Dynamical Modeling and Simulation of Fluid Bio-Membranes

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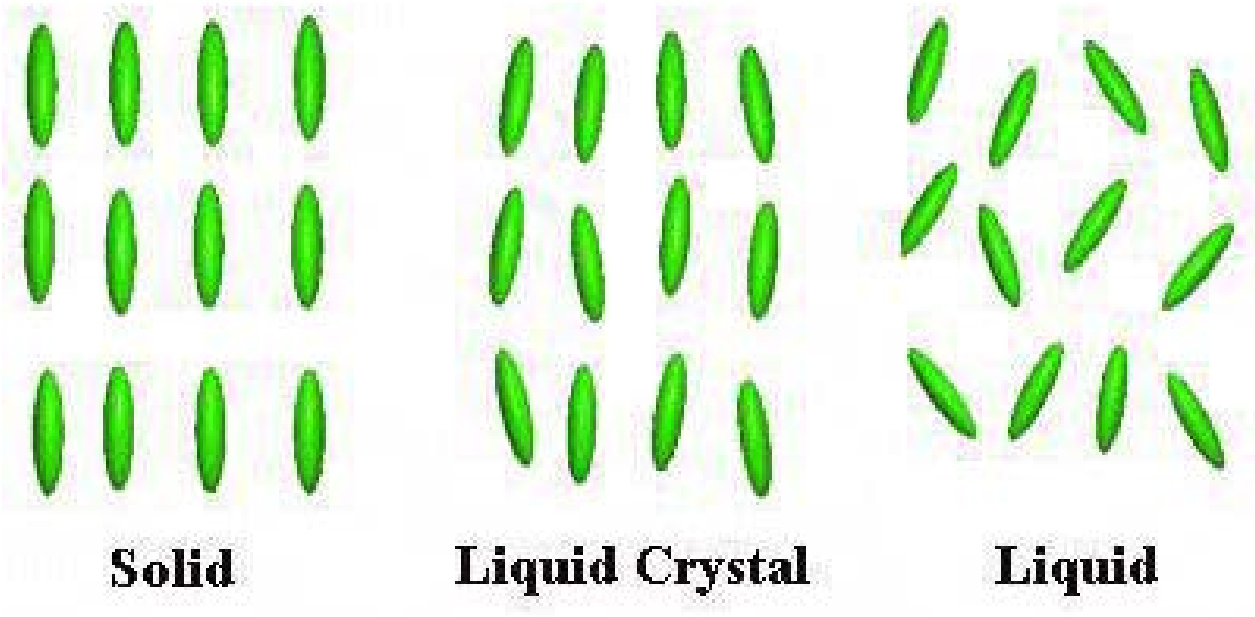
Outline

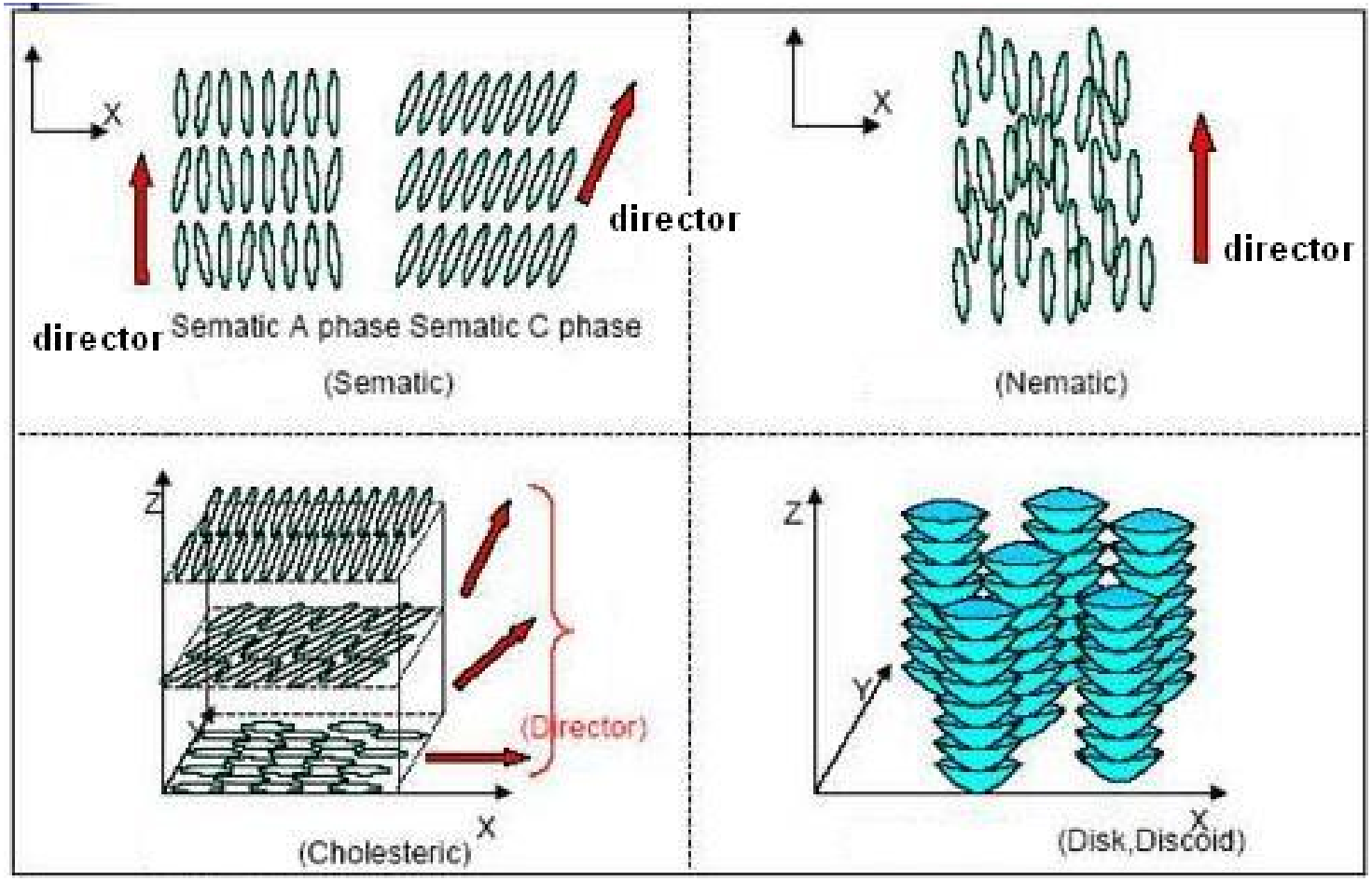
The Mathematical Modeling of Membrane

What is A Liquid Crystal

- A liquid crystal was first reported about 120 years ago by Reinitzer when he was studying the physical properties of cholesteryl esters.
- There are many different liquid crystalline subphases that have been identified and characterized, for example: **nematic, smectic and columnar phases**.
- Thermotropic LCs exhibit a phase transition into the LC phase as temperature is changed, whereas lyotropic LCs exhibit phase transitions as a function of concentration of the mesogen in a solvent (typically water) as well as temperature.
- The type of LC that may be observed depends heavily on the structure of the constituent molecules or groups of molecules (building block: rod-like, disk like, main-chain or side-chain polymers etc.).

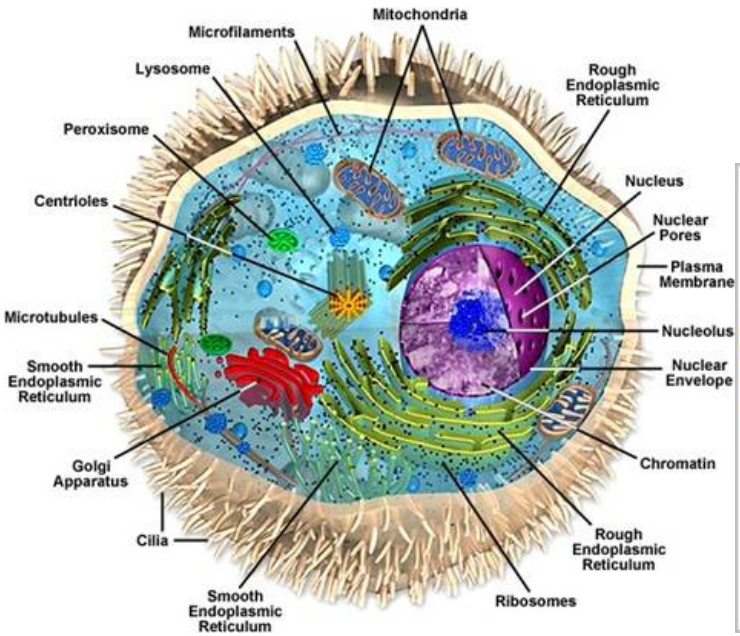


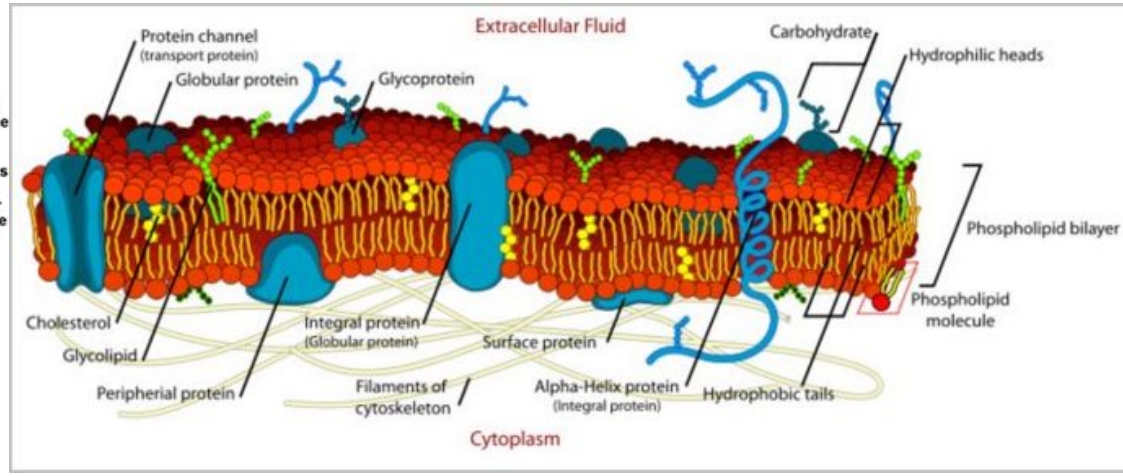
The Different Phases of LCP



What is a Cell Membrane

The cell membrane is the biological membrane separating the interior of a cell from the outside environment. It is a semipermeable lipid bilayer found in all cells. It contains a wide variety of biological molecules, primarily proteins and lipids, which are involved in a vast array of cellular processes such as cell adhesion, ion channel conductance and cell signaling.





