Modelling (Skin) Lipid Bilayers

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Skin …

Design problem for nature

    1. Impermeable to passive transport.
    2. Mechanically stable against perturbation.

Can we get some insight from computer simulations?

What's in it ?

Beauty is skin deep (not really)

*If you are a queen
and especially Cleopatra*

What's in it ?

Beauty is skin deep (not really)

Understanding how products
work is important for the industry.
And that means good business !

Exciting and relatively uncharted biophysical territory to explore.

Plan of the talk

- *What makes skin lipids so special (contrast with phospholipids)*

- *Simulation of skin lipid bilayers*

- *Passive permeation of water*

- *Possible 3-D arrangement of skin lipids*

- *Conclusions*

Compartmentalization of life

- Pack and protect genetic signature
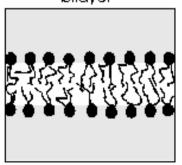- In water environment
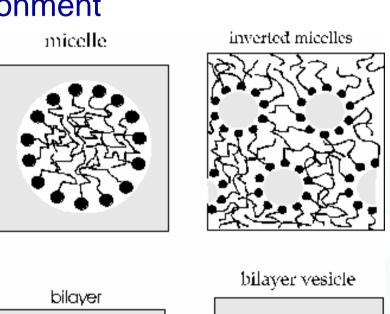
Amphiphilic molecule
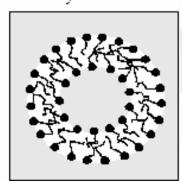
(molecules having love-hate relationship with water)

Compartmentalization of life

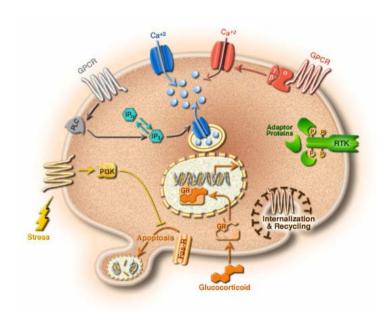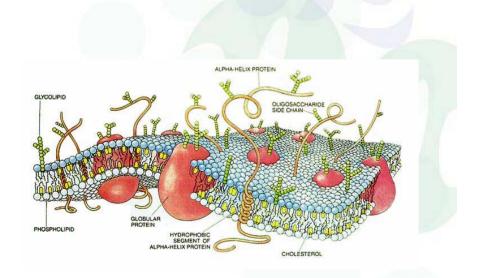- Pack and protect genetic signature
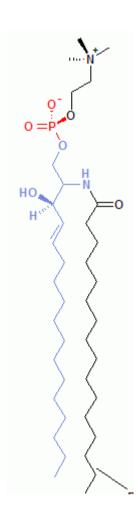- In water environment

Compartmentalization of life

- Pack and protect genetic signature
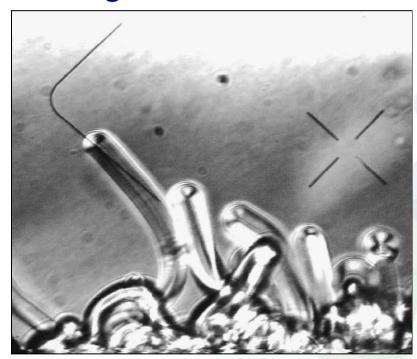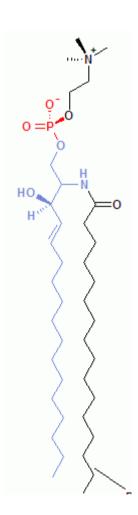- In water environment

Typical Phospholipid

1. Swelling in water

Add water to bulk lipid
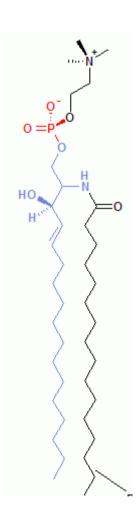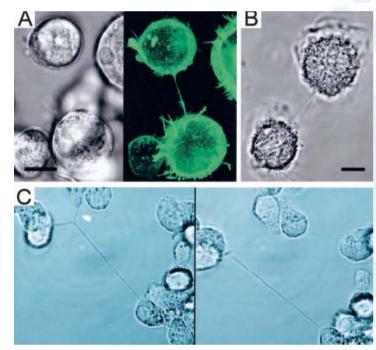*Chen, Schmidt, Olmsted, MacKintosh*

Typical Phospholipid

1. Swelling in water
2. Barrier for both hydrophilic and hydrophobic molecules
3. Fast passive transport of water

Typical Phospholipid

1. Swelling in water
2. Barrier for both hydrophilic and hydrophobic molecules
3. Fast passive transport of water
4. Fluid nature : nanotubes

