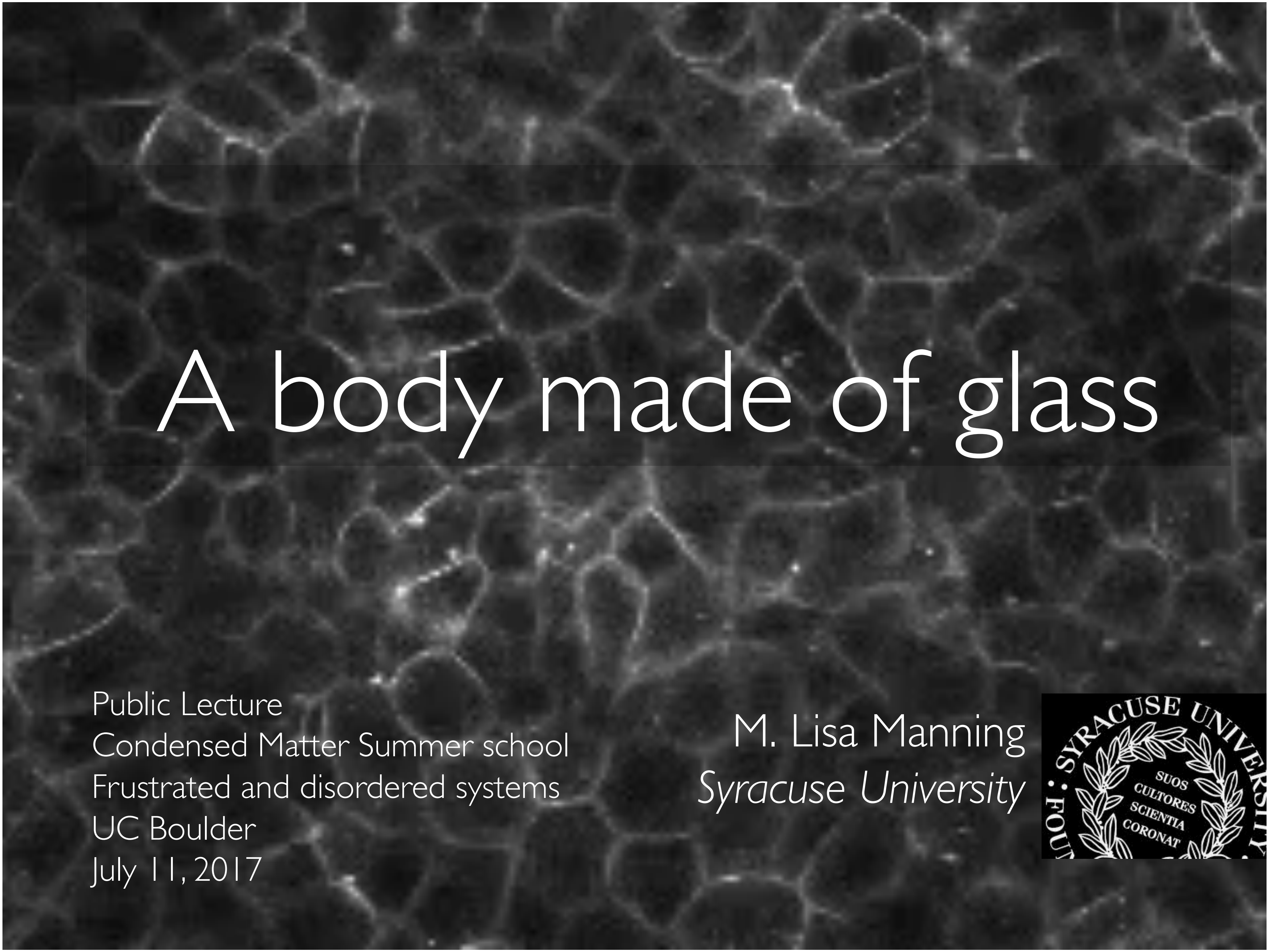


# A body made of glass

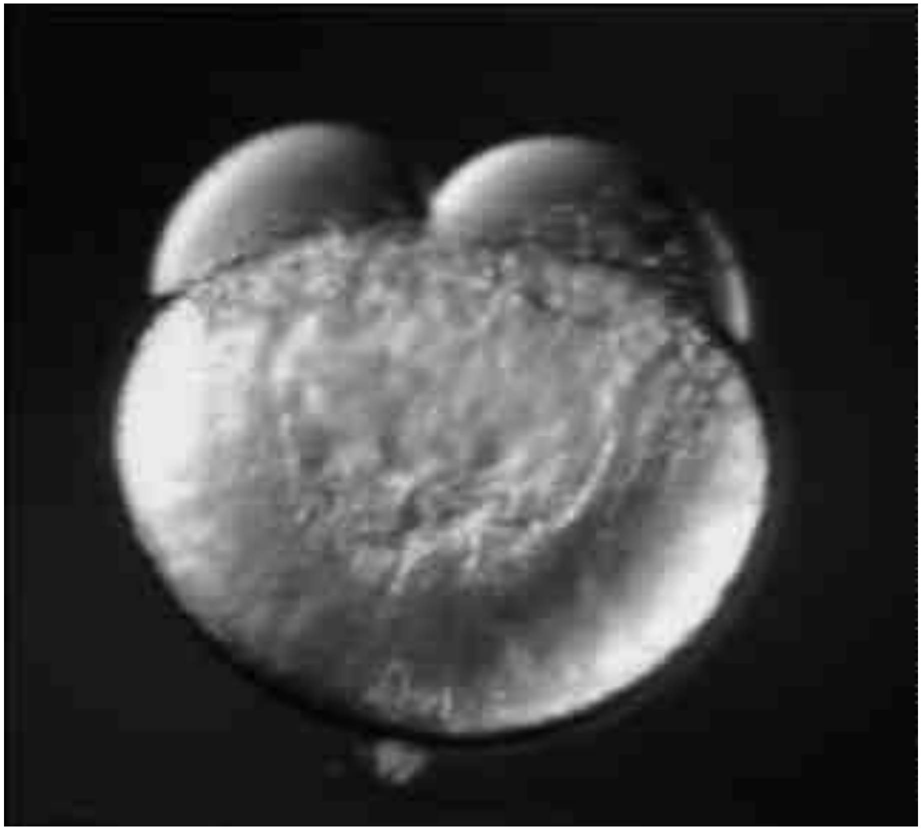
Public Lecture
Condensed Matter Summer school
Frustrated and disordered systems
UC Boulder
July 11, 2017

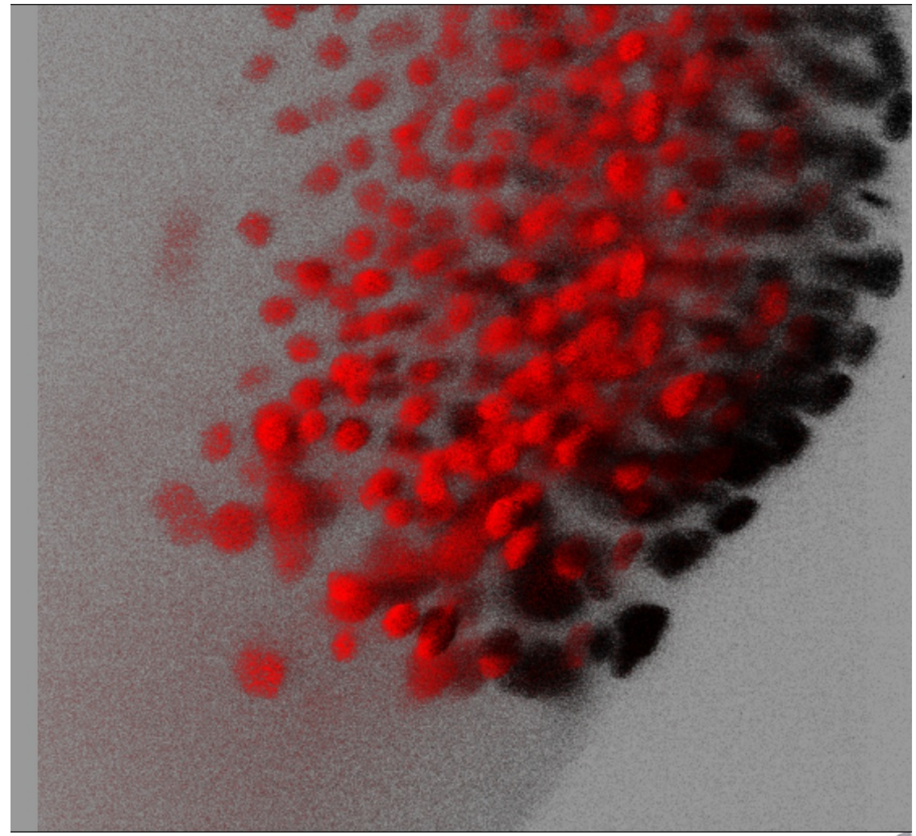
M. Lisa Manning
*Syracuse University*

Are you a solid or a fluid?

# What about during development?

EM Schoetz PhD Thesis 2008

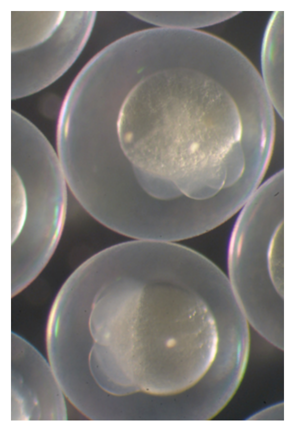




Karlstrom et al, Development (1996)

Tissue fluidity important
segregatior
brain cells ar
cells are in the abdomen, etc.

Scientific Paper

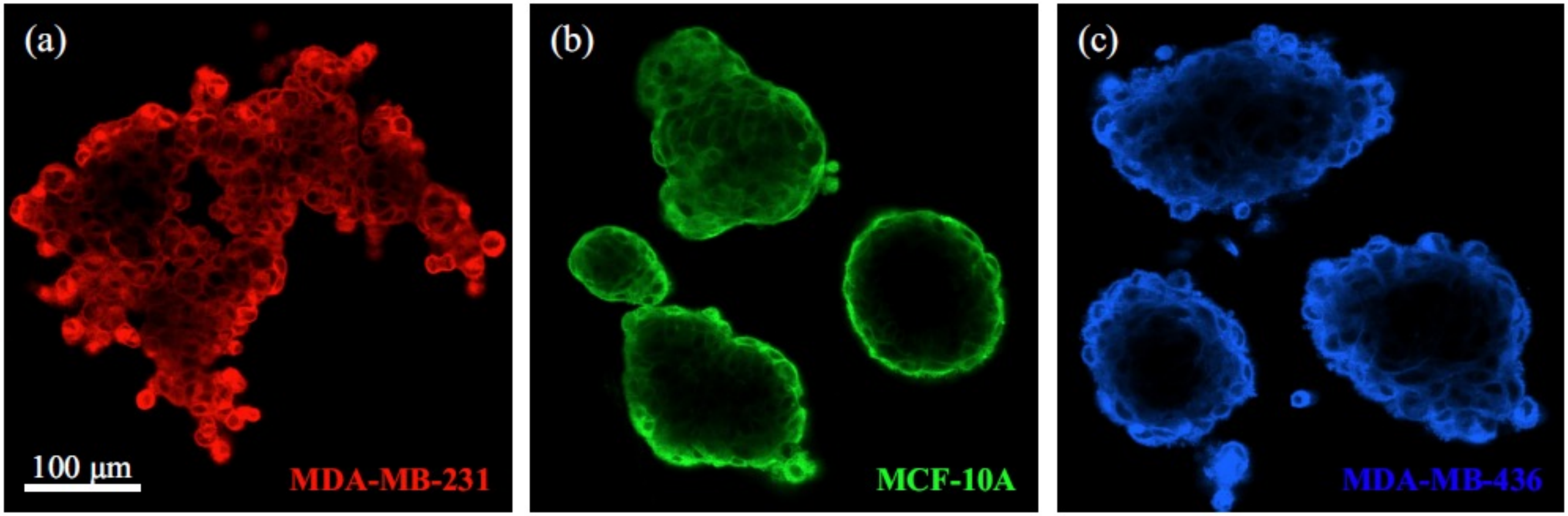


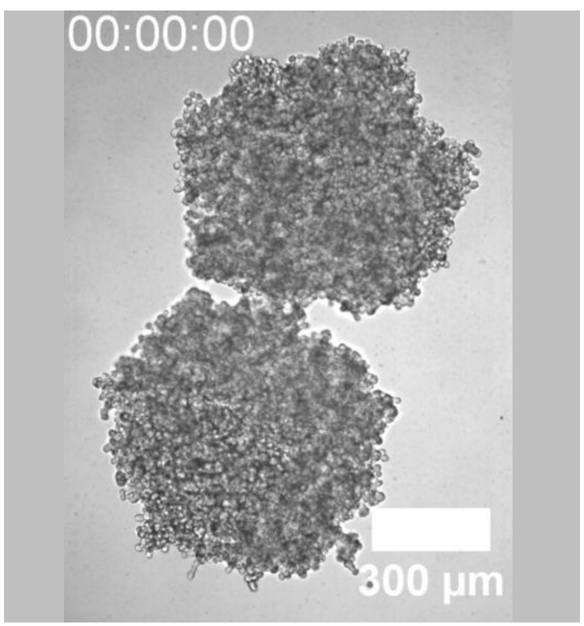
# What about cancer cells?

