APS March Meeting, Boston
March 8, 2019

Physics of active emulsions: Implications for stress granules

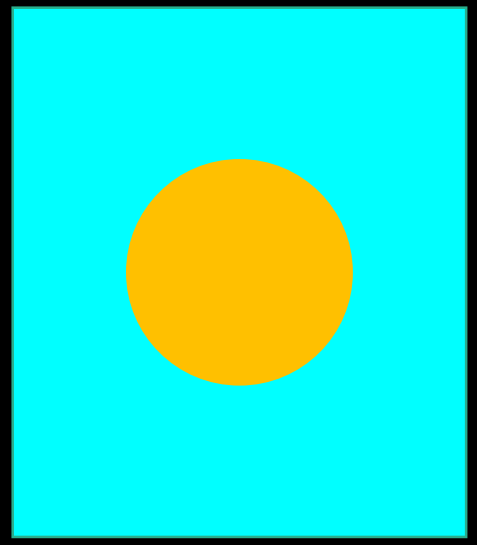
Chiu Fan Lee

Department of Bioengineering

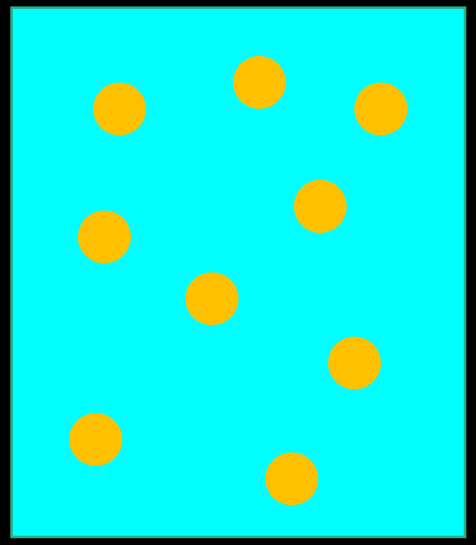
Imperial College London

Phase separation vs. emulsions

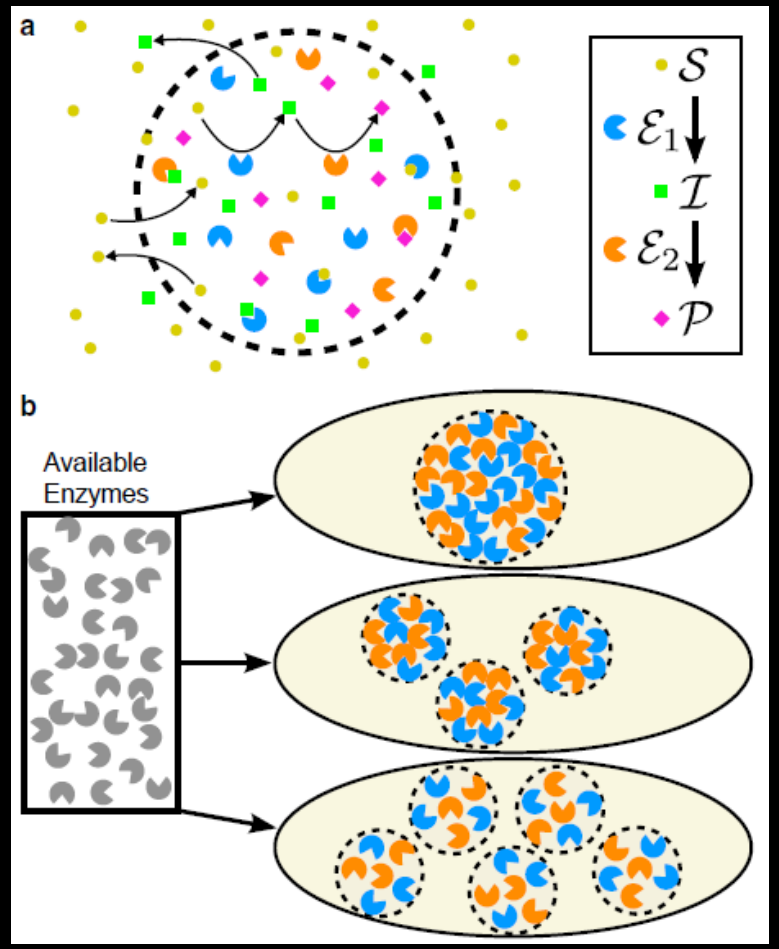
Phase separation



A stable emulsion

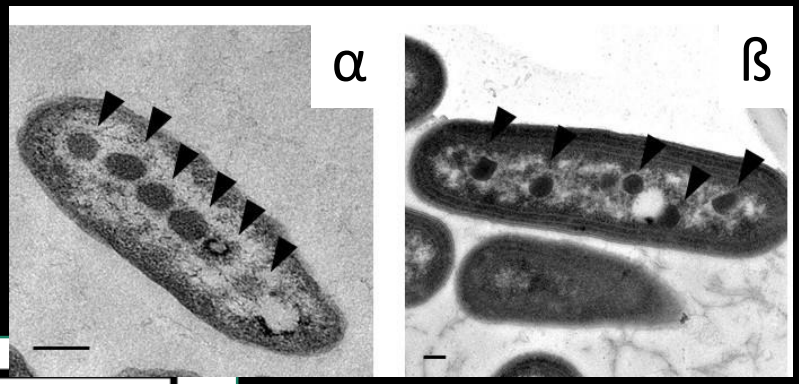


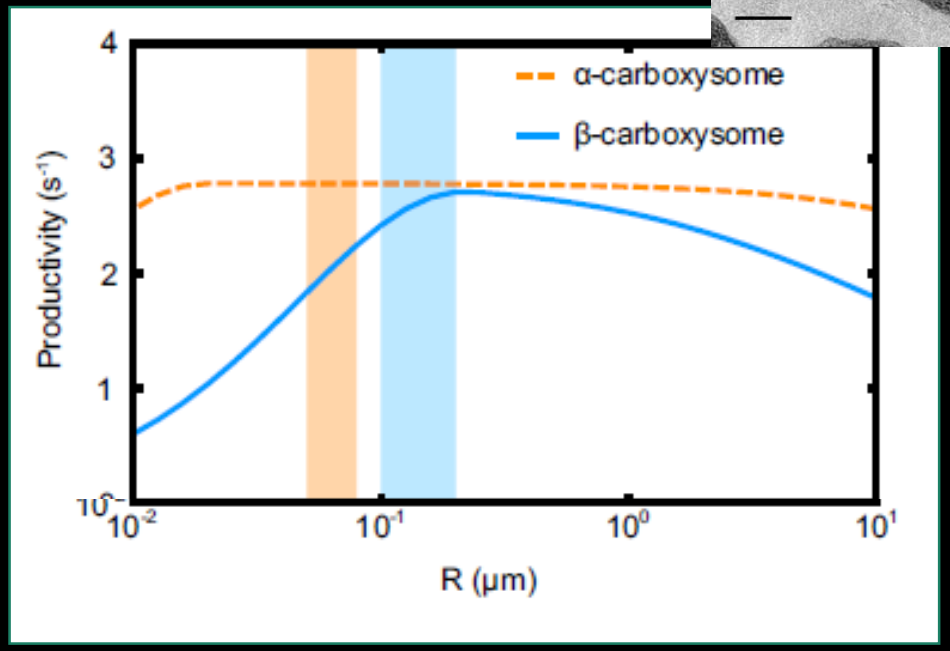
Why an emulsion can be a good thing?



F Hinzpeter, U Gerland & F Tostevin (2016) Biophys. J.

Carboxysomes in bacteria





Many small drops can be better than one big drop

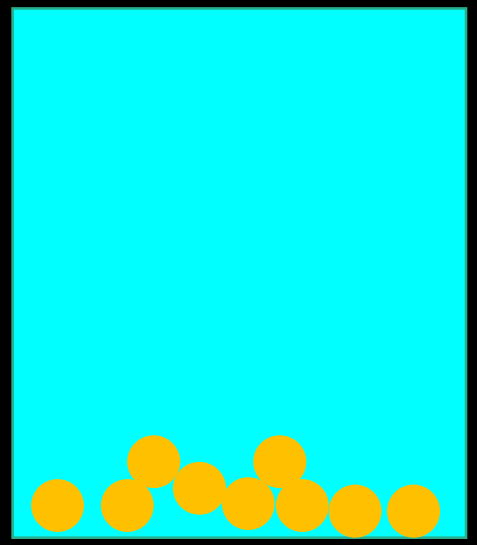
Plan

1. Instabilities in emulsions
2. Non-equilibrium (active) phase separation
3. Implications for stress granule formation
4. Summary & Outlook

