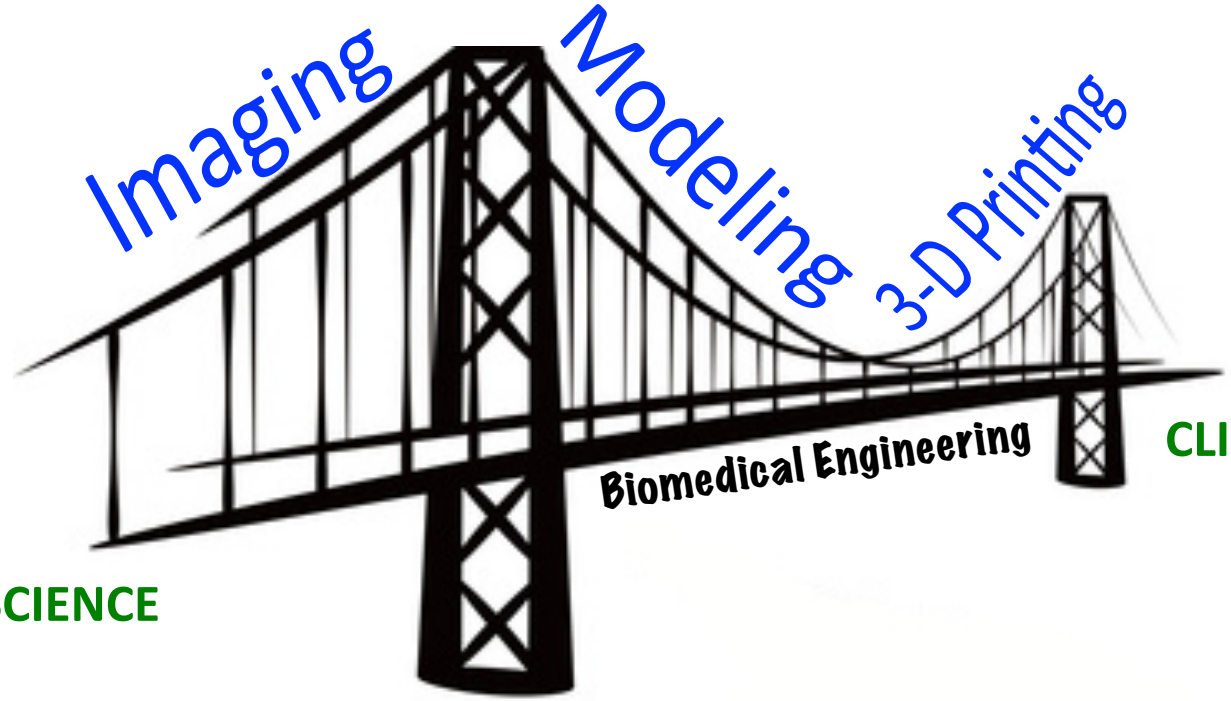


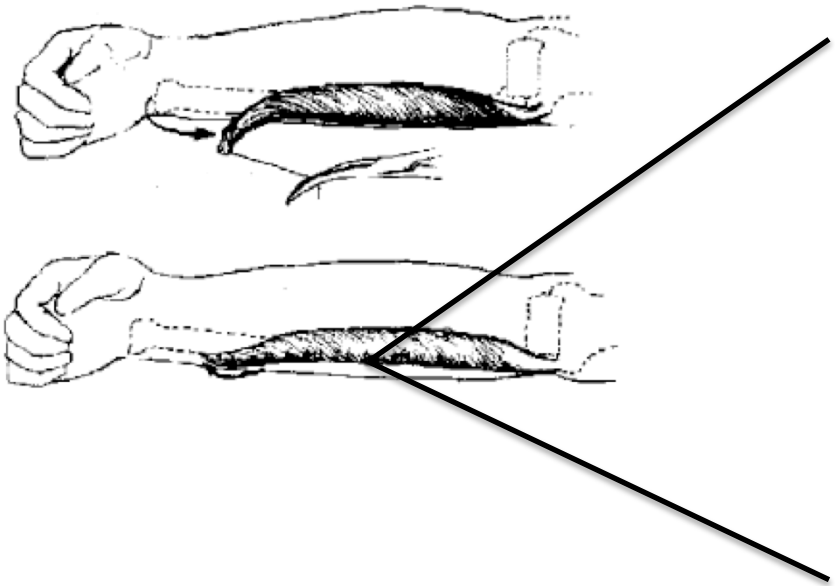
BASIC SCIENCE

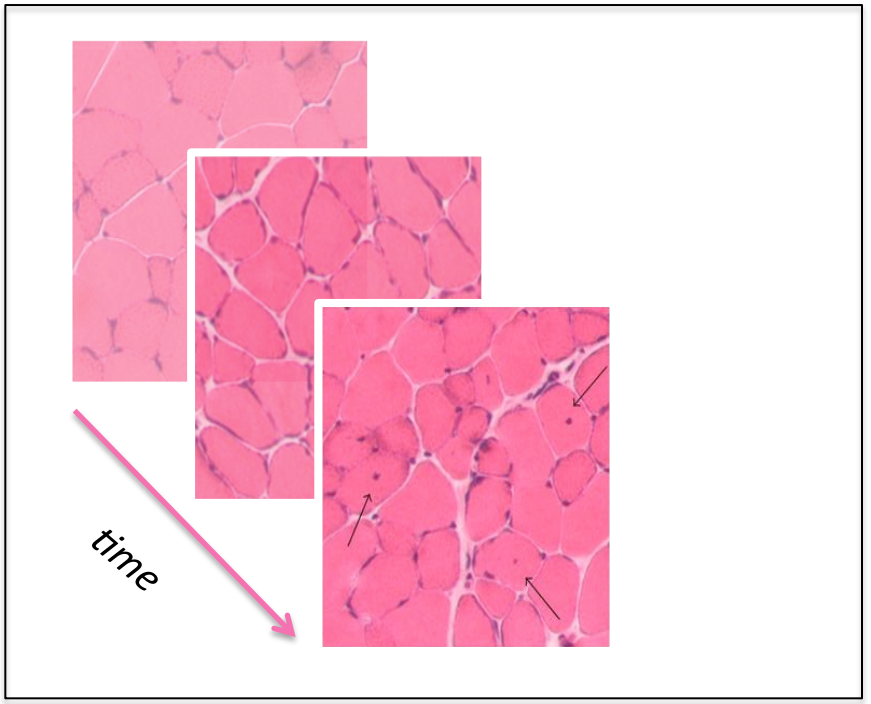
CLINICAL RESEARCH

A current project example: muscle-tendon remodeling following tendon transfer surgery

