Line tension of multicomponent bilayer membranes

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The line tension or edge energy of bilayer membranes self-assembled from binary amphiphilic molecules is studied using self-consistent-field theory (SCFT). Specifically, solutions of the SCFT equations corresponding to an infinite membrane with a circular pore, or an open membrane, are obtained for a coarse-grained model in which the amphiphilic species and hydrophilic solvents are represented by AB and ED diblock copolymers and C homopolymers, respectively. The edge energy of the membrane is extracted from the free energy of the open membranes. Results for membranes composed of mixtures of symmetric and cone- or inverse cone-shaped amphiphilic molecules with neutral and/or repulsive interactions are obtained and analyzed. It is observed that an increase in the concentration of the cone-shaped species leads to a decrease of the line tension. In contrast, adding inverse cone-shaped copolymers results in an increase of the line tension. Furthermore, the density profile of the copolymers reveals that the line tension is regulated by the distribution of the amphiphiles at the bilayer edge.

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I. INTRODUCTION

Bilayer membranes self-assembled from phospholipids are ubiquitous in the cell, separating the cell from the exterior environment as well as encasing its internal organelle structures [1]. Many functions of the membrane depend on its physical and mechanical properties. In recent years, a great number of theoretical and experimental studies have focused on the relationship between the molecular properties (such as composition, geometrical shape, and interactions between lipid species) of the amphiphiles and the elastic properties of the self-assembled membranes [2–5]. In particular, the study of pore formation in bilayer membranes has been a subject of great interest for its fundamental importance in processes such as membrane fusion [6–9], transleaflet lipid diffusion [10], and transport of small molecules across the membranes [1]. Many medical and biotechnological applications also take advantage of artificially formed membrane pores for delivering materials into the cell [11,12].

The property of the self-assembled bilayer membrane is strongly affected by the structure and composition of the amphiphilic molecules, with consequences directly impacting the formation and stability of membrane pores. From a phenomenological point of view, the formation and stability of a membrane pore can be understood by considering the membrane's surface tension γ and the line tension σ of an open membrane edge [13]. It should be pointed out that, in the literature, the term "line tension" has been used to refer to the energy of the phase boundary between two phases of lipids coexisting in the same membrane and to the edge energy of an open lipid membrane. In the current study, the line tension refers to the edge energy of an open membrane, and the terms line tension and edge energy will be used interchangeably. In general, the energy associated with creating an open membrane edge originates from the bending of the lipid monolayers at the edge, thus shielding the hydrocarbons from the water molecules. Therefore, the formation of an open edge is associated with a highly curved lipid monolayer with a large positive curvature. The toroidal structure of an open membrane edge has been examined in a number of computational studies [14,15]. In general, large surface tension and low edge energy would favor the formation of pores. The competition between the surface tension and the edge energy determines the stability of the membrane. In many cases, self-assembled structures such as biological membranes or liposomes are considered to be tensionless, having zero or nearly zero surface tension. Thus for these systems, the formation and stability of pores is mainly determined by the energy of the open edge or the line tension. For bilayer membranes self-assembled from one type of lipid, the line tension is mainly determined by the property of the lipids. However, for multicomponent membranes, the line tension can be further regulated by the composition and molecular property of the amphiphilic species. From this perspective, it is desirable to study the relationship between the composition and molecular property of the amphiphiles and the line tension of an open membrane edge.

In recent years, a number of studies using continuum theory [16–18], computer simulations [14,19–26], and self-consistent field theory [5,27–29] have focused on examining the line tension of model bilayer membranes. In the studies using continuum theory, the structure of the bilayer at the pore edge is modeled by a highly curved monolayer. This approach provides a simple model for estimating the line tension, however it ignores the molecular structure of the amphiphilic molecules. Furthermore, applying the continuum theory to highly curved surfaces could lead to inaccurate results. Computer simulations such as molecular dynamics (MD) or Monte Carlo (MC) simulations provide a more detailed description of the membrane pores, but these simulations are computationally expensive and are limited by the number of amphiphiles. Self-consistent-field theory (SCFT) has also been used for studying the line tension of bilayer membranes, where lipids are modeled as amphiphilic block copolymers. Although SCFT provides a less detailed picture

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of the bilayer membrane as compared with the MC or MD simulations, it is computationally less expensive and provides a complementary method for examining the elastic properties of bilayer membranes.

Many of the theoretical and computational studies examining the elastic properties of bilayers have been focused on single-component membranes [5,19–21,24,25,27,29–33]. For example, Li *et al*. investigated the elastic properties of bilayers using SCFT and the continuum Helfrich model [5]. Modeling lipids as AB-diblock copolymers, the authors studied the effects of molecular architecture on the line tension of single-component bilayers [5]. In a similar simulation study, Hu *et al*. used the line tension of bilayer disks as a driving force to construct flat and closed vesicles [33]. By studying this mechanism, the authors were able to develop an accurate theoretical method for calculating the membrane's Gaussian modulus [33]. Very recently, Pera *et al*. examined the edge energy and the stability of pores of single-component lipid membranes using a lattice self-consistent-field theory. These previous studies indicate that the elastic properties of the lipid bilayers are sensitive to the molecular architecture of the lipids within the membrane. On the other hand, it is expected that for membranes formed by multicomponent lipids, lipid-lipid interactions and the interplay between different lipid architectures can play a significant role in determining the membrane properties. It is therefore desirable to extend the study to multicomponent systems.