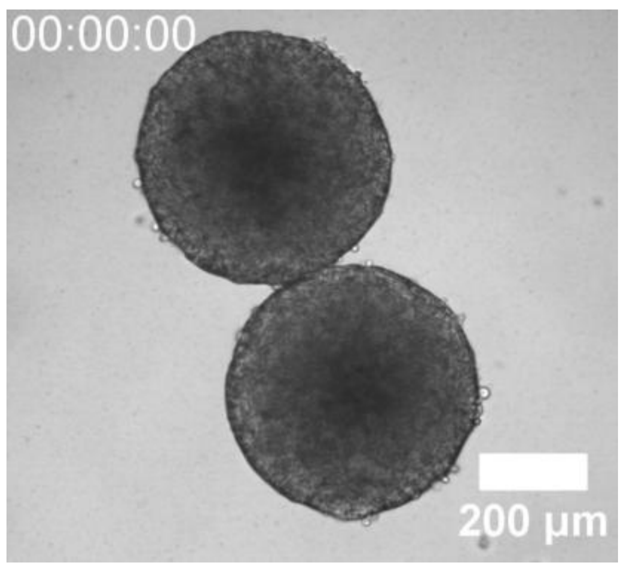
model for **metastatic** breast cancer cells

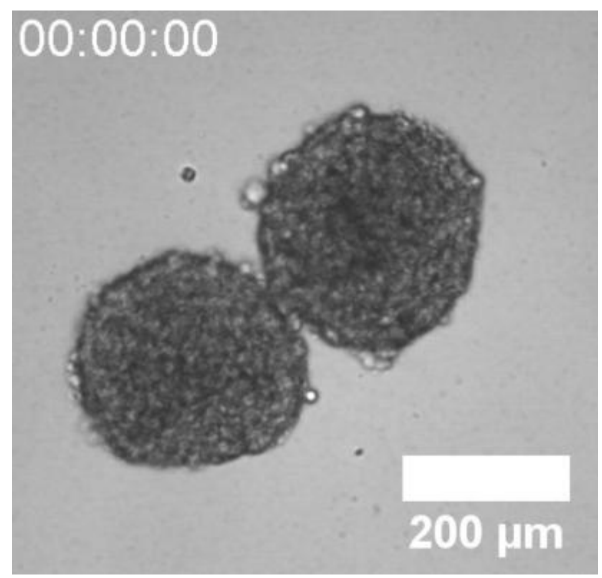
model for **normal** breast cells

model for **malignant** breast cancer cells



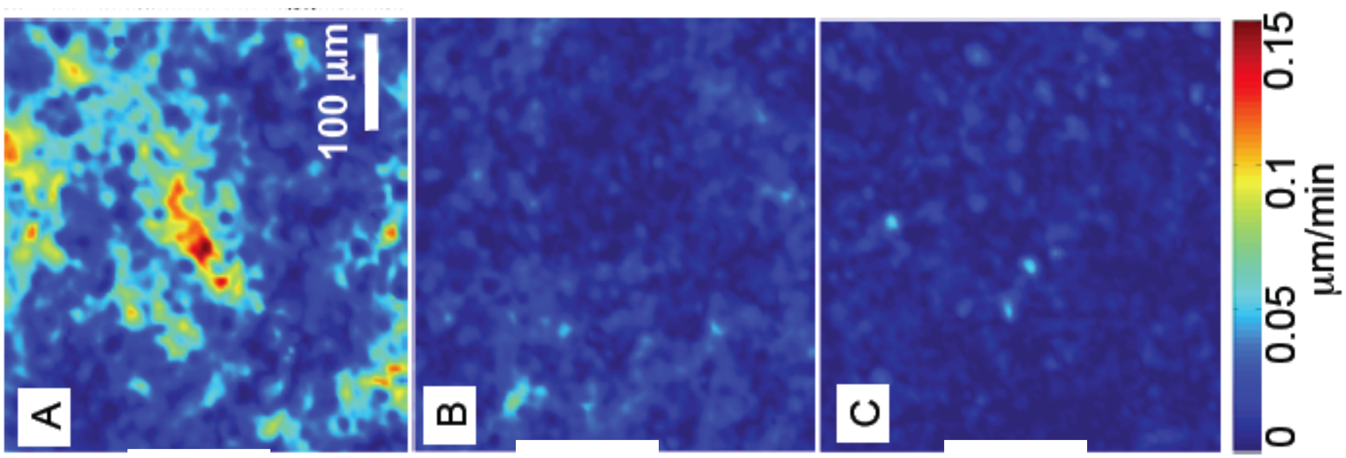

Käs lab, Leipzig University

# What about a healing wound?

woundsource.com

ture Phys. 8 628 (2012)

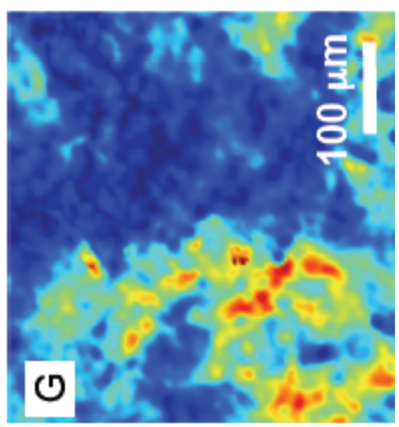
# What about cells in diseases like asthma?

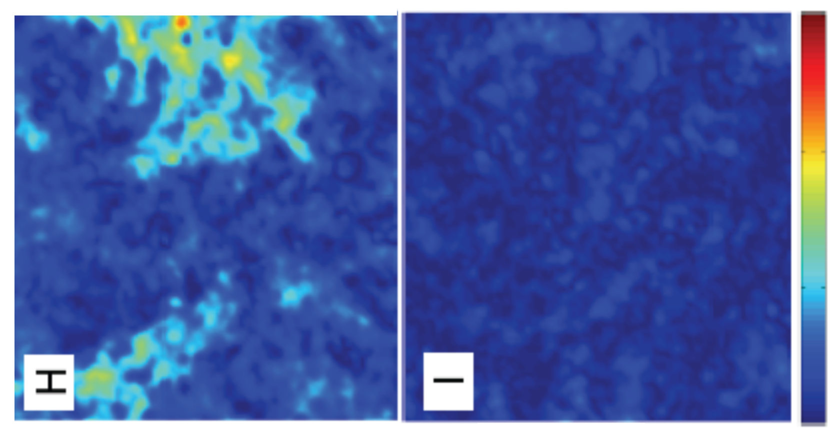

Day 3 Day 6 Day 8

non-asthma patients

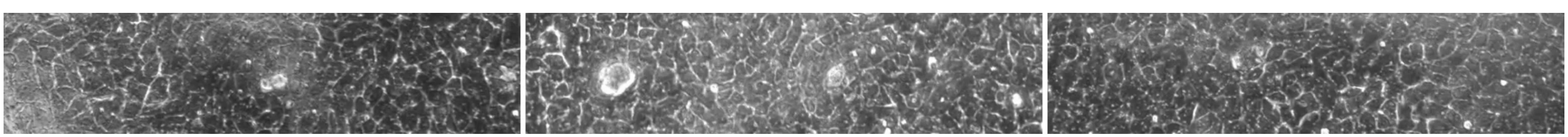
asthma patients




Day 6




Day 10 Day 14



How do you tell the difference between a fluid and a solid?

# Fluid example: Water

- Pour it out of a cup
- Is it easier to run or walk through the pool?

Liquids:

- Force (how hard it is to push) is higher as you move faster
- It doesn't return to where it started!
- Constituent particles rearrange and change neighbors

# Solid example: Rubber Band

- Stretch it! It's elastic!
- What happens as you stretch it?

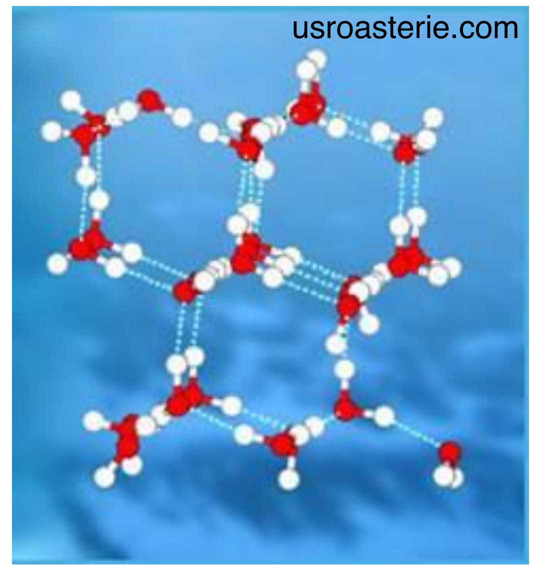
Solids:

- Force (how hard it is to push) is higher as you move farther.
- It does return to where it started!
- Constituent particles do not change their neighbors.

How can you change a fluid into a solid?

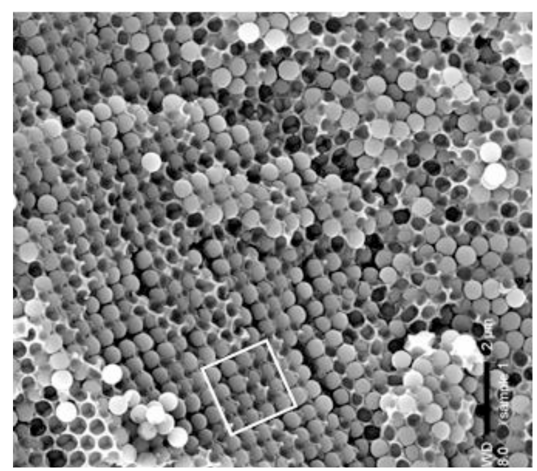
# Many materials crystalize when they are cooled.

Water




1 million times smaller than a yard!
A thousand times smaller than a hair

Metals



Large scale

small scale

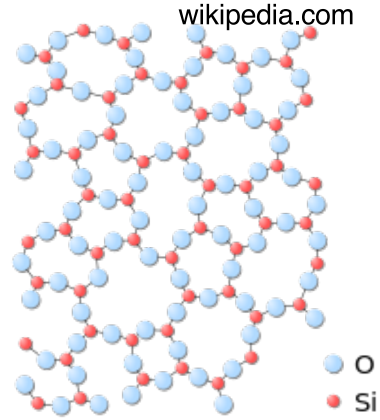
# Many materials **DO NOT** crystalize when they are cooled.

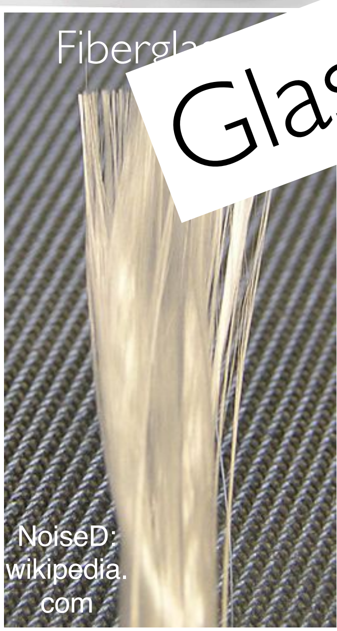
Glassy materials

window (soda-lime) glass

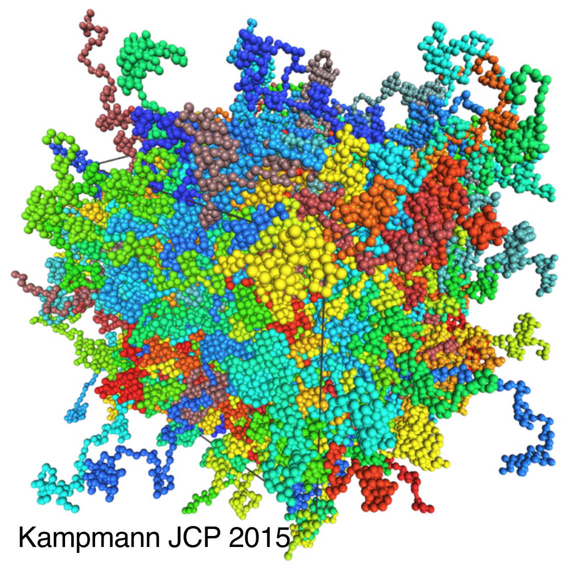

plastics

wikipedia.com







Kampmann JCP 2015

Large scale

Small scale

Are there any other ways to turn a fluid into a solid?