Flexor carpi ulnaris

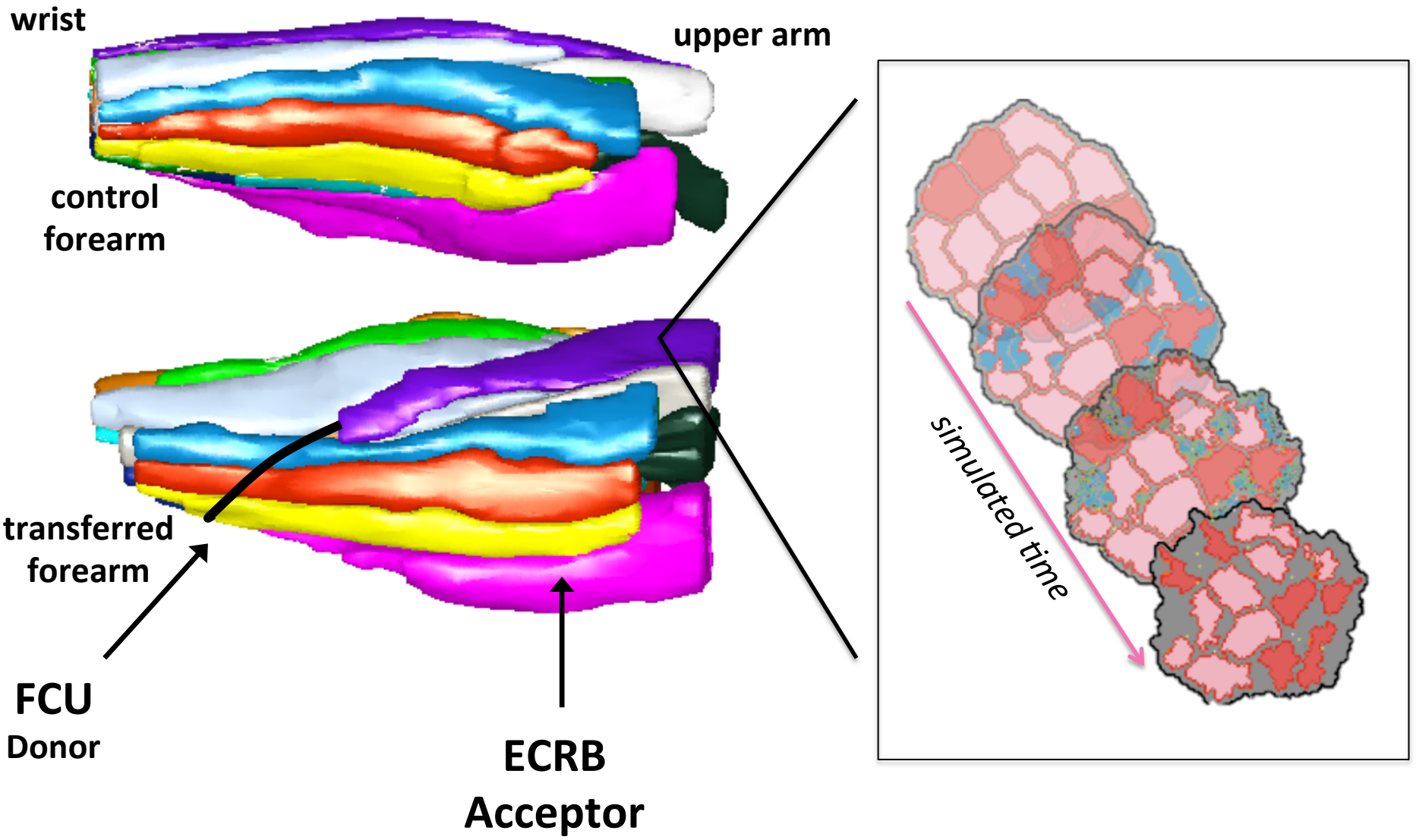
Goal: develop a modeling framework that can predict how muscle adapts to surgery.





Currently funded by the National Science Foundation

We are creating a multi-scale computer model of muscle remodeling following surgery



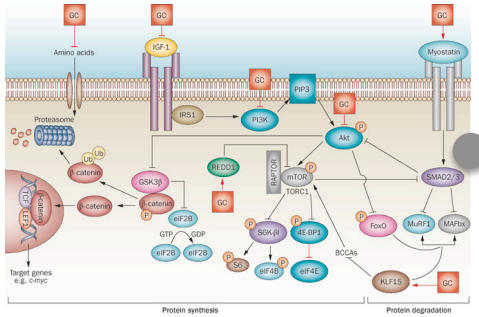
The multi-scale computer models reveal the relationship between molecular & cell biology, composition, form, and function.

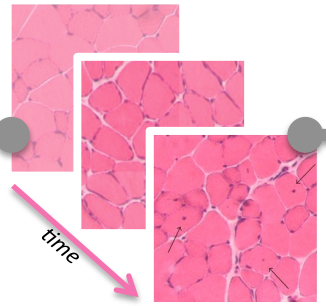
molecular & cell biology

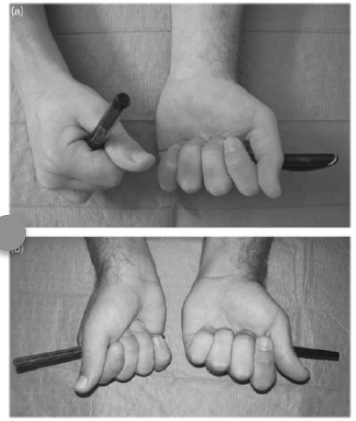
composition

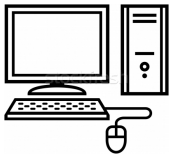
form

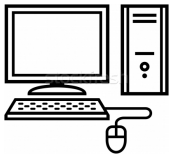
function











Why model???

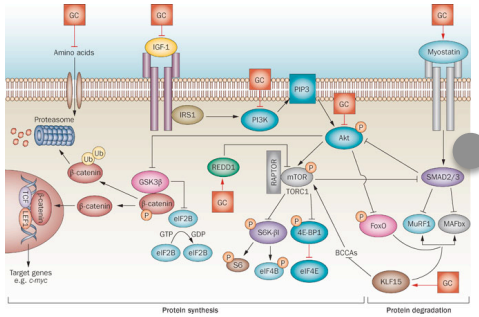
1. Computer models can point you to what is most important.

