Field theoretical approach for a polymer-containing vesicle

Yutaka Oya and Toshihiro Kawakatsu

Abstract

We simulate the structure of a vesicle that encloses polymers as an example of endocytosis and exocytosis. Simulations are performed by coupling two types of continuum field methods, i.e. the phase field theory for vesicle shape and the self-consistent field theory for polymer conformation. Comparing free energies between prolate and oblate shapes of vesicles as the candidates of equilibrium shape of the vesicle that contains polymers, we show that prolate shape is more stable, where the dominant contribution is the conformation entropy of polymers. We extend the above static simulation to a dynamic one by introducing a flow field that is described by Navier–Stokes equation.

Keywords: vesicle, polymer, phase field, self-consistent field, Navier–Stokes equation

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1. Introduction

A vesicle is a closed-form of a bilayer membrane composed of amphiphilic molecules. It is often used as a model system of bio-membranes. A vesicle that contains polymers inside is an important target of biological studies as well as industrial applications, such as drug delivery system. In a recent experiment, it was found that inverse micelles take anisotropic shapes induced by the enclosed polymers [1]. To clarify the physical origin of such a deformation, we modeled the system and performed simulations.

In the past, typical computer simulations on the vesicle shapes were done mainly using molecular models, where the vesicle surface is discretized using triangular lattices [2]. In the present study, on the other hand, we adopt a continuum field approach. For example, vesicle shape is described with phase field (PF) theory [3] and polymer conformations are calculated using the self-consistent field theory (SCFT) [4]. With the use of these field methods, interaction between the vesicle and the enclosed polymer chains is effectively taken into account in a natural manner. Furthermore, the PF theory and the SCF theory can give an accurate value of the free energy of polymer-containing vesicles. Through such a calculation, we can obtain the equilibrium shape of a vesicle that contains polymers. In the following we will discuss two different approaches to this system: one is a static simulation to obtain equilibrium shape of the vesicle and the other is a dynamic simulation, which is coupled with a flow field that obeys the Navier–Stokes equation.

2. Static simulation

In our study, we consider a three-component system such as a system composed of a vesicle, polymers and solvents. Here we assume that the polymers are completely surrounded by the vesicle and the outer space is filled with the solvent. We also assume the following local incompressible condition:

\[ \Phi_m + \Phi_p + \Phi_s = 1, \]

where \( \Phi \) is the local volume fraction and notation \( m, p \) and \( s \) represent the vesicle, polymers and solvents, respectively. In equation (1), volume fraction of the vesicle \( \Phi_m \) is calculated using the phase field theory and those of polymers \( \Phi_p \) and solvents \( \Phi_s \) are calculated using SCFT.

First, we consider how to describe the vesicle shape using the phase field theory. In the phase field theory, vesicle shape is described by scalar order parameter field \( \psi(r) \), where the inside and the outside regions of the vesicle are represented by positive and negative regions of \( \psi \), respectively, and the interface corresponds to \( \psi(r) = 0 \). For simplicity, we assume that the profile of \( \psi(r) \) across the interface has
With the use of SCFT calculation, we obtain free energies of vesicle, polymers and solvents as follows:

$$\Phi_{m}(r) = \varepsilon^{2} |\nabla \psi(r)|^{2} + \frac{1}{2} \left(1 - \psi(r)^{2}\right)^{2},$$  \hspace{1cm} (2)

$$S = \text{const.} \times \int \Phi_{m}(r) \, d r.$$  \hspace{1cm} (3)

On the other hand, the vesicle shape is determined by minimizing the following Helfrich bending energy [5]:

$$F_{b} = \frac{k}{2} \int H^{2} \, d a,$$  \hspace{1cm} (4)

where $\kappa$, $H$ and $da$ are the bending modulus, the local mean curvature and the area element of the vesicle, respectively.

Following a geometric consideration, we find that the local mean curvature $H$ is given by an infinitesimal change of the total surface area of equation (3). Therefore, with the use of the phase field $\psi$, Helfrich bending energy of equation (4) is rewritten as follows [3]:

$$F_{b} [(\psi(r))] = \frac{k}{2} \int (-\psi + \psi^{3} - \varepsilon^{2} \nabla^{2} \psi)^{2} \, d r,$$  \hspace{1cm} (5)

where the integrand on the right-hand side of equation (5) represents the mean curvature $H$. To minimize the free energy of equation (5) under fixed enclosed volume and fixed surface area, we obtain the equilibrium shape of the vesicle.

