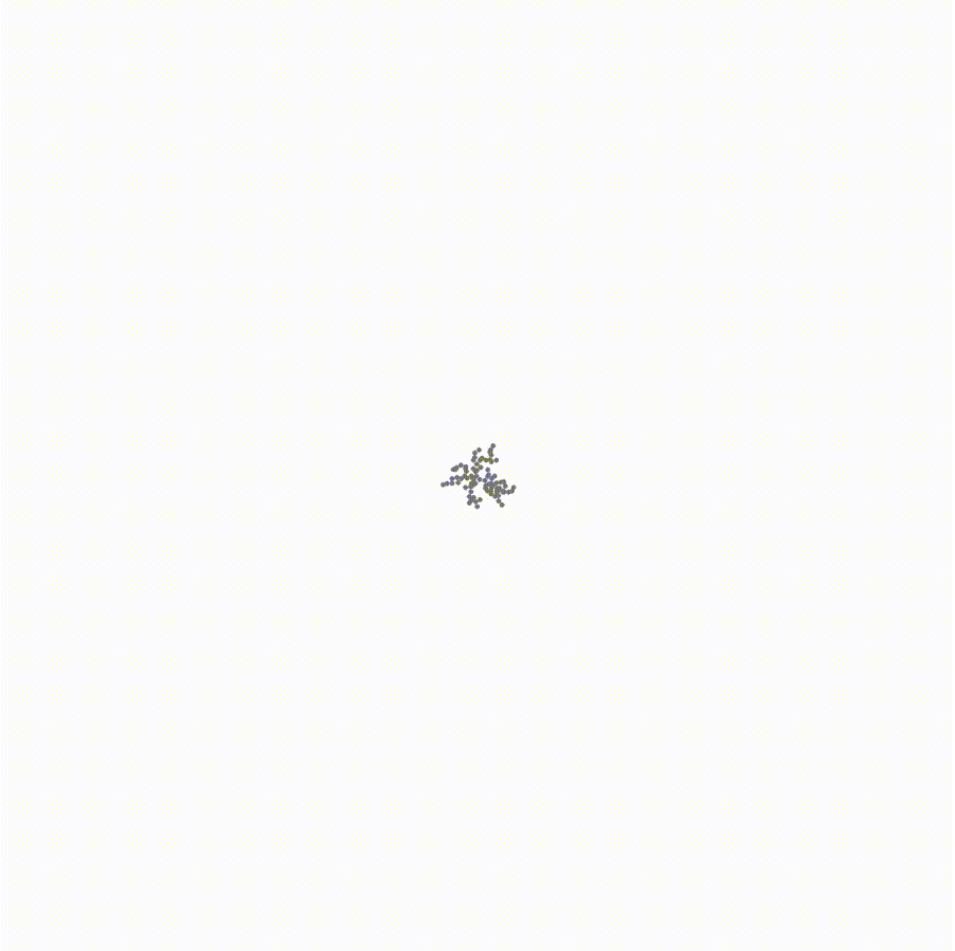
Active materials shape themselves

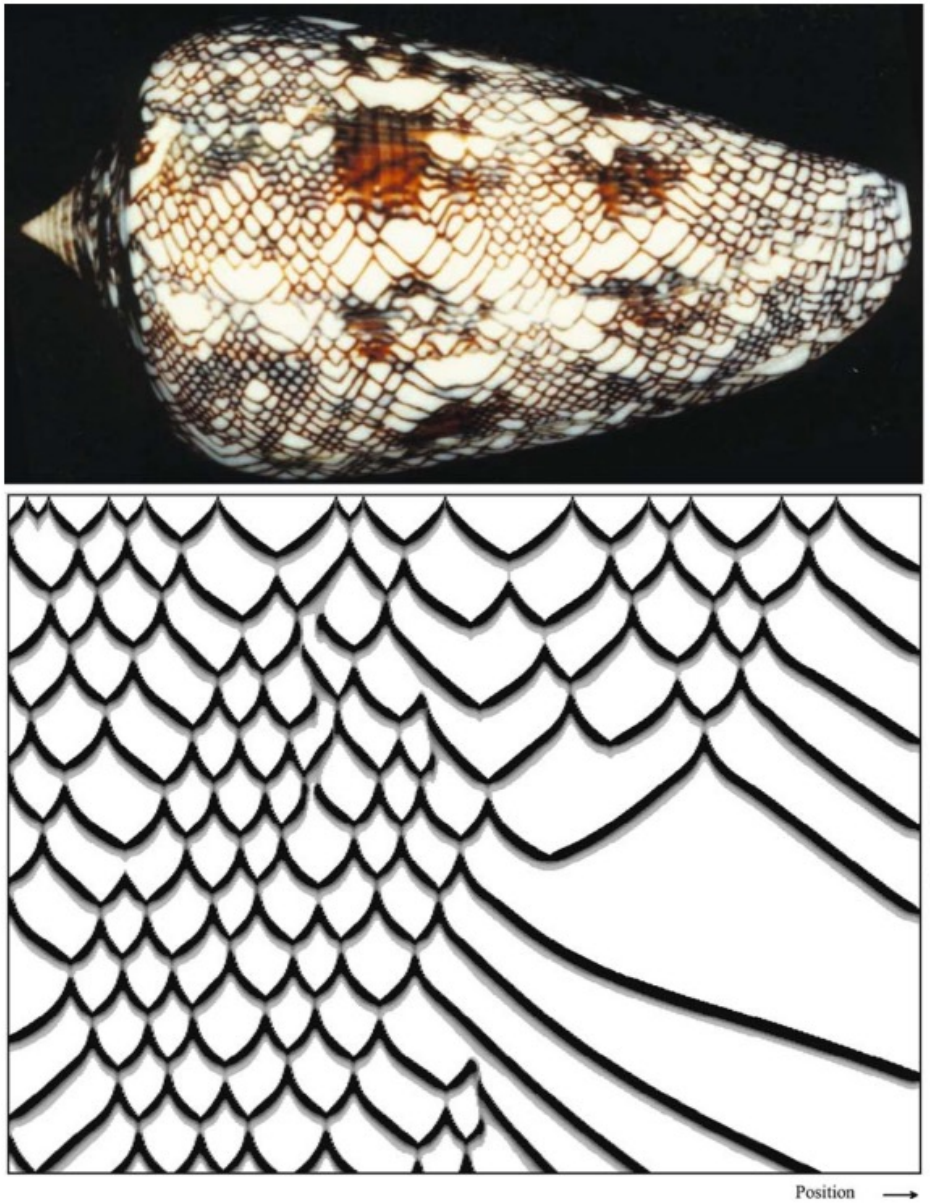
Dag Kristian Dysthe

Pattern forming growth processes in Nature



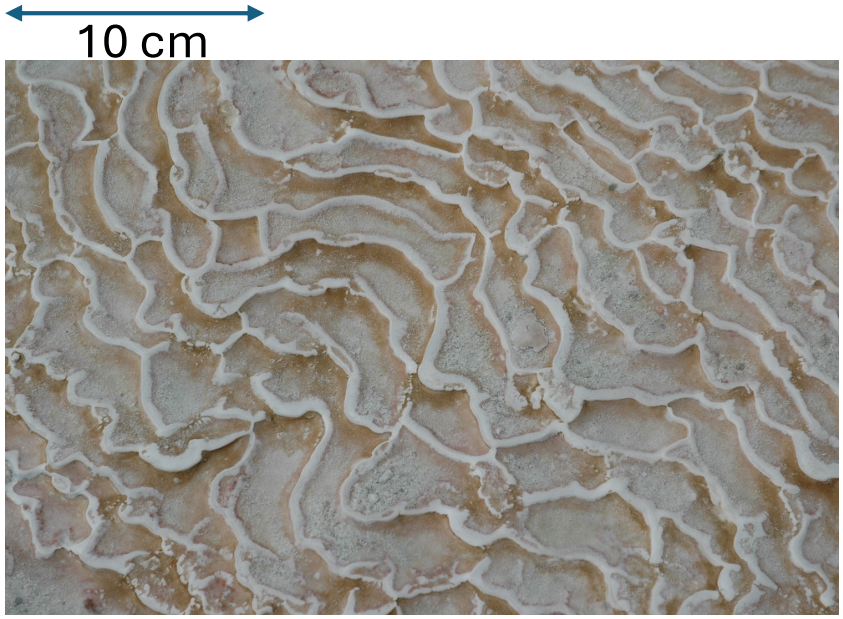
https://github.com/jasonwebb/morphogenesis-resources

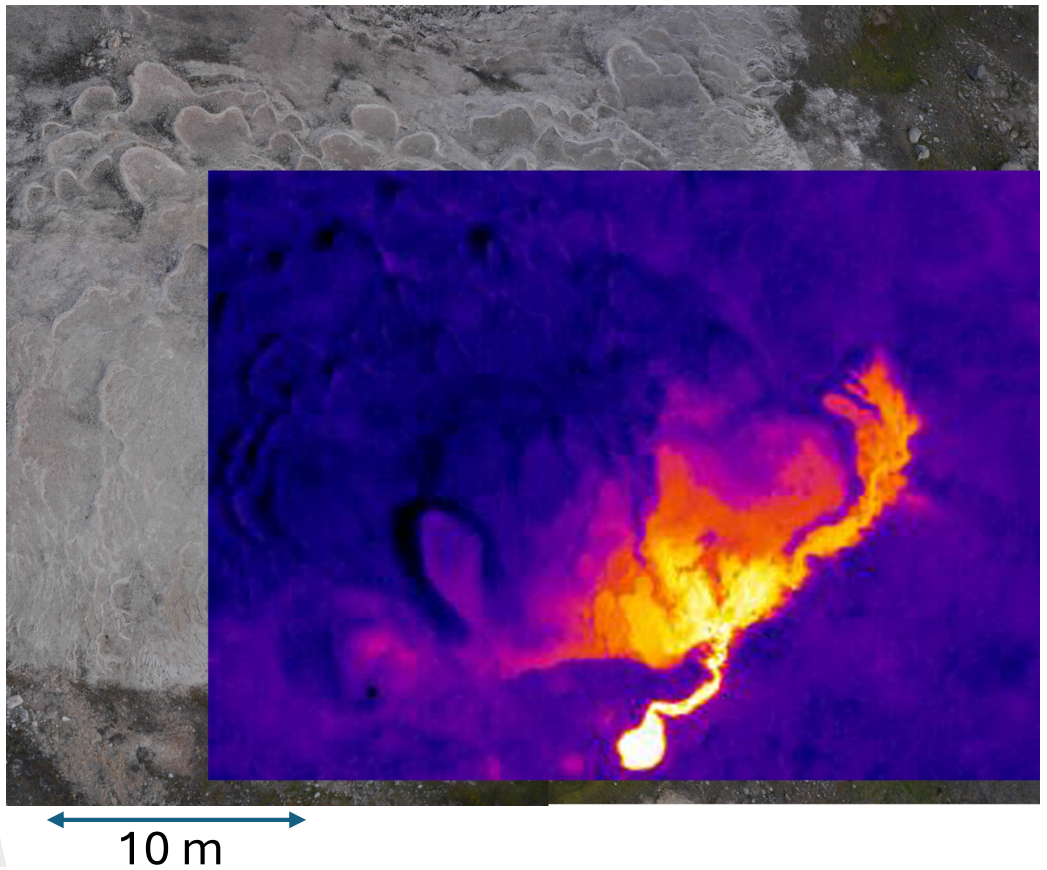
Pattern forming growth processes in Nature



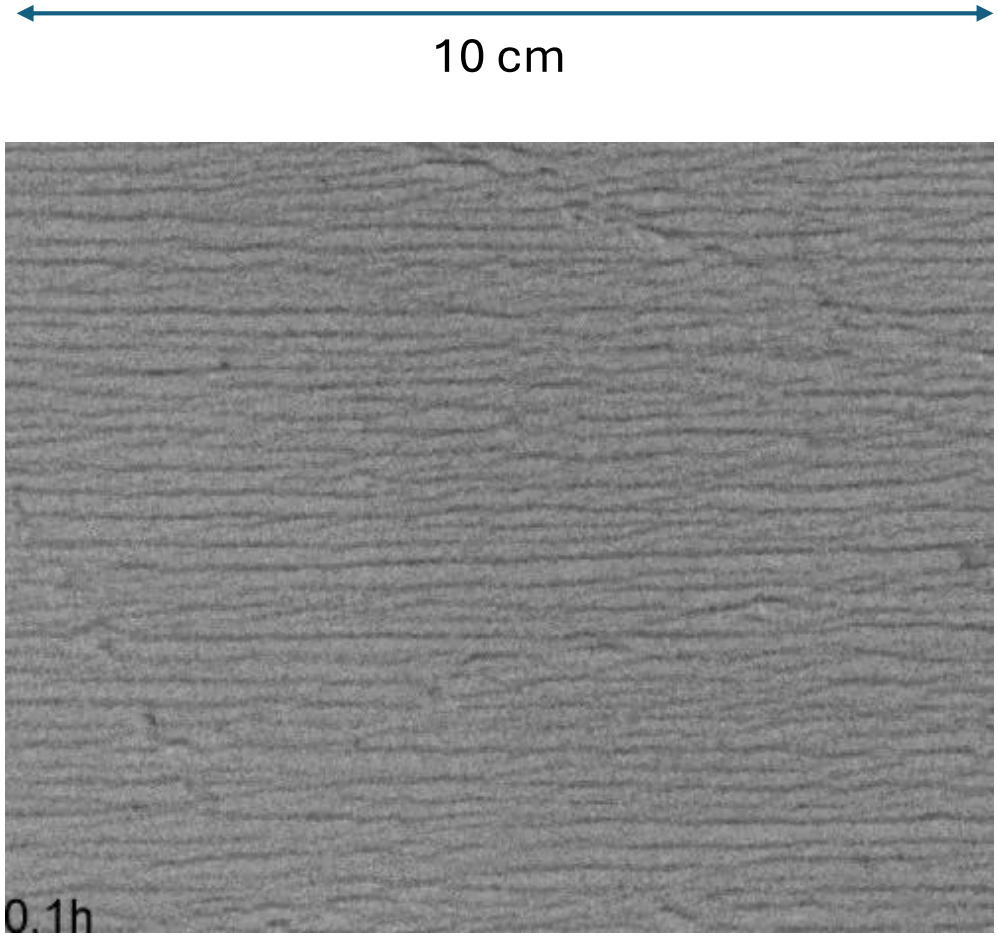
Hans Meinhardt: The algorithmic beauty of sea shells

Pattern forming growth processes in Nature





Pattern forming growth processes in Nature



Pattern forming growth processes in Nature

Competing external forces

Instabilities

Complexity

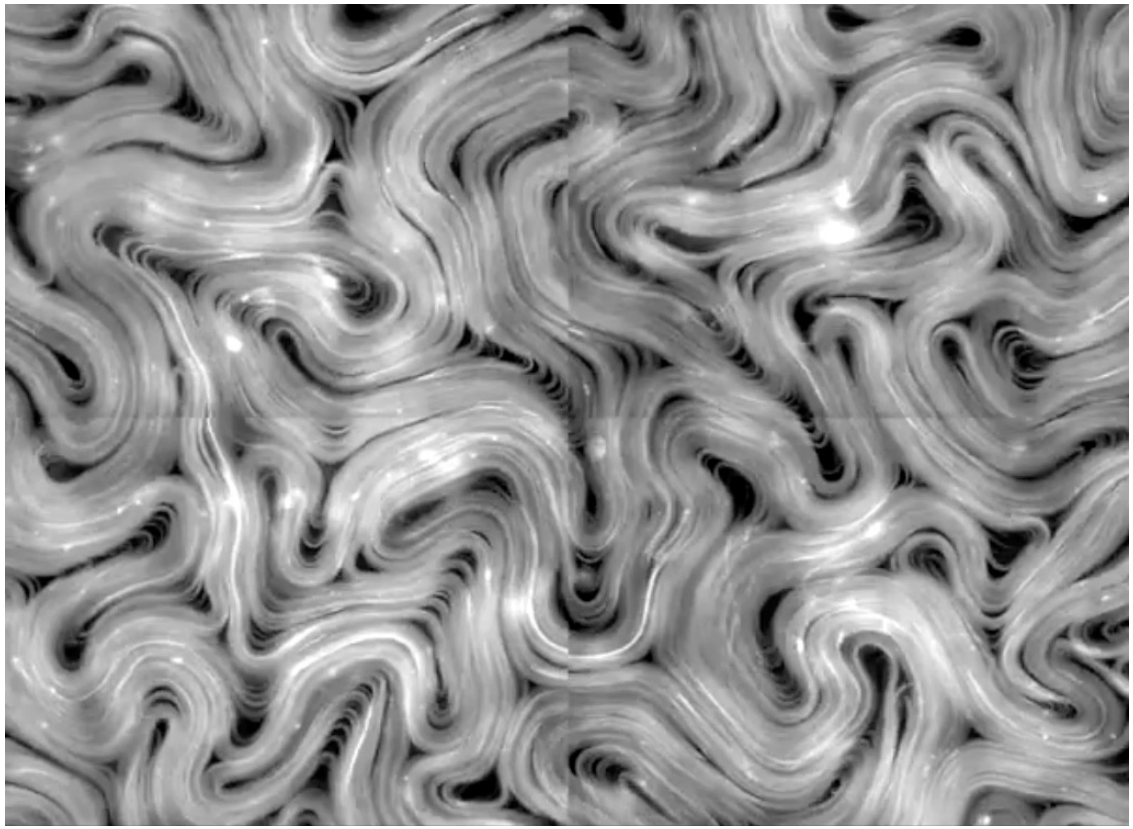
Emergence


Soft matter
nano-/micro-scale parts
interaction energy ~ kT

Active materials

- nano-/micro-scale parts/agents
- interaction energy ~ kT
- energy → forces in local agents