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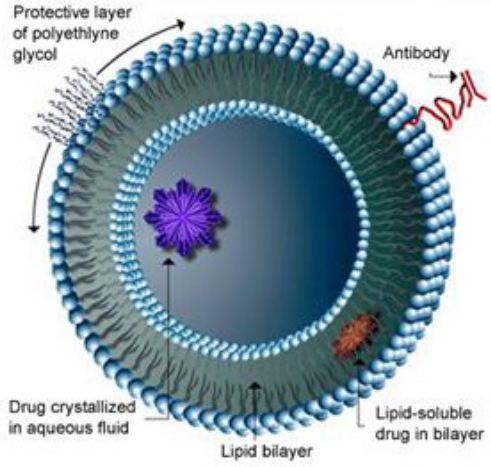
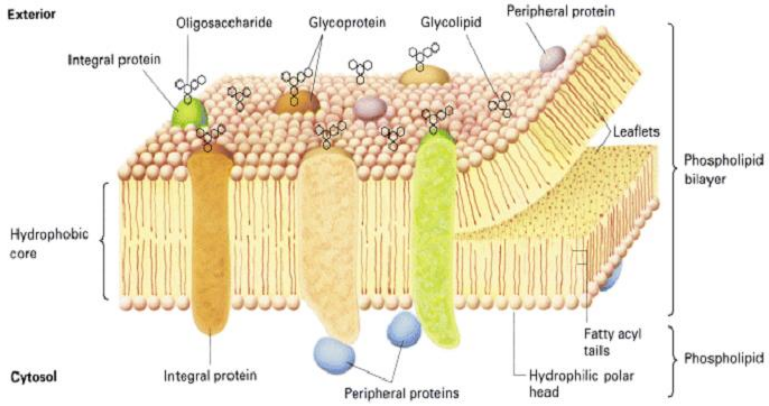
Fluid Mosaic Model

The accepted picture of biomembrane is the fluid mosaic model proposed by Singer and Nicolson in 1972. The biomembrane is considered simply as a bilayer of amphiphilic lipids in which the lipid molecules can move freely on the membrane surface just like ordinary liquid molecules, while the protein molecules and the enzyme molecules are embedded in the lipid bilayer. Some of protein molecules and the enzyme molecules may traverse in the entire lipid bilayer and communicate with both the inside of the cell and its environment. Other protein molecules and enzyme molecules are partially embedded in the bilayer and play other biological function.





- The bilayer is about $6 \sim 10$ nm in thickness;
- The diameter of a normal red blood cell is about $7 \sim 8$ μm.

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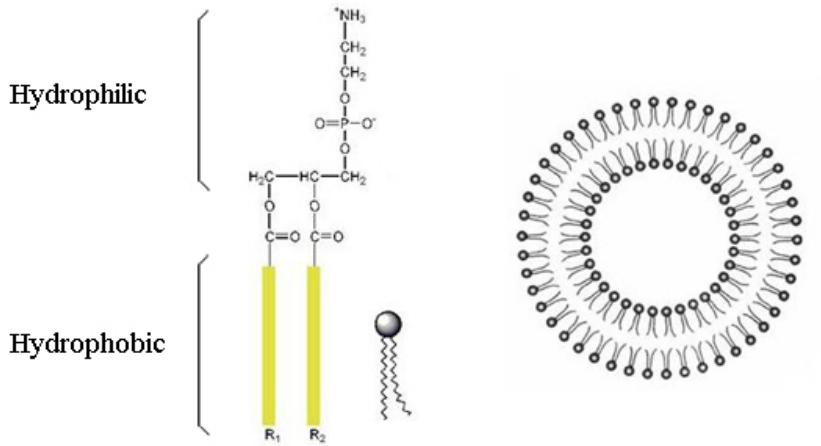
The Lipid Bilayer

The lipid molecules of the model biomembrane must organize themselves into bilayer in which the hydrophilic polar shield the hydrophobic tails from the water surrounding the membrane.

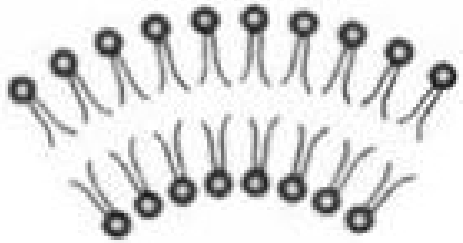


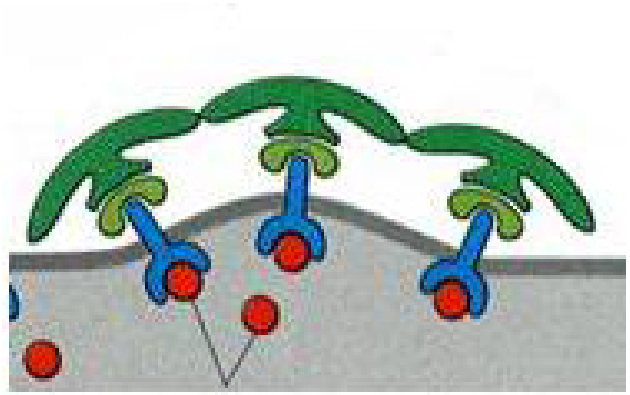
The basic properties of membrane:

- Fluidity (diffusion, viscous or visco-elastic effects)
- Incompressibility (the surface area is locally conserved)
- Asymmetry of the two monolayers
  - The numbers and kinds of lipids are different
  - Different associated proteins
  - Environment

Spontaneous Curvature and Complexity in Biomembrane

The asymmetry of the two monolayers causes spontaneous curvature.





- The difference between the numbers of lipids in two monolayers;
- Some proteins, such as extrinsic protein spectrin in red blood cell's membrane.

It should be pointed out that real biomembrane are structurally much more complicated than we have already mentioned. They are mixtures of a lot of different lipids and components such as cholesterol, cytoskeleton, etc.

Atomistic and Coarse-Grained Modeling

Atomistic models describe the full chemical details of the membrane. In coarse-grained models, a small number of atoms are lumped together into an effective particle. These particles then interact via coarse-grained, simplified interactions. Simulations with microscopic modeling are often done with molecular dynamics simulation. The microscopic approach provides more detailed information about the local structural properties of membranes, but they can only access limited time and length scales.

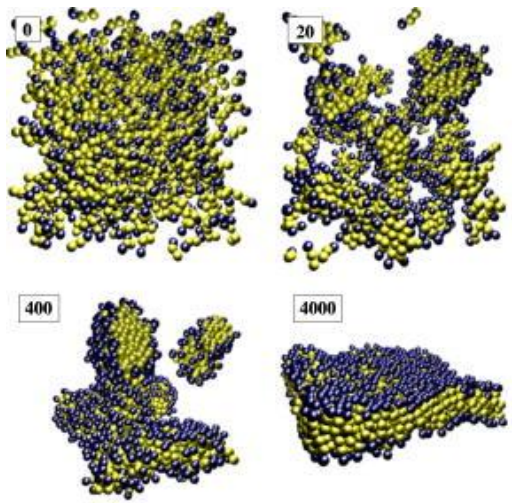


Fig. 1. Snapshots from a simulation using coarse-grained model showing the spontaneous self-assembly of lipids. The lipid head groups are shown in blue, while tails are shown in yellow. The image is taken from I. R. Cooke and M. Deserno, J. Chem. Phys, 123, 224710 (2005).

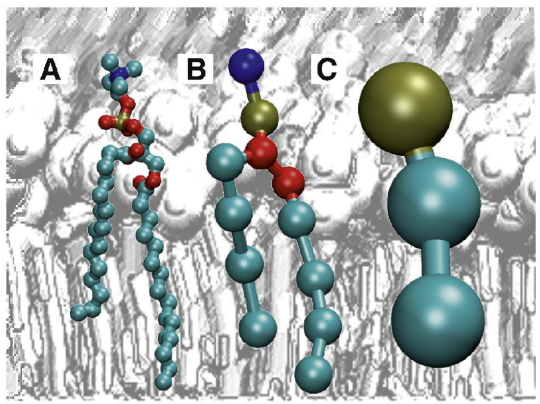


Fig. 2. Different levels of modeling. (A) atomistic model (B) and (C) coarse-grained models. The image is taken from S. J. Marrink, A. H. de Vries and D. P. Tieleman, Biochimica et Biophysica Vol 1788 (2009), Issue 1, 149-168.

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Helfrich Elastic Model of Membrane

Wolfgang Helfrich (1973) deduced the expression for the elastic energy of curvature per unit area of the membrane as

$$g_c = \frac{1}{2}\kappa(c_1 + c_2 - c_0)^2 + \tilde{\kappa} c_1 c_2$$

where c_1, c_2 are two principal curvatures of the surface of the membrane, and the constant c_0 is called the spontaneous curvature of the membrane surface. The total bending energy of the membrane $\mathcal{F}$ is often referred to as the total bending energy of the membrane, is given by

$$\mathcal{F} = \int g_c dA$$

The constant c_0 can be attributed to the mean curvature of the membrane with asymmetric chemical composition of layers in bilayer or the environment and is closely related to the 'spontaneous splay' of the liquid crystals. The constant κ is the bending rigidity and $\tilde{\kappa}$ is the elastic modulus of the Gaussian curvature. By comparing with the curvature elasticity of liquid crystals, both κ and $\tilde{\kappa}$ are found to be in the order of the product of the elastic constants of lipid bilayer and the thickness of the membrane. The Helrich free energy of lipid membranes and is generally recognized as the basic quantity in dealing with the mechanical behavior of biomembranes in the liquid crystal phase.

The Dynamic Model of Membrane

Two alternative opinions:

- The membrane moves with stresses and couples exerted by bulk fluid. (Waxman, Steigmann, Cai and Lubensky, etc.)
- The membrane moves along with the bulk fluid and produces surface stresses. (Porzrikidis, Seifert, Miao, etc.)

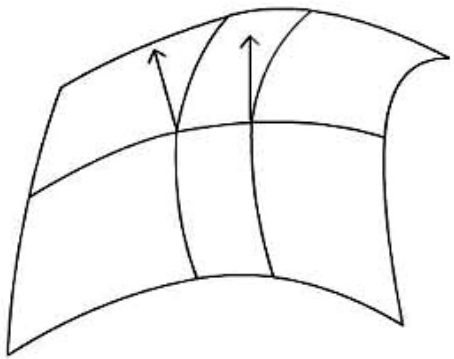
Effects considered and energy dissipation in different models:

	surface kinematics	bulk fluids	elastic effects	viscous effects	energy dissipation
Waxman	✓		✓	✓	
Steigman			✓		✓
Porzrikidis		✓	✓		
Seifert		✓	✓		✓
Cai			✓	✓	✓
Miao		✓	✓	✓	✓

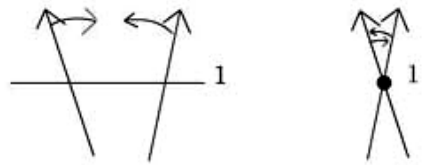
Outline

Basic Viewpoints

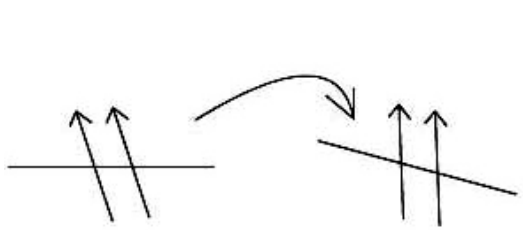
- The membrane is a 2-D **fluid** defined on an **evolving surface**.
- Material points are endowed with unit **directors** (**O**, simplest model of a lipid) .
- Directors have **favorite configuration**: parallel & trim.

