On the thermodynamics of lipid mixtures on curved substrates

Piermarco Fonda

Hydrodynamics at All Length Scales: From High-Energy to Hard and Soft Matter
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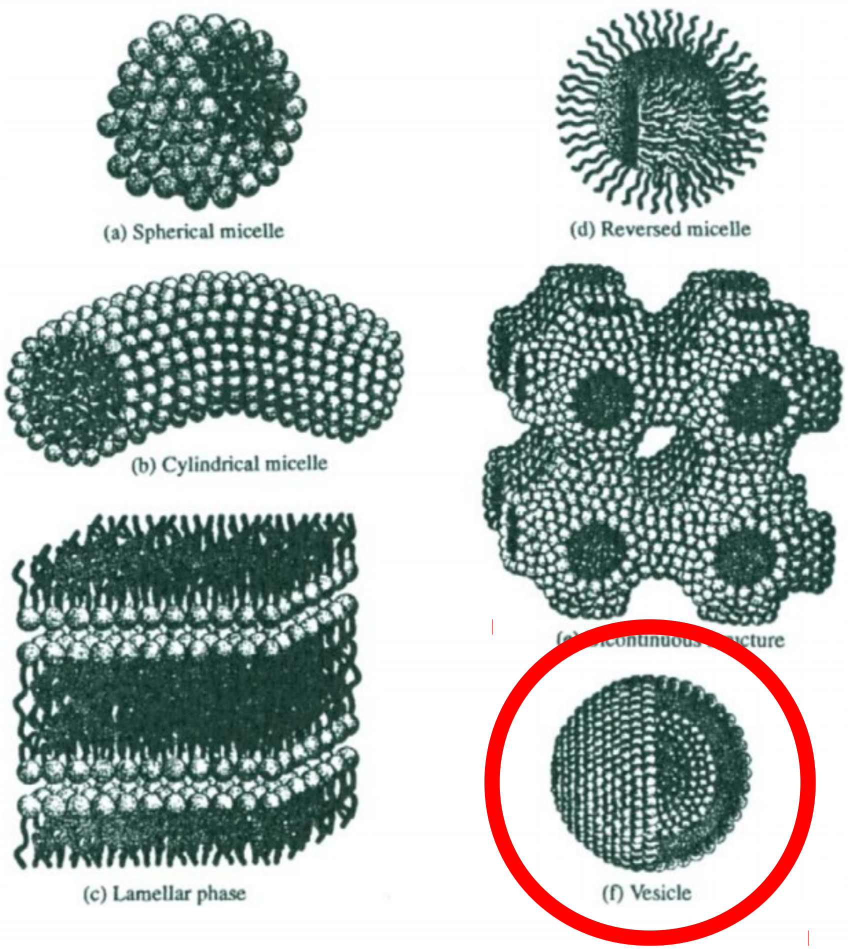
Universiteit Leiden

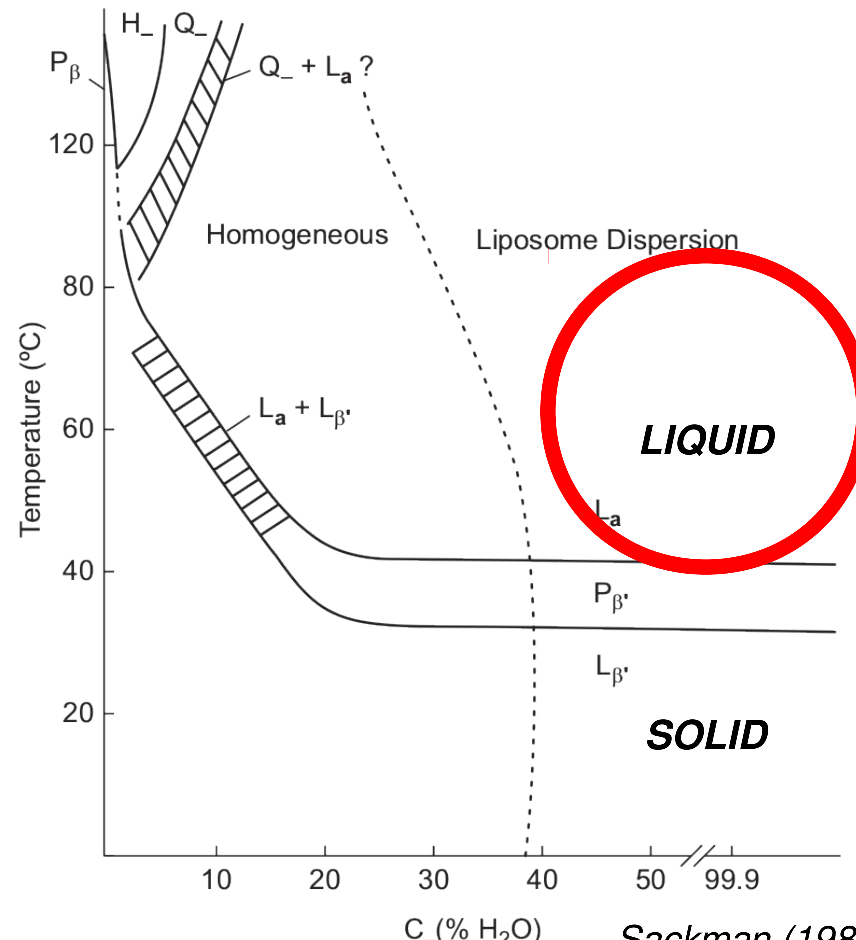
Instituut-Lorentz

Self-assembled lipid membranes

Structural DOFs



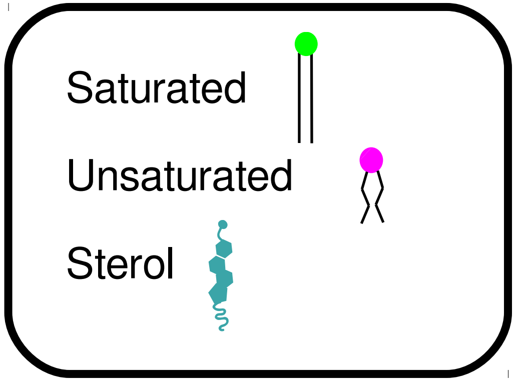
Thermodynamical DOFs

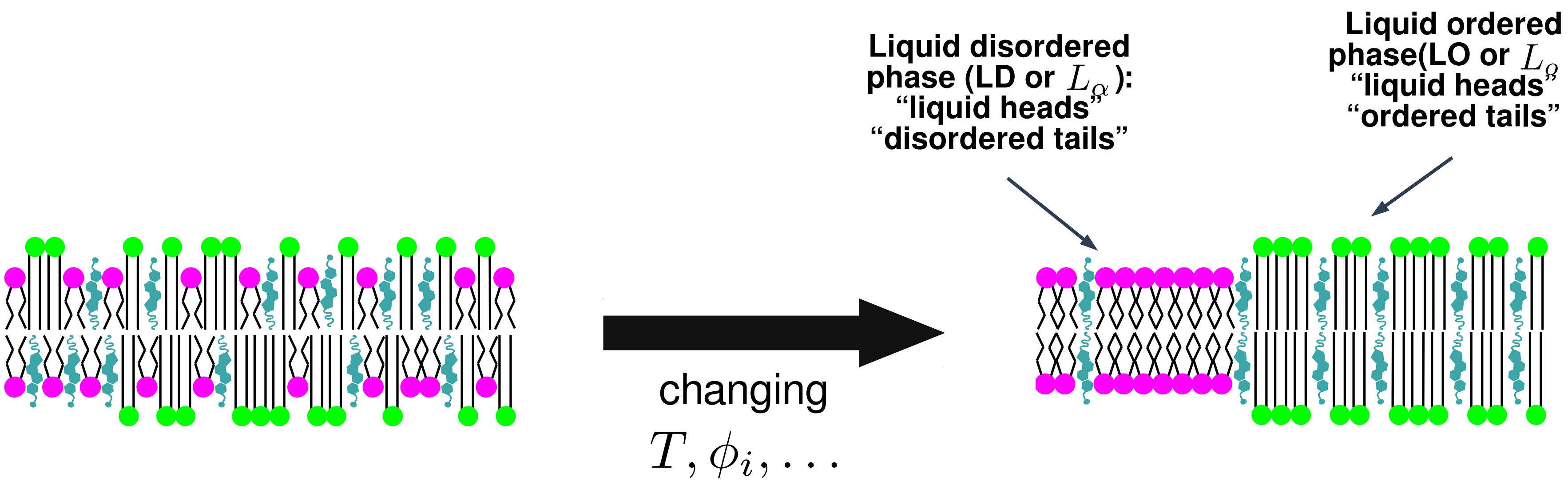


Sackman (1983)

Multicomponent artificial lipid membranes

Ternary mixtures
on a vesicle



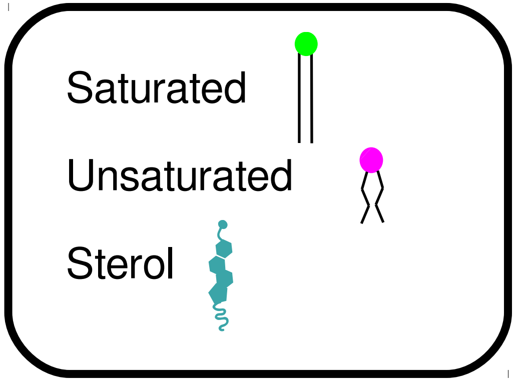


Single 2D liquid
(mixed)

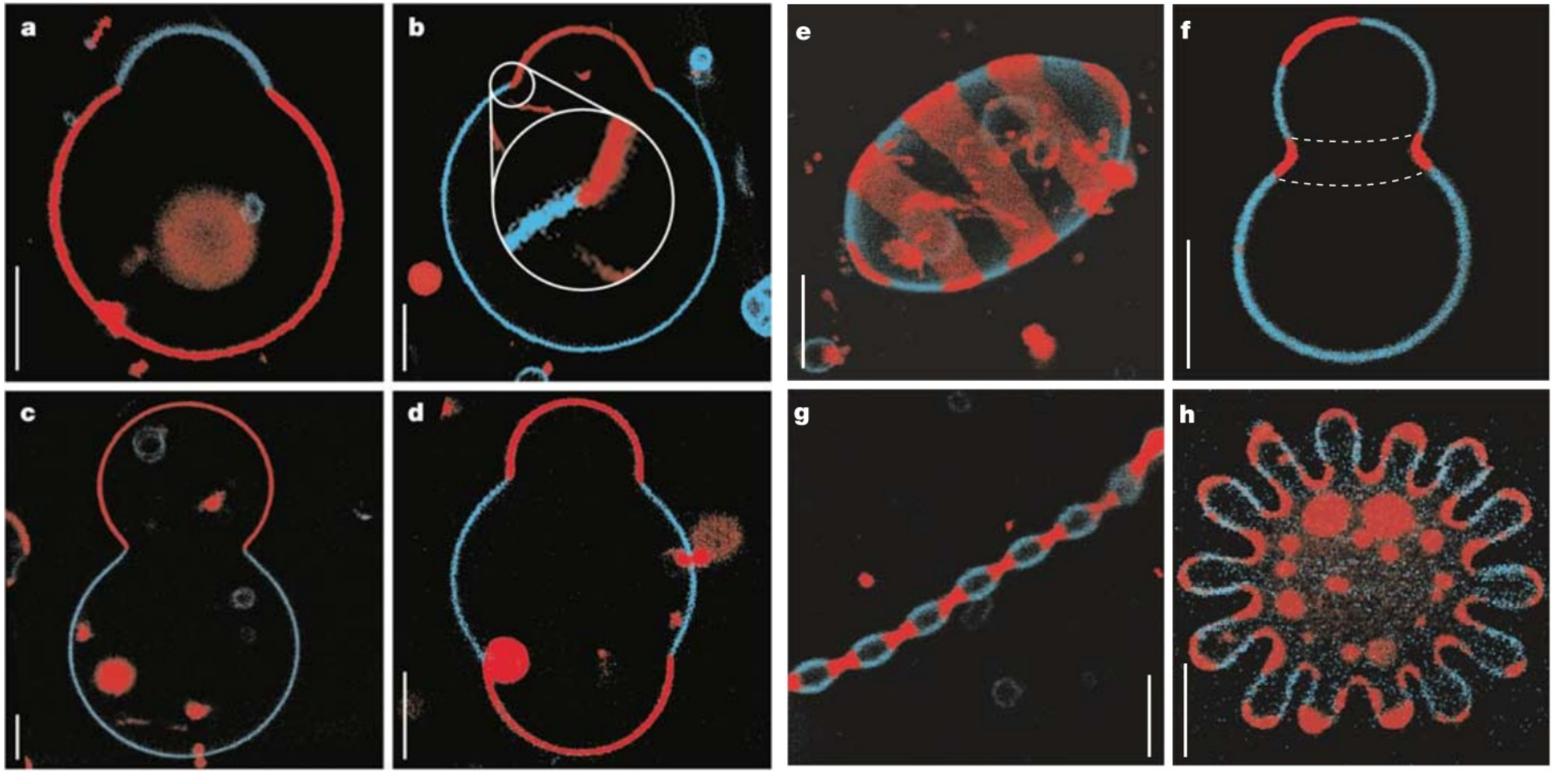
2D Liquid/Liquid coexistence
(phase separated)

