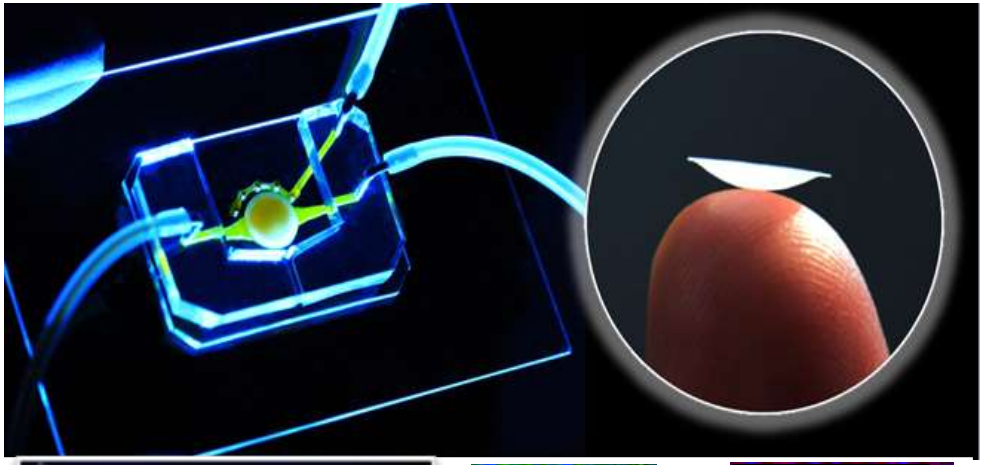
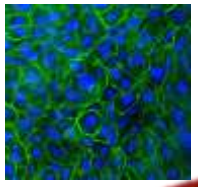
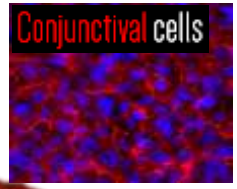
Center for Engineering Mechanobiology

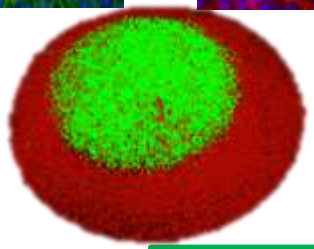
ASU Alabama State University · Bryn Mawr College · Boston University · NJIT New Jersey Institute of Technology · Penn University of Pennsylvania · Texas The University of Texas at Austin · Washington University in St. Louis

Blinking human eye-on-a-chip

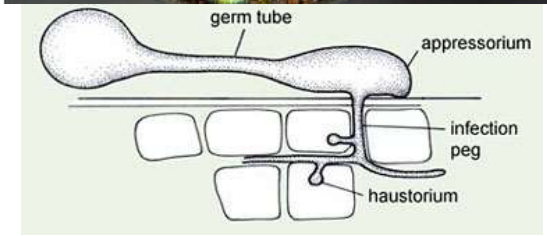


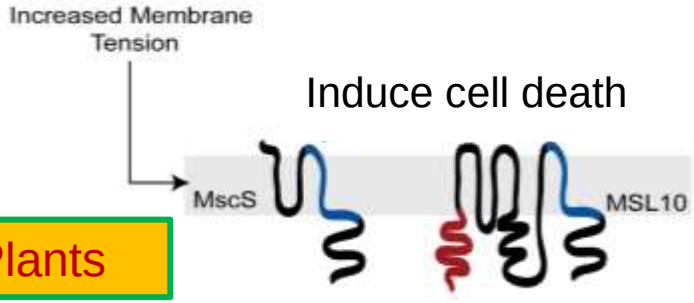






Engineered mechano-protectants





Animals ↔ Plants

CEMB Center for Engineering MechanoBiology

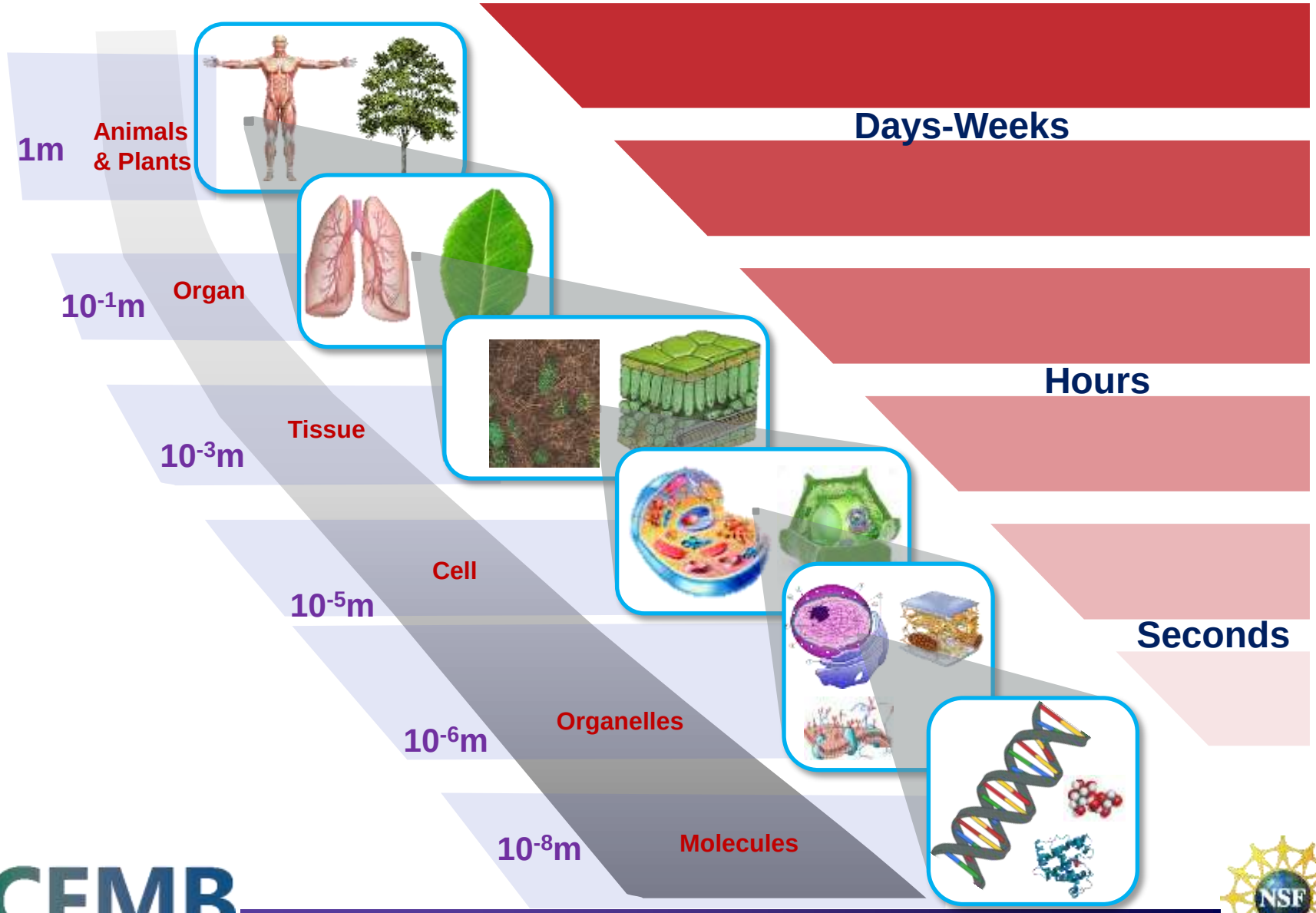
Harnessing Mechanical Responses of Cells For Crops and Health