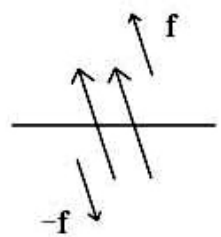


directors on surface



(A) parallel



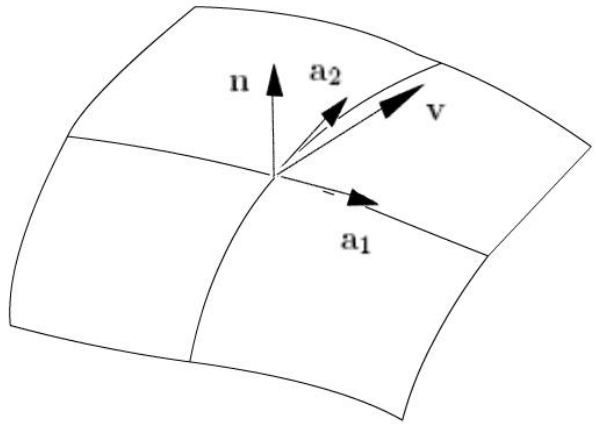


(B) trim

Kinematics & Geometry of Surface

The velocities determine the evolving of surface.

- Surface: $\mathbf{R}(u^\alpha, t)$
- Tangent: $\mathbf{a}_\alpha(u^\beta, t)$
- Normal: $\mathbf{n}_\alpha(u^\beta, t)$
- Decompose: $\mathbf{v} = v^\alpha \mathbf{a}_\alpha + v^{(n)}\mathbf{n}$



The metric tensor and covariant alternating tensor

$$\mathbf{a}_\alpha = \frac{\partial \mathbf{R}}{\partial u^\alpha}, \ \mathbf{n}\cdot\mathbf{a}_\alpha = 0, \ \mathbf{n}\cdot\mathbf{n} = 1$$

$$a_{\alpha\beta} = \mathbf{a}_\alpha \cdot \mathbf{a}_\beta, \ a^{\alpha\beta} = \left(a_{\alpha\beta}\right)^{-1}, \ \varepsilon_{\alpha\beta} = \mathbf{a}_\alpha \times \mathbf{a}_\beta \cdot \mathbf{n}$$

The Gauss-Codazzi equation (curvature tensor and Christoffel symbols, the subscript '$,\alpha$' is the covariant derivative)

$$\begin{aligned} \mathbf{a}_{\alpha,\beta} &= \frac{\partial \mathbf{a}_\alpha}{\partial u^\beta} - \Gamma^\gamma_{\alpha\beta}\mathbf{a}_\gamma = b_{\alpha\beta}\mathbf{n} \\ \mathbf{n}_{,\beta} &= -b^\gamma_\beta \mathbf{a}_\gamma \\ b_{\alpha\beta,\gamma} &= b_{\alpha\gamma,\beta} \end{aligned}$$

Elastic Energy with Spontaneous Curvature

From the **Frank energy** of liquid crystal, considering the spontaneous curvature, we obtain the elastic energy density of the directors

$$E_{\text{el}} = \underbrace{\frac{k_2}{2} O^\alpha O_\alpha}_{\text{tilt energy}} + \underbrace{\frac{k_1+\varepsilon_1}{2} a^{\alpha\beta} \left(\mathbf{O}_{,\alpha} + \mathbf{b}_\alpha\right) \cdot \left(\mathbf{O}_{,\beta} + \mathbf{b}_\beta\right)}_{\text{surface Frank energy}} + \underbrace{\frac{k_1-\varepsilon_1}{2} \varepsilon^{\alpha\beta} \left(\left(\mathbf{O}_{,\alpha} + \mathbf{b}_\alpha\right) \times \left(\mathbf{O}_{,\beta} + \mathbf{b}_\beta\right)\right) \cdot \mathbf{O}}_{\text{topological energy}}$$

$\mathbf{b}_\alpha$ is the spontaneous curvature, which is induced by the asymmetries of the membrane and changes the favorite configuration of directors. $\mathbf{b}_\alpha$ satisfies the equation

$$\mathbf{O} \times \left(\frac{\partial \mathbf{b}_\alpha}{\partial t} - S_\alpha^\pi \mathbf{b}_\pi - \frac{\zeta}{2} \mathbf{O} \times \mathbf{b}_\alpha \right) = 0 \text{ and } \mathbf{O} \cdot \mathbf{b}_\alpha = 0$$

S_α^π is the rate of strain, ζ is the vorticity.

Stresses

- Total in-plane stress: $T^{\alpha\beta}$

$$T^{\alpha\beta} = \underbrace{-\Pi a^{\alpha\beta}}_{\text{(pressure)}} + \underbrace{J^{\alpha\beta}}_{\text{(viscous stress)}} + \underbrace{T_1^{\alpha\beta}}_{\text{(elastic stress)}}$$

  - Viscous stress: $J^{\alpha\beta}$
    1. Pure lipid bilayer ($S_{\alpha\beta}$ is the rate of strain)

$$J^{\alpha\beta} = C^{\alpha\beta\gamma\delta} S_{\gamma\delta}$$

    2. Bilayer with cortex and other proteins (Oldoyd-B)

$$\begin{aligned} J^{\alpha\beta} &= 2\varepsilon_0 S^{\alpha\beta} + \Sigma^{\alpha\beta} \\ \lambda \frac{\partial \Sigma^{\alpha\beta}}{\partial t} + \Sigma^{\alpha\beta} &= 2\mu S^{\alpha\beta} \end{aligned}$$

  - Elastic stress is determined by principle of virtual work

$$\begin{aligned} T_1^{\alpha\beta} = & \left(-\frac{k_1 + \varepsilon_1}{2} \left(a^{\alpha\gamma} a^{\beta\delta} + a^{\alpha\delta} a^{\beta\gamma} \right) + (k_1 - \varepsilon_1) \varepsilon^{\alpha\beta} \varepsilon^{\gamma\delta} \right) (\mathbf{O}_{,\gamma} + \mathbf{b}_\gamma) \cdot \mathbf{O}_{,\delta} \\ & + \left(\frac{k_1 - \varepsilon_1}{2} \left(\varepsilon^{\alpha\gamma} a^{\beta\delta} + \varepsilon^{\beta\gamma} a^{\alpha\delta} \right) - (k_1 + \varepsilon_1) \varepsilon^{\alpha\beta} a^{\gamma\delta} \right) ((\mathbf{O}_{,\gamma} + \mathbf{b}_\gamma) \times \mathbf{O}_{,\delta}) \end{aligned}$$

- Transverse stress: q^α

$$q^\alpha = k_2 O^{(n)} O^\alpha$$

Director Model

Dynamical equations

$$\begin{aligned}
\gamma\frac{\partial \mathbf{v}}{\partial t} &= \mathbf{f}+\left(T^{\alpha\beta}\mathbf{a}_{\beta}\right)_{,\alpha}+\left(q^{\alpha}\mathbf{n}\right)_{,\alpha}\\
\gamma\varphi\mathbf{O}\times\frac{\partial^{2}\mathbf{O}}{\partial t^{2}} &= -k_{2}O^{\alpha}\mathbf{O}\times\mathbf{a}_{\alpha}+\left(k_{1}+\varepsilon_{1}\right)a^{\alpha\beta}\mathbf{O}\times\left(\mathbf{O}_{,\alpha}+\mathbf{b}_{\alpha}\right)_{,\beta}-\left(k_{1}-\varepsilon_{1}\right)\varepsilon^{\alpha\beta}\mathbf{b}_{\alpha,\beta}\\
v^{\alpha}_{,\alpha}-2Hv^{(n)} &= 0\ \ \text{(incompressible condition)}
\end{aligned}$$

The energy dissipative relation

$$\frac{d}{dt}\int\left(\frac{\gamma}{2}\left|\mathbf{v}\right|^{2}+\frac{\gamma\varphi}{2}\left|\mathbf{O}\times\frac{\partial\mathbf{O}}{\partial t}\right|^{2}+E_{\mathrm{el}}\right)dS=-2\varepsilon_{0}\int S^{\alpha\beta}S_{\alpha\beta}\,dS$$

Reduced Elastic Surface Model

Let $k_2 \to \infty$, then $\mathbf{O} \to \mathbf{n}$. The equations reduce to

$$\begin{aligned} \gamma \frac{\partial \mathbf{v}}{\partial t} &= \mathbf{f} + \left(T^{\alpha\beta} \mathbf{a}_\beta \right)_{,\alpha} + \left(q^\alpha \mathbf{n} \right)_{,\alpha} \\ v^\alpha_{,\alpha} - 2Hv^{(n)} &= 0 \quad \text{(incompressible condition)} \end{aligned}$$

where the stresses converge to

$$\begin{aligned} T^{\alpha\beta} &= -\Pi a^{\alpha\beta} + 2\varepsilon_0 S^{\alpha\beta} + M^{\alpha\gamma} b^\beta_\gamma \\ q^\alpha &= M^{\alpha\beta}_{,\beta} \\ M^{\alpha\beta} &= C^{\alpha\beta\gamma\delta} \left(B_{\gamma\delta} - b_{\gamma\delta} \right) \end{aligned}$$

Waxman (Porzrikidis) loses the red term. The spontaneous curvature tensor $B_{\alpha\beta}$ ($\mathbf{b}_\alpha = B^\beta_\alpha \mathbf{a}_\beta$) satisfies

$$\frac{D_s B_{\alpha\beta}}{Dt} = \frac{\partial B_{\alpha\beta}}{\partial t} - B^\mu_\alpha S_{\mu\beta} - B^\mu_\beta S_{\alpha\mu} = 0$$

The energy dissipative relation is

$$\frac{d}{dt} \left(\int \frac{\gamma}{2} |\mathbf{v}|^2 dS + \frac{(k_1 + \varepsilon_1)}{2} \int (2H - C_0)^2 \, dS \right) = -2\varepsilon_0 \int S^{\alpha\beta} S_{\alpha\beta} dS$$

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Local Existence & Uniqueness of 1-D Reduced Model

In 2-D space, the reduced model describes the dynamics of an incompressible elastic string. Using the tangent angle α and the arc length parameter s to express the string, we can get the 1-D reduced model.

$$\gamma\alpha_{tt} = 2T_s\alpha_s + T\alpha_{ss} - \varepsilon\left[(B_s + \alpha_{ss})_{ss} - (B_s + \alpha_{ss})\alpha_s^2\right]$$
$$-\gamma\left(\alpha_t\right)^2 = T_{ss} - T\left(\alpha_s\right)^2 + \varepsilon\left[(B_s + \alpha_{ss})\alpha_{ss} + 2(B_s + \alpha_{ss})_s\alpha_s\right]$$

We proved the solution's existence and uniqueness of this system.

