UNITED NATIONS EDUCATIONAL, SCIENTIFIC AND CULTURAL ORGANIZATION
INTERNATIONAL ATOMIC ENERGY AGENCY
INTERNATIONAL CENTRE FOR THEORETICAL PHYSICS
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SMR.961 - 9

WORKSHOP ON:
PROTEINS, MEMBRANES and their INTERACTIONS

22 JULY - 2 AUGUST 1996

"Single-chain mean-field theories of chain packing in amphiphilic aggregates"

PART I

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Theoretical Approaches to Chain Packing in Amphiphilic Aggregates

Single-Chain Mean-Field Theories:

a) Molecular Organization:

Packing in one and two component aggregates

b) Thermodynamic Properties:

Free energy, lateral pressures.

Elastic Constants of Amphiphilic Bilayers:

a) Phenomenological expressions.

b) Microscopic determination of k, $\bar{k}$ and c_0.

Tethered Polymer Layers:

a) Structural and Thermodynamic Properties

b) Prevention of Protein Adsorption.

Reviews on theories of chainpacking and elasticity

1) Ben-Shaul A, Gelbart W.M.: *Theory of Chain Packing in Amphiphilic Aggregates*. In Ann. Rev. Phys. Chem, 1985. 36:179-211.

2) Ben-Shaul A, *Molecular Theory of Chain Packing, Elasticity and Lipid-Protein Interaction in Lipid Bilayers*. In Structure and Dynamics of Membranes. Edited by Lipowsky R, Sackmann E. Elsevier, 1995, 1A:359-401.

Reviews on tethered polymers, structure, thermodynamics and elasticity

3) Milner ST: *Polymer brushes*. Science 1991, 251:905-914.

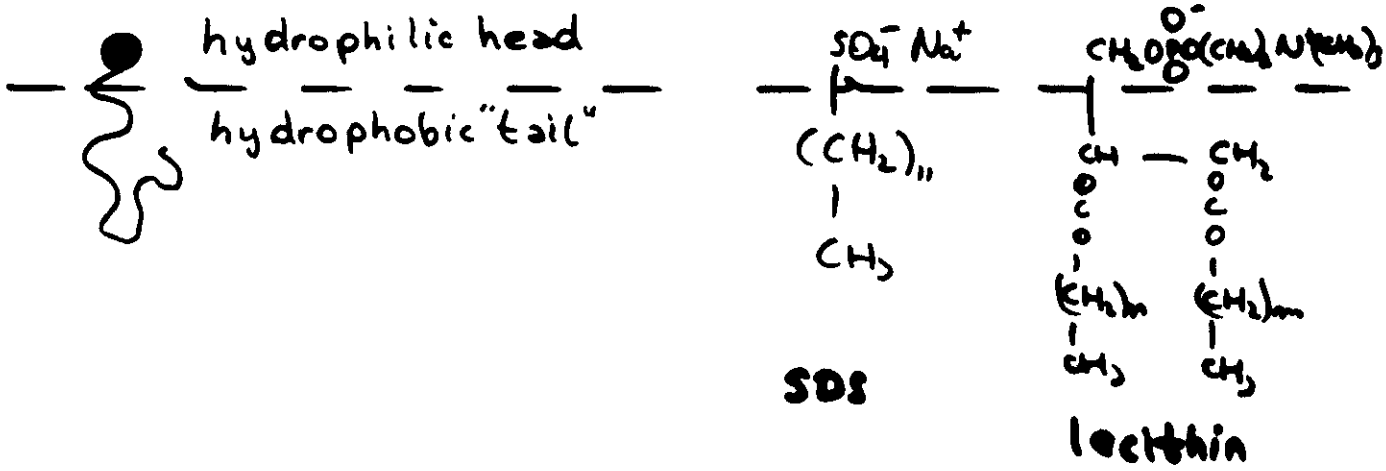
4) Halperin A: *On Polymer brushes and blobology. An introduction.* In Soft Order in Physical Systems. Edited by Rabin Y, Bruinsima R. New York: Plenum press; 1994:33-56. [NATO ASI Series B: Physics, vol 323.]

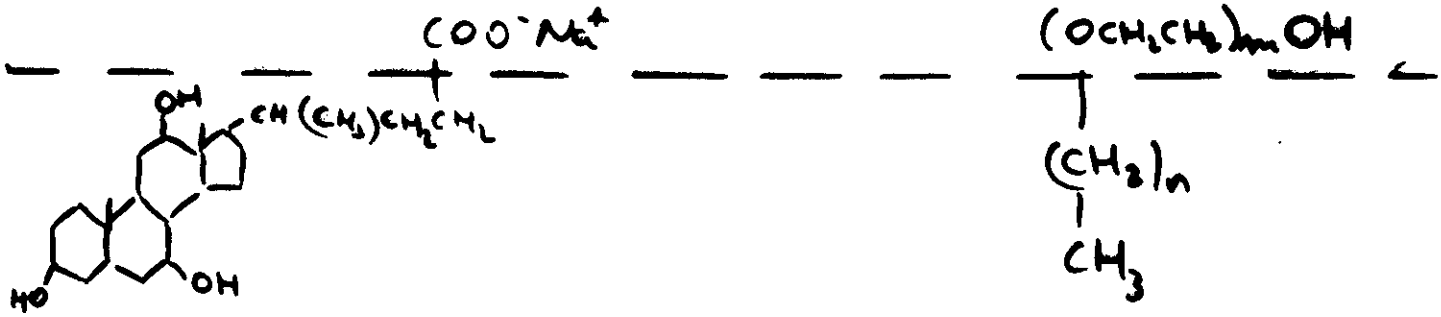
5) Grest GS, Murat M: *Computer simulations of tethered chains*. In Monte Carlo and Molecular Dynamics Simulations in Polymer Science. Edited by Binder K. New York: Oxford Press; 1995:476-569.

6) Szleifer I, Carignano MA: *Tethered polymer layers*. In Advances in Chemical Physics, vol XCIV. Edited by Prigogine I, Rice SA. New York: John Wiley and Sons; 1996:165-259.

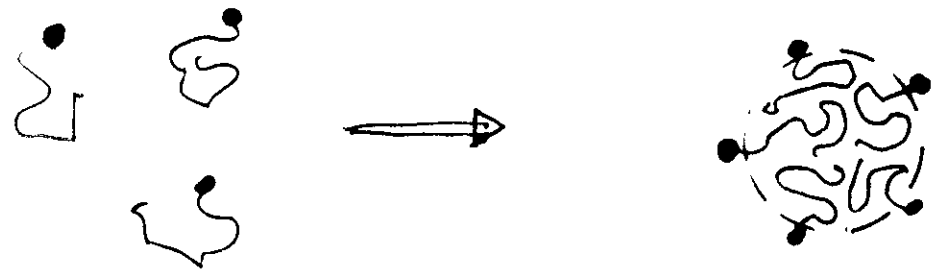
7) Szleifer I, *Statistical thermodynamics of polymers near surfaces*. In Current Opinion in Colloid & Interface Science. 1996, 1:416-423.

Amphiphilic molecules (surfactants)



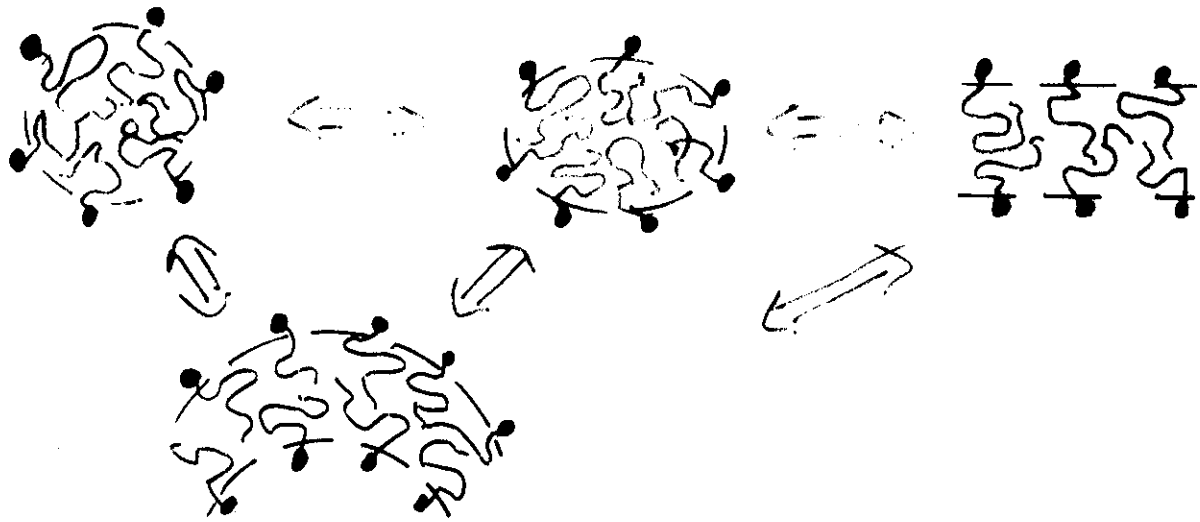


Hydrophobic effect ⟶ Aggregation



Free energy change ~ kT/CH_2 !!

Shape changes



Free energy change ~ 0.1 - 1.0 kT/molecule !!

