A Continuum Variational Approach to Vesicle Membrane Modeling

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Ultimate Goal: Modeling Shape Changes in Membranes

- fusion ★ changes in topology ★
- rafts ★ adhesion ★

Derive kinetics explicitly--don’t assume intermediates. Intermediate shapes and states are an output of the model.
Ultimate Goal: Modeling Shape Changes in Membranes

Assume Intermediates

Calculate Intermediates

Kozlovsky, Chernomordik, Koslov, Biophys. J. 2002

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Ultimate Goal: Modeling Shape Changes in Membranes

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kinetics
Intermediate Goal: Verification for a Simpler Problem

★ Growth and Shrinkage of a Lipidic Pore in a Single Bilayer from Osmotic Pressure ★
Intermediate Goal:
Verification for a Simpler Problem

★ Growth and Shrinkage of a Lipidic Pore in a Single Bilayer from Osmotic Pressure ★
Phase Field & Diffuse Interfaces

★ Encodes material property in smoothly varying phase field function $\phi$.

★ Translates Helfrich energy of membrane into a Hamiltonian in terms of $\phi$.

★ Does not assume a particular shape

★ Treats membrane as a **bulk material** (versus a mathematical interface)

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Phase Field Hamiltonian

\[
E = \frac{B}{2} \int \epsilon (\tanh(\phi) + 1) \left( \Delta \phi - \frac{1}{\epsilon^2} F'(\phi) \right) \, dx \\
+ \frac{J}{2} \int \left( \frac{\epsilon}{2} |\nabla \phi|^2 + \frac{1}{\epsilon} F(\phi) \right) \left( \frac{\epsilon}{2} |\nabla \phi|^2 + \frac{1}{\epsilon} F(\phi) \right) \, dx \\
+ \frac{S}{2A_0} \left( \int (\tanh(\phi) + 1) \left( \frac{\epsilon}{2} |\nabla \phi|^2 + \frac{1}{\epsilon} F(\phi) \right) \, dx - A_0 \right)^2
\]

Equations of Motion

Navier Stokes Equations

\[ \rho (\mathbf{u}_t + \mathbf{u} \cdot \nabla \mathbf{u}) + \nabla p = \nu \Delta \mathbf{u} + \mathbf{f}, \quad \text{(force balance)} \]

\[ \nabla \cdot \mathbf{u} = 0, \quad \text{(incompressibility)} \]

\[ \phi_t + \mathbf{u} \cdot \nabla \phi = 0, \quad \text{(membrane moves with fluid)} \]

★ Flexible way to encode classical and new energies

★ Coupling with water is made easy (vesicle and water are one fluid)

★ Forces and time dependence, outputs, are strictly based on first principle physics
Dynamics of a Lipidic Pore
Calculated Pore Radius as a Function of Time

pore radius (µm)

time (s)

pore radius from phase field

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Dynamics of a Lipidic Pore
Calculated Pore Radius as a Function of Time

pore radius from phase field
Dynamics of a Lipidic Pore

Calculated Pore Radius as a Function of Time

![Graph showing the dynamics of a lipidic pore radius as a function of time. The graph is divided into four phases: I, II, III, and IV.](image)

I: pore radius from phase field

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Dynamics of a Lipidic Pore

Calculated Pore Radius as a Function of Time

- **Pore radius** (µm)
- **Time** (s)

**I**

**II**

**III**

**IV**

Pore radius from phase field

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Dynamics of a Lipidic Pore

Calculated Pore Radius as a Function of Time

pore radius (µm)

0
0.5
1
1.5
2
2.5
3
3.5
4

0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6

time (s)

I
II
III
IV

pore radius from phase field

I
II
III
IV

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Dynamics of a Lipidic Pore
Calculated Pore Radius as a Function of Time

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Dynamics of a Lipidic Pore

Calculated Pore Radius as a Function of Time

Dynamics of a Lipidic Pore
Calculated Surface Areas as a Function of Time

membrane surface area

time (s)

surface area

resting surface area

stretching tension

membrane stretching tension (3.2 nN/µm²)

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Dynamics of a Lipidic Pore
Surface Tension and Line Tension as Pointwise Outputs
Rapid Opening Phase (I): Stretching Tension Dominates
Reversal Phase (II): Surface Area Equilibrates
Slower Linear Closing Phase (III): Line Tension Driven Motion
Rapid Closing Phase (IV) : Line Tension Dominates

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Dynamics of a Lipidic Pore
Water Velocity as Pointwise Outputs
Rapid Opening Phase (I): pressure drives water near hole
Reversal Phase (II): stretching driven motion is fully developed - vesicle becomes aspherical
Slower Linear Closing Phase (Ill) : motion of water not effected by vesicle
Rapid Closing Phase (IV) : outflow during closure is quite small