Theorem

If $B(s) \in W^{2,1}(0,1)$, initial data $\alpha_0 \in H^{k+1}(0,1)$, $(\alpha_t)_0 \in H^{k-1}(k \geq 2)$, there exist a constant t^*, such that this system of equations has a unique set of solutions (α^*, α_t^*), and

$$\alpha^* \in L^\infty\left([0, T^*], H^{k-2}(0,1)\right),\ k \geq 2$$

Coupling with Bulk Fluid

Membranes can be seen as immersed boundaries and they produce stresses. Ignoring the membrane's thickness and considering the no-slipping condition between the membrane and bulk fluid, we can obtain the equations

$$
\begin{aligned}
\frac{\partial \mathbf{u}(\mathbf{x},t)}{\partial t} + (\mathbf{u}\cdot\nabla)\mathbf{u} &= -\nabla p + \mu\Delta\mathbf{u} + \mathbf{f}(\mathbf{x},t), \quad \mathbf{x}\in\Omega\subseteq\mathbb{R}^3 \\
\nabla\cdot\mathbf{u} &= 0 \\
\mathbf{f}(\mathbf{x}) &= \int_\Gamma \mathbf{F}(u^\alpha,t)\delta(\mathbf{x}-\mathbf{X}(u^\alpha,t))\,dS \\
\mathbf{F}(u^\alpha,t) &= \left(T^{\alpha\beta}\mathbf{a}_\beta\right)_{,\alpha} + (q^\alpha\mathbf{n})_{,\alpha} \\
\mathbf{v}(u^\alpha,t) &= \int_\Omega \mathbf{u}(\mathbf{x},t)\delta(\mathbf{x}-\mathbf{X}(u^\alpha,t))\,d\mathbf{x} \\
\frac{\partial \mathbf{X}(u^\alpha,t)}{\partial t} &= \mathbf{v}(u^\alpha,t) \\
v^\alpha_{,\alpha} - 2Hv^{(n)} &= 0
\end{aligned}
$$

where $\mathbf{X}(u^\alpha,t)$ is the membrane's position. This system has the following energy dissipation

$$
\frac{d}{dt}\left(\int_\Omega \frac{1}{2}|\mathbf{u}|^2\,dV + \int_\Gamma E_{\text{el}}\,dS\right) = -\mu\int_\Omega |\nabla\mathbf{u}|^2\,dV - 2\varepsilon_0\int_\Gamma S^{\alpha\beta}S_{\alpha\beta}\,dS
$$

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Outline

The Elastic Surface Model for Planar Membrane

The dynamic equation and the boundary conditions of a planar membrane in the bulk fluid

$$\begin{aligned}
\rho\frac{\partial \mathbf{U}}{\partial t} &= -\nabla P + \nu\triangle\mathbf{U}, \nabla\cdot\mathbf{U} = 0, \\
\frac{\partial h(x,y,t)}{\partial t} &= U_z(x,y,0,t), \\
[\frac{\partial P}{\partial z}] &= 0, [P] = \gamma\triangle_p h(x,y,t) - \mu\triangle_p^2 h(x,y,t), \\
\left[\frac{\partial}{\partial z}\begin{pmatrix} U_x \\ U_y \end{pmatrix}\right] &= -\frac{\varepsilon_0}{\nu}\triangle_p\begin{pmatrix} U_x \\ U_y \end{pmatrix},
\end{aligned}$$

where $[g]$ denotes the jump of the function g across the membrane, the subscript p denotes operators on the x-y plane.

The Director Model for Planar Membrane

The surface is endowed with a director field $\mathbf{O} = (O_x, O_y, 1) = (\mathbf{o}, 1)$, which models the orientation of the lipids. The energy density $\frac{k_2}{2}|\mathbf{o} - \mathbf{n}|^2 + \frac{\mu}{2}|\nabla \mathbf{o}|^2$ is consistent with that of the liquid crystals and is used to represent the bending resistance. When $\mathbf{O} = \mathbf{e}_z$ or $\mathbf{O} = \mathbf{N}$, it reduces respectively to an additional tensile or Helfrich energy density. We need only to modify the pressure jump of equation to

$$[P] = \gamma \triangle_p h(x, y) + k_2 f,$$

where $f = \nabla \cdot (\mathbf{o} - \mathbf{n})$. For simple membranes, the directors oscillate around the instantaneous equilibrium with very high frequency

$$\eta_0 \frac{\partial^2 \mathbf{o}}{\partial^2 t} = -k_2 (\mathbf{o} - \mathbf{n}) + \mu \triangle_p \mathbf{o},$$

where η_0 is the moment of inertia of the lipids. The mean effects in the macroscopic time scale is determined by the equilibrium condition, which simplifies equation to

$$k_2 f - \mu \triangle_p (f - \triangle_p h) = 0.$$

Neglect the inertia effects

$$\eta_1 \frac{\partial \mathbf{o}}{\partial t} = -k_2 (\mathbf{o} - \mathbf{n}) + \mu \triangle_p \mathbf{o},$$

where η_1 is the friction coefficient. Below we call this model the frictional director model. Similarly, we obtain

$$-\eta_1 \frac{\partial (f - \triangle_p h)}{\partial t} + k_2 f - \mu \triangle_p (f - \triangle_p h) = 0.$$

Energetics

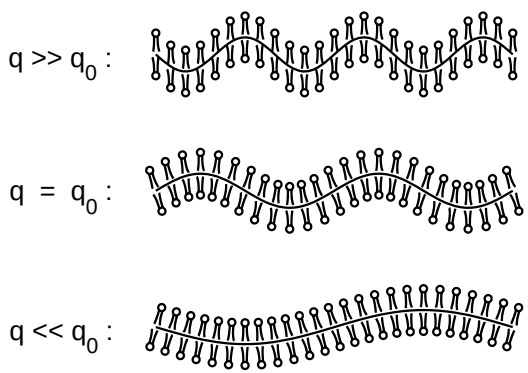
For a given surface the equilibrium states of the directors are determined by minimizing the director energy. Let $h(\mathbf{x}) = h_0 \sin(\mathbf{q} \cdot \mathbf{x})$, the director energy is minimized by

$$\mathbf{o} = \frac{-k_2 h_0}{k_2 + \mu q^2} \cos(\mathbf{q} \cdot \mathbf{x})\, \mathbf{q},$$

where $q = |\mathbf{q}|$ is the wavenumber. The minimum director energy is

$$E_d(q) = \frac{k_2 \mu h_0^2 q^4}{2(k_2 + \mu q^2)}. \tag{1}$$

In the low wavenumber regime ($q \ll q_0 = \sqrt{k_2/\mu}$), the director is close to the surface normal and the director energy reduces to the Helfrich energy $\frac{\mu}{2}(\triangle h)^2$; in the high wavenumber regime ($q \gg q_0$), the directors are close to the z-direction, and the energy reduces to an additional tensile energy $\frac{k_2}{2}|\nabla h|^2$. These wavenumber configurations are sometimes called "collective protrusion ". In some sense, whether to call it "protrusion" or "tilt" depends on the viewpoint–when we look along the z-direction, we see "protrusion"; and when we look along the surface normal direction, we see "tilt".



Dispersion Relation

The dispersion equation of the above models is

$$2m\omega^2 = \mu_c \frac{\nu^2}{\rho^2} q^4 (q - m), m = \sqrt{q^2 - i\omega\rho/\nu},$$

where $\mu_c = \rho\gamma^* / (\nu^2 q)$ is a nondimensional constant. γ^* is the effective tension and is defined in the next table:

Model	γ^*
Elastic surface model	$\gamma + \mu q^2$
Director model	$\gamma + \frac{k_2 \mu q^2}{k_2 + \mu q^2}$
Frictional director model	$\gamma + \frac{k_2 (\mu q^2 - i\omega\eta_1)}{k_2 + (\mu q^2 - i\omega\eta_1)}$

These results are consistent with the work of Fan. In Kramer's work, the bending elasticity is not considered and $\gamma^* = \gamma$.
Let $\omega = \nu q^2 \omega_1 / \rho = f_0 - i\Gamma$, then we have

$$(1 - i\omega_1) (2\omega_1^2 + \mu_c)^2 = \mu_c^2.$$

Oscillation-Overdamping Transition

The membrane is overdamped when $\mu_c < \mu_{c0} \approx 0.3$ and oscillatory when $\mu_c > \mu_{c0}$. Now we define another wavenumber $q_1 = \rho\gamma/\left(\nu^2\mu_{c0}\right)$. Typically, we have $q_1 \ll q_0$ and the modification on the tension is negligible at $q = q_1$. Therefore, q_1 defines the wavenumber of the oscillation-overdamping transition. When $q \ll q_0$, the differences between the three models are negligible; when $q \approx q_0$ or $q > q_0$, the differences in the damping constant become significant.

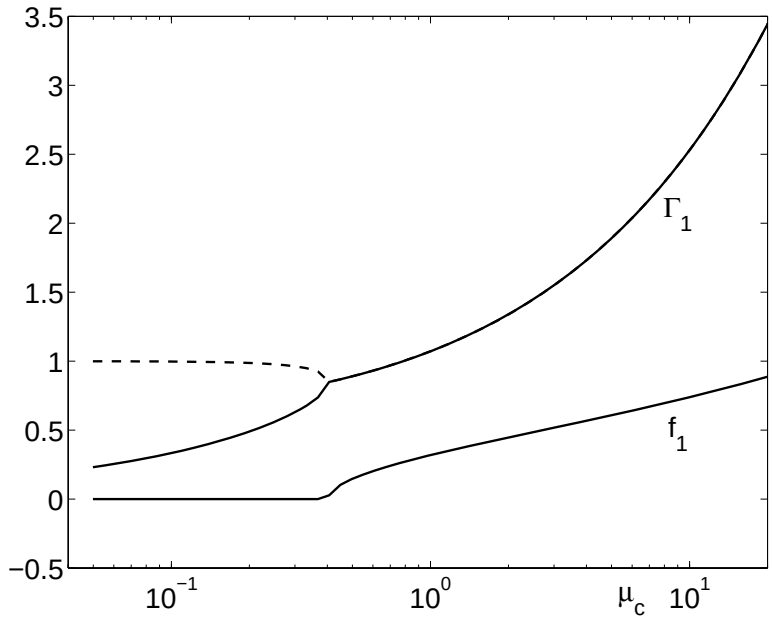


Figure: The nondimensionalized frequency f_1 and damping constant Γ_1 versus the nondimensional constant μ_c. $\omega_1 = f_1 - i\Gamma_1$ is the solution of equation. When μ_c is smaller than some constant μ_{c0} (≈ 0.3), the membrane displays overdamped behavior. The lower branch of Γ_1 is the physical one. When μ_c is greater than the constant, the membrane shows oscillatory behavior.

Experimental Results

The range of experimentally observable wavenumbers is still far from the characteristic wavenumber q_0, at which the bending elasticity becomes important. Since the differences among the three models are very small in this case, Kramer's model is quite sufficient in explaining existing experimental results.

In some of the previous works, the tension is allowed to contain an imaginary part $\gamma^* = \gamma - i\omega\gamma'$, in order to fit the experimental results. γ' is explained as the transverse viscosity. However, origin of this viscosity is lacking from a molecular viewpoint. We will see now that in the frictional director model, μ_c also contains an imaginary part. This gives a satisfactory explanation for the origin of the imaginary part of the tension.

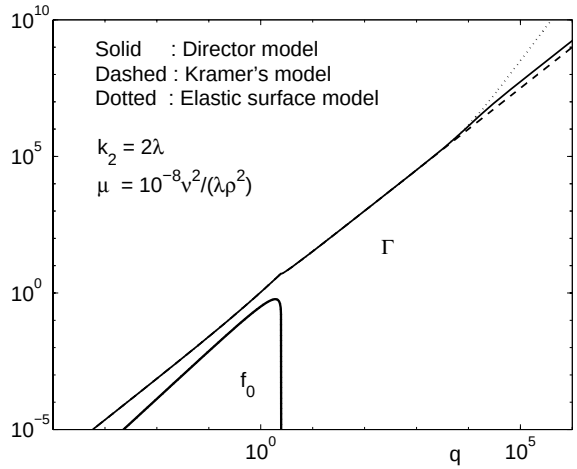


Figure: f_0 and Γ obtained from different models for different wavenumbers. The units of q and f_0 (and Γ) are respectively $\frac{\rho\gamma}{\nu^2}$ and $\frac{\rho\gamma^2}{\nu^3}$. The curves overlaps at small q, which suggests that the three models for the planar membrane are consistent in this regime. At high wavenumber ($q \gtrapprox q_0$), the damping constants of the three models are different. The critical wavenumber for oscillating-overdamping transion is approximately $\frac{1}{\mu_{c0}}\left(\frac{\rho\gamma}{\nu^2}\right)$.

