Strongly coarse-grained membrane simulations

Markus Deserno

Carnegie Mellon University
Department of Physics

with many thanks to
Ira Cooke, Benedict Reynwar, Gregoria Illya, Vagelis Harmandaris, Kurt Kremer

and our afternoon experts
Mingyang Hu and **Patrick Diggins**

International Workshop on Coarse Grained Biomolecula Modeling, October 17–21, 2011, Lausanne, Switzerland

October 19, 2011

Carnegie Mellon

Why coarse-graining?

If you haven't figured that out by now, you should ask for your money back.

No, seriously.
Why coarse graining?

Carnegie Mellon

Why coarse-graining?

Efficiency

Insight

Carnegie Mellon

Efficiency

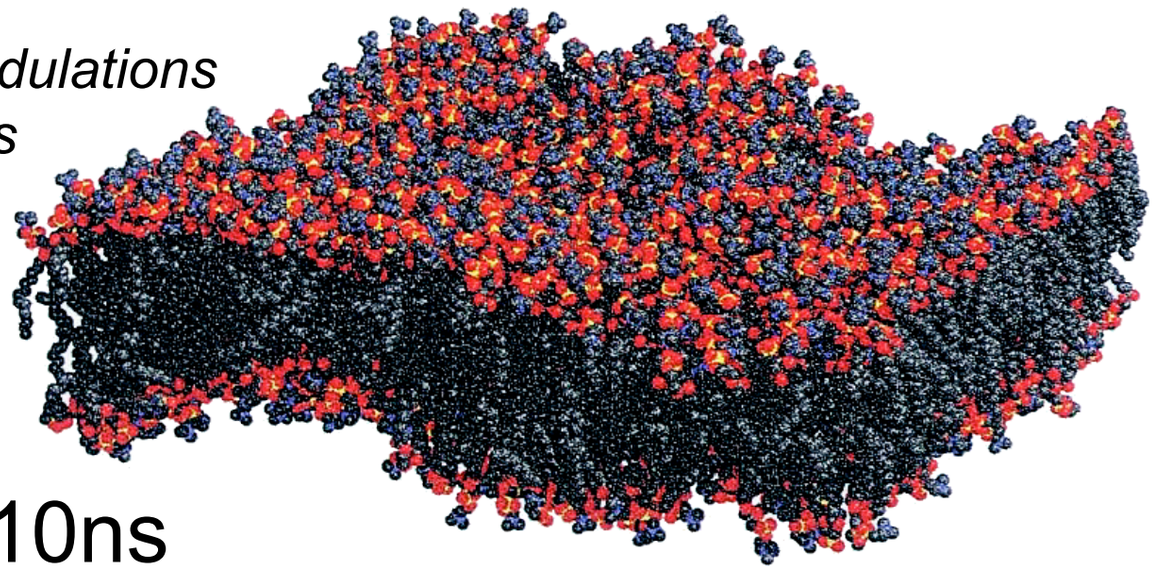
Does that mean just "bigger systems"?

No. Not *just*.

Carnegie Mellon

Efficiency

Lindahl, E. & Edholm, O. *Mesoscopic undulations and thickness fluctuations in lipid bilayers from molecular dynamics simulations*. Biophys. J. **79**, 426-433 (2000).



All-atom lipid bilayer
20nm×20nm, 1024 lipids, 10ns

What if we want a boxlength of L=200nm?

How does computing effort scale with L?

$$\text{effort} \sim L^2 \times L^4 \sim L^6$$

Amount of material

Equilibration time

Carnegie Mellon

Efficiency

20nm → 200nm

Million times more computationally expensive!

$$10^6 \approx 2^{20}$$

20 doublings of computer power!

20 x 2 years **(Moore's law)**

40 years

I'll be retired by then!

(best case scenario)

Carnegie Mellon

Efficiency

Stated differently:

The amount of material scales with the membrane area *A*. Using a domain decomposition scheme, this can (in the best case) be compensated by increasing the number of processors proportional to *A*.

But the simulation time towards equilibration scales like A^3. This still leaves an uncompensated factor of A^2 that you must do more work or have faster chips or better ideas.

Efficiency

Coarse graining cannot just help you to look at *much* bigger systems. It can help you to get well equilibrated data for *somewhat* bigger systems.

If someone offers you 1000 times more computational power, you should make your membrane length ~3 times bigger and simulate it for ~100 time longer!

Efficiency

Coarse graining cannot just help you to look at *much* bigger systems. It can help you to get well equilibrated data for *somewhat* bigger systems.

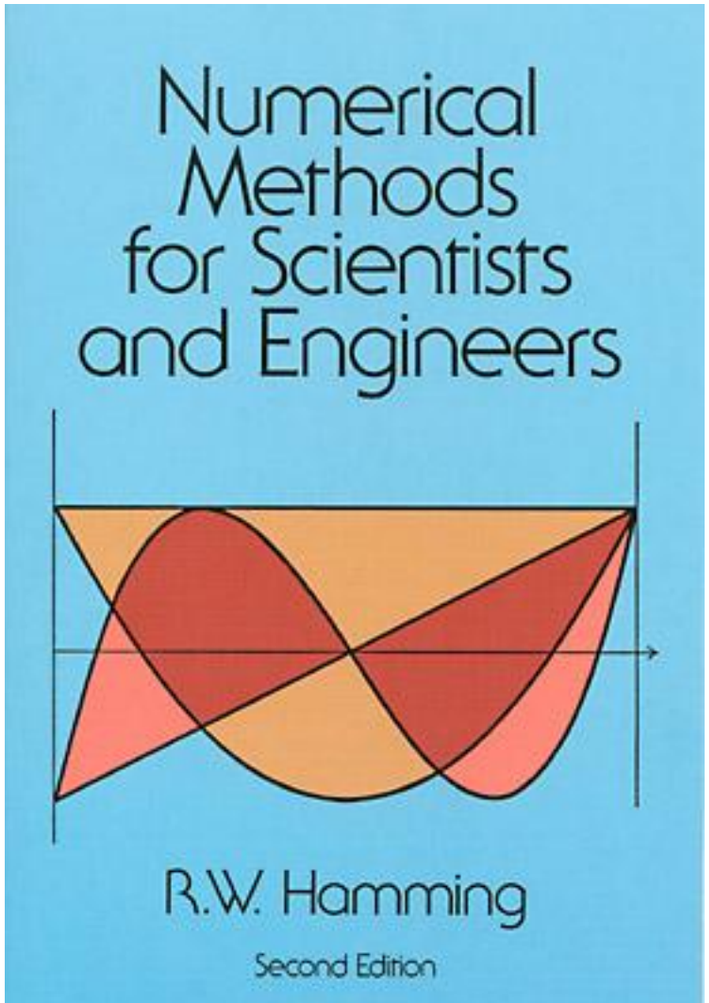
(Unfortunately, the latter doesn't look as obviously sexy.)

(Is it better to have non-equilibrated data of an impressively big or complex system, or to rather have equilibrated data of a system that is not accurate or big enough?)

Insight

"The purpose of computation is insight, not numbers."

Richard W. Hamming (1915-1998)



Mellon

Insight

Assume that there's some biophysical problem that can *only* be solved by sifting through many Terabytes of all-atom simulation trajectories.

This of course might happen!

But if it does, how much have we *understood* of the problem, after we have done the simulation?

As *scientists* we ought to be curious about how many Terabytes of detail we can throw away *before* we begin to model the system.

Because our brains are finite.

(Engineering, on the other hand, might be a whole different issue. Numbers often matter!)

Carnegie Mellon

Insight

Coarse graining is the art of throwing such supposedly unnecessary detail away.

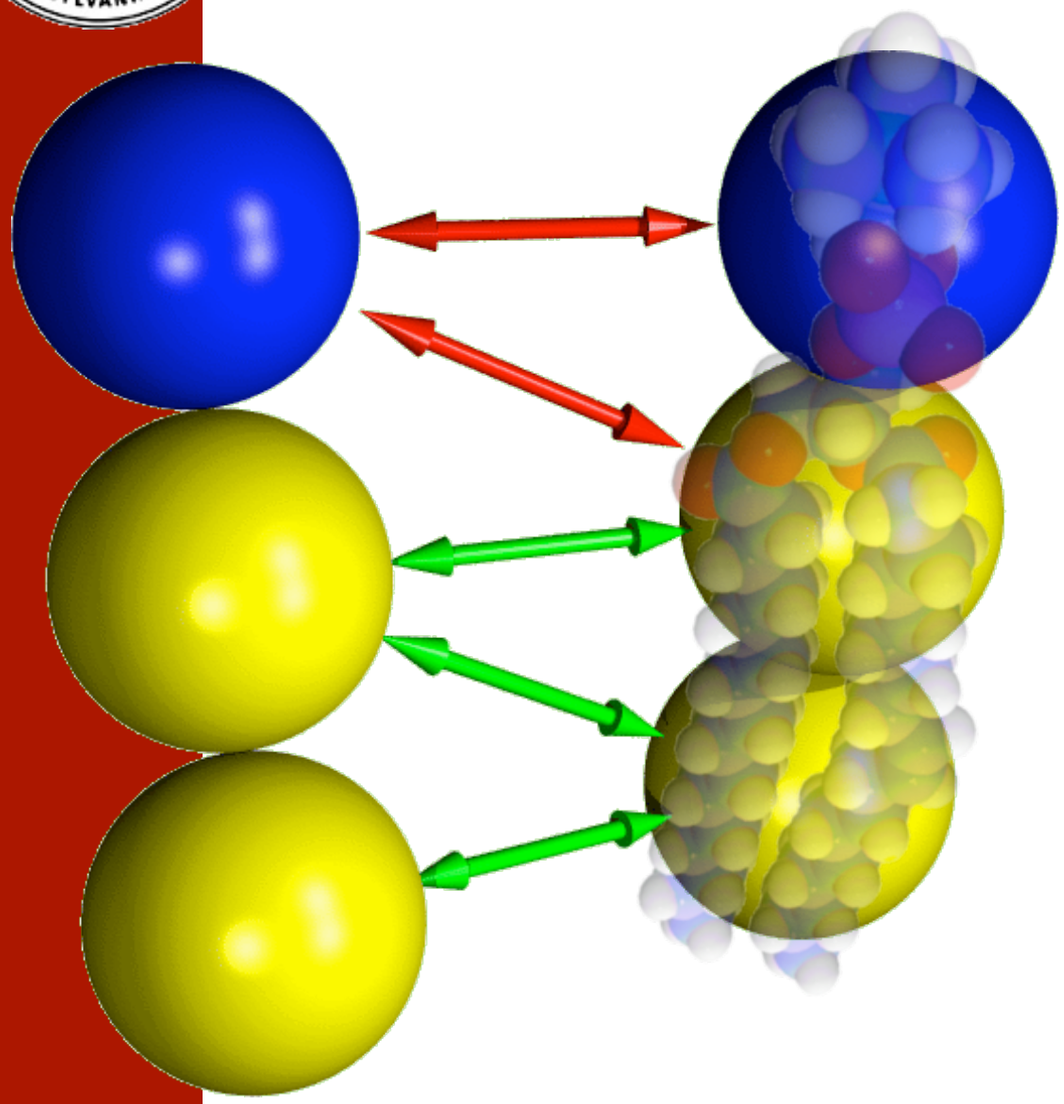
(In fact, I believe that *Physics* is the art of throwing unnecessary detail away)

It's an *art*.
There's no sure-fire way of getting it right.

You throw the wrong stuff away, you're *doomed*!

<u>Well, *not really*:</u> If you make sure that your simulation is correct, then you have a *falsifiable result*! So you're scientific!

Today:



I'll illustrate a way to treat the mesoscopic regime in an efficient and insightful way. (OK, that's a tall order.)

- **Generic top-down bead-spring**
- **solvent free**
- **only pair forces**
- **robust & physically meaningful**

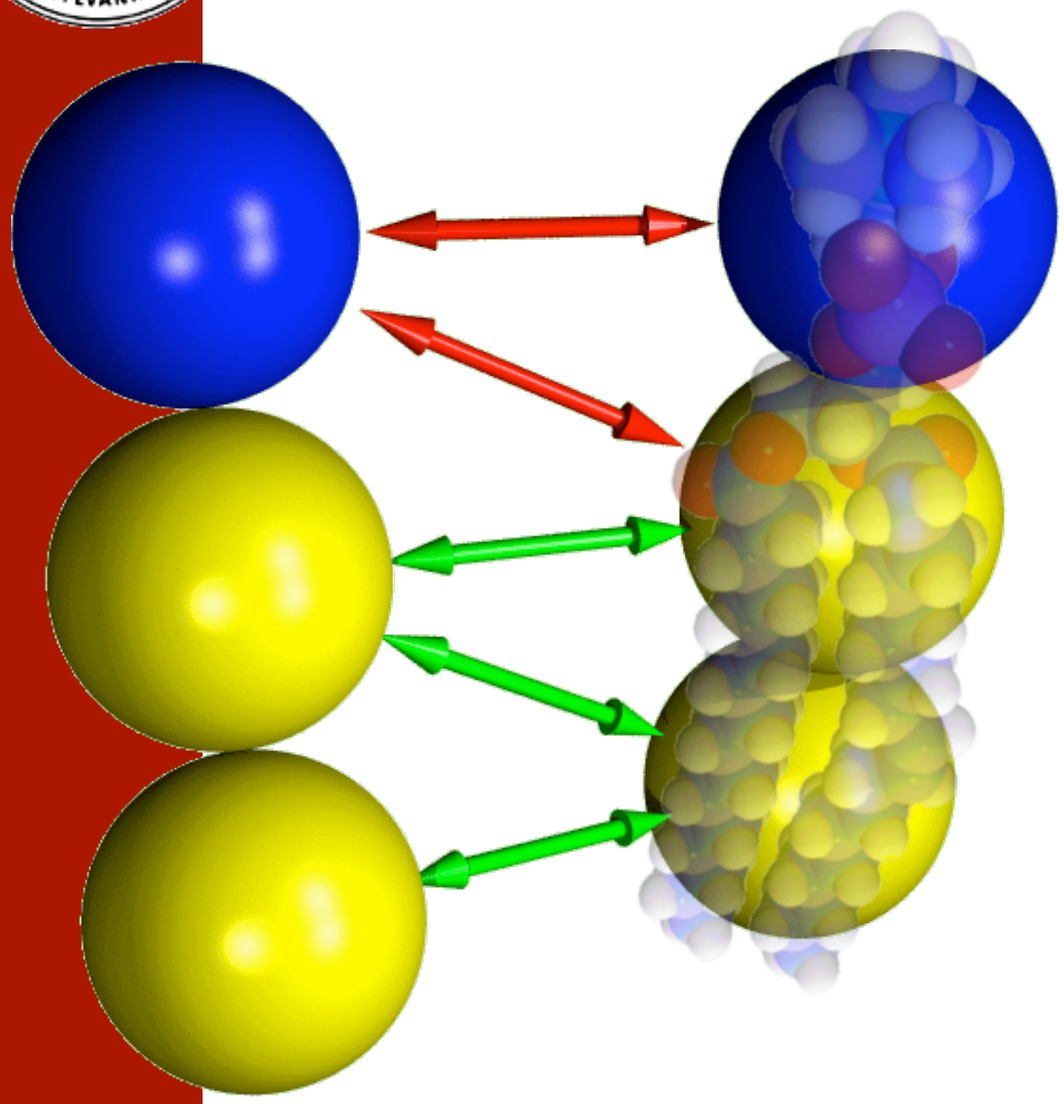
I.R. Cooke, K. Kremer, M. Deserno, Phys. Rev. E **72**, *011506* (2005);
I.R. Cooke and M. Deserno, J. Chem. Phys. **123**, *224710* (2005).

Today:

- J.-M. Drouffe, A. C. Maggs, and S. Leibler, Science **254**, 1353 (1991)
- H. Noguchi and M. Takasu, Phys. Rev. E **64**, 041913 (2001)
- Z.-J. Wang and D. Frenkel, J. Chem. Phys. **122**, 234711 (2005)
- H. Noguchi and G. Gompper, Phys. Rev. E **72**, 021903 (2006)
- G. Ayton and G.A. Voth, Biophys. J. **83**, 3357 (2002)
- O. Farago, J. Chem. Phys. **119**, 396 (2003)
- G. Brannigan and F.L.H. Brown, J. Chem. Phys. **120**, 1059 (2004)
- G. Brannigan, P.F. Philips, and F.L.H. Brown, Phys. Rev. E **72**, 011915, (2005)

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).

Today:



Physics based?

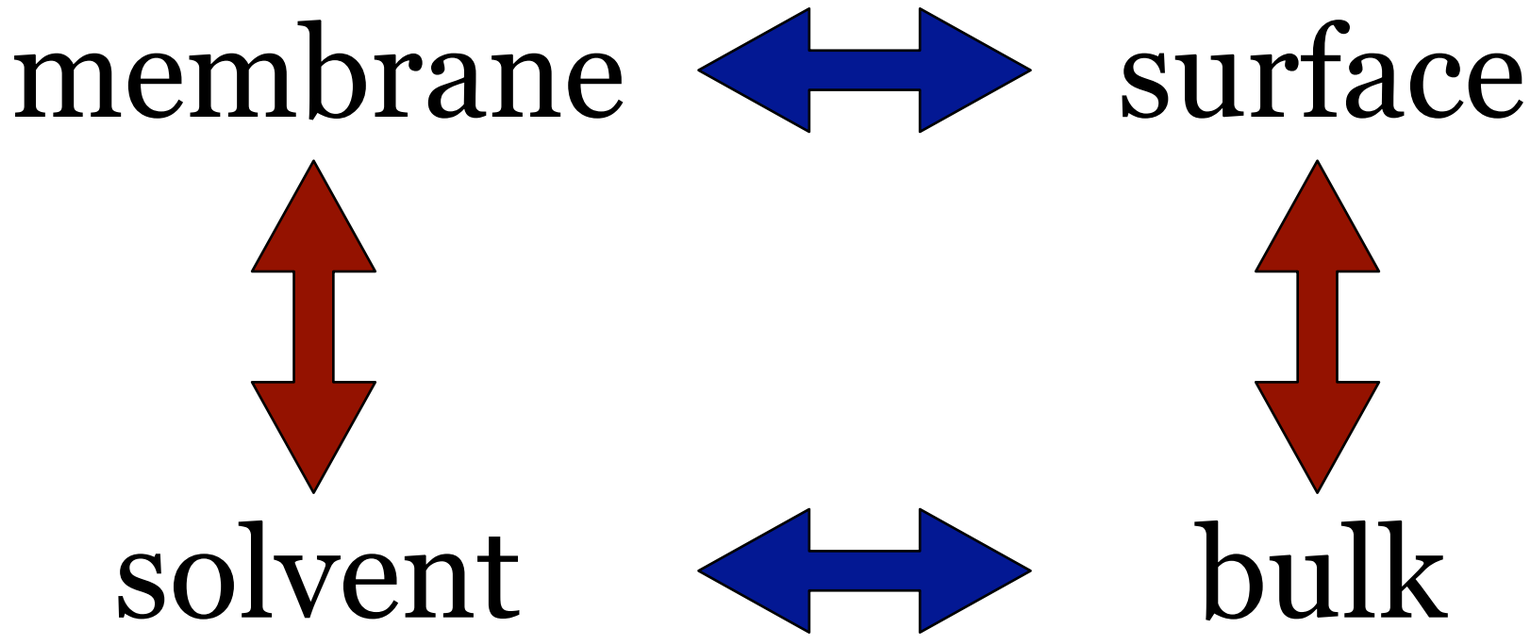
Definitely Yes!

But is there room for physical reasoning or physics-based effects in biology?

I think: Definitely Yes!

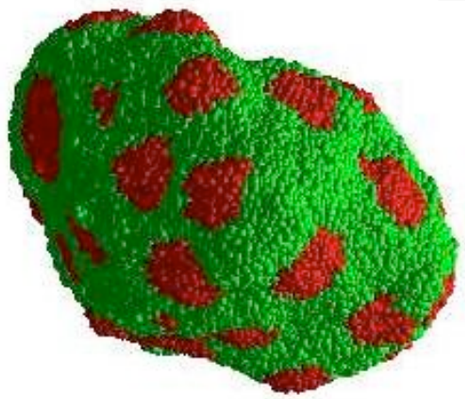
I.R. Cooke, K. Kremer, M. Deserno, Phys. Rev. E **72**, *011506* (2005);
I.R. Cooke and M. Deserno, J. Chem. Phys. **123**, *224710* (2005).

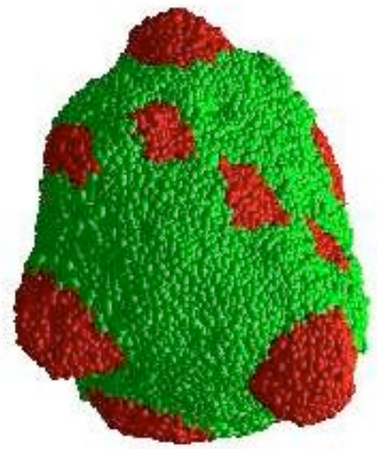
Why is “solvent free” good?

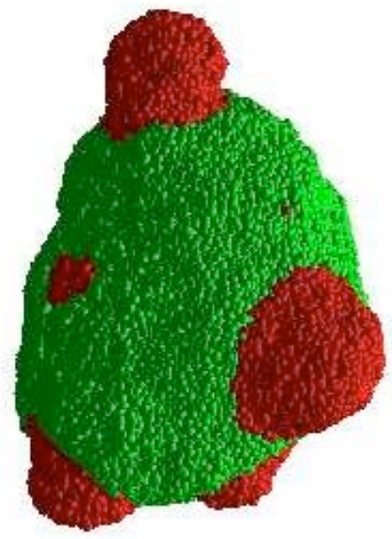


Unless you’re careful, you might end up simulating a finite size effect!

Example







membrane ↔ surface

↕ ↕

solvent ↔ bulk

16,000 DPD lipids 4 beads per lipid.

64,000 degrees of freedom for lipids.

But in total 1,536,000 particles in box!

96% of simulation time spent with solvent!

(They had a good reason for doing this. But do you, too?)

M. Laradji & P.B. Sunil Kumar
Phys. Rev. Lett. **93**, *198105* (2004).

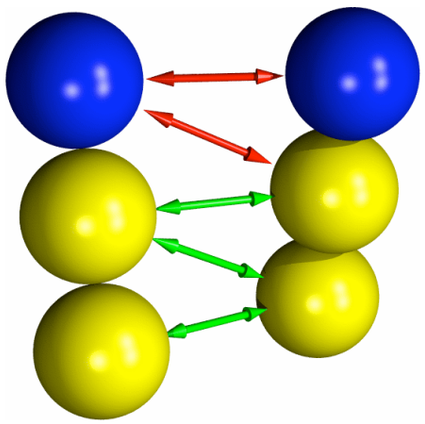
Carnegie Mellon

Difficulties

Implicit solvent models are incredibly common and useful in polymer physics.

Why has it taken so long for them to appear in the field of membrane research?

☞ Polymers don't first have to self assemble!



One needs additional cohesion to make the lipids come together.

☞ Fluidity has proven to be the major challenge.

Difficulties

Implicit solvent models are incredibly common and useful in polym

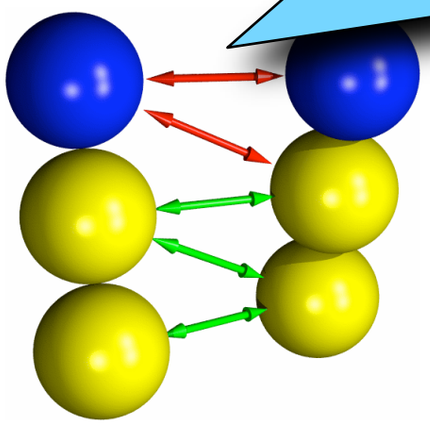
Why has
field of r

☞ Polymer

weak attraction ➠ gas phase

no fluid phase inbetween !?!?

strong attraction ➠ solid (gel) phase



One needs additional cohesion to make the lipids come together.

☞ Fluidity has proven to be the major challenge.

