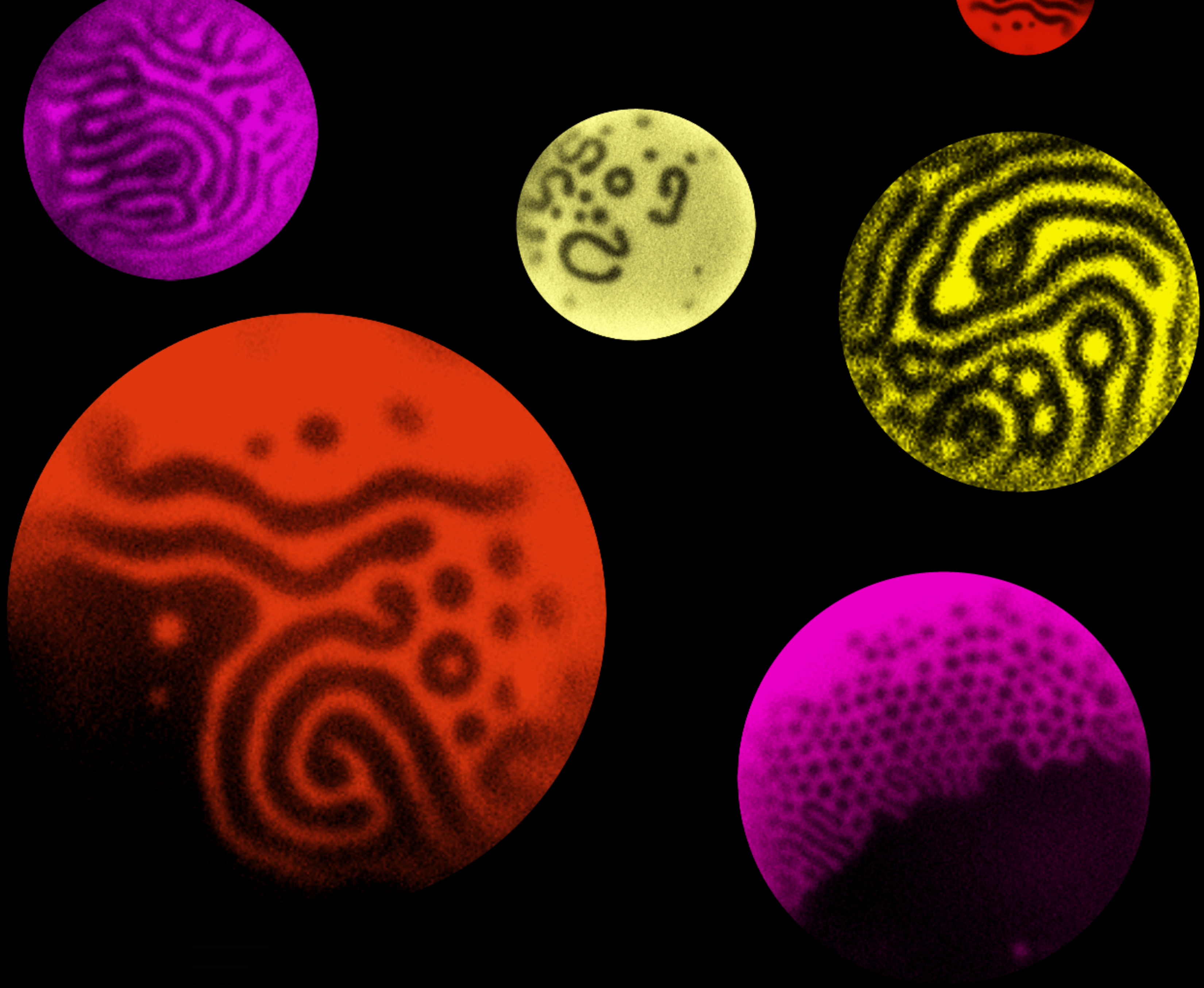

Tuning length scales of small domains in lipid membranes

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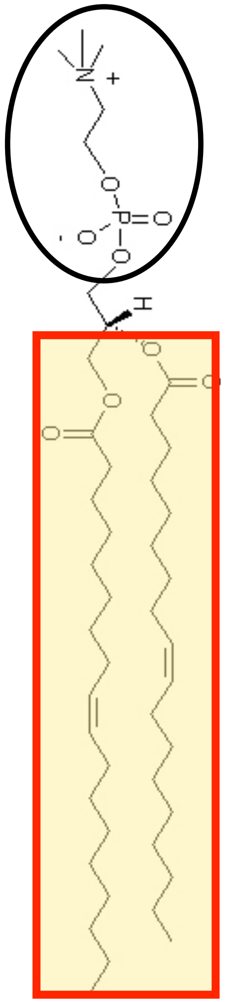
Ph.D. Candidate

University of Washington

SIAM LS18 Aug. 6, 2018

Lipids self-assemble into bilayers in water

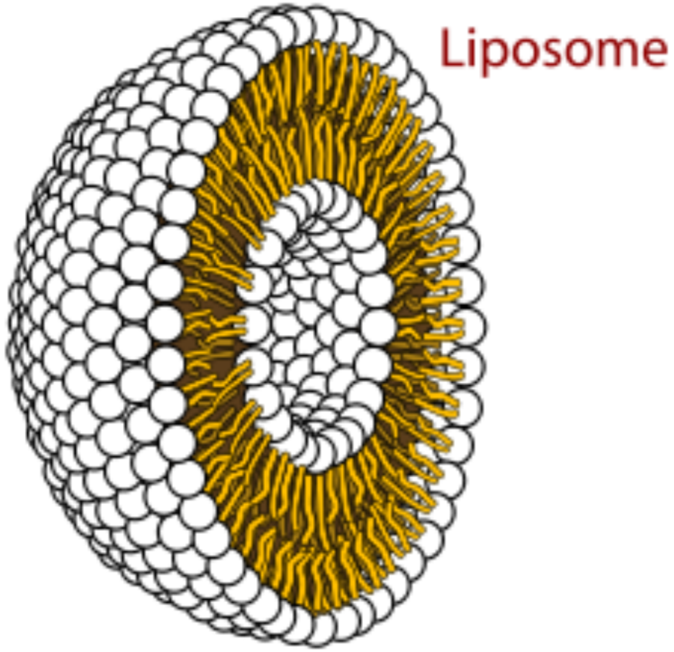


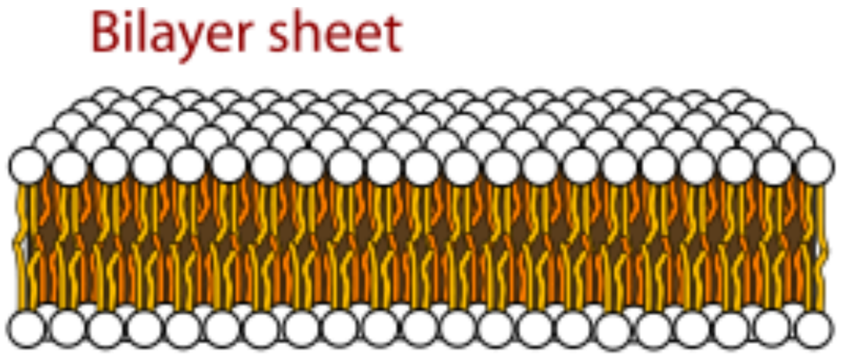
polar
head group

hydrophobic
acyl tail

~~Dipalmitoylphosphatidylcholine~~ → Dioleoylphosphatidylcholine
(DPPC) (DOPC)

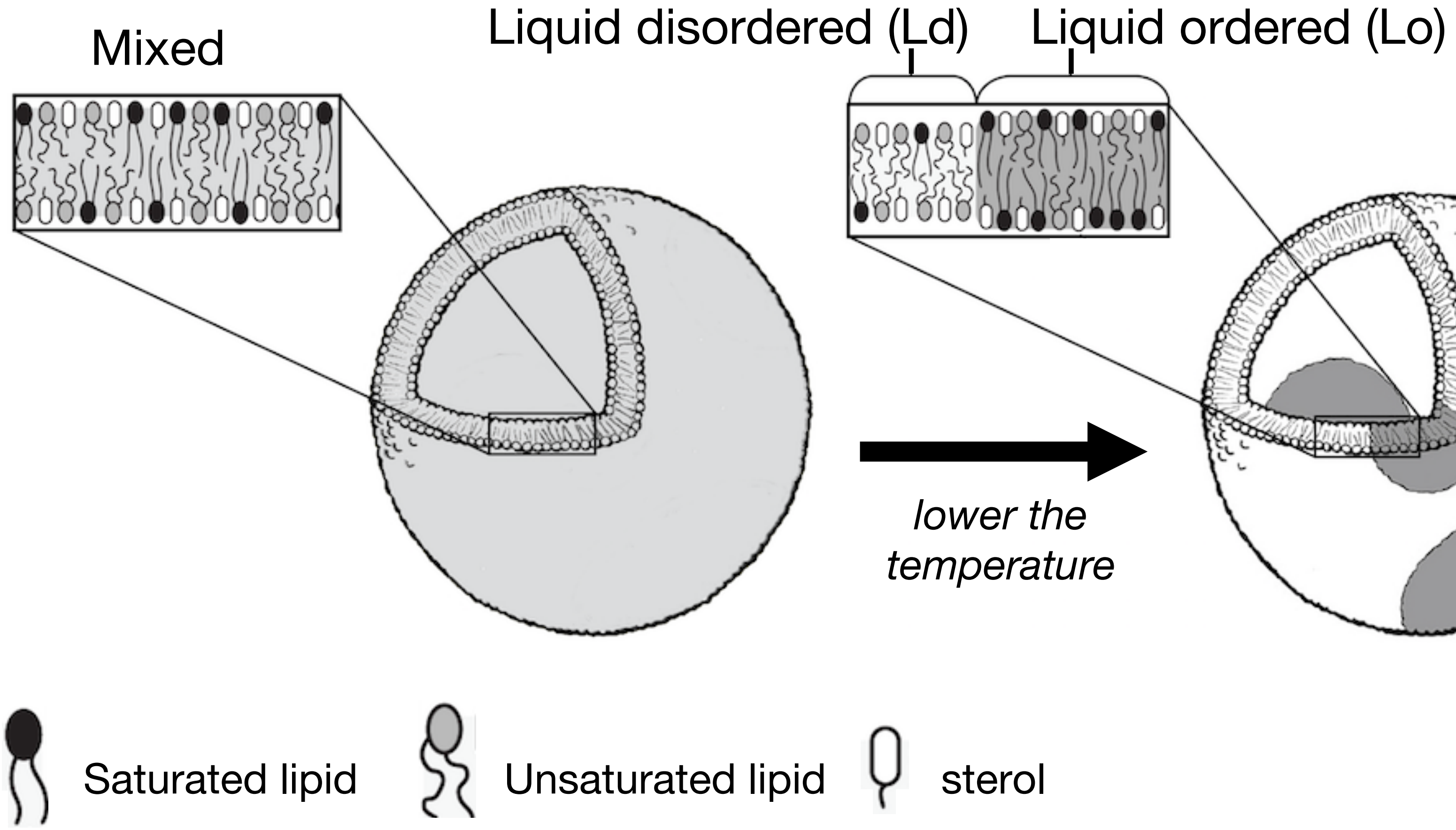
- Self-assemble
- Essentially 2D
- Liquid crystal