Active materials

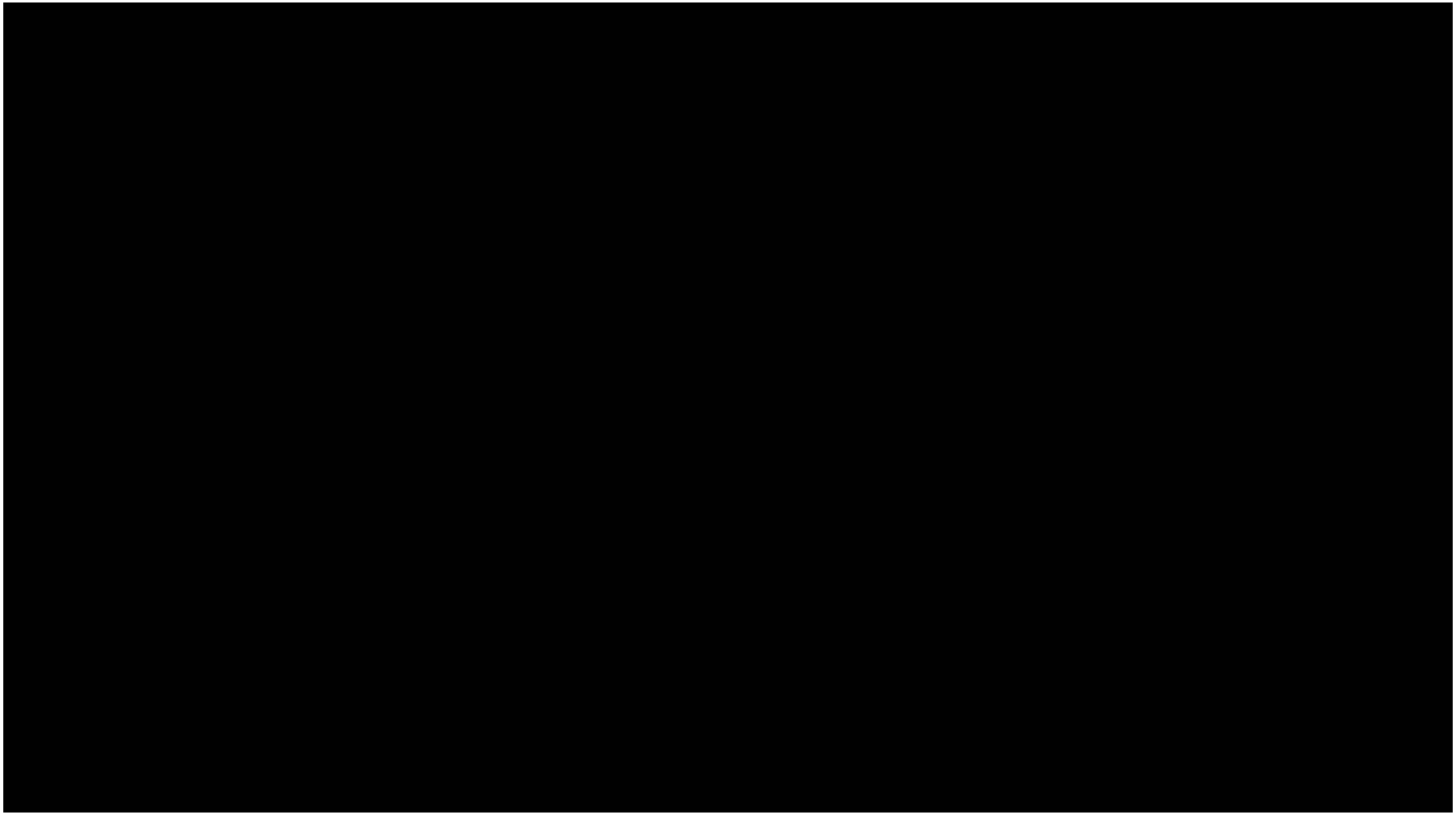


Active 2D Nematic Liquid Crystal: microtubules and kinesin motors, Dogic lab

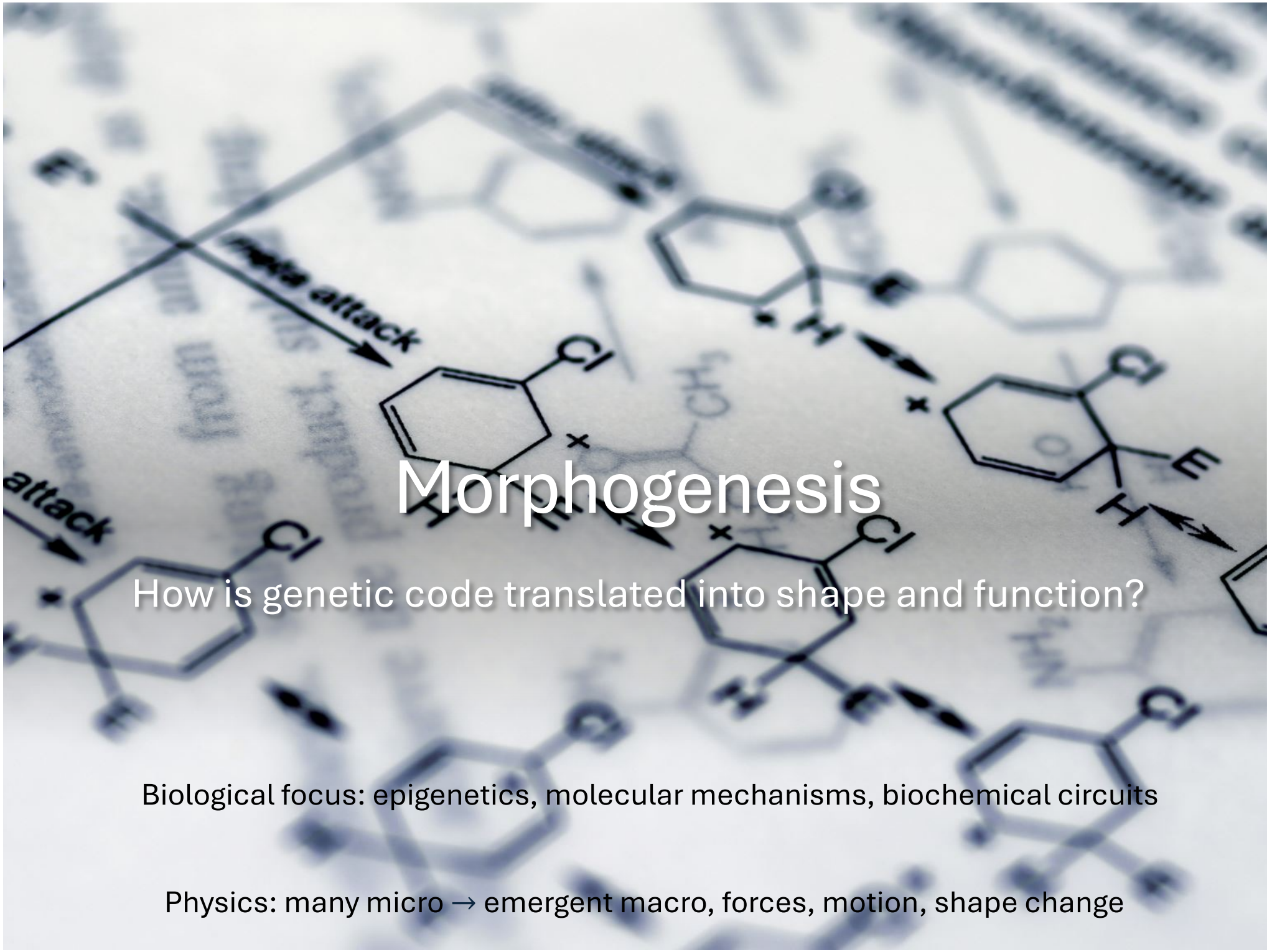
Active materials

- microscale parts
- interaction energy ~ kT
- energy → forces in local agents
- self organized
- no program

Morphogenesis



Imperial College https://youtu.be/1zpV5rzWXMA



Morphogenesis

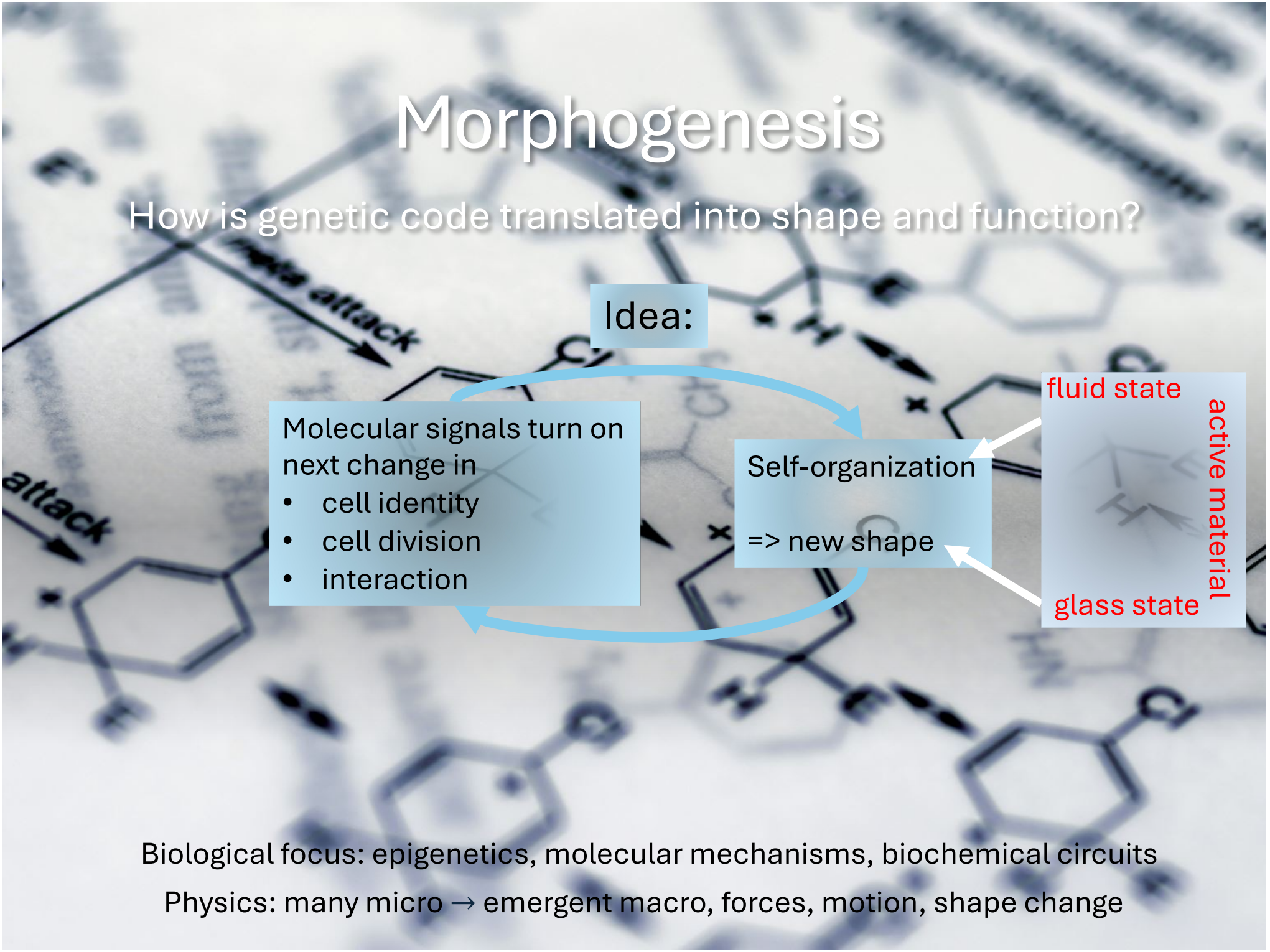
How is genetic code translated into shape and function?

Biological focus: epigenetics, molecular mechanisms, biochemical circuits

Physics: many micro → emergent macro, forces, motion, shape change

Morphogenesis

How is genetic code translated into shape and function?



Biological focus: epigenetics, molecular mechanisms, biochemical circuits

Physics: many micro → emergent macro, forces, motion, shape change

Morphogenesis

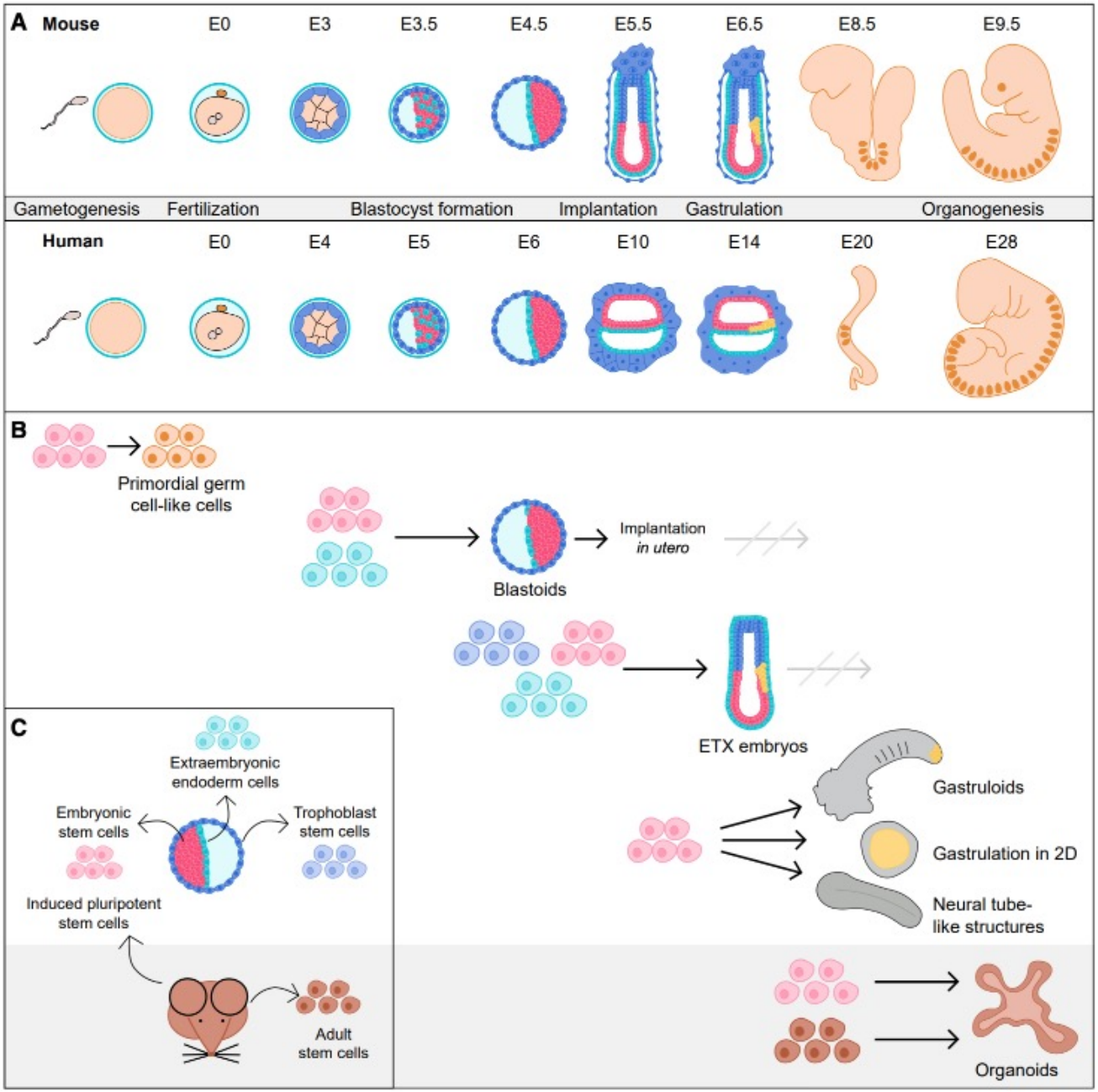
How is genetic code translated into shape and function?

