Symmetry of membrane polyhedra

Christoph A. Haselwandter and Rob Phillips
California Institute of Technology

Outline

1. From biological membranes to bilayer vesicles.

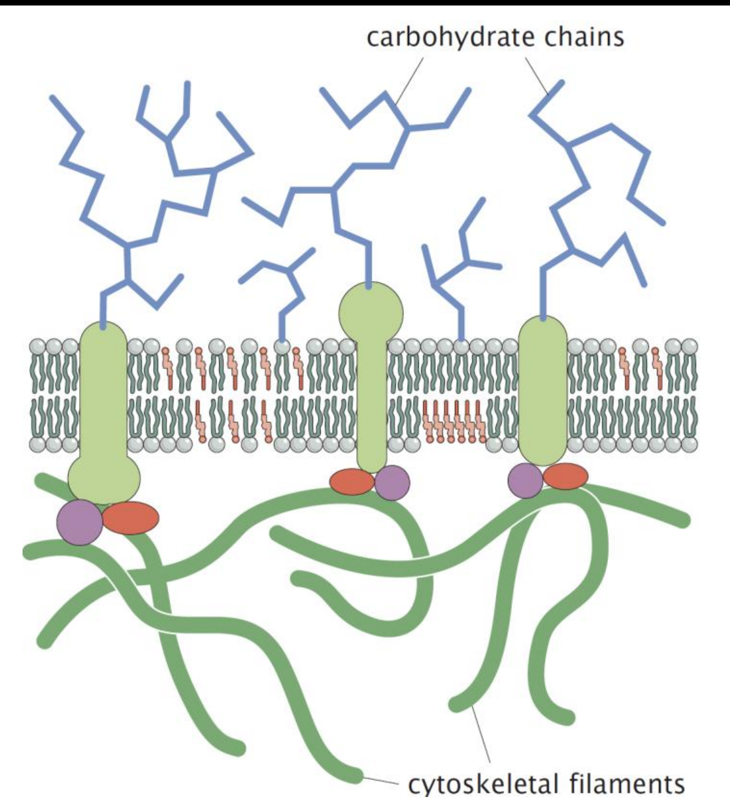
2. Experimental phenomenology of bilayer polyhedra.

3. Contributions to the elastic energy of bilayer polyhedra.

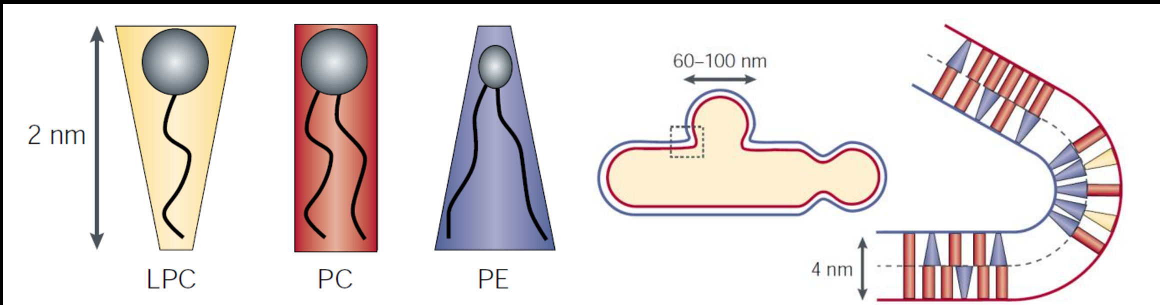
4. Polyhedral symmetries with minimal bilayer bending energy.

Phenomenology of biological membranes

…separate "animate matter" from "inanimate matter."

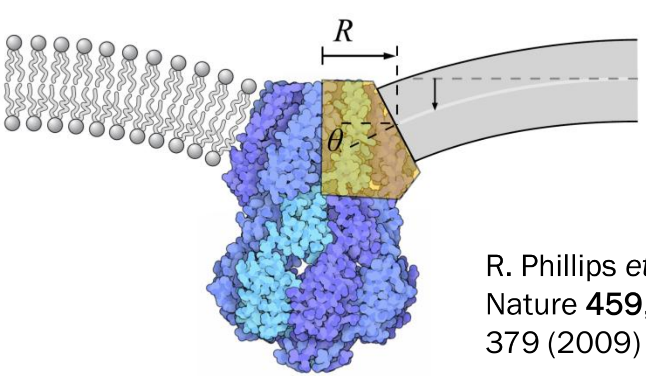


1. Lipids: Self-assemble into bilayers; >1000 different types of lipids in cell membranes

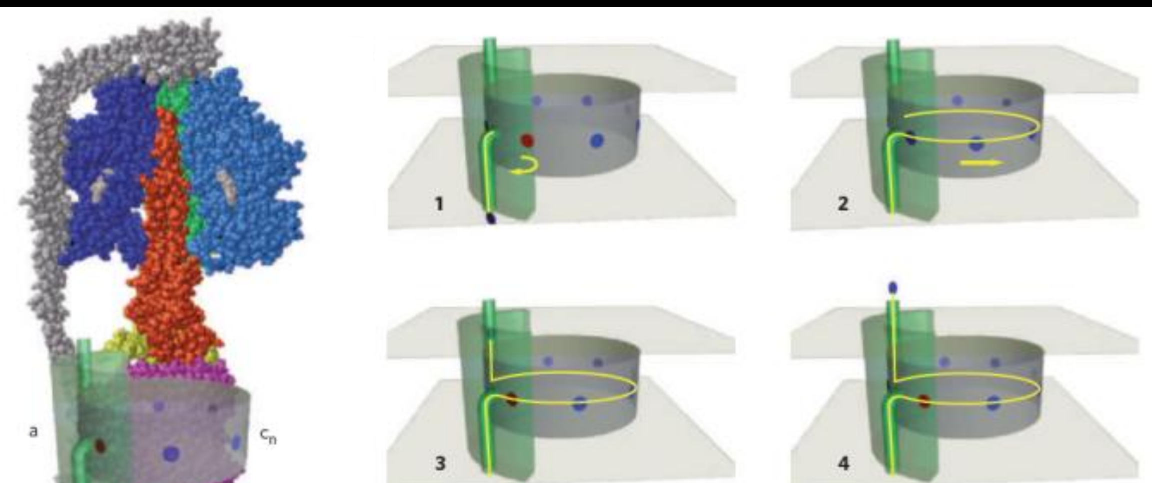


H. Sprong *et al.*, Nat. Rev. Mol. Cell Bio. **2,** 504 (2001)

2. Proteins: ~30% of all human genes code for membrane proteins; crowd membrane.

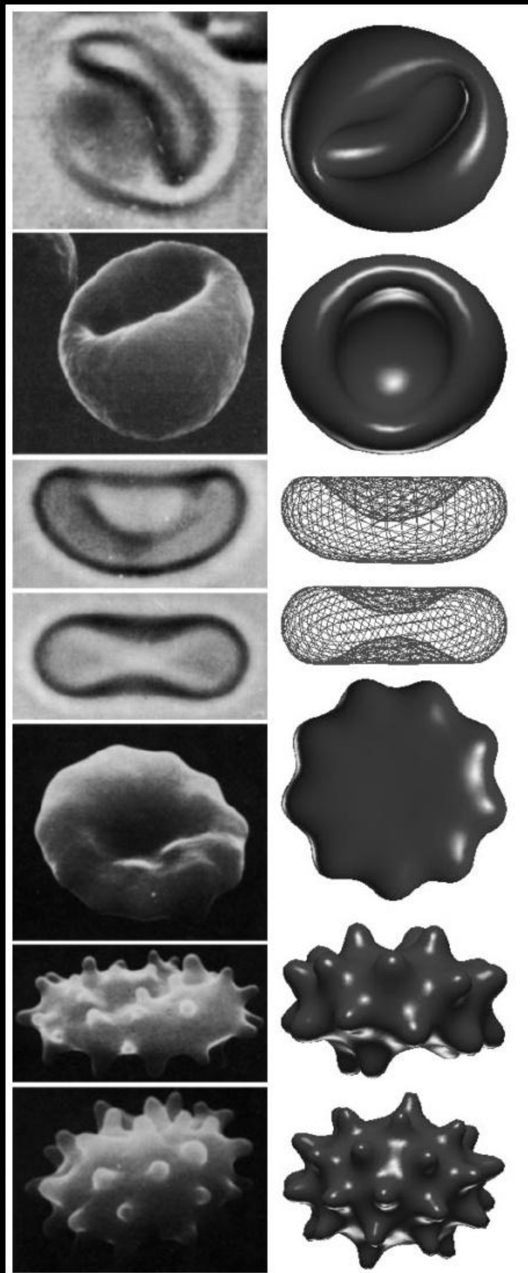


R. Phillips *et al.*, Nature **459**, 379 (2009)



W. Junge *et al.*, Nature **459**, 364 (2009)

Cell membranes have controlled shapes



Stomatocytes

Discocyte

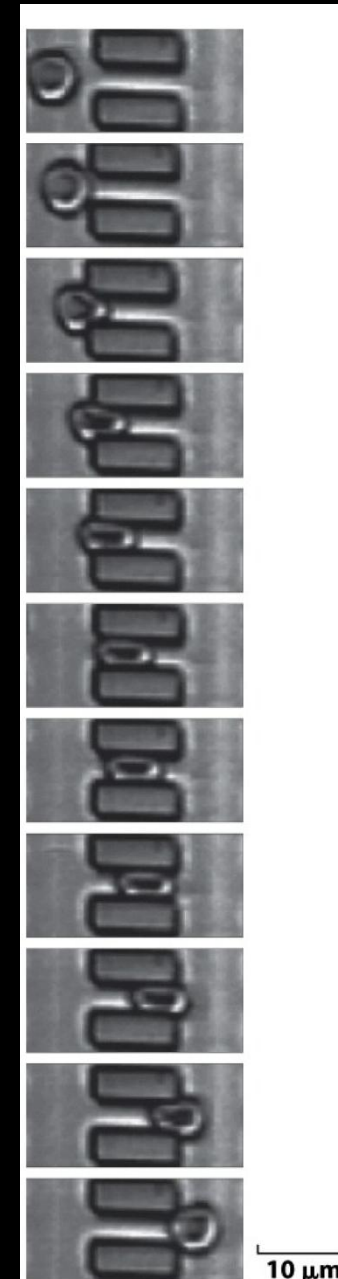
Echinocytes

High pH, cholesterol enrichment, high salt,...

Physiological conditions

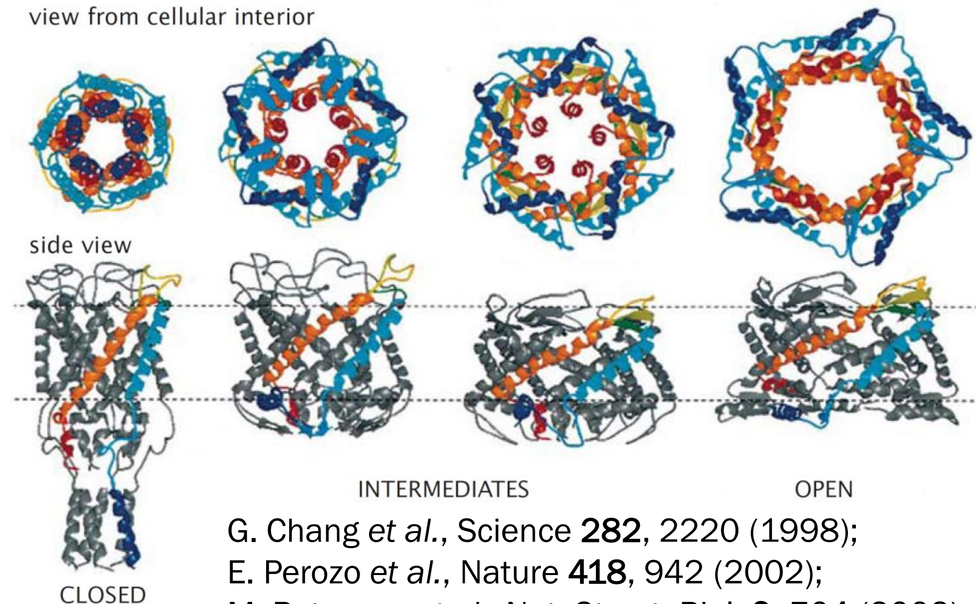
Low pH, cholesterol depletion, low salt,...

G. Lim H. W. *et al.*, PNAS **99**, 16766 (2002)

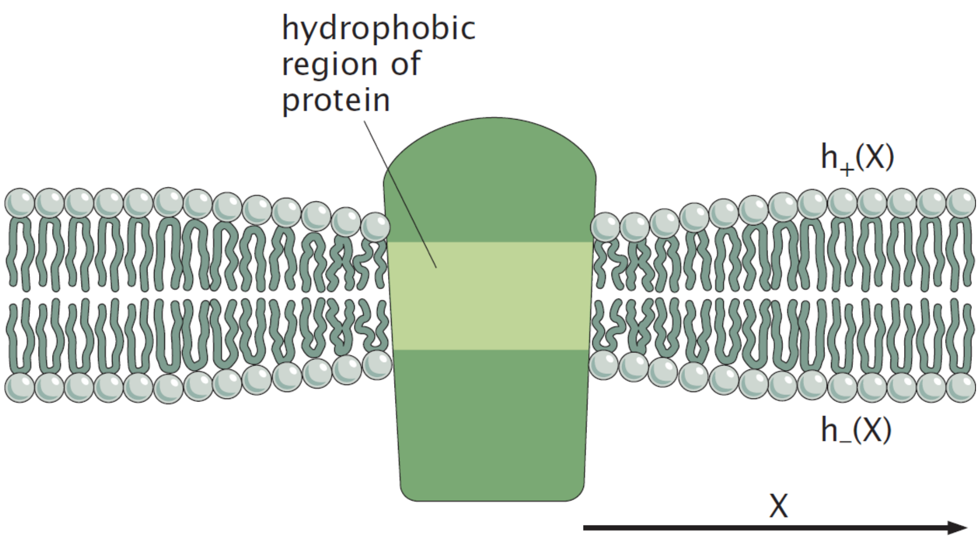


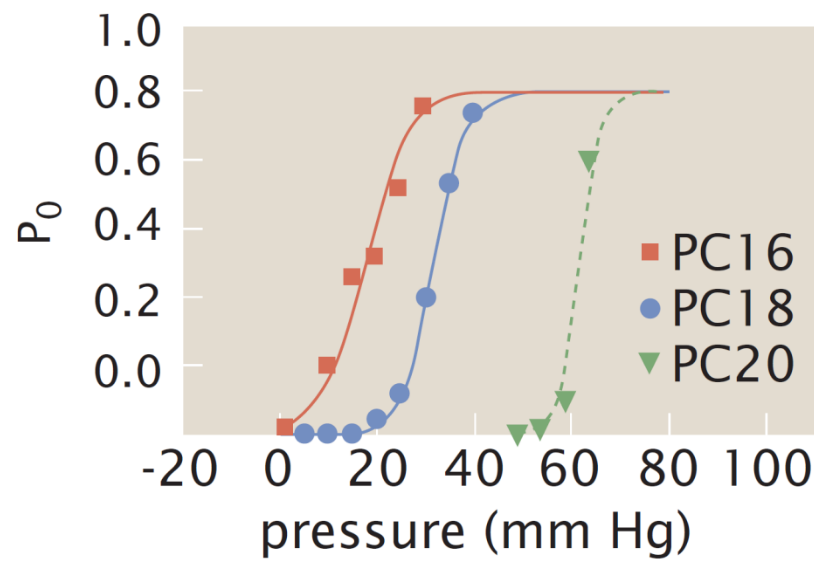
Membranes control exchange of chemical substances

Mechanosensitive channel of large conductance (MscL)



G. Chang *et al.*, Science **282**, 2220 (1998);
E. Perozo *et al.*, Nature **418**, 942 (2002);
M. Betanzos *et al.*, Nat. Struct. Biol. **9**, 704 (2002).

