Curvature-Driven Phase-Separation on Spherical Vesicles: Insights from a Single-Bead Model

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Motivations

We investigate the equilibrium behaviors and kinetics of heterogeneous lipid bilayer membranes important in many biological processes (raft formation, bud formation, vesicle fission, endocytosis).

Multiple-species vesicles can exhibit rich behaviors with phase separation into domains [3] and shape transformations [2,4].

Coarse-grained modeling provides mesoscale approaches for capturing essential physics with minimal computation, allowing access to larger spatial and temporal scales than fully atomistic models. We develop methods based on the single-bead lipid-cluster model [1] along with numerical simulation methods based on LAMMPS and [6,7,8].

Different phases and kinetic regimes are present in the single-bead model. We aim to gain insights into how phase separation interplays with surface geometry and mechanics. We also want to better understand the accuracy and limitations of continuum mechanics approaches.

Pairwise Potential and Parameterization

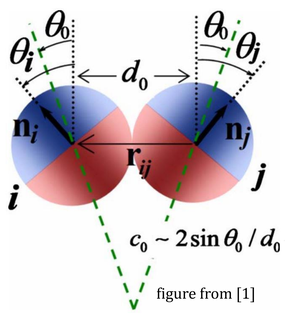


figure from [1]

Interaction Potentials

$$U(\mathbf{r}_{ij},\mathbf{n}_i,\mathbf{n}_j) = \begin{cases} u_R(r) + [1-\phi(\hat{\mathbf{r}}_{ij},\mathbf{n}_i,\mathbf{n}_j)]\epsilon, & r < r_{\min} \\ u_A(r)\phi(\hat{\mathbf{r}}_{ij},\mathbf{n}_i,\mathbf{n}_j), & r_{\min} < r < r_c \end{cases}$$

$$u(r) = \begin{cases} u_R(r) = \epsilon\left[\left(\frac{r_{\min}}{r}\right)^4 - 2\left(\frac{r_{\min}}{r}\right)^2\right], & r < r_{\min} \\ u_A(r) = -\epsilon\cos^{2\zeta}\left[\frac{\pi}{2}\frac{(r-r_{\min})}{(r_c-r_{\min})}\right], & r_{\min} < r < r_c \end{cases}$$

$$a = (\mathbf{n}_i \times \hat{\mathbf{r}}_{ij}) \cdot (\mathbf{n}_j \times \hat{\mathbf{r}}_{ij}) + \sin\theta_0(\mathbf{n}_j - \mathbf{n}_i) \cdot \hat{\mathbf{r}}_{ij} - \sin^2\theta_0$$

$$\phi = 1 + \mu[a(\hat{\mathbf{r}}_{ij},\mathbf{n}_i,\mathbf{n}_j) - 1]$$

Overview
Particle separation and relative orientation dictate interaction.

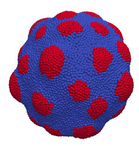
Potential Parameters
r_c: interaction cutoff distance
ζ: steepness of repulsive branch
θ_0: preferred relative orientation
μ: bending penalty

Simulation Parameters
Δt: timestep for simulation
k_BT: temperature of system
$\zeta_{r,n}$: thermostat damping

More details in [1,2].

Bending Elasticity of Heterogeneous Vesicles

Discrete vesicle to Continuous Surface

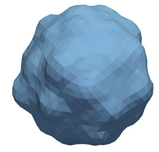


$(\mathbf{r},\theta,\phi)$

$$\boldsymbol{\sigma}(\theta,\phi) = \sum_i \alpha_i Y^i(\theta,\phi)\mathbf{e}_r(\theta,\phi)$$

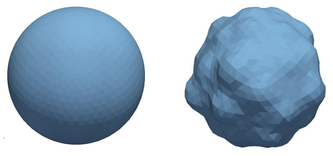
$$\alpha_i = \int_{\theta=0}^{\pi}\int_{\phi=0}^{2\pi}(Y^i)^2 d\phi d\theta$$

Evaluated with Lebedev quadrature [8]



$\boldsymbol{\sigma}[\boldsymbol{\alpha}]$

Mean Curvature Expansion about Sphere (Energy minimizer)



$\boldsymbol{\sigma}[\boldsymbol{\alpha}_0]$ $\boldsymbol{\sigma}[\boldsymbol{\alpha}_0 + \mathbf{b}]$

$$H[\boldsymbol{\sigma}[\boldsymbol{\alpha}_0 + \boldsymbol{b}]] \approx H[\boldsymbol{\sigma}_0] + \nabla_{\boldsymbol{\alpha}} H|_{\boldsymbol{\alpha}_0} \cdot \mathbf{b}$$