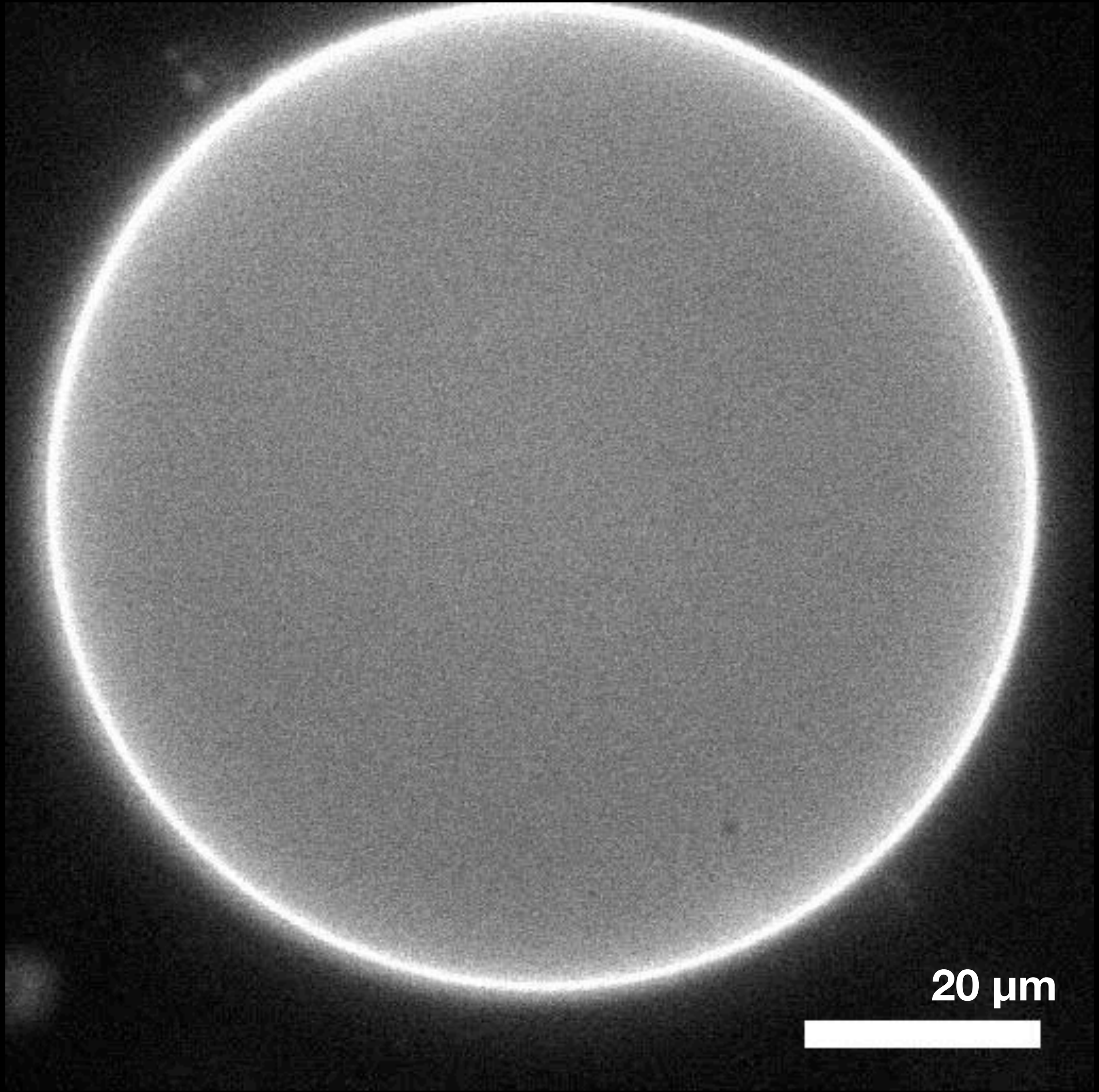
https://en.wikipedia.org/wiki/Lipid_bilayer

Phase separation in model lipid membranes: Giant Unilamellar Vesicles (GUVs)



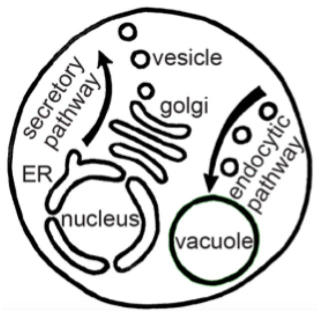
Drawing: Aurelia Honerkamp-Smith

Simple lipid bilayers undergo complex physical behavior

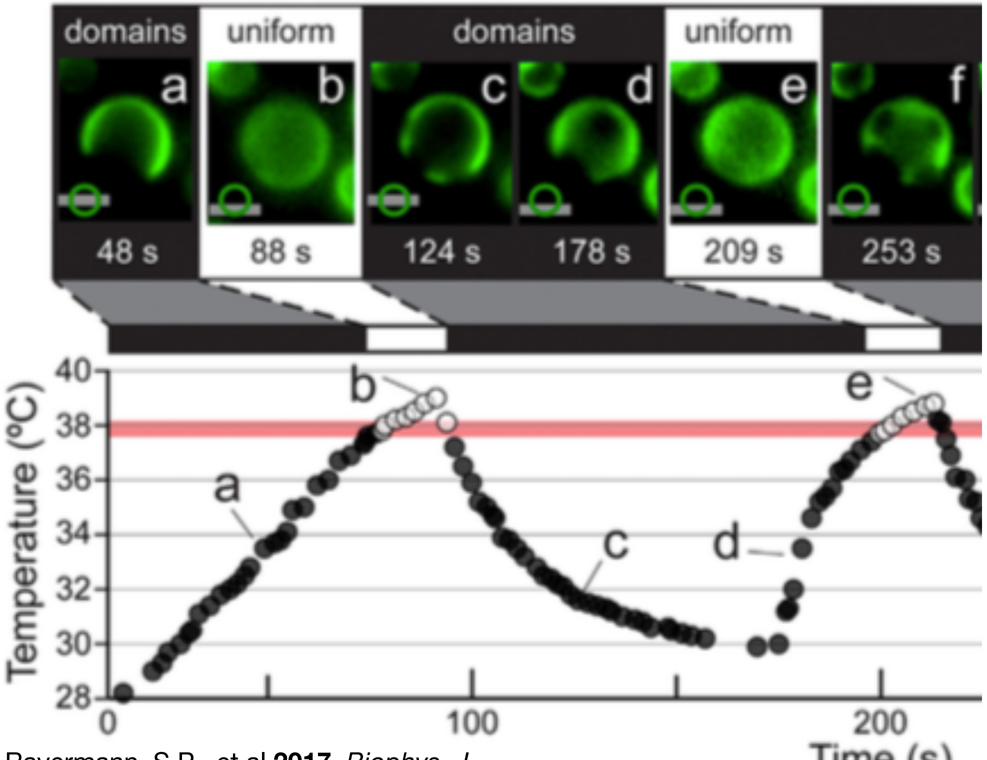


Video: Aurelia Honerkamp-Smith

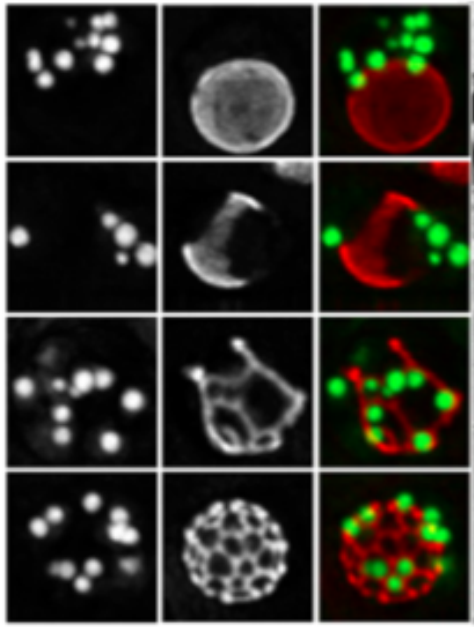
A role for lipid domains in biology: yeast vacuoles



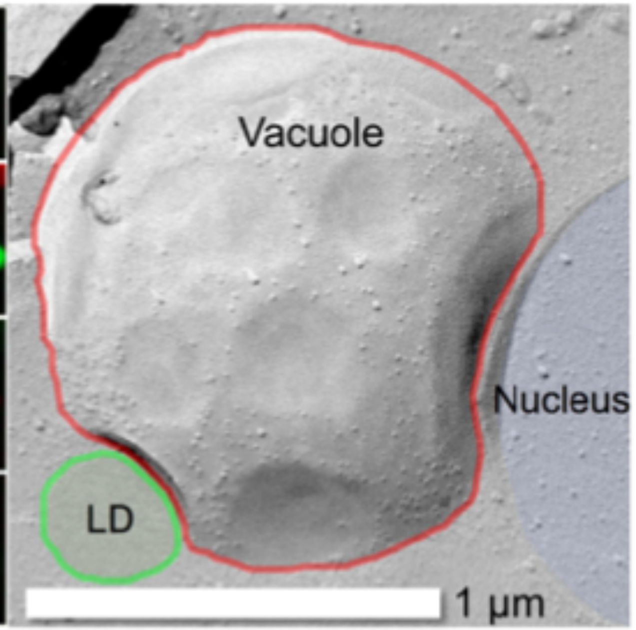
Vacuole membranes reversibly separate into coexisting liquid phases



