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Method of Numerical Simulation of Stable Structures of Fluid Membranes and Vesicles

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Abstract: - In this paper we study a methodology for the numerical simulation of stable structures of fluid membranes and vesicles in biological organisms. In particular, we discuss the effects of spontaneous curvature on vesicle cell membranes under the bending energy for given volume and surface area. The geometric modeling of the vesicle shapes are undertaken by means of surfaces generated as Partial Differential Equations (PDEs). We combine PDE based geometric modeling with numerical optimization in order to study the stable shapes adopted by the vesicle membranes. Thus, through the PDE method we generate a generic template of a vesicle membrane which is then efficiently parameterized. The parameterization is taken as a basis to set up a numerical optimization procedure which enables us to predict a series of vesicle shapes subject to given surface area and volume.

Key-Words: - Surface modeling, Fluid membranes, Vesicles, Partial differential equations, Spontaneous curvature, Optimization

1 Introduction

Biological membranes divide living tissues into different smaller parts or cells thus acting as cell border. These cell membranes facilitate the nature of all communications between the inside and the out side of the cells. These communications can take place via the actual passage of ions or molecules between two parts or via conformational changes induced in membrane components. Model bilayer lipid membranes in aqueous environments exhibit many of the attributes of the biological membranes. For example these membranes can form vesicles or more complex structures that divide the space into separate parts by means of blending or dividing.

A lipid molecule is normally based on a polar hydrophilic head and hydrophobic tail consisting of hydrocarbon chains. Such molecules when put in water based solutions can spontaneously combine to form encapsulating bags called vesicles. Due to the physical and chemical properties of these molecules and their environments, an amphiphilic compound can accumulate into a wide range of different types aggregates like spherical, branched, flat miscelles etc [3]. Bilayer type of membrane is the primary structural mechanism of the boundaries of all cell and cell parts. Accordingly the behavior of vesicles composed of lipid bilayers under the effects of different chemical and physical environments have been used as simplified models for the behavior of cells. Theoretical reasoning for the shape or outline adopted by vesicles have tended to follow a continuum model in which the main effect is the bending elasticity of membrane. This is in contrast to the other types of fluid interfaces where surface tension plays the key role.

First time, in 1970 Canham presented these ideas [4]. According to this model and also following later work it has been shown that the vesicles obtain their shapes for which their surface energy is minimal subject to suitable constraints.

Our aim in this paper is to show how Partial Differential Equation (PDE) based geometric modeling combined with numerical optimization can be utilized to study the stable shapes adopted by vesicle membranes. Thus, through the PDE method we generate a generic template of a vesicle membrane which is then efficiently parameterized.

The parameterization is taken as a basis to set up a numerical optimization procedure which enables us to predict a series of vesicle shapes subject to a given surface area and volume.

2 PDE Surfaces

A PDE surface is a parametric surface patch $\mathbf{X}(u,v)$, defined as a function of two parameters u and v on a finite domain $\Omega \subset R^2$, by specifying boundary data around the edge region of $\partial\Omega$. Typically the boundary data are specified in the form of $\mathbf{X}(u,v)$ and a number of its derivatives on $\partial\Omega$. Here one should note that the coordinate of a point u and v is mapped from that point in Ω to a point in the physical space. To satisfy these requirements the surface $\mathbf{X}(u,v)$ is regarded as a solution of a PDE of the form,

$$D^m_{u,v}\mathbf{X}(u,v) = \mathbf{F}(u,v), \tag{1}$$

where $D^m_{u,v}\mathbf{X}(u,v)$ is a partial differential operator of order m in the independent variables u and v, while $\mathbf{F}(u,v)$ is vector valued function of u and v. Since boundary value problems are of concern here, it is natural to choose $D^m_{u,v}\mathbf{X}(u,v)$ to be elliptic.