Bending Rigidity from Energy (Helfrich)

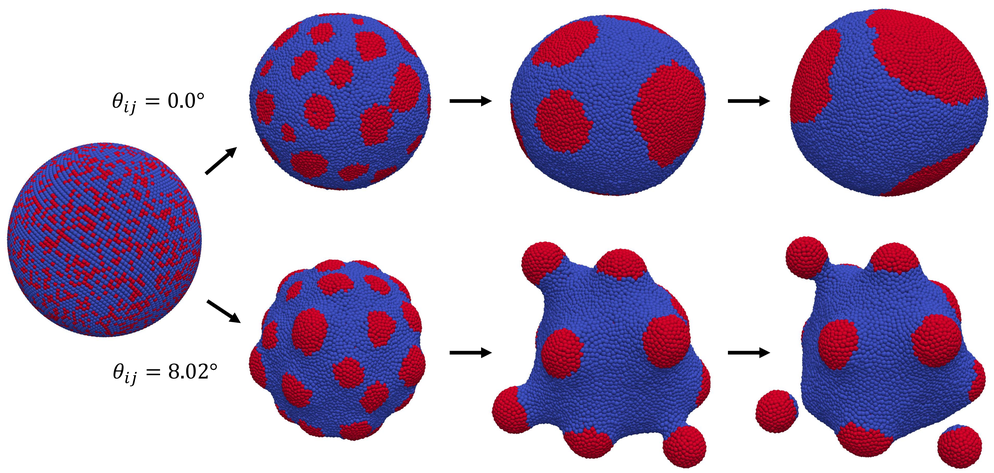
$$E[\boldsymbol{\sigma}] = \int \frac{k_c}{2}[2H(\theta,\phi;\boldsymbol{\sigma}) + c_0]^2 dA$$

$$\approx \mathbf{b}^T\left(\int 2k_c \nabla_{\boldsymbol{\alpha}} H|_{\boldsymbol{\alpha}_0} \nabla_{\boldsymbol{\alpha}} H|_{\boldsymbol{\alpha}_0}^T dA\right)\mathbf{b}$$

Boltzmann factor for linearized energy gives multivariate Gaussian.

$$e^{-\beta E[\boldsymbol{\sigma}]} \longrightarrow \mathrm{cov}(\mathbf{b}\mathbf{b}^T)$$

Phase Separation: Domain Organization vs Spontaneous Curvature



Experimental data from high resolution fluorescence imaging of phase separation and domain formation by T. Baumgart.

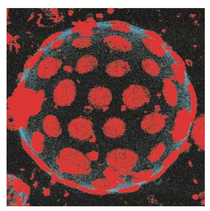


Figure from [4]

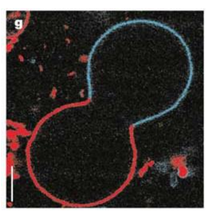


Figure from [4]

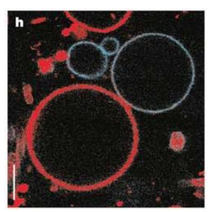
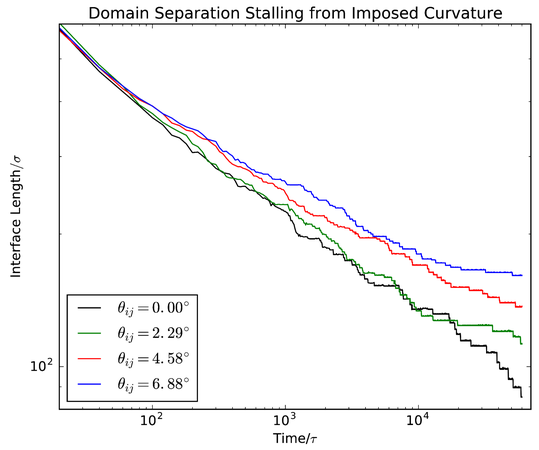


Figure from [4]



Domain interactions initially follow a power law, Interface Length $\sim t^{-\omega}$.

Domains become saturated, and cease combining. **Saturated domain size decreases with $\boldsymbol{\theta_{ij}}$.**

Mechanics of the membrane appear to play a role; **bending elasticity and energy barriers prevent merging of domains.**

Summary and References

Summary

We observe domain separation with imposed curvature; domain separation stalling occurs more rapidly with greater imposed curvature. We analyze thermal fluctuations of the binary spherical vesicles. In future work we plan to further explore the role of hydrodynamics using our integrator for orientations in LAMMPS and SELM-Fluctuating Hydrodynamics [6,7,8].

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