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Energy Functional and Patterns of Cellular Membranes

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Pattern Formation of Cellular Membrane's Composition and Decomposition Curvature Coupling

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Abstract

The energy of cell membranes depends on their "shape". We developed a theoretical framework for describing curvature-composition coupling in multi-component fluid lipid bilayers. We will introduce an energy functional for undulating two−component lipid membrane and theoretically analyze instability of the flat membrane to patterning driven by composition curvature coupling. We will systematically explore the parameter space where the flat membrane becomes unstable and will talk about the effect of lipid segregation in the leaflets. Finally, we will discuss future work going into studying the behavior of and fluctuations in asymmetric lipid bilayers (e.g., that of a eukaryotic cell).

Introduction

A variety of experimental studies have highlighted the role of biological membranes in subcellular protein organization and protein function. They have led to the recognition that membrane curvature can guide the spatial organization of lipids and membrane-associated proteins and that spatial organization can in turn influence membrane shape. While there are a number of experimental and computational studies, theoretical studies of how curvature-composition coupling can lead to instabilities of the flat membrane and to spontaneous micro-organization, are still incomplete. Our model and results can provide a deeper understanding of lipid and protein organization in cell membranes.

Energy Functional Models

Terminology
α = constant related to spontaneous curvature $[L^{-1}]$
h= height [L]
C_o=spontaneous curvature $[L^{-1}]$
q = wave-vector [dimensionless]
h_q = strength of undulation (some constant) [L]
K= bending modulus [E]
γ = line tension/de-mixing strength (some constant) [E]
σ = surface tension $[L^2]$
λ = pinning strength $[E \times L^{-4}]$
r = parameter related to the tendency of two components to mix/de-mix
b =parameter related to the spontaneous curvature
The pivotal notion for this is for the bending energy as function of curvature.

$$E = a\ \underbrace{Tr\left(C^2\right)}_{C_1^2+C_2^2} + b\ \underbrace{Tr\left(C\right)}_{C_1+C_2} + c\ det\left(C\right).$$

For an almost-flat membrane its energy can be written as

$$E \approx \underbrace{\int dA k_b \left(\nabla^2 h - C_o\right)^2}_{\text{bending}} + \underbrace{\sigma \int dA \left(\frac{1}{2}\left(\nabla h\right)^2\right)}_{\text{surface tension}} + \underbrace{\lambda \int dA h^2}_{\text{attachment to soft surfaces/cytoskeleton}} . \tag{1}$$

Now consider an undulating membrane with height profile given by

$$h\left(x,y\right) = h_q \cos\left(q_1 x + q_2 y\right), \tag{2}$$

with the notion $\vec{q} = (q_1, q_2)$ for 2D wavevector. For simplicity we consider $q_2 = 0$. The energy of the undulation is

$$E = \frac{A}{2}\left(Kq^4 + \frac{\sigma}{2}q^2 + \lambda\right)h_q^2, \tag{3}$$

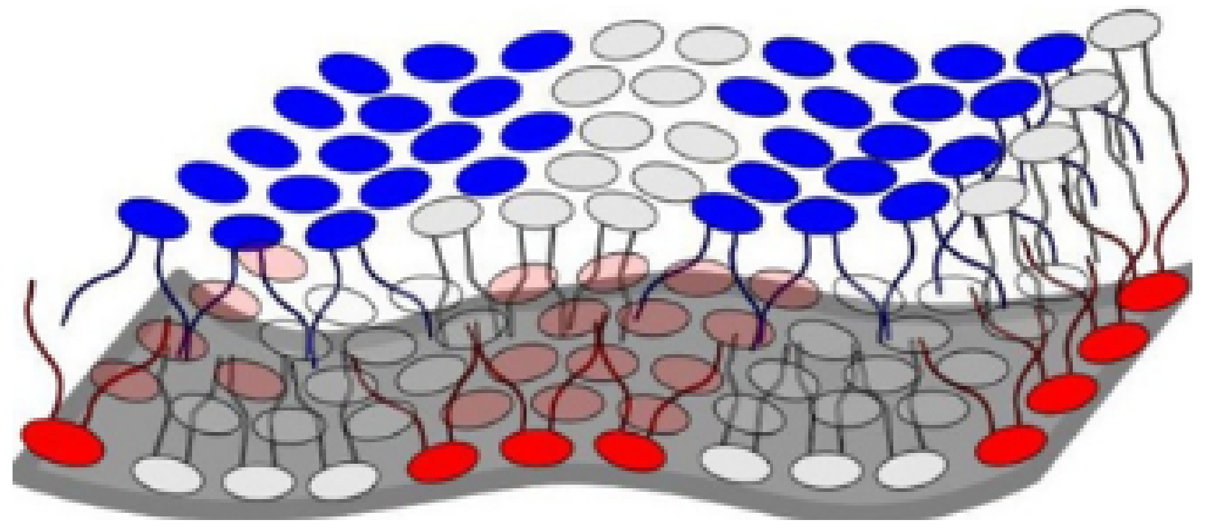
which is always positive.