How do we study morphogenesis?

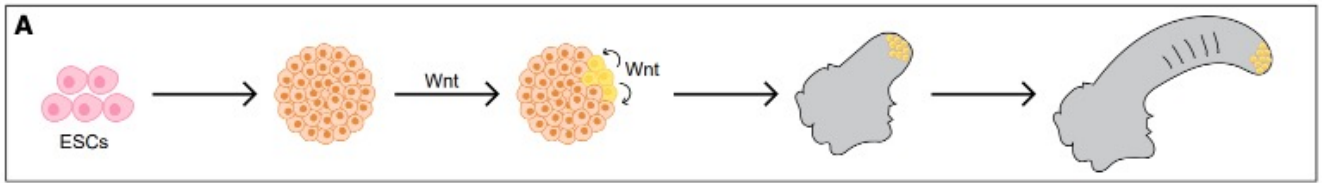
Until now: Follow the natural embryo development

New tool: Gastruloid technology (embryo models)

Gastruloid technology: experimenting with development



Gupta, Lutolf, Hughes & Sonnen (2021) https://doi.org/10.1016/j.stemcr.2021.04.005



Gastruloid technology: experimenting with development

Grow stem cells (ESC or IPSC)

Make an aggregate 100-500 cells

Add signal molecules

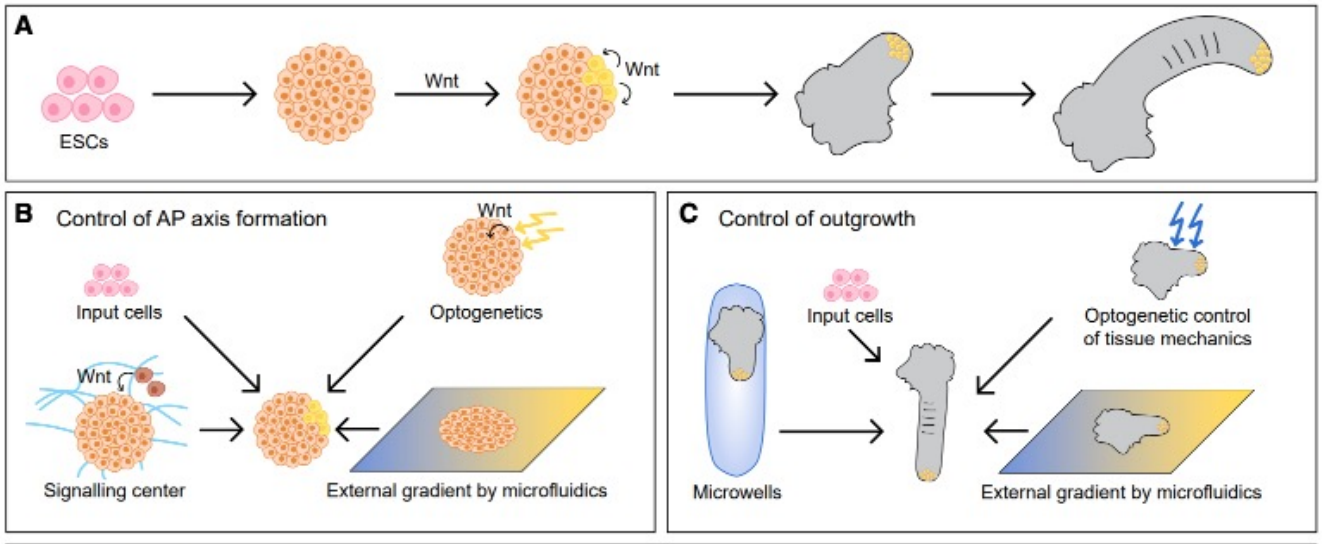
→ polarization (self-organization)

→ differentiation (fluctuations? self-organization?)

→ body patterning (self-organization)

Gupta, Lutolf, Hughes & Sonnen (2021) https://doi.org/10.1016/j.stemcr.2021.04.005

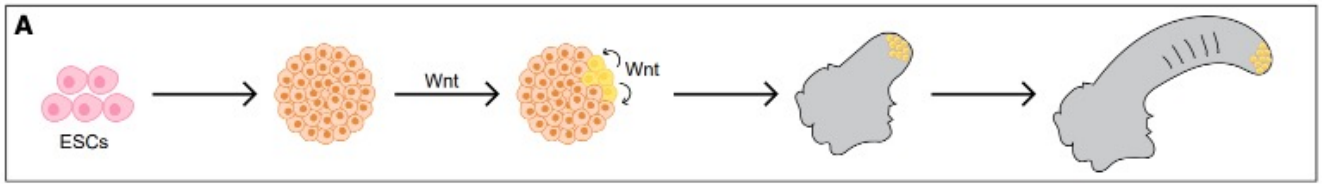
Gastruloid technology: experimenting with development

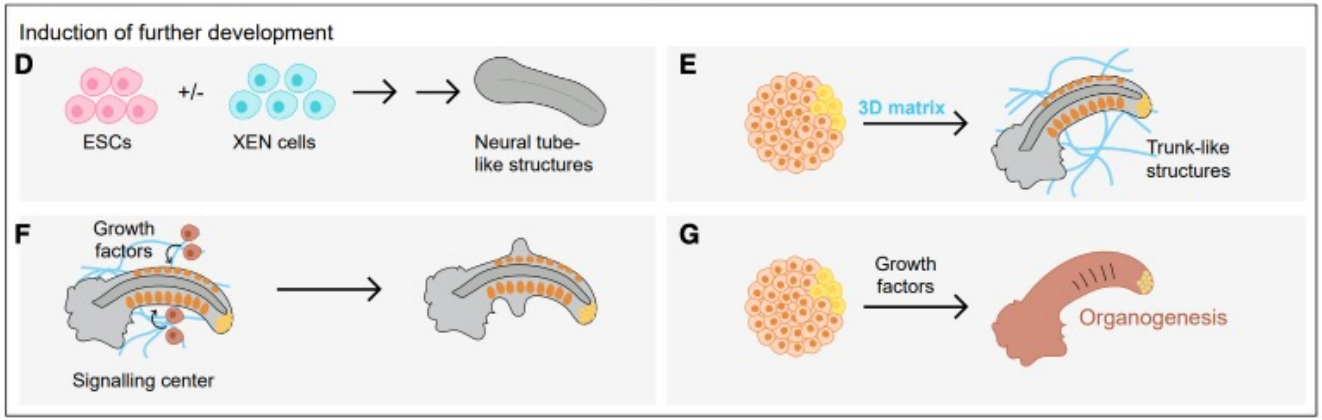


Gradients of signal molecules important for
→ differentiation
→ body patterning

Gupta, Lutolf, Hughes & Sonnen (2021) https://doi.org/10.1016/j.stemcr.2021.04.005

Gastruloid technology: experimenting with development

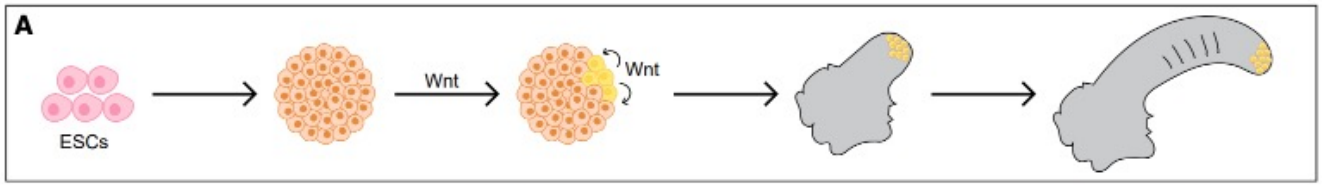




Try and fail development of technology

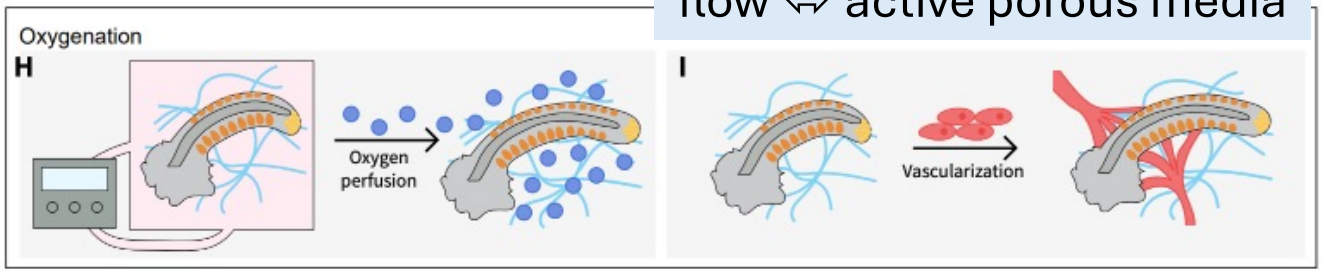
Gupta, Lutolf, Hughes & Sonnen (2021) https://doi.org/10.1016/j.stemcr.2021.04.005

Gastruloid technology: experimenting with development



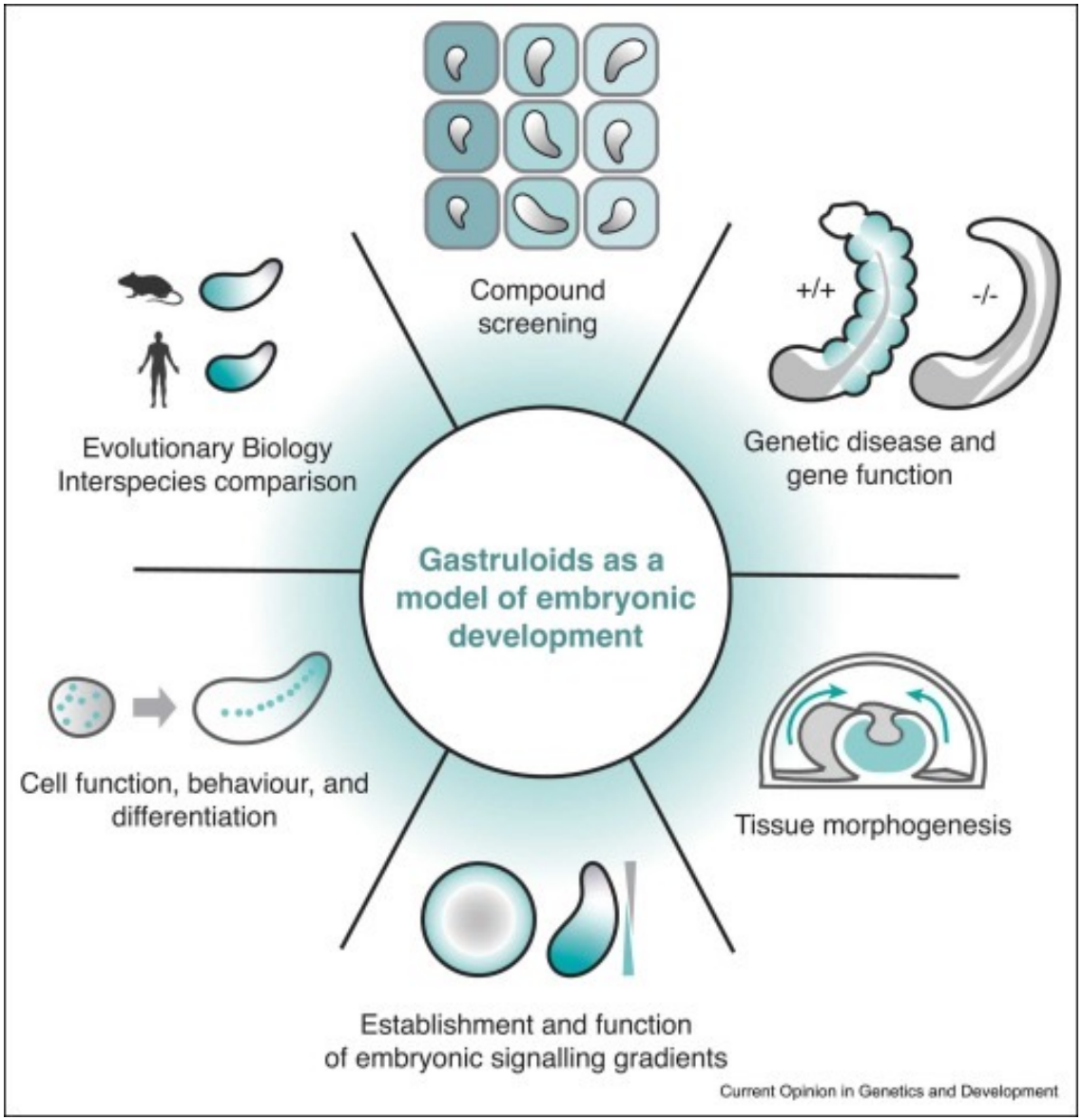
Living cells consume O_2
Diffusion transport of $O_2 \propto r^{-2}$
=> advection is necessary
=> vascularization

feedback
flow ⇔ active porous media



Gupta, Lutolf, Hughes & Sonnen (2021) https://doi.org/10.1016/j.stemcr.2021.04.005

Gastruloid technology: experimenting with development



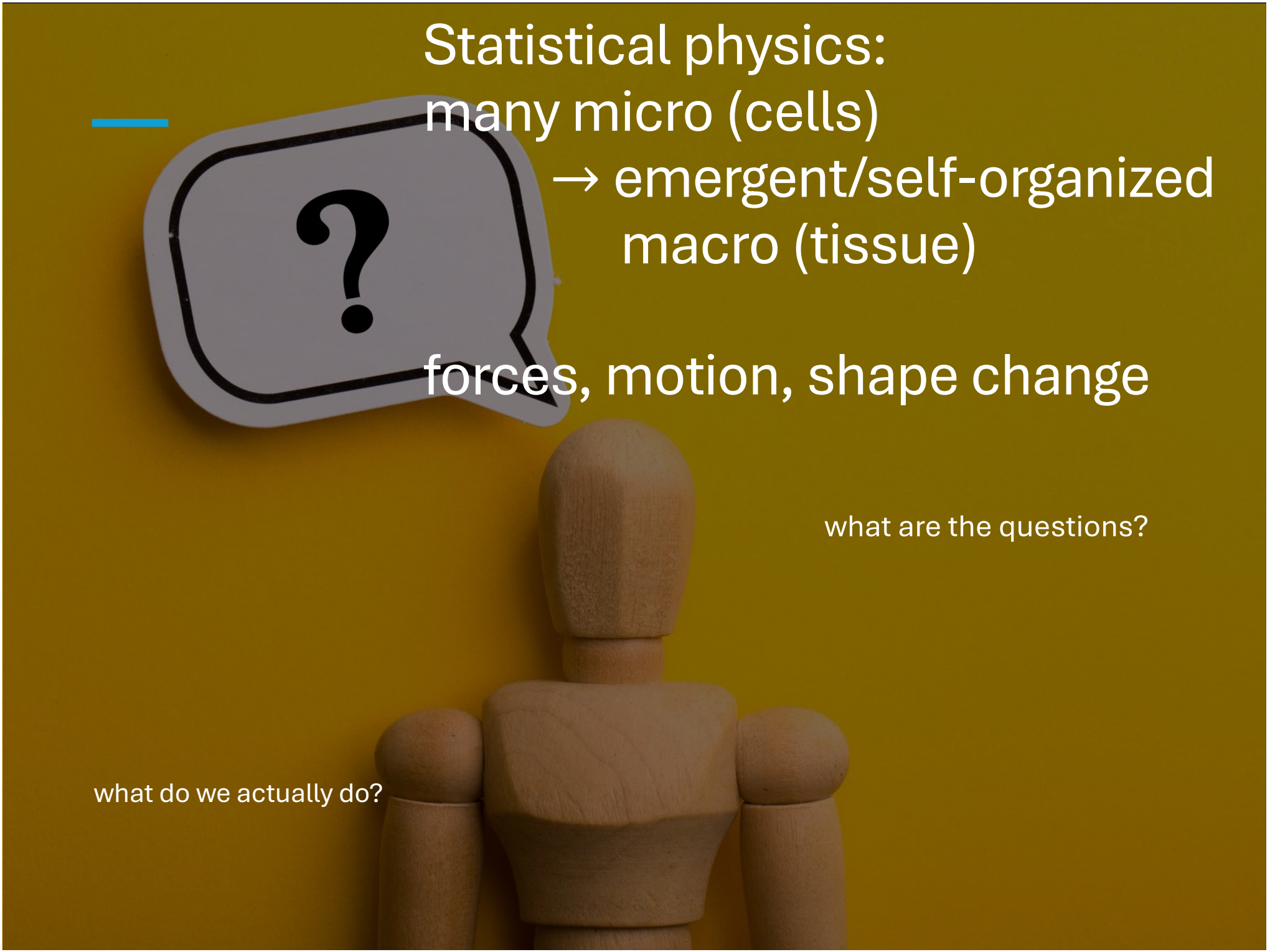
Sullivan & Santos (2023) https://doi.org/10.1016/j.gde.2023.102102

Statistical physics:

many micro (cells)

→ emergent/self-organized macro (tissue)

forces, motion, shape change



what are the questions?

what do we actually do?