Rayermann, S.P., et al **2017,** *Biophys. J.*



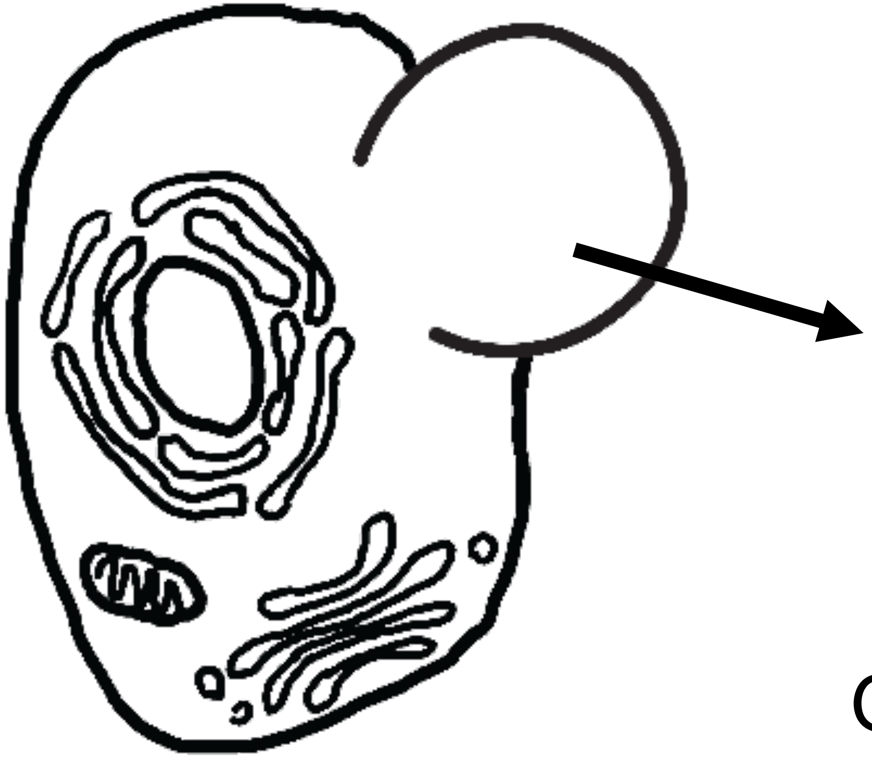
Wang et al **2014,** *J. Cell Bio.*

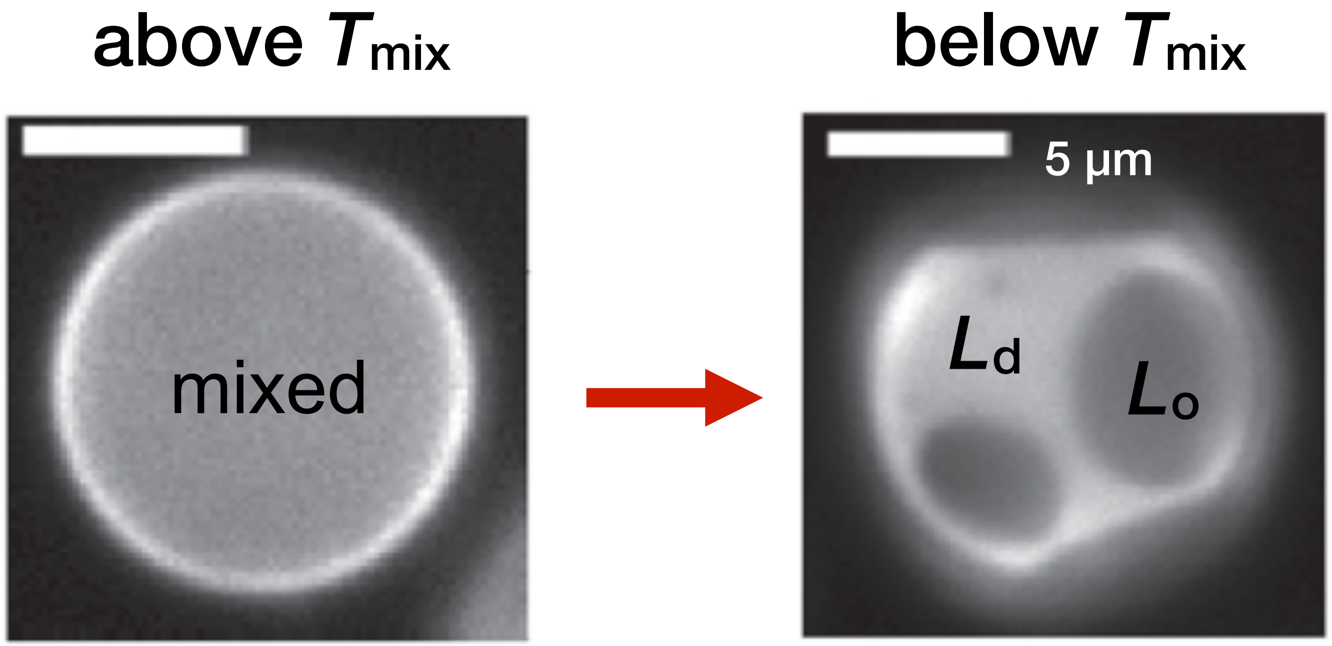


Tsuji, et al **2017,** *eLife*

Lipid droplets (an energy store for the cell) dock to vacuole domains

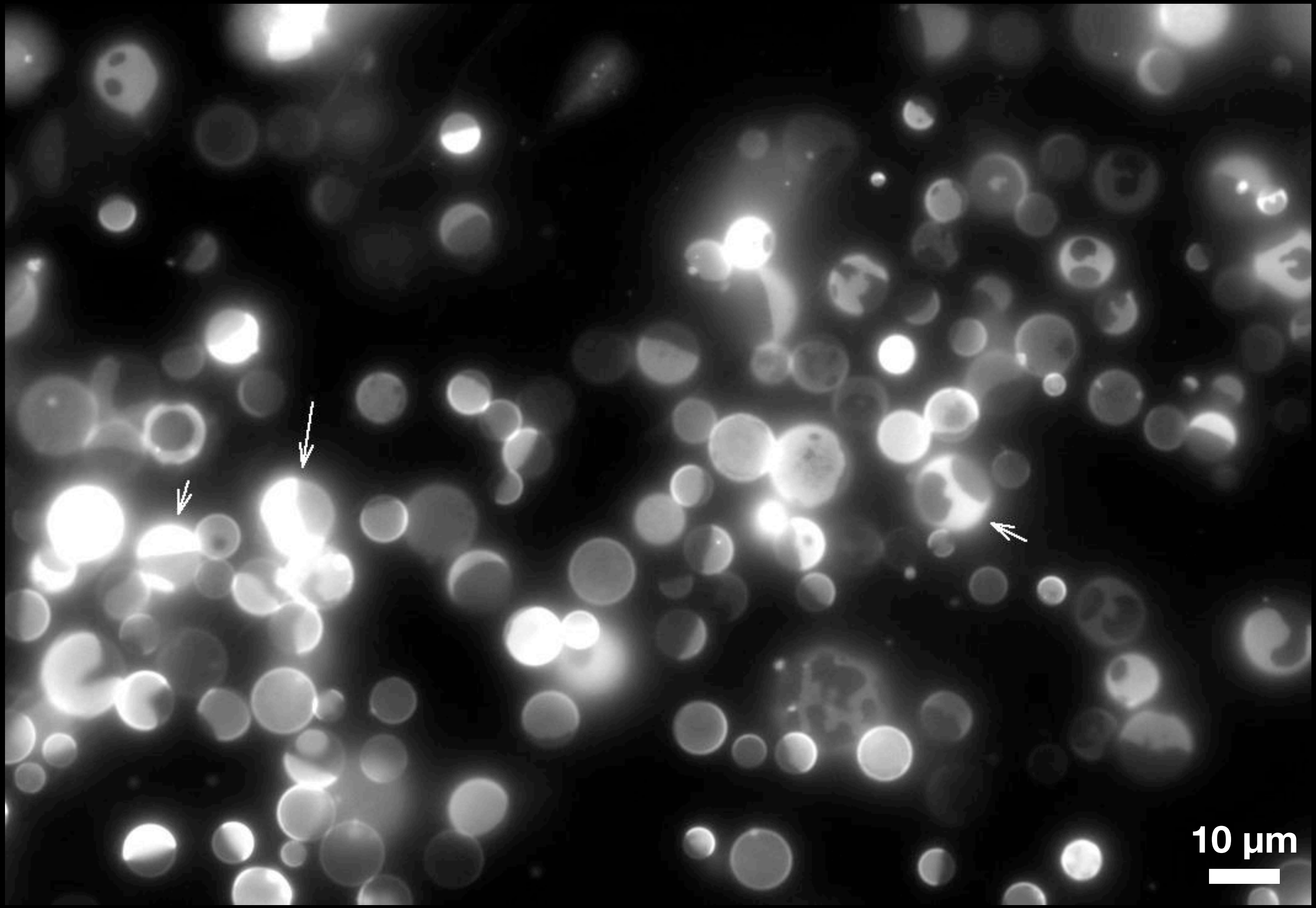
Cell-derived membrane: Giant Plasma Membrane Vesicle (GPMV)



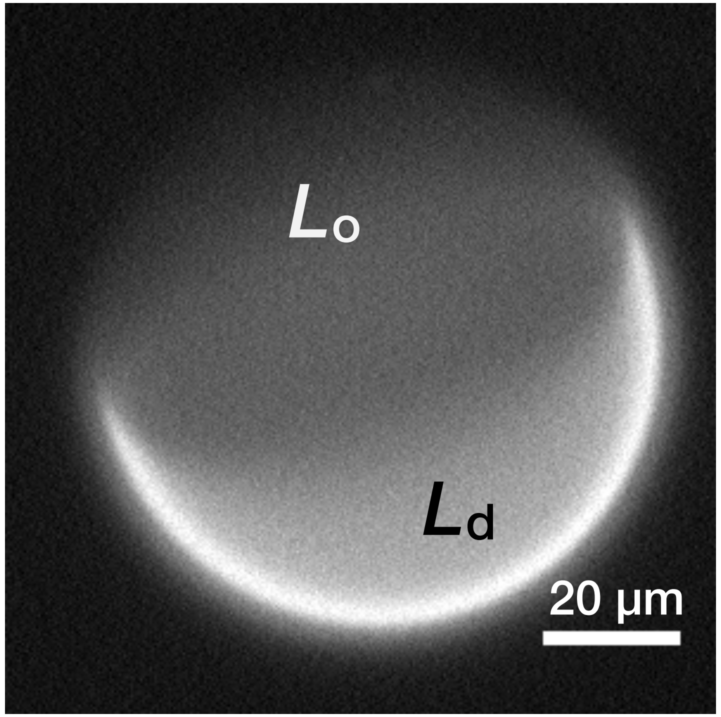


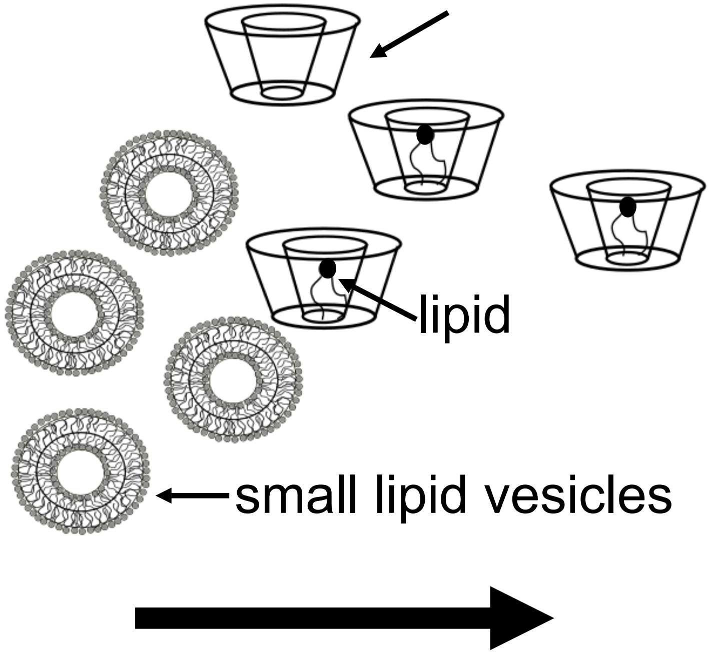
GPMVs retain the biological complexity (>100 lipid types) of the cell membrane *without* the cytoskeleton

