Obtaining the Bending Modulus from a Buckled Lipid Membrane

Patrick Diggins, Mingyang Hu, Markus Deserno

Department of Physics, Carnegie Mellon University, Pittsburgh PA, USA

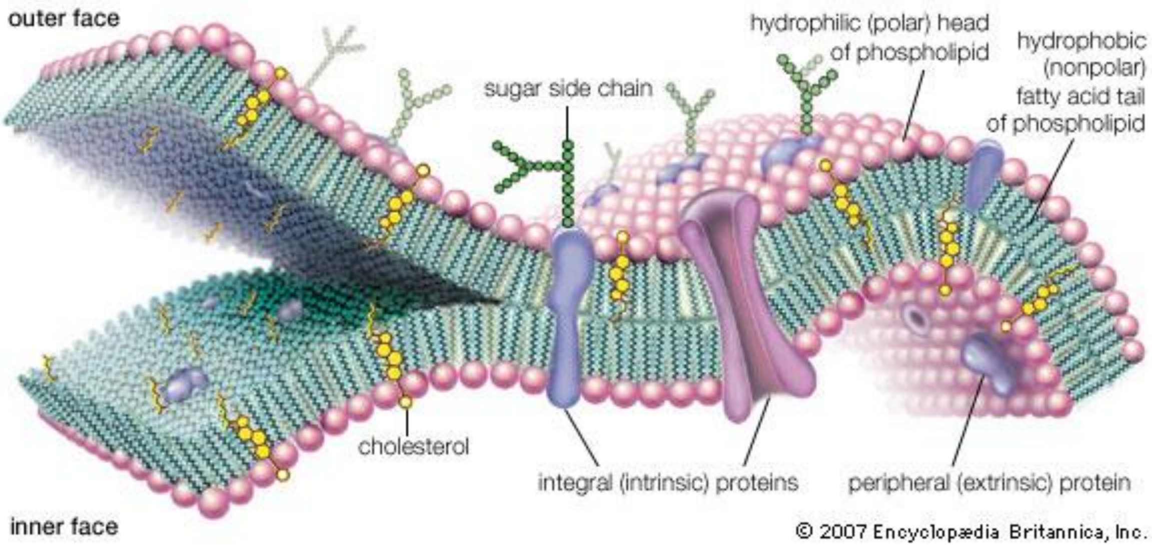
October 11, 2013

Carnegie Mellon

Outline

- Lipid Membranes
  - Membrane elasticity
- Review of other techniques
  - Fluctuations
  - Active Bending
- Theory
  - Shape equation
  - Stress-strain relation
  - Fluctuation corrections
- Simulation Setup
- Results
- Energetics
  - Temperature Dependence of Bending Rigidity

Lipid Membrane



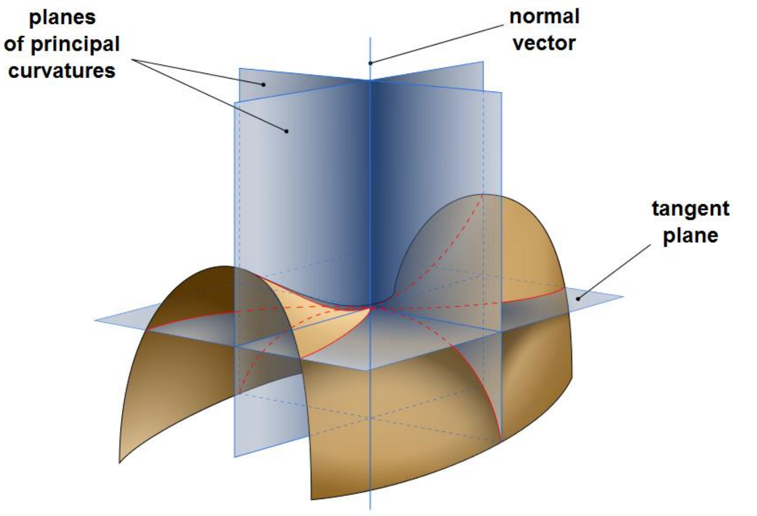
- Forms barriers around cells and cellular organelles
- Formed by two layers of lipid molecules
- Forms due to the hydrophilic nature of lipid molecules

Elasticity of Lipid Membranes

- We can model the membrane as an elastic sheet.
- The energy can be described as:

$$\mathrm{E}[S] = \int_S dA \left\{ \frac{1}{2} \kappa (K - K_0)^2 + \bar{\kappa} K_G \right\}$$