Multicomponent artificial lipid membranes

Ternary mixtures on a vesicle



2D Liquid/Liquid phase coexistence on a curved surface

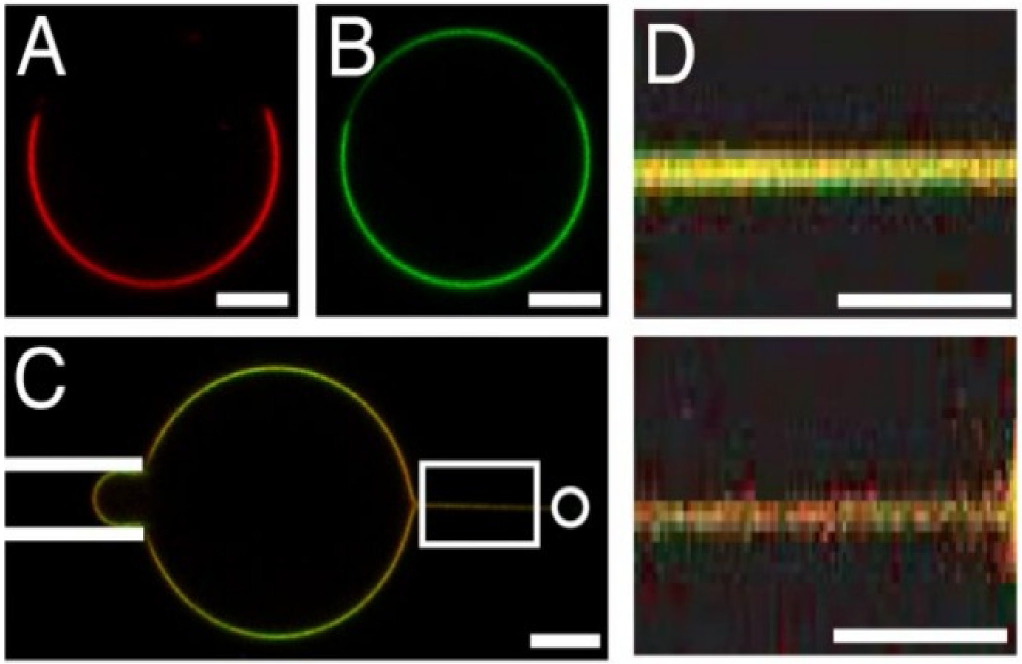


Baumgart,Das,Webb (Nature, 2003)

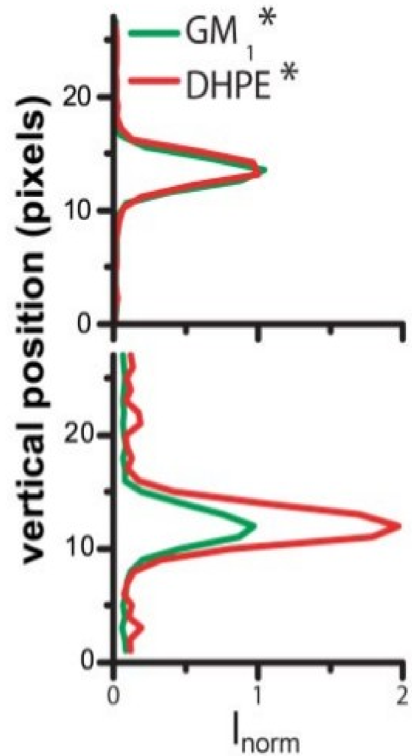
Shape effects on mixed states

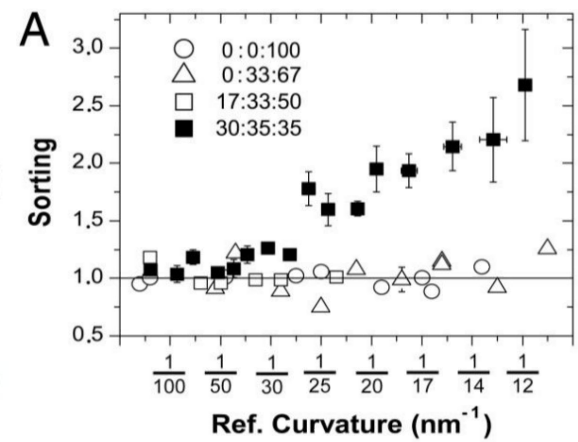
Pulling out a tube from a spherical vesicle:

Large diameter



Small diameter





Curvature-driven lipid sorting needs proximity to a demixing point and is aided by proteins

Benoit Sorre[a,b,1], Andrew Callan-Jones[a,1], Jean-Baptiste Manneville[b], Pierre Nassoy[a], Jean-François Joanny[a], Jacques Prost[a,c], Bruno Goud[b], and Patricia Bassereau[a,2]

Sorre et al. (PNAS, 2009)

Degrees of freedom

Two *liquid* phases with different *mechanical* properties

Geometry

Shape
Area & volume
Membrane topology

Thermodynamics

(at equilibrium)

Local composition
Domain size, shape & number
Interface topology

Degrees of freedom

Two *liquid* phases with different *mechanical* properties

Geometry

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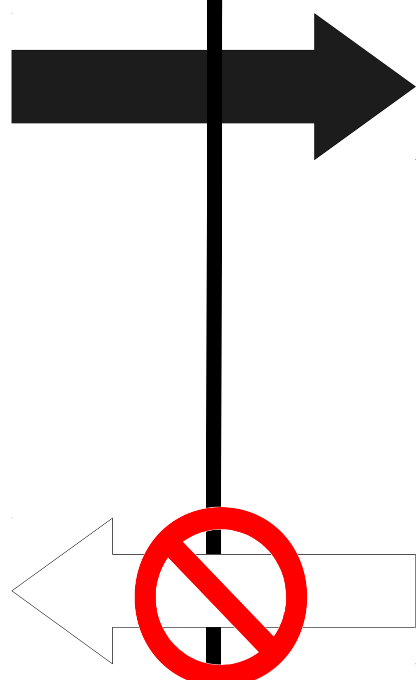

Shape
Area & volume
Membrane topology

Local composition
Domain size, shape & number
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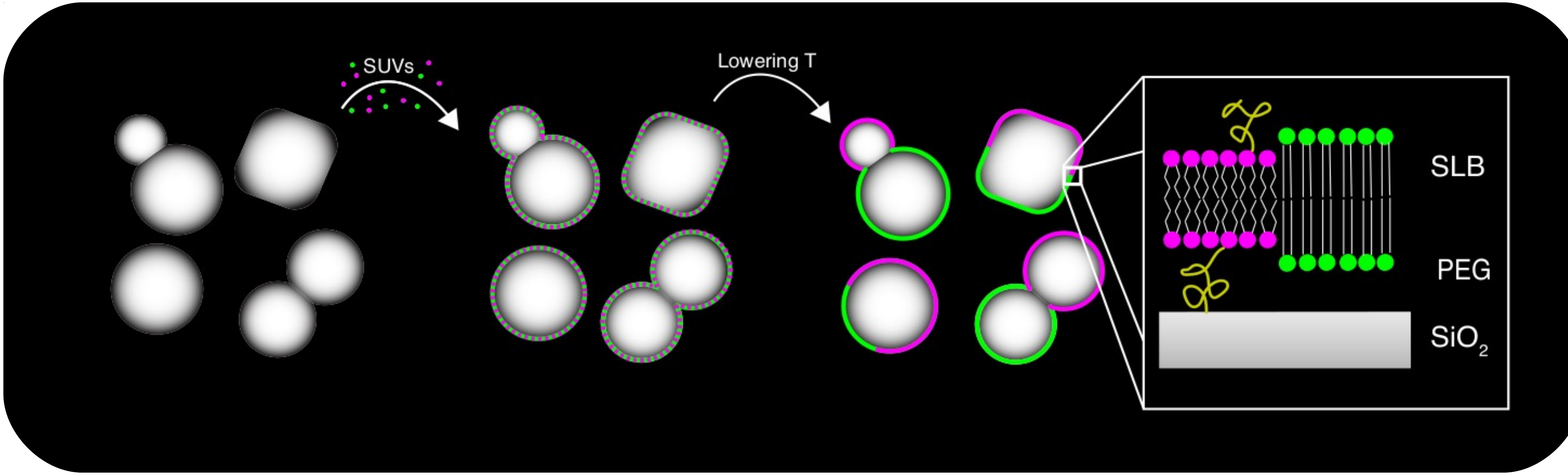
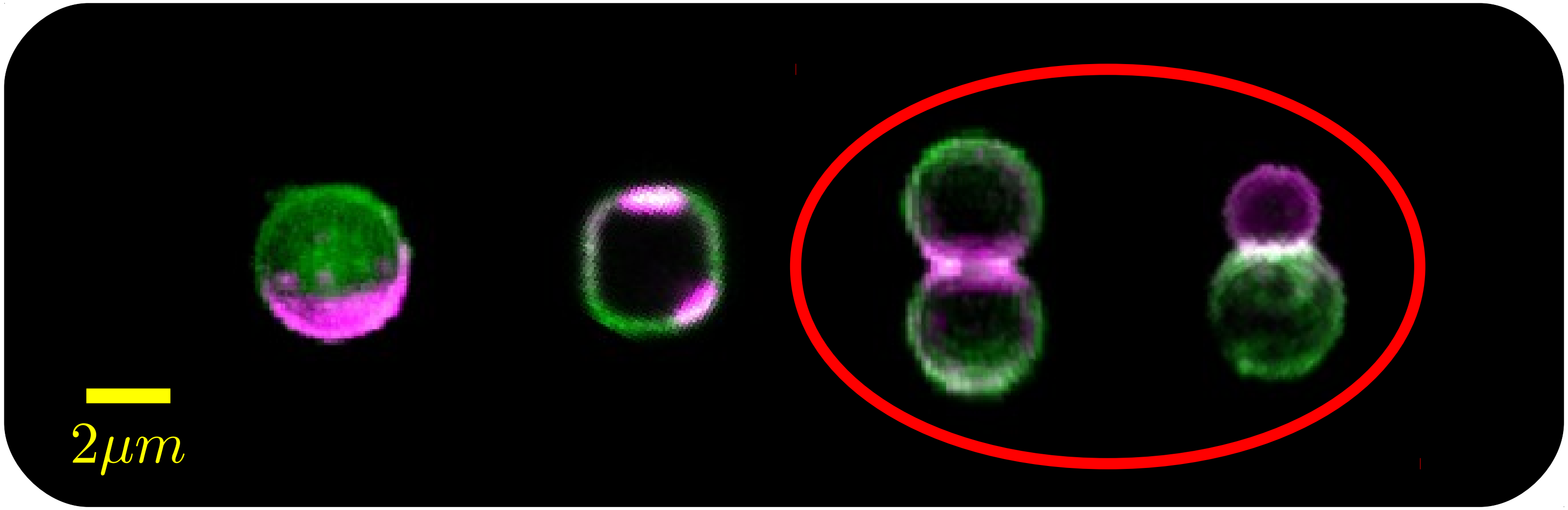
Scaffolded Lipid Vesicles (SLVs)



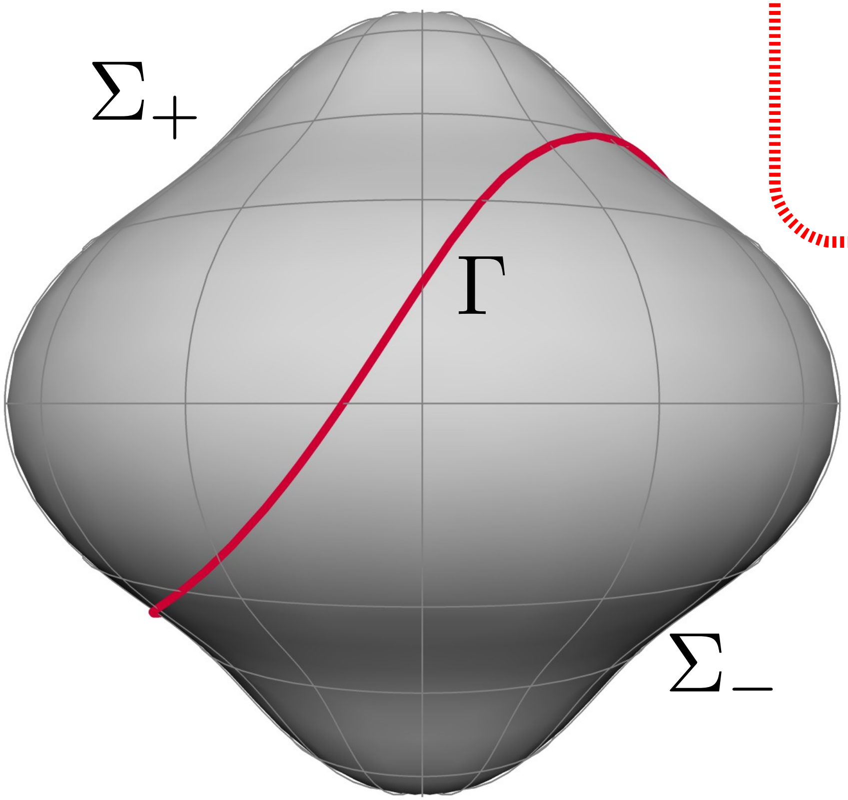


Rinaldin, P.F., Kraft, Giomi (arXiv 1804.08596, under review)