Question: can we ‘explain’ gastruloid morphogenesis?

What we actually do

Modelling (Richard)

interactions

$$V_{ij} = V_{ij}^{(0)} + V_{ij}^{(1)},$$

$$V_{ij}^{(0)} = \lambda_0 \left(e^{-r_{ij}} - e^{-r_{ij}/a_0} \right)$$

$$V_{ij}^{(1)} = e^{-r_{ij}} - (\lambda_1 S_1 + \lambda_2 S_2 + \lambda_3 S_3) e^{-r_{ij}/a_0}$$

$$S_1 = (\mathbf{p}_i \times \mathbf{r}_{ij}) \cdot (\mathbf{p}_j \times \mathbf{r}_{ij})$$

$$S_2 = (\mathbf{p}_i \times \mathbf{q}_i) \cdot (\mathbf{p}_j \times \mathbf{q}_j)$$

$$S_3 = (\mathbf{q}_i \times \mathbf{r}_{ij}) \cdot (\mathbf{q}_j \times \mathbf{r}_{ij}),$$

equations of motion

$$\dot{\mathbf{r}}_i = - \sum_{j=\text{n.n. of } i} \frac{\partial V_{ij}}{\partial \mathbf{r}_i} + \boldsymbol{\eta}_i^{(1)}$$

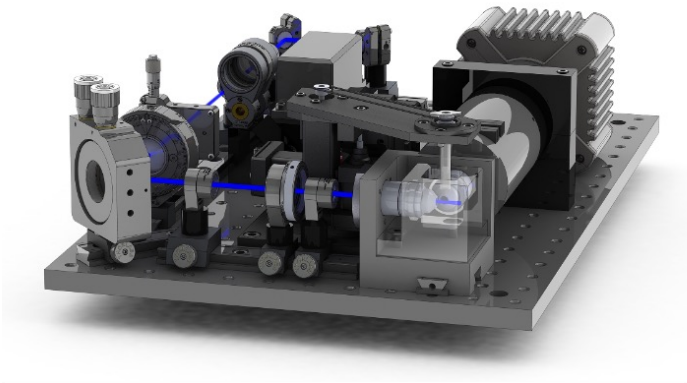
$$\dot{\mathbf{p}}_i = - \sum_{j=\text{n.n. of } i} \frac{\partial V_{ij}}{\partial \mathbf{p}_i} + \boldsymbol{\eta}_i^{(2)}$$

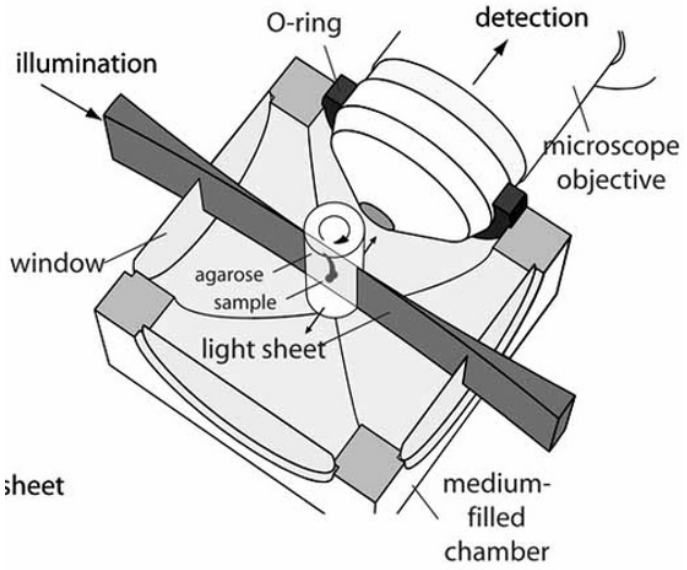
$$\dot{\mathbf{q}}_i = - \sum_{j=\text{n.n. of } i} \frac{\partial V_{ij}}{\partial \mathbf{q}_i} + \boldsymbol{\eta}_i^{(3)},$$

$$\langle \eta_i^{(\alpha)}(t) \eta_j^{(\beta)}(t') \rangle = 2\sigma\delta(t-t')\delta_{ij}\delta_{\alpha\beta}$$

Idea: Self-organization driven by polar adhesion

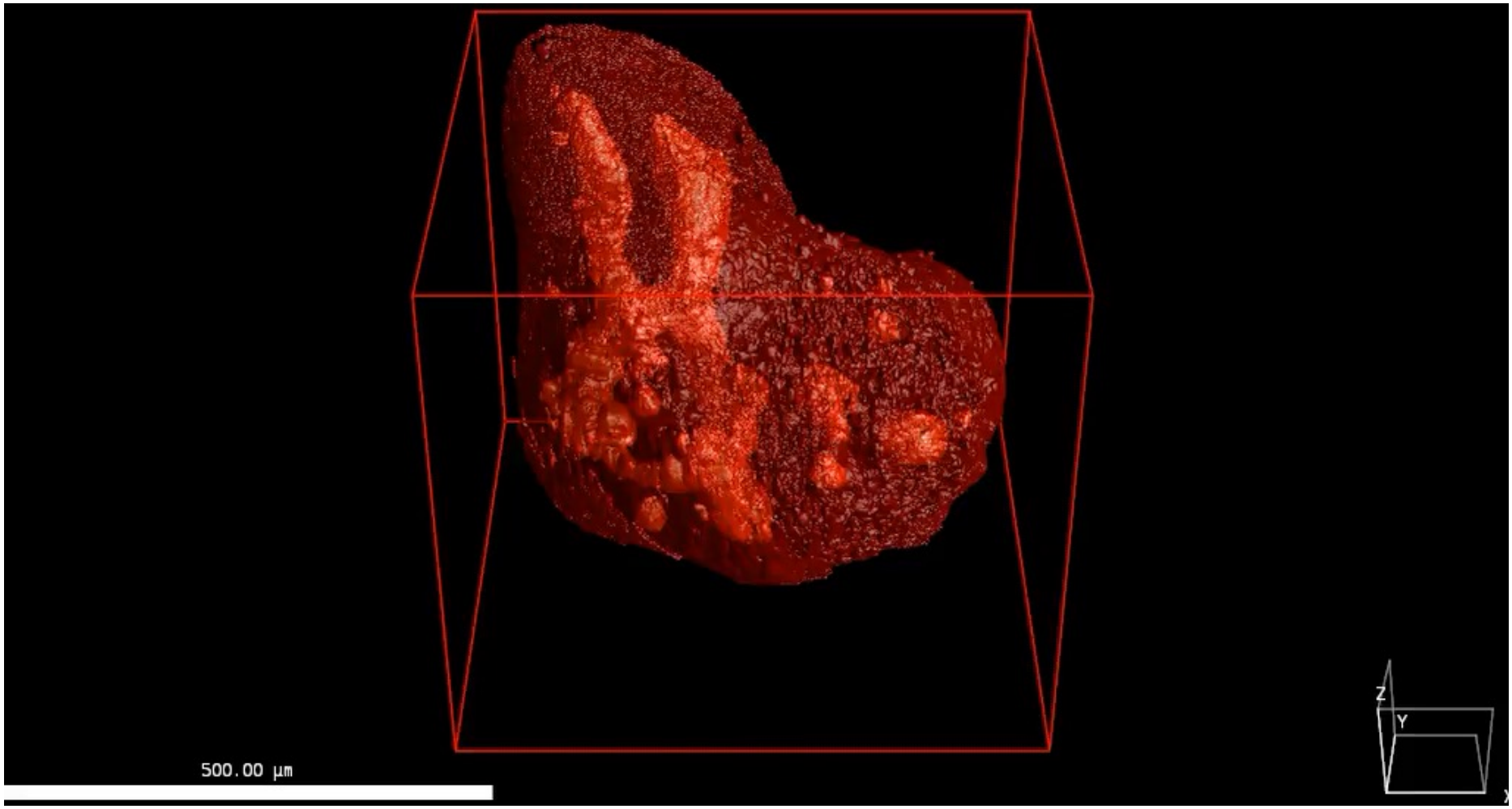
Imaging (Joachim)





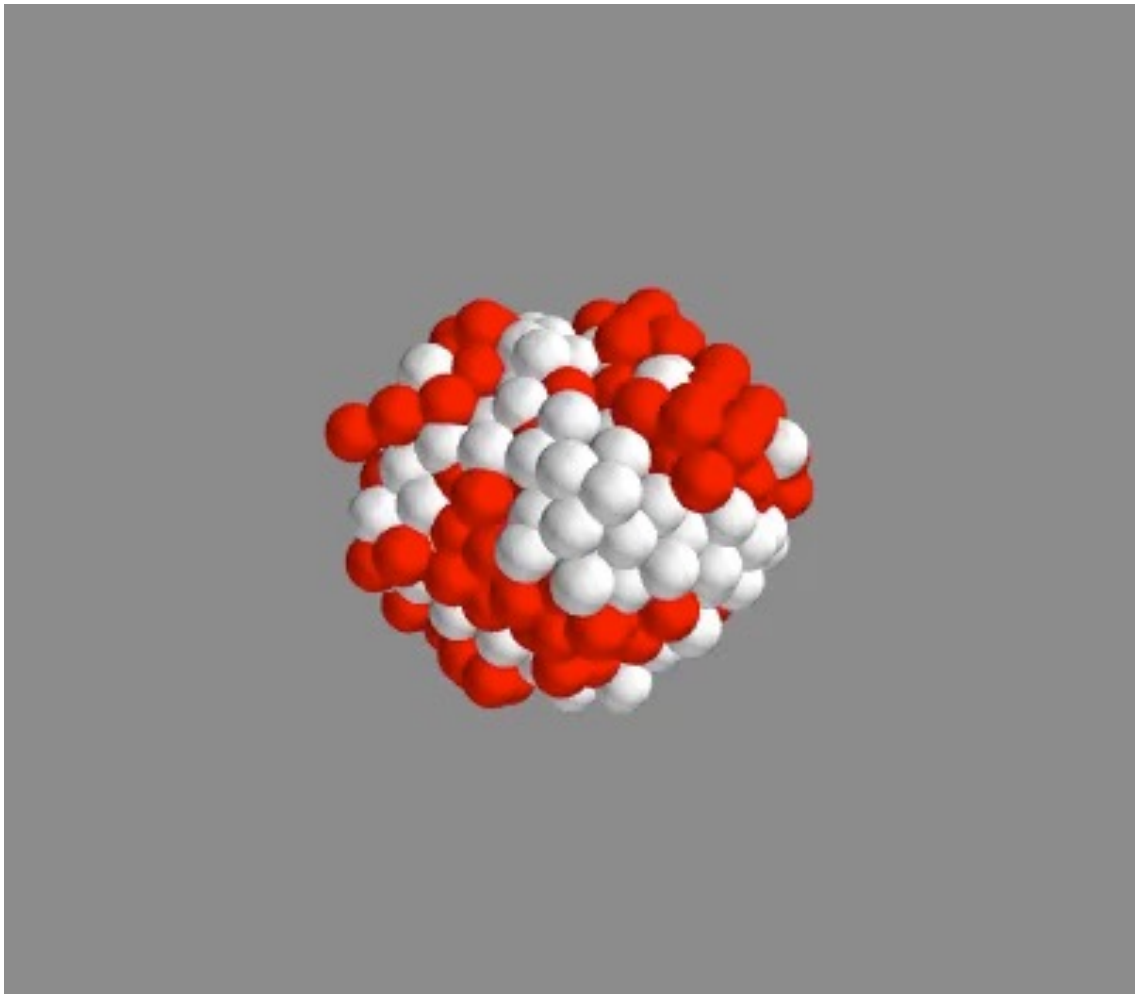
Gastruloid with 2 cell types

Joachim



Why are the gut cells distributed? Will they gather?

Cell sorting and shape change

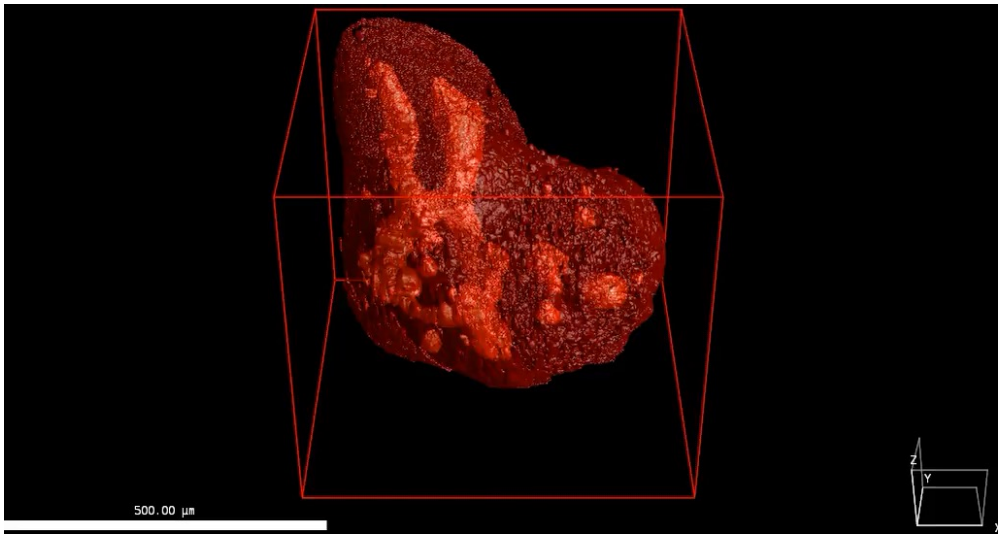


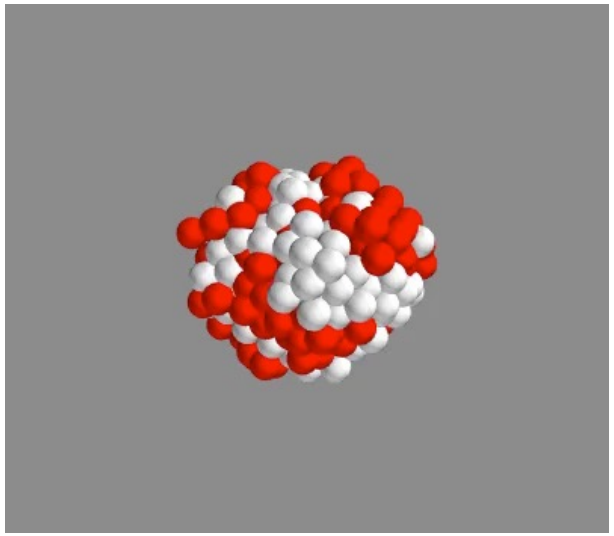
Richard

Physics: Self organization driven by differential & polar adhesion

Question: can we ‘explain’ gastruloid morphogenesis?