NSF

CEMB Vision

A new discipline and a new generation of scientific leaders to understand and control force in living systems

Length and Time Scales in Mechanobiology



Forces Influence Biological Pathways on All Scales

CEMB Center for Engineering MechanoBiology
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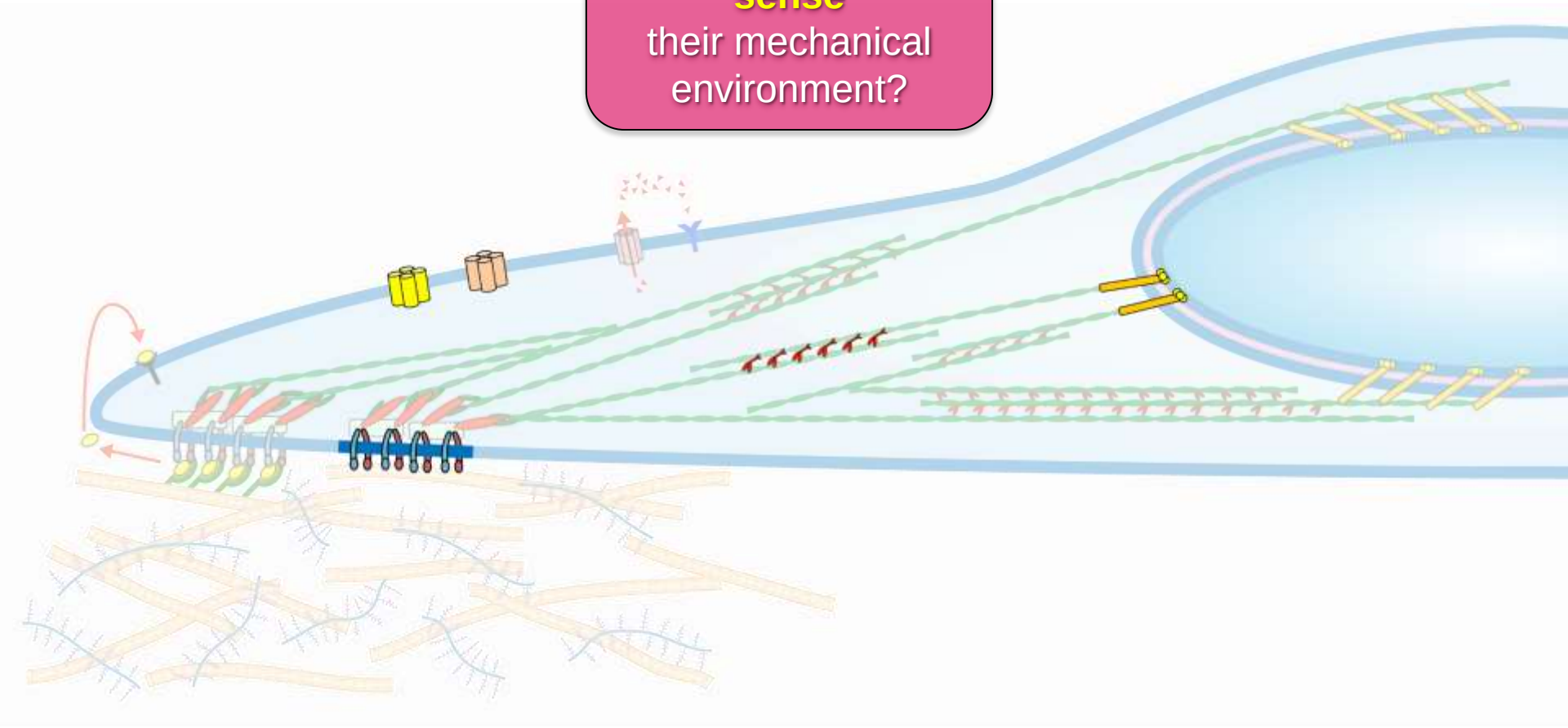
CEMB: Organization of Research

WG1: How do cells **sense** their mechanical environment?