The JL sharp interface model

$$F = \sigma \int_\Gamma \mathrm{d}s + \sum_{\alpha=\pm} k_\alpha \int_{\Sigma_\alpha} \mathrm{d}A H^2 + \bar{k}_\alpha \int_{\Sigma_\alpha} \mathrm{d}A K$$

Jülicher, Lipowsky (PRL, 1993)



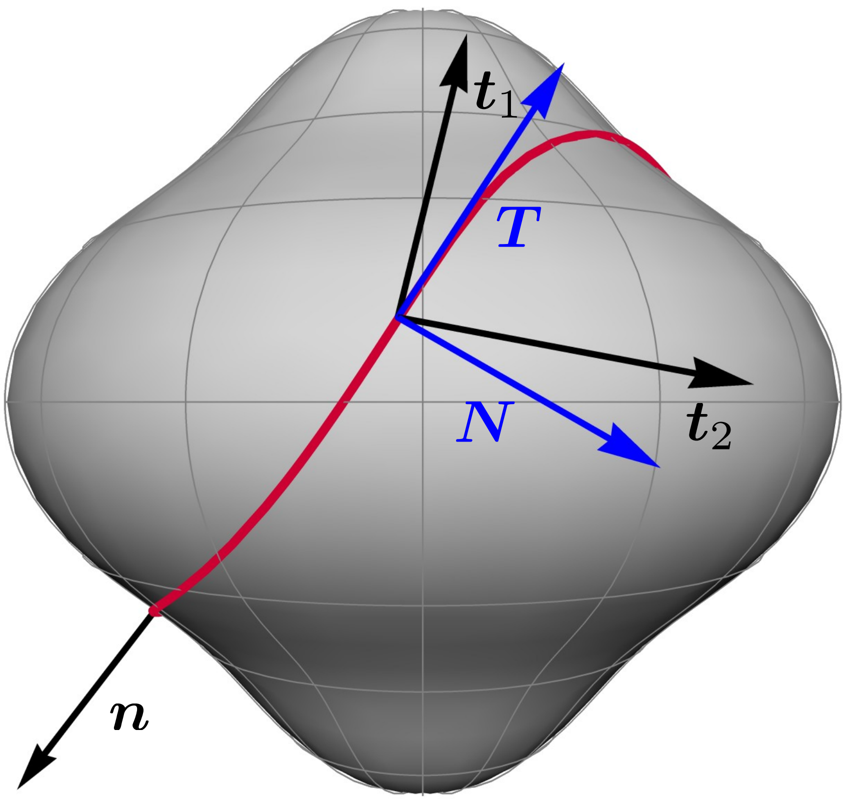
$k_\pm$	bending moduli
$\bar{k}_\pm$	saddle splay moduli
σ	line tension

$\mathrm{Area}(\Sigma_\pm)$	fixed
$\lambda_\pm$	Lagrange multipliers

$$H = \frac{1}{2}\left(\frac{1}{R_1} + \frac{1}{R_2}\right)$$ Mean curvature

$$K = \frac{1}{R_1 R_2}$$ Gaussian curvature

Shape equations



2D Bulk:

$$\lambda_{\pm} H = k_{\pm}\left(\nabla^2 H + 2H(H^2 - K)\right)$$

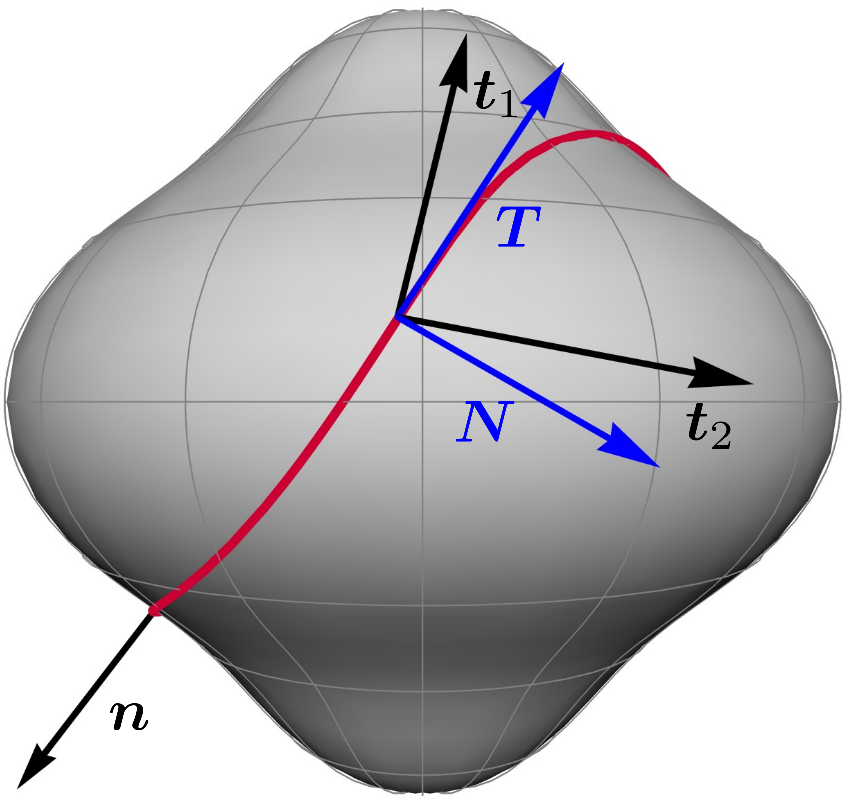
1D Interface:

$$\sigma \kappa_n = \Delta \bar{k} \dot{\tau}_g + \Delta k_\alpha \nabla_{\boldsymbol{N}} H$$

$$\sigma \kappa_g = \Delta k H^2 + \Delta \bar{k} K + \Delta \lambda$$

$$0 = 2\Delta k H + \Delta \bar{k} \kappa_n$$

Shape equations



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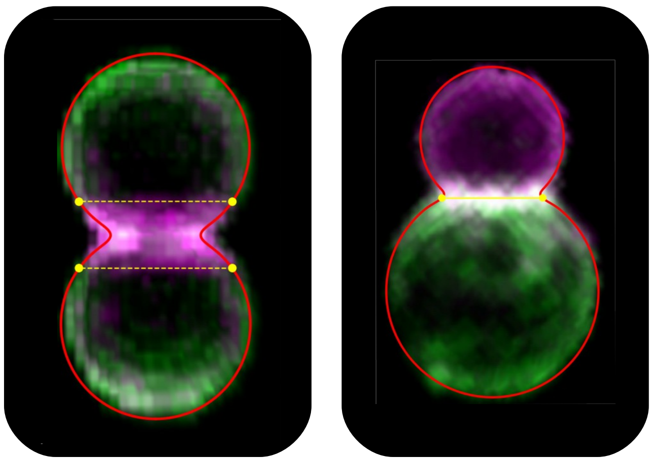
$$0 = 2\Delta k H + \Delta\bar{k}\kappa_n$$

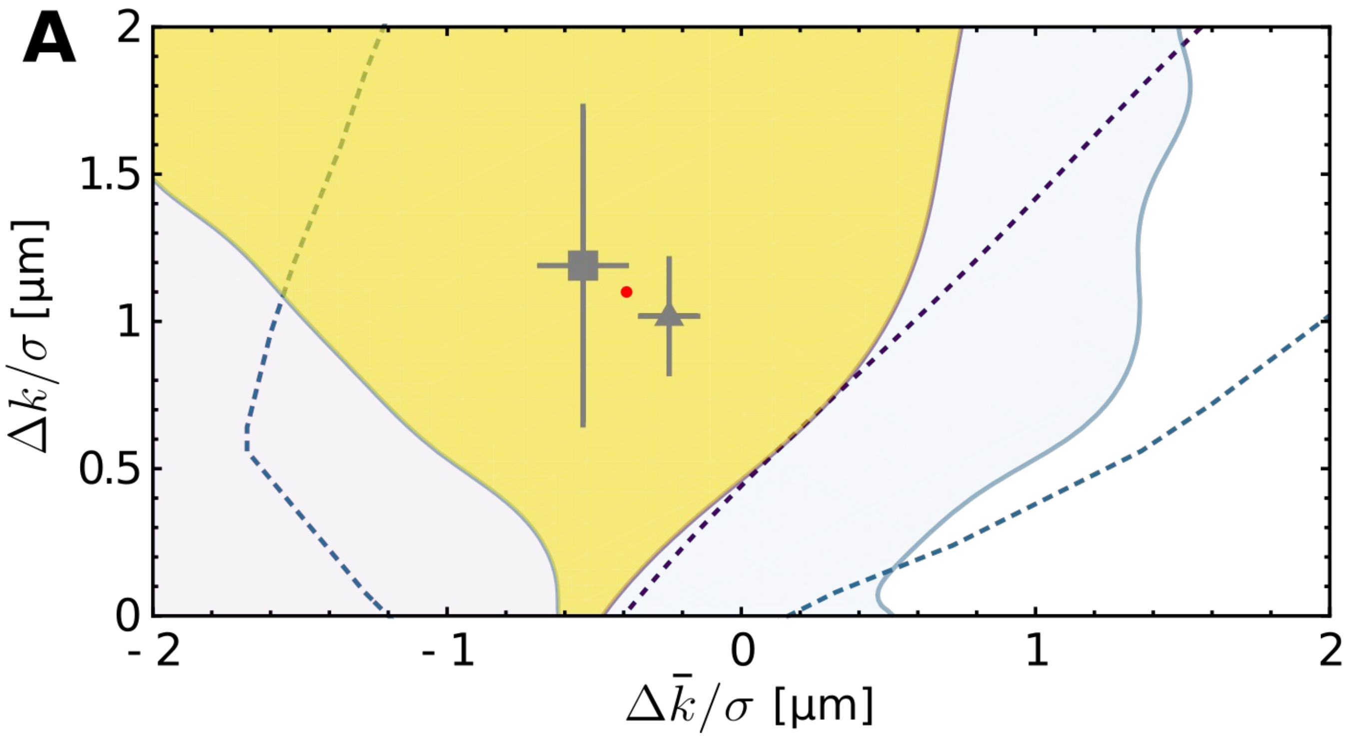
The JL sharp interface model

The JL energy is *geometric*, and as such can be studied with tools from surface theory (see *PF et al. Phys. Rev. E* ***98****, 032801*).



The model has **two** Independent parameters:

$$\frac{\Delta k}{\sigma} \quad \frac{\Delta \bar{k}}{\sigma}$$

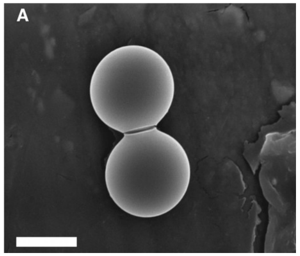


Baumgart, Das, Webb, Jenkins (Biophysical Journal, 2005)

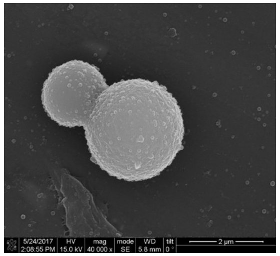
Semrau, Schmidt (Soft Matter, 2009)