For multicomponent membranes, a number of experimental, computational, and theoretical studies have been carried out in recent years to examine the effects of composition, geometrical shape, and interactions of lipids and other membrane-associated molecules on their line tension [23,34–36]. For example, Sakuma *et al*. studied the effects of DHPC or DPPC (cone- or cylindrical-shaped) lipids on the stability of pores in giant unilamellar vesicles (GUVs) [36]. Complementing the experimental results, the authors also used a two-dimensional continuum model to support the idea that pore formation can be stabilized by the aggregation of the cone-shaped lipids at the pore edge [36]. In a similar work investigating the effects of inclusion molecules on the line tension of bilayers, Karatekin *et al*. demonstrated that the addition of cholesterols, approximated as inverse cone-shaped molecules, resulted in an increase in the line tension [34]. In contrast, the addition of cone-shaped molecules was shown to reduce the line tension of the bilayer membrane [34]. Using molecular dynamics simulations, de Joannis *et al*. examined the line tension of bilayers composed of short and long tail phospholipids [23]. These authors showed that an increase in the concentration of short tail lipids results in a decrease in the line tension of ribbon-shaped aggregates [23]. Furthermore, they found that the short tail lipids concentrate at the edge of the aggregates [23]. The studies highlighted above indicate that the composition, geometrical shape, and interactions of lipids and other membrane-associated molecules have significant effects on the line tension of multicomponent bilayer membranes. These previous studies have provided valuable insight into the property of multicomponent membranes. Despite these studies, a systematic study of the physical properties of multicomponent model membranes has been scarce.

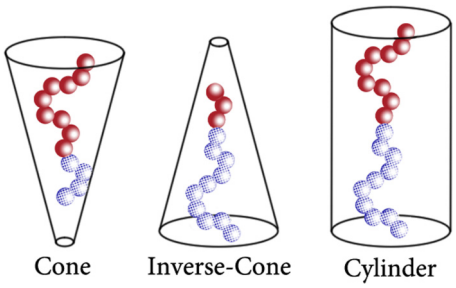

FIG. 1. (Color online) Schematics showing the different molecular architectures studied.

In this paper, we utilize self-consistent-field theory to study the line tension of self-assembled multicomponent bilayers. We model the lipids as amphiphilic AB and ED diblock copolymers, which self-assemble to form bilayer membranes in a hydrophilic solvent modeled as C-homopolymers. Modeling the lipids and water molecules by polymeric species provides a coarse-grained mesoscopic model, in which some of the atomistic details of the system are ignored. The simplified coarse-grained model could lead to significant computational speed-up so that larger systems are accessible. Furthermore, the mesoscopic model and interactions allow the study of collective phenomena of the system, including self-assembled structures and their mechanical properties, as well as phase transitions between these structures [37]. We use the coarse-grained model system to examine the effects of composition, geometrical shape, and interactions of the amphiphilic molecules on the line tension of the bilayer membranes. We control the geometrical shape of the lipid species by varying the relative size of the hydrophilic or hydrophobic blocks of diblock copolymers, as shown schematically in Fig. 1. Similarly, we control the interactions between the lipids by adjusting the Flory-Huggins parameter χ between the blocks. The composition of lipid species within the bilayer is regulated by tuning the relative chemical potential of diblock copolymers, allowing us to examine the effects of lipid composition on the line tension of the membrane edge.

The remainder of this paper is organized as follows. The theoretical model and numerical procedure are presented in Sec. II. Results on the effects of the composition of different lipid species and their geometrical shape and interactions on the line tension of bilayer membranes are reported in Sec. III. Finally, a conclusion and summary of the current study are given in Sec. IV.

II. THEORETICAL FRAMEWORK

The self-consistent-field theory (SCFT) is a well-established theoretical framework for the study of many-body systems, especially polymeric systems. Details of the SCFT formalism have been reported in numerous references [38–40]. In this section, we will give a brief introduction of the theory, focusing on the main aspects of the model and numerical procedure.

The multicomponent system considered in this work is composed of two amphiphilic diblock copolymers (AB and ED) and a homopolymer (C). The hydrophilic or hydrophobic

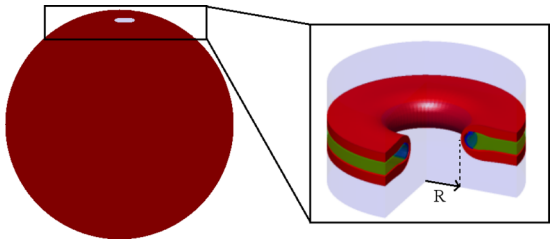

FIG. 2. (Color online) Schematics of the model system investigated. A small pore formed in a giant unilamellar vesicle.

nature of the molecular species is ensured by specifying the interactions between the blocks of the diblock copolymers and the homopolymers, respectively [5]. The thermodynamic properties of the system are most conveniently described using the grand-canonical ensemble, in which the model system contains AB,ED-diblock copolymers and C-homopolymers at a fixed temperature, volume, and activities or chemical potentials. In this study, we assume the membrane geometry is locally flat, corresponding to systems in which the radius of the vesicle is much larger than the region of the pore captured within the computational box. A schematic description of such a configuration is presented in Fig. 2.