1. Instabilities in emulsions

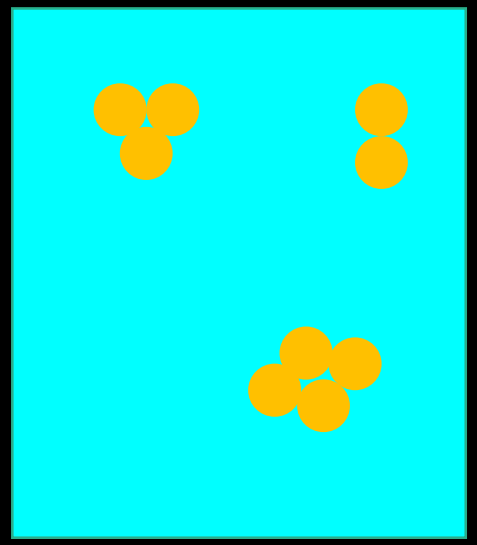
Emulsions tend to be unstable

Creaming / Sedimentation



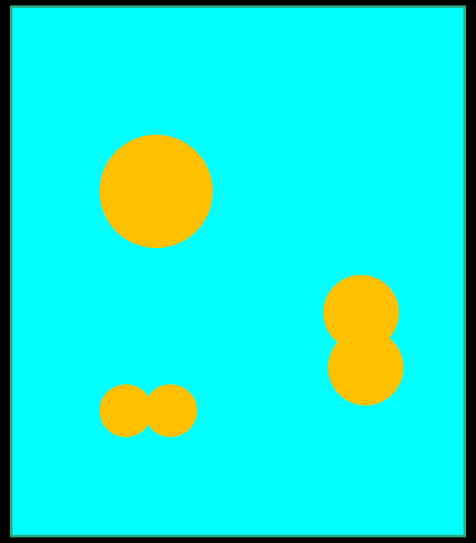
Differential buoyancy

Flocculation



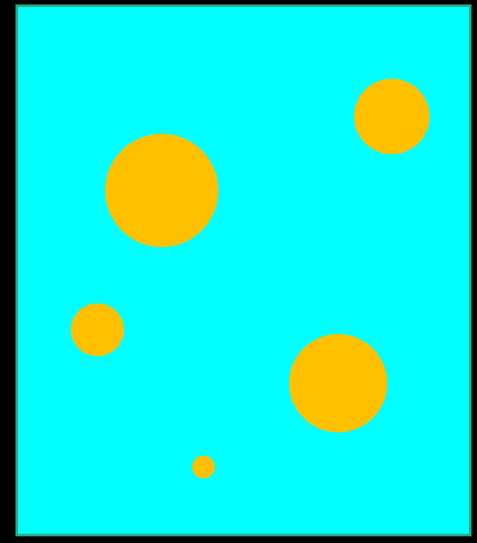
Coagulation of drops

Coalescence



Fusion of drops

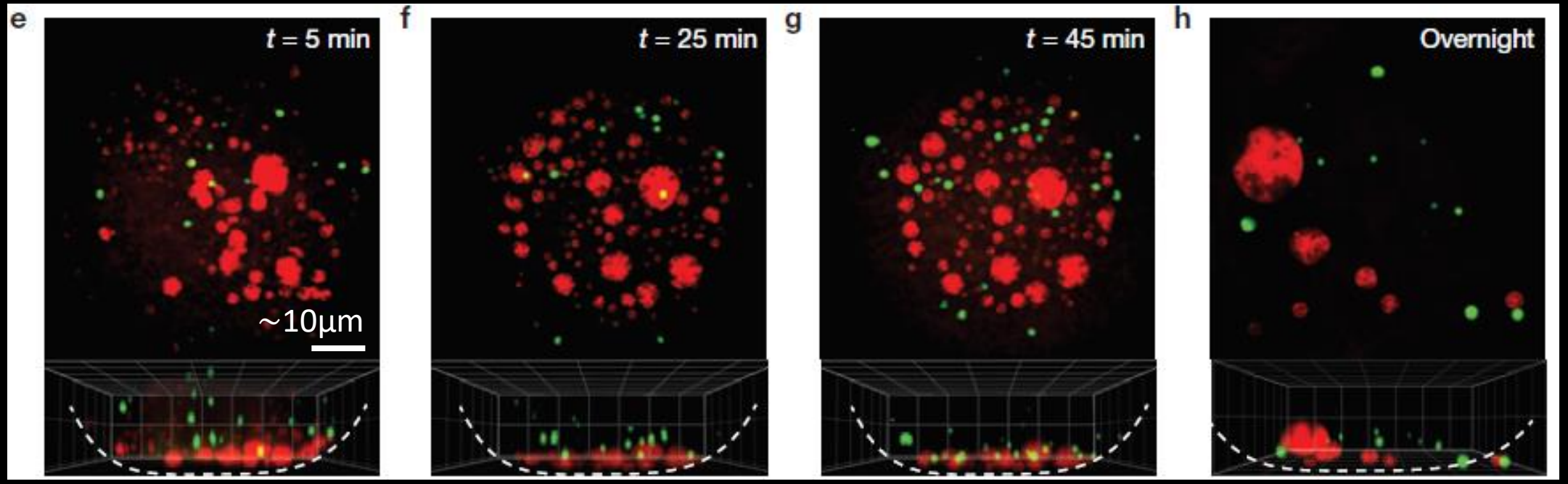
Ostwald ripening



Big drops grow by sucking material from small drops at a distance

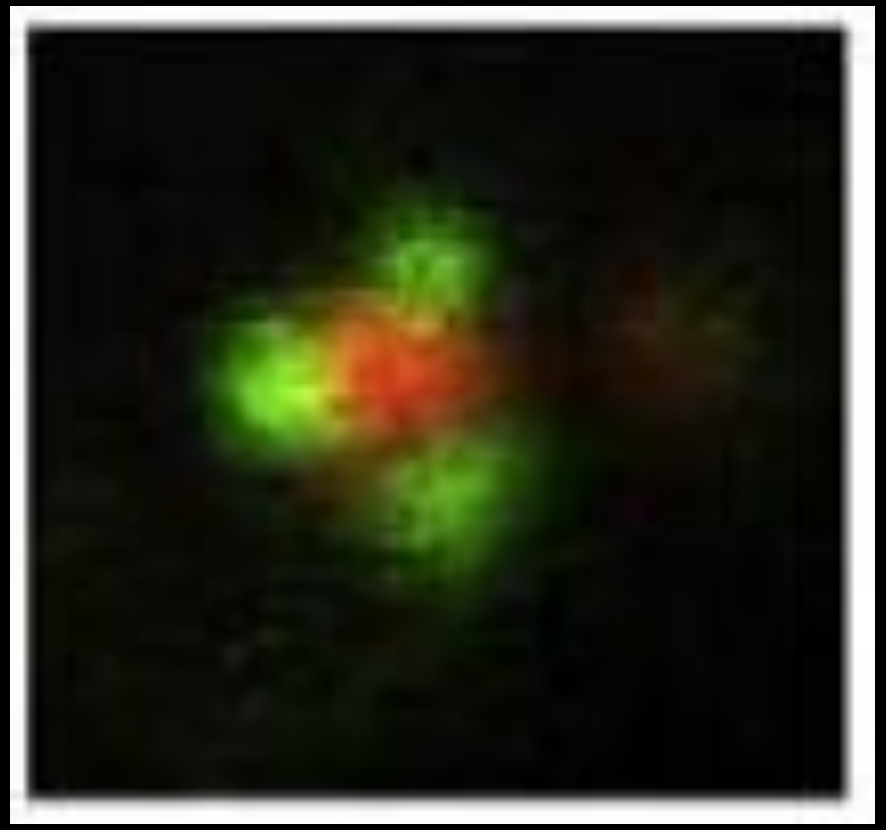
Sedimentation

Precipitation of nucleoli (Red) and Histone locus bodies (Green) in *Xenopus* germinal vesicles upon actin filament disruption



M Feric & CP Brangwynne (2013) Nature Cell Biol.

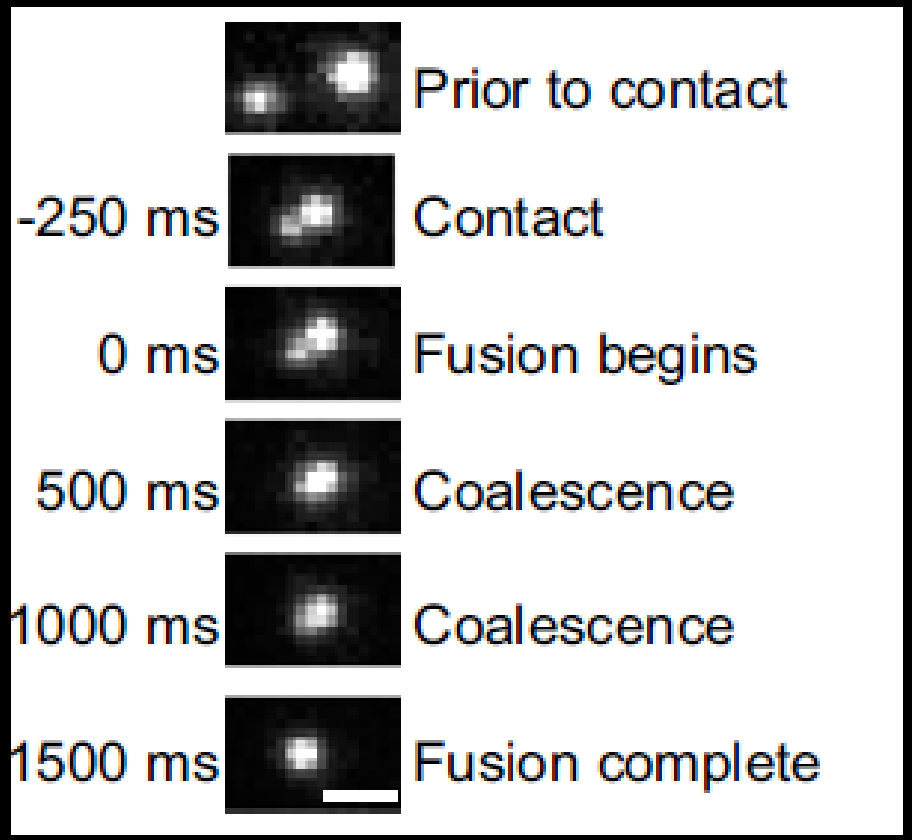
Flocculation



Processing bodies (Green) & P granules (Red) in *C. elegans* embryos

CM Gallo, E Munro, D Rasoloson, C Merritt, G Seydoux (2008) Dev. Biol.