Agreement with results from free vesicles

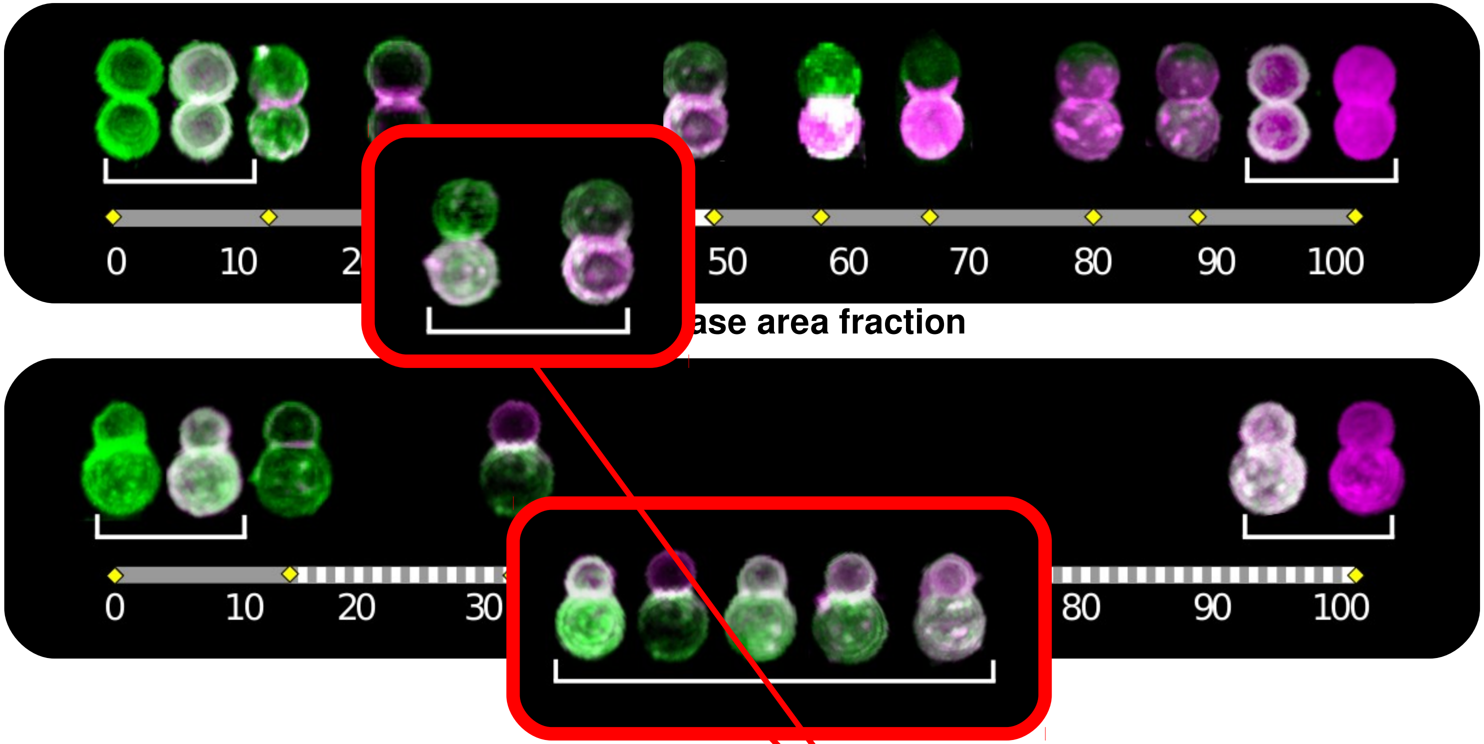
Area fraction diagrams



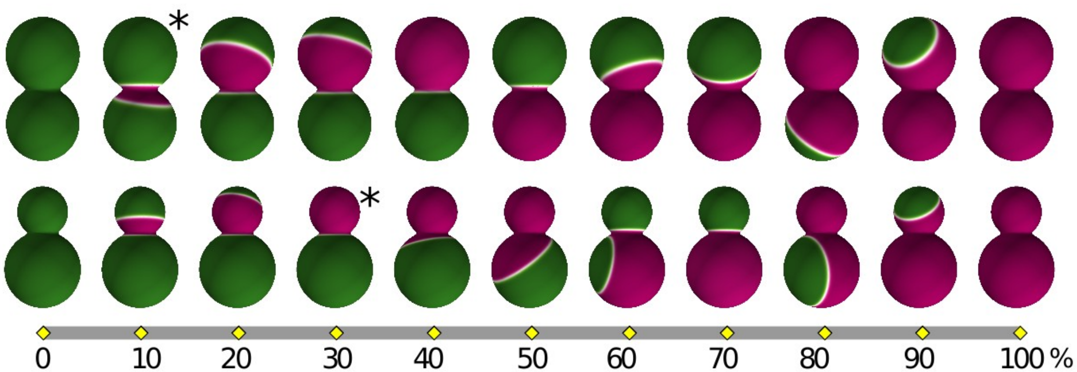
Dumbbell



Snowman



From JL model we get:



%LD phase area fraction

Is this phase separation?

Why something like

is **never** observed?

Constructing a model

Effective free energy density with a *single* scalar order parameter (binary system)

$$F = \int_\Sigma \mathrm{d}A \mathcal{F}(\phi, \nabla_i \phi, \Sigma)$$

Gradients and curvatures are small compared to microscopical scales

$$\boxed{\mathcal{F} \simeq \frac{D(\phi)}{2} \nabla_i \phi \nabla^i \phi + f(\phi) + k(\phi) H^2 + \bar{k}(\phi) K + \dots}$$

Fixed concentration

$$\Phi = \frac{1}{A_\Sigma} \int_\Sigma \mathrm{d}A \phi(x)$$

$$G = F - \mu \Phi$$

$D(\phi)$ compressibility

$f(\phi)$ homogeneous free energy density

$k(\phi)$ bending modulus

$\bar{k}(\phi)$ saddle splay modulus

It has long history:
Markin (1981)
Leibler (1986)
Leibler, Andelman (1986)
⋮

However: the vast majority of literature focuses on local behavior and open systems

What is a *reasonable* choice of these coefficients?
How does this choice affect the phase diagram?

A simple model

We still need a way to choose the concentration (and temperature!) dependence of the coefficients. *A seemingly natural* starting point: **mean field approximation** of a **2D lattice-gas model** with curvature-dependent NN interactions:

$$\mathcal{H} = -\frac{1}{4}\sum_{\langle i,j\rangle} J_i s_i s_j + \sum_i h_i s_i$$

$$J_i = a^2 \left(J + L_\kappa H^2_{(i)} + L_{\bar{\kappa}} K_{(i)}\right) \qquad h_i = a^2 \left(M_\kappa H^2_{(i)} + M_{\bar{\kappa}} K_{(i)}\right)$$

After evaluation of Z and in the continuum limit:

$$\boxed{\begin{aligned} f(\phi) &= -k_B T \mathcal{S}(\phi) + J\phi(1-\phi) \\ \kappa(\phi) &= L_\kappa \phi(1-\phi) + M_\kappa \phi \\ \bar{\kappa}(\phi) &= L_{\bar{\kappa}} \phi(1-\phi) + M_{\bar{\kappa}} \phi \end{aligned}}$$

Local mixing entropy

$$\mathcal{S}(\phi) = -\phi \ln \phi - (1-\phi)\ln(1-\phi)$$

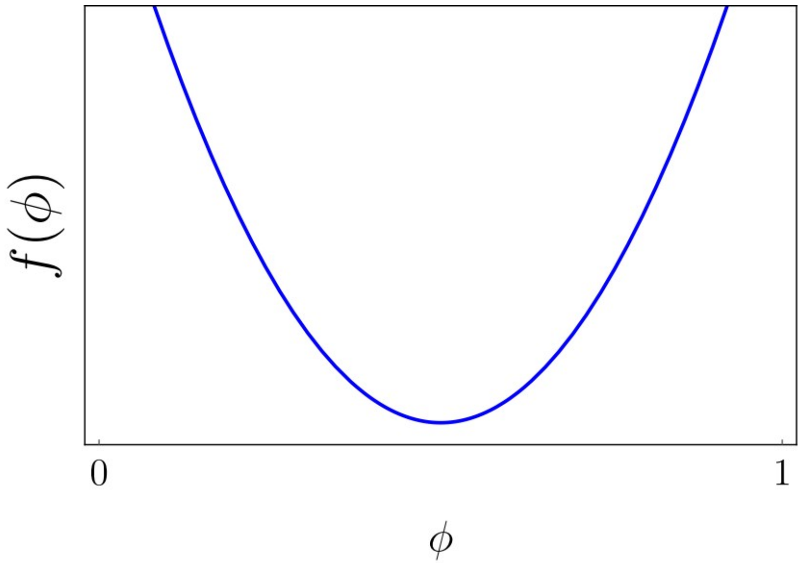
4 new coupling constants which reduce to 2 for spheres:
now we can compute phase diagrams

Classical homogeneous phase separation

To understand bulk phases (far from interfaces), we **neglect gradients** for now.
Thermodynamic equilibrium is given by minima of the free energy density:

$$\boxed{f'(\phi) = \mu}$$

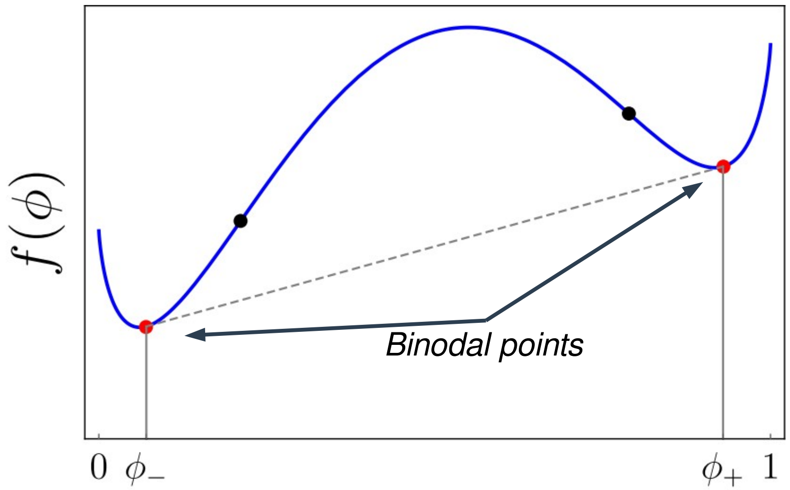
convex



$$\phi(x) = \Phi$$

The local order parameter is a constant everywhere
***Mixed** phase always stable*

concave



$$\phi(x) = \begin{cases} \phi_+, & x \in \Sigma_+ \\ \phi_-, & x \in \Sigma_- \end{cases}$$

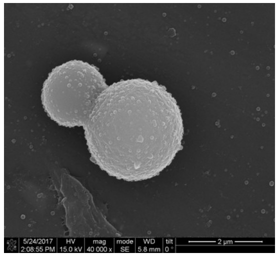
Maxwell construction

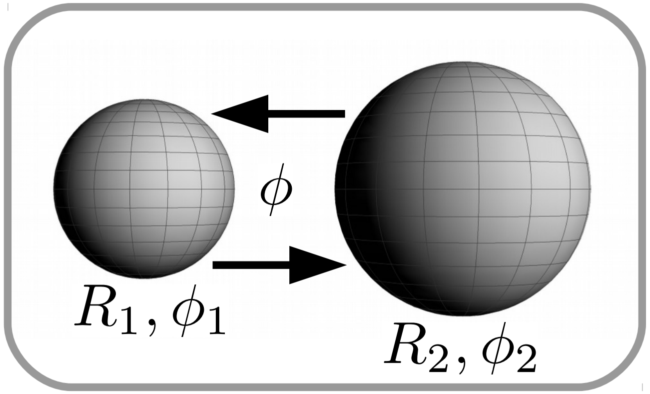
$$f'(\phi_\pm) = \frac{f(\phi_+) - f(\phi_-)}{\phi_+ - \phi_-}$$

***Demixed** phase for*

$$\phi_- < \Phi < \phi_+$$

Minimal inhomogeneous systems: two spheres





A *crude* approximation: two spheres isolated from the environment but freely exchanging order parameter with each other

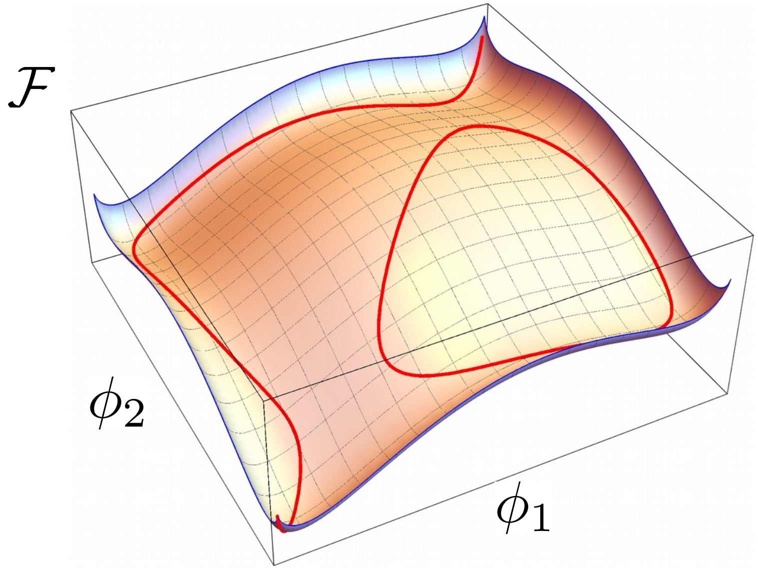
Equilibrium:

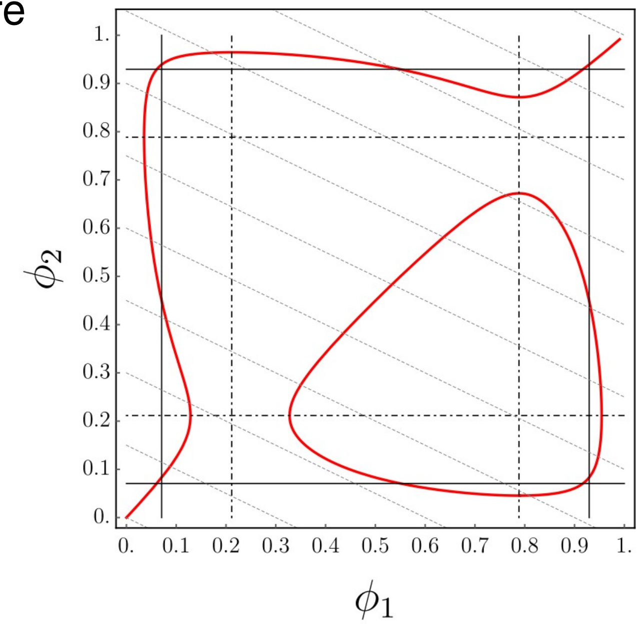
$$f'(\phi_1) + \frac{k'(\phi_1)}{R_1^2} = \mu = f'(\phi_2) + \frac{k'(\phi_2)}{R_2^2}$$

Total concentration constraint

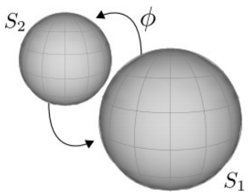
$$\frac{R_1^2}{R_1^2 + R_2^2}\phi_1 + \frac{R_2^2}{R_1^2 + R_2^2}\phi_2 = \Phi$$

With concave potentials, **check stability against demixing** on each sphere

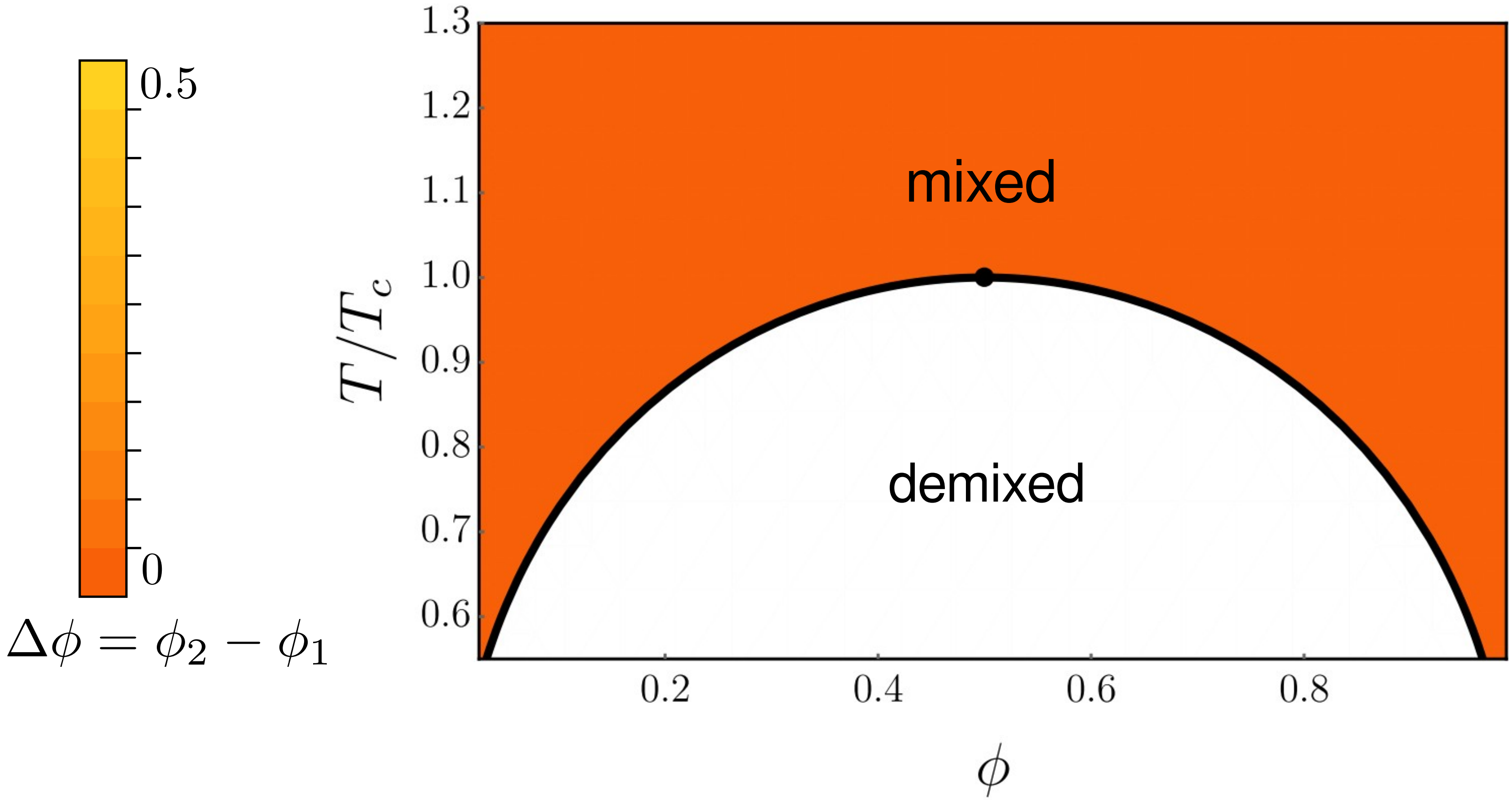




Inhomogeneous thermodynamic potentials

The phase diagram of  for $M_\kappa = 0$

$$\mathcal{F} = f(\phi) + M_k \phi \frac{1}{R^2}$$



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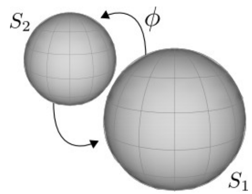
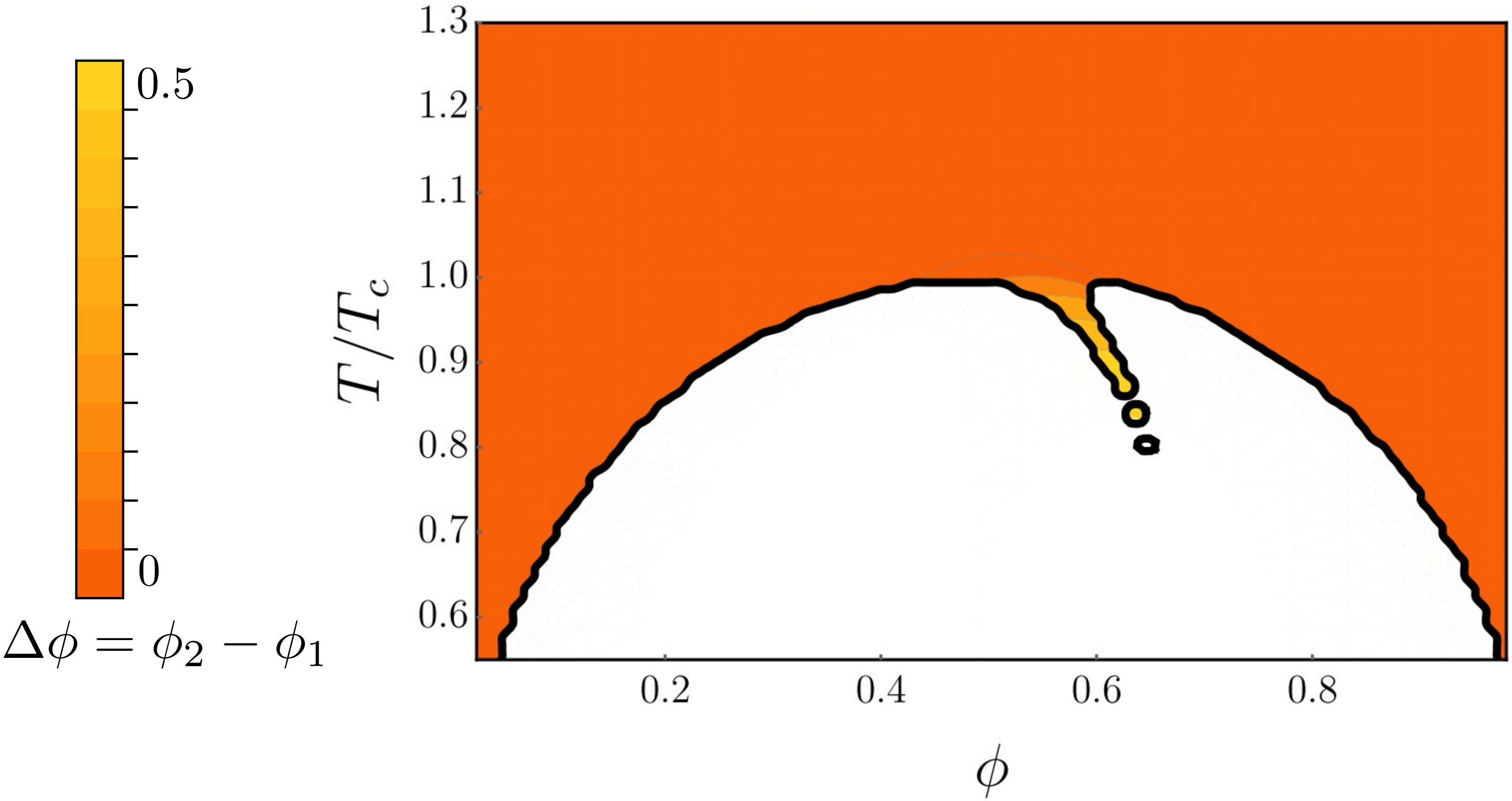
The phase diagram of 

for* $M_\kappa \sim O(0.01)$

$$\mathcal{F} = f(\phi) + M_k \phi \frac{1}{R^2}$$

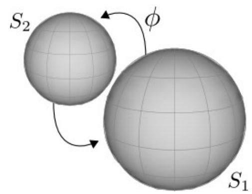


$\Delta\phi \neq 0$

Inhomogeneous mixing

*in units where $f \sim O(1), R_1 = 1$

Inhomogeneous thermodynamic potentials

The phase diagram of  for* $M_\kappa \sim O(0.1)$

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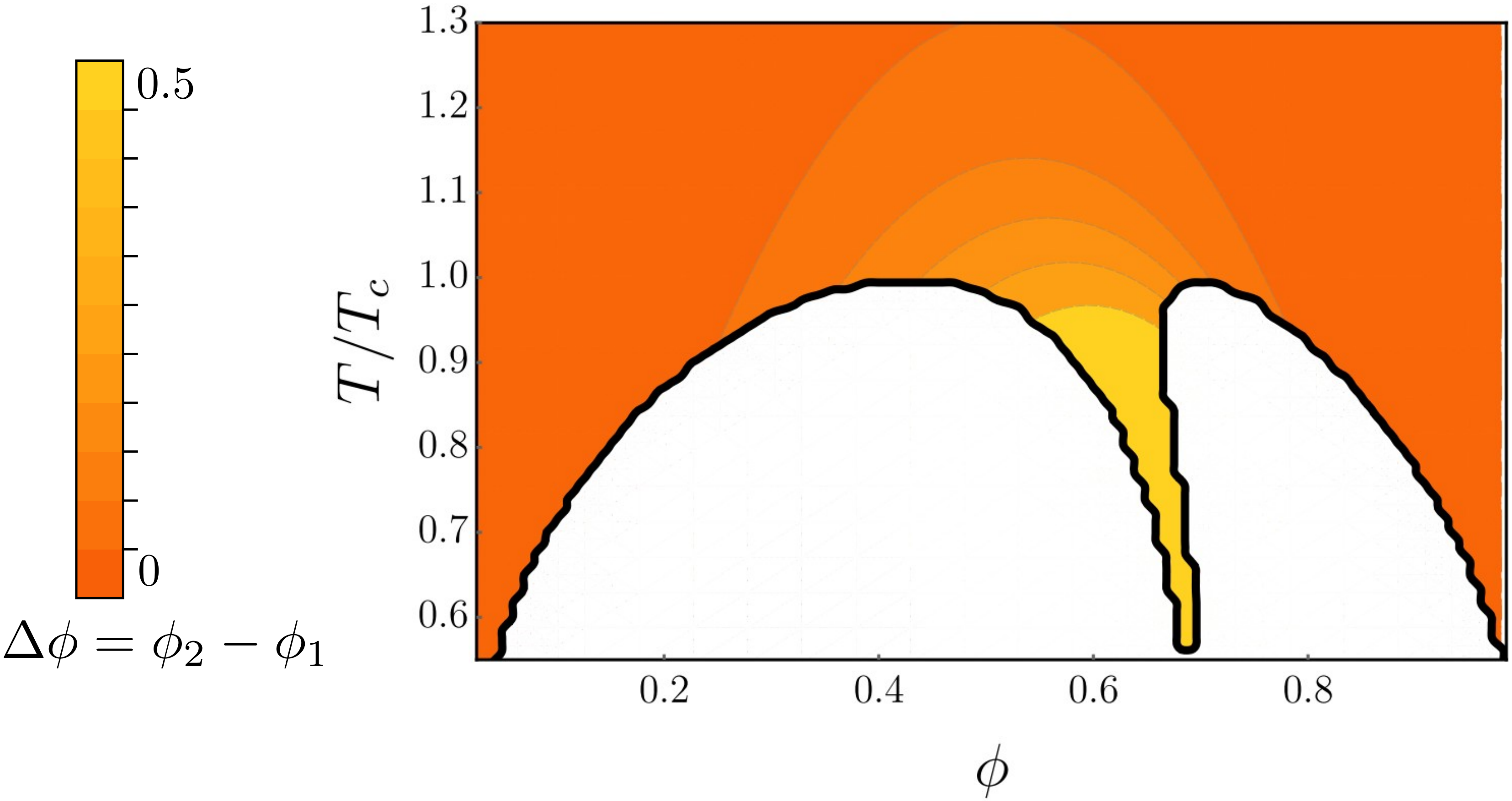