In our model, the conformation of the amphiphilic molecules is described by the Gaussian chain model. Furthermore, the interactions between the different segments are modeled using the Flory-Huggins interaction parameters $\chi_{\alpha\beta}$. An application of the SCFT formalism [38–40] to the model system leads to an expression of the grand-canonical partition function of the system,

$$\Xi = \sum_{n_1=0}^{\infty}\sum_{n_2=0}^{\infty}\sum_{n_3=0}^{\infty}\frac{1}{n_1!n_2!n_3!}\int \mathcal{D}[\phi(\mathbf{r})]\mathcal{D}[\omega(\mathbf{r})] \prod_{\mathbf{r}}\delta\left[\sum_{\alpha}\phi_\alpha(\mathbf{r})-1\right]\delta\left[\sum_{\beta}\phi_\beta(R)-\phi_C(R)\right] \mathbf{e}^{-G[\phi,\omega]}, \tag{2.1}$$

where $\phi_\alpha(\mathbf{r})$ and $\omega_\alpha(\mathbf{r})$ correspond to the volume fraction and conjugate auxiliary fields of the polymer species, with $\alpha = \{A,B,E,C,D\}$ and $\beta = \{A,B,E,D\}$. The local incompressibility constraint is ensured by the first δ function in Eq. (2.1). The second δ function is used as a pining condition to stabilize a pore of radius R [5]. Furthermore, the quantity $G[\phi,\omega]$ in Eq. (2.1) is the grand potential functional or the grand canonical free-energy functional of the system. It is more convenient, however, to consider the free-energy density $g[\phi,\omega] = N_{AB}G[\phi,\omega]/\rho_0 V$, where the lengths of the polymer chains are scaled with respect to the length of the AB-diblock copolymers. Here, ρ_0 is the monomer density of the polymers, which we assume to be the same for all species. The relative degree of polymerization of the species with respect to the length of the AB-diblock copolymers can be written as $\kappa_{ED} = N_{ED}/N_{AB}$ and $\kappa_C = N_C/N_{AB}$.

Using Lagrangian multipliers η and ξ to enforce the incompressibility and pinning condition, the free-energy density can be written as

$$\begin{aligned} g[\phi,\omega,\eta,\xi] &= \frac{1}{V}\int d\mathbf{r}\left[\eta(\mathbf{r})\left(\sum_\alpha \phi_\alpha(\mathbf{r})-1\right)\right. \\ &\quad +\xi(R)\left(\sum_\beta \phi_\beta(R)-\phi_C(R)\right)-\sum_\alpha N_{AB}\omega_\alpha(\mathbf{r})\phi_\alpha(\mathbf{r}) \\ &\quad \left.+\frac{1}{2}\sum_{\alpha\neq\beta}\phi_\alpha(\mathbf{r})\phi_\beta(\mathbf{r})\chi_{\alpha\beta}N_{AB}\right]-Q_{AB} \\ &\quad -\frac{z_{ED}}{\kappa_{ED}}Q_{ED}-\frac{z_C}{\kappa_C}Q_C, \end{aligned} \tag{2.2}$$

where Q_{AB}, Q_{ED}, and Q_C are the single-chain partition functions for the AB, ED, and C molecules, and z_{ED} and z_C are the activities of the ED and C species. We note that the chemical potential of the AB-diblock copolymers is chosen such that $z_{AB} = 1$. Using the saddle point approximation, the density profiles $\phi_\alpha(\mathbf{r})$ and their conjugate fields $\omega_\alpha(\mathbf{r})$ are determined by demanding that the free energy Eq. (2.2) be invariant with respect to variations in the ϕ, ω, η, and ξ fields. This minimization leads to a set of self-consistent field equations,

$$\begin{aligned} \phi_\alpha(\mathbf{r}) &= \int_0^{f_\alpha} ds\, q_\alpha(\mathbf{r},s)q_\alpha^\dagger(\mathbf{r},f_\alpha-s), \\ \phi_\beta(\mathbf{r}) &= \frac{z_{ED}}{\kappa_{ED}}\int_0^{\kappa_{ED}f_\beta} ds\, q_\beta(\mathbf{r},s)q_\beta^\dagger(\mathbf{r},\kappa_{ED}f_\beta-s), \\ \phi_C(\mathbf{r}) &= \frac{z_C}{\kappa_C}\int_0^{\kappa_C} ds\, q_C(\mathbf{r},s)q_C^\dagger(\mathbf{r},\kappa_C-s), \\ \omega_\alpha(\mathbf{r}) &= \frac{1}{2}\sum_{\theta\neq\alpha}\phi_\theta(\mathbf{r})\chi_{\alpha\theta}+\eta(\mathbf{r})-\xi(R), \\ \omega_\beta(\mathbf{r}) &= \frac{1}{2}\sum_{\theta\neq\alpha}\phi_\theta(\mathbf{r})\chi_{\beta\theta}+\eta(\mathbf{r})-\xi(R), \\ \omega_C(\mathbf{r}) &= \frac{1}{2}\sum_{\theta\neq C}\phi_\theta(\mathbf{r})\chi_{C\theta}+\eta(\mathbf{r})+\xi(R), \\ \phi_A(R)+\phi_B(R)+\phi_E(R)+\phi_D(R) &= \phi_C(R), \\ \sum_\theta \phi_\theta(\mathbf{r}) &= 1, \end{aligned} \tag{2.3}$$

where $\alpha = \{A,B\}$, $\beta = \{E,D\}$, and $\theta = \{A,B,C,D,E\}$. In the above set of self-consistent equations, the functions $q(\mathbf{r},s)$ and $q^\dagger(\mathbf{r},s)$ are the forward and backward end-integrated propagators. These propagators satisfy the modified diffusion equations,

$$\begin{aligned} \frac{\partial q(\mathbf{r},s)}{\partial s} &= R_g^2\,\nabla^2 q(\mathbf{r},s)-\omega(\mathbf{r})q(\mathbf{r},s), \\ \frac{\partial q^\dagger(\mathbf{r},s)}{\partial s} &= -R_g^2\,\nabla^2 q^\dagger(\mathbf{r},s)+\omega(\mathbf{r})q^\dagger(\mathbf{r},s), \end{aligned} \tag{2.4}$$

with the initial conditions $q(\mathbf{r},0) = 1$ and $q^\dagger(\mathbf{r},1) = 1$ [38]. In the above equations, R_g is the radius of gyration and is defined

as $R_g = b\sqrt{N/6}$, where b is the Kuhn length of the Gaussian chain.

