The mathematics of biological self-organization

a journey across disciplines, spatial scales and countries

Giulia Laura Celora

Wolfson Centre For Mathematical Biology

Mathematical Institute, Oxford

PiWorks Seminar Series

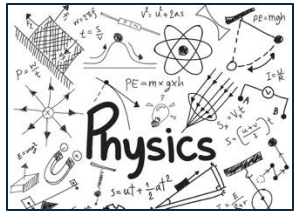
April 2025

Oxford Mathematics

Wolfson Centre for Mathematical Biology

MATHEMATICAL INSTITUTE

BSc in Mathematical Engineering (Milan)



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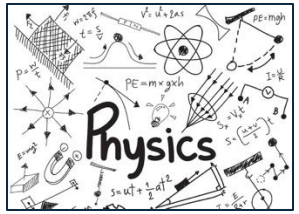
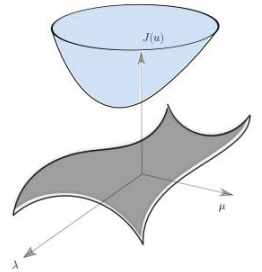


MSc in Applied Mathematics (Oxford)



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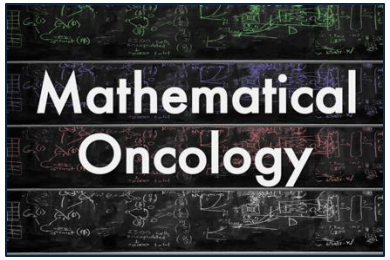

Research Fellow (UCL)

Hooke Research Fellow (Oxford)

Oxford, UK

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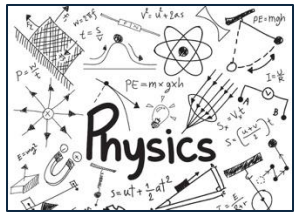

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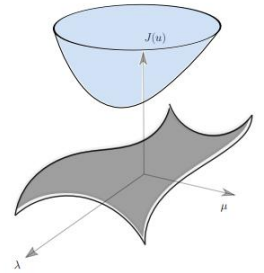

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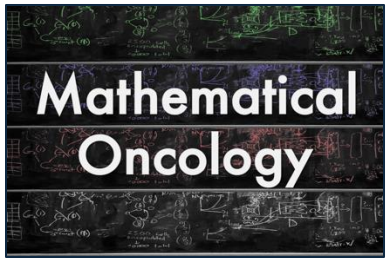

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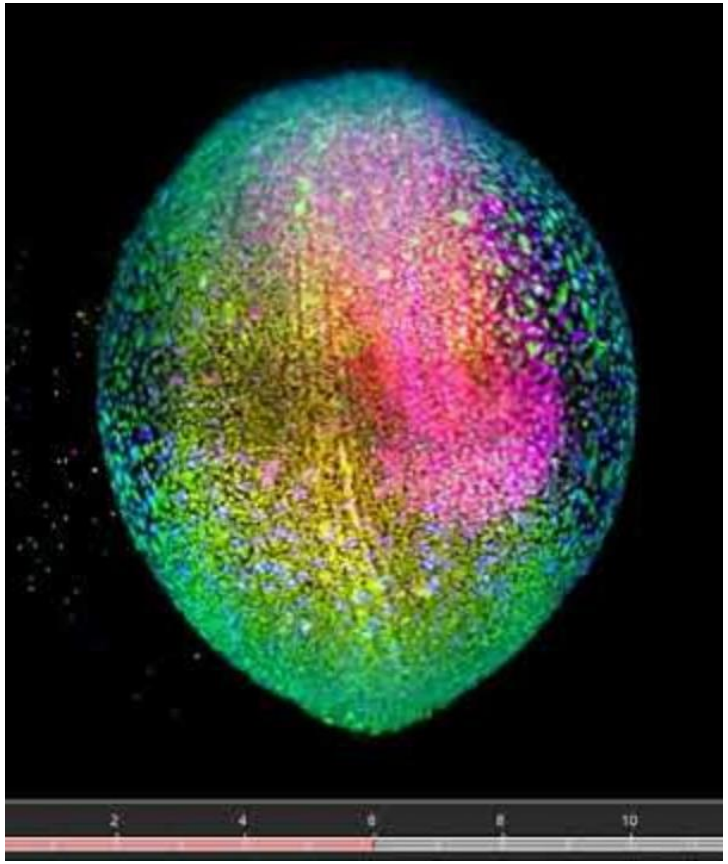
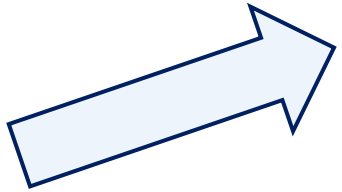
Veiled chameleon, QuantaMagazine

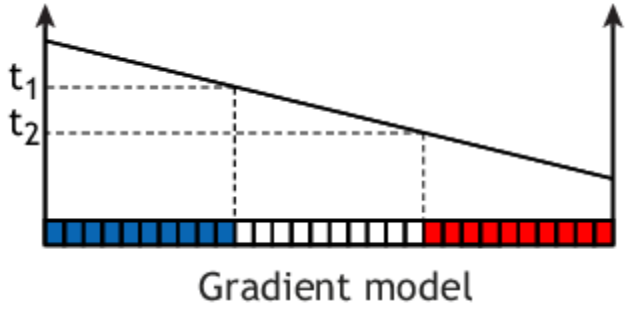


Zebrafish development. Gopi Shah, MPI of Molecular Cell Biology and Genetics

Self-organisation in biology

French Flag Problem





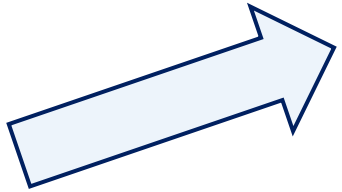
Gradient model

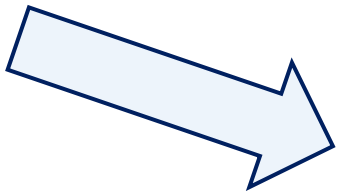
positional information

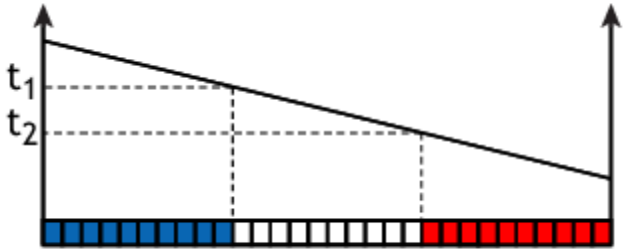
$$\mathcal{O}(\text{input}) \geq \mathcal{O}(\text{output})$$

Self-organisation in biology

French Flag Problem







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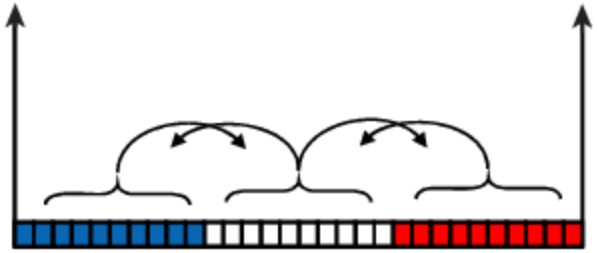

Balancing model

self-organization

Self-organisation in biology

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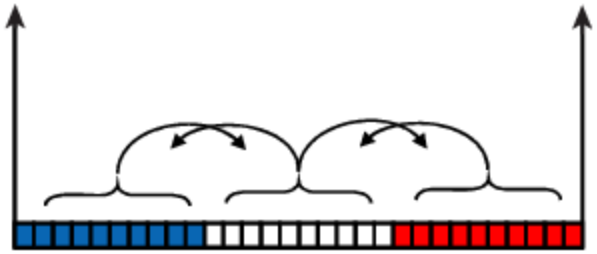


Balancing model

self-organization

“Mathematics is the science of patterns, and nature exploits just about every pattern that there is”

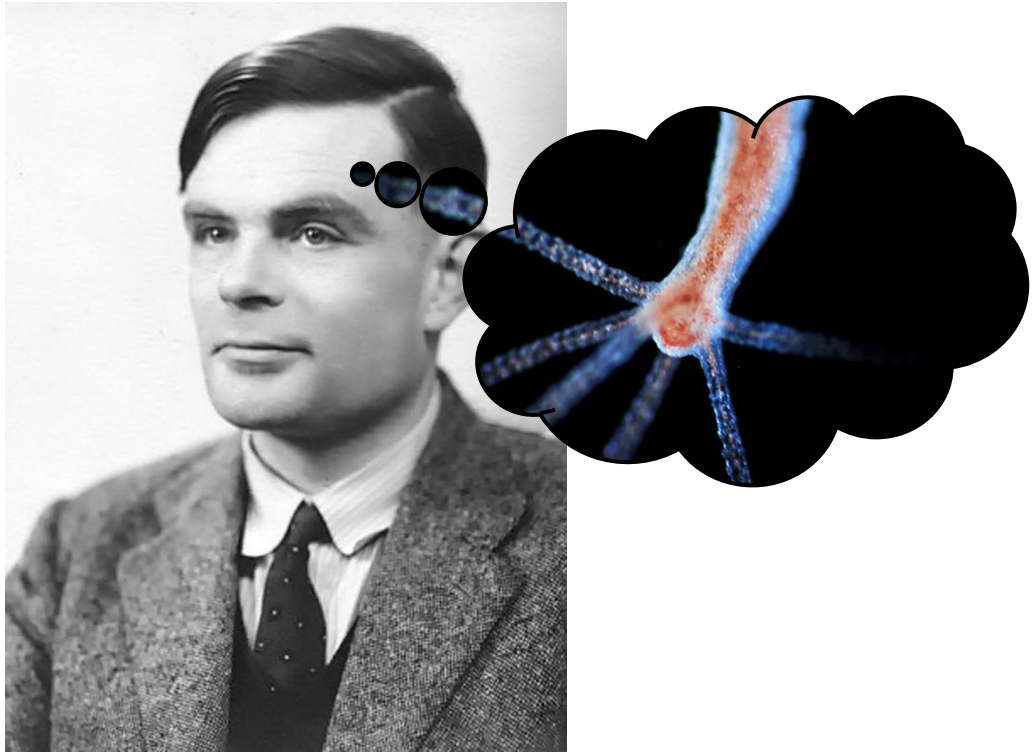
Ian Stewart

Self-organisation in biology

Non-linear dynamics

Pattern Formation

Partial Differential Equations



THE CHEMICAL BASIS OF MORPHOGENESIS

By A. M. TURING, F.R.S. *University of Manchester*

(*Received* 9 *November* 1951—*Revised* 15 *March* 1952)

$$\frac{\partial X}{\partial t} = a(X-h) + b(Y-k) + \mu' \nabla^2 X,$$

$$\frac{\partial Y}{\partial t} = c(X-h) + d(Y-k) + \nu' \nabla^2 Y.$$

chemical interactions

movement

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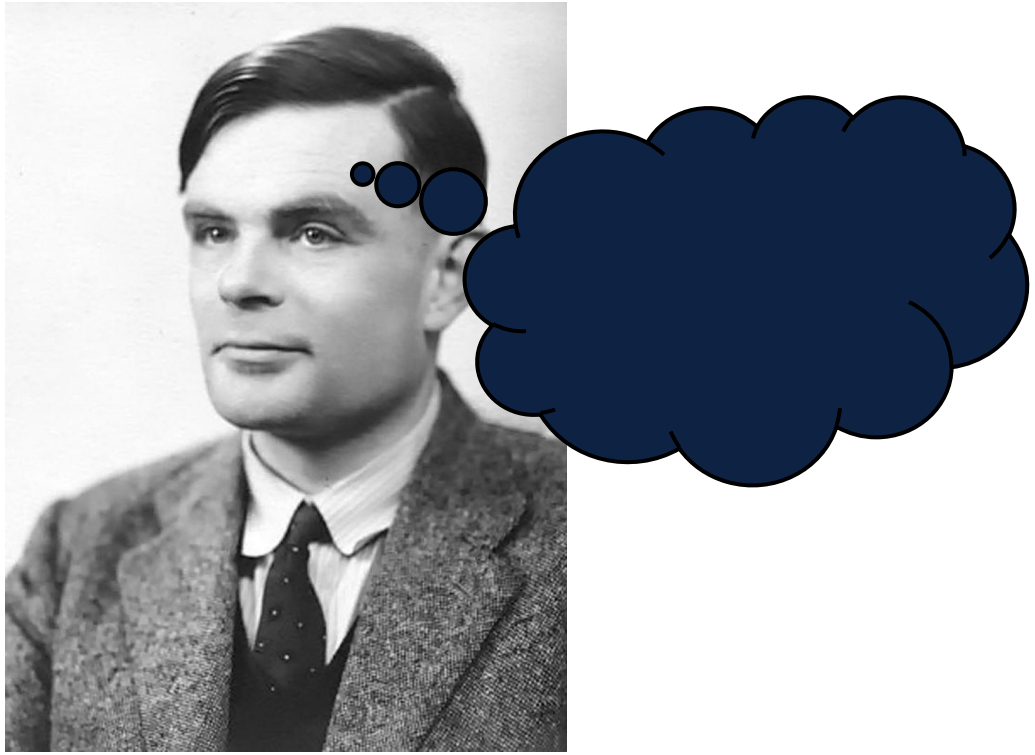