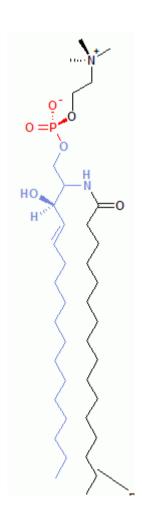Lipid nanotubes connecting human immune cells
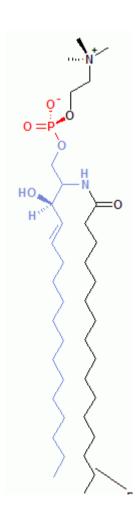*Onfelt et al, J. Immunology, 2004*

Sometimes you need skin

1. Land animals : How to maintain water level?
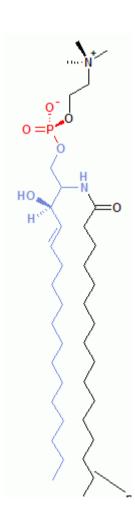
Sometimes you need skin

1. Land animals : How to maintain water level?
2. Lipid multilayers : What if it rains?

Sometimes you need skin

1. Land animals : How to maintain water level?
2. Lipid multilayers : What if it rains?
3. Can we shake hands without horizontal transfer of genes??

Human skin

Stratum Corneum

- Permeation through SC 3-5 orders of magnitude slower than phospholipid membranes.
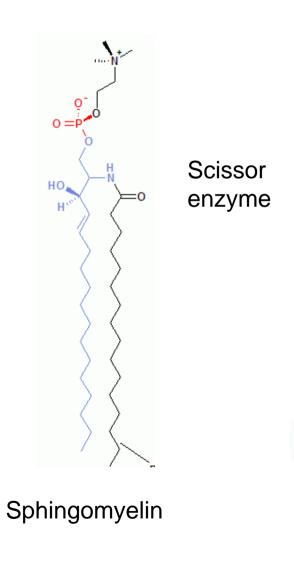- Allows warm bath and hand shakes!
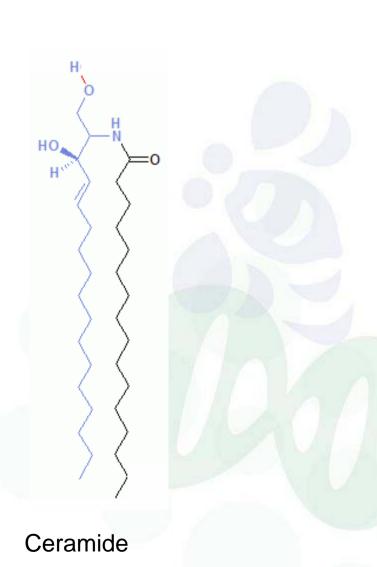
Composition

Sphingomyelin
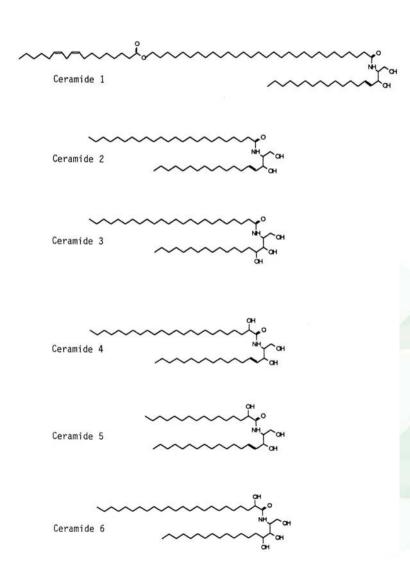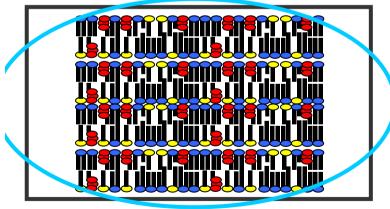
Don't throw away what works!

Composition

Sphingomyelin

Scissor enzyme

Ceramide

Composition

Ceramide 1

Ceramide 2

Ceramide 3

Ceramide 4

Ceramide 5

Ceramide 6

And the family

BECAUSE :
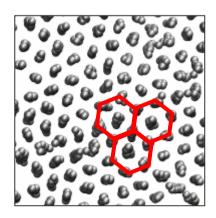
• All 3 components necessary for proper barrier function.

