

Predicting shapes of polymer-chain-anchored fluid vesicles

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We propose a general method for predicting shapes of fluid vesicles with anchored polymers. The method combines the Helfrich curvature elasticity theory for fluid membranes and the self-consistent field theory for polymers, to determine stable and metastable shapes of the vesicles as well as the segment distributions of the anchored chains. We illustrate the method by investigating the shape change of a fluid vesicle induced by a single anchoring polymer chain. Extension to more complicated systems, such as vesicles with multiple anchored chains, block copolymers, or semiflexible chains, is straightforward.

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Lipid bilayers that form the walls of living cells are often “decorated” by a large number of macromolecules, such as proteins, DNA, and polymers. For example, a polymer brush called *glycocalyx* is grafted to the plasma membrane of animal cells through coupling with the membrane-spanning proteins [1]. These bilayers usually are impenetrable by most biomacromolecules in cytoplasm. As a very much simplified model of biological cells, polymer chains anchored to fluid vesicles have recently attracted experimental investigation [2,3]. Complex shape changes, such as budding, pearling, and coiling of the vesicles, can be induced even when a very small amount of polymer chains are anchored and/or adsorbed onto the membranes. These subtle shape changes of vesicles with anchored polymers have also drawn theoretical attention [4–6]. Analytical calculations and Monte Carlo simulations reveal that the anchored chains can induce local inhomogeneities of the bending rigidity and spontaneous curvature of the membrane [4,5]. Adsorption of polymers anchored to membranes was also investigated and for strong adsorption a decrease of the entropically induced membrane curvature was predicted [7]. Furthermore, the anchored polymers with adhesive segments were thought to act as adhesive stickers between membranes, a mechanism that underlies the adhesion of biomembranes [8]; however, repeller molecules anchored to the membranes, such as polyethylene glycol lipids, can induce purely repulsive interaction potentials [9].

Up to now, theoretical studies have accounted for the altering of the spontaneous curvature and bending rigidity of an infinitely large planar membrane. For vesicles, however, due to the closure of the membranes, a different model for closed vesicles with anchored polymers, which has more biological relevance, is needed. In this paper, we propose an approach that combines the Helfrich curvature elasticity theory for fluid membranes and the self-consistent field theory (SCFT) for polymers to satisfy this need. The Helfrich

theory has been extensively used to explore the shape changes of closed membranes under various conditions. It has successfully predicted the diskocyte shape of the red blood cell [10]. For polymer systems, SCFT is the method of choice for numerical studies of equilibrium phases and has yielded quantitative agreement with experiments [11,12]. The combined Helfrich-SCFT theory allows the simultaneous prediction of the shapes of vesicles with anchored polymer chains as well as the segment distributions of these chains.

We consider a polymer-vesicle system in solvent. We assume that the vesicle membrane is infinitively thin but not penetrable by the polymer chains that are outside of the vesicle. The number of solvent molecules is n_s and that of the polymer chains is n_p with each chain of N_p segments. The partition function of such a system can be written as

$$\begin{aligned} \Xi = & \frac{1}{n_s!n_p!} \int \prod_{i=1}^{n_s} DR_s^i \int \prod_{i=1}^{n_p} [DR_p^i(\tau) e^{-\beta H_p^0[R_p^i(\tau)]}] \\ & \times \int DR_m(u,v) e^{-\beta H_m^0[R_m(u,v)]} e^{-\beta H_{\text{int}}} \\ & \times \prod_r \delta[\hat{\rho}_p(r) + \hat{\rho}_s(r) - \rho_0] \\ & \times \delta\left(\int_{r \in V_{\text{in}}[R_m(u,v)]} dr \hat{\rho}_p(r)\right), \end{aligned} \quad (1)$$

where $\beta=1/k_B T$, and $\int DR$ denotes functional integration over configurations of the solvents, polymers, and fluid membrane. R_s^i and $R_p^i(\tau)$ denote the spatial positions of the solvent i and the segment τ of the i th chain, respectively. $R_m(u,v)$ denotes the spatial position of the membrane and u,v are curvilinear coordinates in the membrane surface. $r \in V_{\text{in}}[R_m(u,v)]$ or $r \in V_{\text{out}}[R_m(u,v)]$ denotes that r is inside or outside the volume enclosed by the vesicle membrane, respectively. The first δ function ensures the incompressibility constraint and ρ_0 is the reference density, and the second δ function guarantees that the membrane is impenetrable by polymer chains. The density operators are defined as $\hat{\rho}_s(r)$