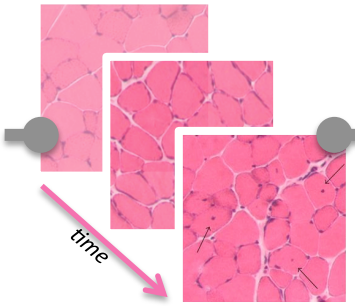
molecular & cell biology

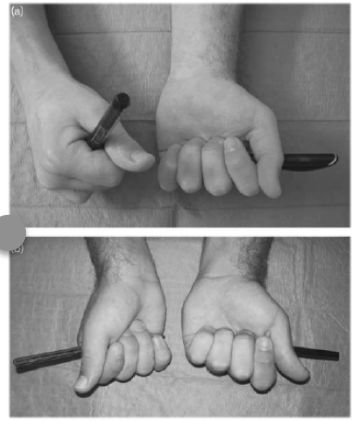
composition

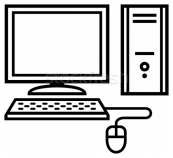
form

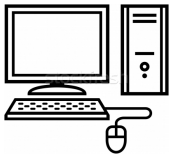
function







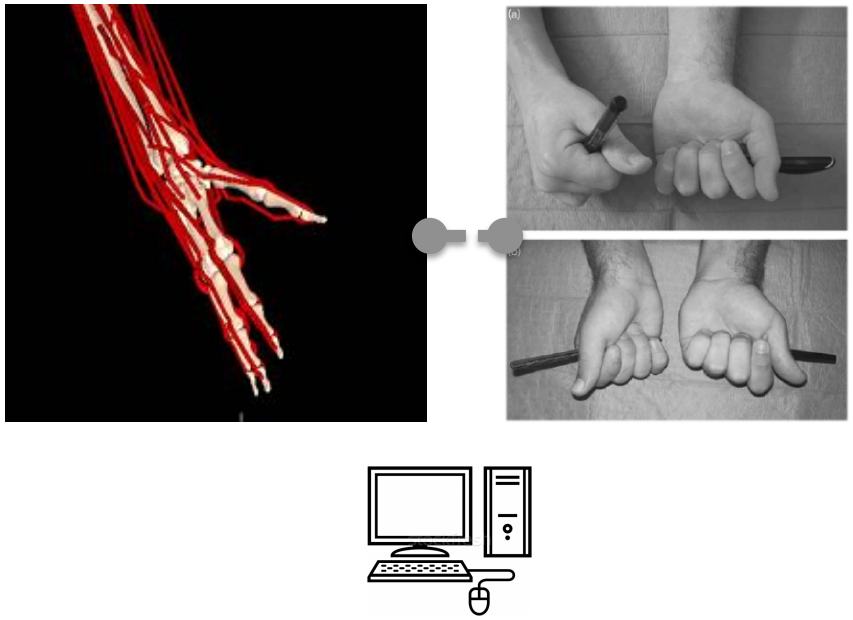




1. Computer models can <u>point you to what is most important</u>.

"How does surgical tensioning influence post-operative function"

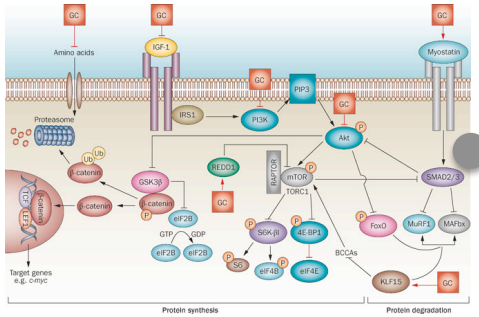
form **function**



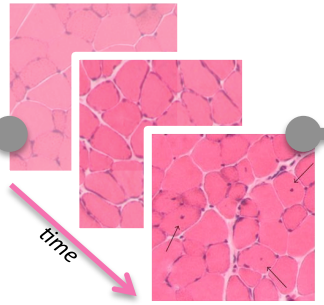
1. Computer models can point you to what is most important.

"Which molecule is the best target for minimizing scar following surgery?"

molecular & cell biology

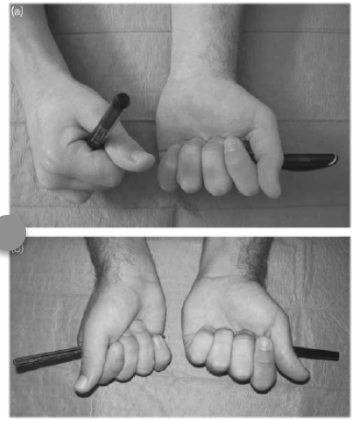


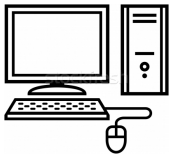
composition

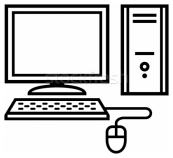


form

function



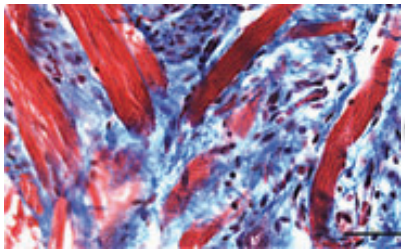
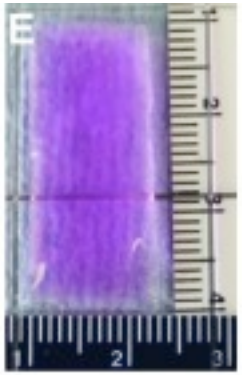
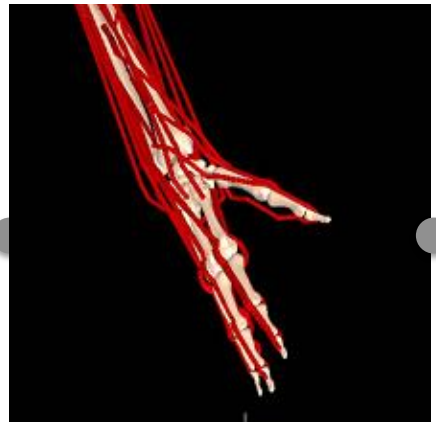
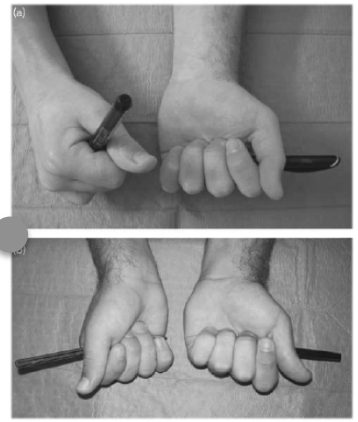
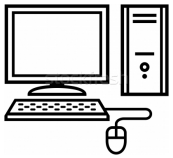




2. Computer models can run *in silico* experiments so that you can run fewer real (expensive and time-consuming) experiments

"Which combinations of cells & scaffolds should be included in a tissue engineered implant provide the most functional improvement?"

molecular & cell biology | **composition** | **form** | **function**

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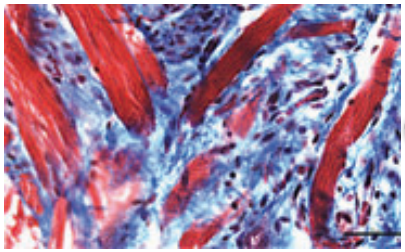
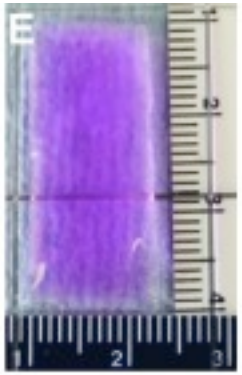
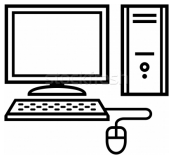
molecular & cell biology

composition







3 scaffold types
3 cell conditions
6 animals per treatment group
4 time points per treatment group
2 muscle beds

