論文内容の要旨
Dissertation Abstract

論文題目:

Dissertation title: Effects of Anchored Polymers on Biomembranes

(生体膜に対するグラフト高分子の効果)

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Since the past decades, our knowledge on the heterogeneous structure of biomembranes has been developed from the primitive fluid mosaic model to the modern raft model. It is considered that membrane proteins are not randomly distributed in lipid membranes but concentrated in local microdomains, called lipid rafts, with diameter of 10~100nm. The raft contains high concentrations of glycosphingolipids, which contain bio-functional glycan chains, and cholesterol, and play important roles on many intra- and intercellular processes including signal transaction and membrane protein trafficking. However, the formation mechanism of such microdomains has not been understood so far. There are still lack of systematical studies on the polymeric effects on the finite lipid domains and line tension on membranes with various shapes. In this thesis, we focus on the effects of anchored polymers on properties of biomenbranes, in particular on lipid domains and the strip membranes with open edges.

In this thesis, we first revisited linear and scaling theories for ideal and excluded-volume polymers in Chapter 3. Then we developed one biomembrane model by anchored polymers based on the solvent-free meshless model to simulate the polymer-induced effects in Chapter 4. Since we focus on the entropic effects of polymer chains, the detailed structures of the bilayer can be neglected and treated as a curved surface. In the meshless model, a membrane particle represents a patch of bilayer membrane whose properties can be easily controlled, and the parameters related to mechanical properties of membranes can independently change and can be tuned in a wide range. In Chapter 5, the bending rigidity and spontaneous curvature are investigated for anchored ideal and excluded-volume polymer chains. Our results agree with the previous theoretical predictions well. It is found that the anchored polymers reduce the line tension of membrane edges, as well as

the interfacial line tension between membrane domains, leading to microdomain formation as shown in Chapter 6. Instead of the mixing of two phases as seen in typical binary fluids, densely anchored polymers stabilize small domains. A mean field theory is also proposed in Chapter 6 for the edge line tension reduced by anchoring ideal chains, which well explains our simulation results.

(1) <u>Cylindrical shape of single-component membranes with anchored polymer chains</u>

In Chapter 5, a cylindrical shape of single-component membranes with anchored polymers is applied as a convenient tool to measure the effective spontaneous curvature C_0 and bending rigidity κ. We first obtained an axial force equation by minimizing the Helfrich curvature free energy for the cylindrical shape of biomembranes. Through estimating the coefficients by the linear fitting, we obtained the effective bending rigidity κ and spontaneous curvature C_0 for the membrane with anchored polymers, as shown in Figure 1 (a) and (b), respectively. Our simulation

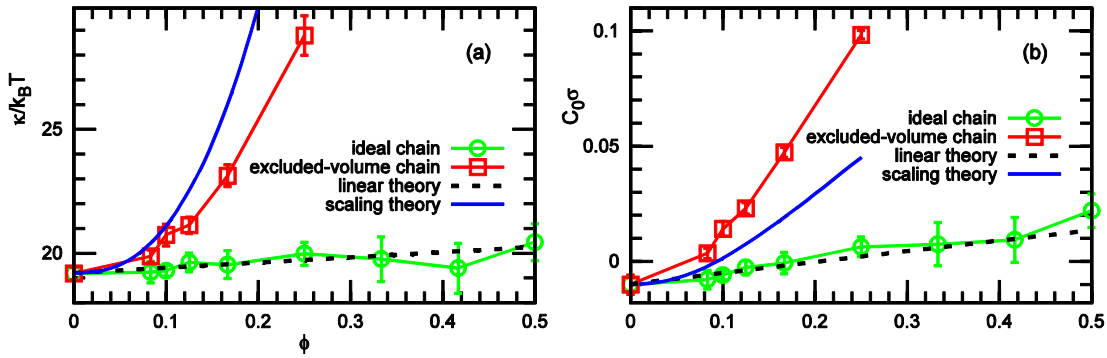

Figure 1. (a) Dependence of the bending rigidity κ on the anchored polymer density ϕ. (b) Dependence of the spontaneous curvature C_0 on the anchored polymer density ϕ.

results agree with the previous linear theory very well when the anchored polymers are ideal chains at any anchored density or are excluded-volume chains at the lower anchored density than the overlapping density. The difference at high density parts for excluded-volume chains between our simulation and the scaling theory arises from the short polymer chains used in this work, so the short polymers cannot effectively reflected the blob picture of polymer brush well. To avoid this difference, we have to simulate longer anchored polymer chains.