Coalescence

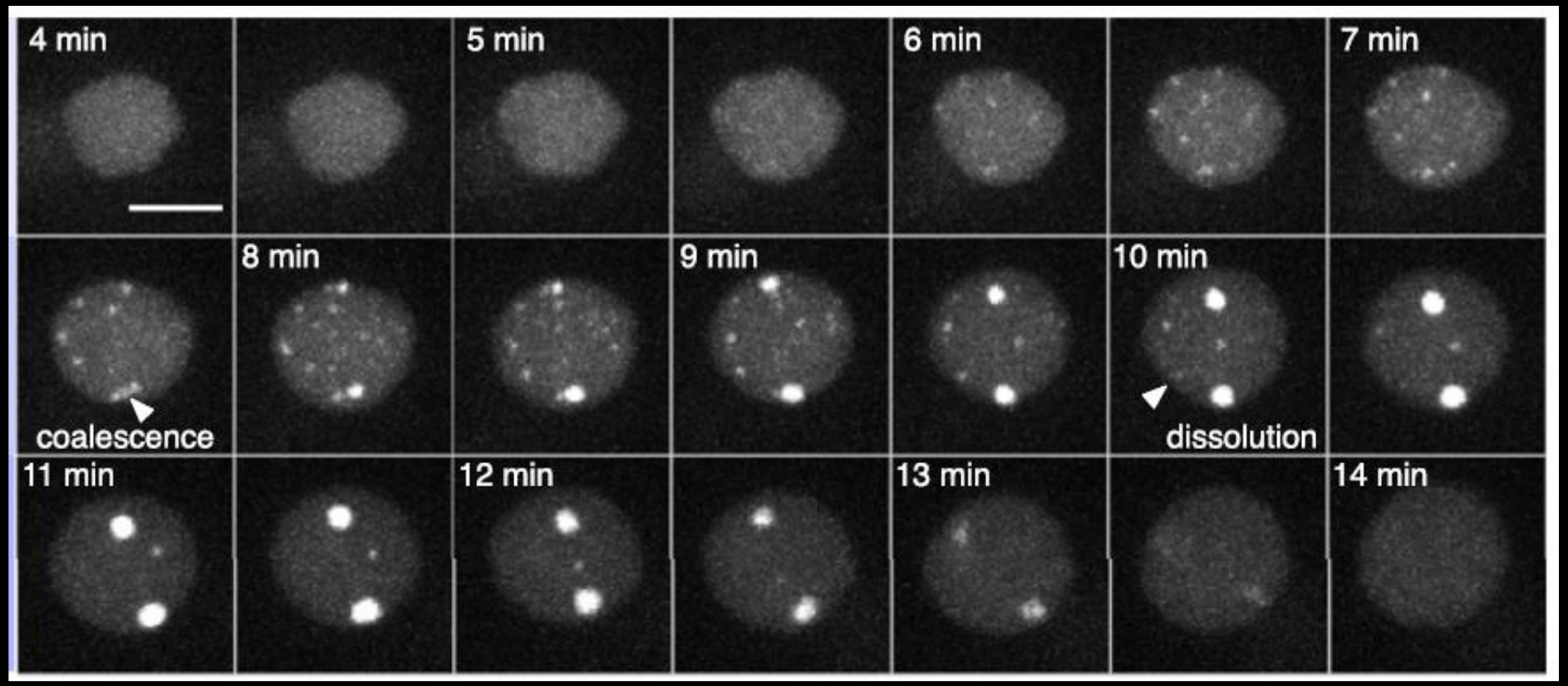


TAR-DNA binding protein 43 (TDP-43) Ribonucleoprotein granules in neurons

PP Gopal, JJ Nirschl, E Klinman & ELF Holzbaurt (2017) PNAS

Ostwald ripening

Nucleoli in *C. elegans* embryo



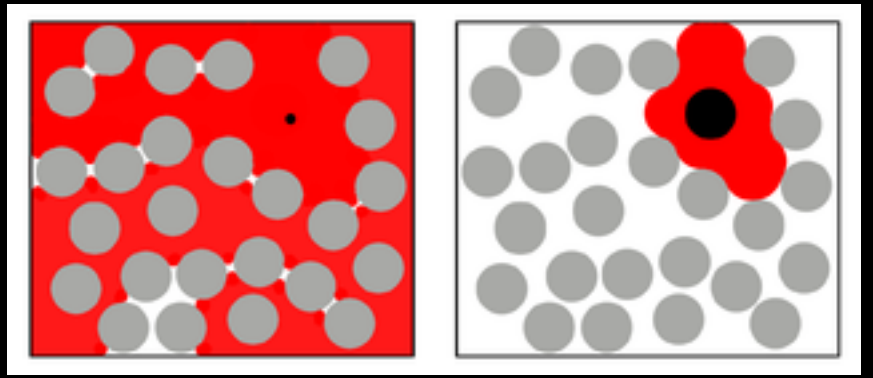
J Berry, SC Weber, N Vaidya, M Haataja & CP Brangwynne (2015) PNAS

Focus on the late-stage / steady-state

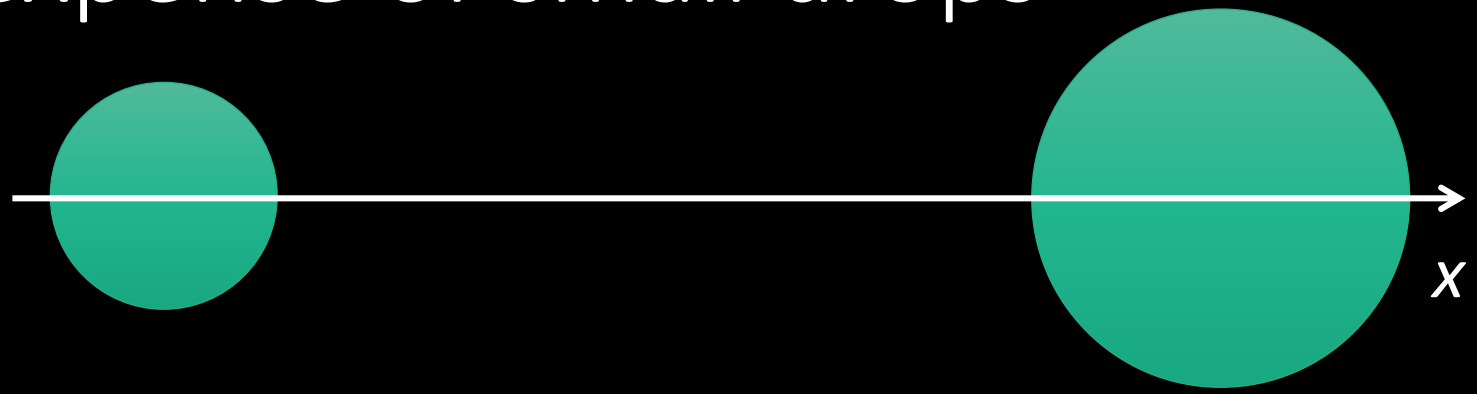
- ~~Creaming / sedimentation~~
- ~~Flocculation~~
- ~~Coalescence~~
- Ostwald ripening

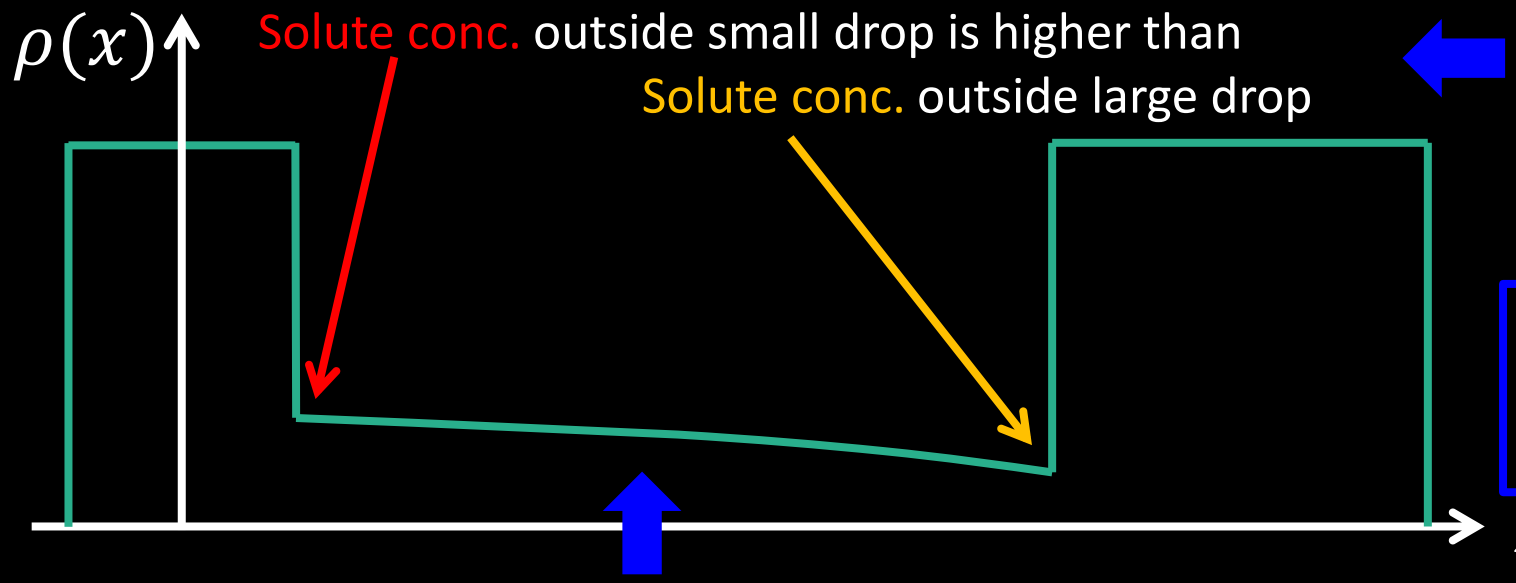
Gravity not important

Macromolecular crowding ->
drops diffuse less as they grow



Ostwald ripening: big drops grow at the expense of small drops





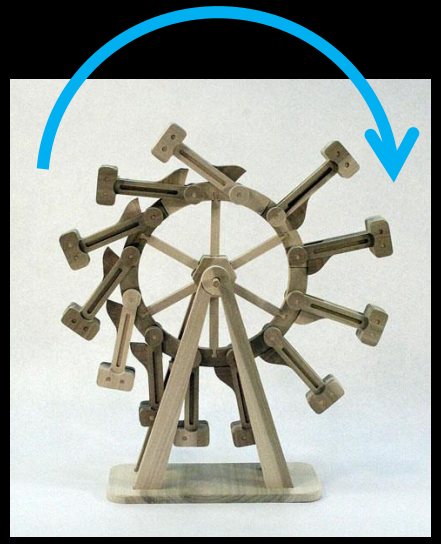
1. Gibbs-Thomson relation:

$$\rho(R) = \rho(R = \infty)\left(1 + \frac{l_c}{R}\right)$$

1.+2. -> Ostwald ripening

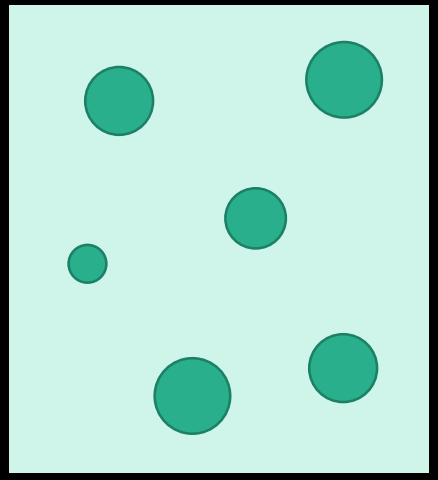
$$\langle R(t)\rangle \sim t^{1/3}$$

Second law of thermodynamics

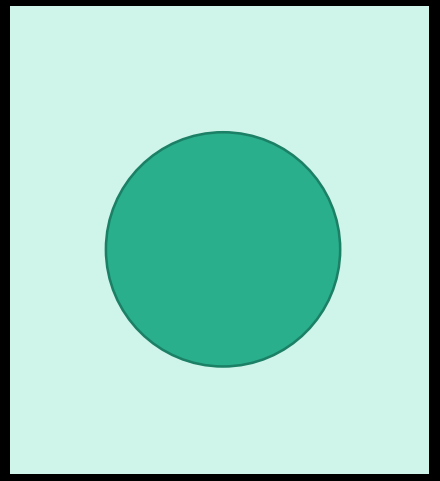


Time

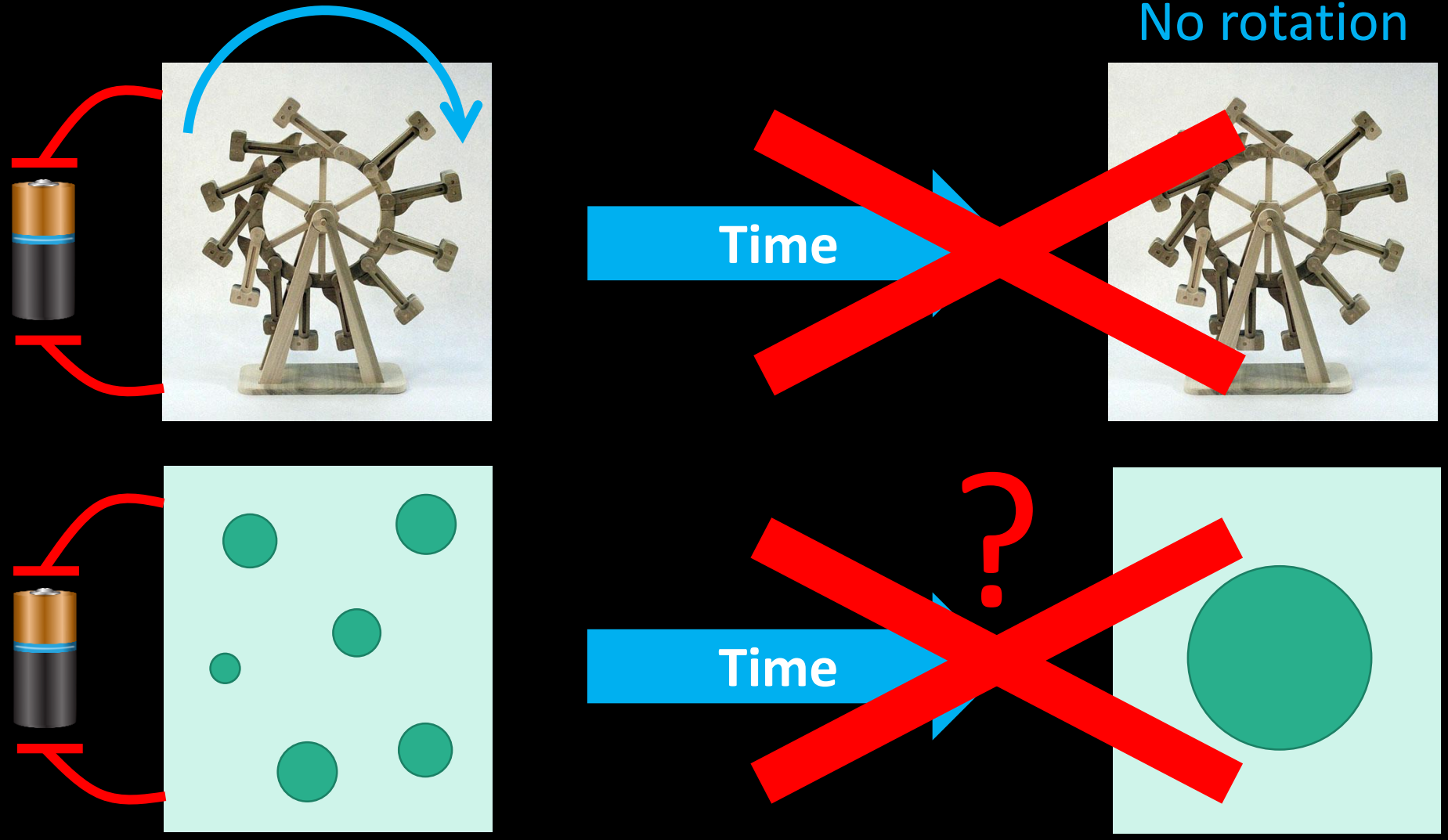
No rotation

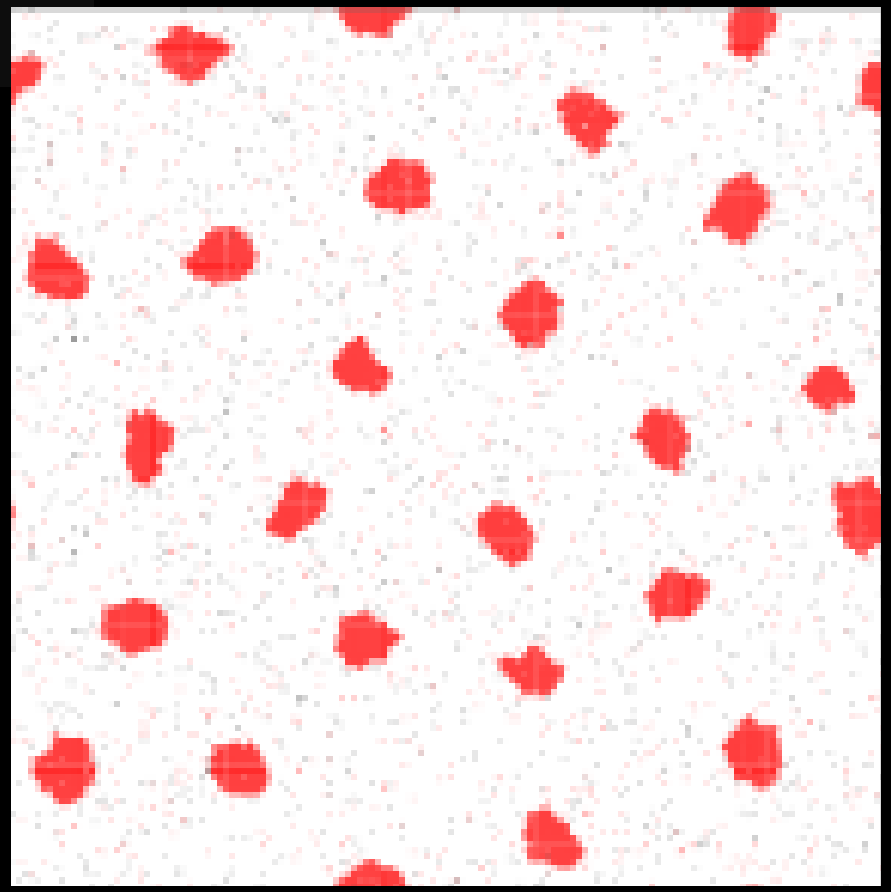


Time



~~Second law of thermodynamics~~





2. Non-equilibrium (active) phase separation

Two hallmarks of living matter

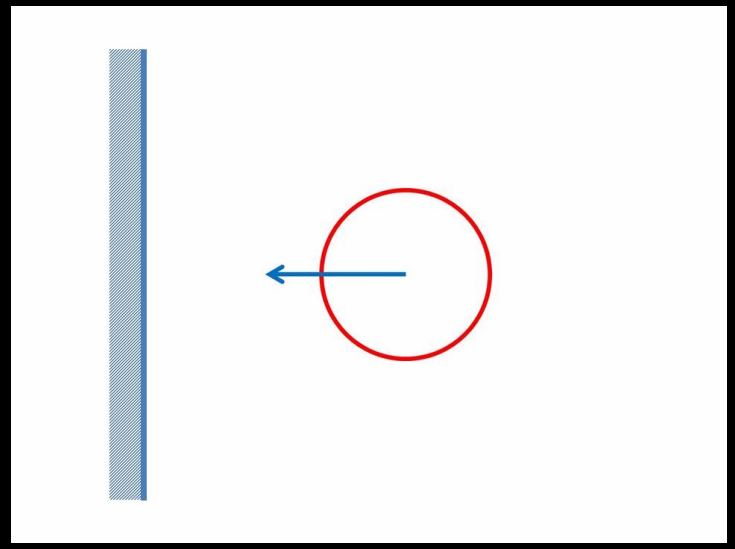
- Self-generated mechanical force
  - motility via ATP-driven molecular motors

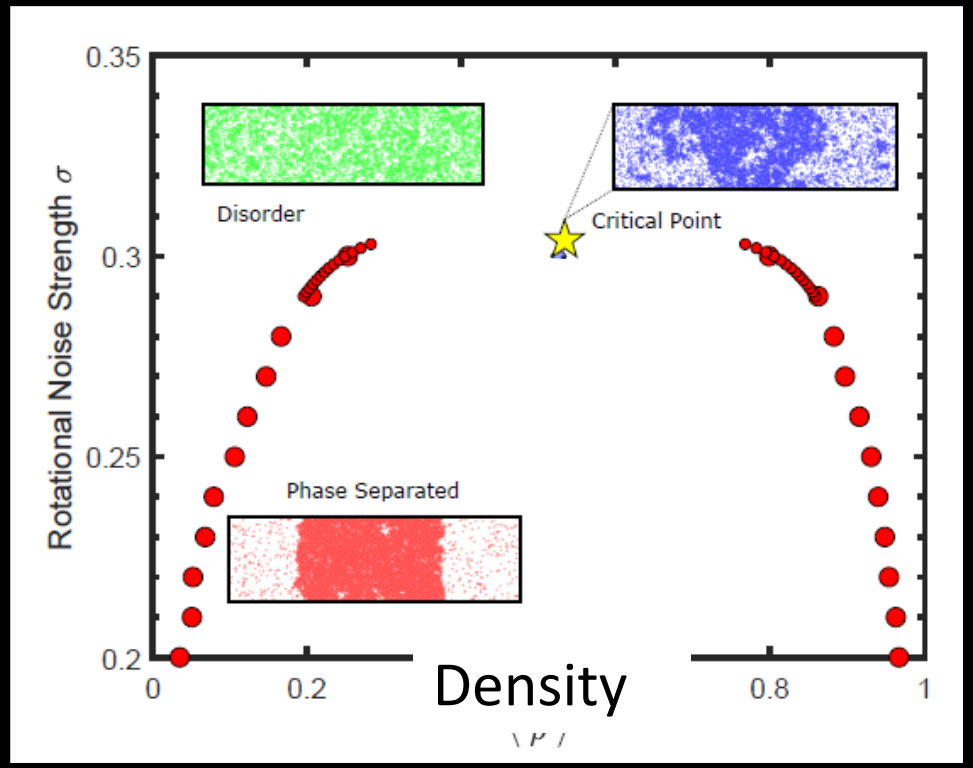
- Driven chemical reactions
  - metabolism, ATP-driven phosphorylation)

Motility-induced phase separation [MIPS]