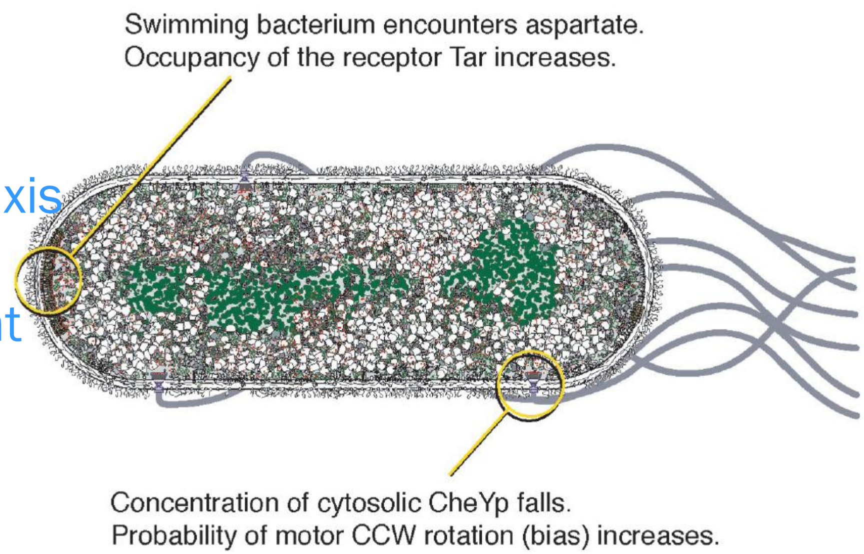


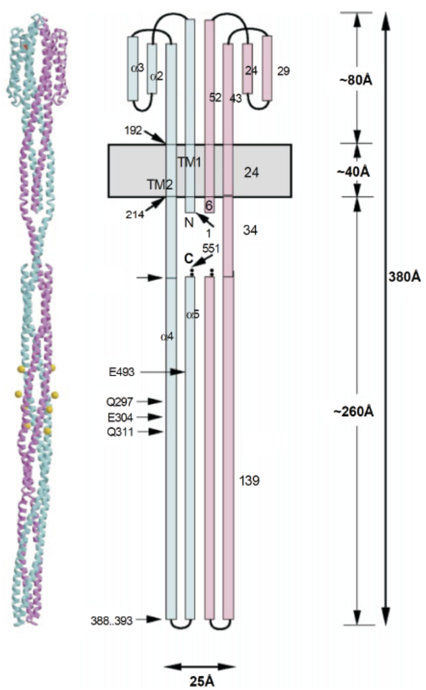


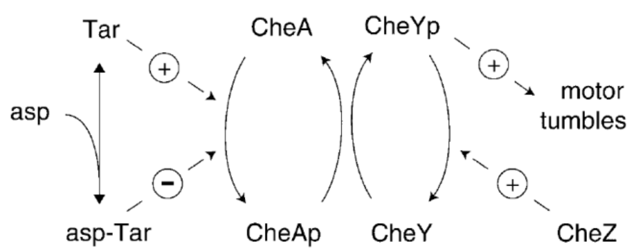
E. Perozo *et al.*, Nat. Struct. Biol. **9**, 696 (2002).

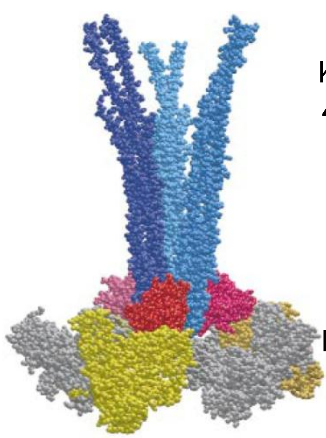
Membranes control exchange of information

Chemotaxis towards attractant



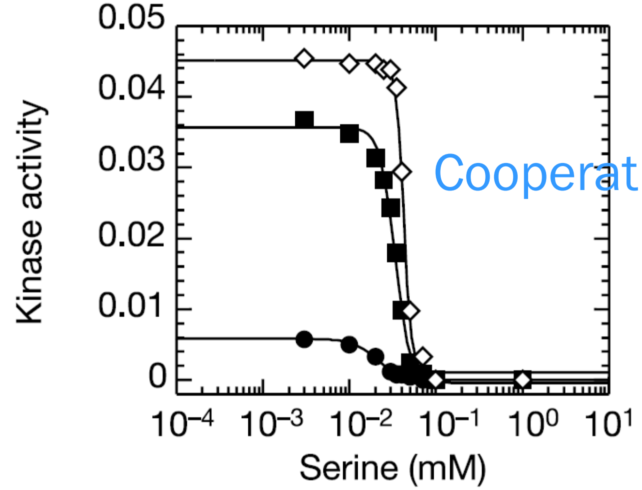


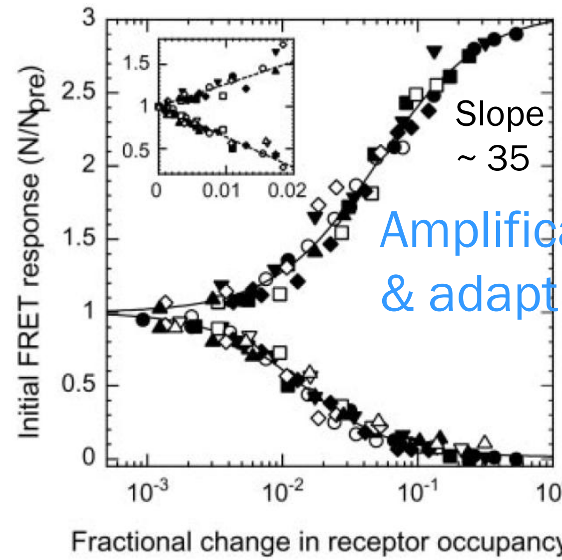




K. K. Kim *et al.*, Nature **400**, 787 (1999); T. S. Shimizu *et al.*, Nat. Cell Biol. **2**, 792 (2000); D. Bray, PNAS **99**, 7 (2002); V. Sourjik & H. Berg, PNAS **99**, 123 (2002); Nature **428**, 437 (2004).

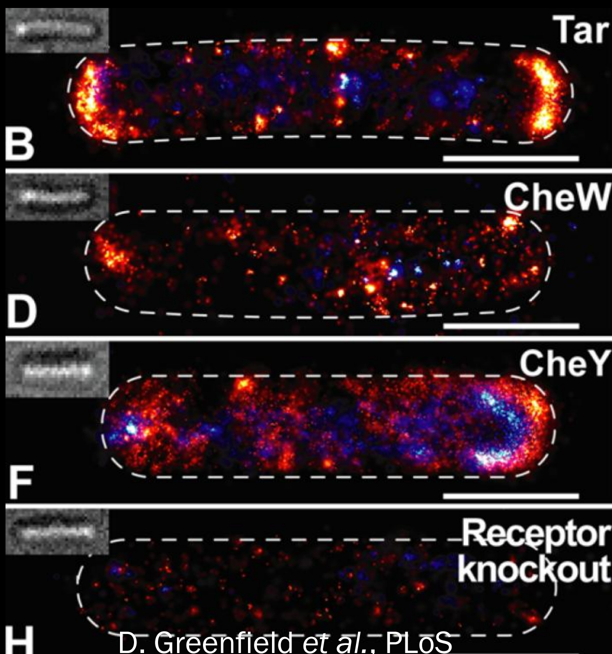
Sensitivity (5 orders of magnitude in ambient concentration, concentration changes of ~3 molecule in volume of cell)



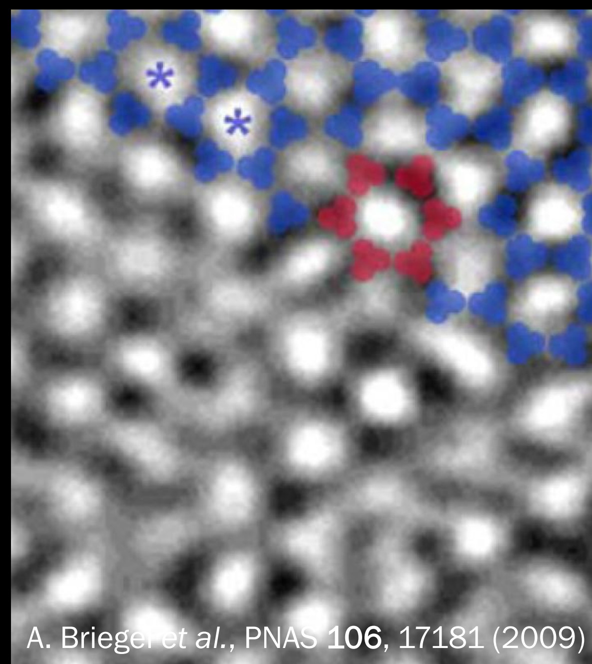


Membranes are highly organized

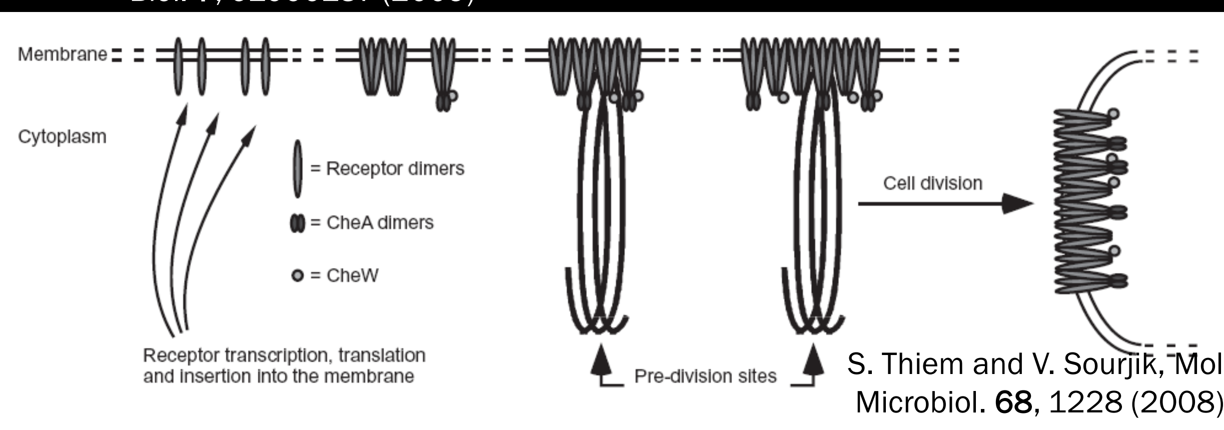
Spatial organization of trimers of chemo-receptor trimers into hexagonal lattices



D. Greenfield *et al.*, PLoS Biol. **7**, e1000137 (2009)

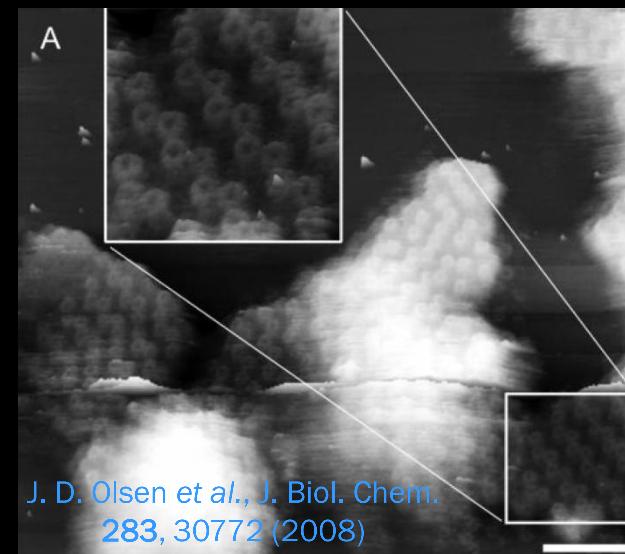


A. Briegel *et al.*, PNAS **106**, 17181 (2009)

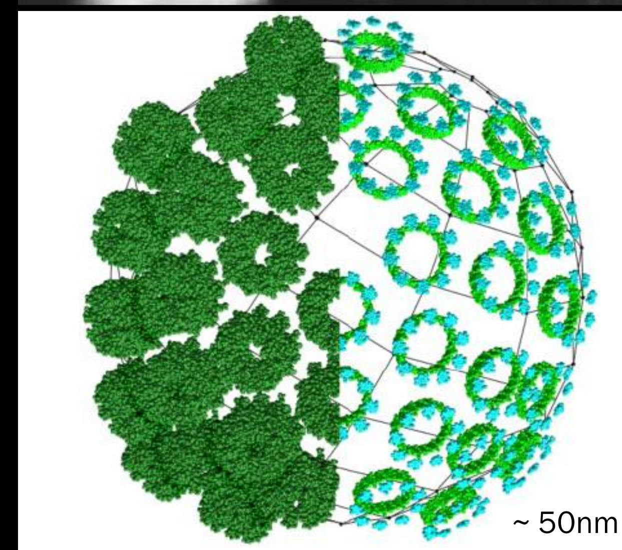


S. Thiem and V. Sourjik, Mol. Microbiol. **68**, 1228 (2008)

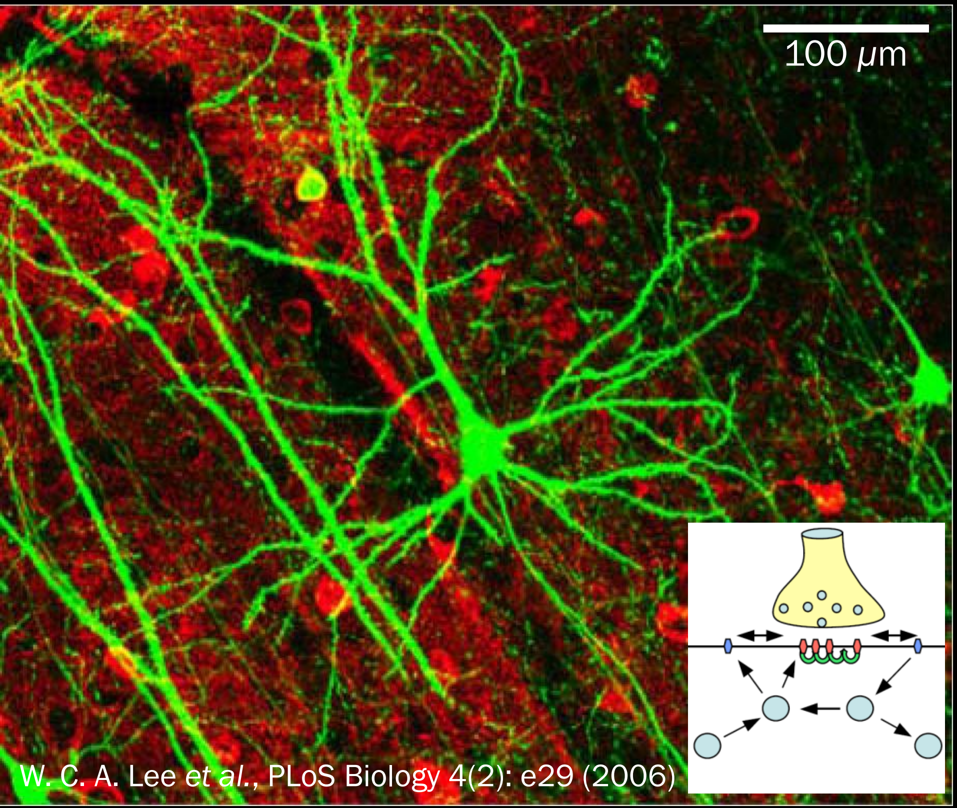
Spatial organization of LH2 complex



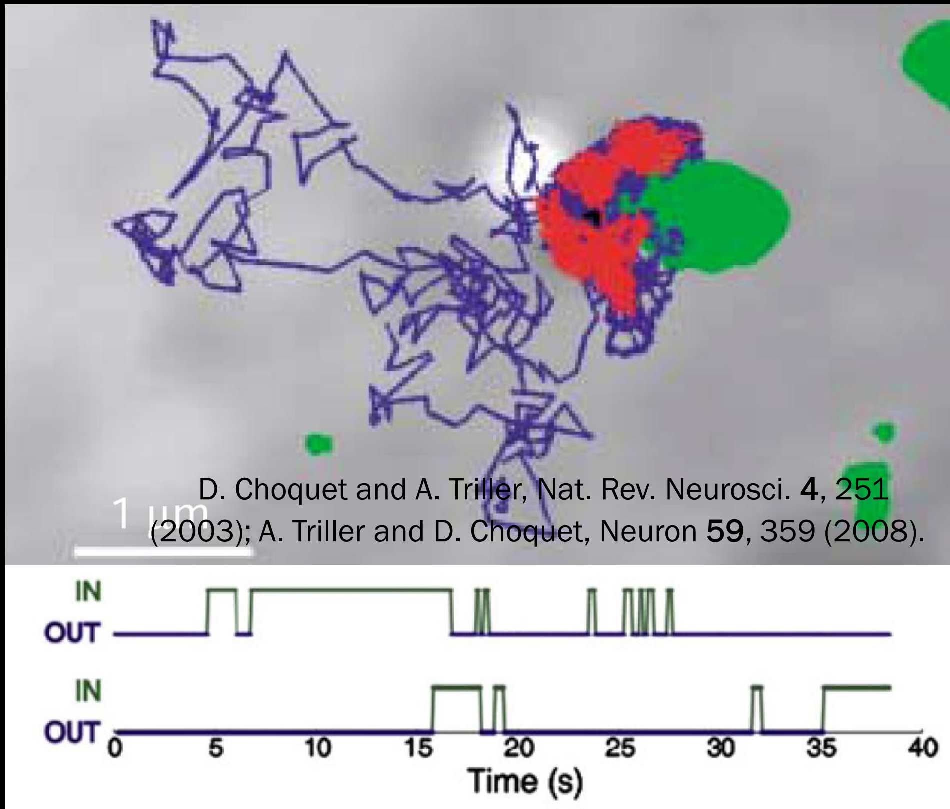
J. D. Olsen *et al.*, J. Biol. Chem. **283**, 30772 (2008)



Membranes are highly dynamic

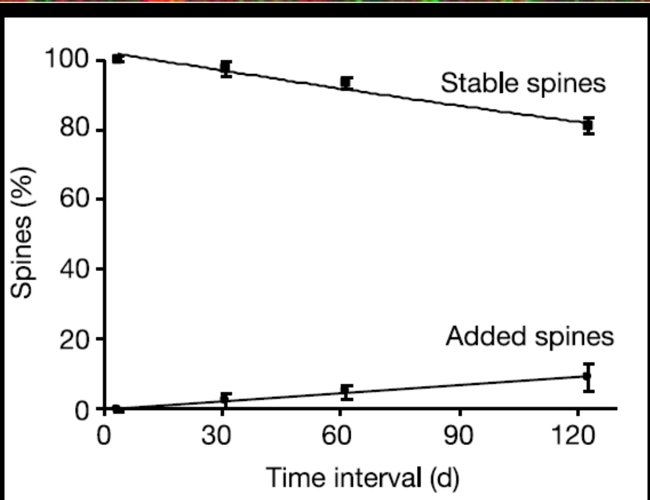


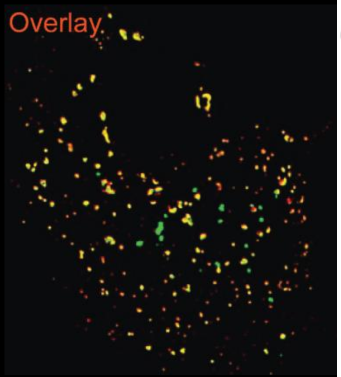
W. C. A. Lee *et al.*, PLoS Biology 4(2): e29 (2006)



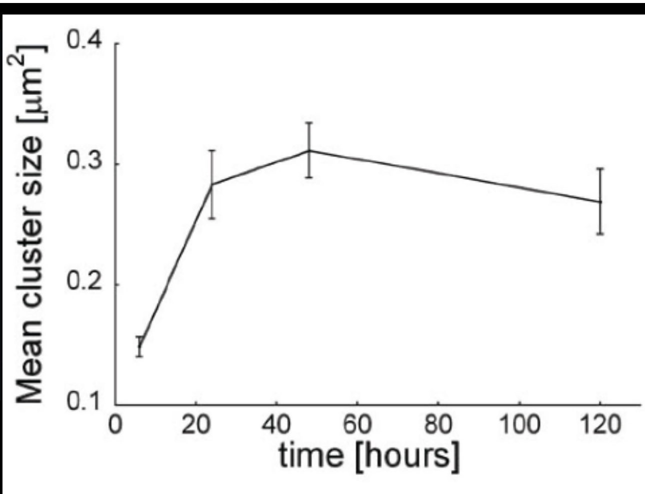
D. Choquet and A. Triller, Nat. Rev. Neurosci. **4**, 251 (2003); A. Triller and D. Choquet, Neuron **59**, 359 (2008).