Joachim



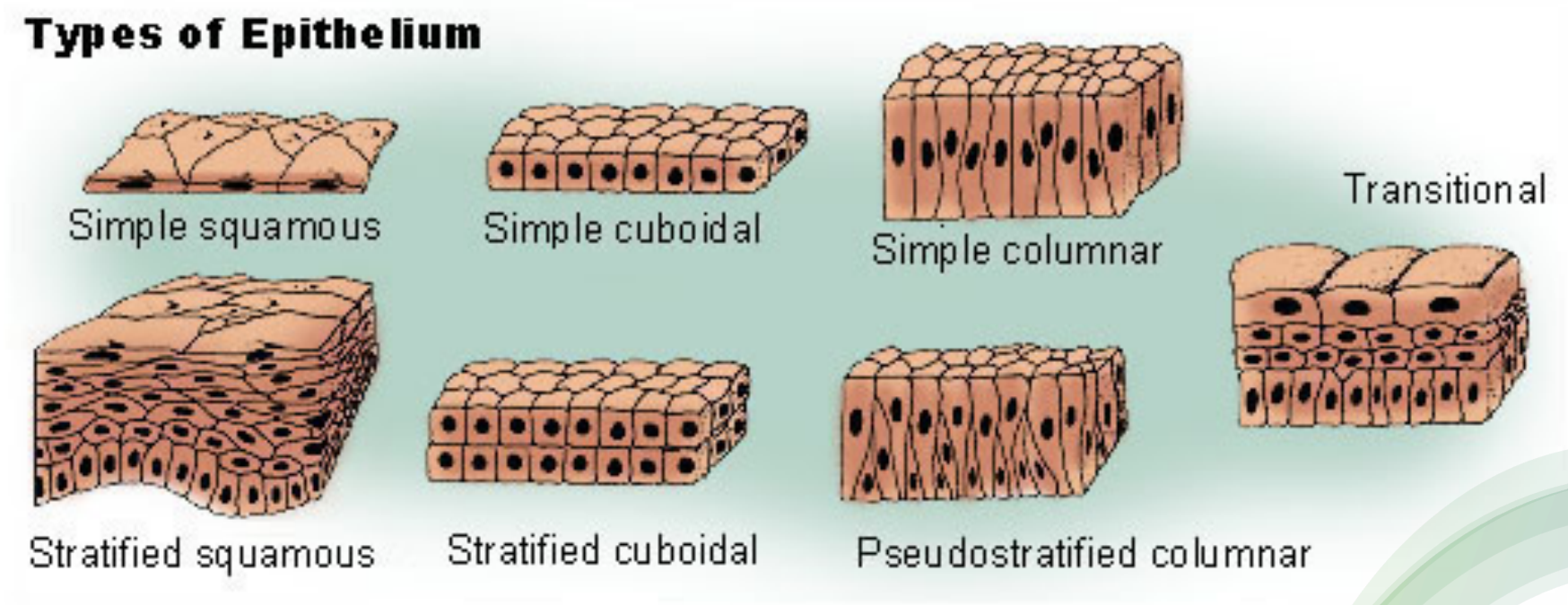


Richard

- Model: Self organization driven by differential & polar adhesion. Add:
  - cell division
  - signal gradient => cell fate & interactions
- Experiments: Fixed samples. Add:
  - live imaging
  - track motion of different cell types
- Quantify: shapes, motion, distributions, fluctuations, variations
- Compare

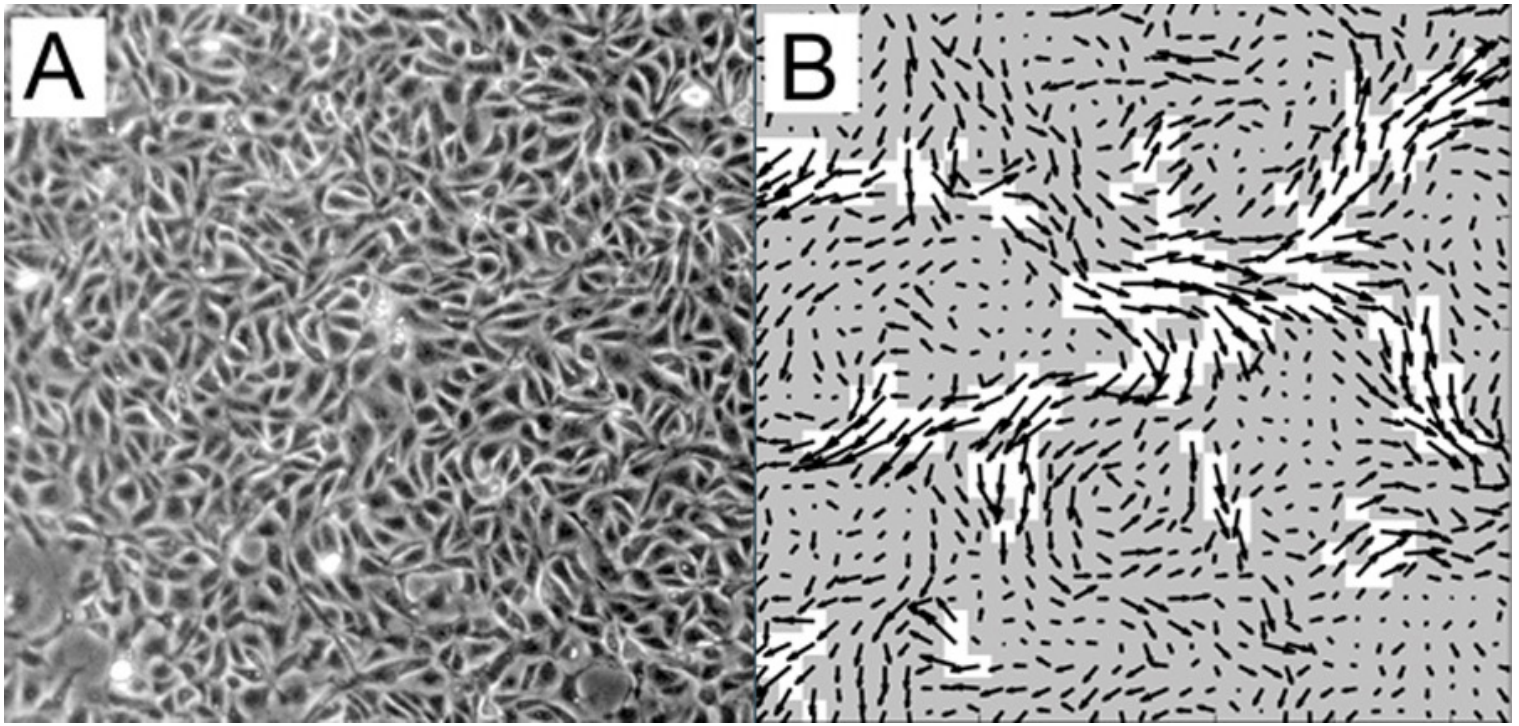
Question: Are there other universal principles than differential & polar adhesion?

Simplify: 2D studies of epithelia

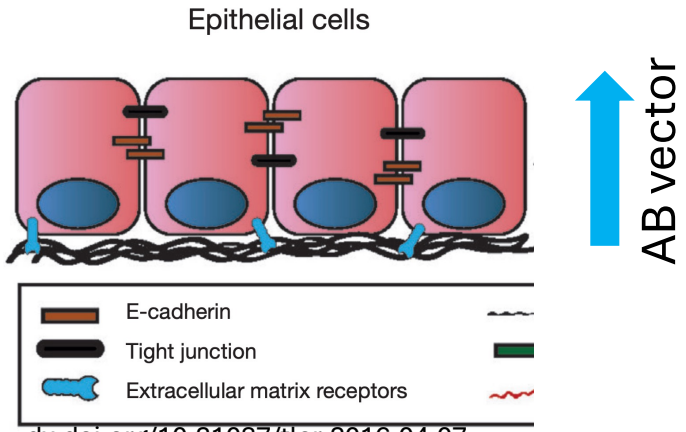


Wikipedia: epithelium

Simplify: 2D study of epithelia

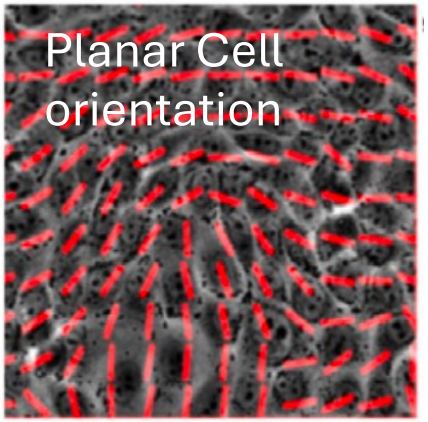


dx.doi.org:10.1073/pnas.1010059108



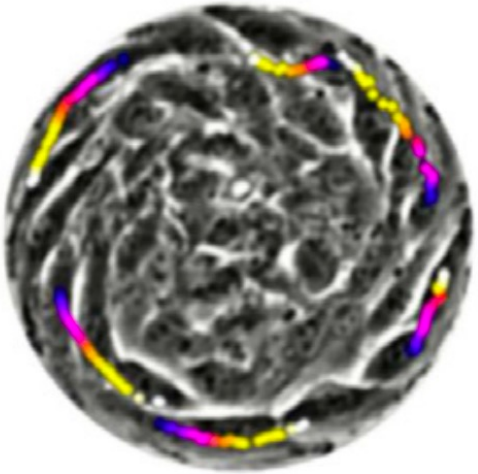
dx.doi.org/10.21037/tlcr.2016.04.07

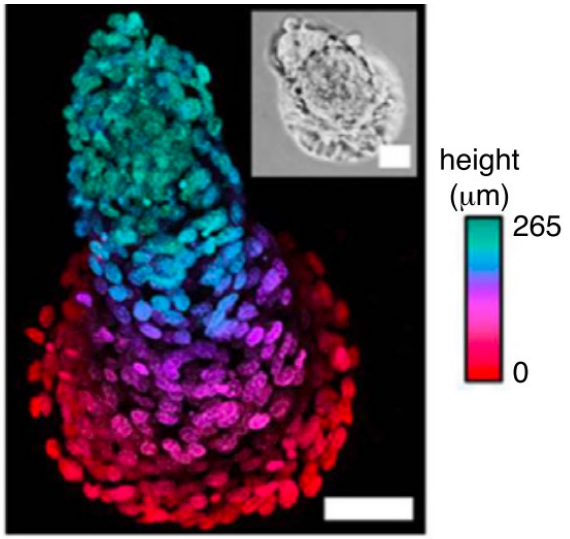
AB vector

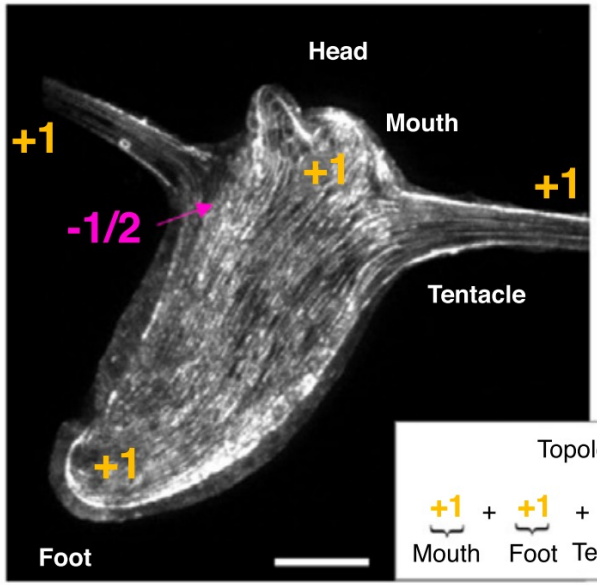


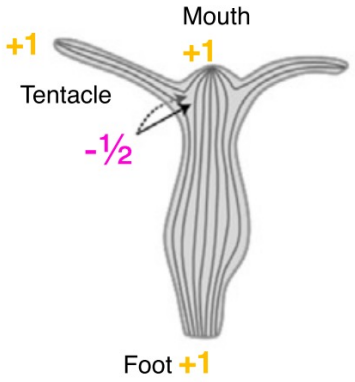
dx.doi.org/10.1016/j.gde.2021.101897

Idea: 2D topology governs 3D growth









Topological charge in mature *Hydra*

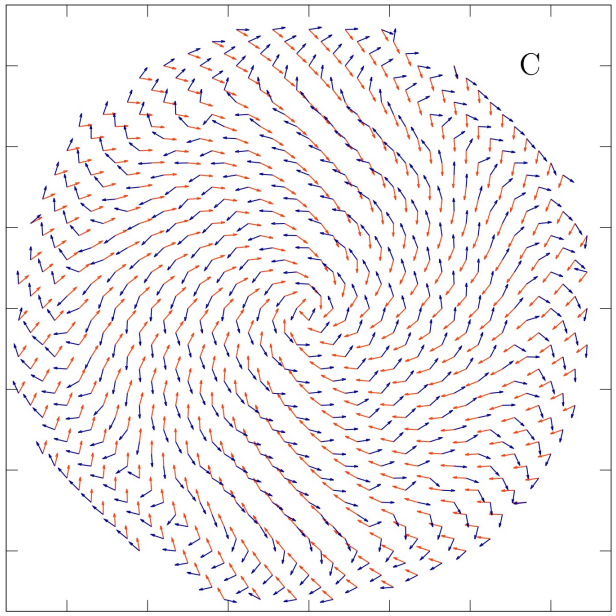
$$\underbrace{+1}_{\text{Mouth}} + \underbrace{+1}_{\text{Foot}} + \underbrace{N}_{\text{Tentacles}} \times \left(\underbrace{+1}_{\text{Tip}} + 2 \times \left(\underbrace{-\tfrac{1}{2}}_{\text{Base}} \right) \right) = +2$$

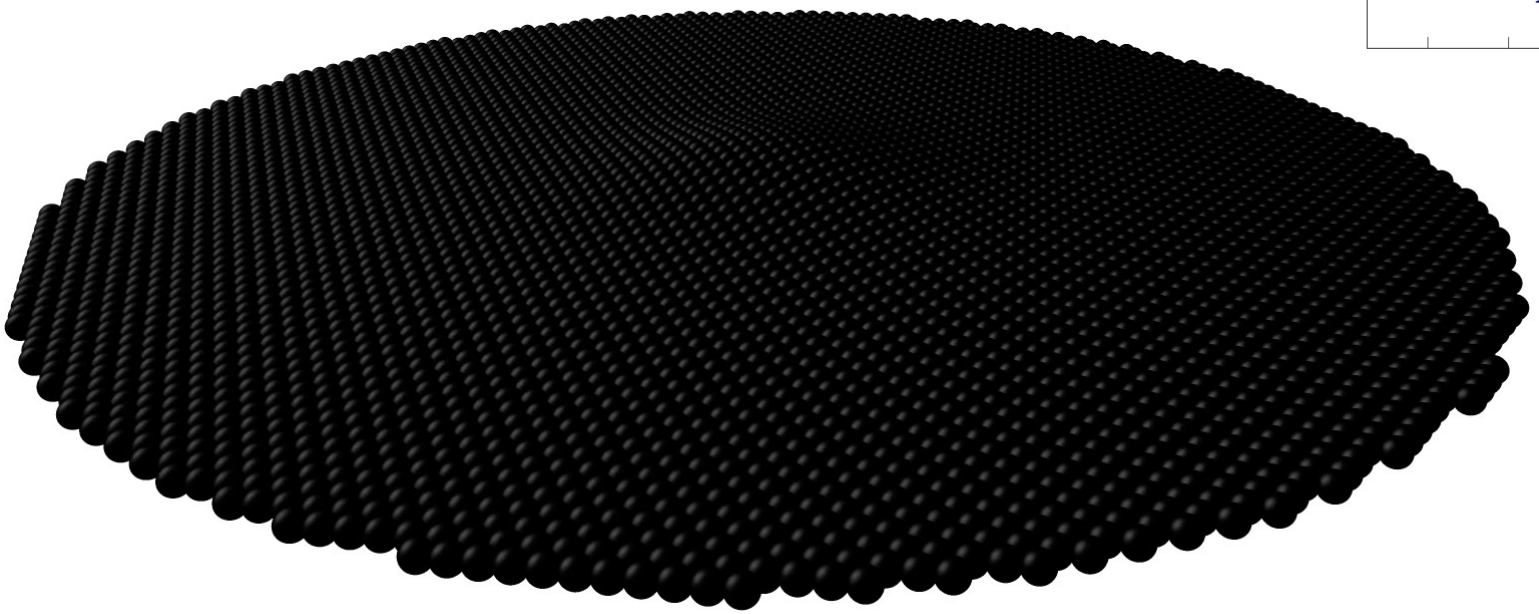
Question: Is this a universal principle?