(2) <u>Strip shape of single-component membranes with anchored polymer chains</u>

In Chapter 6, we systematically studied a strip shape of single-component membranes with anchored polymers. Such shape of membranes with open edges can be easily employed to estimate the polymer-induced line tension on the edge. We applied the pressure tensors to calculate the effective line tensions with different anchored polymer densities for ideal chains and excluded-volume chains, respectively. In addition, we proposed a mean field theory to analytically estimate the effective line tension on the edge and polymer distribution on the strip membranes.

Figure 2. (a) compares our theory and simulation for ideal chains, and they are very well consistent with each other (see the overlapping between black dashed line and red solid line). Our

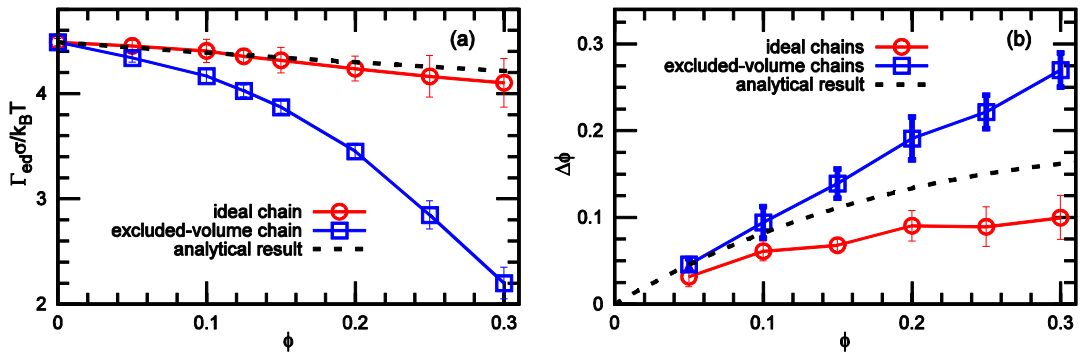

Figure 2. (a) Dependence of the edge line tension Γ_{ed} on the anchored polymer density ϕ. (b) Dependence of the excess polymer density $\Delta\phi$ on the anchored polymer density ϕ. Black dashed lines represent theoretical results, red solid lines represent simulation data for ideal chains, and blue solid lines represent simulation data for excluded-volume chains.

mean field theory assumes that the strip shape can be approximately divided into two uniform parts: the edge part with a high polymer density and the center part with a low polymer density. The density difference between these two parts is called the excess polymer density $\Delta\phi$. But polymer distribution cannot be simply divided into two parts, but connected by the region with the polymer density gradually changing, in the actual simulation. Thus, the actual excess polymer density for ideal chains should be lower than the mean field theory prediction. This result is well shown in Figure 2 (b). Our mean field model is proposed for ideal chains. The excluded-volume chains have a strong steric interaction between polymer segments, so the excess polymer density should be higher than our theory prediction for ideal chains due to the repulsion. This effect is also captured in Figure 2 (b) very well.

(3) <u>Multi-component membranes with anchored excluded-volume polymer chains</u>

Domains on multi-component membranes with anchored excluded-volume polymer chains are the most exciting topic in this thesis. In Chapter 7, we investigated the effective line tension of the boundaries of the strip domain and the circular domain, respectively. We found that the polymer-induced line tension of the strip domain decreases more quickly than the circular domain with the same area with the anchored polymer density increasing. It shows that the bulky polymers in the domain center have more contribution than the boundary polymers because of the steric repulsion between excluded-volume chains.

We further found that when the interfacial line tension decreases less than about 1 k_BT), the circular domain will separate into some small domains. Compared with two-component membrane without anchored polymers, we found that anchored polymers can stabilize the small domain (called microdomains) and do not continue to divide when the polymer density is high enough, but the domain in the binary fluid membrane without anchored polymers approaches the complete mixing state at last. This interesting phenomena is well exhibited in Figure 3, where (a) the arrow routes show two different evolution process for the pure domain with the chemical affinity decreasing and the polymer-decorated domain with the anchored polymer density increasing, respectively. An elongated and multi-arm intermediate state for the domain with anchored

polymers occurs when the polymer density is 0.45. (b) and (c) show the changes of the mean size