- Phase separation without attractive interactions

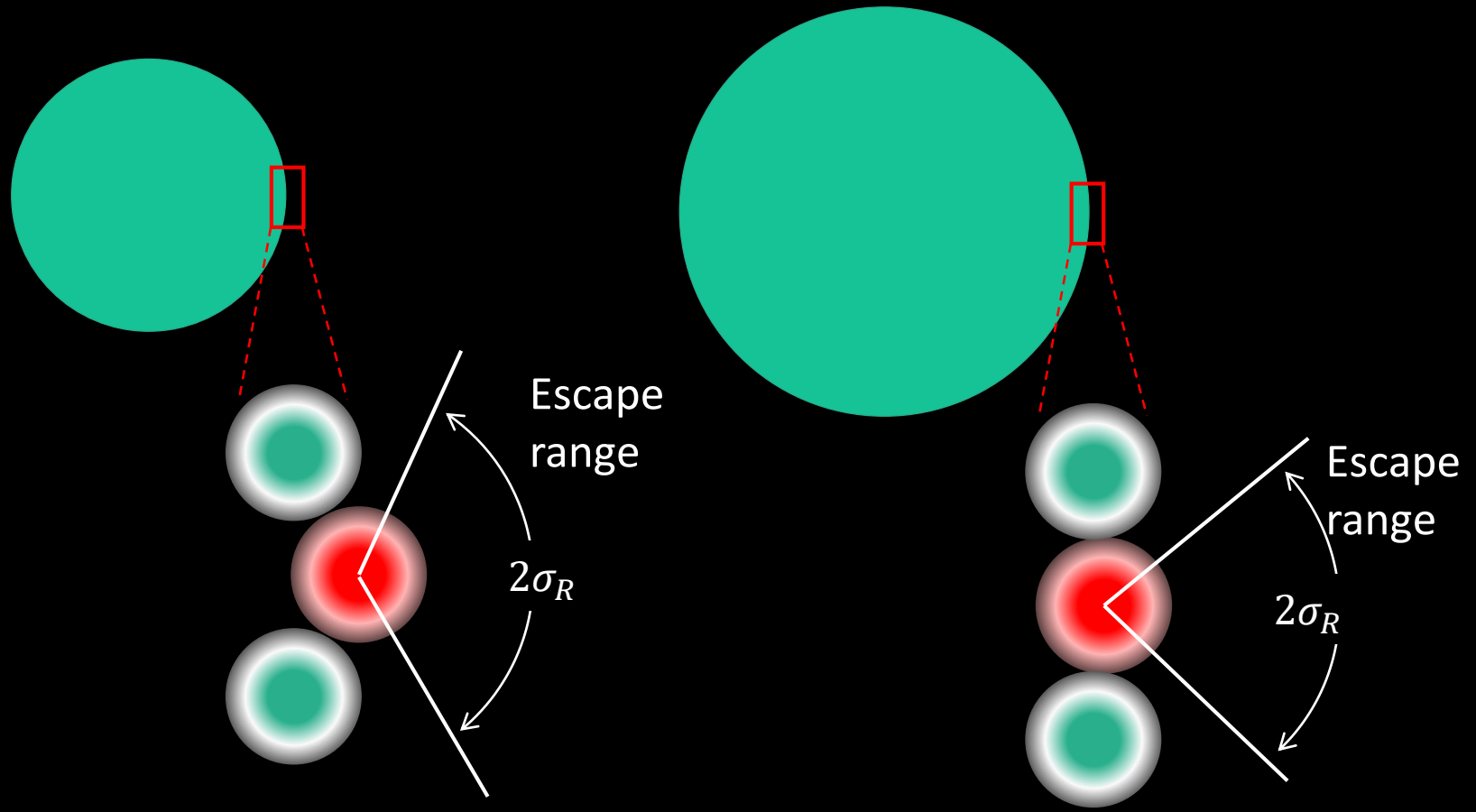
  [J Tailleur & ME Cates (2008) Phys. Rev. Lett.; Y Fily & MC Marchetti (2012) Phys. Rev. Lett.; GS Redner, MF Hagan & A Baskaran (2013) Phys. Rev. Lett.]





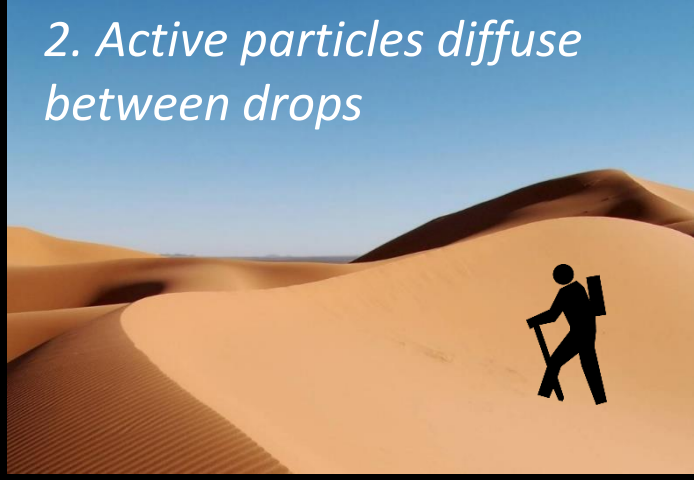
B Partridge & CFL. arXiv:1810.06112

Ostwald-ripening in MIPS

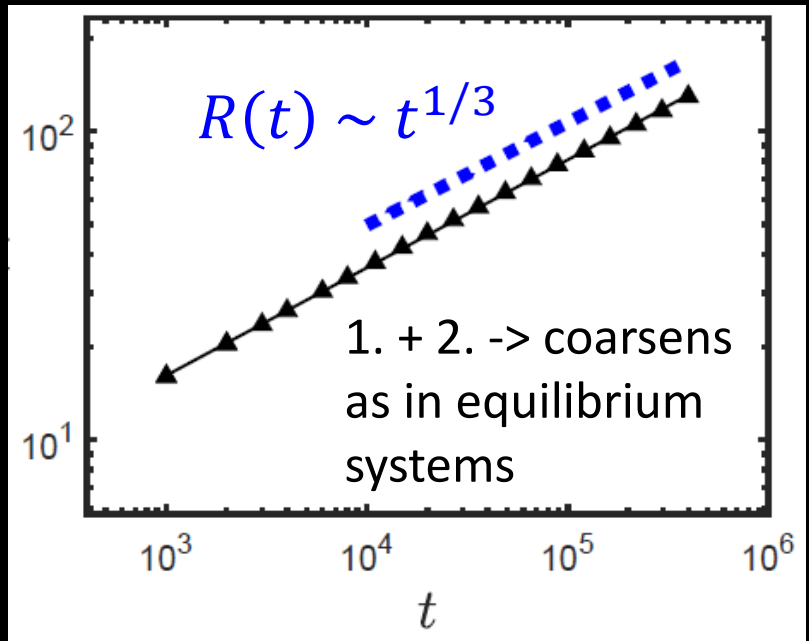


1. Gibbs-Thomson relation: [Solute] outside a big drop < [Solute] outside a small drop

CFL (2017) Soft Matter



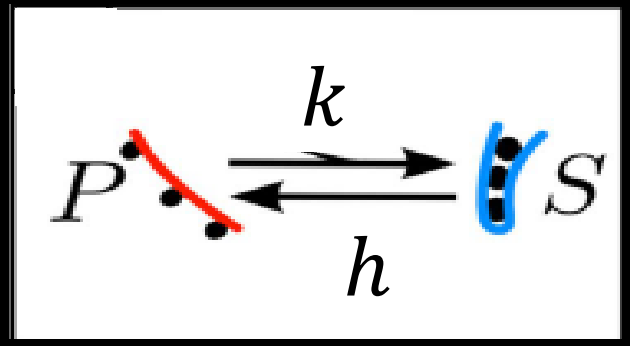
See also E Tjhung, C Nardini & ME Cates (2018) *Cluster Phases and Bubbly Phase Separation in Active Fluids: Reversal of the Ostwald Process.* Phys. Rev. X



B Partridge & CFL. ArXiv:1810.06112

Chemical reaction-controlled phase separation

Separating state (*P*) & Soluble state (*S*)

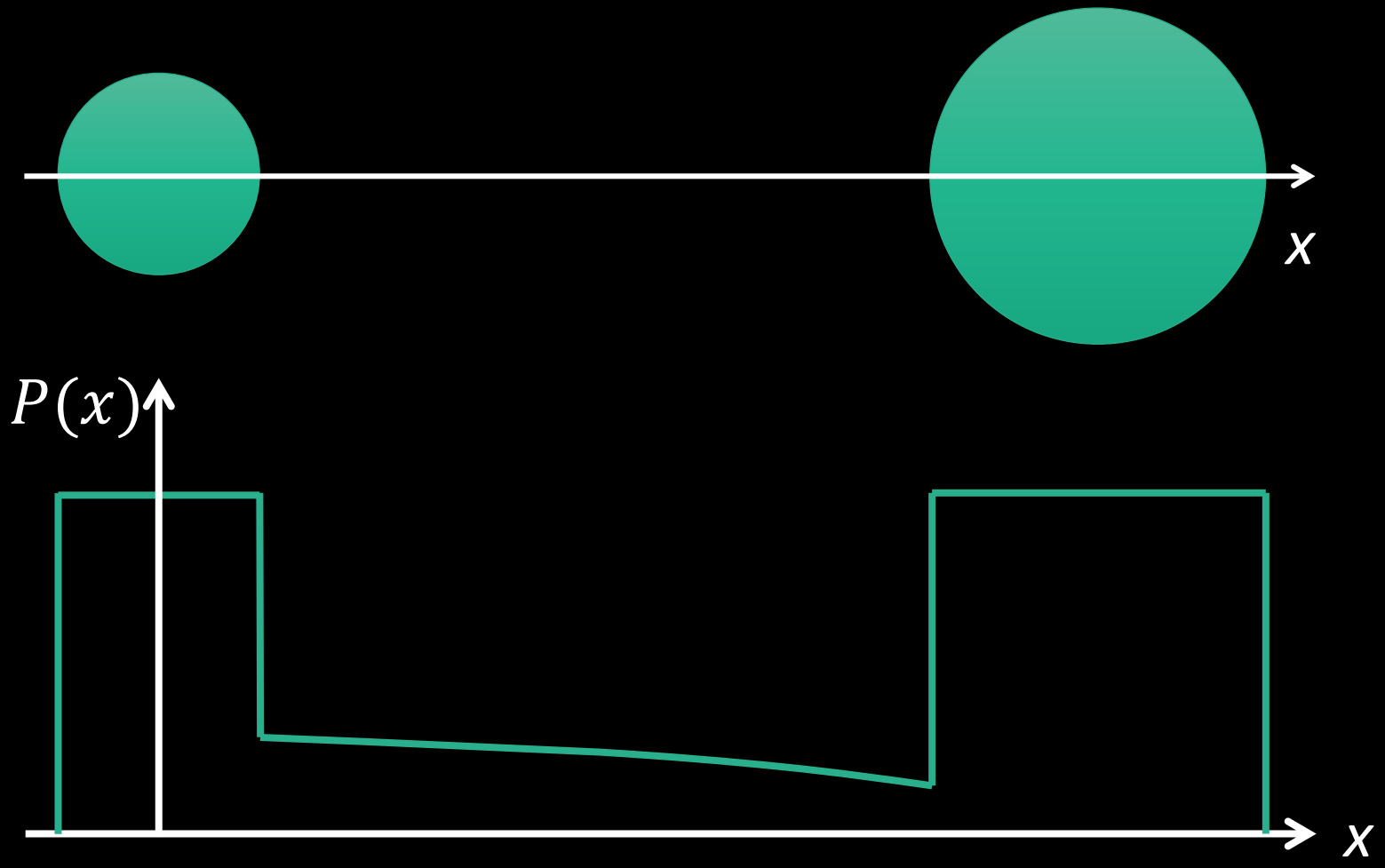


$$\frac{\partial P_{\text{in,out}}}{\partial t} = D\nabla^2 P_{\text{in,out}} - kP_{\text{in,out}} + hS_{\text{in,out}},$$

