Line activity of hybrid lipids: stabilization of membrane rafts?

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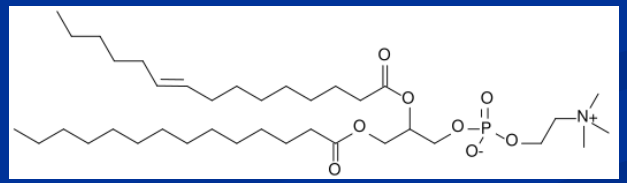
Hybrid lipids

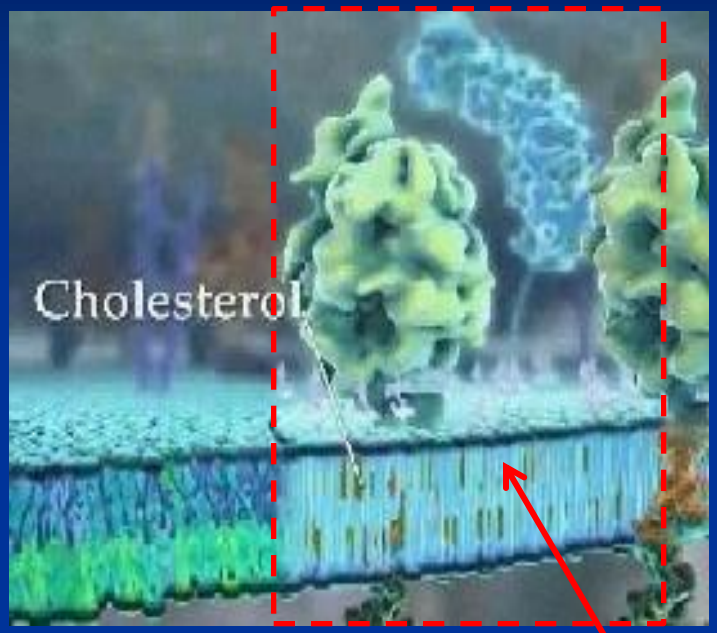
Unsaturated tail

POPC



Saturated tail

Lipid raft hypothesis – biological systems

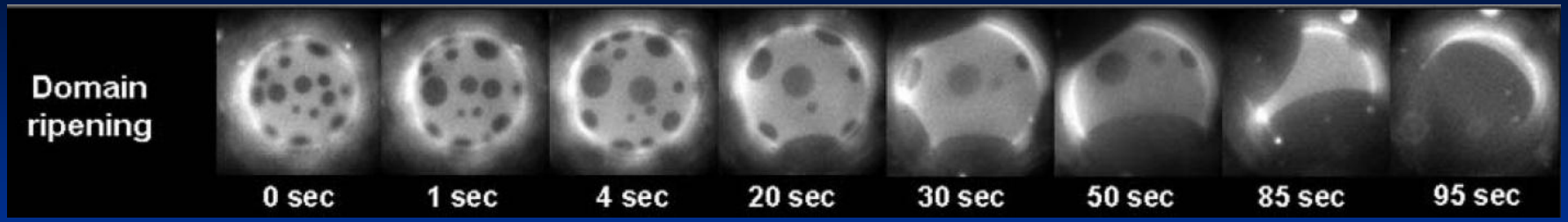


(From: The Inner Life of the Cell http://multimedia.mcb.harvard.edu/anim_innerlife.html)

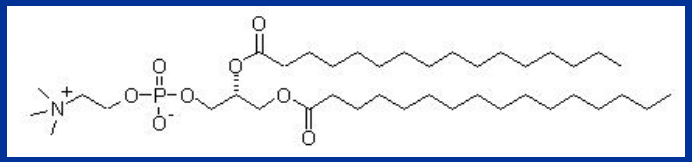
Lipid raft : small domains in biological membranes – controversial !

- Rich in saturated lipids
- Metastable or even stable
- The size of the domain is of the linear order of 10 – 100 nm.