J. Grutzendler, Nature **420**, 812 (2002)





C. A. H. *et al.* (unpublished)



- Membrane composition is very heterogeneous.

- Membrane shape is tightly controlled.

- Membranes control the flow of chemical substances.

- Membranes control the flow of information.

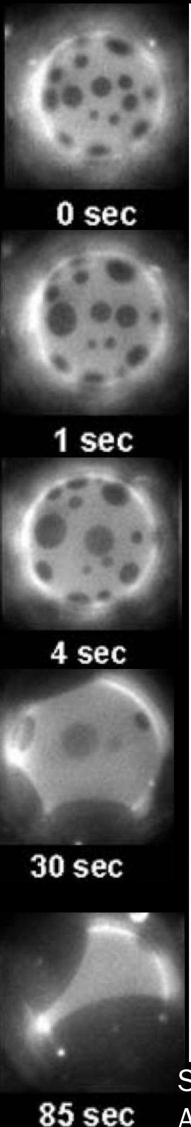
- Membranes are highly organized.

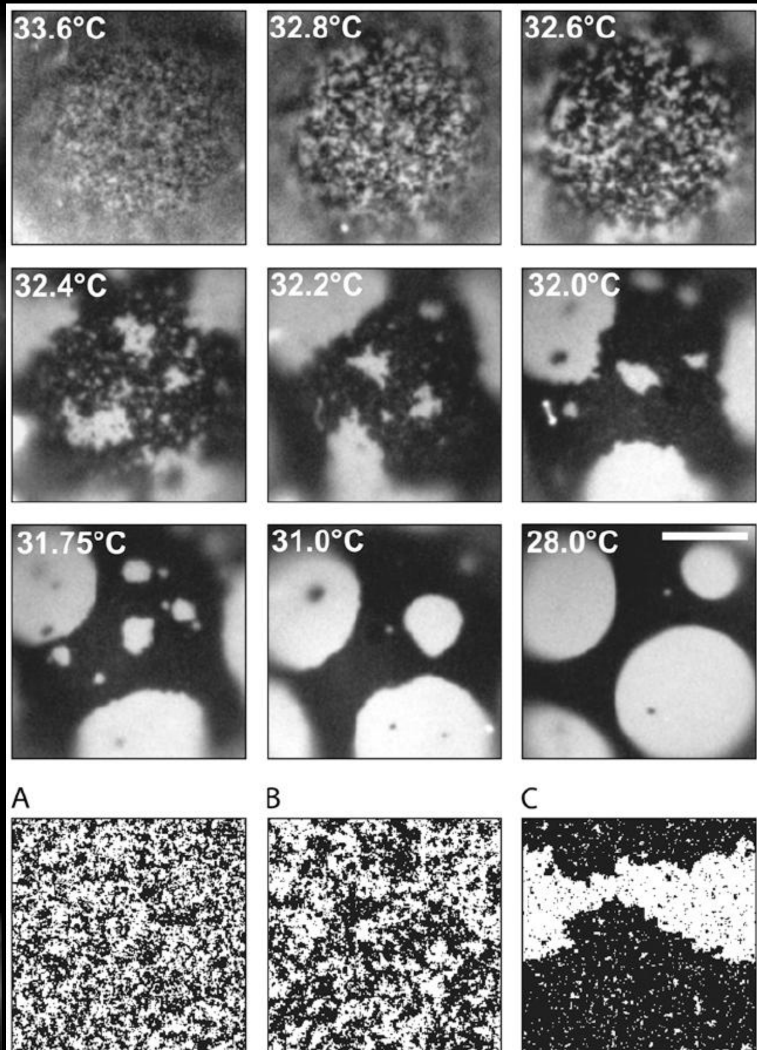
- Membranes are highly dynamic.

How can we quantitatively understand such complex nonequilibrium systems?

Bilayer vesicles are model systems for cell membranes

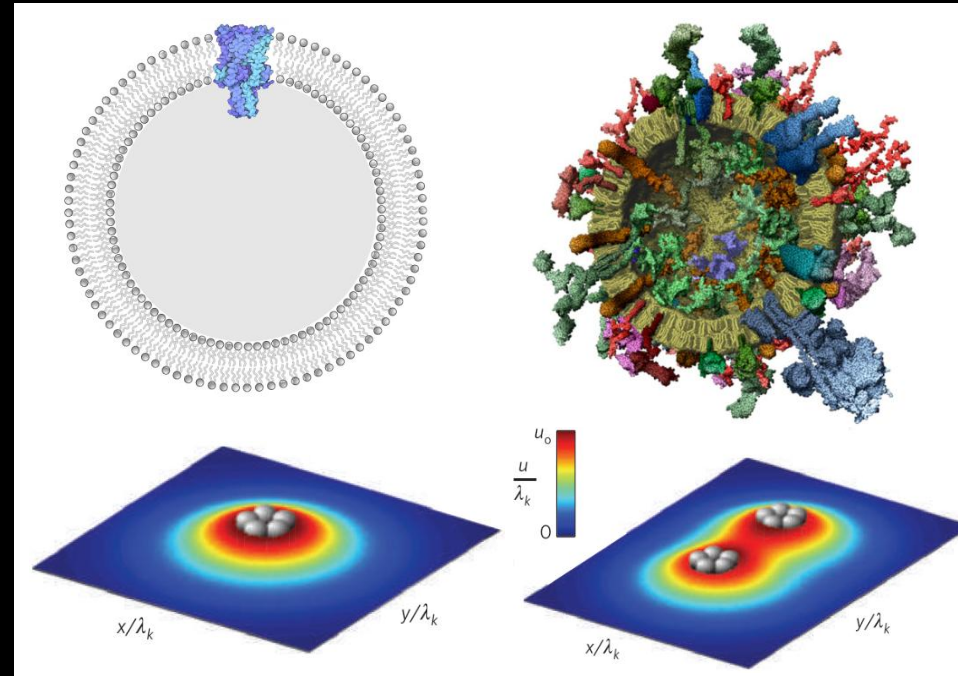
Lipid phase separation, critical fluctuations (rafts?)

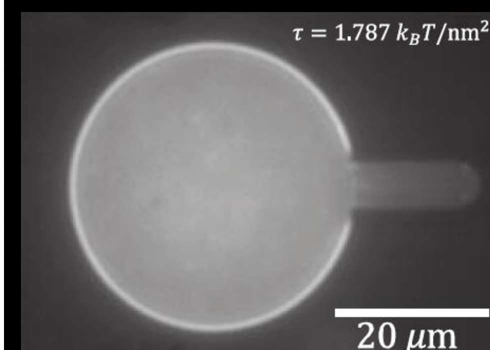


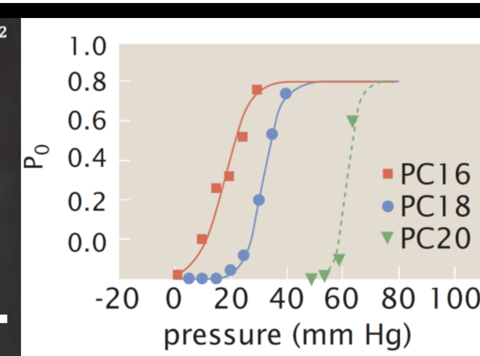


S. L. Veatch and S. L. Keller, Biophys. J. **85**, 3074 (2003)
A. R. Honerkamp-Smith et al., Biophys. J. **95**, 236 (2008)

Functional & physical properties of membrane proteins



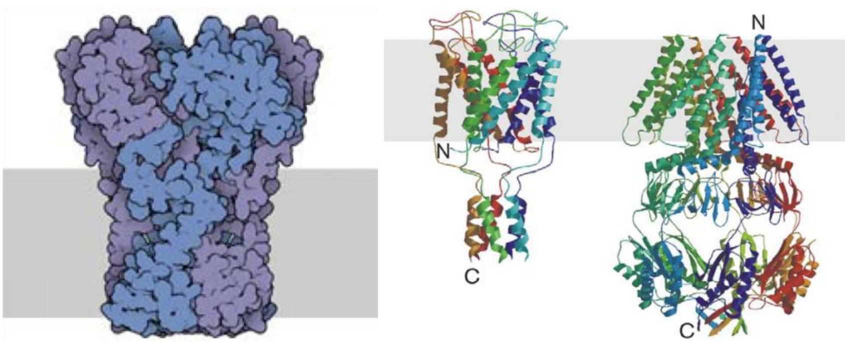




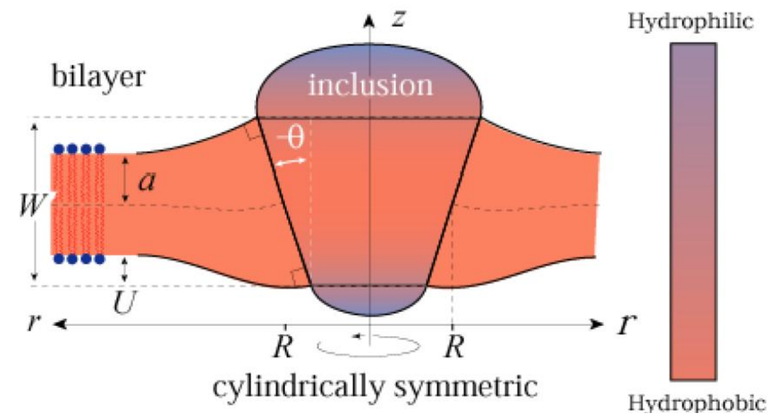
E. Perozo *et al.*, Nat. Struct. Biol. **9**, 696 (2002)
R. Phillips *et al.*, Nature **459**, 379 (2009)

Mechanistic understanding of cell membranes

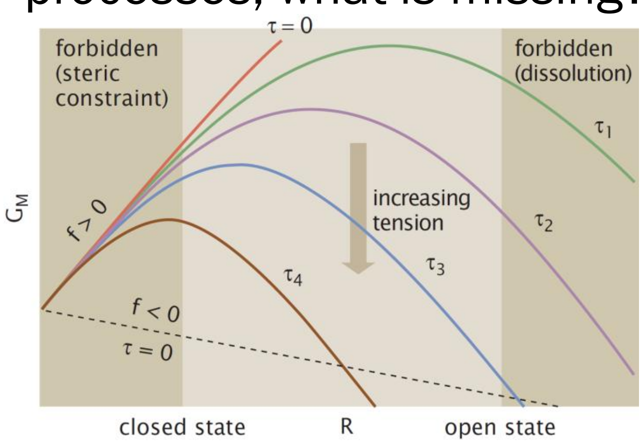
Protein/lipid structure & lipid-protein interactions (e.g., experiments or quantum mechanics)



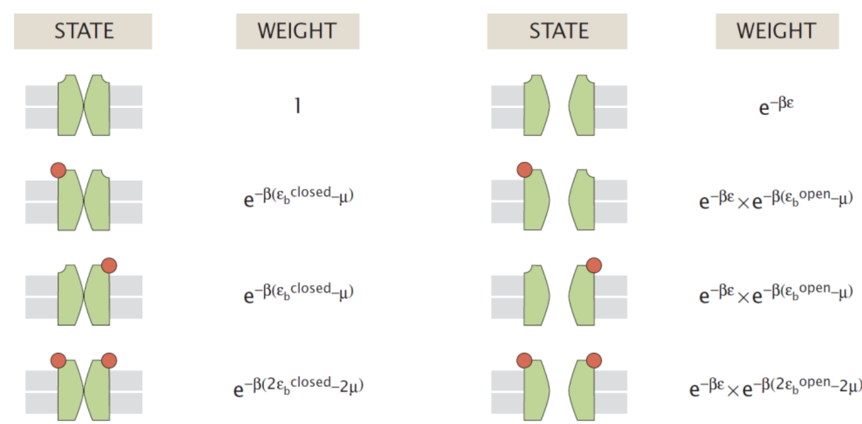
Coarse-grained description with few parameters (e.g., elasticity theory)



Physical mechanisms for biological processes, what is missing?



Ensemble of interacting membrane proteins (statistical mechanics)



Outline

1. From biological membranes to bilayer vesicles.

2. Experimental phenomenology of bilayer polyhedra.

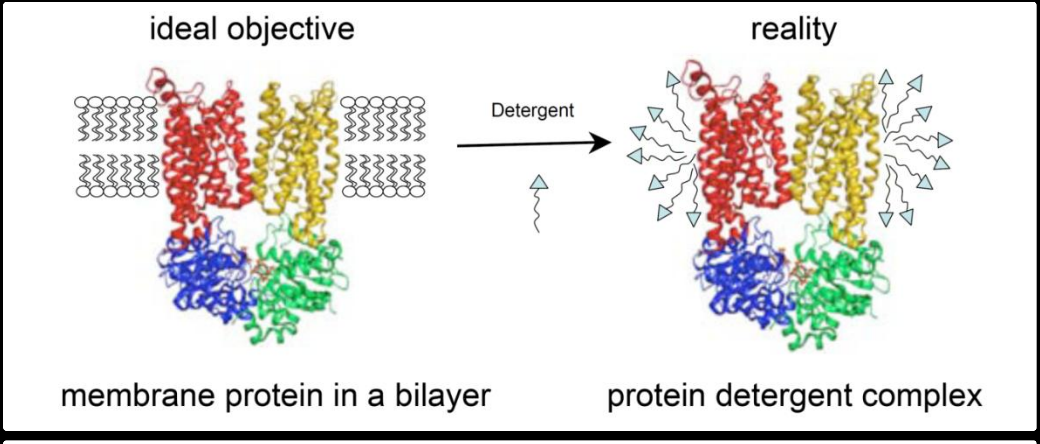
3. Contributions to the elastic energy of bilayer polyhedra.

4. Polyhedral symmetries with minimal bilayer bending energy.

Motivation for polyhedral bilayer vesicles

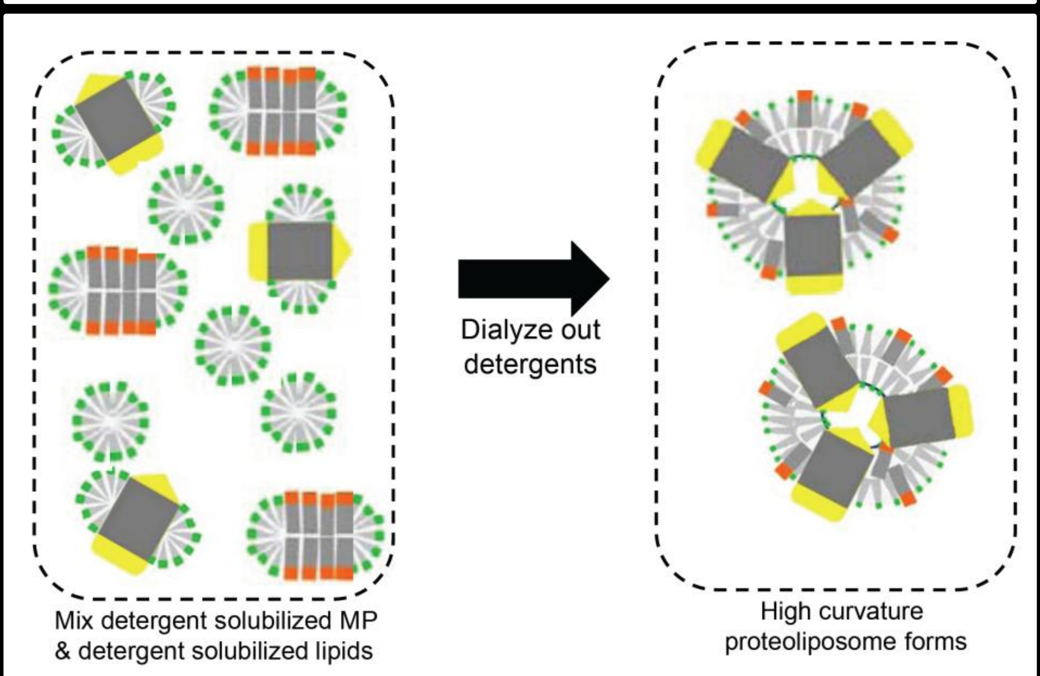
HHMI Collaborative Innovation Award 'High Resolution Structural Studies of Membrane Proteins in Native Phospholipid Membranes'

D. C. Rees & R. Phillips (Caltech), M. H. B. Stowell & H. Yin (UC Boulder)

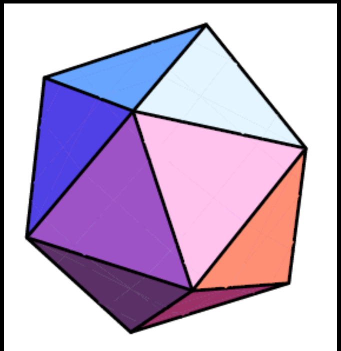


Goal: Structure of membrane components & energetics of their interactions.