Two-Component Membranes

Now consider bilayers made of two kinds of lipids, one of which may be more cylindrical and the other more conical in shape.
Let ψ_1 be the fraction of conical lipids in upper leaflets and ψ_2 be the fraction of conical lipids in lower leaflets, where the difference between is written as $\phi = \psi_1 - \psi_2$. We can write the spontaneous curvature as $C_o = \alpha\phi$, where α is some constant. We will see that rewriting the bending energy using those notions are useful in understanding if energy of a lipid bilayer is allowed to be negative at any point — i.e., if there is a point of unstable fluctuation. More over we now have an additional energy contribution corresponding to the mixing/de-mixing of the two lipid components which could take a form [by taylor expanding about the minimum]

$$E_\phi = \gamma(\nabla\phi)^2 + r\phi^2 \tag{4}$$

We now found that the energy corresponding to undulations can become negative, implying that the flat-membrane can become unstable to undulations. Now we investigate under what conditions this is possible.



Results

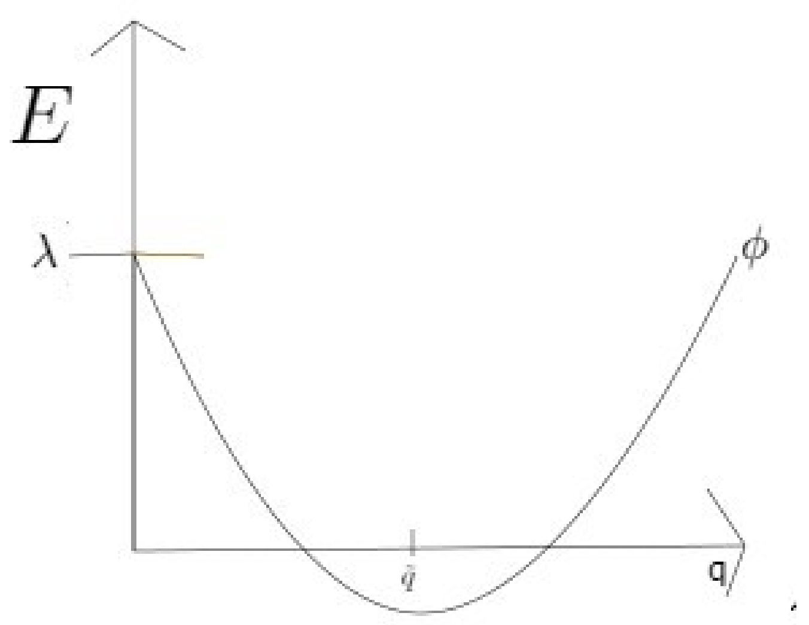
We found that the energy for a joint undulation in h and ϕ is

$$E \approx \frac{A}{2}(kq^4 + \frac{\sigma}{2} * q^2 + \lambda)h_q^2 + \text{A h}_q q^2 \alpha\tilde{\phi}_q + \frac{A * \gamma}{2}(q^2\tilde{\phi}_q^2) + \frac{1}{2}r * \phi_q^2 A. \tag{5}$$

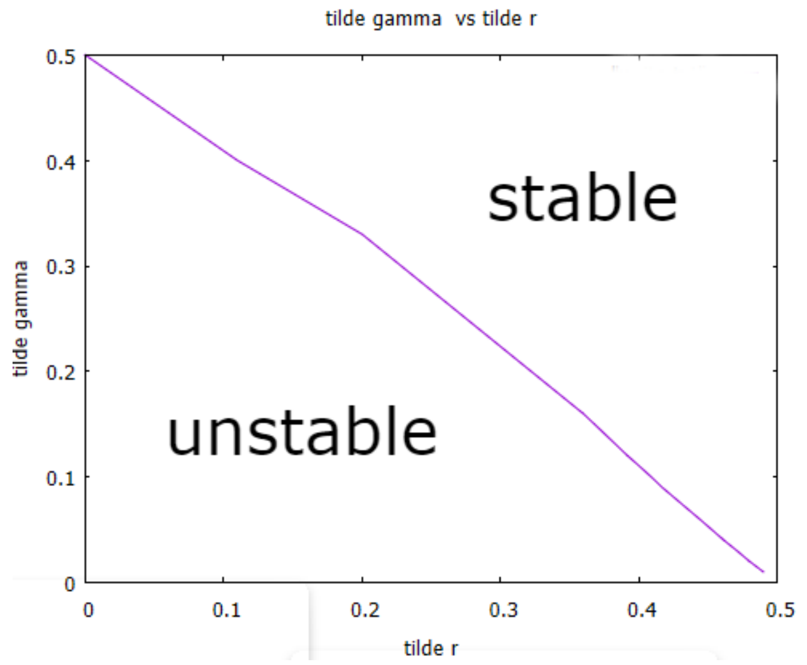
Minimizing with respect to ϕ_q and substituting, the energy takes the form [with $\sigma = 0$],

$$E(q) \approx \frac{A}{2}h_q^2((kq^4 + \lambda) - \frac{q^4\alpha^2}{\gamma q^2 + r}). \tag{6}$$

This energy functional can become negative for intermediate values of q. Which indicates instability to stripe type patterns.



As for decoupling, we found that r has a very clear significance in that as r equals zero; the two components want to segregate. Negative r means a mixed state is unstable which has nothing to do with the curvature; it would be true even for a flat membrane. For positive r, the flat membrane would be stable but due to the coupling of curvature to lipid composition, the components partially de-mix to generate patterns such as stripes. We find that for this to happen, values of r and line tension must be reasonably small.



Conclusion

We found a range of parameter space where the two components de-mix and stabilize height undulations, even when the two components would have been completely mixed for a flat-membrane. Thus we find curvature composition coupling can lead to pattern formation. For future work we want to study more carefully lipid de-mixing in each individual leaflet and also look at how it affects dynamic membrane fluctuations.

References

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