In the geometry examined in our study, the axial symmetry about the center of the pore permits us to write the self-consistent equations in cylindrical coordinates [5]. With this, we apply the alternating direction implicit (ADI) technique to solve the modified diffusion equations [Eqs. (2.4)] in the r-z plane [41]. By solving Eq. (2.4) using appropriate boundary conditions, we can determine solutions of the SCFT equations in terms of the density profiles $\phi_\alpha(\mathbf{r})$ and their conjugate fields $\omega_\alpha(\mathbf{r})$ for a given set of model parameters. In particular, solutions corresponding to a pore of a given radius can be obtained. To extract physical quantities such as membrane surface tension, bending moduli, and pore line tension, we fit the free energy of the system calculated using the SCFT method to that given by the Helfrich model [13]. In the Helfrich model, the membrane can be represented as a two-dimensional elastic sheet, with a free energy given by

$$f_H = \int d\mathbf{A}[2\kappa_M(M - c_0)^2 + \kappa_G G + \gamma] + \int d\mathbf{L}\,\sigma, \quad (2.5)$$

where M and G are the local mean and Gaussian curvatures. These curvatures can be specified in terms of the principal curvatures c_1 and c_2 as $M = (c_1 + c_2)/2$ and $G = c_1 c_2$ [13,42]. In Eq. (2.5), c_0, γ, and σ are the spontaneous curvature, membrane's surface tension, and line tension, respectively. For large vesicles or flat membranes, the membrane pore, as shown schematically in Fig. 2, can be considered to be in a flat geometry, thus allowing us to set $c_1 = c_2 = 0$. Using this information, we can rewrite the Helfrich free energy as a function of membrane surface tension and pore line tension,

$$f_H = \gamma \int d\mathbf{A} + \sigma \int d\mathbf{L}.$$

Although the self-assembled biological membranes can often be characterized as tensionless, many studies focus on bilayers with nonzero surface tension [31,34,43]. In the current study, however, we focus on tensionless membranes. Specifically, we vary the chemical potential of the C-homopolymers so that the membrane is tensionless [5]. For a tensionless membrane and with the assumption that the pore is circular and locally flat, we can write the free energy of the pore as $f_H = 2\pi R\sigma$. In this simple form, the free energy of the pore is linearly proportional to the radius. The line tension or the edge energy of the membrane is proportional to the slope of the line. By fitting the free energy calculated using the SCFT method to f_H, we can obtain the line tension for membranes for various copolymer composition, geometrical shape, and interactions. It should be pointed out that extension of the study to membranes with tension is straightforward. Specifically, the free energy of the pore with tension will be given by $f_H = -\pi R^2\gamma + 2\pi R\sigma$. A fitting of the free energy of the pore to this expression can then be used to obtain the surface tension γ and the line tension σ.

III. RESULTS AND DISCUSSION

In this section, we present the results for the line tension of bilayer membranes composed of two types of amphiphilic molecules. We vary the architecture of the lipid species by adjusting the volume fractions f_α and the relative block lengths κ of the diblock copolymers. Similarly, the interactions between the segments are controlled by adjusting the Flory-Huggins parameters χ. To investigate the effects of amphiphile composition, we introduce an order parameter, $\psi = (\phi_{AB} - \phi_{ED})/(\phi_{AB} + \phi_{ED})$, to characterize the relative volume fraction of the AB and ED amphiphilic molecules within the bilayer. Furthermore, to isolate the effects of molecular geometries, interactions, and membrane composition, we investigate bilayer systems with zero surface tension ($\gamma = 0$). Starting with a system in the bilayer configuration, as shown in Fig. 3(a), we adjust the chemical potential of the solvent such that the membrane is tensionless. We then construct a pore of radius R, illustrated in Fig. 3, using the pinning condition as described in the preceding section.

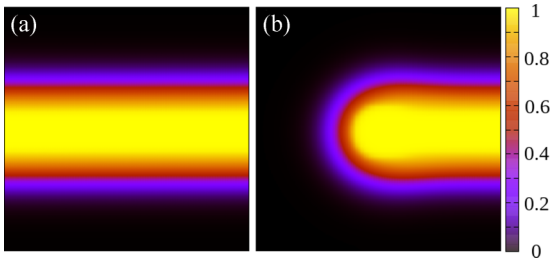

FIG. 3. (Color online) 2D density profiles for the (a) bilayer and (b) pore configuration. The profile illustrates the overall density of the diblock copolymers $AB + ED$ in the lighter regions and solvent C in the dark regions. These plots correspond to the cross-sectional view of the bilayer and the pore, respectively.

