

IPLS Retreat
Bath, Oct 17, 2017

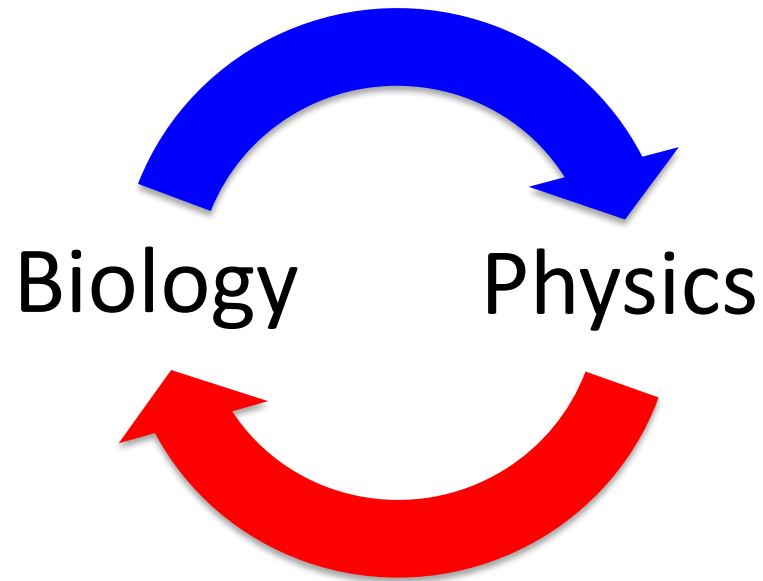
Novel Physics arising from phase transitions in biology

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Imperial College
London

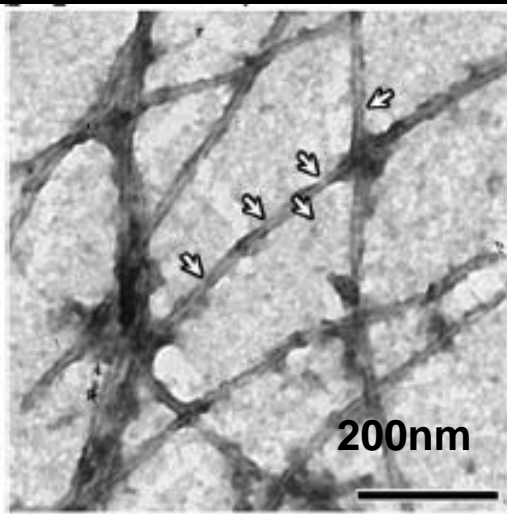
Biology inspires new physics



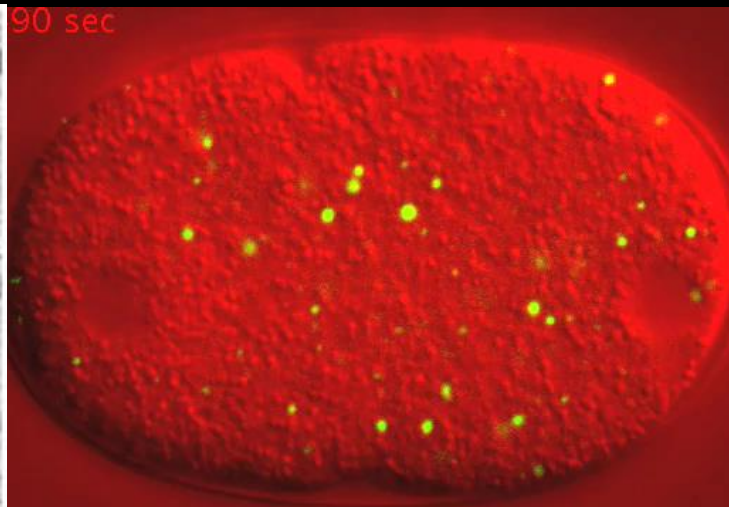
Physics leads to quantitative biology

Phase transitions in biology

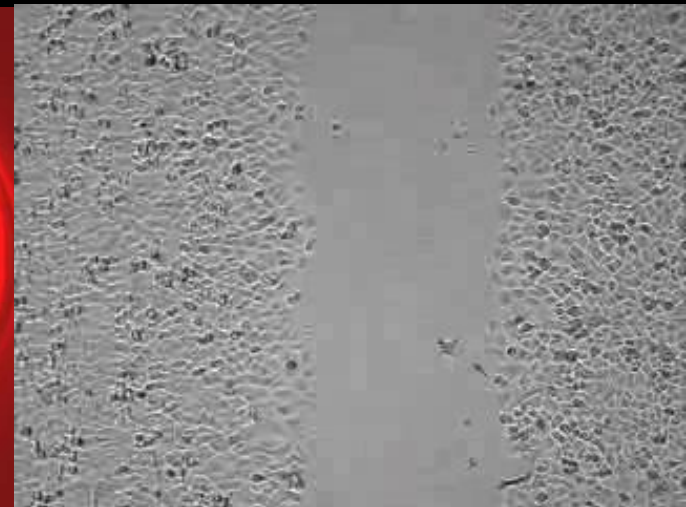
Amyloid fibrils



RNA granules



Active matter

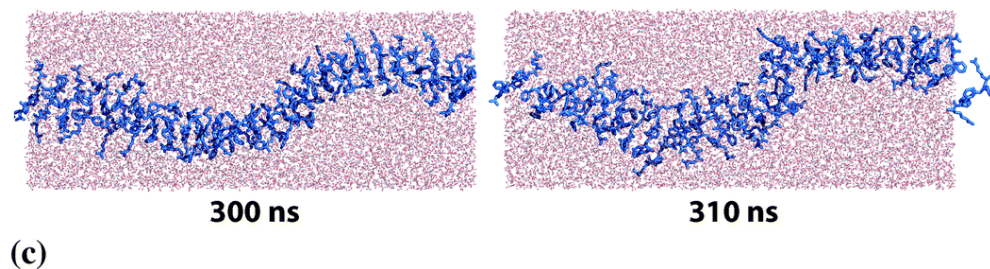
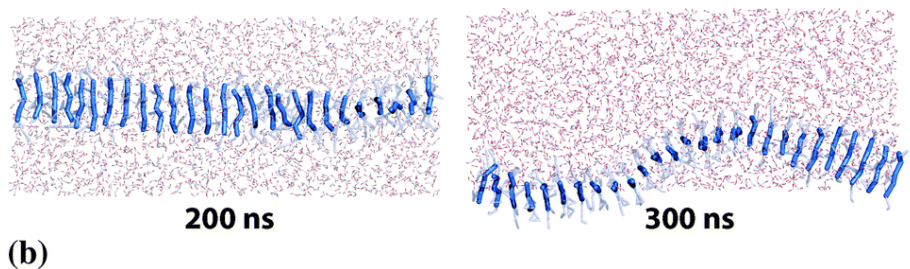
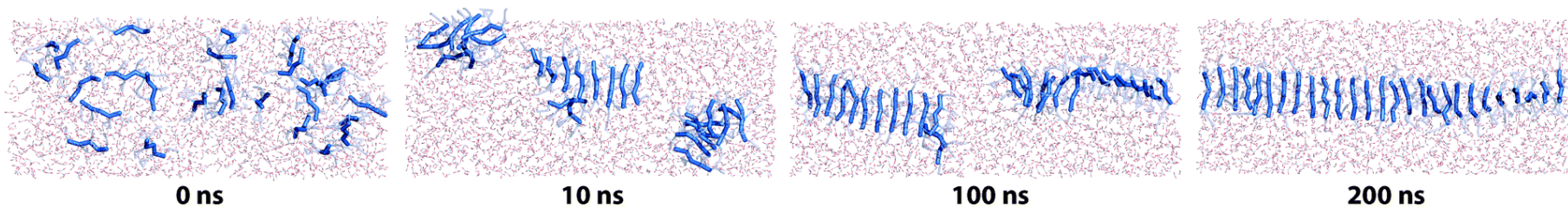


Brangwynne [Hyman Lab]

<https://www.youtube.com/watch?v=EimBzUSmak8>

Plan

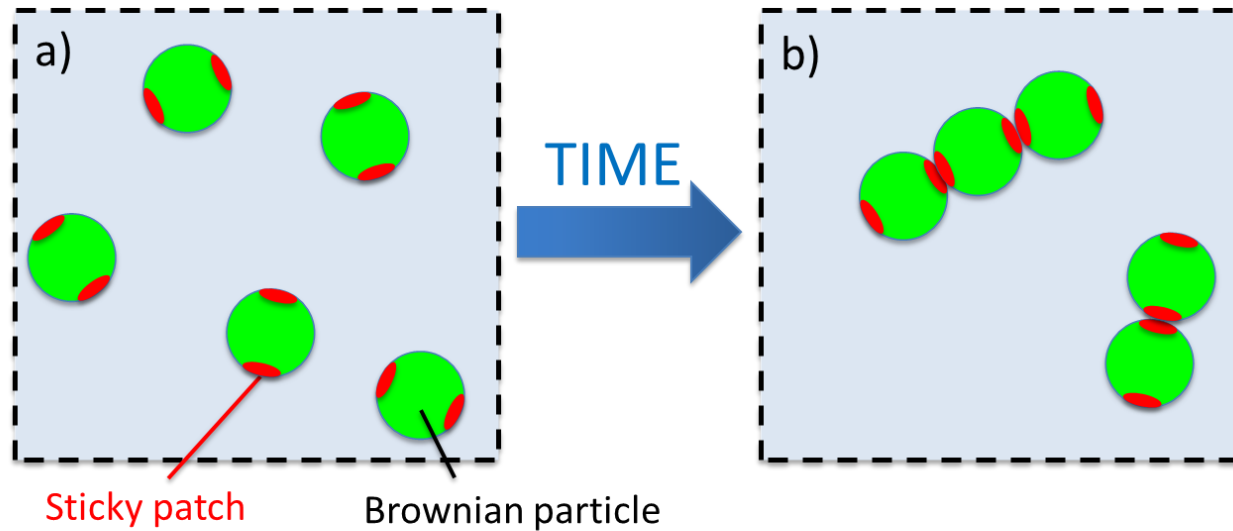
1. Physics of polymer self-assembly
2. Non-equilibrium phase separation
3. Universality in active matter
4. Summary & Outlook



Slyngborg & Fojan (2015) Phys. Chem. Chem. Phys.

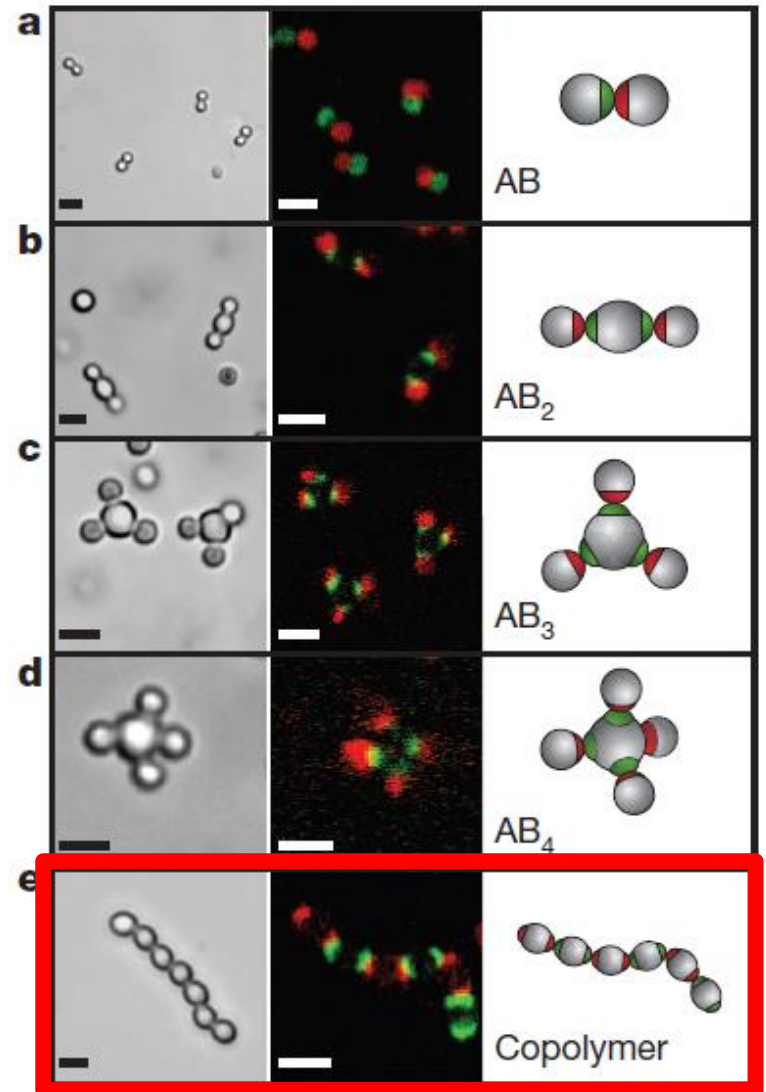
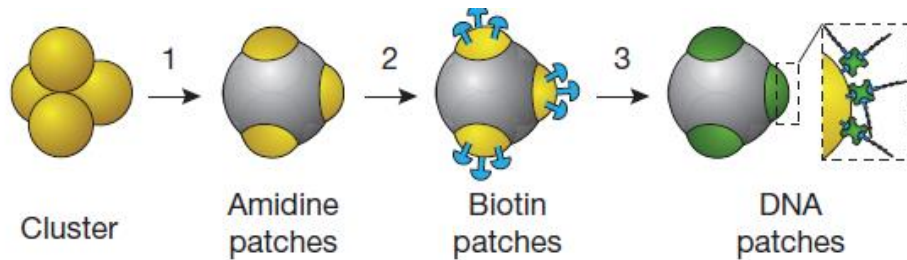
1. Physics of polymer self-assembly