- κ: Bending modulus
- $\bar{\kappa}$: Gaussian curvature modulus
- $K = c_1 + c_2$: Total curvature
- K_0: Intrinsic curvature
- $K_G = c_1 c_2$: Gaussian curvature



en.widipedia.org/wiki/Curvature

Carnegie Mellon

Outline

- Lipid Membranes
  - Membrane elasticity
- **Review of other techniques**
  - **Fluctuations**
  - **Active Bending**
- Theory
  - Shape equation
  - Stress-strain relation
  - Fluctuation corrections
- Simulation Setup
- Results
- Energetics
  - Temperature Dependence of Bending Rigidity

Carnegie Mellon

Simulation Techniques to obtain κ

- Fluctuation Methods
  - Undulations
  - Tilt
- Active Bending
  - Cylindrical tethers
  - Buckling

Carnegie Mellon

Fluctuations

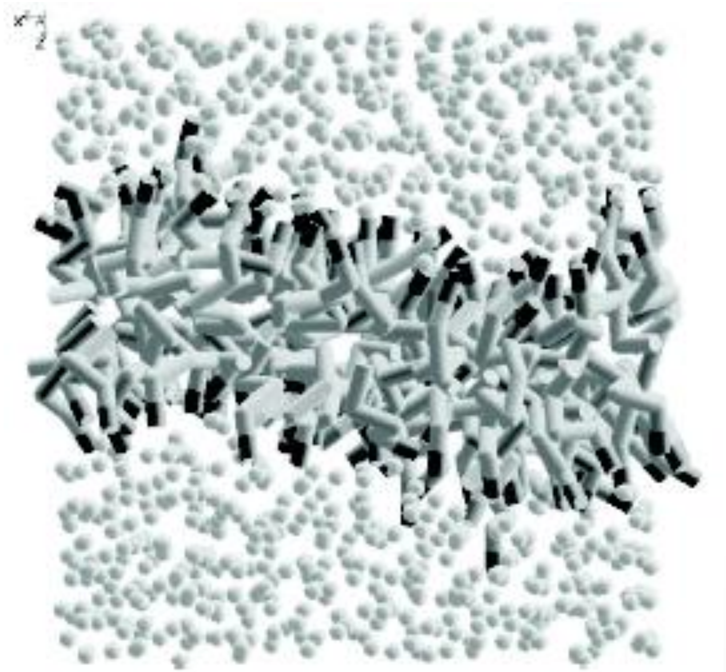
- Power spectrum of undulation modes[1,2]:
  - $\kappa = \frac{k_b T}{L^2 q^4 \left\langle \left| h_q \right|^2 \right\rangle}$
- Power spectrum of tilt fluctuations[3]:
  - $\kappa = \frac{k_b T}{q^2 \left\langle \left| \hat{n}_q{}^{||} \right|^2 \right\rangle}$

[1]Goetz R., Gompper G., Lipowsky R. (1999) *Phys. Rev. Lett*. **82**: 221-224
[2]Lindahl E., Edholm O. (2000*) Biophys. J*. **79**:426-433
[3]Watson M.C., Brandt E.G., Welch P.M., Brown F.L.H. (2012) *Phys. Rev. Lett*. 109: 028102

Carnegie Mellon

Active Bending

- Enforce particular shape and measure the constraining force
- Early attempt: enforce large undulation mode using umbrella sampling[1]
- Problem separating effect of bending from effect of stretching