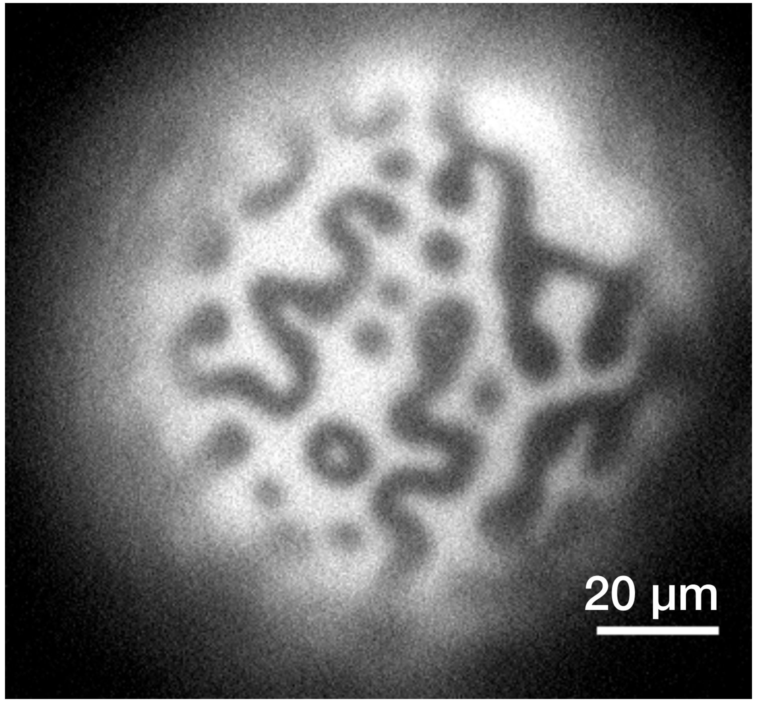
A zoo of length scales



We induce small-scale features in model GUVs

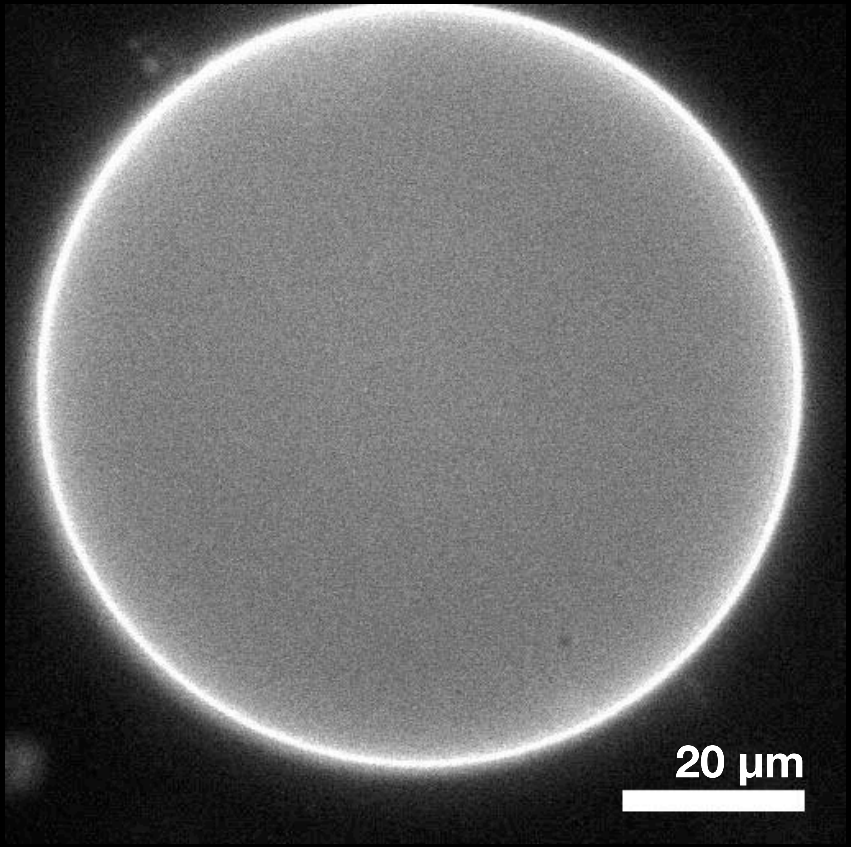


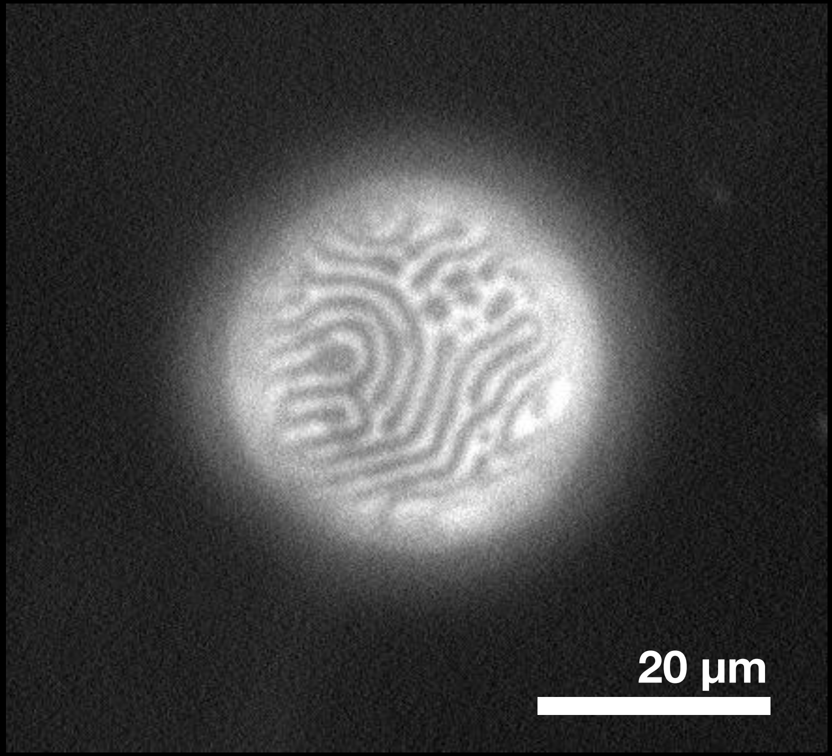


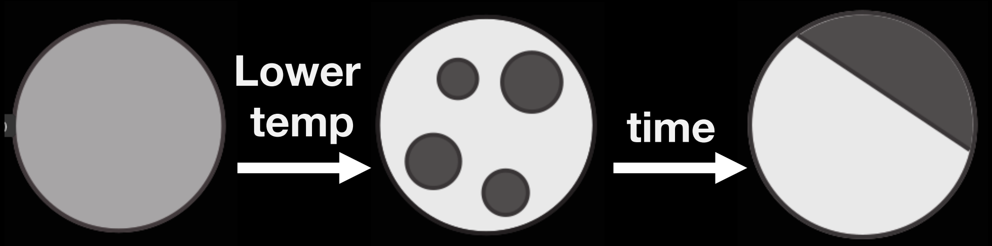


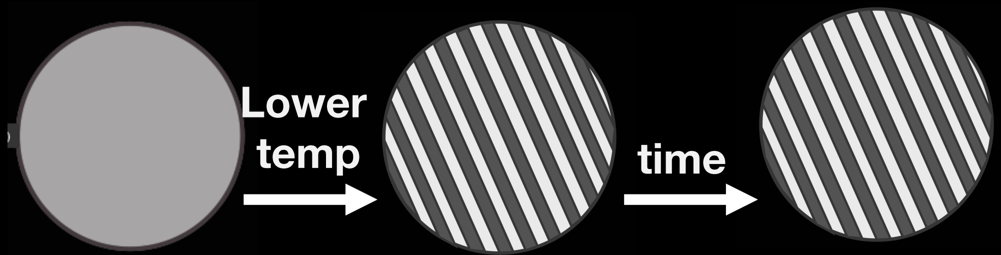
Excess lipid loaded into the outer leaflet of the bilayer

Small-scale features persist



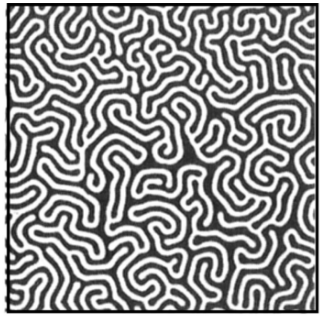




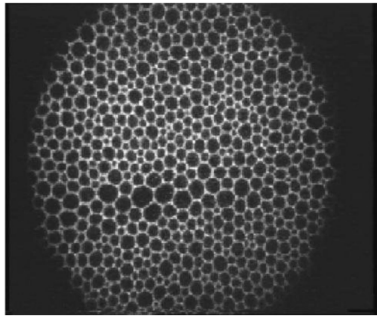


What conditions give rise to small length scales in membranes?

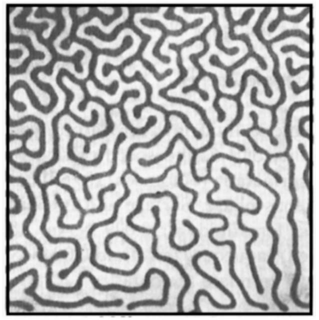
Andelman & Rosenweig **2009,** *J. Phys. Chem. B*



Ferrofluid



Alkyl lipid monolayer



Dielectric oil

Modulated phase:

A thermodynamic equilibrium state in which the appropriate order parameter shows a spatial modulation.

And in a lipid bilayer?

Free energy with two lipid components:

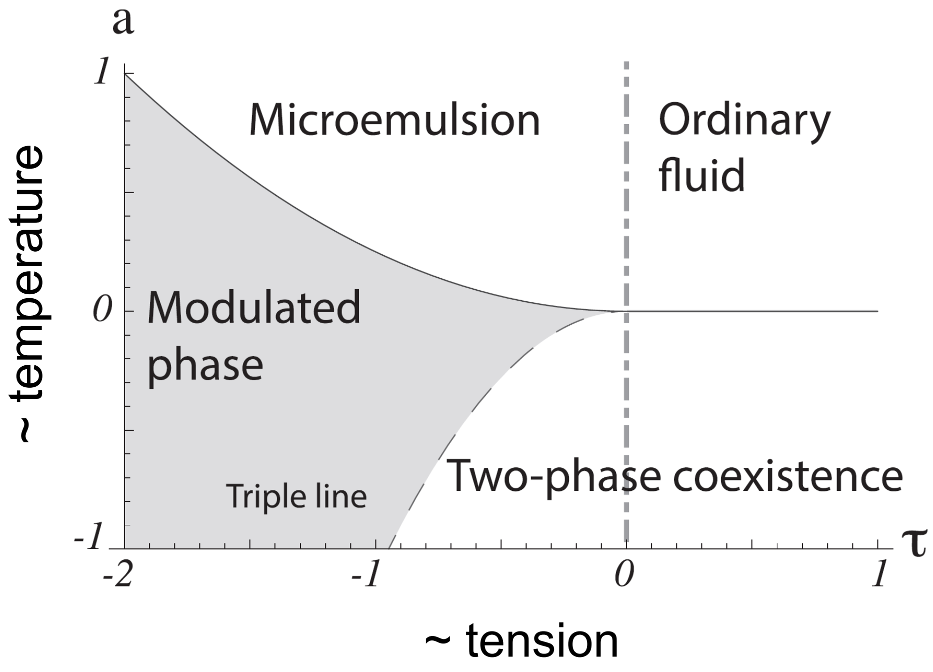
Order parameter

$$\phi(\mathbf{R}) \equiv [\phi_A(\mathbf{R}) - \phi_B(\mathbf{R})]$$

$$F[\phi] = b\, k_B T \int d^2r \left[\frac{a(T)}{2}\phi^2 + \frac{1}{4}\phi^4 + \frac{\tau}{2}(\nabla\phi)^2 + \frac{1}{2}(\nabla^2\phi)^2\right]$$