Toy model



Liu, Lee & Huang, in Biophysics and biochemistry of protein aggregation (World Scientific, 2017)

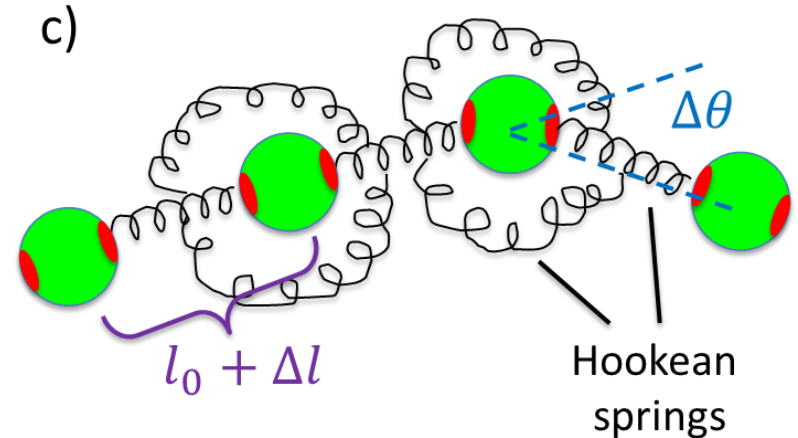
A colloidal example



Statistical mechanics

Energy of a s -mer:

$$U(\{\mathbf{x}\}) = \sum_{k=1}^{s-1} A\Delta l_k^2 + \sum_{h=1}^{s-2} B\Delta\theta_h^2 - E(s-1)$$



Monomer number conservation:

$$\sum_{s=1}^{\infty} sN_s = N$$

Partition function (dilute limit):

$$Z_{\text{tot}} = \prod_s \frac{1}{N_s!} \left(\frac{Vz_s}{\Lambda^3} \right)^{N_s}$$

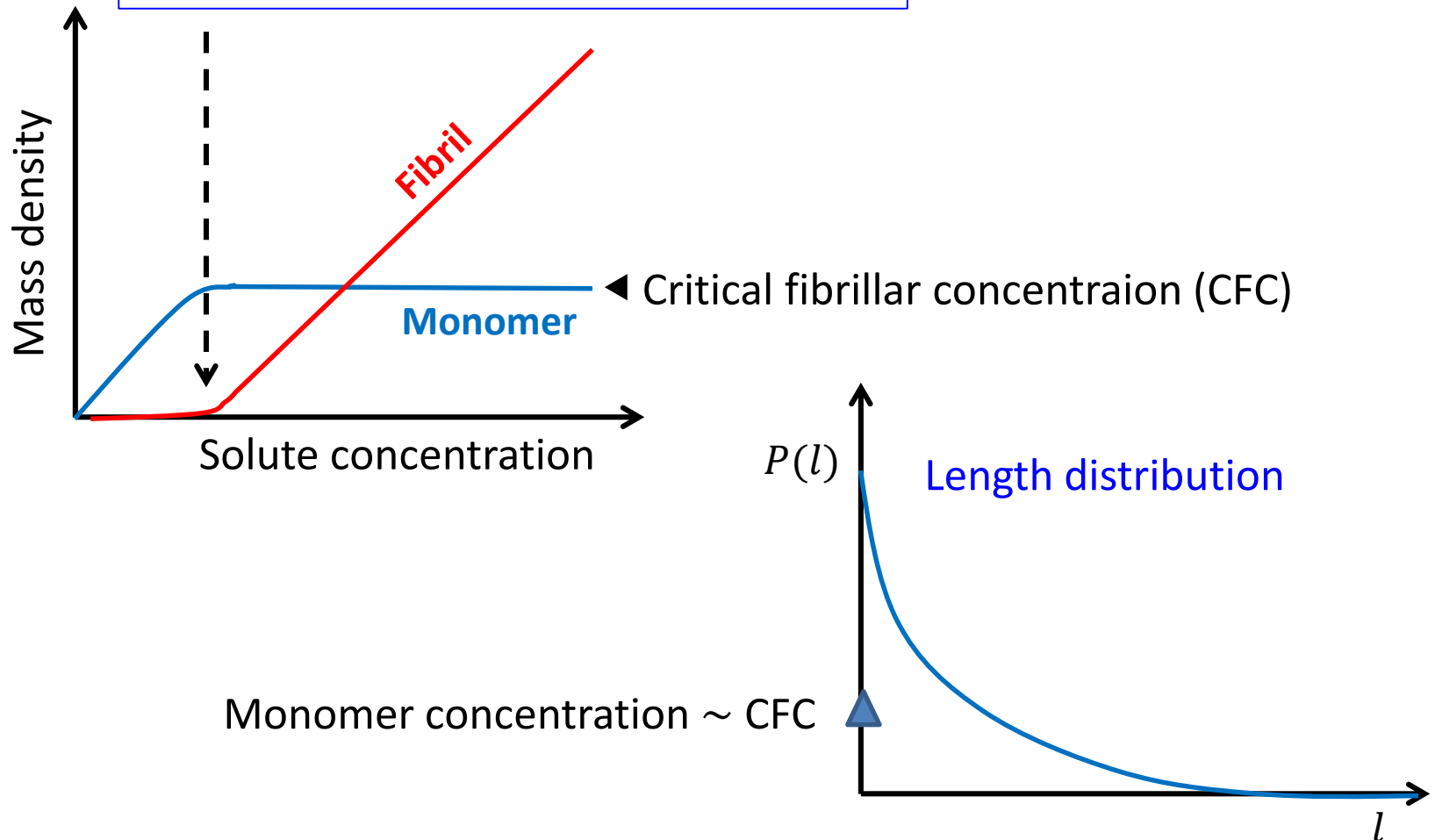
Factorial because of indistinguishability by our choice (nothing to do with quantum mechanics!)

$$\begin{aligned} z_s &= \frac{4\pi l_0^2 e^{(s-1)\beta E}}{\Lambda^{3(s-1)}} \left(\int_{-l_c}^{l_c} d\Delta l e^{-\beta A \Delta l^2} \right)^{s-1} \left(l_0^2 \int_0^{\theta_c} d\Delta\theta \sin(\Delta\theta) e^{-\beta B \Delta\theta^2} \right)^{s-2} \\ &= \frac{4\pi^{3/2} l_0^2 e^{\beta E}}{\Lambda^3 \sqrt{\beta A}} \left(\frac{l_0^2 \sqrt{\pi} e^{\beta E}}{\Lambda^3 \beta^{3/2} \sqrt{AB}} \right)^{s-2} \end{aligned}$$

Liu, Lee & Huang, in Biophysics and biochemistry of protein aggregation (World Scientific, 2017)

Static configuration

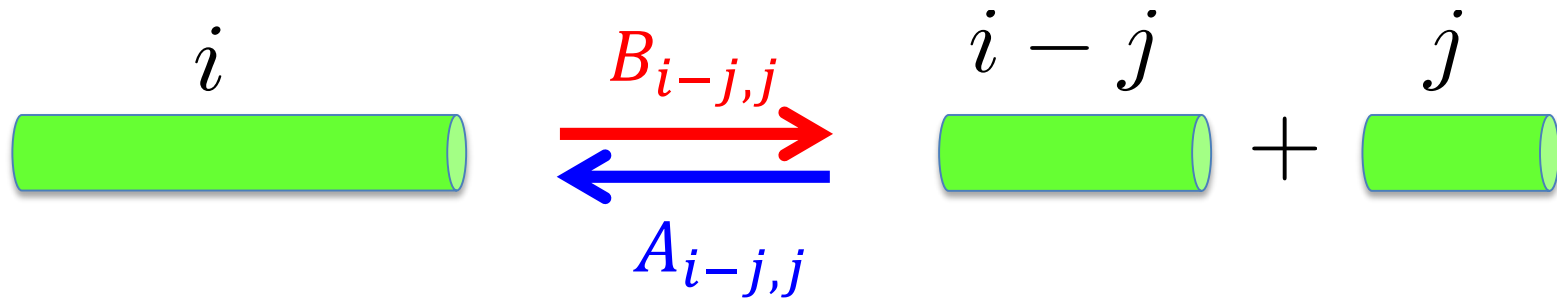
NOT a thermodynamic phase transition



Cates & Candau (1990) J. Phys.: Condens. Matter

Lee (2009) Phys. Rev. E; Lee (2012) J. Phys.: Condens. Matter

Steady-State Kinetics



$$\frac{d\rho_k}{dt} = \frac{1}{2} \sum_{i+j=k} A_{ij} \rho_i \rho_j - \rho_k \sum_{j \geq 1} A_{kj} \rho_j + \sum_{j \geq 1} B_{kj} \rho_{j+k} - \frac{\rho_k}{2} \sum_{i+j=k} B_{ij}$$

ρ_k : Concentration of k -mers

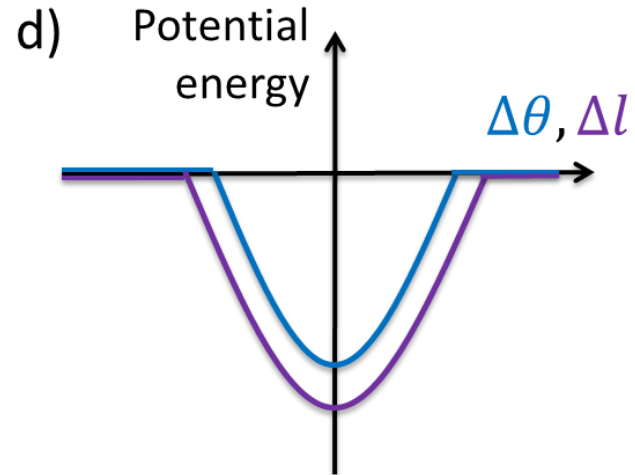
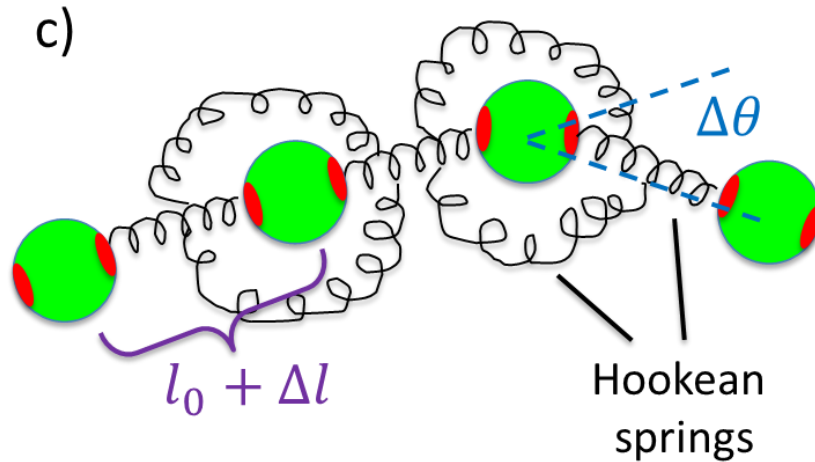
Thermal equilibrium: $\rho_k^* \equiv \lim_{t \rightarrow \infty} \rho_k(t) \propto \exp\left(-\frac{k}{\langle L \rangle}\right)$

➔

$$0 = \frac{1}{2} \sum_{i+j=k} A_{ij} \rho_i^* \rho_j^* - \rho_k^* \sum_{j \geq 1} A_{kj} \rho_j^* + \sum_{j \geq 1} B_{kj} \rho_{j+k}^* - \frac{\rho_k^*}{2} \sum_{i+j=k} B_{ij}$$

A_{ij} and B_{ij} are not independent!