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Molecular Dynamics Simulation Results

Since it is hard to capture the damping process by MD simulation, the structure factor $S(q) \equiv \left\langle \left| \tilde{h}(q) \right|^2 \right\rangle$ for the undulation of the membrane is obtained from the static states in MD simulations, where $\tilde{h}(q)$ is the Fourier transform of the height function h. From the energy equipartition theory, we may evaluate the static structure factor for different models:

Model	$S(q)$	$S^*(q)$
Elastic surface model	$\frac{k_B T}{\gamma q^2 + \mu q^4}$	$\frac{k_B T}{\mu q^4}$
Director model	$\frac{k_B T \left(k_2 + \mu q^2\right)}{\gamma k_2 q^2 + (k_2 + \gamma) \mu q^4}$	$\frac{k_B T}{\mu q^4} + \frac{k_B T}{k_2 q^2}$

where (and below) the star stands for the structure factor of a tensionless state ($\gamma = 0$) which is achieved in the MD simulations. From equation and table, the director model also allows us to evaluate the structure factor of the directors ($S_o(q) = \left\langle |\tilde{\mathbf{o}}(q)|^2 \right\rangle$)

$$
\begin{aligned}
S_o(q) &= \frac{k_2^2 k_B T}{\left(k_2 + \mu q^2\right)\left(\gamma k_2 + (k_2 + \gamma)\mu q^2\right)} + \frac{2 k_B T}{k_2 + \mu q^2}, \\
S_o^*(q) &= \frac{k_2 k_B T}{\mu q^2 \left(k_2 + \mu q^2\right)} + \frac{2 k_B T}{k_2 + \mu q^2}.
\end{aligned}
$$

Note that, in both $S_o(q)$ and $S_o^*(q)$, the first term comes from the undulation of the membrane, and the second term comes from the oscillation of the lipids around its equilibrium orientation.

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Summary of Elastic Surface and Director Model

Goetz et al provides the first explicit connection between molecular dynamics results and elastic membrane models. The static structure factor (in the absence of tension) obtained from their simulations agrees very well with that of the director model. Similar results also appeared in the work of Lindahl etc. These results suggest that the director model (but not the elastic surface model) is also quite accurate at high wavenumbers. As a side product, we can use the director model to help understand results from molecular dynamics.

Both the Helfrich elastic surface model and the director model result in a wavenumber-dependent modification to the tension. When the wavenumber is not too high, this modification is negligible. In fact, existing experimental results of neutron scattering and dynamic light scattering are well explained by Kramer's theory, which neglects the bending energy and the tilt of the lipid molecules. At high wavenumbers, the difference of the models become significant. Results from molecular dynamics simulation have provided direct evidence that the director model is valid in the high wavenumber regimes but the Helfrich model does not.

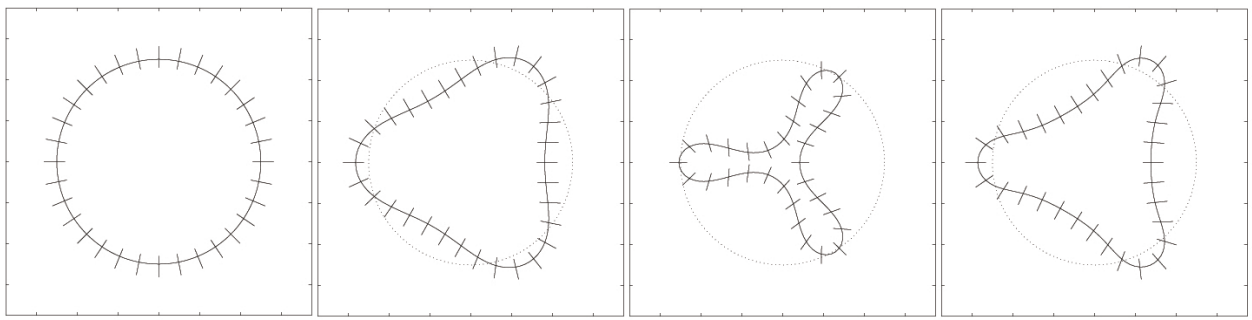
Outline

Equations for the Cylindrical Vesicle

The cylindrical vesicle can be described by its directrix. Thus it can be seen as a incompressible elastic curve in a plane. Using the tangent angle α and θ to express the curve and the director, we can obtain the angle's equations of the vesicle.

$$\begin{aligned} -\gamma\alpha_{tt} &= 2T_s\alpha_s + T\alpha_{ss} + (k_2 O^1 O^{(n)}\mathbf{n})_{ss}\cdot\mathbf{n} \\ -\gamma(\alpha_t)^2 &= T_{ss} - T(\alpha_s)^2 + (k_2 O^1 O^{(n)}\mathbf{n})_{ss}\cdot\mathbf{a} - P\alpha_s \\ \gamma\phi\theta_{tt} &= -\frac{k_2}{2}\sin 2(\alpha-\theta) + (k_1+\varepsilon_1)(\theta_{ss}+b_s) \end{aligned}$$

In fact, this is a dynamical system of an incompressible elastic string. The evolving of a translation invariable membrane for given osmotic pressure and initial velocities: PLAY



Relations Between Director Model and Reduced Model

Elastic energy

$$E_{\text{el}} = \frac{k_2}{2} O^\alpha O_\alpha + \frac{k_1+\varepsilon_1}{2} a^{\alpha\beta} \left(\mathbf{O}_{,\alpha} + \mathbf{b}_\alpha\right) \cdot \left(\mathbf{O}_{,\beta} + \mathbf{b}_\beta\right) + \frac{k_1-\varepsilon_1}{2} \varepsilon^{\alpha\beta} \left(\left(\mathbf{O}_{,\alpha} + \mathbf{b}_\alpha\right) \times \left(\mathbf{O}_{,\beta} + \mathbf{b}_\beta\right)\right) \cdot \mathbf{O}$$

The difference between the director model (with different parameter k_2) and the reduced model (both are computed to time $t = 1.0$)

k_2	$\|\|\mathbf{x}_{\text{director}} - \mathbf{x}_{\text{reduced}}\|\|_2$
1.6	1.29714×10^{-2}
3.2	4.60772×10^{-3}
6.4	2.42708×10^{-3}
12.8	1.34529×10^{-3}
25.6	7.24118×10^{-4}
51.2	4.27454×10^{-4}
102.4	2.88752×10^{-4}

Difficulties in the Simulation of Two Dimensional Membrane

Difficulties in numerical simulation of a separate moving membrane

- difficulties
  - incompressibility
  - fourth-order spatial derivative
  - evolving surface
  - no effective coordinate system
- possible ways
  - projection method
  - using the evolving equation for curvature
  - high accuracy numerical method
  - moving mesh method

We have applied the numerical method to axisymmtric membrane.

Theorem

Hodge decomposition Let Ω be a close surface in the three dimensional Euclidian space, and $\mathbf{B}$ be a vector function defined on the surface, then we have the decomposition

$$\mathbf{B} = \mathbf{A} + \mathbf{C},$$

with $A^{\alpha}_{,\alpha} - 2HA^{(n)} = 0$ and $\mathbf{C} = \left(\Pi a^{\alpha\beta}\mathbf{a}_{\alpha}\right)_{,\beta}$. The decomposition also satisfies $\int \mathbf{A}\cdot\mathbf{C}ds = 0$. Π is decided by

$$a^{\alpha\beta}\pi_{,\alpha\beta} - 4H^2\pi = B^{\alpha}_{,\alpha} - 2HB^{(n)}.$$

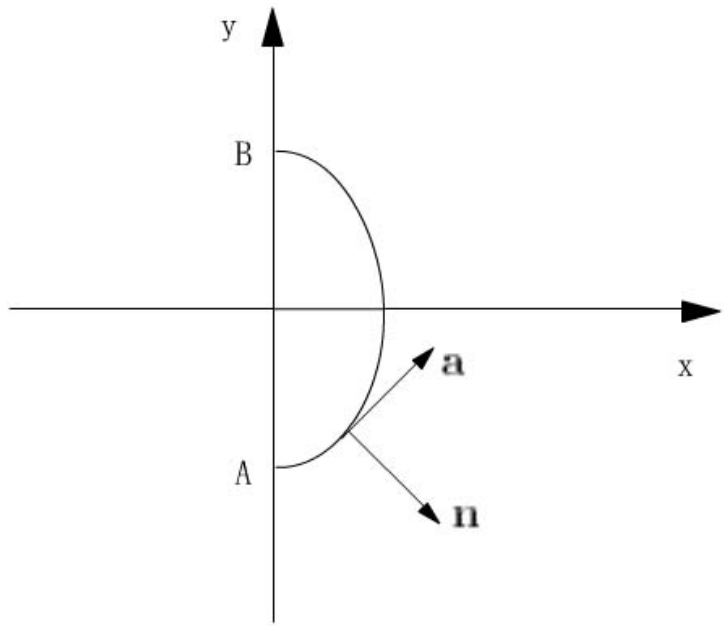
Projection Method

Main steps:

1. Compute the accelerations (without the pressure);
2. Update the velocities and move the membrane (without the effect of pressure);
3. Update the geometric quantities;
4. Compute the pressure and adjust the velocities (projection);
5. repeat.

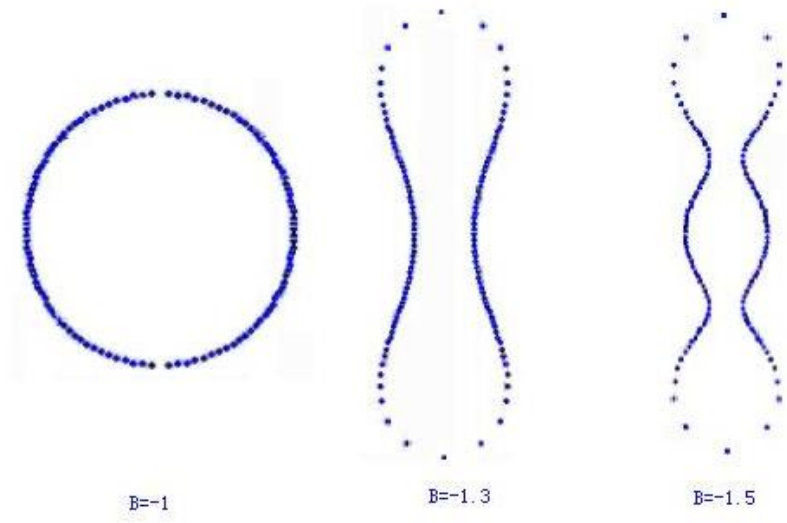
The Axial Symmetric Case

For the axial symmetric case, we can just compute the quantities on one generatrix. In the convected coordinate system, the generatrix may escape from the x-y plane, thus it is not a suitable coordinate system for computation.



