NUMERICAL SIMULATIONS FOR VESICLE MEMBRANES USING THE PHASE FIELD MODEL

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The Goal of the Research

- To understand the way vesicle membranes deform if given an arbitrary initial shape
- Reconfirm that the phase field model is an excellent method in describing changes in the topology of the cell membrane
- Visualize the results to help further deepen our knowledge of vesicle shapes
The Cell Membrane

- Components of the Membrane
  - Phospholipid bilayer
  - Hydrophilic Head
  - Hydrophobic Tails
- Properties of the Membrane
  - Strength
    - Internal bulk
    - External fields
  - Permeability
Minimizing the elastic bending energy

\[ E = \int_{\Gamma} \left( a + b(H - c_0)^2 + cK \right) ds, \]

\[ H = \frac{k_1 + k_2}{2} \]

\( H = \text{Mean Curvature}, \ a = \text{Surface Tension}, \ b = \text{Bending Rigidity} \)
\( c = \text{Stretching Rigidity}, \ Co = \text{Spontaneous Curvature}, \ K = \text{Gaussian Curvature} \)

- Minimizing the elastic bending energy
- The first and last term may be neglected because they only matter with changing surface area, in some cases \( Co \) may also be neglected.

\[ E = \int_{\Gamma} \frac{k}{2} (H - c_0)^2 \ ds \]
Phase Field Model

- Can be viewed as a level-set method
- Allows topological changes on the interface
- Describes complex surfaces relatively simply
- Much easier than other numerical methods of implementation
- The Phase Field model quickly finds the equilibrium membrane shape
Phase Field Model

1. Introduction of phase function \( \varphi(x) \), which is defined in the computational domain \( \Omega \)

2. Define \( \Gamma \) to be the level set that gives the cell membrane

3. We visualize the level set
   1. \( \{ x : \varphi(x) = 0 \} \) gives the membrane
   2. \( \{ x : \varphi(x) > 0 \} \) represents the inside of the membrane
   3. \( \{ x : \varphi(x) < 0 \} \) represents the outside of the membrane
Ideal phase field function

- $d$: distance function
- $+1$ inside, $-1$ outside
- Sharp interface as $\varepsilon \to 0$

$$\phi(x) = \tanh\left(\frac{d(x, \Gamma)}{\sqrt{2\varepsilon}}\right)$$
Minimize

\[ E = \int_G \frac{k}{2} (H - c_0)^2 \, ds \]

\[ E(\phi) = \frac{1}{\epsilon} \int_{\Omega} (\epsilon \Delta \phi + \frac{1}{\epsilon} (1 - \phi)^2 \phi)^2 \, dx \]

As we minimize, we will notice that H goes to zero.

If our Phase Field Model is accurate the mean curvature will eventually be zero, or as close to it as possible.
Minimization of Bending Energy

\[ E'(\varphi) = \lim_{h \to 0} \frac{E(\varphi + h\psi) - E(\varphi)}{h} \]

\[ E'(\varphi) = \frac{1}{\varepsilon} \int R \Delta\varepsilon \left( 2\varepsilon \Delta\varphi + \frac{2}{\varepsilon} \varphi - \frac{4}{\varepsilon} \varphi^2 + \frac{2}{\varepsilon} \varphi^3 \right) + \left( -\frac{4}{\varepsilon} \varphi + \frac{3}{\varepsilon} \varphi^2 + \frac{1}{\varepsilon} \right) (2\varepsilon \Delta\varphi + \frac{2}{\varepsilon} \varphi - \frac{4}{\varepsilon} \varphi^2 + \frac{2}{\varepsilon} \varphi^3) \cdot \psi \, dx \]

\[ \lim_{h \to 0} \frac{E(\varphi + h\psi) - E(\varphi)}{h} = \int G(\varphi) \cdot \psi \, dx \]