Mass Action Model:

Equilibrium of aggregates of different sizes (and shapes) implies:

Equal chemical potentials: in dilute solution

$$\mu = \mu_n = \mu_n^\circ + \frac{kT}{n} \ln\left(\frac{X_n}{n}\right) = \text{const.}$$

$n = 1, 2, 3, \ldots$

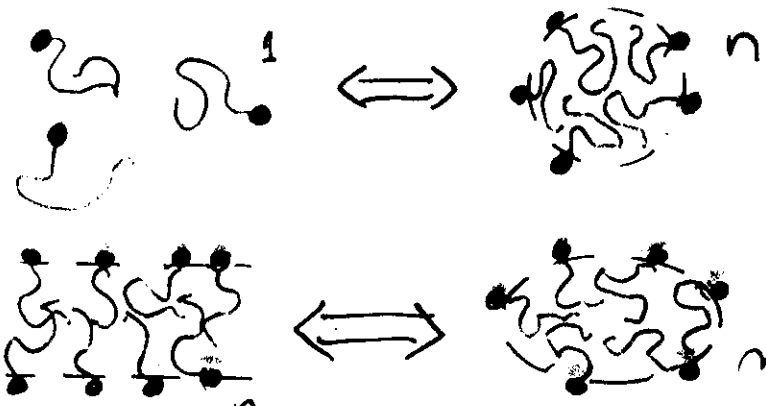
$$X_n = n\left\{ X_1 \exp\left[- \frac{\mu_n^\circ - \mu_1^\circ}{kT} \right] \right\}^n$$

or

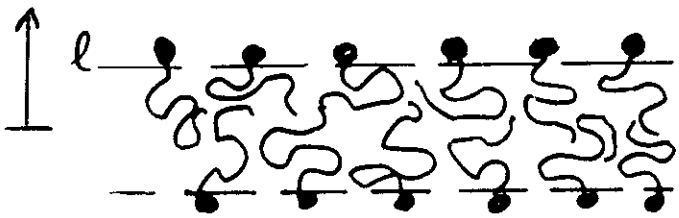
$$X_n = n\left\{ \frac{X_m}{m} \exp\left[\frac{m(\mu_m^\circ - \mu_n^\circ)}{kT} \right] \right\}^{n/m}$$

$\mu_n^\circ - \mu_1^\circ \sim kT/CH_2$ for micellar n

$\mu_n^\circ - \mu_m^\circ \sim 0.1 - 1.0\ kT$/molecule



Free energy contributions:



Surface tension → minimize water-hydrocarbon contact: $f_{ST} = \gamma a(l)$, γ = water-oil surface tension

Head-group interactions:

hard-core (2D) repulsions: $f_{HC} = kT \ln(a - a_h)$

a_h = hard-core excluded area (parameter)

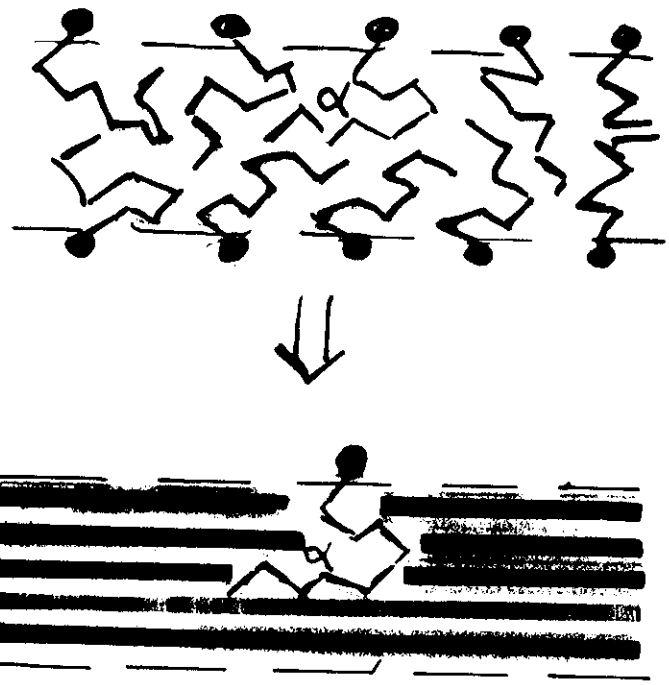
Electrostatic contributions:

(i) Poisson-Boltzmann equation

(ii) Phenomenological models: e.g. capacitor model $f_{el} = \frac{c}{a}$, c = phenomenological const.

Chain Packing:

Single-Chain Mean-Field Theories:



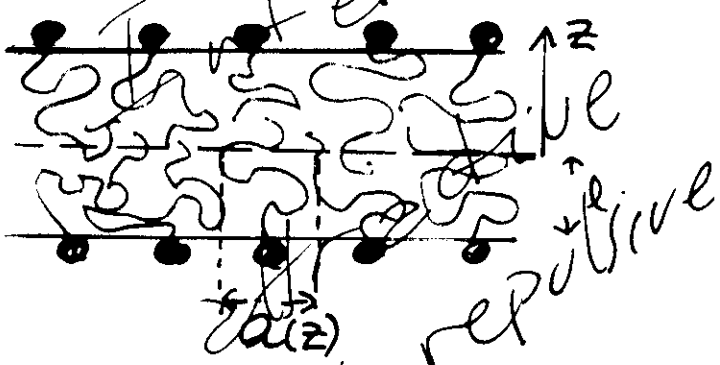
Find $P(\alpha)$!!

$P(\alpha)$ is a function of area per molecule, geometry of aggregate, type of chain system, etc.

From $P(\alpha)$ any desired average (single-chain) conformational and thermodynamic property can be calculated! $\langle A \rangle = \sum_{\alpha} P(\alpha) A(\alpha)$

Assumption:

(c) Hydrophobic core has uniform (CH_2) segment density. $\Longrightarrow$ packing constraints!!



The "volume" occupied (on average) by the tails must be equal to the available volume

$$\sum_{\alpha} P(\alpha)\, a(\alpha, z) = a(z)\,dz \quad \text{for } -l \le z \le l$$

Now how do we find $P(\alpha)$?

1) Minimize tails free energy subject to packing constraints!!

Tail's free energy:

$$\beta f_t = \underbrace{\sum_\alpha P(\alpha) \ln P(\alpha)}_{\text{conformational entropy}} + \underbrace{\sum_\alpha P(\alpha) E_{int}(\alpha)}_{\text{internal energy}}$$

Minimizing subject to: $\sum_\alpha P(\alpha) n(\alpha, z) N_0 = a(z) dz$

Result (introducing Lagrange multipliers $\beta\Pi(z)$):

$$P(\alpha) = \frac{1}{q} e^{-\beta E_{int}(\alpha) - \beta \int_0^\ell \Pi(z) n(\alpha; z) dz}$$

$\Pi(z)$ are the lateral pressures that "force" the tails to fulfill packing constraints.

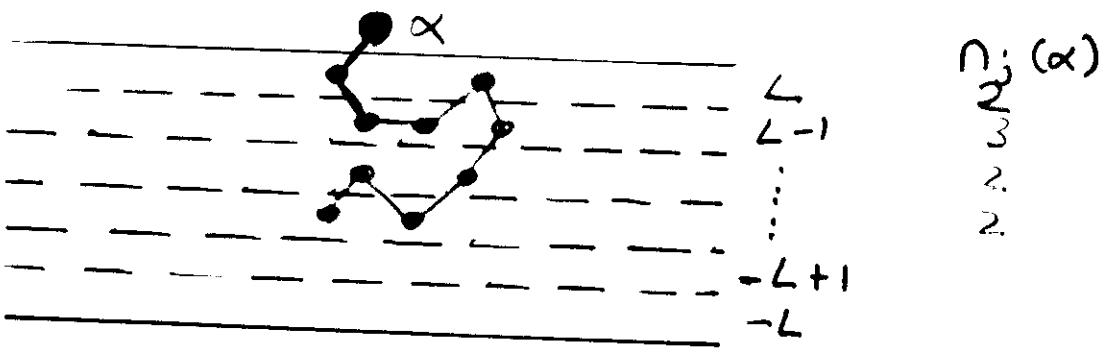
They are the "mean-field" repulsive interactions of the neighboring molecules on the central tail.

How do we get $\Pi(z)$?

Replace pdf, $P(N)$, into constraint equation

$$\sum_{\alpha} \frac{e^{-\beta \mathcal{E}_{int}(\alpha) - \beta \sum \Pi_i n_i(\alpha)}}{q} \; n_j(\alpha) = m_j \qquad j = -L, -L+1, \ldots, L-1, L$$

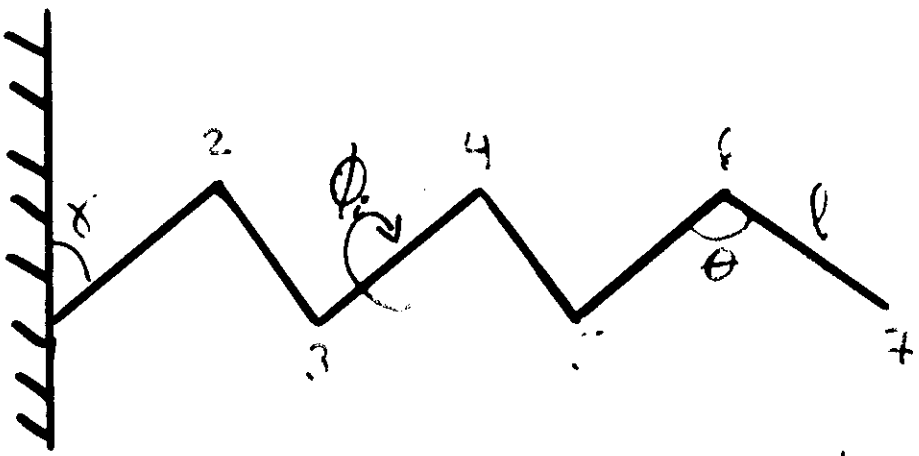
$$q = \sum_{\alpha} e^{-\beta \mathcal{E}_{int}(\alpha) - \beta \sum \Pi_i n_i(\alpha)}$$



Input: set of single chain conformations (1 chain model), average over permutations of interface and geometry.

Solve set of non-linear equations for Π_i.

Rotational isomeric state model:



θ is fixed, l is fixed, ϕ_i can be: 0° (trans)

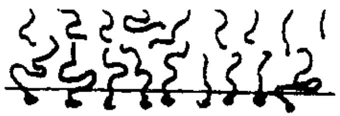
+120° (gauche +), −120° (gauche −)

The chains are fully flexible, i.e. we assume that there is no energy difference between the three possible states of each bond.

Total number of configurations is 3^{N-2}, only self avoiding are accepted.

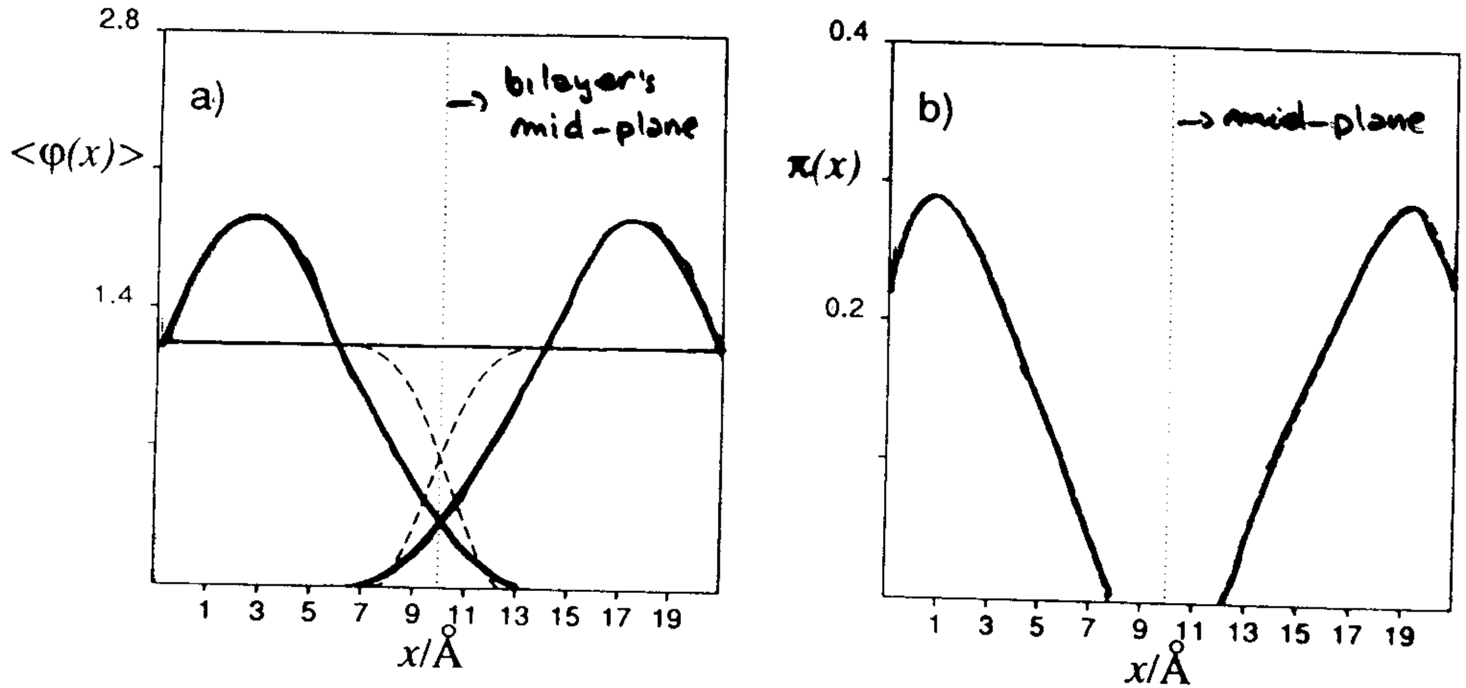
Results are obtained with respect to the end-to-end.