Results-Spontaneous Curvature

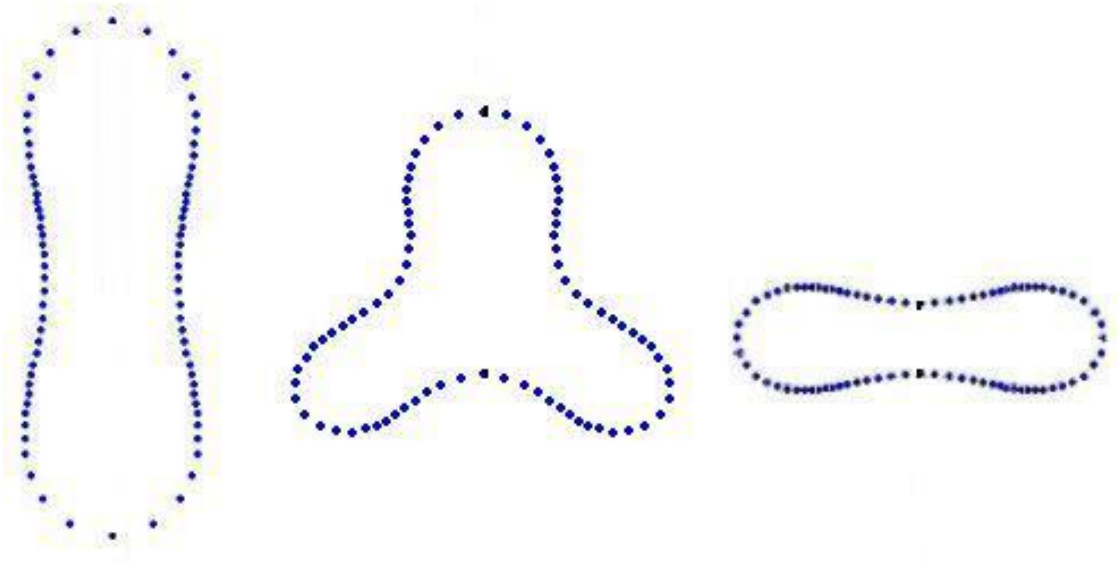
Steady states for different spontaneous curvature (without the osmotic pressure). There might be different steady states for the same spontaneous curvature.



The total mean curvature decreases as the spontaneous curvature decreases.

Results-Osmotic Pressure

Different initial value result in different steady states for the same volume (the spontaneous curvature is 0).



Elastic energy: (1) $\approx$ (3) $<$ (2).
A little positive spontaneous curvature makes the biconcave shape to be the global minimal.

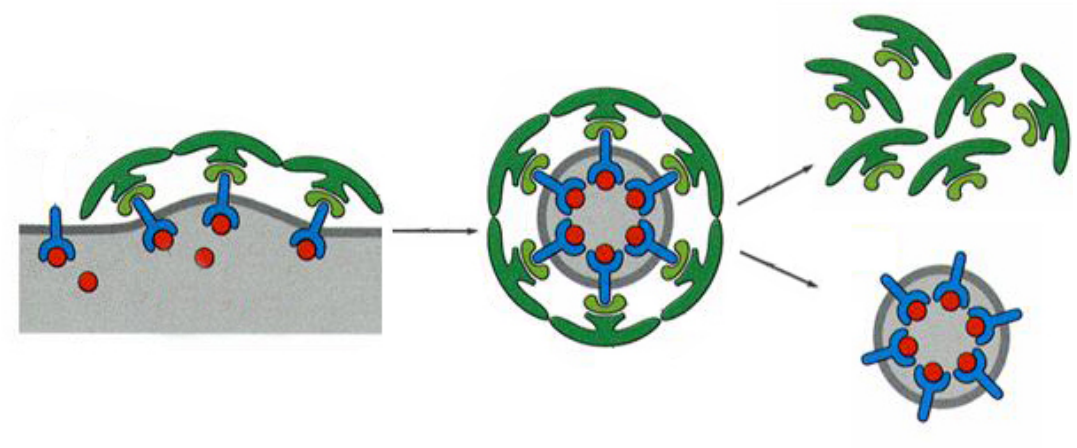
Spontaneous Curvature

The spontaneous curvature tensor has the form

$$B_{\alpha\beta} \quad = \quad B\left(u^1, u^2\right) a_{\alpha\beta}$$

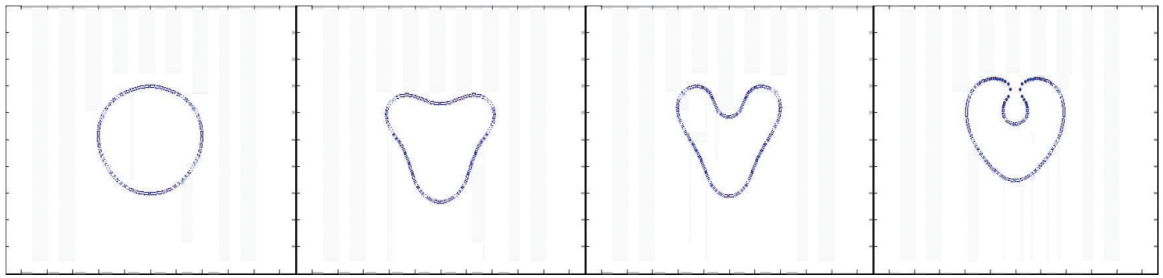
where $B\left(u^1, u^2\right)$ is independent of the time t.

- Global spontaneous curvature: the difference between the numbers of lipids in two monolayers; $B\left(u^1, u^2\right)$ is a constant;
- **Local spontaneous curvature**: $B\left(u^1, u^2\right)$ is a local function; Certain proteins induce endocytosis and exocytosis

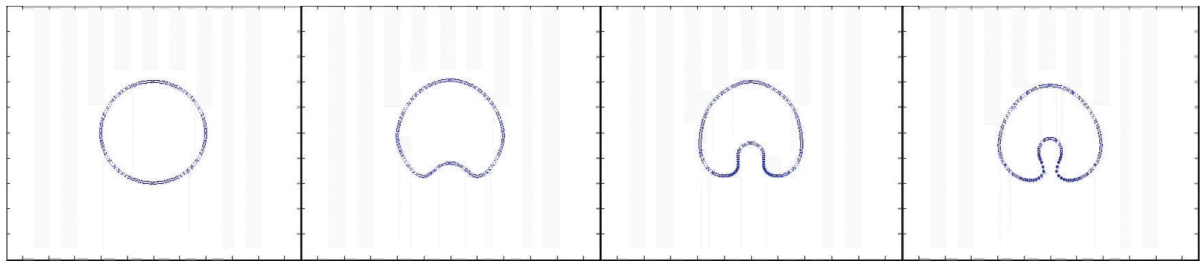


Endocytosis and Exocytosis

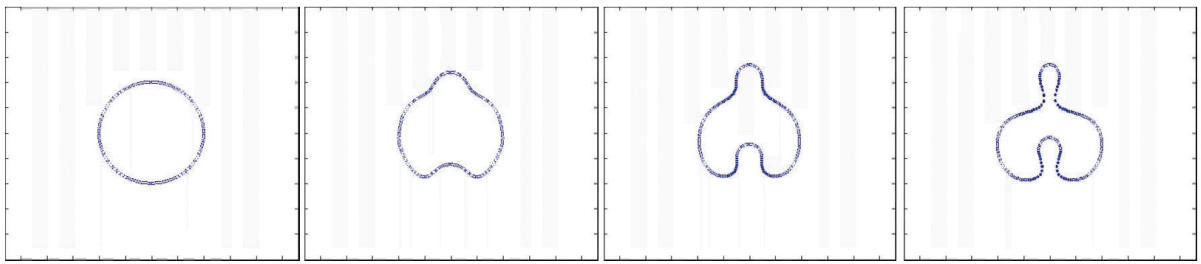
- Global spontaneous curvature (endocytosis): PLAY



- Local spontaneous curvature
  1. endocytosis: PLAY



  2. both endocytosis and exocytosis: PLAY



1-D Reduced Model Coupling with Stokes Flow

The 1-D reduced model describes the cylindrical vesicle's directrix. By the no-slipping condition, the coupling system is

$$
\begin{aligned}
-\nabla p + \mu \Delta \mathbf{u} + \mathbf{f} &= 0 \\
\nabla \cdot \mathbf{u} &= 0 \quad \text{(bulk fluid's incompressible condition)} \\
\mathbf{f}(\mathbf{x}, t) &= \int_0^L \mathbf{F}(s, t)\delta(\mathbf{x} - \mathbf{X}(s, t))\, ds \\
\mathbf{F}(s, t) &= (T\mathbf{a})_s + (-\varepsilon\kappa_s \mathbf{n})_s \\
\mathbf{v}(s, t) &= \int_{\mathbb{R}^2} \mathbf{u}(\mathbf{x}, t)\delta(\mathbf{x} - \mathbf{X}(s, t))\, ds \quad \text{(no-slipping condition)} \\
\frac{\partial \mathbf{X}(s, t)}{\partial t} &= \mathbf{v}(s, t) \\
\frac{\partial \mathbf{v}}{\partial s} \cdot \mathbf{a} &= 0 \quad \text{(membrane's incompressible condition)}
\end{aligned}
$$

Difficulties

- Two pressures p & T are coupled implicitly by two incompressible conditions and no-slipping condition;
- Variables defined on different spaces ($\mathbb{R}^2$, Γ);
- strong nonlinearity ($\mathbf{F}$);
- The force depends on κ_{ss}, which is the fourth-order derivative of $\mathbf{X}$. The time step must be very small in explicit scheme.

$$
\begin{aligned}
-\nabla p + \mu \Delta \mathbf{u} + \mathbf{f} &= 0 \\
\nabla \cdot \mathbf{u} &= 0 \quad \text{(bulk fluid's incompressible condition)} \\
\mathbf{f}(\mathbf{x}, t) &= \int_{\Gamma} \mathbf{F}(s, t)\delta(\mathbf{x} - \mathbf{X}(s, t))\, ds \\
\mathbf{F}(s, t) &= (T\mathbf{a})_s + (-\varepsilon \kappa_s \mathbf{n})_s \\
\mathbf{v}(s, t) &= \int_{\mathbb{R}^2} \mathbf{u}(\mathbf{x}, t)\delta(\mathbf{x} - \mathbf{X}(s, t))\, ds \quad \text{(no-slipping condition)} \\
\frac{\partial \mathbf{X}(s, t)}{\partial t} &= \mathbf{v}(s, t) \\
\frac{\partial \mathbf{v}}{\partial s} \cdot \mathbf{a} &= 0 \quad \text{(membrane's incompressible condition)}
\end{aligned}
$$

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Tangent Angle Description and Boundary Integral Equation

We use the tangent angle α to express the curve Γ. The movement of the curve $\mathbf{X}_t = \mathbf{v}$ can be changed into

$$\alpha_t = -\mathbf{v}_s \cdot \mathbf{n}$$

The velocity can be expressed by the boundary integral equation

$$\mathbf{v}(s,t) = \mathbf{u}^{\infty}(\mathbf{X}(s,t),t) + \frac{1}{4\pi\mu}\int_0^L \overleftrightarrow{G}(s,s') \cdot \mathbf{F}(s',t)\, ds'$$

