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A phase field model for vesicle–substrate adhesion ☆

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ABSTRACT

In this paper, a phase field model is developed for vesicle adhesion involving complex substrate and vesicle geometries. The model takes into account an adhesion potential that depends on the distance of vesicle to the substrate. A variational problem is solved in a 3D computational domain by minimizing the contribution of bending elastic energy and the adhesion energy under the constraints of total surface area and volume, described via a phase function. An adaptive finite element method is used to efficiently compute the numerical solutions of the model. The computational results are validated through comparison of several axisymmetric shapes with the sharp-interface ODE solution. Moreover, we compute shapes for non-axisymmetric situations to support the observation that concave substrates favor adhesion.

1. Introduction

The Giant Unilamellar Vesicles (GUVs) made up by lipid bilayers have been used as a simplest model for cell membranes without the complexity of membrane bound proteins [23]. They permit the investigations of mechanistic and physicochemical aspects of cell membrane functions. One such function is adhesion which plays an important role in fundamental biological processes [1,17]. There have been much investigation on the adhesion of lipid bilayer vesicles to substrates which could lead to better understanding of the roles played by cell membrane in adhesion [24,30,33,35]. In this work, we develop a phase field approach for the adhesion of vesicles.

In a continuum mechanics description, the GUVs are modeled as two dimensional surfaces embedded in a three dimensional space [32], with their shapes being controlled mainly by the bending elastic energy. For isotropic membranes, the bending energy is formulated by the surface integral of the mean curvature square [20,32]:

$$E = \int_\Gamma c_1 H^2 ds, \tag{1}$$

where Γ is the vesicle surface, H is the mean curvature, and c_1 the bending modulus. During adhesion, the segment of a bound vesicle that interacts with the substrate can experience a variety of intramolecular forces [33] which thus gives rise to an effective adhesion potential $W(\mathbf{x})$ for any $\mathbf{x} \in \Gamma$. With such a consideration, the equilibrium vesicle–substrate adhesion model is given by minimizing the total energy functional

$$\mathcal{E}(\Gamma) = \int_\Gamma c_1 H^2 ds - \int_\Gamma W ds + \Sigma \int_\Gamma ds + p \int dV. \tag{2}$$

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The quantities Σ and p correspond to the Lagrange multipliers for area and volume constraints, respectively, when the vesicle is assumed to conserve its surface area and enclosed volume during adhesion. In a recent study [11], we have investigated the influence of substrate geometry and curvature on the adhesion of vesicle, with the above form of bending elastic energy, in axisymmetric configurations. The contribution due to the Gaussian curvature has been ignored there, with the assumption that the vesicle does not change topology during adhesion.

In this paper, we extend our previously developed phase field diffuse interface models of vesicle membrane deformations to incorporate the effect of vesicle substrate adhesion as modeled by Eq. (2). The phase field model employs a diffuse interface description of the vesicle via a phase field function (order parameter) whose zero level set implicitly defines the vesicle surface Γ [13,14]. The phase field approach has the advantage that a single set of variational equations are defined in the whole computational domain without explicit reference to an interface. This in turn avoids complications in the design of numerical algorithms and provides a natural and systematic account for topology changes. For membrane deformation, this approach has become increasingly popular in the research community in recent years, we refer to [5,8,9,12–14,19,22,26,39] and the references cited therein.

To make a distinction in our presentation, the problem of finding the vesicle surface Γ to minimize the functional in (2) is referred as the sharp interface model. As the interfacial width parameter approaches to zero, the phase field model studied in this paper is consistent to (2). Due to the implicit surface representation of the vesicle, the phase field setting has the advantage of offering greater flexibility in the description of the contact domain (contact zone) with varying topology, which could not be easily addressed by the approach given in [11]. We further discuss an adaptive finite element method for the discretization of the phase field model. Some simulation results based on the adaptive FEM are reported to serve as the validation of both the consistency and the effectiveness of the phase field approach.

2. Discussion on the adhesion potential

There have been many studies on the various forms of adhesion energy between the vesicle and substrate. A particular popular form is modeled via an effective contact potential, that is

$$W(\mathbf{x}) = \begin{cases} w & \text{if} \quad d_s(\mathbf{x}) = 0, \\ 0 & \text{otherwise}, \end{cases} \tag{3}$$

with $d_s(\mathbf{x})$ being the distance of $\mathbf{x}$ to the prescribed substrate and w being a positive constant (here, the subscript s refers to the substrate in order to distinguish from the distance function to the interface Γ used later). Other forms such as the polynomial form [31], or the Morse potential [4] have also been introduced which provide an extra spatial length scale for which the adhesion effect is accounted for and are thus more realistic. As our purpose here is to introduce a general phase field framework that can take into account the adhesion energy which depends on the proximity of the vesicle with the substrate, we consider an adhesion potential W which has the form

$$W(\mathbf{x}) = w \exp(-d_s^2(\mathbf{x})/\delta^2), \tag{4}$$

with δ being a small parameter that determines the range of this potential. We refer to this as a Gaussian potential model due to the particular exponential form used. Notice that in the limit of $\delta = 0$, we effectively recover the contact area formula with the same w. As a verification of this consistency and an examination on how close the results are for small δ, we computed some three dimensional axisymmetric equilibrium shapes based on (3) and (4), respectively. As the parameter δ approaches zero, the solution with the contact area formula (3) is indeed recovered from the limit of the solutions corresponding to the Gaussian potential (4). The comparison of shapes are shown in Fig. 1 and the total bending energies and adhesion energies are provided in Table 1. The data corresponding to $\delta = 0$ refer to the results computed using the contact area formula.

The computation of the axisymmetric shapes with the contact potential is performed with a MATLAB code developed in [11] which handles only the case that the boundary of the contact area is given by a circle. The computation with the Gaussian potential is performed using similar techniques. We note that in the latter case, no assumptions are made on the vesicle being on one side of the substrate, thus, we see the slight protrusion of the vesicle surface into the substrate which are features associated with the use of Gaussian potential. Naturally, it might be unrealistic or less-physical if the protrusion starts to become significant. A geometric constraint can be explicitly imposed to eliminate the protrusion entirely should this become a significant issue. With proper choices of the initial profile and parameters, solutions with substantial protrusions have not been observed even without imposing the non-protrusion assumptions. Moreover, we note that other forms of the adhesion potential, such as the Morse potential would automatically prevent the protrusion because of the fact that the potential grows unbounded as the distance $d_s(\mathbf{x})$ approaches zero.

3. A phase field formulation

For the sharp-interface model, the investigation in the axisymmetric configuration reduced the Euler–Lagrange equations to a system of ordinary differential equations (ODEs) similar to the analysis given in [11]. These ODEs can thus be solved easily using an ODE solver for boundary value problems. In order to study more general substrates and vesicle shapes, we need to work with the more general form of the Euler–Lagrange equations which consist of a set of highly-nonlinear partial