For $N = 50$ we generate 2.95×10^6 single chain configurations (that are self avoiding also with the surface)

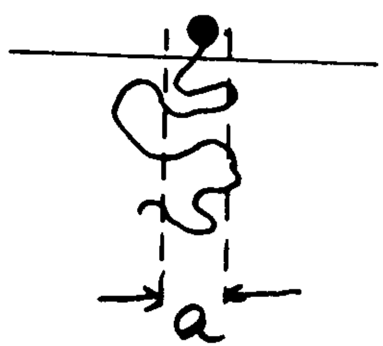


$H-(CH_2)_{11}CH_3$ packed in planar bilayer

$a = 33 Å^2$



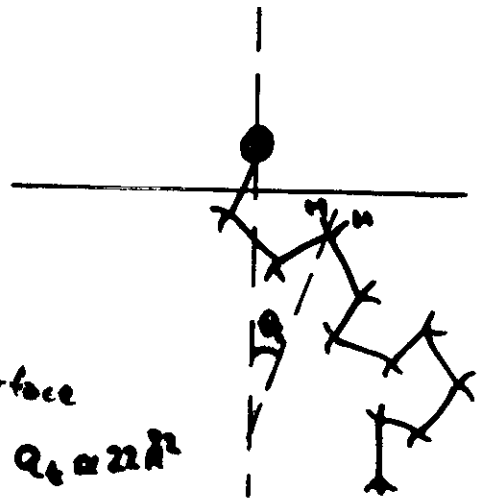
free chain: same boundary cond.
but no packing const. ⇒ $\pi(x) \equiv 0$ for all x



Planar Bilayer

$$H-(CH_2)_8-CH_3$$

$$S_{C_iH} = \frac{3}{2}\langle \cos^2\theta_i \rangle - \frac{1}{2}$$



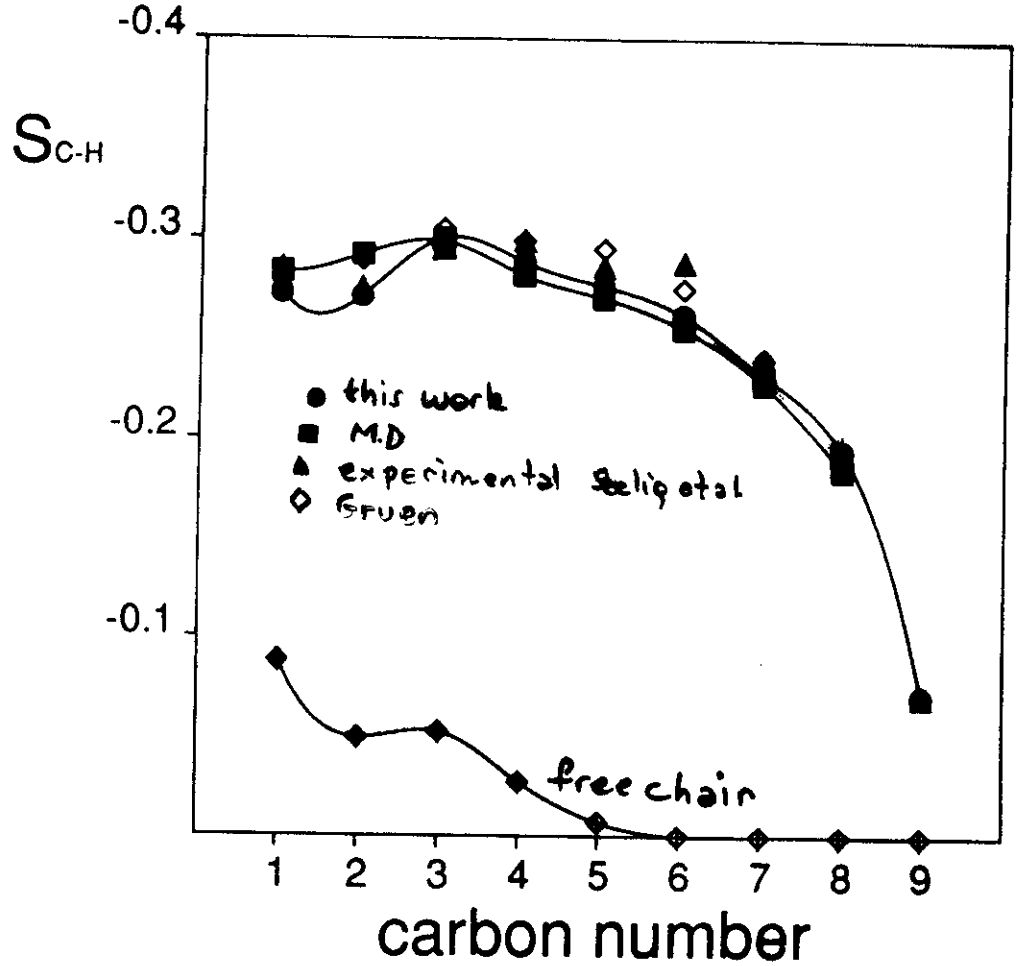
$S_{C_iH} = 0$ random distribution

$S_{C_iH} = -0.5$ bond parallel to the interface

theoretical results for $a = 25\text{Å}^2$ $a_0 = 22\text{Å}^2$

$T = 300\text{K}$

$E_g = 700 \frac{\text{cal}}{\text{mole}}$



Thermodynamics:

MD	$f_c = -2.62 k_0 T$	$S \simeq 4.37k$	$\langle \epsilon \rangle = 1.75kT$
This work	$= -2.55 k_0 T$	$\simeq 4.23k$	$= 1.69kT$

Marcelja's theory:
extension of Maier-Saupe theory of liquid crystals.

$$P(\alpha) = \frac{e^{-\beta E_{int}(\alpha)}}{q} \; e^{-\beta v_0 \eta \sum_{i=1}^{n-1} P_2[\cos\theta_i(\alpha)]/(n-1)}$$

$$P_2[\cos\theta_i(\alpha)] = \frac{3}{2}\cos^2\theta_i(\alpha) - \frac{1}{2} \quad ; \quad v_0 = -700 \frac{cal}{mol}$$

$$\eta = \left\langle \sum_{i=1}^{n-1} P_2(\cos\theta_i) \right\rangle / (n-1)$$ self-consistent condition!

1) gel-liquid crystal phase transition

2) order parameters in bilayers.

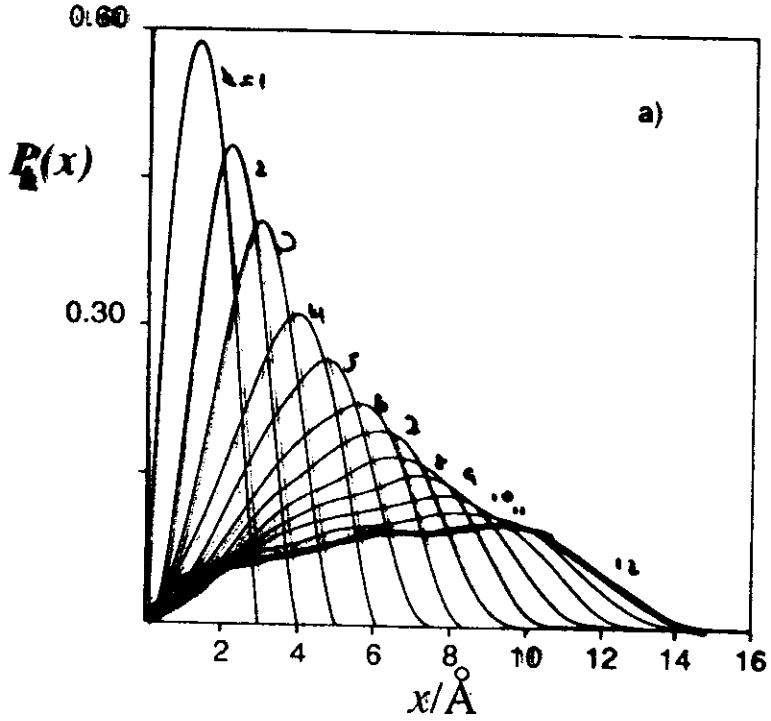
Gruen: (i) replace η by η_i

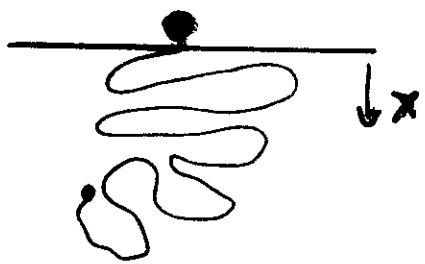
(ii) for general geometries postulates

$$P(\alpha) = \frac{e^{-\beta E_{int}(\alpha)}}{q} \; e^{-\beta \int \pi(z) V(z,\alpha) dz}$$