CEMB: Organization of Research

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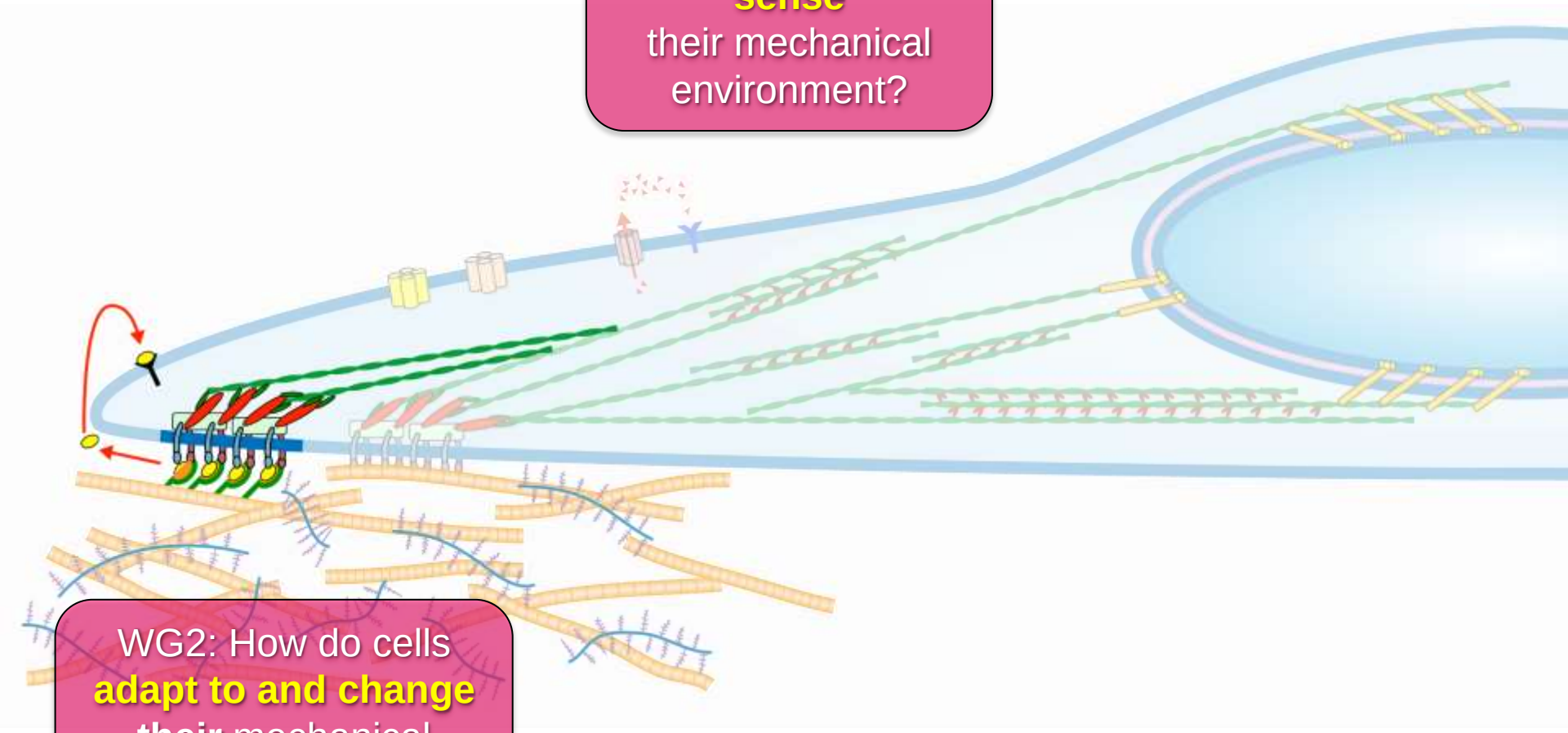
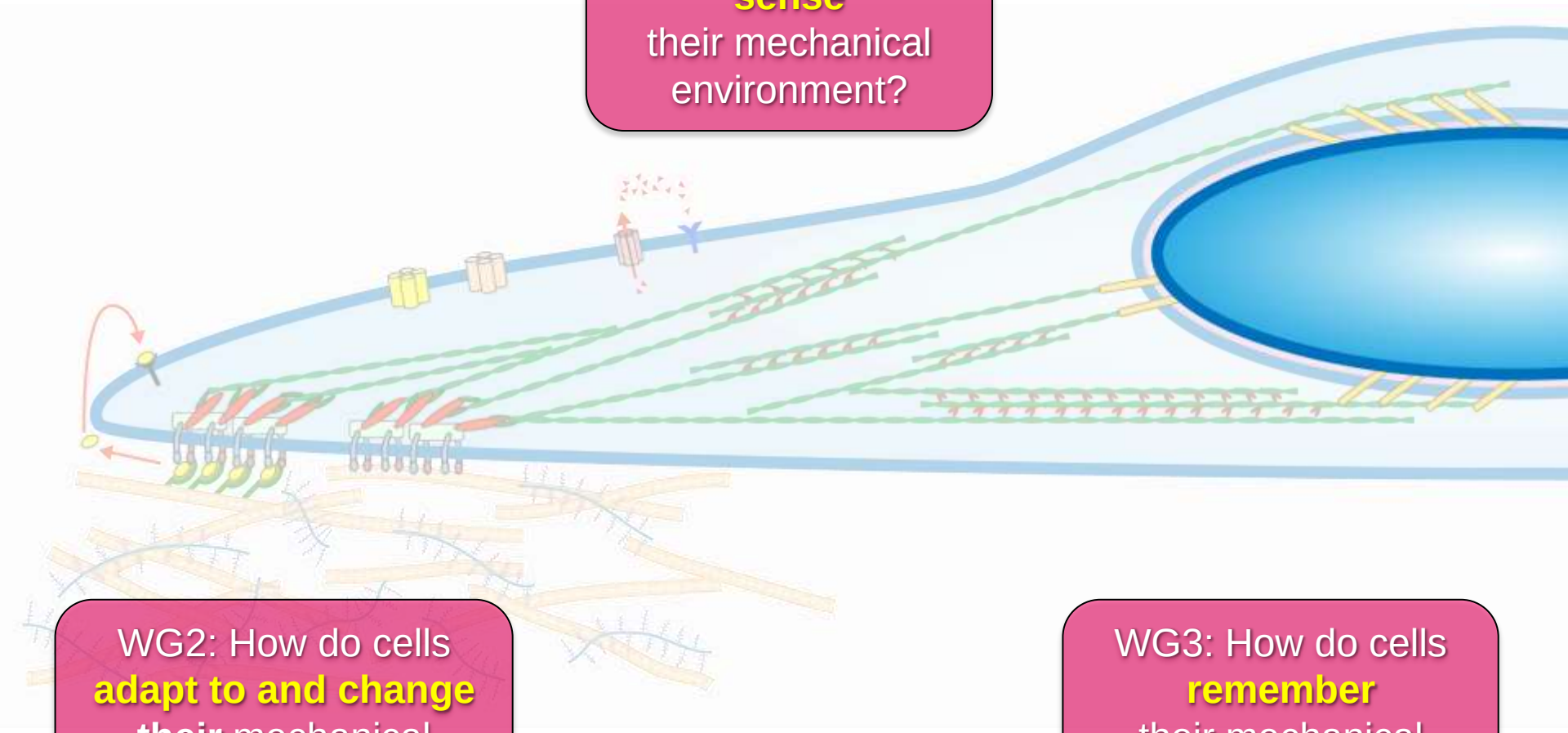


