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Simulating vesicle–substrate adhesion using two phase field functions ☆

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ABSTRACT

A phase field model for simulating the adhesion of a cell membrane to a substrate is constructed. The model features two phase field functions which are used to simulate the membrane and the substrate. An energy model is defined which accounts for the elastic bending energy and the contact potential energy as well as, through a penalty method, vesicle volume and surface area constraints. Numerical results are provided to verify our model and to provide visual illustrations of the interactions between a lipid vesicle and substrates having complex shapes. Examples are also provided for the adhesion process in the presence of gravitational and point pulling forces. A comparison with experimental results demonstrates the effectiveness of the two phase field approach.

1. Introduction

It is common in biological systems to see one or more micro-structures contained in a fluid, one type of which is the blood [24]. However, it remains challenging to model and simulate situations in which red blood cells or leucocytes interact with vessel walls or other cells [4,15,26]. The cell membrane is a fluid mosaic of lipids, proteins, and other carbohydrates, with more than 70% of the area composed of lipid molecules [1,36]. Cell membranes composed only by lipids are referred to as *lipid vesicles*. It is known that the properties of lipid molecules determine the shape of the lipid vesicles which were first studied in [18] based on a principle that the equilibrium shape of such a membrane is determined by minimizing the elastic bending energy

$$E = \int_\Gamma a_1 + a_2(H - c_0)^2 + a_3 G \, ds, \tag{1}$$

where H denotes the mean curvature of the membrane surface, a_1 the surface tension, a_2 the bending rigidity, a_3 the stretching rigidity, c_0 the spontaneous curvature that describes the asymmetry effect of the membrane or its environment, and G the Gaussian curvature. For a single-vesicle system, the shape of the vesicle reaches its equilibrium state when the bending energy is minimized subject to a prescribed cell volume and surface area [32].

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In this paper, we investigate the adhesion of a vesicle to a substrate so as to simulate the adhesion of a blood cell to a vessel wall. The physical principle for vesicle–substrate adhesion is that when a vesicle comes near enough to a substrate, probably within a distance of a few nanometers, both adhesive and repulsive forces spontaneously occur between them. The two forces compete with each other until the system reaches an equilibrium state. In the early study [28], a simple model was developed to describe the adhesion of vesicles to interfaces. Additional studies were later carried out to explain the effect of volume change of the vesicle on the adhesion state [19]. Deeper theoretical discussions [20] were proposed to study a large membrane segmentation and a closed membrane surface that is attached to another surface. Later, a more general expression for the adhesion energy and the membrane configuration was presented in Fourier space [33]. The vesicle–substrate adhesion has been extensively studied from several other viewpoints such as the strong adhesion of giant charged vesicles [6], the adhesion of latex spheres to giant vesicles [8], and adhering lipid vesicles with free edges [25].

An important issue in dealing with vesicle–substrate adhesion is to consider the contact potential of the system. In early days, scientists investigated the adhesion of a vesicle to a flat substrate [2,28]. Later, a two-dimensional model was developed to simulate vesicles adhering to a curved substrate [29]. Recently, scientists introduced methods for dealing with a vesicle adhering to a substrate whose shape can be varied [7,27]. The contact energy was formed and explained in [7]. Then, in [37], a phase field function was used to simulate the shape of the vesicle. To discuss the adhesion potential, they introduced a function

$$W(\mathbf{x}) = we^{-d^2(\mathbf{x})/\delta^2} \tag{2}$$

with $d(\mathbf{x})$ denoting the distance from a point $\mathbf{x}$ to a prescribed substrate and w denoting a positive constant; δ is a small parameter that determines the range of the adhesion force. Once the distance between the vesicle and the substrate surpasses this range, the potential energy will decrease exponentially fast. The function W was then inserted into the energetic phase field equation built in [12] and an adaptive finite element method was used to solve the adhesion problem.

In our approach, we introduce a different means from that used in [37] to model vesicle–substrate adhesion. We introduce two independent phase field functions, one simulating the deformation and adhesion process of the vesicle and the other simulating the fixed substrate. The phase field method has been proved to be successful in modeling fluid flows [30,31,35]. For the deformation of a vesicle, we will turn to the energetic phase field model which was very successful in modeling the shape transformation of lipid vesicles. For example, a series of papers have already reported on the success of the energetic phase field model for the simulation of a single vesicle, including the phase field model and its theoretical analysis [9], simulations of equilibrium vesicle shapes [10,12,14], vesicle transformations in fluid fields [11], multi-component vesicles [21,22,34], and retrieval of topological information within the phase field framework [13]. For the adhesion of the vesicle to the substrate, we introduce a contact potential which will be determined using an integral of the two phase field functions on the entire domain multiplied by a potential coefficient. This topic will be discussed in detail in Section 2.1.

One advantage of using two phase field functions to simulate vesicle–substrate adhesion is that the small $d(\mathbf{x})$ indicated in [37] (see (2)) will be implicitly carried in the model by a phase field function. Unlike in [37], we do not need to calculate the distance of every point to the substrate, thus significantly reducing the computational complexity. Moreover, this enables us to simulate substrates with extremely complicated geometric shapes. In Section 4.4, we offer several examples demonstrating the capability of our method for simulating complex substrate shapes.

In our numerical approach, we use a gradient flow method proposed by [5]. The forward Euler scheme is used for time discretization whereas a central difference scheme is used for spatial discretization. Based on our experience in the numerical simulation of single vesicle system in three dimensions, we saw the need for high-performance parallel computing for the simulations. The simulation code is parallelized on shared memory systems via OPENMP.

The paper is organized as follows. First, we formulate our two phase field model for vesicle–substrate adhesion. Detailed discussions are given about the formulation of the contact potential energy. Second, we select an appropriate numerical scheme for discretizing our continuous model in three dimensions. Third, we display our computational results, including several substrate shapes. Moreover, we provide a numerical comparison of our method with the results offered by [37]. Finally, we add two more examples incorporating physical forces, one being a gravitational force coupled with the system and the other being a pointwise pulling force applied to the top of the vesicle. We contrast our results of the second example to experimental results given in [3].

2. Energetic phase field method

We consider a system for which, at the initial time, there is a single vesicle located very close to but separated from a substrate. Due to the adhesion force between these two particles, the vesicle will move closer to the substrate and eventually attach to it. We introduce two phase field functions, $\phi_1(x)$ and $\phi_2(x)$, both defined on the physical domain Ω. The zero surface $\{x : \phi_1(x) = 0\}$ describes the vesicle membrane Γ_1, whereas $\{x : \phi_1(x) > 0\}$ represents the interior of the vesicle and $\{x : \phi_1(x) < 0\}$ its exterior. The zero surface $\{x : \phi_2(x) = 0\}$ describes the surface of the substrate Γ_2, whereas $\{x : \phi_2(x) > 0\}$ describes the region that the vesicle cannot protrude into and $\{x : \phi_2(x) < 0\}$ the region in which the vesicle can move freely. In the phase field modeling, the functions ϕ_i, $i = 1, 2$, are assumed to be nearly constant valued, $+1$ where they are positive and -1 where they are negative, except in thin regions close to the surfaces Γ_i, $i = 1, 2$. The small positive constant parameter ϵ characterizes the widths of the thin regions, i.e., the diffusive interfaces.