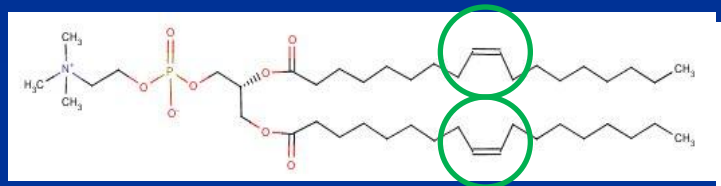
Domains in lipid vesicles – DPCC, DOPC



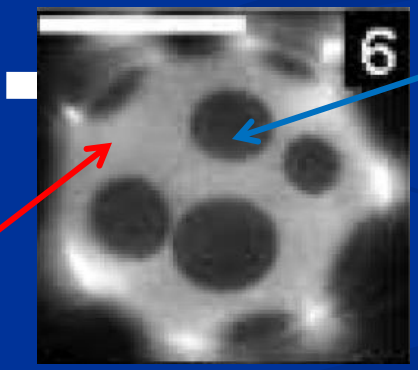
Saturated lipids, *e.g.* DPPC, S



Unsaturated lipids, *e.g.*,DOPC U



20 μm



L_d phase: Rich in U and lipid chains are disordered.

L_o phase: Rich in S and the lipid chains are ordered.

Veatch and Keller, BPJ, ***85****, 3074 (2003).*

Silva et al., submitted .

Phase separation: macroscopic or finite domains in lipid mixtures

- **Phase separation implies positive line tension: separate into macroscopic domains**

- **How can finite domains be stable (in equilibrium)?**

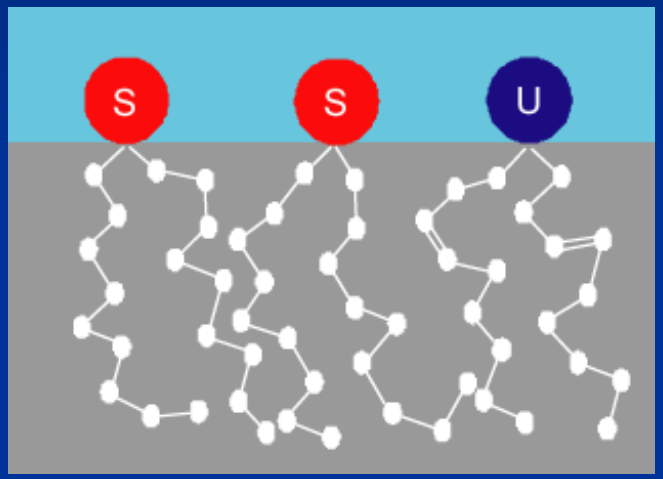
- **Line active species reduces interfacial free energy: line analogy of surfactants**
- **Here, "lineactant*" chains match the two phases: only chain packing needed to explain effect**

*lineactant:

D. Schwartz, PRL 2008

Chain packing theory of macroscopic phase separation

Chain packing “frustration” of saturated/unsaturated lipids is the driving force of phase separation of lipid membrane



- Phenomenological potential chain order
- Packing entropy
- Incompressibility of hydrophobic core

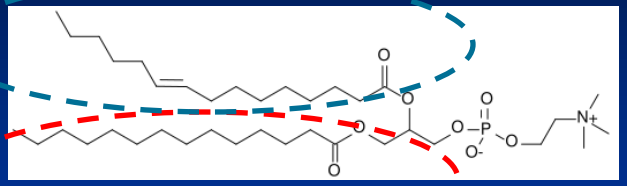
R. Elliot, I Szleifer, and M. Schick, PRL, 96, 098101 (2006).