The PDE method for geometric design is originally developed by Bloor and Wilson as a mechanism of blend shape generation [1]. Since this initial development, the applications of the method have broadened (e.g. see [1, 6, 10, 14, 16, 17]). Thus, apart from the method being utilized in blend and free form shape design, it has been successfully utilized for automatic design for function in various design scenarios. This is achieved by means of incorporating engineering design criteria such as functional constraints into the geometric design of PDE surfaces. Examples of automatic design using the PDE method include automatic design of ship hulls [11], propeller blades [5], aircraft [2] and thin-walled structures [15].

In this paper we use the sixth order PDE for modeling. This PDE provides enough degrees of freedom not only to accommodate tangent, but also curvature boundary conditions and offers more shape control parameters to serve as user controls for the manipulation of surface shapes. In order to achieve real-time performance, we have constructed a surface function and developed a high-precision approximate solution to the 6th order PDE.

PDE-based techniques are able to create free-form surfaces as fast and almost as accurately as the closed-form analytical solutions. Due to the fact that it has sufficient degrees of freedom to accommodate the continuity of 3-sided and 4-sided surface patches at their boundaries, this method is able to model complex surfaces consisting of multiple patches.

2.1 Sixth Order PDE Surfaces

In this work in order to model the complex shapes of membranes we use the elliptic partial differential equations, in particular equations based on the Laplace equation. For ease of setting up the problem with adequate degrees of freedom we use the 6th order PDE which is of the form,

$$\left(\frac{\partial}{\partial u^2} + a^2\frac{\partial}{\partial v^2}\right)^3 \mathbf{X}(u,v) = 0, \tag{2}$$

where $\mathbf{X}(u,v)$ is the surface function for each of the Cartesian coordinates x, y and z. The "smoothing parameter" a controls the relative smoothing of the independent variables u and v and altering a changes the length scale over which the boundary conditions influence the interior of the surface.

Taking the parameter space Ω to be the region $\{u,v : 0 \le u \le 1; 0 \le v \le 2\pi\}$ and a solution that is periodic in v, the solution of Equation (2) can be obtained analytically subject to boundary conditions,

$$\begin{aligned}
&\mathbf{X}(0,v) = f_0(v),\\
&\mathbf{X}(1,v) = f_1(v),\\
&\mathbf{X}_u(0,v) = g_0(v),\\
&\mathbf{X}_u(1,v) = g_1(v),\\
&\mathbf{X}_{uu}(0,v) = h_0(v),\\
&\mathbf{X}_{uu}(1,v) = h_1(v),
\end{aligned} \tag{3}$$

where the subscript u denotes a partial derivative with respect to u. Assuming the solution we are looking for is subject to periodic boundary conditions, the method of separation of variables can be utilized to write the down the solution as,

$$\begin{aligned}
\mathbf{X}(u,v) &= A_0(u)\\
&+ \sum_{n=1}^{N} A_n(u)\cos(nv) + B_n(u)\sin(nv),
\end{aligned} \tag{4}$$

where the coefficient functions $A_n(u)$ and $B_n(u)$ are of the form,

$$A_0 = a_{00} + a_{01}u + a_{02}u^2 + a_{03}u^3 + a_{04}u^4 + a_{05}u^5, \quad (5)$$

$$A_0(u) = a_{00} + a_{01}u + a_{02}u^2 + a_{03}u^3 + a_{04}u^4 + a_{05}u^5,$$

$$A_n(u) = a_{n0}e^{anu} + a_{n1}e^{-anu} + a_{n2}u\ e^{anu} + a_{n3}ue^{-anu} + a_{n4}u^2e^{anu} + a_{n5}u^2e^{-anu}, \quad (6)$$

$$B_n(u) = b_{n0}e^{anu} + b_{n1}e^{-anu} + b_{n2}u\ e^{anu} + b_{n3}ue^{-anu} + b_{n4}u^2e^{anu} + b_{n5}u^2e^{-anu}. \quad (7)$$