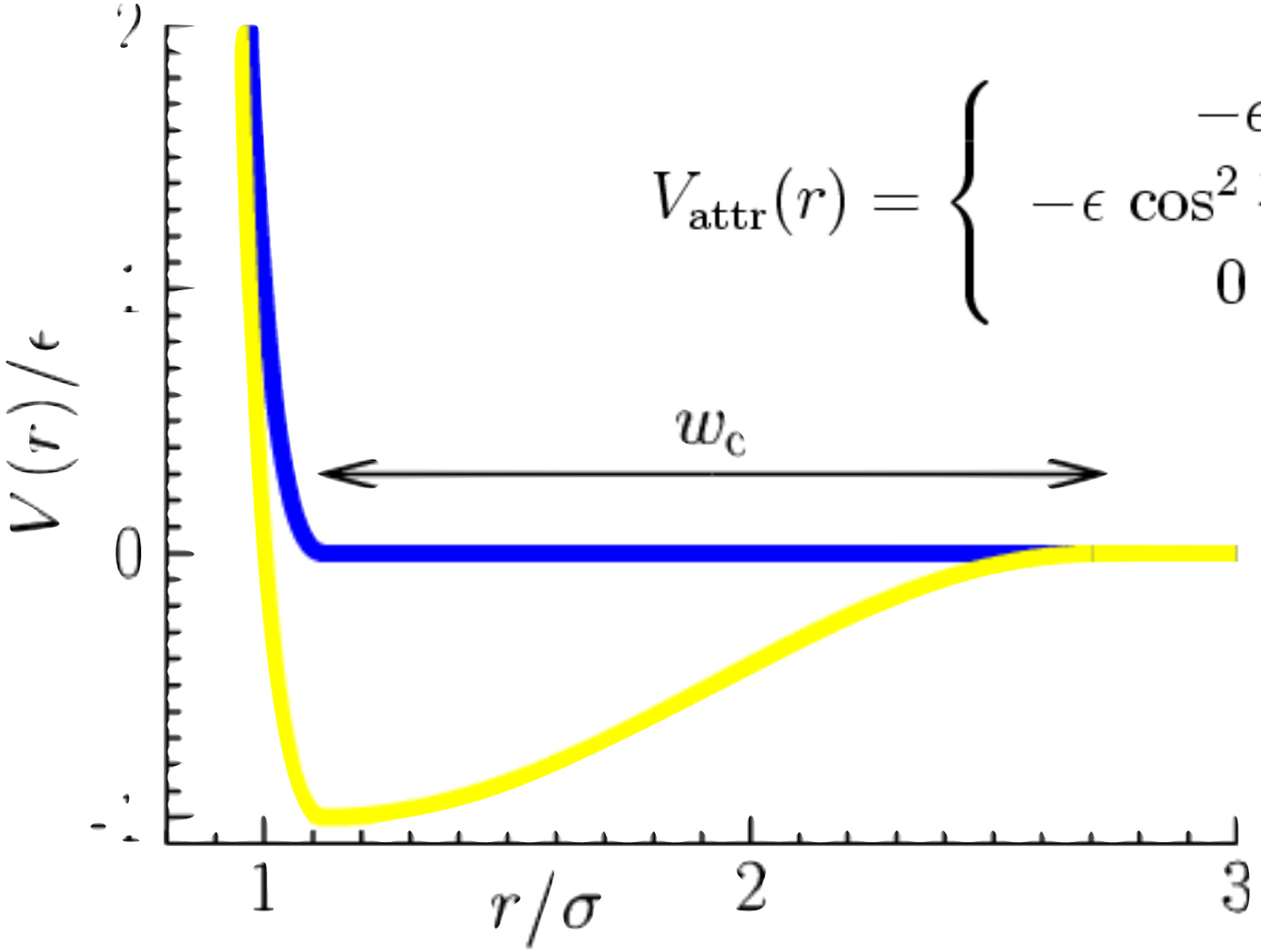
Our model

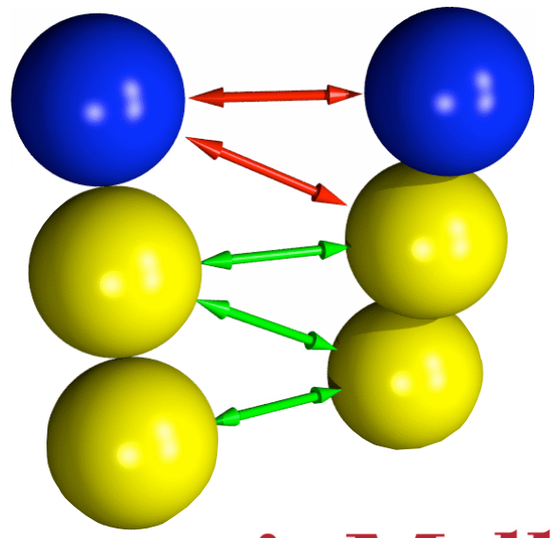
Link three beads $V_{\rm bond}(r) = -\frac{1}{2}k_{\rm bond}r_\infty^2 \log\left[1-(r/r_\infty)^2\right]$

Make lipid stiff $V_{\rm bend}(r_{13}) = \frac{1}{2}k_{\rm bend}(r_{13}-4\sigma)^2$

Nonbonded $V_{\rm rep}(r) = 4\epsilon\left[\left(\frac{r_{\rm c}}{r}\right)^{12} - \left(\frac{r_{\rm c}}{r}\right)^{6} + \frac{1}{4}\right]\Theta(r_{\rm c}-r)$

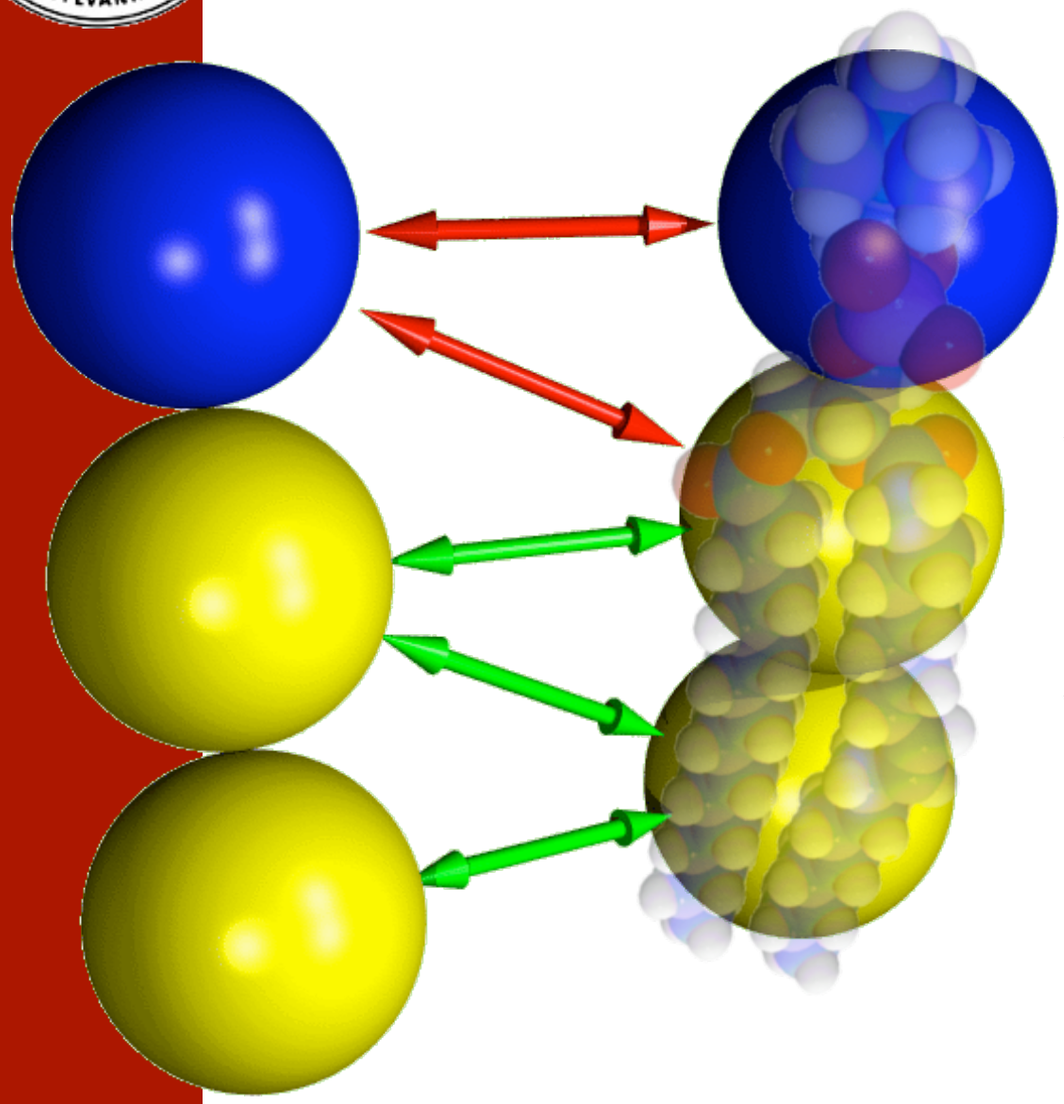
$$V_{\rm attr}(r) = \begin{cases} -\epsilon & , \quad r < r_{\rm c} \\ -\epsilon\,\cos^2\frac{\pi(r-r_{\rm c})}{2w_{\rm c}} & , \quad r_{\rm c} \le r \le r_{\rm c}+w_{\rm c} \\ 0 & , \quad r > r_{\rm c}+w_{\rm c} \end{cases},$$

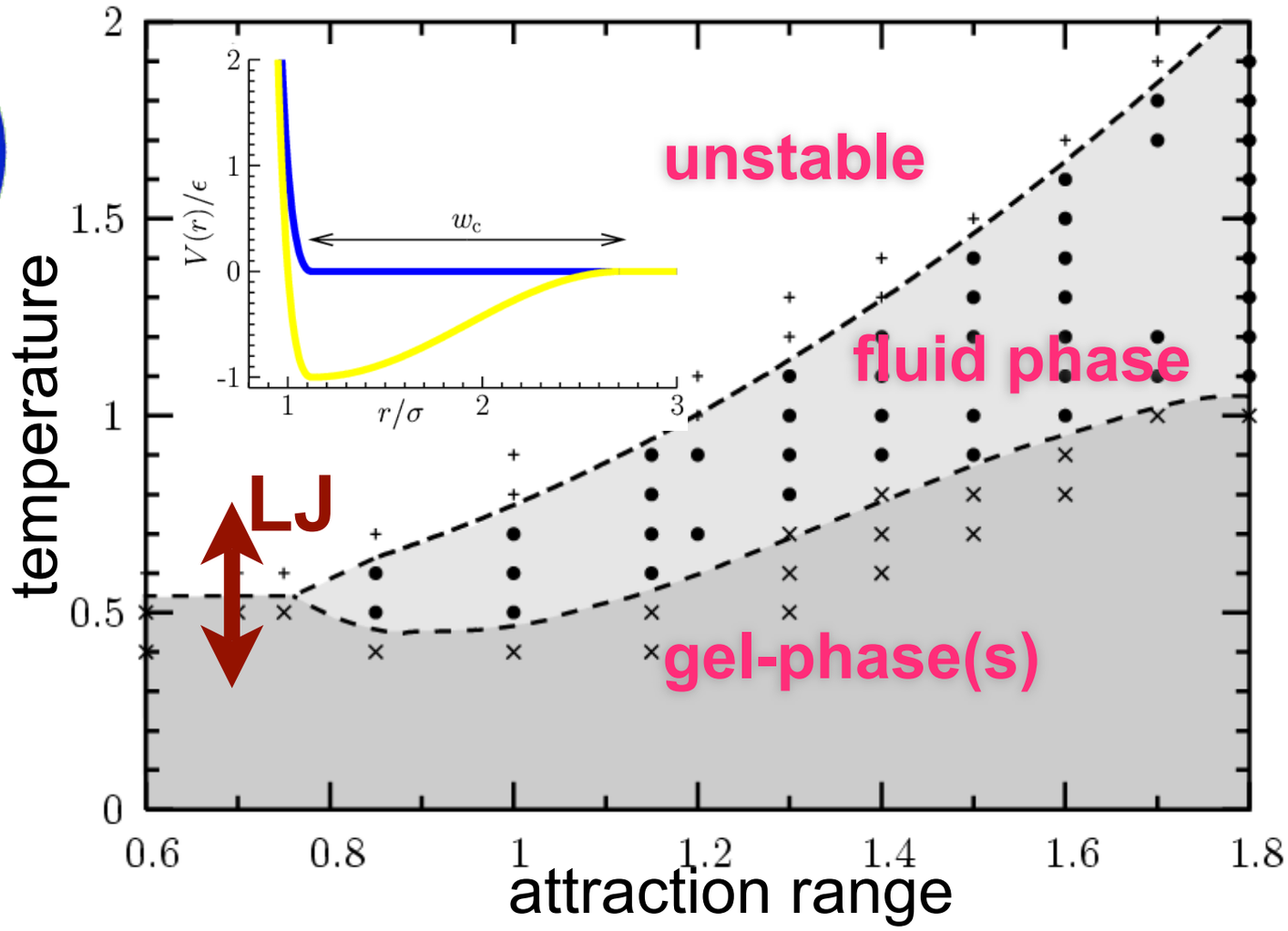




Carnegie Mellon

Overall phase behavior





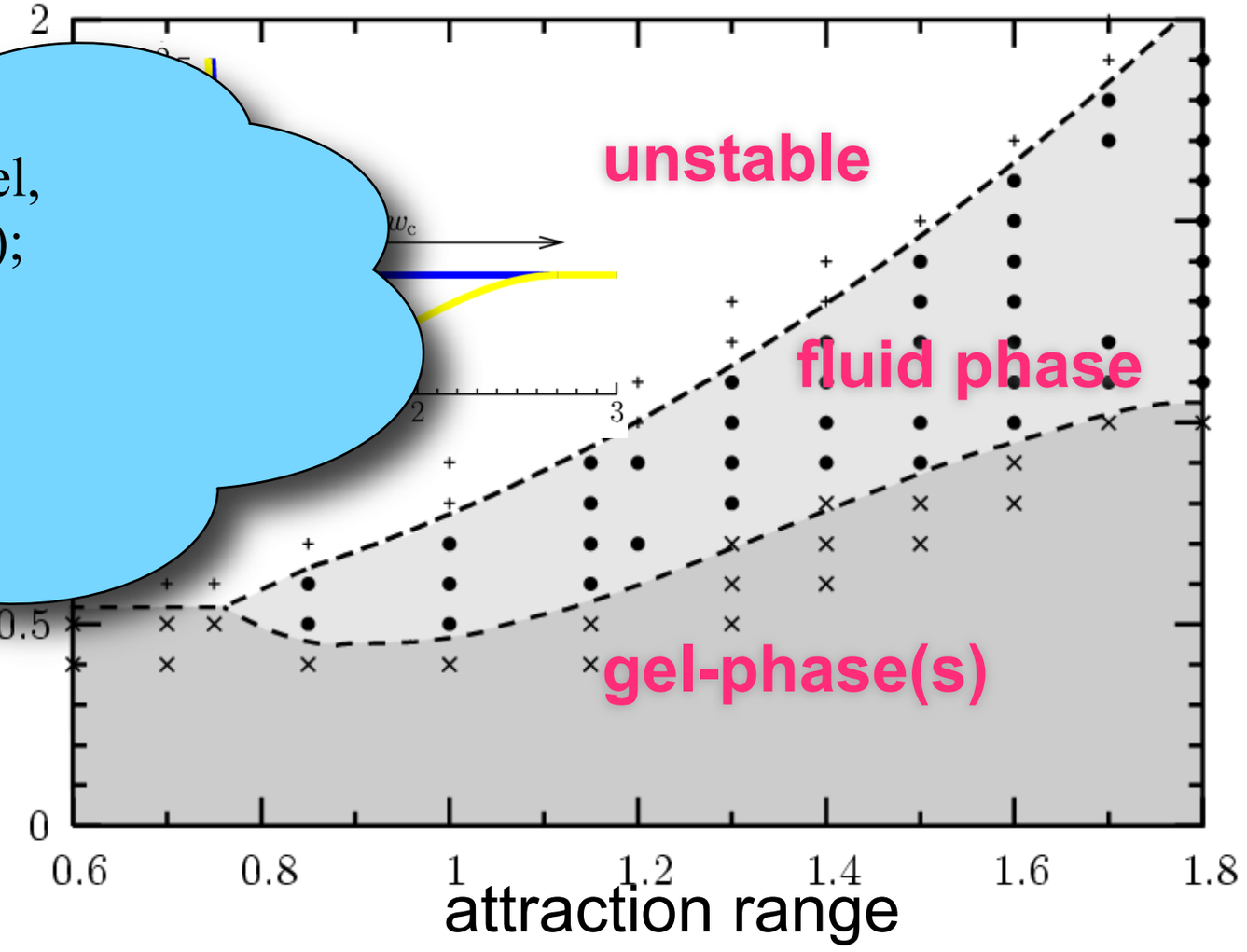
Long-ranged attractions "save" the system some entropy!

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).

Carnegie Mellon

Overall phase behavior

A.P. Gast, C.K. Hall, and W.B. Russel,
J. Coll. Interface Sci. **96**, *251* (1983);
M.H.J. Hagen, D. Frenkel,
J. Chem. Phys. **101**, *4093* (1994);
A.A. Louis, Phil. Trans. R. Soc.
Lond. A **359**, *939* (2001).



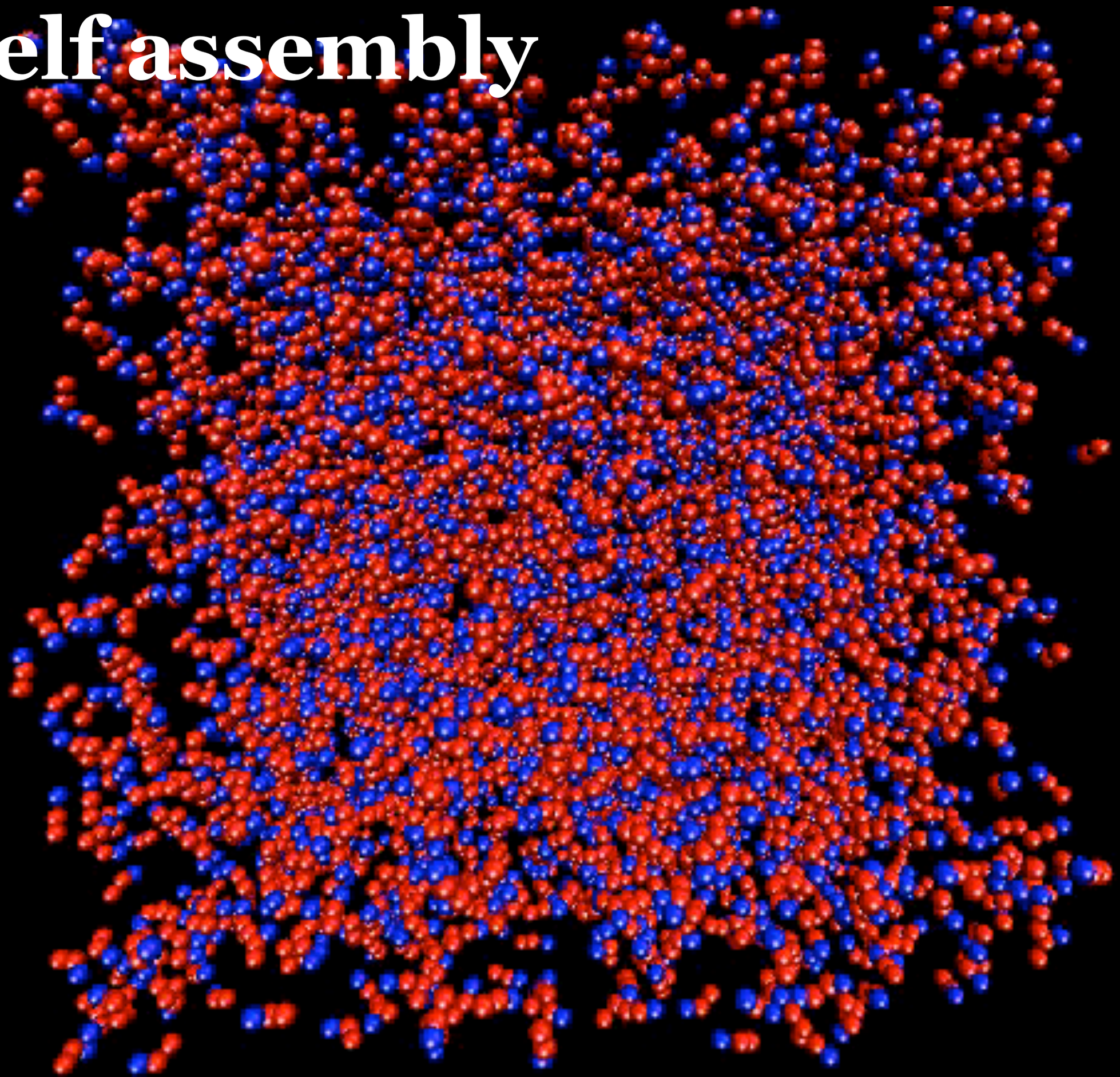
Long-ranged attractions "save" the system some entropy!

Shape of CG potential is *qualitatively* important!

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).

Carnegie Mellon

Self assembly



Properties

Are these things really lipid membranes?

Carnegie Mellon

Bending modulus

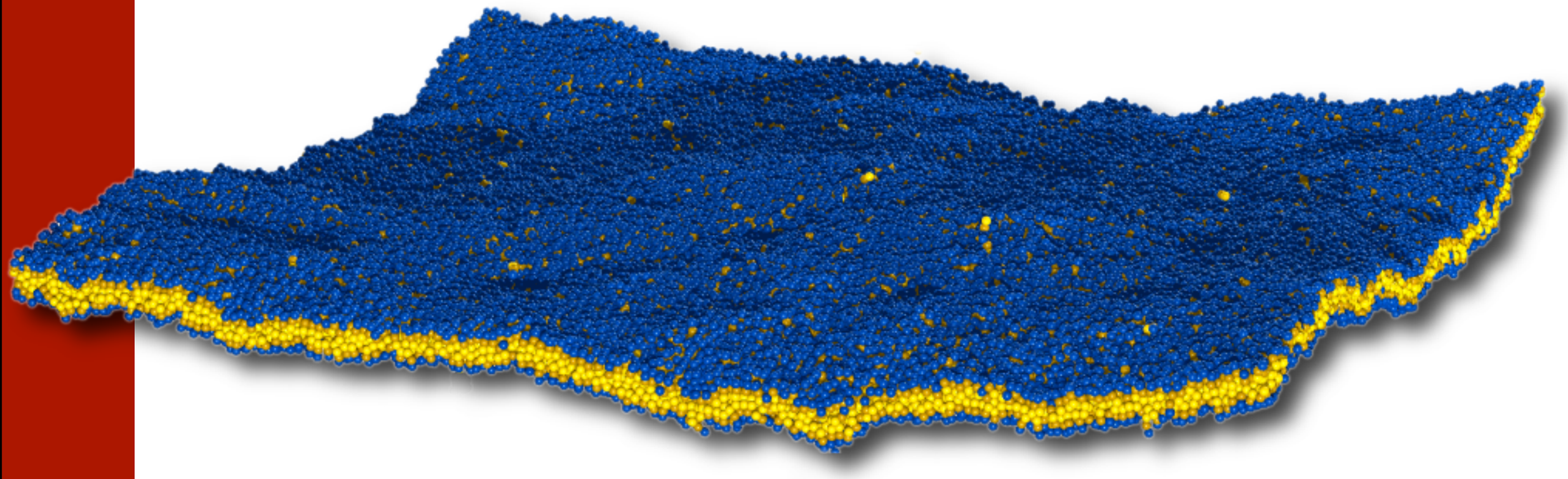
Fluctuation spectrum from continuum theory

$$E = \int \mathrm{d}A \left\{ \tfrac{1}{2}\kappa K^2 + \sigma \right\} \approx \tfrac{1}{2} \int \mathrm{d}x\, \mathrm{d}y \left\{ \kappa (\nabla^2 h)^2 + \sigma (\nabla h)^2 \right\}$$

total curvature

surface tension

"linearized Monge gauge"



Carnegie Mellon

Bending modulus

Fluctuation spectrum from continuum theory

$$E = \int \mathrm{d}A \left\{ \tfrac{1}{2}\kappa K^2 + \sigma \right\} \approx \tfrac{1}{2} \int \mathrm{d}x\, \mathrm{d}y \left\{ \kappa (\nabla^2 h)^2 + \sigma (\nabla h)^2 \right\}$$

total curvature

surface tension

"linearized Monge gauge"

Fourier expansion and equipartition theorem

$$\left\langle |h_{\boldsymbol{q}}|^2 \right\rangle = \frac{k_\mathrm{B}T}{L^2[\kappa q^4 + \sigma q^2]} = \frac{k_\mathrm{B}T}{L^2\kappa}\, q^{-4}$$

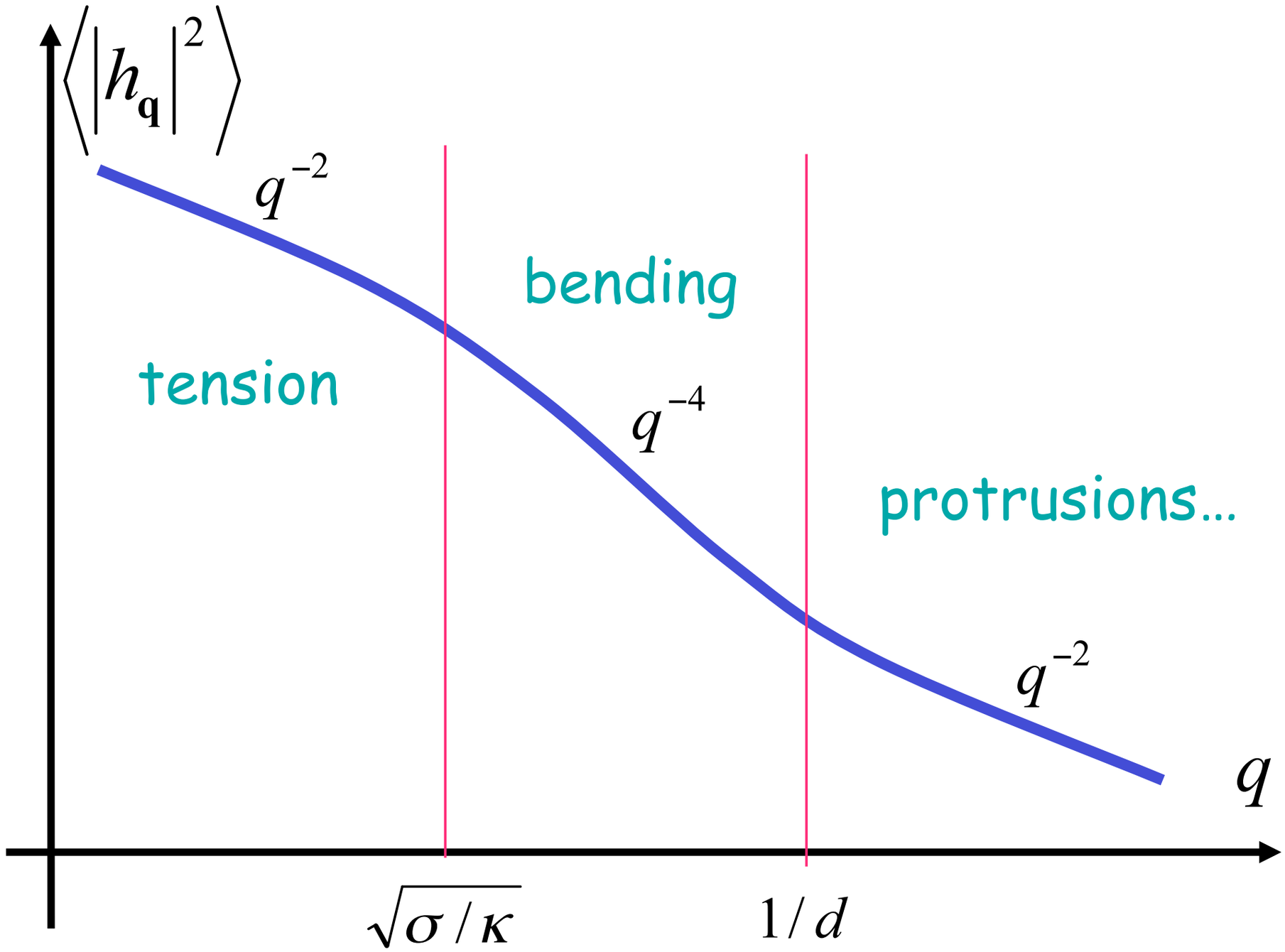
zero surface tension

determine bending modulus!