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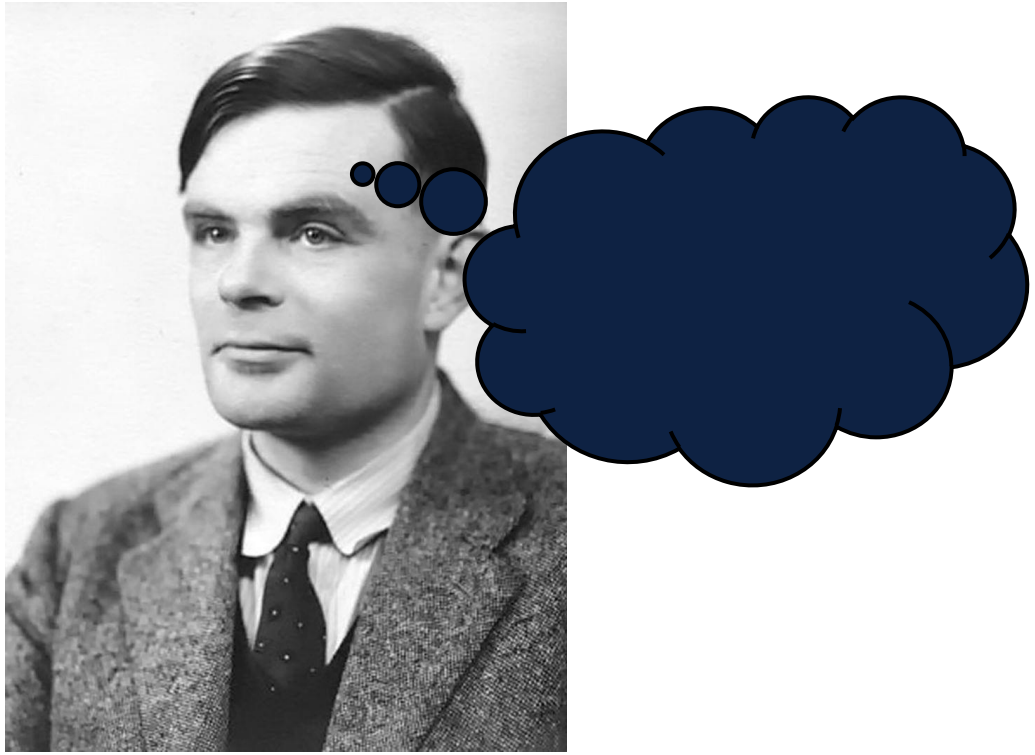

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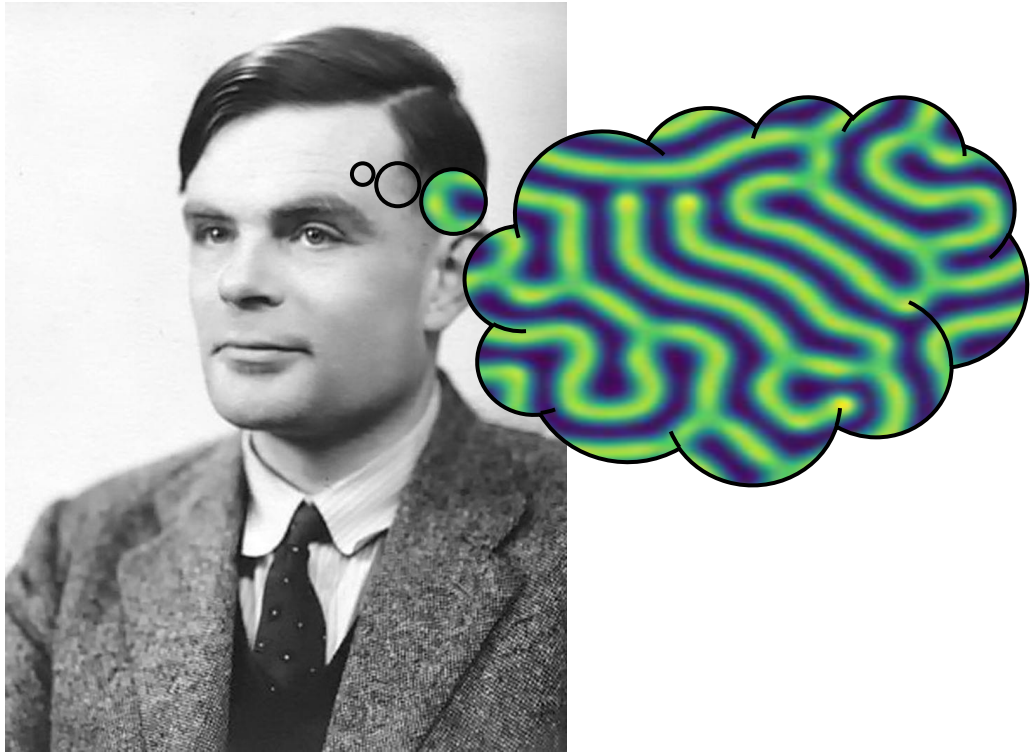

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diffusion-driven instabilities

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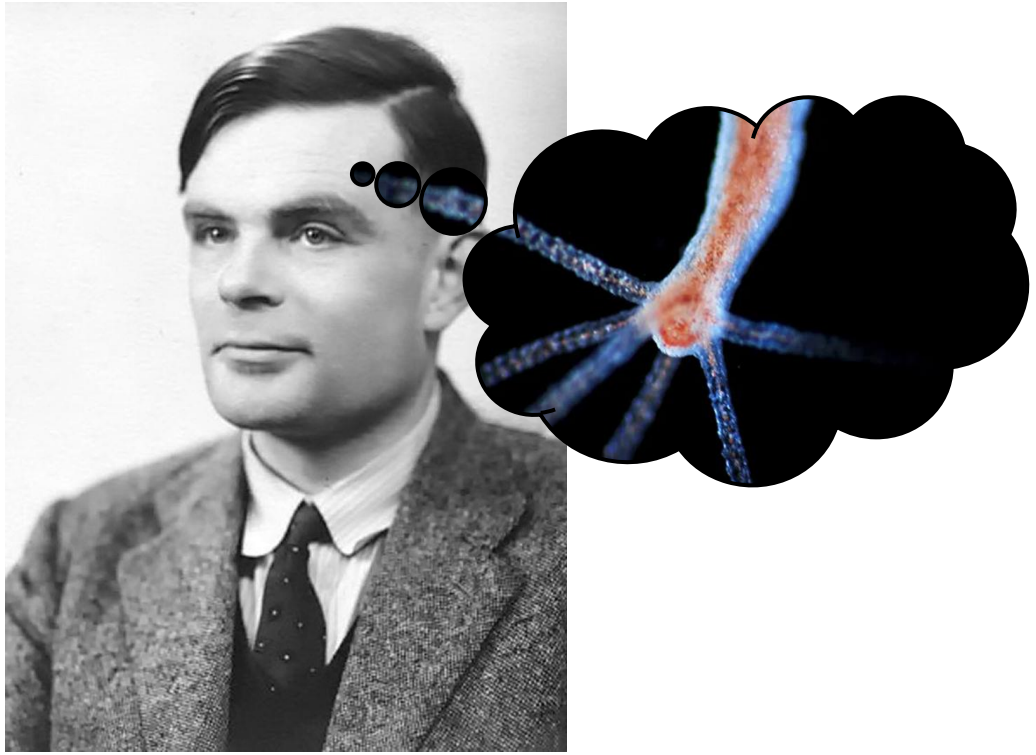

70 years

Self-organisation in biology

Non-linear dynamics

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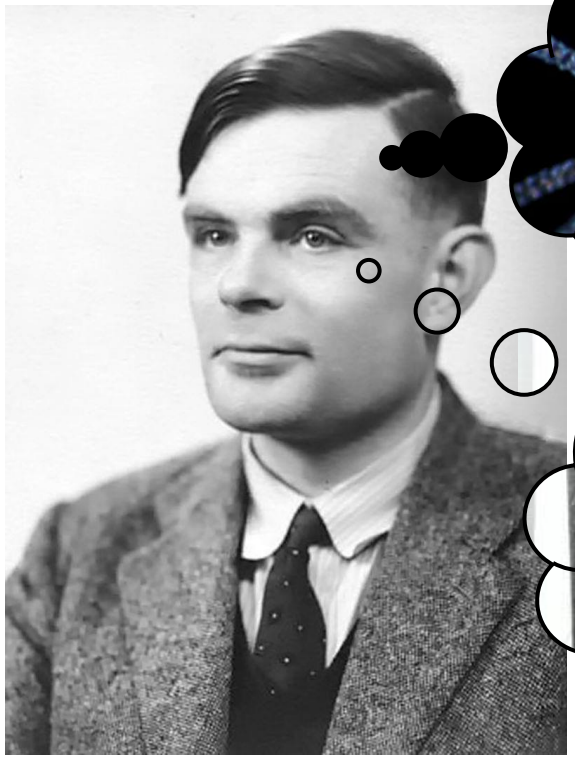
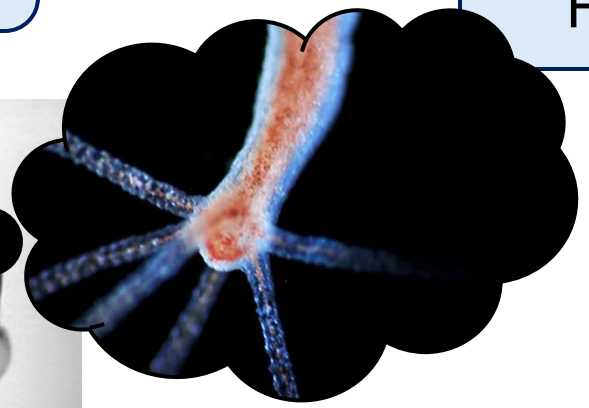
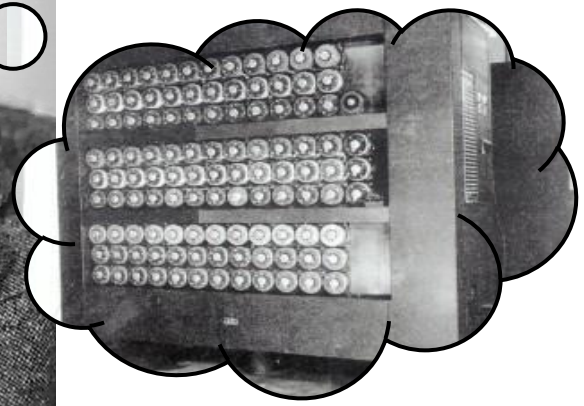
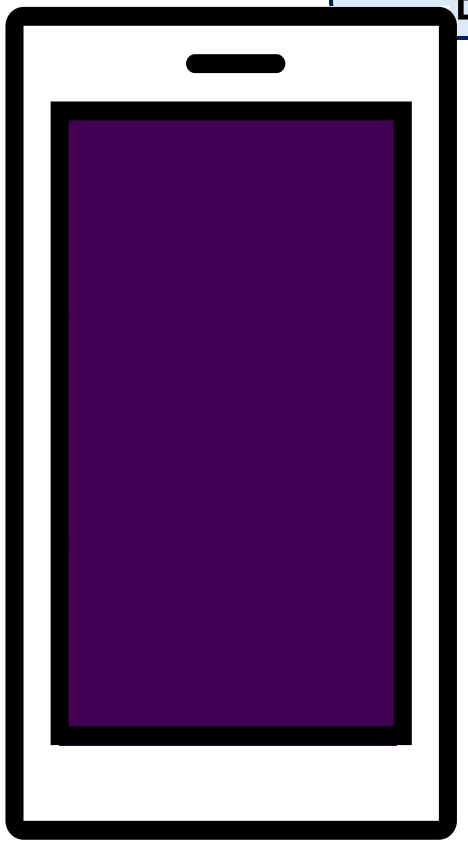
Partial Differential Equations







70 years



Self-organisation in biology

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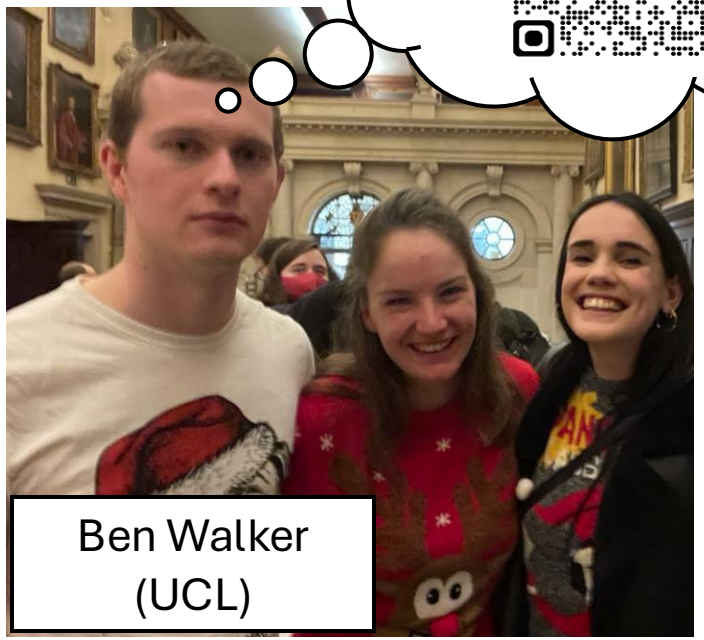
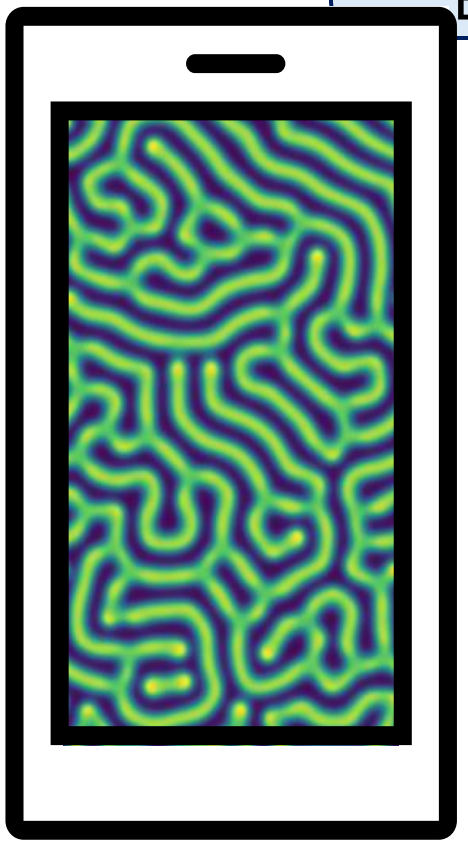
Visual PDE

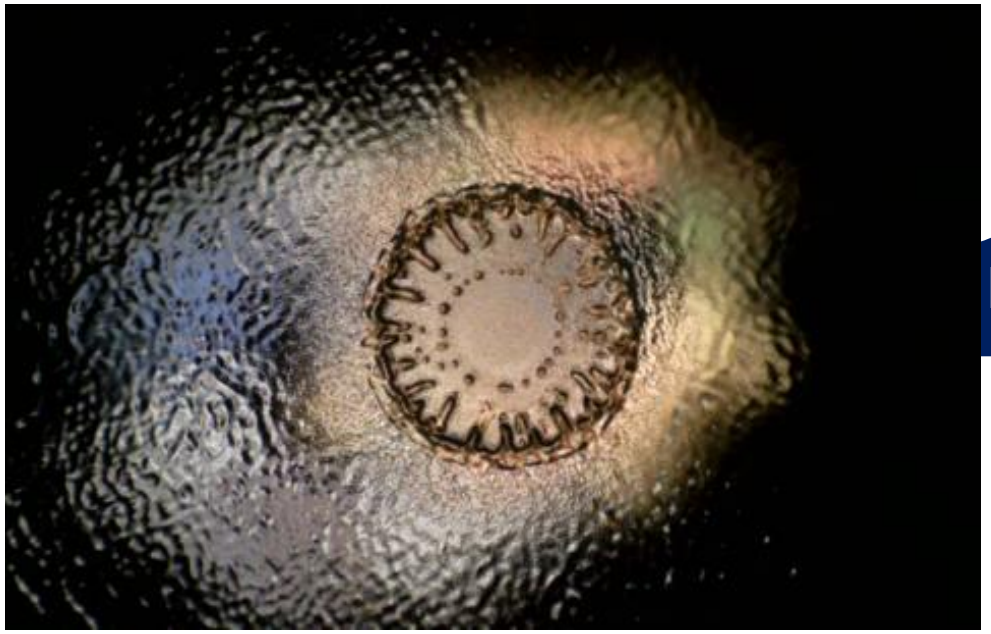


Ben Walker (UCL)