The free energy of the pore, as described by the continuum model, is $f_H = (2\pi\sigma)R$. In this form, the line tension σ can be determined by evaluating the free energy of the system as a function of radius R. Figure 4 presents the free energy obtained from the SCFT calculations, as a function of pore radius

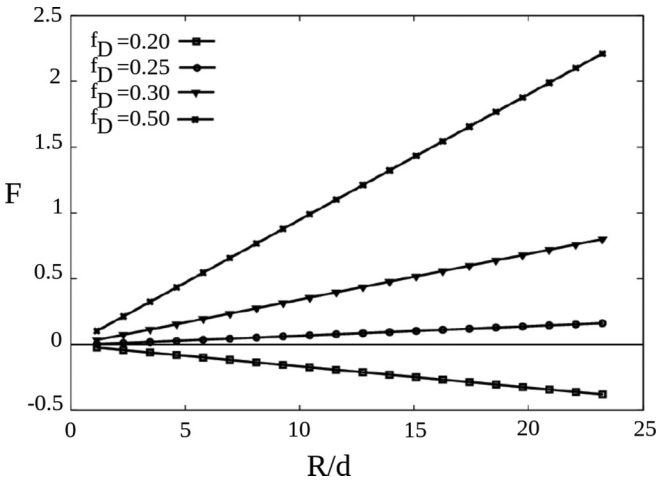

FIG. 4. The free energy as a function of pore radius R for blends with $\chi_{AB} = \chi_{ED} = \chi_{AD} = \chi_{BE} = \chi_{BC} = \chi_{CD} = 30$, $f_A = f_B, \kappa_C = 1$, and various ED-molecular architectures. The molecular fraction of the D species is defined as $f_D = N_D/N_{AB}$. The pore radius R is measured in units of R_g and is normalized with respect to the bilayer thickness d, given as $d \sim 4.3R_g$.

for a model system with $\chi_{AB} = \chi_{ED} = \chi_{AD} = \chi_{BE} = \chi_{BC} = \chi_{CD} = 30$, $\chi_{AE} = \chi_{BD} = \chi_{AC} = \chi_{CE} = 0$, $f_A = f_B$, $\kappa_C = 1$, $\mu_{AB} = \mu_{ED}$, and different ED-molecular architectures. By adjusting f_D while keeping the length of the E-block constant, we change the geometry of the ED-molecules from a cylindrical- to a cone-shaped structure. The results can then be used to examine the effects of mixing cylindrical- and cone-shaped lipids on the line tension.

Figure 4 shows the free energy of 1:1 mixtures of cylindrical- and cone-shaped molecules as a function of pore radius R. The first feature to notice is that the line tension, which is proportional to the slope of the free-energy curve, decreases with an increase in the asymmetry (f_D) of the ED-molecules. For a tensionless membrane, the only contribution to the free energy is from the line tension. In this case, the stability of the pore is determined by analyzing the free energy as function of the pore radius. For blends with $f_D = 0.5$, 0.3, and 0.25, the slope of the free energy is positive, corresponding to pores that would shrink upon the release of the pining constraint. In contrast, blends with $f_D = 0.2$ have a negative line tension, which correspond to pores that would grow in size, resulting in the rupture of the membrane. Most interestingly, binary lipid mixtures with zero line tension would correlate with long-lasting stable pores. These results suggest that an increase in the lifetime of a pore can be obtained by tuning the concentration of cone-shaped detergent molecules within the membrane.

To further explore the effects of lipid asymmetry on the pore line tension, we investigate membranes composed of various concentrations of ED-molecules. By controlling the chemical potential of the ED-diblock copolymers (μ_{ED}), we can adjust the relative composition of the ED-molecules in the membrane. Figure 5 presents the line tension σ as a function of the order parameter ψ for model systems with $\chi_{AB} = \chi_{ED} = \chi_{AD} = \chi_{BE} = \chi_{BC} = \chi_{CD} = 30$, $\chi_{AE} = \chi_{BD} = \chi_{AC} = \chi_{CE} = 0$, $f_A = f_B$, $\kappa_C = 1$, and $f_D = 0.25$, 0.30, and 0.40. The molecular composition within the membrane is characterized by the order parameter ψ, where $\psi = 1$ and -1 correspond to membranes composed purely of AB and ED species, respectively. As shown in Fig. 5, membranes composed of asymmetric molecules (cone-shaped) have lower line tension than those composed of symmetric molecules (cylindrical-shaped). A decrease in σ for membranes composed of asymmetric lipids has been reported previously for single-component membranes by Li *et al.* [5]. These authors investigated the effect of molecular fraction f on the line tension for single-component bilayers, and they showed that a decrease in the relative size of the head groups results in a decrease in the line tension [5].

As illustrated in Fig. 5, an increase in the concentration of cone-shaped lipid species in the membrane leads to a decrease in the line tension σ. Furthermore, the decrease of σ is more pronounced for cone-shaped lipids with smaller head groups (characterized by smaller f_D), in that the line tension can be changed from positive to negative. For example, for a binary mixture of symmetric AB- and asymmetric ED-molecules with $f_D = 0.25$, the pure AB and ED membranes have positive and negative line tensions, respectively. As shown in Fig. 5, for this system the line tension vanishes at a critical composition, ψ_c. At this concentration, a pore with a finite radius formed in a tensionless membrane would be stable.

A decrease in the line tension as a function of an increase in the concentration of cone-shaped molecules has been reported in a number of experiments [34–36]. It has been suggested that the decrease in the line tension is caused by the aggregation of the cone-shaped molecules at the pore edge [34–36]. The availability of the SCFT solutions allows us to investigate the segregation of lipid species within the membrane by analyzing the density profile of the lipid species. Figure 6 presents the density profiles for a system with $\chi_{AB} = \chi_{ED} = \chi_{AD} = \chi_{BE} = \chi_{BC} = \chi_{CD} = 30$, $\chi_{AE} = \chi_{BD} = \chi_{AC} = \chi_{CE} = 0$, $f_A = f_B$, $\kappa_C = 1$, $f_D = 0.25$, and $\psi = 0.18$. As shown in Fig. 6, the cone-shaped ED-molecules have a higher concentration at the pore edge. This effect can be seen more clearly in the one-dimensional profile (Fig. 6)