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$= \sum_{i=1}^{n_s} \delta(r - R_s^i)$ and $\hat{\rho}_p(r) = \sum_{i=1}^{n_p} \int_0^{N_p} d\tau \delta[r - R_p^i(\tau)]$, and the interaction Hamiltonian includes interactions between the polymer segments and solvent molecules and the membrane, i.e., $H_{\text{int}} = V_{ps} + V_{pm}$, which can be written as $\beta V_{ps} = \chi \int dr \hat{\rho}_s(r) \hat{\rho}_p(r)$ and $\beta V_{pm} = \eta \oint dA \hat{\rho}_p\{r \in A[R_m(u, v)]\}$, where χ and η are the interaction parameters of polymer-solvent and polymer-membrane pairs, respectively, and $A[R_m(u, v)]$ represents the surface of the closed vesicle membrane. The Hamiltonian of the polymer chain can be written as $\beta H_p^0[R_p] = (3/2b^2) \int_0^{N_p} d\tau [\partial R_p(\tau) / \partial \tau]^2$, where b is the Kuhn length of the chain. The Hamiltonian of the vesicle has been proposed by Ou-Yang and Helfrich [14], $\beta H_m^0[R_m] = (\kappa/2) \oint_{R_m(u, v)} dA (2H + c_0)^2 + \lambda \oint_{R_m(u, v)} dA + \Delta p \int_{r \in V_{\text{in}}[R_m(u, v)]} dr$, where H and c_0 are the local mean curvature and spontaneous curvature of the fluid membrane, respectively. κ is the bending rigidity of the membrane, λ can be considered as the tensile stress acting on the membrane, and $\Delta p = p_{\text{out}} - p_{\text{in}}$ is the pressure difference across the membrane.

Following the standard procedure of the SCFT [11], by introducing external fields ω_p and ω_s , which are the self-consistent molecular fields conjugated to the collective densities ρ_p and ρ_s , and the Lagrangian multipliers ξ for the incompressibility of the system, as well as ζ for the impenetrability of the membrane, Eq. (1) can be written as $\Xi = \int DR_m D\rho_s D\rho_p D\omega_s D\omega_p D\xi D\zeta e^{-\beta F\{R_m, \rho_s, \rho_p, \omega_s, \omega_p, \xi, \zeta\}}$, with the functional βF defined as

$$\begin{aligned} \beta F = & -n_p \ln Q_p[\omega_p] - n_s \ln Q_s[\omega_s] + \int dr [\chi \rho_s \rho_p - \omega_s \rho_s \\ & - \omega_p \rho_p + \xi(\rho_p + \rho_s - \rho_0)] + \frac{\kappa}{2} \oint_{R_m} dA (2H + c_0)^2 \\ & + \lambda \oint_{R_m} dA + \Delta p \int_{r \in V_{\text{in}}[R_m]} dr + \eta \oint_{R_m} dA \rho_p \\ & + \zeta \int_{r \in V_{\text{in}}[R_m]} dr \rho_p. \end{aligned} \quad (2)$$

In Eq. (2), the partition function for the solvent molecules $Q_s[\omega_s]$ is defined as $Q_s[\omega_s] = \int dr e^{-\omega_s}$ and the single chain partition function $Q_p[\omega_p]$ is calculated as $Q_p[\omega_p] = \int dr q_p(r, N_p)$, where the propagator $q_p(r, \tau)$ satisfies the modified diffusion equation $(\partial/\partial\tau)q_p(r, \tau) = (b^2/6)\nabla^2 q_p(r, \tau) - \omega_p q_p(r, \tau)$, with the initial condition $q_p(r = R_m(u, v), 0) = 1$ and $q_p(r \neq R_m(u, v), 0) = 0$ for a polymer chain with one of the ends anchored on the vesicle. Since the other end of the polymer is free, a different propagator $q_p'(r, \tau)$ is needed, which obeys a similar diffusion equation with $\partial/\partial\tau$ multiplied by -1 and the initial condition $q_p'(r, N_p) = 1$.