Andrew Krause (Durham)

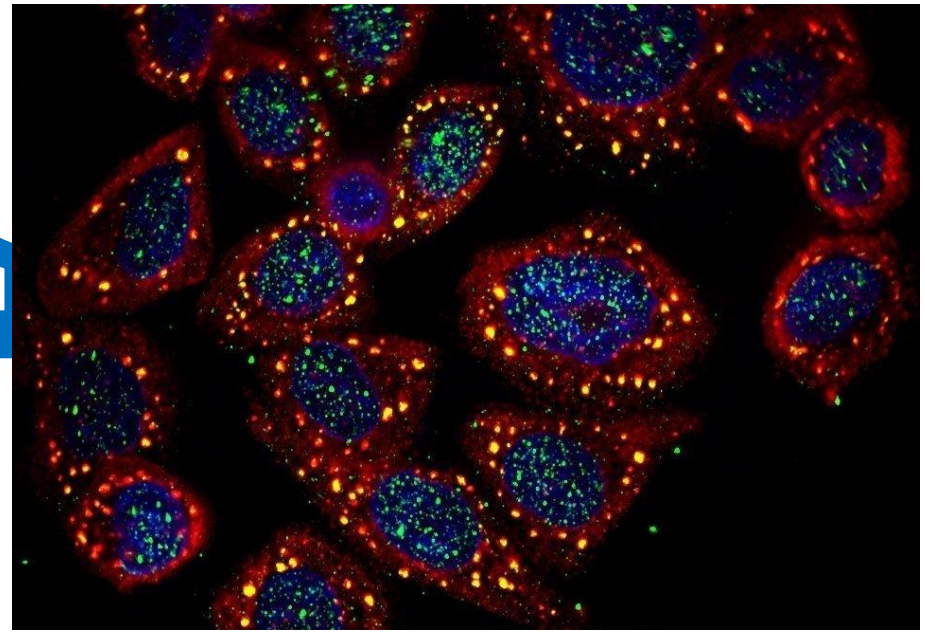


STORY 1: **Patterning in migration of multicellular communities**



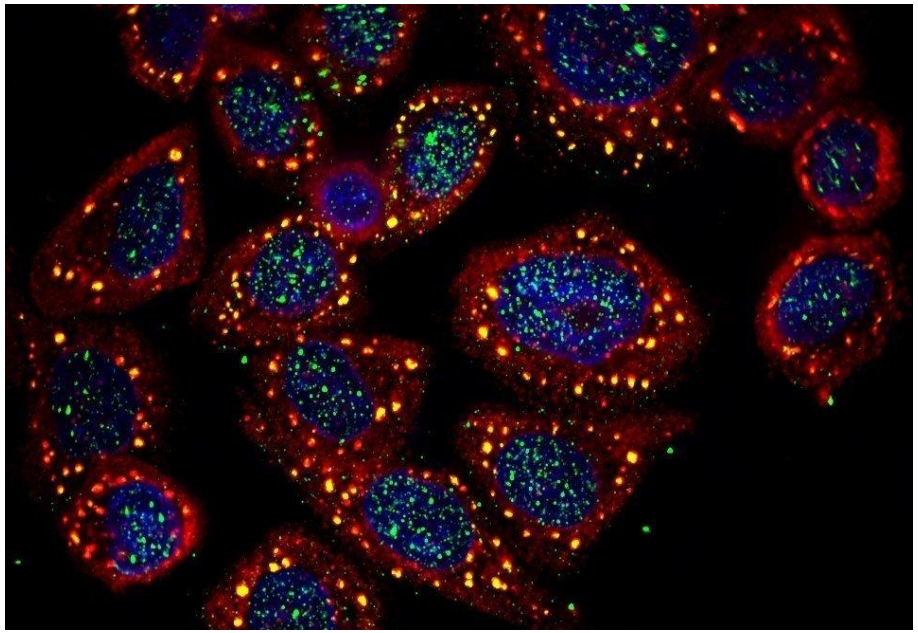
from VisualPDE

STORY 2: **Patterning of the intracellular space**



STORY 1: **Patterning in migration of multicellular communities**

STORY 2: **Patterning of the intracellular space**



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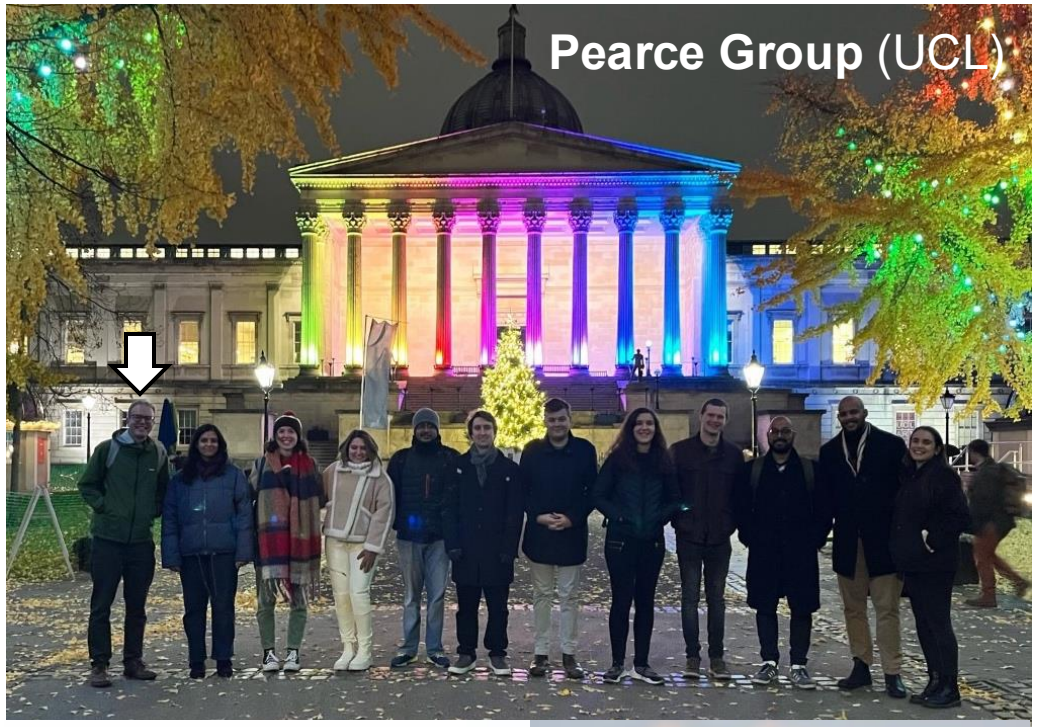
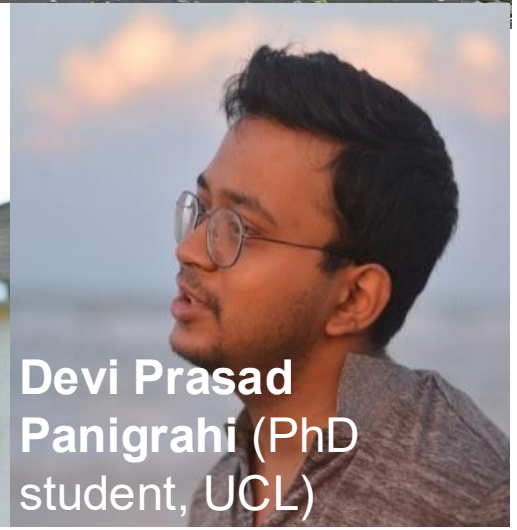
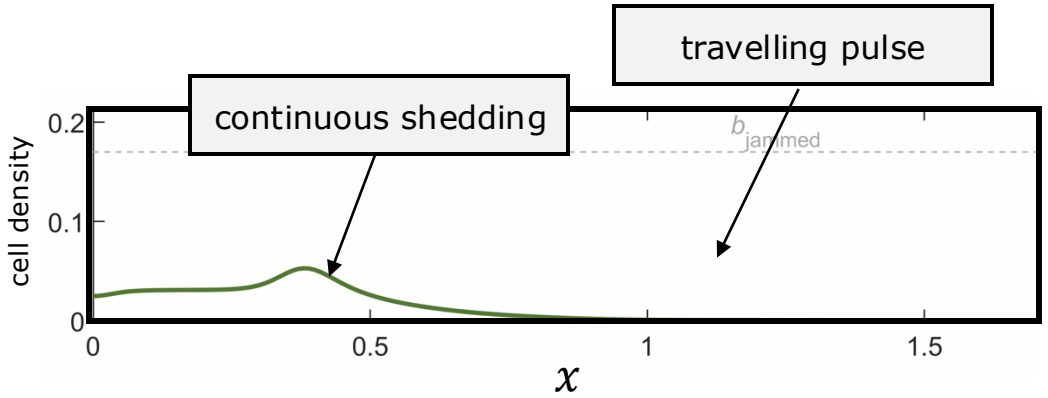


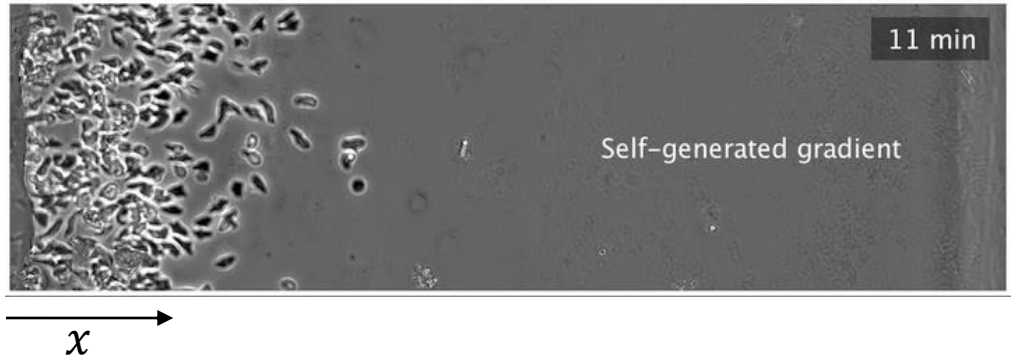


Motivation

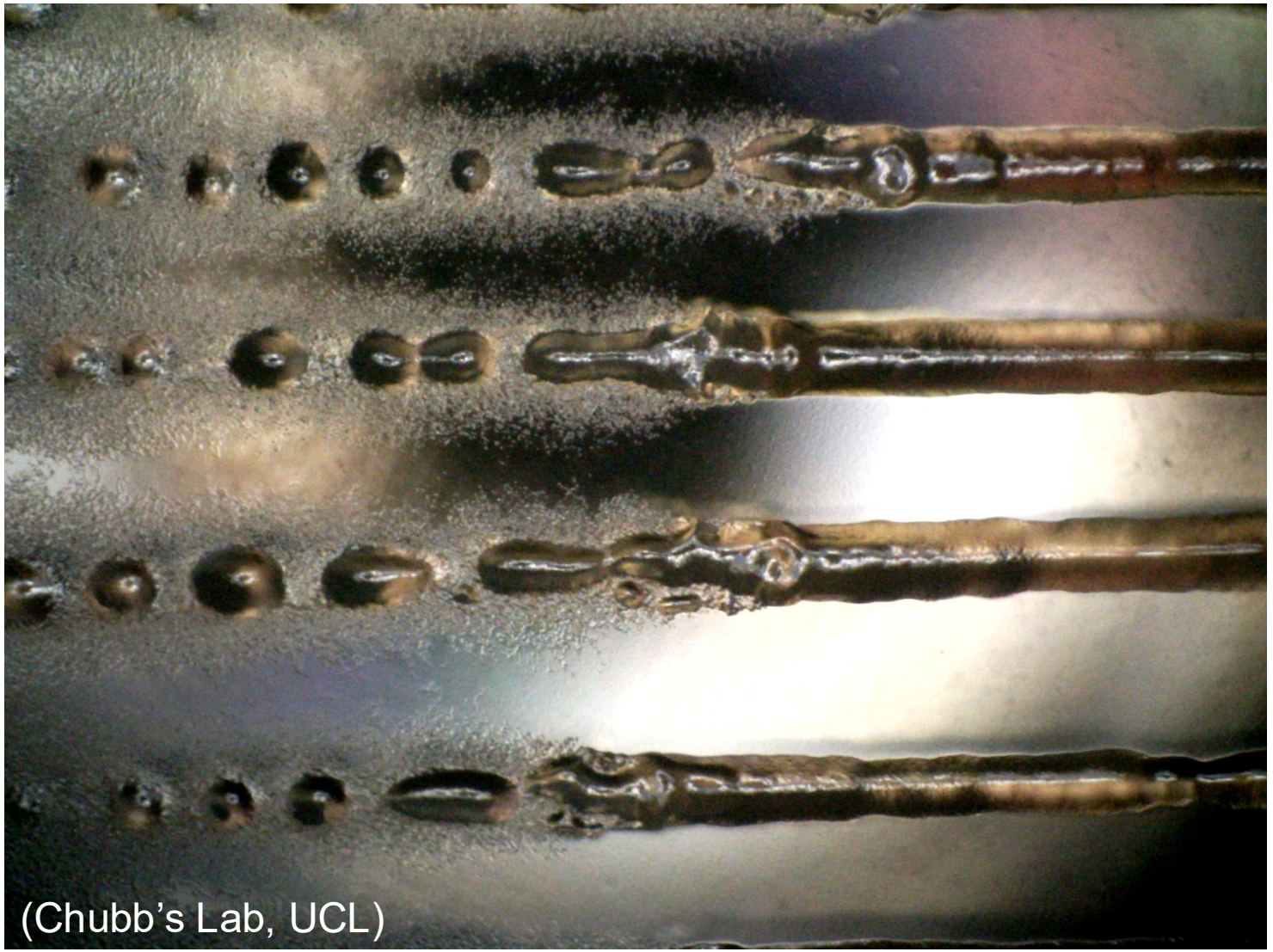
- Directed cell migration up chemical signals (i.e., chemotaxis) is a fundamental process in biological systems, e.g., in development and cancer invasion.