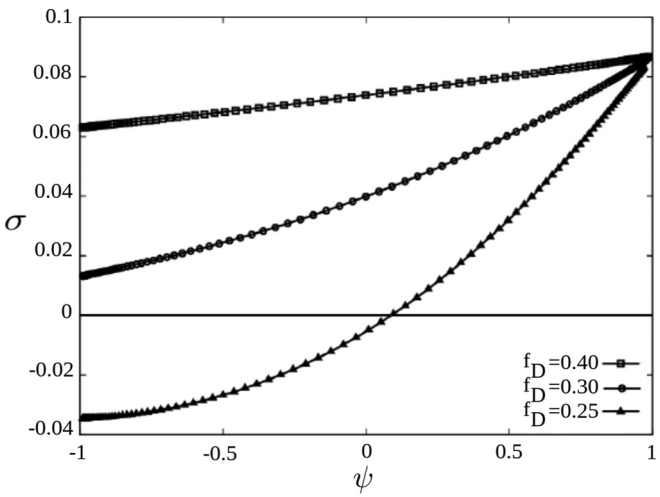

FIG. 5. The line tension σ as a function of order parameter ψ for blends with $\chi_{AB} = \chi_{ED} = \chi_{AD} = \chi_{BE} = \chi_{BC} = \chi_{CD} = 30$, $f_A = f_B$, $\kappa_C = 1$, and $f_D = 0.25$, 0.3, and 0.4.

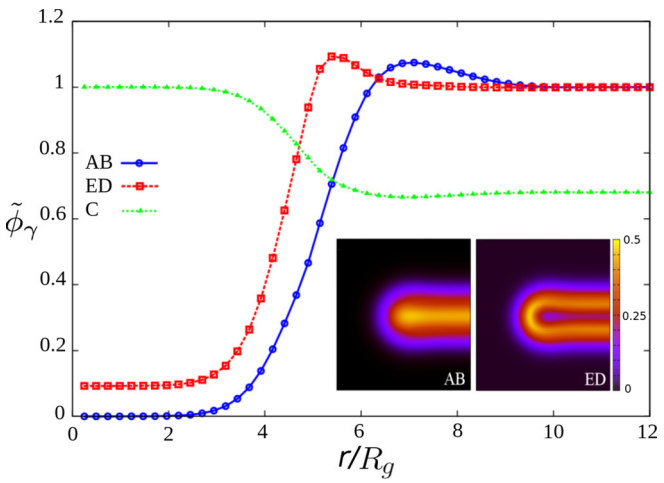

FIG. 6. (Color online) Relative concentrations of the AB, ED, and C molecules $\tilde{\phi}_\gamma$ ($\gamma = AB$, ED, and C) as a function of position for blends with $f_D = 0.25$. Inset: 2D density profiles of the (a) AB and (b) ED blends for $\chi_{AB} = \chi_{ED} = \chi_{AD} = \chi_{BE} = \chi_{BC} = \chi_{CD} = 30$, $f_A = f_B$, $\kappa_C = 1$, $f_D = 0.25$, and $\psi = 0.18$.

of the relative concentrations of the molecular species $\tilde{\phi}_\gamma = \phi_\gamma/\phi_{\gamma,\text{bulk}}$ ($\gamma = AB, ED$, and C), which is the concentration of the molecular species normalized by their bulk values for a planar membrane. The results shown here clearly reveal an increase in the concentration of ED-molecules at the pore edge. This observation of molecular segregation to the pore edge provides strong evidence that the mechanism of line tension decrease is the coupling of molecular density with the curvature of the amphiphilic monolayers.

To understand why the segregation of the cone-shaped molecules at the pore edge reduces the line tension, we need to consider the spontaneous curvature of the AB and ED monolayers. When a pore is formed, the hydrophobic tails are exposed to the solvent. To reduce the unfavorable interaction between the hydrophobic tails and solvent, the molecules rearrange to shield the hydrophobic segments. This results in the formation of an edge with a large positive curvature. If the bilayer is composed only of symmetric molecules, with zero spontaneous curvature, the penalty for bending the membrane is large. On the other hand, if cone-shaped molecules with positive spontaneous curvature are added to the membrane, they could aggregate at the pore edge and act as pore stabilizers, thus reducing the line tension.

The above analysis can be extended to the case of species with inverse cone-shaped geometries. In addition to inverse cone-shaped lipids, the shape of cholesterol molecules is often described as an inverse cone-shaped structure. Given the abundance of cholesterol in biological membranes, it is interesting to explore the effects of inverse cone-shaped molecules on the line tension. As a model system for inverse cone-shaped lipids, we calculated the line tension for membranes composed of AB and ED molecules, where $N_A = N_B$ and $N_D > N_E$. Figure 7 gives the line tension of this bilayer system as a function of the order parameter ψ, for blends with $\chi_{AB} = \chi_{ED} = \chi_{AD} = \chi_{BE} = \chi_{BC} = \chi_{CD} = 30$, $\chi_{AE} = \chi_{BD} = \chi_{AC} = \chi_{CE} = 0$, $f_A = f_B$, $\kappa_C = 1$, $f_E = 0.25$, 0.35, and 0.45. As before, $\psi = 1$ and -1 correspond

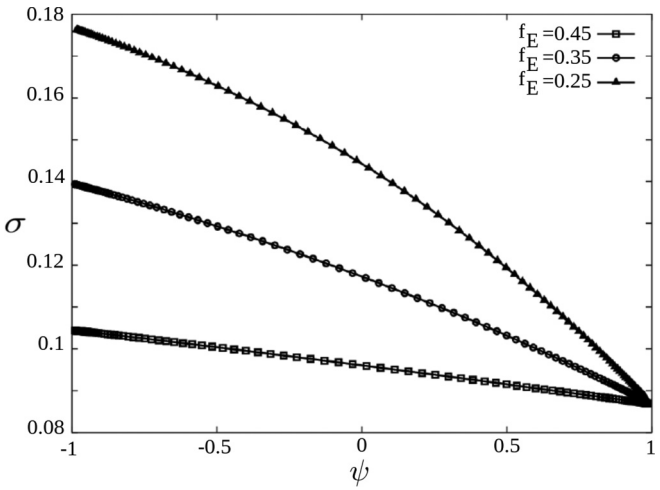

FIG. 7. Line tension σ as a function of order parameter ψ for blends with $\chi_{AB} = \chi_{ED} = \chi_{AD} = \chi_{BE} = \chi_{BC} = \chi_{CD} = 30$, $f_A = f_B$, $\kappa_C = 1$, and $f_E = 0.25$, 0.35, and 0.45.