In SCFT one approximates Ξ by the extremum of the integrand $e^{-\beta F}$. Thus the free energy $-(1/\beta)\ln \Xi$ is given by $F\{R_m, \rho_p, \rho_s, \omega_p, \omega_s, \xi, \zeta\}$, where $R_m, \rho_p, \rho_s, \omega_p, \omega_s, \xi$, and ζ are functions for which F attains its minimum. Following Eq. (2), these functions satisfy the self-consistent equations [13]

$$\omega_p = \begin{cases} \eta/b + \chi\rho_s + \xi, & r \in A[R_m], \\ \zeta + \chi\rho_s + \xi, & r \in V_{\text{in}}[R_m], \\ \chi\rho_s + \xi, & r \in V_{\text{out}}[R_m], \end{cases} \quad (3)$$

$$\omega_s = \chi\rho_p + \xi, \quad (4)$$

$$\rho_p = \frac{n_p}{Q_p} \int_0^{N_p} d\tau q_p(r, \tau) q_p'(r, \tau), \quad (5)$$

$$\rho_s = \frac{n_s}{Q_s} e^{-\omega_s}, \quad (6)$$

$$\rho_p + \rho_s = \rho_0, \quad (7)$$

$$\int_{r \in V_{\text{in}}[R_m]} dr \rho_p = 0, \quad (8)$$

and following the standard procedure of the functional minimization for fluid membranes [13,14], we obtain the shape equation of the vesicle in the presence of polymers,

$$\begin{aligned} \{\Delta p + \zeta\rho_p(r = R_m) + \eta\mathbf{n} \cdot \nabla \rho_p(r = R_m)\} - 2\{\lambda + \eta\rho_p(r = R_m)\} \\ \times H + 2\kappa\nabla^2 H + \kappa(2H + c_0)(2H^2 - c_0H - 2K) = 0, \end{aligned} \quad (9)$$

where \mathbf{n} is the unit normal vector and K is the Gaussian curvature of the membrane.

Compared with the general shape equation of vesicles derived by Ou-Yang and Helfrich [14], extra (inhomogeneous) pressure and tensile stress terms appear in Eq. (9). The extra pressure $[\zeta\rho_p(r = R_m)]$ originates from the reduction of the chain conformation entropy due to the spatial confinement of the polymer chains by the impenetrable membrane. The extra tensile stress $[\eta\rho_p(r = R_m)]$ comes from the adhesion of the chain segments onto the vesicle membrane, which simply reflects that if the membrane adsorbs the chain, it reduces the tensile stress and thus the membrane tends to be extended to decrease the free energy (energy benefit). This result coincides with the mean field analysis by Bickel and Marques [15] for an impenetrable fluid membrane ornamented with grafted chains. Moreover, the adhesion of polymer chains onto the membrane also results in additional pressure $\eta\mathbf{n} \cdot \nabla \rho_p(r = R_m)$, which also reflects that the membrane tends to contact more polymer segments if it adsorbs polymer segments.

To demonstrate our combined Helfrich-SCFT approach for exploring vesicle shapes under the effect of polymer chains, we have chosen to first investigate the system in which only a single polymer chain is anchored to the vesicle and restrict our study to a vesicle with axisymmetric shape [13]. For convenience, we set ξ as an inherent property of the fluid vesicle instead of determining it by applying the constraint in Eq. (7). Removing these restrictions is possible but causes more computational efforts and will be presented elsewhere. The numerical scheme we use is as follows. We begin with an initial guess for the vesicle shape (say, sphere), then the self-consistent equations (3)–(8) are solved to obtain $\rho_p(r)$, in which the diffusion equations are solved using an alternate direction implicit scheme [12]. The obtained $\rho_p(r)$ is then inserted into Eq. (9) for calculating the new shape of the vesicle under the influence of $\rho_p(r)$. For axisymmetric vesicles, the shape equation is solved using the algorithm of Seifert *et al.* [16]. These steps are repeated until the conver-