• Select most abundant representatives.
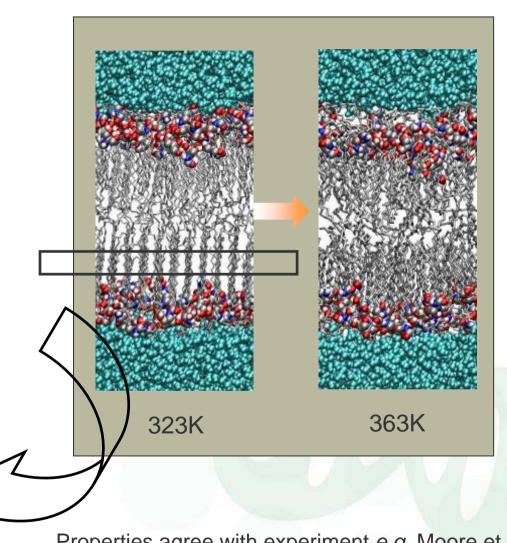

Cholesterol

Fatty Acid

Ceramide 2

Atomistic MD models

- "Gel" phase with hexagonally packed chains at 323K.
- Transition to fluid phase at 363K.
- Fluid region in centre of bilayer.
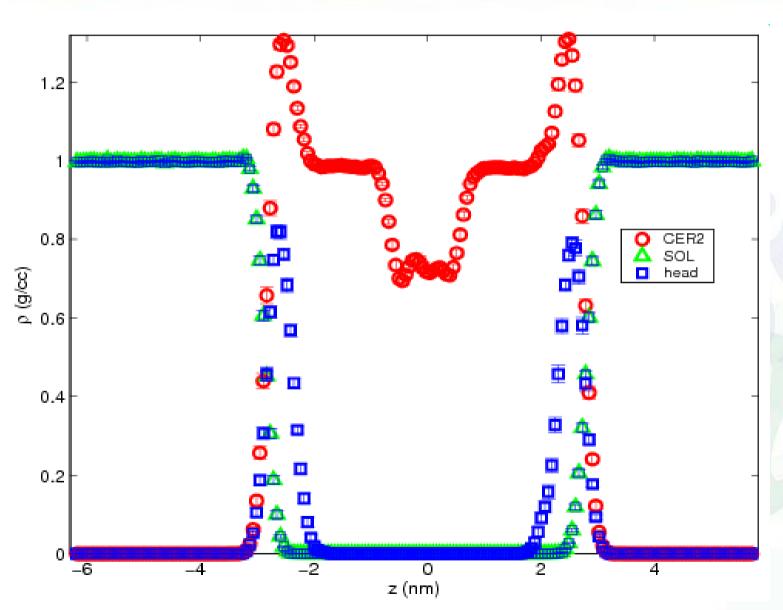- Bilayer thickness = 5.7 nm.
- Area per lipid = 0.37 nm^2.

323K   363K

Properties agree with experiment *e.g.* Moore et al. *J. Phys. Chem. B* **1997,** 101, 8933.
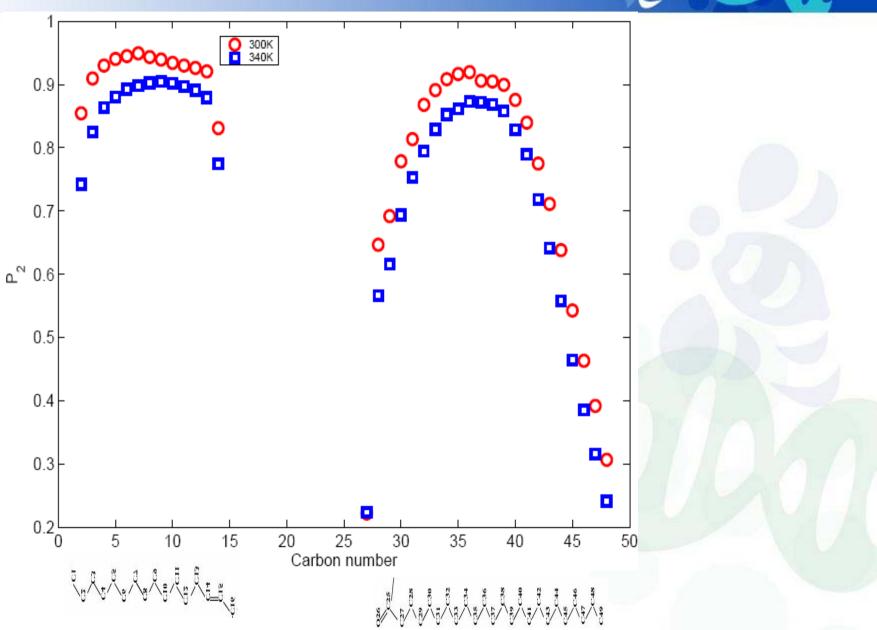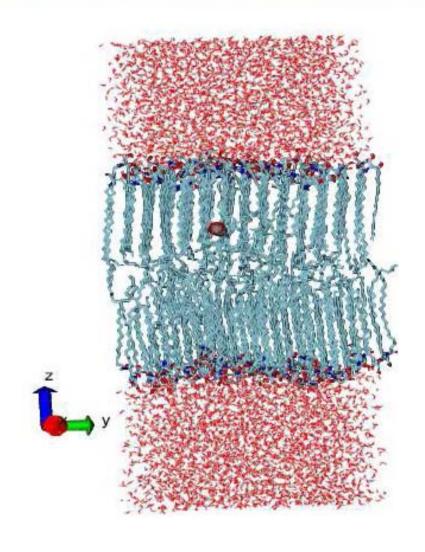
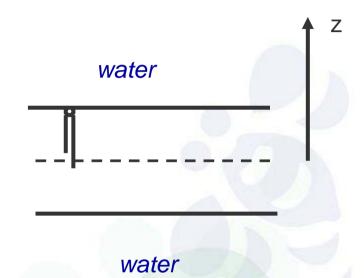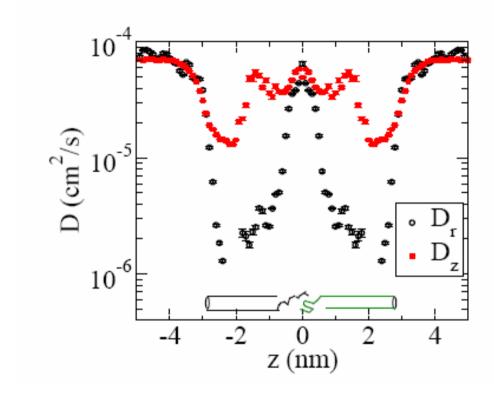# Density profile

