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# Elastic Biomembranes Involving Lipid Separation

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Supported by
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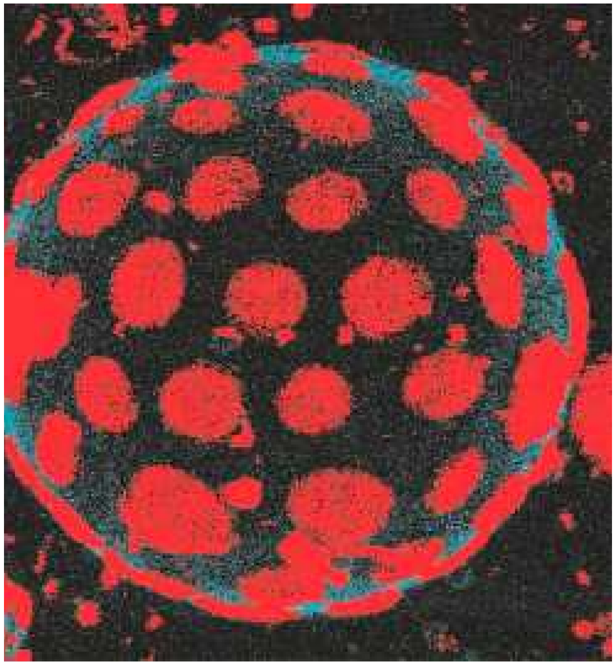
# Introductory Example

Shape determined by elastic energy (bending energy).

Phase separation of lipids (red and blue domains)
$\rightsquigarrow$ phase interface carrying energy (line energy).



[ Baumgart, Hess, Webb 2005 ]

**Goal:** Compute equilibrium shapes of vesicles,
define and study an appropriate relaxational dynamics.

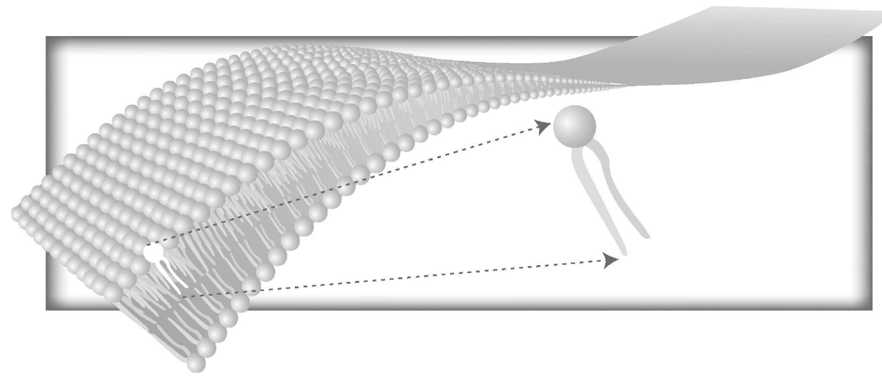
**Example:** Diffuse interface approach for phase separation,
areas of the two phases and enclosed volume preserved. Budding?

# Outline

1. Biomembranes with Lipid Decomposition
   - elastic properties biomembranes
   - phase field approach for the phase separation
2. Relaxational Dynamics
   - dynamics of the phase separation
   - dynamics of the surface
3. Numerical Approach
   - linear finite elements on triangulated surfaces
   - discretisation of evolution equations
4. Simulation Results
   - convergence (in interfacial thickness)
   - influence of physical parameters

# Lipid Bilayers

- consist of lipid molecules
- constitute boundaries of cells and cell organs



[ Peletier, Röger ]

**Bending energy:** [ Canham, Evans, Helfrich 1970s ]

Membrane modelled as two-dimensional hypersurface $\Gamma \subset \mathbb{R}^3$ with energy (to leading order)

$$F_b = \int_\Gamma \frac{k}{2}(\kappa - \bar{\kappa})^2 \left[ + \int_\Gamma k_G \kappa_G \right]$$

$\kappa$ mean curvature, $\kappa_G$ Gauss curvature, $k$, $k_G$ rigidities, $\bar{\kappa}$ spontaneous curvature.

Gauss-Bonnet: $k_G$ constant, $\partial\Gamma$ empty $\Rightarrow \int_\Gamma k_G \kappa_G = k_G \, 2\pi\chi(\Gamma)$.

# Lipid Decomposition

Ordered-disordered phase transition observed in giant unilamellar vesicles.

[ Jülicher, Lipowsky 1996 ]:

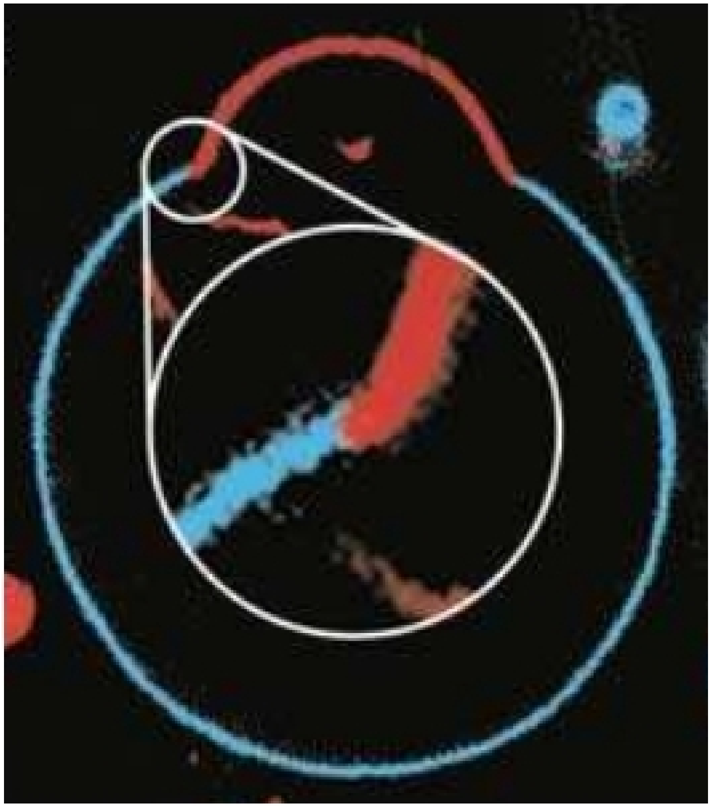
$\Gamma$ is split into two domains (phases) $\Gamma_1$, $\Gamma_2$ with a common boundary $\gamma = \partial\Gamma_1 = \partial\Gamma_2$.

**Assumption:** $\Gamma$ smooth across $\gamma$.

**Line Energy:**

$$F_l = \int_\gamma \sigma$$

$\sigma$ line energy coefficient (constant).



[ Baumgart, Hess, Webb 2003 ]

# Some Work of Relevance

[ Jülicher, Lipowsky 1996 ], equilibrium shapes and budding, axisymmetric case only,
[ Taniguchi, 1996, 1997 ], sphere-like membranes, diffuse interface model for phase separation,
[ Jiang, Lookman, Saxena 1999 ], other symmetries, diffuse interface model for phase separation.
[ Du, Wang 2004, 2006 ], diffuse interface model for representation of the membrane,
[ Campelo, Saxena 2006 ], FD methods, no intermembrane domains,
[ Lowengrub, Xu, Voigt 2007 ], IIM, phase separation on vesicles in 2D flow,
[ Ma, Klug 2008 ], $C^1$ FE, direct minimisation, mesh regularisation.

# Ideas and Methods

**Goal:** Computation of equilibrium shapes by gradient flow dynamics.

- Phase Separation: use a phase field model,
  $\leadsto$ parabolic equation for an order parameter on an evolving surface.
  Overview article: [ Chen 2002 ].
  Use [ Dziuk, Elliott 2006 ] for solving pdes on evolving surfaces .