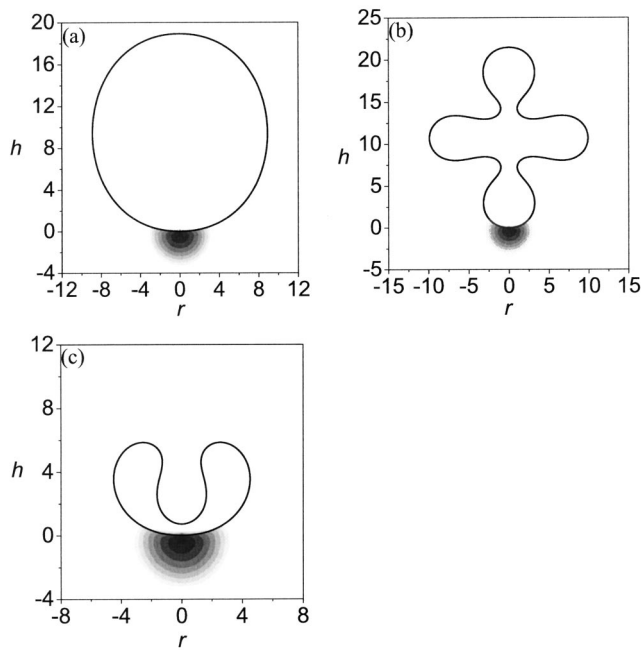


FIG. 1. Typical stationary solutions, including shapes of the vesicle and segment distributions of the anchored polymer chain, to the self-consistent equations. The shape of the vesicle is represented by the solid curve and the density of the polymer chain is drawn in gray scale on a logarithmic scale. The radial (horizontal) and height axes are scaled by $\sqrt{N_p}b$. In all three cases, we use $b=1$, $N_p=200$, $c_0=0$, $\chi=0$, $\eta=0$, and $\zeta=1.5$. (a) $\kappa=5$, $\lambda=-0.003465$, and $\Delta p=0.00005$. (b) $\kappa=1$, $\lambda=-0.00039$, and $\Delta p=0.00001$. (c) $\kappa=1.67$, $\lambda=-0.00036$, and $\Delta p=0.00002$.

gence conditions have been reached. In our numerics, we adopt b (which is the Kuhn length of the chain and also the thickness of the membrane) as the length unit and $k_B T$ as the energy unit. In practice, the diffusion equations are solved with $\Delta r=0.05\sqrt{N_p}b$ and $\Delta \tau=1$.

To verify our numerical procedure, we have solved the shape equation without anchored polymers and observed a set of stationary (either stable or metastable) shapes that is consistent with the result of Seifert *et al.* [16]. For vesicles with a single anchored chain, the combined Helfrich-SCFT approach leads to a variety of interesting shapes, such as dumbbells, pears, diskocytes, and stomatocytes. Several typical shapes of the vesicle and segment density distributions of the anchored polymer are illustrated in Fig. 1. The shapes of the vesicles are described by $h(r)$ with h being the height of the membrane and r the coordinate along the horizontal direction.

In Fig. 1 and the figures following, all the parameters are dimensionless, but can be transformed back to the real physical values by the following rescaling: $\kappa \rightarrow \kappa k_B T$, $\lambda \rightarrow \lambda k_B T / b^2$, $\Delta p \rightarrow \Delta p k_B T / b^3$, $\eta \rightarrow \eta k_B T b$, $\chi \rightarrow \chi k_B T b^3$, $\zeta \rightarrow \zeta k_B T$. Using a length unit (the Kuhn length of the chain and also the thickness of the membrane) $b=5$ nm, the coil size of the polymer chain is calculated to be $\sqrt{N_p}b \sim 100$ nm for $N_p=200$; thus the size of the vesicles in the present calculation can have the order of magnitude of $1 \mu\text{m}$ (note that in all the figures the length is rescaled by $\sqrt{N_p}b$), which is at the limit of optical microscopy. Our calculation therefore suggests longer chains have to be used to facilitate the optical observation of the vesicle shape changes induced by the anchored polymers. Throughout this paper, we have