Breakage rate B_{ij}

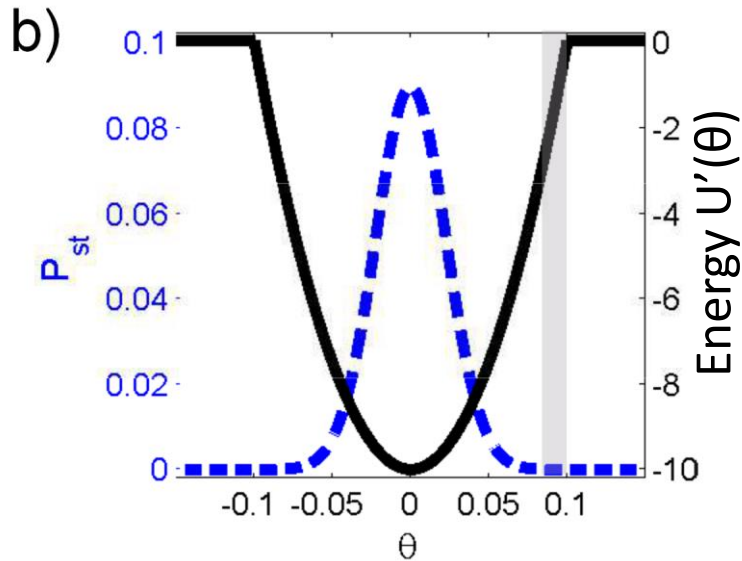


$$U(\{\mathbf{x}\}) = \sum_{k=1}^{s-1} A\Delta l_k^2 + \sum_{h=1}^{s-2} B\Delta\theta_h^2 - E(s-1)$$

Over-damped EOM:
$$\frac{d\vec{r}_i}{dt} = -\frac{1}{\zeta} \vec{\nabla}_{\vec{r}_i} U + \sqrt{\frac{2k_B T}{\zeta}} \vec{\eta}_i$$

Breakage rate = (First-passage time)⁻¹

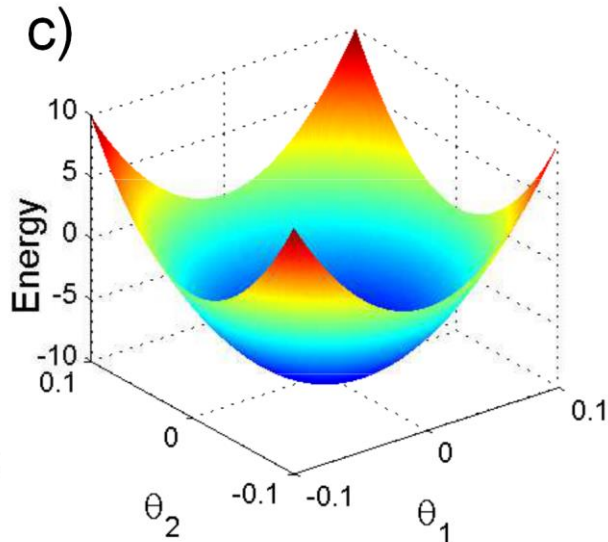
Asymptotic results



1D Kramers escape problem

Quasi-static approximation: $P(\theta) \propto e^{-B\theta^2}$

$$\text{Exit rate: } \frac{3|U'(\theta_c)|}{l^2\zeta} \sqrt{\frac{\beta B}{\pi}} e^{-\beta E}$$



Multidimensional Kramers escape problem

Breakage rate of a s -mer by thermal bending:

$$R_s = \frac{3(s-2)\beta B|U'(\theta_c)|\theta_c}{l^2\zeta} \sqrt{\frac{\beta B}{\pi}} e^{-\beta E}$$

Revisiting the kinetic equation

$$\frac{d\rho_k}{dt} = \frac{1}{2} \sum_{i+j=k} A_{ij} \rho_i \rho_j - \rho_k \sum_{j \geq 1} A_{kj} \rho_j + \sum_{j \geq 1} B_{kj} \rho_{j+k} - \frac{\rho_k}{2} \sum_{i+j=k} B_{ij}$$

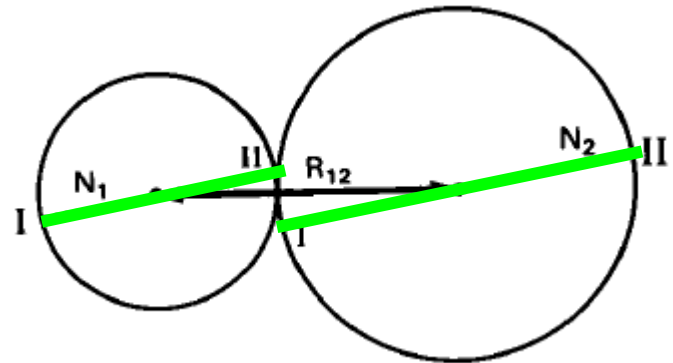
- Uniform breakage profile $\rightarrow B_{ij} = B$
- Steady state configuration $\rho_k^* \equiv \lim_{t \rightarrow \infty} \rho_k(t) \propto \exp\left(-\frac{k}{\langle L \rangle}\right)$
 $\rightarrow A_{ij} = A$
- Namely, all joining rates of any pair of polymers are identical, irrespective of the sizes
- *How does this square with the Smoluchowski picture?*

Smoluchowski reaction kinetics

Diffusion-controlled binary association rate:

$$A_{ij} \sim (D_i + D_j) \left(\frac{i + j}{2} \right)$$

where $D_i \sim \frac{\log i}{i}$




Considering the rod-like nature as well: $A_{ij} \sim \frac{i \log j + j \log i}{ij(i + j)}$

Hill (1983) Biophys. J.

What's wrong with this picture?

Breakage-controlled, NOT diffusion-controlled

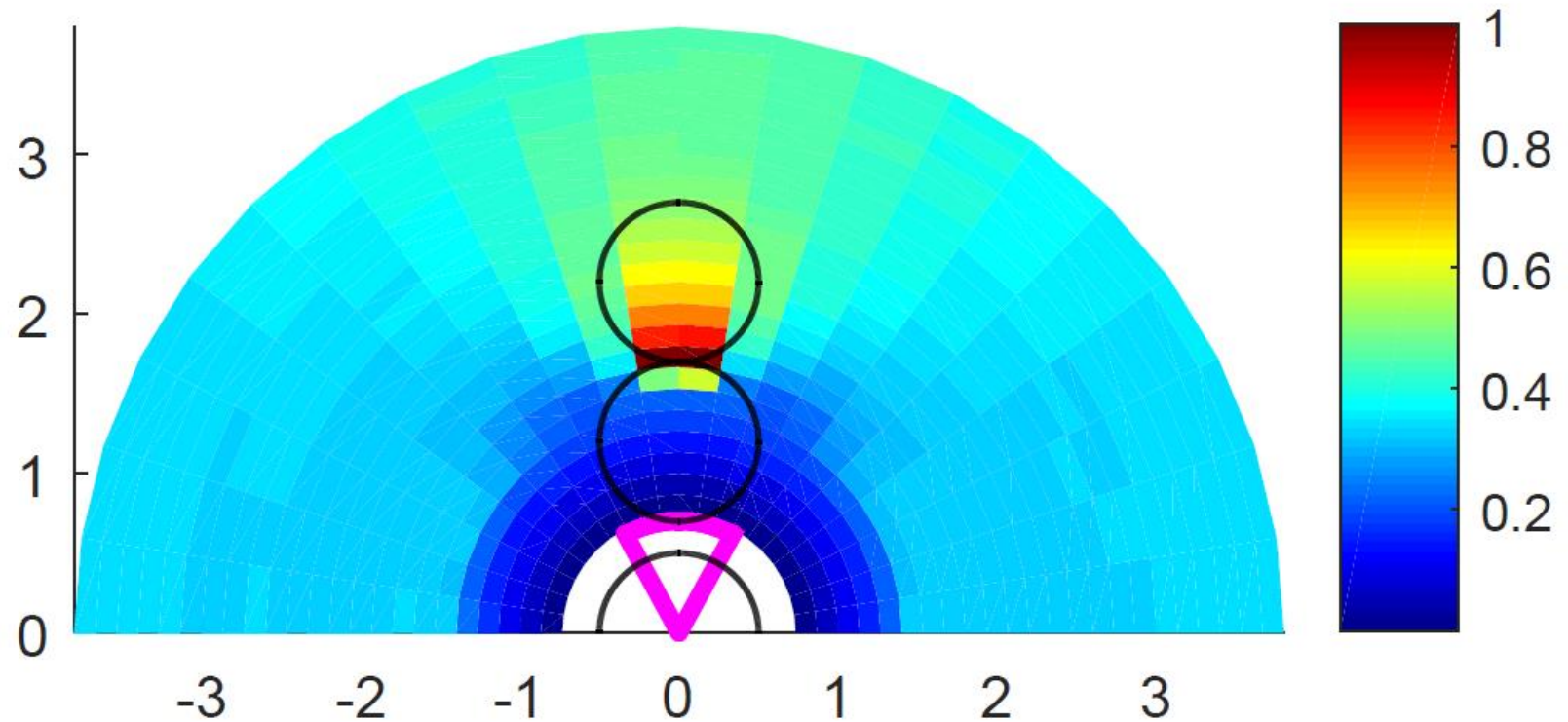
We can compute the breakage rate from the Smoluchowski picture and compare it to the true breakage rate


$$\frac{B_{ij}^{(\text{Smol})}}{B_{ij}^{(\text{ext})}} \propto \frac{i \log j + j \log i}{ij(i+j)\Delta E^{3/2}} \rightarrow_{\Delta E \rightarrow \infty} 0$$

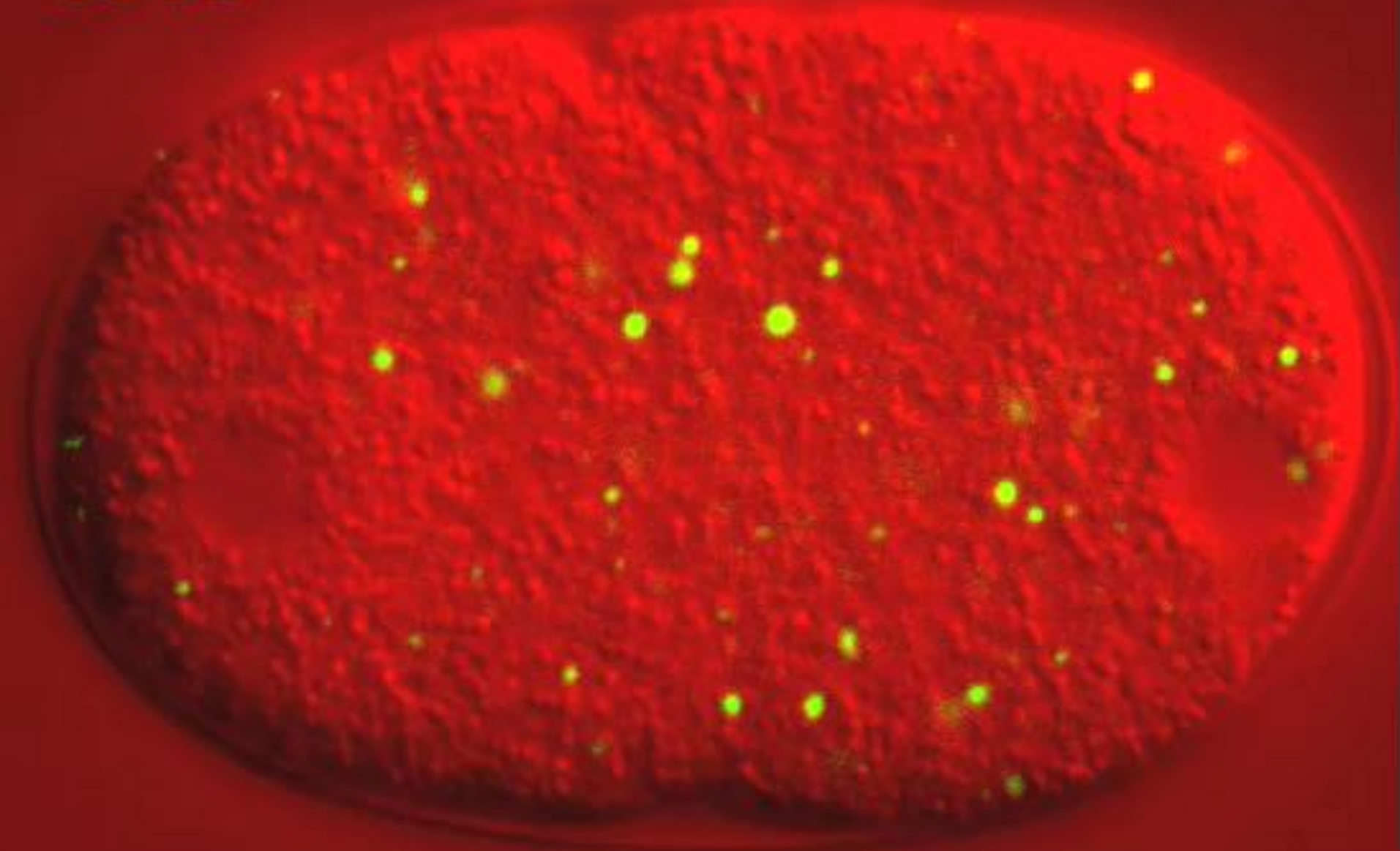
- *Therefore, a polymer interacts predominately with its own fragments!*