WG2: How do cells **adapt to and change their** mechanical environment?

CEMB: Organization of Research

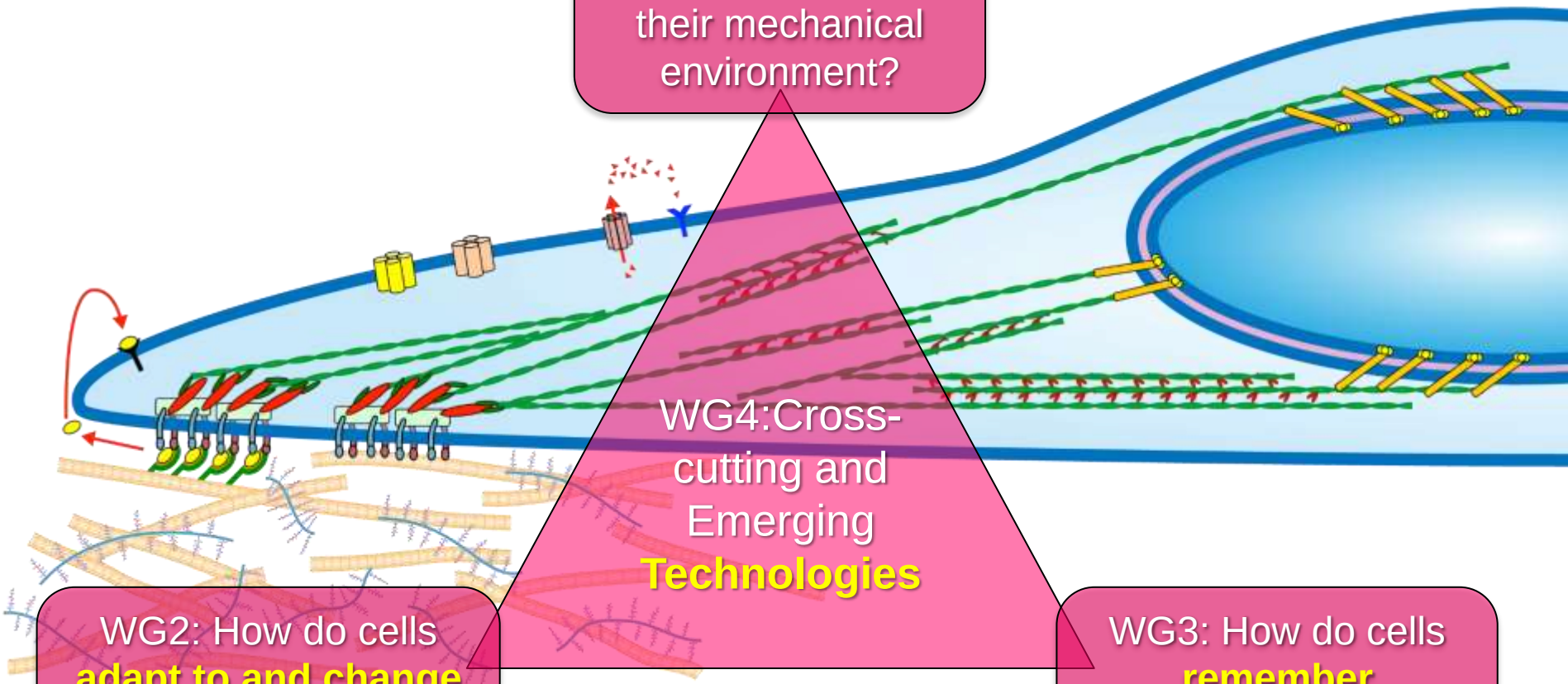
WG1: How do cells **sense** their mechanical environment?



WG2: How do cells **adapt to and change their** mechanical environment?

WG3: How do cells **remember** their mechanical environment?

CEMB: Organization of Research



WG1: How do cells **sense** their mechanical environment?

WG4:Cross-cutting and Emerging **Technologies**

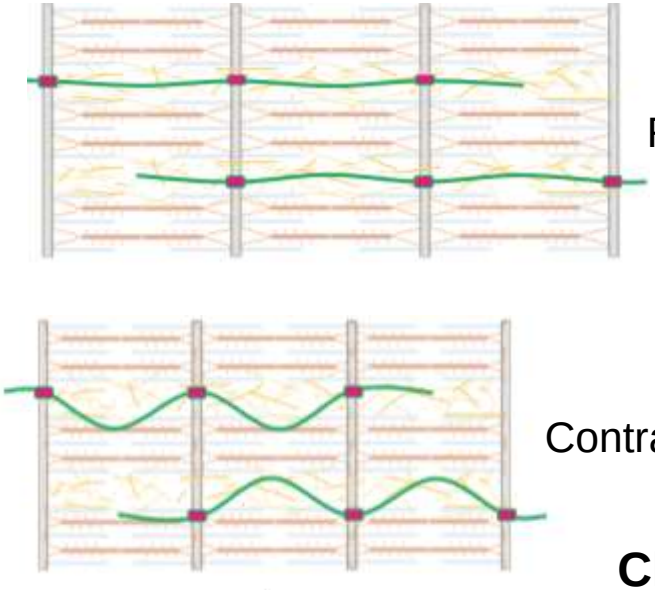
WG2: How do cells **adapt to and change their** mechanical environment?