- Geometric Evolution: surface $\Gamma(t)$ evolves according to

$$\text{normal velocity} \;=\; \text{force (space, orientation, curvature, } \ldots\text{)}.$$

  Here: of Willmore flow type ($L^2$ gradient flow of bending energy).
  Overview article: [ Deckelnick, Dziuk, Elliott 2005 ]. Relevant work (triangulated surfaces):
  [ Mayer, Simonett 2002 ], [ Clarenz, Diewald, Dziuk, Rumpf, Rusu 2004 ],
  [ Bänsch, Morin, Nochetto 2005 ], [ Barrett, Garcke, Nürnberg 2007 ], [ Dziuk 2008 ].

# Line Energy in the Phase Field Approach

Replace by a Ginzburg-Landau energy:

$$F_l^\varepsilon = \int_\Gamma \frac{\varepsilon\sigma}{2}|\nabla_\Gamma c|^2 + \frac{\sigma}{\varepsilon}\psi(c),$$

with a **double-well potential** $\psi \sim (1-c^2)^2$ and the surface gradient

$$\nabla_\Gamma c = \nabla c - \nabla c \cdot \boldsymbol{n}\,\boldsymbol{n} = \boldsymbol{P}\nabla c \quad \text{where } \boldsymbol{P} = \boldsymbol{Id} - \boldsymbol{n}\otimes\boldsymbol{n},$$

$\boldsymbol{n}$ unit normal on $\Gamma$.

Flat case, in the sense of a $\Gamma$-limit:

$$F_l^\varepsilon \xrightarrow{\varepsilon\to 0} F_l = \int_\gamma \sigma.$$

# Membrane Energy

Total membrane energy:

$$F(\Gamma, c : \Gamma \to \mathbb{R}) = \int_\Gamma \underbrace{\frac{k(c)}{2}(\kappa - \bar{\kappa}(c))^2}_{\text{bending energy}} + \underbrace{\sigma\Big(\frac{\varepsilon}{2}|\nabla_\Gamma c|^2 + \frac{1}{\varepsilon}\psi(c)\Big)}_{\text{line energy}}$$

Evolution:

- Evolving hypersurface $\{\Gamma(t)\}_t$ with velocity $\boldsymbol{v} = V\boldsymbol{n}$ (geometric evolution),
- Law for the order parameter $c(t) : \Gamma(t) \to \mathbb{R}$ will involve the **material derivative** (= normal time derivative)
$$\partial_t^\bullet c = \partial_t c + \boldsymbol{v} \cdot \nabla c,$$
- Constraints: $|\Gamma|$ and $\int_\Gamma c$ are preserved ($\leadsto |\Gamma_1|$ and $|\Gamma_2|$ are preserved), enclosed volume is preserved.

# Phase Separation

Postulate a law for the order parameter $c$ such that the energy decreases if $\Gamma$ is stationary.

- **Cahn-Hilliard** equation, $c$ conserved quantity ($\int_\Gamma c$ preserved):

$$\partial_t^\bullet c + \underbrace{c\nabla_\Gamma \cdot \boldsymbol{v}}_{=-c\kappa V} = \nabla_\Gamma \cdot \big(D_c \nabla_\Gamma \mu\big).$$

- **Allen-Cahn** equation:

$$\partial_t^\bullet c = -\mu - \lambda_c$$

  with Lagrange multiplier $\lambda_c$ to preserve $\int_\Gamma c$.

(chemical) potential:

$$\mu = \frac{\delta F}{\delta c} = \frac{k'(c)}{2}(\kappa - \bar{\kappa}(c))^2 - k(c)(\kappa - \bar{\kappa}(c))\bar{\kappa}'(c) - \sigma\varepsilon\Delta_\Gamma c + \frac{\sigma}{\varepsilon}\psi'(c)$$

# Evolution of the Surface

Deduced by computing the time derivative of the energy and using the law for $c$.

Exemplary for the case $k$ constant, $\bar{\kappa} = 0$:

$$\begin{aligned} \frac{d}{dt}F = & \int_\Gamma k\kappa\partial_t^\bullet\kappa + \sigma\varepsilon \underbrace{\partial_t^\bullet|\nabla_\Gamma c|^2}_{=\nabla_\Gamma c\cdot\nabla_\Gamma\partial_t^\bullet c - \nabla_\Gamma c\otimes\nabla_\Gamma c:\nabla \boldsymbol{v}} + \frac{\sigma}{\varepsilon}\psi'(c)\partial_t^\bullet c \\ & + \int_\Gamma \Big(\frac{k}{2}\kappa^2 + \sigma\varepsilon|\nabla_\Gamma c|^2 + \frac{\sigma}{\varepsilon}\psi(c)\Big)\nabla_\Gamma\cdot\boldsymbol{v} \\ = & - \int_\Gamma D_c|\nabla_\Gamma\mu|^2 \\ & + \int_\Gamma V\Big( - \sigma\varepsilon\nabla_\Gamma c\otimes\nabla_\Gamma c : \nabla_\Gamma\boldsymbol{n} + (\mu c - f)\kappa + k\Delta_\Gamma\kappa + k|\nabla_\Gamma\boldsymbol{n}|^2\kappa\Big) \end{aligned}$$

# Summary, Evolution Laws

Surface:

$$\begin{aligned} V = &- \left(\Delta_\Gamma + |\nabla_\Gamma \boldsymbol{n}|^2\right)\big(k(c)(\kappa - \bar{\kappa}(c))\big) \\ &+ (f - \mu c)\kappa + \sigma\epsilon\nabla_\Gamma c \otimes \nabla_\Gamma c : \nabla_\Gamma \boldsymbol{n} \\ &+ \lambda_v - \lambda_a \kappa \end{aligned}$$

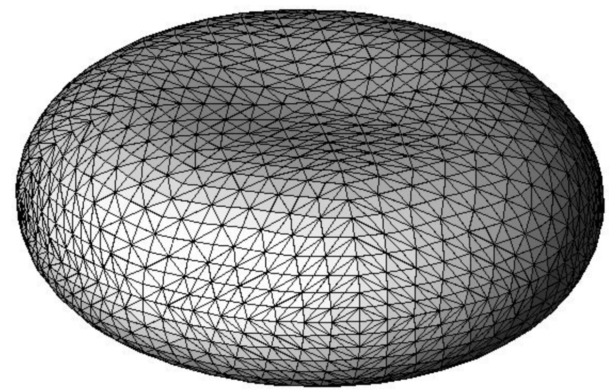
with Lagrange multipliers $\lambda_v$ and $\lambda_a$ for preserving the enclosed volume and the membrane area.

Phase Separation:

$$\partial_t^\bullet c - c\kappa V = \nabla_\Gamma \cdot \big(D_c \nabla_\Gamma \mu\big)$$

$$\mu = \frac{k'(c)}{2}(\kappa - \bar{\kappa}(c))^2 - k(c)(\kappa - \bar{\kappa}(c))\bar{\kappa}'(c) - \sigma\varepsilon\Delta_\Gamma c + \frac{\sigma}{\varepsilon}\psi'(c)$$

# Linear Surface Finite Elements



Approximation of $\Gamma$ by a polyhedral surface $\Gamma_h$
(admissible triangulation)

$$\Gamma_h = \bigcup_{T_h \in \mathcal{T}_h} T_h$$

given in terms of vertex positions $\{\boldsymbol{x}_i\}_i$ and topology.

Finite element space (isoparametric, linear):

$$S_h = \left\{ \phi_h \in C^0(\Gamma_h) \,\middle|\, \phi_h\big|_{T_h} \text{ linear for all } T_h \in \mathcal{T}_h \right\}.$$

Identity $\boldsymbol{x}_h \in S_h^3$, given by $\boldsymbol{x}_h(\boldsymbol{x}_i) = \boldsymbol{x}_i$ for all $i$.

# Weak Formulation, Surface Evolution

Based on $\kappa \boldsymbol{n} = \Delta_\Gamma \boldsymbol{x}$.