Spatial correlation

Distribution of dimer's center of mass



-490 sec



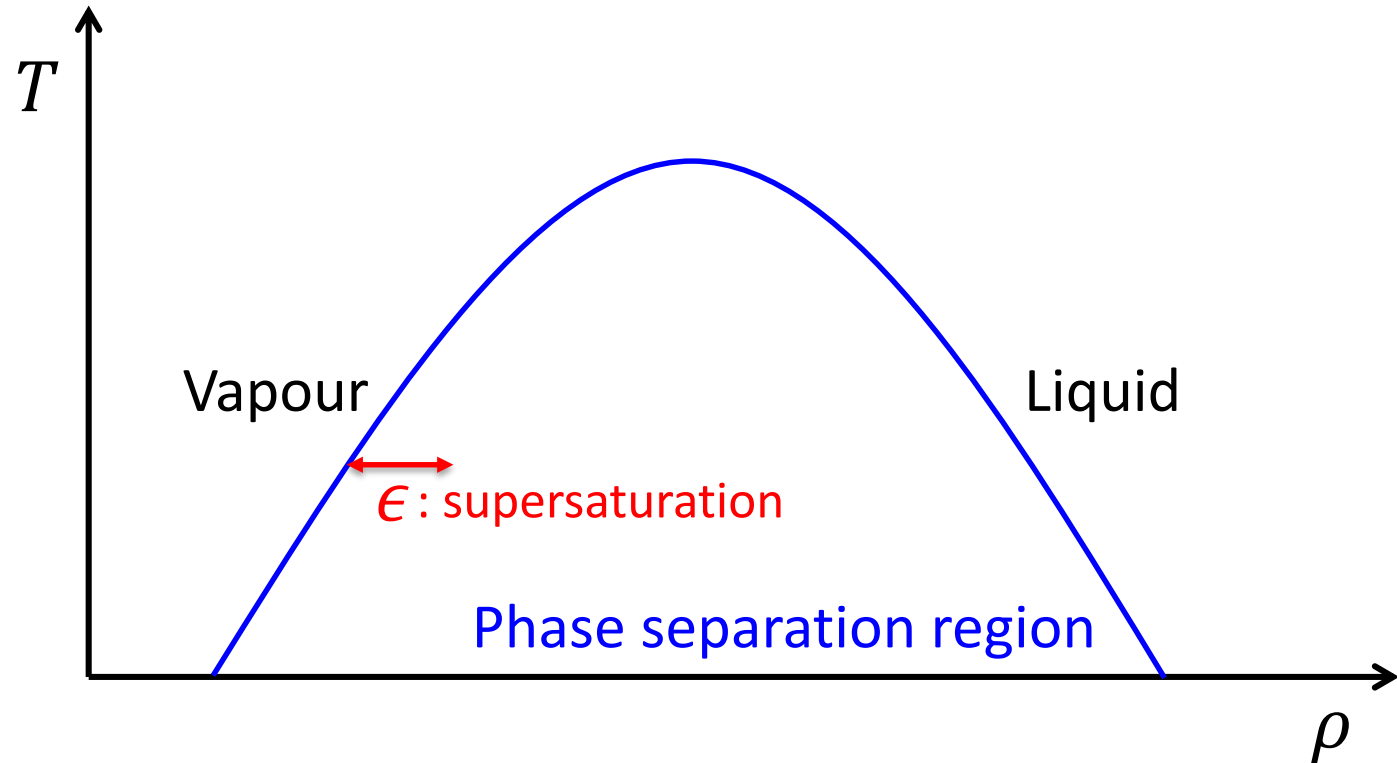
2. Non-equilibrium phase separations

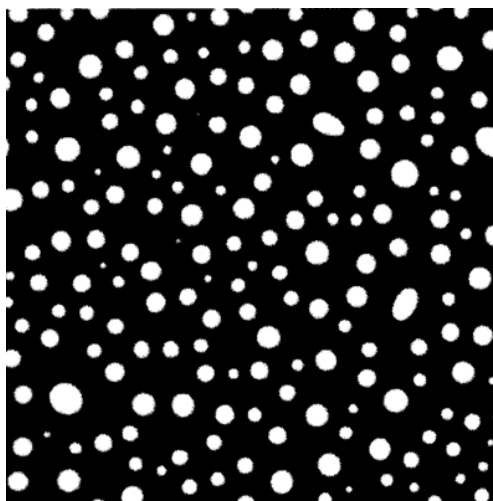
Formation by phase separation



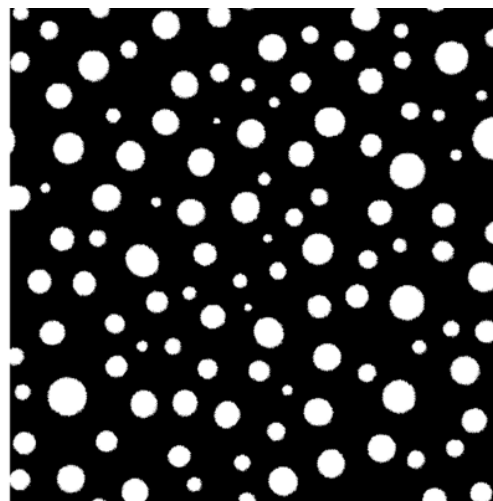
- No membrane
- Rapid turnover
- Coalescence