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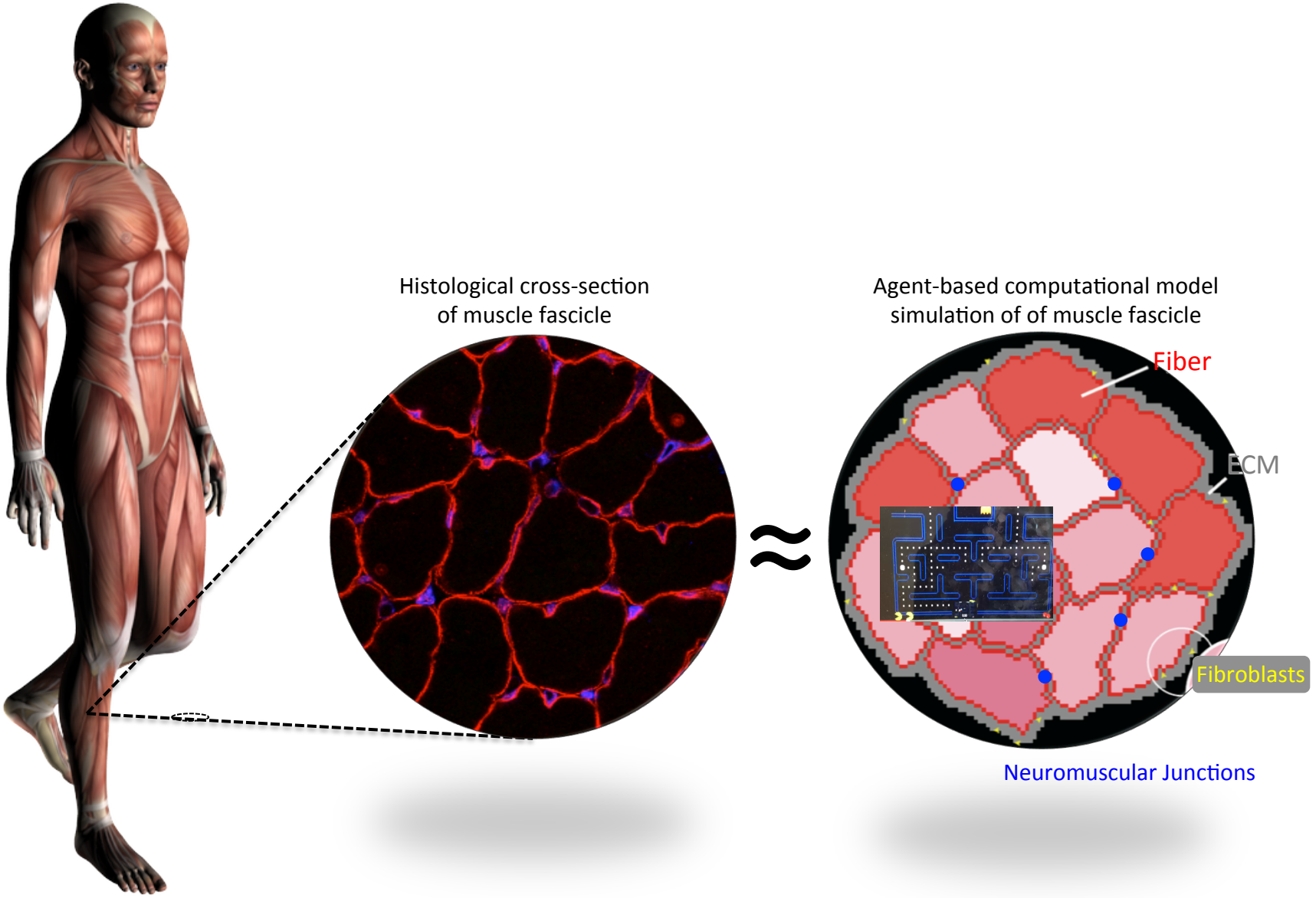
432 rats *= 1 year of a technician's time*
= 1 day on the computer

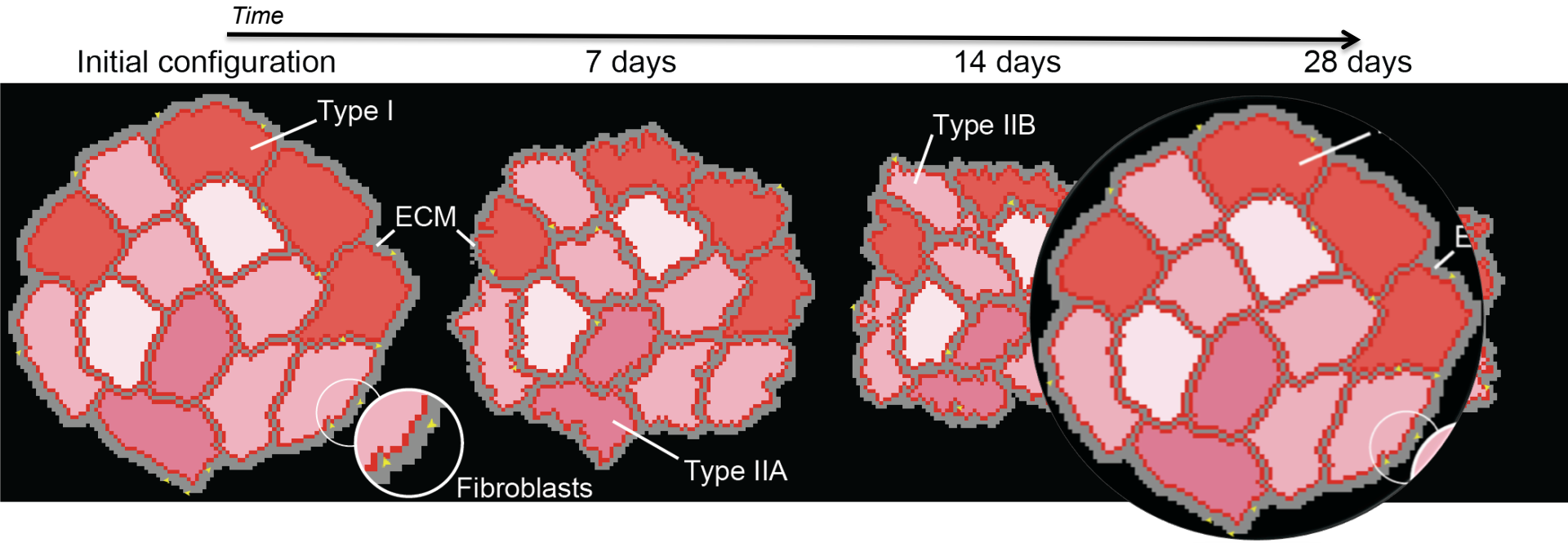
Agent-based computational model simulates cells and proteins in muscle to predict degeneration and regeneration