Carnegie Mellon

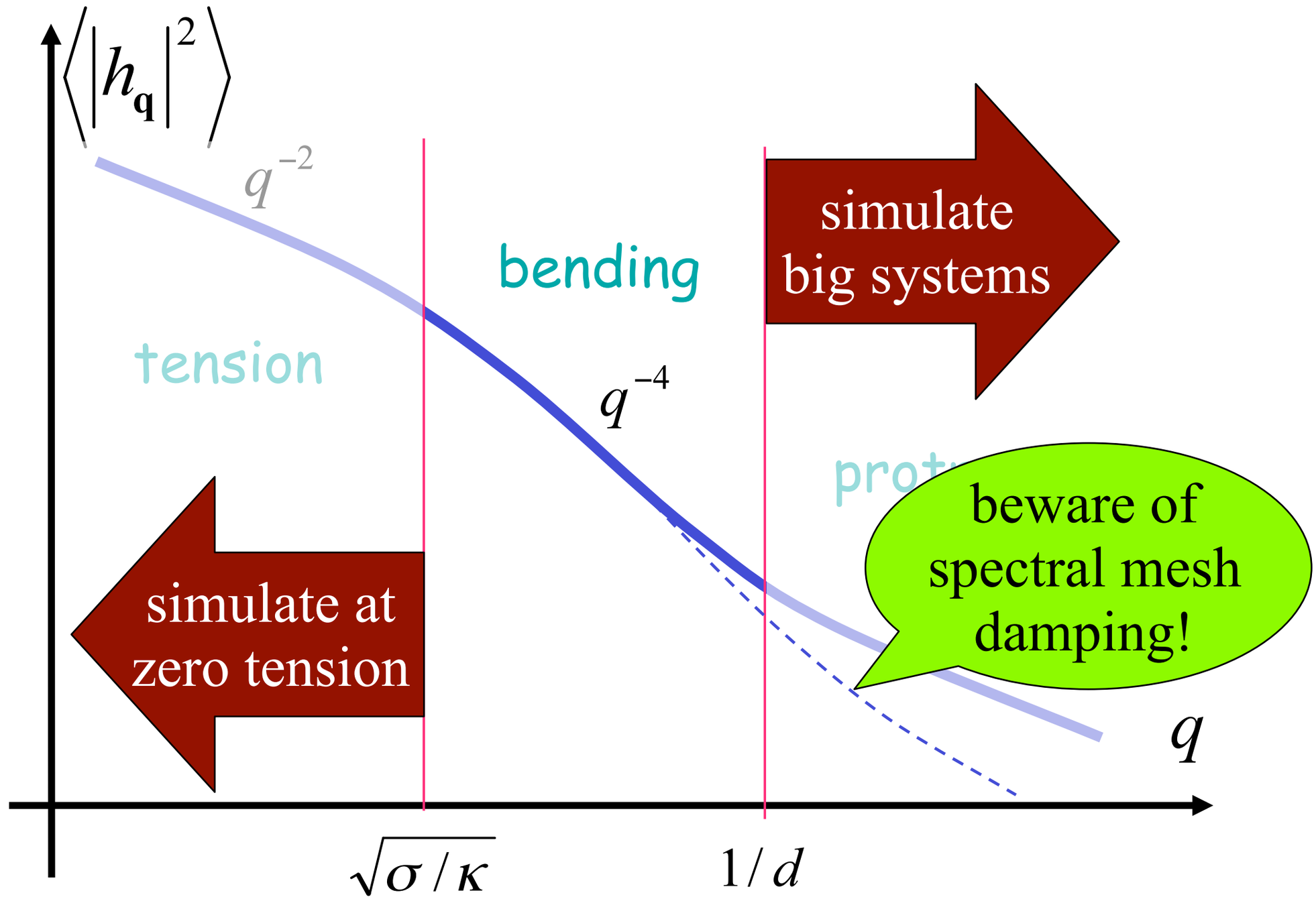
Bending modulus

Fluctuation spectrum from continuum theory



Bending modulus

Fluctuation spectrum from continuum theory



Carnegie Mellon

Bending modulus

However…

- Equilibration time of Fourier modes scales like q^{-4} (remember?)
- Large bending modulus (κ) from small perturbation (kT) → small signal!
- Result relevant for strong bending?

$$h(x) = h_q \, \mathrm{e}^{\mathrm{i}\, qx} \quad \longrightarrow \quad K = -h''(x) = h_q \, q^2 \, \mathrm{e}^{\mathrm{i}\, qx}$$

$$\langle K^2 \rangle = \langle |h''(x)|^2 \rangle = q^4 \, \langle |h_q|^2 \rangle = \frac{k_\mathrm{B} T}{L^2 \, \kappa}$$

$$\overline{R} \;=\; \frac{1}{\langle K^2 \rangle^{1/2}} \;=\; \sqrt{\frac{\kappa}{k_\mathrm{B} T}} \, L \;\simeq\; 3 \ldots 5 \, L$$

Bending modulus

However…

- Equilibration time of Fourier modes scales like q^{-4} (remember?)
- Large bending modulus (κ) from small perturbation (kT) → small signal!
- Result relevant for strong bending?

Maybe we need an alternative technique?

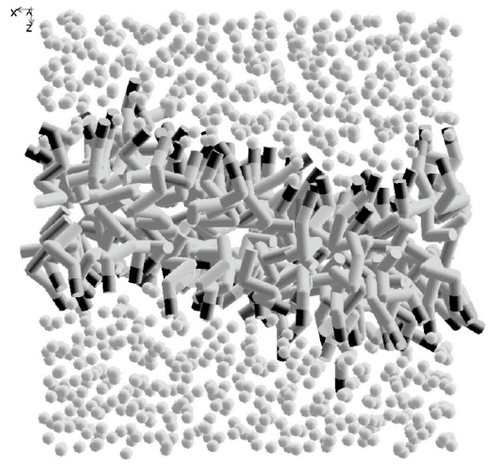
Bending modulus

...from actively bent membranes

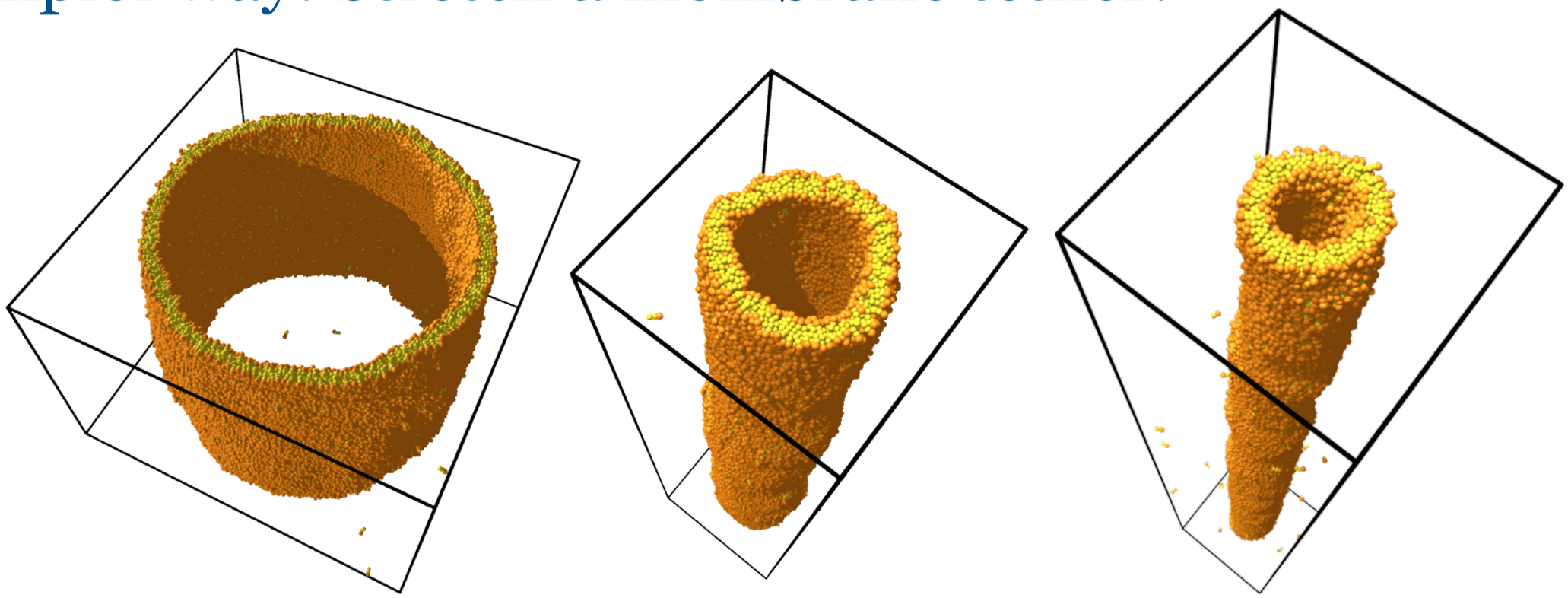
first implementation:

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

Enforce large undulation mode, measure constraining force.



Simpler way: Stretch a membrane tether!



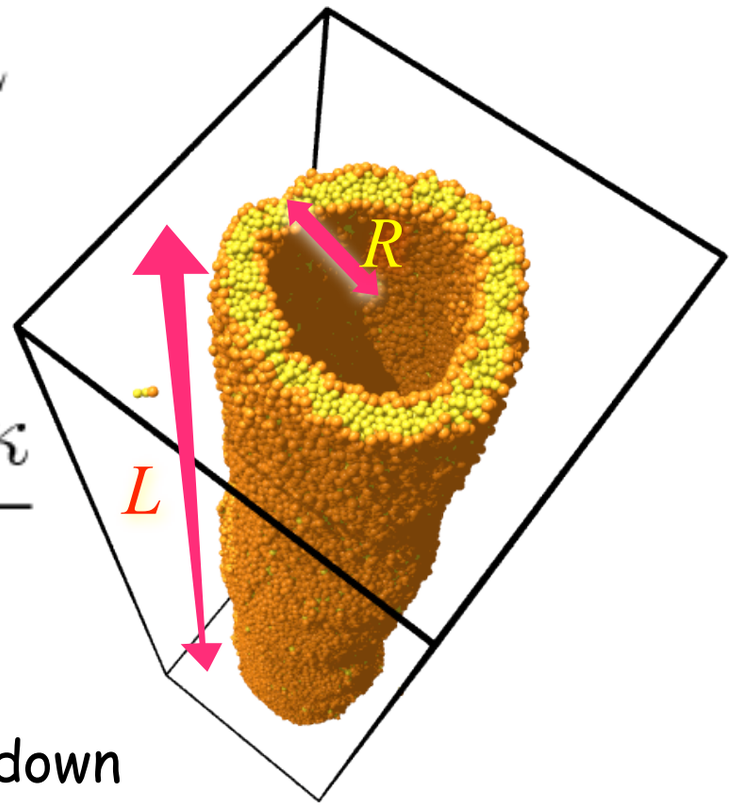
V. A. Harmandaris and M. Deserno, J. Chem. Phys. **125**, *204905* (2006)

Carnegie Mellon

Bending modulus

...from actively bent membranes

Energy: $E = \frac{\kappa}{2} \times \frac{1}{R^2} \times A$ $\quad A = 2\pi RL$



Force: $F = \left(\frac{\partial E}{\partial L}\right)_A = \cdots = \frac{2\pi\kappa}{R}$

goes up goes down

Bending modulus: $\kappa = \frac{FR}{2\pi} \simeq \frac{\overline{F}\,\overline{R}}{2\pi}$

what about fluctuations?

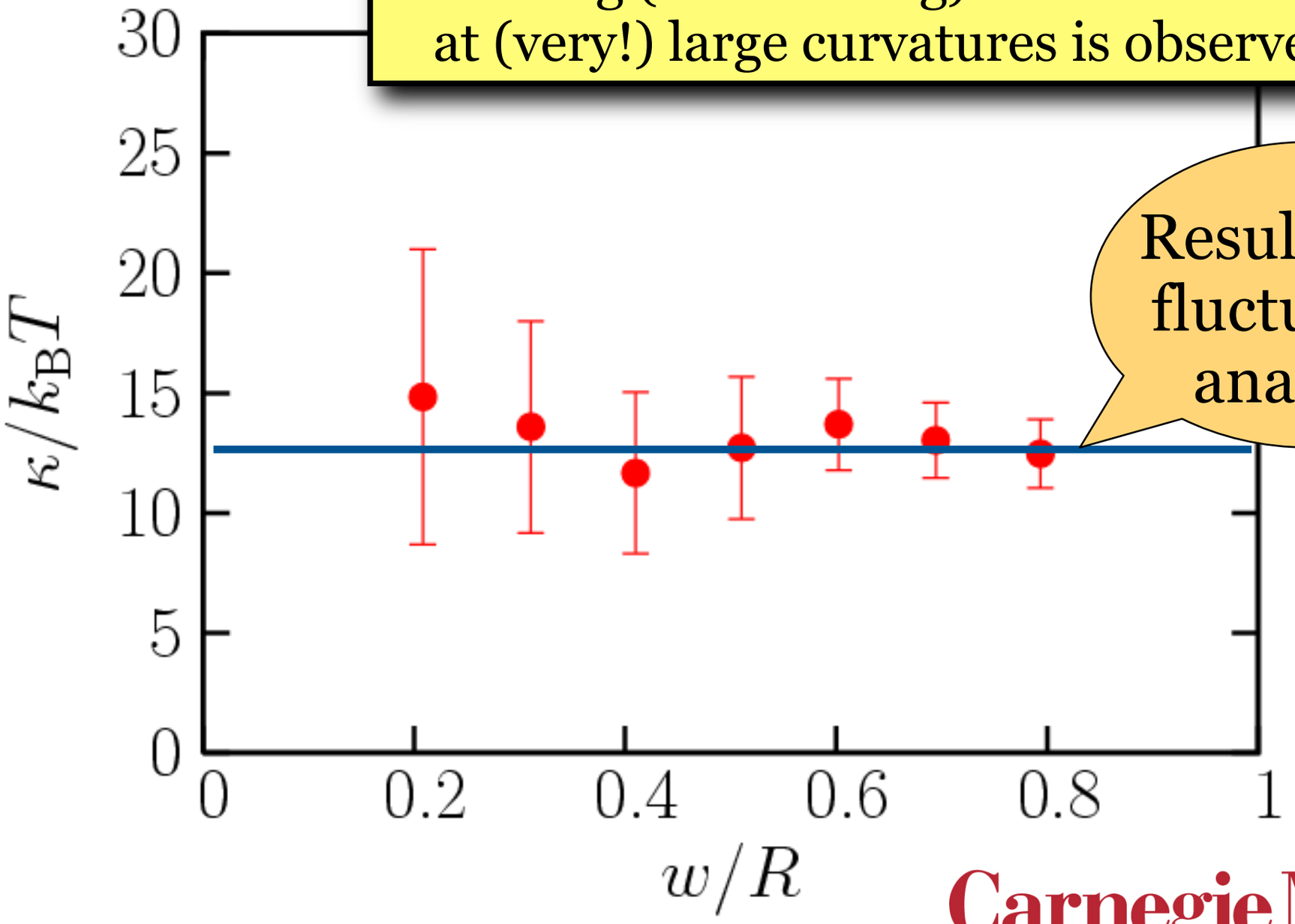
V. A. Harmandaris and M. Deserno, J. Chem. Phys. **125**, *204905* (2006)

Bending modulus

...from actively bent membranes

Results:

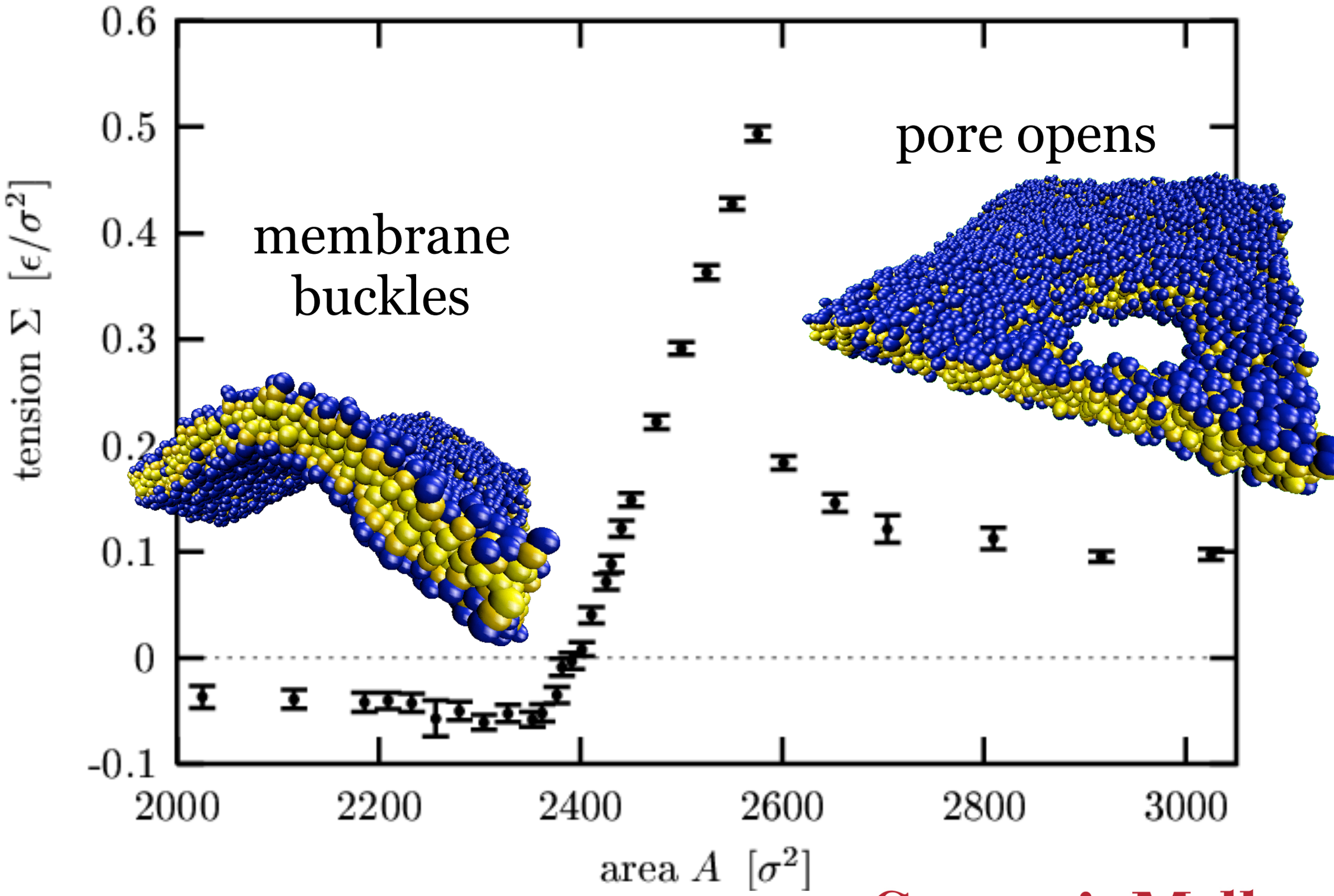
Within the limits of our resolution no stiffening (or softening) of the membrane at (very!) large curvatures is observed.



Result from fluctuation analysis

Carnegie Mellon

Stretching modulus



I.R. Cooke and M. Deserno, J. Chem. Phys. **123**, *224710* (2005)

Carnegie Mellon

Stretching modulus

Simple theory for this:

Farago, JCP, 2003; Tolpekina/den Otter/Briels, JCP 2004; Cooke/Deserno, JCP 2005

Membrane stretching plus line energy

$$E = \frac{1}{2} M \frac{(A - A_S - \pi R^2)^2}{A_S} + 2\pi\gamma R$$

rescaling of energy:

$$\lambda^3 = \frac{\gamma A_S}{\pi M} \quad , \quad \tilde{R} = \frac{R}{\lambda} \quad , \quad B = \frac{A - A_S}{\pi \lambda^2}$$

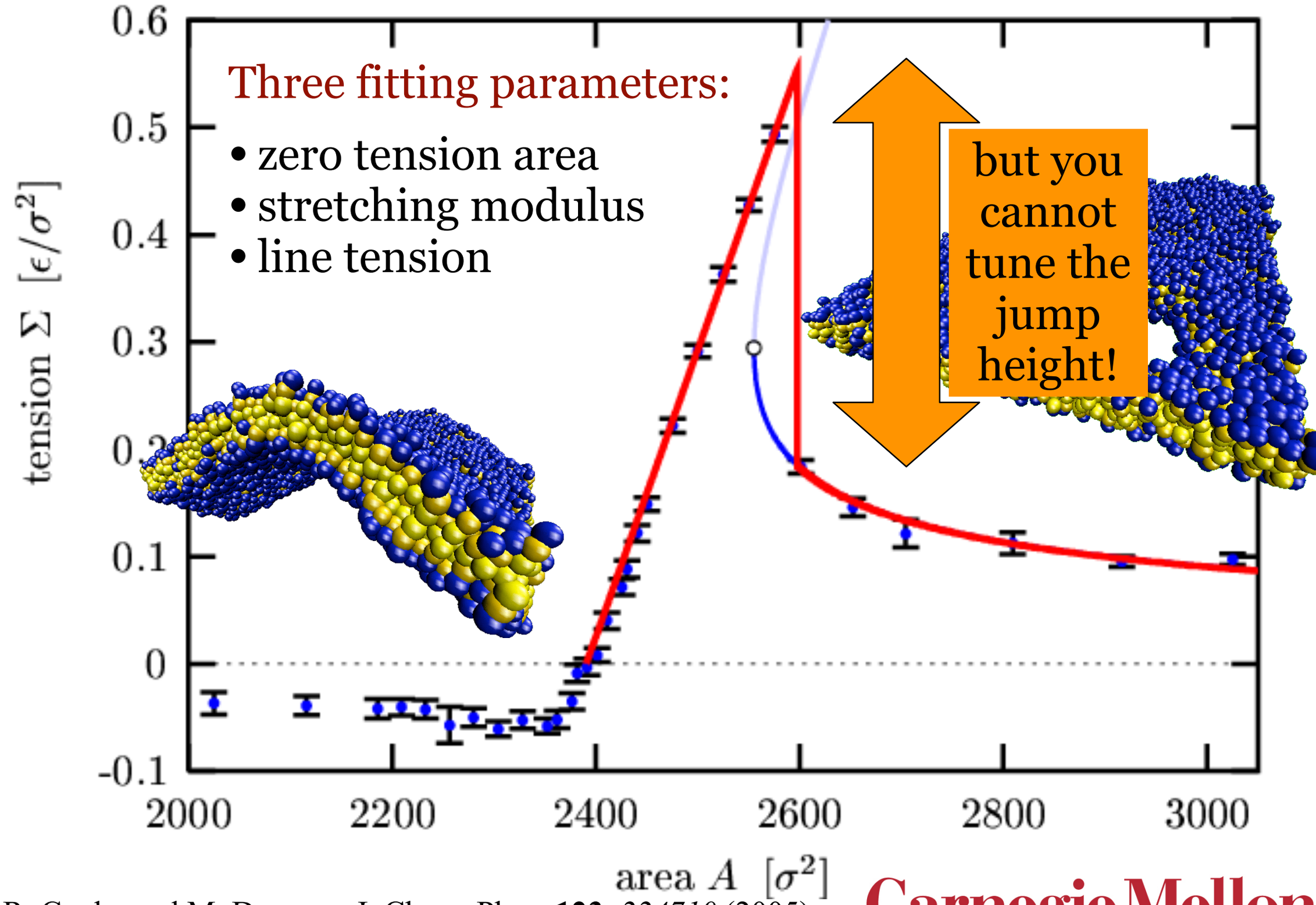
equilibrium condition for pore radius:

$$\tilde{R}^3 - B\tilde{R} + 1 = 0$$

Only one length scale, only one dimensionless driving parameter!

Carnegie Mellon

Stretching modulus

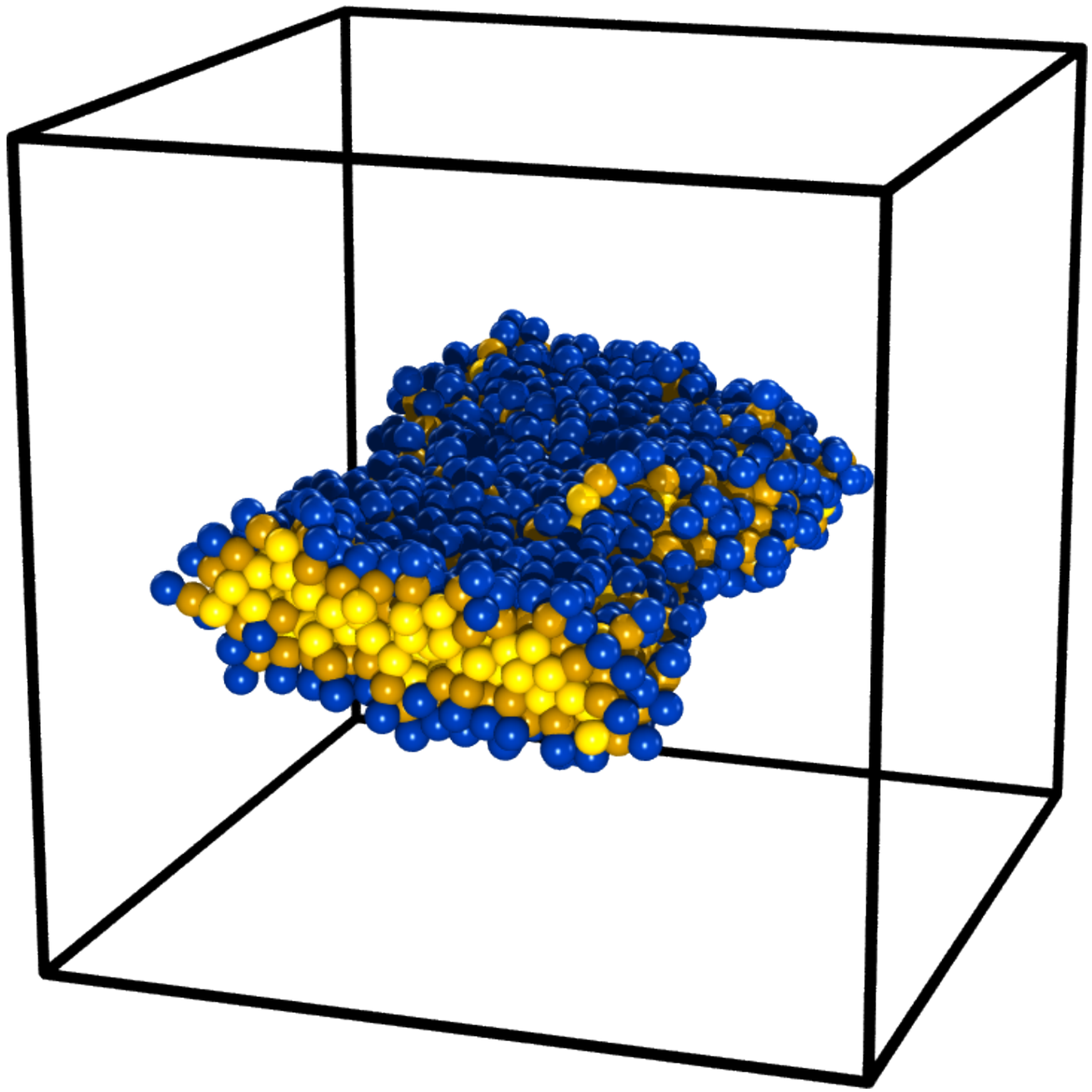


I.R. Cooke and M. Deserno, J. Chem. Phys. **123**, *224710* (2005)

Carnegie Mellon

Line tension

However, if all you want is the line tension, there's a simpler way of doing this:



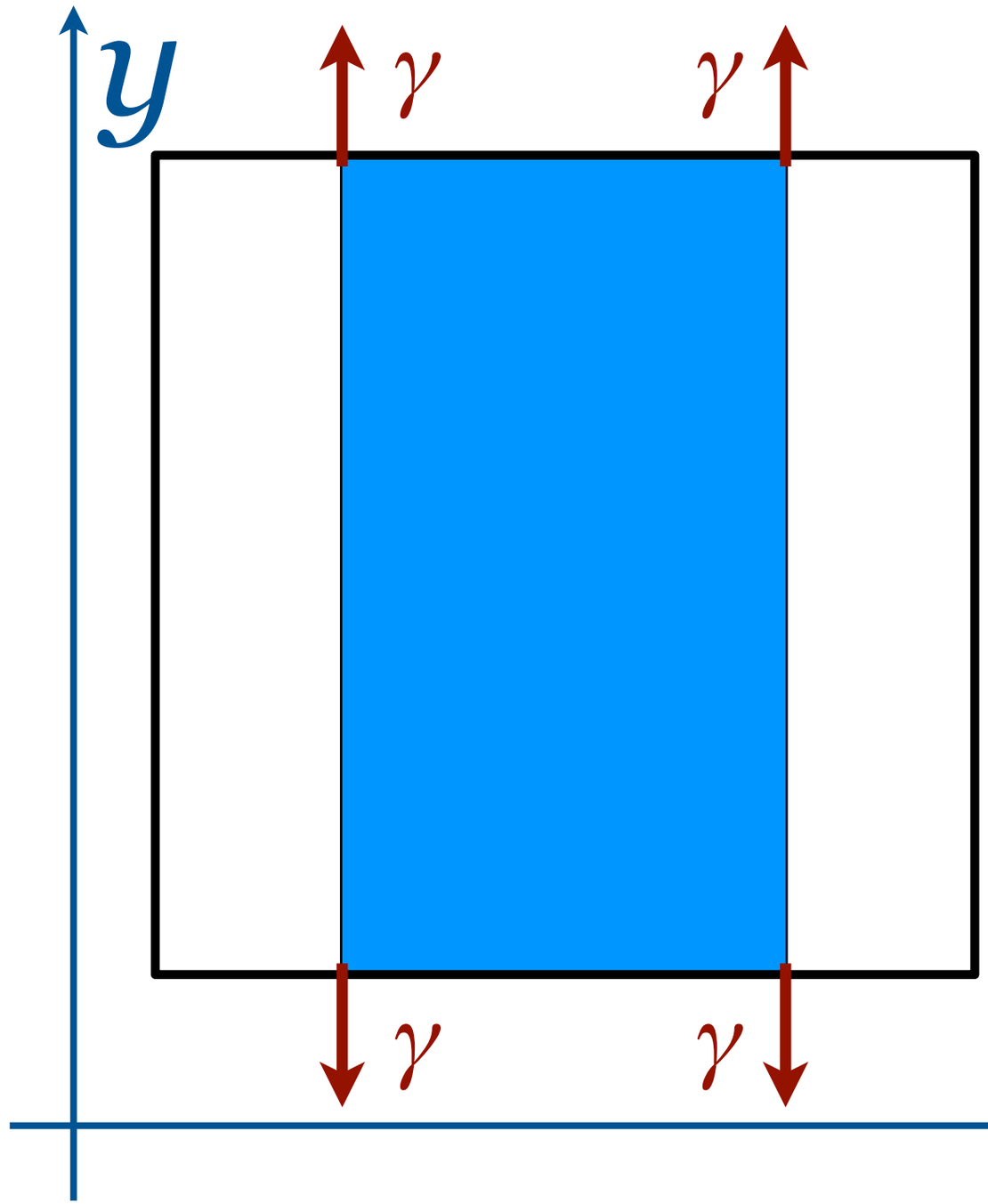
Simulate a periodically half-connected bilayer in a box.