Tail Order Parameter

Water Permeation

Water Permeation
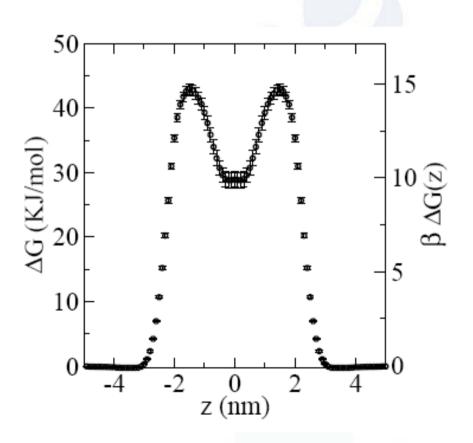

$$\frac{1}{P} = \int_{z1}^{z2} dz \frac{e^{\Delta G / RT}}{D_\perp}$$

Penetration coefficient is 3 orders of magnitude larger than DOPC;
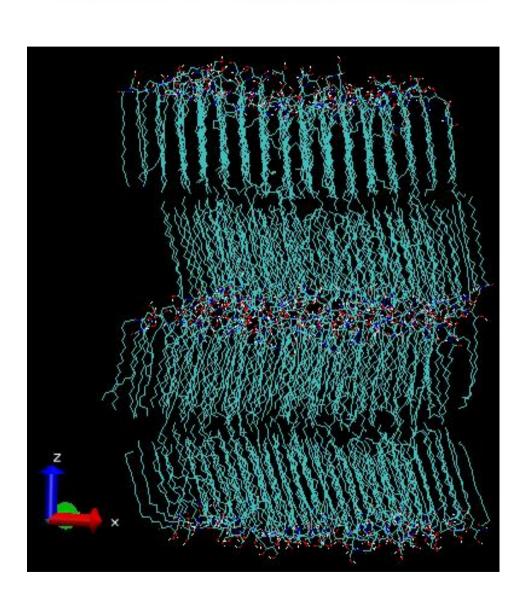
qualitatively right for skin permeation experiments

Dry Multilayer
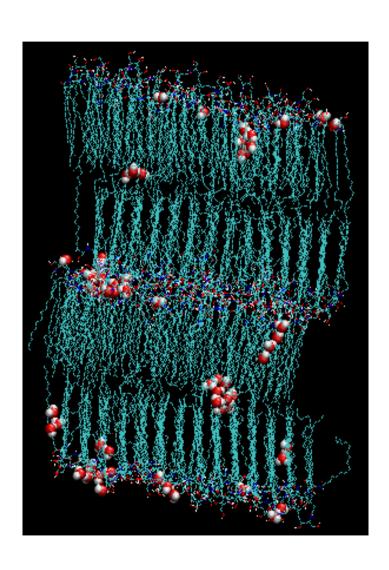
Strong hydrogen bond between bilayers.
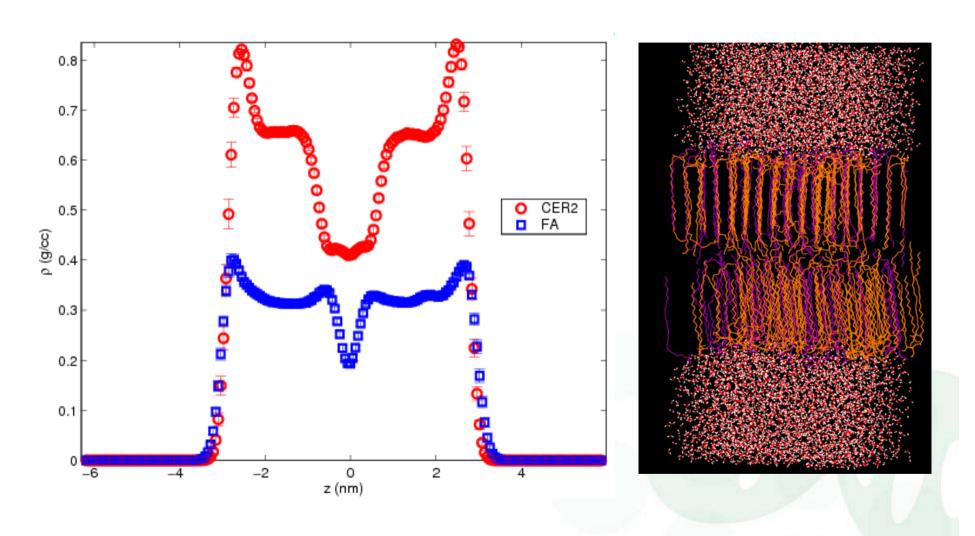
Hydration of a Multilayer