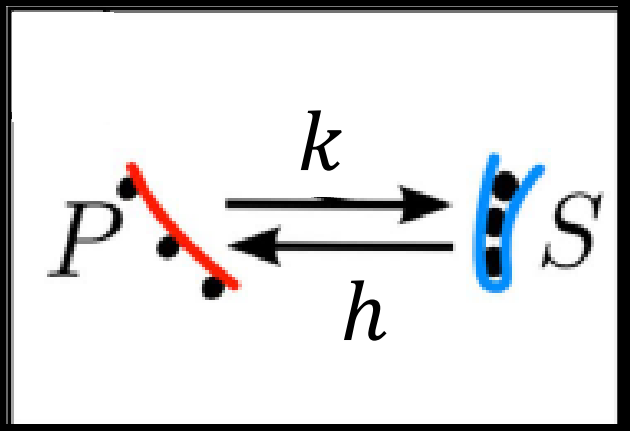
$$\frac{\partial S_{\text{in,out}}}{\partial t} = D\nabla^2 S_{\text{in,out}} + kP_{\text{in,out}} - hS_{\text{in,out}},$$

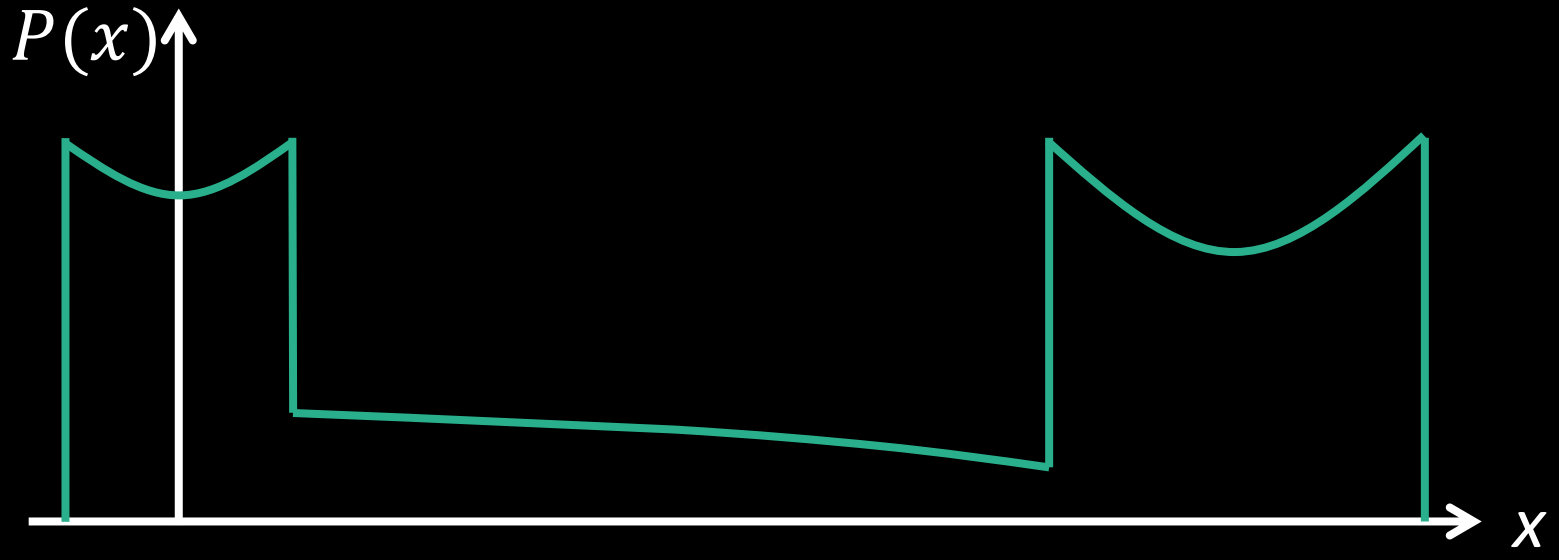
- SC Glotzer, EA Di Marzio & M Muthukumar (1995) Phys. Rev. Lett
- D Zwicker, AA Hyman & F Jülicher (2015) Phys. Rev. E
- JD Wurtz & CFL (2018) Phys. Rev. Lett.
- Review: CA Weber, D Zwicker, F Jülicher & CFL (2019) Rep. Prog. Phys.

Phase separation with chemical reactions

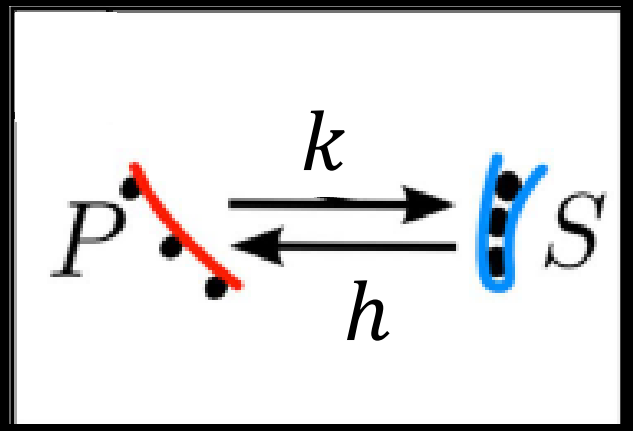


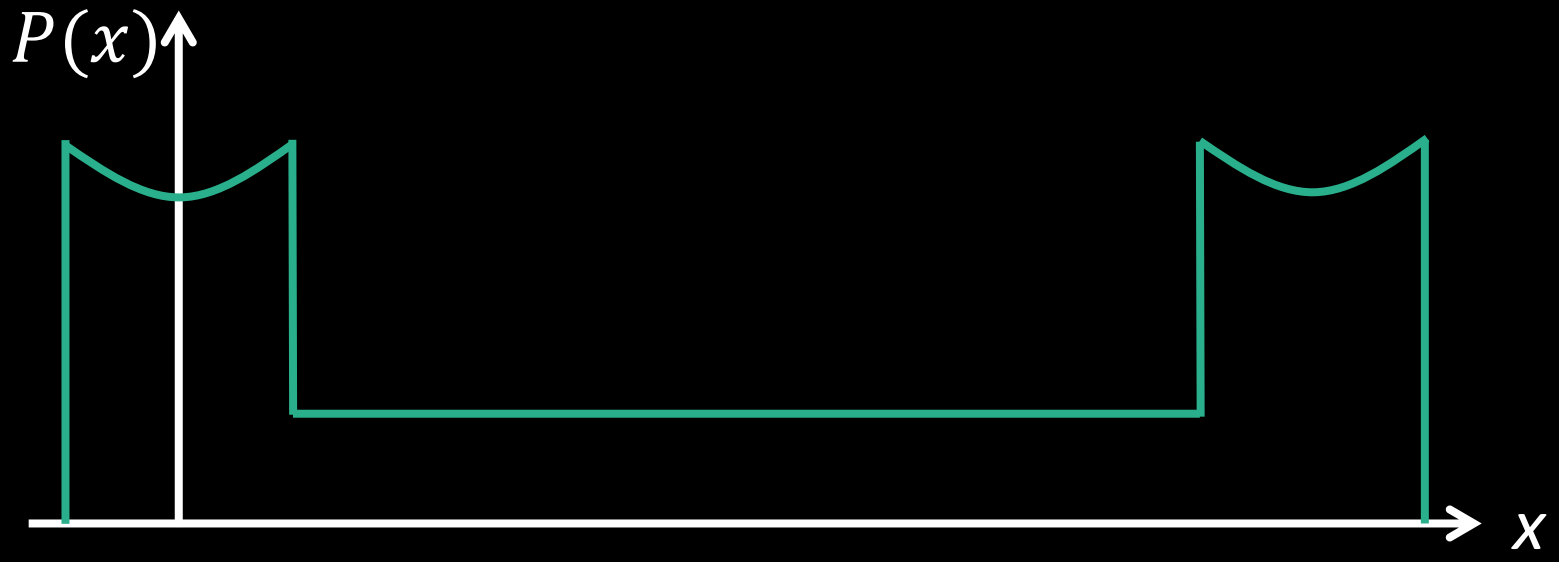
Phase separation with chemical reactions