# Sand

- Stand on it at the beach
- Sift it through your fingers

# Mayonnaise


Dense emulsion (Thijssen)

Other materials like this: sand, foams, fault gouge on earthquake faults, pharmaceutical pills

# summary:

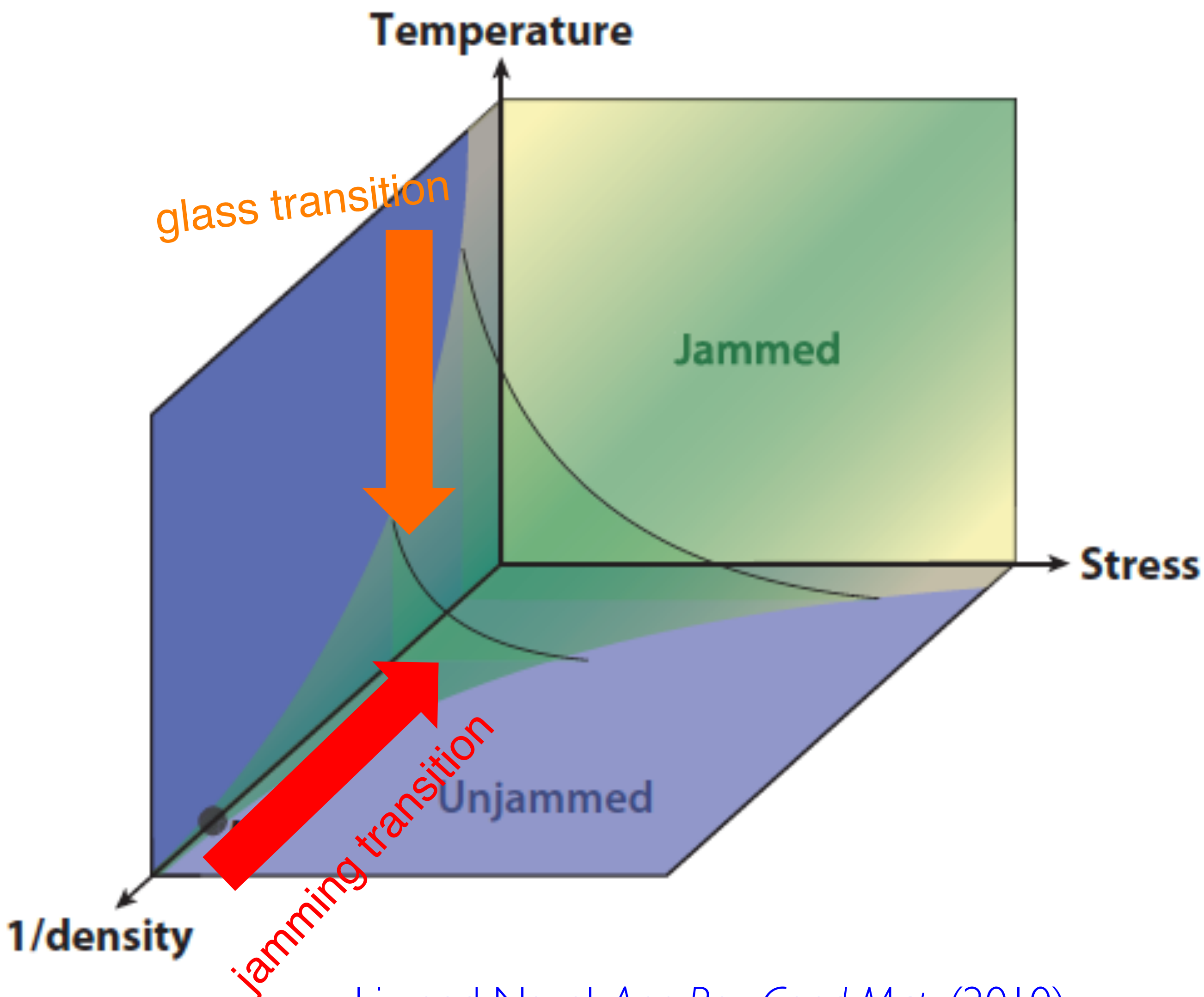
fluidity depends on:

the temperature (energy available for constituent objects to move around)

and

density (how tightly packed the objects are)

# Can we unify these ideas?




Liu and Nagel, *Ann Rev. Cond Mat.* (2010)

Scientists here in Boulder now:

Why do these materials solidify?
Is there a most dense glass?
How does the stiffness of the glass depend on these parameters?
How does the motion of particles depend on these parameters?
How does the glass fail if you push it too far?
What is the relationship between these disordered systems and others (machine learning, encryption)?

But wait, you say --
you promised us a talk about biology!

Cells can do many things that mayonnaise cannot:

divide
die
differentiate (turn into different cell types)
respond to their environment
move around on their own

# For the rest of this talk, I'll ask **what can we explain**

by adding two simple ingredients to this glass picture:

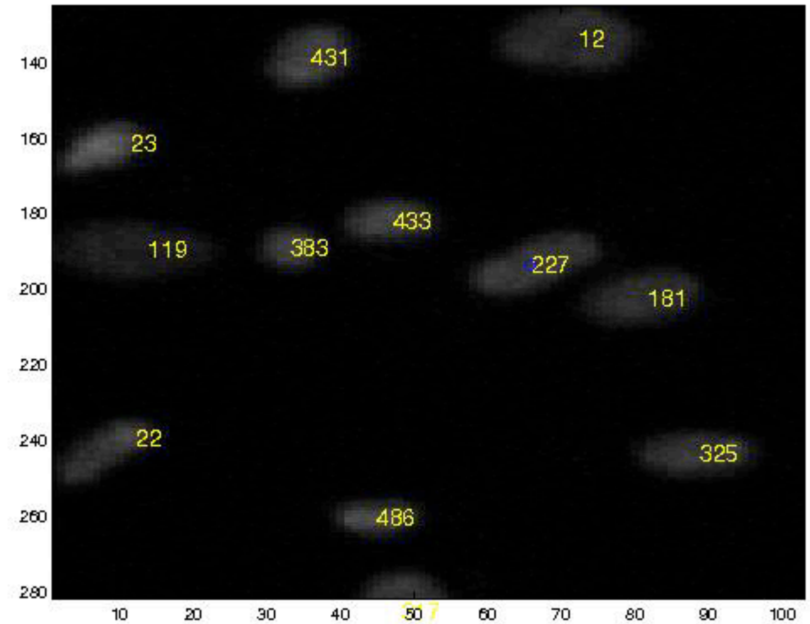
1. Cells can exert forces and move on their own
2. The interaction between cells depends on cell shape (instead of density)

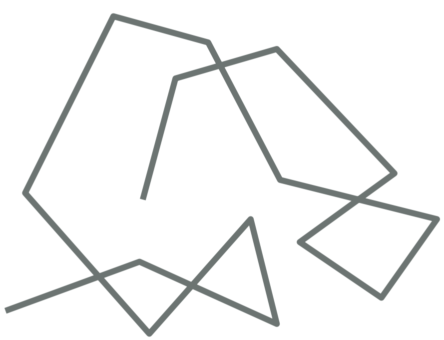
# How can we describe cells that generate their own forces?

Use two parameters:

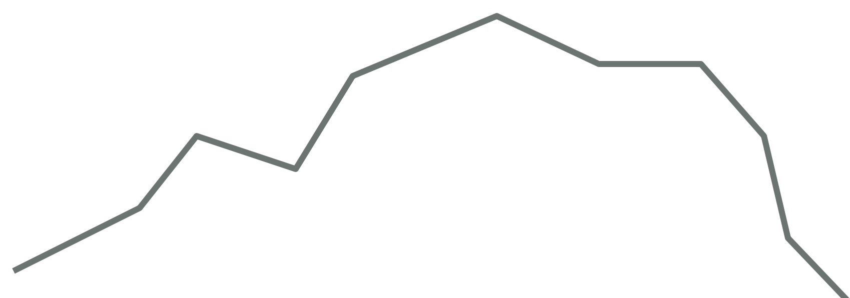
cell speed

persistence length



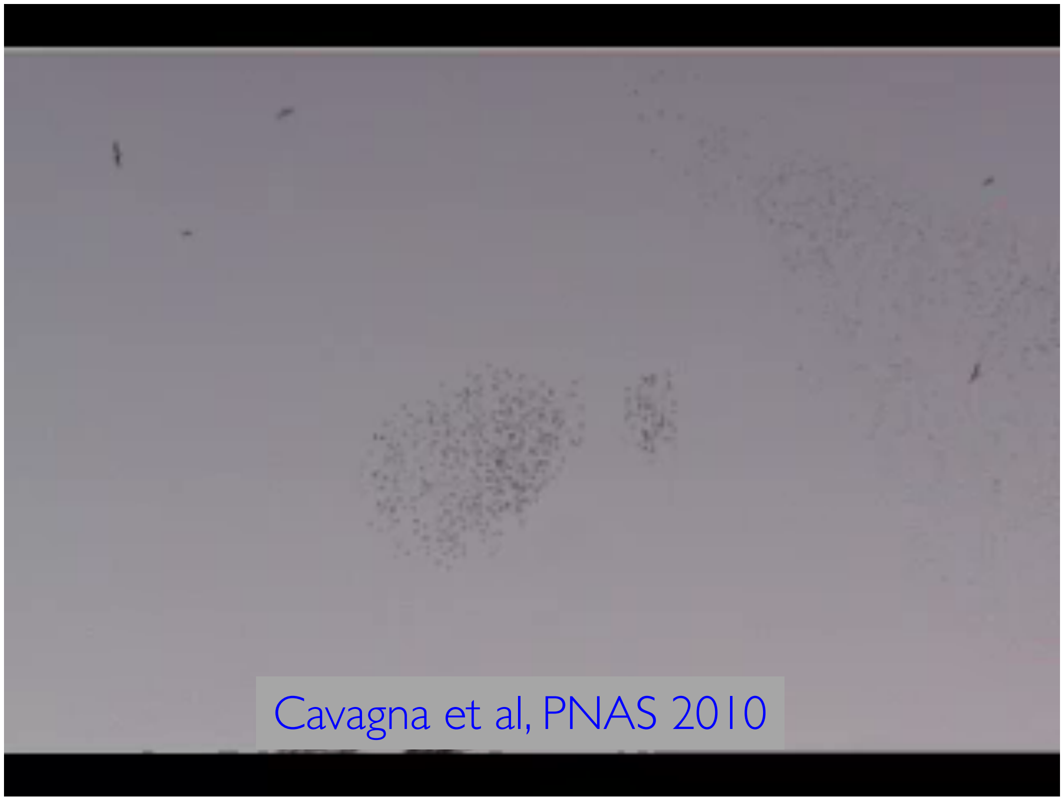
cell trajectory with **small** persistence length



cell trajectory with **large** persistence length

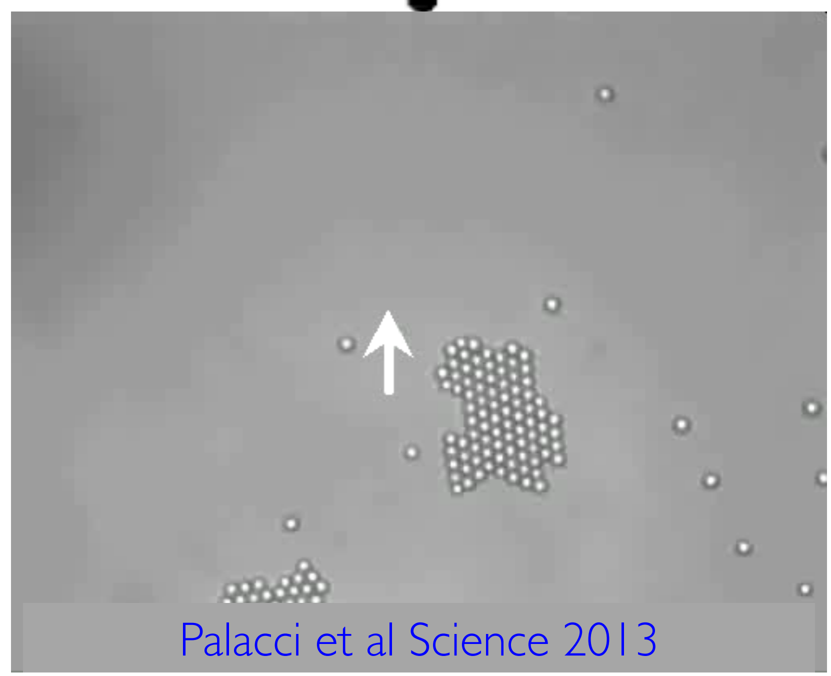
# What happens when objects generate their own forces?

Part of a new class of "active matter" models



Cavagna et al, PNAS 2010

Cristian Huepe, Vicsek et al PRL 1995

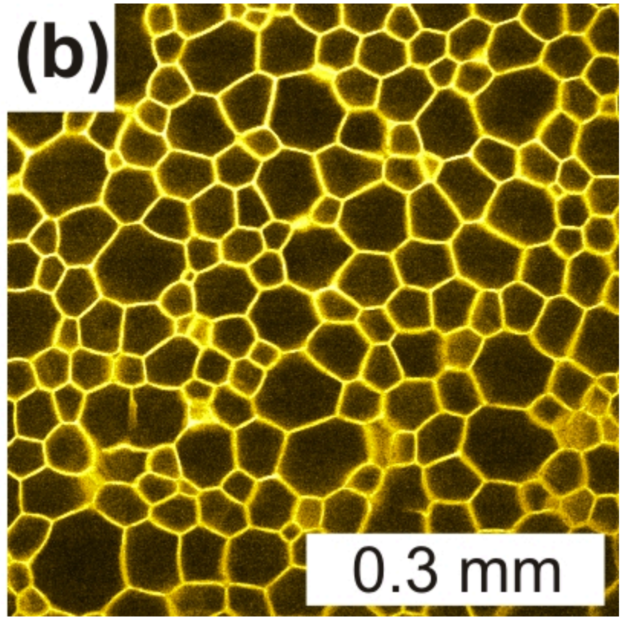


Palacci et al Science 2013

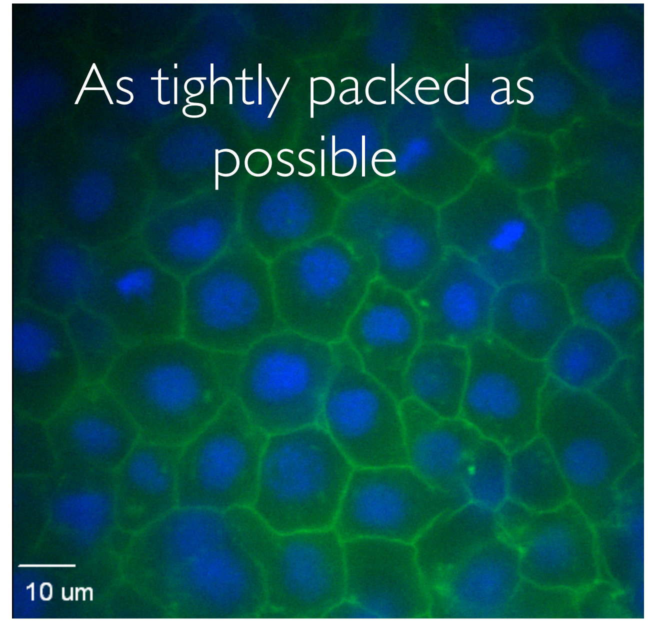
Cells also interact with each other differently than particles or droplets:

The microscopic structure looks like a glassy solid (very high density), but cells can change neighbors like in a fluid – why?