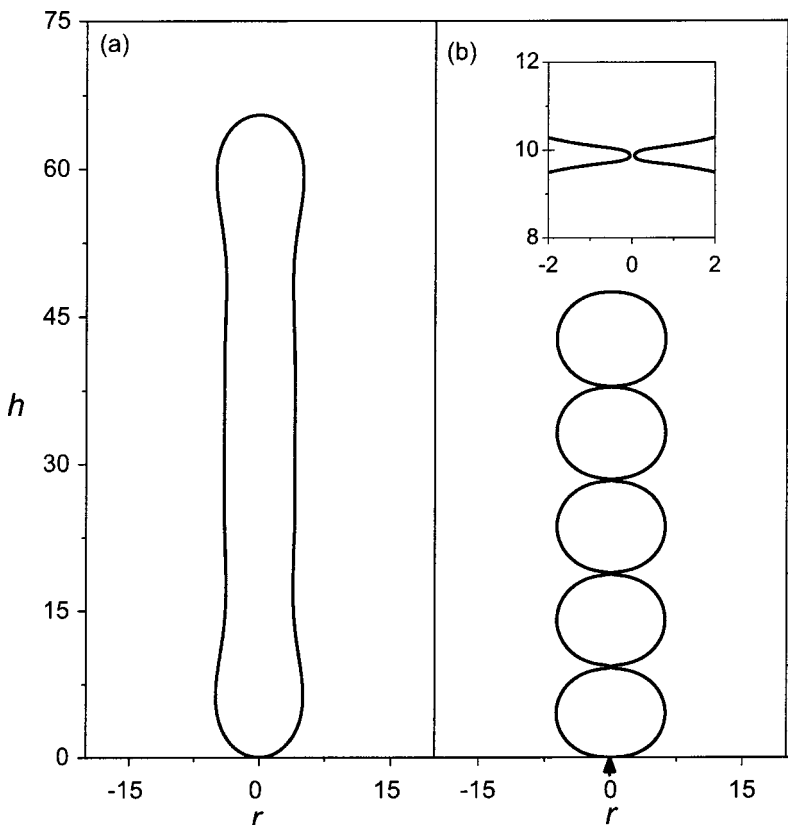


FIG. 2. Pearling transition of tubular vesicles due to polymer anchoring. The tubular vesicle shown in (a) is obtained with parameters $\kappa=1.67$, $c_0=0$, $\chi=0$, $\eta=0$, $\Delta p=0.00001$, $\lambda=-1.5(\Delta p/2)^{2/3}$. The pearly vesicle in (b) is with the same parameters, but a polymer chain with chain length $N_p=200$ anchored, and $\zeta=1.5$ (for clarity, the polymer segment distribution is not drawn and the anchoring point is indicated by an arrow). The radial (horizontal) and height axes are scaled by $\sqrt{N_p}b$. The inset depicts the pore between the bottom pearl and its neighbor.

chosen the κ value to be $1 \sim 25k_B T$, where T is a physiological temperature, as well as λ in the range of $(10^{-5} - 10^{-3})k_B T/\text{nm}^2$. These values of κ and λ can be compared to the typical bending rigidity of a bilayer of phospholipids, which was estimated to be $\kappa \sim 10k_B T$, and the surface tension $\lambda \sim 10^{-3}k_B T/\text{nm}^2$, based on micropipette experiments [17,18]. The pressure difference Δp we used corresponds to 1–10 Pa, and the adsorption-desorption strength (represented by the η term) is in the range of $(-0.1 - 0.1)k_B T$, which are all accessible in real experiments.

Note that due to the disturbing of the polymer chain, a spherical shape is not stable and thus is not observed. In fact, the disturbance of the polymer chain always results in elongation of the spherical vesicles along the axis direction if the surface area of the vesicle is fixed. In general the symmetry of the vesicle shapes is lowered due to the anchored polymer chain.

More dramatic shape change occurs when a polymer chain is anchored to tubular vesicles. For a membrane with zero spontaneous curvature, when $\lambda = -1.5(\Delta p/2)^{2/3}$, the vesicle can form an infinitely long tube with radius $(\Delta p/2)^{-1/3}$ [16]. However, with the same parameters, if a polymer chain is anchored to such a tubular vesicle, the vesicle is always unstable and changes into a shape comprising a chain of “pearls” with radius close to that of the original tube, as shown in Fig. 2. Note that each pearl is still connected with its neighbor through a narrow pore, which is depicted in the inset of Fig. 2(b). “Pearling” states of tubular vesicles have been achieved experimentally either by using laser tweezers [17] or by anchoring polymers [2].

One advantage of the Helfrich-SCFT method is that not only does it predict the shape of the vesicle, but it also provides simultaneously the segment density distribution of the anchored chain. Therefore, we have also investigated the chain segment density distribution for various values of the interaction parameter between the chain segment and the membrane, η . When $\eta \geq 0$, as expected, the polymer is repelled from the membrane surface and thus forms a “mushroom.” When $\eta < 0$, however, the attractive interaction between the segment and membrane could make the chain form a “pancake” covering on the vesicle surface. Figure 3 shows two examples of a polymer coil changing from “mushroom” to “pancake” shape with decrease of η . We have calculated the amount of polymer adsorption on the membrane and found that, when η changes from 0.05 to -0.15 , adsorption increases 5.3 and 4.6 times in Figs. 3(a) and 3(b), respectively. This means that adsorption is indeed happening. Note that, however, by decreasing η (< 0), in Fig. 3(a) the membrane bends toward the polymer, while in Fig. 3(b) it bends away from the polymer. Although counterintuitive, we believe this is reasonable because the bending rigidity κ ($=25$) used in Fig. 3 is much higher than that in all previous cases (where $\kappa \leq 5$); thus the membrane is very rigid and the shape of the vesicle is mostly determined by the membrane itself. Therefore, if (global) free energy minimization requires the membrane bending away from the polymer, although the adsorption interaction favors the membrane engulfing the polymer, it cannot compete with the effect of bending rigidity. However, previous scaling arguments pre-