Using Fourier analysis, the boundary conditions, $f_0(v), f_1(v), g_0(v), g_1(v), h_0(v)$ and $h_1(v)$ can be written in the form,

$$f_0(v) = c_{00}(u) + \sum_{n=1}^{N}[c_{n0}(u)\cos(nv) + d_{n0}(u)\sin(nv)], \quad (8)$$

$$f_1(v) = c_{01}(u) + \sum_{n=1}^{N}[c_{n1}(u)\cos(nv) + d_{n1}(u)\sin(nv)], \quad (9)$$

$$g_0(v) = c_{02}(u) + \sum_{n=1}^{N}[c_{n2}(u)\cos(nv) + d_{n2}(u)\sin(nv)], \quad (10)$$

$$g_1(v) = c_{03}(u) + \sum_{n=1}^{N}[c_{n3}(u)\cos(nv) + d_{n3}(u)\sin(nv)], \quad (11)$$

$$h_0(v) = c_{04}(u) + \sum_{n=1}^{N}[c_{n4}(u)\cos(nv) + d_{n4}(u)\sin(nv)], \quad (12)$$

$$h_0(v) = c_{05}(u) + \sum_{n=1}^{N}[c_{n5}(u)\cos(nv) + d_{n5}(u)\sin(nv)]. \quad (14)$$

The vector constants of the general solution a_{ni} and b_{ni} are calculated from the vector constant c_{ni} and d_{ni} of the Fourier terms associated with the boundary conditions, where $i = 0,1,2,3,4,5$.

Figure 1 shows sample PDE surfaces generated by varying the Fourier modes associated with the boundary conditions. As one can see that a wide variety of surface shapes can be generated by varying the Fourier modes associated with the boundary conditions. Thus, in this work we use the Fourier modes associated with boundary conditions as a basis of parameterzing the shape of the surface.

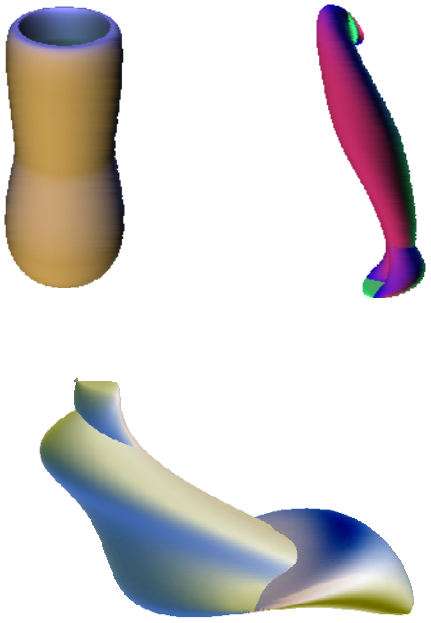

Figure 1. Sample PDE surfaces generated by varying the Fourier modes associated with the boundary conditions.

3 Mathematical Modeling of Vesicle Energy

The simplest models for the biological cells and molecules are single component vesicles, which are bilayers assembled by certain amphiphilic molecules in water. The equilibrium shape of such a membrane may be determined by the asassociated energy

function. These usually consist of the following bending energy [7, 8],

$$E_{elastic} = \int_{\Gamma} \frac{k}{2} H^2 ds, \quad (15)$$

where $H = \frac{(k_1+k_2)}{2}$ is the mean curvature of the membrane surface, with k_1 and k_2 being the principal curvatures. The principal curvatures are the eigenvalues of the Weingarten matrix of the surface [7, 8]. The parameter k is called the bending rigidity. Note that k usually depends on the local heterogeneous concentration of the molecules.

The bending energy in Equation (15) is a special case of a general form obtained using the Hooke's Law [12],

$$E = \int_{\Gamma} (l + m(H - k_0)^2 + nG) ds, \quad (16)$$

where G, l, m, n and k_0 are the Gaussian curvature, surface tension, bending rigidity, stretching rigidity and spontaneous curvature respectively. The spontaneous curvature describes the asymmetry effect of the membrane.

In the energy model we have utilized here the first term l can be neglected, as it remains constant for the vesicles with a given surface area. For a smooth compact surface with a constant n, the last term is related to the Euler index which represents the topological structure of the membrane [7]. For simplicity, here we only consider the energy given in Equation (16) and the case where the bending rigidity is a constant. Thus, if $l = 0 = n$ and $m = 1$ in Equation (16), the bending energy can be simplified as,

$$E = \int_{\Gamma} (H - k_0)^2 ds. \quad (17)$$

From the above Equation we can see that only the effect of the spontaneous curvature is retained and the bending rigidity is assumed to be a constant.