- $\mathbf{u}^{\infty}(\mathbf{x},t)$: the incident velocity field;
- $\overleftrightarrow{G}(s,s')$: the Green's function, which is defined as

$$G_{ij} = -\ln|\mathbf{r}|\delta_{ij} + \frac{r_i r_j}{|\mathbf{r}|^2}, \quad \mathbf{r} = \mathbf{X}(s,t) - \mathbf{X}(s',t)$$

Take this integral equation into the curve's incompressible condition, we can get the equation for pressure T

$$\mathbf{a}\cdot\frac{\partial \mathbf{u}^{\infty}}{\partial s} + \mathbf{a}\cdot\frac{1}{4\pi\mu}\frac{\partial}{\partial s}\int_0^L \overleftrightarrow{G}(s,s')\cdot[(T\mathbf{a})_{s'} + \varepsilon(\alpha_{s's'}\mathbf{n})_{s'}]\, ds' = 0$$

Small Scale Decomposition: Solve Pressure

By the decomposition $\mathbf{v} = V\mathbf{a} + U\mathbf{n}$, the incompressible condition is

$$V_s + \alpha_s U = 0$$

Using Taylor expansion, we can find the leading order term of this equation is

$$-\frac{1}{4\mu}\mathcal{H}(T), \quad \hat{\mathcal{H}}(T) = -i \cdot \mathrm{sgn}(\xi)\hat{T}(\xi)$$

where $\mathcal{H}(\cdot)$ is the Hilbert transform. Therefore, We get the following iteration

$$\frac{1}{4\mu}\frac{\partial}{\partial s}\mathcal{H}(T^{n,i+1}) + \eta T^{n,i+1} = V_s(\alpha^n, T^{n,i}) + \alpha_s U(\alpha^n, T^{n,i}) + \frac{1}{4\mu}\frac{\partial}{\partial s}\mathcal{H}(T^{n,i}) + \eta T^{n,i}$$

where η is a relaxation factor. In each iterative step, we can use DFT to solve $T^{n,i+1}$.

Small Scale Decomposition: Move Curve

Similarly, the velocity of the angle can also be expressed by V, U as

$$\alpha_t = -U_s + \alpha_s V;$$

The leading order is

$$-\frac{\varepsilon}{4\mu}\mathcal{H}(\alpha_{ss})$$

We use the following semi-implicit scheme to move the curve

$$\frac{\alpha^{n+1}-\alpha^n}{\Delta t} - \frac{\varepsilon}{4\mu}\frac{\partial}{\partial s}\mathcal{H}(\alpha_{ss}^{n+1}) = -U_s(\alpha^n, T^n) + \alpha_s V(\alpha^n, T^n) - \frac{\varepsilon}{4\mu}\frac{\partial}{\partial s}\mathcal{H}(\alpha_{ss}^n)$$

we can also use DFT to solve this equation.

Static Flow

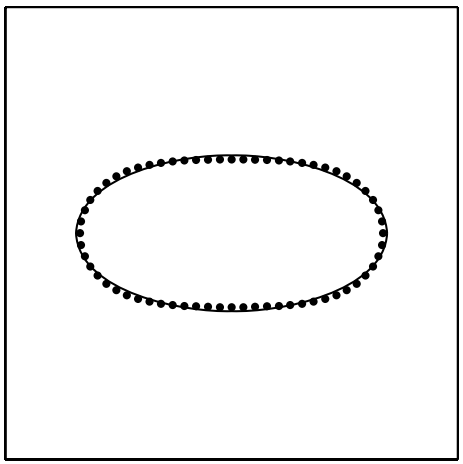
An important parameter

$$c = \frac{L}{2\pi\sqrt{A/\pi}}$$

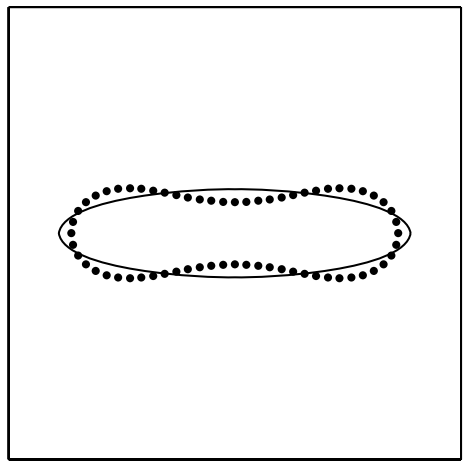
where L and A are the arc length and the area circled by the curve.

- $c \geq 1.0$;
- The bigger of c, the more prolate of the curve;
- $c \to 1.0$: the curve tends to be a circle.

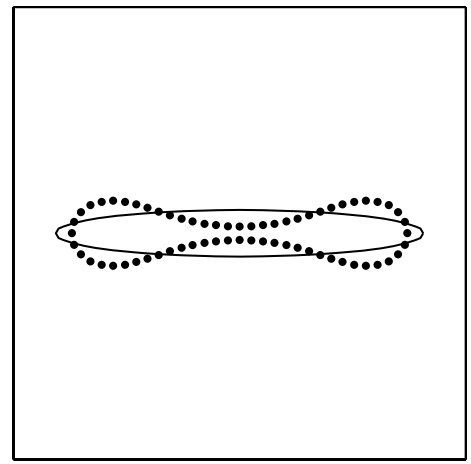
In static flow, different ellipses' steady states (different c)



$c = 1.0903$



$c = 1.3652$



$c = 1.8425$

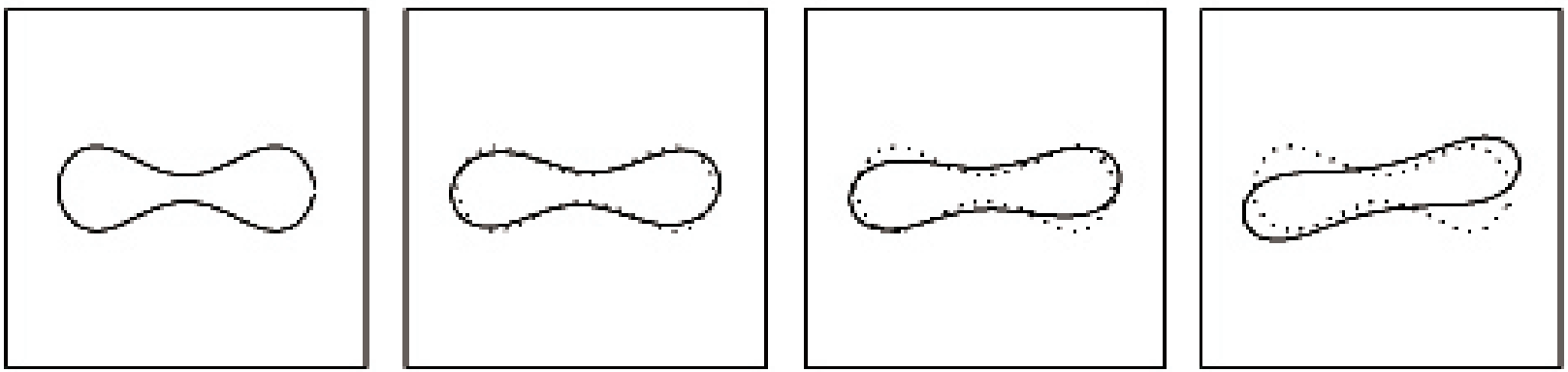
Shear Flow: Experiment Results

In experiment, Schmid-Schönbein & Wells (1969) and Goldsmith (1971) observed that the blood red cell have two different dynamic processes in different shear flow

- Low shear rate: rotation like rigid particles;
- High shear rate: the dimples of the biconcave disk disappear, and the membrane presents the shape of a prolate ellipsoid with tank-treading motion.

Shear Flow: Biconcave Shape, Low Shear Rate

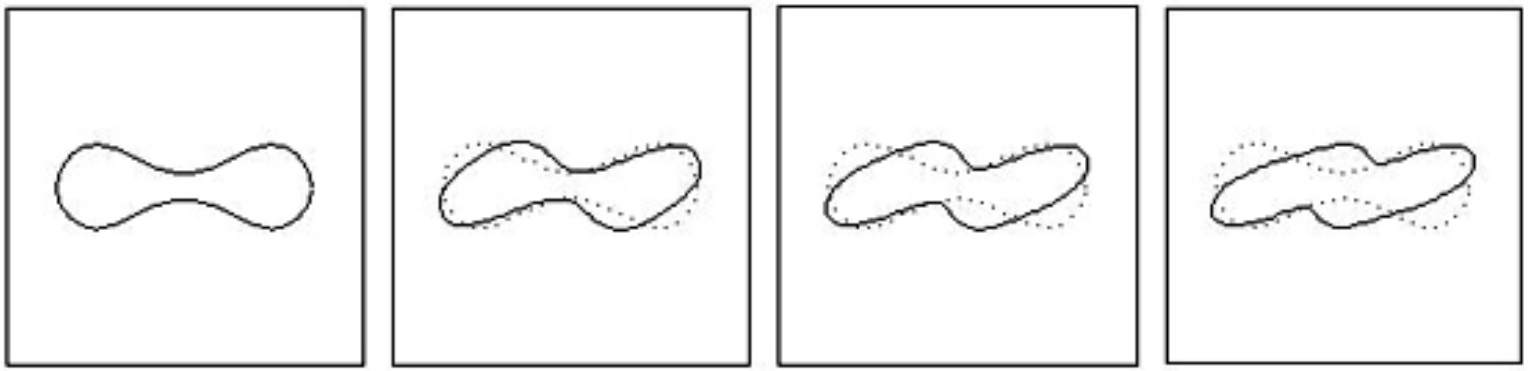
Low shear rate: rotation like rigid particles. PLAY



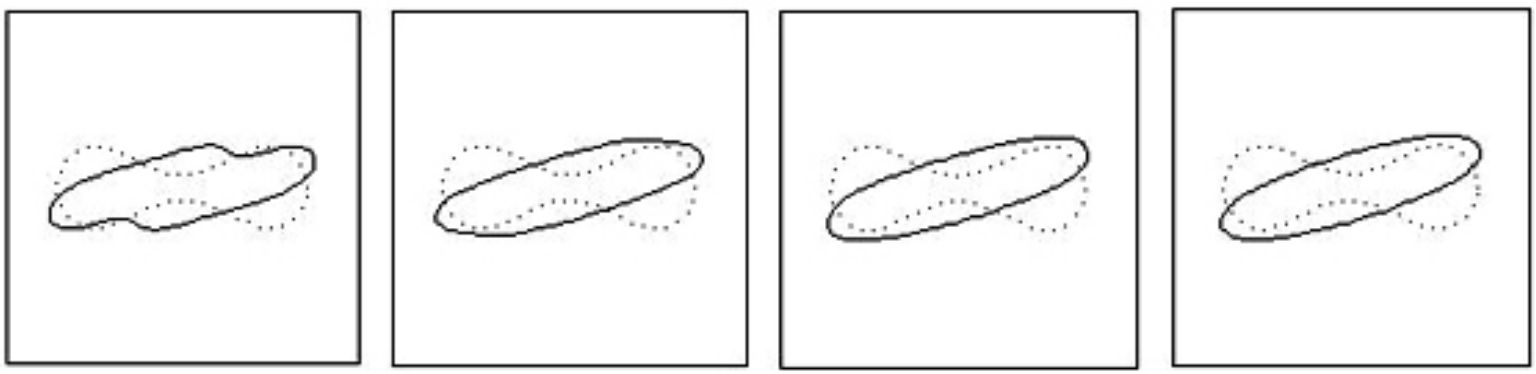
$t = 0.0$ $t = 0.5$ $t = 2.0$ $t = 5.5$

Shear Flow: Biconcave Shape, High Shear Rate

High shear rate: the dimples of the biconcave disk disappear, and the membrane presents the shape of a prolate ellipsoid with tank-treading motion.
PLAY