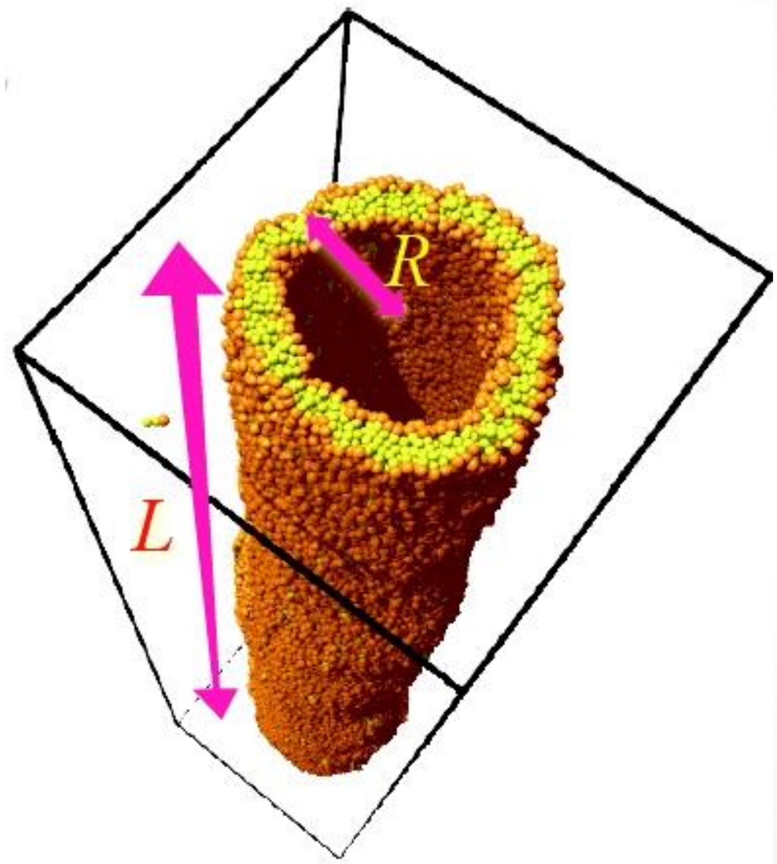


[1]Otter W.K. and Briels W.J. (2003) J. Chem. Phys. **118**, 4712

Carnegie Mellon

Active Bending of Cylinder

- Hold a cylindrical tether at a fixed length.
- $\kappa = \frac{FR}{2\pi}$
  - F is the force needed to hold the tether in a fixed position.
  - R is the radius of the tether.
- Useful for implicit solvent models.



V.A. Harmandaris and M. Deserno, J. Chem. Phys. 125, 204905 (2006)

Carnegie Mellon

Outline

- Lipid Membranes
  - Membrane elasticity
- Review of other techniques
  - Fluctuations
  - Active Bending
- **Theory**
  - **Shape equation**
  - **Stress-strain relation**
  - **Fluctuation corrections**
- Simulation Setup
- Results
- Energetics
  - Temperature Dependence of Bending Rigidity

Carnegie Mellon

Buckled Membranes

- The energy of a buckled membrane can be parameterized as a function of the arc length:

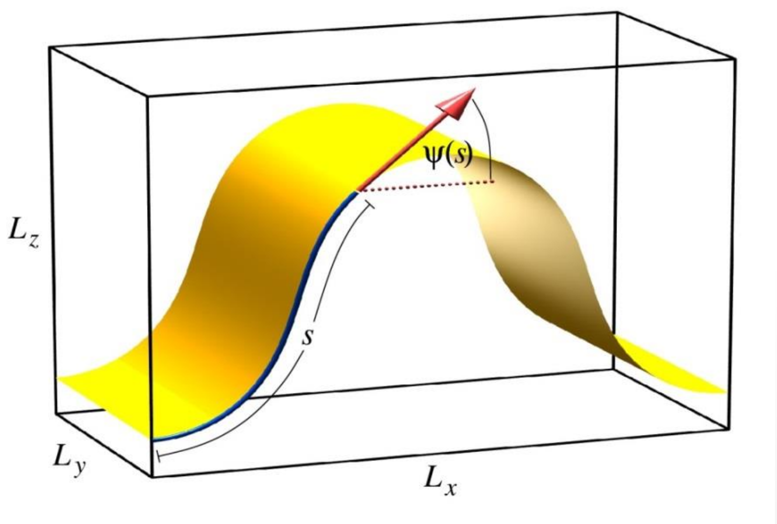
$$E[\psi(s)] = L_y \int_0^L ds \left\{ \frac{1}{2} \kappa \dot{\psi}^2 + f_x \left[cos\psi - \frac{L_x}{L} \right] \right\}$$

f_x is the lateral compressive stress along the membrane

- Functional variation shows that $\psi(s)$ satisfies:

$$\ddot{\psi} + \lambda^2 \sin\psi = 0$$

$$\lambda^2 = \frac{\kappa}{f_x}$$



M. Hu, P. Diggins, M. Deserno. *J. Chem. Phys.* **138**, 214110 (2013)

H. Noguchi,. Phys. Rev. E. 83, 061919 (2011)

Carnegie Mellon

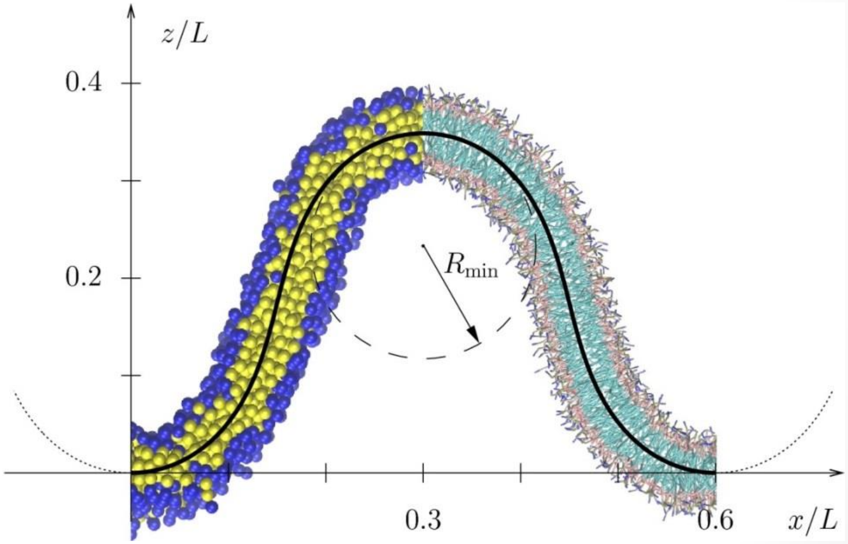
Shape of a buckle

- The shape of the buckle can be parameterized in terms of the arc length.