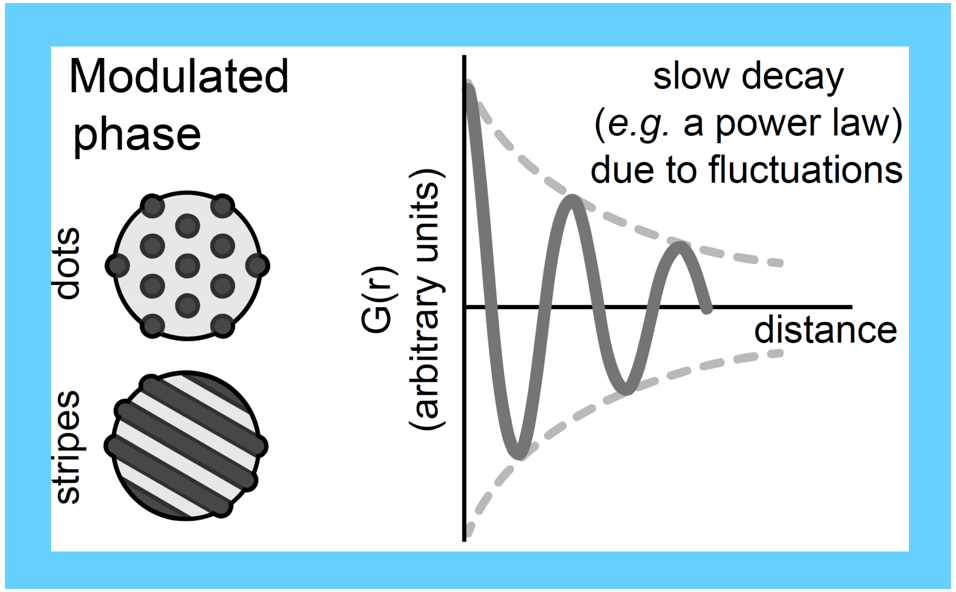
Macroscopic phase behavior

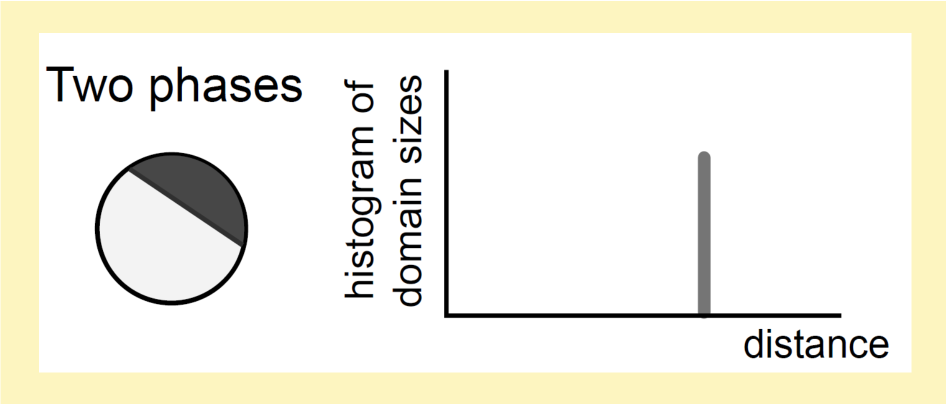
Non-macroscopic phase behavior

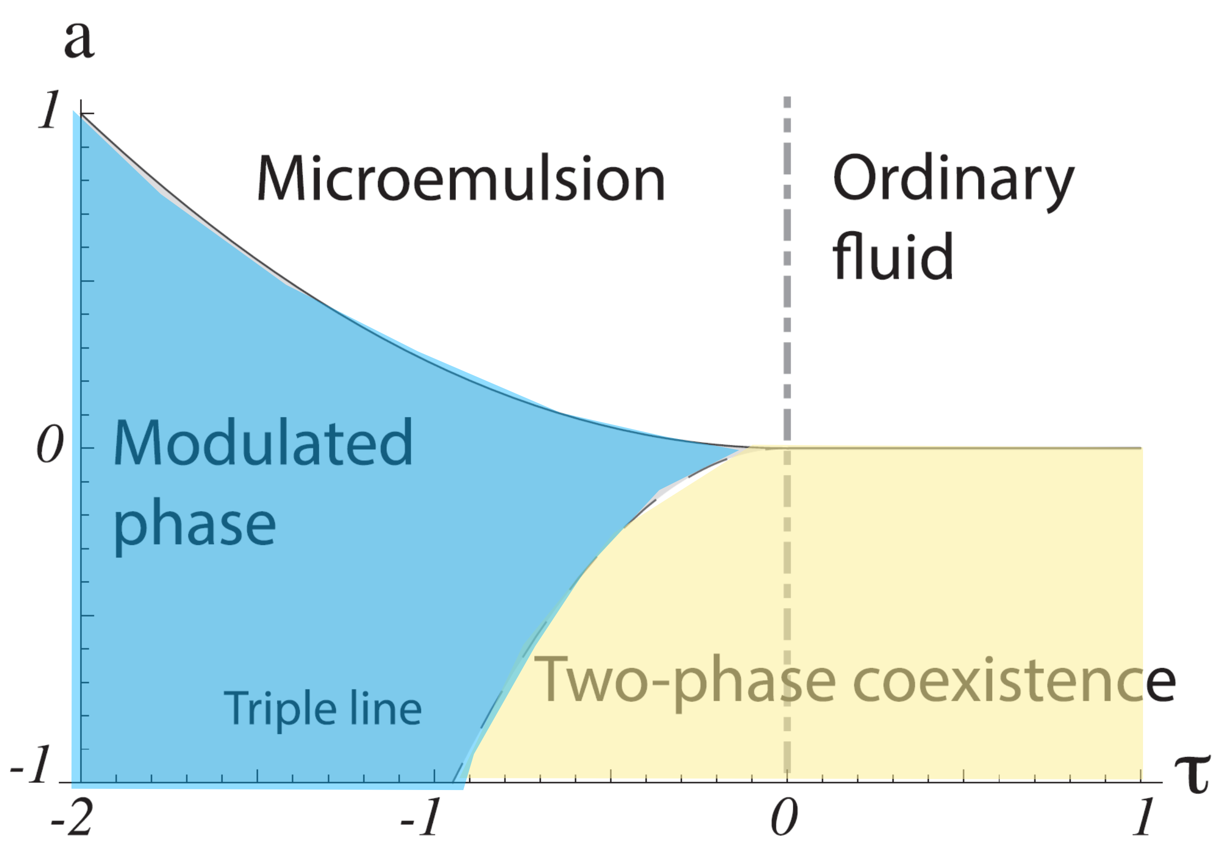


Shlomovitz, R. et al **2014,** *Biophys. J.*

Length scales of lipid membrane phases

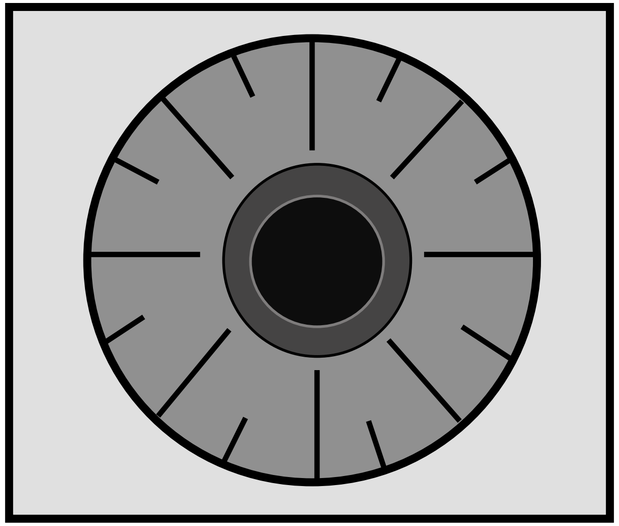




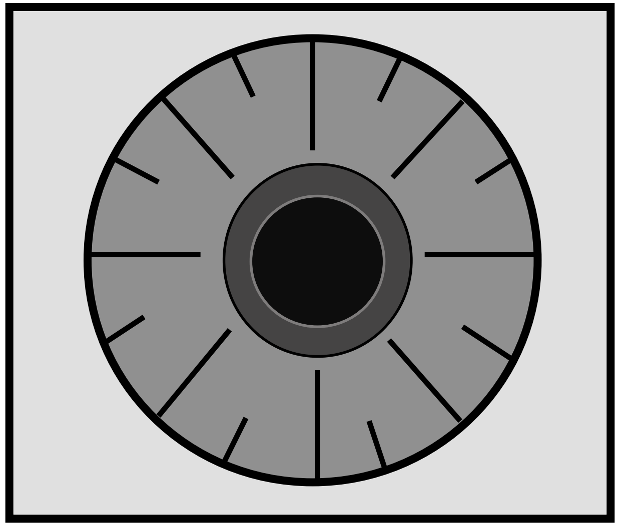


What “knobs” can I turn to change the physical parameters of the membrane?