dx.doi.org/10.1016/j.gde.2021.101897

Idea: 2D topology governs 3D growth

Question: Is this a universal principle?
Answer 1: Simple models predict this





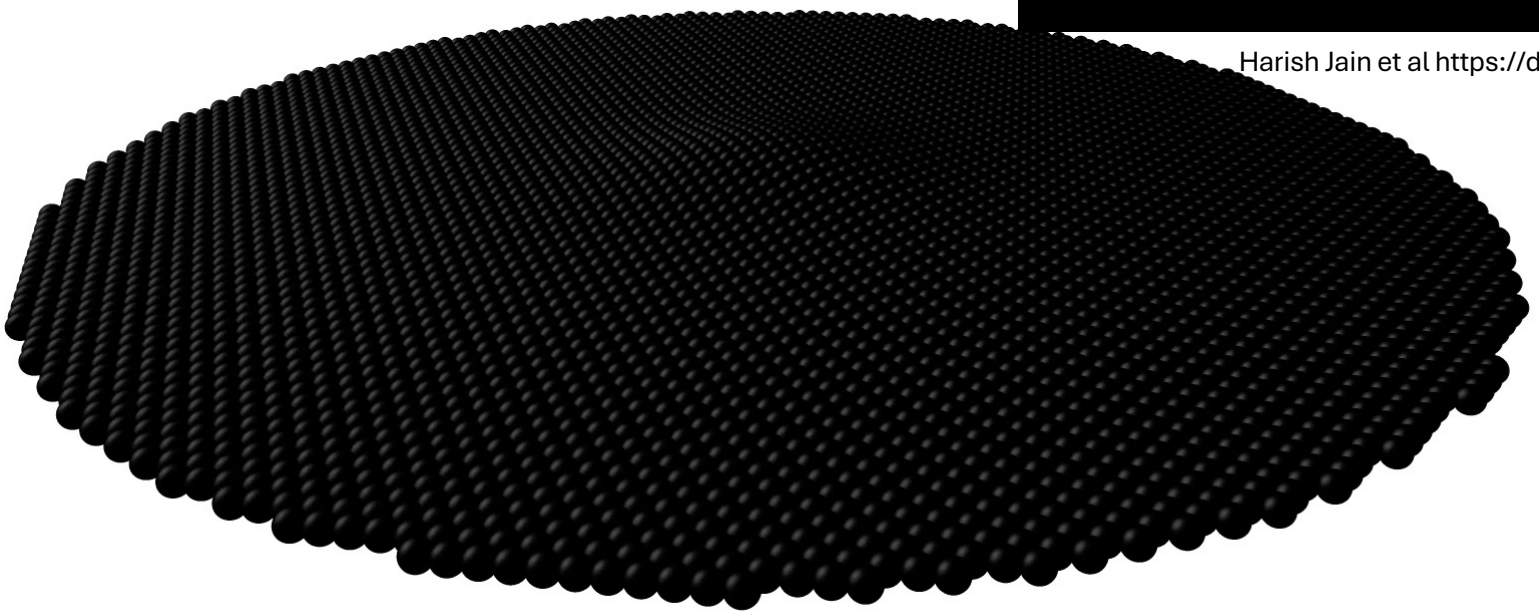
Richard D.J.G. Ho et al, https://doi.org/10.48550/arXiv.2403.05276

Idea: 3D gives space for fluidization

Fluidization = neighbour exchanges / T1 transitions



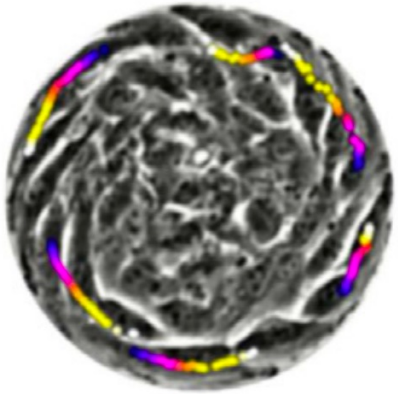
Harish Jain et al https://doi.org/10.1038/s41598-023-37064-6

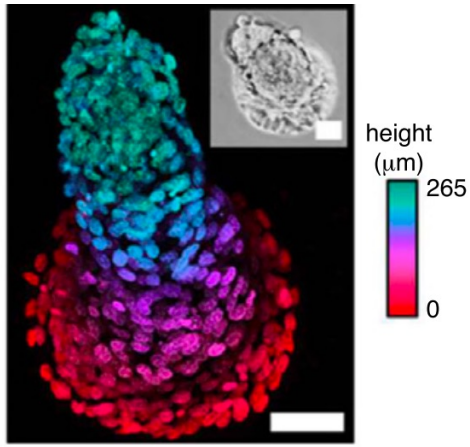


Richard D.J.G. Ho et al, https://doi.org/10.48550/arXiv.2403.05276

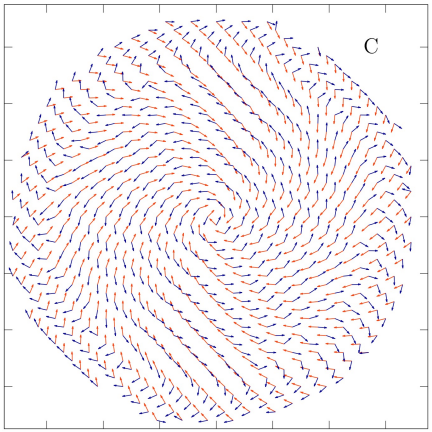
Idea: 2D topology governs 3D growth

Question: Is this a universal principle?
Answer 2: For myoblasts, yes





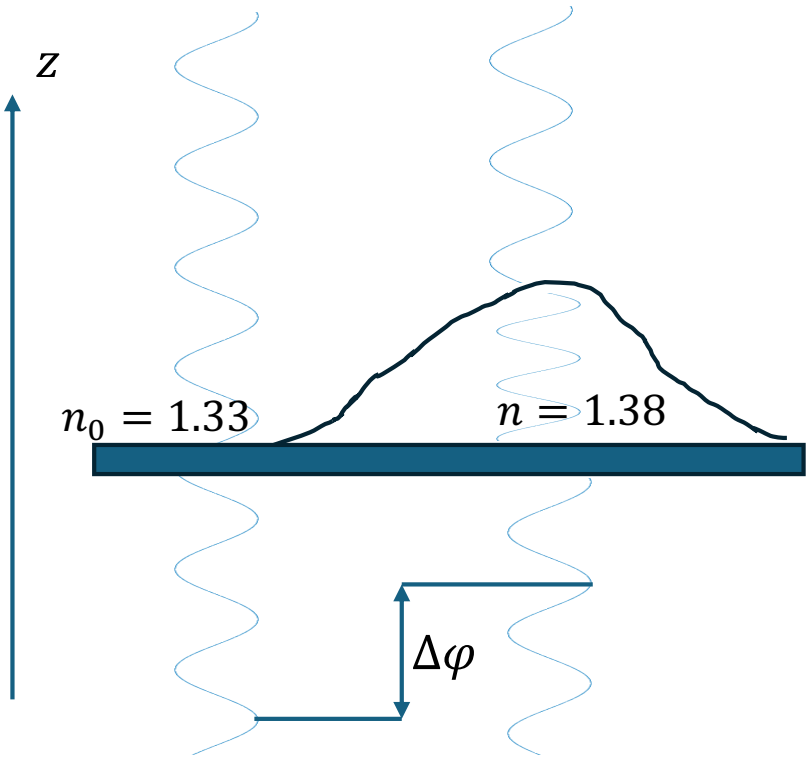
How about epithelia?



Plan:

- Embed vortex pattern like in simulation
- Study dynamics

Epithelial dynamics:
Quantitative phase imaging



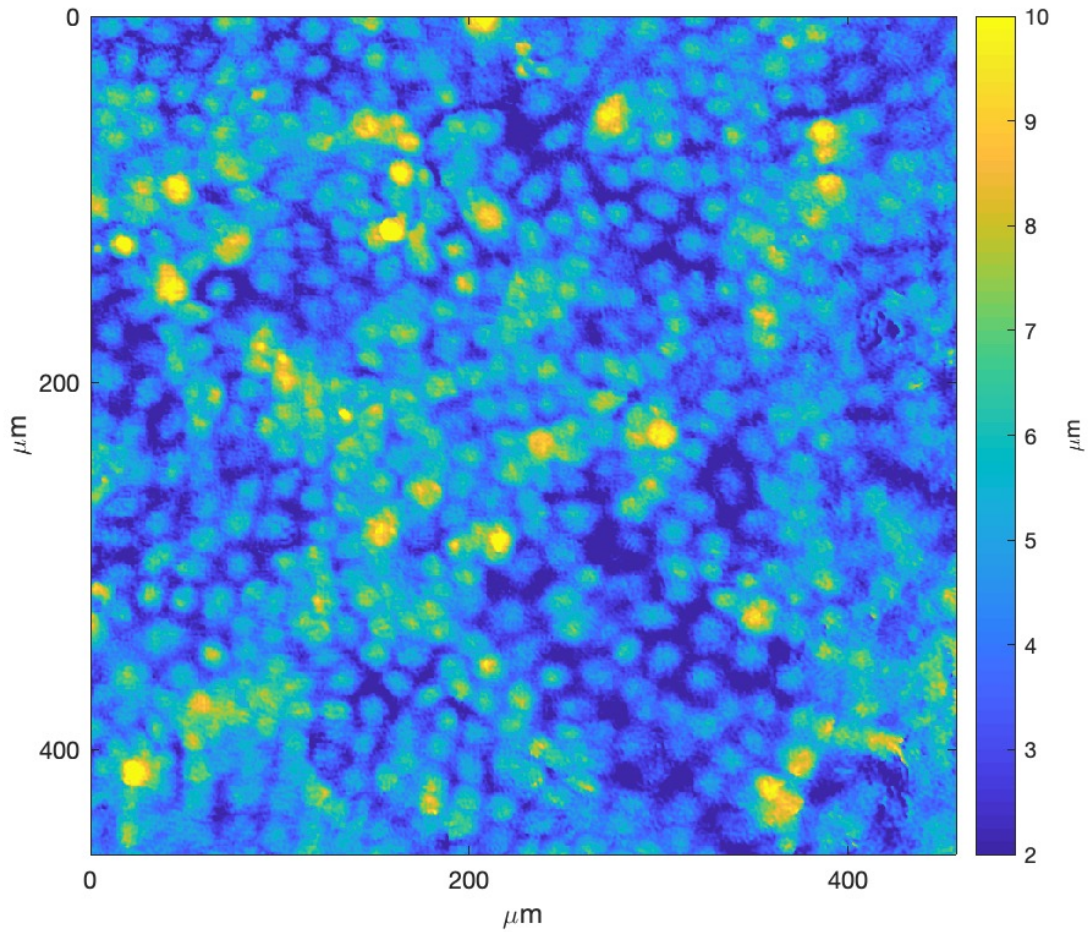
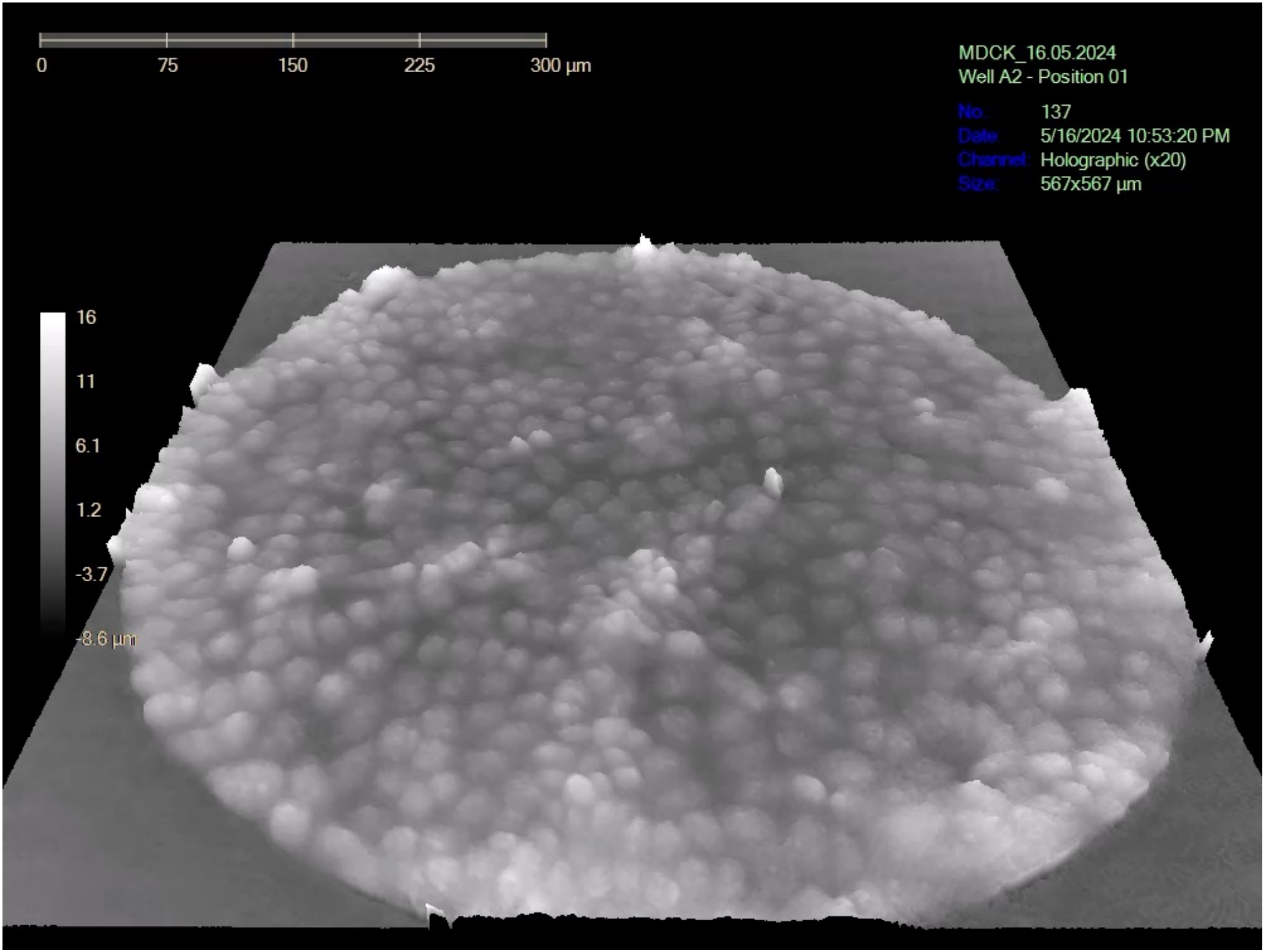