Stress tensor will be imbalanced precisely by twice the line tension!

Carnegie Mellon

Line tension

However, if all you want is the line tension, there's a simpler way of doing this:



$$\Pi_{xx} = P$$

$$\Pi_{yy} = P - 2\gamma / L_x L_z$$

$$\gamma = \frac{1}{2} L_x L_z \left(\Pi_{xx} - \Pi_{yy} \right)$$

(Notice that $P = 0$ in the solvent free case!)

Vesicles

After having measured bending rigidity and line tension, we can make a prediction about the size of certain vesicles.

"The size of bilayer vesicles generated by sonication",

W. Helfrich, Physics Letters A, Volume 50, Issue 2, p. 115-116

Sonicate vesicle solution, rip vesicles into bits and pieces!

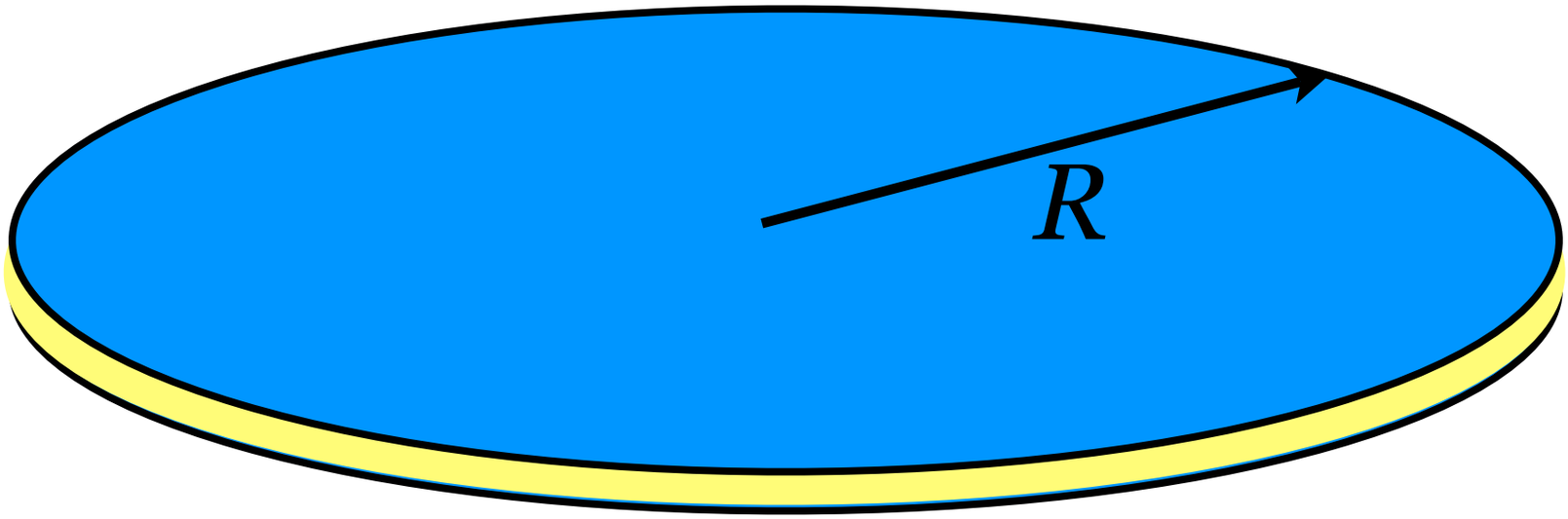
These (flat!) pieces will merge and grow bigger.

At what point will they again close up and form vesicles?

Why would they close up in the first place?

Vesicles

After having measured bending rigidity and line tension, we can make a prediction about the size of certain vesicles.



$$E_{\text{pancake}} = 2\pi R\,\gamma$$

$$E_{\text{vesicle}} = 4\pi\left(2\kappa + \bar{\kappa}\right)$$

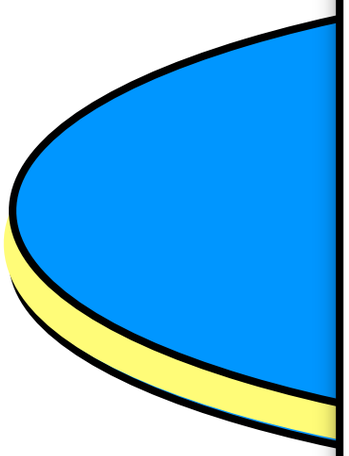
Vesicles

After having me
we can make a p

$$e_{\text{curvature}} = \frac{1}{2}\kappa\left(\frac{1}{R_1}+\frac{1}{R_2}\right)^2 + \bar{\kappa}\frac{1}{R_1}\cdot\frac{1}{R_2}$$

$$E_{\text{vesicle}} = 4\pi R^2 \cdot \left[\frac{1}{2}\kappa\left(\frac{1}{R}+\frac{1}{R}\right)^2 + \bar{\kappa}\frac{1}{R}\cdot\frac{1}{R}\right]$$

$$= 4\pi\left[2\kappa + \bar{\kappa}\right]$$



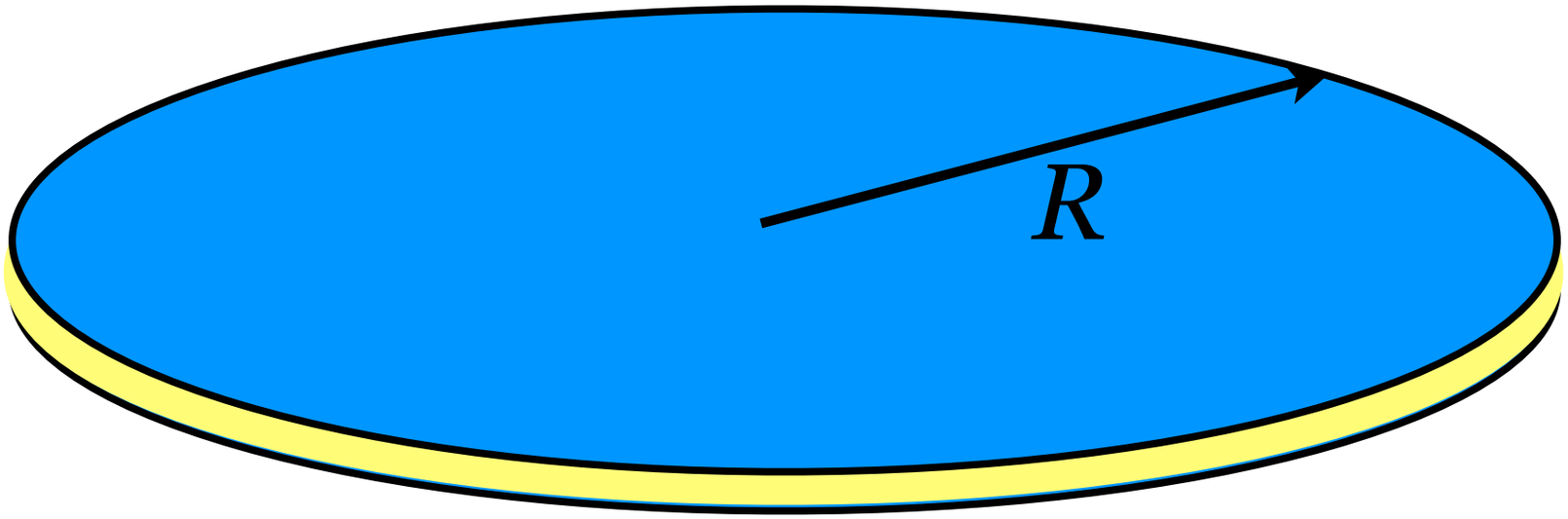
$$E_{\text{pancake}} = 2\pi R\,\gamma$$

$$E_{\text{vesicle}} = 4\pi\left(2\kappa + \bar{\kappa}\right)$$

Carnegie Mellon

Vesicles

After having measured bending rigidity and line tension, we can make a prediction about the size of certain vesicles.



$$E_{\text{pancake}} = 2\pi R\,\gamma$$

$$E_{\text{vesicle}} = 4\pi\left(2\kappa + \bar{\kappa}\right)$$

Energies are equal, if

$$R_{\text{pancake}} = \frac{2\left(2\kappa + \bar{\kappa}\right)}{\gamma}$$

(real stability analysis: 2 → 4)

Carnegie Mellon

Vesicles

What values do we expect?

Very little is known about this value!

$$\kappa \approx 20\, k_B T \approx 80\,\mathrm{pN\,nm} \qquad \bar{\kappa} \approx -\kappa \qquad \gamma \approx 10\,\mathrm{pN}$$

$$R_{\mathrm{pancake}} = \frac{4\left(2\kappa + \bar{\kappa}\right)}{\gamma} \approx \frac{4\kappa}{\gamma} \approx \frac{320\,\mathrm{pN\,nm}}{10\,\mathrm{pN}} \approx 32\,\mathrm{nm}$$

This is then also the diameter of the vesicles we expect to find!

Carnegie Mellon

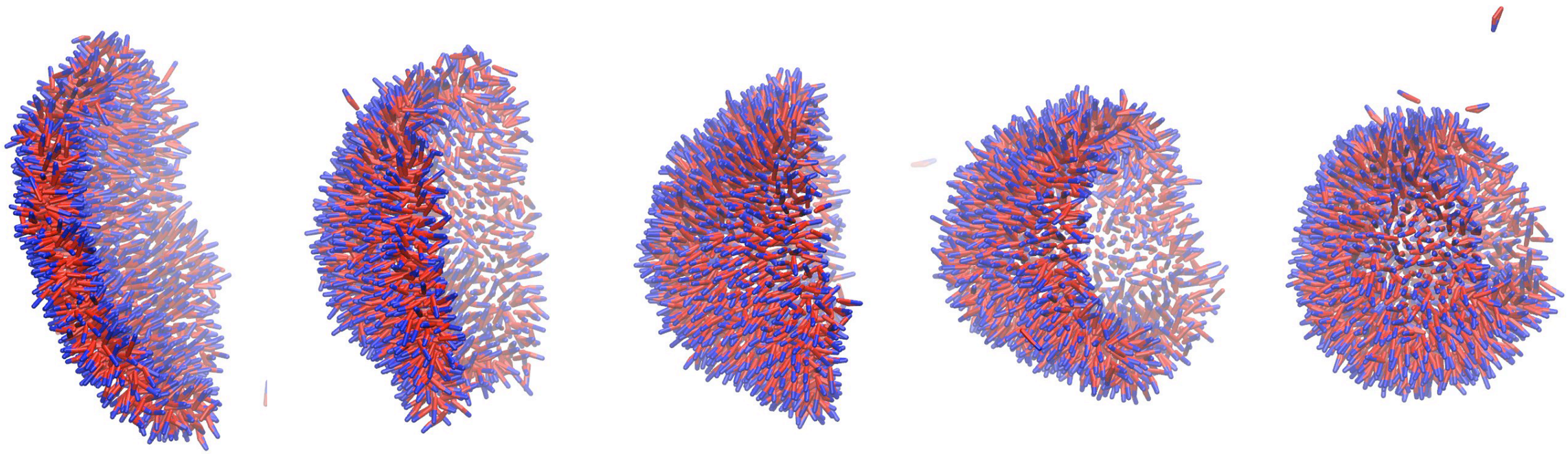
Vesicles

What values do we expect?

Very little is known about this value!

$$\kappa \approx 20\,k_{\mathrm{B}}T \approx 80\,\mathrm{pN\,nm} \qquad \bar{\kappa} \approx -\kappa \qquad \gamma \approx 10\,\mathrm{pN}$$

$$R_{\mathrm{pancake}} = \frac{4\left(2\kappa + \bar{\kappa}\right)}{\gamma} \approx \frac{4\kappa}{\gamma} \approx \frac{320\,\mathrm{pN\,nm}}{10\,\mathrm{pN}} \approx 32\,\mathrm{nm}$$

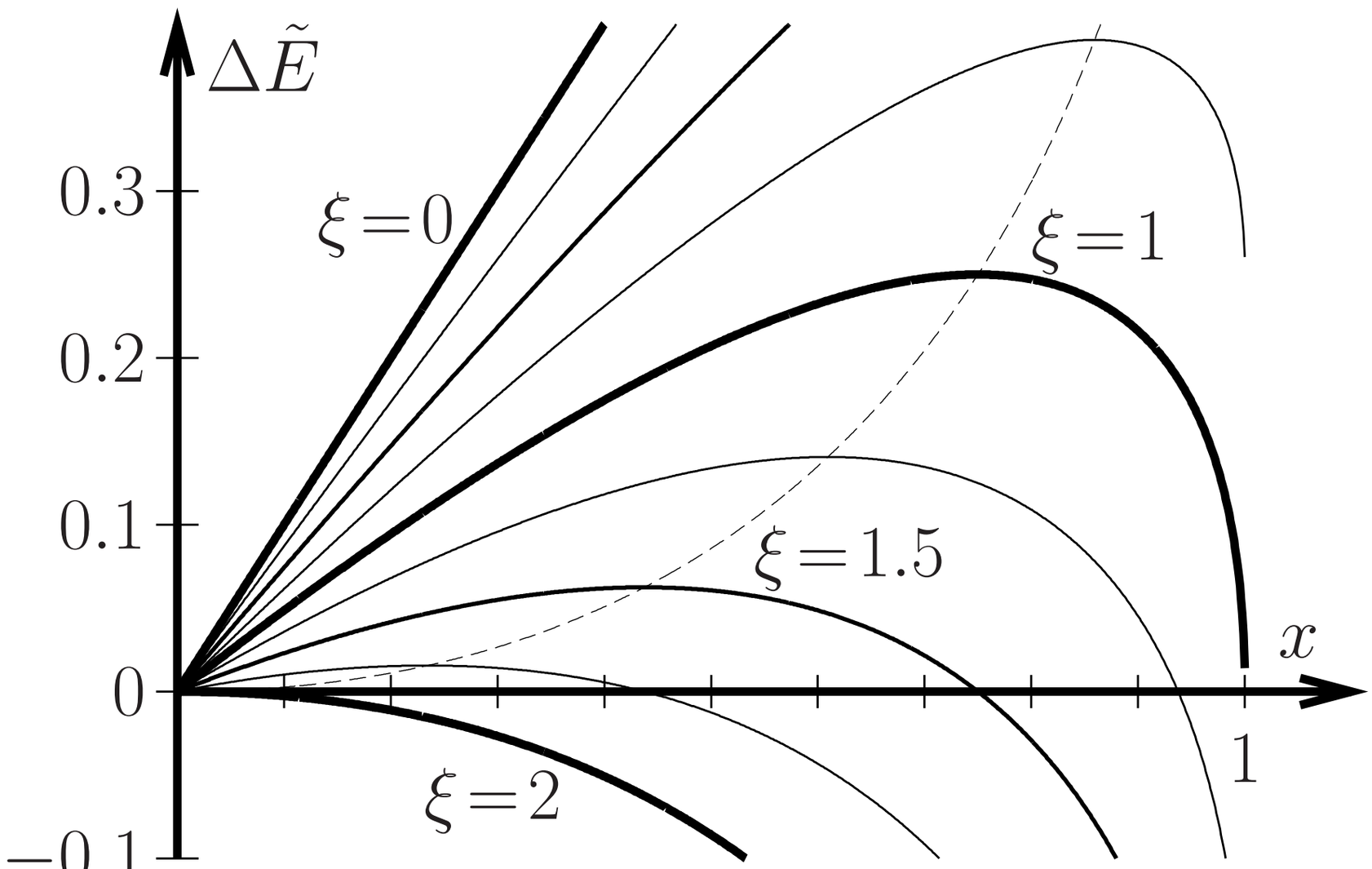


Carnegie Mellon

How we measure $\bar{\kappa}$

The energy of a partially curved patch can be calculated as:

$$\frac{\Delta E(x,\xi)}{8\pi\kappa + 4\pi\bar{\kappa}} = \Delta\tilde{E}(x,\xi) = x + \xi\left[\sqrt{1-x} - 1\right]$$



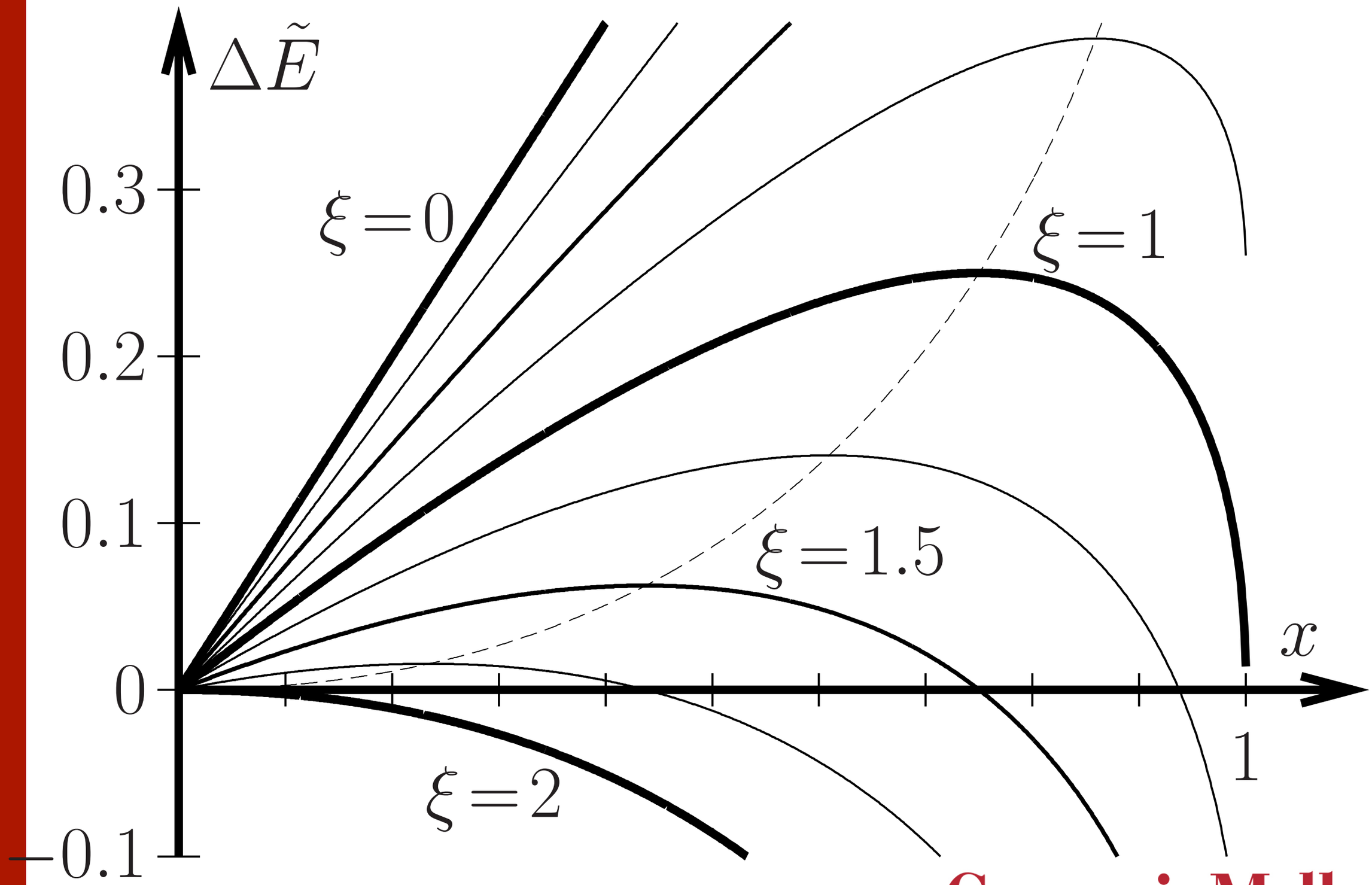
$$x = (Rc)^2$$

$$R = \sqrt{\frac{A}{4\pi}}$$

$$\xi = \frac{\gamma R}{2\kappa + \bar{\kappa}}$$

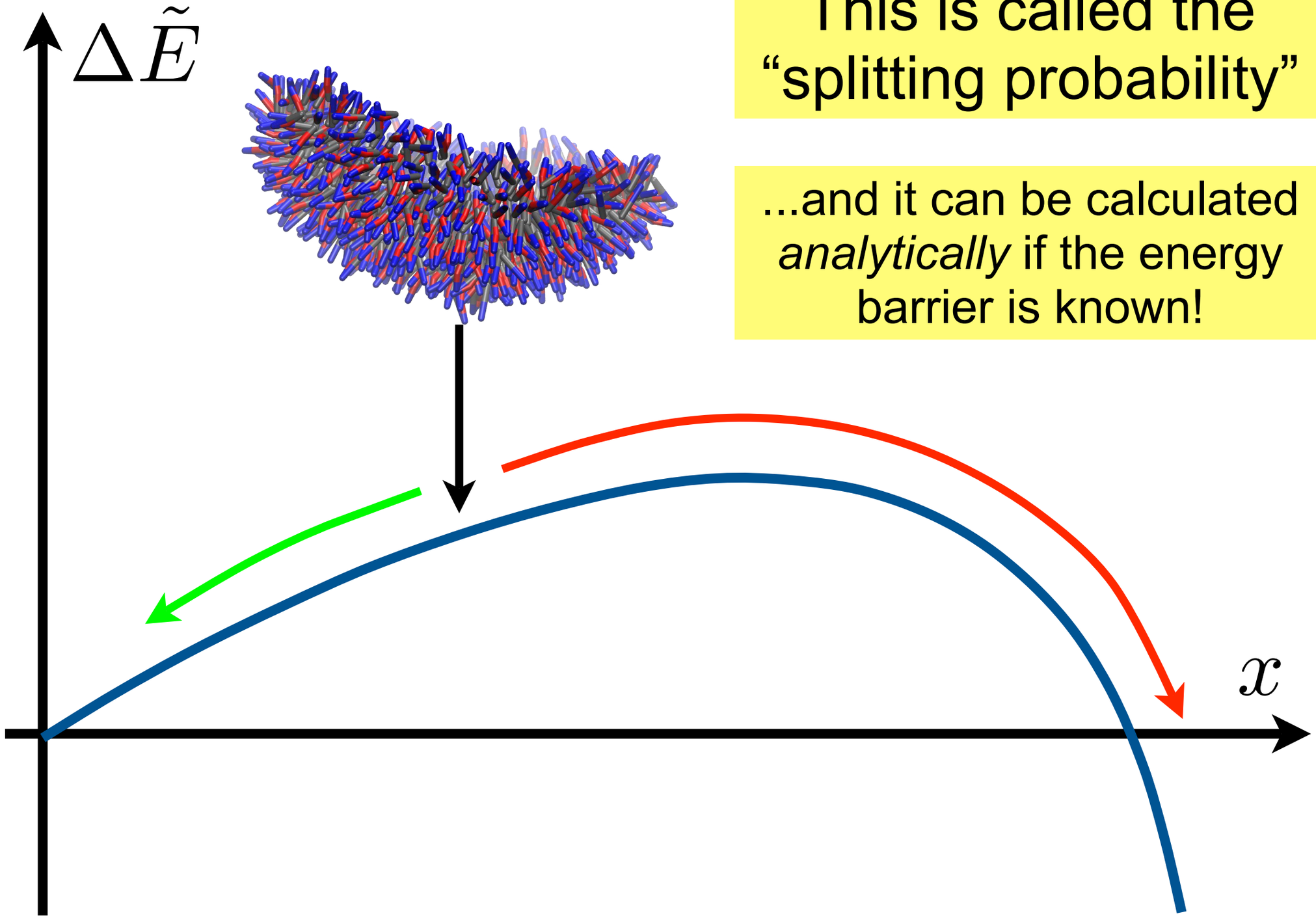
Carnegie Mellon

How we measure $\bar{\kappa}$



Carnegie Mellon

How we measure $\bar{\kappa}$



This is called the "splitting probability"

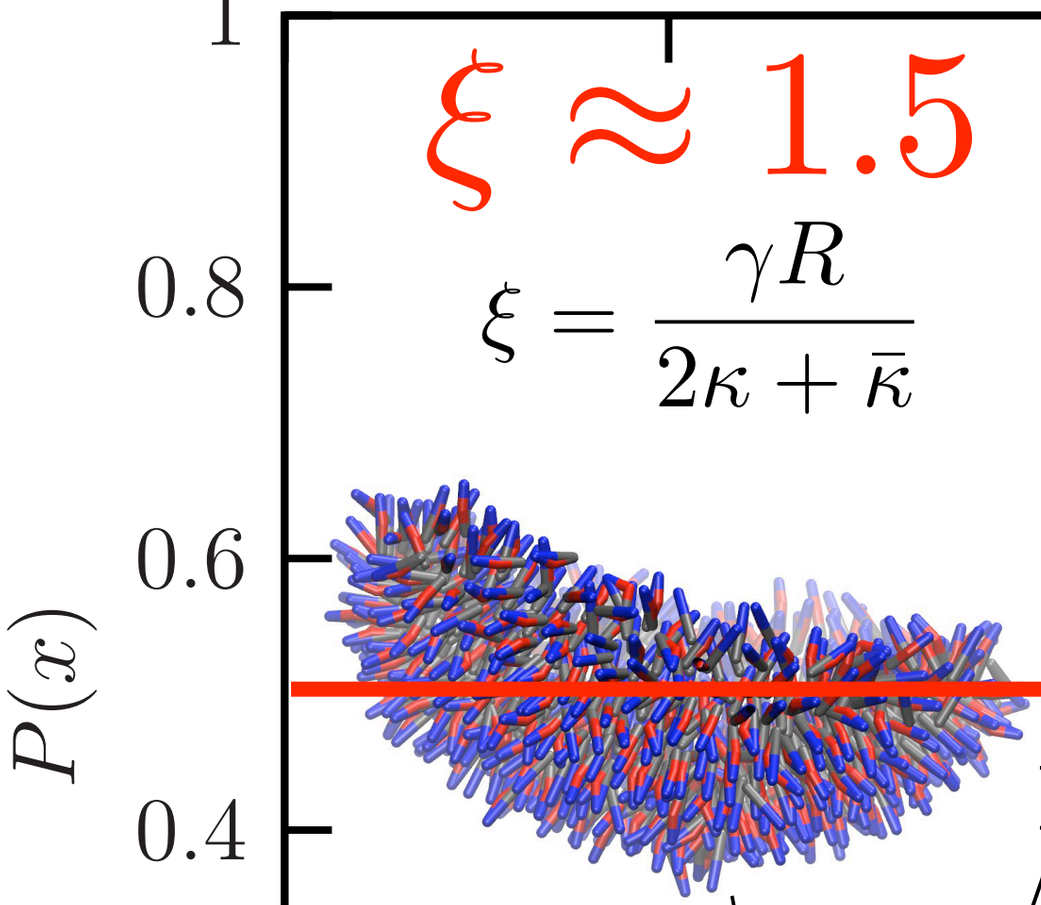
...and it can be calculated *analytically* if the energy barrier is known!