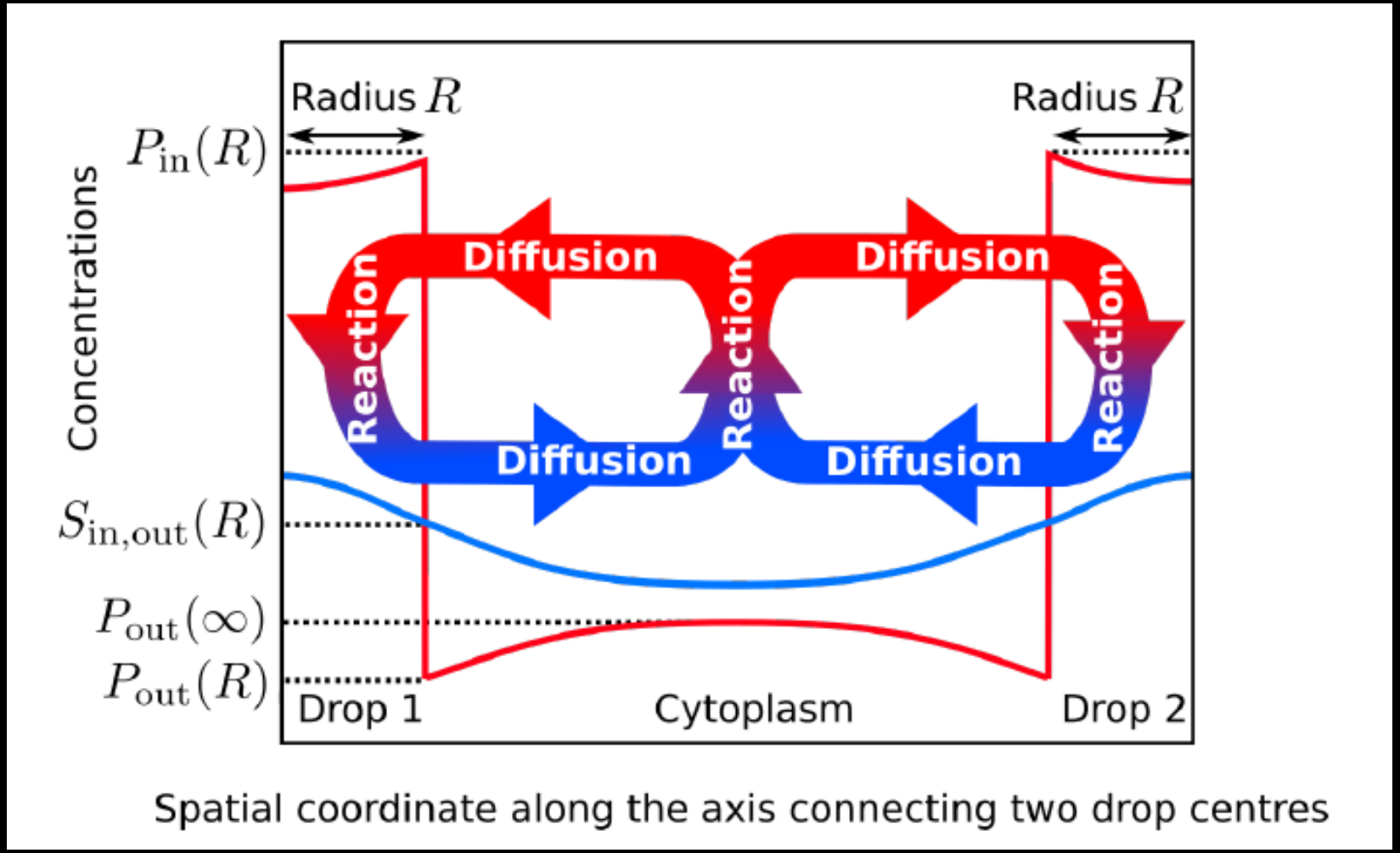


Phase separation with chemical reactions



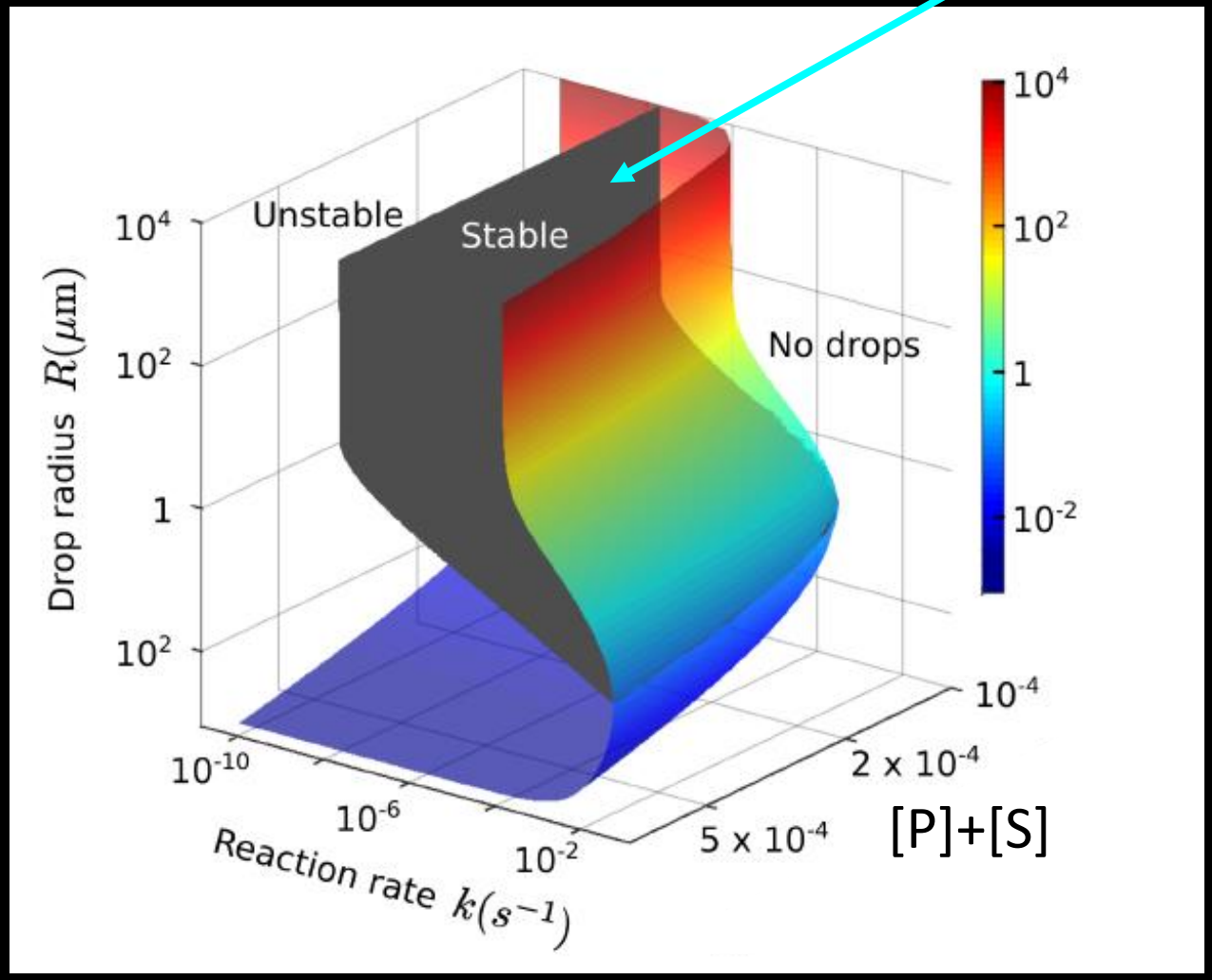


Chemical reaction can stop coarsening

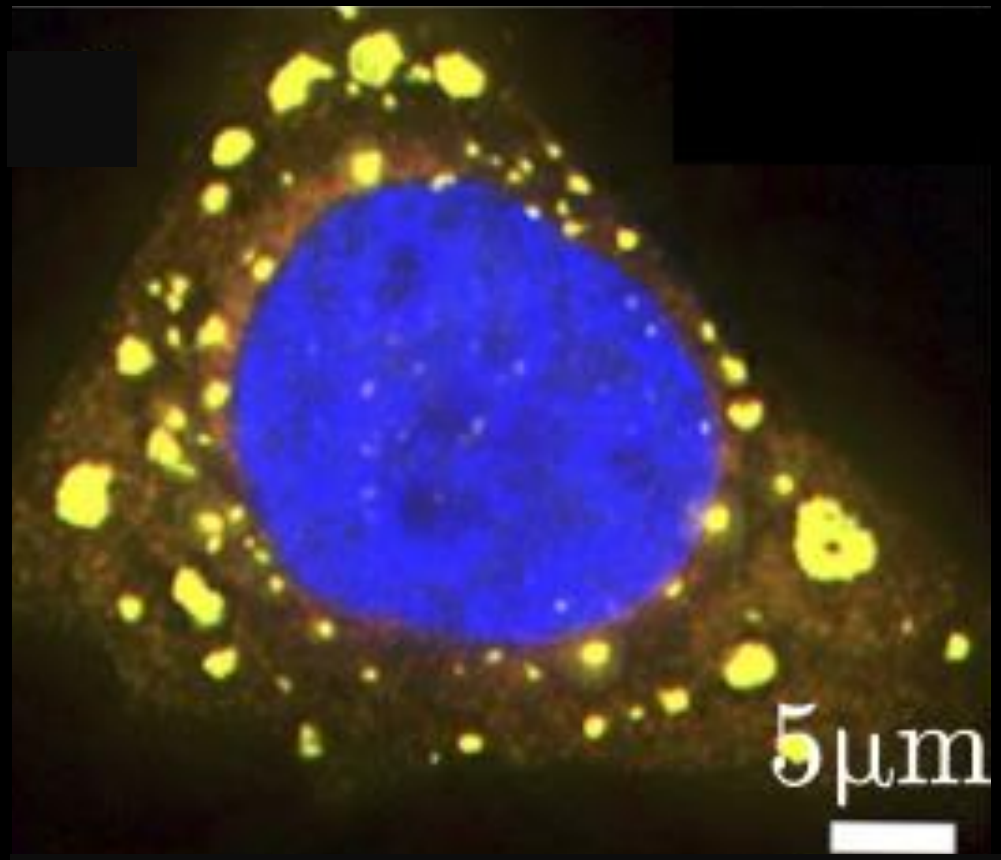


CFL & JD Wurtz (2019) Journal of Physics D

Novel phase diagram



JD Wurtz & CFL (2018) Phys. Rev. Lett.