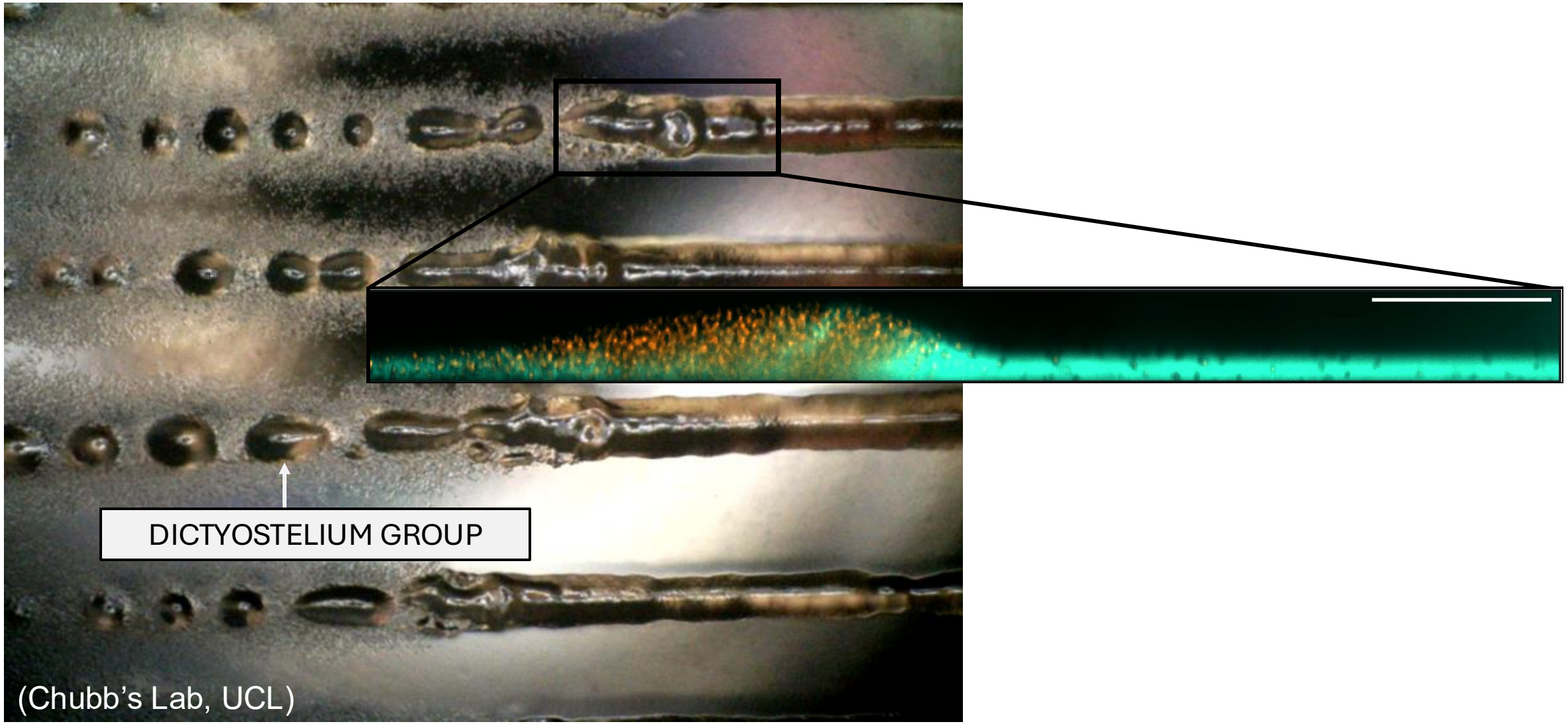
- Our current theoretical understanding of the self-organization of multicellular communities during chemotaxis is based on the Keller-Segel model (1970s).

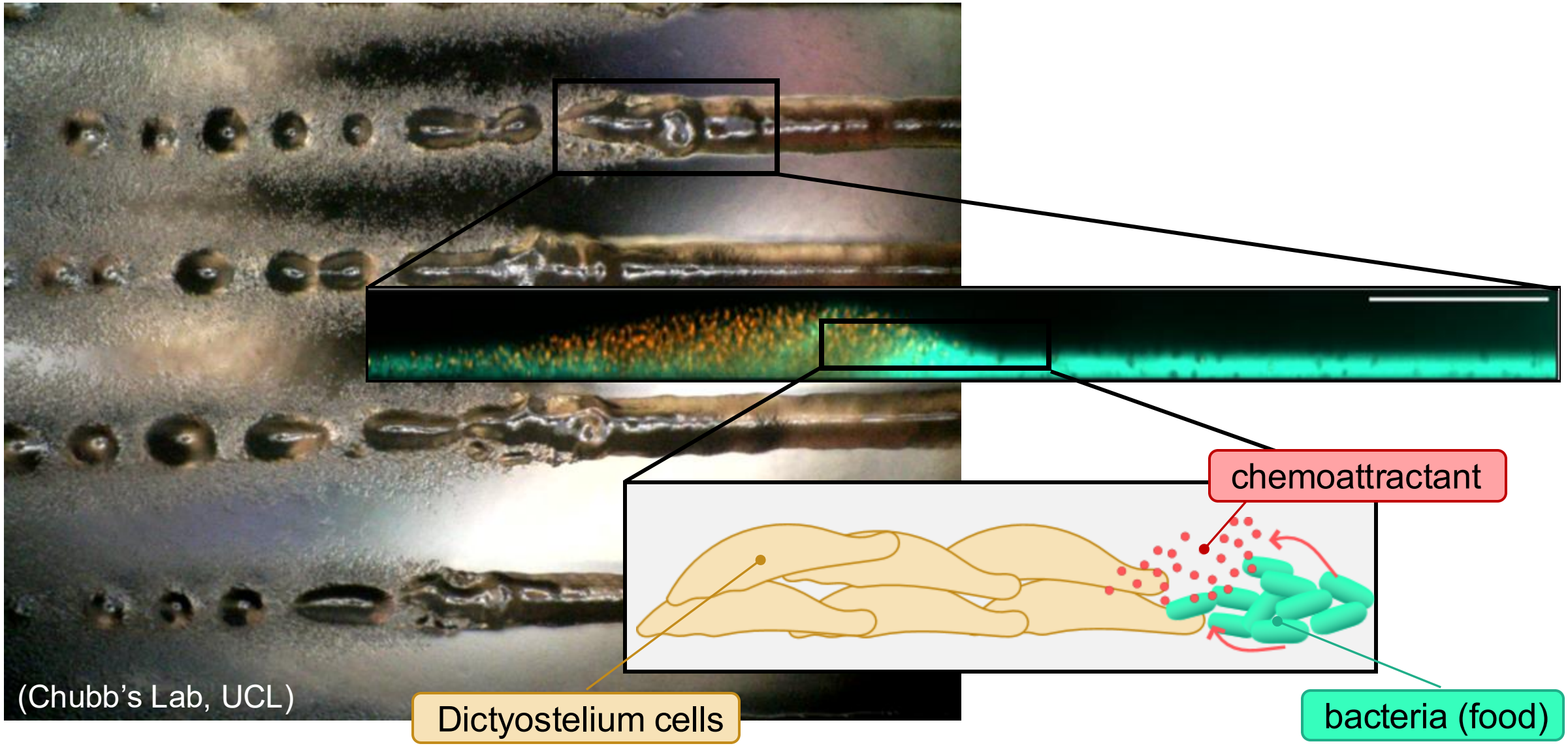




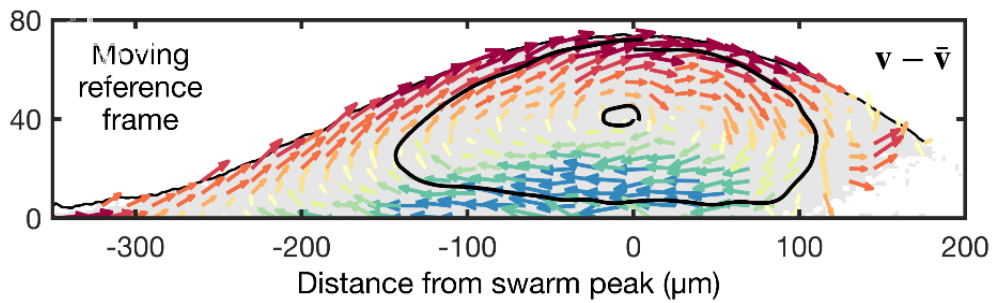
(left) solution of the Keller-Segel model with proliferation (Amchin et al., PLoS Comput Bio., 2022); **(right)** Dictyostelium cells migration up self-generated gradients (Tweedy et al., Science, 2020);

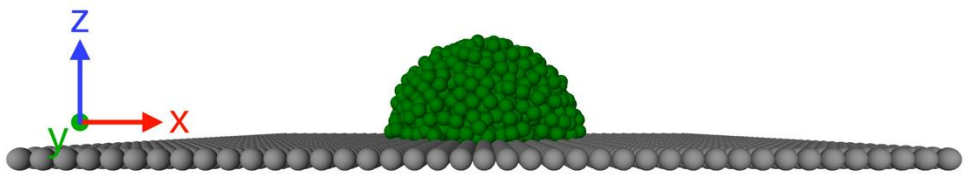

(Chubb’s Lab, UCL)


DICTYOSTELIUM GROUP
(Chubb's Lab, UCL)


chemoattractant
Dictyostelium cells
bacteria (food)
(Chubb's Lab, UCL)

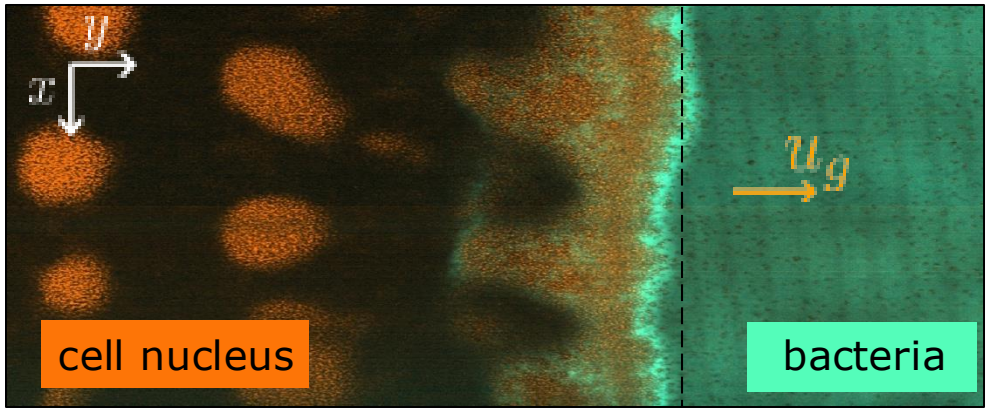
Q1: How do cell-level interactions give rise to the rheology of the swarm?





by Devi Prasad Panigrahi
(UCL PhD student co-supervised by Philip Pearce)

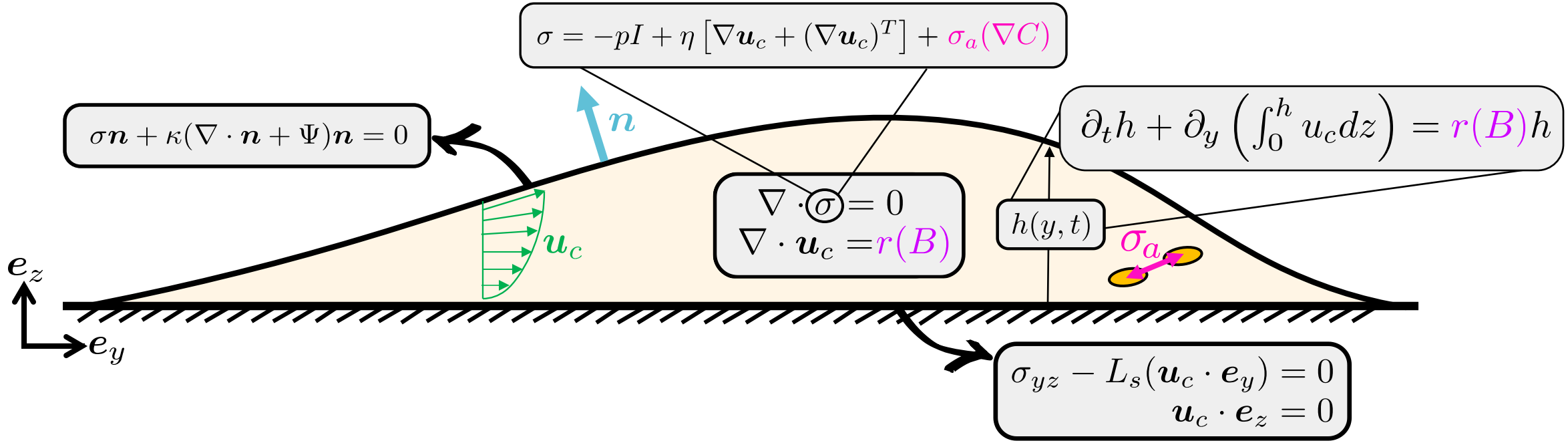
Q2: What mechanisms dictate the periodic shedding of groups?