WG3: How do cells **remember** their mechanical environment?

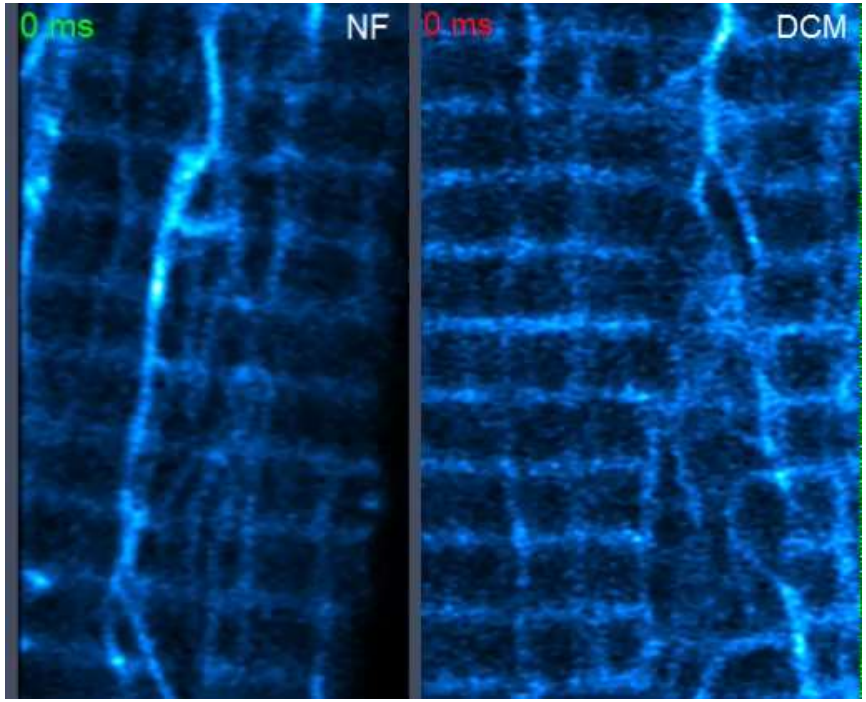
Heart Failure Linked to Buckling of Microtubules

Prosser, Margulies, Shenoy

- Microtubules ”buckle” during contraction and resist heart cell motion
- In cells of patients with heart failure, there is a dramatic increase in detyrosinated microtubule
- Reducing detyrosination restores the contractile function of failing heart cells by 50%