Next, we introduce SCFT to describe the polymer conformations and the mixing entropy of solvents. In SCFT, effects of the interaction between polymers and solvents are replaced by the interaction between them and the mean field $V(r)$, and the Boltzmann factors for all possible conformations of a single polymer chain are evaluated by using path integral $Q$. Here, it should be noted that the path integral $Q$, the local volume function $\Phi_{a}$ and the mean field $V$ are determined in a self-consistent manner using an iteration. With the use of SCFT calculation, we obtain free energies of the polymers and the solvents in the following form:

$$F_{\text{SCFT}} = -k_{B}M_{p}\log\left(\int Q \, d r\right) + \int \Phi_{a}(\log \Phi_{a} - 1) \, d r
- \int \left(\Phi_{p}V_{p} + \Phi_{s}V_{s}\right) \, d r + \frac{1}{2} \int \chi \Phi_{p} \Phi_{s} \, d r.$$  \hspace{1cm} (6)

where $M_{p}$ is the number of polymers. The first term and the second term on the right-hand side of equation (6) are the contributions to the free energy from the conformation entropy of polymers and the mixing entropy of solvents. The fourth term represents the interaction energy between polymers and solvents, where $\chi$ is the interaction parameter.

Following the above discussion we obtain total free energies of vesicle, polymers and solvents as follows:

$$F_{\text{total}} = F_{\text{PF}} + F_{\text{SCFT}} + \int \mu(r)(\Phi_{m} + \Phi_{p} + \Phi_{s} - 1) \, d r,$$  \hspace{1cm} (7)

where $F_{\text{PF}}$ includes $F_{0}$ and the contributions to the free energy from the fixed surface area and the fixed volume conditions, and the third term accounts for the interaction between the polymer and the vesicle due to the local incompressible condition of equation (1). In the static simulation, we use the following phenomenological time evolution equation for the phase field $\psi$:

$$\frac{\partial \psi}{\partial t} = -\frac{\delta F_{\text{total}}}{\delta \psi}.$$  \hspace{1cm} (8)

We performed a minimization of the free energy of equation (7) by iterating equation (8) and SCFT calculation alternatively.

### 3. Static simulation results

In this section, we show results of the static simulations to obtain the equilibrium shape of the vesicle that contains polymers. As a candidate of the equilibrium shape of the vesicle, we chose a prolate shape and an oblate shape of the vesicles as is shown in figure 1. Here, we introduce important parameters for the confinement effects on the polymers. One of these parameters is the reduced volume $\nu$ of the vesicle defined by the following equation:

$$\nu = \frac{3}{4\pi} \left(\frac{4\pi}{S}\right)^{3/2},$$  \hspace{1cm} (9)

where $V_{in}$ is the inner volume of the vesicle. When reduced volume is small, which means that the surface area is larger than that of a spherical vesicle, the vesicle becomes strongly deformed. Such a strong deformation forces the polymers to be strongly confined inside the vesicle. The other parameters are the chain length ($N$) and the concentration ($\rho$) of the polymers and the interaction parameter ($\chi$) between the polymers and the solvents.

In figure 2, we show the differences of each contribution of the free energies between prolate and oblate shapes of the vesicles with fixed polymer concentration $\rho$ and fixed repulsive interaction parameter $\chi$. Minus value of this free energy difference represents that prolate shape is more stable than oblate shape. In figure 2, increasing $N$ or decreasing reduced volume $\nu$, which means that the polymer confinement
inside the vesicle becomes stronger, the prolate shape tends to be more stable. It is also shown that a dominant factor that determines this behavior is the contribution from the conformation entropy of the polymers. Our results are consistent with the experiments, in which polymer-containing inverse micelles show the prolate shape rather than the oblate shape. According to a blob argument, it can be explained why conformation entropy of polymers prefers the prolate shape rather than the oblate shape of vesicle. Polymers confined in narrow spaces can be modeled by sequences of blobs. For example, in the case of a single polymer chain in a narrow slab with separation $L$, the polymer can be regarded as a sequence of the blobs with size $L$ and the number of these blobs is $\sim N/L^2$. Therefore the increase in the free energy due to the loss of the conformation entropy of polymers in the narrow slab is given by