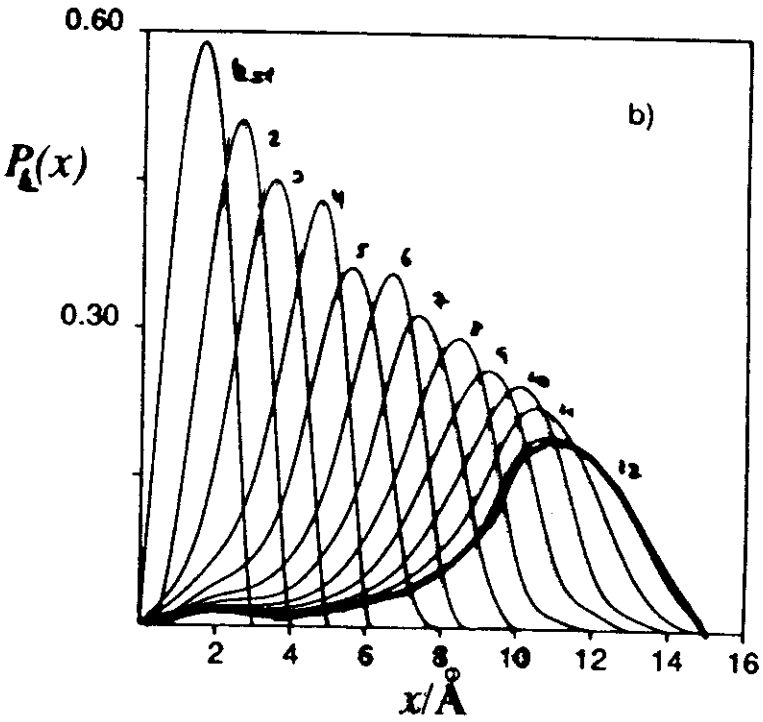
$H-(CH_2)_n-CH_3$

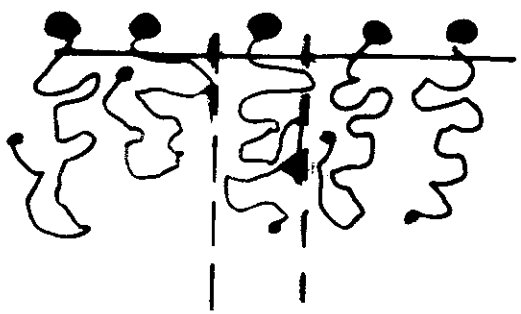
free chain





constrained chain $a = 33\,\text{Å}^2$





"Self-Consistent field" theory:

Replace $P(\alpha)$ by a random walk in the field $\Pi(z)$.

Green's function:

$$G(z', z''; s) = \sum_{\alpha} \delta_{z', z_1(\alpha)} \, \delta_{z'', z_{s+1}(\alpha)} \, e^{-\sum_z \Pi(z) n(z;\alpha)}$$

Recurrence relation (for cubic lattice)

$$G(z; z''; s) = e^{-\Pi(z'')} \left[\frac{4}{6} G(z; z''; s-1) + \frac{1}{6} G(z'; z''+1; s-1) \right.$$

$$\left. + \frac{1}{6} G(z', z''-1; s-1) \right]$$

Initial condition

$$G(z' z'', 0) = \delta_{z', z''} \, e^{-\Pi(z'')}$$

Density profiles:

$$\phi(z) = \frac{1}{G} \sum_{s=1}^{n} \frac{G(1, z; s-1) \sum_{z'} G(z, z'; n-s)}{e^{-\Pi(z)}}$$

Normalization:

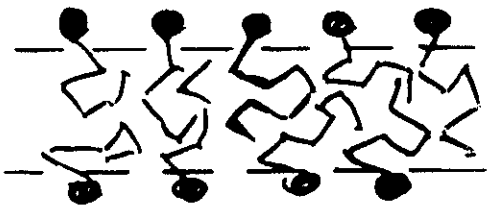
$$\sum_z \phi(z) = \frac{N_\epsilon n}{A}$$

Formal derivation of $P(\alpha)$

$$P(\alpha_1, \alpha_2, \cdots, \alpha_{N_c}) = \frac{e^{-\beta U(\alpha_1, \alpha_2, \cdots, \alpha_{N_c})}}{Q(N_c, V, T)}$$

$$Q(N_c, V, T) = \sum_{\alpha_1} \sum_{\alpha_2} \cdots \sum_{\alpha_{N_c}} e^{-\beta U(\alpha_1, \alpha_2, \cdots \alpha_{N_c})}$$

$$P(\alpha_1) = \frac{\sum_{\alpha_2} \cdots \sum_{\alpha_{N_c}} e^{-\beta U(\alpha_1, \alpha_2, \ldots, \alpha_{N_c})}}{Q(N_c, V, T)}$$



We separate the interaction of the central chain:

$$U(\alpha_1, \alpha_2, \cdots, \alpha_{N_c}) = u(\alpha_1 / \alpha_2, \ldots \alpha_{N_c}) + U(\alpha_2, \ldots, \alpha_{N_c})$$

Then

$$P(\alpha_1) = \frac{e^{-\beta u(\alpha_1 / \alpha_2 \ldots \alpha_{N_c})} \sum_{\alpha_2} \cdots \sum_{\alpha_{N_c}} e^{-\beta U(\alpha_2, \ldots \alpha_{N_c})}}{Q(N_c, V, T)}$$

Assume "excl. vol." interactions:

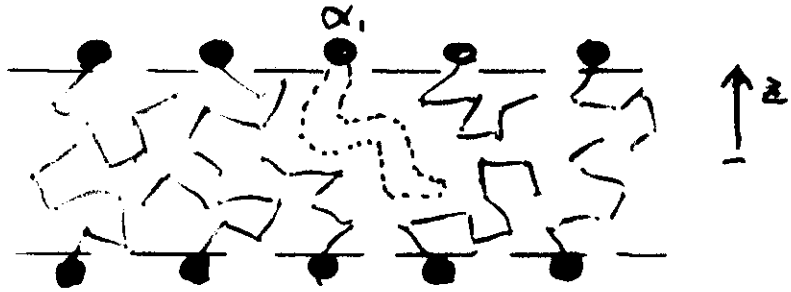
$$u(\alpha_1 / \alpha_2, \ldots, \alpha_{N_c}) = \begin{cases} 0 & \text{if no overlap } \alpha_1 \text{ with } \alpha_j \\ \infty & \text{if overlap } \alpha_1 \text{ with } \alpha_j \end{cases}$$

$$P(\alpha) = \frac{e^{-\beta U(\alpha_1/\alpha_2,\dots,\alpha_{N_c})} \sum_{\alpha_2}\cdots\sum_{\alpha_{N_c}} e^{-\beta U(\alpha_2,\dots,\alpha_{N_c})}}{Q(N_c,V,T)}$$

$$e^{-\beta U(\alpha_1/\alpha_2,\dots,\alpha_{N_c})} = \begin{cases} 1 & \text{no overlap } \alpha_i \text{ with } \alpha_j \\ 0 & \text{overlap } \alpha_i \text{ with } \alpha_j \end{cases}$$

$$P(\alpha) = \frac{\sum_{\alpha_2}'\cdots\sum_{\alpha_{N_c}}' e^{-\beta U(\alpha_2,\dots,\alpha_{N_c})}}{Q(N_c,V,T)}$$

$$\sum_{\alpha_2}'\cdots\sum_{\alpha_{N_c}}' e^{-\beta U(\alpha_2,\dots,\alpha_{N_c})} = Q\left(N_c-1, \int (A(z)-a(\alpha_1,z))dz, T\right)$$



$$P(\alpha_1) = \frac{Q\left(N_c-1, \int (A(z)-a(z,\alpha_1))dz, T\right)}{Q(N_c,V,T)} \Longrightarrow \text{expansion on "volume"}$$

$$\ln P(\alpha) = -\underbrace{\left(\frac{\partial \ln Q}{\partial N_c}\right)_{V,T}}_{\mu} - \int \underbrace{\left(\frac{\partial \ln Q}{\partial A(z)}\right)_{A(z'),N_c,T}}_{\Pi(z)} a(z,\alpha_1)dz + \dots$$

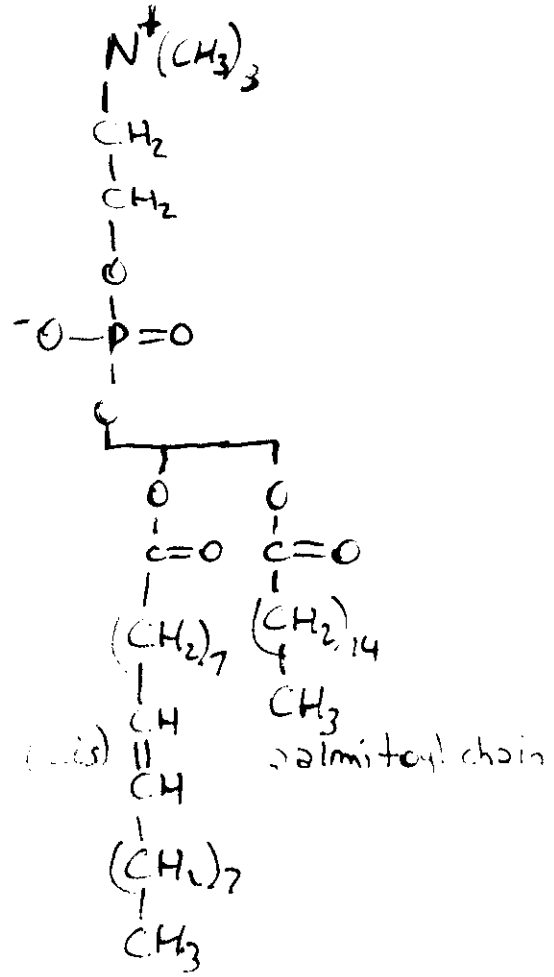
$$\boxed{P(\alpha_1) \equiv \frac{e^{-\beta\int \Pi(z)a(z,\alpha_1)dz}}{Q}}, \quad \beta\mu \equiv -\ln Q$$