Thus, the problem considered in this paper is to study the vesicle shapes minimizing the bending energy given in Equation (17) with constraints on the cell volume and surface area.

We now assume that we have a domain Ψ in $\Re^3$, and a smooth compact surface $\Gamma \subset \Psi$ which is the candidate surface that minimizes the bending energy given in Equation (17). By following the work from [7], the bending energy can be defined as,

$$E(\phi) = \int_{\Psi} \frac{1}{\varepsilon} \left(\varepsilon \Delta \phi + \left(\frac{1}{\varepsilon} \phi + K \right) \left(1 - \phi^2 \right) \right)^2 dx \quad (18)$$

where $K = \sqrt{2} k_0$, $\phi(x) = \tanh(\frac{d(x)}{\sqrt{2}\varepsilon})$ is the so called phase field function defined for all $x \in \Psi$ and $d(x)$ is the signed distance between point x and Γ. $\phi(x)$ is utilized to mark the vesicle membrane through its sharp transition layer. ε is a transition parameter and it is taken to be a very small.

With the above formulation the cell energy function, which is to be minimized, is of the form,

$$F(\phi) = E(\phi) + (V(\phi) - v)^2 + (A(\phi) - a)^2, \quad (19)$$

where v and a are the cell volume and area respectively and $V(\phi)$ and $A(\phi)$ are the target vesicle volume and surface area respectively.

4 Results

The approach to predicting the stable shapes of vesicles is to utilize the 6th order PDE method for surface parameterization which is coupled with a design optimization algorithm. The parameterization is achieved through the Fourier series representing the boundary conditions of the chosen PDE. The optimization is performed by solving a constrained optimization problem using an augmented Lagrange multiplier method [9] along with the Broyden-Fletcher-Goldfarb-Shanno (BFGS) method [13] whereby the objective function is taken to be that given in Equation (19).

With the above formulation, the optimization is started at some initially chosen point in the parameter space within the Fourier domain. The routine allows to detect the local minimum of the surface energy for a given value of the spontaneous curvature, vesicle volume and surface area. To achieve this a starting value of spontaneous curvature, vesicle volume, surfaces area and a starting set of values of Fourier modes for the design parameters of the PDE are chosen. The optimisation procedure then enables to locate a stationary state for the energy of the vesicle. Hence for a given value of spontaneous curvature, once this initial stationary state is found the optimization is repeated

by incrementing the volume until further stationary states are found.

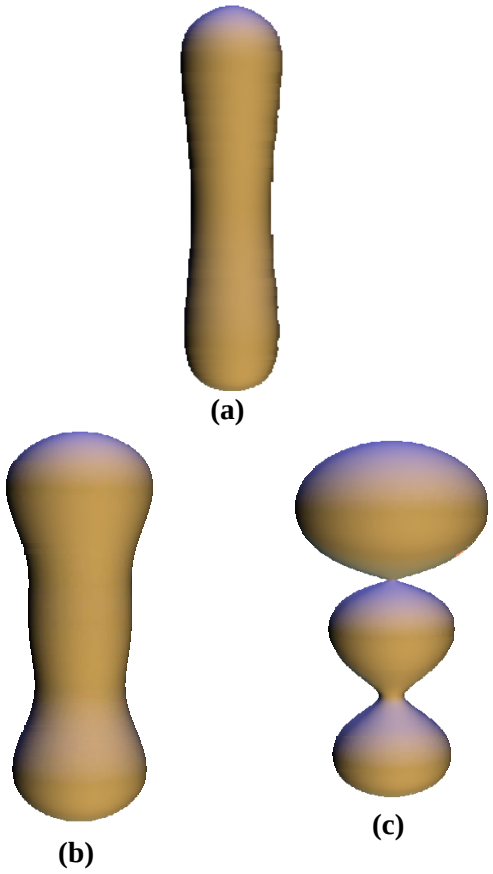

Figure 2. Sample stationary vesicle shapes obtained with varying spontaneous curvature and volume.