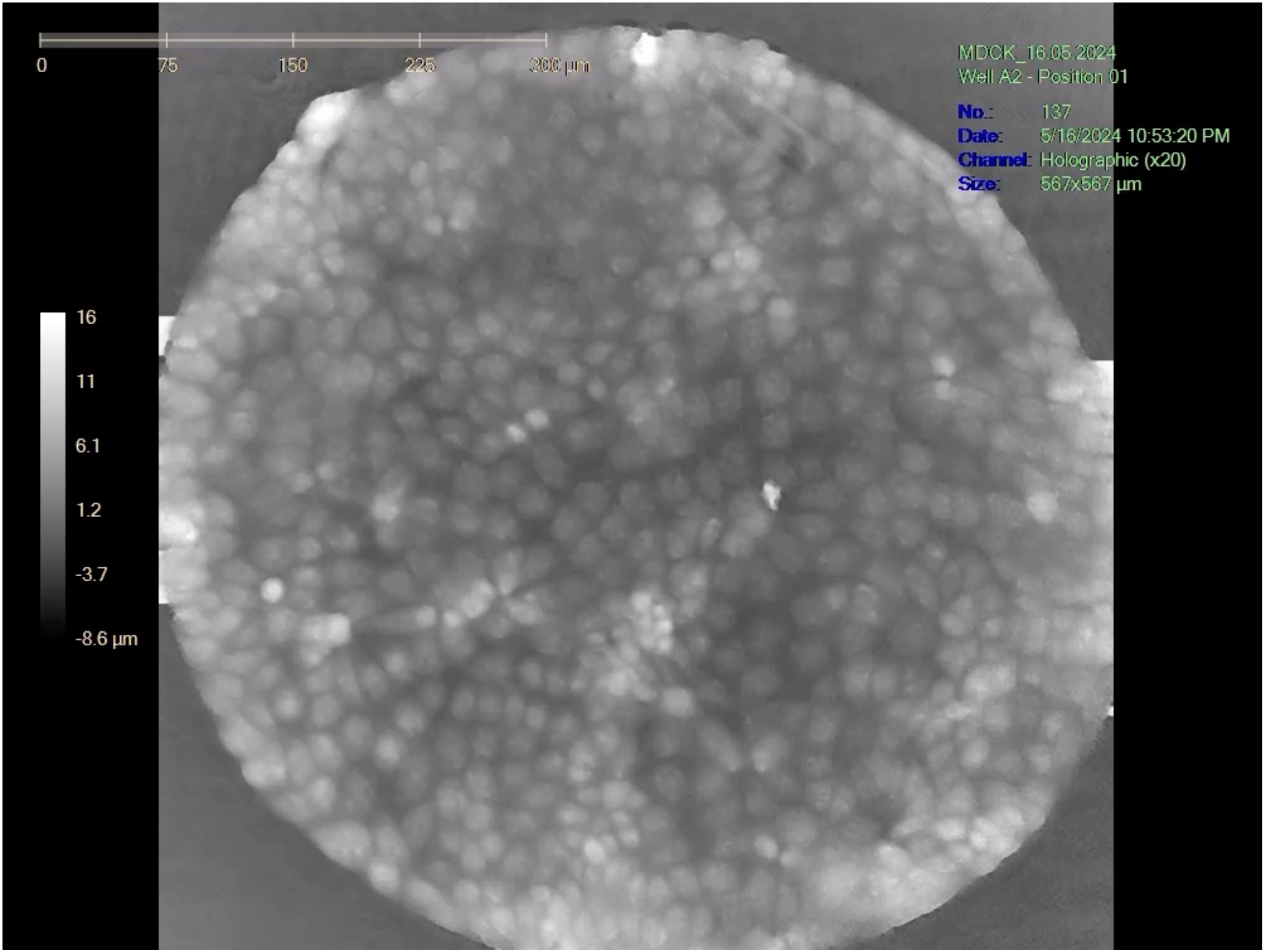
Image intensity

$$I \propto \Delta\varphi \propto \int (n(z) - n_0)dz \approx h$$

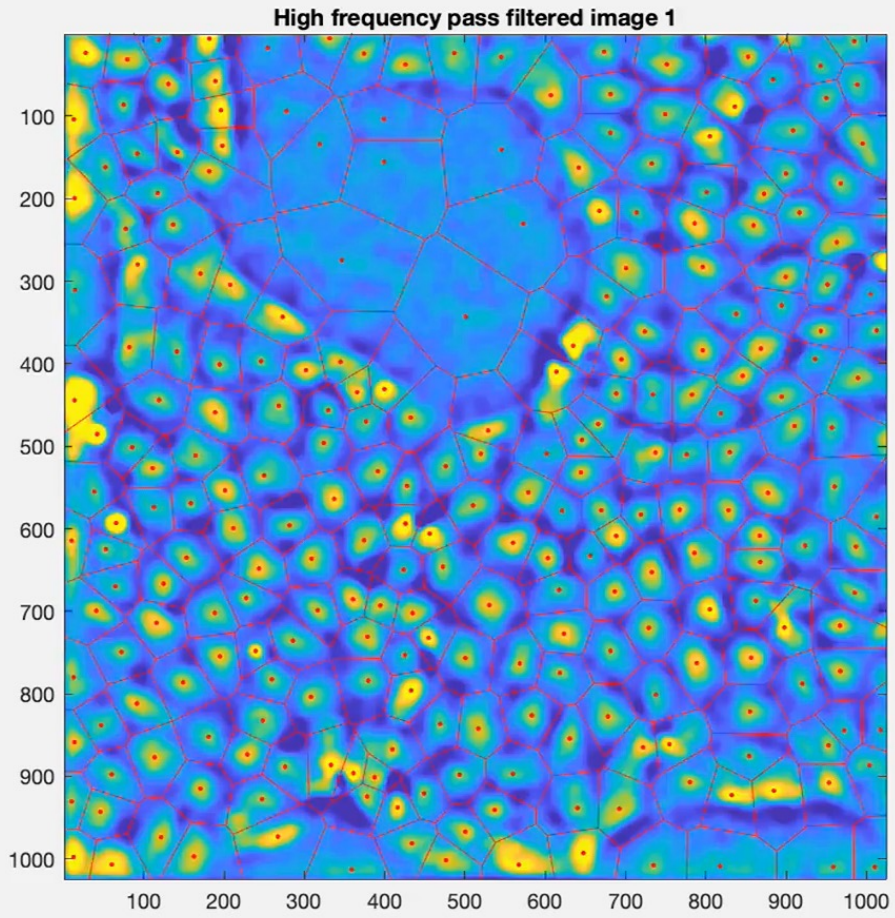
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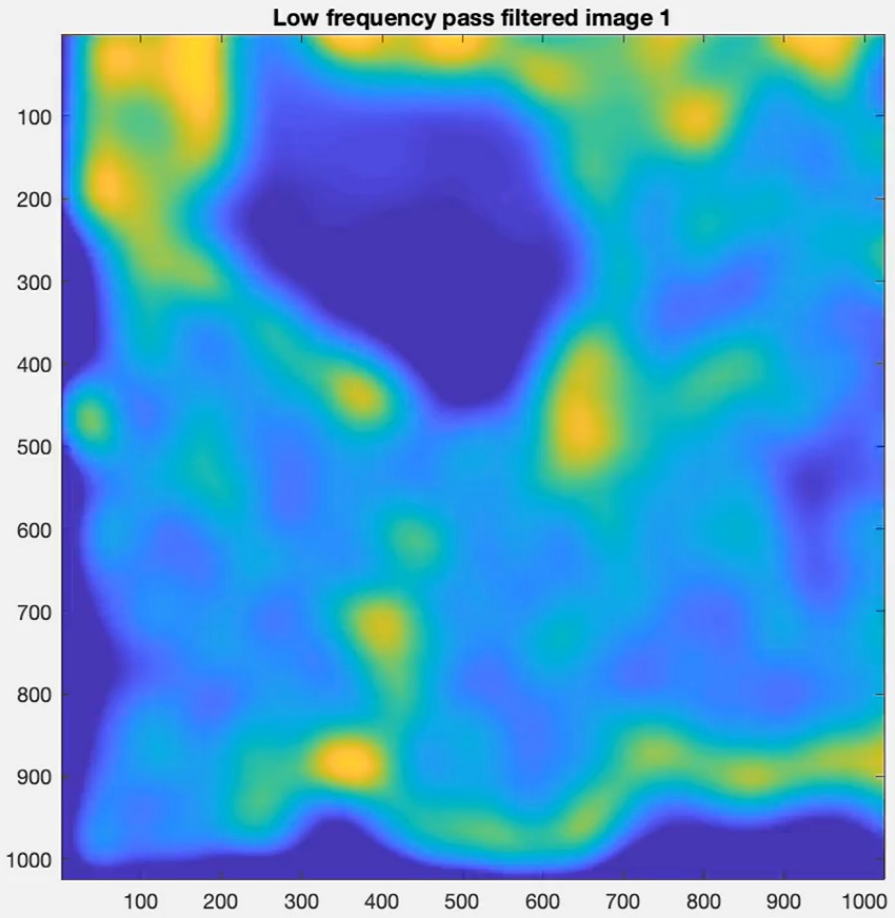
Nigar


0
75
150
225
300 µm
MDCK_16.05.2024
Well A2 - Position 01
No: 137
Date: 5/16/2024 10:53:20 PM
Channel: Holographic (x20)
Size: 567x567 µm
16
11
6.1
1.2
-3.7
-8.6 µm


0
75
150
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300 µm
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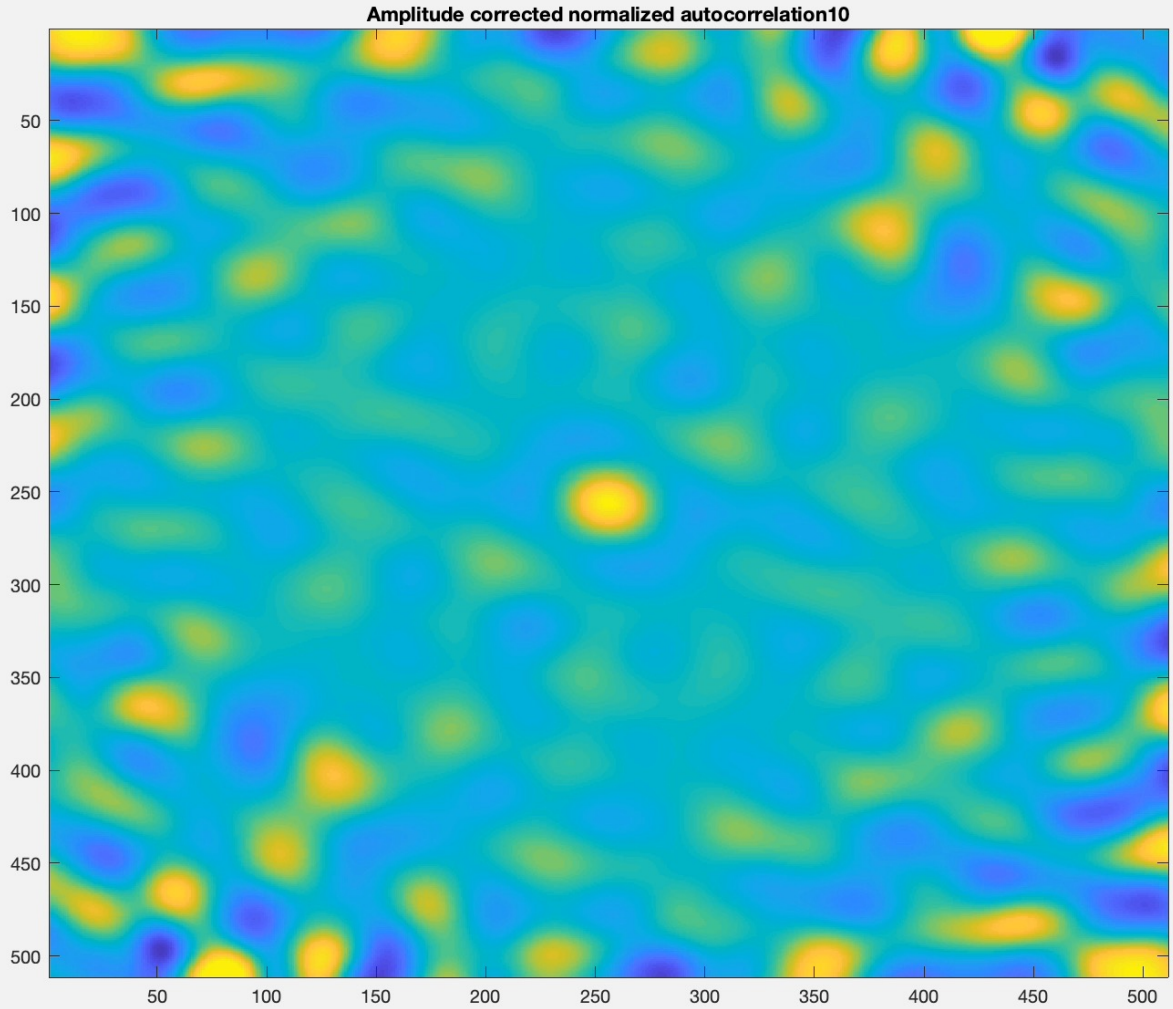
Epithelial dynamics:
Neighbor exchanges & density waves





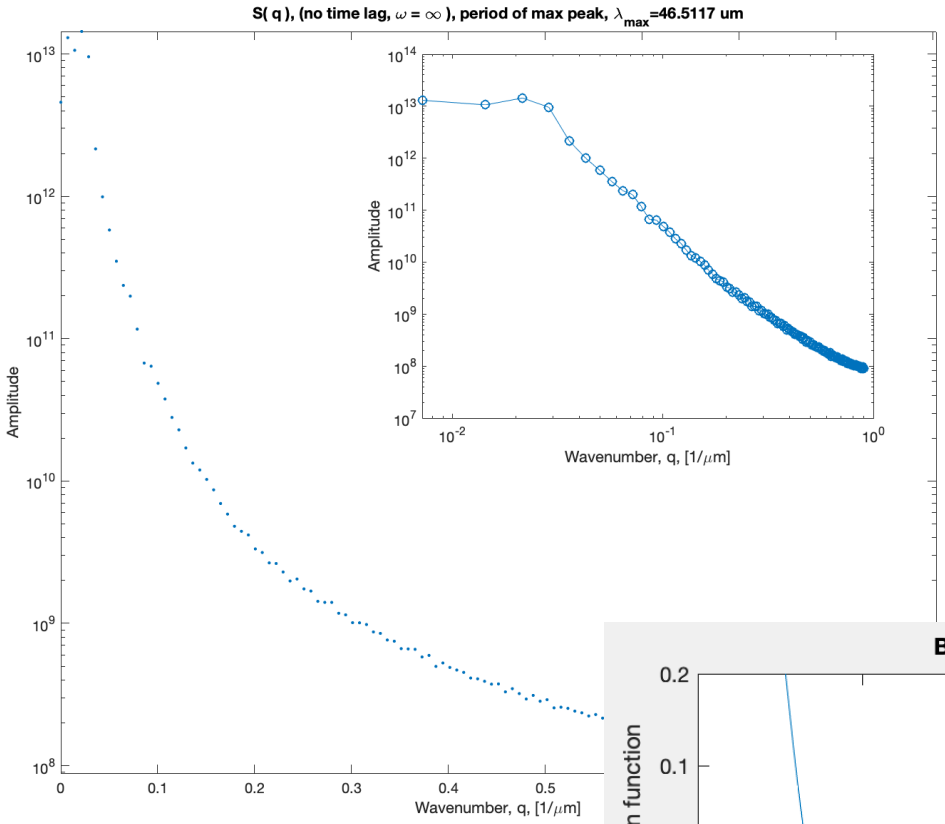
Nigar

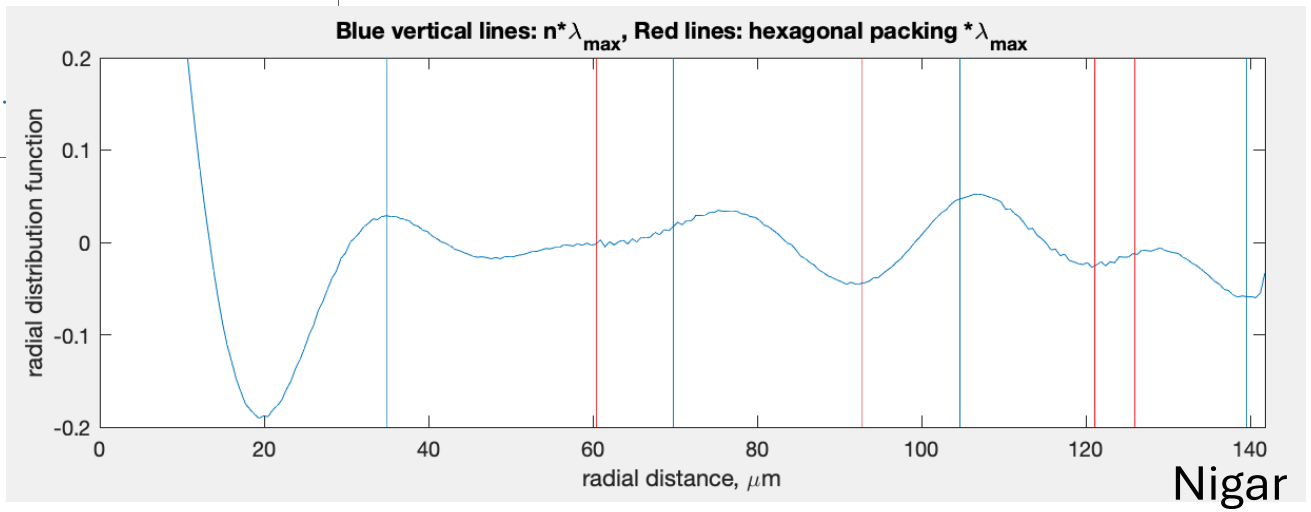
Epithelial dynamics:
Liquid or crystalline structure?