Phase diagram

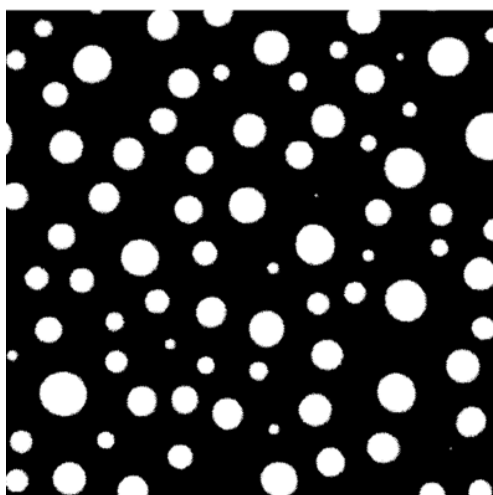




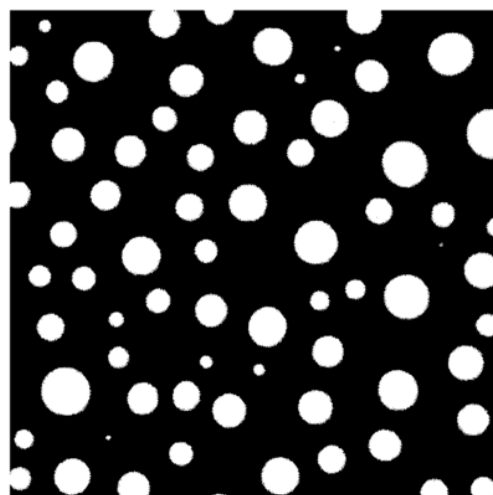
$t=10000$



$t=40000$

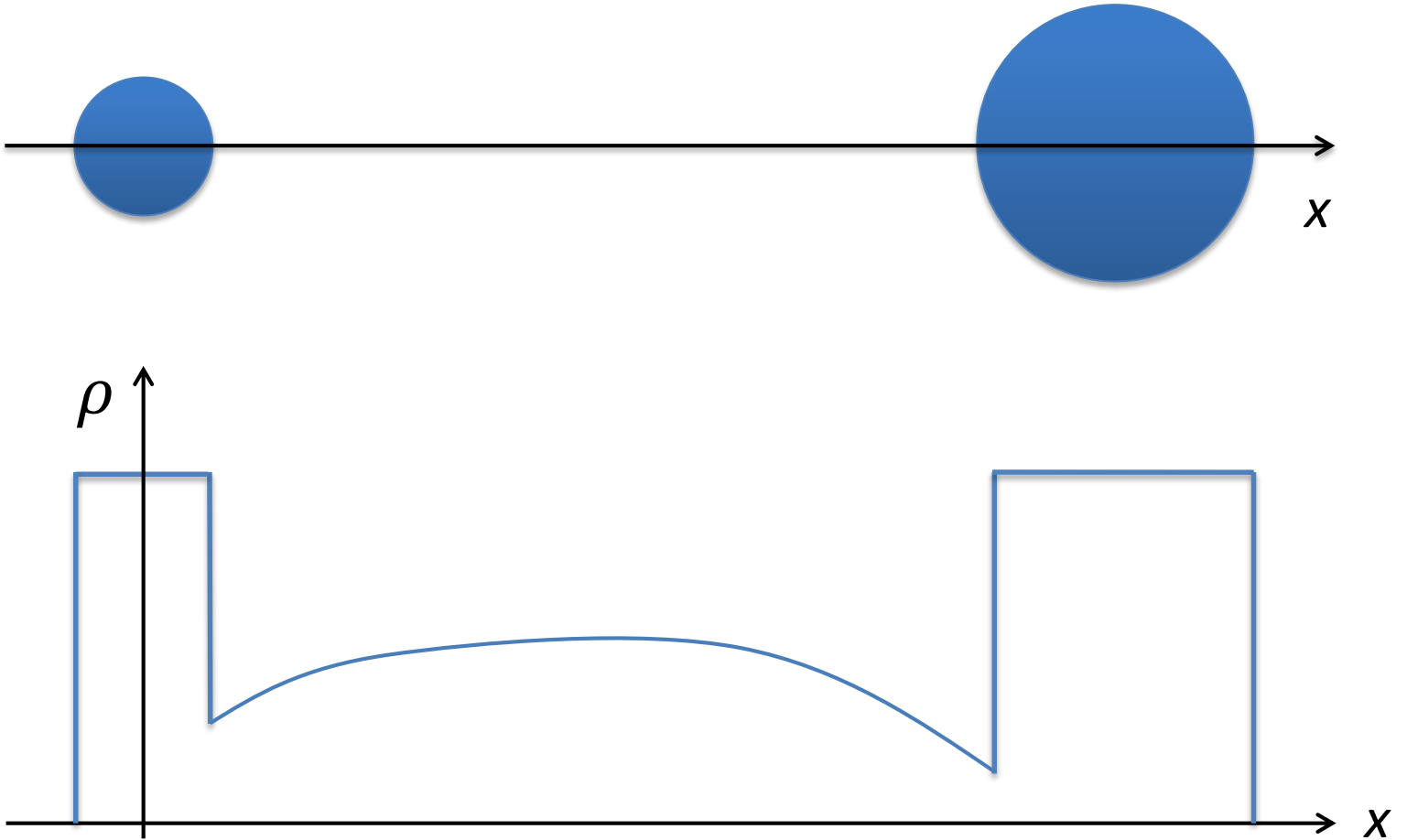


$t=80000$

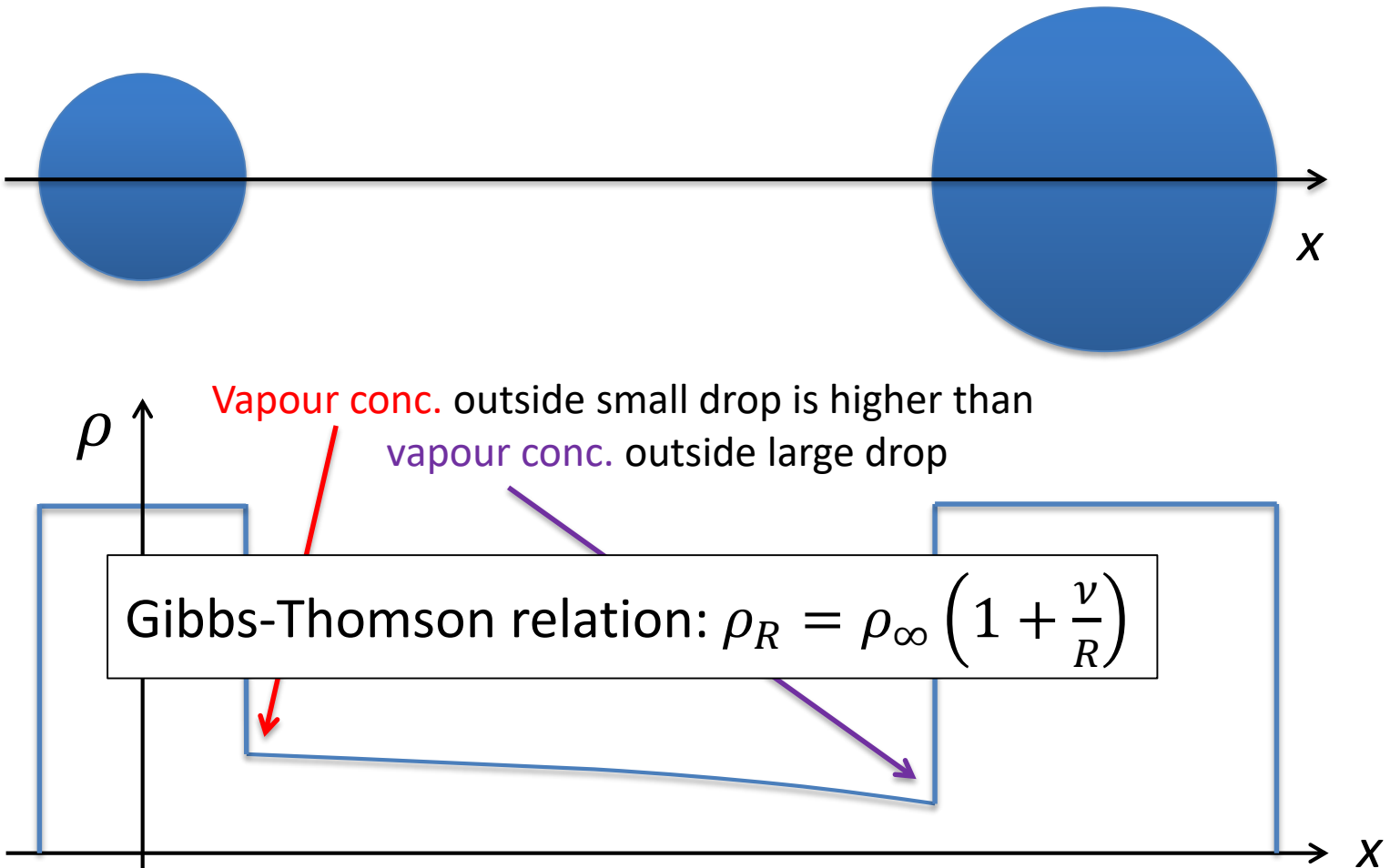


$t=100000$

Drop growth

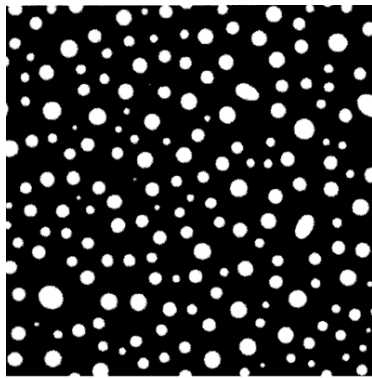


Drop growth

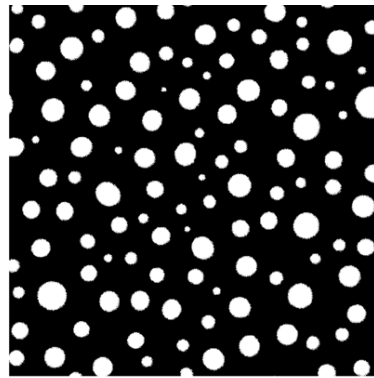


Universality of surface-tension driven droplet growth

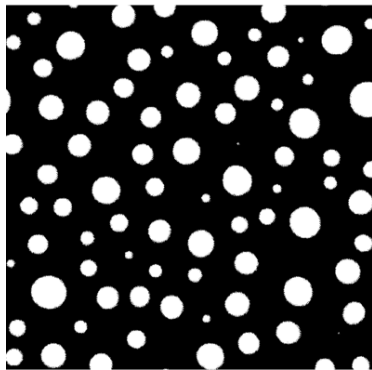
Ostwald coarsening



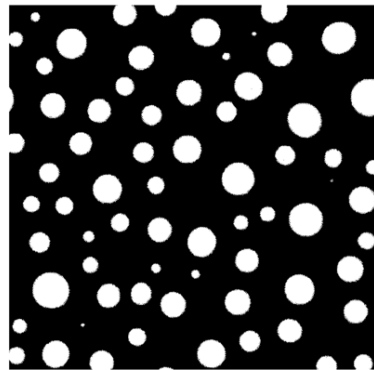
t=10000



t=40000

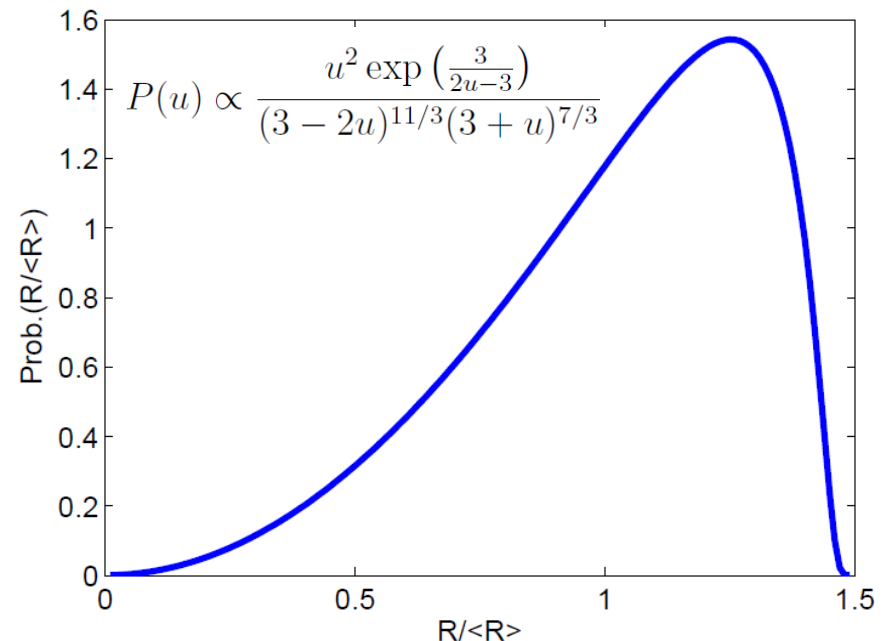


t=80000

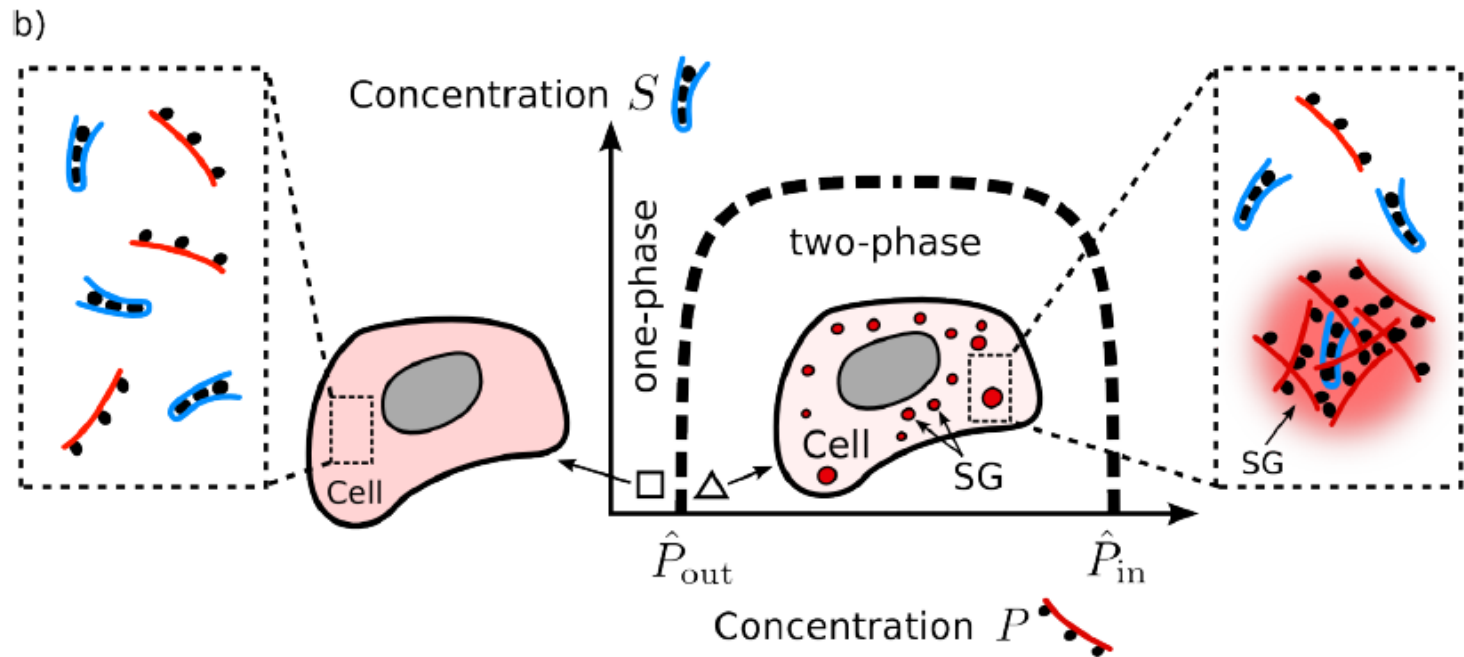


t=100000

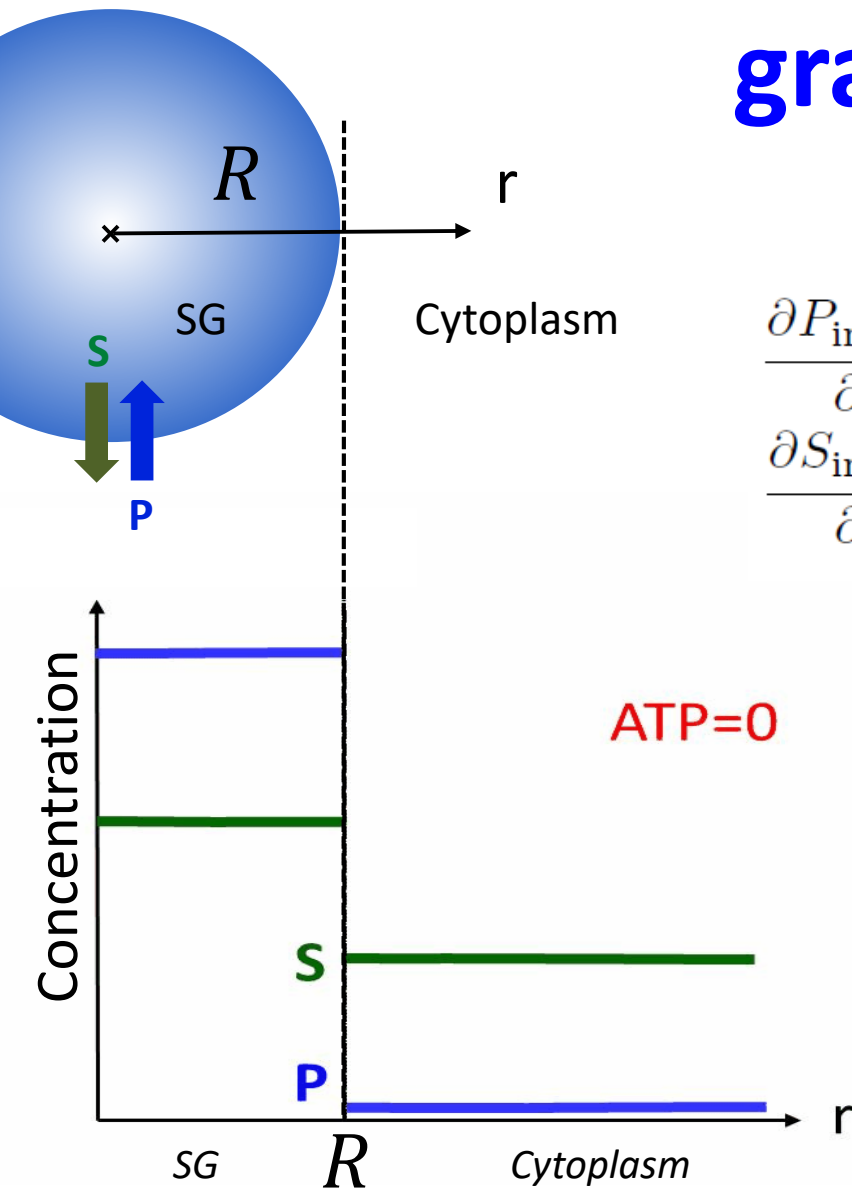
- Lifshitz-Slyozov universal growth law: $\langle R(t) \rangle \sim t^{1/3}$
- Universal droplet size distribution



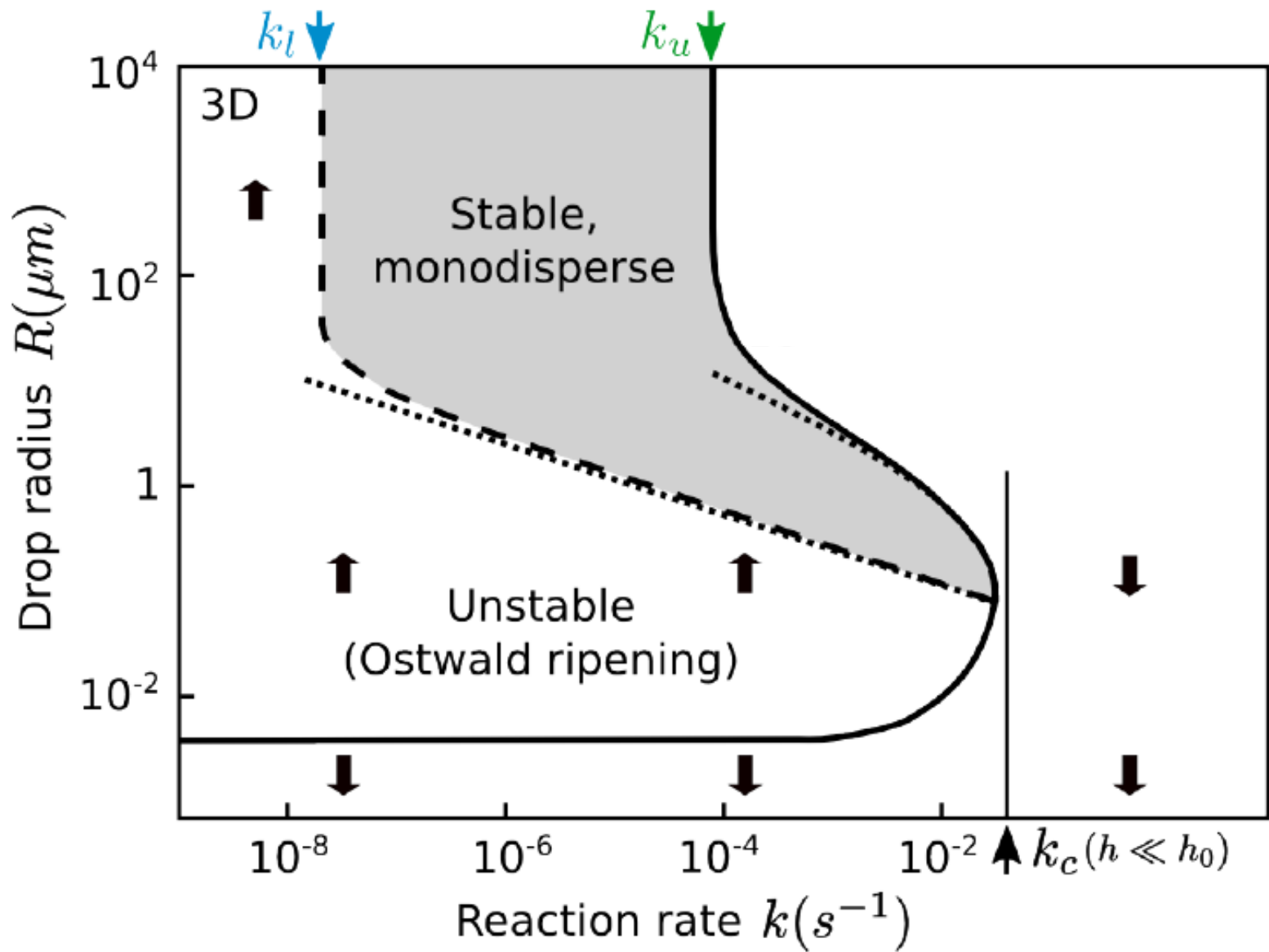
Chemical reaction-controlled phase separation