Bilayer

= 30Å T = 300K

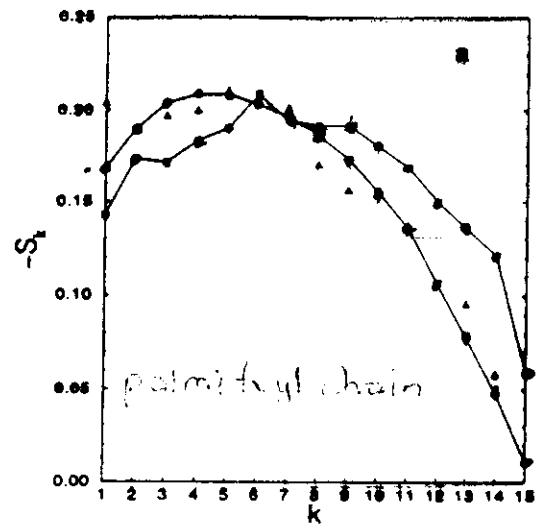
= 60.5 Å²

POPC

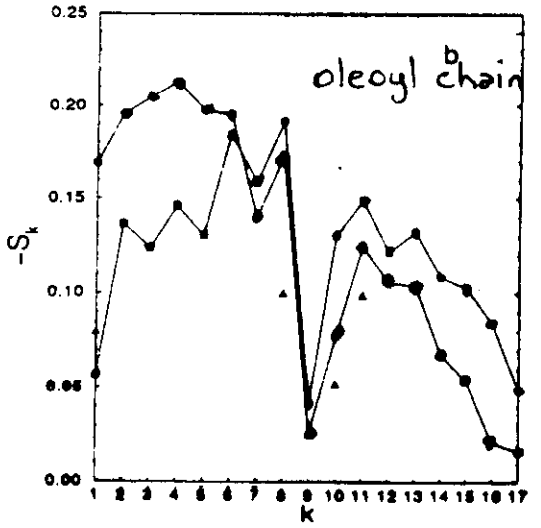


palmitoyl chain

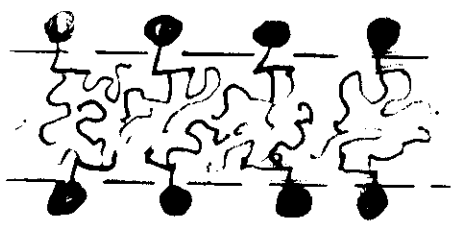
oleoyl chain



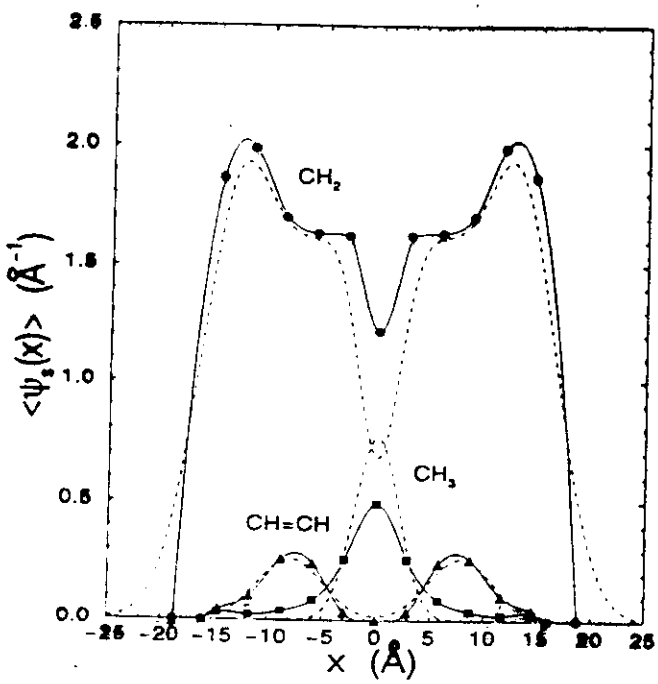
$-S_k = 0$ random
$= 1$ perp. to surface



● SCMF
■ MD (Heller et al.)
▲ experiments
Seelig and Waespe-Sarcevic



D.R. Fenal, A. Ben-Shaul/Physica A 220 (1995) 192–216



—— SCMF

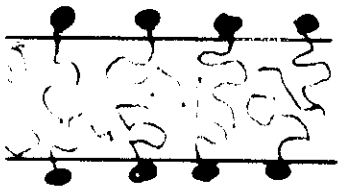
- - - - experim. x-ray and neutron scattering. (Wiener and White)

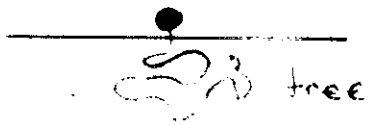
Distribution of segments along the bilayer