Line activity of hybrid lipid: reduces packing frustration

Hybrid lipids 

Unsaturated tail

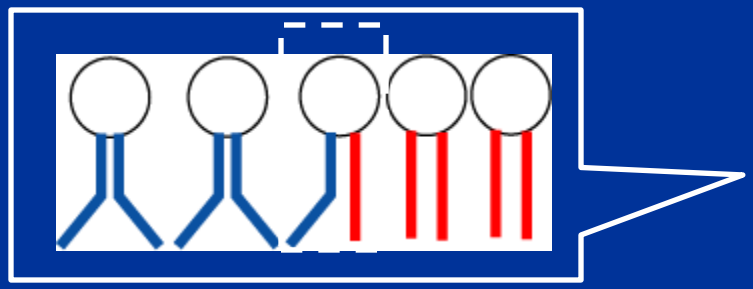
POPC



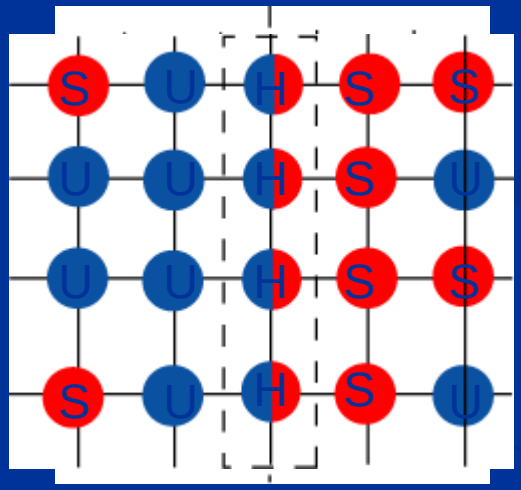
Saturated tail

Biologically abundant

Side view



Top view



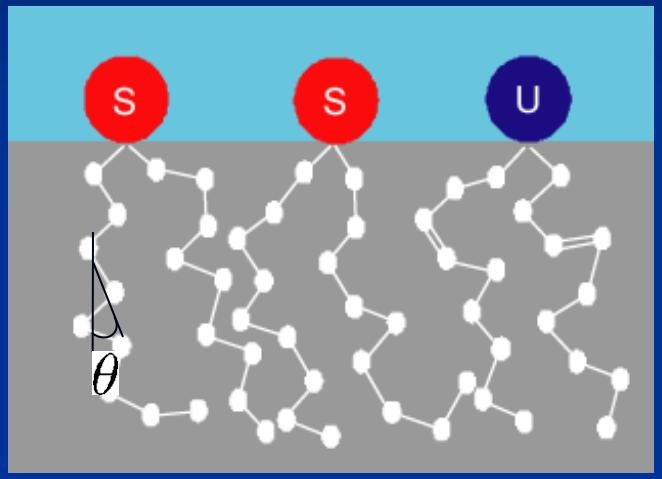
Line tension is reduced to zero for strong interaction (or low temperature).

R. Brewster, P. A. Pincus, and S. A. Safran, Biophys. J., ***97****, 1087 (2009) and R. Brewster, S. A. Safran, Biophys. J. Lett., in press.*

Objective

What is role of chain ordering in line activity of 

?



Liquid crystal order parameter

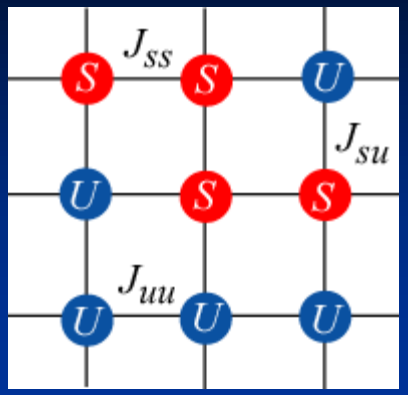
$$S = \langle \frac{3\cos^2\theta - 1}{2} \rangle \quad -0.5 \le S \le 1$$

θ: The angle between the bilayer normal and chain segment

Liquid crystal model to analyze how chain ordering drives phase separation and line activity of hybrid lipids

Lattice model for membrane without hybrid lipids

Lipids



Assumption:

The order parameter for U is ~ 0 , ($S_u \sim 0$), because entropy >> interaction.