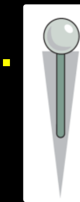
⇨ Membrane protein polyhedra.



Bottleneck: Controlled symmetry & size of membrane protein polyhedra.



Bilayer nanodisks and icosahedra

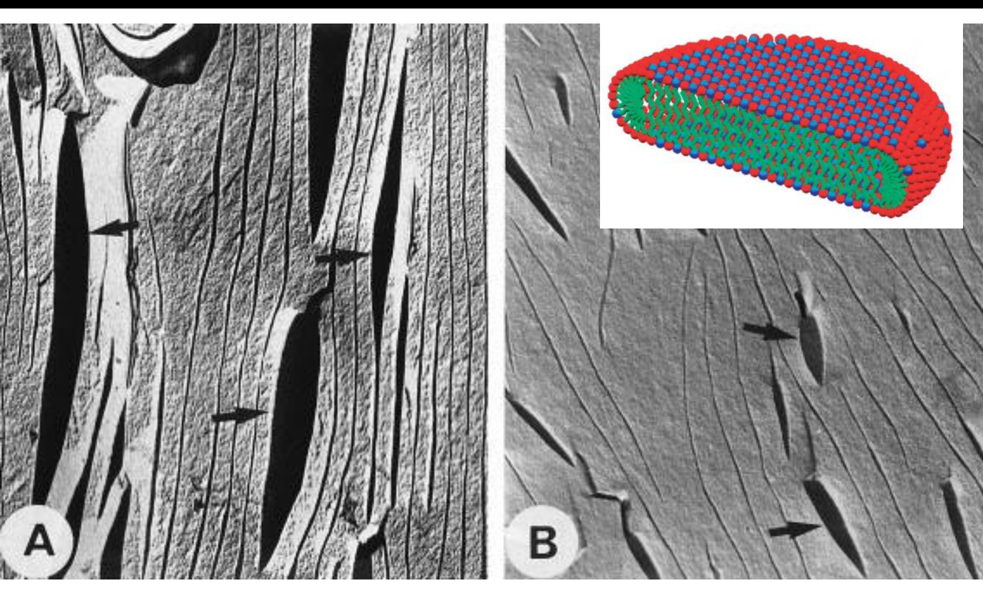
Water + single-tailed anionic+ single-tailed cationic amphiphiles. 

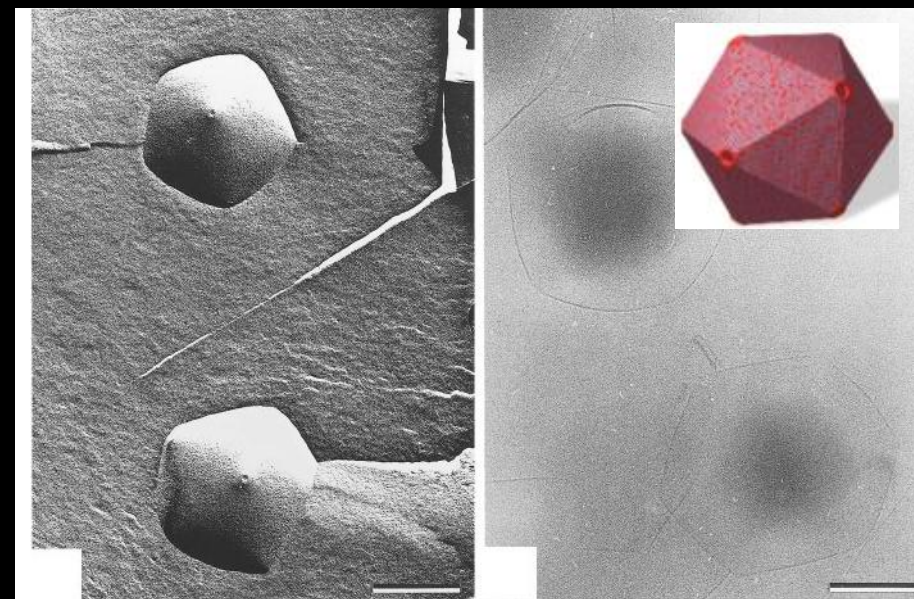
Solution is dilute in amphiphiles ($c<0.05$).

Excess of one amphiphile species ($0.4<r<0.5$; $0.5<r<0.65$).

Bilayer disks with size controlled by r

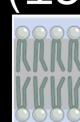
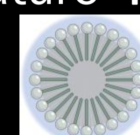
Icosahedra of ~fixed size





T. Zemb *et al.*, Science **283,** 816 (1999)

M. Dubois *et al.*, Nature **411,** 672 (2001)

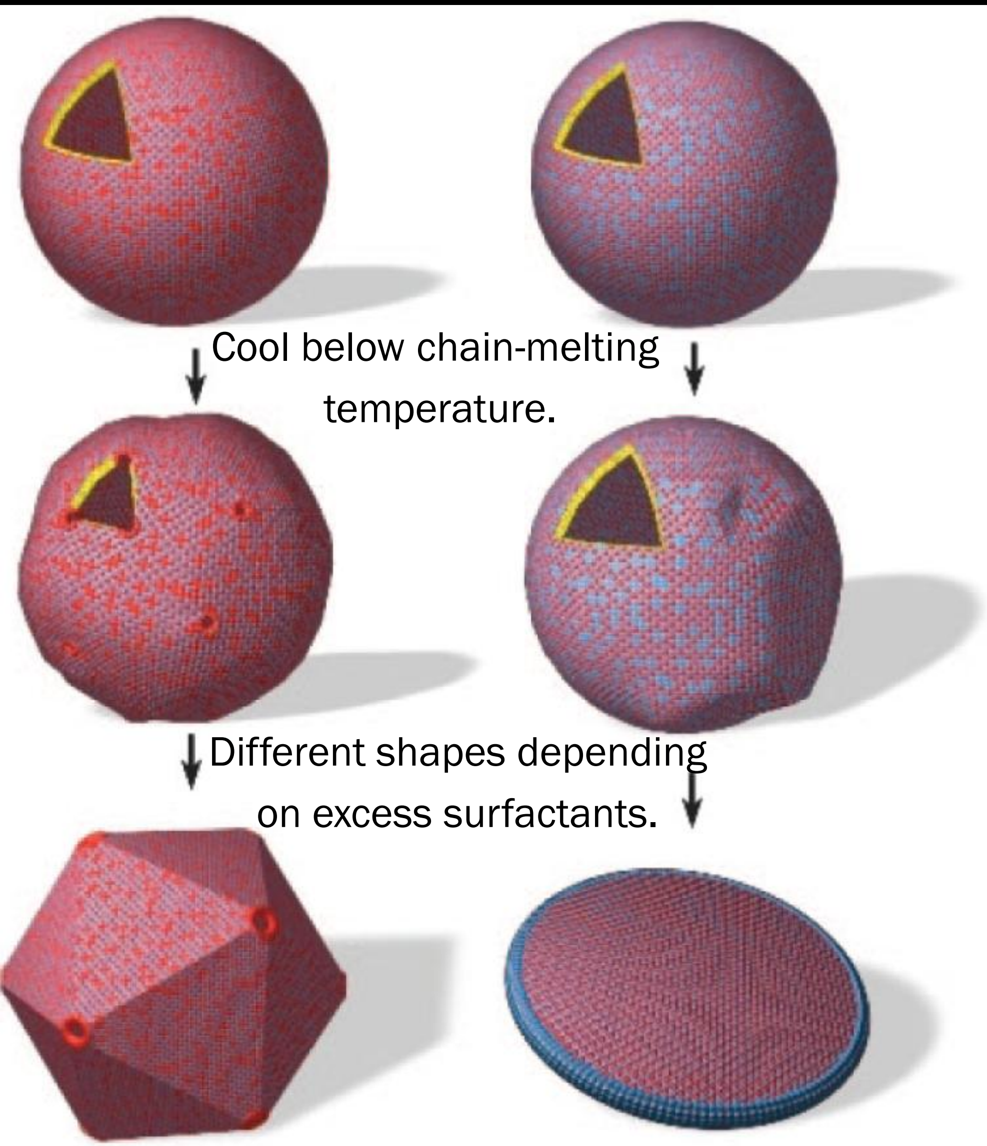
Why flat bilayers  rather than micelles  ?

Why polyhedra rather than spheres [c.f., U. Seifert, Adv. Phys. **46**, 13 (1997)]?

What determines polyhedral symmetry? Why icosahedron?

Phenomenology of bilayer icosahedra

M. Dubois *et al.*, PNAS **101**, 15087 (2004)



Characteristic icosahedron size: 1 μm

Disk size: 30 nm – 3 μm

Bending modulus: 500 $k_B T$

Bilayer thickness: 4 nm

Total number of amphiphiles: 10^7

Pore radius: 15 nm – 30 nm

Excess amphiphiles mainly segregate at pores.

Icosahedron energy:

$$E = \underbrace{N_l E_{\text{bending}}}_{\text{ridges}} + \underbrace{N_p E_p}_{\text{pores}} + \underbrace{\cancel{T\Delta S}}_{\text{thermo.}} + \underbrace{\cancel{E_{es}}}_{\text{electro.}}$$

"Mechanism for the formation of icosahedra is minimization of elastic bending energy."

What vesicle *shape and size* minimizes the elastic bending energy for the Dubois *et al.* system?

Outline

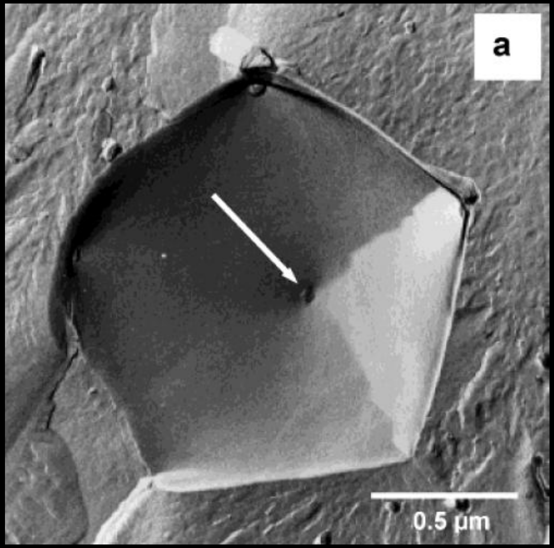
1. From biological membranes to bilayer vesicles.

2. Experimental phenomenology of bilayer polyhedra.

3. Contributions to the elastic energy of bilayer polyhedra.

4. Polyhedral symmetries with minimal bilayer bending energy.

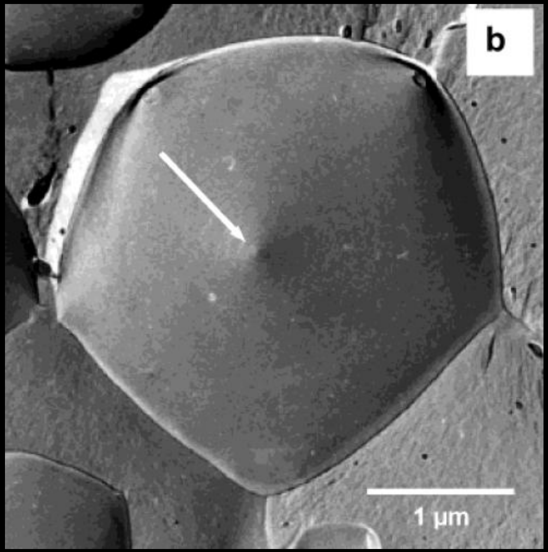
Contributions to the elastic energy of bilayer polyhedra



Ridges

Vertex pores

Closed vertices



K. Glinel *et al.*, Langmuir **20,** 8551 (2004)

Elastic theory of polyhedral ridges, vertices, and pores

Elastic theory of thin sheets

$$\kappa\nabla^4 f = [\chi, f] + P,$$

$$\frac{1}{Yh}\nabla^4\chi = -\frac{1}{2}[f, f],$$

$$[a,b] = \varepsilon_{\alpha\mu}\varepsilon_{\beta\nu}(\partial_\alpha\partial_\beta a)(\partial_\mu\partial_\nu b).$$

$$C_{ij} = \partial_i\partial_j f. \quad \sigma_{ij} = \varepsilon_{ik}\varepsilon_{jl}\partial_k\partial_l\chi.$$

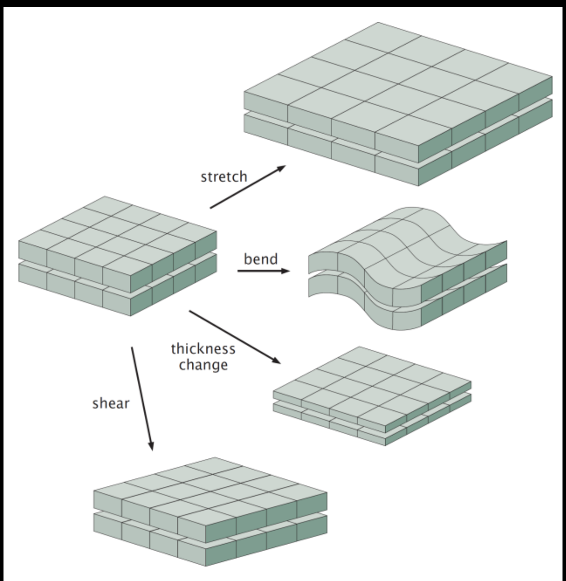
von Kármán equations

1. "These equations are very complicated, and cannot be solved exactly, even in very simple cases." (Landau & Lifshitz, *Theory of Elasticity*)

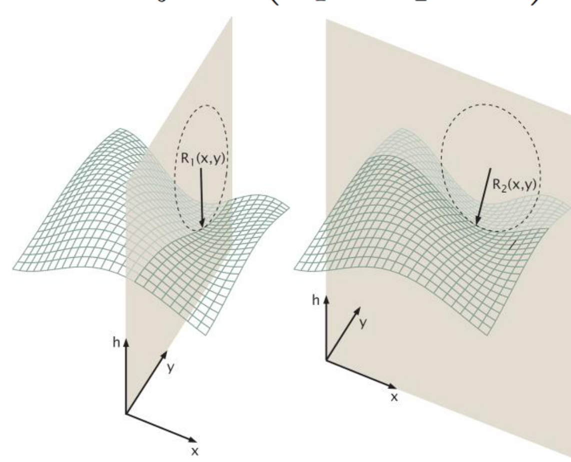
2. Several essentially unknown parameters.

3. Complicated solution would not necessarily lead to a gain in intuitive understanding.

Helfrich-Canham-Evans theory: { Several alternative elastic models }



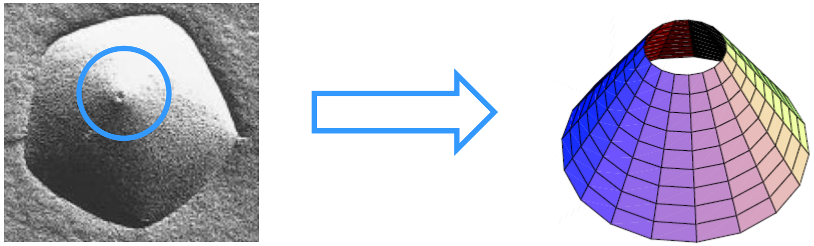
$$G = \frac{K_b}{2}\int dS\left(\frac{1}{R_1} + \frac{1}{R_2} - H_0\right)^2$$



\+

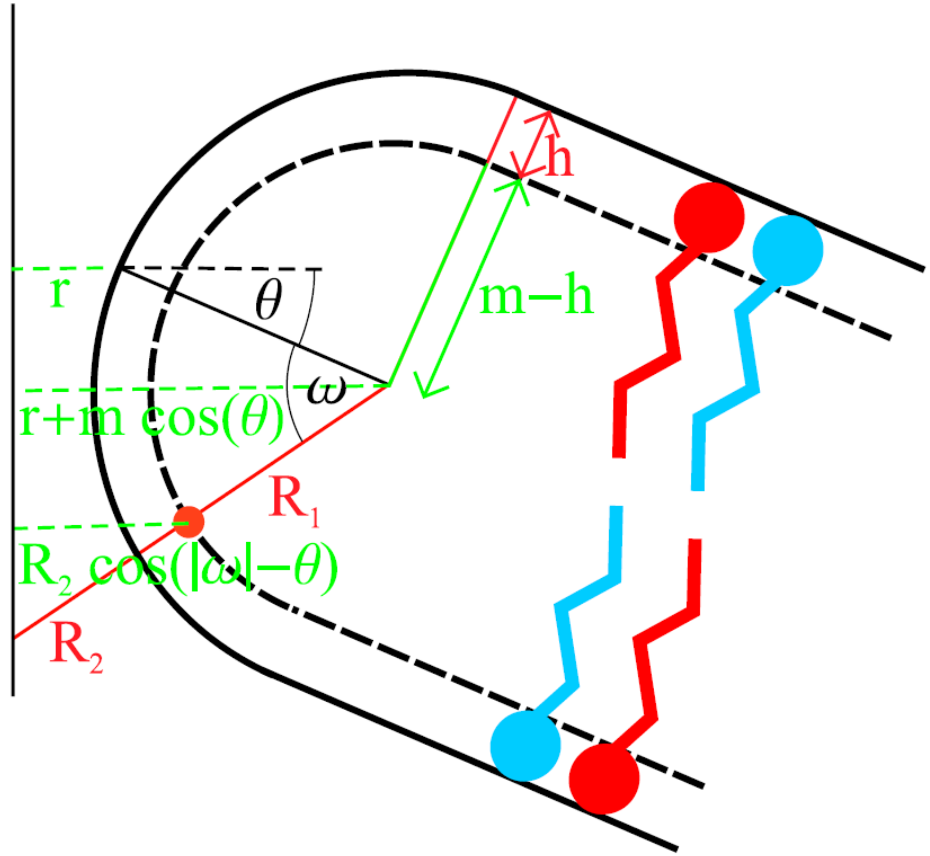
[Comparisons to known asymptotic limits of elasticity theory.]