$$\psi(s) = 2\arcsin\{\sqrt{m}\,\mathrm{sn}[s/\lambda, m]\}$$

$$x(s) = 2\lambda\,\mathrm{E}[\mathrm{am}[s/\lambda, m], m] - s$$

$$z(s) = 2\lambda\sqrt{m}\,(1 - \mathrm{cn}[s/\lambda, m])$$



$$m = \sin^2\left(\frac{\psi_i}{2}\right)$$

E, sn, am, cn are elliptic integrals.

ψ_i is the angle at the inflection point

Imposing Constraints on the Buckle

- There are still two unknowns in the equations of shape:
  - *m* (the elliptic parameter) which is equivalent to the inflection angle
  - λ (the characteristic length) which depends on the f_x.
- Two constraints must be enforced:
  - $\psi(s)$ is periodic with period *L*
  - when *s* has increased by *L*, x must increase by L_x.

Stress-strain relation

- We first express m as a function of strain:

$$m(\gamma) = \gamma - \tfrac{1}{8}\gamma^2 - \frac{1}{32}\gamma^3 - \frac{11}{1024}\gamma^4 \cdots$$

- f_x can be expressed as:

$$f_x = \kappa\left(\frac{2\pi}{L}\right)^2 \left[1 + \frac{1}{2}\gamma + \frac{9}{32}\gamma^2 + \frac{21}{128}\gamma^3 \cdots\right]$$

- Since this is a fluid membrane, there is also a force in the perpendicular direction:

$$f_y = \kappa\frac{(2\pi)^2}{A}\frac{L_y}{L_x}\left[1 - \frac{5}{2}\gamma - \frac{23}{32}\gamma^2 - \frac{39}{128}\gamma^3 \cdots\right]$$

Carnegie Mellon

Fluctuation Corrections

- Need to account for thermal membrane undulations.
- The correction in the direction of the buckle is extremely small

$$\delta f_x = \frac{3k_BT}{2LL_y}\left[1 + \frac{5}{8}\gamma + \frac{27}{64}\gamma^2 + \frac{295}{1024}\gamma^3 \cdots\right]$$

- The correction for the stress perpendicular to the buckle is larger and also depends on a microscopic cutoff length a

$$\delta f_y = \frac{-k_BTL}{L_xL_ya}\left[1 + \frac{3L_ya}{2L^2}\left(1 - \frac{11}{8}\gamma \cdots\right)\right] \qquad a = \frac{2\pi}{q_c}$$

Carnegie Mellon

Outline

- Lipid Membranes
  - Membrane elasticity
- Review of other techniques
  - Fluctuations
  - Active Bending
- Theory
  - Shape equation
  - Stress-strain relation
  - Fluctuation corrections
- **Simulation Setup**
- Results
- Energetics
  - Temperature Dependence of Bending Rigidity

Setting up Simulations

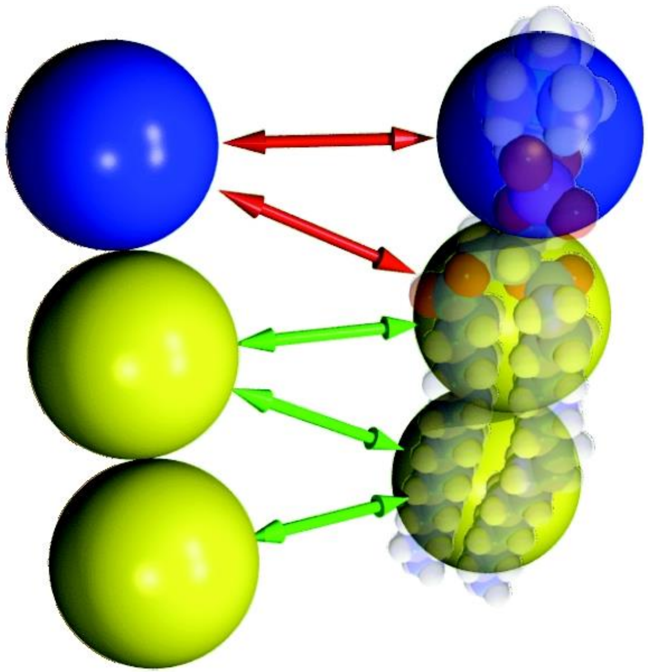
- Width of membrane strip should be small
  - Saves computational effort
  - Reduces the fluctuations in the y-direction
- Three processes need to be performed
  - Obtain the length of a flat membrane under zero stress
  - Create the buckled membrane
    - Many different techniques
  - Calculate the stress from a buckled membrane at a fixed stain

