Dynamic critical exponents in a two-dimensional lipid membrane with conserved order parameter

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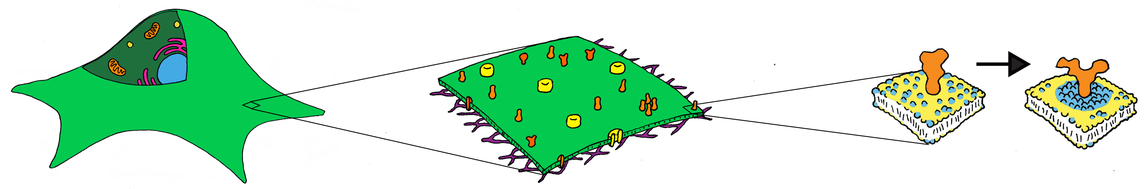
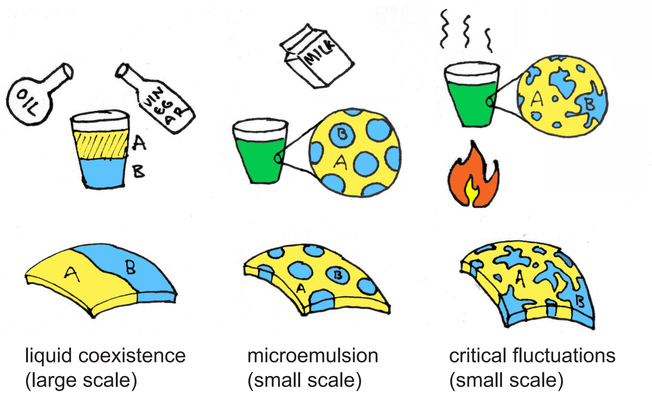
Biological motivation: how do cells regulate membrane proteins?



Almost all plasma membranes exist in a liquid phase at cell growth temperatures, and large-scale liquid phase coexistence is never observed in living cells.

Cell membranes contain multiple types of lipids, cholesterol, and membrane proteins.

The conformation and functional activity of some membrane proteins depends on the identity of the surrounding lipids [1]. Cells may use nanoscale compositional heterogeneity to control membrane protein localization and activity.



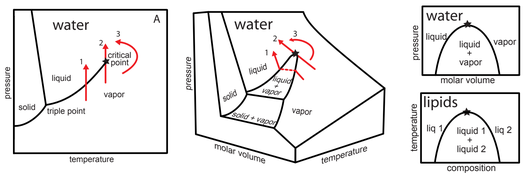
liquid coexistence (large scale)

microemulsion (small scale)

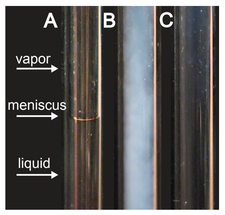
critical fluctuations (small scale)

A membrane containing small-scale fluctuations is consistent with a current popular picture in which sub-micron, dynamic heterogeneity in lipid and protein composition, rather than micron-scale phase separated domains, arises within the plasma membranes of resting cells [2].

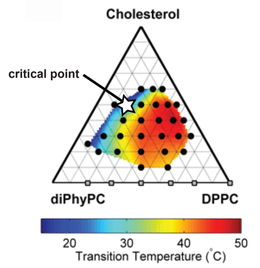
Physics methodology: phase coexistence and critical universality



At the critical point, large fluctuations occur. Liquid/vapor systems are characterized by an order parameter, *m*, that is a density difference between the two phases. In membranes the order parameter is the deviation from the average lipid composition as reported by each pixel's grey scale [3].



A is below the critical temperature, C is above, and B is at the critical temperature. In B, density fluctuations in CO_2 result in "critical opalescence," [3].



The phase diagram for a ternary mixture of DiPhyPC/DPPC/cholesterol contains a miscibility critical point (figure from [4]).

The two-dimensional Ising model consists of spins with short-range interactions only. Systems near a critical point display universality: the properties of the system are determined only by the dimension and number of coexisting phases. Universality is exhibited through universal critical exponents, which govern the temperature dependence of system properties [5].

Ising Model Critical Exponents

$$\xi \propto \left(\frac{T - Tc}{Tc}\right)^{-\nu}$$

Eq. 1: Correlation length increases near the critical temperature. For the 2-D Ising model, $\nu = 1$. [5]

$$\Delta m \propto \left(\frac{T - Tc}{Tc}\right)^{-\beta}$$

Eq. 2: The width of the distribution of order parameter values increases as Tc is approached. For the 2-D Ising model, $\beta = 1/8$. [5]

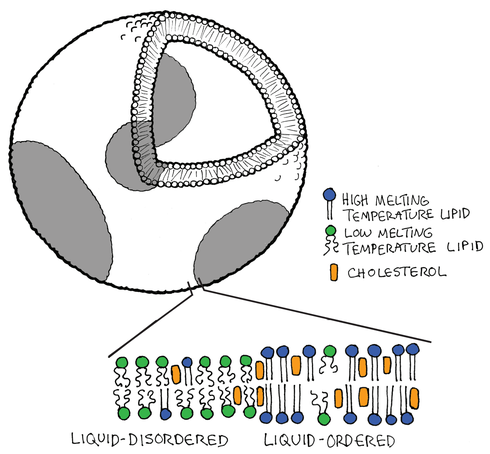
$$\Gamma = k^z \overline{\Omega}(k\xi)$$

Eq. 3: Fluctuation lifetime depends on correlation length and on wavevector [6].