Agent-based computational model simulates cells and proteins in muscle…

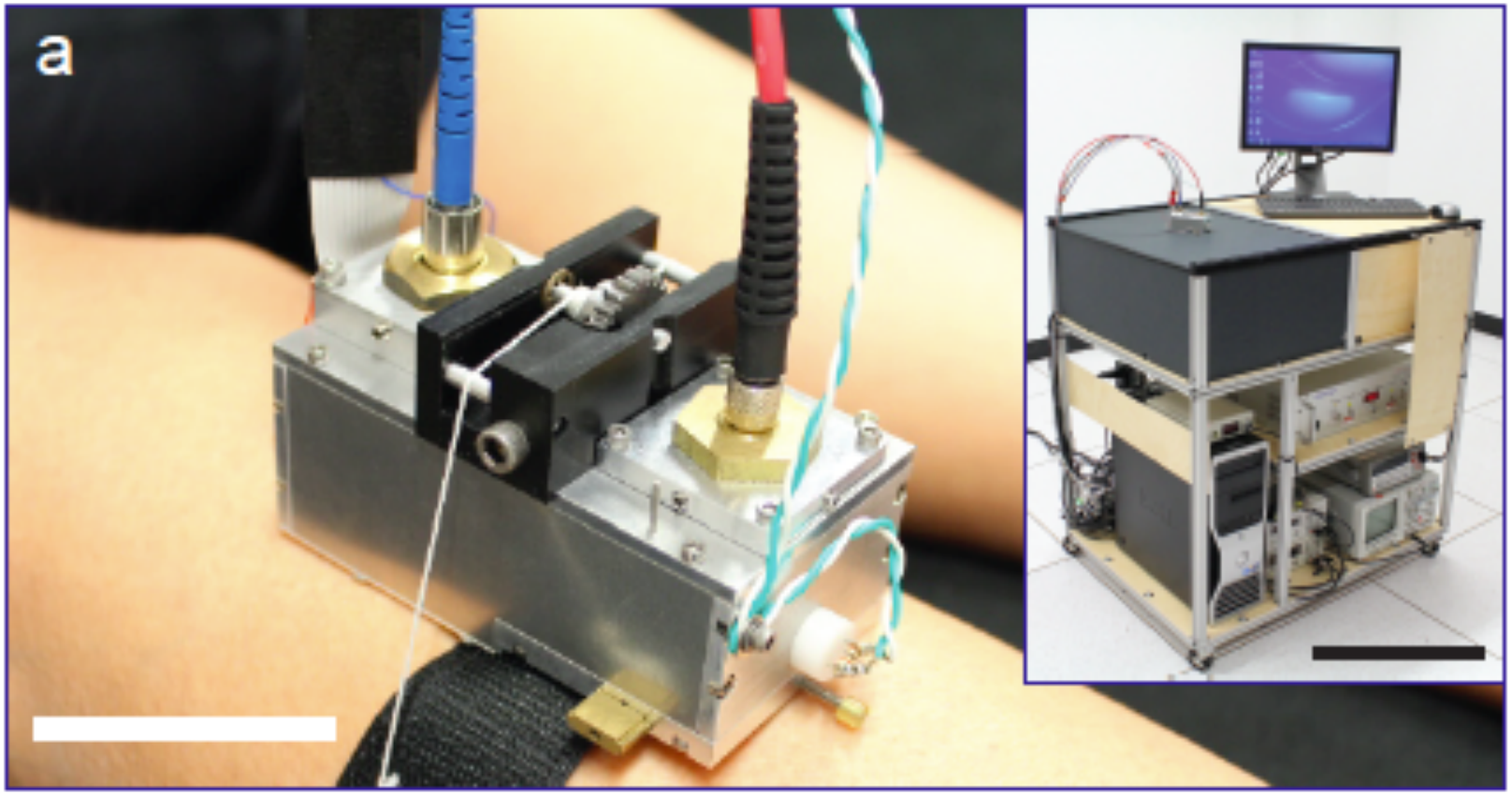
and how they change over time (i.e. growth, repair, remodeling)…