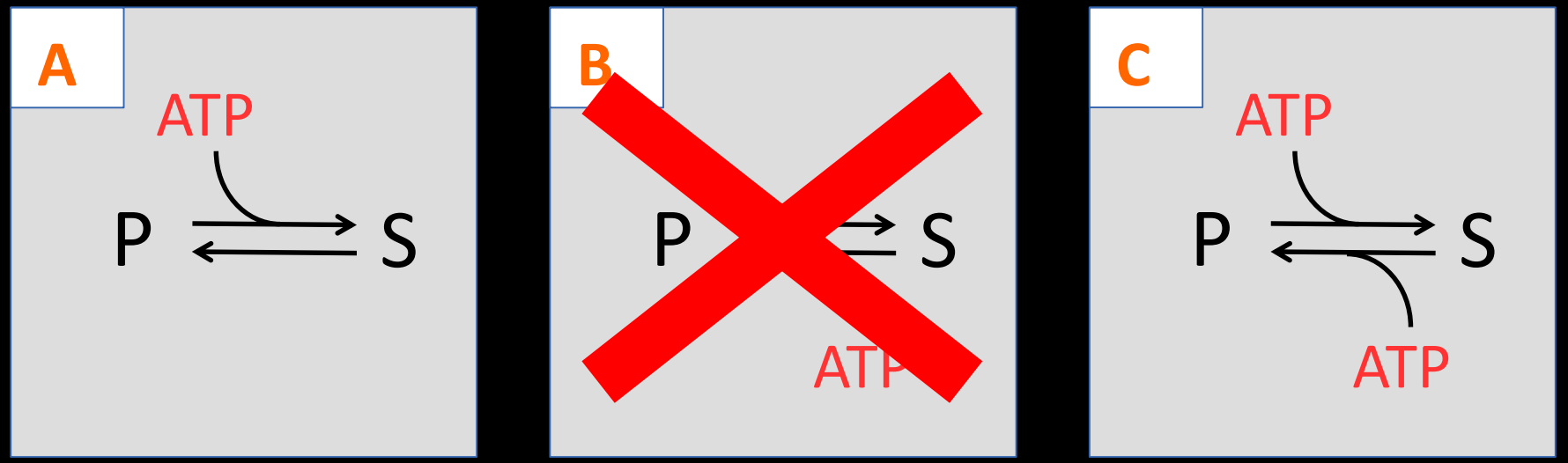
JR Wheeler et al. (2018) eLife

3. Implications for stress granule formation

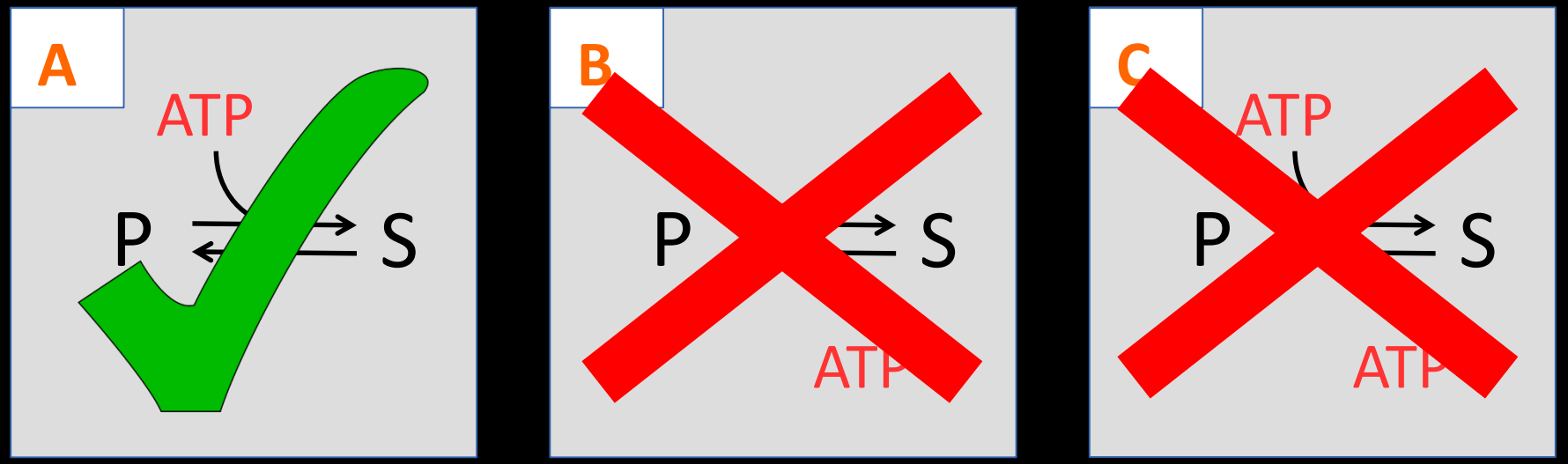
ATP depletion-triggered stress granule formation

Two assumptions

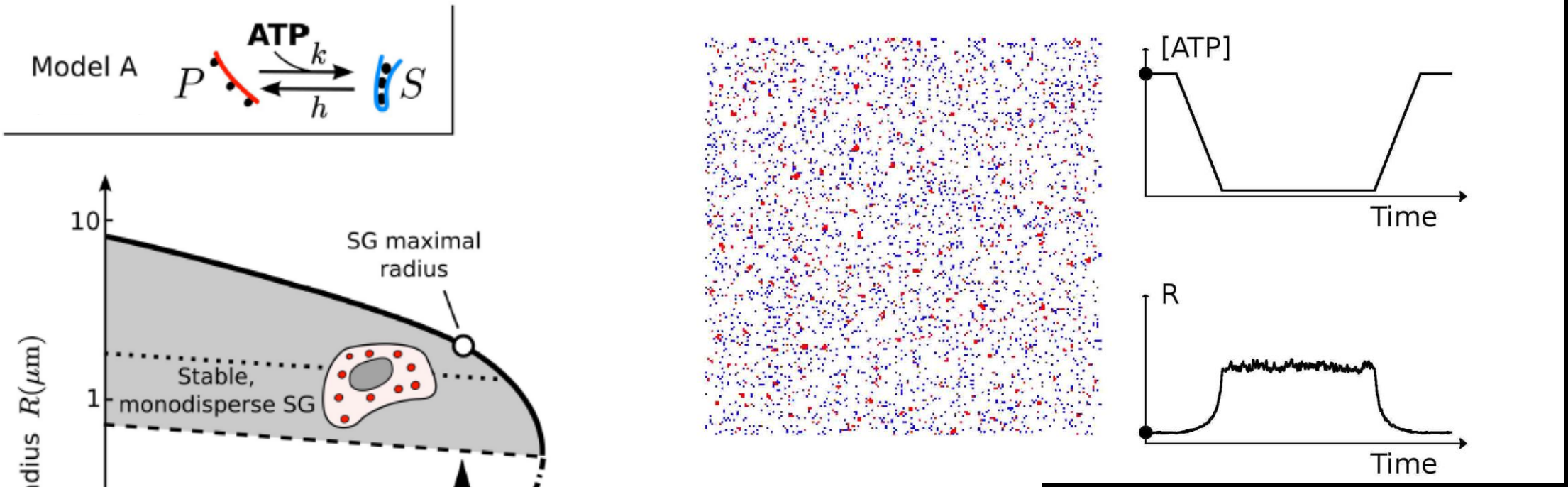
1. ATP-driven conversion(s) between phase separating form (P) and soluble form (S)
2. No SG at normal [ATP], but SG form at 50% [ATP]



1. ATP-driven conversion between phase separating form (P) and soluble form (S)
2. No SG at normal [ATP], but SG form at 50% [ATP]



Model C: 50% drop in [ATP] -> SGs with < 140nm in size



JD Wurtz & CFL (2018)
New J. Phys.

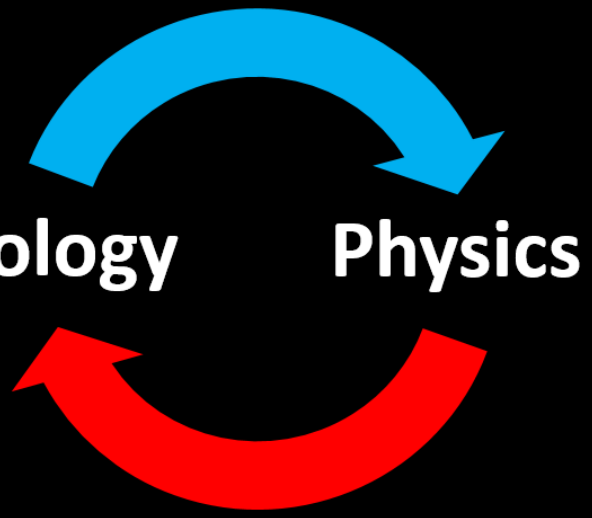
Insurance mechanism

	Cell	**Car**
Normal conditions	ATP consumption	Monthly payment
Stress conditions / Accident	SG formation for free	Insurance coverage

Insurance scheme: SG are tied to unpredictable environment

Summary

Biology inspires new physics



Physics allows us to do quantitative biology

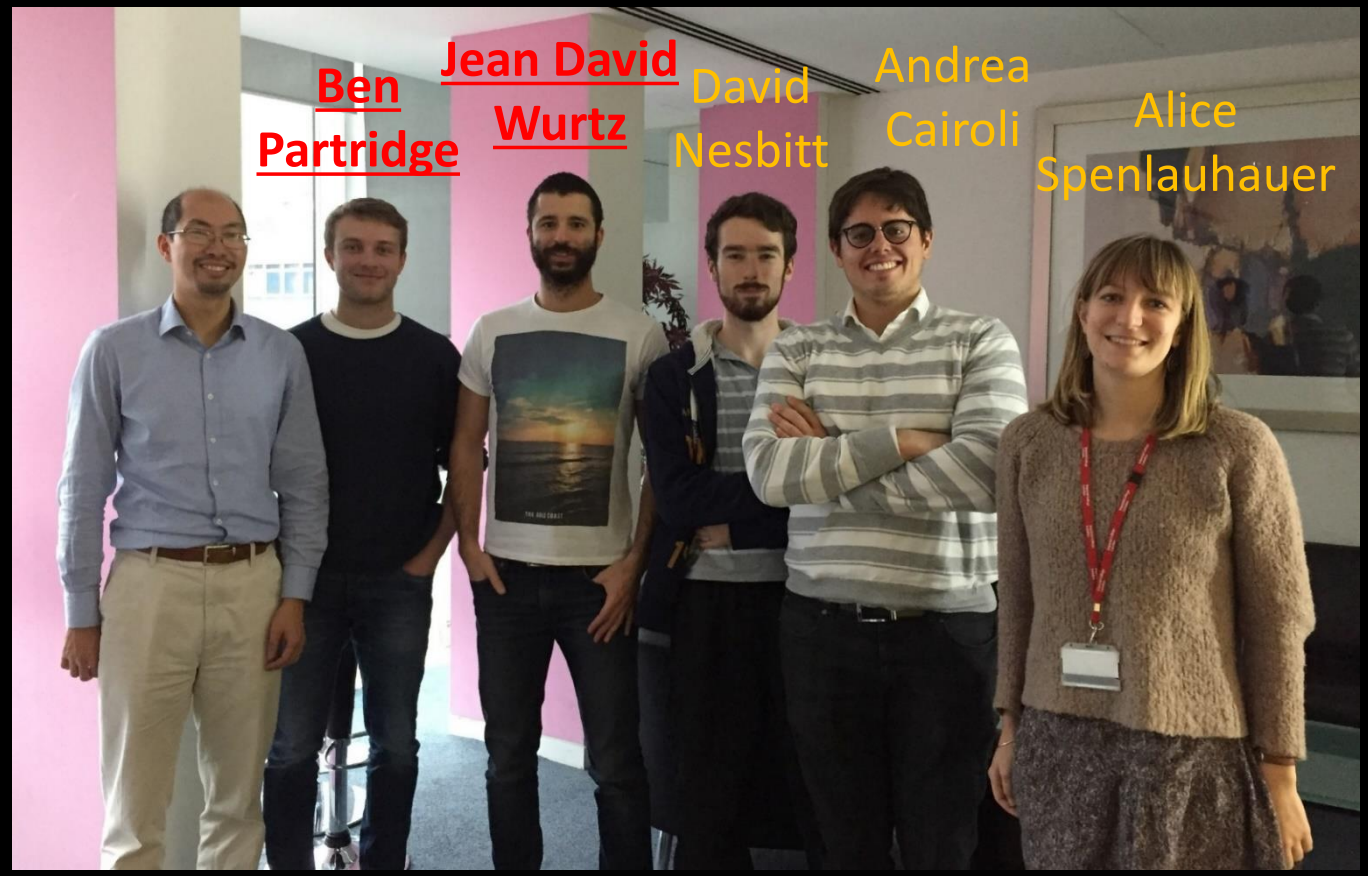
- Driven phase separation
  - Chemical reaction can lead to a stable, multidrop system

- ATP depletion-triggered stress granule formation
  - ATP promotes solubility of SG constituents
  - Regulation by crossing phase boundary

CFL & JD Wurtz (2019) *Novel physics arising from phase transitions in biology.* J. Phys. D: Appl. Phys. 52, 023001

Imperial College London

Universality in biology group



Thanks:

Christoph Weber (MPI-PKS)
David Zwicker (MPI-DS)
Frank Jülicher (MPI-PKS)

Thank you for your attention!

BBSRC bioscience for the future

EPSRC