Outline

- Lipid Membranes
  - Membrane elasticity
- Review of other techniques
  - Fluctuations
  - Active Bending
- Theory
  - Shape equation
  - Stress-strain relation
  - Fluctuation corrections
- Simulation Setup
- **Results**
- Energetics
  - Temperature Dependence of Bending Rigidity

Carnegie Mellon

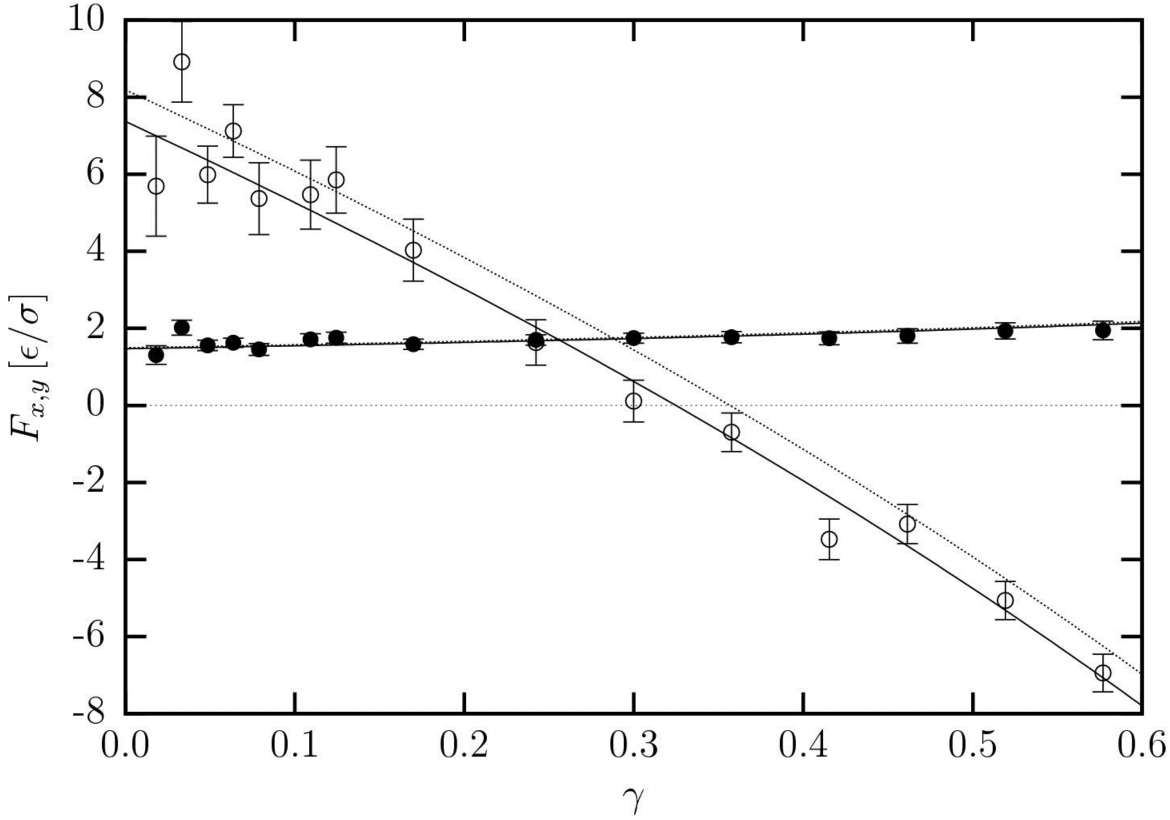
The Cooke Model



- Coarse-grained lipid
- 3 beads: reasonable aspect ratio
- Generic bead-spring
- Only pair forces
- Solvent free

I.R. Cooke, K. Kremer, M Deserno, Phys. Rev. E 72, 011506 (2005)
I.R. Cooke and M. Deserno, J. Chem. Phys. 123, 224710 (2005)