- Small amount of water prefer tail region.
- Large barrier for initial swelling.
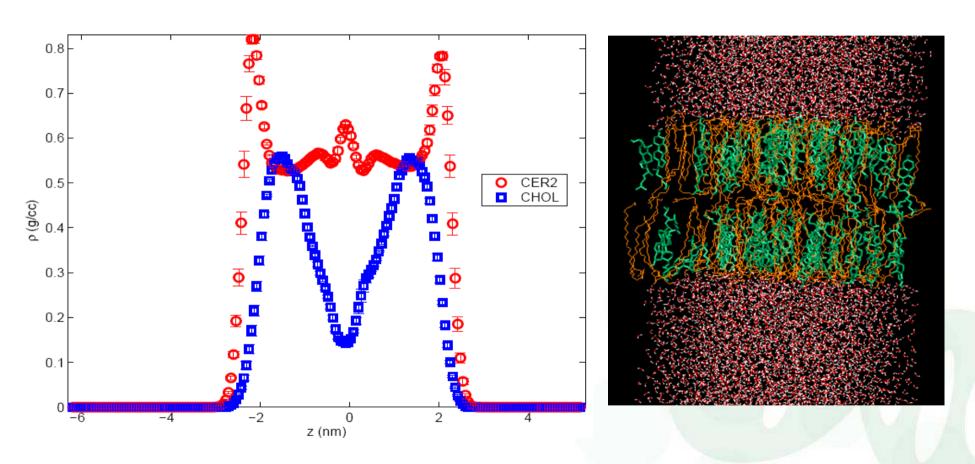
Ceramide + FA mixture

FFA aligns with CER tails and increases nematic order.
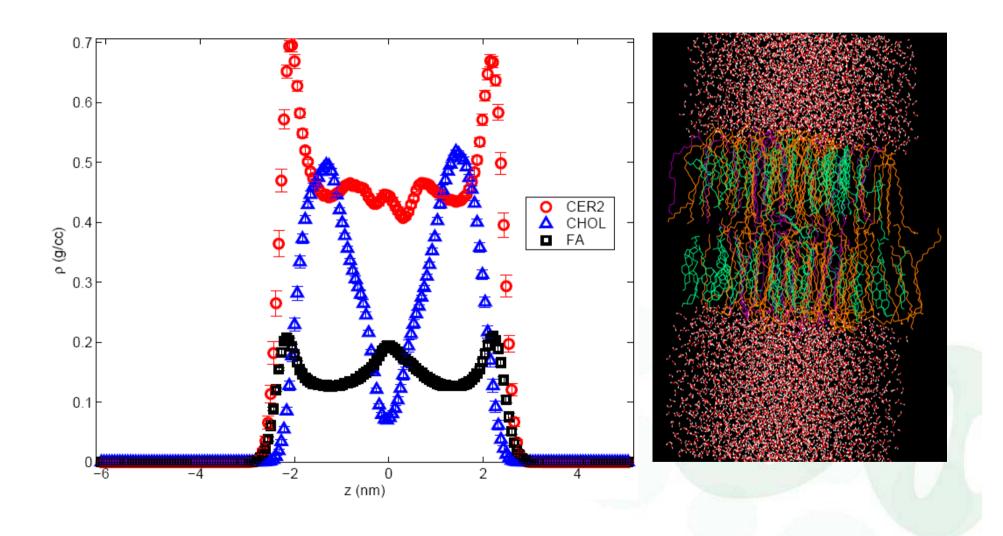
Ceramide + Cholesterol mixture