Healthy heart cell **Failing heart cell**

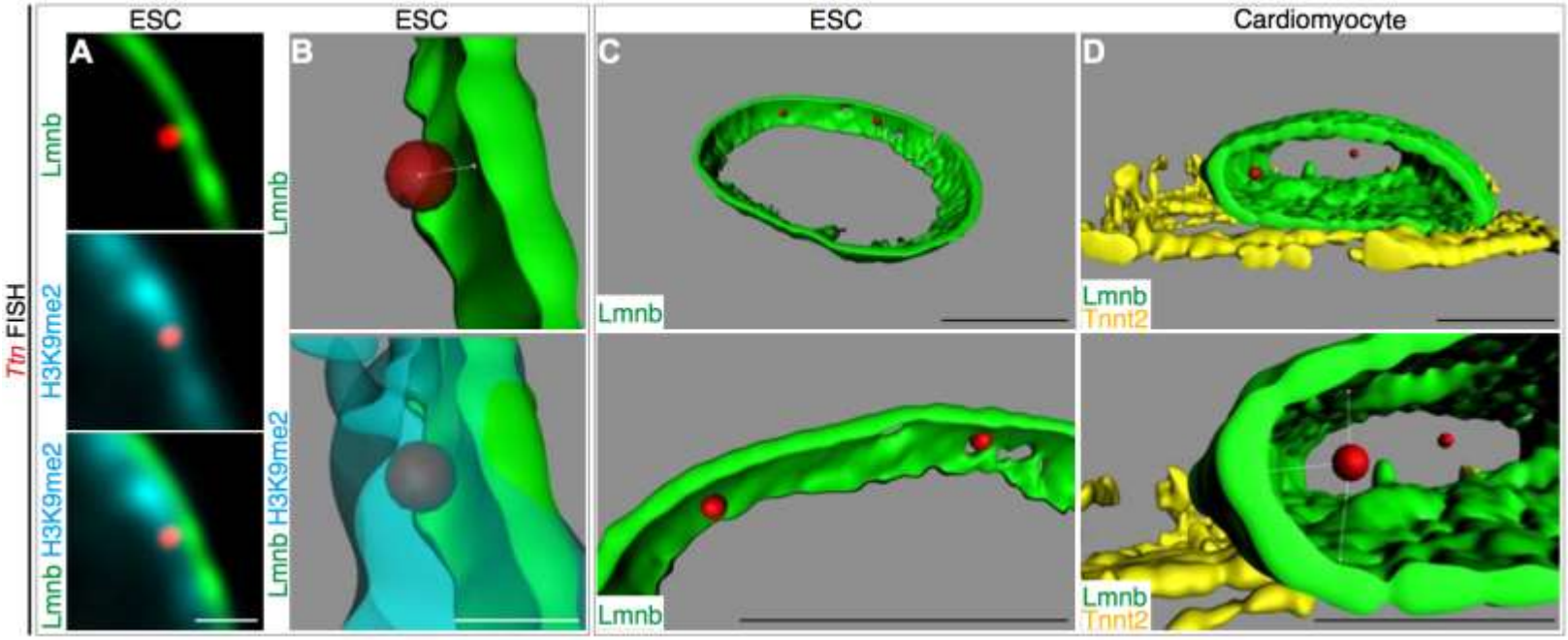


microtubules – EMTB-3X-GFP

Chen et al. Nature Medicine 2018
Robinson et al. Science 2016

3D Packaging of DNA Regulates Cell Identity

Jain, Prosser, Mauck, Discher,
Shenoy, Thirumalai, Strader



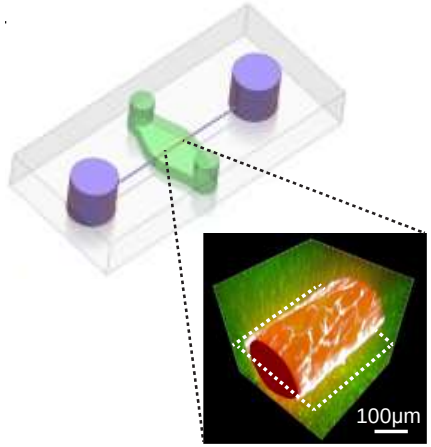
Poleshko et al. Cell 2017

- ❑ Impact of mechanics on 3D gene organization in the nucleus
- ❑ Titin loci have moved away from the edge of the nucleus in differentiated cells

Engineered Blood Vessel on a Chip

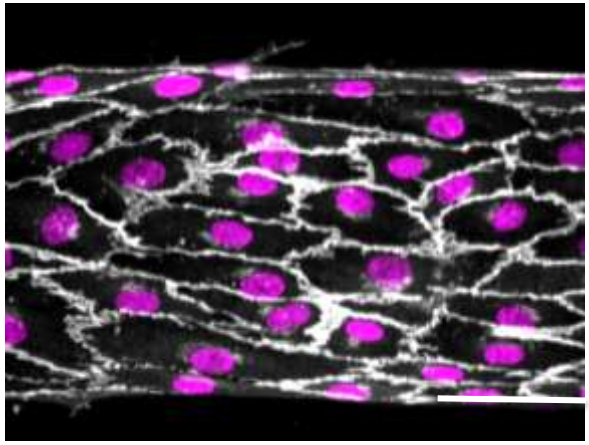
Chen, Assoian, Wells, Shenoy

- Novel microfluidic platform to control flow in engineered blood vessels
- We found a new biological pathway governed by fluid shear stress
- We are exploring this model in detail with computational modeling