Nigar

Epithelial dynamics:
Liquid or crystalline structure?



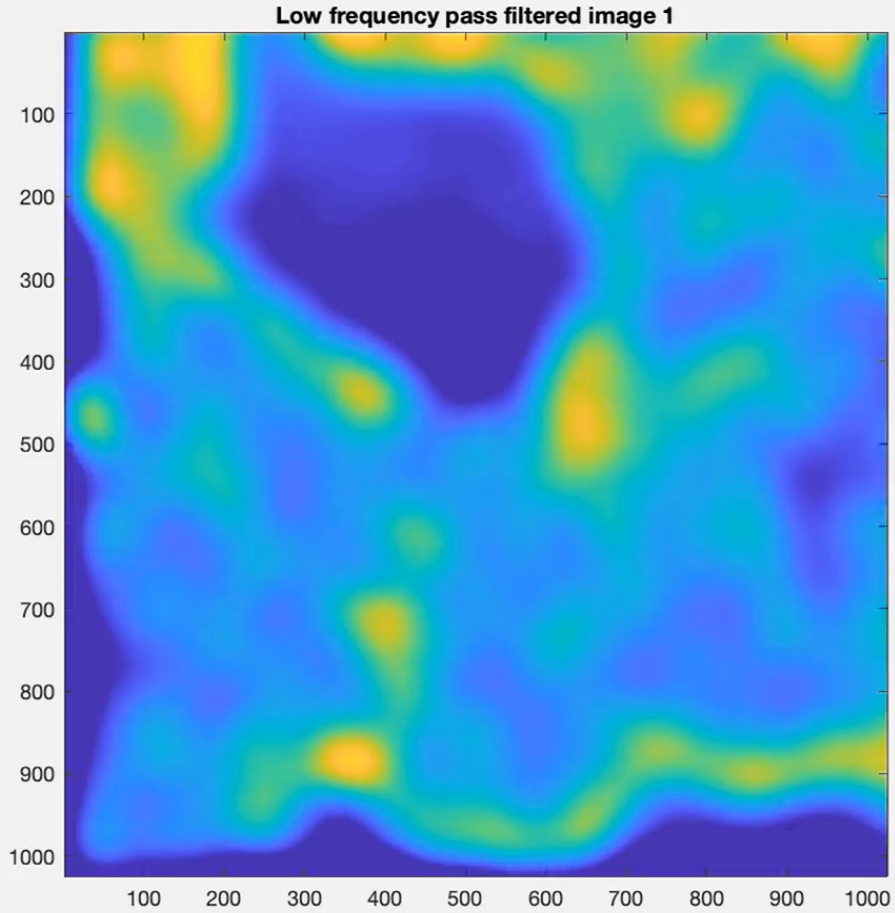


Nigar

Epithelial dynamics:

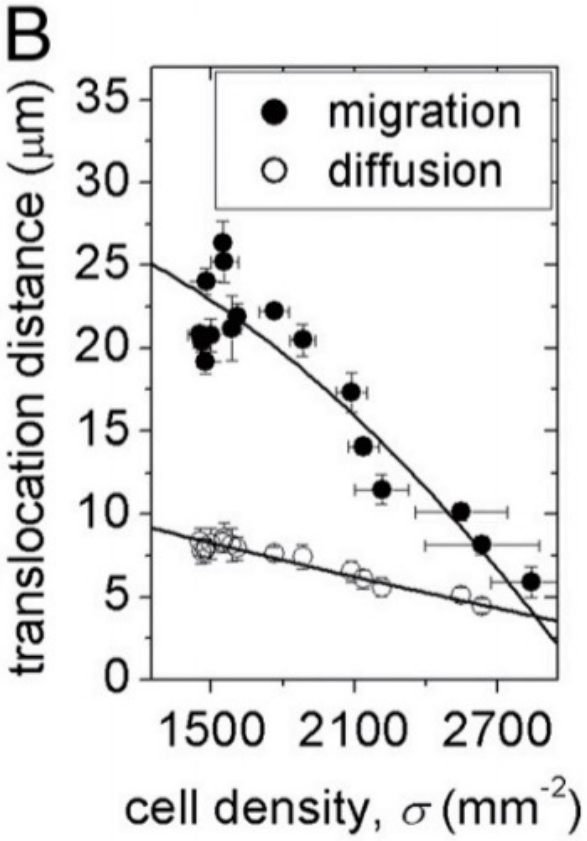
collective velocities, activity (kT) & structure





Silja, Richard, Thomas

Epithelial dynamics:
Glass transition?



dx.doi.org:10.1073/pnas.1010059108

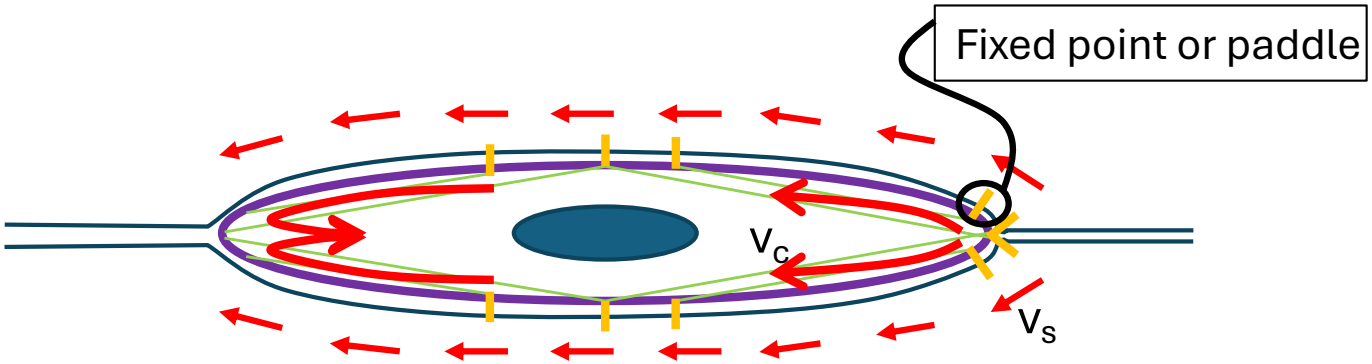
Glass transition at constant kT ?
Or activity in cells ($\propto kT$) reduced due to density?

Repeating with
- QPI (extra information from $h(x, y, t)$)
- MDCK (standard epithelial model)
- HaCaT (activity can be controlled independently)

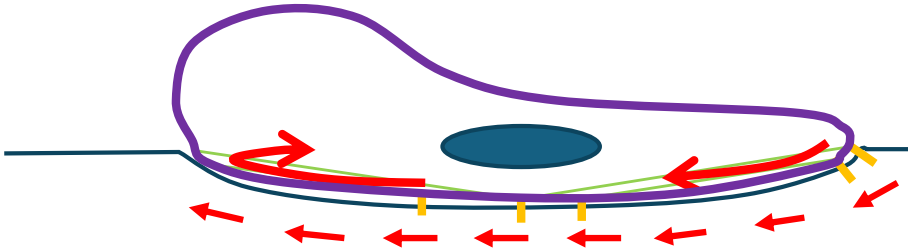
We know that tissue can switch between fluid and glass like states. Mechanical and chemical triggers.

Active material: acto-myosin

In ECM

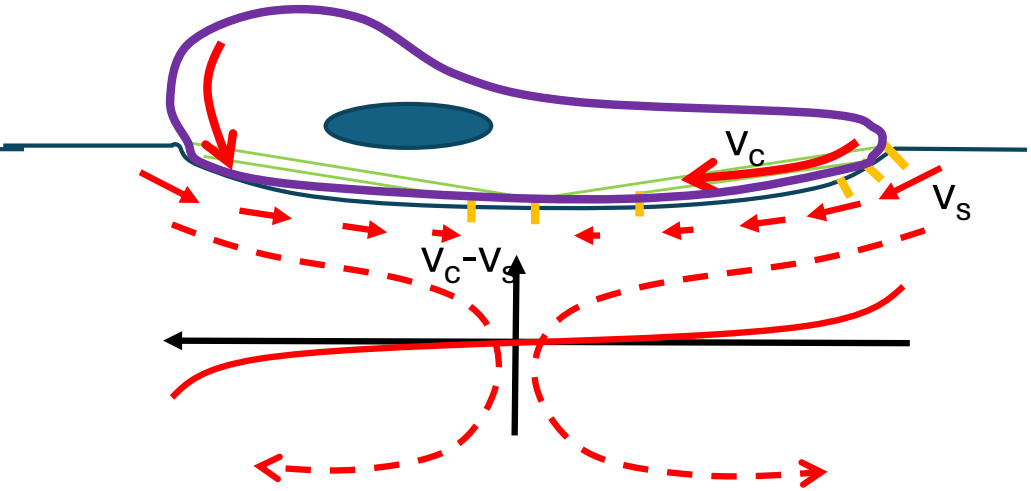


On substrate



Fixed anchors + treadmilling

Friction/viscosity mediated propulsion

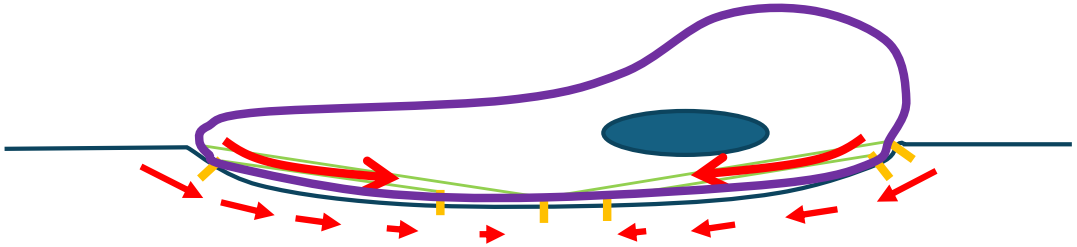


Flow in viscous media

Silja

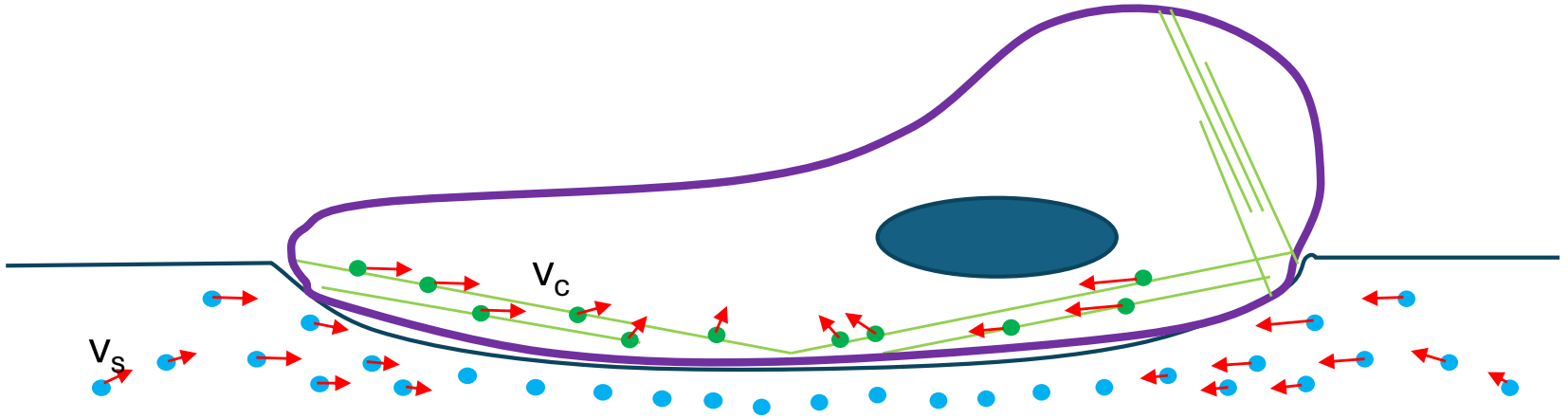
Actin flow + friction = motion

Idea



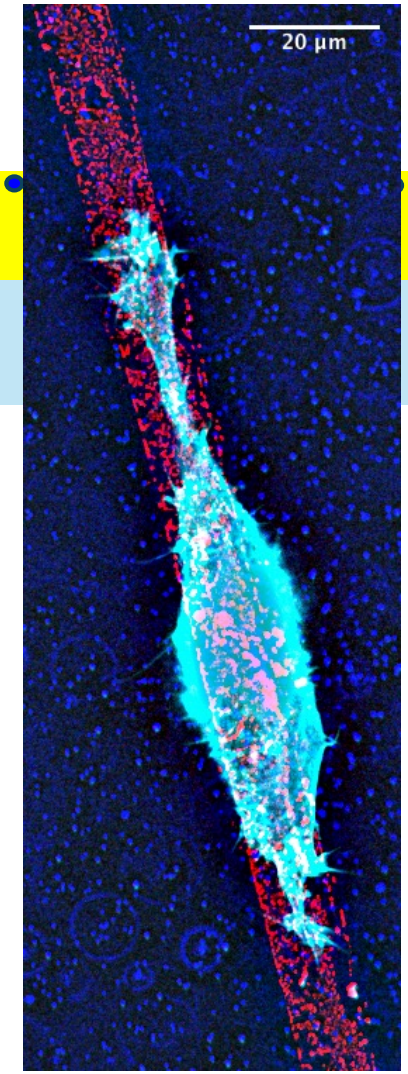
Concept of realization:

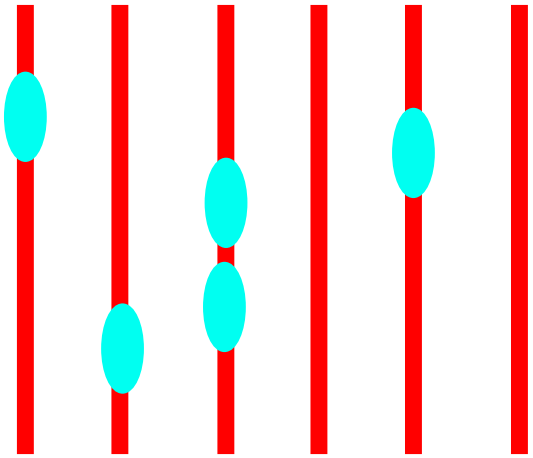
- Structure in cytoskeleton and substrate
  - Actin speckle
  - Fluorescent beads in gel
- Velocity of structures quantified by image correlation => relative motion $(v_c\text{-}v_s)$
- Absolute displacement of beads to determine force F
- Friction: $F = \zeta(v_c - v_s)$



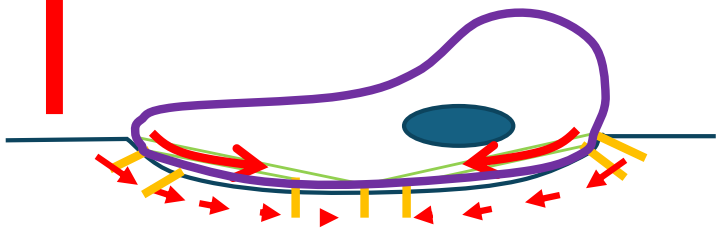
Migration of GFP actin stained cells on fibronectin lines







Anchoring cell,
look for relative
motion + friction…



Silja

Bone generation