Rigid CHOL works as molecular clamp
(entropic clamp)
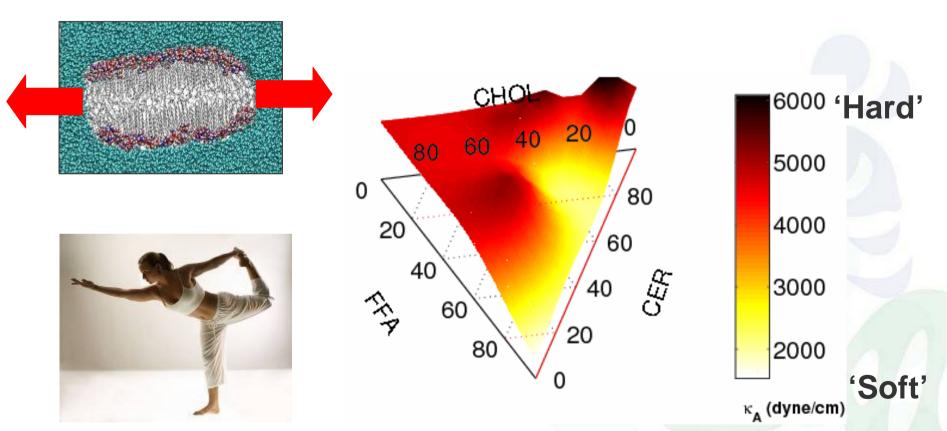
Cer + Chol + FA mixture (2:2:1)

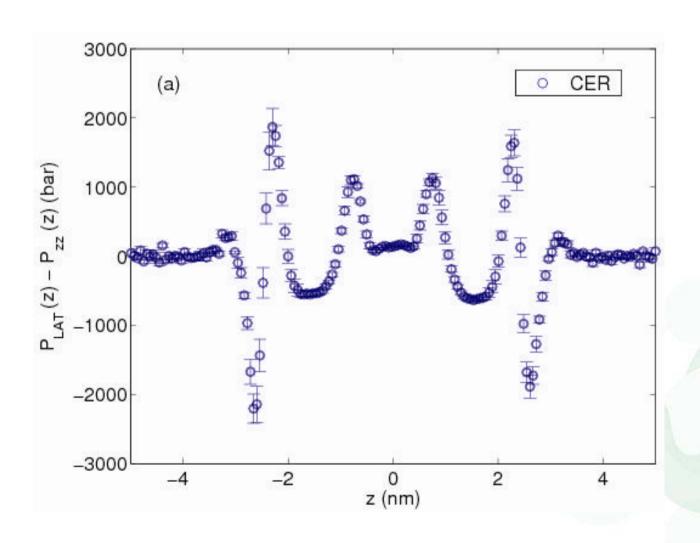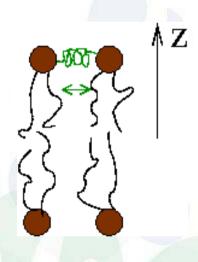# How far can it stretch ?

- Area compressibility modulus κ_A

'Hard'

'Soft'

κ_A (dyne/cm)

$$\kappa_A = k_B T \frac{<A>}{<A^2> - <A>^2}$$

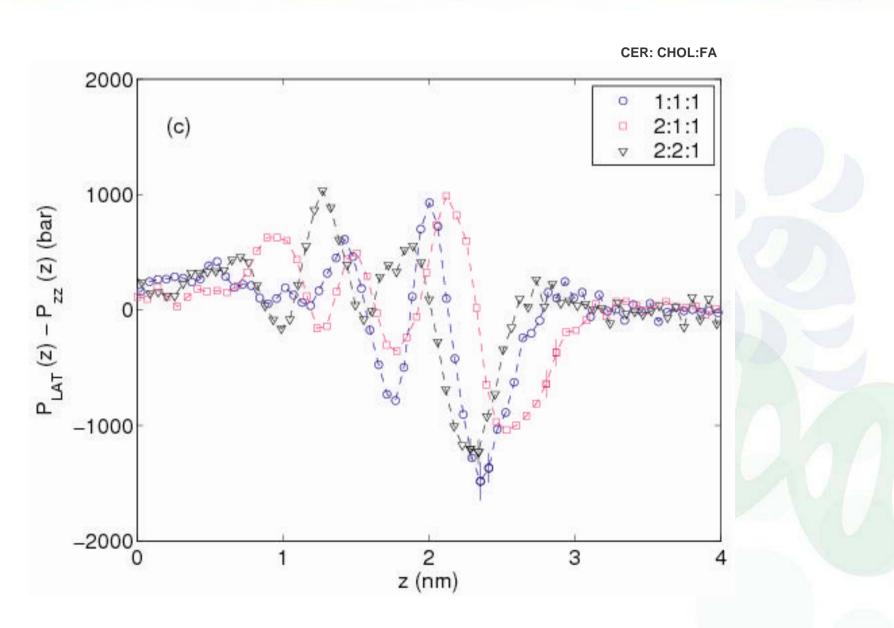# Pressure Tensor (components)