\[ G(\varphi) = \frac{1}{\varepsilon} \left( 2 \left( \varepsilon \Delta\varphi + \frac{1}{\varepsilon} (1 - \varphi)^2 \varphi \right) \right) + \frac{1}{\varepsilon^2} (3\varphi - 1)(\varphi - 1) \left( 2 \left( \varepsilon \Delta\varphi + \frac{1}{\varepsilon} (1 - \varphi)^2 \varphi \right) \right) \]
The Minimization Algorithm

\[ G(\varphi) = \frac{1}{\varepsilon} \left( 2 \left( \varepsilon \Delta \varphi + \frac{1}{\varepsilon} (1 - \varphi)^2 \varphi \right) \right) + \frac{1}{\varepsilon^2} (3\varphi - 1)(\varphi - 1) \left( 2 \left( \varepsilon \Delta \varphi + \frac{1}{\varepsilon} (1 - \varphi)^2 \varphi \right) \right) \]

- When \( h \) is small \( E(\varphi + h\psi) \leq E(\varphi) \), which means \( E(\varphi_{next}) < E(\varphi_{previous}) \)

- Thus \( G(\varphi_{next}) < G(\varphi_{previous}) \), and we keep doing these iterations until the change between the two becomes very very small.

- Fast Fourier Transform package, FFTW, is used to accelerate the program’s runtime.
void Define_phi_Random4(double *phi)
{
    double x,y,z, radius;
    for(int k=0; k< nz; ++k)
    {
        z=-M_PI+hz*k;
        for(int j=0; j<ny; ++j)
        {
            y=-M_PI+hy*j;
            for(int i=0; i<nx; ++i)
            {
                x =-M_PI+hx*i;
                radius =(1/((x*x) + (y*y)))-z;
                if(radius >=0)
                    phi[(k*ny+j)*nx+i]= 1;
                else
                    phi[(k*ny+j)*nx+i]= -1;
            }
        }
    }
}

• Defines Phi as you chose, to give any initial shape

• Defines all numerical entries in the computational domain Omega

• We defines X, Y, and Z to be 64…..

• How many entries will we have in our computational domain?
  • 262,144
Visualization Method

• Open the Data file Matlab and run this code on it

```matlab
v = reshape(data, 64, 64, 64);
p = patch(isosurface(v, 0));
isonormals(v, p);
set(p, 'FaceColor', 'blue', 'EdgeColor', 'none');
daspect([1 1 1])
view(24, 12);
grid on;
camlight
lighting phong;
```

• The Isosurface is shows the level set \( \{ x : \varphi(x) = 0 \} \)

• An Isosurface is a 3D version of a contour map
The equilibrium shape of a flat ellipse shape is a torus

Ref: Wang, 2006
A nonsymmetrical torus eventually becomes a symmetric torus.
Previous Work...(3)

Initial vesicle shape with a slightly larger surface area

Initial vesicle shape with a slightly smaller surface area
Previous Work...(4)

LEFT : Two or three spheres merge into a torus

RIGHT : Six spheres merge into a cylinder
Previous Work...(5)

Nine spheres merge into a membrane with pump and holes
Previous work has focused on membranes with spherical geometries. Ex., Liposomes and Micelles.

These results can be easily compared to experiments.

My study focuses on bilayer membrane which are difficult to investigate using experiments.
Test 1: Cayley Cubic

Cayley Cubic
Test 2: Clebsch
Test 3: DingDong
Test 4:

Spheroid
Test 5: Trumpet
Test 6:

Whitney's Umbrella
Test 7: Simpson's
Conclusion

- The equilibrium membrane shape is largely unpredictable and can vary widely with the smallest of differences.
- The equilibrium shape is always the closest shape possible to a minimum surface.
- A minimum surface is a surface with a mean curvature of zero.
- The phase field model is a very powerful method of extracting intricate topological changes.
- Any research in biological sciences is always beneficial and aids in medical advances.
References

- Phase field models and simulations of vesicle bio-membranes, Xiaoqiang Wang, Pennsylvania State University, 2005.
- Modeling and Simulations of Multi-component Lipid Membranes and Open Membranes via Diffusive Interface Approaches, Qiang Du and Xiaoqiang Wang, submitted to *Journal of Mathematical Biology*, 2006