$$\Delta F = k_B T \log 2^{N/L^2}. \quad (10)$$

We apply the above estimation of the loss of the conformation entropy of polymers in a narrow slab to the cases of oblate and prolate shapes. Here we use simple models of the prolate and oblate shapes of vesicles, where we approximate these shapes by cylinders with diameter $L_p$ and height $L_o$, respectively. In the limit of large surface area, a comparison between the prolate shape and the oblate shape of the cylinders with the same volume and the same surface area gives the following relation:

$$L_p \approx 4L_o. \quad (11)$$

Using the fact that the number of chains is inversely proportional to the chain length $N$, the difference of loss of free energy between prolate and oblate shapes is as follows:

$$\frac{1}{N} \left[ 2\Delta F_{pr} - \Delta F_{ob} \right] = -\frac{7k_B T}{8L_0} \log 2 < 0, \quad (12)$$

where the factor 2 in the proportionality coefficient for the prolate case comes from the fact that the polymers are constrained from two mutually perpendicular directions. In the result of equation (12), the conformation entropy of the polymers prefers the prolate shape rather than the oblate shape and this tendency is not changing even if we change the chain length in the limit of large surface area. This tendency is consistent with the long chain region in figure 2(a).

### 4. Dynamic simulation

In this section, we introduce a dynamic simulation of the vesicle coupled with the flow field. In a dynamic simulation, local volume fraction of the vesicle should be conserved. Therefore time evolution of the local volume fraction is described by the following continuum equation:

$$\frac{\partial \Phi_m}{\partial t} = \nabla \cdot \Phi_m \nabla \frac{\delta F}{\delta \Phi_m} - \nabla \cdot (\mathbf{v} \cdot \Phi_m), \quad (13)$$

where $\mathbf{v}$ is the flow velocity that obeys the Navier–Stokes equation. Now, we rewrite the above equation into a time
evolution equation of the phase field. With the use of equation (2), which is the relation between the volume fraction of the vesicle and the phase field, we obtain the following equation:

\[
\frac{\partial \psi(r)}{\partial t} = \frac{1}{2\varepsilon^2} |\nabla \psi|^2 \cdot \int \frac{\mathbf{r} - \mathbf{r}' \cdot \partial \Phi_m(r')}{|\mathbf{r} - \mathbf{r}'|^3} \cdot \frac{|\nabla' \psi|}{|\nabla' \psi|^2} \cdot \int |\mathbf{r} - \mathbf{r}'| \cdot |\nabla \psi|^2 
+ o(H^2). 
\]

This equation is a perturbation expansion of equation (13) up to the first order in the mean curvature \(H\). On the other hand, Navier–Stokes equation in the presence of the vesicle is expressed as

\[
\rho \frac{\partial \mathbf{v}}{\partial t} = -\nabla P - \mathbf{v} \cdot (\nabla \mathbf{v}) + \nabla \cdot (\mu \nabla \mathbf{v}) - \Phi_m \nabla \frac{\delta F}{\delta \Phi_m},
\]

where \(\rho\) is the concentration of the fluid, and \(\mu\) is the viscosity and the fourth term on the right-hand side is the body force imposed by the vesicle. Combining equations (14) and (15), we obtain the shape deformation of the vesicle in the flow field as shown in figure 3.

Figure 3 represents the shape change of the polymer-containing vesicle in a two-dimensional Poiseuille flow. This is a model of the drug delivery system in a blood vessel. In this simulation, we observe that the vesicle deforms and becomes parachute-like shape similar to that of a red-blood cell in the blood vessel.

5. Conclusion

We calculated equilibrium shapes of vesicles that enclose polymers by using the PF theory and SCFT. As a result, we found that the vesicle prefers to have a prolate shape. The origin of such a shape change is found to be the conformation entropy of the polymers. It is confirmed by an analytical estimation of the conformation entropy, which is consistent with recent experimental result. Moreover, we derived a dynamic equation for the phase field by coupling with the Navier–Stokes equation and simulated the deformation of the vesicle in a two-dimensional Poiseuille flow.

References

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