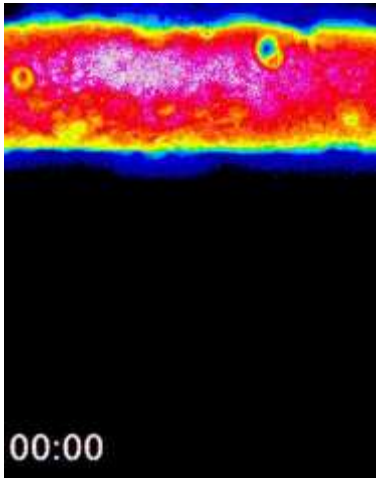


Polacheck et al. Nature 2017

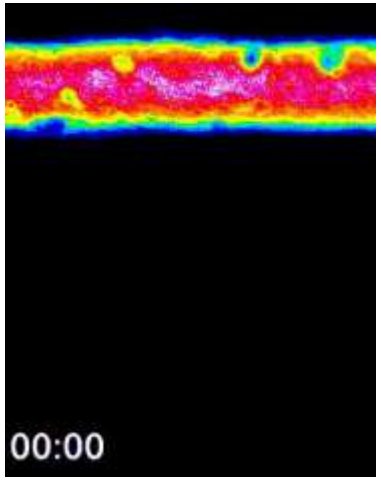
Engineered blood vessel



Static



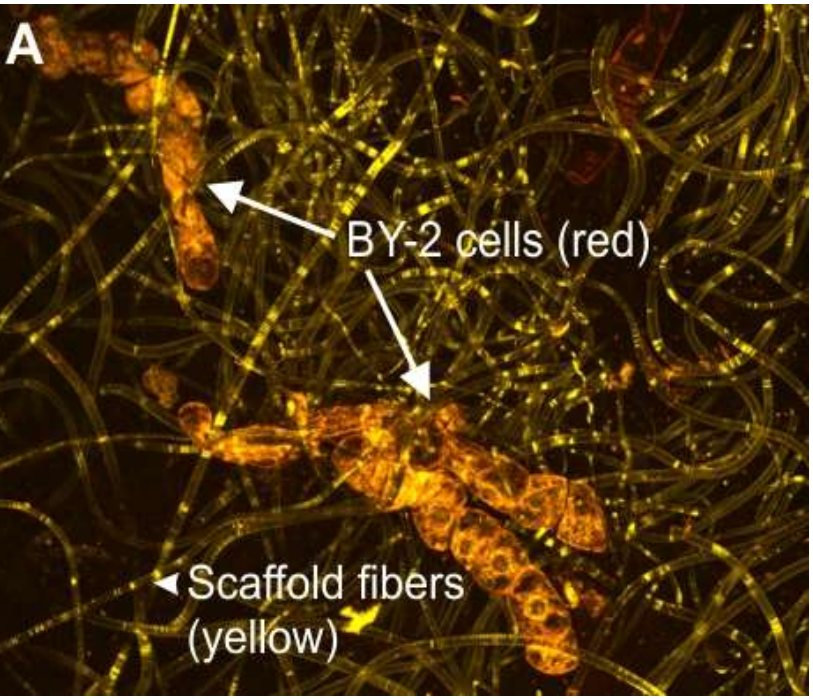
Flow

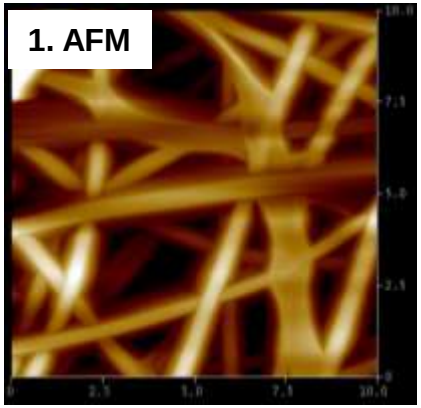


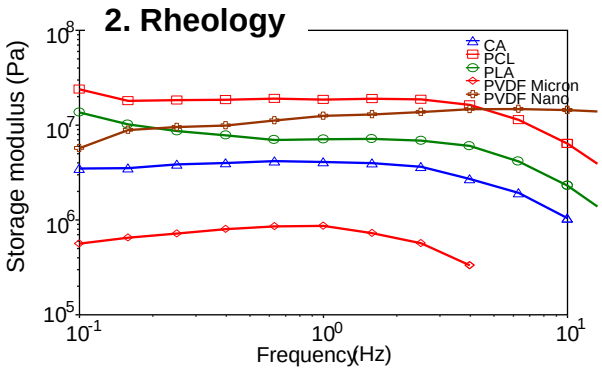
Artificial Scaffolds For Plant Cells

Arinzeh, Dean, Dixit, Foston, Huh

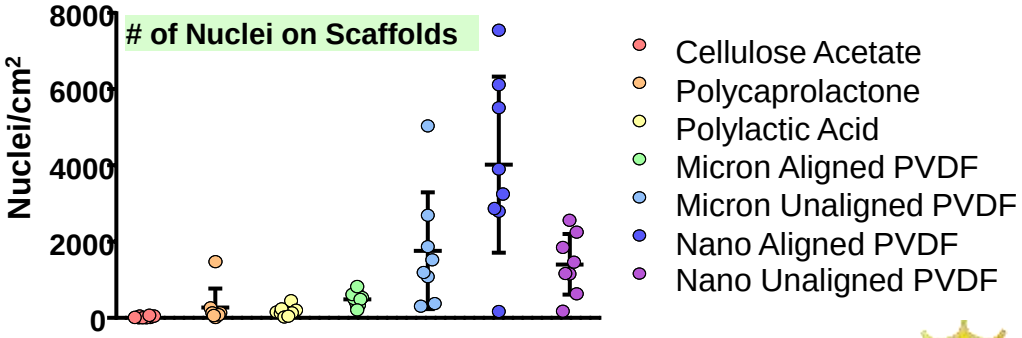
Identified the first artificial scaffolds for plant cell growth





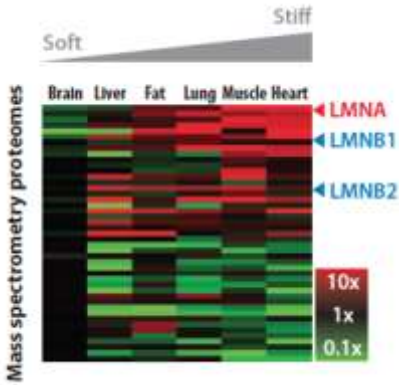


3. Hydrophobicity

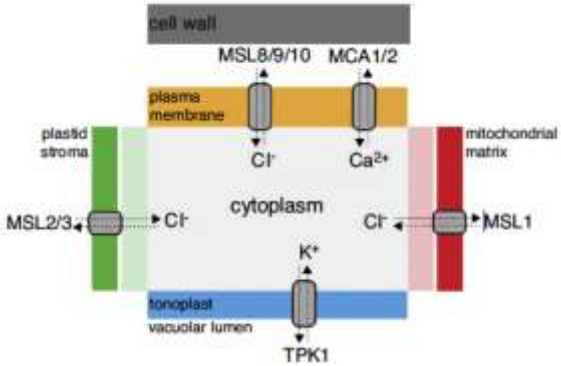


Hydrophobic materials support better plant cell growth

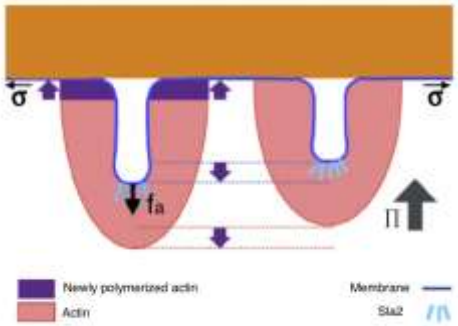
Reviews and Position Papers



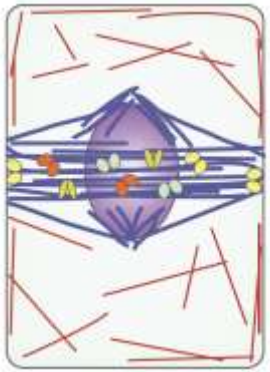
Matrix mechanosensing (Discher) ***Ann. Rev. BioPhys 2017***



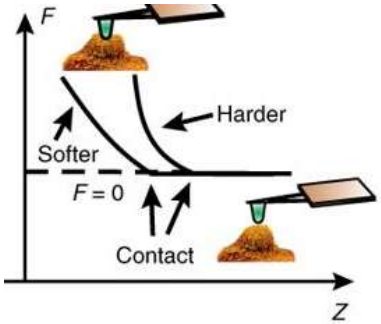
Mechanosensitive channels (Haswell) ***Curr. Opi. Plant Bio 2017***



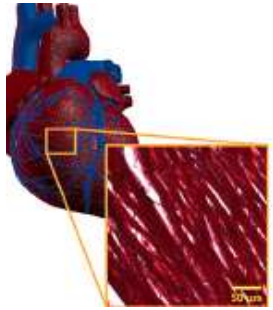
Membrane Bending (Carlsson) ***Curr. Opi. Cell Bio 2018***



Motors in Plants (Dixit) ***Ann. Rev. Plant Bio, 2018***



Methods to measure cell mechanics (Janmey) ***Nature Methods 2018***



Needs for basic and translational mechanobiology (Janmey&Discher) ***Nano Letters 2018***