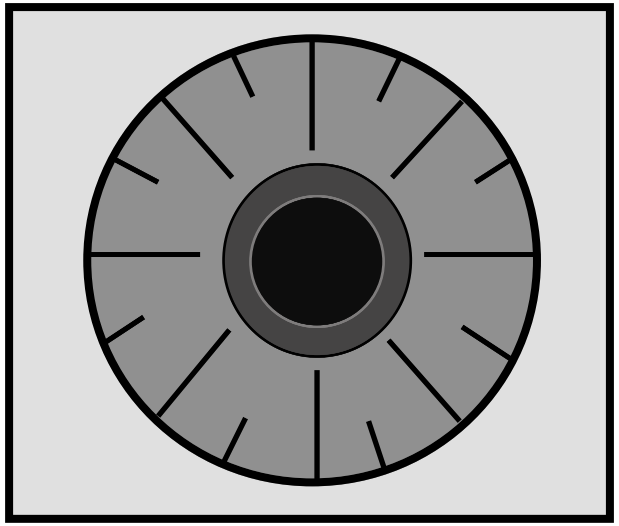
Temperature



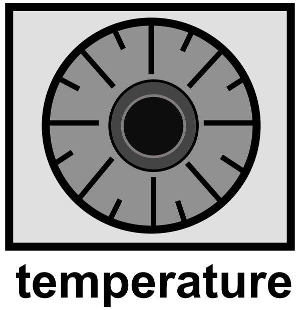
Tension

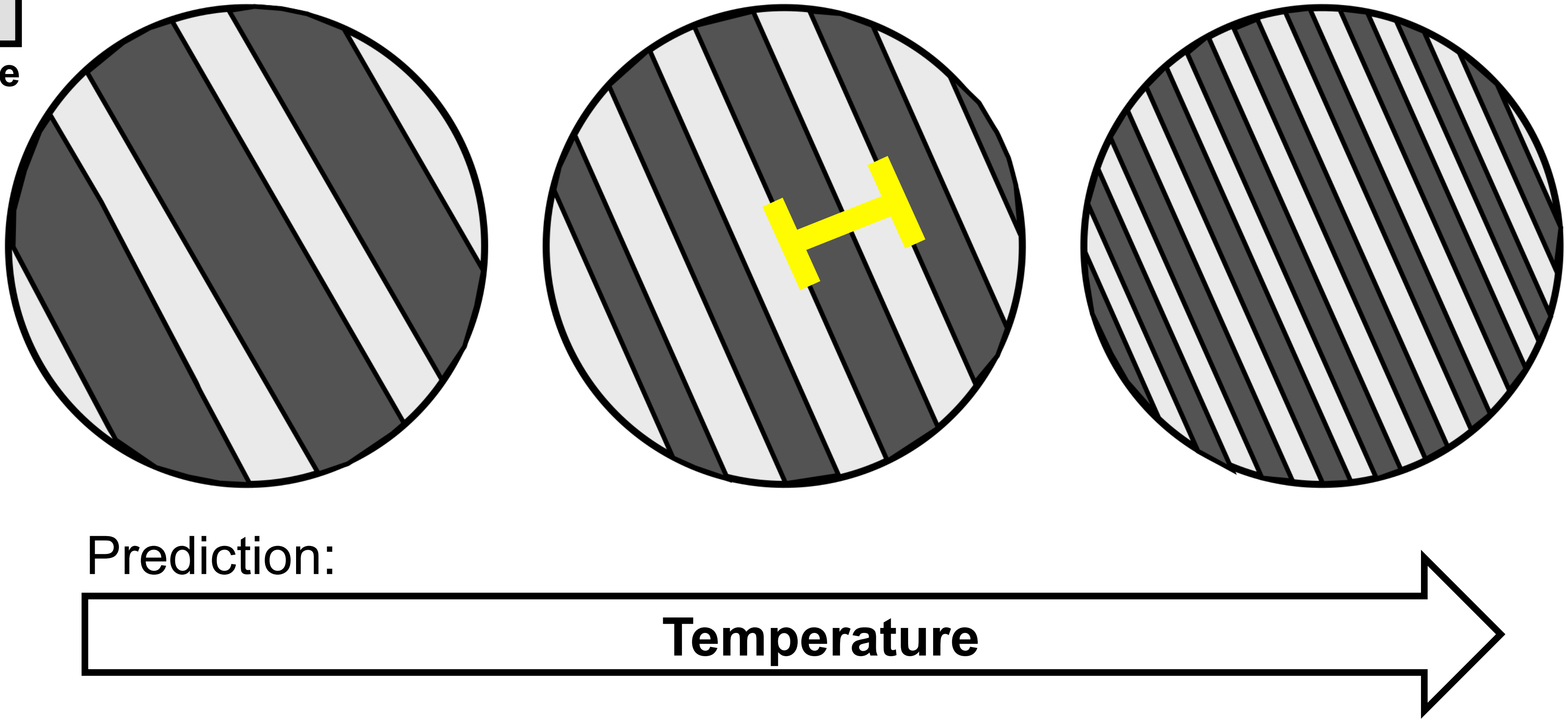


Lipid ratios

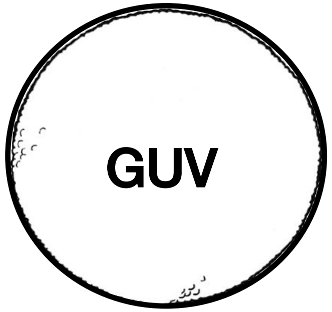


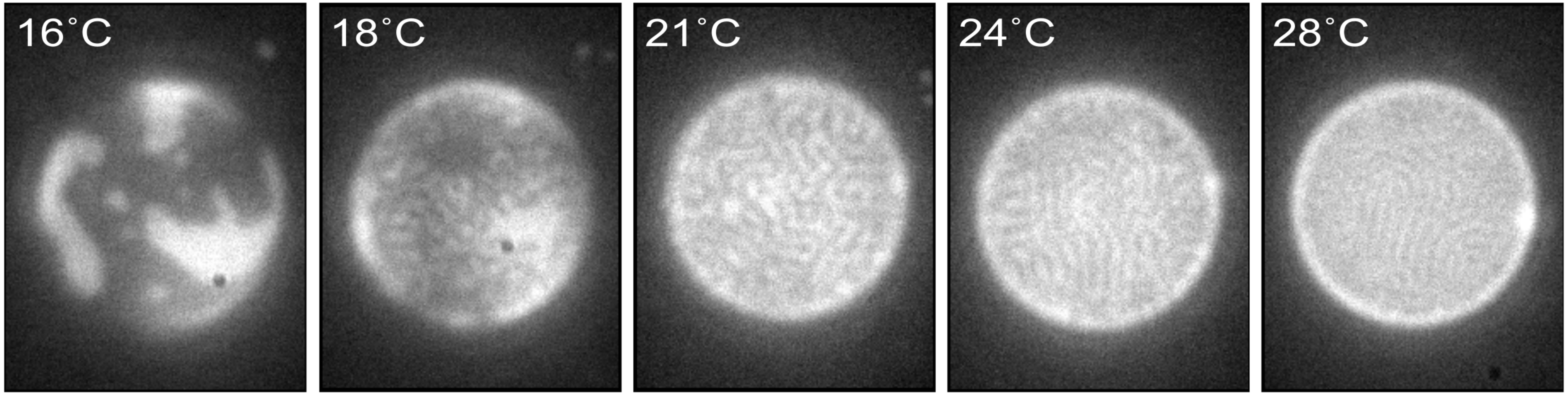
How do domain lengths scale with temperature?