Discretisation as in [ Barrett, Garcke, Nürnberg 2007 ]:
Vertices move in normal direction according to geometric evolution law,
in tangential direction to maintain a good grid quality (equidistribution in 1D).

$$\int_\Gamma \partial_t \boldsymbol{x} \cdot \boldsymbol{n} \chi - f \kappa \chi - k(c) \nabla_\Gamma \kappa \cdot \nabla_\Gamma \chi = \int_\Gamma \cdots + \lambda_v \int_\Gamma \chi + \lambda_a \int_\Gamma \kappa \chi,$$

$$\int_\Gamma \kappa \boldsymbol{n} \cdot \boldsymbol{\xi} + \nabla_\Gamma \boldsymbol{x} : \nabla_\Gamma \boldsymbol{\xi} = 0.$$

# Discrete Surface Evolution

Given the vertices and fields at time $t = m\Delta t$:

$$\int_{\Gamma_h^m} \frac{\boldsymbol{x}_h^{m+1} - \boldsymbol{x}_h^m}{\Delta t} \cdot \boldsymbol{n}\chi_h - f_h^m \kappa_h^{m+1}\chi_h - k(c_h^m)\nabla_{\Gamma_h^m}\kappa_h^{m+1} \cdot \nabla_{\Gamma_h^m}\chi_h = \dots$$

$$\int_{\Gamma_h^m} \kappa_h^{m+1}\boldsymbol{n} \cdot \boldsymbol{\xi}_h + \nabla_{\Gamma_h^m}\boldsymbol{x}_h^{m+1} : \nabla_{\Gamma_h^m}\boldsymbol{\xi}_h = 0.$$

Tangential motion of the vertices determined by second equation.

System:

$$\begin{pmatrix} (\boldsymbol{N}^m)^T & -B^m \\ \boldsymbol{A}^m & \boldsymbol{N}^m \end{pmatrix} \begin{pmatrix} \underline{\boldsymbol{x}}^{m+1} \\ \underline{\kappa}^{m+1} \end{pmatrix} = \begin{pmatrix} \underline{a}^m + \lambda_v \underline{l}^m + \lambda_a M^m \underline{\kappa}^m \\ 0 \end{pmatrix}$$

Resolving first equation w.r.t. $\underline{\kappa}^{m+1}$ yields

$$\boldsymbol{I}^m \underline{\boldsymbol{x}}^{m+1} = \underline{\boldsymbol{r}}^m + \lambda_v \underline{\boldsymbol{\nu}}^m + \lambda_a \underline{\boldsymbol{k}}^m.$$

# Constraints

Formula for new vertices:

$$\boldsymbol{I}^m \underline{\boldsymbol{x}}^{m+1} = \underline{\boldsymbol{r}}^m + \lambda_v \underline{\boldsymbol{\nu}}^m + \lambda_a \underline{\boldsymbol{k}}^m.$$

**Goal:** $\lambda_v$ and $\lambda_a$ such that

$$\int_{\Gamma_h^{m+1}} \boldsymbol{n}^{m+1} \cdot \boldsymbol{x}_h^{m+1} = \int_{\Gamma_h^0} \boldsymbol{n}^0 \cdot \boldsymbol{x}_h^0, \quad |\Gamma_h^{m+1}| = |\Gamma_h^0|.$$

[ Barrett, Garcke, Nürnberg 2007 ] employ explicit formulae $\rightsquigarrow \lambda_v^m$, $\lambda_a^m$.

Here implicitely (similar to ideas of [ Bonito, Nochetto ])

1. solve $(\boldsymbol{I}^m)^{-1}\underline{\boldsymbol{r}}^m$, $(\boldsymbol{I}^m)^{-1}\underline{\boldsymbol{\nu}}^m$, $(\boldsymbol{I}^m)^{-1}\underline{\boldsymbol{k}}^m$ with CG,
2. compute $\lambda_v^{m+1}$ and $\lambda_a^{m+1}$ with a Newton method (involves computing $\underline{\boldsymbol{x}}^{m+1}$),
3. find the new curvature values $\underline{\boldsymbol{\kappa}}^{m+1}$.

Price: three linear systems instead of one $\rightsquigarrow$ switch when the surface has 'almost relaxed'.

# Weak Formulation, Phase Separation

Discretisation based on [ Dziuk, Elliott 2006 ] for surface pdes,
requires motion of the grid points according to material velocity, here $\boldsymbol{v} = V\boldsymbol{n}$.

**But:** grid points involve tangential motion, $\partial_t \boldsymbol{x} = V\boldsymbol{n} + \boldsymbol{T}$, which must be taken into account.

$$\begin{aligned} \partial_t^\bullet c - cV\kappa &= \partial_t c + V\boldsymbol{n} \cdot \nabla c + c\nabla_\Gamma \cdot (V\boldsymbol{n}) \\ &= \partial_t c + (\partial_t \boldsymbol{x}) \cdot \nabla c + c\nabla_\Gamma \cdot (\partial_t \boldsymbol{x}) - \nabla_\Gamma \cdot (c\boldsymbol{T}) \end{aligned}$$

Cahn-Hilliard system:

$$\int_\Gamma \big(\partial_t c + \partial_t \boldsymbol{x} \cdot \nabla c + c\nabla_\Gamma \cdot (\partial_t \boldsymbol{x})\big)\chi + D_c \nabla_\Gamma \mu \cdot \nabla_\Gamma \chi = \int_\Gamma -c\partial_t \boldsymbol{x} \cdot \nabla_\Gamma \chi,$$

$$\int_\Gamma \mu\phi - \sigma\varepsilon\nabla_\Gamma c \cdot \nabla_\Gamma \phi = \int_\Gamma \Big(\frac{k'(c)}{2}(\kappa - \bar{\kappa}(c))^2 - k(c)(\kappa - \bar{\kappa}(c))\bar{\kappa}'(c) + \frac{\sigma}{\varepsilon}\psi'(c)\Big)\phi.$$

# Discrete Phase Separation

Semi-discrete Cahn-Hilliard system:

$$\frac{d}{dt}\Big(\int_{\Gamma_h(t)} c_h(t)\chi_h(t)\Big) + \int_{\Gamma_h(t)} D_c \nabla_{\Gamma_h(t)}\mu_h(t)\cdot\nabla_{\Gamma_h(t)}\chi_h(t)$$
$$= -\int_{\Gamma_h(t)} c_h(t)\partial_t \boldsymbol{x}_h \cdot \nabla_{\Gamma_h(t)}\chi_h(t),$$

$$\int_{\Gamma_h(t)} \mu_h(t)\phi_h(t) - \sigma\varepsilon\nabla_{\Gamma_h(t)}c_h(t)\cdot\nabla_{\Gamma_h(t)}\phi_h(t) = \ldots$$

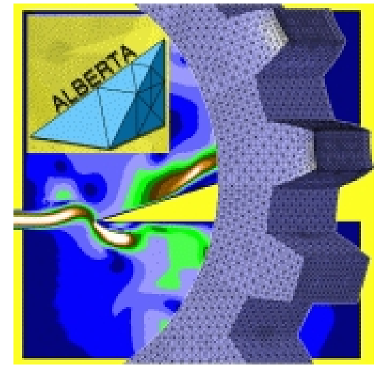
Fully discrete system:

$$\begin{pmatrix} \frac{1}{\Delta t}M^{m+1} & D_c A^{m+1} \\ -\sigma\varepsilon A^{m+1} & M^{m+1} \end{pmatrix}\begin{pmatrix} \underline{c}^{m+1} \\ \underline{\mu}^{m+1} \end{pmatrix} = \begin{pmatrix} \underline{r_c} \\ \underline{r_\mu} \end{pmatrix}$$

Total mass is conserved (insert $\chi_h \equiv 1$).

# Implementation, Adaptivity

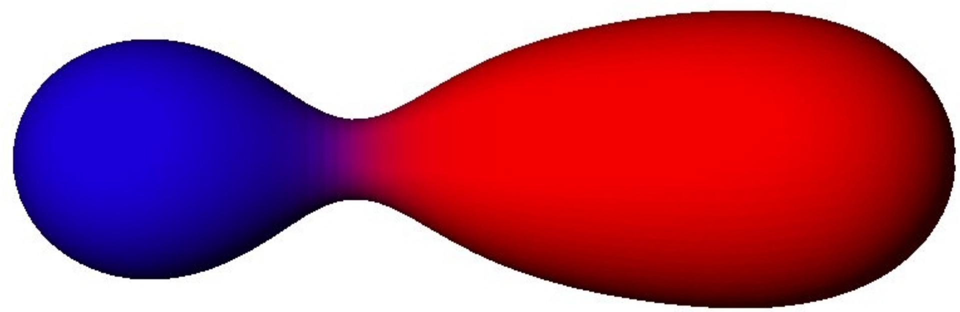
Implementation with the ALBERTA finite element toolkit,
[ Schmidt, Siebert 2005 ].