in response to disuse, surgery, exercise, *therapy*…

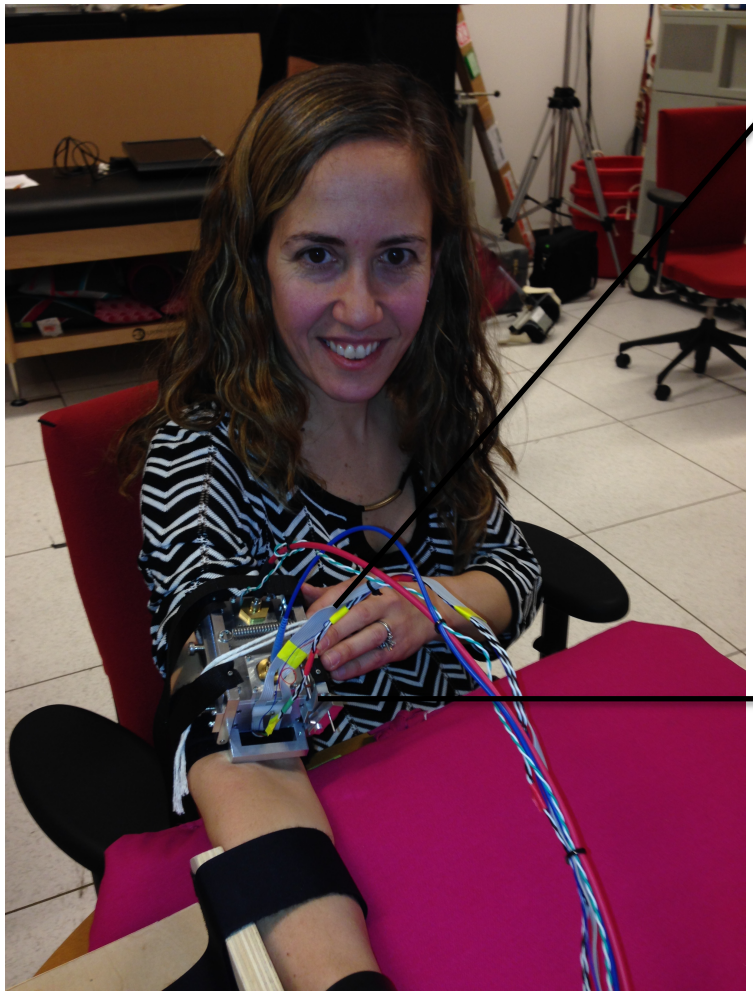


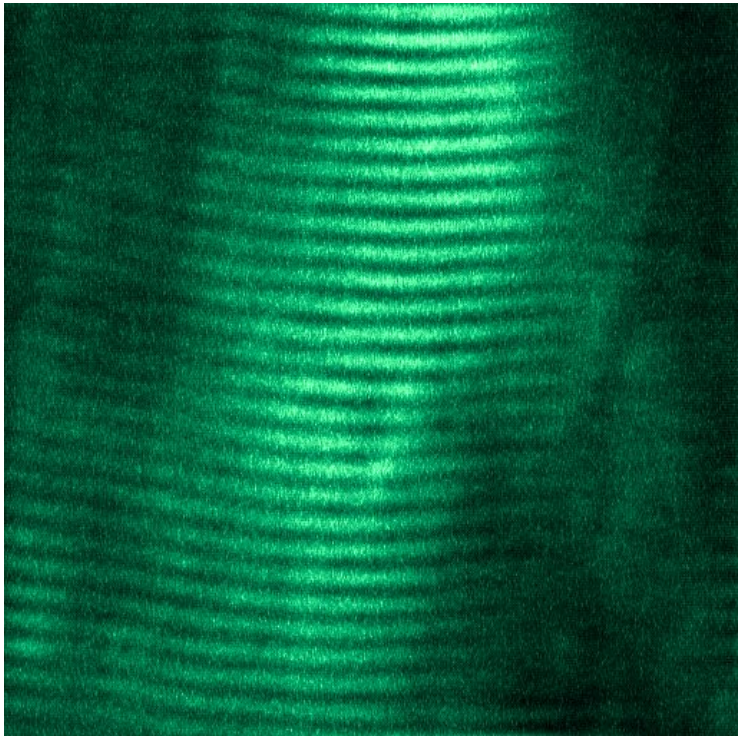
Models are integrated with novel imaging and 3D printing technologies

The “Zebra-scope”… a wearable microscope with a multi-functional microendoscope probe for minimally invasive observation of tissues



Real-time imaging of muscle tissue in “alert” subjects





Laser-scanning second-harmonic generation (SHG) imaging

First-ever serial measurements of sarcomere lengths

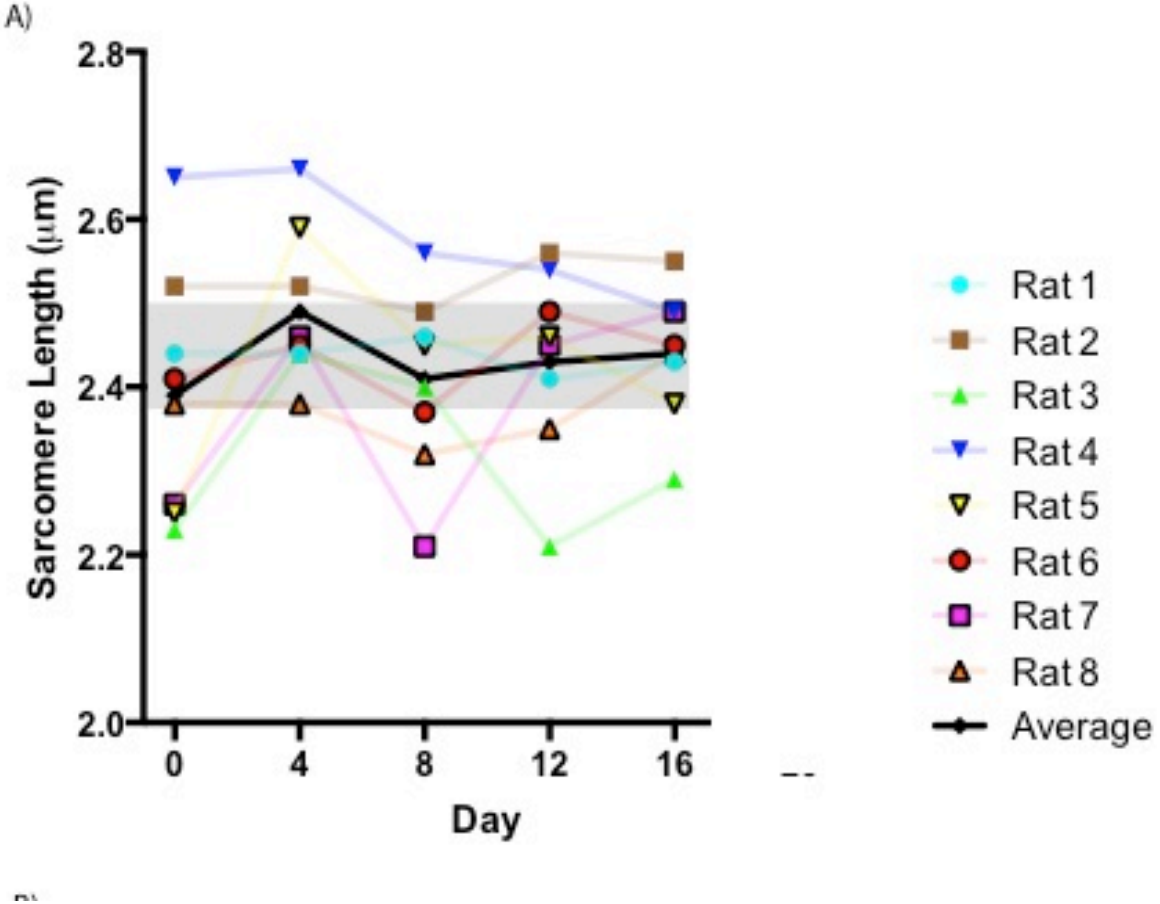
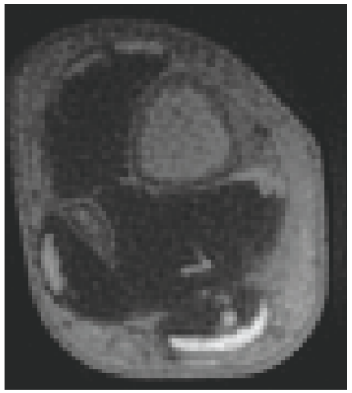


Image-based reconstructions of muscle allow us to quantify muscle volume in vivo

extreme hypertrophy (z > 4)
hypertrophy (2.5<z<4)
slight hypertrophy (1<z<2.5)
normal (-1<z<1)
slight atrophy (-2.5<z<-1)
atrophy (-4<z<-2.5)
extreme atrophy (z<-4)