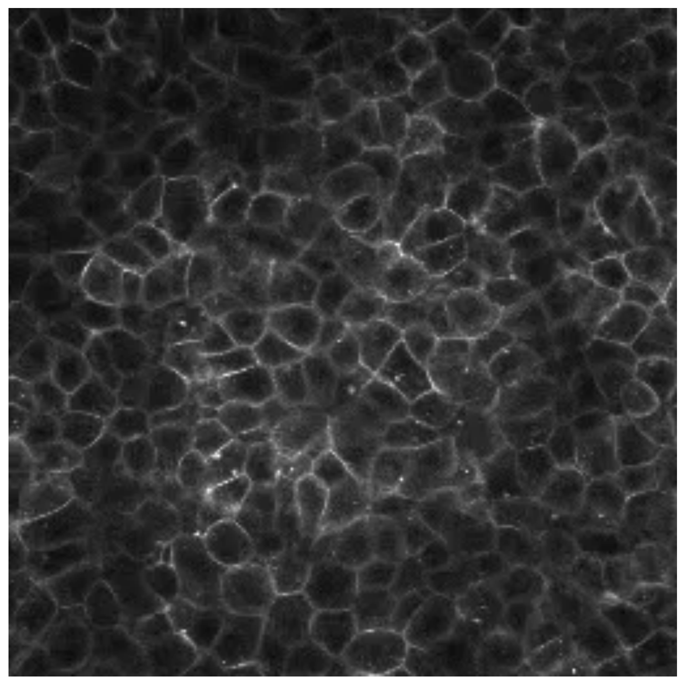
Need a good model for how the cells interact with each other




Dense emulsion (Thijssen)




Cells (Schoetz Lab UCSD)

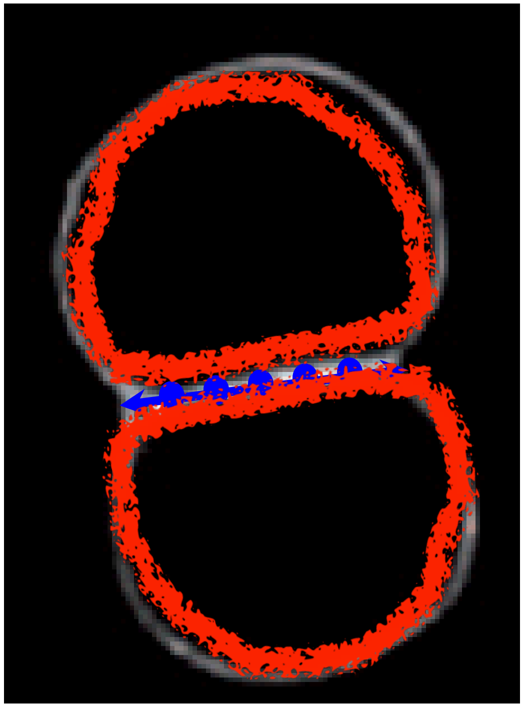


Cells (Schoetz Lab UCSD)

# What mechanical forces act to regulate cell shapes?

T. Nagai, H. Honda, Philos. Mag. B 81, 699 (2001)
Hufnagel et al, PNAS vol. 104 (10) pp. 3835 (2007)
Farhadifar et al, Current Biology (2007)
Jülicher et al Phys. Rep. (2007)
Hilgenfeldt et al, PNAS 105 3 907–911 (2008)
**MLM** et al, PNAS (2010)
Staple et al EPJE 33 (2) 117 (2010)
Chiou et al PLOS Comp Bio 8 (5) e1002512 (2012)

1. Cell-cell adhesion: sticky molecules help cells stick together
2. Active cytoskeleton: cells have a dynamic internal "skeleton" that prevents them from changing shape too much
3. Fluid filled: many cell types do not change their volume easily.



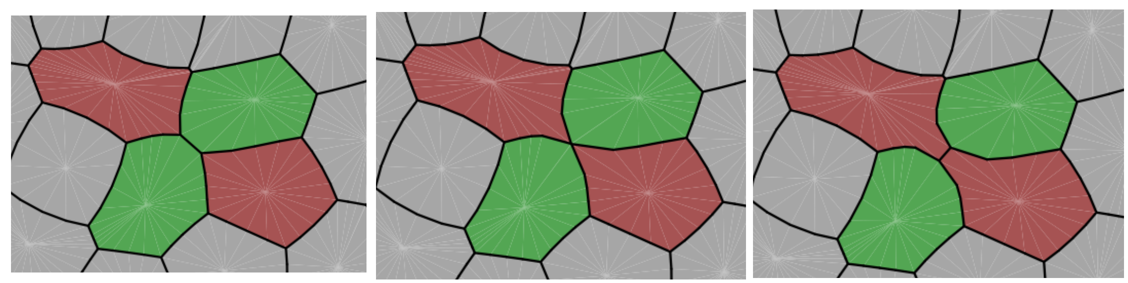
Devries et al, Development **131**, 4435–4445 (2004)

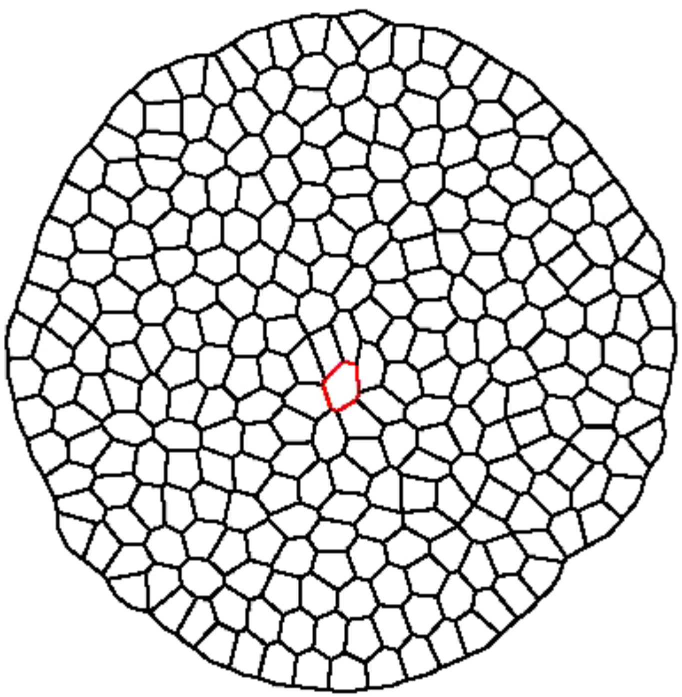
# This leads to a simple mathematical model that allows us to predict how much work is required for a cell to migrate

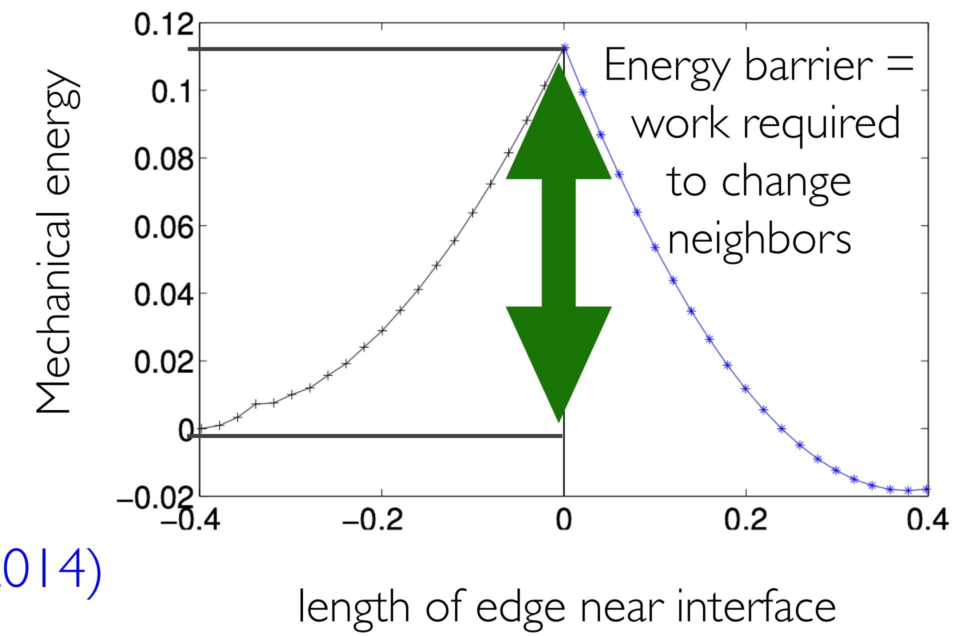
$$E_{cell} = k_A(A - A_0)^2 + k_P(P - P_0)^2$$
$$= k_A(A - A_0)^2 + k_P(P^2 - 2P_0P + P_0^2)$$

A = cross-sectional area

P = cross-sectional perimeter

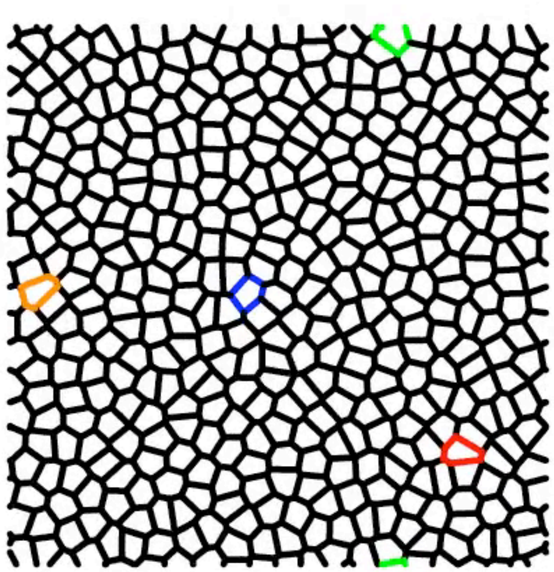




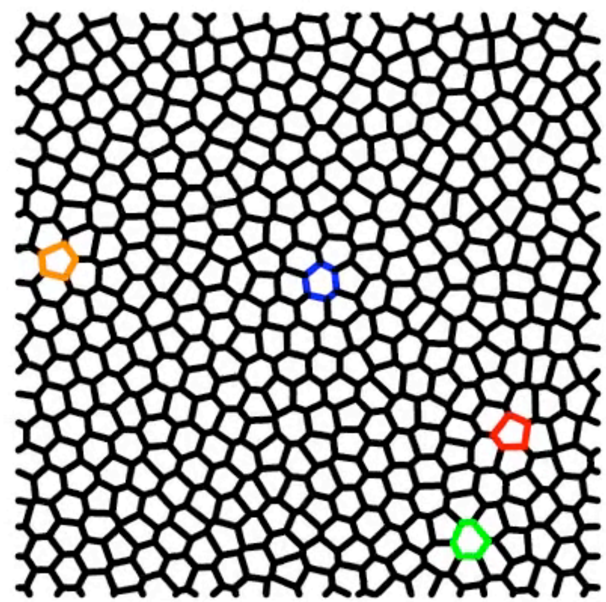



Bi, Lopez, Schwarz, **MLM** Soft Matter (2014)