Mixing entropy

$\psi(\mathbf{r})$: Local concentration of S

$$G_{\text{mix}} = k_B T[\psi(\mathbf{r}) \ln \psi(\mathbf{r}) + (1 - \psi(\mathbf{r})) \ln(1 - \psi(\mathbf{r}))]$$

Interaction energy

(favorable when neighboring chains are ordered - *only interactions due to chain ordering*)

$$G_{\text{int}} = -\frac{1}{2} J_{\text{ss}} \psi^2(\mathbf{r}) S_s^2(\mathbf{r})$$

$S_s(\mathbf{r})$: Chain order parameter for S

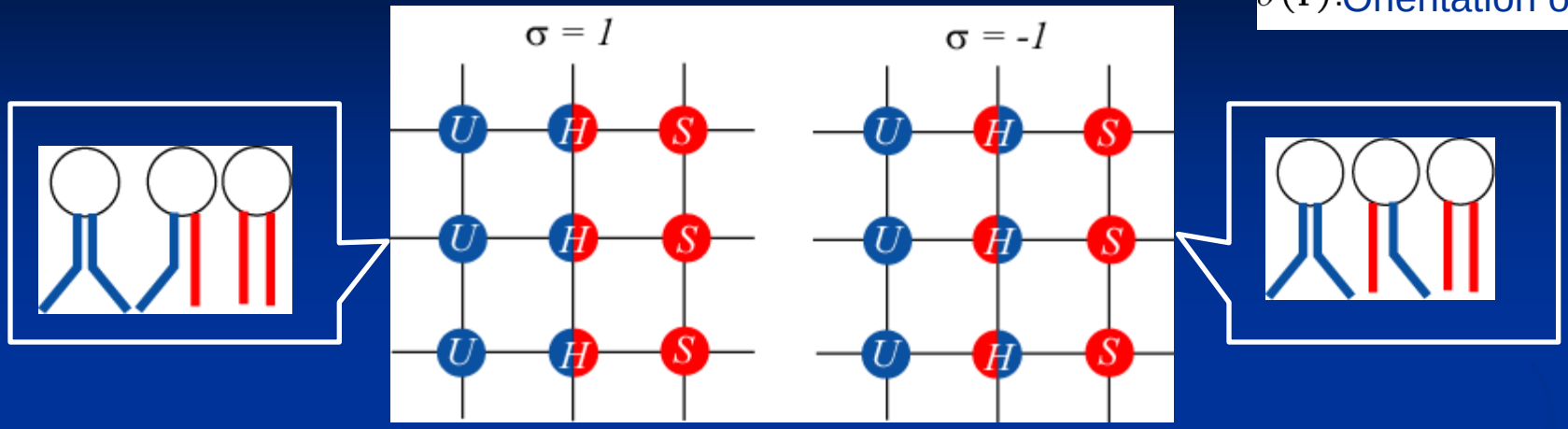
Entropy loss due to chain ordering

$$G_{\text{conf}} = 2k_B T[u_s S_s^4 - w_s S_s^3 + r_{0s} S_s^2]\psi(\mathbf{r})$$

P. G. de Gennes and J. Prost, The Physics of Liquid Crystals

Lattice model for membrane with H

$\sigma(\mathbf{r})$:Orientation of H



Orientation **dependent** part of the interaction energy

$$-\frac{1}{2}J_{ss}S_s(\mathbf{r})\psi_h(\mathbf{r})\sigma(\mathbf{r})\nabla(S_s(\mathbf{r})\psi(\mathbf{r}))$$

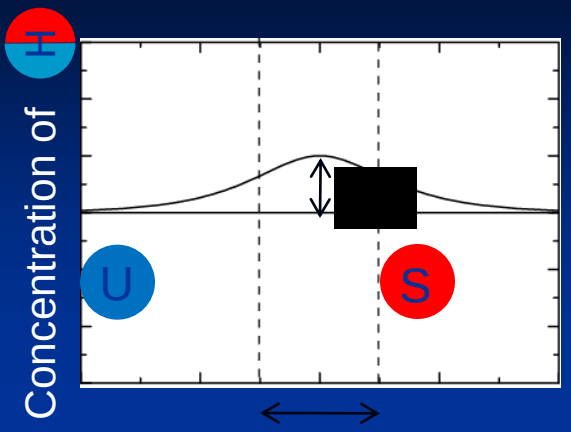
$\psi_h(\mathbf{r})$:

Local composition of H

Orientational entropy

$$k_BT[\frac{1+\sigma(\mathbf{r})}{2}\ln\frac{1+\sigma(\mathbf{r})}{2}+\frac{1-\sigma(\mathbf{r})}{2}\ln\frac{1-\sigma(\mathbf{r})}{2}]\psi_h(\mathbf{r}).$$

Weak interaction (high temperature)



$\bar{\psi}_h$:bulk H concentration

Line tension $\lambda = \lambda_0 \sqrt{1 - \alpha \psi_h^{\mathrm{int}}}$ $\alpha > 0$

λ_0 :Line tension for S + U system with no hybrid

However, concentration of H adsorbed at interfaces is not enough to reduce the line tension to zero near critical point.