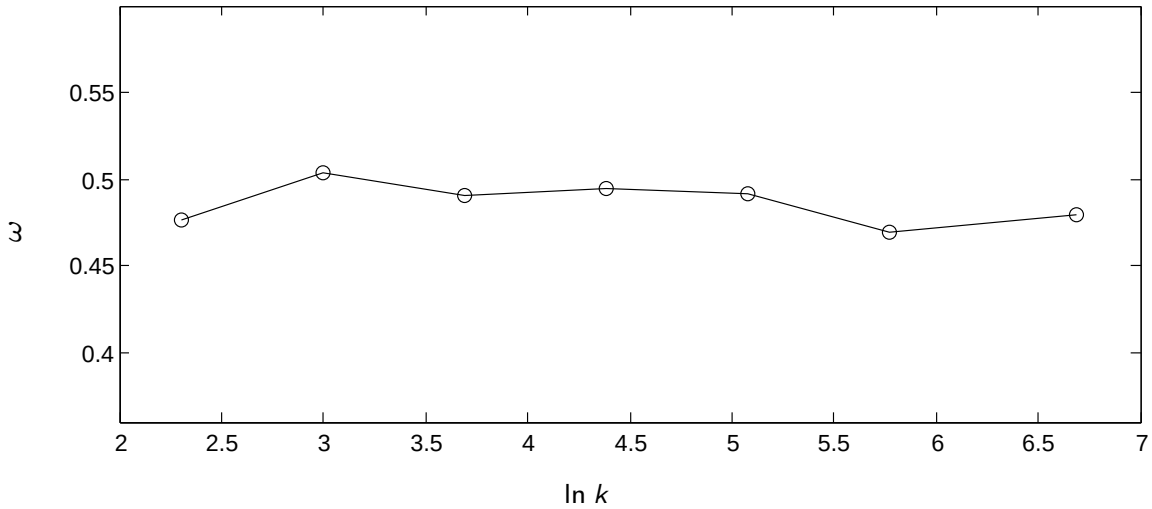
$t = 0.00$ $t = 0.01$ $t = 0.02$ $t = 0.03$



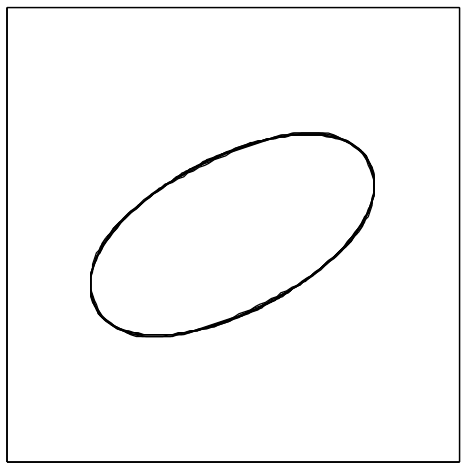
$t = 0.04$ $t = 0.059$ $t = 0.08$ $t = 0.10$

Shear Flow: Different Shear Rate

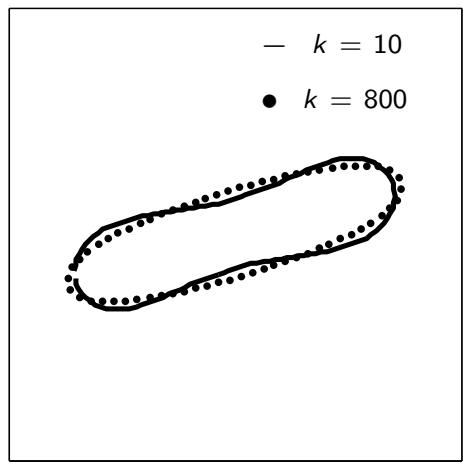
- the direction of the steady state in different shear flow is invariable



Put steady states together



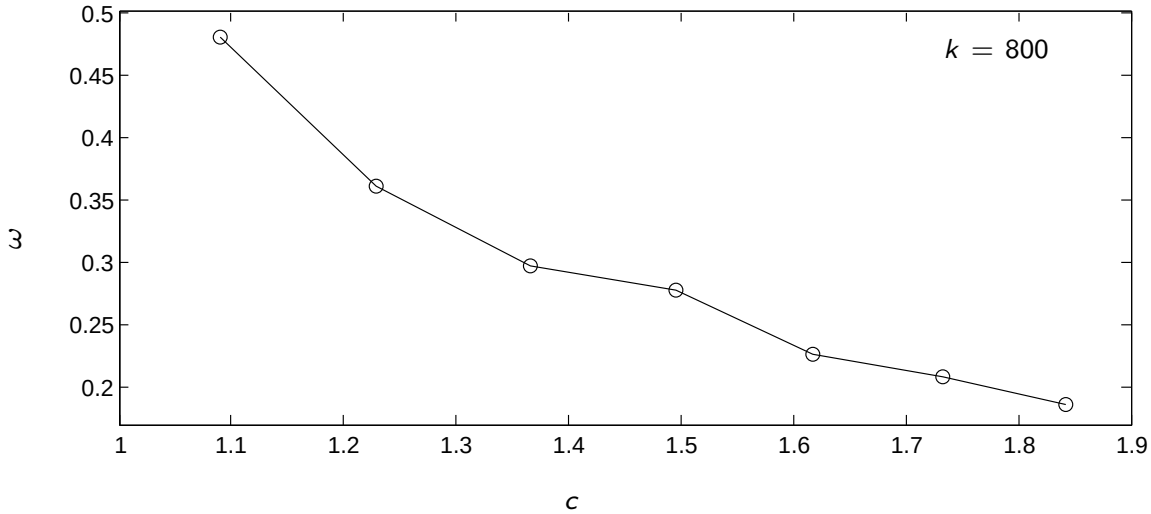
7 steady states, $c = 1.0903$

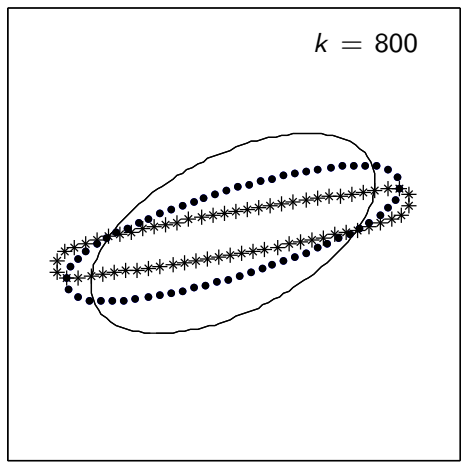


2 steady states, $c = 1.3652$

Shear Flow: Different Ellipses

- If c is bigger, the oblique angle of the steady state will be smaller

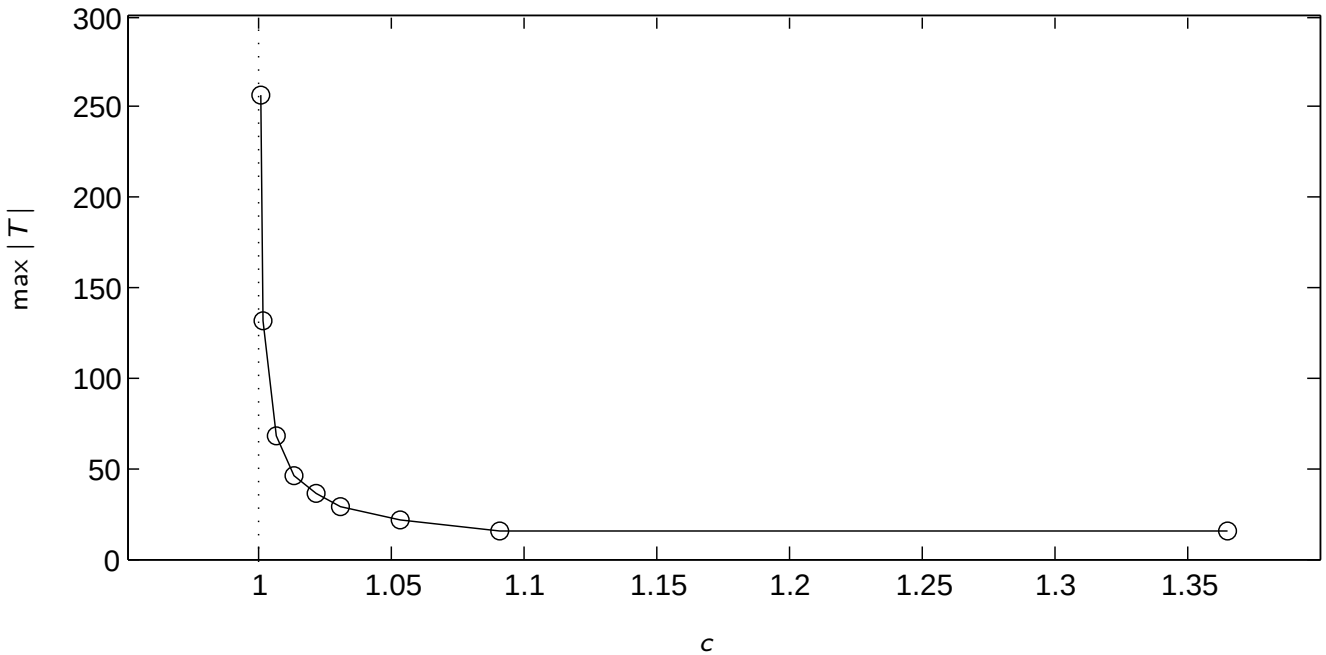




— $c = 1.0903$
· $c = 1.3653$
∗ $c = 1.8426$

Shear Flow: the Singularity of the Circular Shape

While the initial state tends to be a circular curve, the pressure will tends to infinity, i.e. $\lim_{c \to 1+0} \max |T| = +\infty$, $(k = 10.0)$



It means there is no circular membrane in shear flow. Actually, while c is small, the pressure is so large that the membrane will be snapped.

Summary

- We derived a director model with viscous effects, elastic effects and natural energy dissipation;
- A reduced model was obtained from a limit case and an additional elastic stress was found for the Waxman's model;
- The planar membrane shows intrinsic difference between the director model and the reduced elastics surface model;
- We use the tangent angle to express the cylindrical vesicle and simulate its motion;
- We use the projection method for the simulation of incompressible moving surface;
- Local spontaneous curvature was introduced to explain the exocytosis and endocytosis;
- Based on the small scale decomposition and tangent angle description, a numerical method was proposed for the cylindrical vesicle coupling with Stokes flow. The numerical results shows that
  1. The biconcave vesicle has two different dynamic processes in different shear flow;
  2. The steady state's direction is independent on the shear rate, but depends on parameter c.
  3. There is no circular vesicle in shear flow.

Thank You for Your Attention!

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