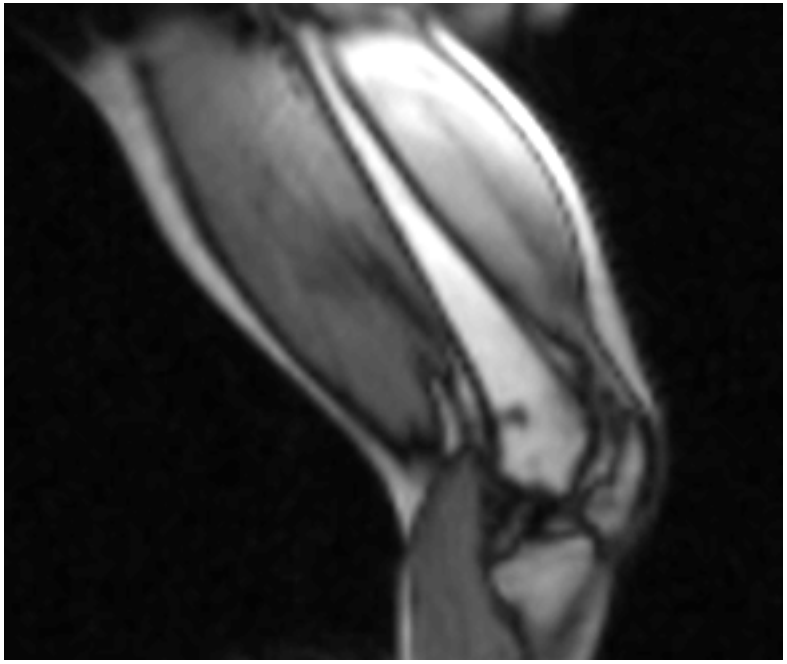
Ultra-short echo-time imaging of tendon



posterior view

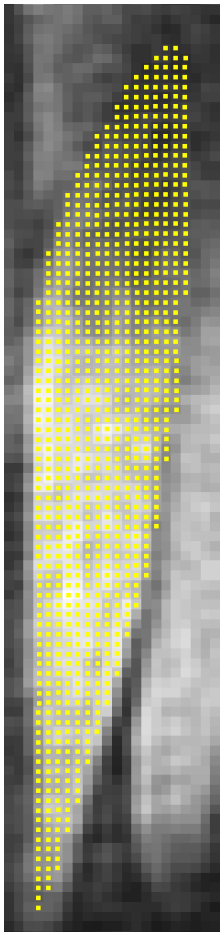
Dynamic MRI

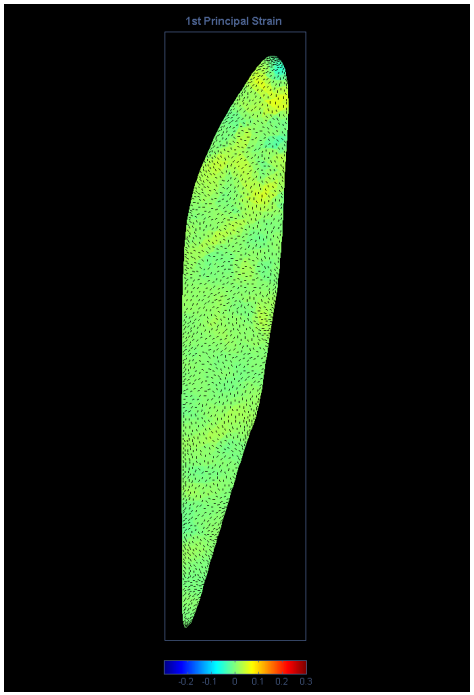
Real-time MRI



Fiorentino et al, J. Biomechanical Engineering, 2014

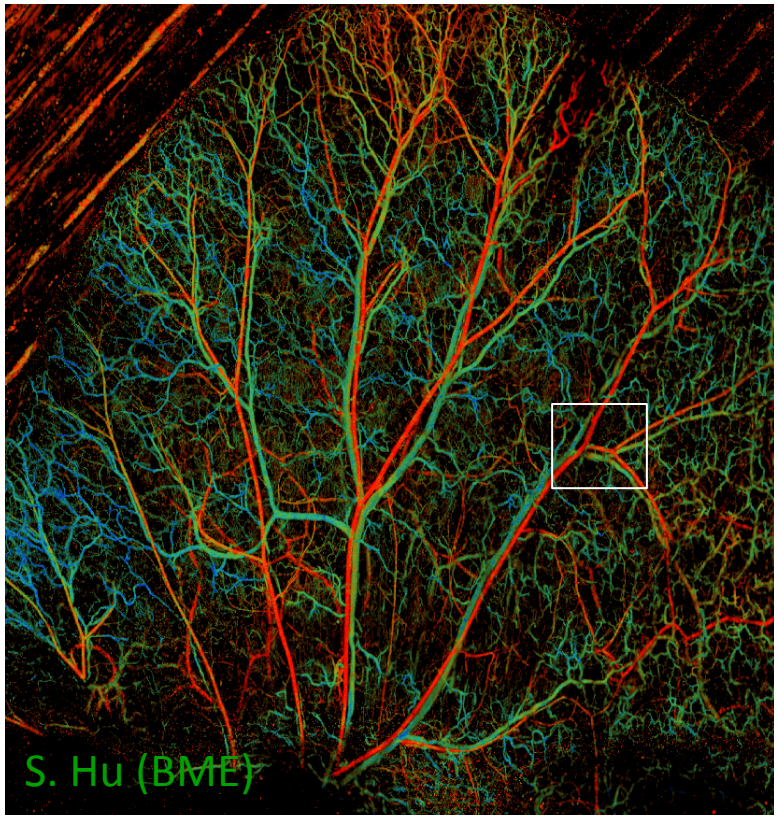
Cine DENSE MRI

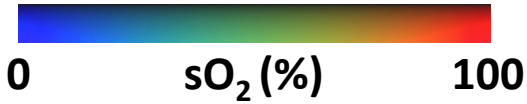


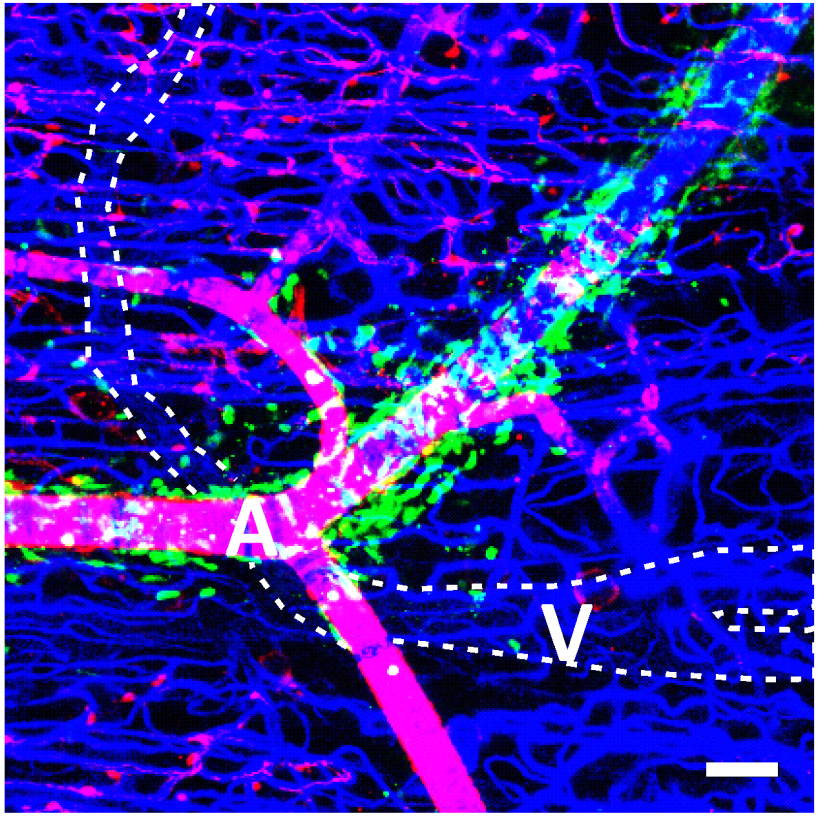