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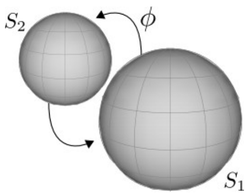
The phase diagram of  for* $M_\kappa \sim O(1)$

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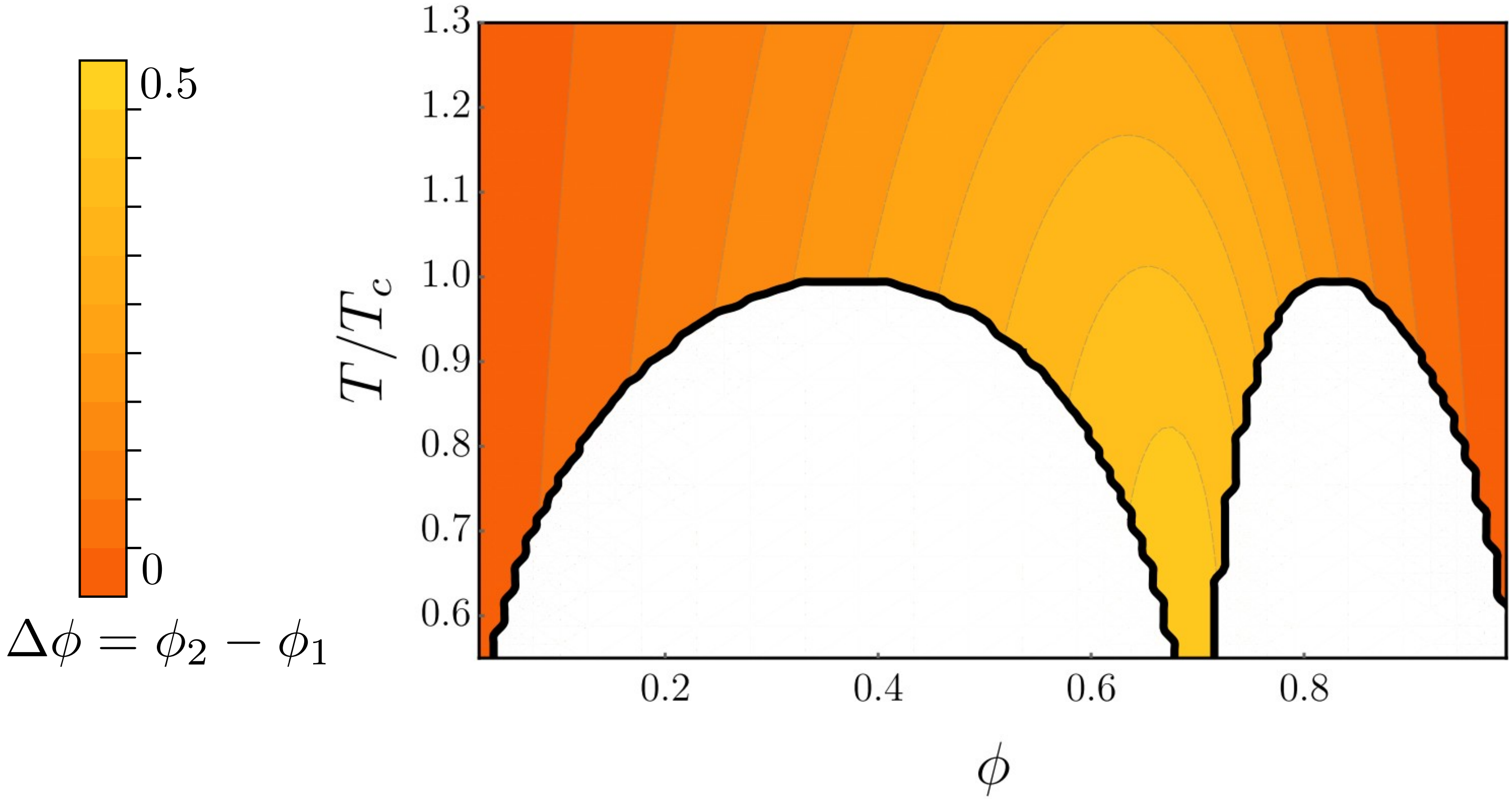

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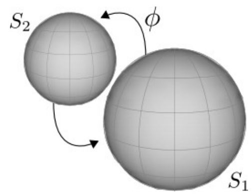
The phase diagram of 

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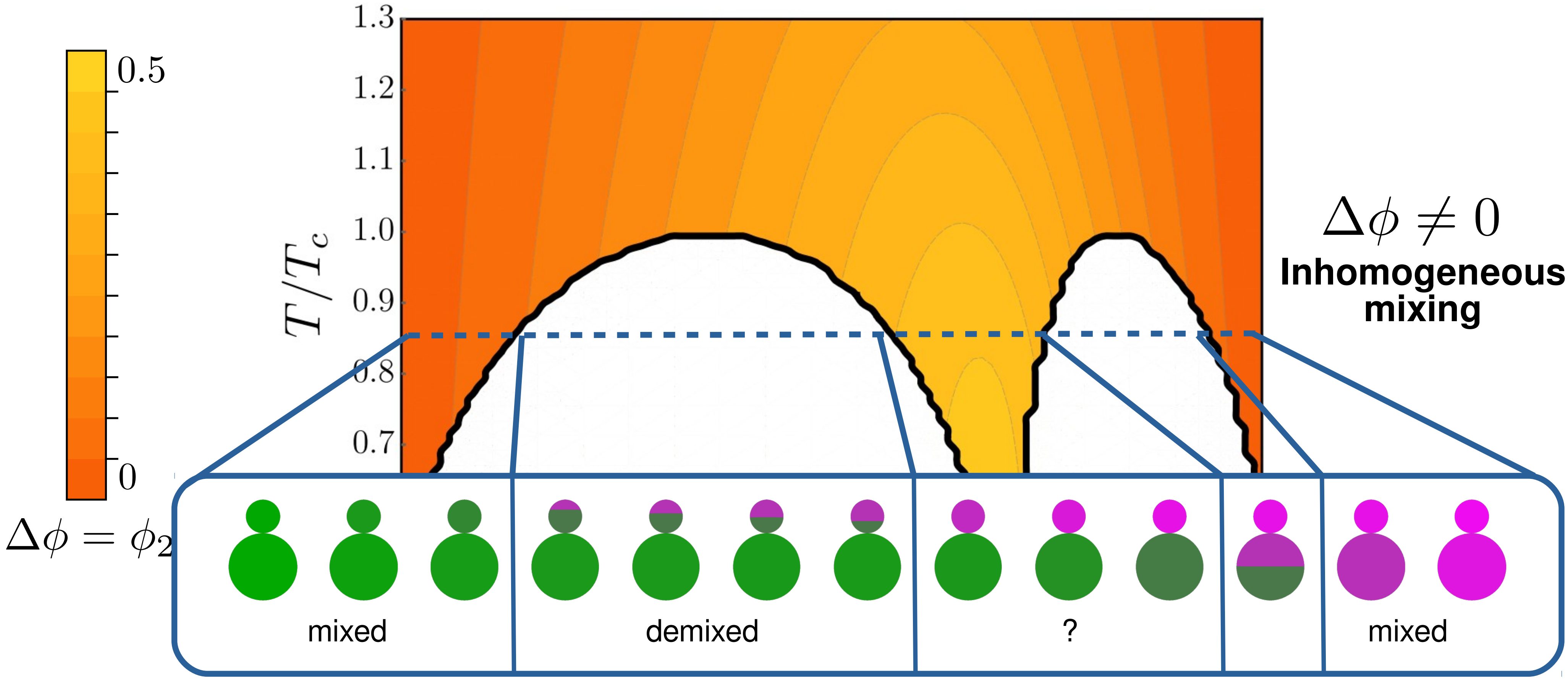

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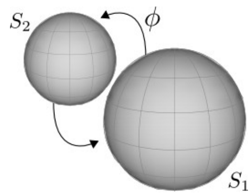
The phase diagram of  for* $M_\kappa \sim O(1)$

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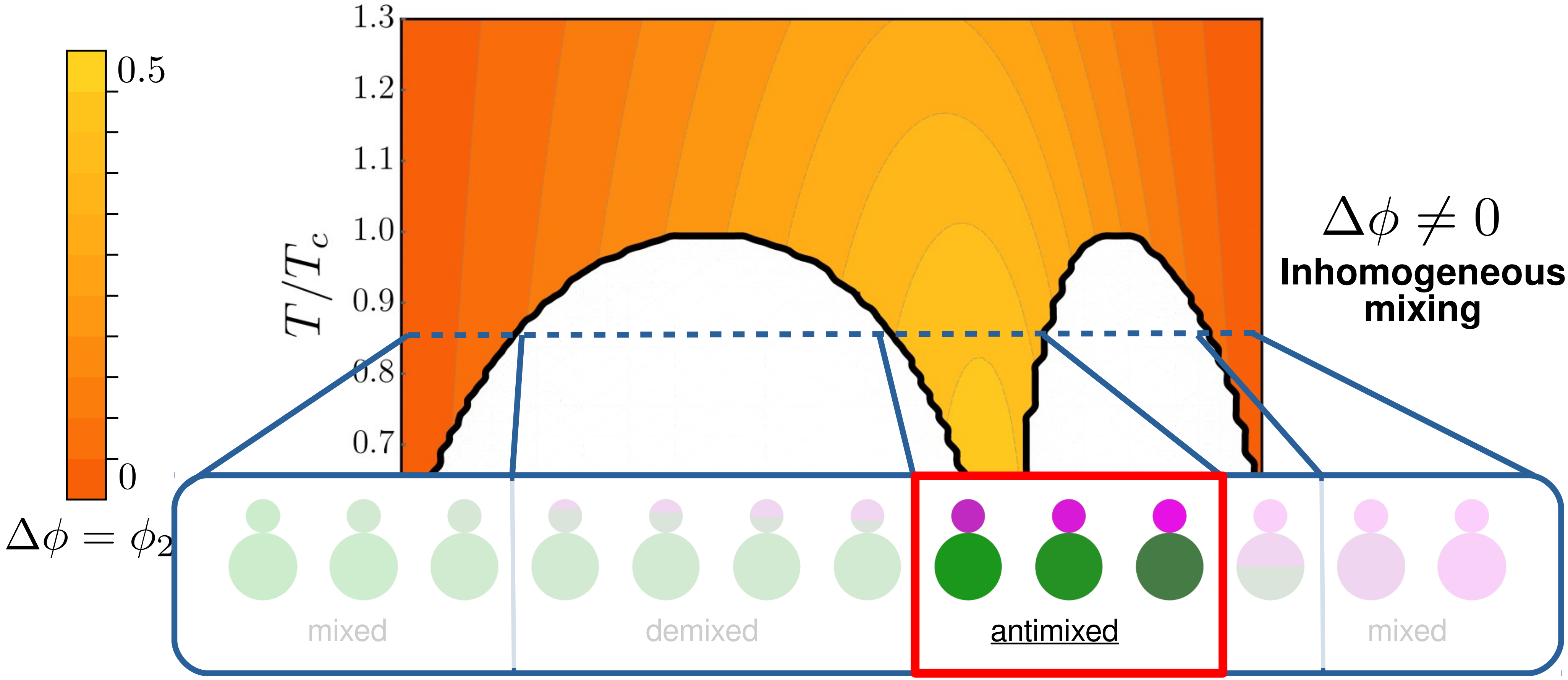