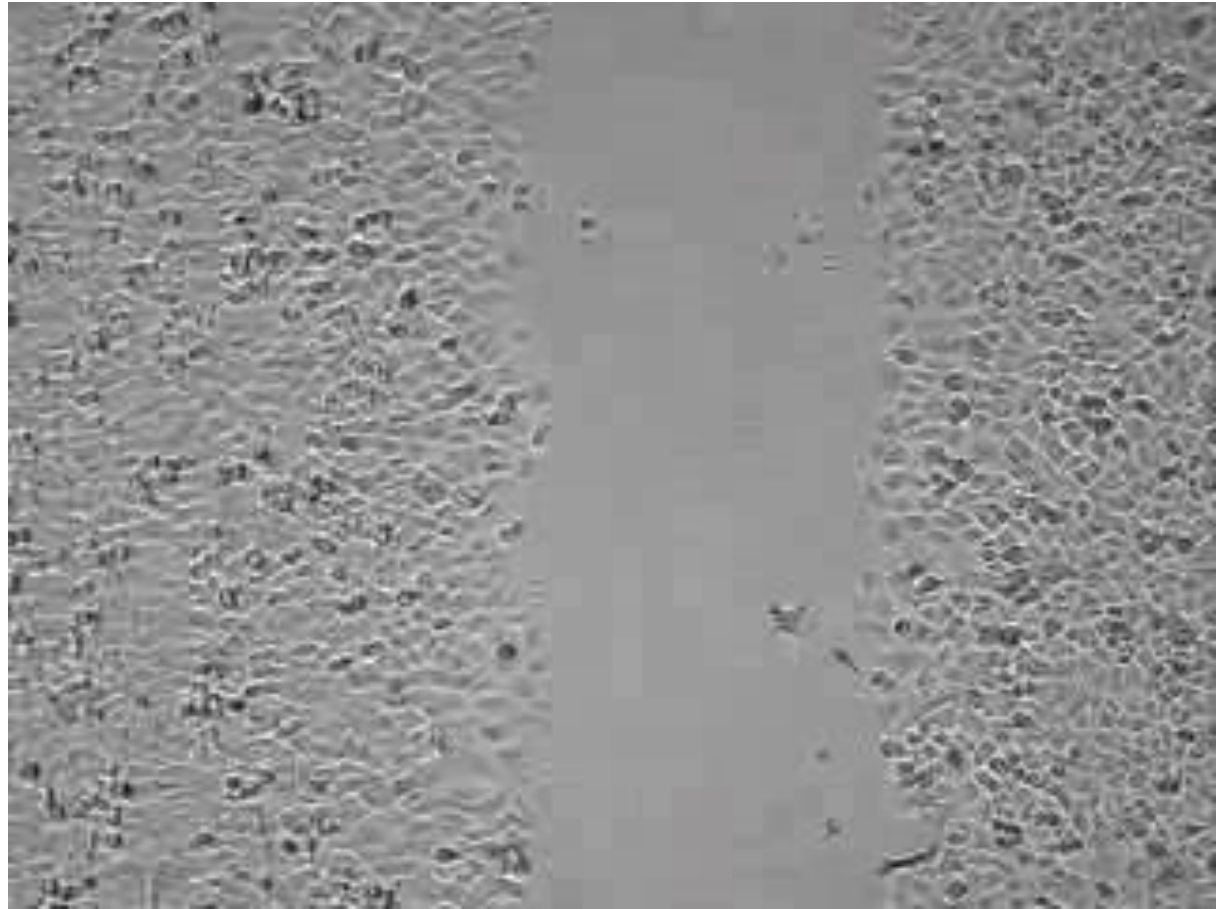


Chemical reactions create gradients



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





https://www.youtube.com/watch?v=v9xq_GiRXeE

3. Universality in active matter

Incompressible fluids

$$\partial_t \vec{v} = -\vec{\nabla} P + \vec{f} - \lambda(\vec{v} \cdot \vec{\nabla})\vec{v} - (a + bv^2)\vec{v} - \mu \nabla^2 \vec{v} + cv^4 \vec{v} + \xi(\nabla^2)^2 \vec{v} + \dots$$



Symmetries + coarse-graining *via* renormalisation group transformation

$$\partial_t \vec{v} = -\vec{\nabla} P + \vec{f} - (\vec{v} \cdot \vec{\nabla})\vec{v} - \mu \nabla^2 \vec{v}$$

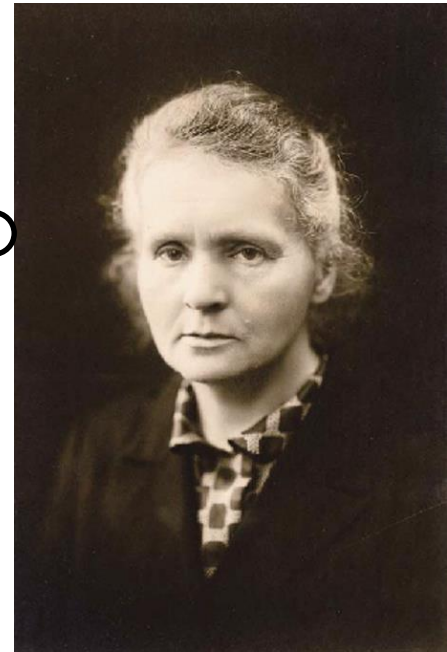
Parameter-free prediction:

$$\langle \vec{v}(t) \cdot \vec{v}(0) \rangle \propto t^{-(d/2)}$$

(Long-time tail)

Physical systems

- Translational invariance
- Rotational invariance
- Galilean invariance
- Fluctuation-dissipation



Incompressible active fluids



$$\partial_t \vec{v} = -\vec{\nabla} P + \vec{f} - \lambda(\vec{v} \cdot \vec{\nabla})\vec{v} - (a + bv^2)\vec{v} - \mu \nabla^2 \vec{v} + cv^4 \vec{v} + \xi(\nabla^2)^2 \vec{v} + \dots$$

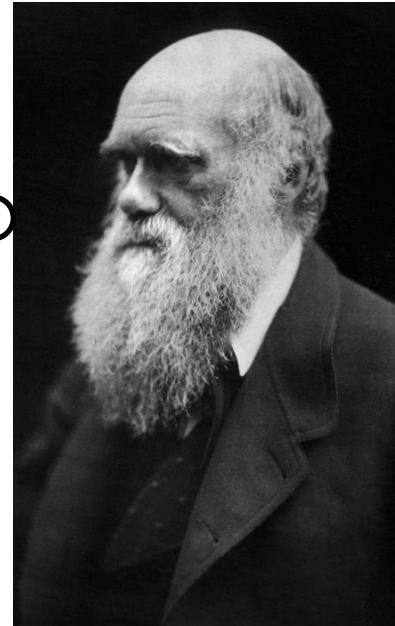


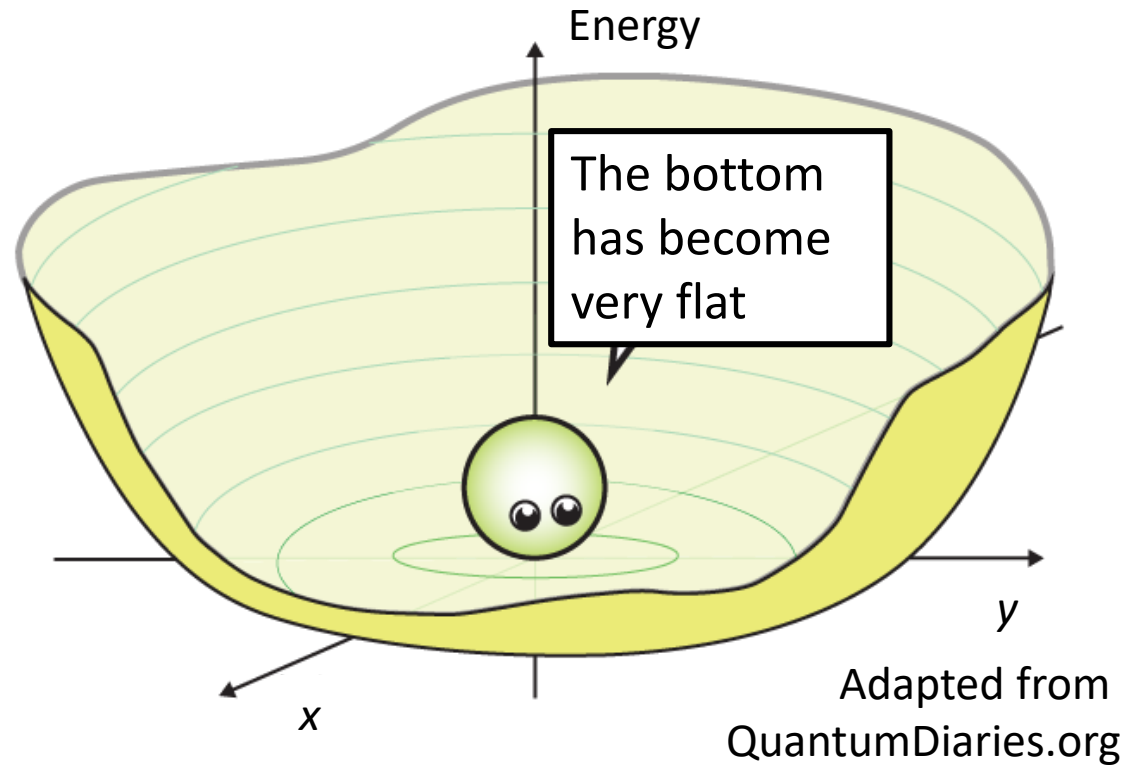
Symmetries + coarse-grain *via* renormalisation group transformation

$$\partial_t \vec{v} = -\vec{\nabla} P + \vec{f} - \lambda(\vec{v} \cdot \vec{\nabla})\vec{v} - (a + bv^2)\vec{v} - \mu \nabla^2 \vec{v}$$

Biological systems

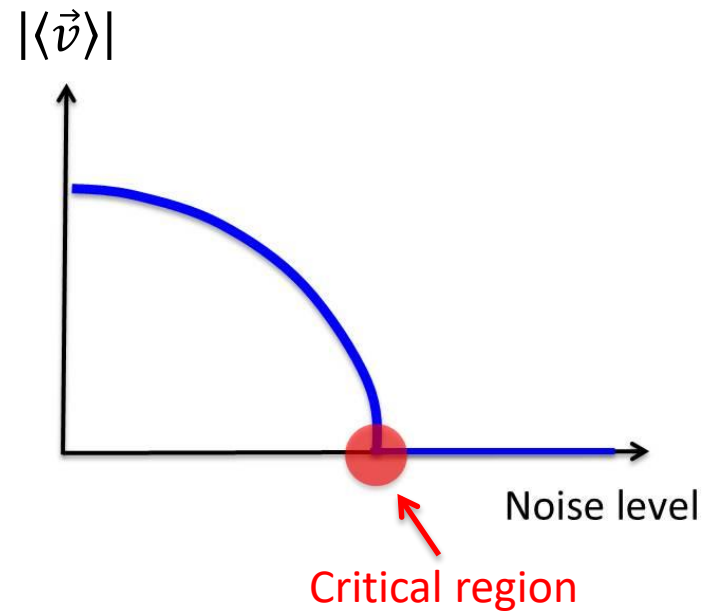
- Translational invariance
- Rotational invariance
- Galilean invariance
- Fluctuation-dissipation





Critical order-disorder transition

Phase diagram of incompressible active fluids



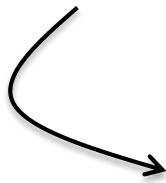
Critical incompressible active fluids

$$\text{EOM: } \partial_t \vec{v} + \vec{\nabla} P - \vec{f} = -\lambda(\vec{v} \cdot \vec{\nabla})\vec{v} - (a + bv^2)\vec{v} - \mu \nabla^2 \vec{v} + cv^4 \vec{v} + \xi(\nabla^2)^2 \vec{v} + \dots$$



RG transformation

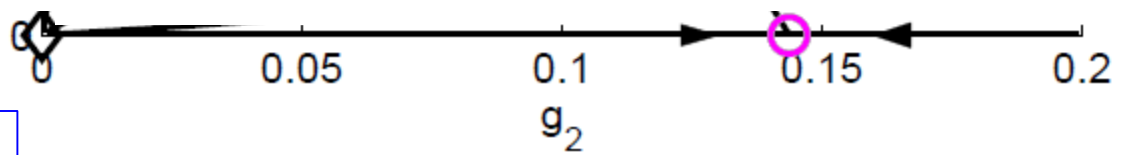
$$\partial_t \vec{v} + \vec{\nabla} P + \vec{f}_l = -\lambda_l(\vec{v} \cdot \vec{\nabla})\vec{v} - (a_l + b_l v^2)\vec{v} - \mu_l \nabla^2 \vec{v}$$