# Surprise: model predicts two phases that depend on cell shape (instead of the density)

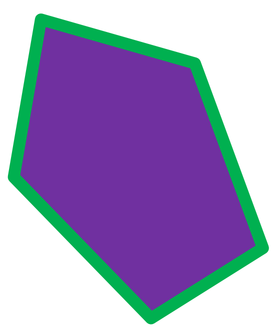


Fluid



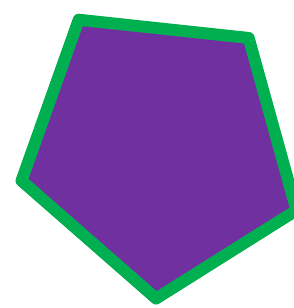
Solid

large shape index > 3.81



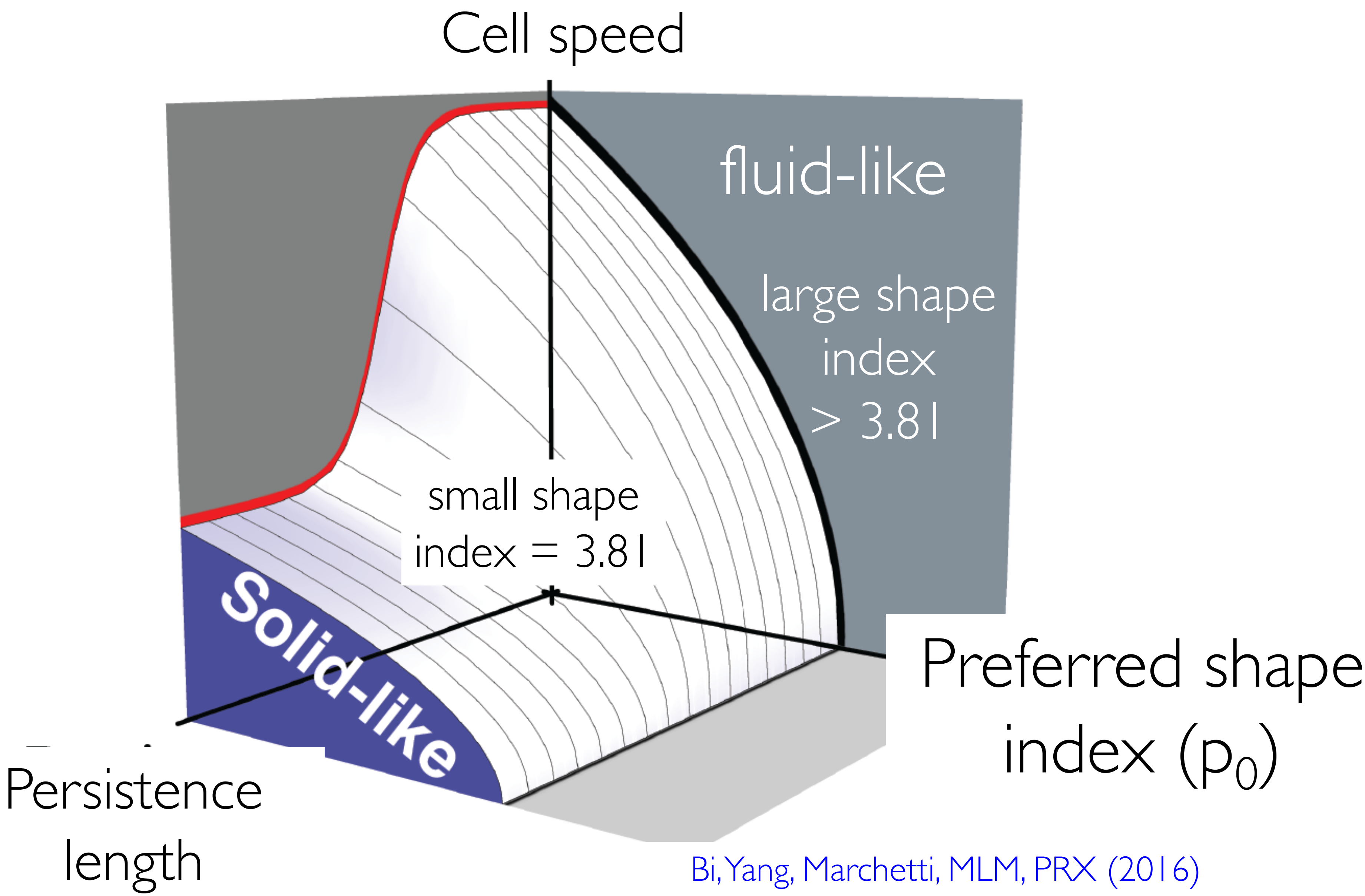
$$< p > = \text{shape index} = \frac{\text{perimeter}}{\sqrt{\text{area}}}$$

Controlled by balance between cell stickiness and cytoskeleton stiffness



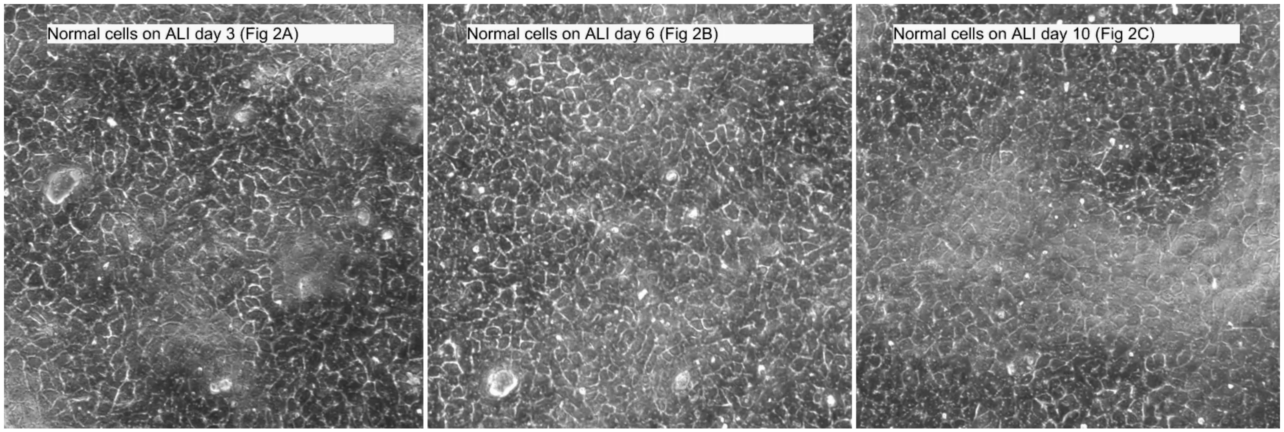
small shape index = 3.81

# Fluid-solid phase diagram for biological tissues




Bi, Yang, Marchetti, MLM, PRX (2016)

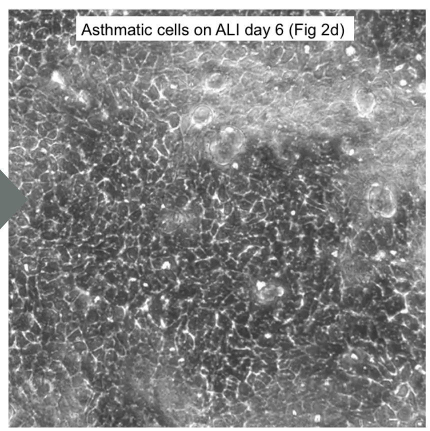
# Asthmatic cells have a delayed fluid-to-solid transition



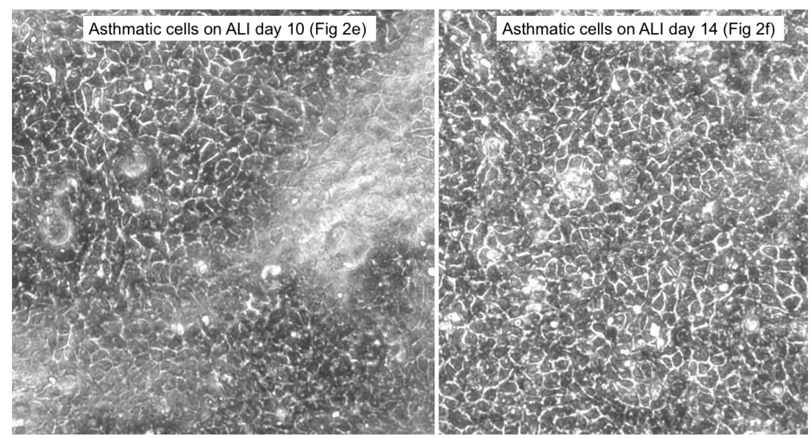

Day 3 Day 6 Day 8

non-asthma patients

asthma patients




Day 6



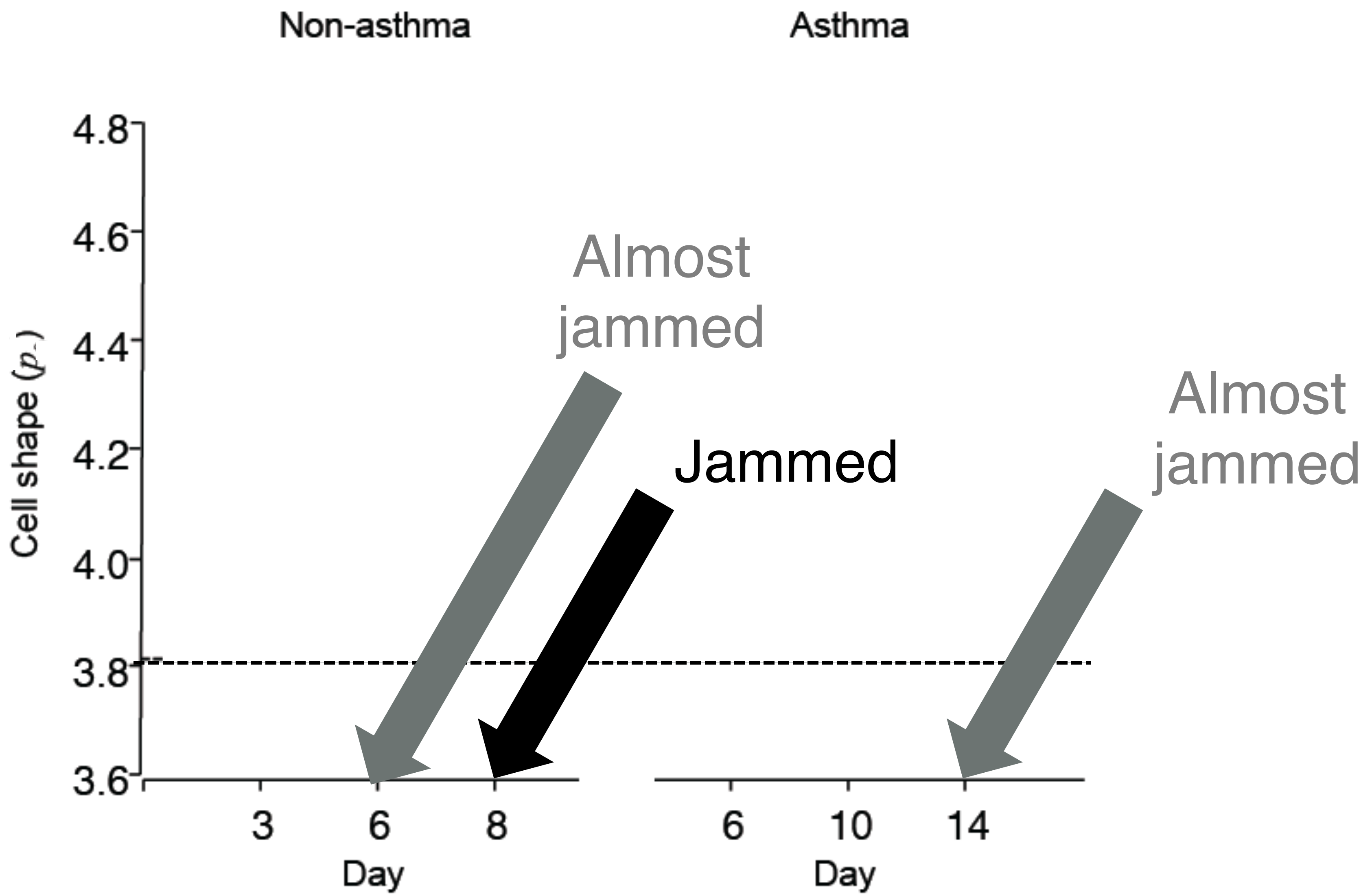

Day 10 Day 14

with Jeff Fredberg's group at Harvard School of Public Health

Park, Kim, Bi, et al, Nature Materials, 2015

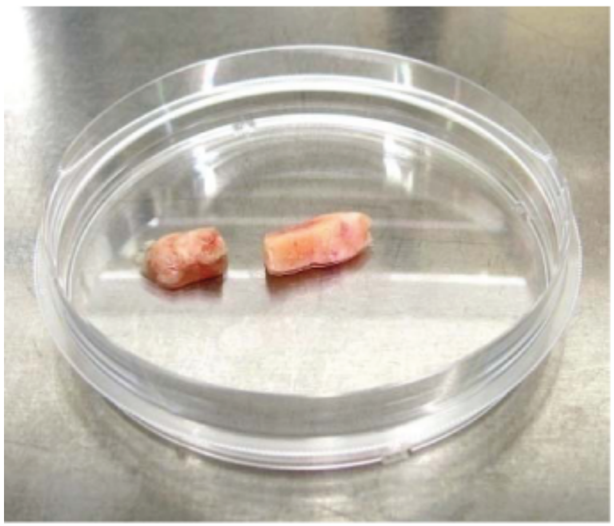
# Shape index p approaches precisely the predicted value at jamming

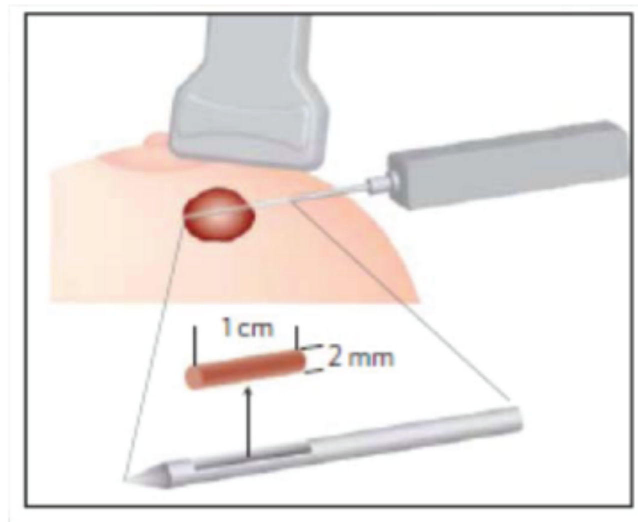
Measure this easily from one snapshot!




Park, Kim, Bi, et al, Nature Materials 2015

# Another application: Can we understand whether mechanical properties of cancer tissues make certain ones more invasive?

