Research Project

Mathematical Modelling of Cell Membrane Dynamics

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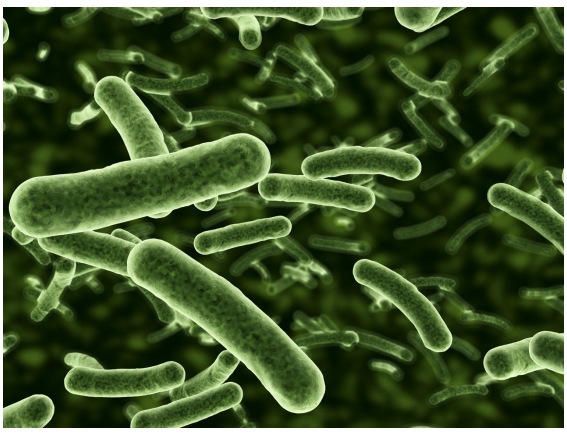

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1 Introduction

First can we detect deceases such as Alzheimer's disease, cancer cells and develop new methods and vaccines [1]. One of the primary components of the cell membranes are lipids which serve many different functions. A key function is that it is consisting of a bilayer of lipids which controls the structural rigidity and the fluidity of the membrane [2]. It also turns out that the lipids often accumulate into so-called lipid rafts which serves as a rigid platform for proteins with special properties such as intracellular trafficking of lipids and lipid-anchored proteins [3].

Modelling of lipid rafts formation can be modelled as a two-phase separation problem based on minimization of the Ginzburg-Landau energy functional [4]

$$\mathcal{E}_{ch}(\Gamma) = \int_{\Gamma} \Psi(c) + \frac{\gamma}{2} |\nabla c|^2,$$

which is describing the chemical energy for a concentration $c : \Gamma \times [0,T] \mapsto [0,1]$ over a surface membrane Γ. Several authors have solved this problem often results by deriving variants of Cahn Hilliard Equation or Allen Cahn Equation if the concentration is not conserved both standstill and evolving domains [4–8] .

Assuming that the system is a single-phase system can the elastic bending energy be modelled using the Canham Helrich energy functional [5, 9]

$$\mathcal{E}_e(\Gamma) = \int_{\Gamma} c_b H^2 + c_k K$$

.

Here is $H = \frac{\kappa_1+\kappa_2}{2}$ denoted as the mean curvature and $K = \kappa_1\kappa_2$ as the gaussian curvature with respectively c_b and c_k as tuning parameters and κ_1 and κ_2 as principal curvatures. Using the Gauss-Bonnet theorem can it be shown that the problem above is equivalent to the so-called Willmore energy functional [10, Ch 8.5 Thm 8.29],

$$\mathcal{E}(\Gamma) = \int_{\Gamma} H^2. \tag{1}$$

This is a well known problem in the mathematical community [11, 12]. In fact, it is a mathematical tool used to study the geometry of surfaces because it can be used to study the properties of minimal surfaces, which are surfaces with the least possible area for a given boundary. This is important in many areas of mathematics, including differential geometry, topology and mathematical physics [13–15].

In this report will we establish a numerical scheme on minimization on this functional. However, we will first establish notation by including a section for definitions and important results from differential geometry. We will then derive the underlying PDE's for this equation. Lastly we will establish the model for the problem and discretize the problem using evolationary parametric FEM methods.

2 Background Theory

We may define $\Gamma(t)$ to be a time evolutionary, smooth compact and oriented surface with no boundary in $\mathbb{R}^3$. We will denote the normal unit vector outer normal vector of $\Gamma(t)$ to be $\boldsymbol{\nu}(\mathbf{x})$ for $\mathbf{x} \in \Gamma$. Now, let v be some vector field defined in $\mathcal{V} \in \mathbb{R}^3$ s.t. the vector $\mathbf{v} = v\boldsymbol{\nu}$ is describing the normal component deformation velocity of the surfaces $\{\Gamma(t)\}_{t=0}^{T}$.

Let us now define a arbitrary energy functional containing some the surface dynamics $\mathbf{v}$ and a evolutionary surface $\Gamma(t)$. We may apply the $L_2(\Gamma)$ gradient flow.