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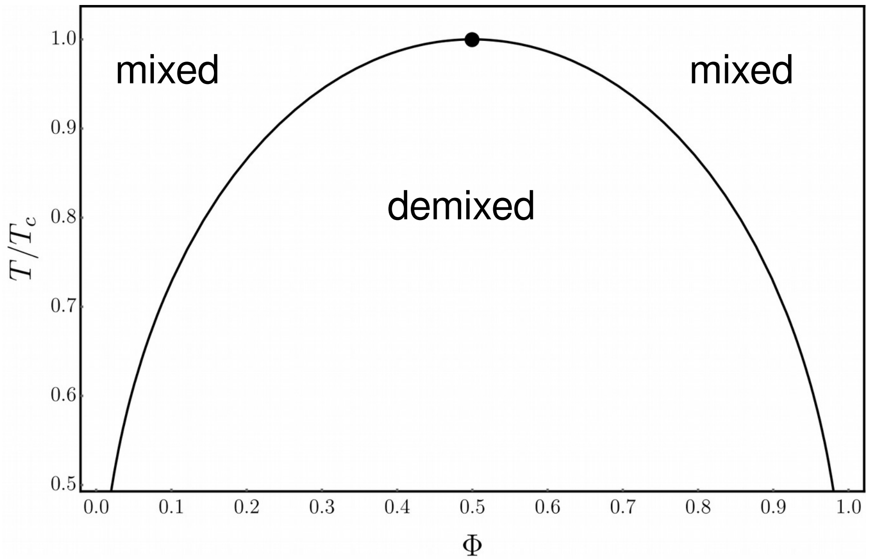
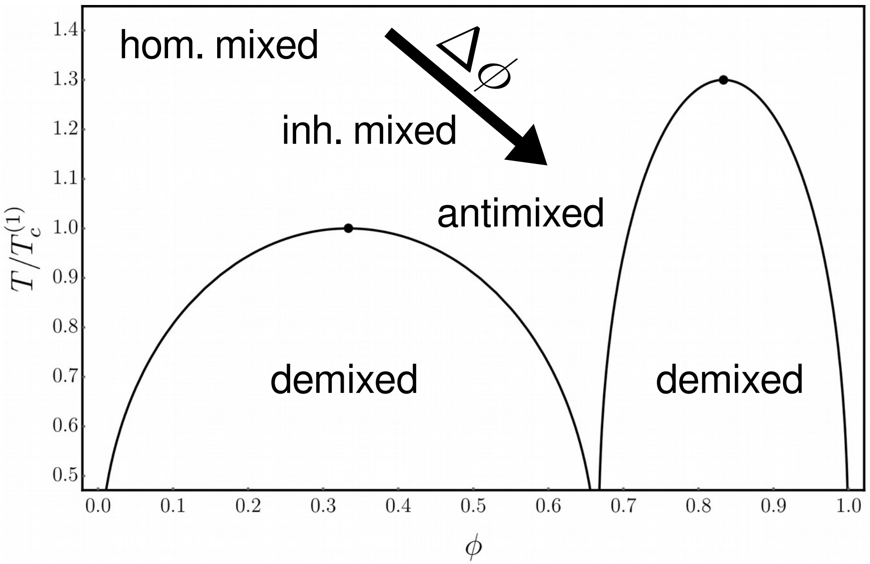
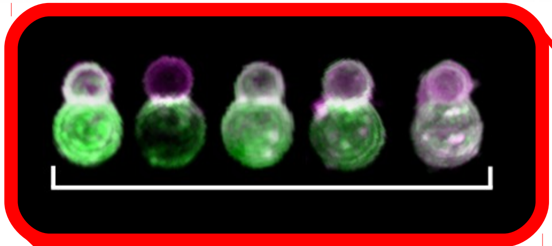
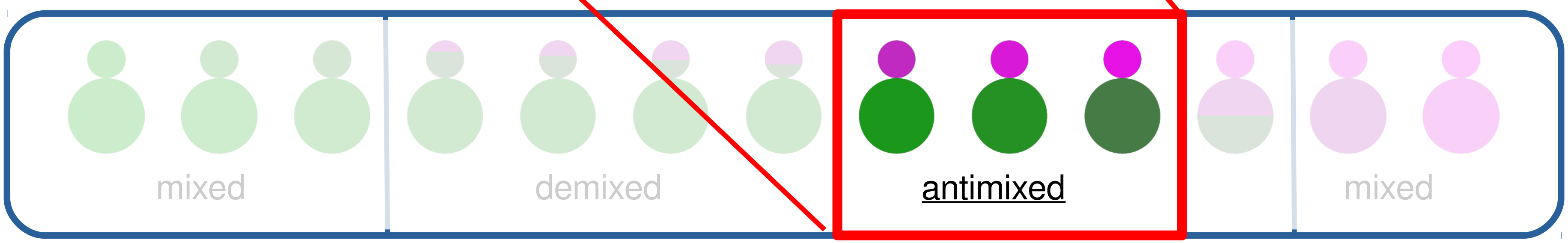
A new framework







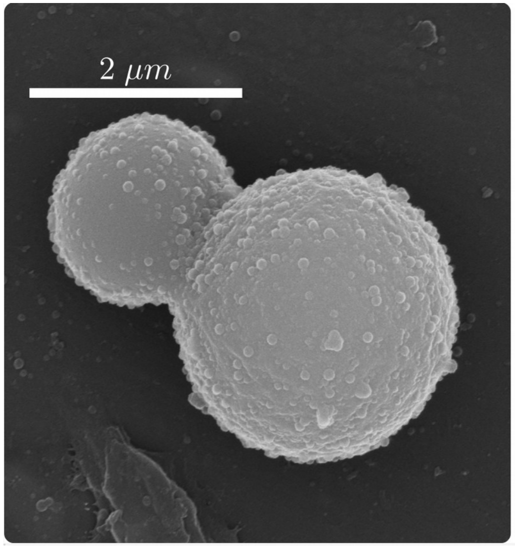


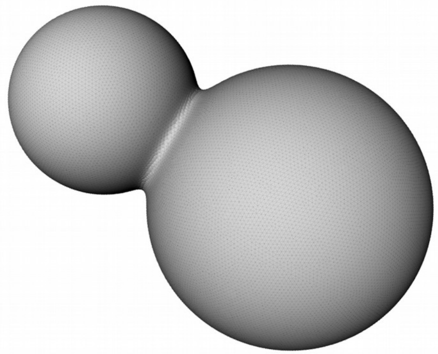
Is this phase separation? No*

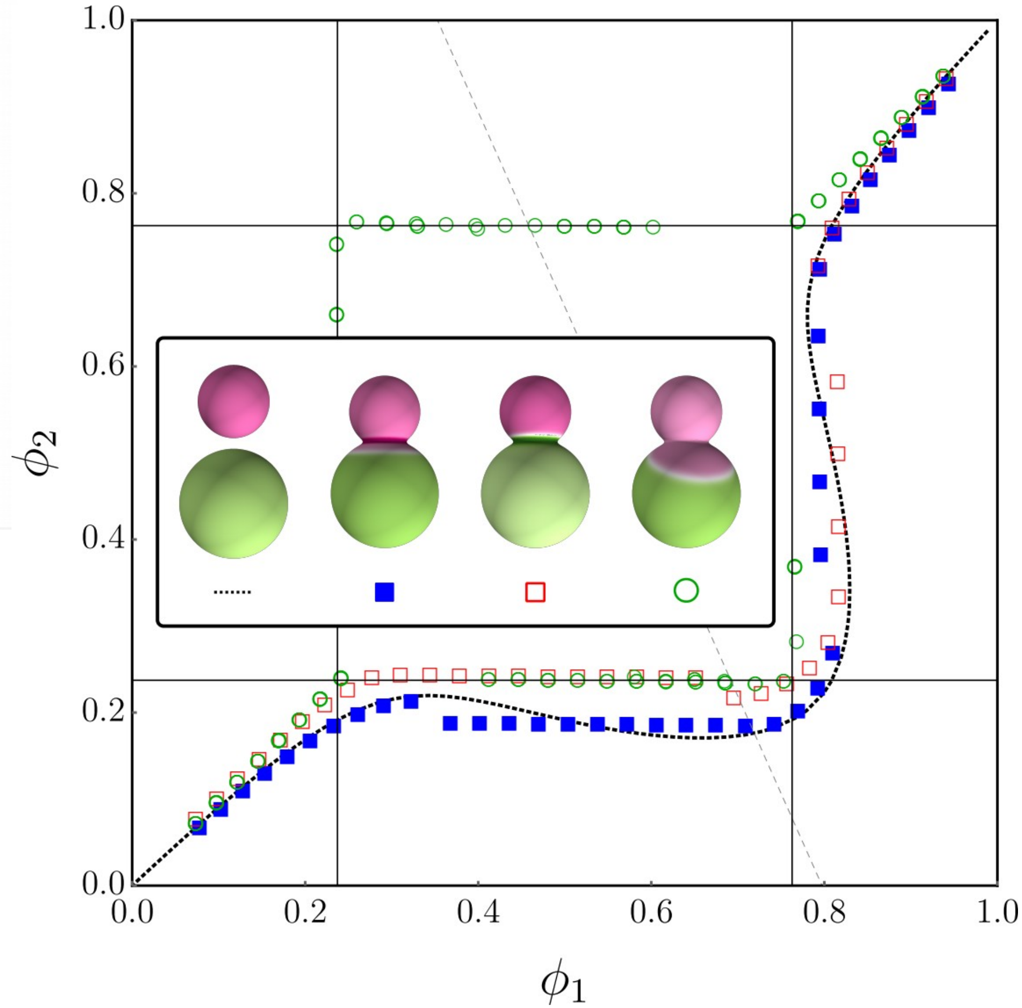
**Dumbbell ≠ Two spheres*

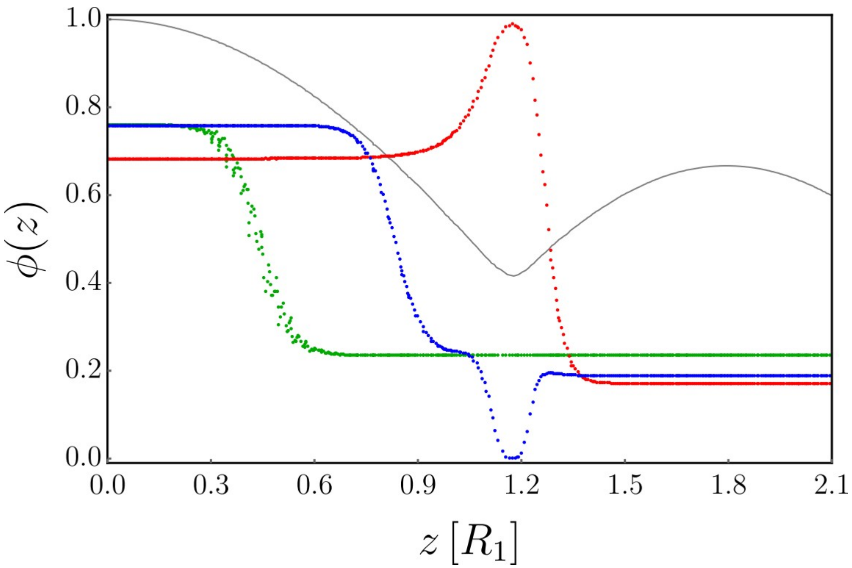
More realistic surfaces

How good of an approximation are two disjoint spheres? Our colloids are dumbbells:









P.F. et al. (arXiv 1812.11563, under review @ PRE)