Isoparametric linear finite elements provided,
including adaption of the grid (bisection).

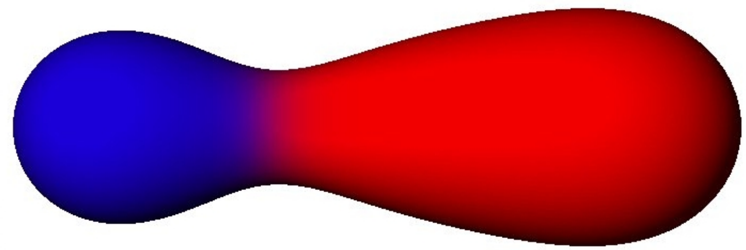
Experience value from flat case:
ensure 8 grid points
across the interfacial layers.

Phase transition regions often most curved.



$\rightsquigarrow$ used order parameter (indicating the phase interface) for grid adaption so far.

# Parameters for Convergence Test



Initial shape relaxed shape.

| | | | |
|---|---|---|---|
| $\lvert\Omega\rvert$ | 2.8760 | $k$ | 1.0000 |
| $\lvert\Gamma\rvert$ | 12.5610 | $\bar{\kappa}$ | 0.0000 |
| | | $\sigma$ | 2.5000 |
| $R_c := \sqrt{\lvert\Gamma\rvert/4\pi}$ | 0.9996 | $\lambda := \frac{4}{3}R_c\sigma/k$ | 3.3319 |
| $\bar{v} := \lvert\Omega\rvert/\frac{4}{3}\pi R_c^3$ | 0.6875 | $x := \lvert\Gamma_1\rvert/\lvert\Gamma\rvert$ | 0.6986 |

# Convergence in $\varepsilon$ I

Fully refined grid:

| $h$ | $\varepsilon$ | $F_h$ | $eoc$ | comment |
|---|---|---|---|---|
| [0.032, 0.089] | 0.4243 | 51.573 | | |
| [0.021, 0.068] | 0.3000 | 51.388 | 0.7229 | |
| [0.014, 0.045] | 0.2121 | 51.244 | 1.9602 | |
| [0.010, 0.035] | 0.1500 | 51.171 | | |
| [0.014, 0.045] | 0.3000 | 51.371 | | finer mesh |

$$eoc(\varepsilon) = \log(\tfrac{F_h(\sqrt{2}\varepsilon) - F_h(\varepsilon)}{F_h(\varepsilon) - F_h(\varepsilon/\sqrt{2})}) / \log(\sqrt{2}).$$

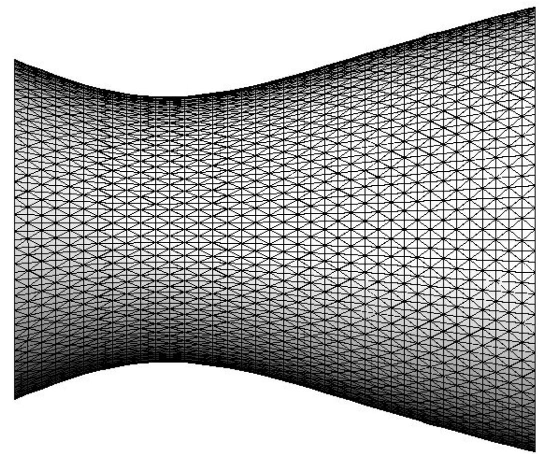
Timestep: $\Delta t \sim h^2$.

# Convergence in $\varepsilon$ II

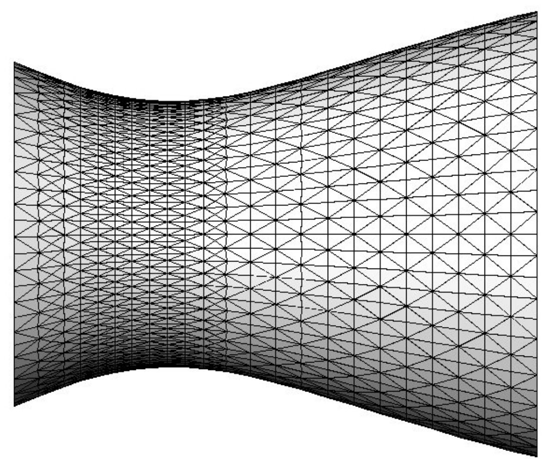
Adaptively refined grid:

| $\varepsilon$ | $F_h$ | $eoc$ | comment |
|---|---|---|---|
| 0.2121 | 51.270 | | |
| 0.1500 | 51.199 | 1.6556 | |
| 0.1061 | 51.159 | 3.0291 | |
| 0.0750 | 51.145 | | |
| 0.2121 | 51.280 | | finer mesh |
| 0.2121 | 51.244 | | globally refined |