Chain Packing in Bilayers $H-(CH_2)_{15}-CH_3$

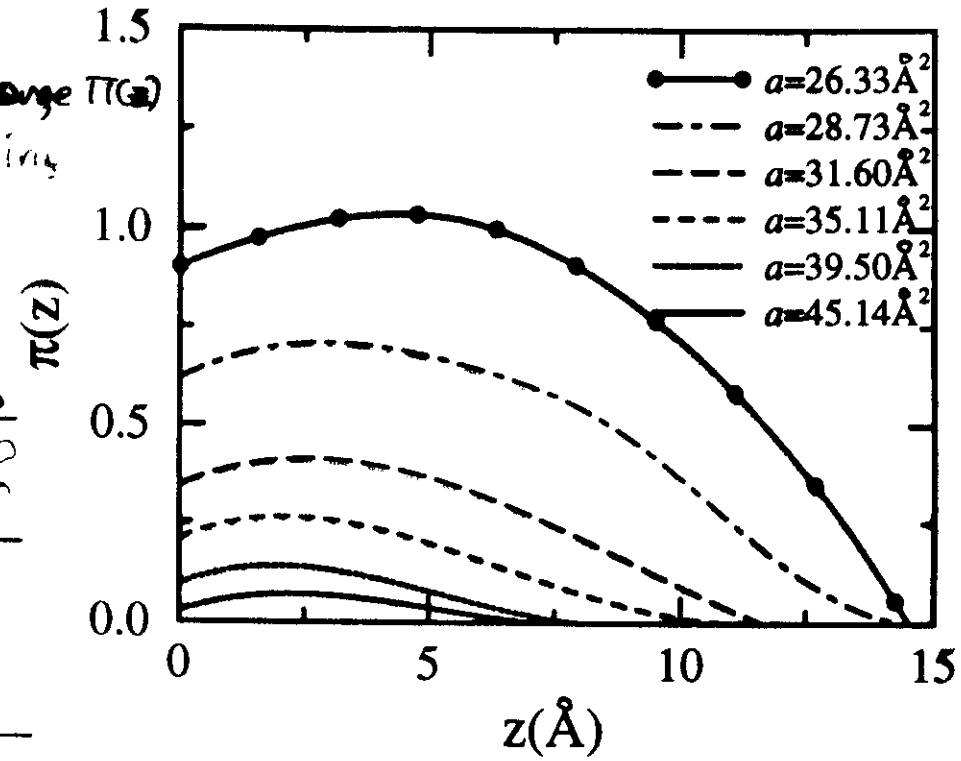
small a → large $\pi(z)$

chain stretching



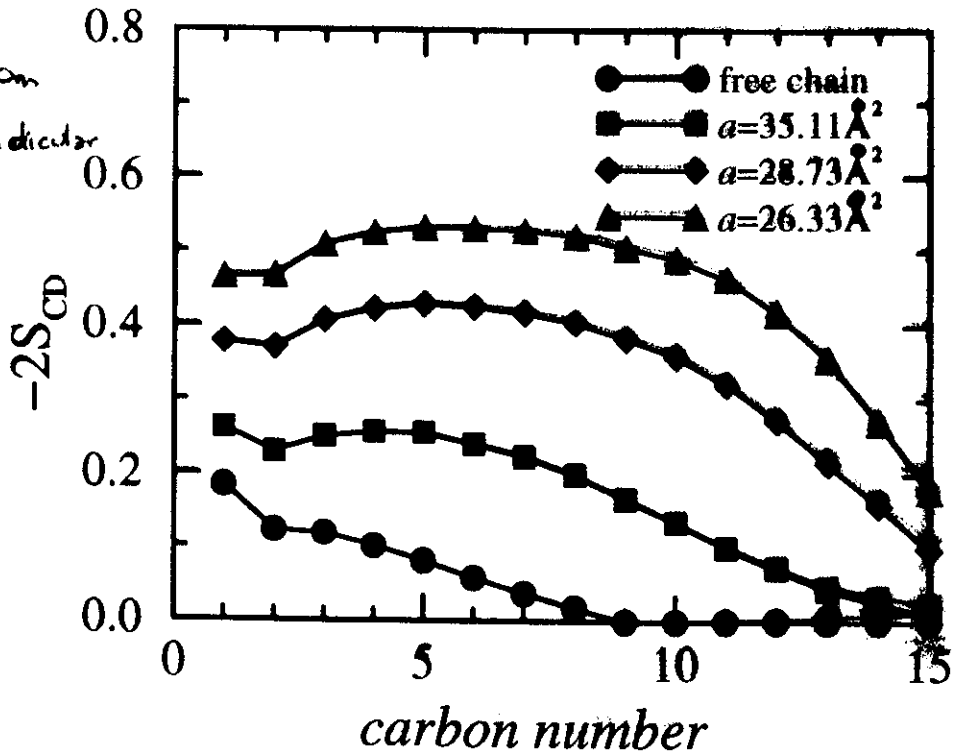


free chain $\pi(z) \approx 0$



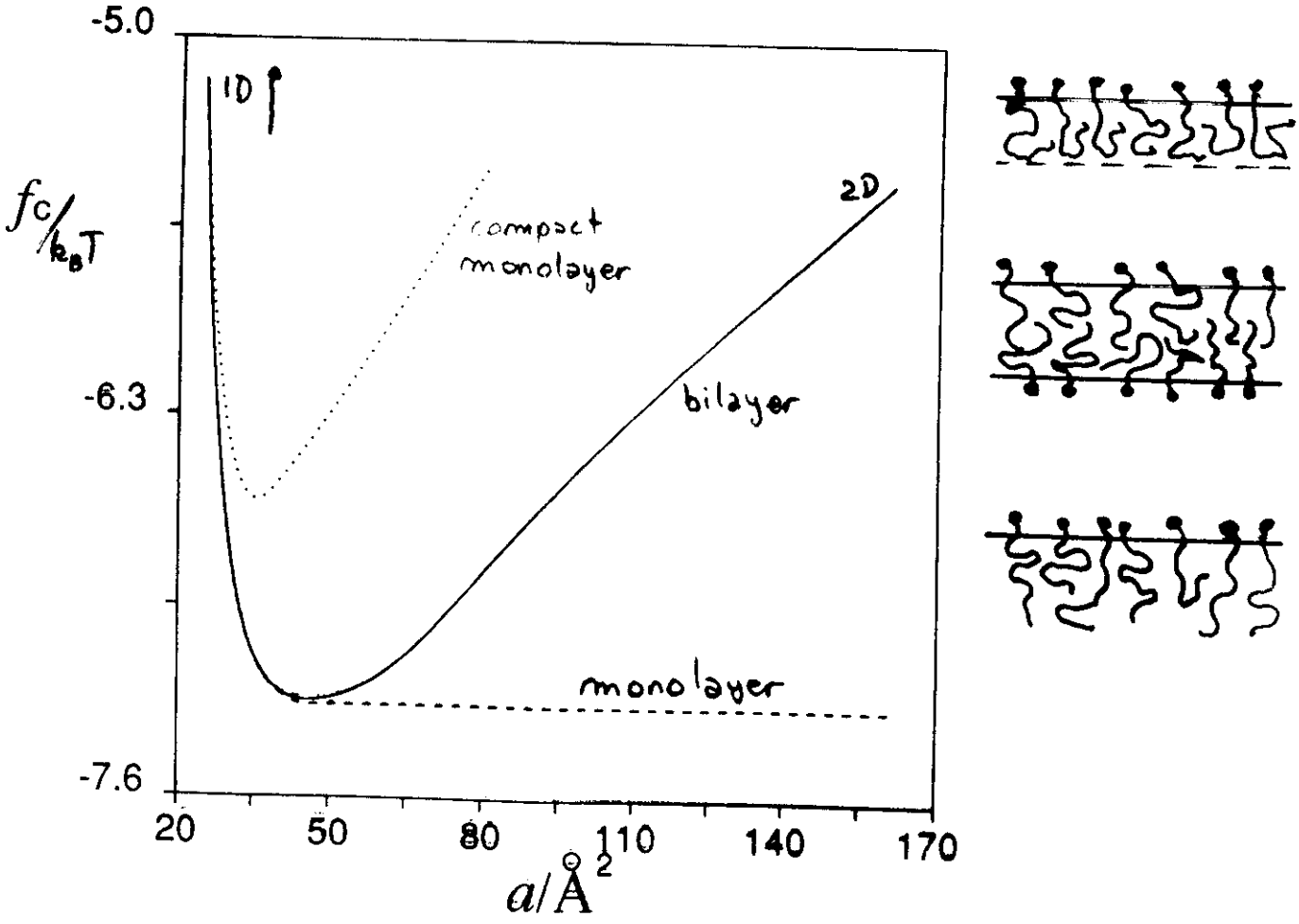
$-2S_{CD} = 0$ random

$-2S_{CD} = 1$ perpendicular

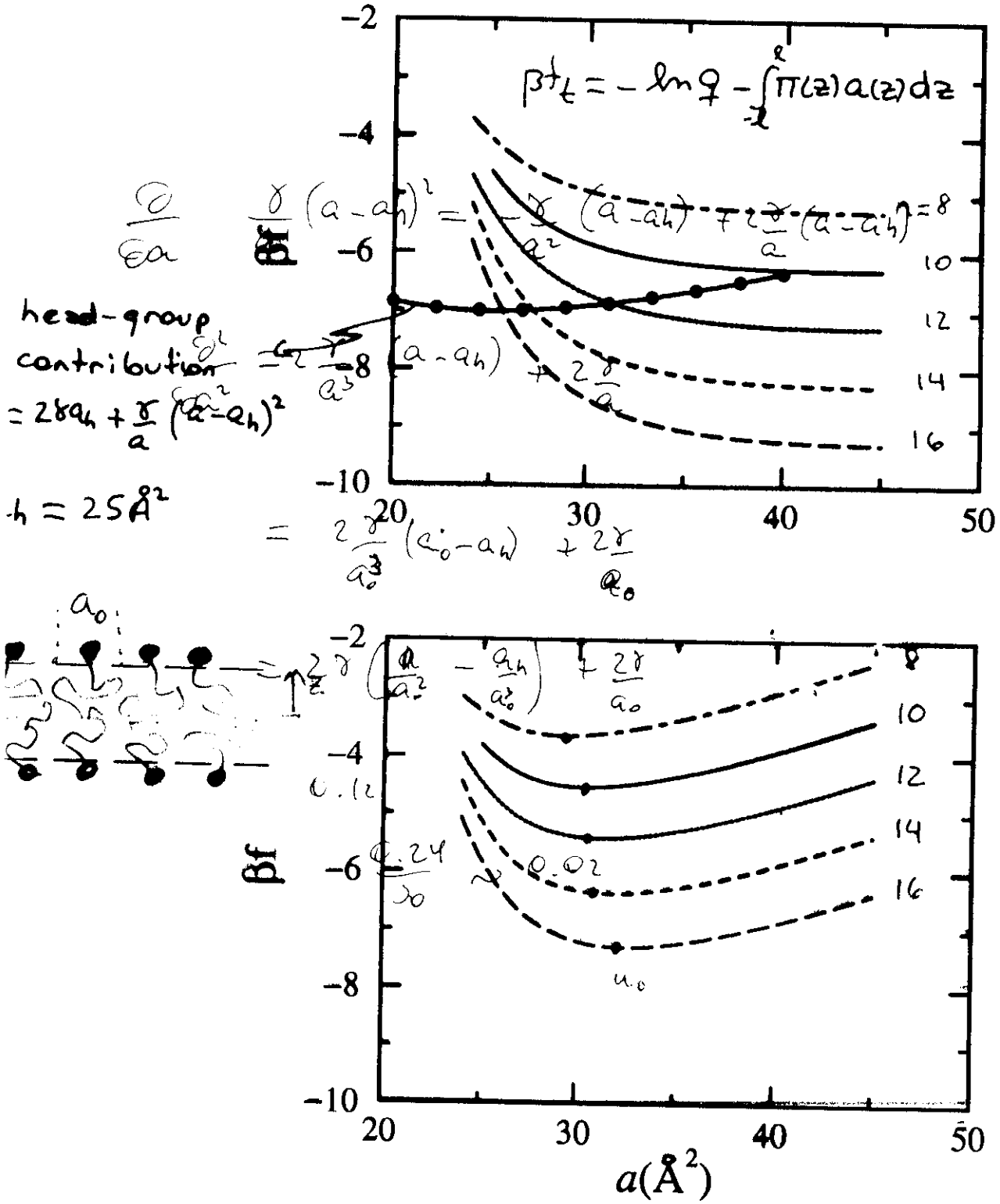


$$H-(CH_2)_{11}-CH_3$$

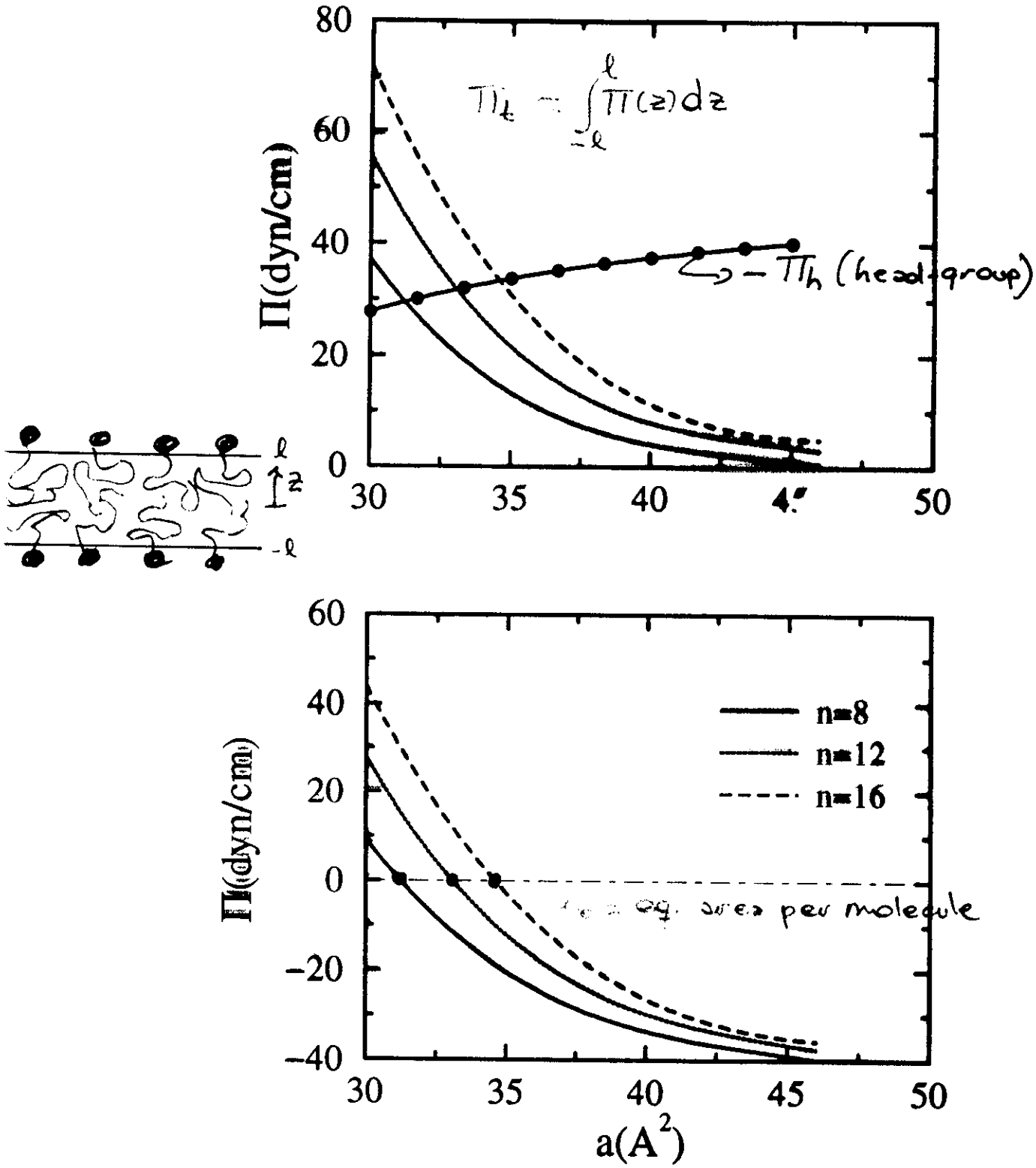
$$f_c = -k_B T \ln z - \int \pi(x)\, a(x)\, dx$$