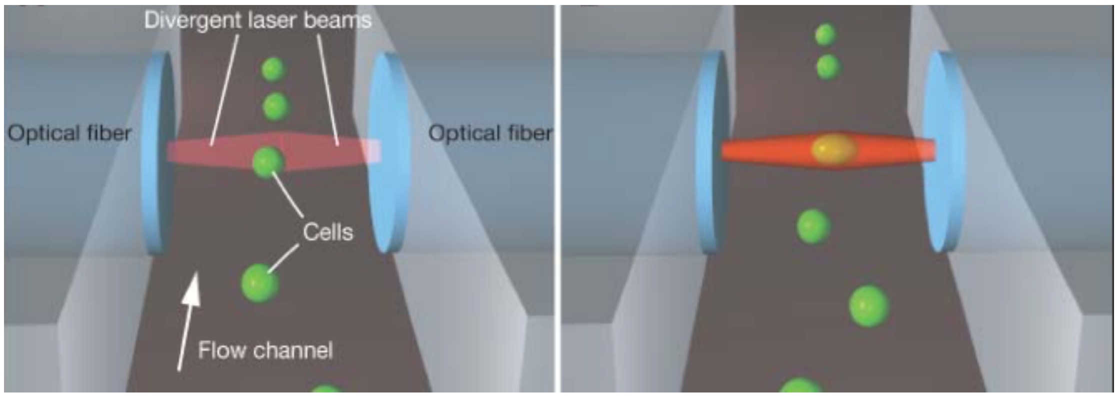


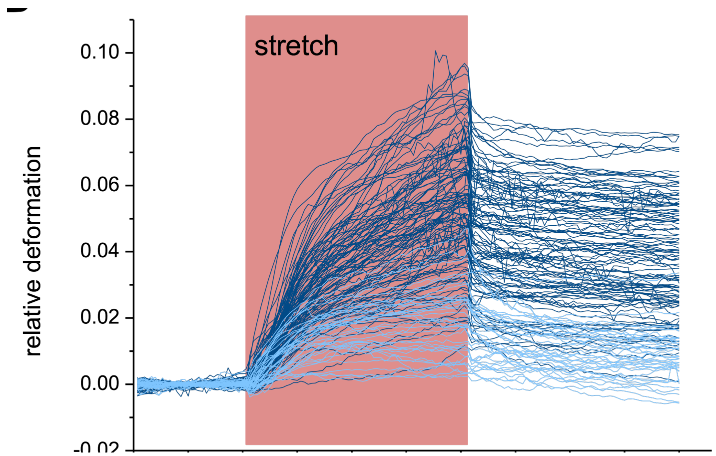



primary tumor cells from patients with breast and cervical cancer

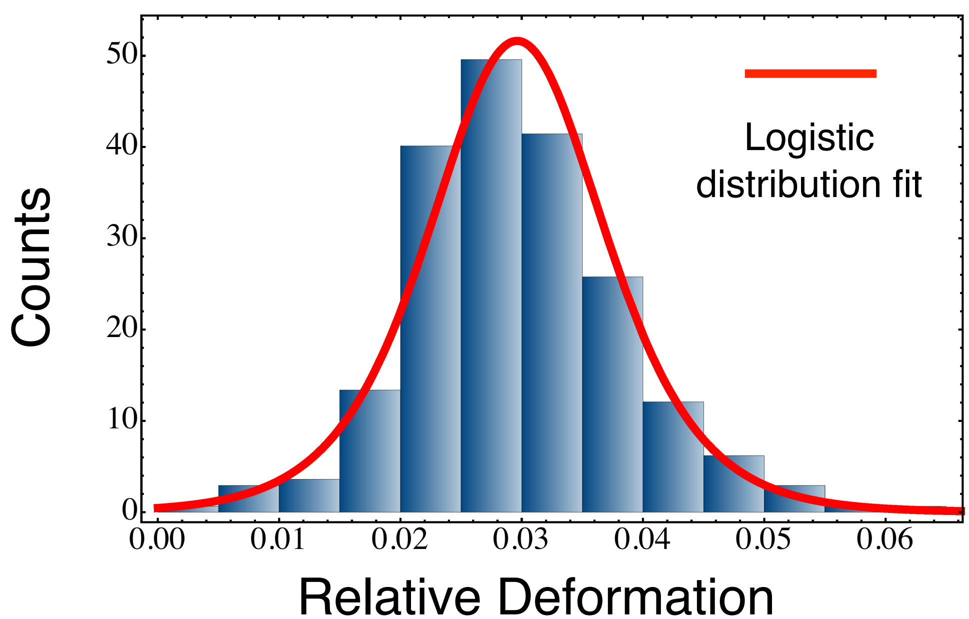
Franziska Wetzel[1], Dapeng Bi[3], Anatol Fritsch[1], Steffen Grosser[1], Linda Oswald[1], Steve Pawlizak[1], Lars-Christian Horn[1], Michael Höckel[1], Susanne Briest[1], Cristina Marchetti[2], Lisa Manning[2], Josef Käs[1],
[1]Leipzig University, [2]Syracuse University, [3]Rockefeller University