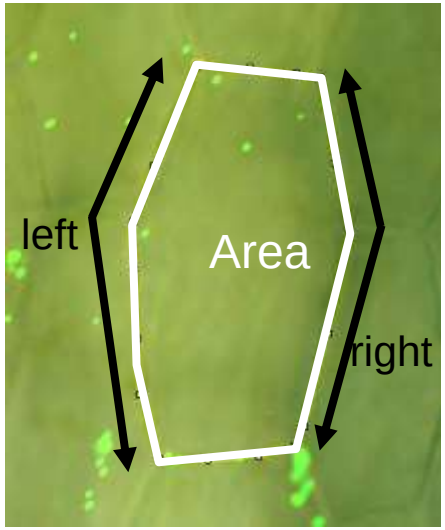
CEMB Center for Engineering MechanoBiology

More Integrative Review Papers in Progress

NSF

Mechanobiology Bootcamp

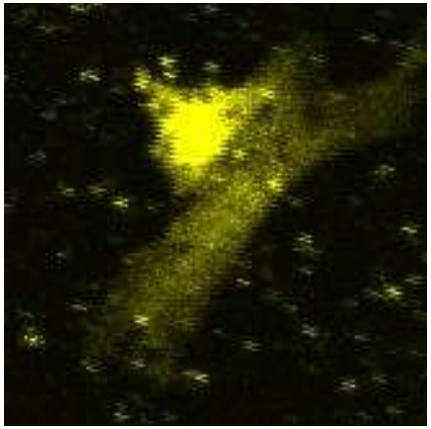
Two week intensive training program for early CEMB graduate students: establish a common language and collaborative cohort



Anisotropic growth in *Arabidopsis* twisted mutants

Week 1: The Basics

- Lectures on plants and animal cell biology and mechanics
- Hands-on lab tutorials for small groups (2-5 students), led by CEMB postdocs and advanced students
  - Plant and animal cell culture, molecular biology techniques, microfabrication, basic and advanced Matlab and image analysis, rheology, TFM, materials
- Lunch talks on the NSF and Networking at Conferences
- Evening social events



Mechanotransduction and juxtacrine signaling

Week 2: Final Projects

- Teams of 4 students each given a research question
- Final presentations at retreat
- Both projects now being pursued

Knowledge Transfer Highlights

Mechanobiology Startups:

- Mauck & Lee: Mechano-Therapeutics LLC (Drug delivery platform that responds to mechanical forces)
- Burdick: Prohibix (Injectable and bio-responsive hydrogels)

prohibix

Industry Partners:

MONSANTO

SANOFI

Johnson & Johnson INNOVATION

emulate

Advanced BioMatrix
Innovative 3D Matrix Products

ST. JUDE MEDICAL

Merck KGaA
Darmstadt, Germany

INTEGRA

stryker

KCI
The Clinical Advantage

Innovation Slams (Penn ICorps, Jess Tytell, BU):
Trainee 'Shark Tank' Public *Pitch Session* – new 'companies focused' on 'mechano-active soil'

Conferences and International Collaborations

Signaling by Adhesion Receptors
Gordon Research Conference

Connecting Structure, Mechanics, and Function in Cells and Tissues

June 24 - 29, 2018

Chair: Christopher S. Chen
Vice Chair: Ann L. Miller

Generation and Control of Forces in Cells

NORDITA
Nordic Institute for Theoretical Physics

Program
11—29 June 2018

Coordinators: Anders Carlsson, Edda Klipp, David Sept

www.nordita.org/gcfc2018

CEMB MECHANOBIOLOGY SYMPOSIUM
September 13-14, 2018
University of Pennsylvania, Philadelphia

Dec 2018 in Philadelphia

institutCurie

MBI
MECHANOBIOLOGY INSTITUTE
National University of Singapore

Dec 2017 in Singapore

NSFC

July 2018 in Xian

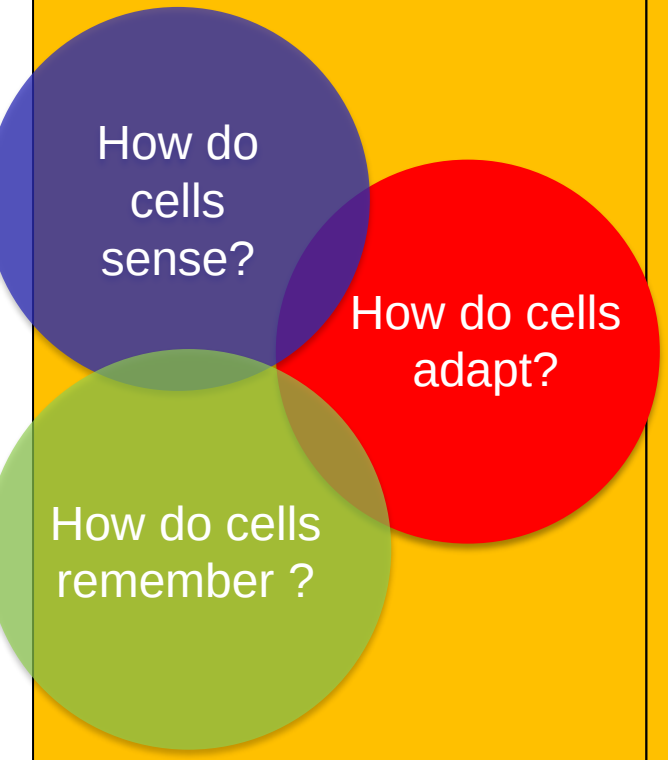
CEMB
Center for Engineering MechanoBiology

a global partnership for mechanobiology

Building an International Mechanobiology Community

Reflections on the First Two Years

Big Questions



Achievements

Integration across working groups, education and outreach

Integration across sites: Cross-site REU,RET, Bootcamp, Innovation slams

National and international visibility

Goals

<u>Research</u>: More plant-animal work

<u>Education</u>: Recruit students nationwide to the bootcamp

<u>Outreach</u>: Expand collaboration with the Franklin Institute

<u>Diversity</u>: New partnership with UC Merced