Chemically-regulated hydrodynamic instability

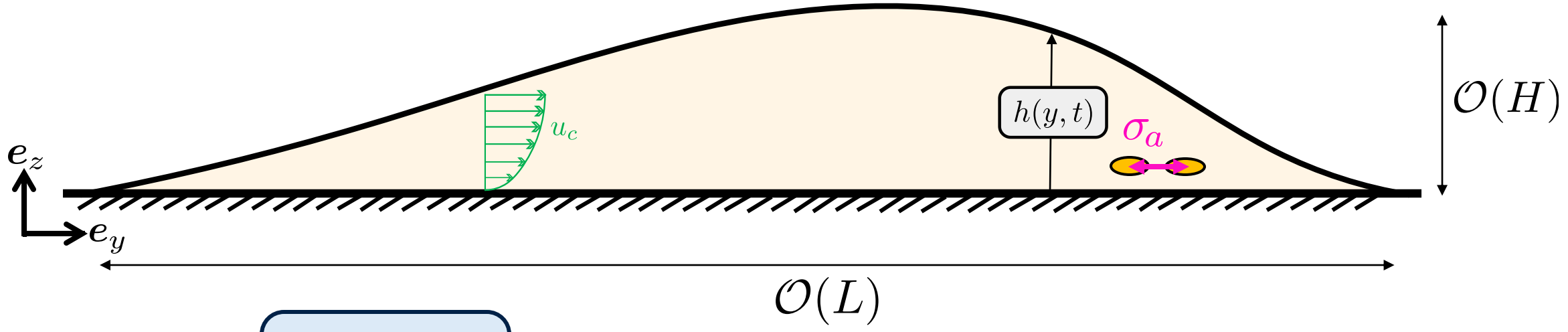
Ford, Celora et al., in press, PNAS

An active living viscous thin-film



Ford, Celora et al., bioRxiv (2024)

An active living viscous thin-film



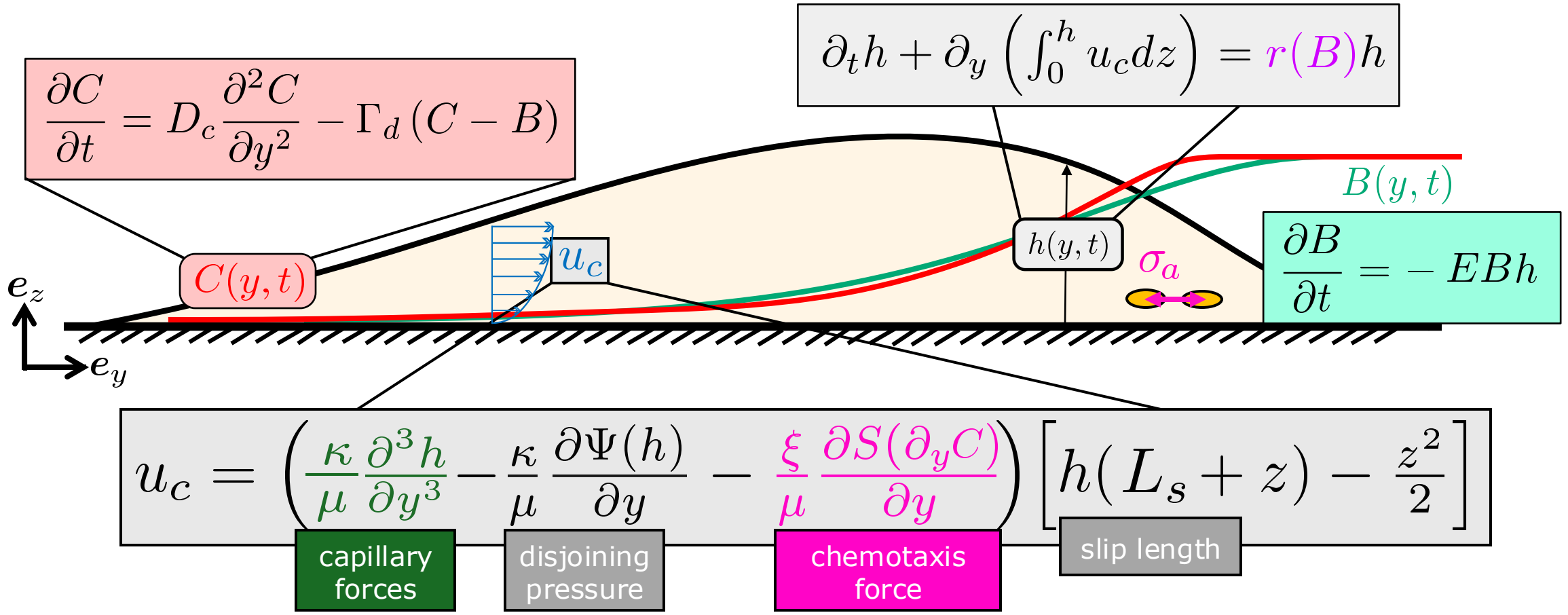
$$\epsilon = \frac{H}{L} \ll 1$$

lubrication approximation

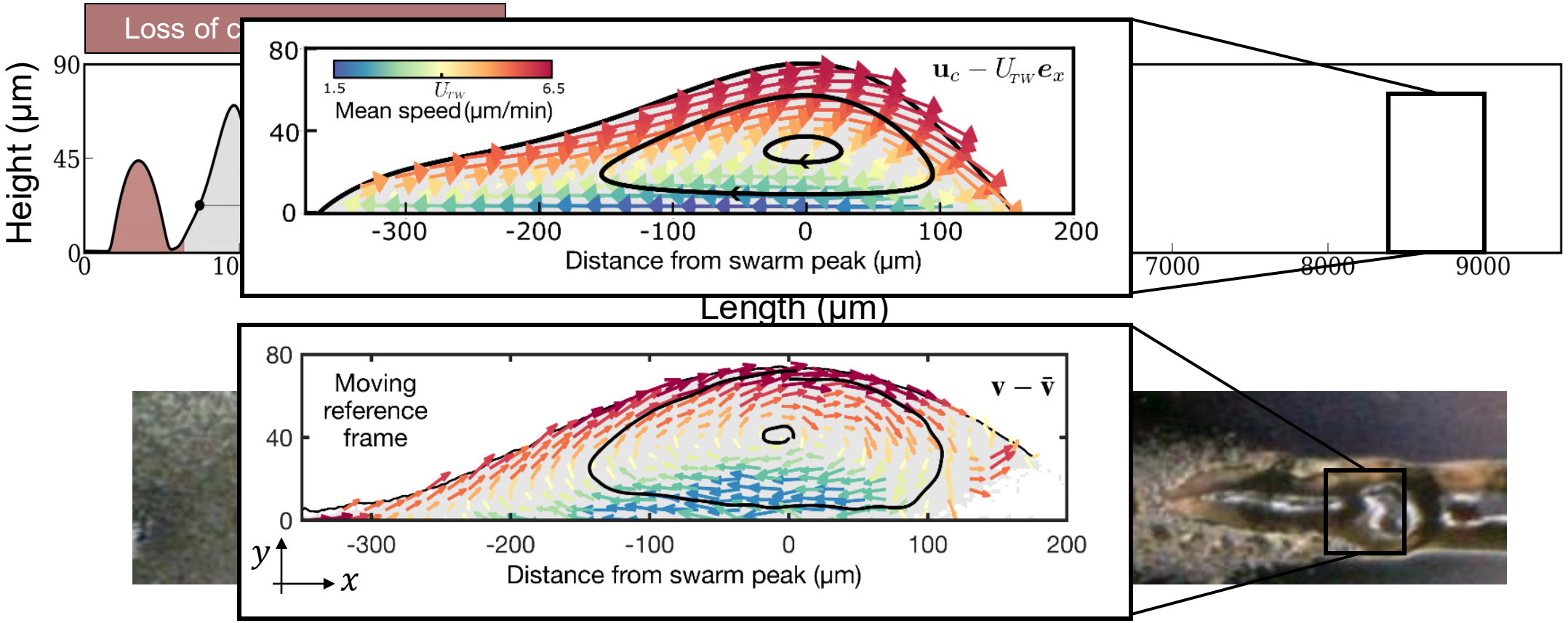
PSEUDO-2D model

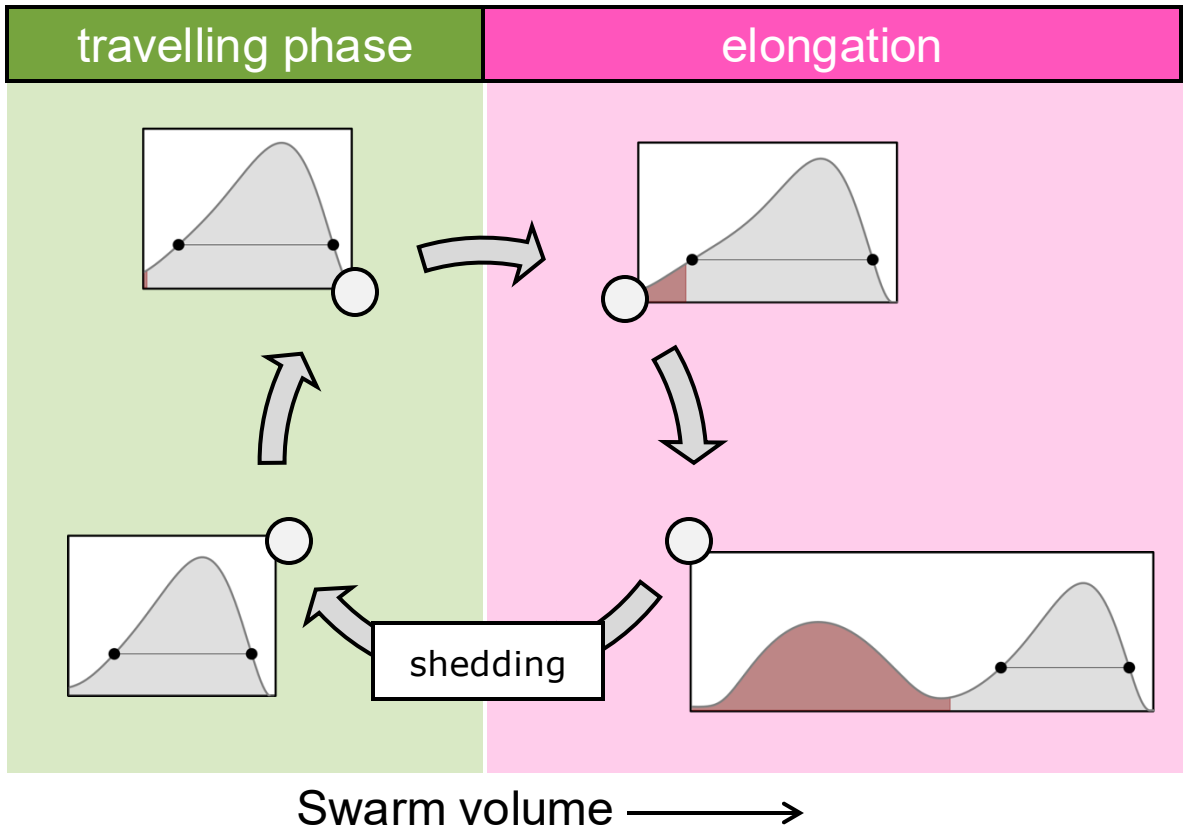
Ford, Celora et al., bioRxiv (2024)