# Using a "light tweezer" to measure distribution of cell stiffnesses in primary tumors

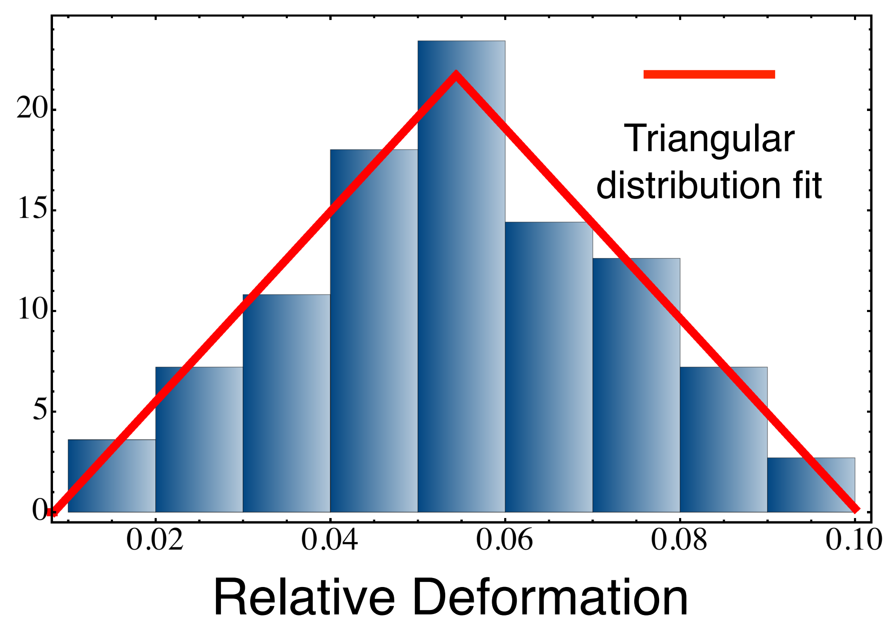


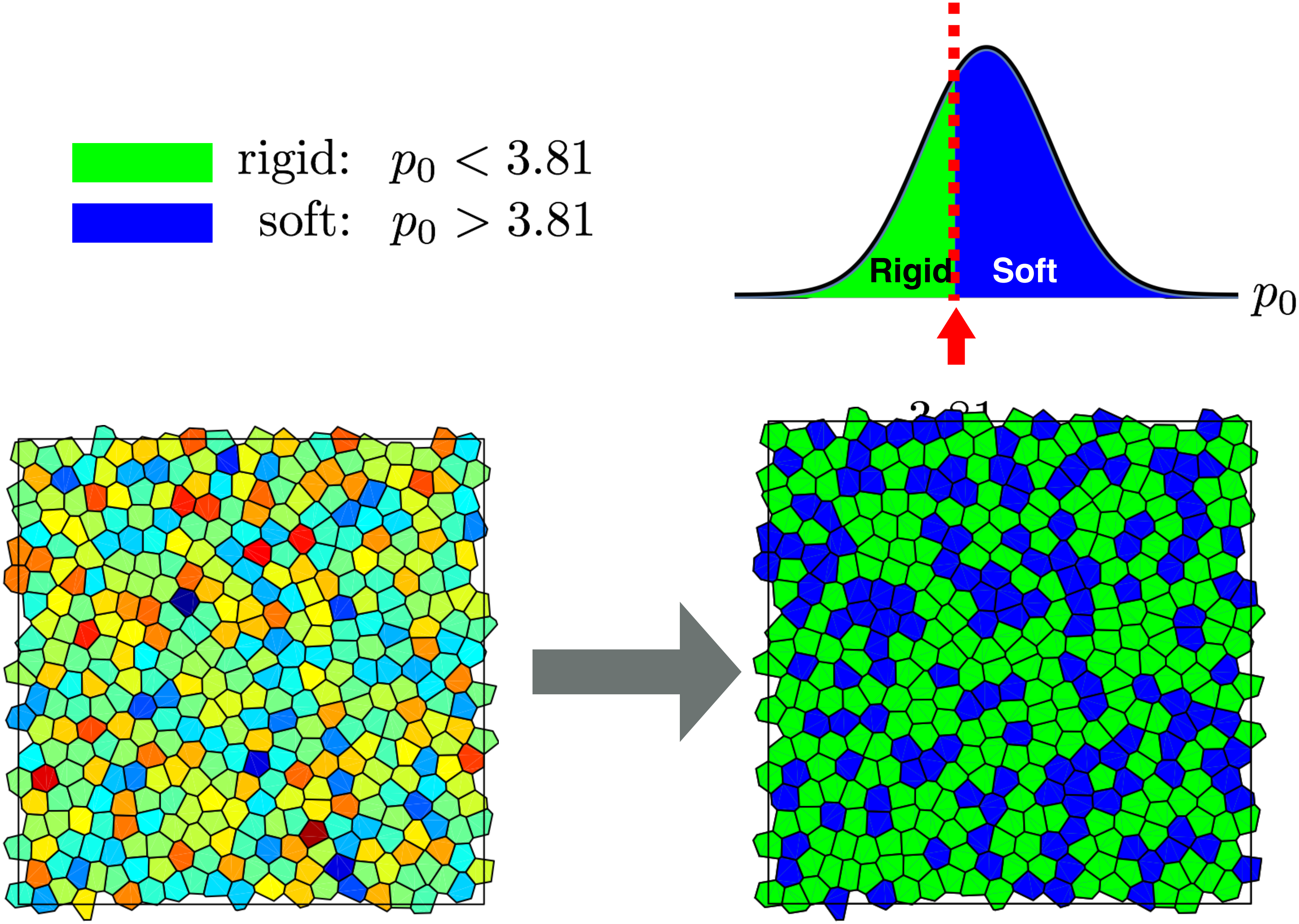




Breast Cancer



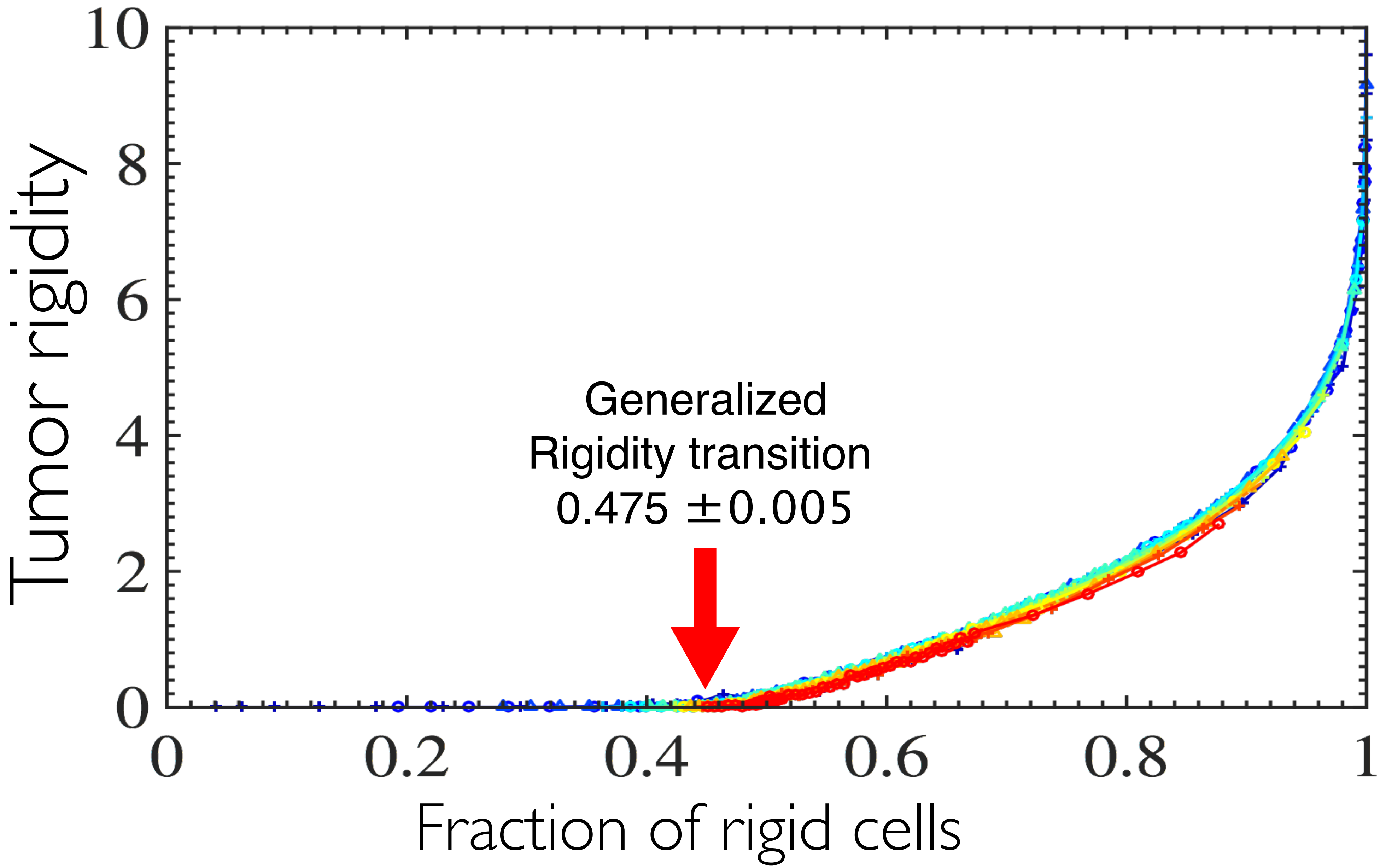

Cervix Cancer



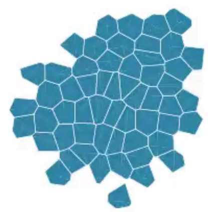


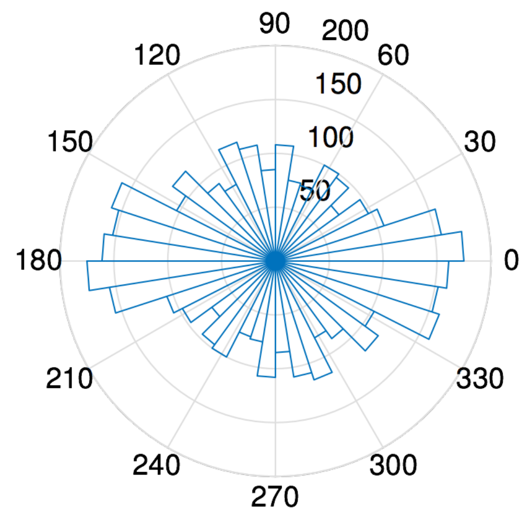

$$F_r = \text{fraction of cells with } p_0 \leq 3.81$$

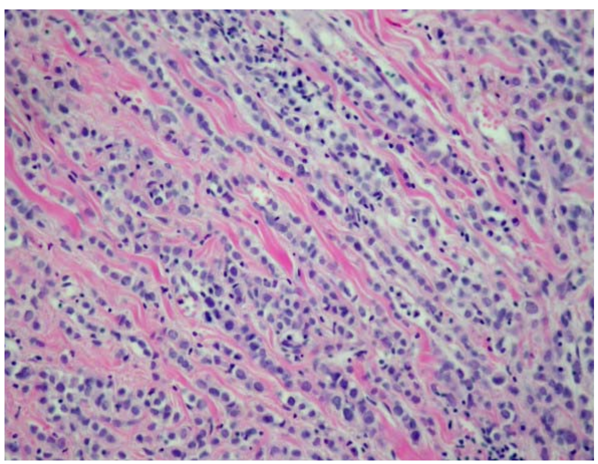
# A tumor can be rigid even when more than 50% of its cells are soft

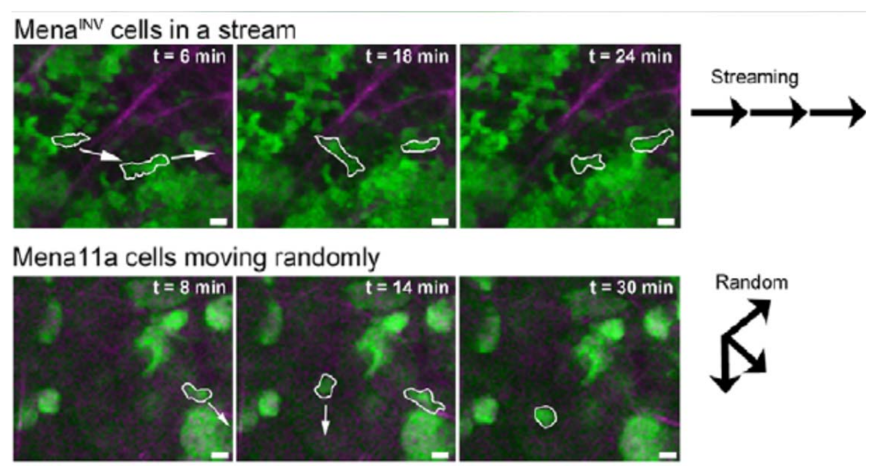


# This same model may also help explain "multi-cellular streaming" seen in some cancer tumors





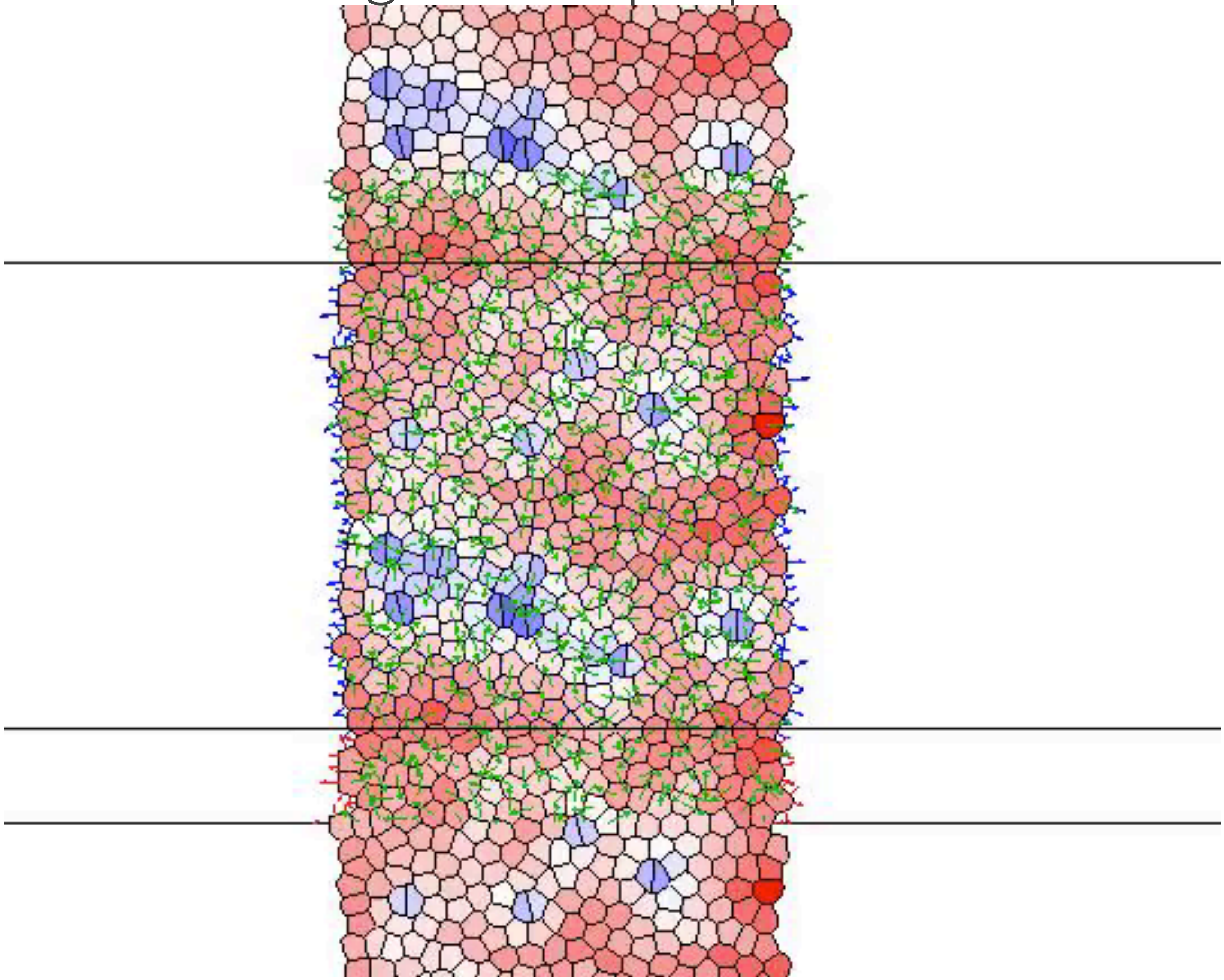


# What other questions are we trying to answer?

In movies….