More realistic surfaces

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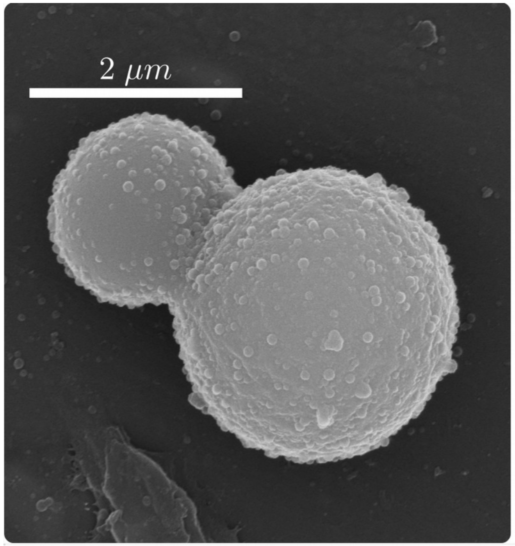
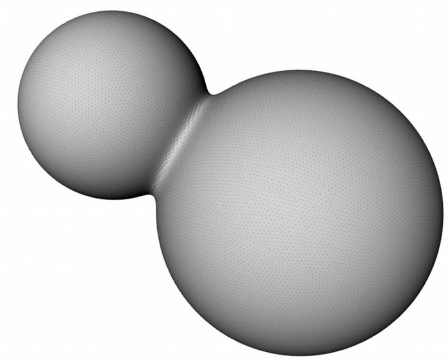
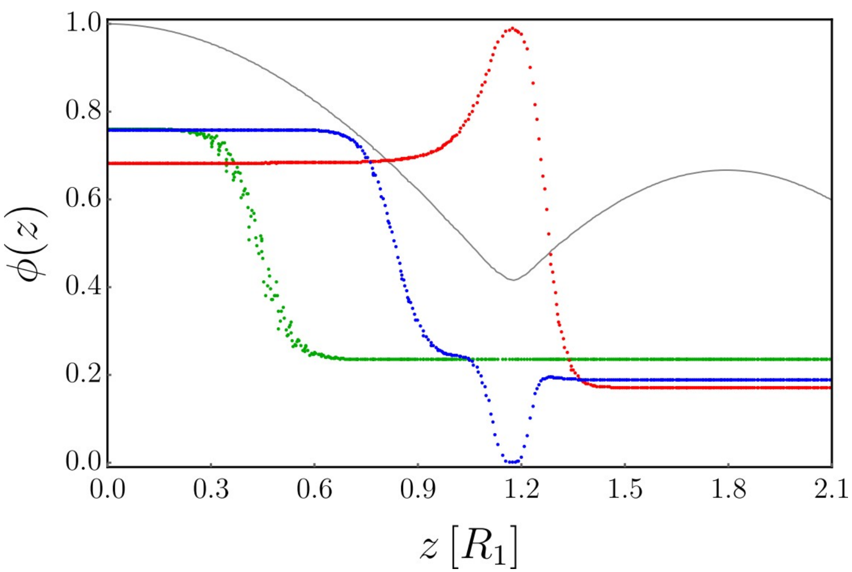
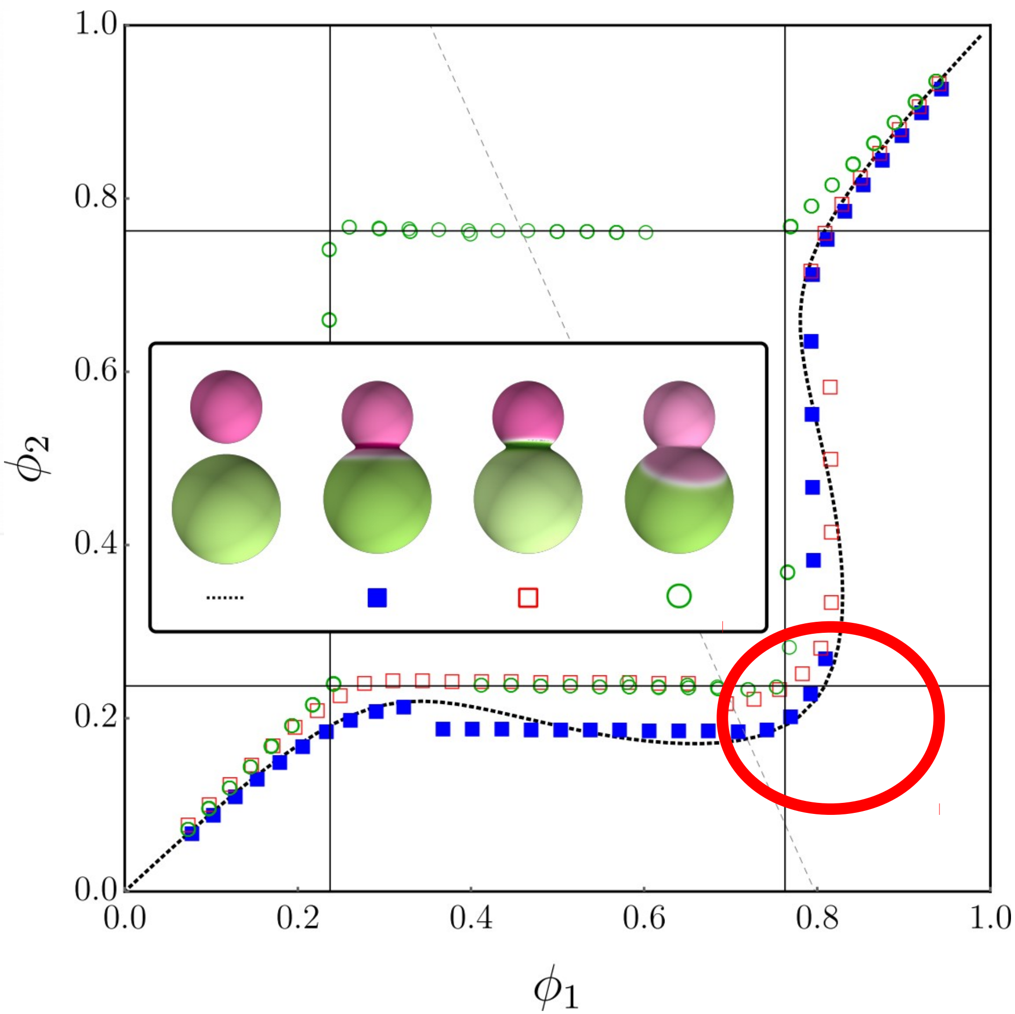








P.F. et al. (arXiv 1812.11563, under review @ PRE)

The antimixed state survives for large enough bending modulus!

Are there quadratic curvature interactions?

$$\mathcal{F} \simeq J\frac{\xi^2}{2}\nabla_i\phi\nabla^i\phi + f(\phi) + k(\phi)H^2 + \bar{k}(\phi)K + \dots$$

If the full free energy has **location-dependent binodal points** we find – through boundary layer analysis of the gradient term – **corrections to the line tension due to curvature**

$$\tilde{\sigma} \simeq \sigma + \delta_k H^2 + \delta_{\bar{k}} K + \dots$$

Where

$$\sigma = \xi \int_{\phi_-}^{\phi_+} \mathrm{d}\varphi \sqrt{2\tilde{f}(\varphi)} \qquad \delta_k = \xi \int_{\phi_-}^{\phi_+} \mathrm{d}\varphi \frac{\tilde{k}(\varphi)}{\sqrt{2\tilde{f}(\varphi)}}$$

with $\tilde{f}(\varphi) = f(\varphi) + \dfrac{f(\phi_-)(\varphi - \phi_-) + f(\phi_+)(\phi_+ - \varphi)}{\phi_+ - \phi_-}$

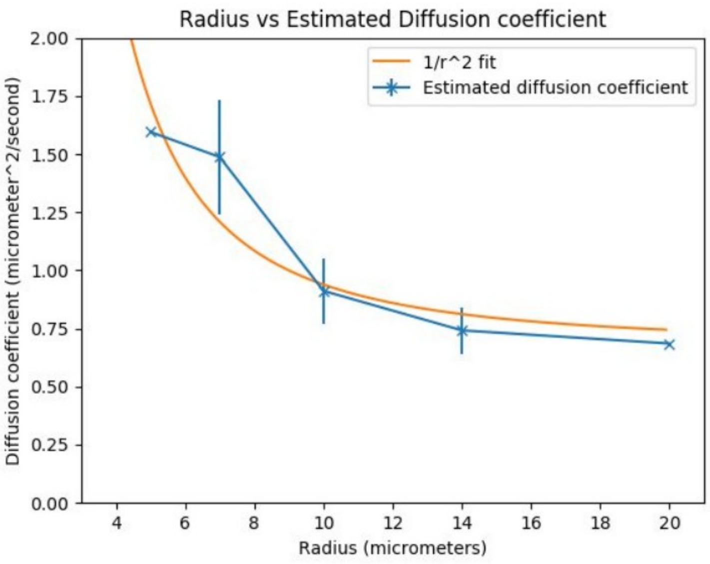
$\delta_{k,\bar{k}}/\sigma$ are the 1D analogues of the **Tolman lengths**

For our MFT lattice gas model we find $\delta_{k,\bar{k}}/\sigma = \dfrac{3q}{4} L_{k,\bar{k}}(T_c - T)^{-1}$

Are there quadratic curvature interactions?

Actual MFT compressibility

$$D = \xi^2 \left(J + L_k H^2 + L_{\bar{k}} K\right)$$



$$D_{flat} = 0.679 \,[\frac{\mu m^2}{s}]$$

$$\alpha = 25.96 \,[\frac{\mu m^4}{s}]$$

$$D_s = D_{flat} + \frac{\alpha}{R^2} \qquad \alpha \propto L_k + L_{\bar{k}}$$

Ten Haaf, Rinaldin, Kraft, PF (unpublished)

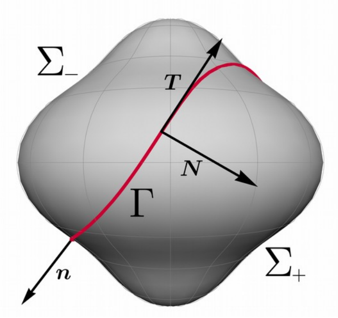
Since NN interaction modulates *both* diffusion and reaction forces, we infer that, in bilayer membranes, there should *be* a **quadratic interaction** and a **curvature dependent critical temperature**

$$T_c = \frac{q}{2}\left(J + L_\kappa H^2 + L_{\bar{\kappa}} K\right)$$

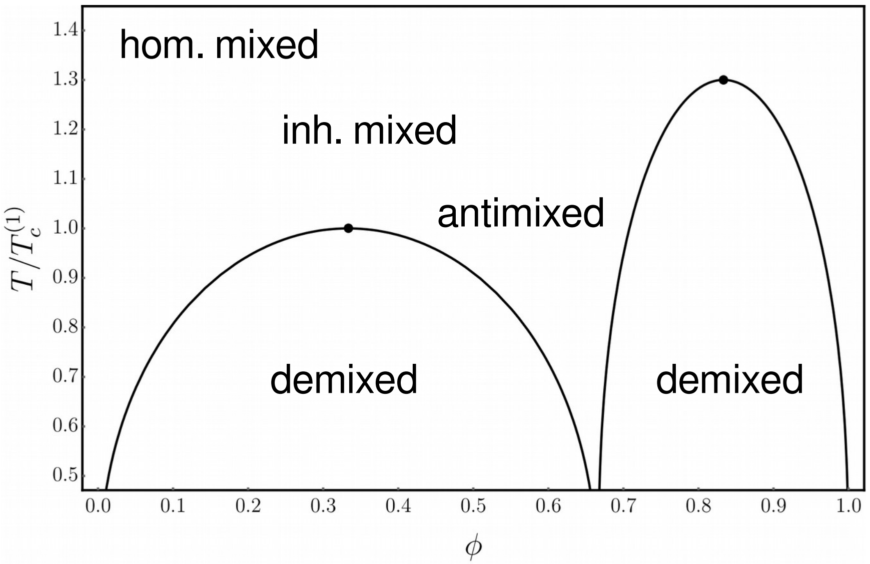
P.F. et al. (arXiv 1812.11563, under review @ PRE)

Summary

- SLVs are **closed** thermodynamical systems
- Sharp interface models have **limited** applicability
- **Curvature-composition** interactions are essential to get the full picture
- **Non-spherical** shapes are necessary to make this effect evident



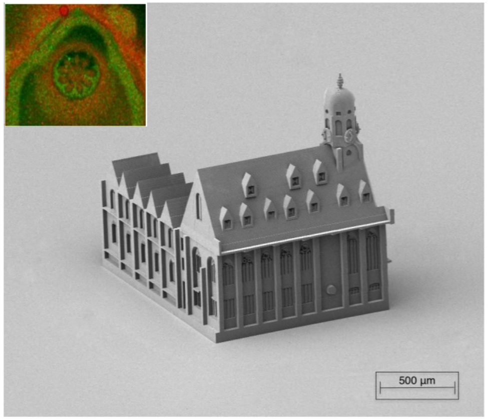
- New equilibrum states can emerge: **antimixing**
- Different couplings (**linear** vs. **quadratic**) produce very different phenomenologies



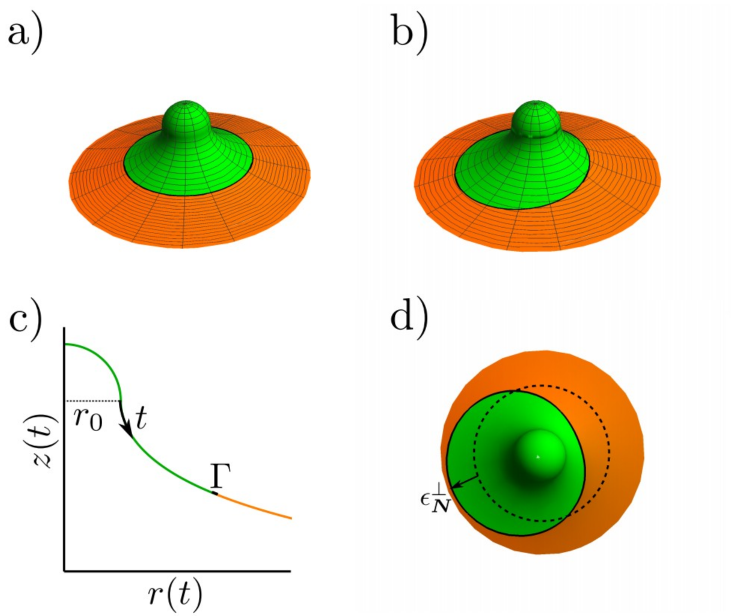
Future directions

- Extend the model to n-nary mixtures
- Is critical temperature affected by curvature? And line tension?
- In Leiden, we can 3D print *any surface* and coat it with lipids: we want to engineer the right surface to highlight specific curvature effects:

Rinaldin, Doherty (unpublished)



A micron-sized version of the Academiegebouw in Leiden



Measuring membrane Gaussian rigidity using curved substrates, *PF et al. (in preparation)*

Honerkamp-Smith et al. (BJ, 2008)

A collaboration with:

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End of presentation