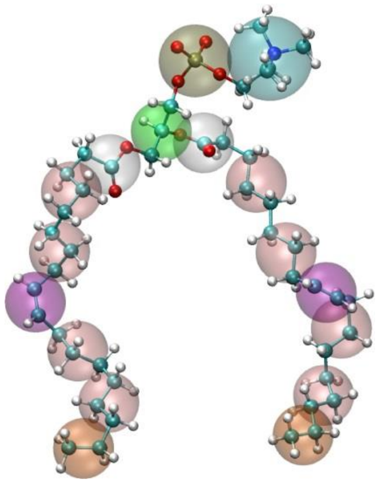
Cooke Model Results



$$\kappa_x = 12.8 \pm 0.4\ k_B T$$
$$\kappa_y = 12.9 \pm 0.8\ k_B T$$

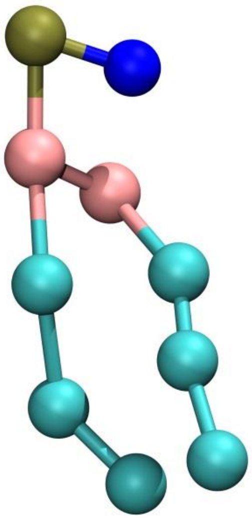
Carnegie Mellon

Other models



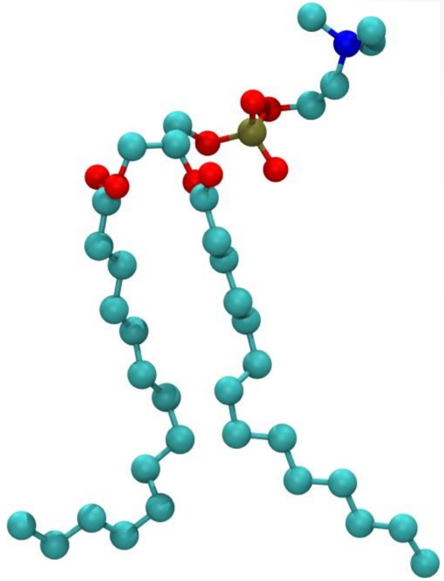
- Wang Model: DOPC
  - 17 beads
  - Implicit Solvent

Z.J. Wang and M. Deserno, *New J. Phys*. **12**, 095004 (2010)



- MARTINI: DMPC
  - 10 beads
  - CG solvent

S.J. Marrink *et. al.* , *J. Phys. Chem. B* **111**, 7812 (2007)

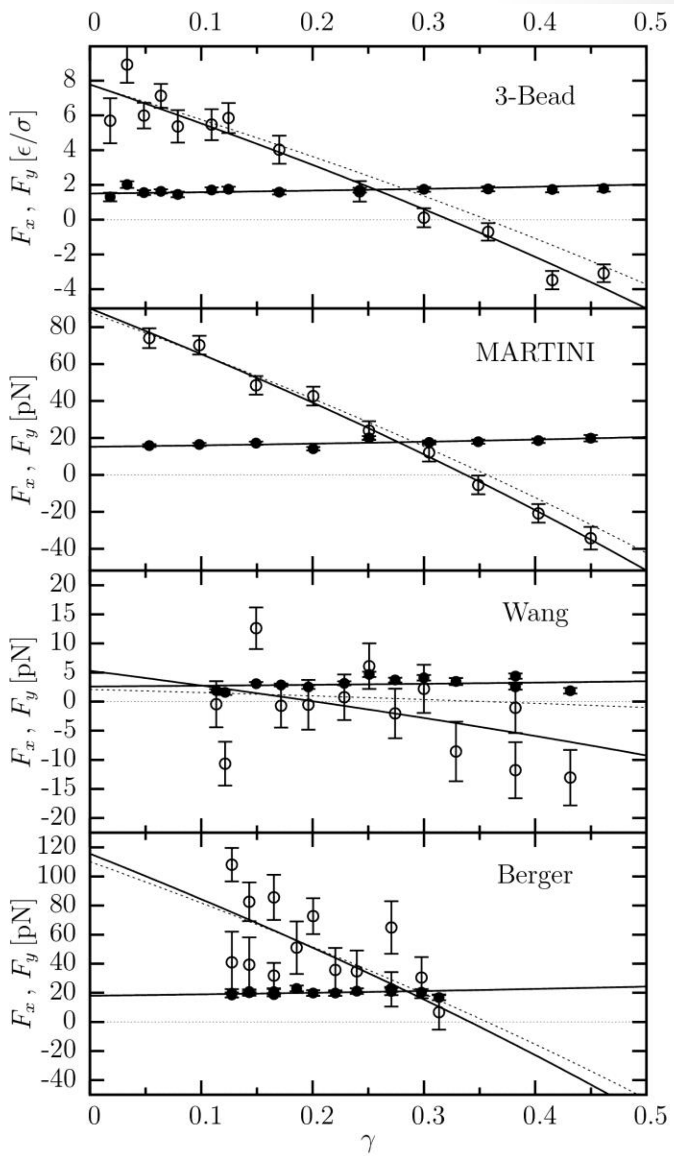


- Berger: DMPC
  - 46 beads
  - United Atom
  - Explicit Solvent

O. Berger, O. Edholm and F. Jähnig, *Biophys. J*. **72**, 2002 (1997)

Results

- MARTINI:
  - $\kappa_x = 29.0 \pm 1.0\ k_B T$
  - $\kappa_y = 27.7 \pm 1.9\ k_B T$
- Wang:
  - $\kappa_x = 5.5 \pm 0.4\ k_B T$
  - $\kappa_y = 3.1 \pm 2.6\ k_B T$
- Berger:
  - $\kappa_x = 24.8 \pm 0.9\ k_B T$
  - $\kappa_y = 26 \pm 11\ k_B T$