Pore energy I: Cone with apex angle π − 2θ



Each pore carries an energetic cost

$$G_p = \frac{K_b^\star}{2} \int dS \left(\frac{1}{R_1} + \frac{1}{R_2} - H_0^\star \right)^2$$



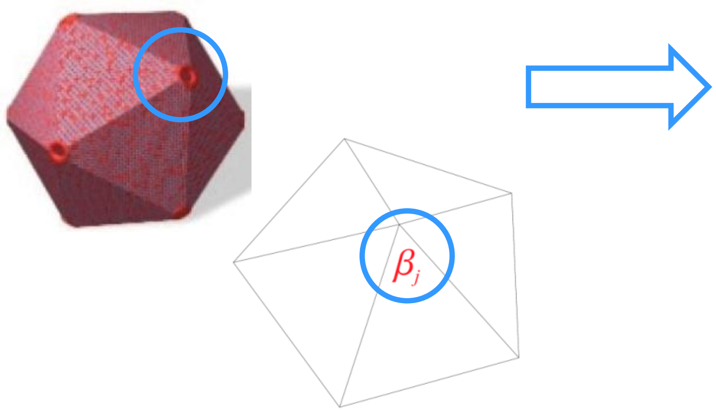
$$R_1 = m - h\,,$$

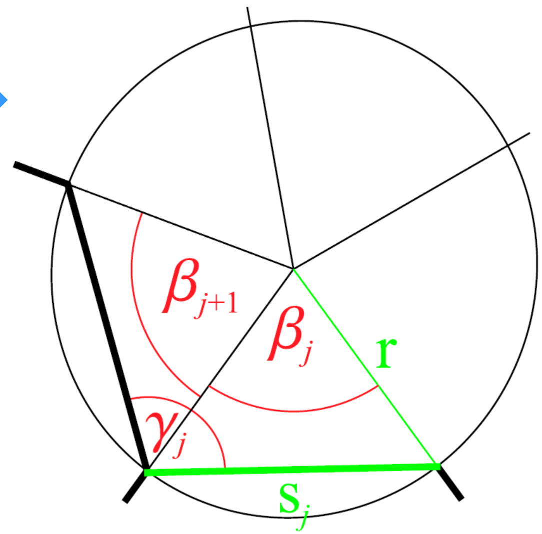
$$R_2 = -\left(\frac{r + m\cos\theta}{\cos(|\omega| \pm \theta)} - m + h \right)\,,$$

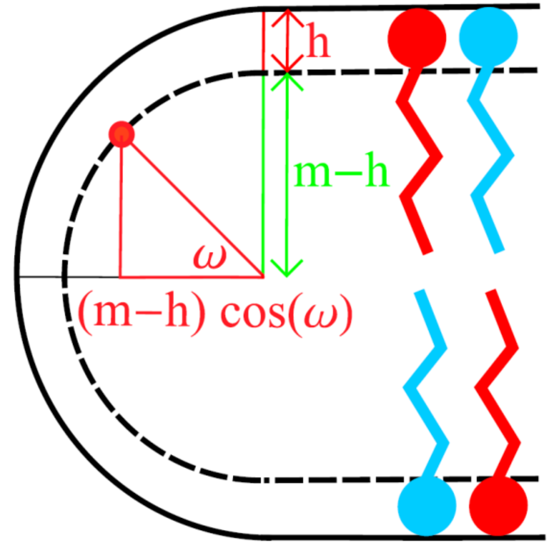
$$dS = 2\pi R_1 \left[-R_2 \cos(|\omega| \pm \theta) \right] d\omega\,.$$

c.f., M. Dubois *et al.*, PNAS **101,** 15087 (2004)

Pore energy II: Polyhedral pores







$$G_p = \frac{K_b^\star}{2} \int dS \left(\frac{1}{R_1} + \frac{1}{R_2} - H_0^\star \right)^2$$

$$G_p^{(1)} = \frac{K_b^\star}{2} \pi (m-h) s_j \left(\frac{1}{m-h} - H_0^\star \right)^2 ,$$

$$s_j = 2r \sin \frac{\beta_j}{2} .$$

$$G_p^{(2)} = \bar{K}_b^\star (m-h) \left(\pi - \gamma_j + \bar{H}_0^\star \right)^2 ,$$

$$\gamma_j = \frac{1}{2} \left(2\pi - \beta_j - \beta_{j+1} \right) .$$

$$\boxed{G_p^{(p)} = \sum_{j=1}^{q} \left(G_p^{(1)} + G_p^{(2)} \right)}$$

Asymptotic results for singular vertices and ridges

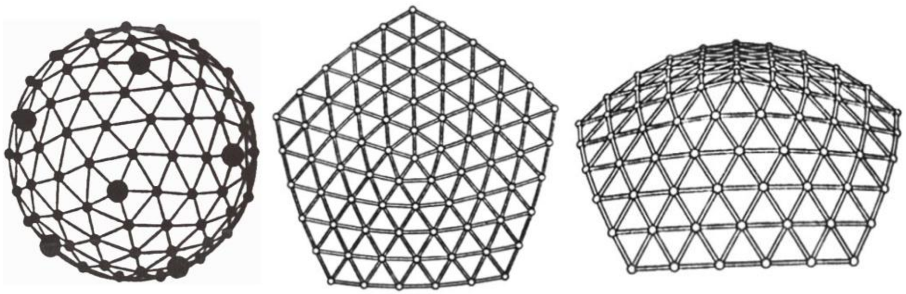
Energy of 5-fold disclinations: Viral capsids

H. S. Seung & D. R. Nelson, Phys. Rev. A **38,** 1005 (1988)

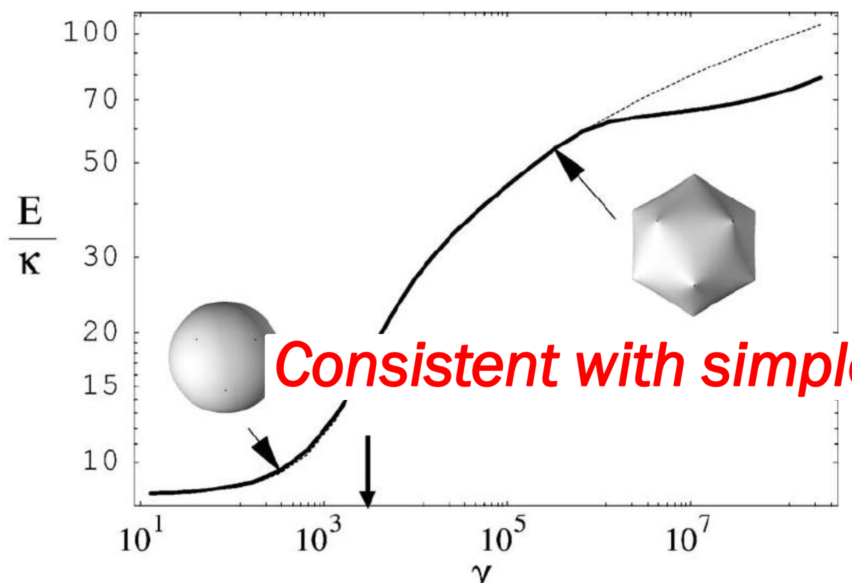
J. Lidmar *et al*., Phys. Rev. E **68,** 051910 (2003)

T. Nguyen *et al*., Phys. Rev. E **72,** 051923 (2005)

$$\frac{E(\gamma)}{K_b} = \begin{cases} \frac{B}{2}\frac{\gamma}{\gamma_b} & \text{for } \gamma < \gamma_b, \\ \frac{B}{2}\left[1 + \log\left(\frac{\gamma}{\gamma_b}\right)\right] & \text{for } \gamma > \gamma_b. \end{cases}$$



Föppl-von Kármán number: $\gamma = \dfrac{YR^2}{K_b}$

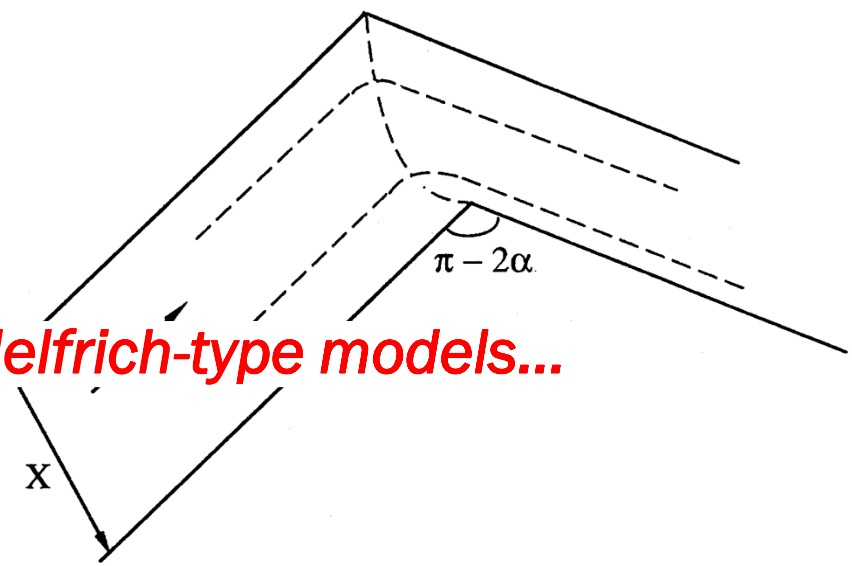


Ridge scaling as $\gamma \longrightarrow \infty$

A. Lobkovsky, Phys. Rev. E **53,** 3750 (1996)

A. Lobkovsky & T. A. Witten, Phys. Rev. E **55,** 1577 (1997)

$$\frac{E_r}{K_b} \approx 1.24 \left(\frac{\pi - \alpha}{2}\right)^{7/3} \left(\frac{Yl^2}{K_b}\right)^{1/6}$$



Consistent with simple Helfrich-type models…

Outline

1. From biological membranes to bilayer vesicles.

2. Experimental phenomenology of bilayer polyhedra.

3. Contributions to the elastic energy of bilayer polyhedra.

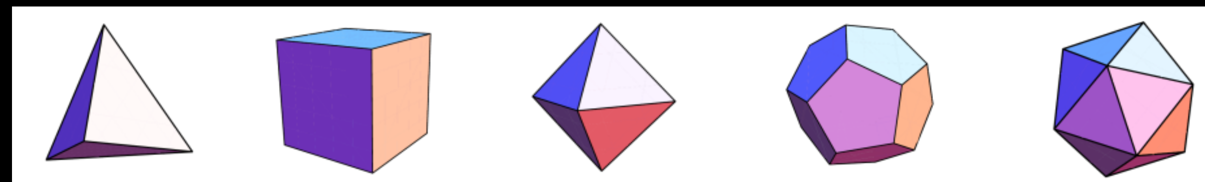
4. Polyhedral symmetries with minimal bilayer bending energy.

Minimizing polyhedral bending energy

Minimize “ridge part” of polyhedral bending energy: *Regular faces*.

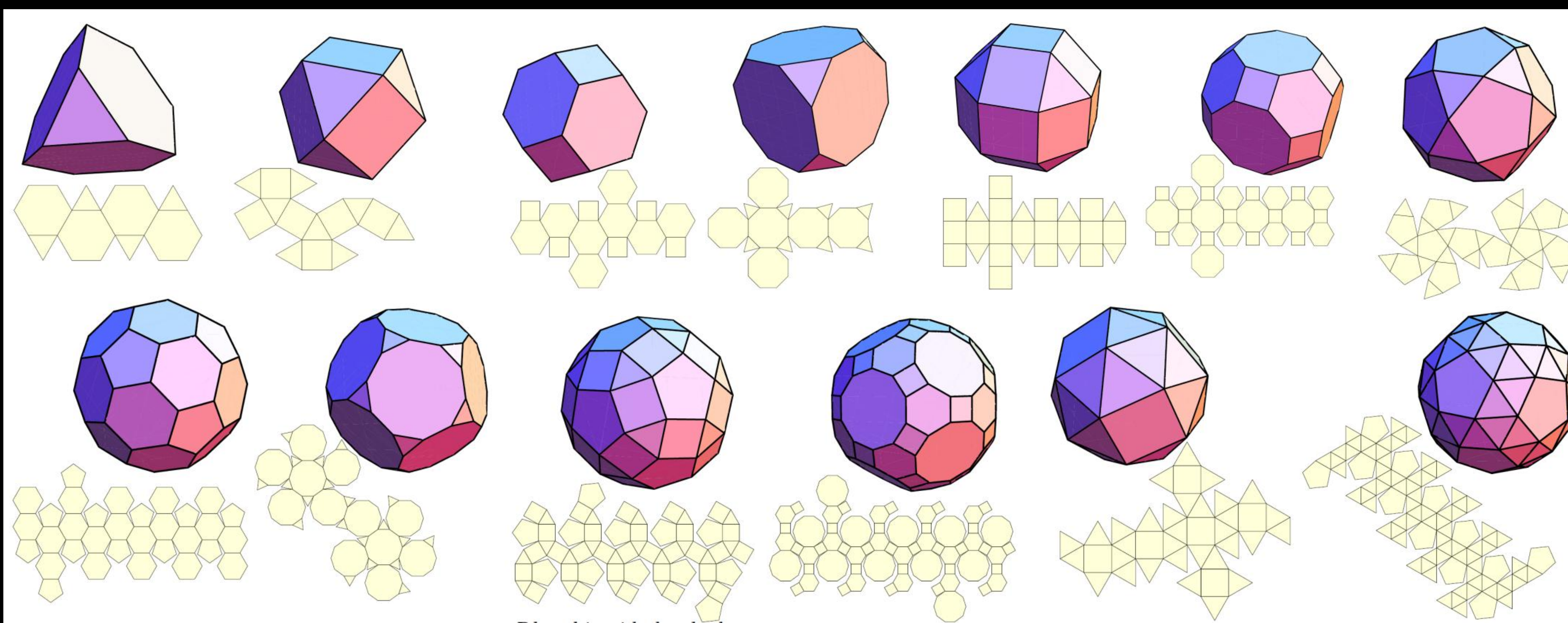
Regular polyhedra (vertex-, edge-, face-transitive):

5 Platonic solids.



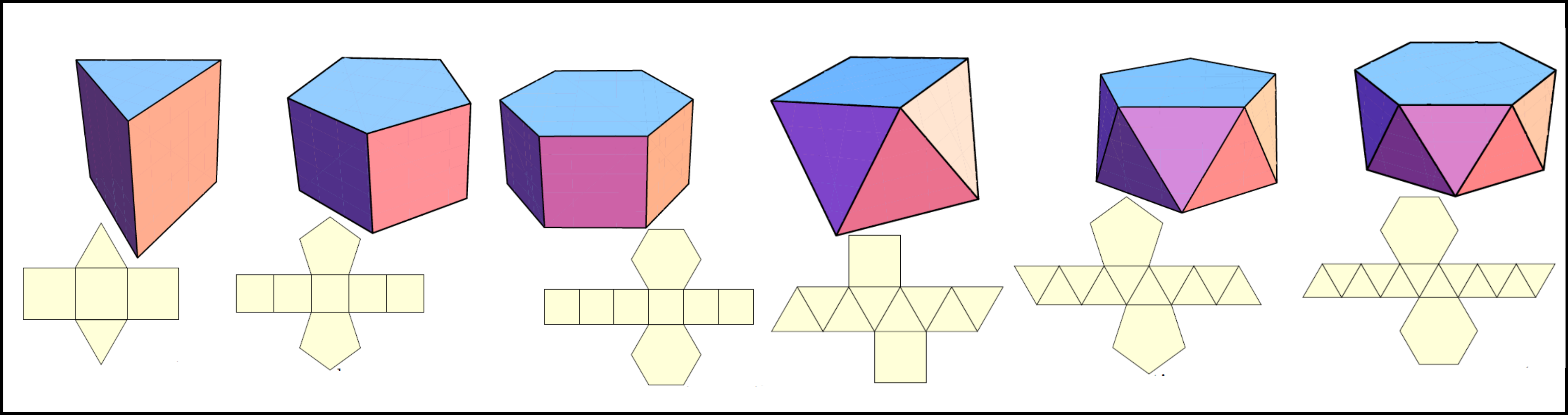
Semiregular polyhedra (vertex-transitive, regular faces):