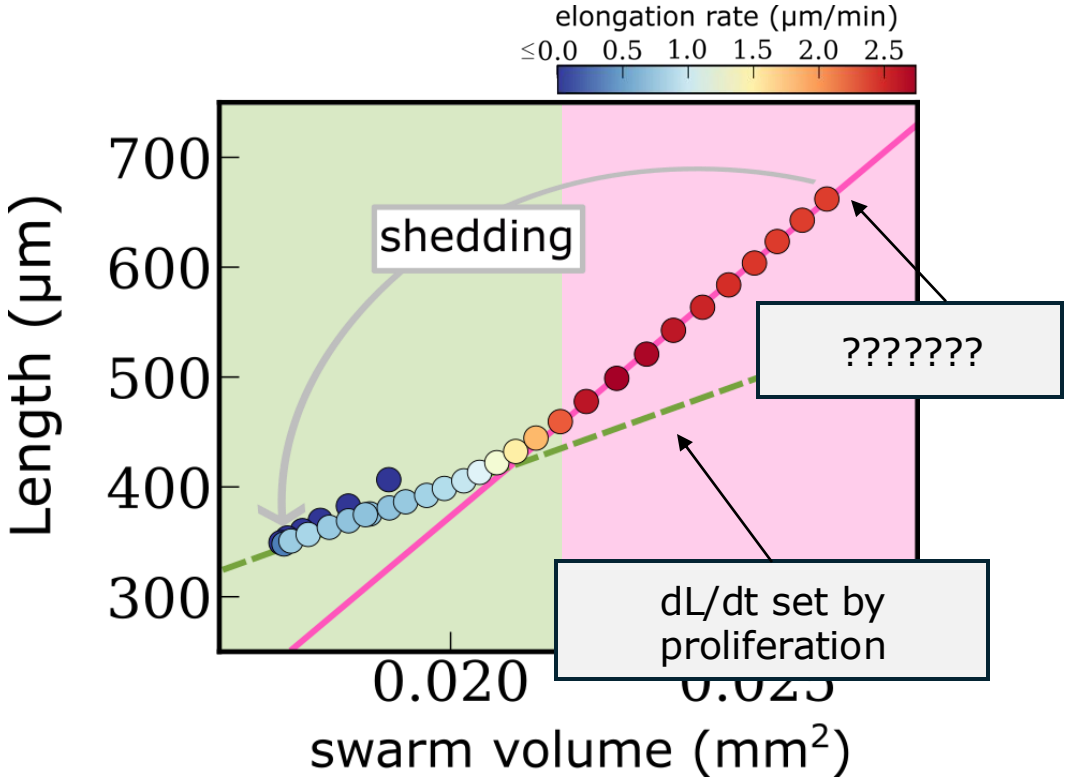
An active living viscous thin-film

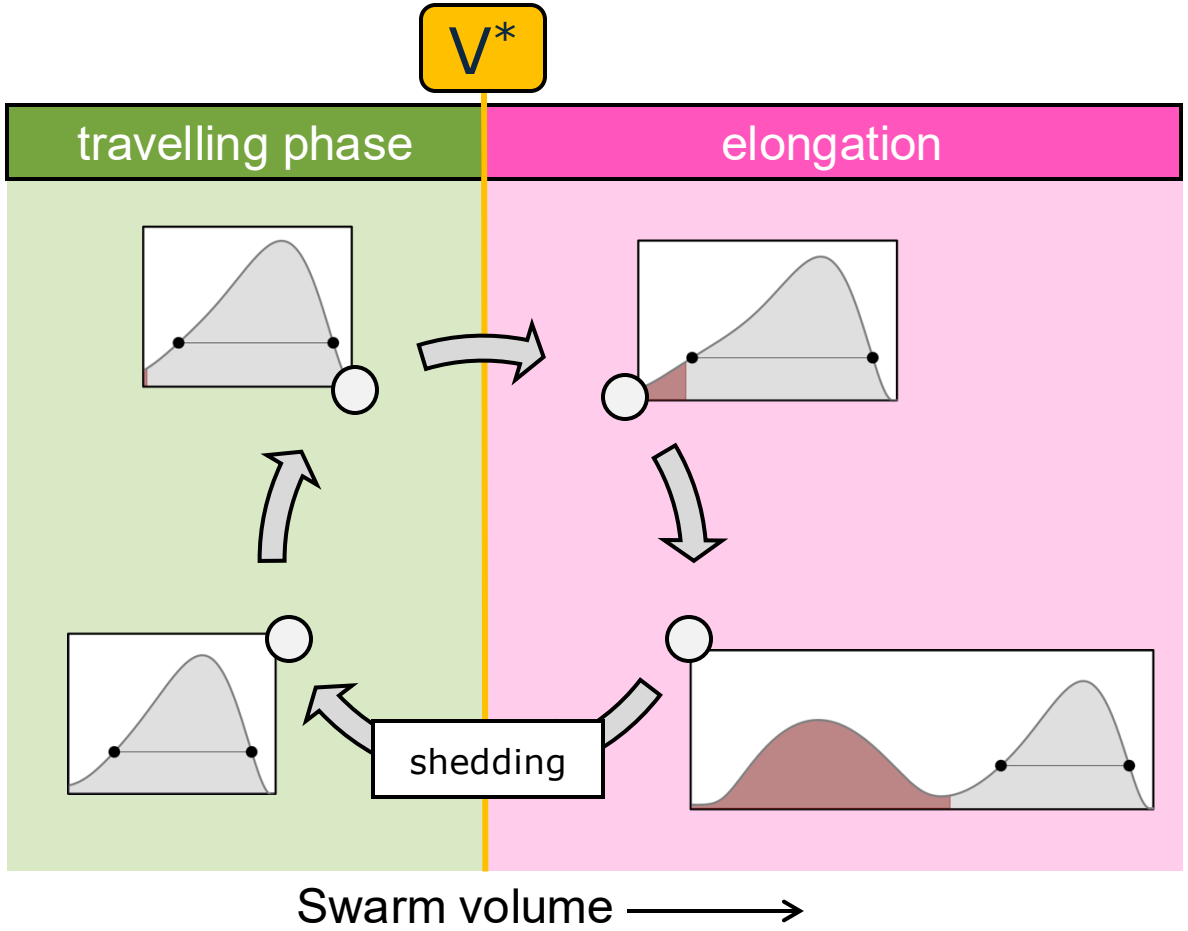


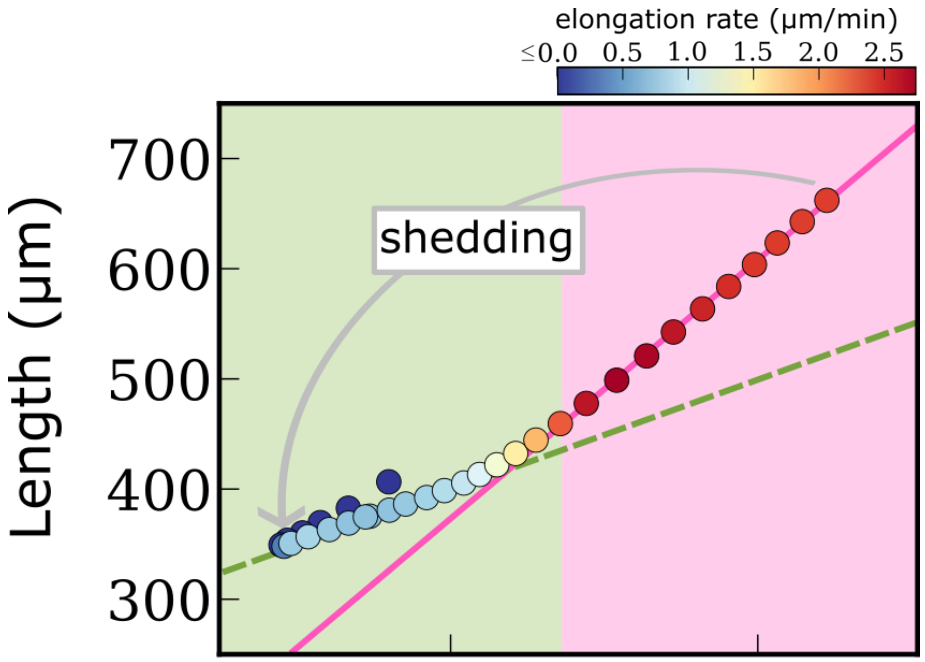
Ford, Celora et al., bioRxiv (2024)

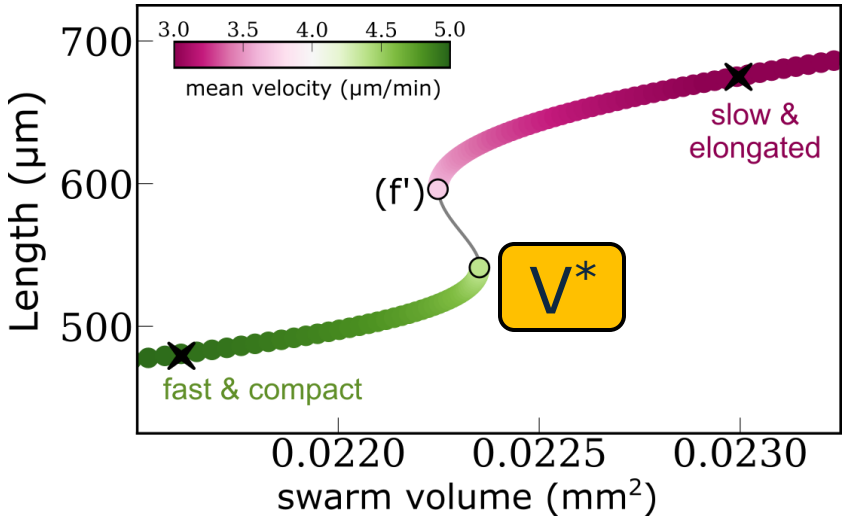

Loss of c
Height (µm)
90
45
0
0
10
80
40
0
1.5
U_{TW}
6.5
Mean speed (µm/min)
$\mathbf{u}_c - U_{TW}\mathbf{e}_x$
-300
-200
-100
0
100
200
Distance from swarm peak (µm)
7000
8000
9000
Length (µm)
Moving reference frame
$\mathbf{v} - \bar{\mathbf{v}}$
y
x
Distance from swarm peak (µm)


travelling phase
elongation
shedding
Swarm volume


elongation rate (µm/min)
≤0.0 0.5 1.0 1.5 2.0 2.5
Length (µm)
700
600
500
400
300
shedding
???????
dL/dt set by proliferation
0.020
swarm volume (mm²)


V*
travelling phase
elongation
shedding
Swarm volume


elongation rate (µm/min)
≤0.0 0.5 1.0 1.5 2.0 2.5
Length (µm)
700
600
500
400
300
shedding


3.0 3.5 4.0 4.5 5.0
mean velocity (µm/min)
Length (µm)
700
600
500
slow &
elongated
(f')
V*
fast & compact
0.0220
0.0225
0.0230
swarm volume (mm²)

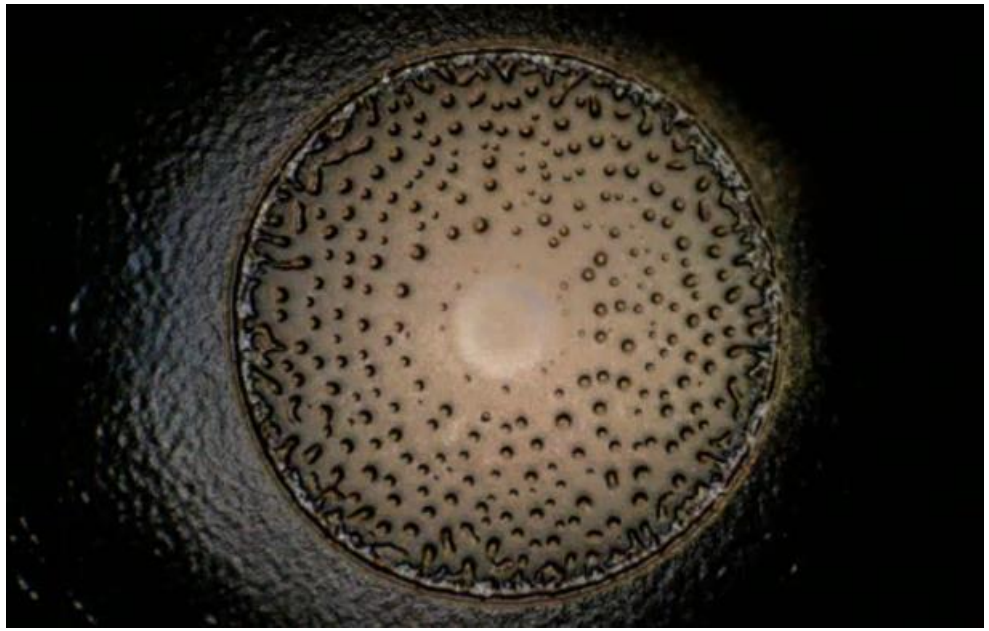
STORY 1: **Patterning in migration of multicellular communities**

Emergent material properties regulate self-organized patterning in migrating multicellular communities.

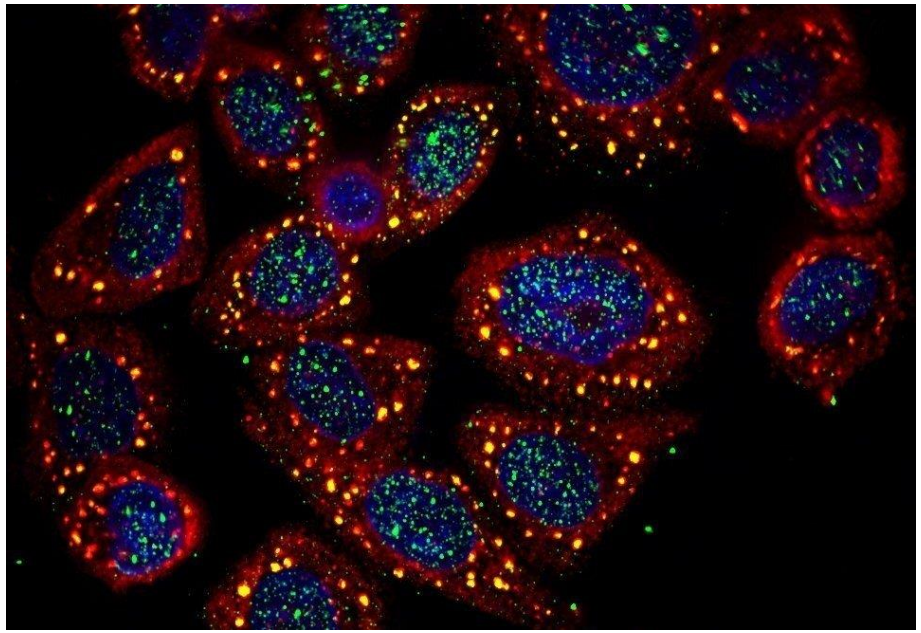
surface tension

self-organized patterning

STORY 1: **Patterning in migration of multicellular communities**



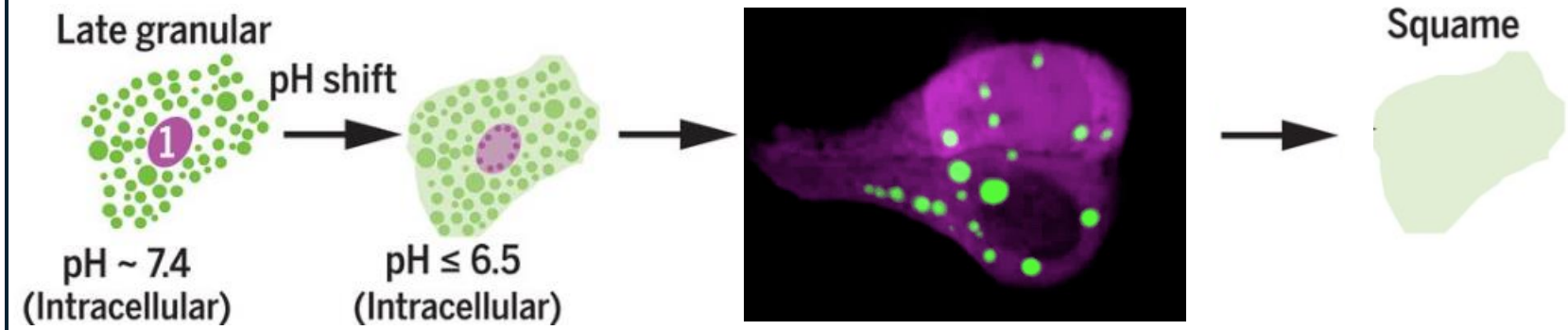
STORY 2: **Patterning of the intracellular space**



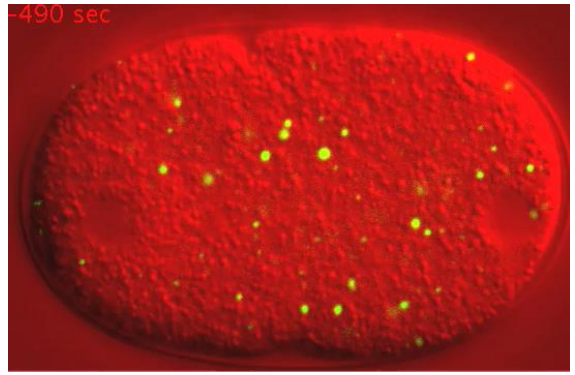
Membrane-less organelles: biological soft matter

- Spontaneous <u>reversible liquid-like</u> structures
- Stimuli-responsive materials with tunable composition and properties

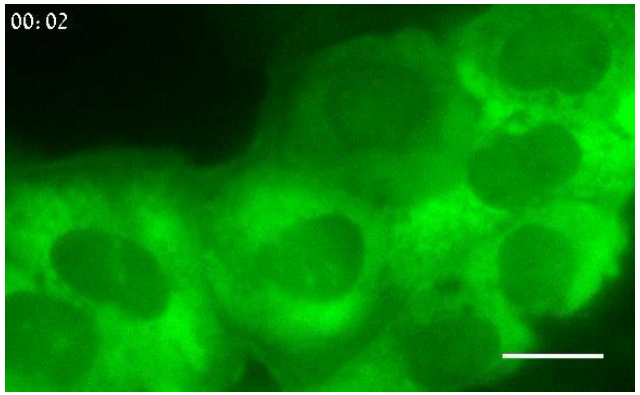
potential for drug discovery and synthetic biology



Keratohyalin granules in skin barrier formation (Quiroz et al., Science 367, 2020).