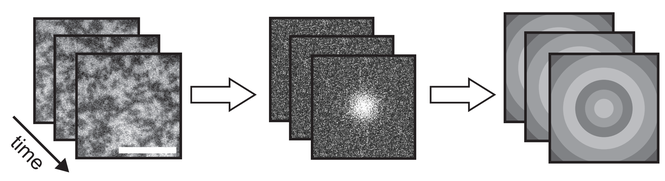
Experiments

I produce giant unilamellar vesicles (GUVs) with coexisting liquid phases using a ternary mixture of a low melting-temperature lipid, a high melting-temperature lipid, and cholesterol. Of the two phases, the liquid-ordered (Lo) phase is more dense, and is rich in DPPC and cholesterol. The liquid-disordered (Ld) phase is rich in DiPhyPC [4]. I identify a lipid composition at which a critical point occurs, here at 20% DPPC, 30% DiPhyPC, and 50% cholesterol. Next, I produce vesicles by electroformation.

I label the Ld phase with 0.6 mol% Texas Red DPPE. Then I record movies by epifluorescence microscopy as I vary the temperature of the vesicles (with precision +/- 0.05 °C).



Analysis



I Fourier transform vesicle movies, then average to create the static structure factor, or time-correlate to create the dynamic structure factor. I radially average to examine structure as a function of wavenumber.

Quick 2-minute summary

Composition fluctuations in membranes are well described in space, composition, and time duration by the 2-D Ising model. Nanoscale, dynamic composition fluctuations exist in membranes within ~ 5 °C of the miscibility transition temperature. Critical composition fluctuations provide a physical mechanism for small-scale liquid phase coexistence in membranes. Vesicles from living cell membranes (plasma membrane vesicles) also exhibit concentration fluctuations consistent with the 2-D Ising model, suggesting that the lipid composition in plasma membranes is poised near a critical point [8].

Citations and further information

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Acknowledgements

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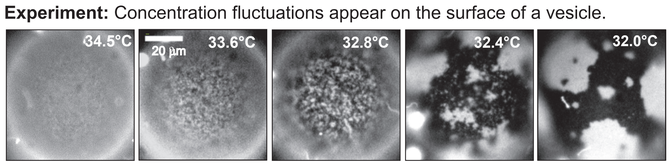
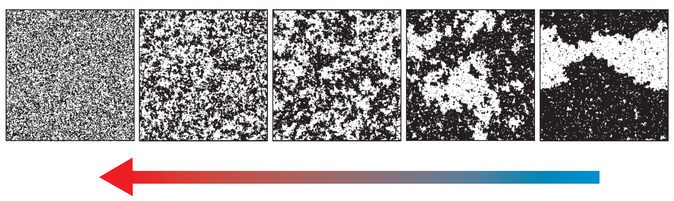
Results: size and duration of membrane fluctuations match 2D Ising model

Images: Vesicles vs. 2-D Ising

Experiment: Concentration fluctuations appear on the surface of a vesicle.



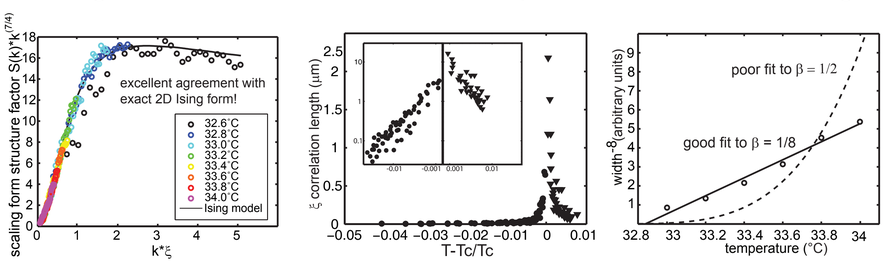
Simulation: Neighboring spins align in a 2-D Ising model.



At high temperatures, vesicle membranes appear uniform by fluorescence microscopy. As the temperature is lowered, composition fluctuations appear. The fluctuations are so large and persist for so long that they are clearly resolvable by microscopy. At lower temperatures, membranes separate into two distinct micron-scale liquid phases that contain different compositions of lipid and fluorescent dye.

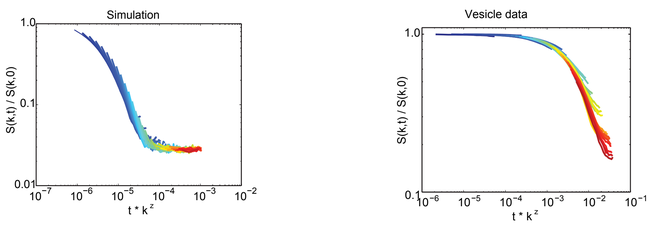
Property	Critical exponent	Predicted value	Measured value [7]
correlation length, ξ	ν	1	1.2 ± 0.2
order parameter, *m*	β	0.125	0.124 ± 0.03

Scaling indicates that static critical exponents match 2-D Ising model



Static critical exponents govern the temperature dependence of the size (correlation length, ξ) of composition fluctuations, and the difference in composition between the two phases (order parameter, *m*). Extrapolating to small length scales by plugging $\nu = 1$ within Eq. 1 yields the result that fluctuations of ~ 50 nm should exist at temperatures on the order of 5˚C above the membrane's critical temperature.

Preliminary results show dynamic critical exponent matches "Model B"



The dynamic structure function for multiple wavenumbers collapse onto the same curve in this scaling plot, indicating the value of the dynamic exponent, z. The dynamic exponent depends on the details of transport in the system. Lipid membranes very close to the critical point show dynamics that appear to resemble those of the the Ising "Model B" variation with conserved order parameter.

Fluctuation duration

I find that the persistence time of 50-300 nm fluctuations is between 0.6 and 18 ms by extrapolating from the measured dynamics for all data for which $2\ \mu m < \xi < 3\ \mu m$. 50 nm domains persist for 0.6 ms, the right order of magnitude to affect protein function [9].