13 Archimedean solids.



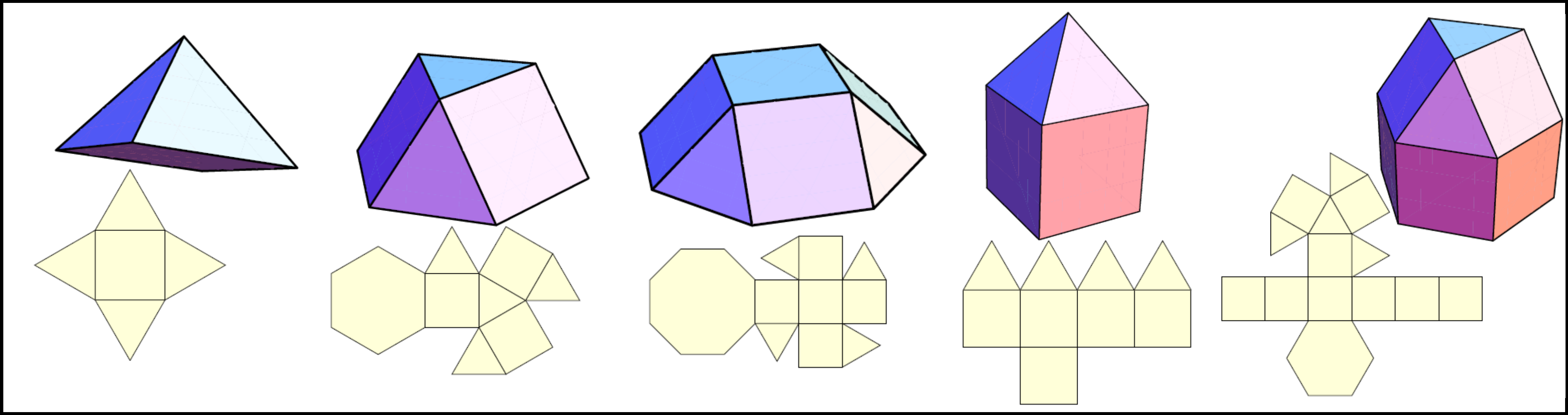
Minimizing polyhedral bending energy

Prisms & antiprisms.

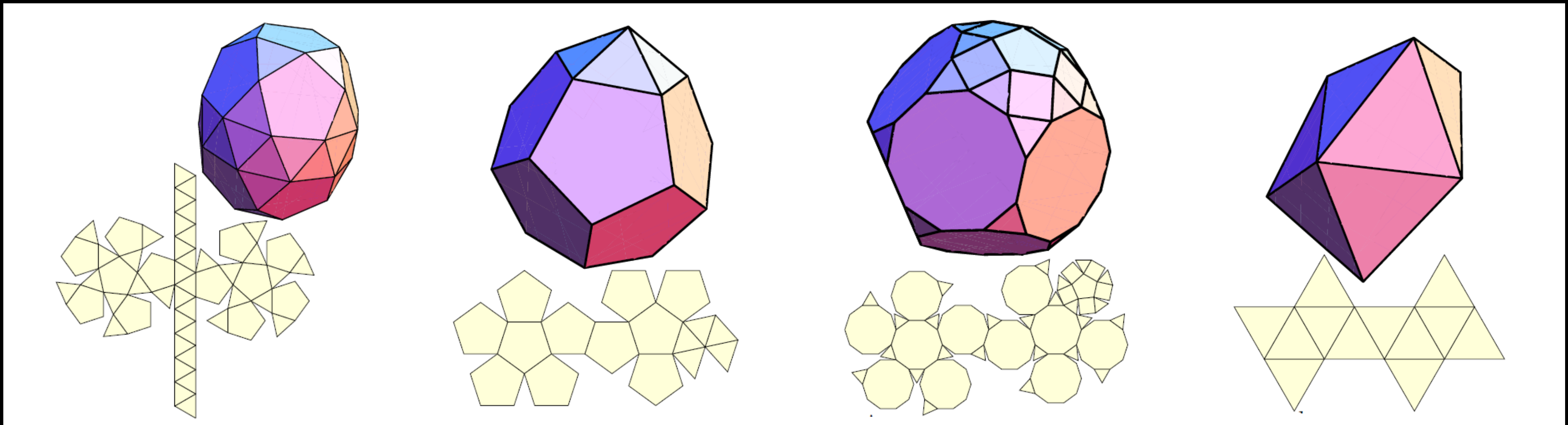


Convex polyhedra with regular polygons as faces:

92 Johnson solids. Such as...

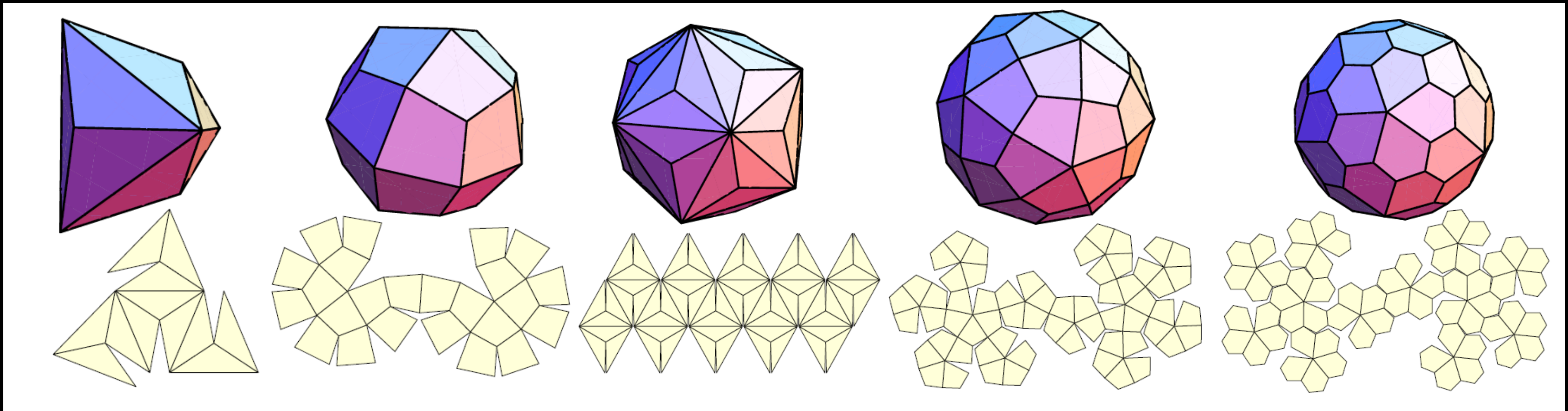


Minimizing polyhedral bending energy

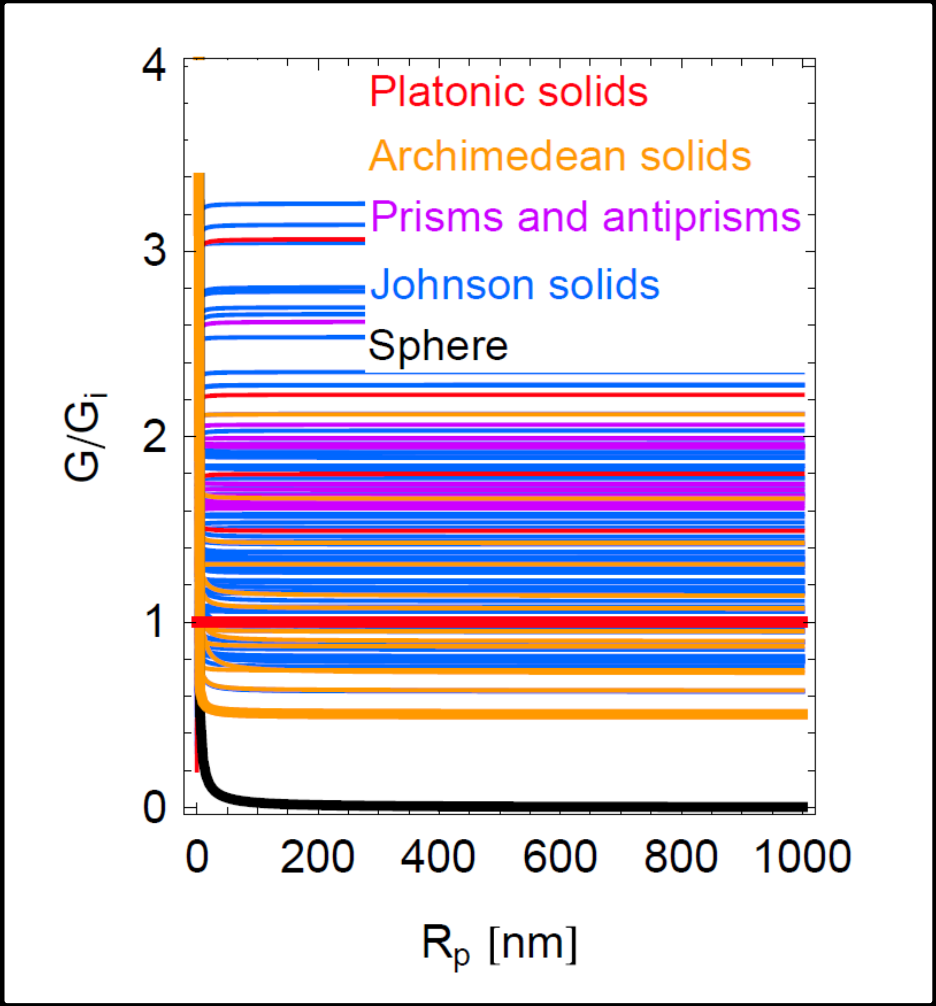


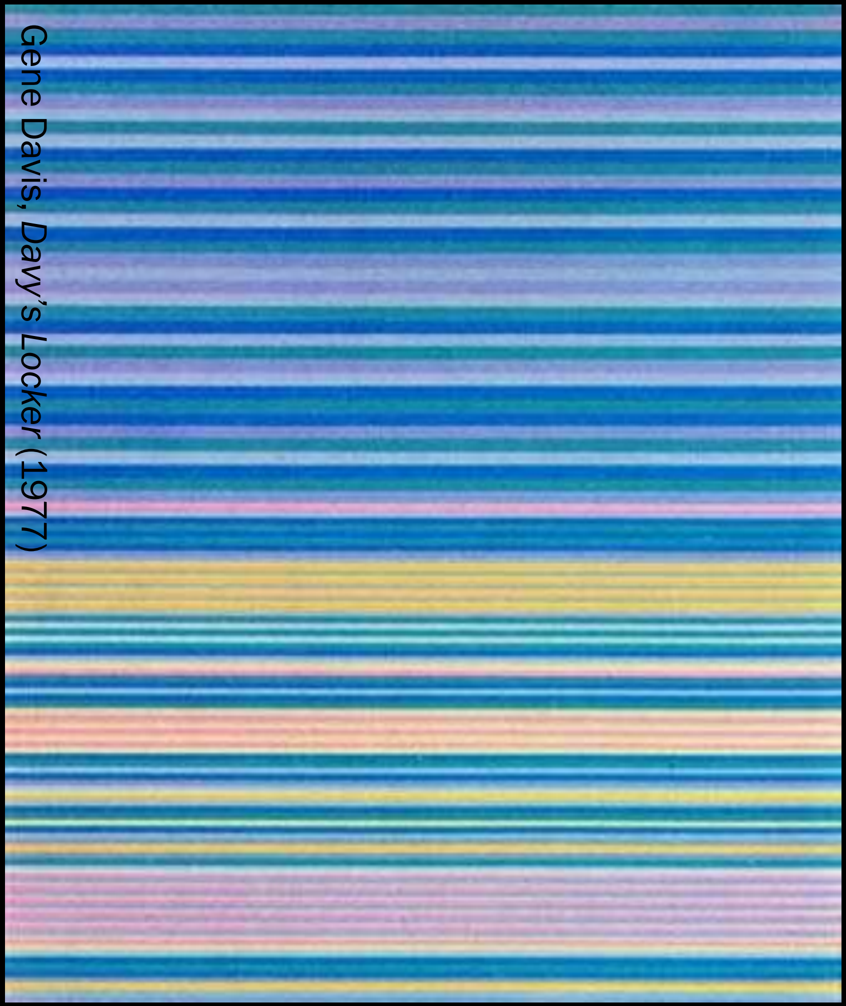
This list is complete. (Johnson & Zalgaller, 1960s)

As an illustration of polyhedra with non-regular faces, consider Catalan solids (duals of Archimedean solids; face-transitive).

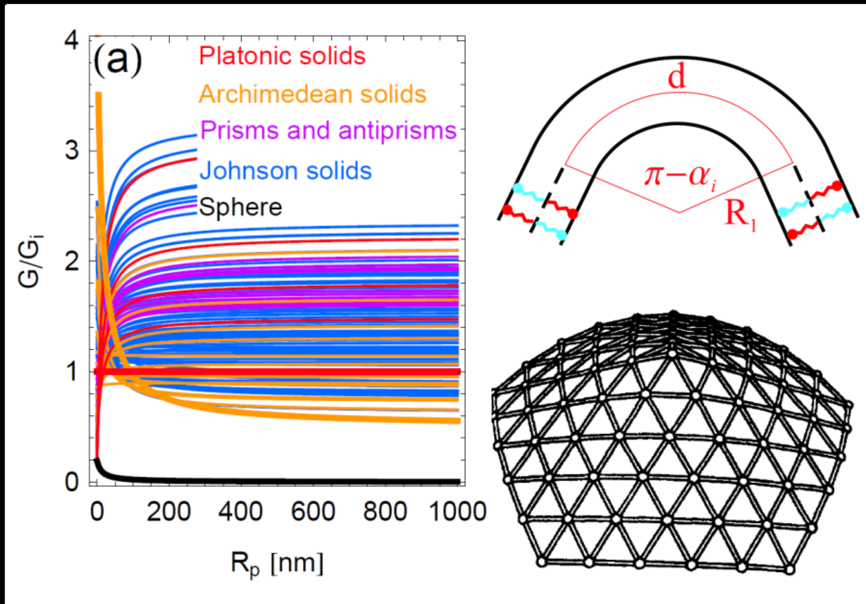


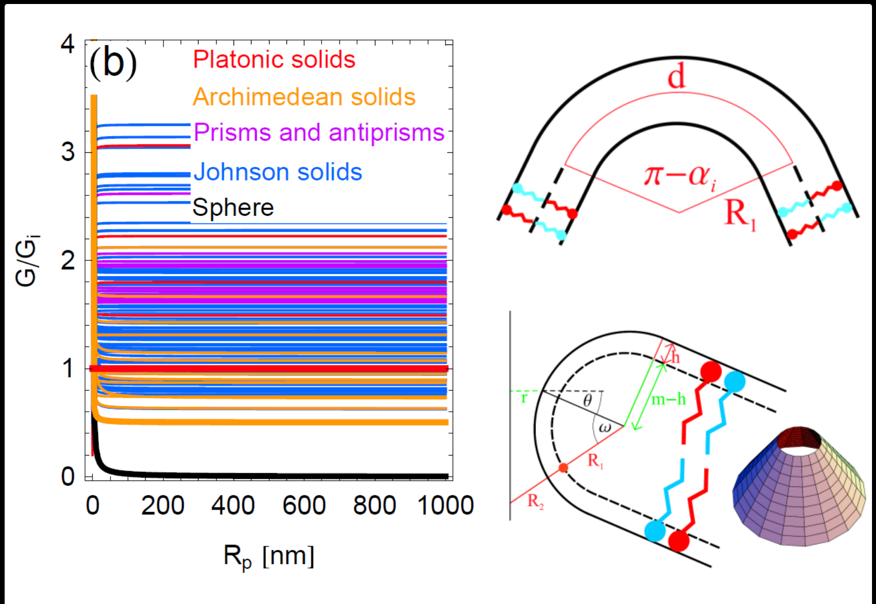
Total polyhedral bending energies: No segregation