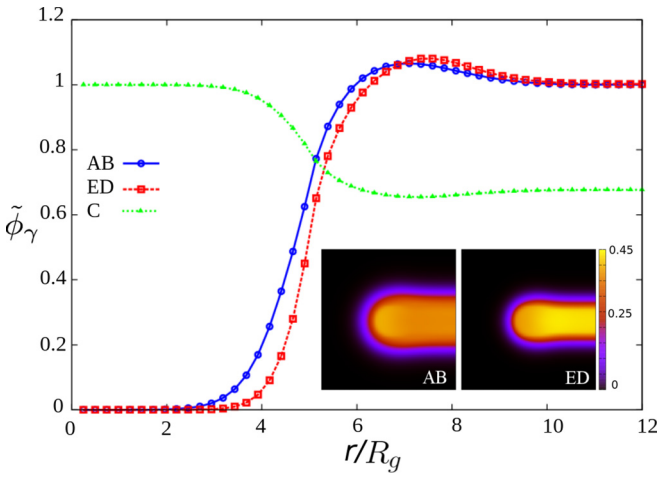

FIG. 8. (Color online) Relative concentrations of the AB, ED, and C molecules $\tilde{\phi}_\gamma$ ($\gamma = AB, ED$, and C) as a function of position. Inset: 2D density profiles of the (a) AB and (b) ED blends for $\chi_{AB} = \chi_{ED} = \chi_{AD} = \chi_{BE} = \chi_{BC} = \chi_{CD} = 30$, $f_A = f_B$, $\kappa_C = 1$, $f_E = 0.25$, and $\psi = 0.3$.

to membranes composed of pure AB and ED molecules, respectively.

The results shown in Fig. 7 reveal that an increase in the concentration of the inverse cone-shaped molecules (ED-molecules) leads to an increase in the line tension of the membrane edge. The increase of the line tension is more pronounced for ED-molecules with a larger block asymmetry. To understand why inverse cone-shaped molecules result in an increase in the line tension, we will focus on the distribution of the AB and ED species within the bilayer. In Fig. 8, we present the density profiles for the AB, ED and C molecules. In contrast with the case of cone-shaped ED-molecules, there is a depletion of the ED-molecules at the pore edge. This effect is shown more clearly in the one-dimensional density profile, where the relative concentrations of the molecules $\tilde{\phi}_\gamma$ ($\gamma = AB, ED$, and C) are plotted as a function of the position. The aggregation of the ED-molecules away from the pore edge is caused by the mismatch between the spontaneous curvature of the ED-molecules and that of the pore edge. This indicates that pore formation in systems with a high concentration of inverse cone-shaped molecules is highly unfavorable.

Experiments on the effects of cholesterol molecules on the stability of membranes indicate that an increase in the concentration of cholesterol molecules results in a more stable membrane [43–45]. For example, Koronkiewicz and Kalinowski showed that the critical radius, at which the membrane rupture, increases for membranes with higher cholesterol concentration [45]. For a bilayer membrane with a finite surface tension, the free energy as given by the continuum model can be written as $f_H = 2\sigma\pi r - \gamma\pi r^2$, resulting in a critical radius of $r_c = 2\sigma/\gamma$. Therefore, the critical radius is proportional to the line tension σ. As shown in Fig. 7, the line tension increases with an increase in the concentration of the inverse cone-shaped molecules. For a system with finite surface tension, this corresponds to an increase in the critical pore radius r_c. These results indicate that an increase in the concentration of inverse cone-shaped molecule such as

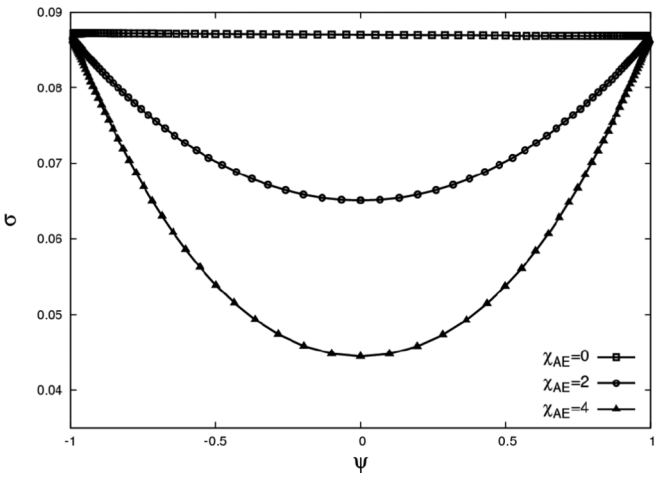

FIG. 9. The line tension σ as a function of the order parameter ψ for blends with $\chi_{AB} = \chi_{ED} = \chi_{AD} = \chi_{BE} = \chi_{BC} = \chi_{CD} = 30$, $f_A = f_B = f_E = f_D$, and $\kappa_C = \kappa_{ED} = 1$ for $\chi_{AE} = 0$, 2, and 4.

cholesterol would correspond to an increase in the energy associated with creating a pore, therefore preventing pore formation and stabilizing the membrane.