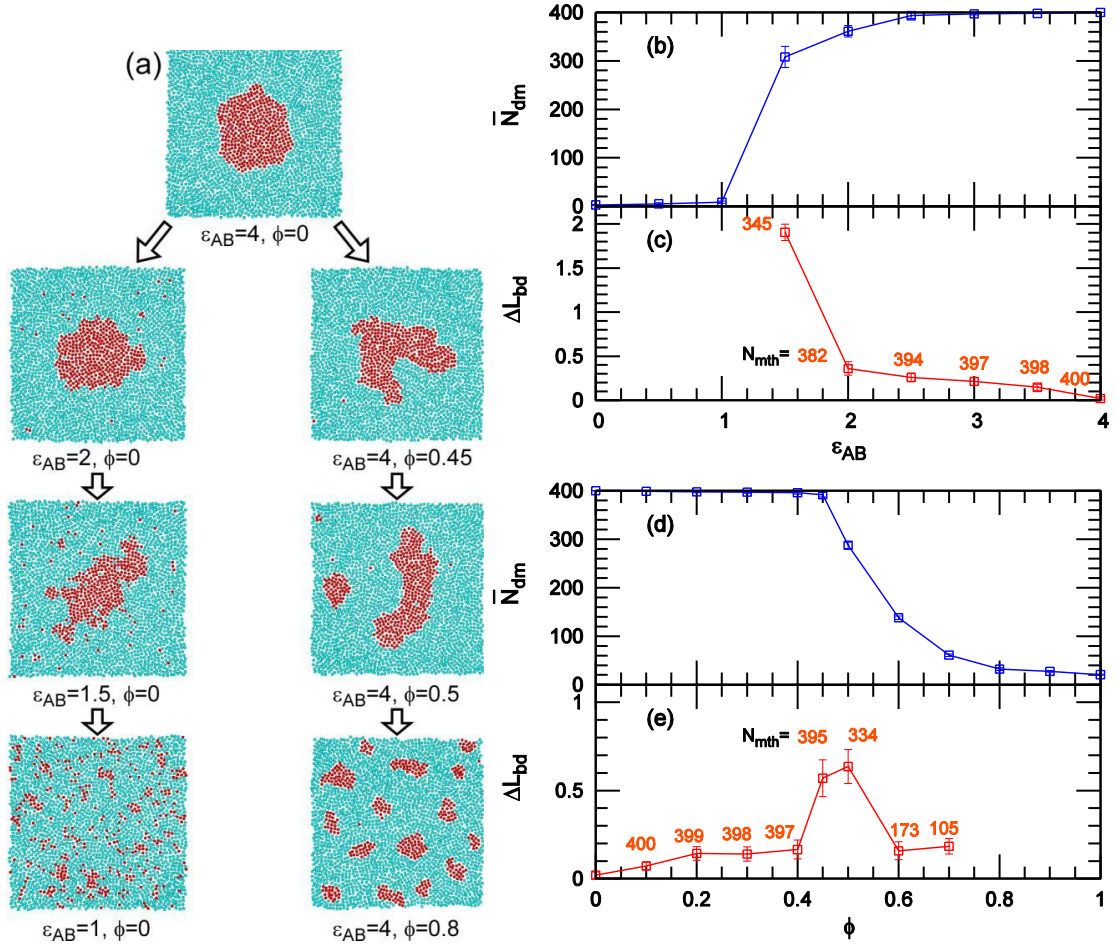

Figure 3. (a) Comparison between two types of domain separations: the left sequence shows the process for the pure binary fluid, while the right sequence shows the one for the binary fluid with anchored polymers. (b) and (c) Dependence of the mean size $\bar{N}_{dm}$ and the excess length ΔL_{bd} of pure binary domain on the chemical affinity ε_{AB}. (d) and (e) Dependence of the mean size $\bar{N}_{dm}$ and the excess length ΔL_{bd} of polymer-anchored binary domain on the anchored polymer density ϕ.

$\bar{N}_{dm}$ and the excess length ΔL_{bd} of the pure domain, while (d) and (e) show these changes for the polymer-decorated domain. Our simulation results on the circular domain with anchor polymers are consistent with the experimental observations from Yanagisawa and coworkers very well. They experimentally confirmed that an intermediate state with the network shape comes up when the polymer density reaches a transition value, and if the polymer density further increases, the big circular domain will separate into several microdomains.

These present investigations highlight entropic effects of anchored polymers on the biomembranes with open edges and the microdomain formation via the reduction in domain boundary tension on quasi-2D biomembranes. It is well known that high line tension can induce budding of membranes. Nonzero spontaneous curvature induced by proteins and anchored polymers can lead to various liposome shapes, such as tube formation and pearling. Shape transformation of vesicles induced by polymer-anchored domains is an interesting topic for further studies.