18434 vertices

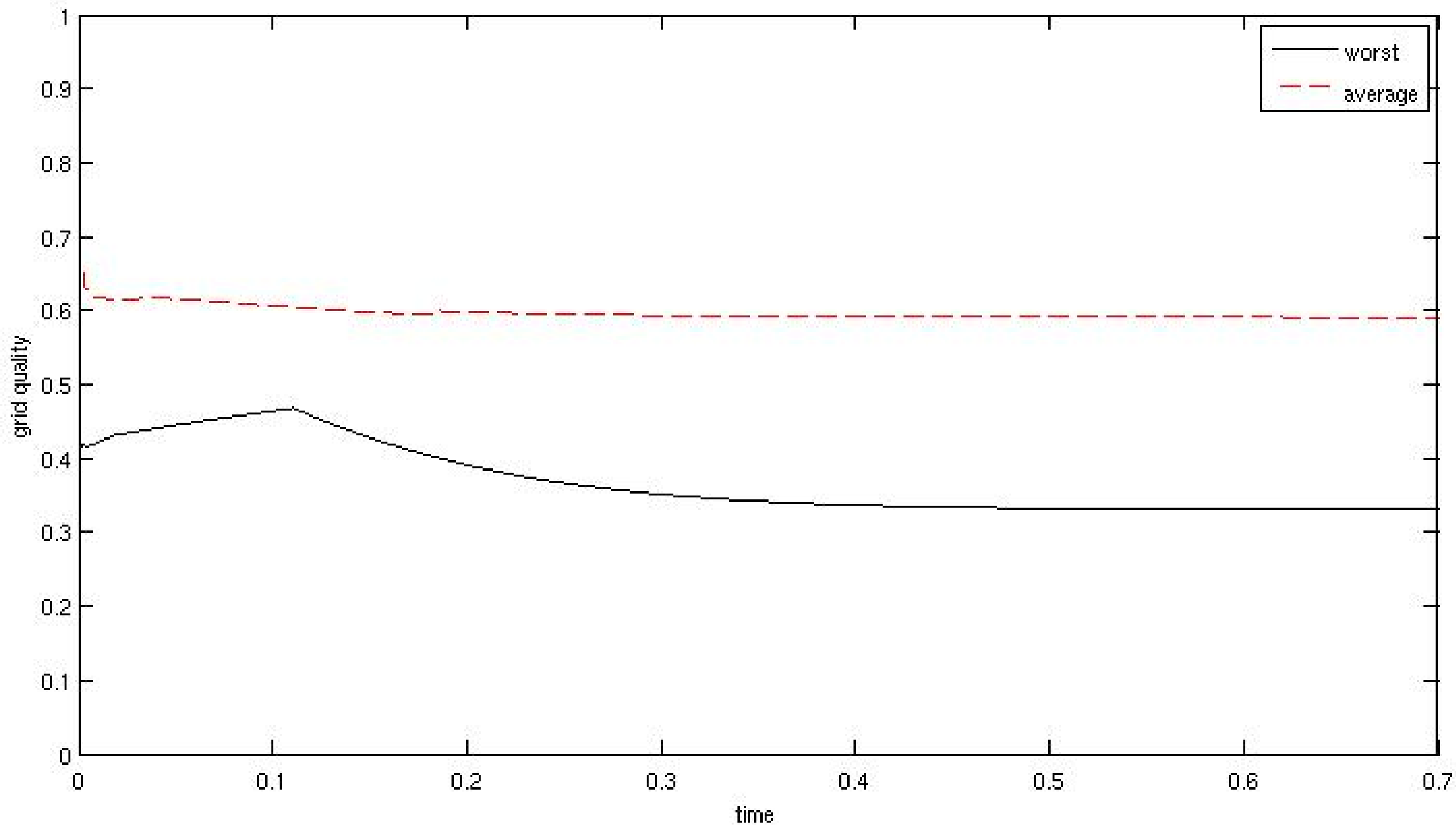


$\approx$ 5314 vertices



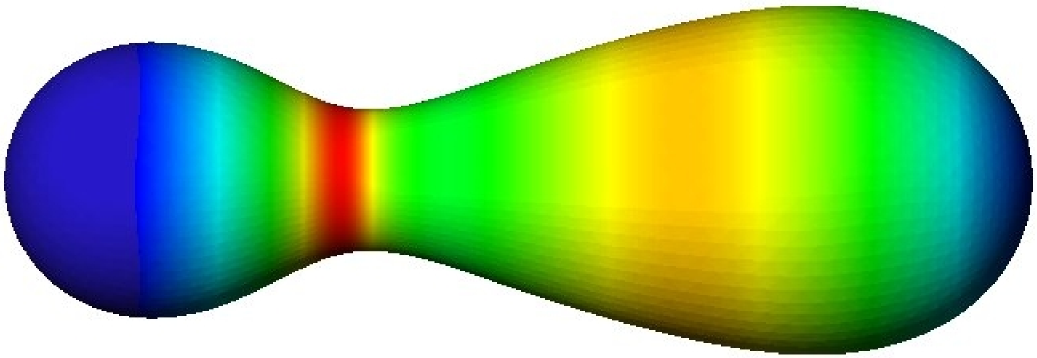
# Grid Quality

$q = \min\{\sin(\alpha) \mid \alpha \text{ inner angle}\}.$

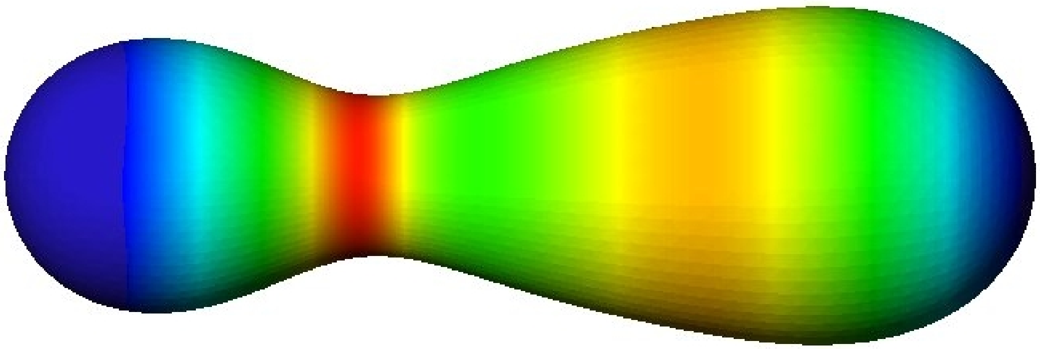


# Spontaneous Curvature Effect

With spontaneous curvature:



No spontaneous curvature:



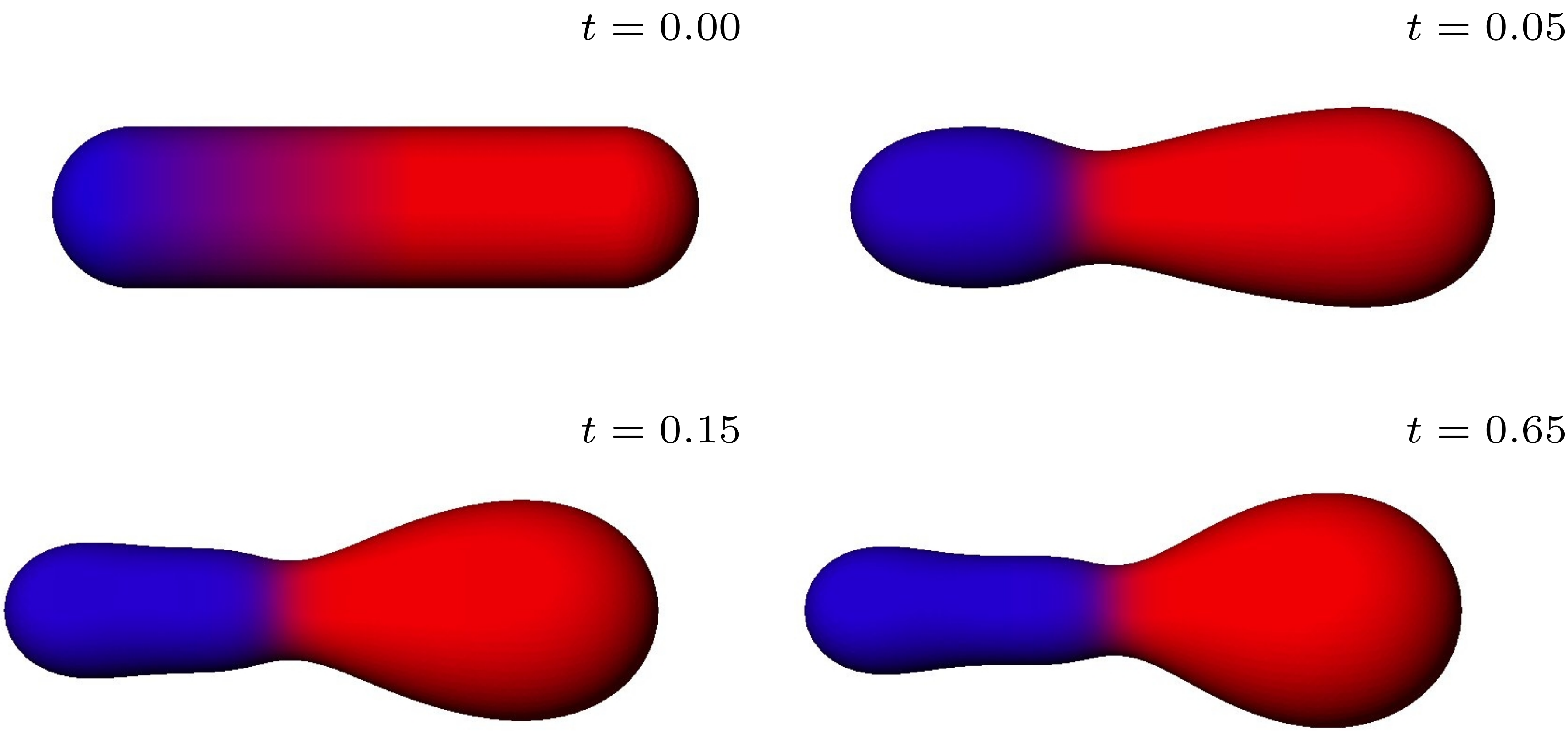
$\bar{\kappa}(c = 1) = -1.206061$,
$\bar{\kappa}(c = -1) = 0.0$,
interpolation with polynomial of degree three in between.

Result:
neck more pronounced,
adjacent membranes slightly more rounded.

Colour indicates the curvature between -0.35 (blue) and -0.15 (red).