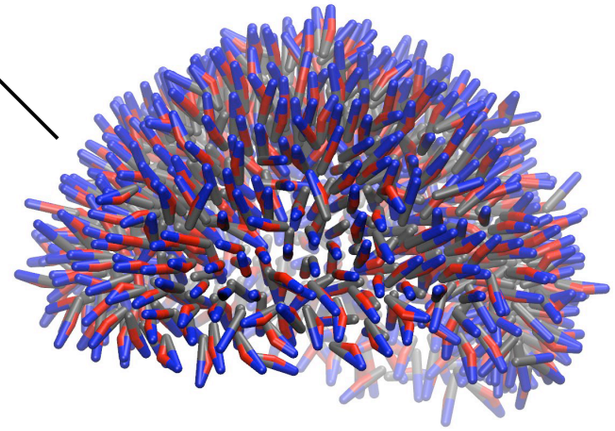
Carnegie Mellon

How we measure $\bar{\kappa}$

$\xi \approx 1.5$

$$\xi = \frac{\gamma R}{2\kappa + \bar{\kappa}}$$





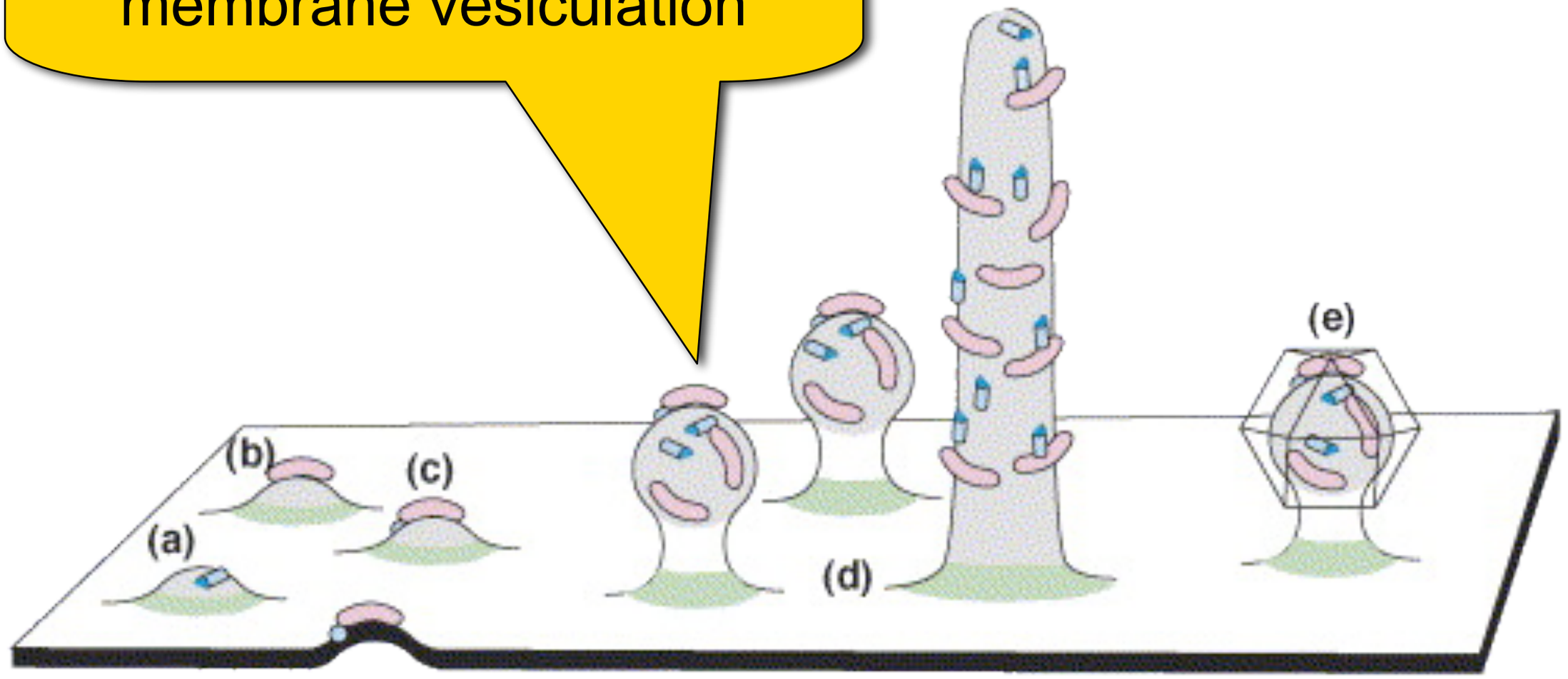
Carnegie Mellon

Applications

Protein-induced budding

Membrane-curving proteins can attract and drive membrane vesiculation

B. Antonny, Curr. Opin. Cell Biol. **18**, *386* (2006)



Intuitive, but no physical justification!

Carnegie Mellon

Protein-induced budding

Interaction potential from linearized theory

(spherical caps, radius a, detachment angle α)

$$U(R) = 2\pi\sigma\, a^2\alpha^2 \left[\mathrm{K}_0\left(\frac{R}{\lambda}\right) + \left(\frac{a}{\lambda}\right) \mathrm{K}_2^2\left(\frac{R}{\lambda}\right) \right]$$

[T.R. Weikl, M.M. Kozlov, W. Helfrich, PRE **57**, *6988* (1998)]

characteristic decay length: $\lambda = \sqrt{\kappa/\sigma}$

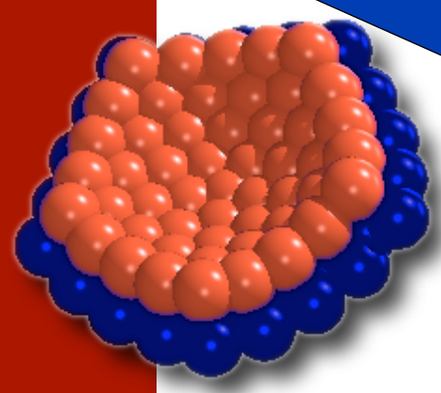
$$\sigma = 0 \;\Rightarrow\; U(R) = 8\pi\kappa\,\alpha^2 \left(\frac{a}{R}\right)^4$$

Goulian, Bruinsma, Pincus, Europhys. Lett. **22**, *145* (1993)

This is always repulsive!

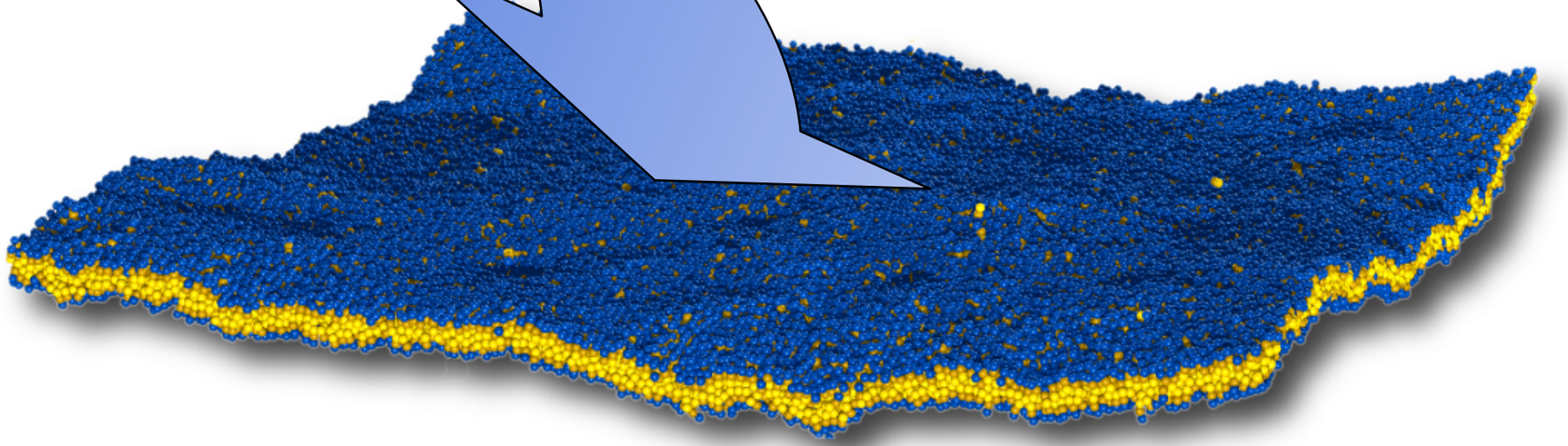
Carnegie Mellon

Protein-induced budding



many caps

(“contact lens”)

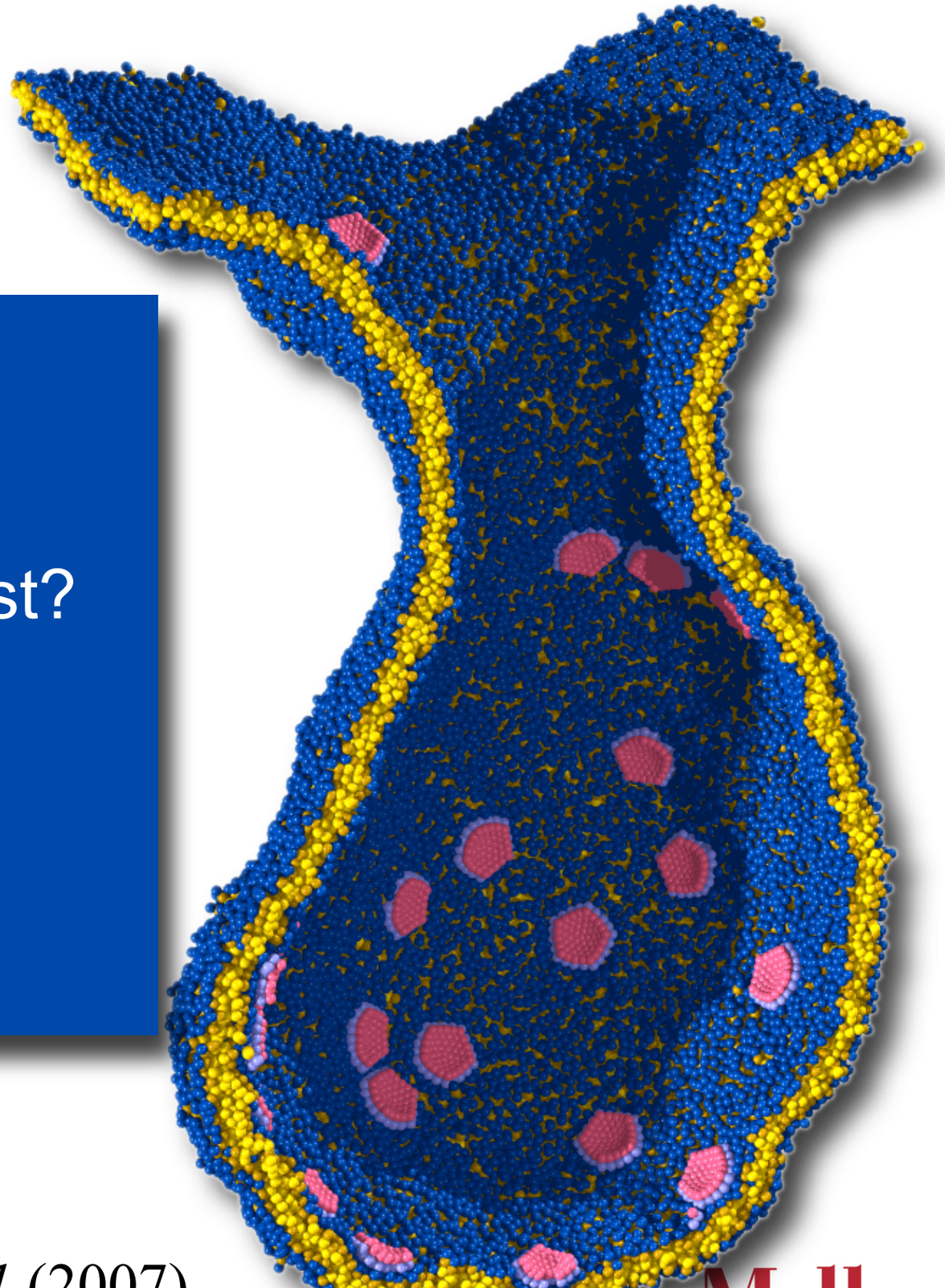


36 curved caps, ~50000 lipids,
160nm side-length, total time ~1ms
no lateral tension
no explicit interaction between caps

B.J. Reynwar *et al.*, Nature **447**, *461* (2007)

Carnegie Mellon

Protein-induced budding



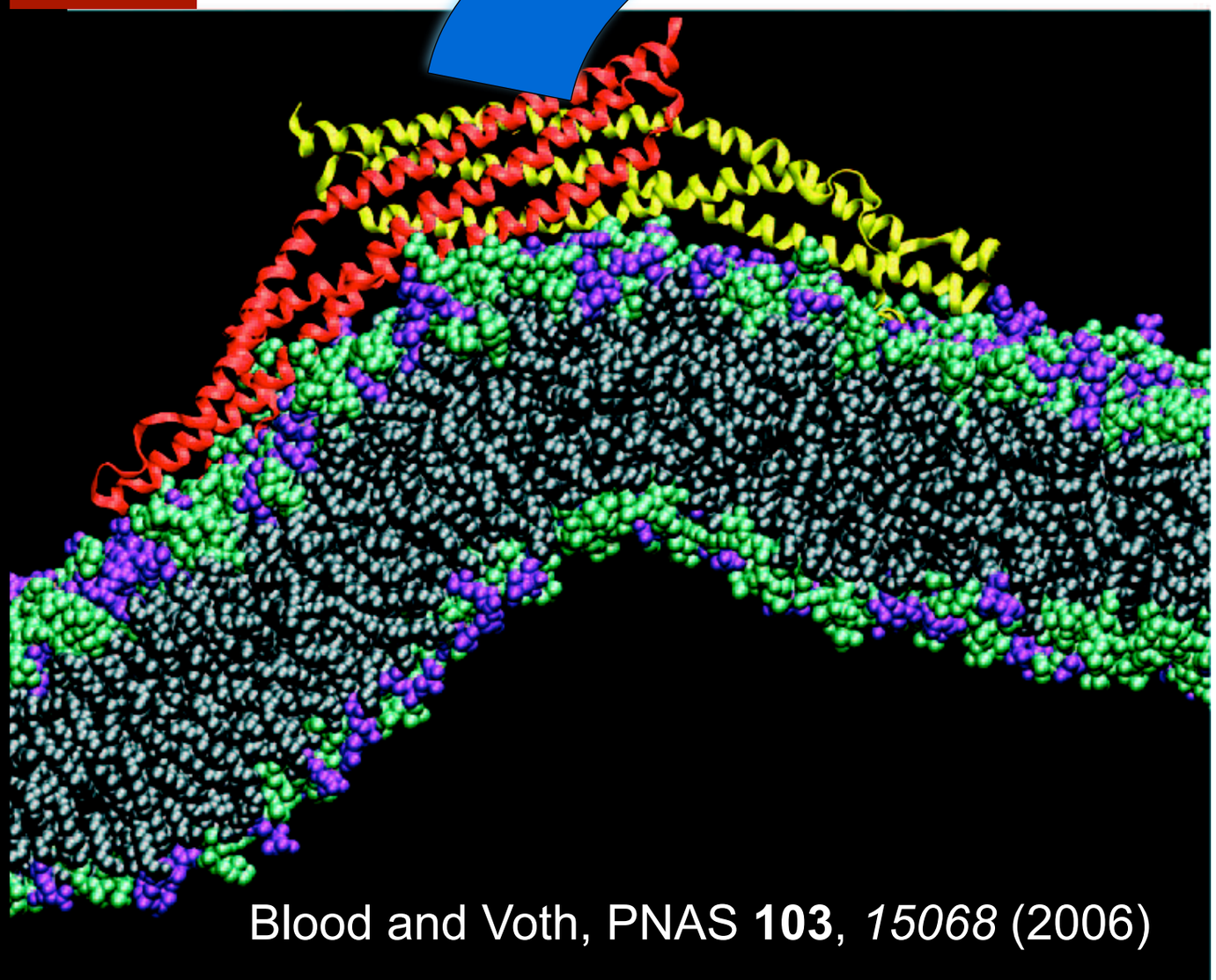
Some observations:

- Caps **attract** collectively
- Attractive pair-forces exist?
- No crystalline structure
- Cooperative vesiculation
- No “scaffolding”
- 50-100nm length scales
- several milliseconds

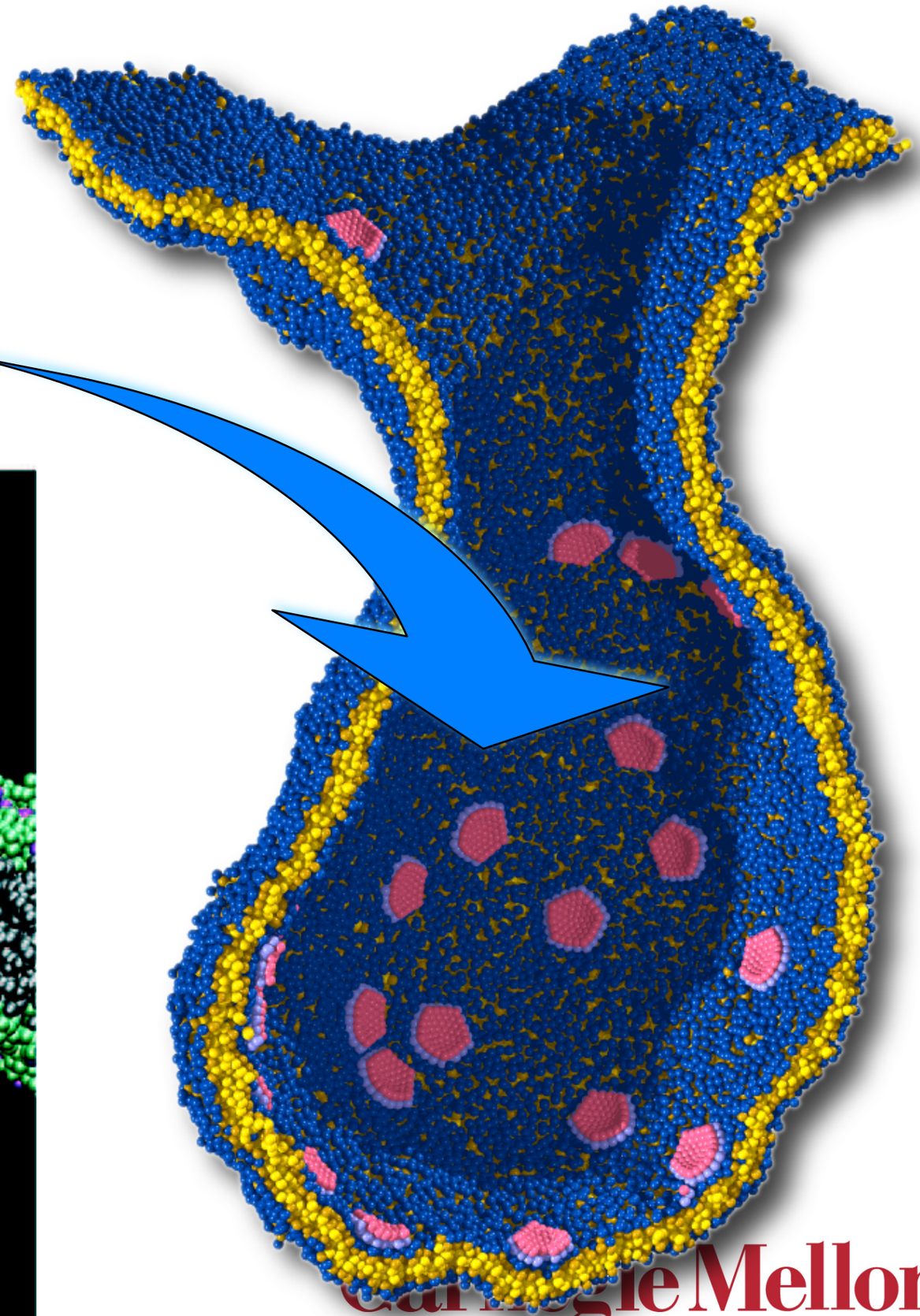
B.J. Reynwar *et al.*, Nature **447**, *461* (2007)

Carnegie Mellon

Protein-induced budding



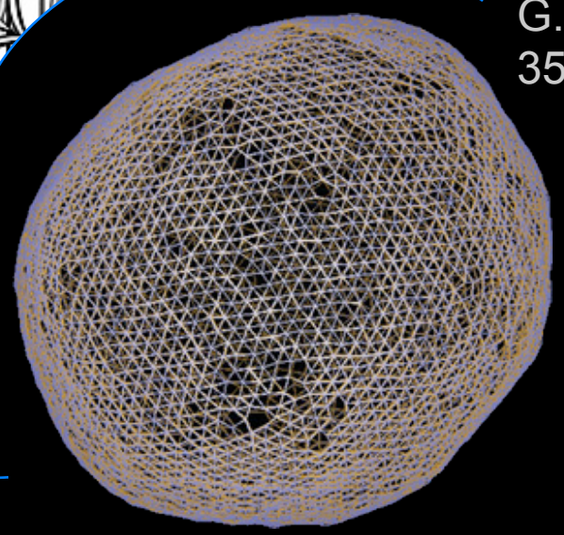
Blood and Voth, PNAS **103**, *15068* (2006)