Strong interaction (low temperature)

Line tension

$\psi_h^{\text{int}} \to 1$

$\sigma \to 1$

Width of interface ξ ~ Molecular size

Complete orientation

$$\lambda \sim -\frac{1}{2} J_{\text{ss}} S_{\text{int}} - k_B T \ln \bar{\psi}_h$$

> 0

$\bar{\psi}_h$ Average of  in the bulk.

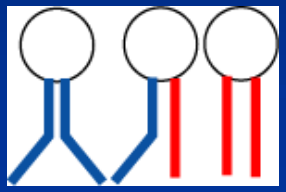
S_{int} Chain order parameter of hybrid at the interface ~ 1

- Line tension is reduced to 0 with decreasing temperature
- Loss of mixing entropy limits this effect to low temperatures

- Interfaces between domains stabilized by hybrid!
- What is the stable size of the domains?

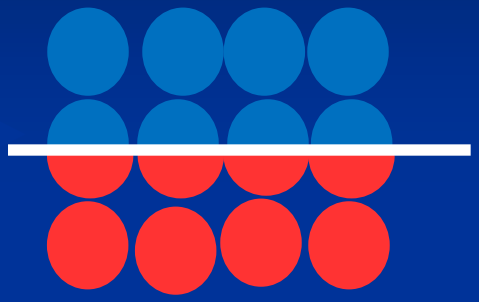
Domain size: 2D spontaneous curvature

Side view



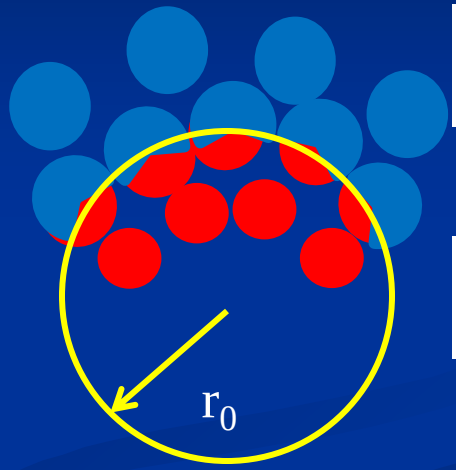
Top view

$\kappa_0 = 0$



κ_0 : Optimal curvature.

$\kappa_0 = -1/r_0$



disordered chain

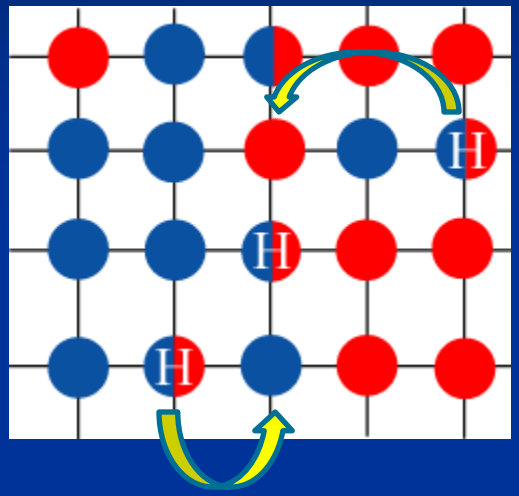
ordered chain

- Spontaneous curvature determines radius of domains stabilized by 
  .
- Subject to conservation constraints of S, U, and H (microemulsion)