Exact hydrodynamic EOM with TWO coefficients governing the model's scale-invariance properties:

$$g_1(l) \sim \frac{D_l \lambda_l^2}{\mu_l^3} \quad , \quad g_2(l) \sim \frac{D_l b_l}{\mu_l^2}$$

Level of
coarse-graining

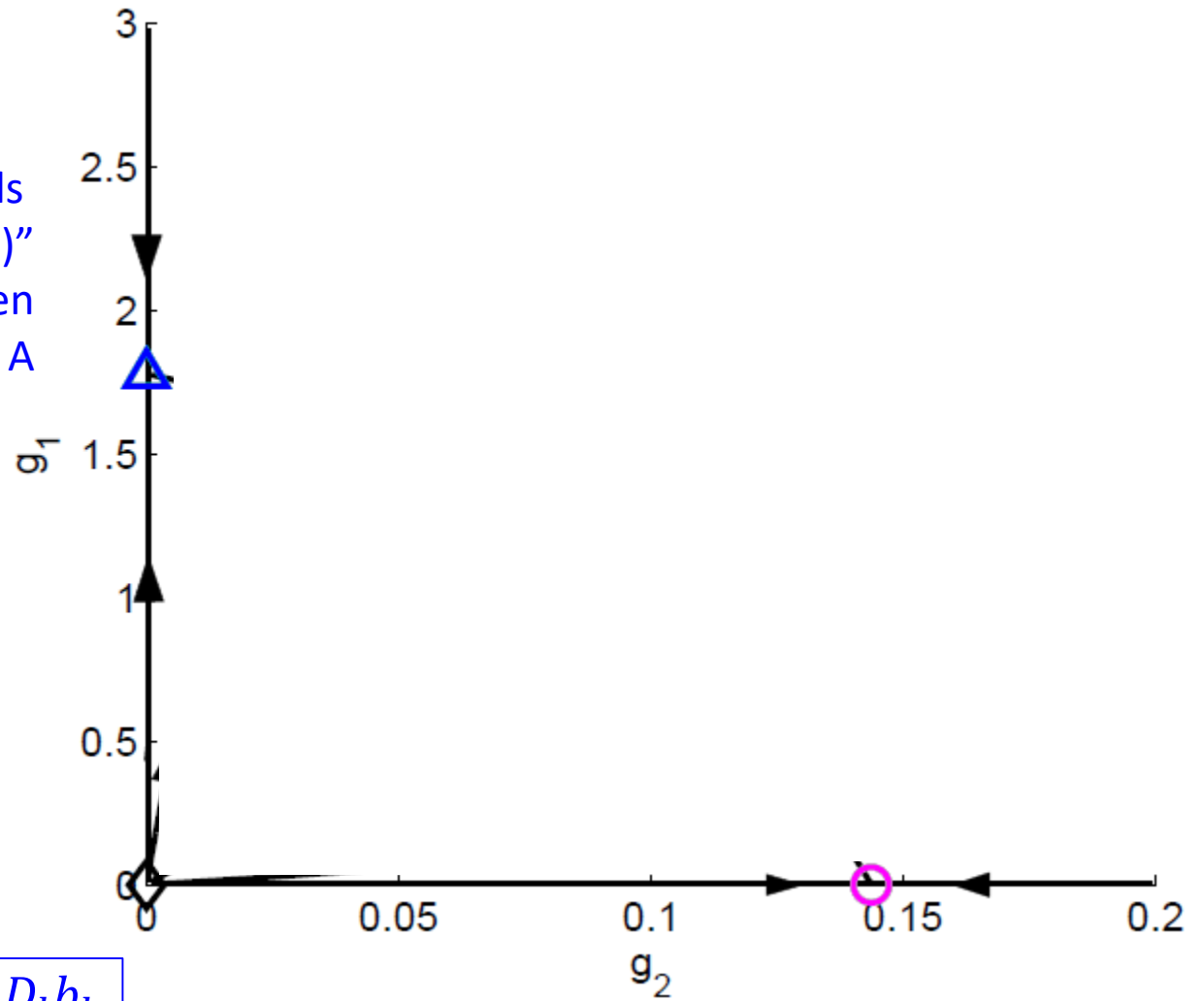


$$g_1(l) \sim \frac{D_l \lambda_l^2}{\mu_l^3}; \quad g_2(l) \sim \frac{D_l b_l}{\mu_l^2}$$

“Ferromagnets with dipolar interactions”
 Aharony and Fisher (1973) Phys. Rev. Lett.

Chen, Toner, Lee (2015)
 New J. Phys. 17, 042002

“Randomly stirred fluids
(Model B)”
Forster, Nelson & Stephen
(1977) Phys. Rev. A

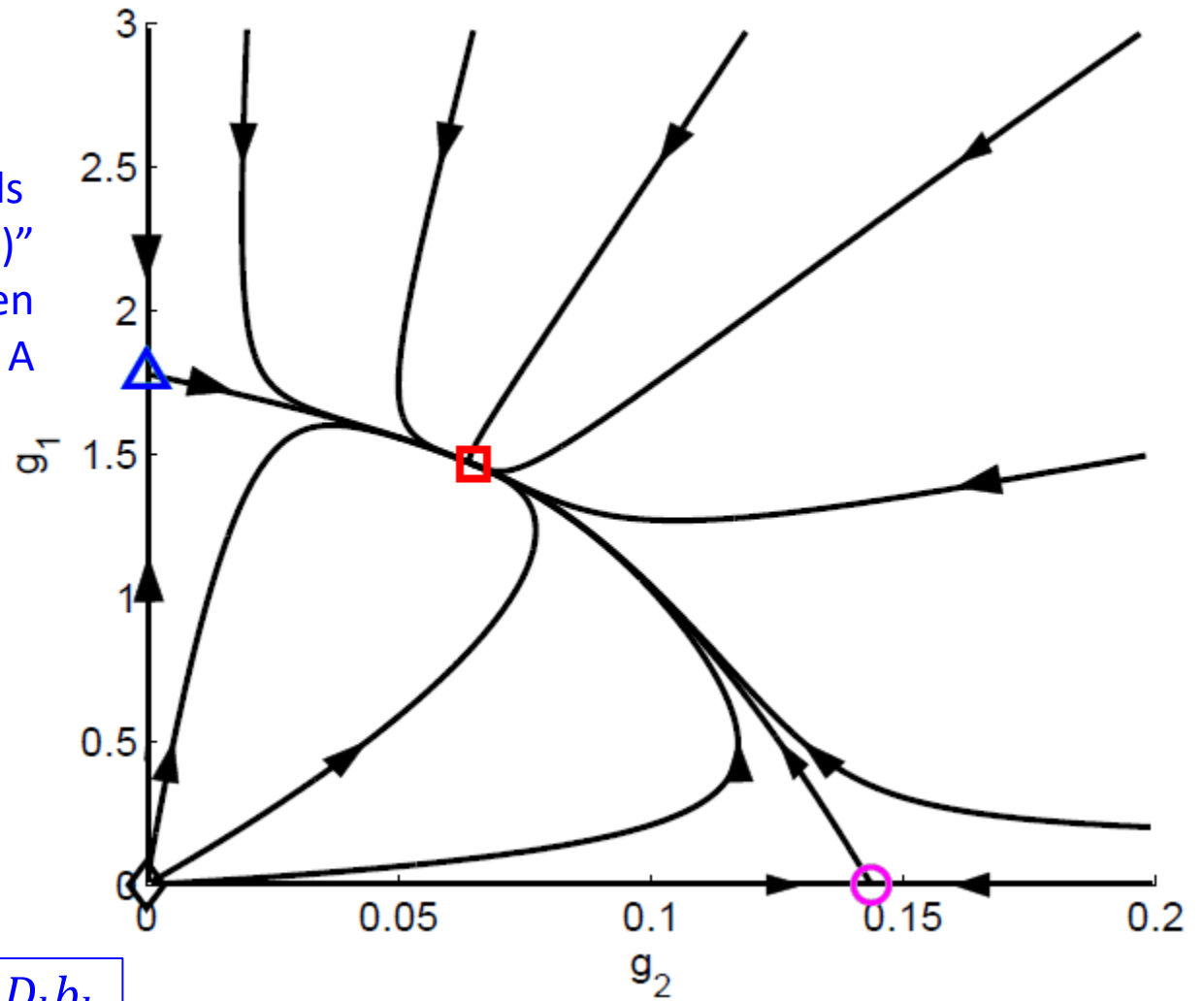


$$g_1(l) \sim \frac{D_l \lambda_l^2}{\mu_l^3}; \quad g_2(l) \sim \frac{D_l b_l}{\mu_l^2}$$

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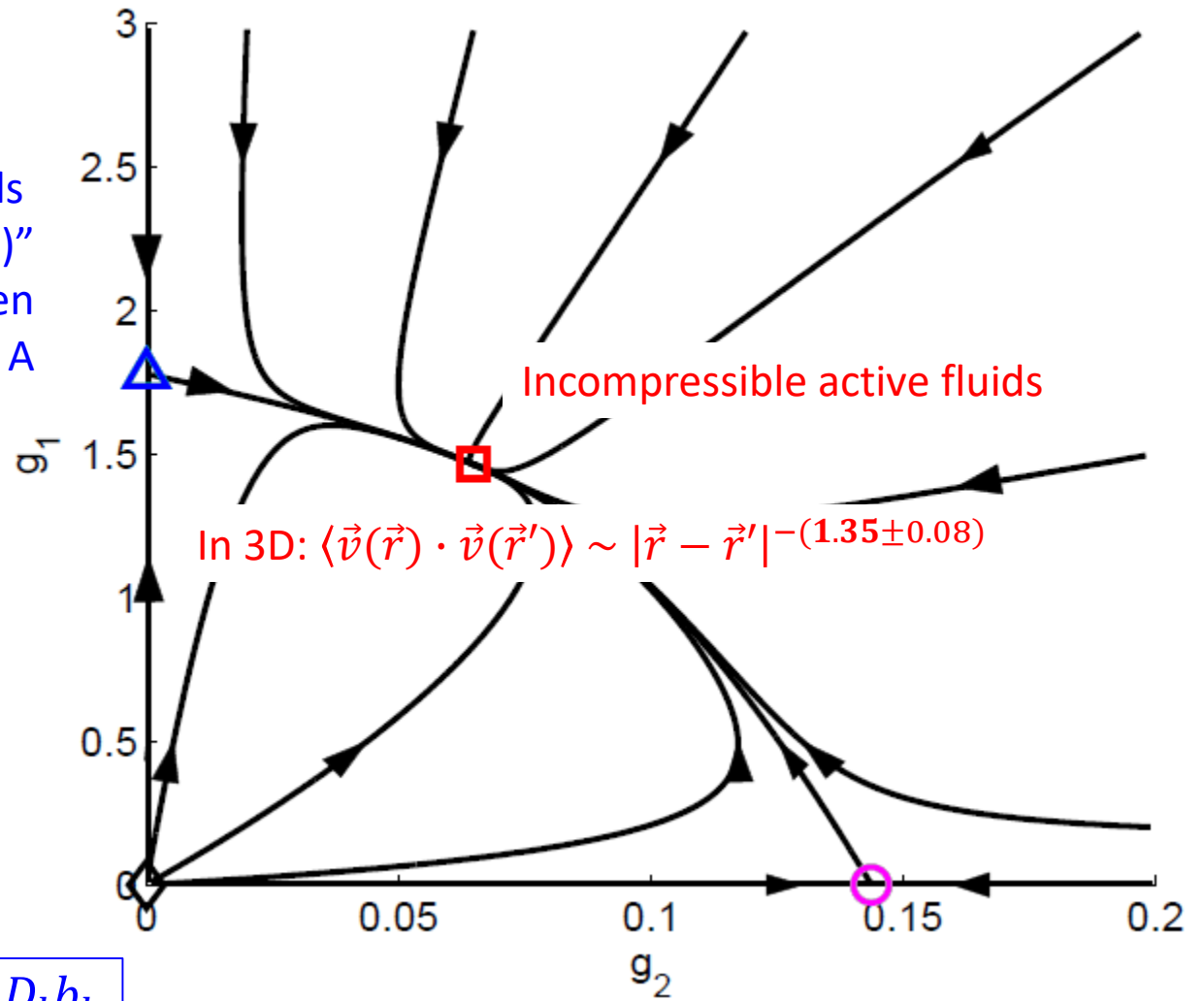


$$g_1(l) \sim \frac{D_l \lambda_l^2}{\mu_l^3}; \quad g_2(l) \sim \frac{D_l b_l}{\mu_l^2}$$

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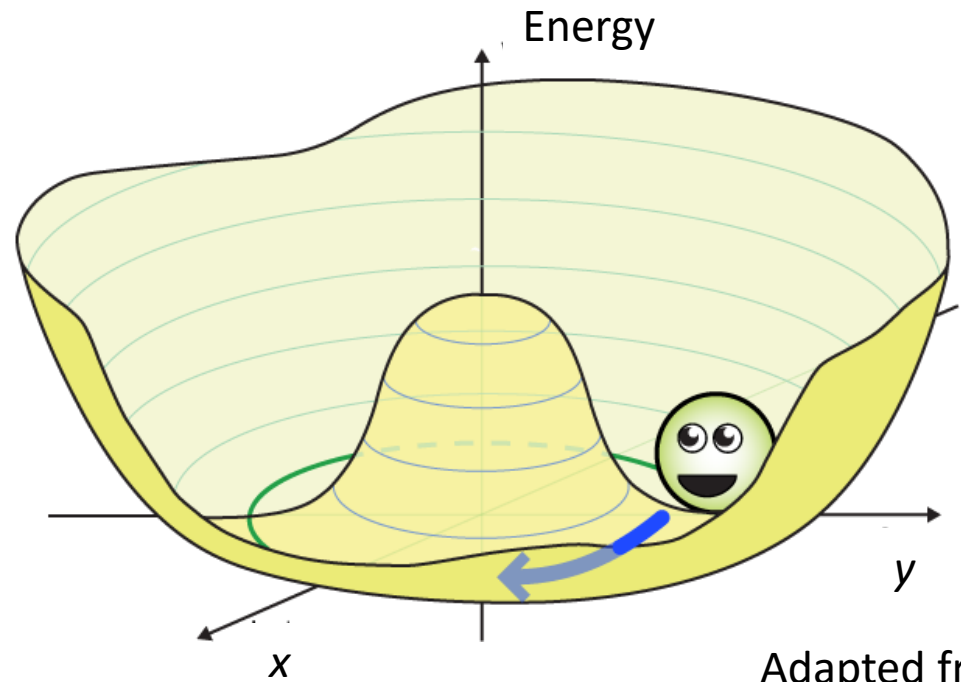
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$$g_1(l) \sim \frac{D_l \lambda_l^2}{\mu_l^3}; \quad g_2(l) \sim \frac{D_l b_l}{\mu_l^2}$$

“Ferromagnets with dipolar interactions”
Aharony and Fisher (1973) Phys. Rev. Lett.