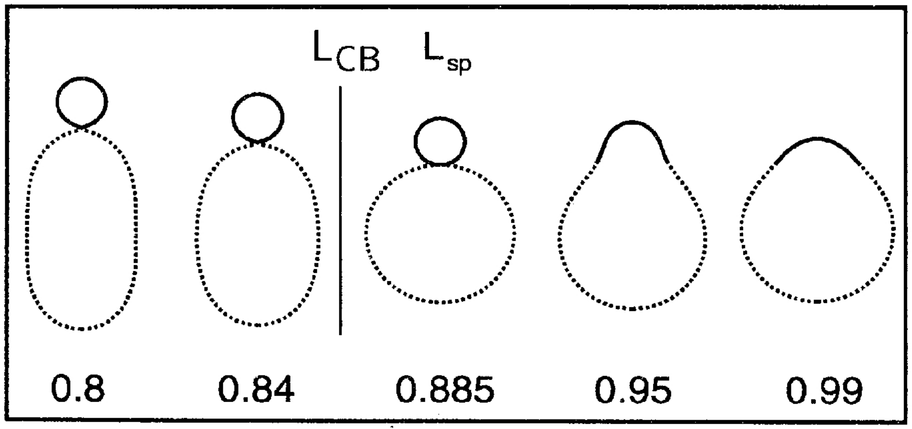
# Effect of Different Bending Rigidities

$k(\text{red}) = 2.0$, $k(\text{blue}) = 0.4$ and interpolation with a polynomial of degree three in between.



# Quantitative Example

[ Jülicher, Lipowsky 1996 ]:

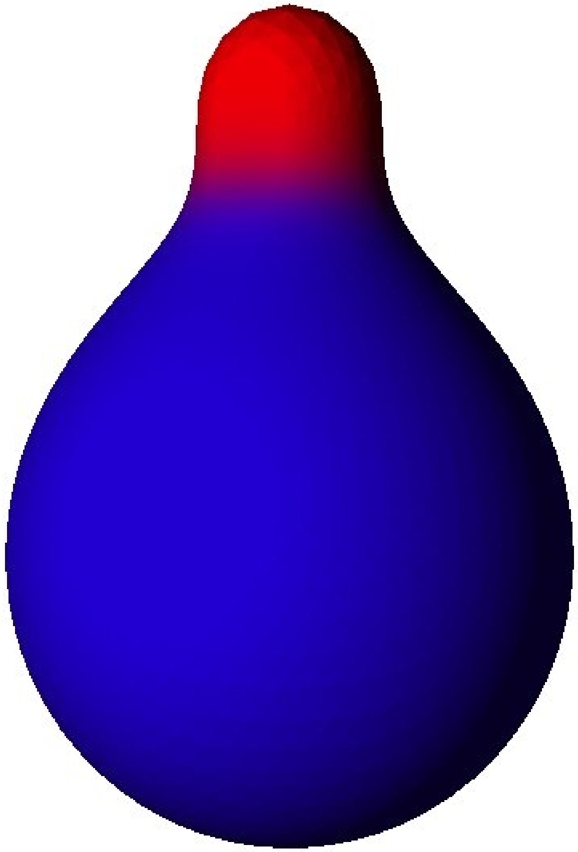



$\bar{v} = 0.92$, $\lambda = 9$, $x = 0.1$.

Predicted energy: $[54.915, 55.047]$.

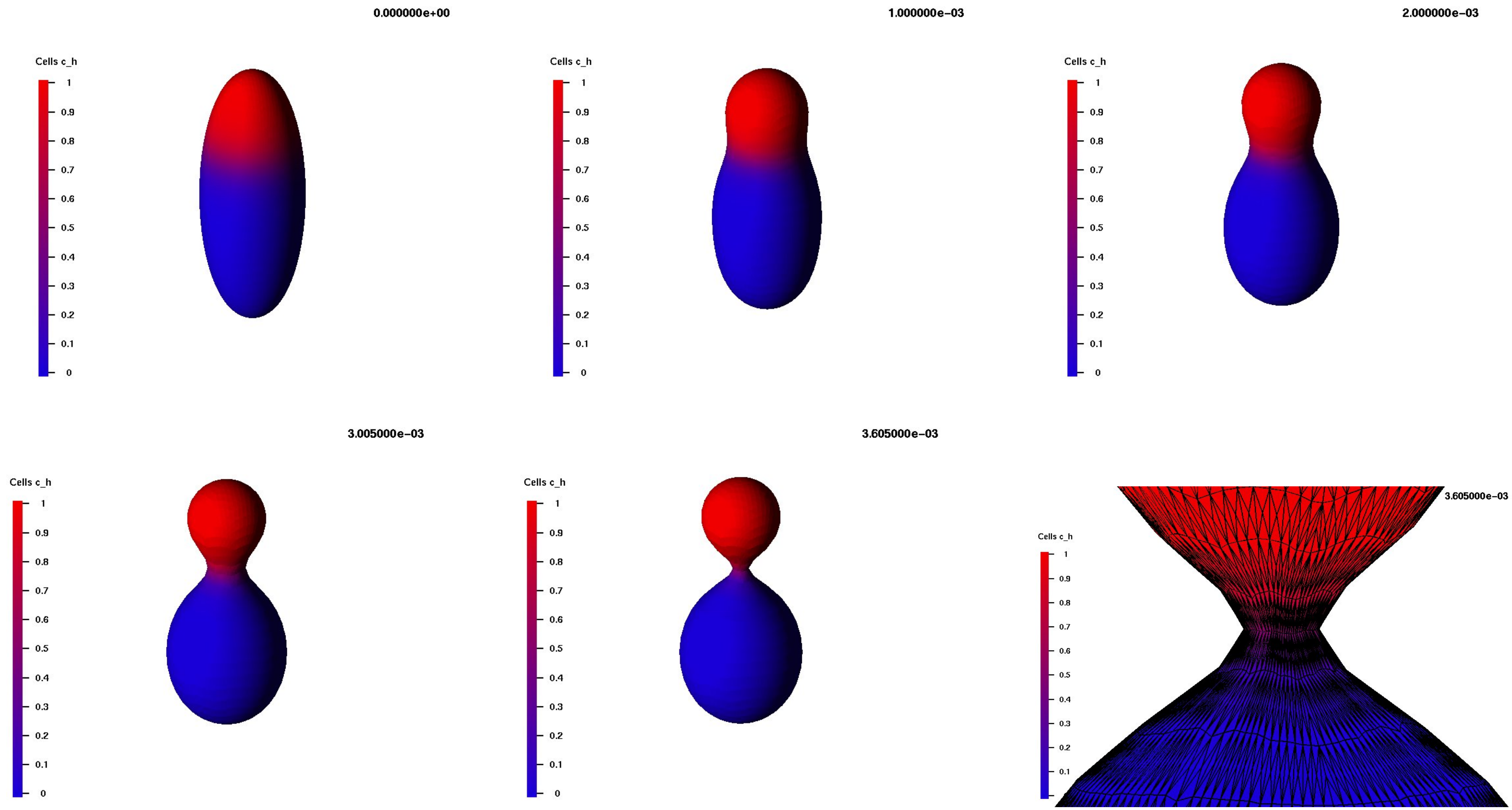
Measured energy: 55.019.