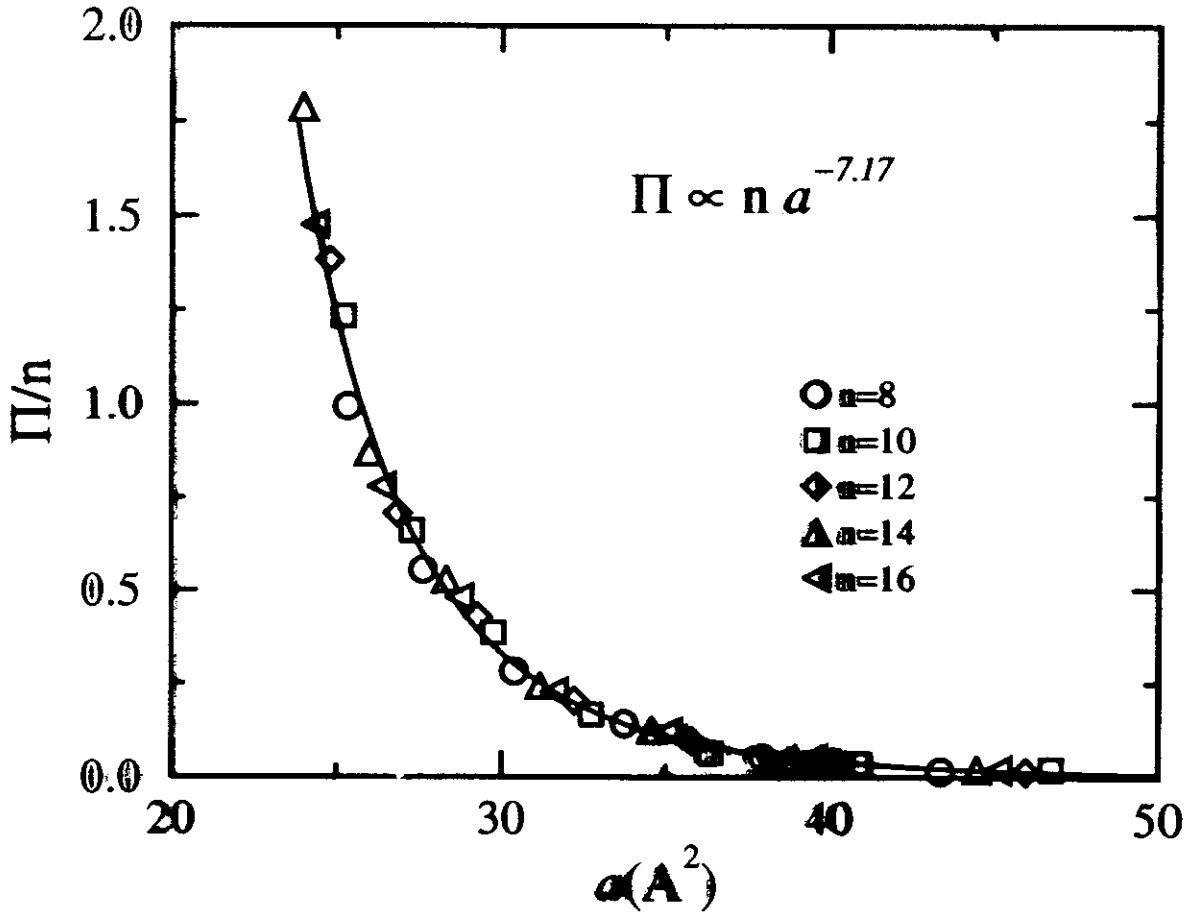
Bilayer's free energy



Pressure-area bilayers: $\Pi = -\frac{\partial f}{\partial a}$

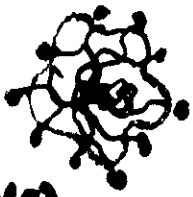


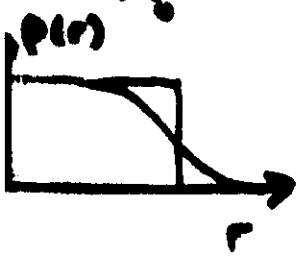
"universal" pressure: only tail contributions

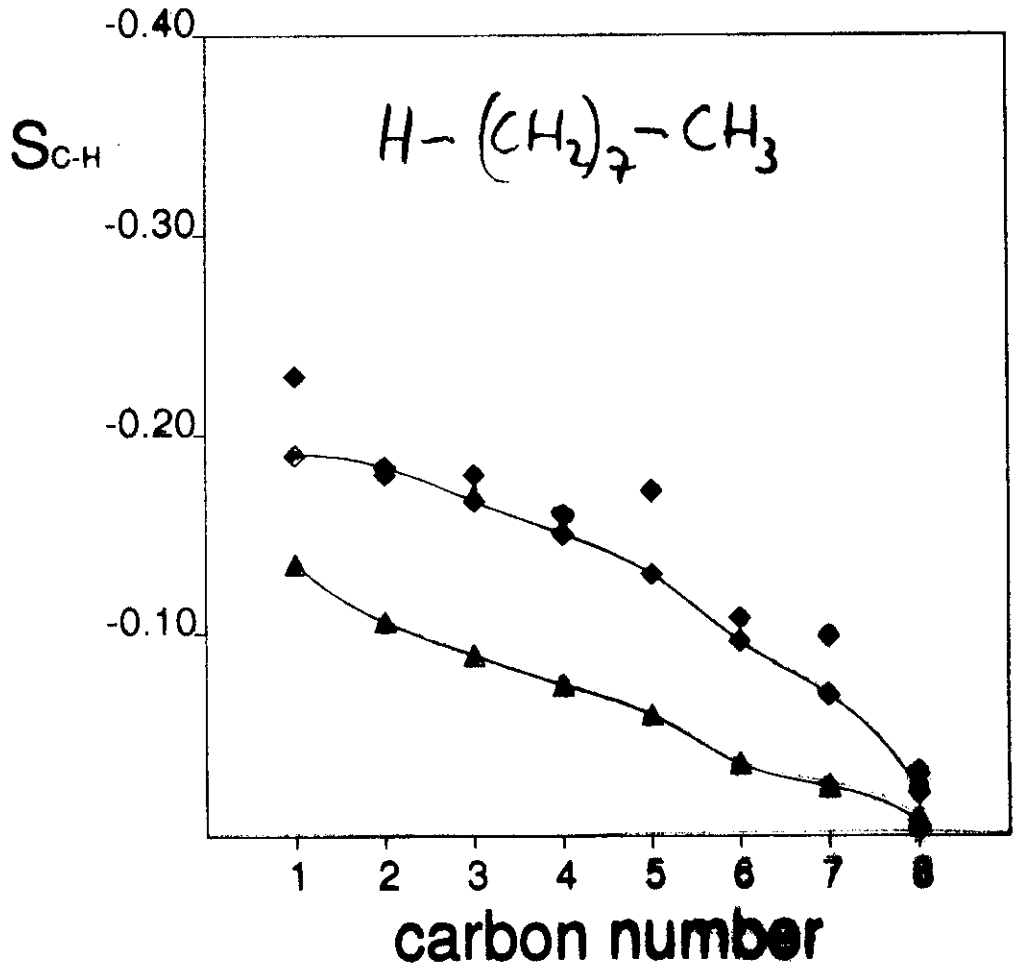


Spherical micelle

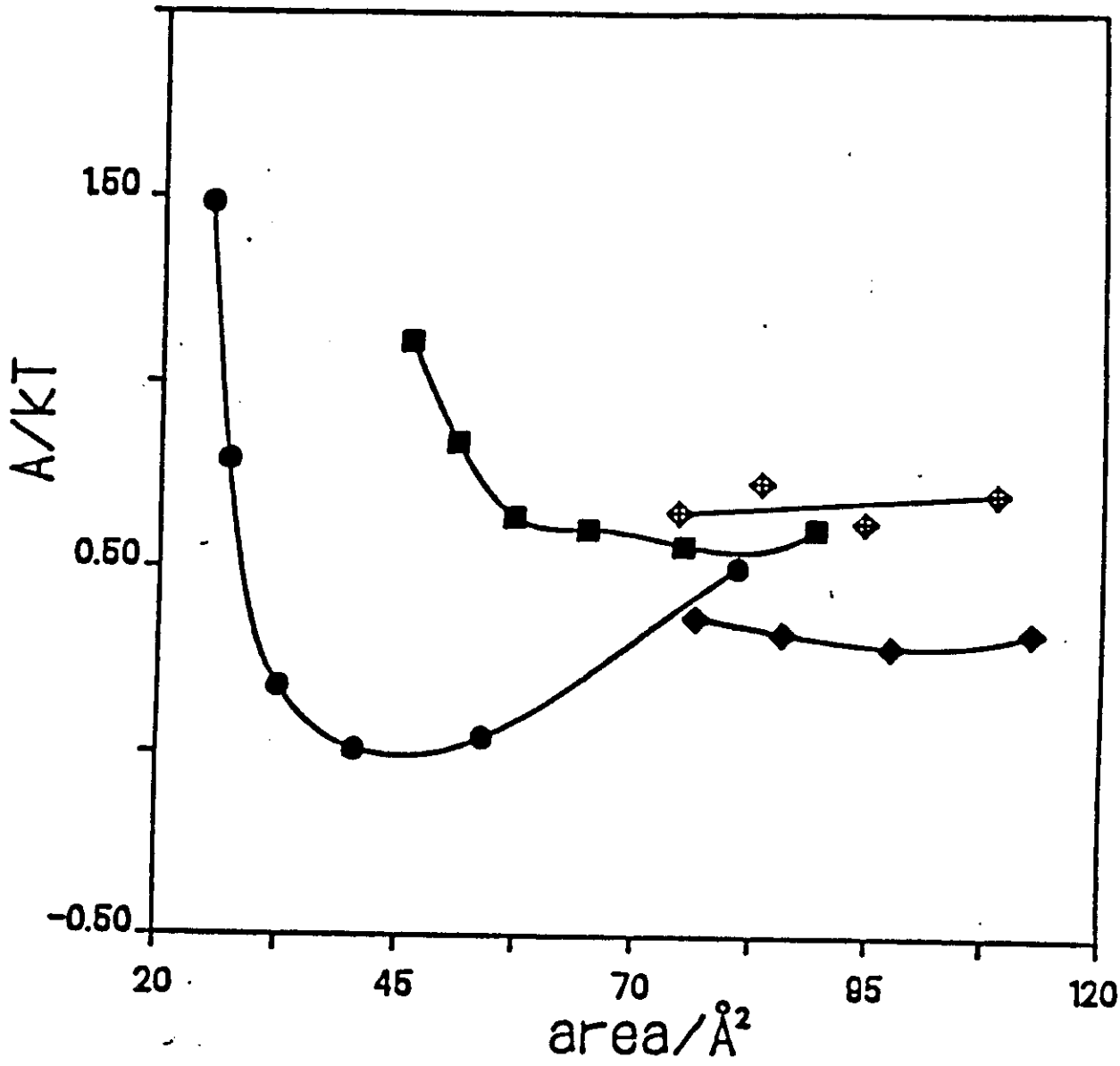
- ◆ experimental results (Walderhaug et. al.)
- ▲ compact micelle
- ◆ "rough" micelle







$-(CH_2)_7-CH_3$ $\varepsilon_g = 500 \frac{cal}{mole}$ $T = 315\,K$



● planar bilayer

■ cylinder $p_1 = 0.094$ $p_2 = 0.92$ $p_{i\geq 3} = 1$

⊕ 'rough' micelle $p_1 = 0.15$ $p_2 = 0.87$ $p_{i\geq 3} = 1$

◆ 'rough' micelle $p_1 = 0.30$ $p_2 = 0.70$ $p_{i\geq 3} = 1$

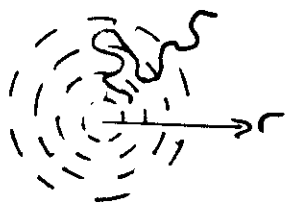
reference state: free chain in bilayer

Self-assembly:

Generalize constraint equations to include all components in mixture:

$$\int N_p(r) \frac{\langle \nu_p(r') \rangle_r}{V(r')} dr + \underbrace{\phi_s(r)}_{\text{solvent}} = 1 \quad \text{for all } r.$$

$$\langle \nu_p(r') \rangle_r = \sum_{\alpha_r} P(\alpha_r)\, \nu_p(r', \alpha_r); \quad \sum_{\alpha_r} P(\alpha_r) = 1 \text{ for each } r$$