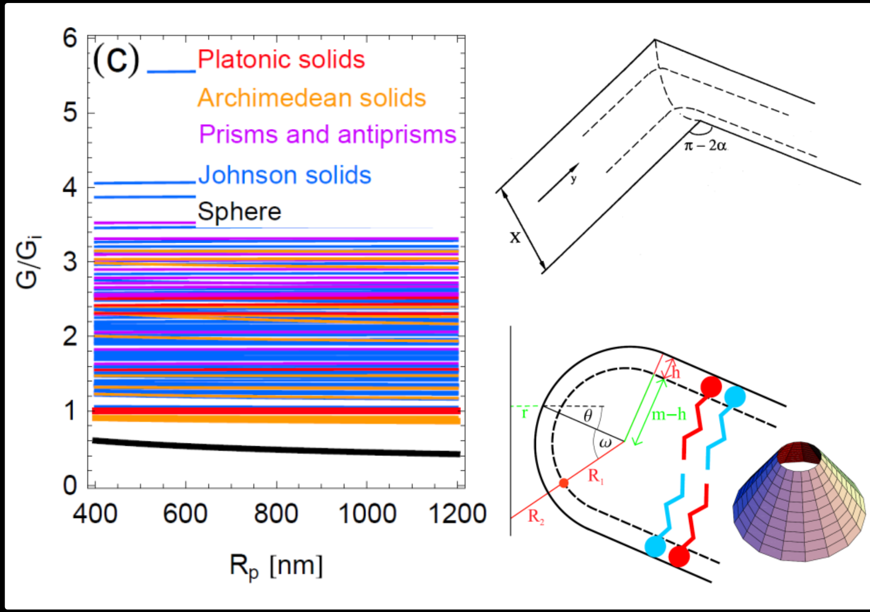


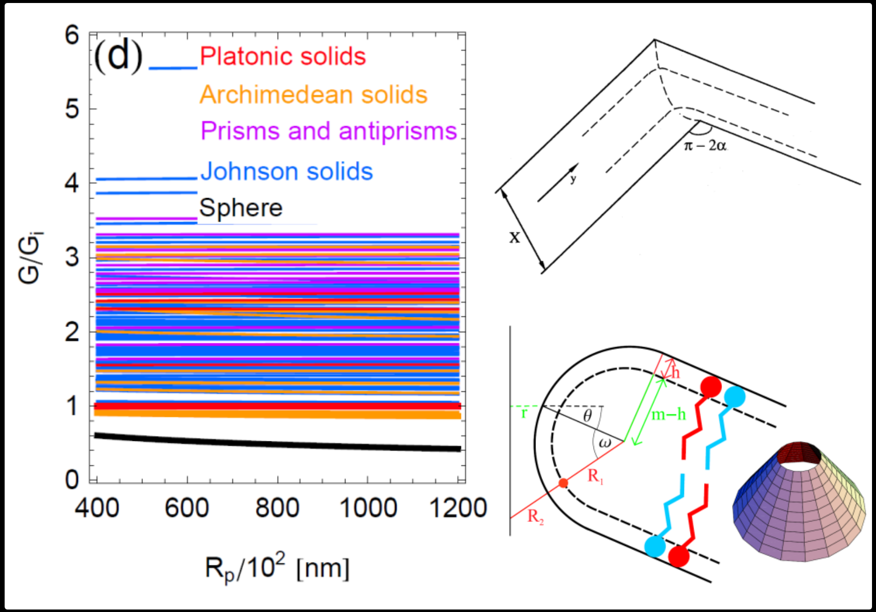


Total polyhedral bending energies: No segregation



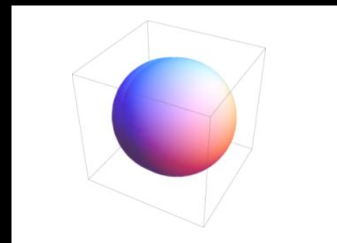




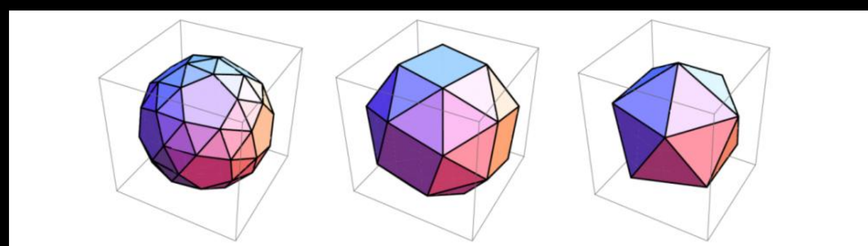


Total polyhedral bending energies: No segregation

1. Spherical vesicles are always energetically favorable [c.f., U. Seifert, Adv. Phys. **46**, 13 (1997)].



2. For small polyhedron radii, the snub dodecahedron, the snub cube, and the icosahedron are in close competition.



3. For large enough polyhedron radii, the polyhedral shape with minimal energy is always the snub dodecahedron.

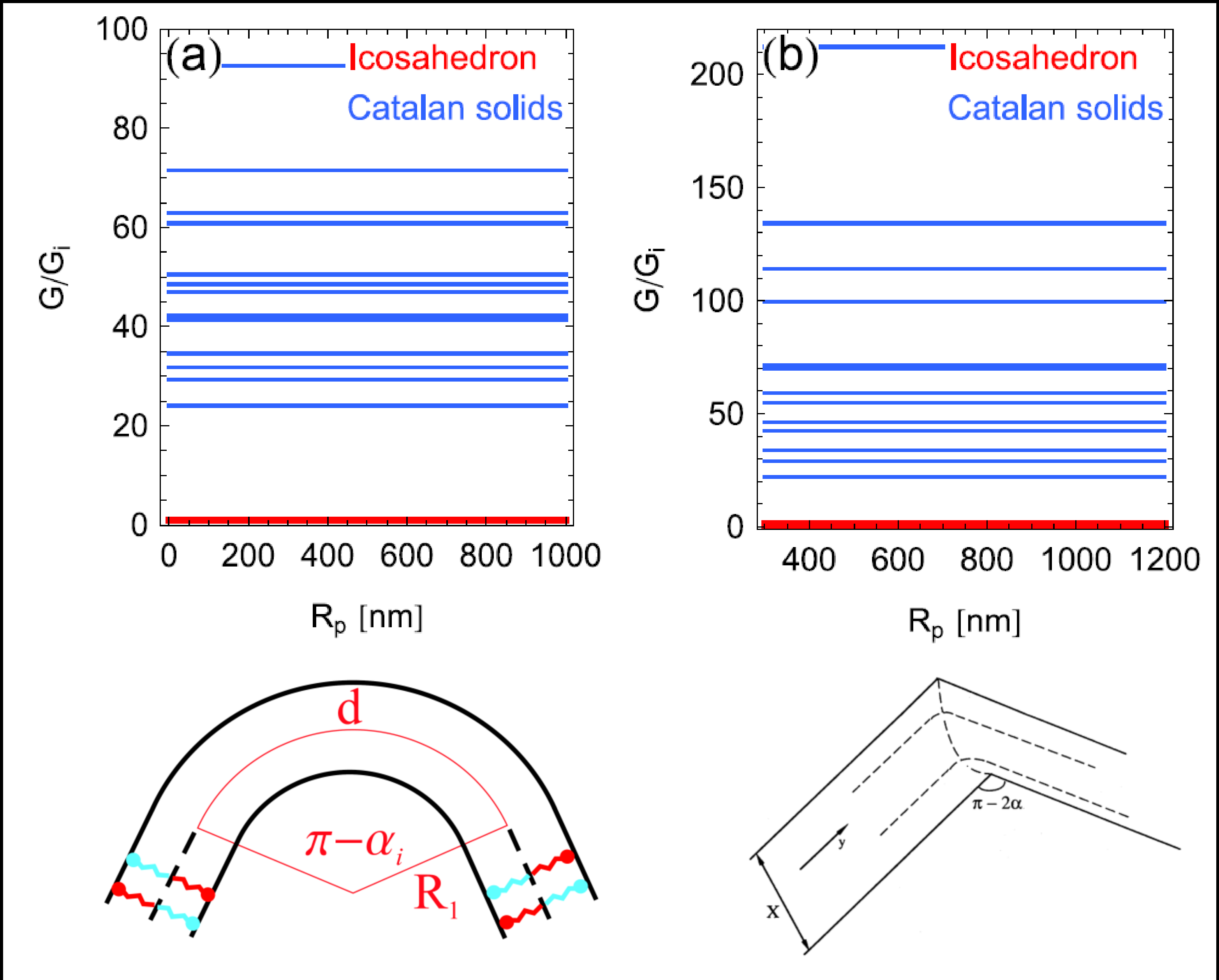
General ridge energy: $G_r \propto (\pi - \alpha)^p l^q$.

Previous cases: $(p, q) = (2, 1)$, $(7/3, 1/3)$.

For $p \gtrapprox 2$: $q \lessapprox 0.2$ or $q \gtrapprox 1.6$, and

for $q \lessapprox 1$: $p \lessapprox 1.3$ to change energy minimum.

Total ridge energies of Catalan solids

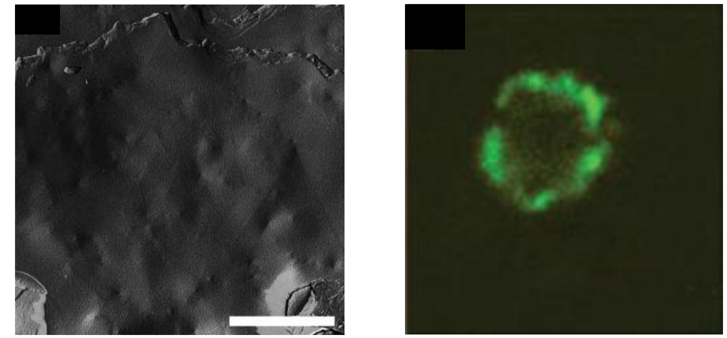


What is the effect of unpaired excess amphiphiles?

Excess amphiphiles: Beyond homogeneous bilayers

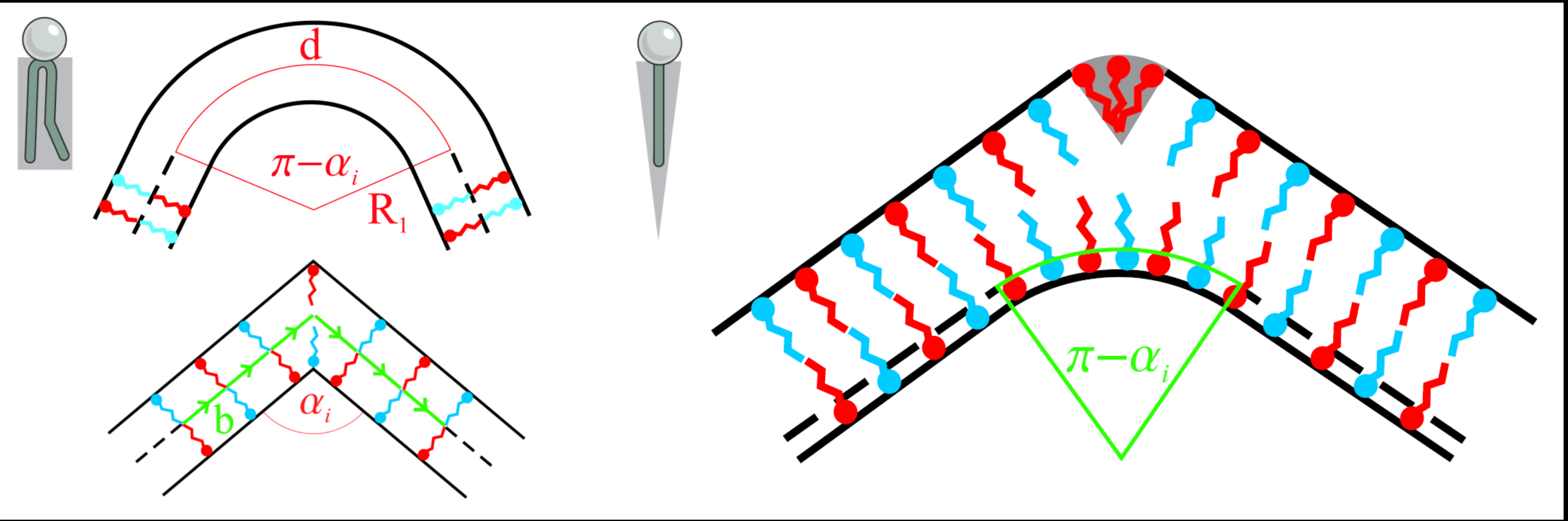
1. Pores are seeded into *all* bilayers, including spheres and disks.

2. At ridges, excess lipids lower bending energy of outer amphiphile layer.



M. Dubois *et al.*, PNAS **101,** 15087 (2004)

Assume that shape of excess amphiphiles commensurate with dihedral angle.

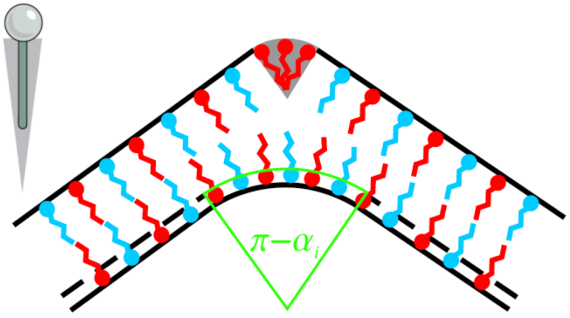


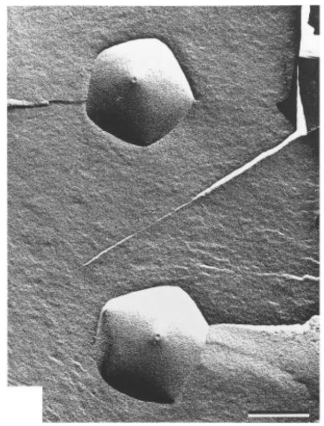
No additional parameters:

$$\boxed{G_r^{(s)} = \frac{\bar{K}_b^\star}{2}(\pi-\alpha_i)^2 l_i}$$

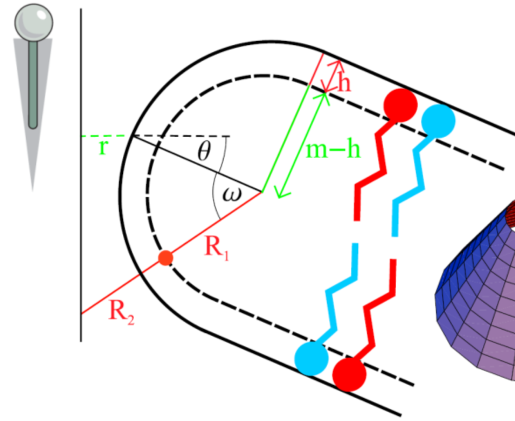
(lower bound)

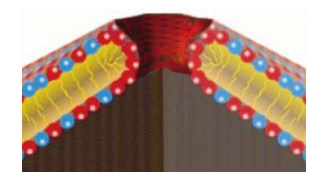
Estimating the amount of excess amphiphiles

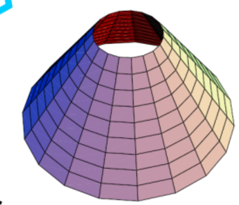


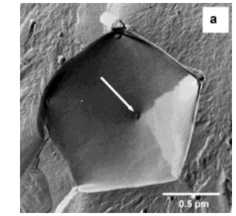


$$n_i = (\pi - \alpha_i)/(bH_0^\star)$$



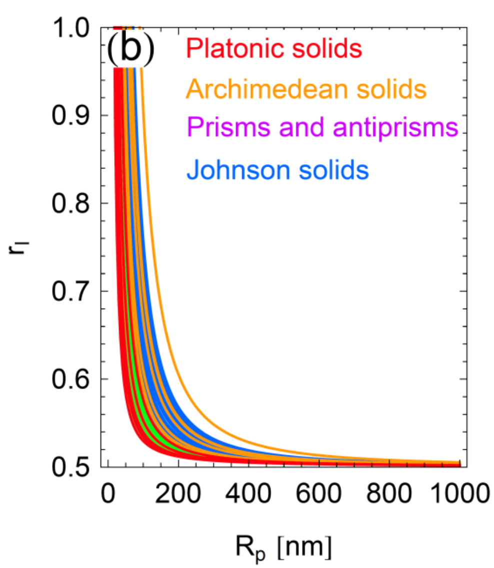


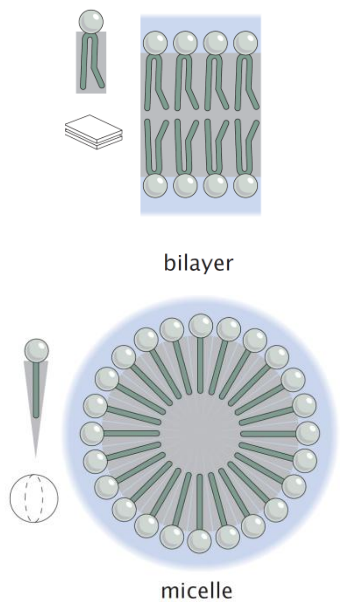




Segregation along ridges: $N_R = \sum_i l_i n_i$

Segregation at pores: $N_P = V \dfrac{2\pi^2 m(m+r)}{b^2}$





$$r_I = \frac{N_T/2 + N_R + N_P}{N_T}; \quad N_T = \frac{A}{b^2}.$$

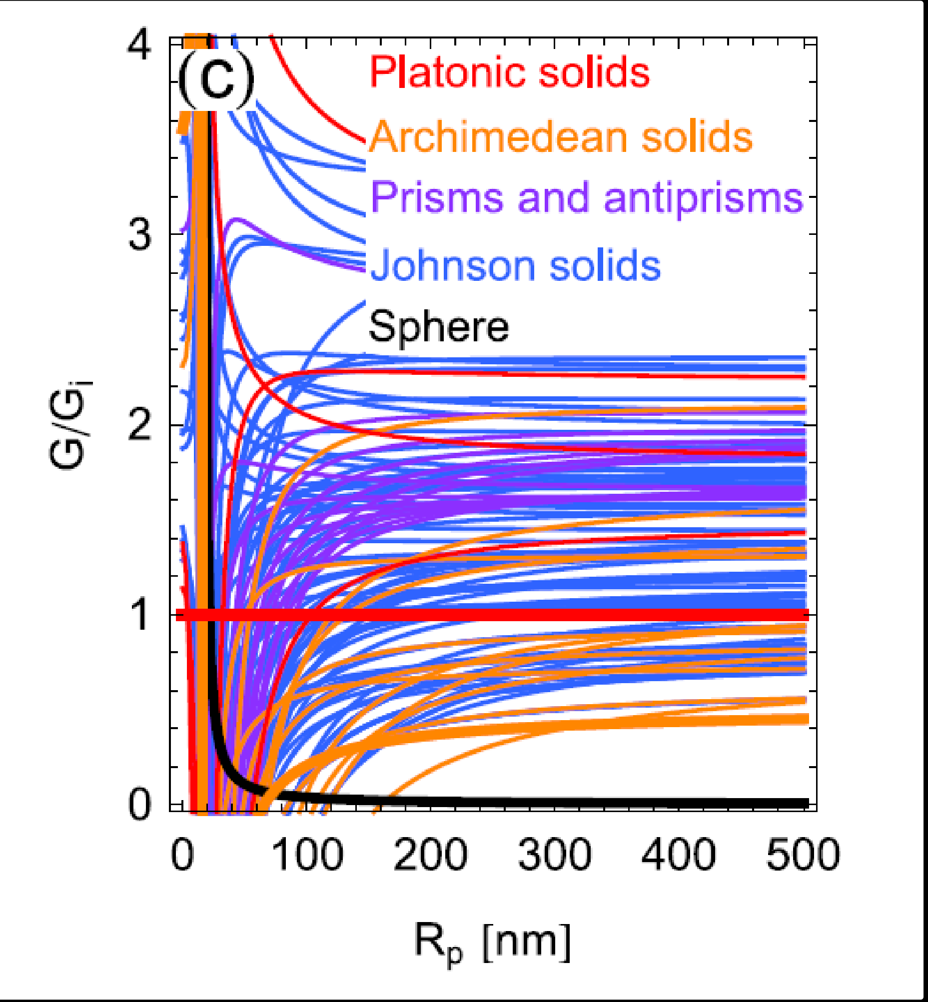
Theory: $r_I \approx 0.51$ for $R_p \approx 500$ nm.