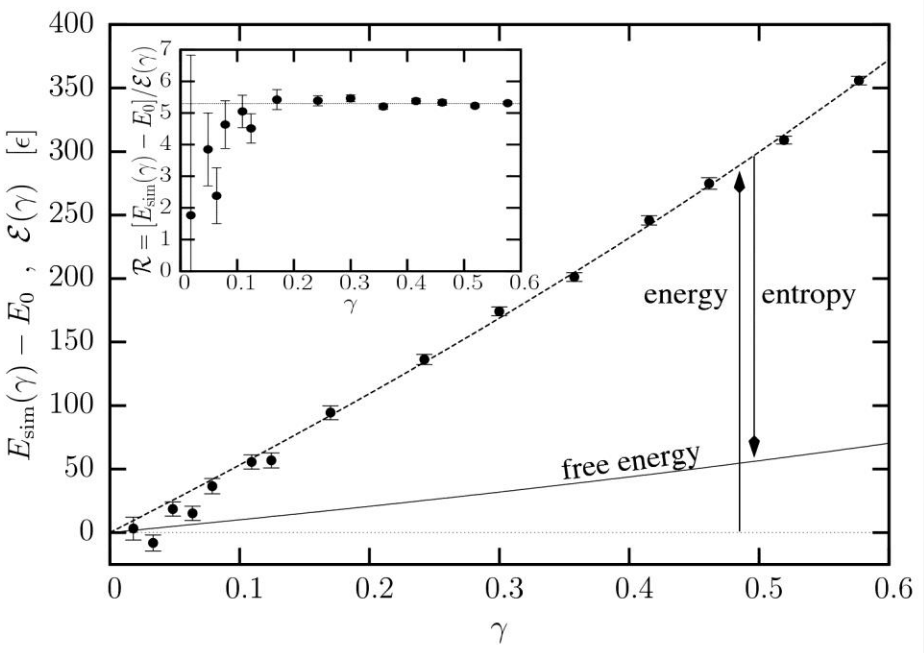
Outline

- Lipid Membranes
  - Membrane elasticity
- Review of other techniques
  - Fluctuations
  - Active Bending
- Theory
  - Shape equation
  - Stress-strain relation
  - Fluctuation corrections
- Simulation Setup
- Results
- **Energetics**
  - **Temperature Dependence of Bending Rigidity**

Carnegie Mellon

Energetics of Bending

- For all models, the free energy of bending is lower than the total energy of bending.
  - Entropy favors bending
- As a function of γ, the two energies differ by a multiplicative factor.
- The ratio between the energies reveals the temperature dependence of the bending modulus.