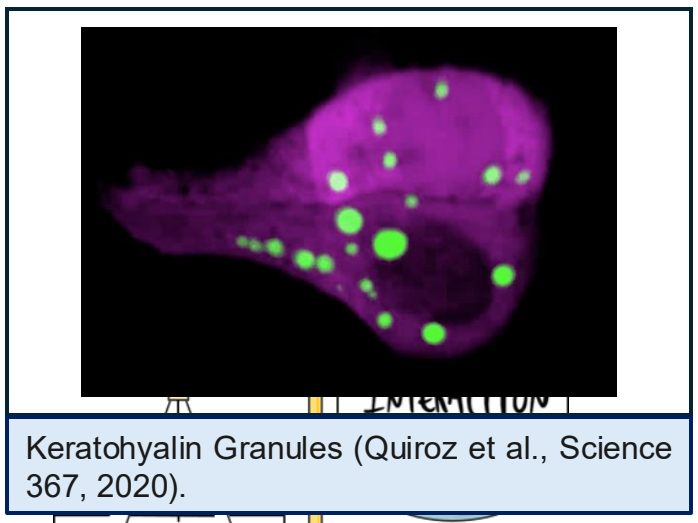


P Bodies (Brangwynne et al. Science, 2009).

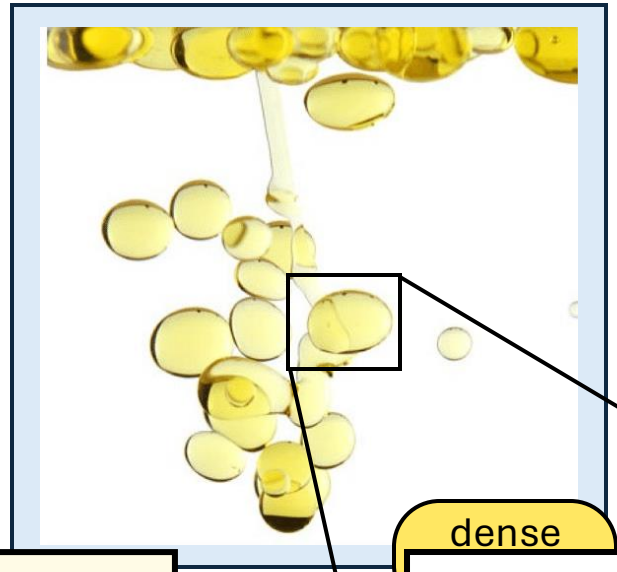


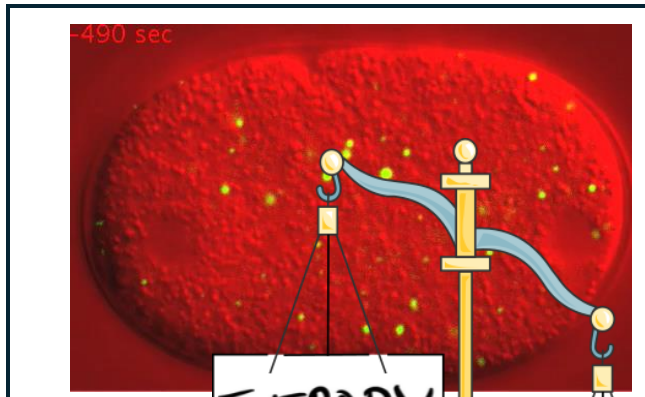
SG formation in cancer cells exposed to chemo (Schwed-Gross et al; *J Cell Sci* 135, 2022)

Membrane-less organelles: biological soft matter

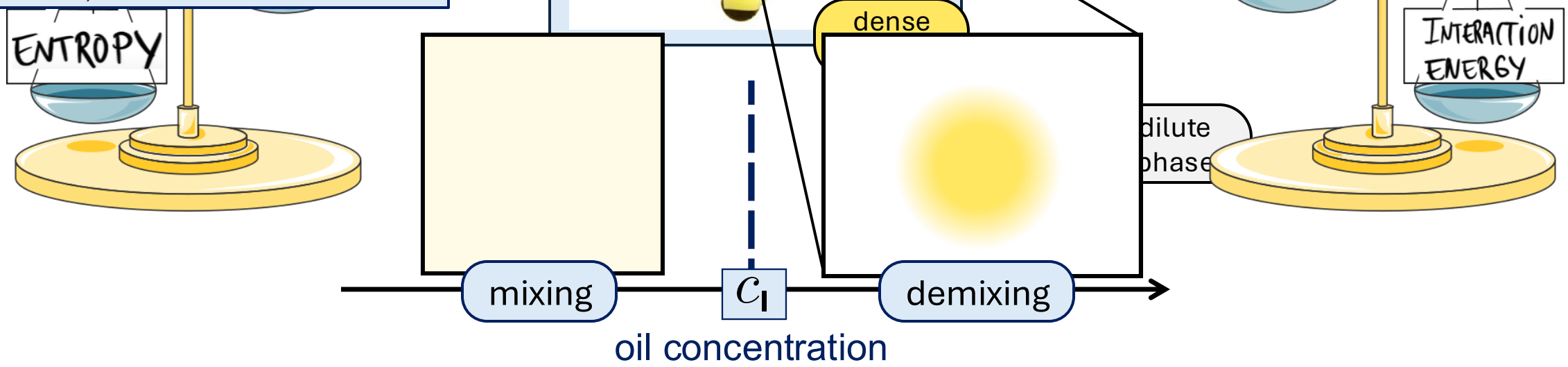


Keratohyalin Granules (Quiroz et al., Science 367, 2020).

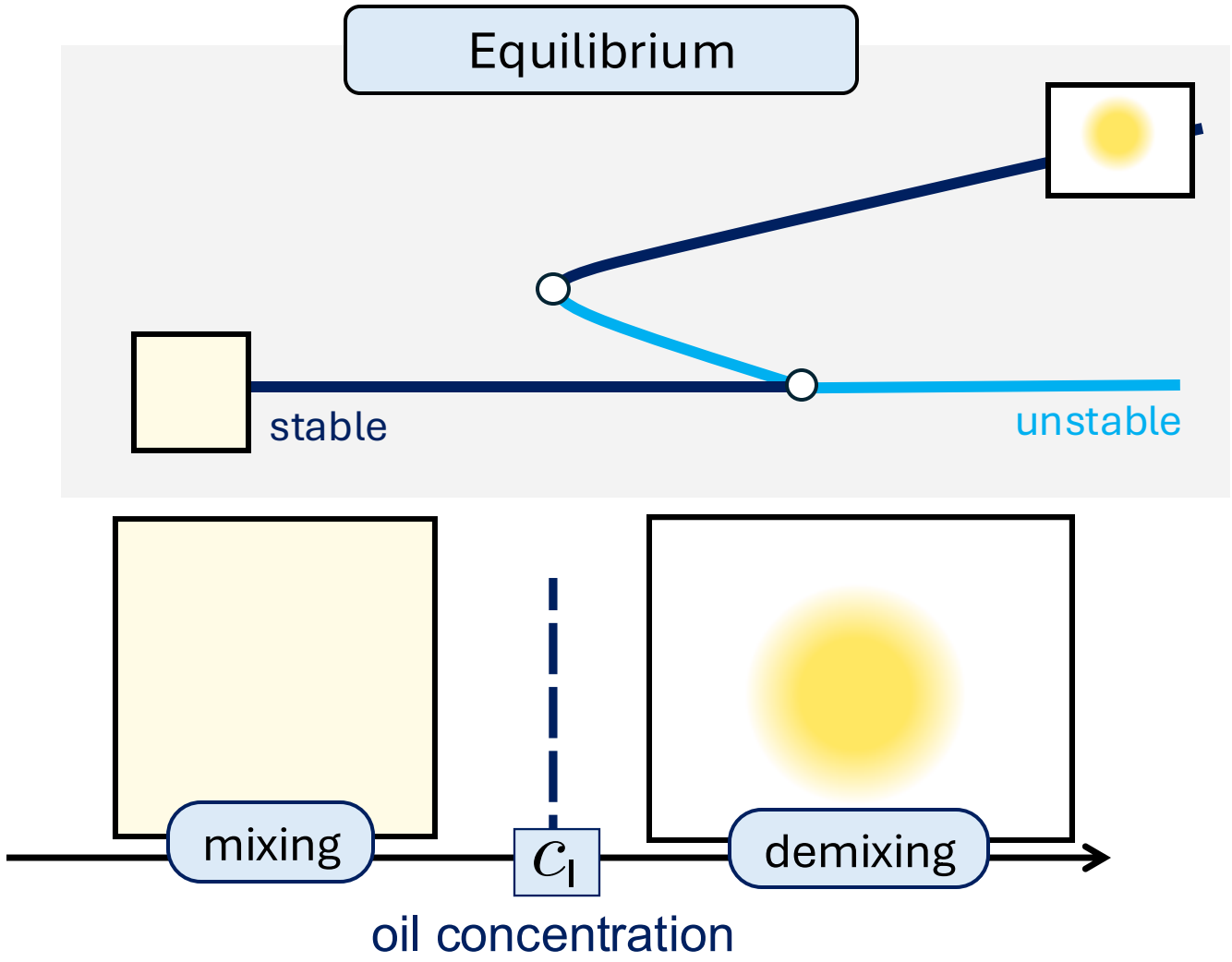


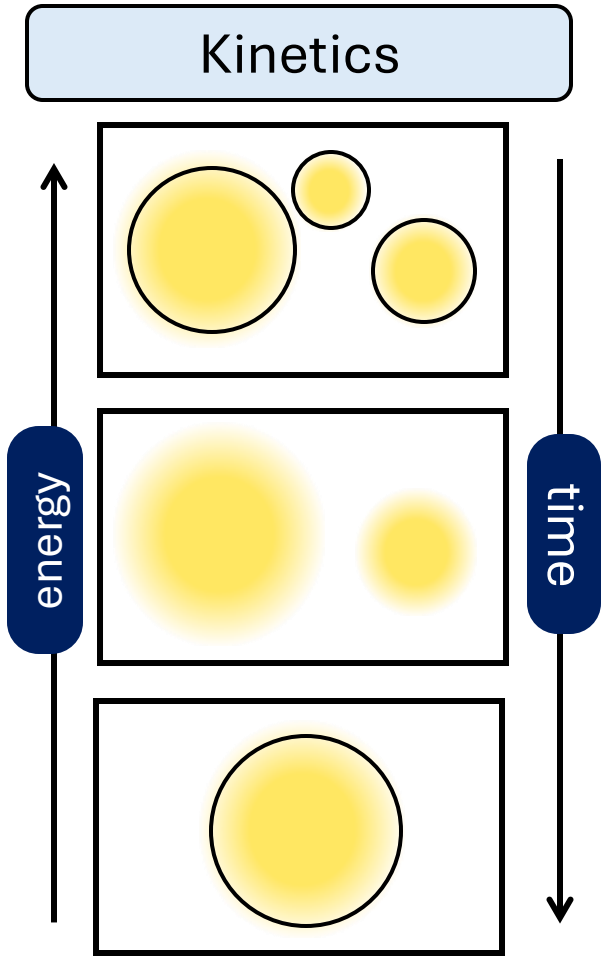


P Bodies (Bra… …nce, 2009).



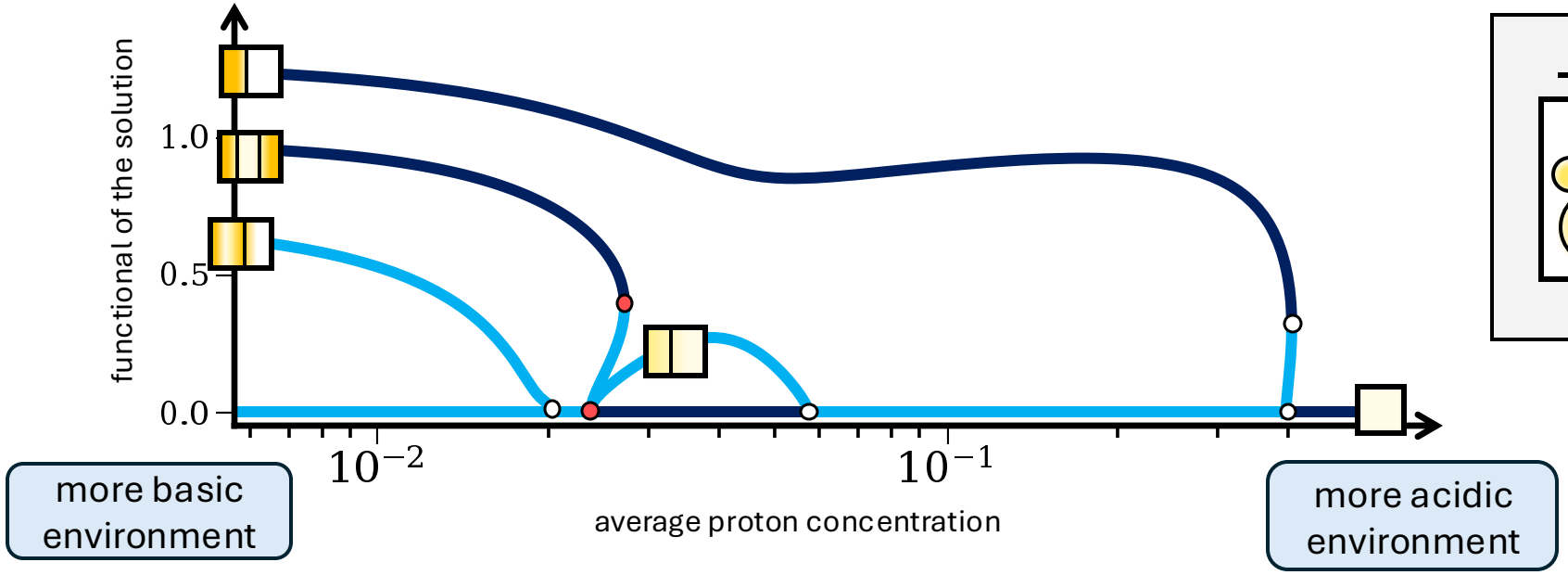
Membrane-less organelles: biological soft matter