Michael
Czajkowski

# How do boundaries and cell divisions change tissue properties?

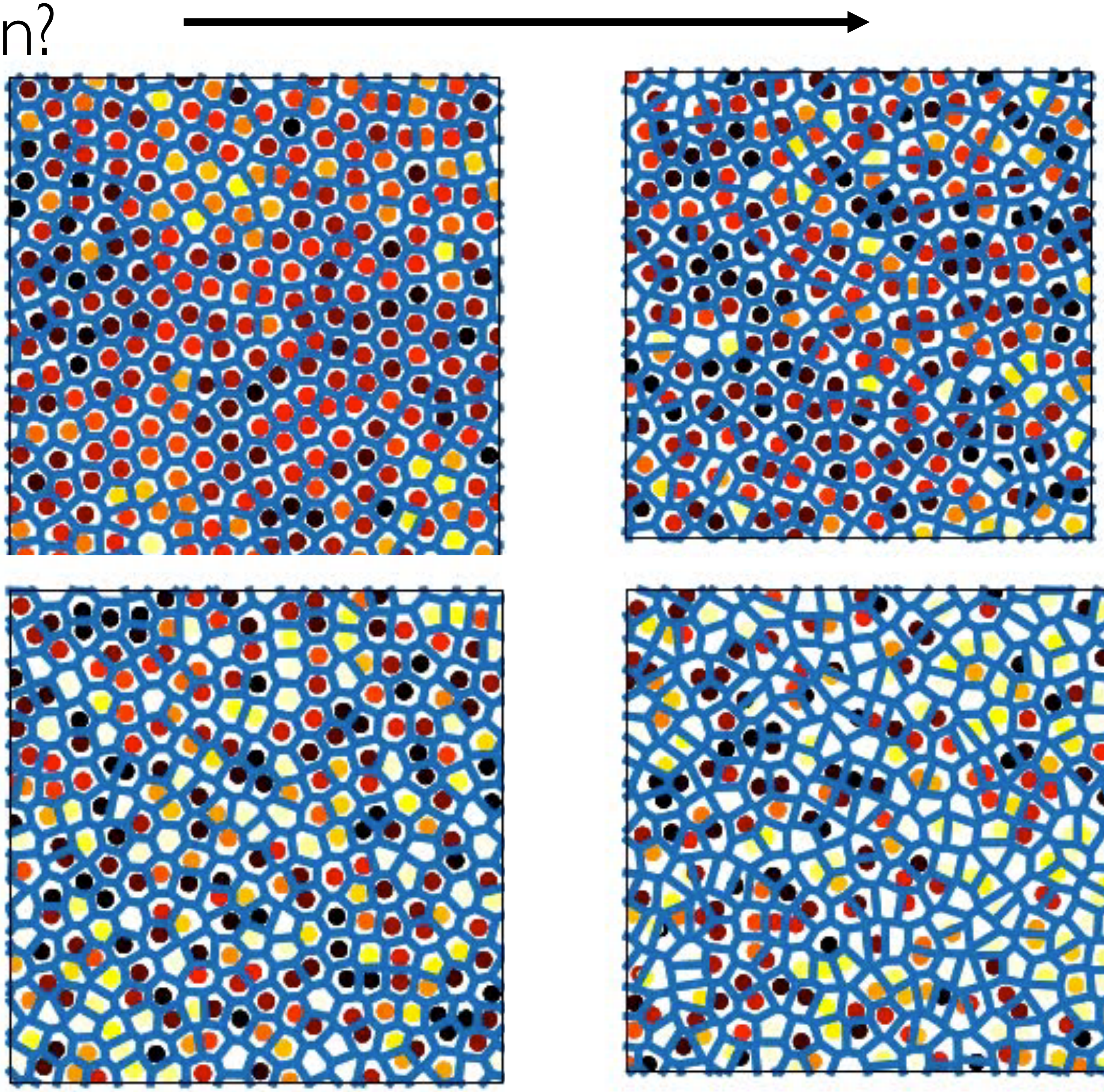


# What happens when cells align?

Matteo Paoluzzi

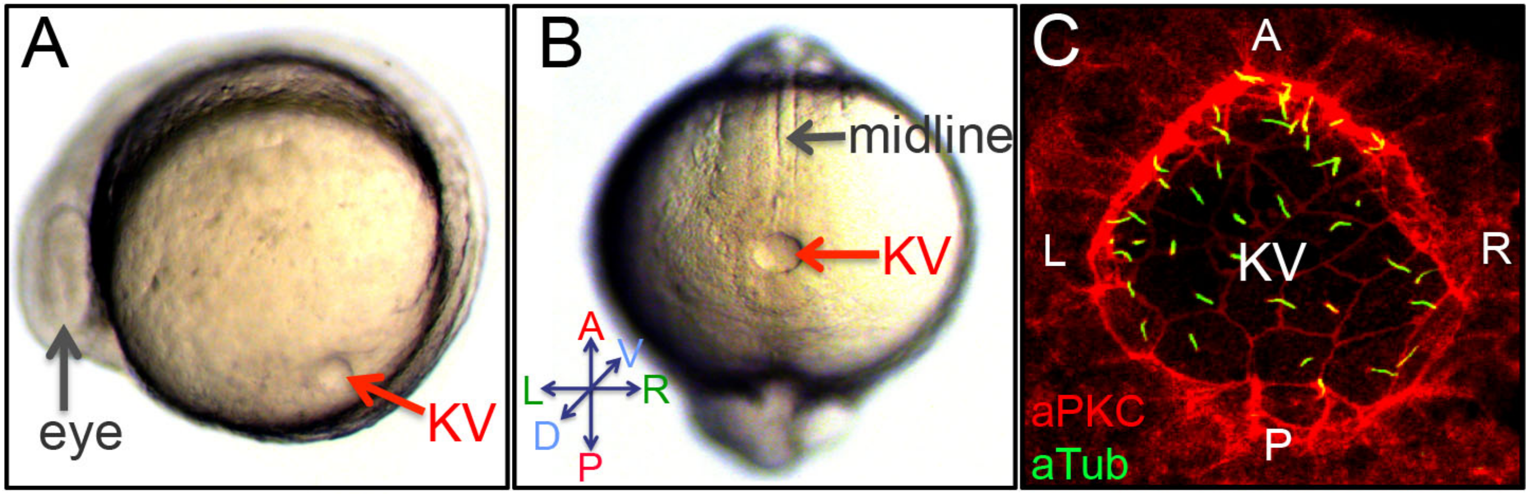
Cristina Marchetti

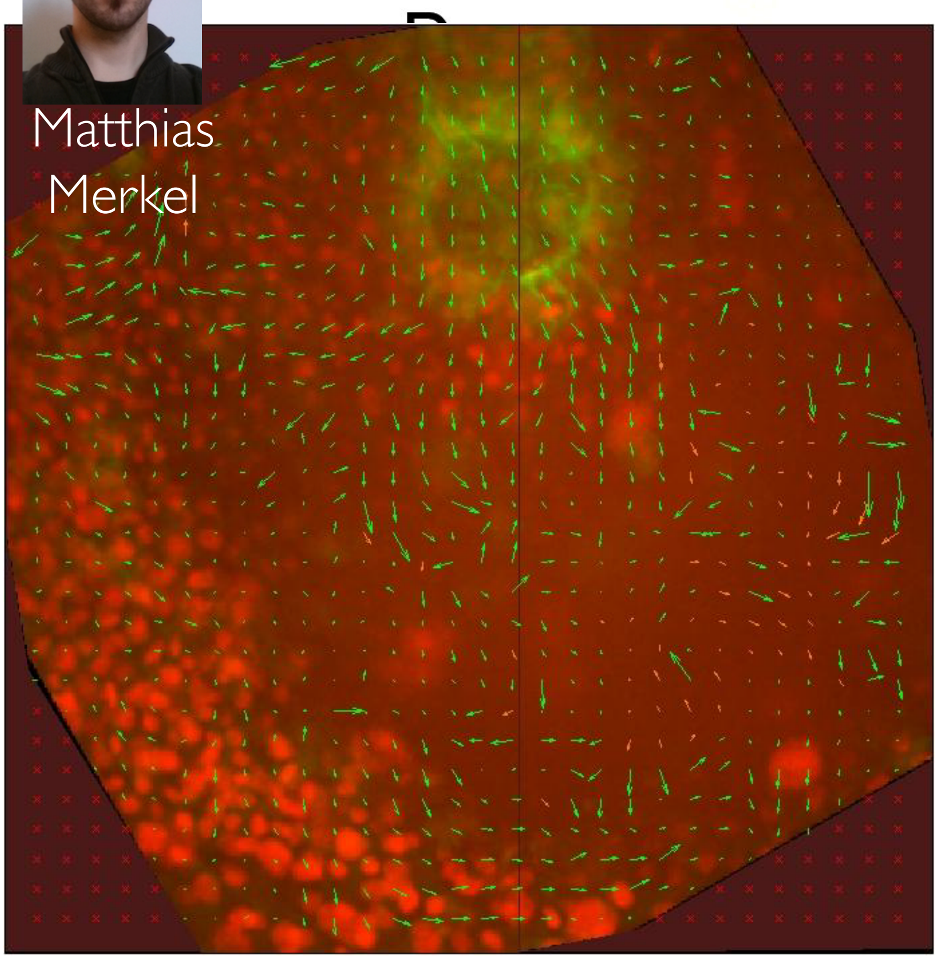
increasing cell anisotropy

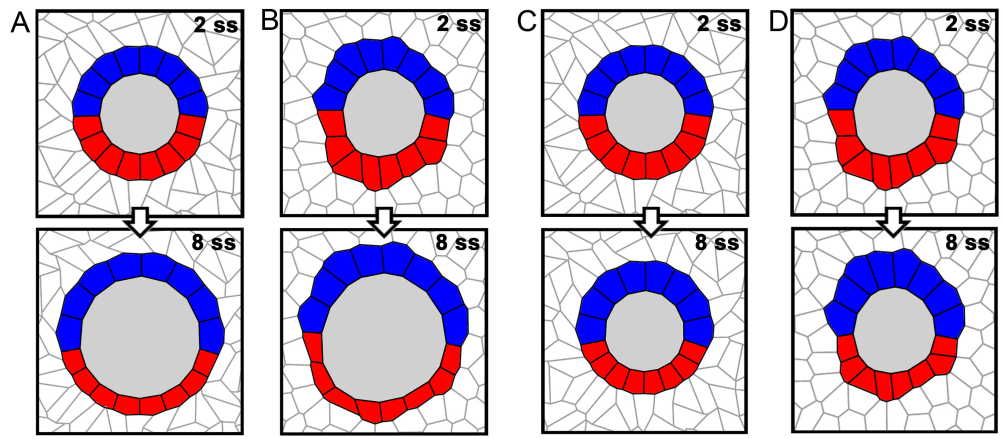


Gonca Erdemci-Tandogan

Matthias Merkel



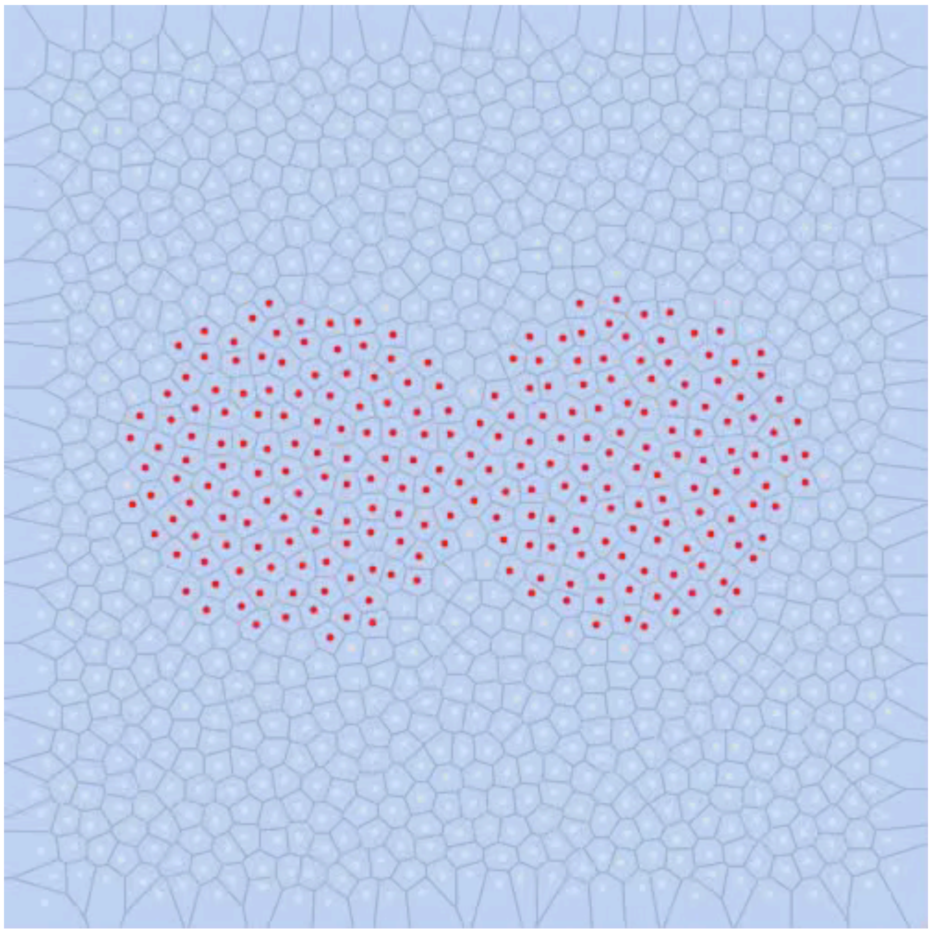



# How does your heart end up on the correct side of your body?

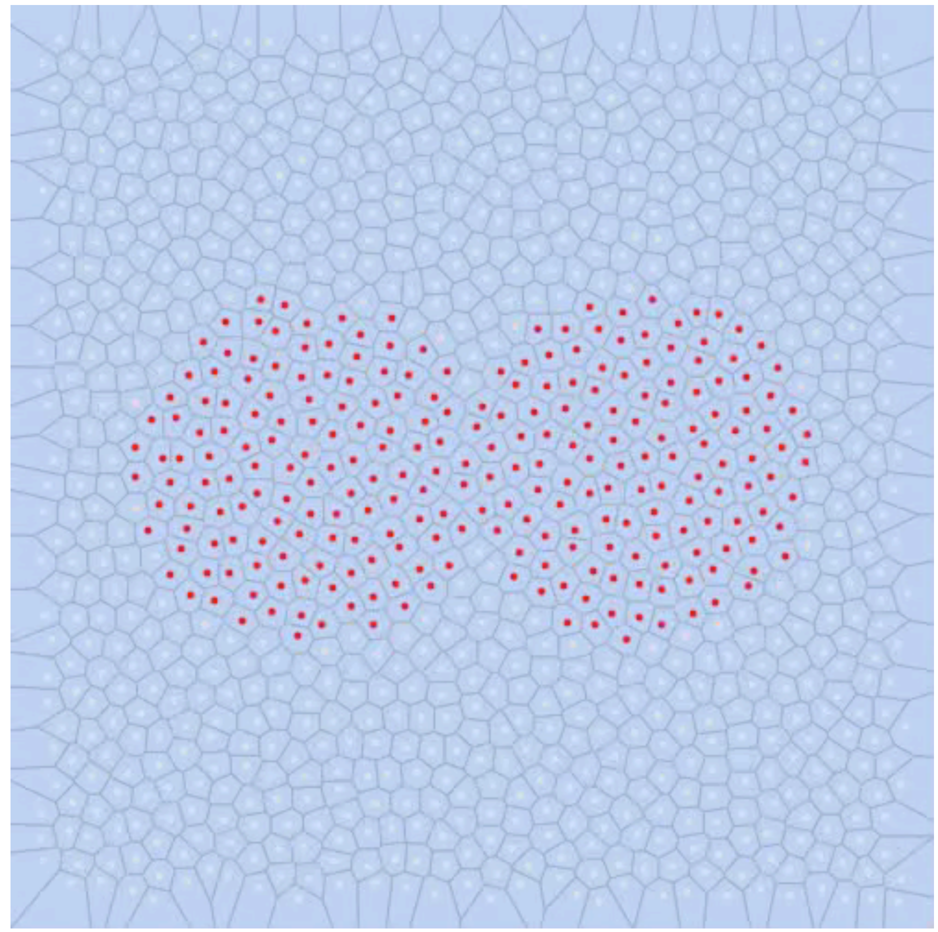
With Jeff Amack, Upstate Medical University

Daniel Sussman

# What are the properties of surfaces between cell types?



tissue is a fluid



tissue is a solid

# summary

- the tissues in your body can be thought of as a "living material"
- sometimes it is useful for the tissues to be fluid-like, and sometimes solid-like
- the physics of glasses is a useful starting point for thinking about transitions between these two phases
- we can use simple models for materials to make incredibly accurate predictions about tissue behavior
- we can use these insights to understand disease
- there's a lot more to do, and the future is exciting!

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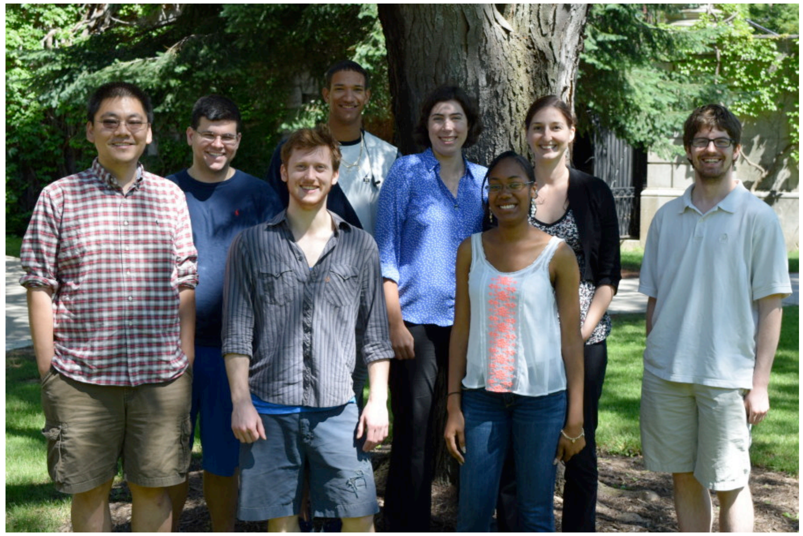

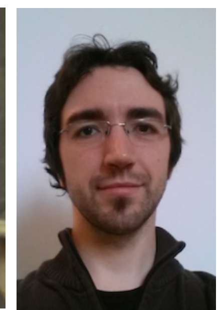

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