Computed shape:



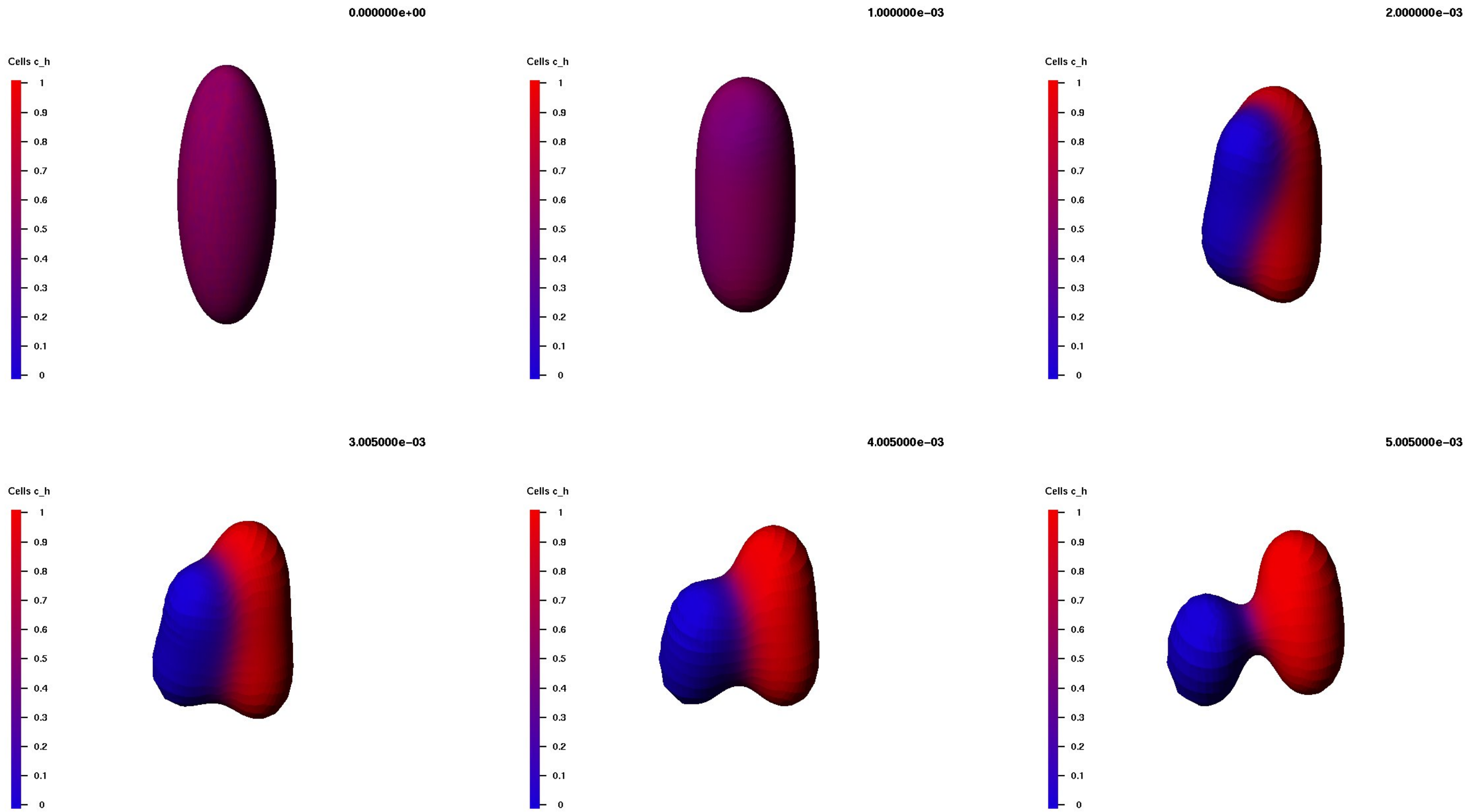
# Budding?

Budding due to high line energy coefficient $\sigma$.
$\bar{v} \approx 0.85$, $\lambda \approx 14.7$, $x \approx 0.275$, $\bar{\kappa} = 0.0$.



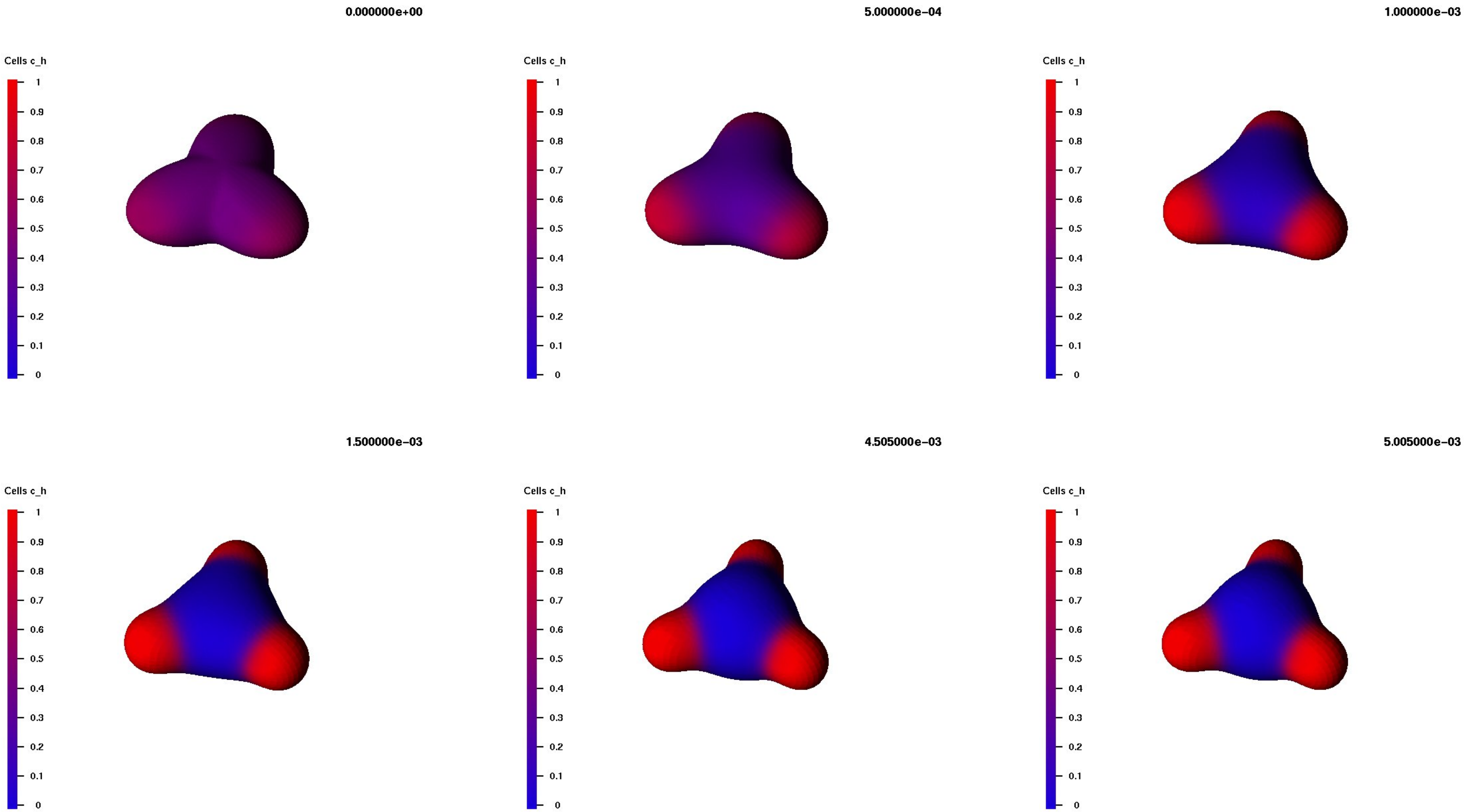
# Random Order Parameter

$\bar{v} \approx 0.85$, $\lambda \approx 14.85$, $x \approx 0.55$ (random initial field $c$), $\bar{\kappa} = 0.0$.



# Non-Axisymmetric Structure

$\bar{v} \approx 0.9$, $\lambda \approx 9.0$, $x \approx 0.45$, $\bar{\kappa} = 0.0$.



## Scale Invariance, Effective Parameters

Consider smooth hypersurfaces $\Gamma$ in $\mathbb{R}^3$ of sphere-topology enclosing a domain $\Omega$, as well as smooth, compact curves $\gamma \subset \Gamma$. Characteristic radius: $R = |\Gamma|/4\pi$.

System energy

$$F = \int_\Gamma \frac{k}{2}(\kappa - \bar{\kappa})^2 + \int_\gamma \sigma$$

is invariant under scaling $\boldsymbol{x} \mapsto \eta \boldsymbol{x}$, $\boldsymbol{x} \in \Gamma$, $\eta > 0$, provided that $\sigma \mapsto \sigma/\eta$ and $\bar{\kappa} \mapsto \bar{\kappa}/\eta$.