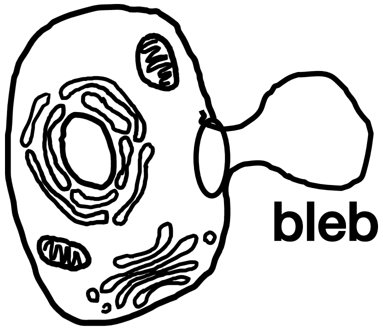


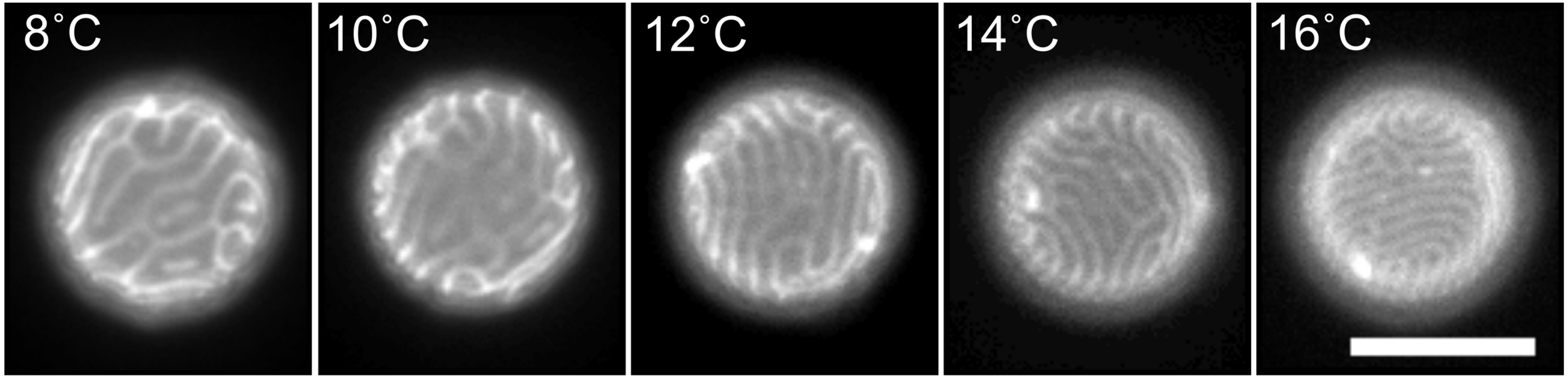


Length scales decrease with increasing temperature



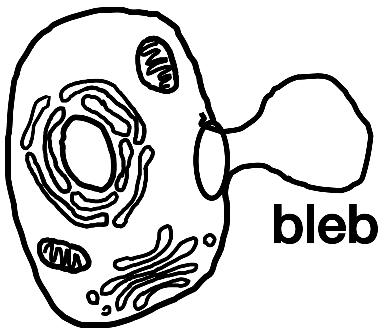


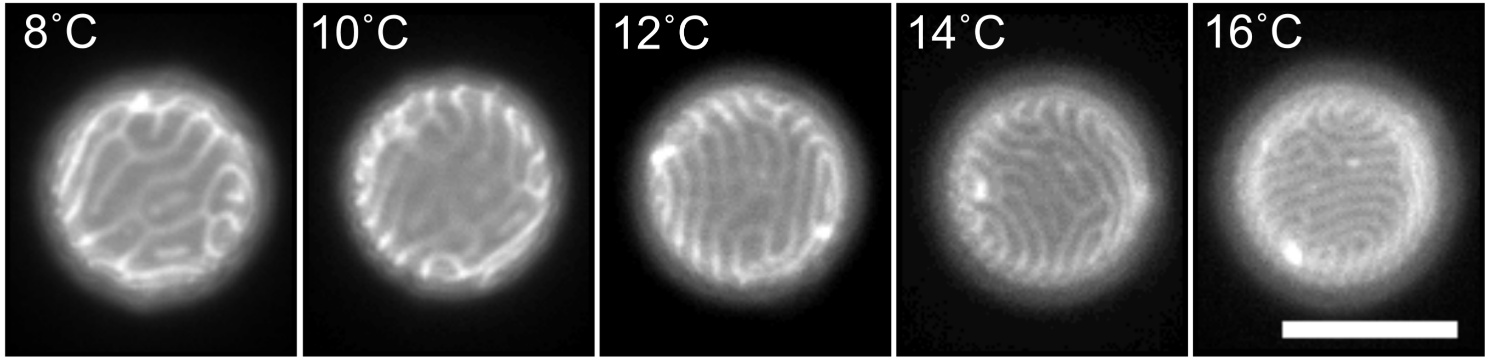


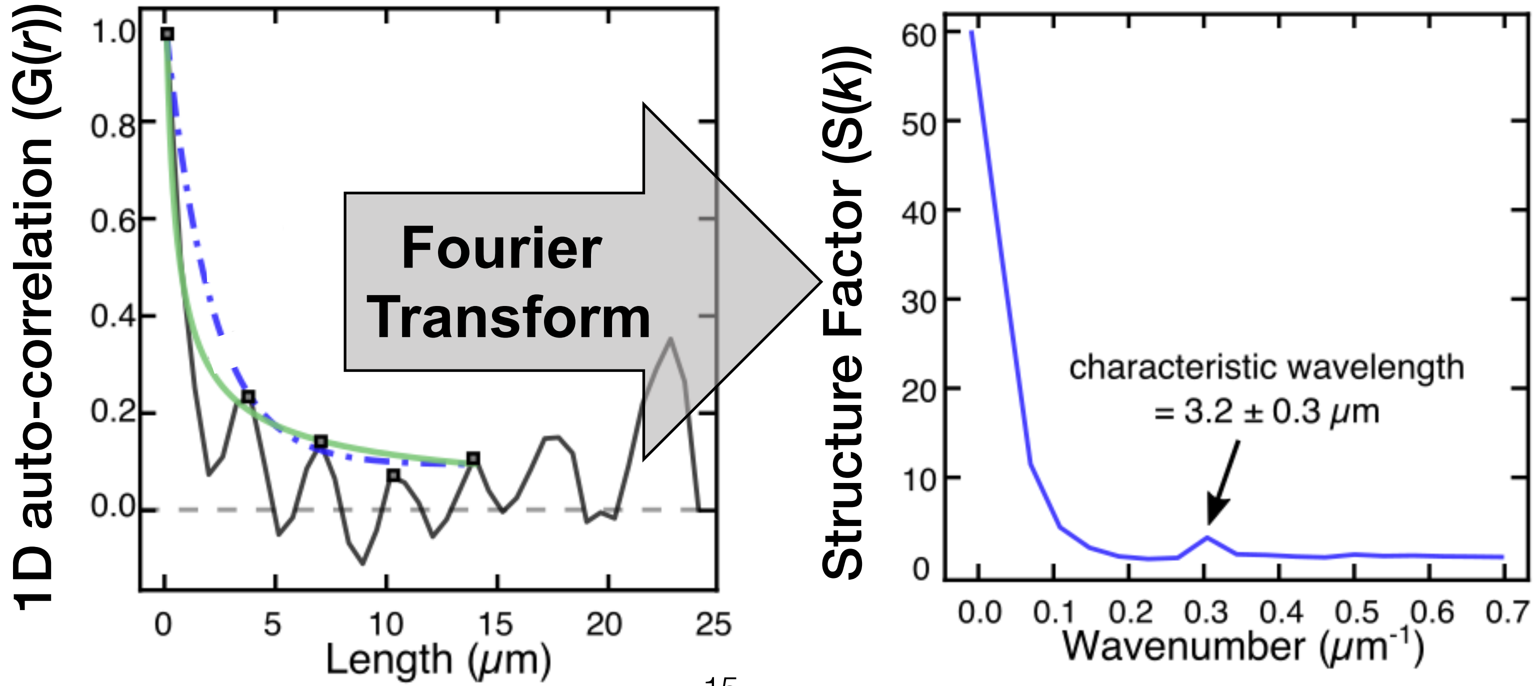


Cornell, C.E., et al **2018,** *Biophys. J.*

Length scales increase with increasing membrane tension

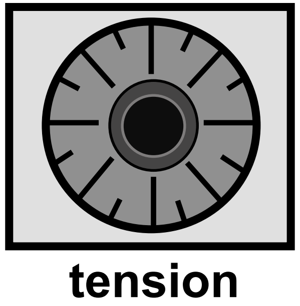


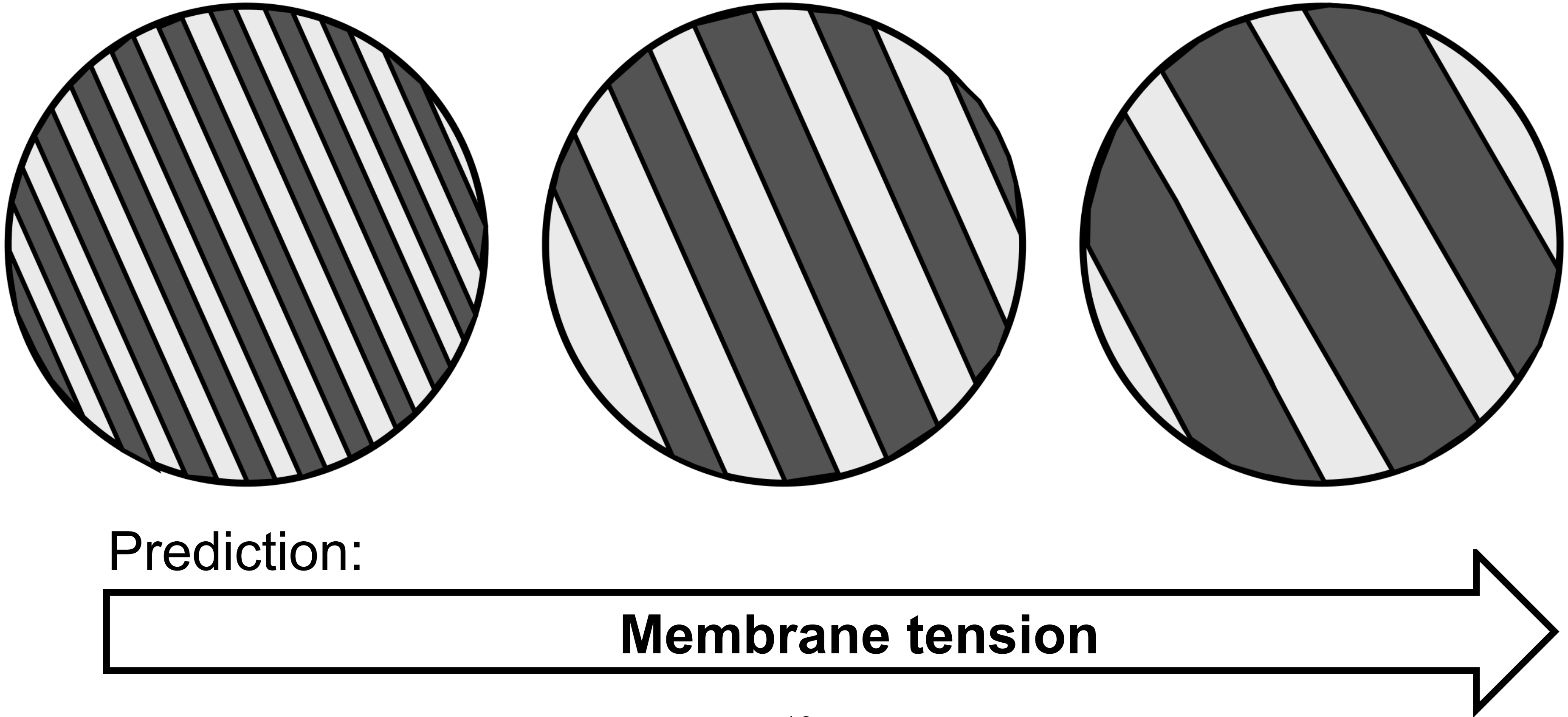




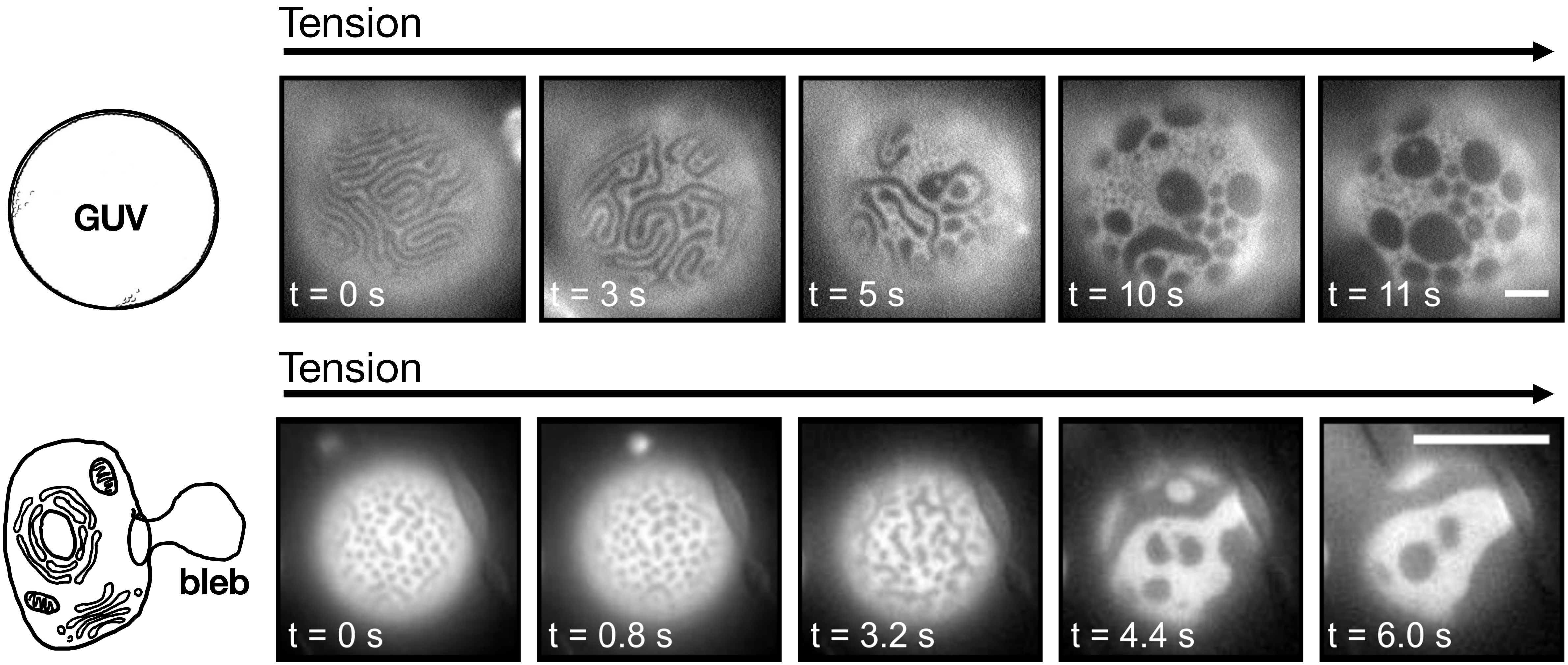
Cornell, C.E., et al **2018,** *Biophys. J.*

How do domain lengths scale with membrane tension?





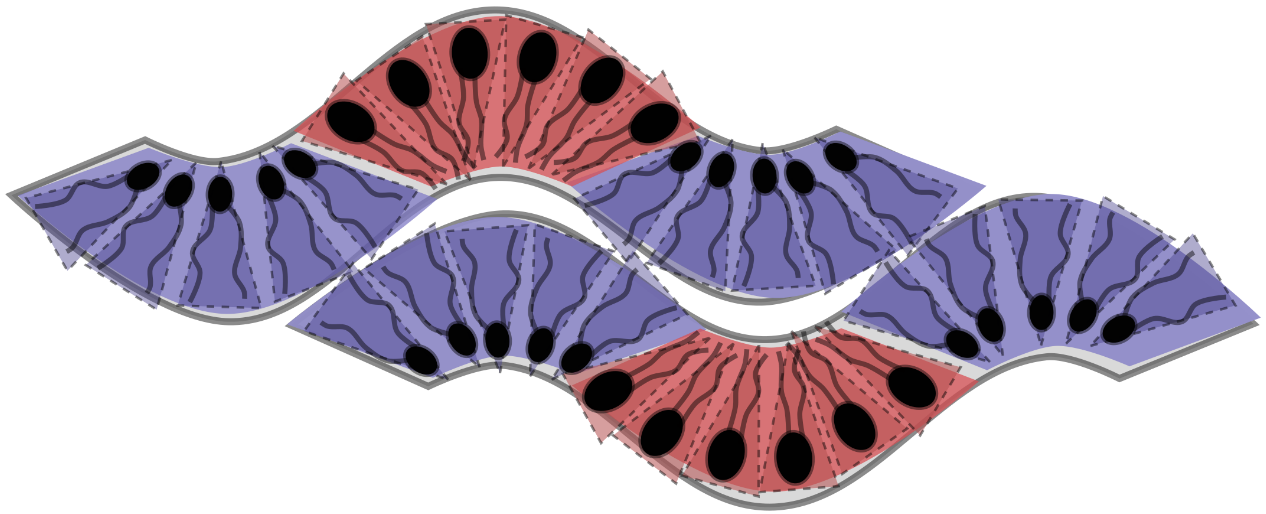
Length scales increase with increasing membrane tension



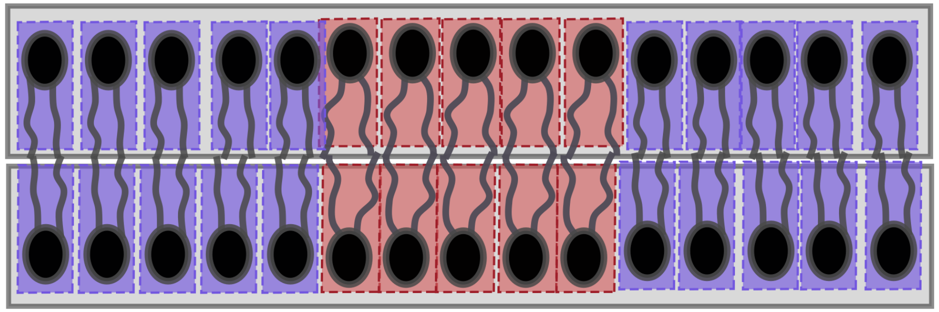
Cornell, C.E., et al **2018,** *Biophys. J.*

What role does the ratio of lipids play?