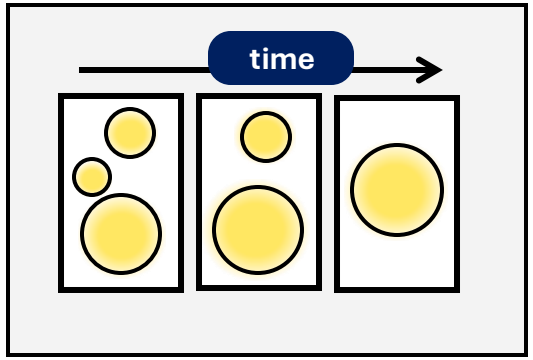




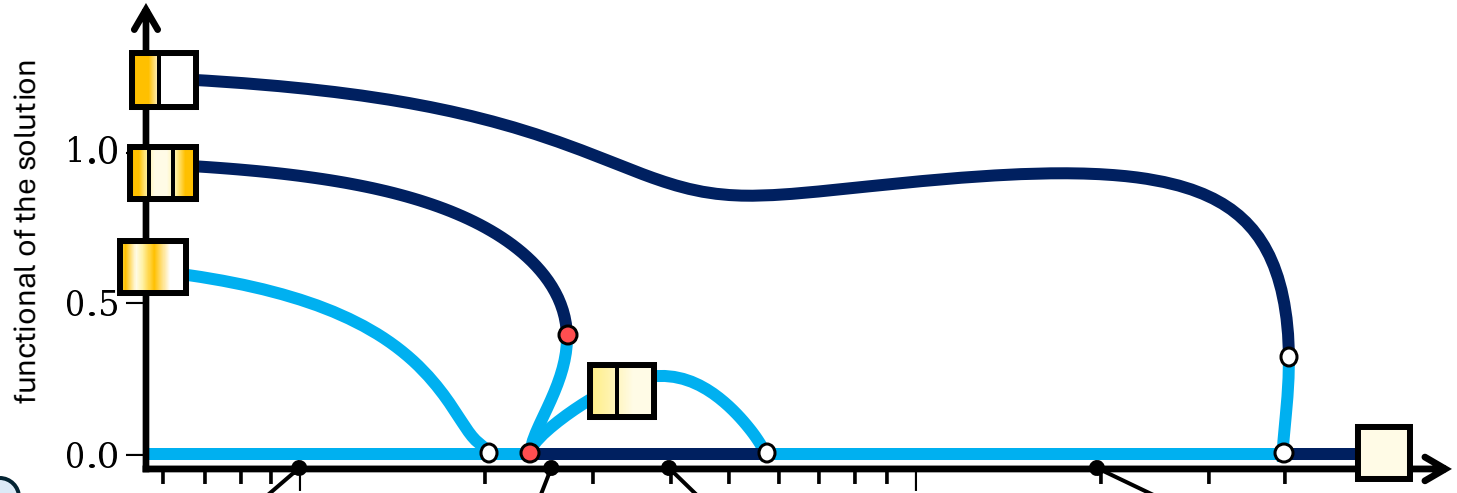
$$\partial_t c = \nabla \cdot \left(c \nabla \frac{\delta E[c]}{\delta c} \right)$$

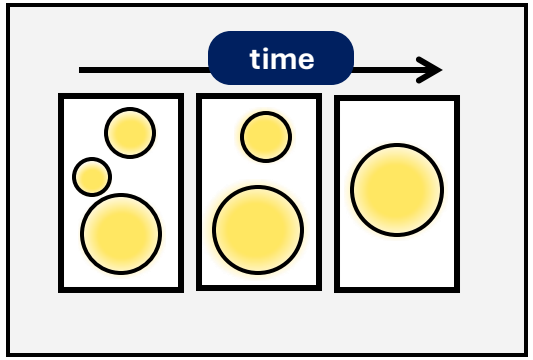
Demixing of complex weakly charged biofluids





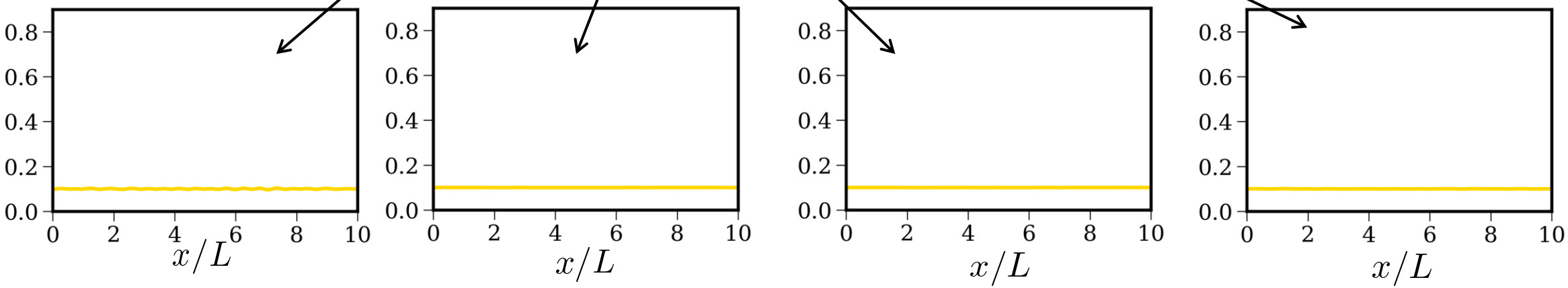
Demixing of complex weakly charged biofluids



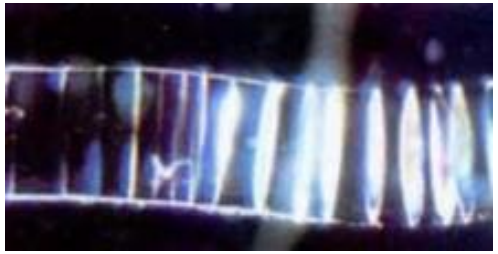


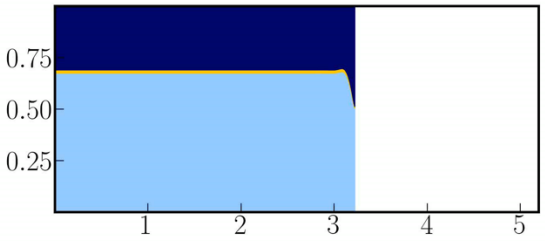
more basic environment

more acidic environment

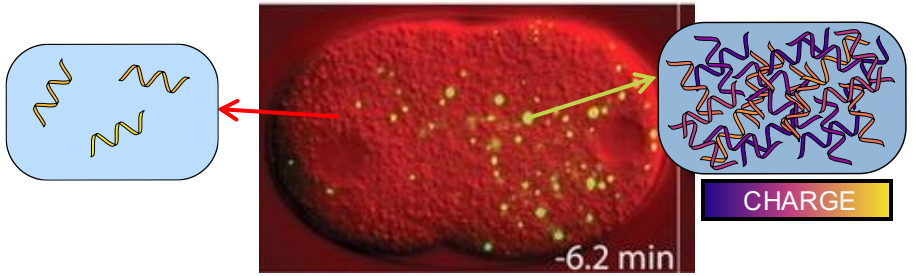


Stimuli-responsive gels

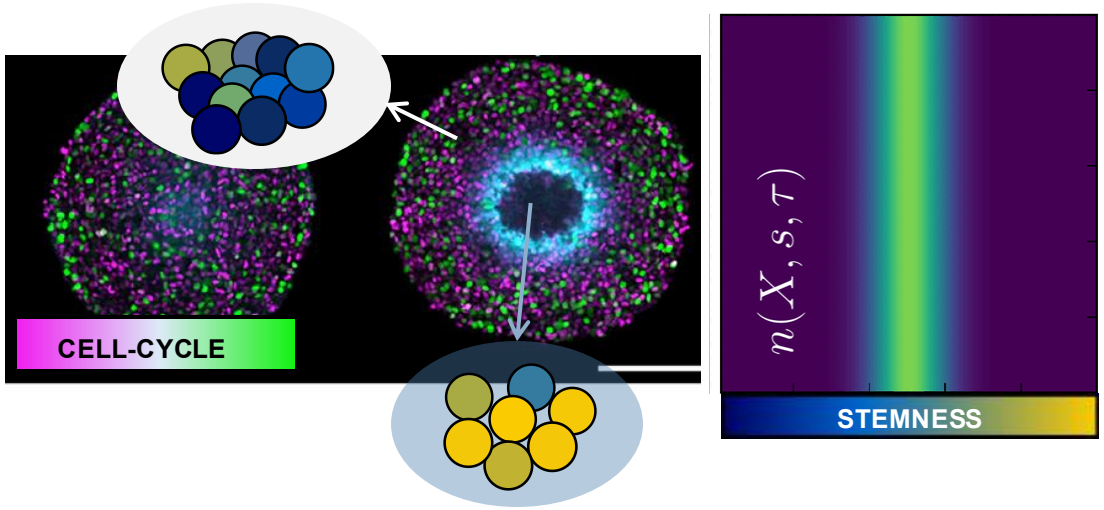




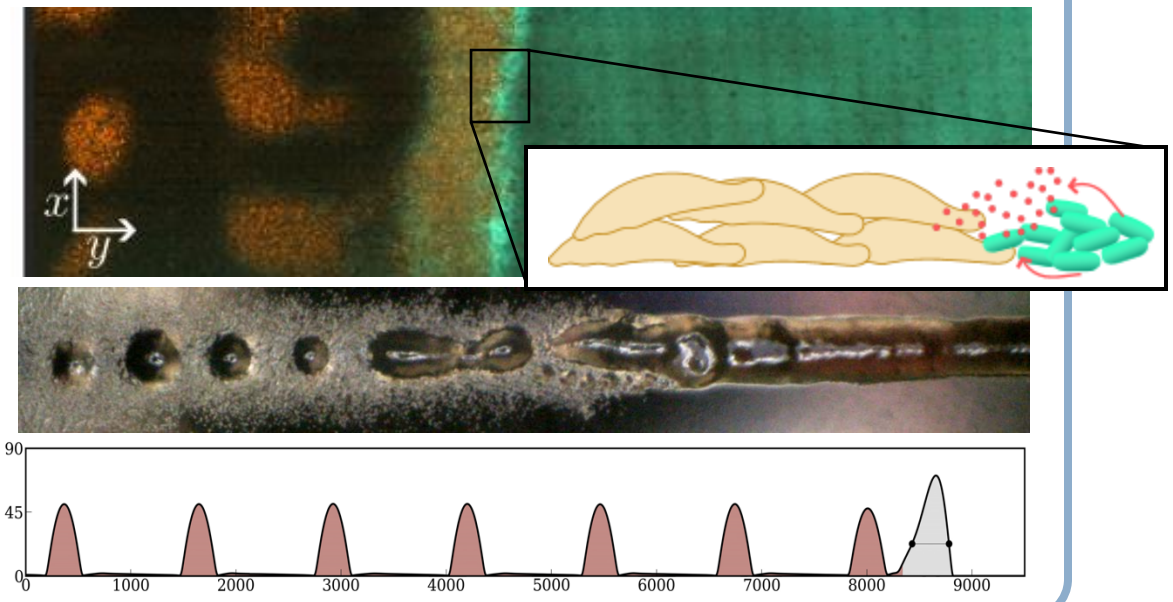
Biomolecular condensates

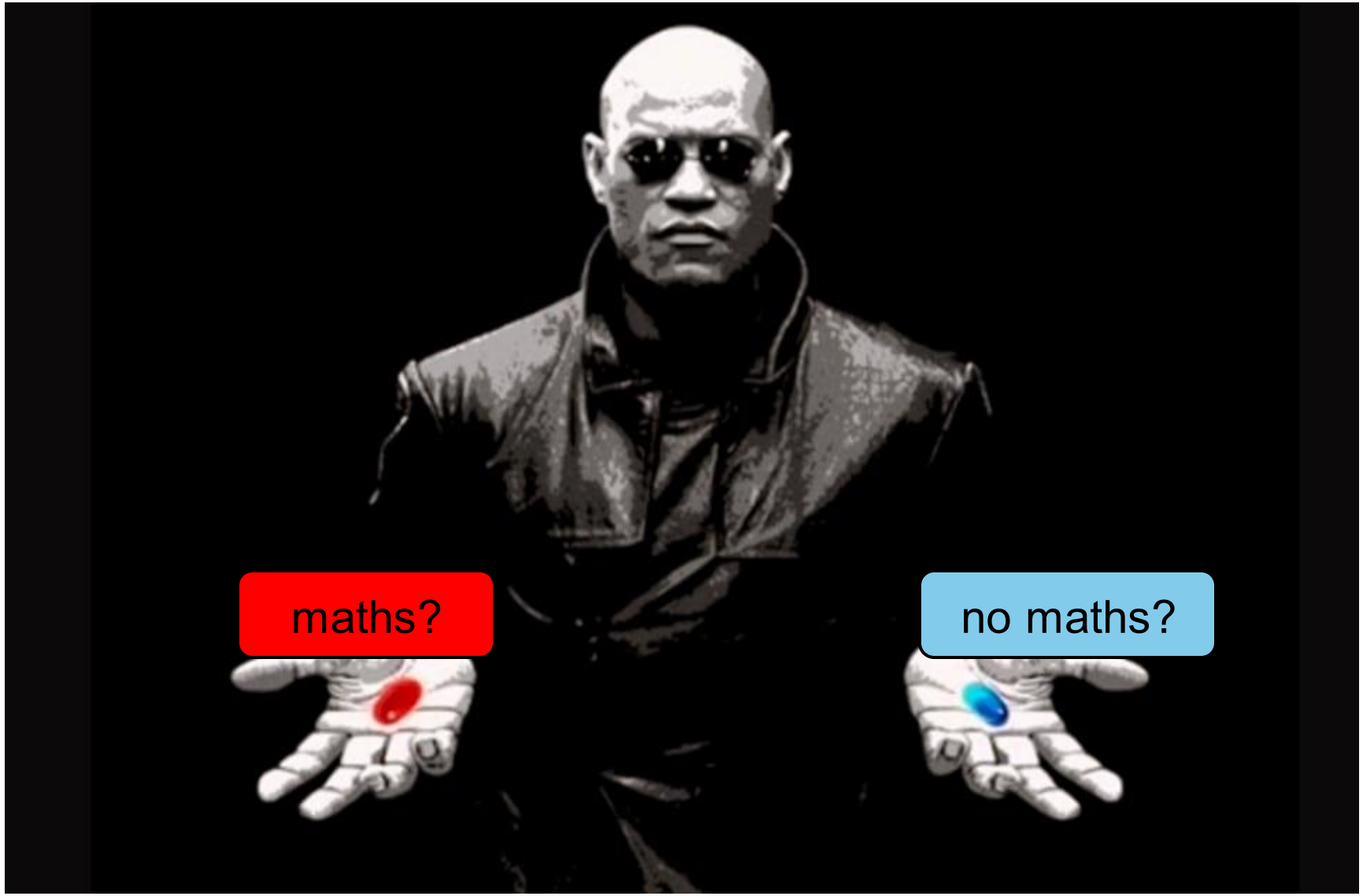


Cancer



Collective cell migration





What's your choice?