(Perfect segregation, no micelles)

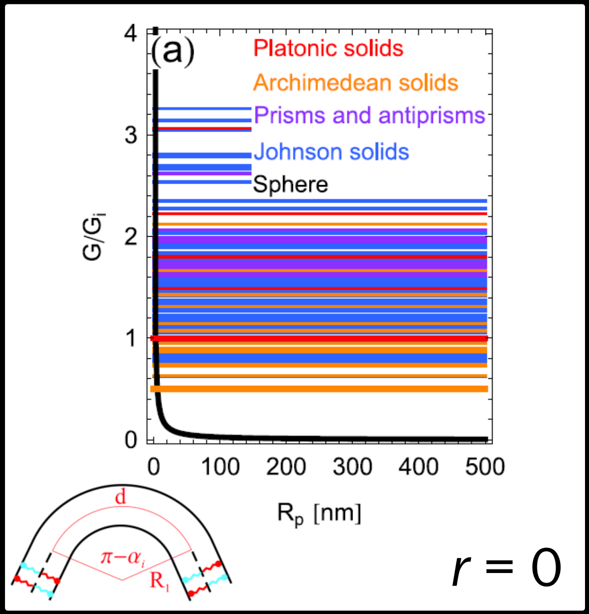
Experiments: $0.5 < r_I < 0.65$.

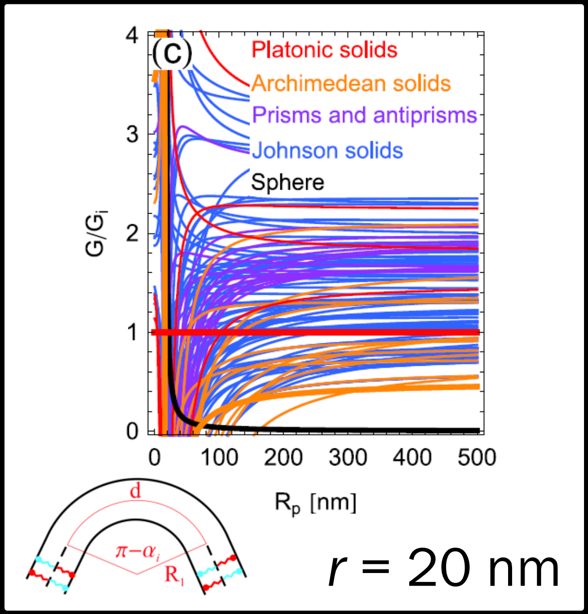
Ideal amphiphile imbalance $r_I \approx 0.57$.

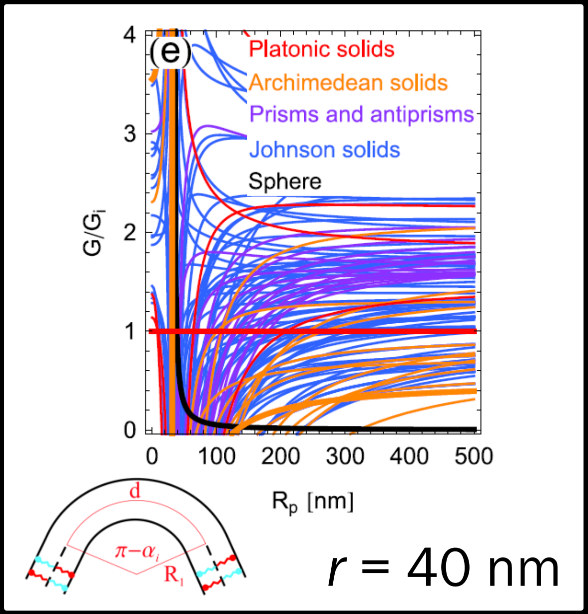
Segregation at pores only [M. Dubois *et al.*, Nature **411**, 672 (2001)]

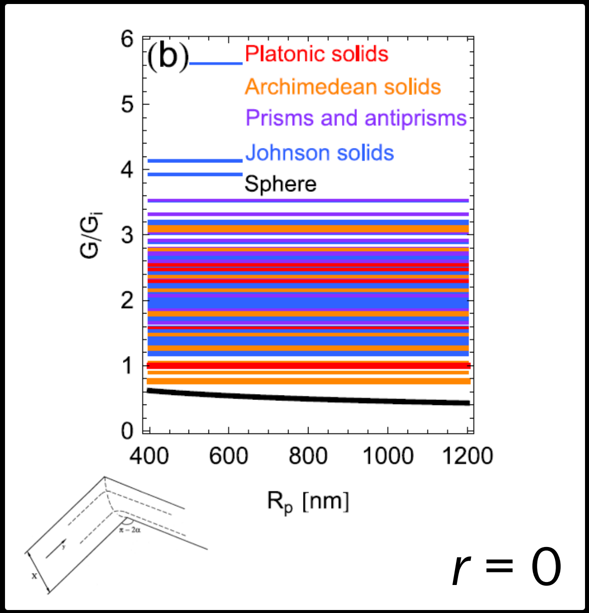


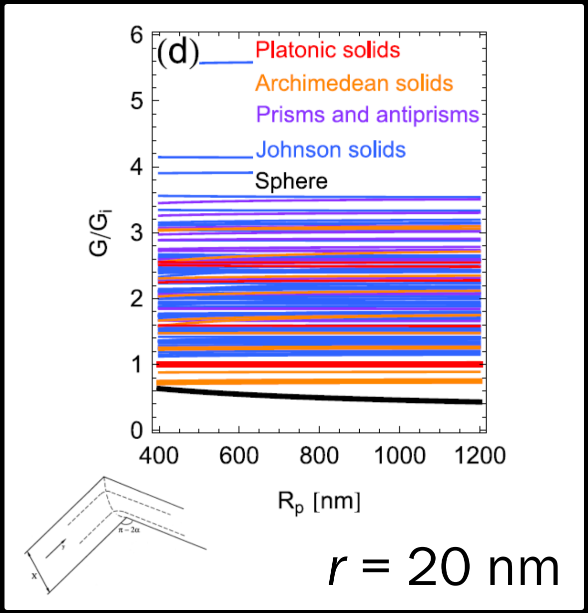
Segregation at pores only [M. Dubois *et al.*, Nature **411**, 672 (2001)]

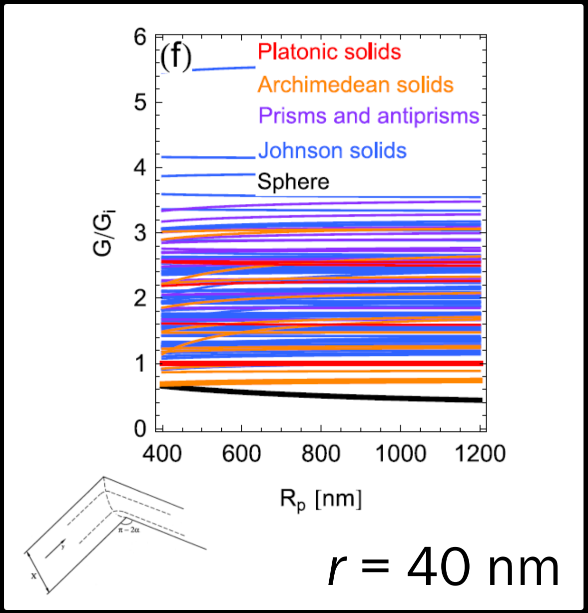




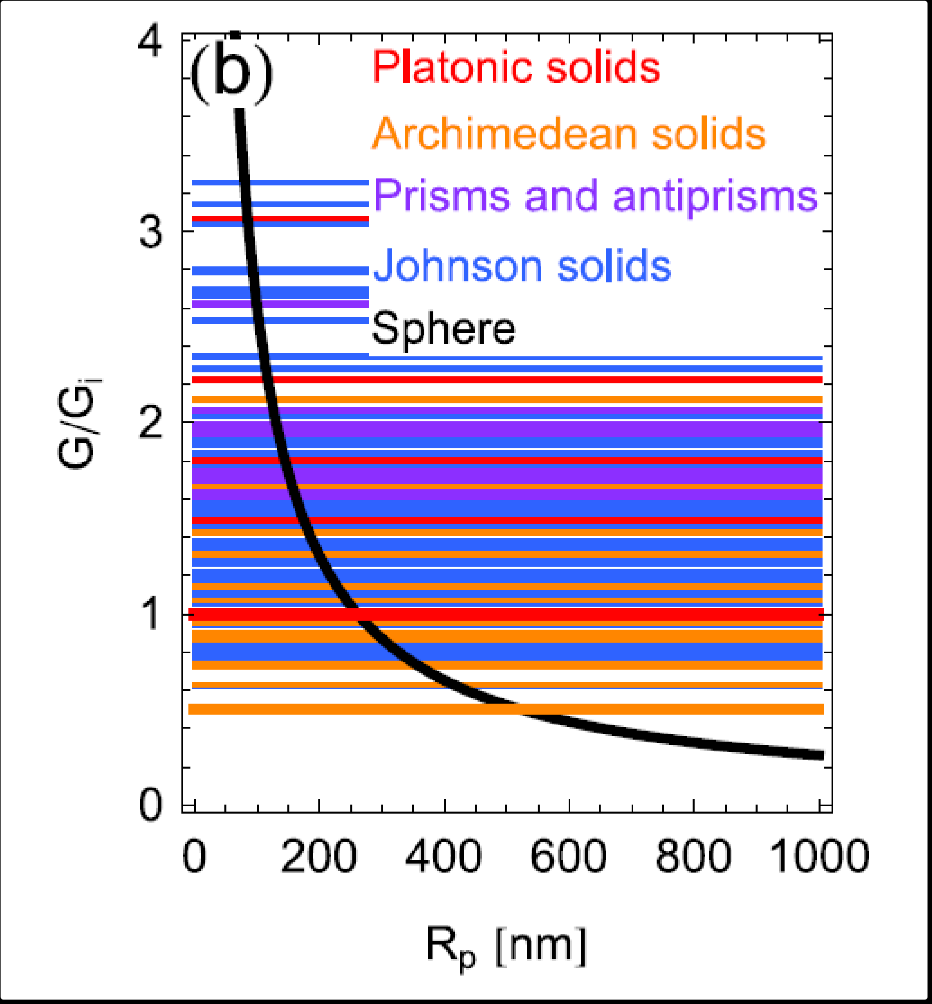




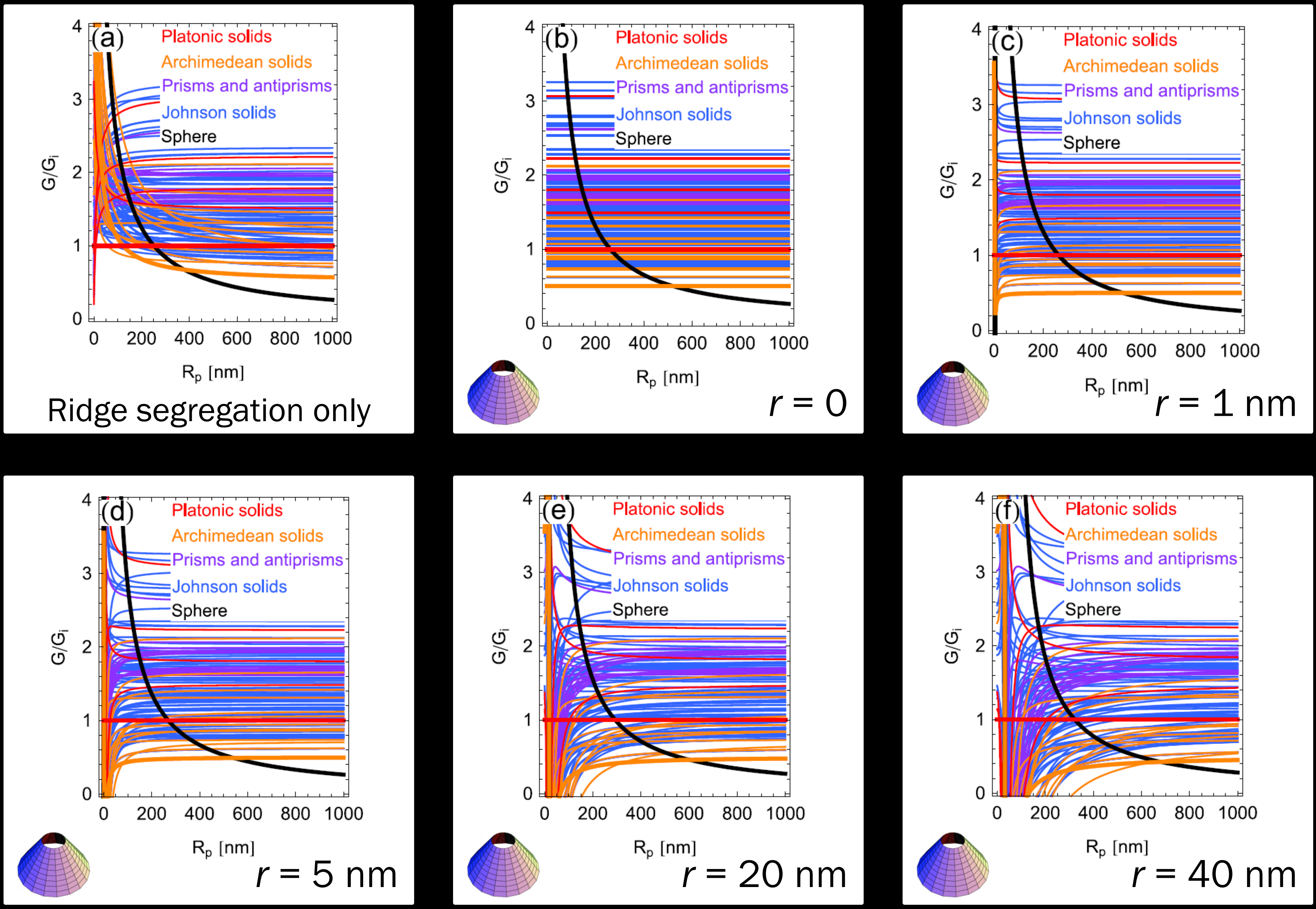




Segregation at ridges [M. Dubois *et al.*, PNAS **101,** 15087 (2004)]



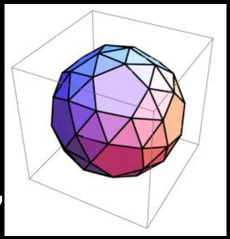
Segregation at ridges [M. Dubois *et al.*, PNAS **101,** 15087 (2004)]



Outlook and summary

1. Segregation at *ridges* is essential for membrane polyhedra.

2. Quite generally, polyhedral shapes with minimal bending energy are snub dodecahedron & snub cube.
   [c.f., R. F. Bruinsma *et al.*, PRL **90**, 248101 (2003); R. Zandi *et al.*, PNAS **101**, 15556 (2004); M. J. W. Dodgson, J. Phys. A **29**, 2499 (1996); G. Vernizzi and M. Olvera de la Cruz, PNAS **104**, 18382 (2007).]



3. Putative mechanism for the characteristic size of polyhedra:
   Sufficient number of excess lipids ($\sim R_p^2$) *versus* energy of sphere (~const.).

4. Other energy contributions? Kinetics? Lipid chemistry?

5. Membrane-*protein*-polyhedra—structural biology
   Arrangement of proteins? Membrane deformations?