Sickle RBC Phase Field Model

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Abstract

In sickle cell disease abnormal beta-globins, known as hemoglobin S (HbS), are produced, and they polymerize to form long, rigid fibers that bend red blood cells (RBCs) into sickle shapes. Many studies and much modeling of the dynamics of HbS polymer fibers have been done to better understand sickle RBCs [1,2,3]. However, the models are computationally expensive and do not describe the HbS fiber-RBC membrane interaction, which occurs at multi-spatial scales, ranging from nanometers to micrometers.

In this poster, we discuss a phase field model for HbS fiber-RBC membrane interaction. Phase field is a global method that describes complex interfaces as a relatively simple function, and it allows topological changes without the need to modify meshes for interface tracking. The RBC membrane is modeled by representing Helfrich elastic bending energy using the phase field function $\Phi(x) = \tanh\left(\frac{d(x,\Gamma)}{2\epsilon}\right)$. The HbS fiber is modeled as a chain of particles, and since the distance information is included in $\Phi(x)$, the interaction between a particle and the membrane is described by $\frac{1}{\Phi_p(x)}$, where $\Phi_p(x)$ is the particle's phase field value interpolated using inverse distance weighting.

Phase-Field Method

Helfrich elastic bending energy of closed lipid bilayer[4] without spontaneous curvature is

$$E = \int_{\Gamma} \frac{k}{2} H^2 \, ds \qquad (1.1)$$

k: bending rigidity
H: mean curvature

The phase field representation of (1.1) using phase field function $\phi = \phi(\mathbf{x}) = \tanh\left(\frac{d(x,\Gamma)}{\sqrt{2}\epsilon}\right)$ defined on a computational domain Ω is

$$E_M(\phi) = \frac{3k}{8\sqrt{2}\epsilon} \int_{\Omega} \left[\epsilon \Delta \phi + \frac{1}{\epsilon} \phi(1-\phi^2) \right]^2 dx \qquad (1.2)$$

As $\epsilon \to 0$,

$$E_M(\phi) \to \int_{\Gamma} \frac{k}{2} H^2 ds$$

where the level sets $\{\mathbf{x} : \phi(\mathbf{x}) = 0\}$ represents the membrane Γ, $\{\mathbf{x} : \phi(\mathbf{x}) > 0\}$ represents the interior of Γ, and $\{\mathbf{x} : \phi(\mathbf{x}) < 0\}$ represents the exterior.

Phase-Field Simulations

Various equilibrium conformations of vesicles can be obtained by minimizing (1.2) with different surface areas and volume constraints[5]. Furthermore, vesicle-vesicle adhesion[6] and dynamics of multi-component lipid membrane[7] can be simulated using multiphase-field methods.
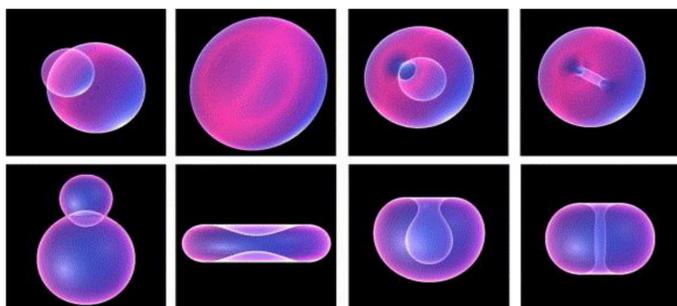
Figure 1. 3D views of equilibrium conformations obtained by minimizing (1.2) with different surface areas and volumes. From left to right: twin-bubble, dimpled-disc, round-pot torus.

HbS Polymer Model

HbS fiber is modeled as a chain of N+1 particles, where the N-1 internal particles function as hinges that allow the chain to bend. By setting the chain segment lengths and the bending angles equal, the chain can be initialized with three central seed particles using Rodrigues' rotation, and the energy of HbS fiber is defined as

$$E_C(\mathbf{P}_0, \mathbf{P}_1, \mathbf{P}_2) = K_b(N-1)(cos\theta + 1)^2 \qquad (2.1)$$

K_b: bending stiffness
$$cos\theta : \frac{(\mathbf{P}_0 - \mathbf{P}_1) \cdot (\mathbf{P}_2 - \mathbf{P}_1)}{l^2}$$

HbS – RBC Membrane Model

The interaction energy between each HbS chain particle and Γ is defined as

$$T(\phi_{\mathbf{P}_i}) = \frac{1}{\phi_{\mathbf{P}_i}} \qquad (2.2)$$

which increases asymptotically as $\mathbf{P}_i$ nears Γ. However, on Ω the particles may not lie on the grid points. Therefore, $\phi_{\mathbf{P}_i}$ is interpolated using inverse distance weighting, and the range of interaction energy can be adjusted with the number of grid points used for interpolating.

Simulation

RBC with a stiff straight HbS chain and RBC with a stiff curved HbS chain is simulated by minimizing the total energy of HbS fiber – RBC membrane model:

$$E_{total} = E_M(\phi) + E_C(\mathbf{P}_0, \mathbf{P}_1, \mathbf{P}_2) + \sum_{i=0}^{N} T(\phi_{\mathbf{P}_i}) \qquad (3.1)$$

with the constraints

$$A(\phi) = \alpha$$
$$V(\phi) = \beta$$
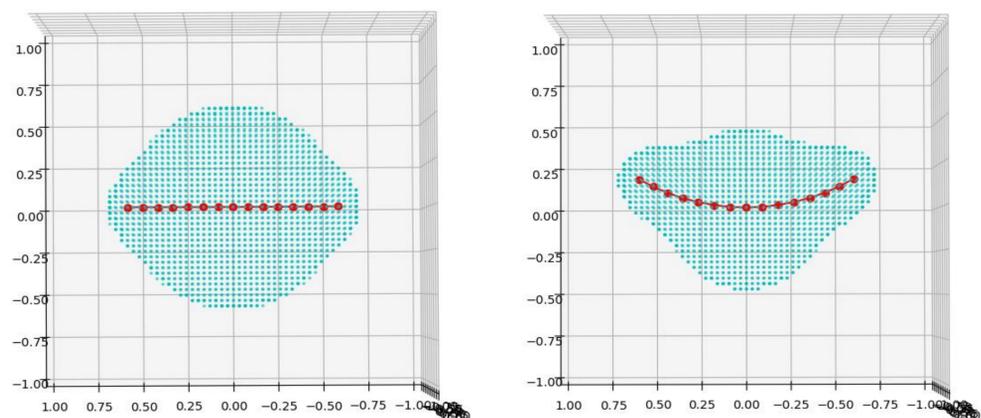
Figure 2. Simulation results of RBC with a stiff straight HbS chain (left) and RBC with a stiff curved HbS chain (right) is shown. 9^3 neighboring grid points were used for each particle's phase field value interpolation, and the total energy was minimized for 100,000 time steps for both simulations.

Future Works

➢ Run various simulations
  ➢ Various HbS chain stiffness
  ➢ Multiple HbS chains (HbS chain – HbS chain interaction)
  ➢ Validate the model by comparing the computational results to experimental results
  ➢ Optimize parameters

➢ Expand the model to include sickle cell – sickle cell and sickle cell – blood vessel interactions

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