Carnegie Mellon

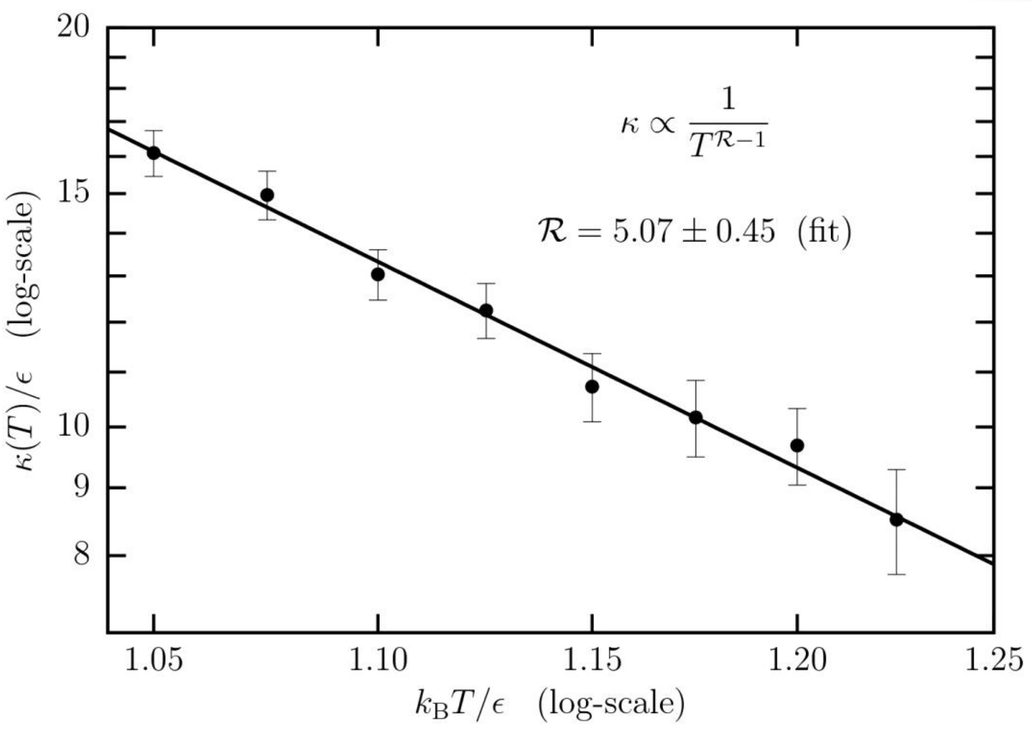
Temperature Dependence of κ

The temperature dependence of κ is:

$$\kappa(T) = \kappa(T_0)\left(\frac{T_0}{T}\right)^{R-1}$$

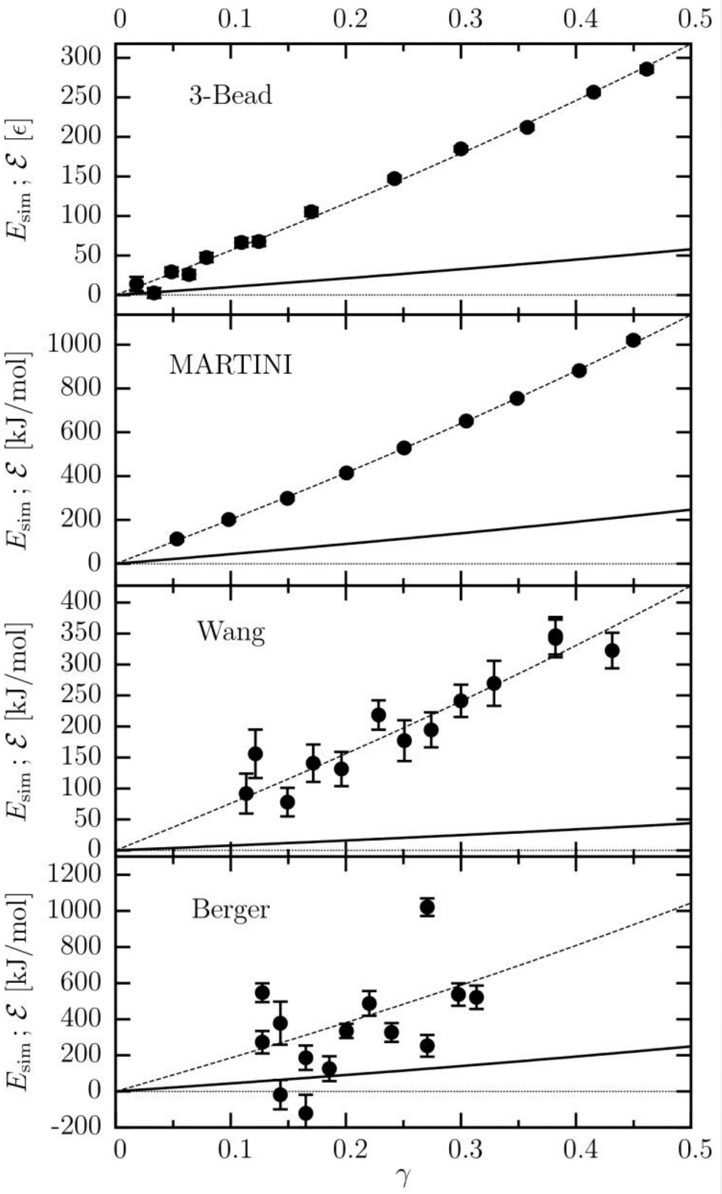
The ratio of the energy versus free energy is:

$$R = 5.43 \pm 0.12$$



Results

- Cooke:
  - $R = 5.43 \pm 0.12$
- MARTINI:
  - $R = 4.59 \pm 0.08$
- Wang
  - $R = 9.3 \pm 1.0$
- Berger
  - $R = 4.5 \pm 3.0$



Carnegie Mellon

Conclusions

- Buckling membranes provides an efficient and accurate method for obtaining bending rigidity.
- The method works for a wide range of lipid models.
- It allows to obtain local temperature dependence of bending rigidity.

Acknowledgements

- We would like to thank:
  - Erik Brandt
  - Jemal Guven
  - John Nagle
  - David Siegel
- KITP

- Funding:
  - NSF Grant PHY11-25915
  - NSF Grant CMMI-0941690