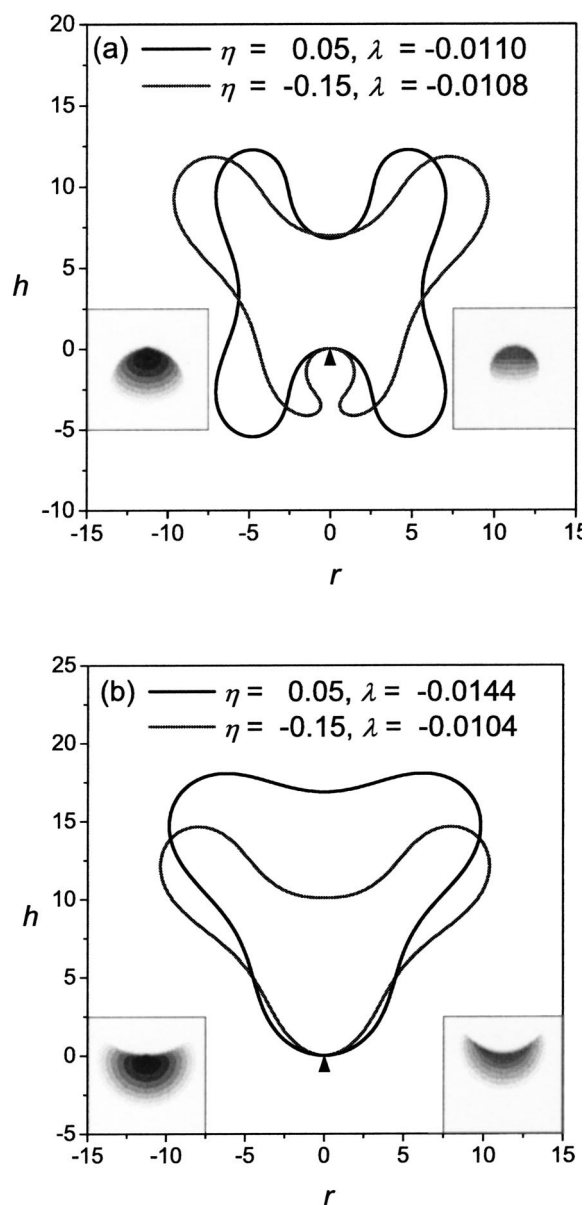


FIG. 3. (Color online) Effect of the polymer-membrane interaction parameter η . The parameters used are $b=1$, $N_p=200$, $c_0=0$, $\chi=0$, $\zeta=1.5$, $\Delta p=0.0003$, $\kappa=25$. The radial (horizontal) and height axes are scaled by $\sqrt{N_p}b$. For clarity, the polymer segment distributions are horizontally moved, and the anchoring points are indicated by arrows.

dicted that the membrane will bend toward the polymer in order to maximize the number of contact points with the pancake shape, while an explicit calculation for ideal chains shows that the sign of the spontaneous curvature may, in general, depend on microscopic parameters [19]. These predictions were all based on a polymer anchored to an infinitely large planar membrane. Our Helfrich-SCFT calculation for finite sized and closed vesicles shows that the local bending of the membrane induced by the anchored chain is subtle. It depends not only on whether the local interactions between the polymer segments and the membrane are attractive or repulsive, but also on the global shape of the vesicle.

In summary, we have proposed a general approach for predicting shapes of fluid vesicles with anchored polymer chains. The central idea is to combine the Helfrich curvature elasticity theory for fluid membranes and the self-consistent field theory for polymers, to determine stable and metastable shapes of the vesicle-polymer systems as well as the segment distributions of the anchored chains. We illustrate the application of the method by investigating the shape change of a fluid vesicle induced by a single anchored polymer chain. We

emphasize that the approach is very general and can be extended straightforwardly to the case of more complicated systems, such as multiple chains, block copolymers, or semi-flexible chains anchored to vesicles.

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