Pressure Tensor (mixture)

CER: CHOL:FA
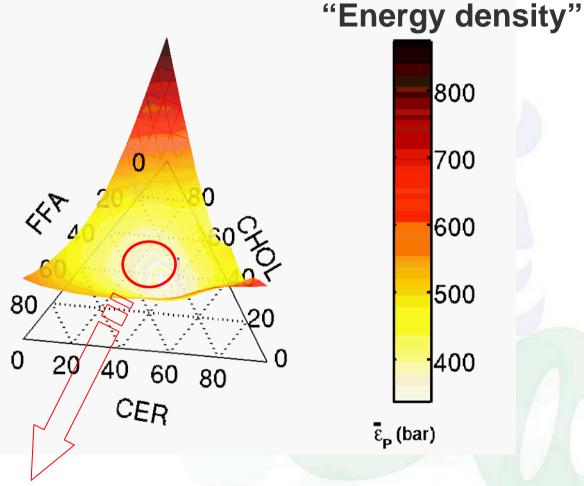
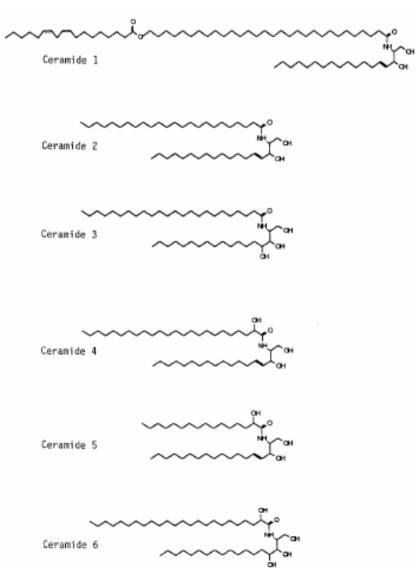**"Energy density"**

This is the natural composition of healthy skin

Density is high, but "stress" is low:
good barrier and mechanical properties.

$$\bar{\epsilon}_P = \frac{1}{2d} \int_0^{2d} dz \left[< (\delta P(z) - < \delta P(z) >)^2 > \right]^{\frac{1}{2}}$$
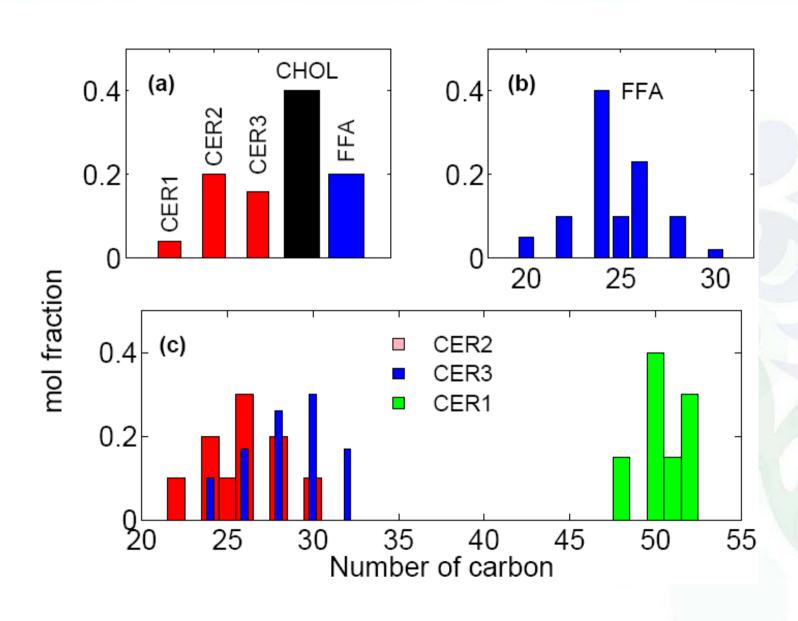
And the whole family, again
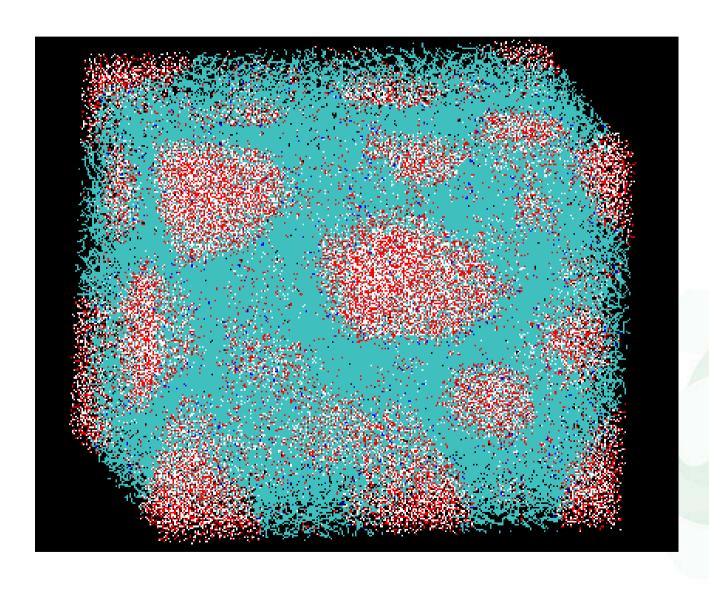
Polydispersity in chain length