Figure	K	$V(\phi)$	$A(\phi)$
2(a)	0.00	0.60	12.55
2(b)	2.51	0.67	12.53
2(c)	4.22	0.74	12.56

Table 1. Values of spontaneous curvature, vesicle volume and surface area for the stationary shapes shown in Figure 2.

Figure 2 shows some sample stationary shapes obtained for a given value of spontaneous curvature, vesicle volume and surface area. The parameter values taken for this simulation is shown in Table 1.

Figure 3 shows some sample stationary shapes obtained for various volumes and surface area with a given spontaneous curvature value. Here the spontaneous curvature value is taken to be 6.0. Table 2 shows the various parameter values taken for this simulation.

Note all the stationary vesicle shapes obtained in the simulations we have undertaken are verifiable. Interested reader is for example referred to [8].

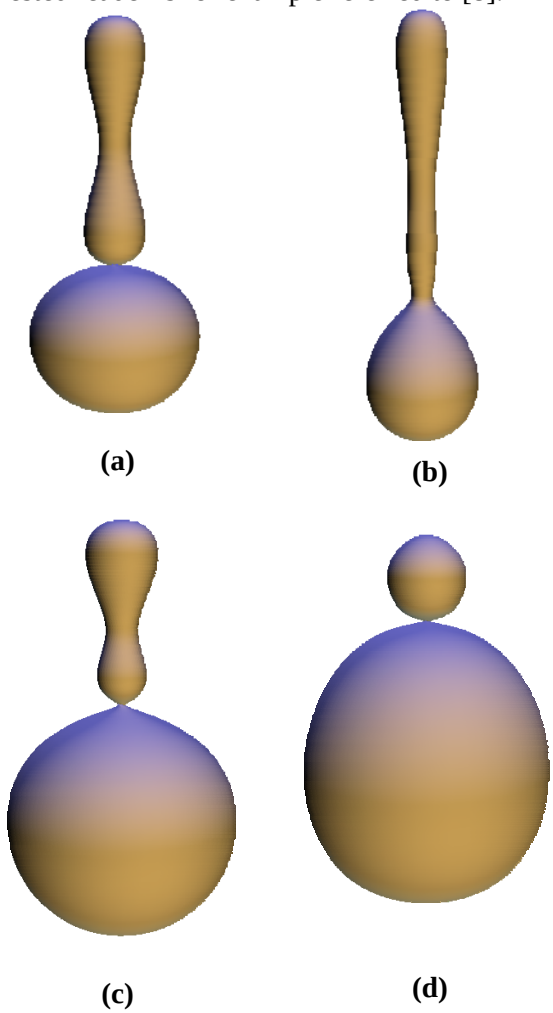

Figure 3. Sample stationary vesicle shapes for spontaneous curvature of 6.0 with varying volume and area.

Figure	$E(\phi)$	$V(\phi)$	$A(\phi)$
3(a)	2.12	0.50	12.01
3(b)	2.37	0.74	12.49
3(c)	2.80	0.82	12.58
3(d)	3.54	0.90	13.11

Table 2. Values of vesicle volume, surface area and bending energy for the stationary shapes shown in Figure 3.

5 Conclusion

In this paper we have demonstrated how one can study the effects of spontaneous curvature on the vesicle cell membrane under the bending energy for given volume and surface area. For this purpose, we utilized a sixth order PDE which is flexible for

efficiently parameterizing the vesicle geometry. Thus, we have demonstrated how the choice of a PDE model enables us to create the geometry corresponding to complex biological vesicles.

In order to simulate the stable structures of vesicle shapes, the geometry parameterization using the PDE is coupled with an optimization routine. This enables us to efficiently predict the stationary structures corresponding to a given spontaneous curvature, vesicle volume and surface area. Several examples of possible stationary shapes that resulted in our simulation are shown.

We have shown that the PDE based method we have presented in this paper is capable of efficient parameterization of complex geometry. Our future work will include extending the shape parameterization methodology in order to cater for complex geometry involving arbitrary topology changes.

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