- R. Brewster, SAS: Biophys. J. Lett., in press

Hybrid lipid more effective in line tension reduction in S+H

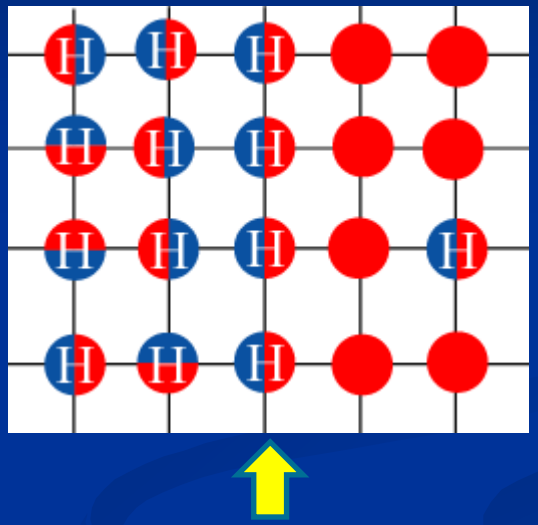
S + U membrane + H



Must bring H to interface

Cost mixing entropy:
Only effective at low T

S + H membrane

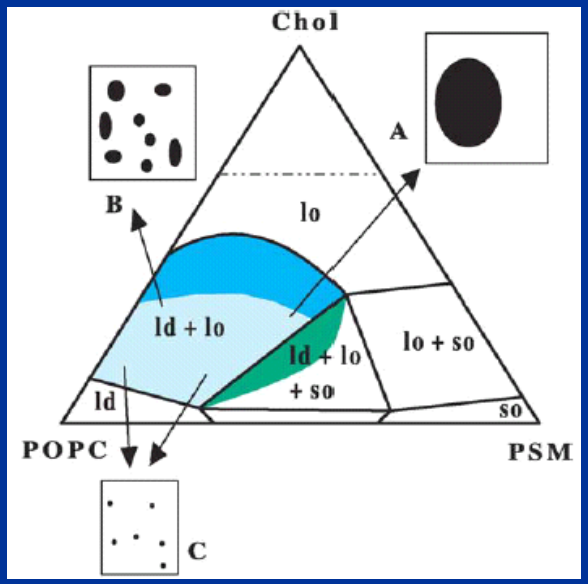


H is already there!

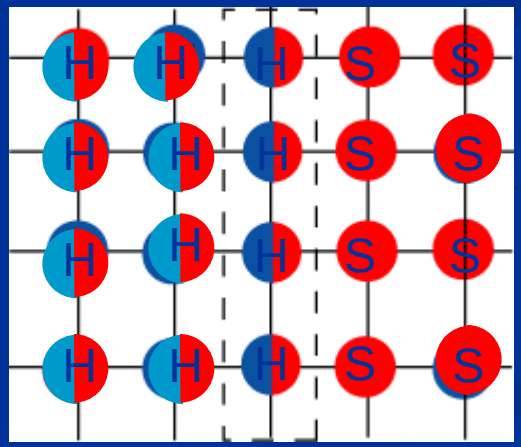
No mixing entropy cost:
Effective even near the onset of the phase separation ($T \sim T_c$)

Hybrid + Saturated Lipids

- Hybrid saturated chain can have different order states
- In bulk (surrounded by other H) can be disordered
- Near interface with S phase will be more ordered
- Hybrid is line active in 2 component system due to the internal degree of freedom of chain order



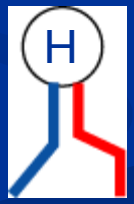
(Almeida et al., JMB 2005)



bulk: saturated chain of H disordered
interface: saturated chain of H ordered
H can be line active

Line active

Bulk



Expts: Hybrid + Saturated

- Macroscopic or small domains
  - S+U+C clearly macroscopic
  - S+H+C ???

- Membranes of POPC, Palmitoyl SM, and cholesterol phase separate, in large domains
  (Veatch and Keller PRL 94, 148101 (2005)

- Type I (sat, unsat, chol) – macroscopic phase separation
  Type II (sat, hybrid, chol) – nanometric domains
  (Feigenson, Biochimia Biophys Acta, 2009)

- Ziblat et al. – POPC needed to stabilize the membrane for experiments

Almeida et al., JMB 2005
Silva et al. – to be published