Equilibrium shapes / local minimiser are characterised by:

| | |
|---|---|
| $v_r = \lvert\Omega\rvert/(4\pi/3)R^3$ | reduced volume, |
| $q_r = \lvert\Gamma_1\rvert/\lvert\Gamma\rvert$ | relative domain size, |
| $\sigma_r = \sigma R/k$ | reduced line tension, |
| $c_r = \bar{\kappa} R$ | reduced spontaneous curvature. |

# Effective Parameters, Phase Diagram

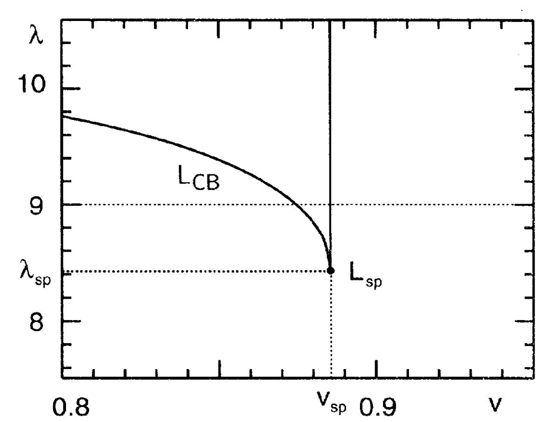
Example from [ Jülicher, Lipowsky 1996 ].

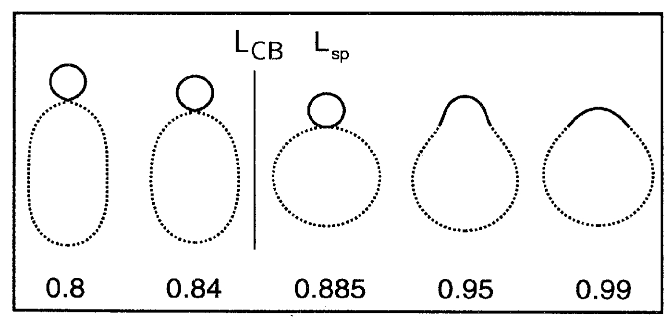
$q_r = 0.1$ fixed, $c_r = 0.0$.

Top: variation of $\lambda = \sigma_r$ and $v = v_r$.
Bottom: $\sigma_r = 0.9$ fixed, variation of $v_r$.

Limit shapes:
$L_{CB}$: prolate and a spherical bud,
$L_{sp}$: two cut spheres.

Axisymmetric shapes only.



# Relaxational Dynamics

Total Energy:

$$F(\Gamma, c) = \int_\Gamma \frac{k}{2}(\kappa - \bar{\kappa})^2 + \sigma\left(\frac{\varepsilon}{2}|\nabla_\Gamma c|^2 + \frac{1}{\varepsilon}\psi(c)\right)$$

Approach to define the motion laws:

First, postulate a motion law for the order parameter such that the energy decreases if the surface does not move.
Here: Allen-Cahn equation with Lagrange multiplier for the constraint.

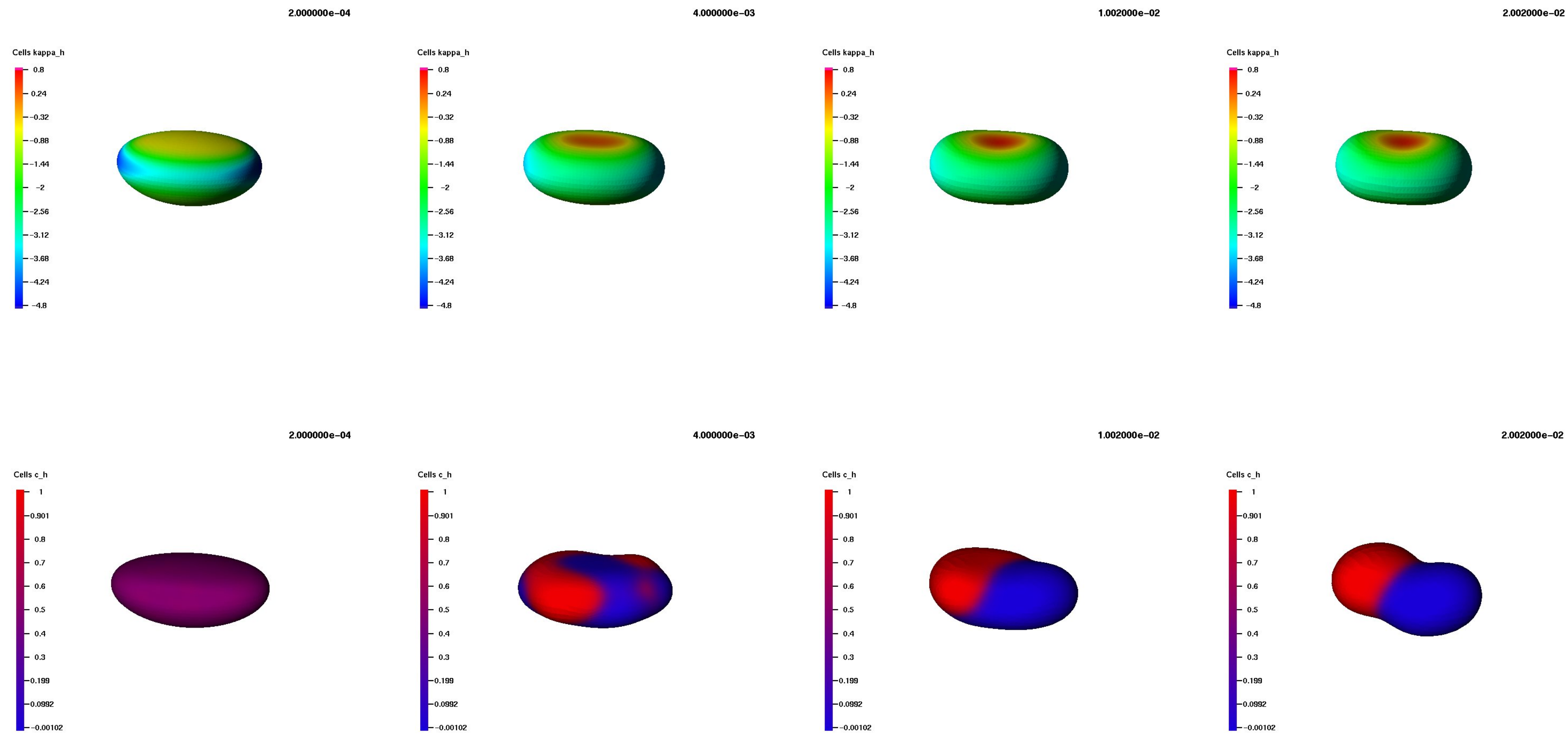
Second, compute the time derivative of the energy and deduce the laws for the velocity such that energy decreases in time.

# Euler-Lagrange Equation, SIM

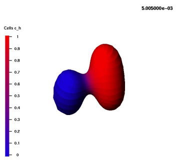
$$
\begin{aligned}
0 &= \sum_{i=1}^{2} \int_{\Gamma_i} k_i \Big( \Delta_\Gamma \kappa_i + |\nabla_\Gamma \boldsymbol{n}|^2 (\kappa_i - \bar{\kappa}_i) - \frac{1}{2} (\kappa_i - \bar{\kappa}_i)^2 \kappa_i \Big) \boldsymbol{n} \cdot \boldsymbol{w} \\
&+ \int_\gamma \Big( \sigma \boldsymbol{\kappa}_\gamma + \sum_{i=1}^{2} k_i (\kappa_i - \bar{\kappa}_i)^2 \boldsymbol{\tau}_i \Big) \cdot \boldsymbol{w} \\
&+ \sum_{i=1}^{2} \lambda_A^{(i)} \Big( \int_{\Gamma_i} -\boldsymbol{\kappa}_i \cdot \boldsymbol{w} + \int_\gamma \boldsymbol{\tau}_i \cdot \boldsymbol{w} \Big) \\
&+ \lambda_V \sum_{i=1}^{2} \int_{\Gamma_i} \boldsymbol{n} \cdot \boldsymbol{w}.
\end{aligned}
$$

# Example IV: Discocyte

Effects by spontaneous curvature.



# Example III: Mesh



without re-meshing