To minimize our energy functional of the surface dynamics will we utilize a method called gradient flows. Gradient flows in surface partial differential equation (PDE) are used to solve physical problems where the surface is changing due to some external force. The PDE describes how the surface changes over time in response to this force, thus allowing us to model real-world phenomena such as fluid and heat flow. The gradient of the surface PDE determines the direction and magnitude of the change over time, while the PDE itself may contain additional terms that modify or influence the solution. [16] An alternative approach would be to solve the problem using standard shape optimization techniques using Γ as a variable surface [17].

To be able do develop the evolutionary PDE's we may introduce the gradient flow of the energy functional (1). Using the definition from [18, 19] can we define the shape derivative of some energy functional

$$\mathcal{J} = \int_{\Gamma} \varphi$$

to be the limit

$$d\mathcal{J}(\Gamma; w) = \lim_{t\to 0} \frac{\mathcal{J}(\Gamma(t)) - \mathcal{J}(\Gamma(0))}{t} \quad \forall w \in \mathcal{V}.$$

Where it is for our case $\varphi = H^2$.

3 Cahn Hilliard Equation on a Closed Membrane

Let c_0 and c_1 indicate the concentration profile of the substances in a 2 -phase system such that $c_0(\mathbf{x},t) : \Omega \times [0,\infty] \to [0,1]$ and similarly $c_1(\mathbf{x},t) : \Omega \times [0,\infty] \to [0,1]$, where $\mathbf{x}$ is a element of some surface Ω and t is time. However, in the 2 phase problem will we will restrict ourself so that $c_0(t,\mathbf{x}) + c_1(t,\mathbf{x}) = 1$ at any $\mathbf{x}$ at time t. A property of the restriction is that we now can express c_0 using c_1, with no loss of information. Hence, let us now define $c = c_0$ so $c(\mathbf{x},t) : \Omega \times [0,\infty] \to [0,1]$. It has been shown that 2 phase system if thermodynamically unstable can be evolve into a phase separation described by a evolutional differential equation [20] using a model based on chemical energy of the substances. However, further development has been done [4] to solve this equation on surfaces. Now assume model that we want to describe is a phase-separation on a closed membrane surface Γ, so that $c(\mathbf{x},t) : \Gamma \times [0,T] \to [0,1]$. Then is the surface Cahn Hilliard equation described such that

$$\rho\frac{\partial c}{\partial t} - \nabla_\Gamma\left(M\nabla_\Gamma\left(f_0' - \varepsilon^2\nabla_\Gamma^2 c\right)\right) = 0 \quad \text{on } \Gamma. \tag{2}$$

We define here the tangential gradient operator to be $\nabla_\Gamma c = \nabla c - (\mathbf{n}\nabla c)\,\mathbf{n}$ applied on the surface Γ restricted to $\mathbf{n}\cdot\nabla_\Gamma c = 0$.

Lets define ε to be the size of the layer between the substances c_1 and c_2. The density ρ is simply defined such that $\rho = \frac{m}{S_\Gamma}$ is a constant based on the total mass divided by the total surface area of Γ. Here is the mobility M often derived such that is is dependent on c and is crucial for the result during a possible coarsening event [4]. However, the free energy per unit surface $f_0 = f_0(c)$ is derived based on the thermodynamical model and should according to [4] be non convex and nonlinear.

A important observation is that equation (2) is a fourth order equation which makes it more challenging to solve using conventional FEM methods. This clear when writing the equation on the equivalent weak form and second order equations arise.

4 Energy Functionals

Let $c(x,t) : \Gamma \times [0,T] \mapsto [0,1]$. From [4] can we observe the energy functionals

$$E_1(c) = \int_\Gamma f(c).$$

where

$$f(c) = f_0(c) + \frac{1}{2}\varepsilon^2\left|\nabla_\Gamma c\right|^2$$

and the conservation law $\rho\frac{\partial c}{\partial t} + div_\Gamma\mathbf{j} = 0$ for the evolution of c, derived from the Ficks Law $\mathbf{j} = -M\nabla_\Gamma\mu$ for the chemical potential derived by the functional derivative $\mu = \frac{\delta f}{\delta c}$. The double well function is denoted as

$$f_0(c) = \frac{\zeta}{4}c^2(1-c)^2$$

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