Inverse micellar arrangement
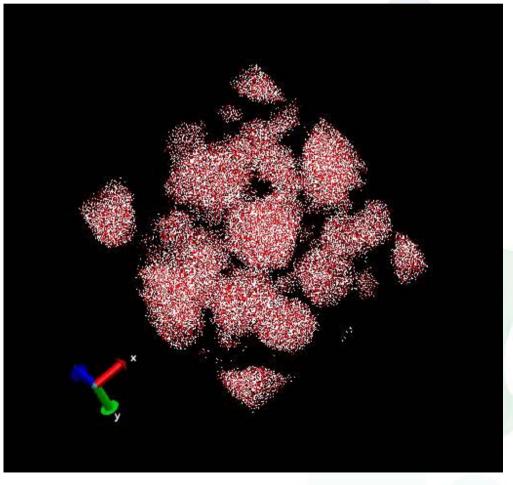
2000 CER
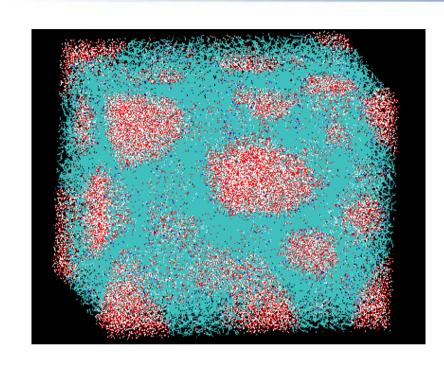2000 CHOL
1000 FFA
43600 SOL
$\sim3 \times 10^6$ atoms
~50 ns

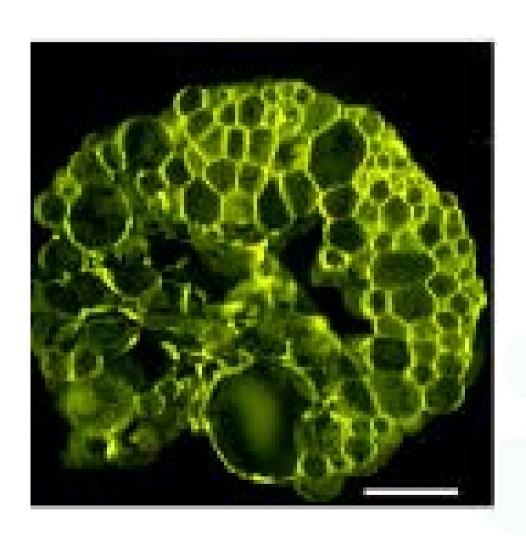# Inverse micellar arrangement

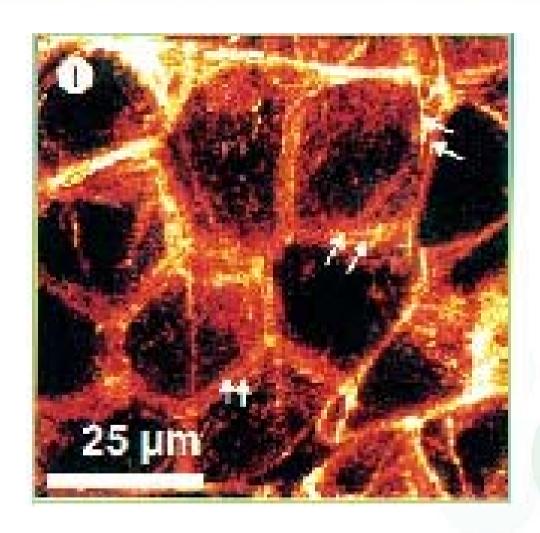# Inverse micellar arrangement

Confocal fluorescence 3D image of SC lipid : in vitro arrangement

Plasencia et al, Biophys J. (07)

Fault lines at the surface

*Schätzlein et al
B. J. Derm (98)*

Confocal laser scanning microscopy of Stratum Corneum : permeation evidence

Summary – Design Problem

- **Impermeable to water**

  Ceramides provide high density (wax like)
  Cholesterol improves packing and
  Fatty acid helps flatten the density profile

  (as boring and as effective as sand bags)

- **Mechanically stable**

  Low states of microscopic (mech.) energy density

  Can stretch easily

Inverse micellar phase :

Do multilayers arise from a wall effect ?

Is there preferential transport at fault lines ?

Thanks to:

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