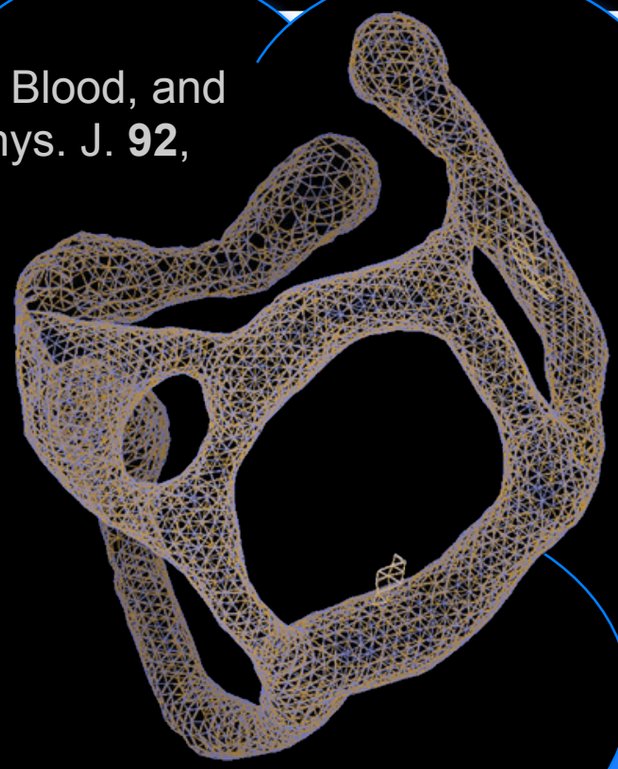


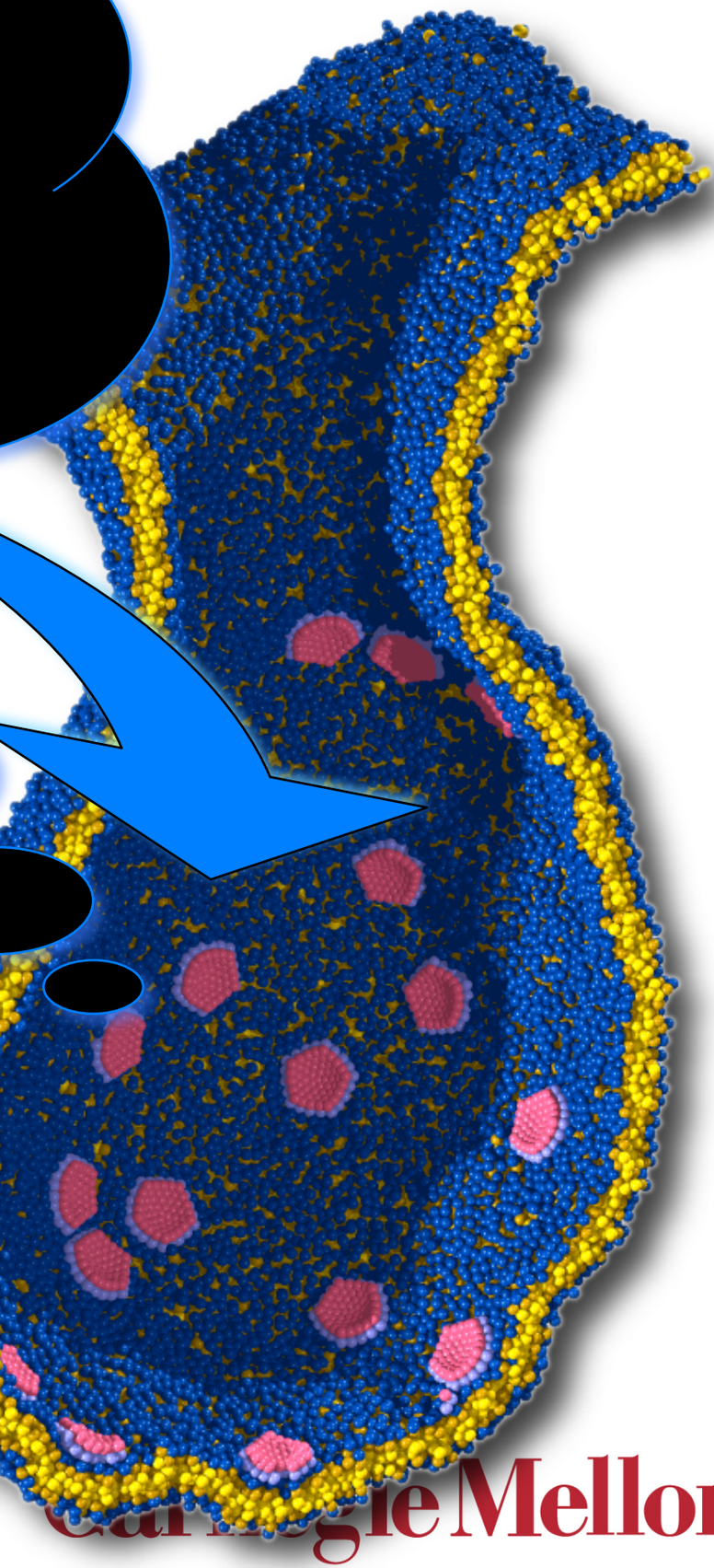
Carnegie Mellon

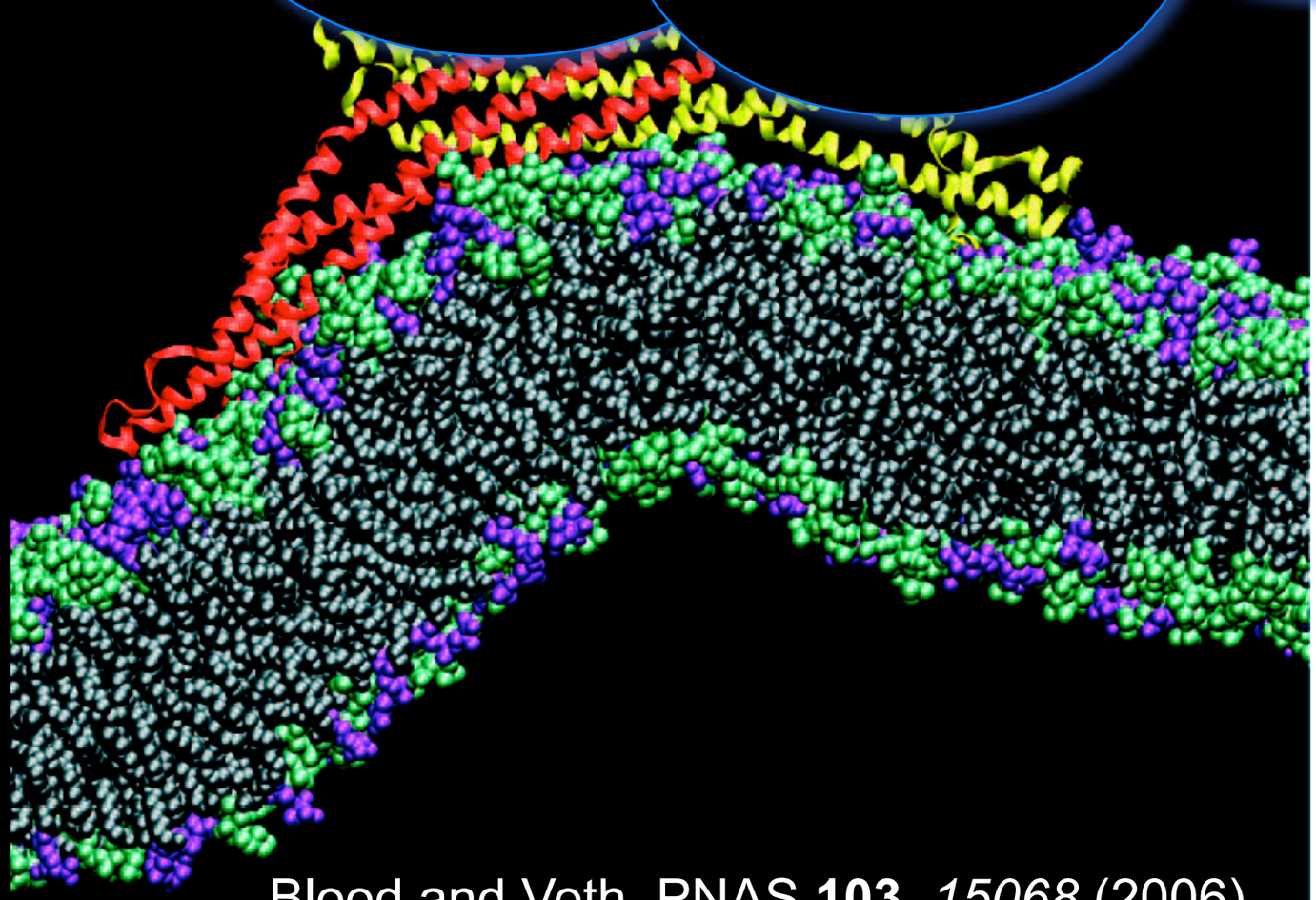
budding

G.S. Ayton, P.D. Blood, and G.A. Voth, Biophys. J. **92**, 3595 (2007)







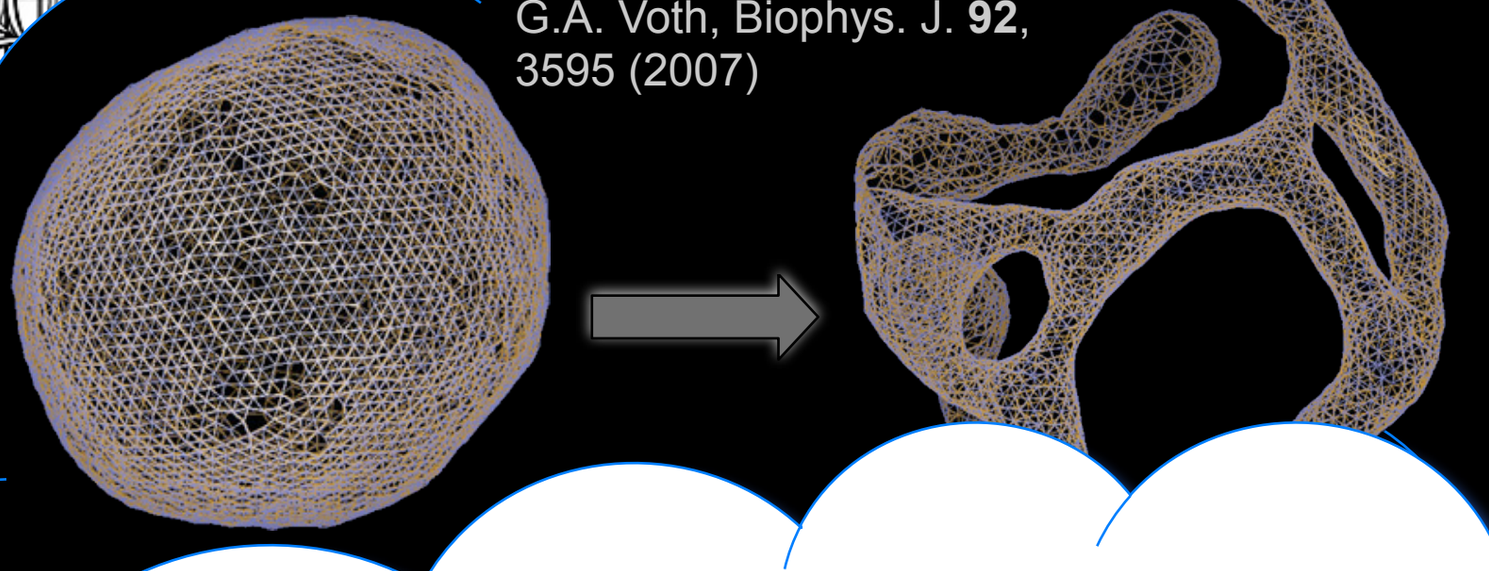


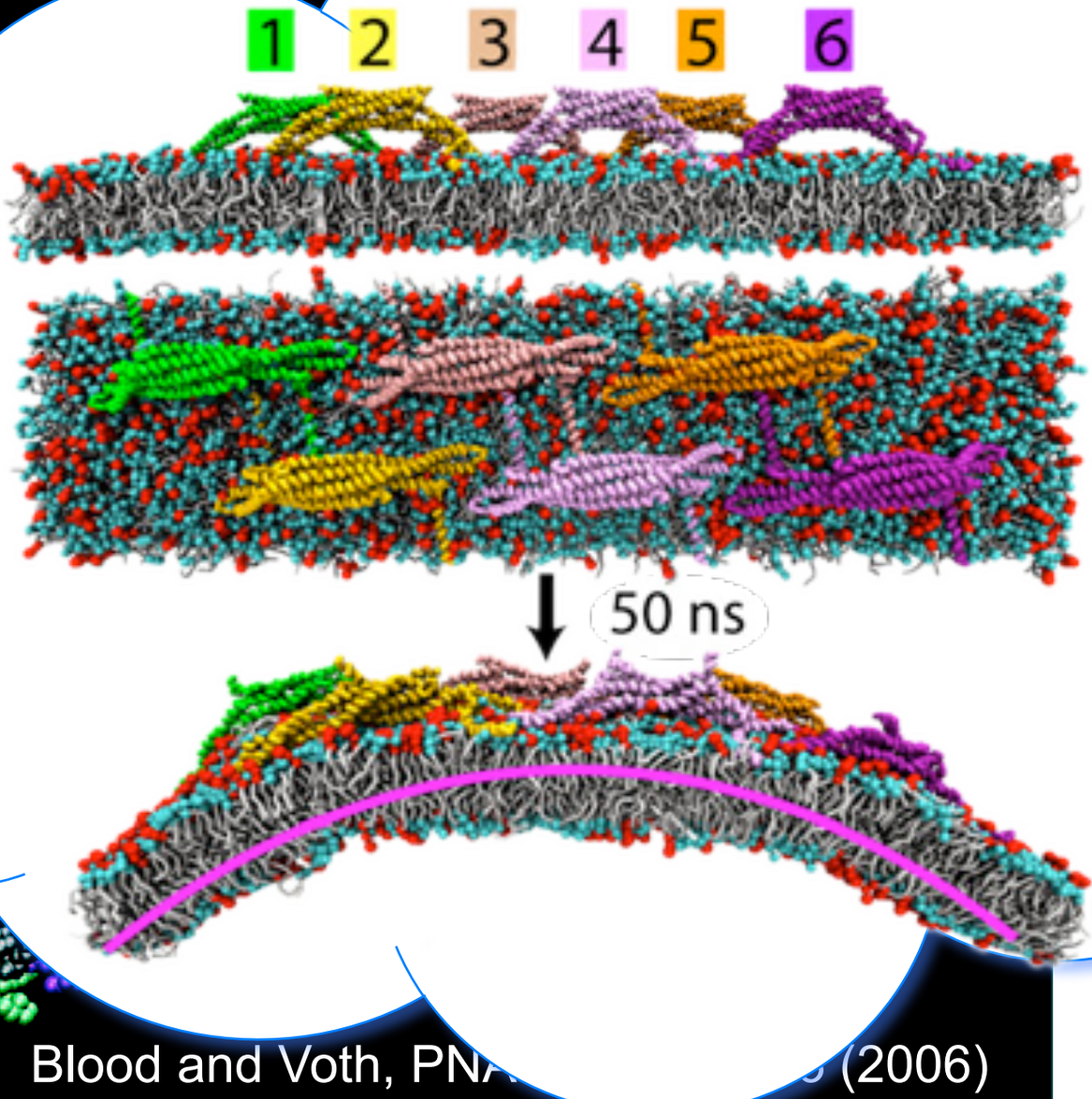
Blood and Voth, PNAS **103**, *15068* (2006)

Carnegie Mellon

budding

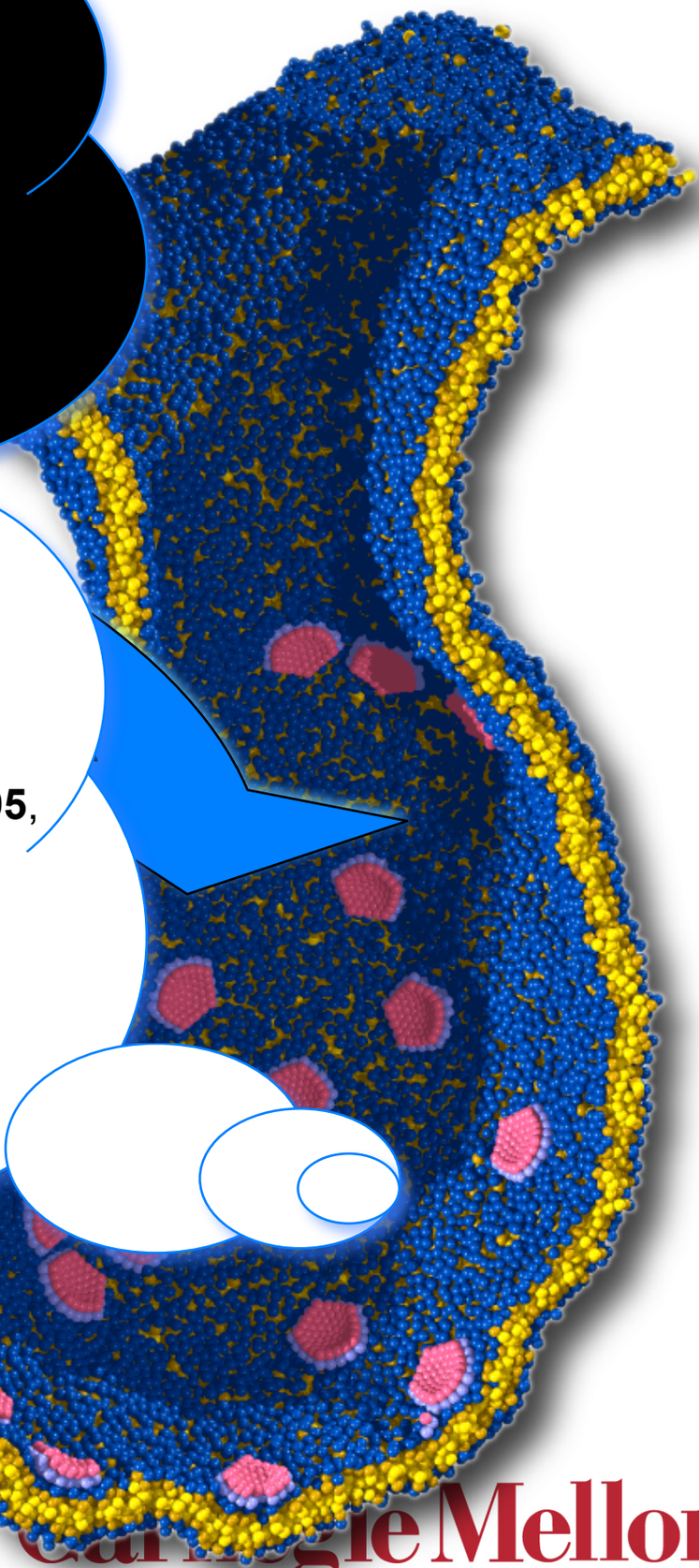
G.S. Ayton, P.D. Blood, and G.A. Voth, Biophys. J. **92**, 3595 (2007)





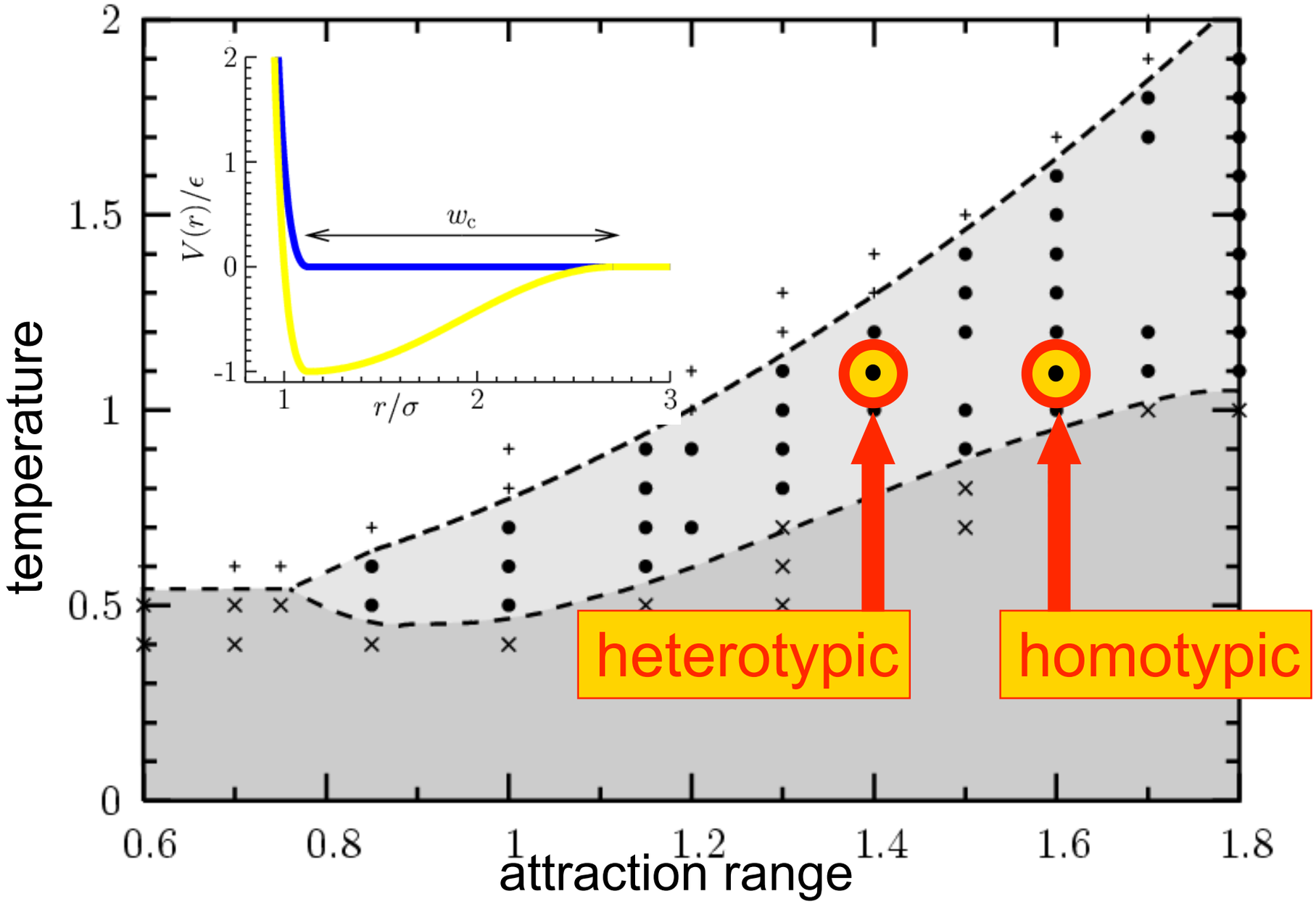
Blood and Voth, PNA (2006)

A. Arkhipov, Y. Yin, K. Schulten. Biophys. J. **95**, 2806 (2008)



Carnegie Mellon

Lipid A-B–mixtures

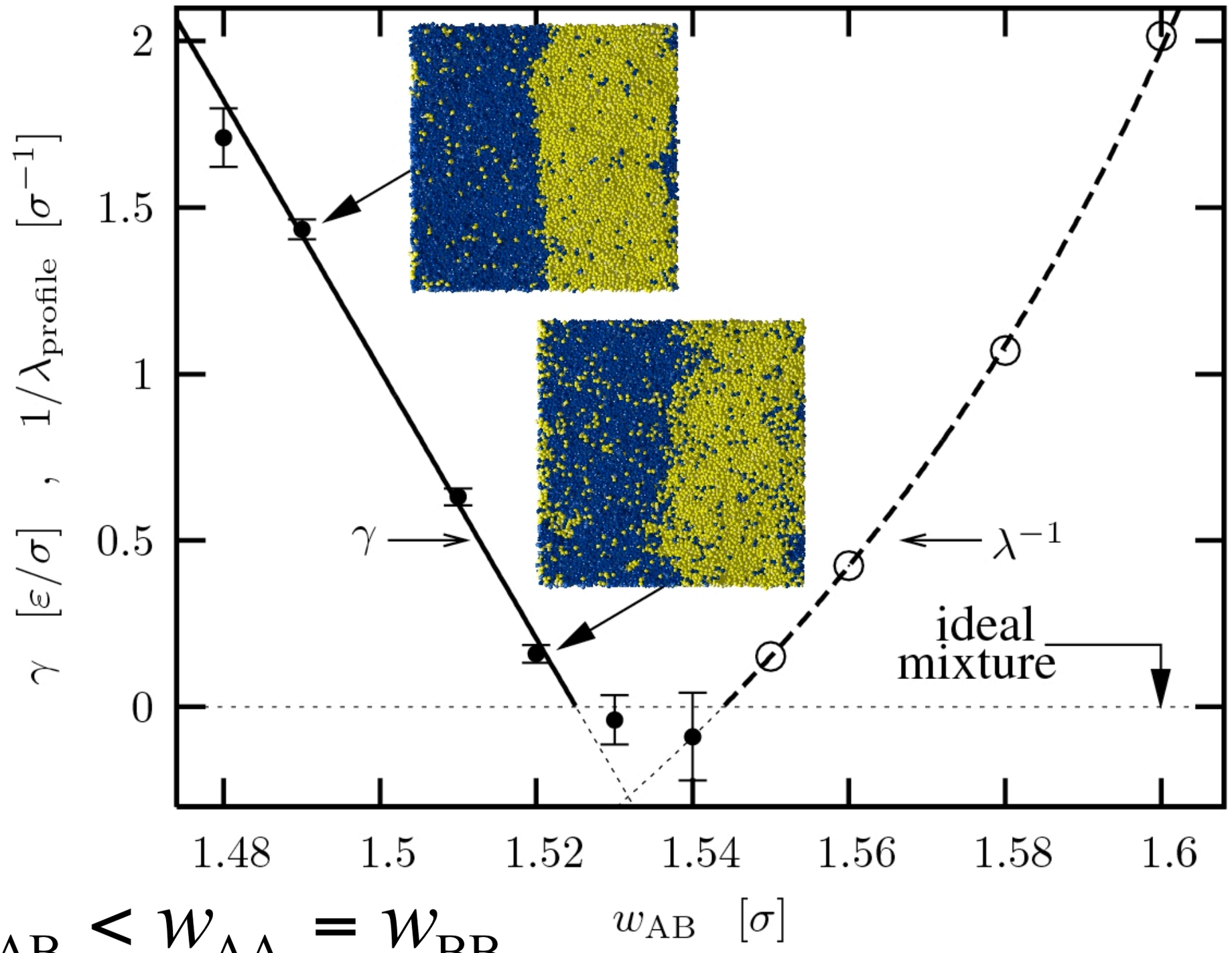


$$w_{AB} < w_{AA} = w_{BB}$$

B.J. Reynwar & M. Deserno,
Biointerphases **3**, *FA118* (2009)

Carnegie Mellon

Lipid A-B–mixtures



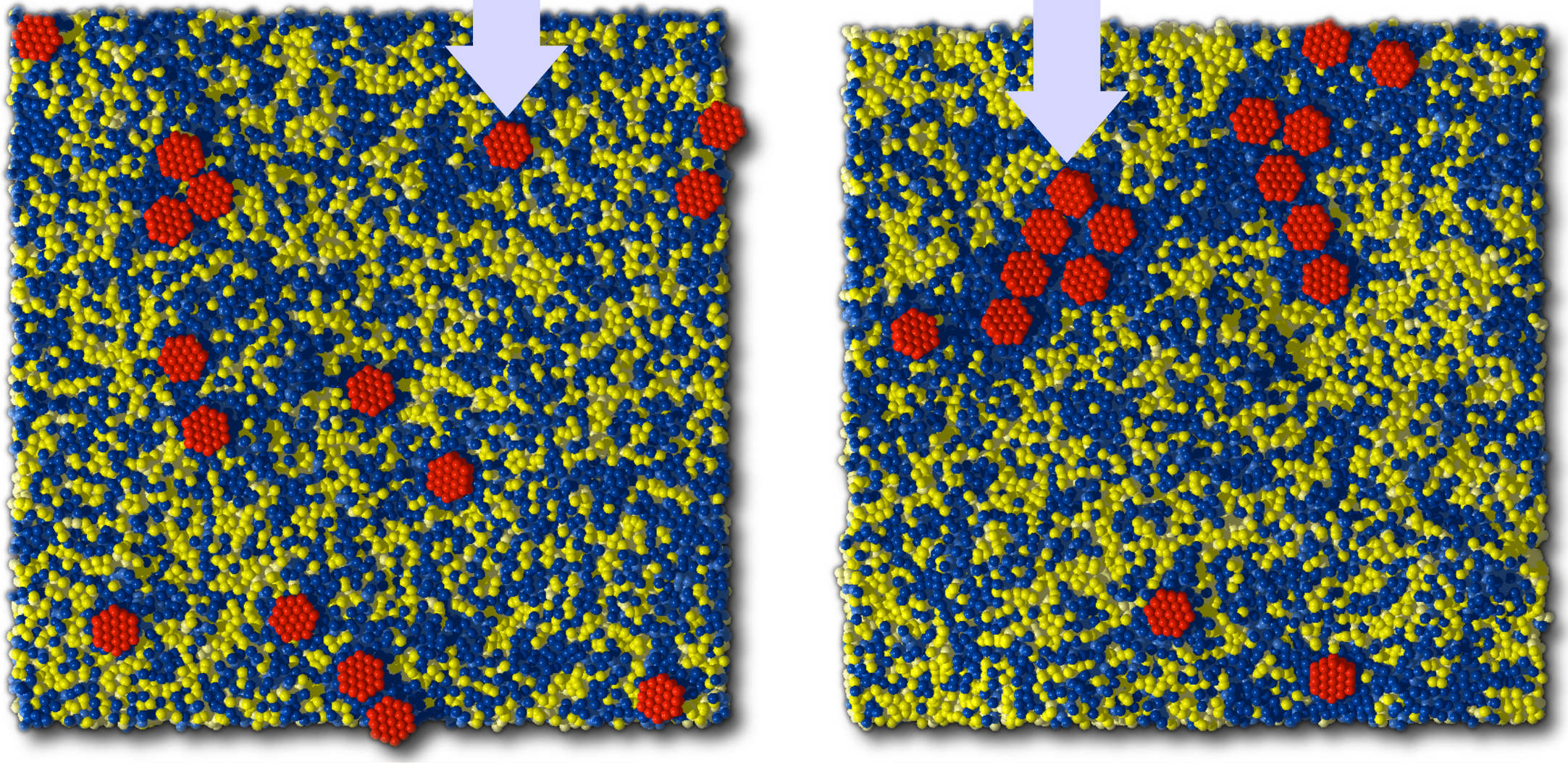
$$w_{\mathrm{AB}} < w_{\mathrm{AA}} = w_{\mathrm{BB}}$$