Fiorentino et al, J. Biomechanics, 2012

High-resolution imaging of microvessel function, structure, & composition

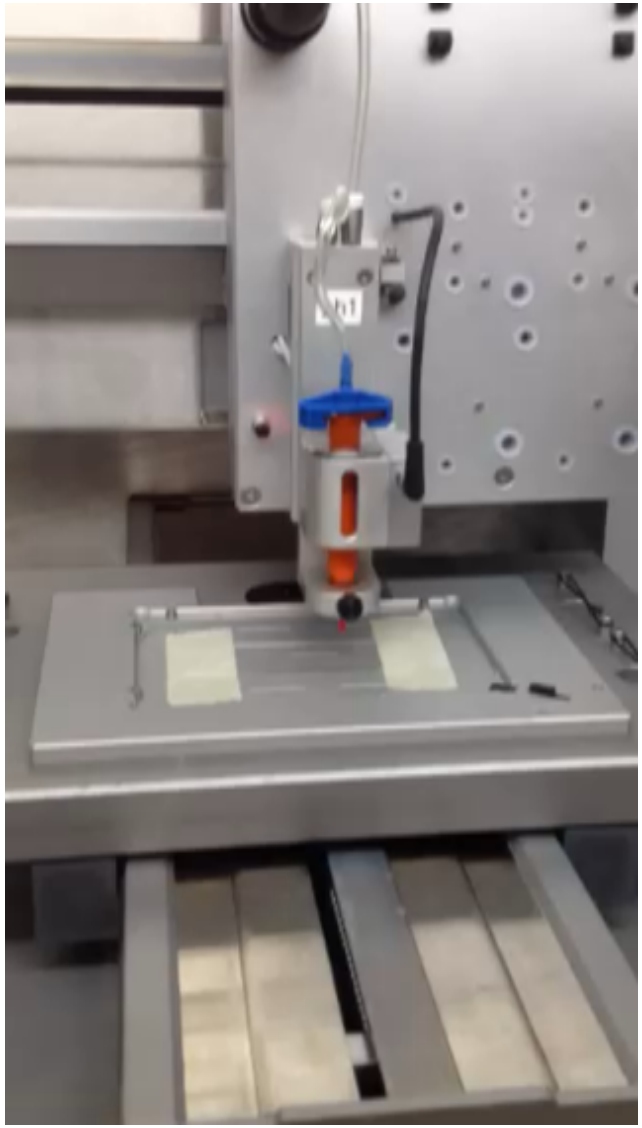


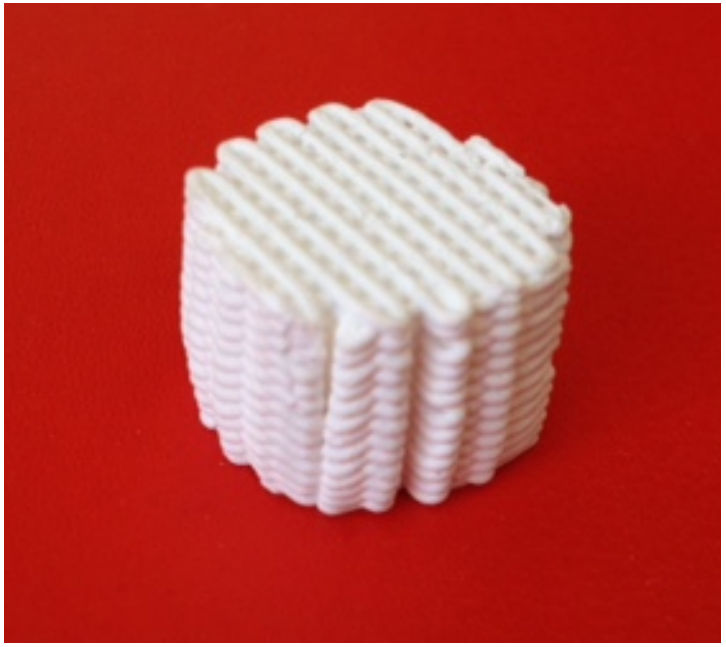


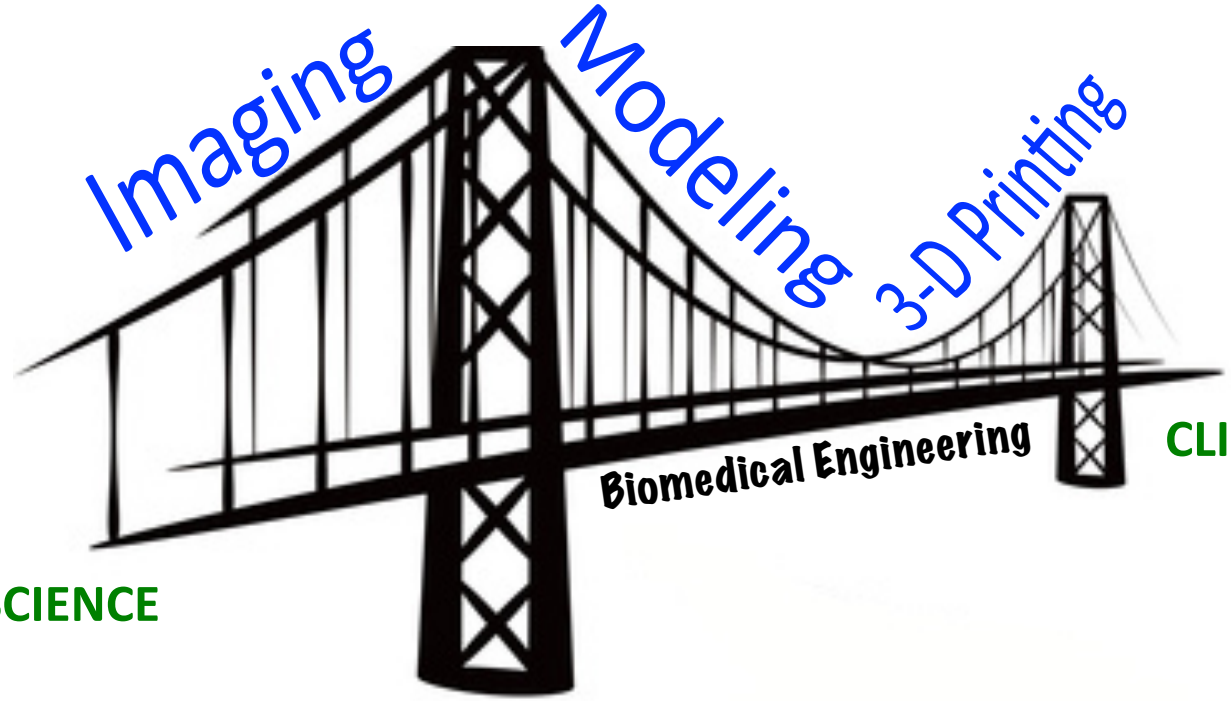


Monocyte-derived Macrophages

3D-Bioprinting in Peirce-Cottler Lab







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CLINICAL RESEARCH