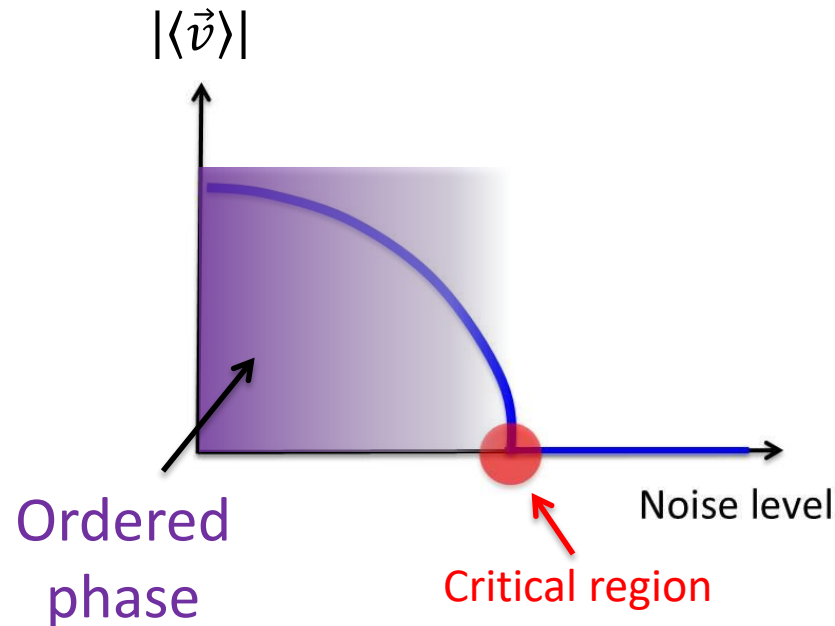
Chen, Toner, Lee (2015)
New J. Phys. 17, 042002



Adapted from
QuantumDiaries.org

Ordered phase (2D)

Ordered incompressible active fluids



- **Universality is more than criticality!**
- Universal behaviour expected in the symmetry-broken phase of a continuous symmetry

Ordered phase of 2D incompressible active fluids


$$\text{EOM: } \partial_t \vec{v} + \vec{\nabla} P - \vec{f} = -\lambda(\vec{v} \cdot \vec{\nabla})\vec{v} - (a + bv^2)\vec{v} - \mu \nabla^2 \vec{v} + cv^4 \vec{v} + \xi(\nabla^2)^2 \vec{v} + \dots$$

$$\text{Ordered phase: } \mathbf{v} = (v_0 + u_x(\mathbf{r}, t))\hat{x} + u_y(\mathbf{r}, t)\hat{y}$$



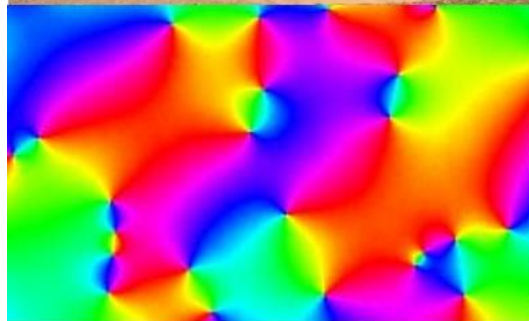
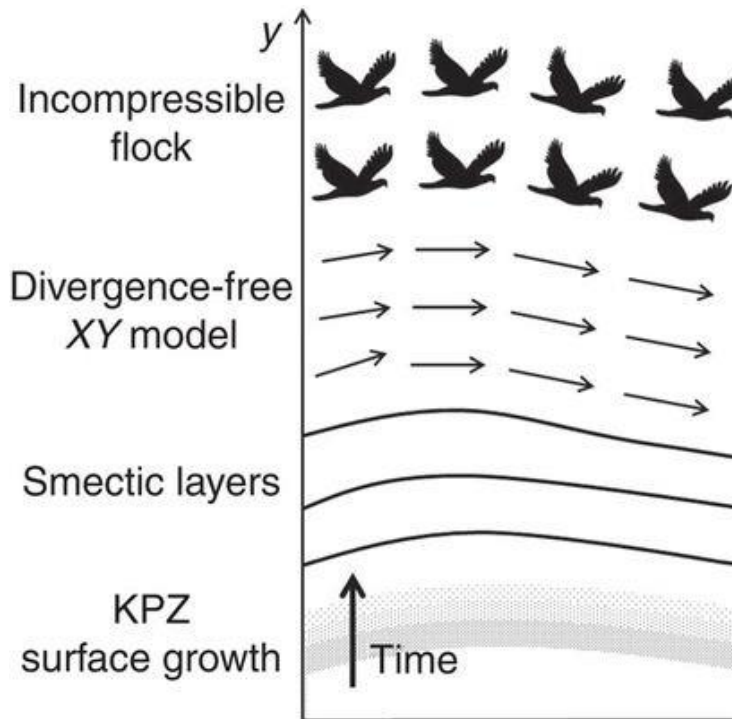
RG transformation

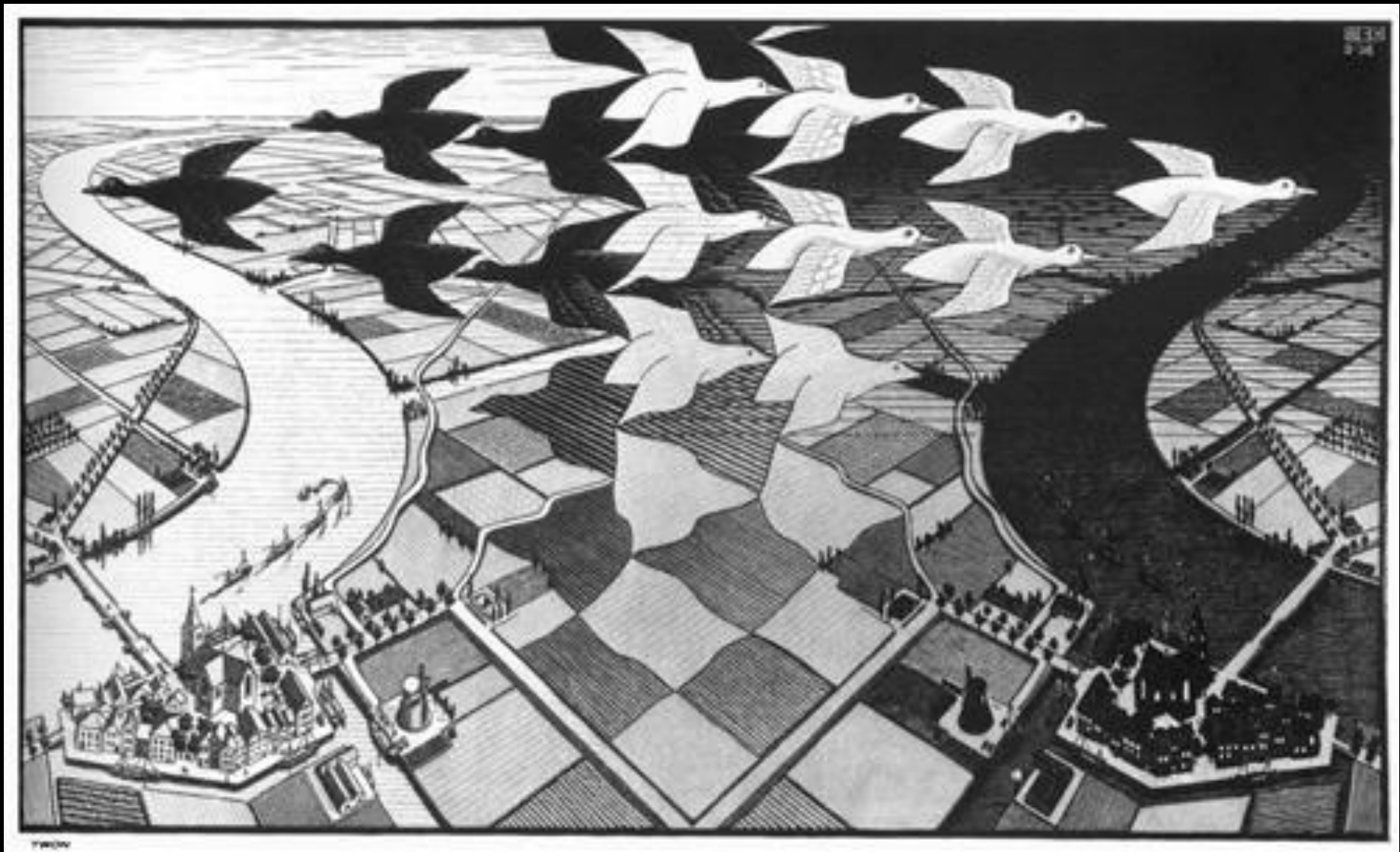
$$\begin{aligned} \partial_t u_x &= -\partial_x P - 2b \left(u_x + \frac{u_y^2}{2v_0} \right) + \mu \nabla^2 u_x + f_x \\ \partial_t u_y &= -\partial_y P - \frac{2b}{v_0} \left(u_x + \frac{u_y^2}{2v_0} \right) u_y + \mu \nabla^2 u_y + f_y \end{aligned}$$



Level of
coarse-graining

Active fluids in 2D





M.C. Escher (1938) *Day and Night*

Summary

1. Biopolymer self-assembly
 - Breakage-controlled thermalisation kinetics
2. Chemically active phase separations
 - Coarsening arrested by chemical reactions
3. Universality in active matter
 - Symmetry-based categorisation of non-equilibrium systems

Outlook 1

*“In physics, we (try to) teach principles and derive the predictions for particular examples. In biology, teaching proceeds (mostly) from example to example. **Although physics has subfields, to a remarkable extent the physics community clings to the romantic notion that Physics is one subject.**” [Biophysics: Searching for Principles (2012)]*



William Bialek

Outlook 2



Anthony Zee, Quantum Field Theory in a Nutshell (Princeton University Press, 2003)

Chapter VIII.3

Effective Field Theory Approach to Understanding Nature

Low energy manifestation

The pioneers of quantum field theory, Dirac for example, tended to regard field theory as a fundamental description of Nature, complete in itself. As I have mentioned several times, in the 1950s, after the success of quantum electrodynamics many leading particle physicists rejected quantum field theory as incapable of dealing with the strong and weak interactions, not to mention gravity. Then came the great triumph of field theory in the early 1970s. But after particle physicists retrieved field theory from the dust bin of theoretical physics, they realized that the field theories they were studying might be “merely” the low energy manifestation of a deeper structure, a structure first identified as a grand unified theory and later as a string theory. Thus was developed an outlook known as the effective field theory approach, *pace* Dirac.

The general idea is that we can use field theory to say something about physics at low energies or equivalently long distances even if we don't know anything about the ultimate theory, be it a theory built on strings or some as yet undreamed of structure. An important consequence of this paradigm shift was that nonrenormalizable field theories became acceptable. I will illuminate these remarks with specific examples.

The emergence of this effective field theory philosophy, championed especially by Wilson, marks another example of cross fertilization between condensed matter and particle physics. Toward the late 1960s, Wilson and others developed a powerful effective field theory approach to understanding critical phenomena, culminating in his Nobel Prize. The situation in condensed matter physics is in many ways the opposite of that in particle physics at least as particle physics was understood in the 1960s. Condensed matter physicists know the short distance physics, namely the quantum mechanics of electrons and ions. But it certainly doesn't help in most cases to write down the Schrödinger equation for the electrons and ions. Rather, what one would like to have is an effective description of how a system would respond when probed at low frequency and small wave vector. A striking example is the effective theory of the quantum Hall fluid as described in Chapter VI.2: The relevant degree of freedom is a gauge field, certainly a far cry from

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Thank you for your attention!