B.J. Reynwar & M. Deserno,
Biointerphases **3**, *FA118* (2009)

Carnegie Mellon

Lipid A-B–mixtures +proteins

Proteins only adsorb on blue lipids



ideal lipid mixture

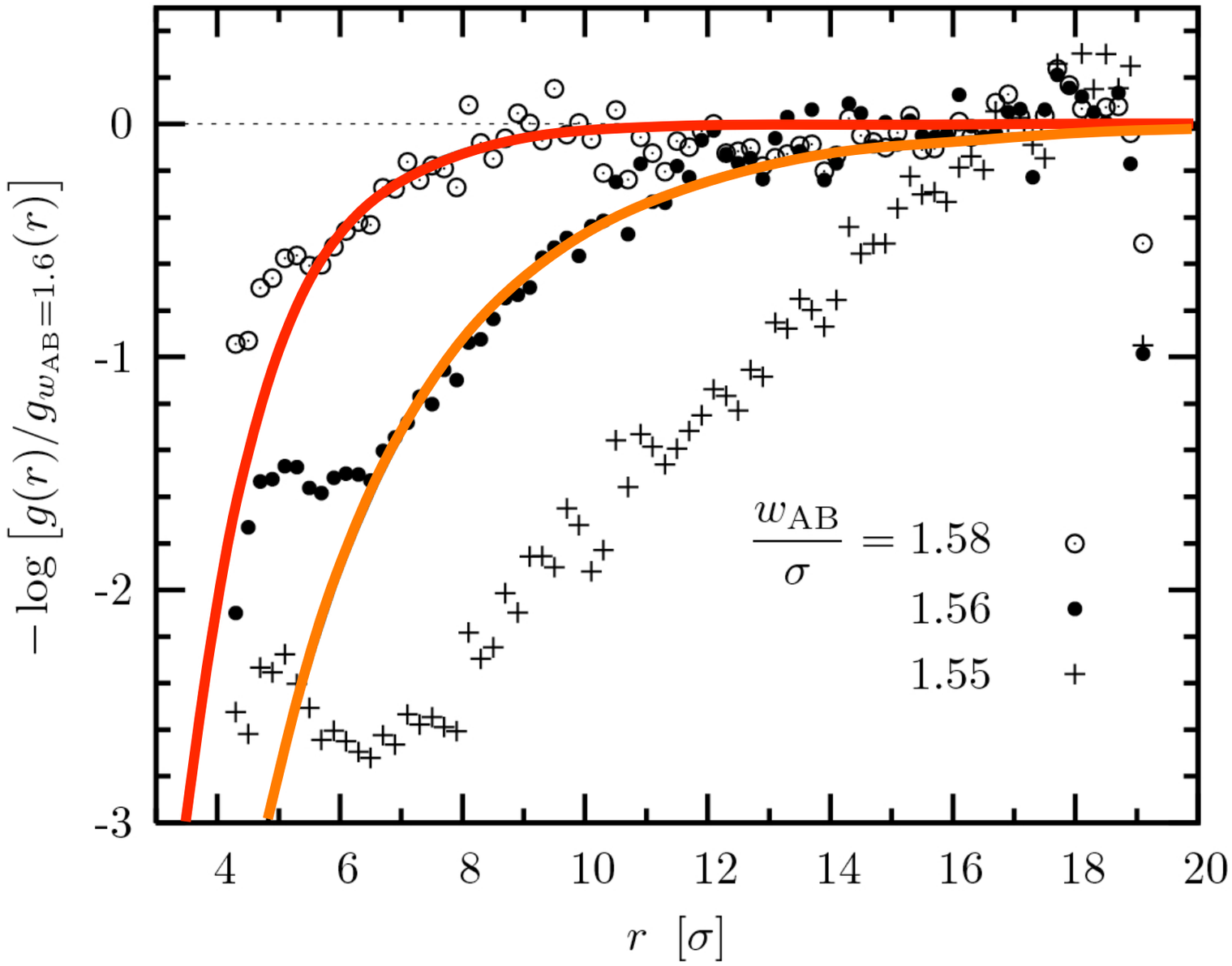
non-ideal lipid mixture

Composition-induced protein aggregation

B.J. Reynwar & M. Deserno,
Biointerphases **3**, *FA118* (2009)

Carnegie Mellon

Lipid A-B–mixtures +proteins

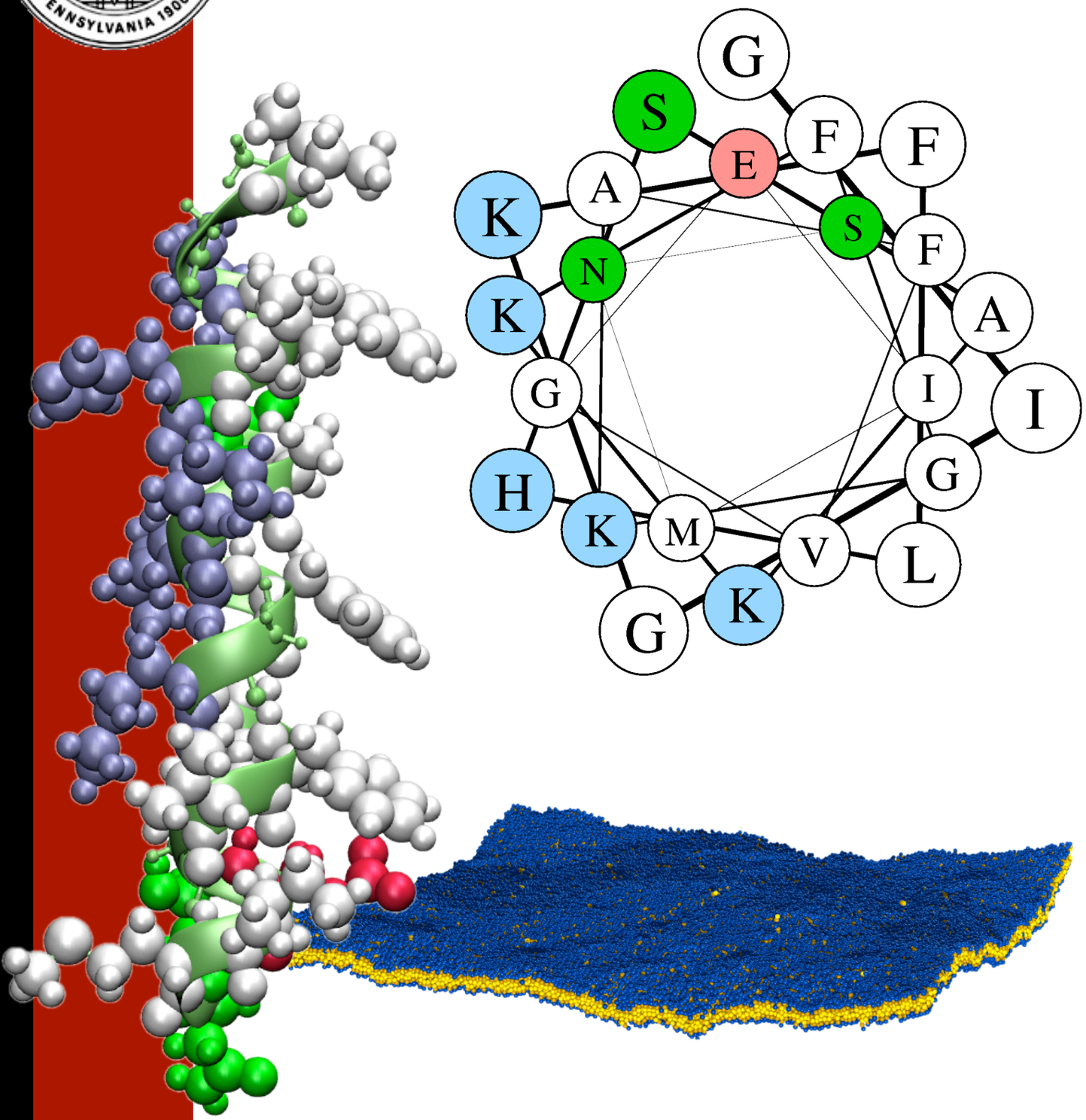


Pair potentials can be fitted by simple ground state theory.

B.J. Reynwar & M. Deserno,
Biointerphases **3**, *FA118* (2009)

Carnegie Mellon

Peptide-induced pore formation

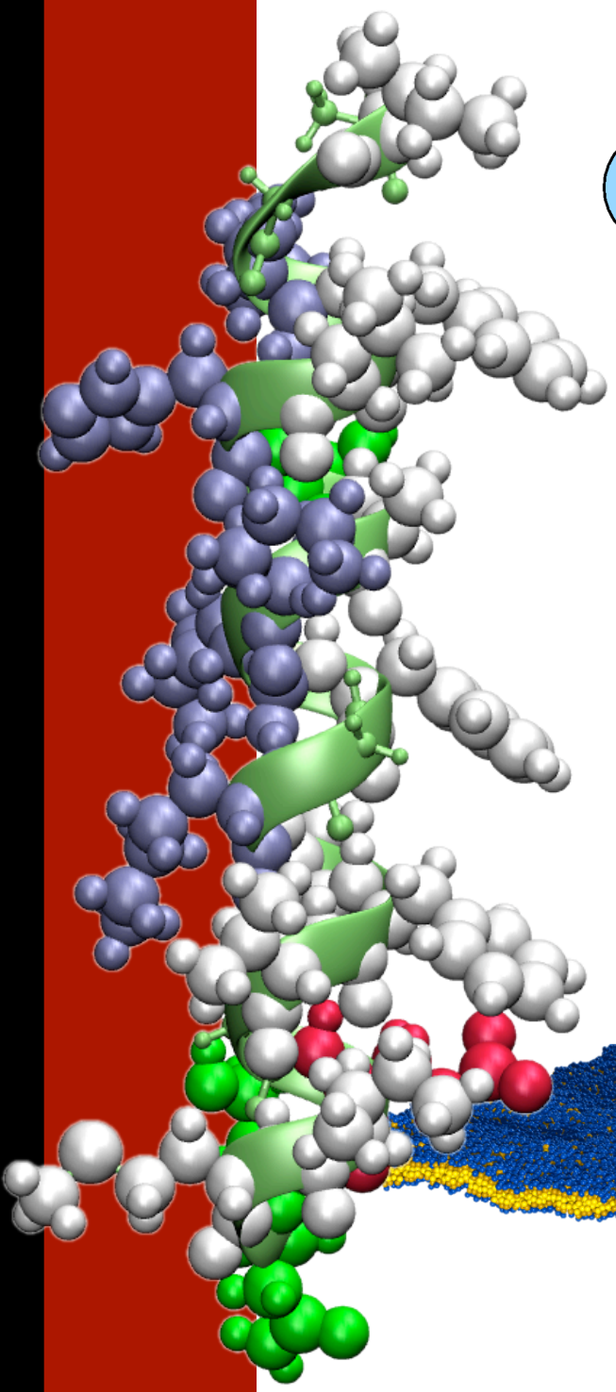


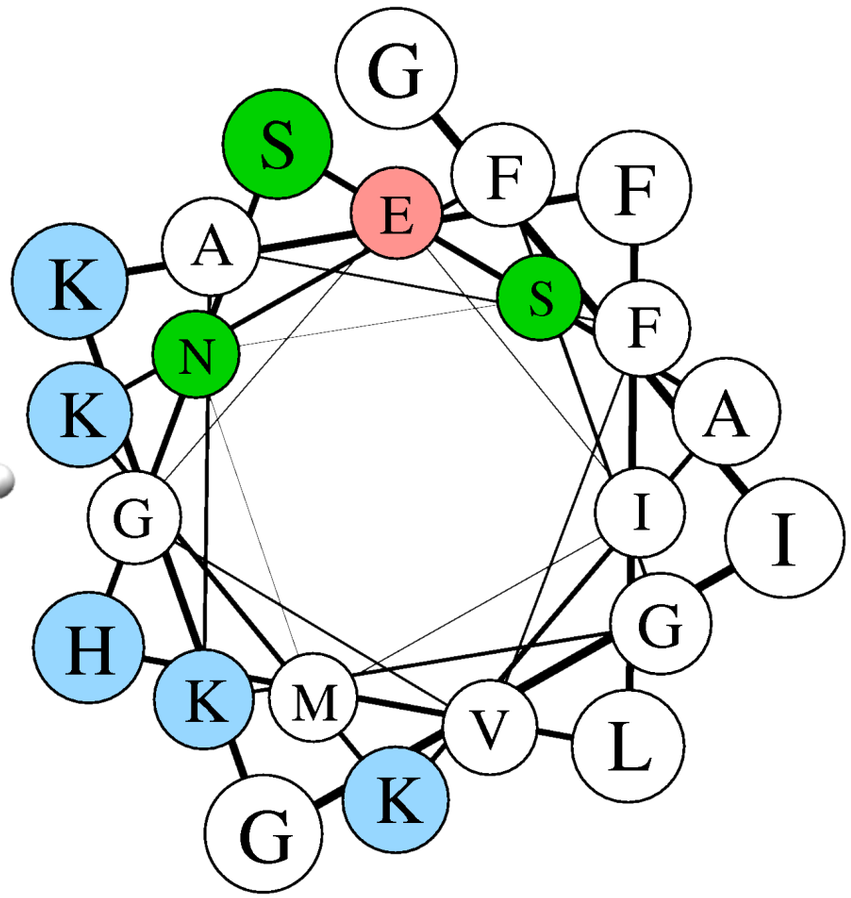
Antimicrobial Peptide "magainin"

G. Illya & M. Deserno, Biophys. J. 95, 4163 (2008)

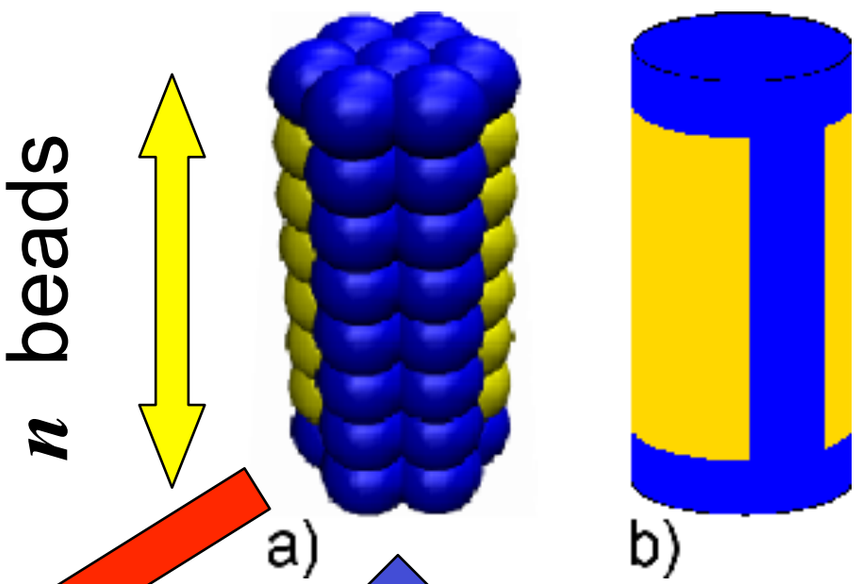
Carnegie Mellon

Peptide-induced pore formation





Peptides:



m beads

P_n^m – peptide

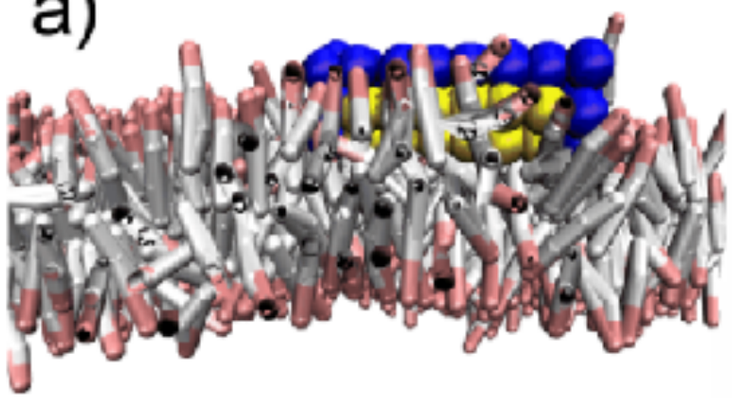
Example above: P_8^2

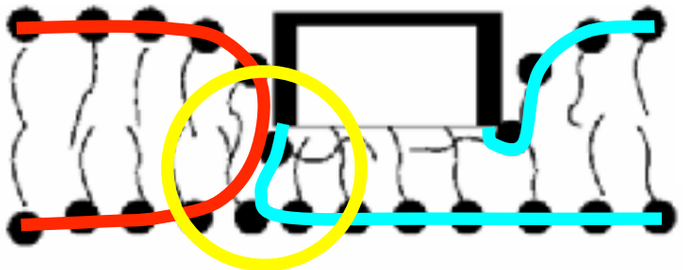
G. Illya & M. Deserno, Biophys. J. 95, 4163 (2008)

Carnegie Mellon

Peptide-induced pore formation

a)

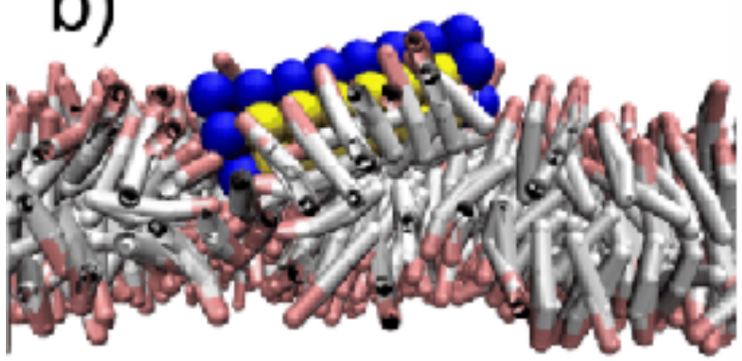




breakthrough

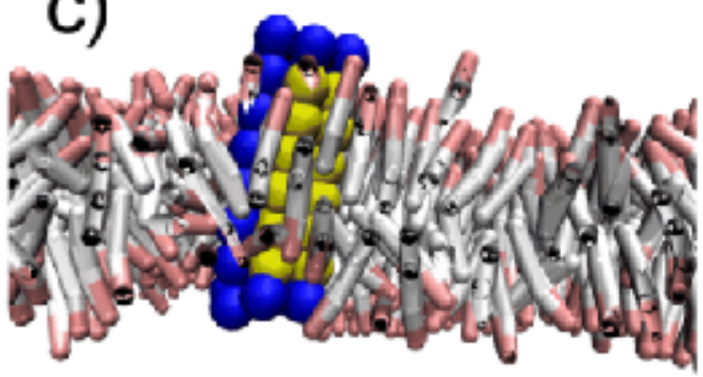
Surface adsorbed

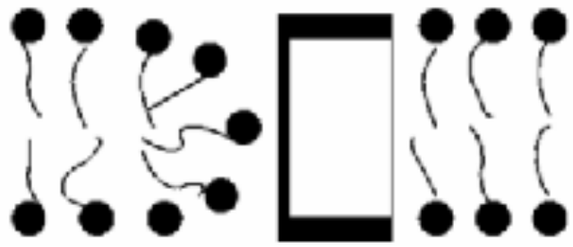
b)



Monolayer contact

c)





Sliding in

G. Illya & M. Deserno, Biophys. J. 95, 4163 (2008)

Carnegie Mellon

Peptide-induced pore formation

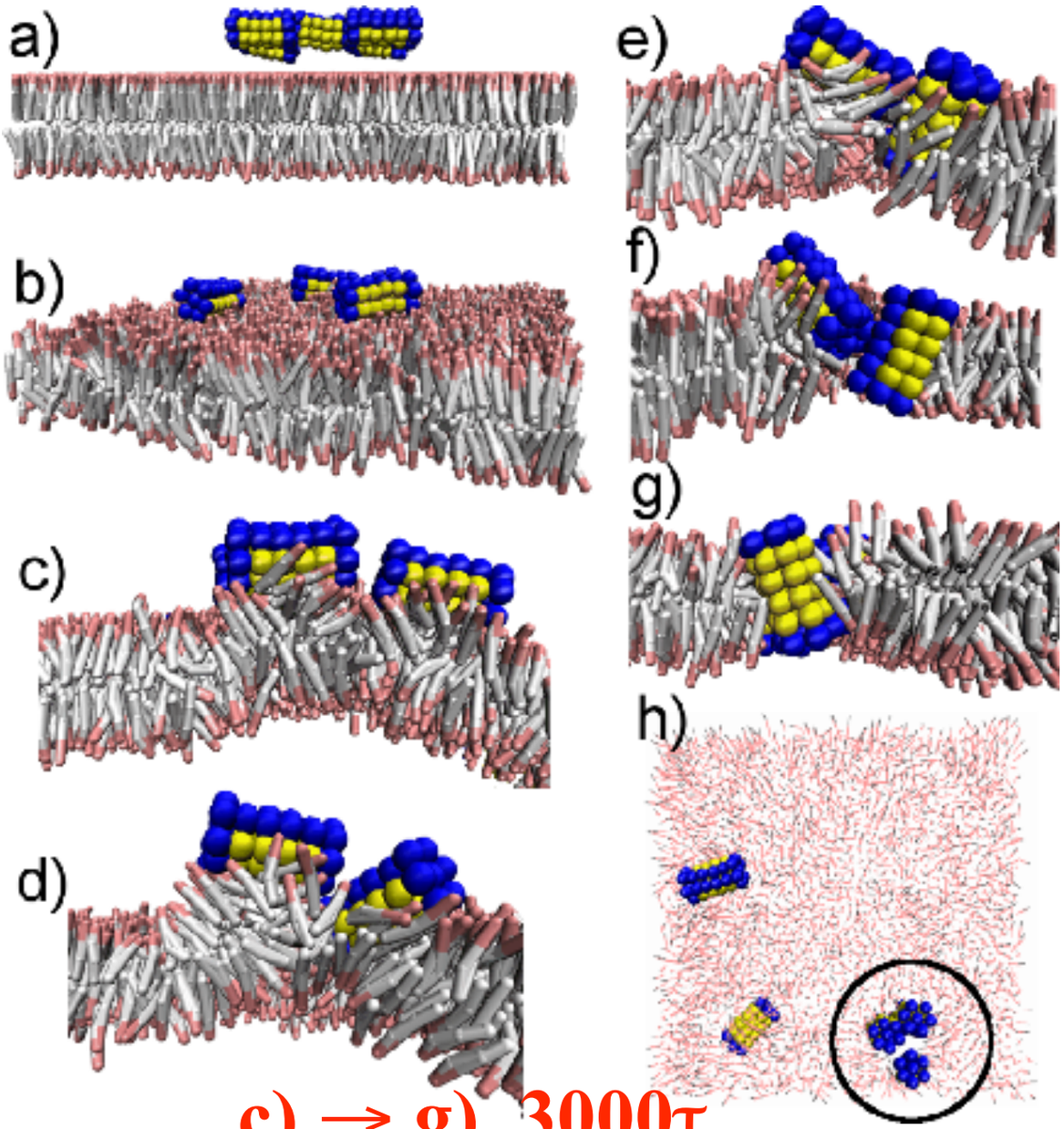
	Binding strength	k_BT=1.7	k_BT=1.9
P_6^2	1.5	stray	stray
	1.6	bound	bound/inserted
	1.7	inserted	inserted
	1.8	inserted	inserted
P_8^2	1.4	stray	
	1.5	bound	
	1.6	inserted	
	1.7	inserted	
	1.8	inserted	

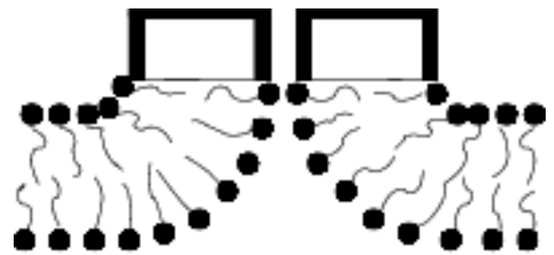
Let us now look at this system consisting of *many* of these peptides

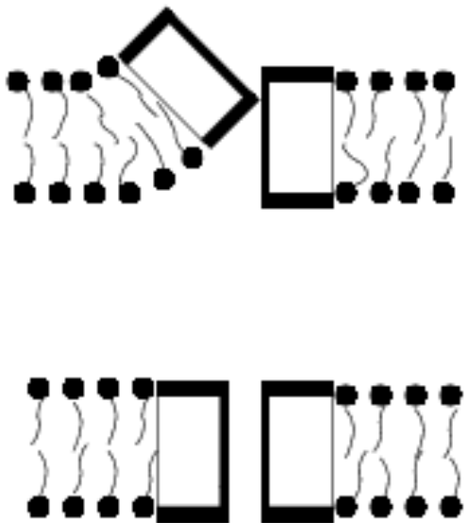
G. Illya & M. Deserno, Biophys. J. 95, 4163 (2008)