We introduce a mean bilayer spontaneous curvature
by adding extra lipids into the outer leaflet of the bilayer

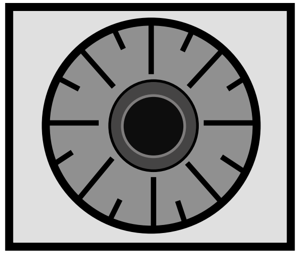


Domains in antiregistration

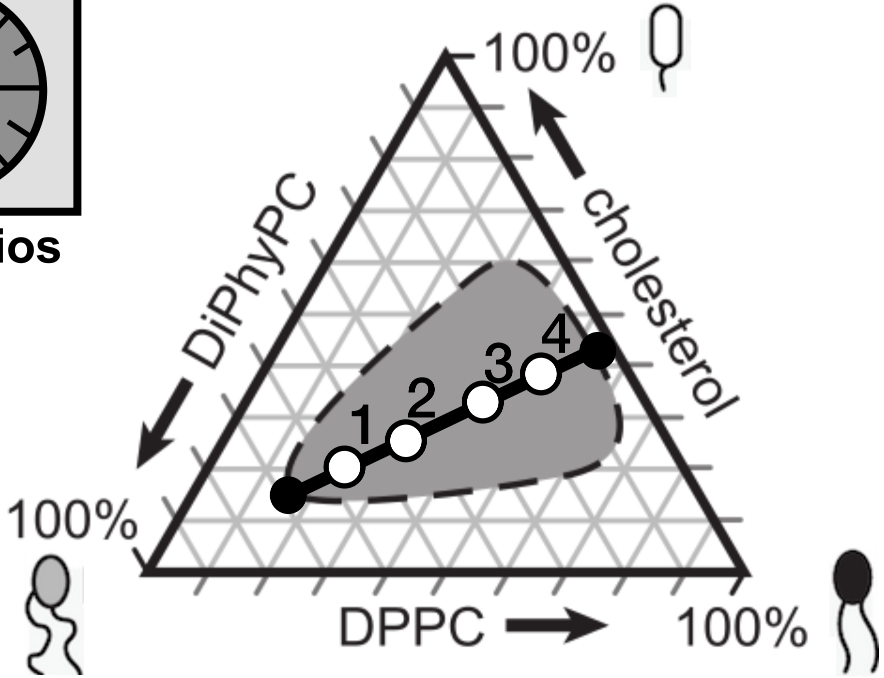


Domains in registration

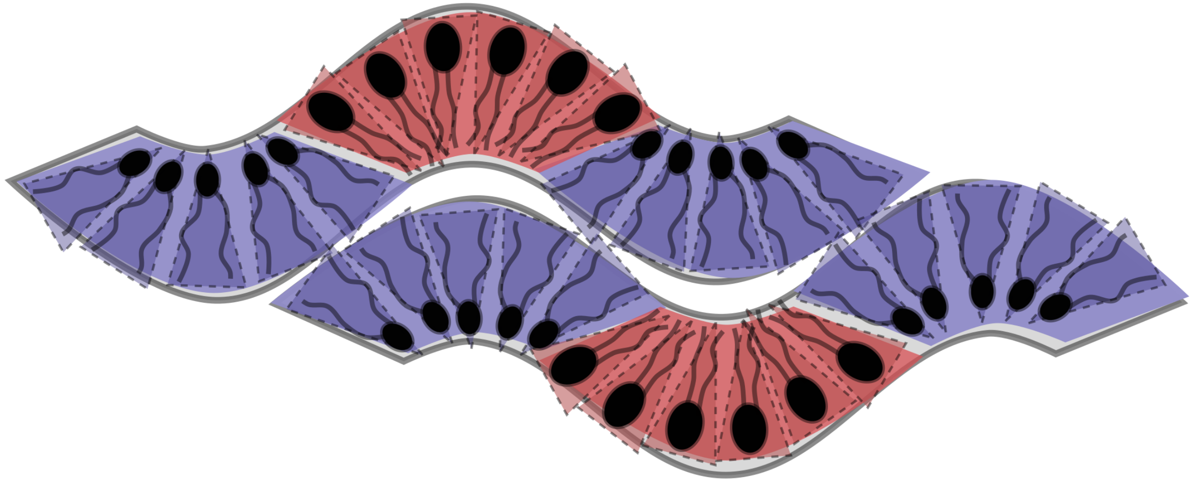
How do we determine bilayer registration?

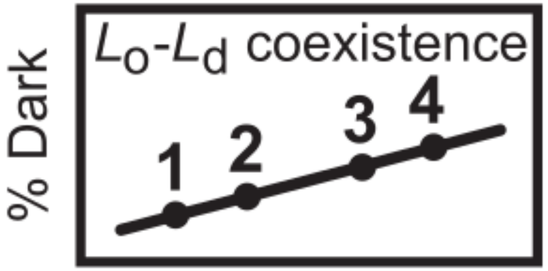


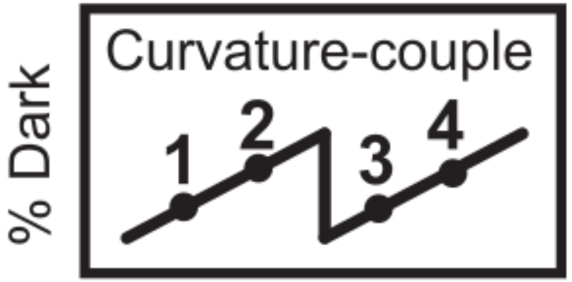
lipid ratios



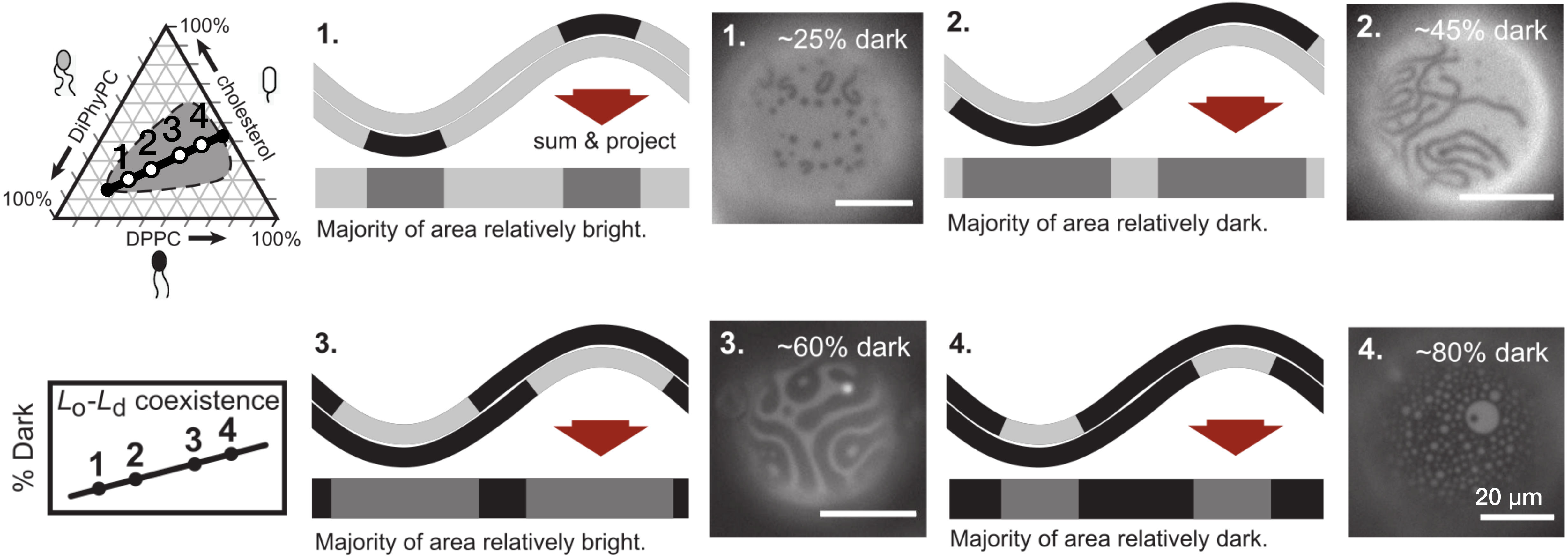
Prediction for anti-registered bilayer:







The area fraction of the dark area increases linearly



Cornell, C.E., et al **2018,** *Biophys. J.*

General conclusions:

Parameter	My results	Schick et al. [1]	Harden et al. [2]	Andelman et al. [3]
Temperature increase	Length scale decrease	✔	✔	✔
Tension increase	Length scale increase	✖	✔	✖
Lipid ratio (increase line tension)	Transition from stripes to hexagonal dots		✖	

Mathematical challenge: What is the mechanism in our system?

[1] Shlomovitz, R. et al **2014,** *Biophys. J.*

[2] Harden, J.L., et al **2005,** *Phys. Rev. E.*

[3] Taniguchi, et al **1994,** *J. Phys. II. Fr.*

Acknowledgements

Keller Lab Members:

Roy Black
Zach Cohen
Sarah Keller
Brenda Kessenich
Chantelle Leveille
Glennis Rayermann

Funding:

Lab: NSF
Personal: NIH MBTG

Collaborators:

Kandice Levental (UT Houston)
Ilya Levental (UT Houston)
Shushan He (UW)
Allison Skinkle (Rice Univ.)

Special Thanks:

Michael Schick
Lutz Maibaum
Sharona Gordon
Sarah Veatch

Calculation of auto-correlation G(r)

Contrast between grey value vector and average image grey value:

$$\delta\rho(\boldsymbol{r}) = \rho(\boldsymbol{r}) - \bar{\rho}$$

Image average grey value:

$$\bar{\rho} = \frac{\int \mathrm{d}\boldsymbol{r}\rho(\boldsymbol{r})}{\int \mathrm{d}\boldsymbol{r}}.$$

2D radial distribution function:

$$g(\boldsymbol{r}) = \frac{\langle \delta\rho(\boldsymbol{r'} + \boldsymbol{r})\delta\rho(\boldsymbol{r'})\rangle}{\langle \delta\rho(\boldsymbol{r})\rangle^2}$$

Grey value vector in matrix representation:

$$g(\boldsymbol{r}) = g(r_{i,j}) = \frac{\left(\sum_{k,l=1}^{m,n} \delta\rho_{k,l} \cdot \delta\rho_{k+i,l+j}\right)}{\left(\sum_{k,l=1}^{m,n} \delta\rho_{k,l}\right)^2}$$

A helpful aside: Gibbs phase triangles and how to read them