Finally, we investigate the effects of head-group interactions on the line tension of multicomponent bilayers. We begin by considering a repulsive interaction between the A/E blocks (head groups) for symmetric blends with $N_{AB} = N_{ED} = N_C$. Figure 9 gives the line tension σ as a function of the order parameter ψ, for blends with $\chi_{AB} = \chi_{ED} = \chi_{AD} = \chi_{BE} = \chi_{BC} = \chi_{CD} = 30$, $\chi_{BD} = \chi_{AC} = \chi_{CE} = 0$, $f_A = f_B = f_E = f_D$, $\kappa_C = \kappa_{ED} = 1$, and $\chi_{AE} = 0$, 2, and 4. In this figure, the line tension for blends with $\chi_{AE} = 0$ is taken as a reference. It is interesting to point out that mixing symmetric molecules with repulsive head group interactions leads to a decrease in the line tension, with a minimum at $\psi = 0$. We can understand the decrease in the line tension for a mixed system by considering the properties of a pore modeled as a folded monolayer. Using a two-dimensional continuum model, Li *et al*. considered the line tension of a pore created by folding a monolayer onto itself, forming a pore edge similar to that seen in Fig. 3(b) [5]. Using this approach, the authors derived an expression for the line tension as a function of the monolayer properties,

$$\sigma = \pi \kappa_M \frac{1 - 4c_0\delta}{2\delta}, \tag{3.1}$$

where κ_M, c_0, and δ are the bending modulus, spontaneous curvature, and thickness of the monolayer, respectively [5,46]. For a symmetric system such as a single-component AB bilayer, the spontaneous curvature of the monolayer c_0 is zero. In a mixed AB/ED system, the effect of the repulsive head group interaction would result in the formation of an effective cone-shaped molecule, shown schematically in Fig. 10. The nonzero spontaneous curvature for the cone-shaped molecule results in a decrease in the line tension as shown in Fig. 9. These results indicate that the line tension of a membrane can be regulated by introducing molecules with repulsive head group interactions.

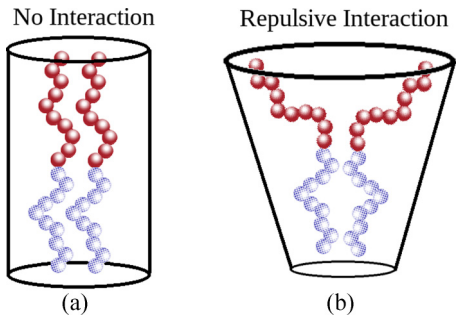

FIG. 10. (Color online) Schematic diagram showing the effect of repulsive head group interaction on the overall geometrical shape of the lipids.

IV. CONCLUSION

Using the self-consistent field theory, we have investigated the line tension or edge energy of self-assembled multicomponent bilayer membranes, focusing on the effects of composition, geometrical shape, and interactions of lipid species. The lipid species in the bilayer were modeled as amphiphilic AB and ED diblock copolymers in a solvent, modeled as C-homopolymers. Solutions of the SCFT equations are obtained for a bilayer membrane with a pore of fixed size. By fitting the SCFT free energy of the pore to the Helfrich model, we have extracted the line tension of the membrane. We then examined the effects of the composition, geometrical shape, and interactions of lipid species on the line tension.

We first investigated bilayer systems composed of cylindrical, cone-, and inverse cone-shaped lipid species, focusing on the effects of relative lipid composition on the line tension of the self-assembled bilayer membranes. Our results revealed that an increase in the concentration of the cone-shaped lipids results in a decrease in the line tension. The mechanism underlying the reduction in the line tension was found to be related to the segregation of the molecules within the membrane. Lipid segregation is driven to relieve the stress caused by the large positive curvature of the pore edge. The local curvature of the pore matches more closely to the spontaneous curvature of the cone-shaped lipids, resulting in the aggregation of the cone-shaped species at the pore edge. The overall effect of adding cone-shaped lipids to the bilayer is consistent with experimental and computational studies [34–36]. In contrast to the behavior of cone-shaped lipids, we discovered that an increase in the concentration of the inverse cone-shaped molecules results in an increase in the pore line tension. The underlying mechanism for this increase, similar to the cone-shaped lipid system, is the segregation of lipids within the bilayer. In contrast, however, the spontaneous curvature of the inverse cone-shaped lipids is different from that of the pore edge. This results in a depletion of the inverse cone-shaped molecules from the pore edge. Experiments have also shown that an increase in the concentration of inverse cone-shaped molecules such as cholesterol could result in an increase in the line tension of the membrane, causing it to be more stable [34]. Finally, we considered the effects of repulsive interaction between the head groups of symmetric lipid species. We discovered that an increase in the repulsive interaction between the head groups results in a decrease in the

pore line tension. This effect was understood to be caused by the formation of effective cone-shaped lipid aggregates, which we know to lower the line tension.

Although the coarse-grained model ignores many molecular details of lipids, the results and conclusion from the current study provide a qualitative understanding of the interplay between the lipid segregation and local curvature. In particular, the results provide clear evidence that the segregation of the lipids can lead to the increase or decrease of the line tension, depending on the geometry of the molecules. The predicted trend of the line tension as a function of the concentration of the second lipids is in good agreement with available experiments. Although this trend of line tension could be understood intuitively, the current study places the mechanism of the line tension behavior in a multicomponent lipid system on a solid theoretical base.

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