Peptide-induced pore formation

…of a peptide which *alone* does *not* insert within 25000τ







- Stronger joint perturbation
- Sliding in very efficient

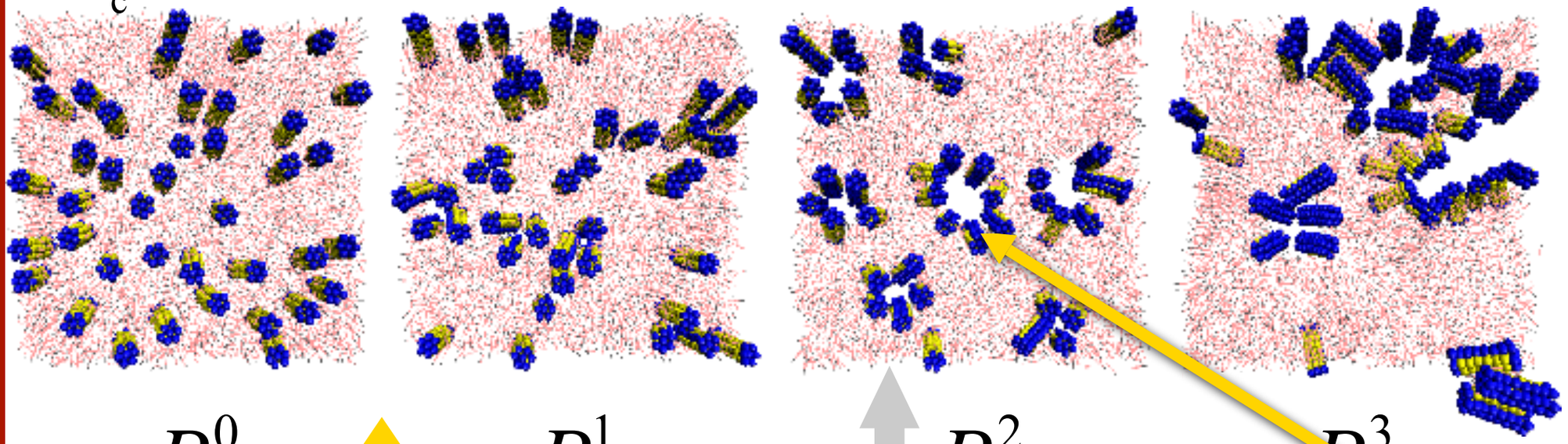
c) → g) 3000τ

G. Illya & M. Deserno, Biophys. J. 95, 4163 (2008)

Carnegie Mellon

Peptide-induced pore formation

$w_c = 1.5$

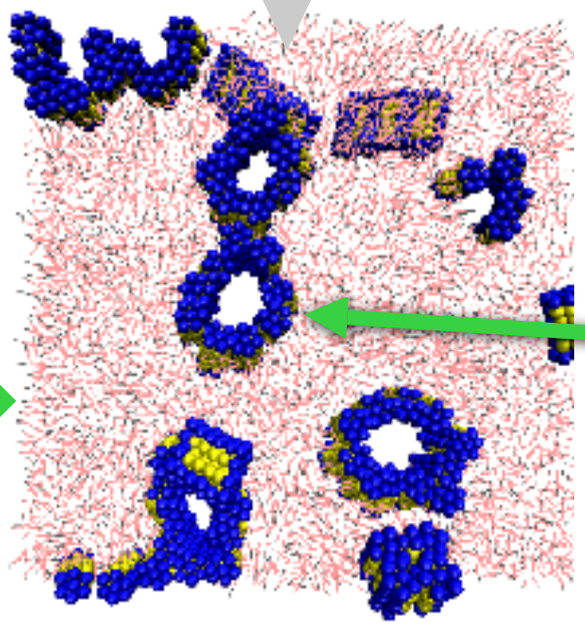


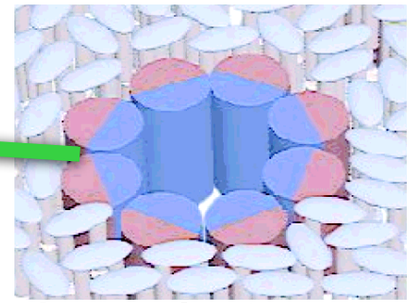
P_8^0 P_8^1 P_8^2 P_8^3

No peptide attraction

toroidal

Some peptide attraction





barrel-stave

P_6^2 $w_c = 1.6$

G. Illya & M. Deserno, Biophys. J. 95, 4163 (2008)

Carnegie Mellon

Lipid curvature effects

The model of Israelachvili, Mitchell and Ninham

J. Chem. Soc., Faraday Trans. **272** *1525* (1976)

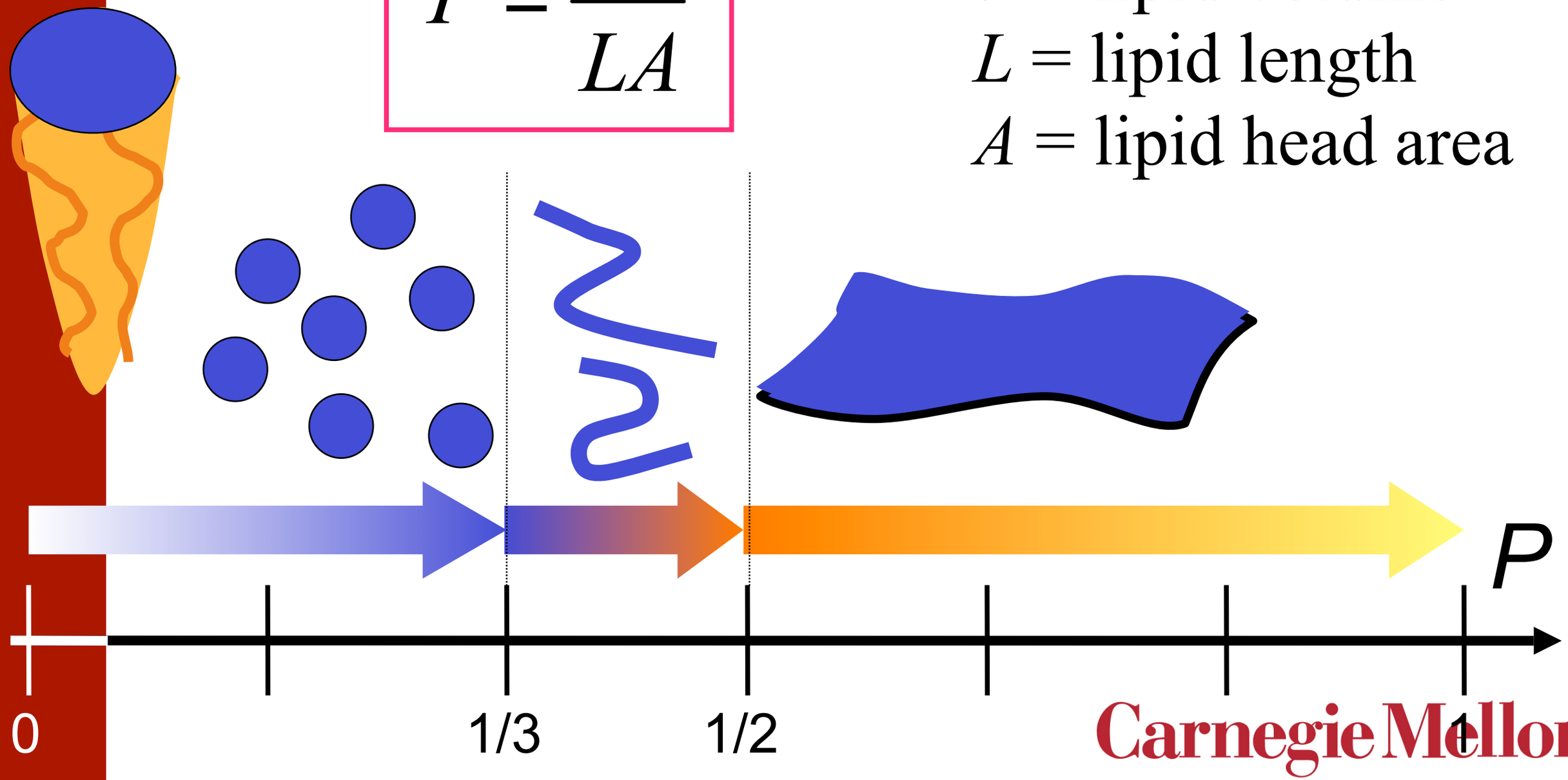
packing parameter

$$P = \frac{V}{LA}$$

V = lipid volume

L = lipid length

A = lipid head area



Carnegie Mellon

Lipid curvature effects

The model of Israelachvili, Mitchell and Ninham

J. Chem. Soc., Faraday Trans. **272** *1525* (1976)

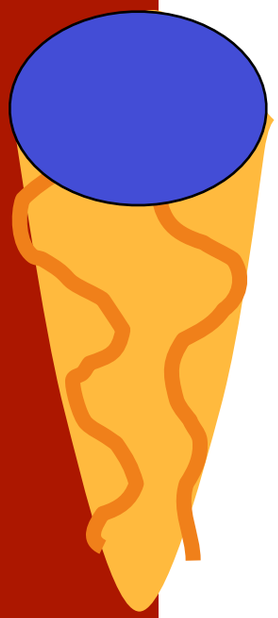
packing parameter

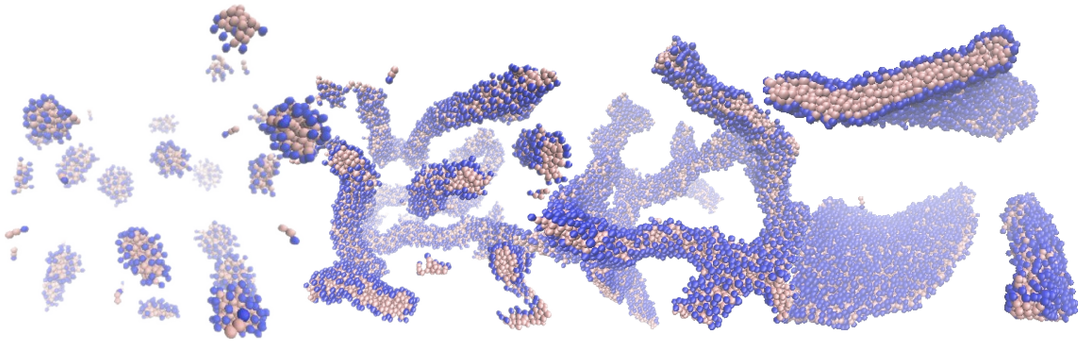
$$P = \frac{V}{LA}$$

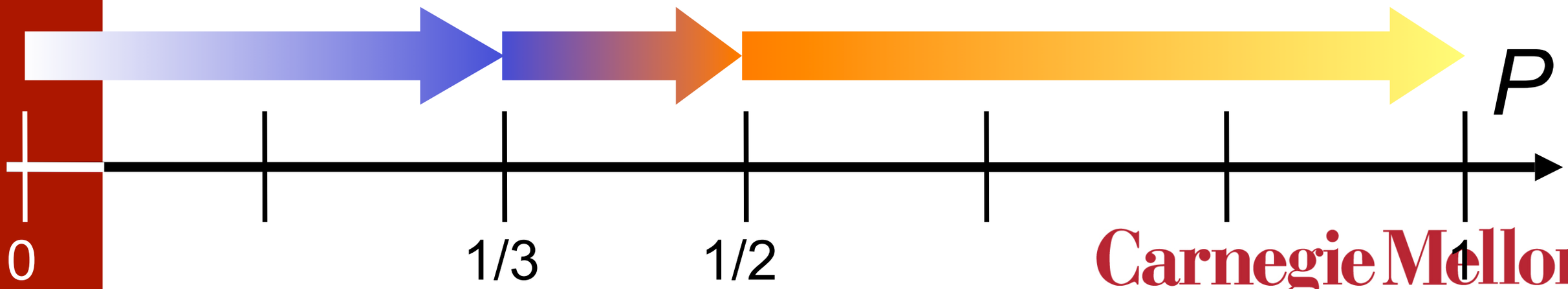
V = lipid volume

L = lipid length

A = lipid head area

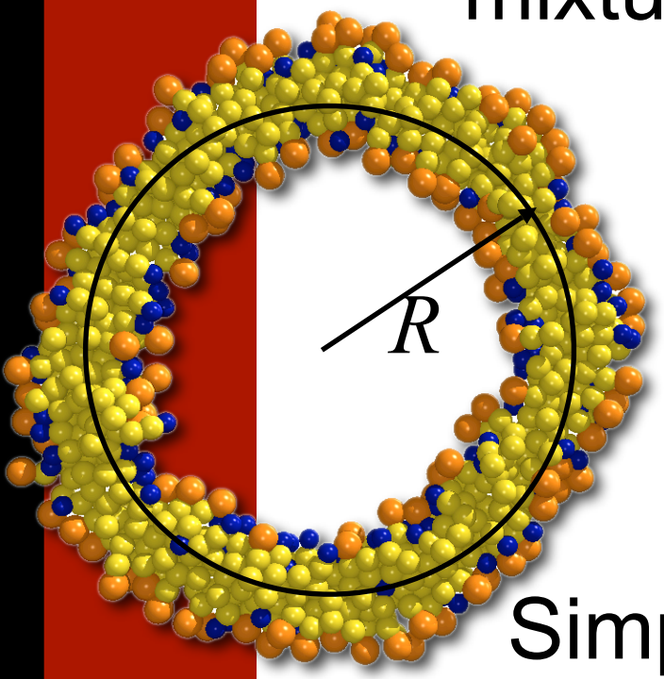


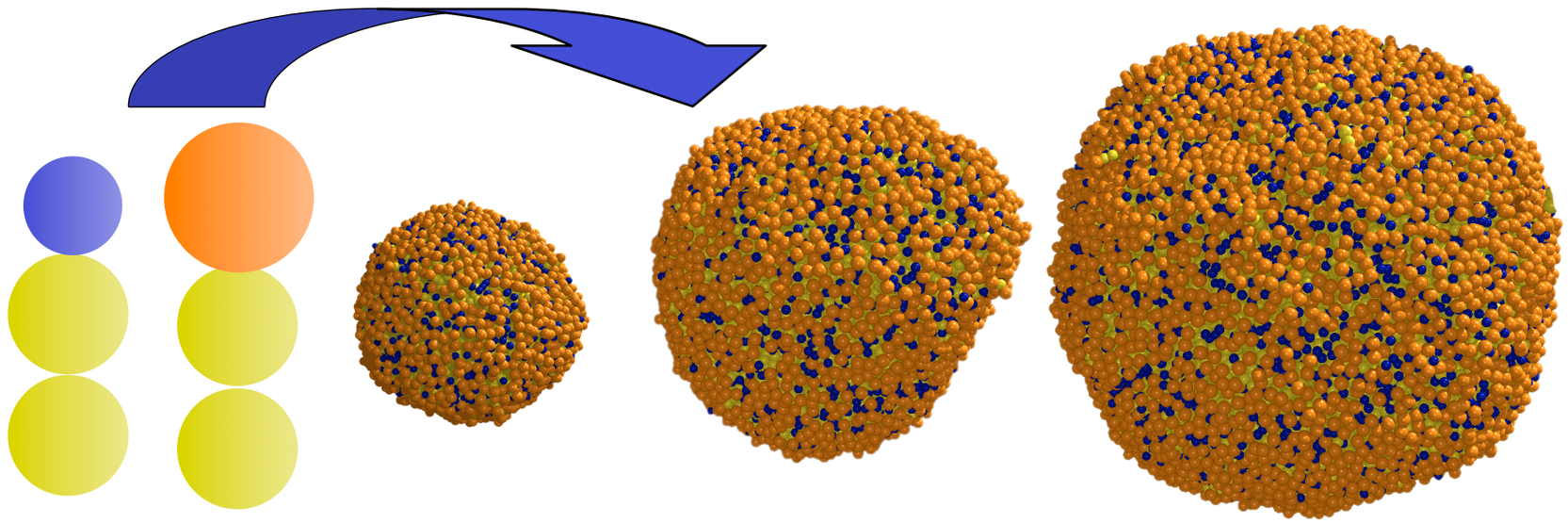




Lipid curvature effects

50:50 mixture





Density of big headed lipids in the **outer** monolayer

Simple model gives:

$$\ln \frac{\phi_{\text{out}}}{\phi_{\text{in}}} = \frac{2\mathcal{M}K_\ell}{k_{\text{B}}T} K$$

Linear in bilayer curvature!

Density of big headed lipids in the **inner** monolayer

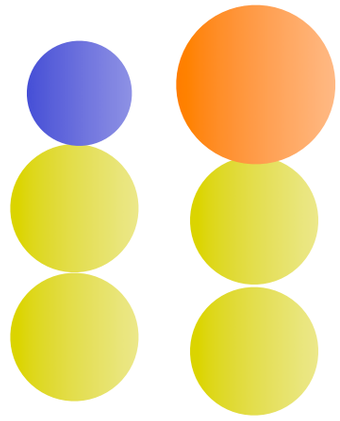
$$E = \frac{1}{2}\mathcal{M}\left(K - K_\ell\right)^2$$

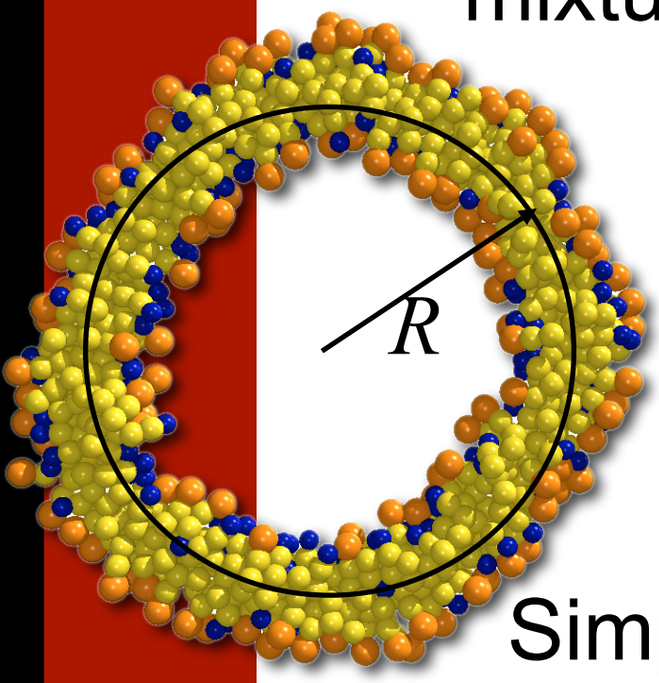
$S = \text{ideal gas}$

I.R. Cooke and M. Deserno, Biophys. J. **91**, *487* (2006)

Lipid curvature effects

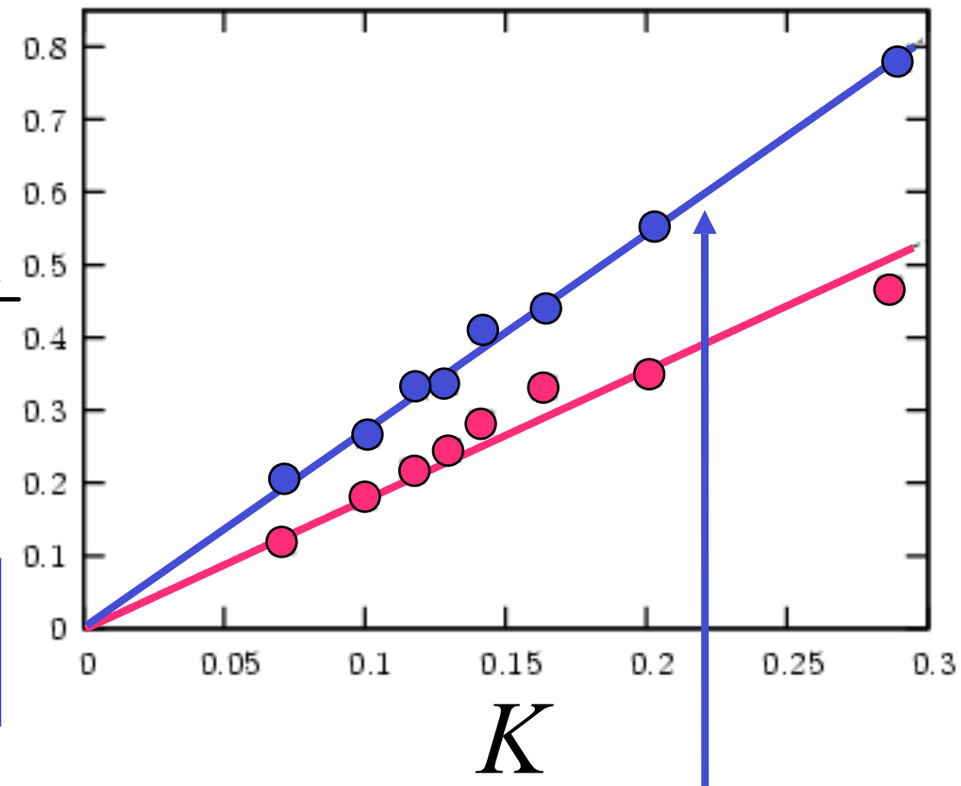
50:50 mixture





Density of big headed lipids in the **outer** monolayer

$$\ln \frac{\phi_{out}}{\phi_{in}}$$



Simple model gives:

$$\ln \frac{\phi_{\text{out}}}{\phi_{\text{in}}} = \frac{2\mathcal{M}K_\ell}{k_{\text{B}}T} K$$

Linear in bilayer curvature!

Density of big headed lipids in the **inner** monolayer

$$E = \frac{1}{2}\mathcal{M}\left(K - K_\ell\right)^2$$

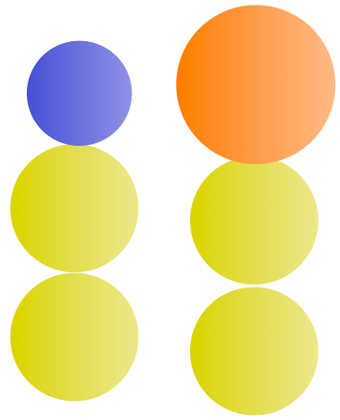
$S = \text{ideal gas}$

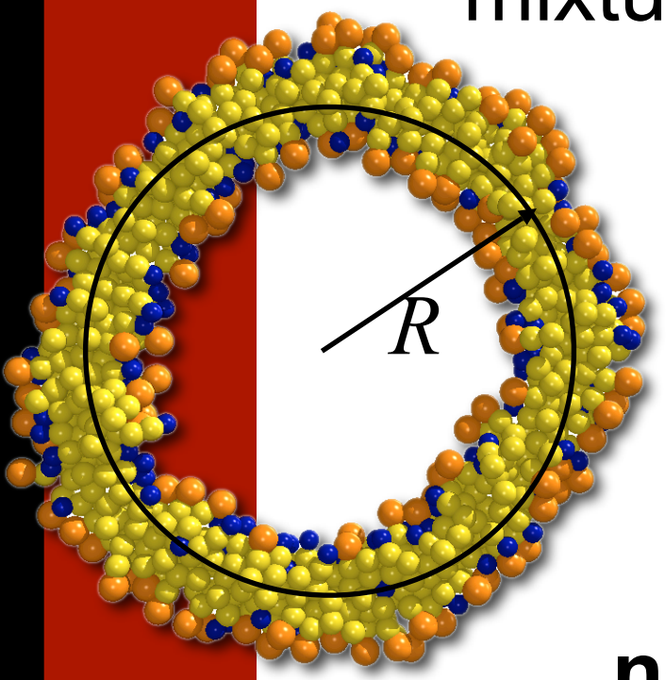
I.R. Cooke and M. Deserno, Biophys. J. **91**, *487* (2006)

Carnegie Mellon

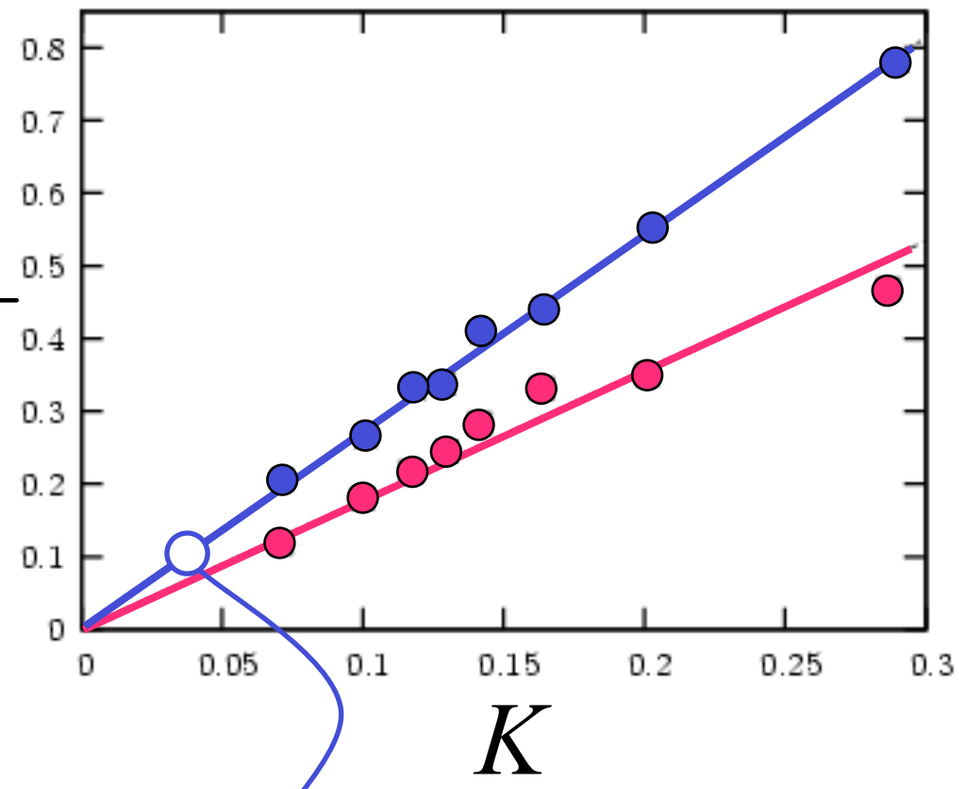
Lipid curvature effects

50:50
mixture



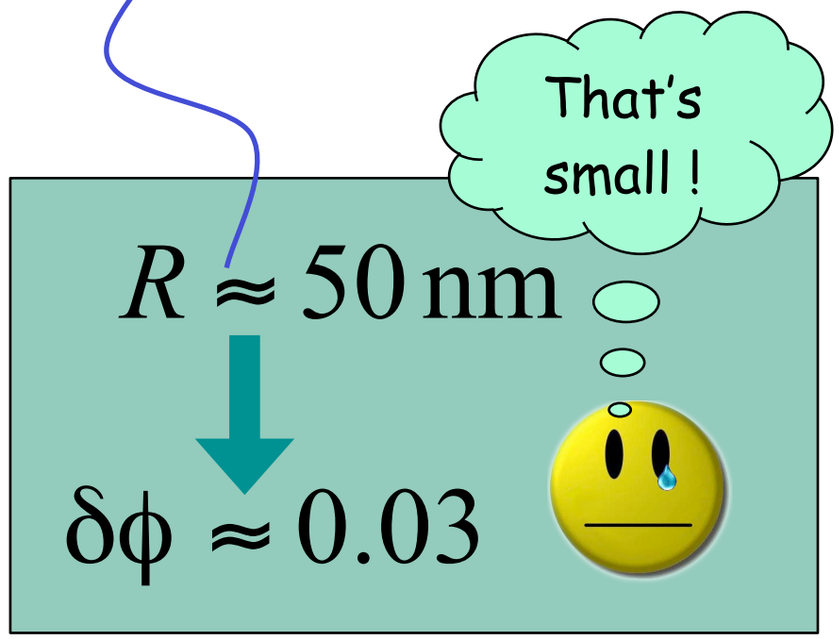


$$\ln \frac{\phi_{out}}{\phi_{in}}$$



…for realistic membrane curvatures the effect is **not** enough to drive sorting!

Tian & Baumgart,
Biophys. J. **96**, *2676* (2009)



I.R. Cooke and M. Deserno, Biophys. J. **91**, *487* (2006)

Carnegie Mellon