Generalize free energy to account for "r translation" of solvent:

$$\beta f = \underbrace{\int N_p(r) \sum_{\alpha_r} P(\alpha_r) \ln P(\alpha_r)\, dr}_{\text{conformational entropy (r)}} + \underbrace{\int N_p(r) \ln \phi_p(r)}_{\text{+translational entropy (r)}}$$

$$+ \frac{1}{2} \underbrace{\iiiint N_p(r) N_p(r'') \chi(r' - r''') \langle n(r') \rangle_r \frac{\langle n(r''') \rangle_{r''}}{V(r'')} dr\, dr\, dr\, dr}_{\text{attractive interaction}}$$

$$+ \underbrace{\int N_s(r) \ln \phi_s(r)\, dr}_{\text{solvent translation}} - \int N_p(r) \mu_p\, dr - \int N_s(r) \mu_s\, dr$$

Minimization subject to constraint gives:

$$P(\alpha_r) = \frac{1}{q(r)} e^{-\int \Pi(r) V(r;\alpha_r) dr' - \epsilon(\{H_r\};\alpha_r)}$$

additional equation from thermodynamic stability

$$\beta \mu_p = -\ln q(r) + \ln \rho_p(r)$$

for solvent

$$f_s(r) = e^{-\Pi(r) + \beta\mu_s}$$

Replacing $P(\alpha_r)$ and $\rho_s(r)$ into constraints gives a set of equations to be solved (now self-consistently becau

$$\epsilon(\{H_r\},\alpha_r) = \frac{1}{2}\iiint \chi(r'..r''') \; n(r';\alpha_r) \; N_p(r'') \frac{\langle n(r''')\rangle_{\alpha_r}}{V(r''')} dr' dr'' dr'''$$

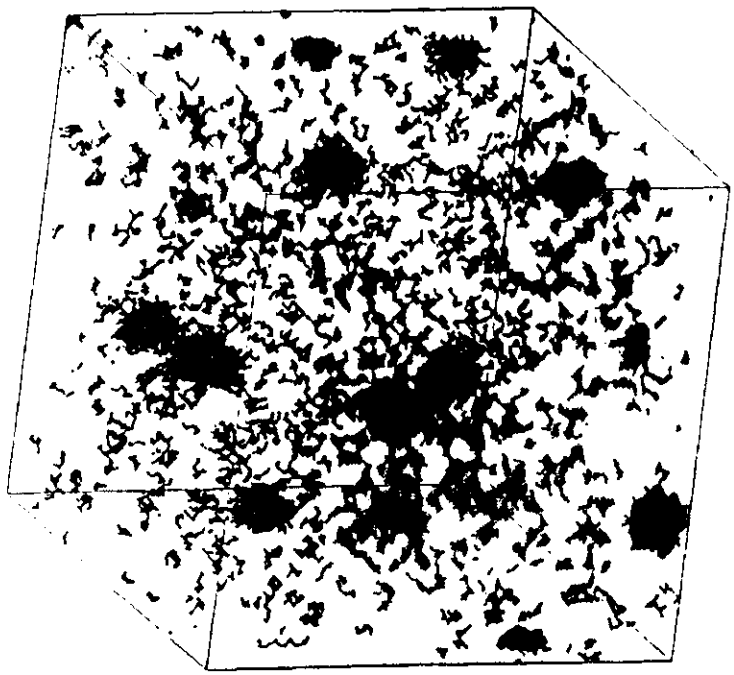
$$+ \frac{1}{2}\iiint \chi(r''..r''') \frac{n(r''';\alpha_r)}{V(r''')} N_p(r') \langle n(r'')\rangle_{\alpha_r} dr' dr'' dr'''$$

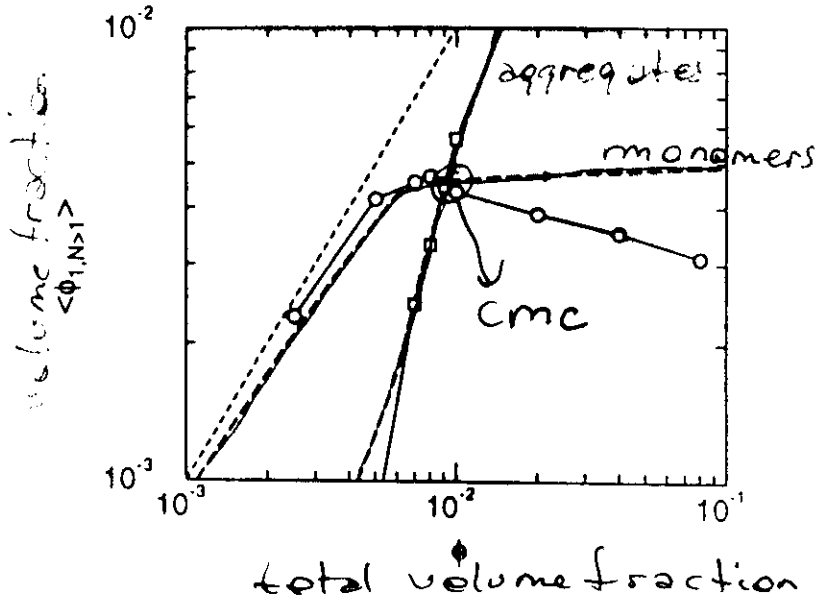
Note that $\rho_p(r)$ and $P(\alpha_r)$ are determined separately!!

Lattice simulations (Mackie and Panagiotopoulos)

H_4T_4 T–T attractive, all others repulsive

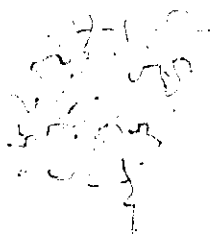
volume fraction 0.01 segments lattice 120^3 sites

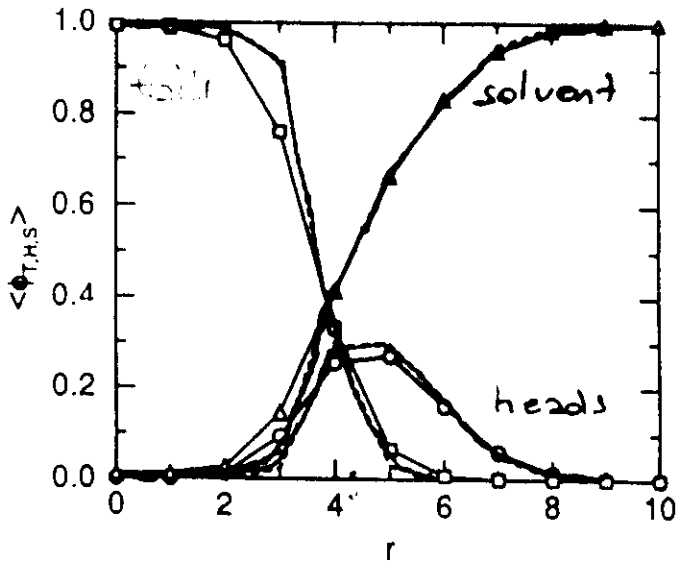




symbols : simulations

- - - - - : SCMF





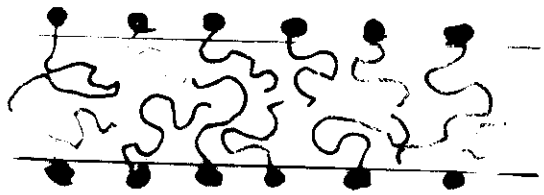
Wijmans and Linse: 2 orders of magnitude difference in cmc between simulations and lattice SCF theory!!

Packing in mixed Aggregates:

"volume sharing" $\Rightarrow$ packing constraints:

$$X_A \langle n_A(z) \rangle + X_B \langle n_B(z) \rangle = a(z) dz, \quad 1 \le z \le \ell$$

$$\langle n_A(z) \rangle = \sum_{\alpha_A} P(\alpha_A)\, n_A(z;\alpha_A) \quad ; \quad \langle n_B(z) \rangle = \sum_{\alpha_B} P(\alpha_B)\, n_B(z;\alpha_B)$$



Free energy:

$$\frac{\beta f}{N_{tot}} = X_A \sum_{\alpha_A} P(\alpha_A) \ln P(\alpha_A) + X_B \sum_{\alpha_B} P(\alpha_B) \ln P(\alpha_B) + X_A \ln X_A + X_B \ln X_B$$

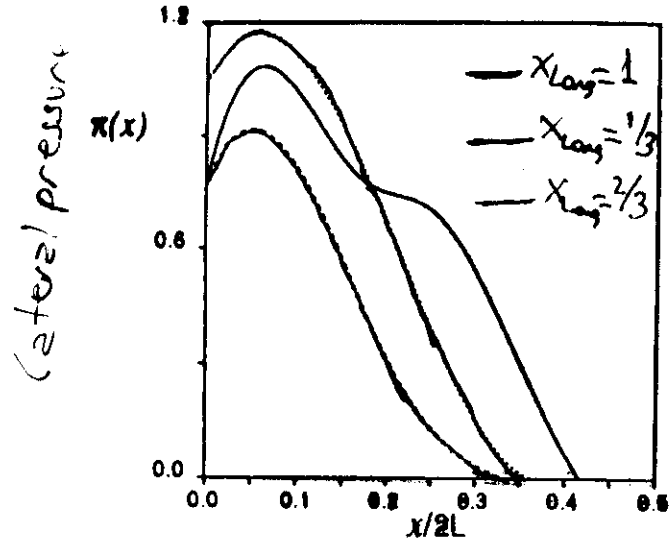
Minimization gives:

$$P(\alpha_A) = \frac{1}{q_A} e^{-\beta \int \Pi(z)\, n_A(z;\alpha_A) dz}$$

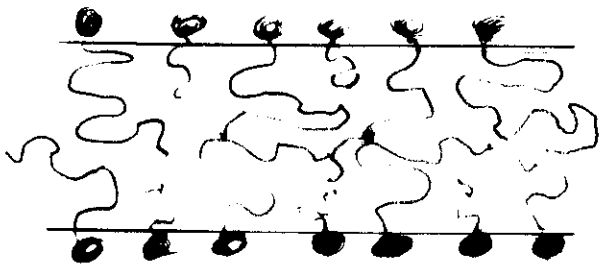
$$P(\alpha_B) = \frac{1}{q_B} e^{-\beta \int \Pi(z)\, n_B(z;\alpha_B) dz}$$

some $\Pi(z)$!! found by replacing $P(\alpha_A)$ and $P(\alpha_B)$ in packing constraints.

Mixed Bilayers : $H-(CH_2)_{10}-CH_3 / H-(CH_2)_{18}-CH_3$

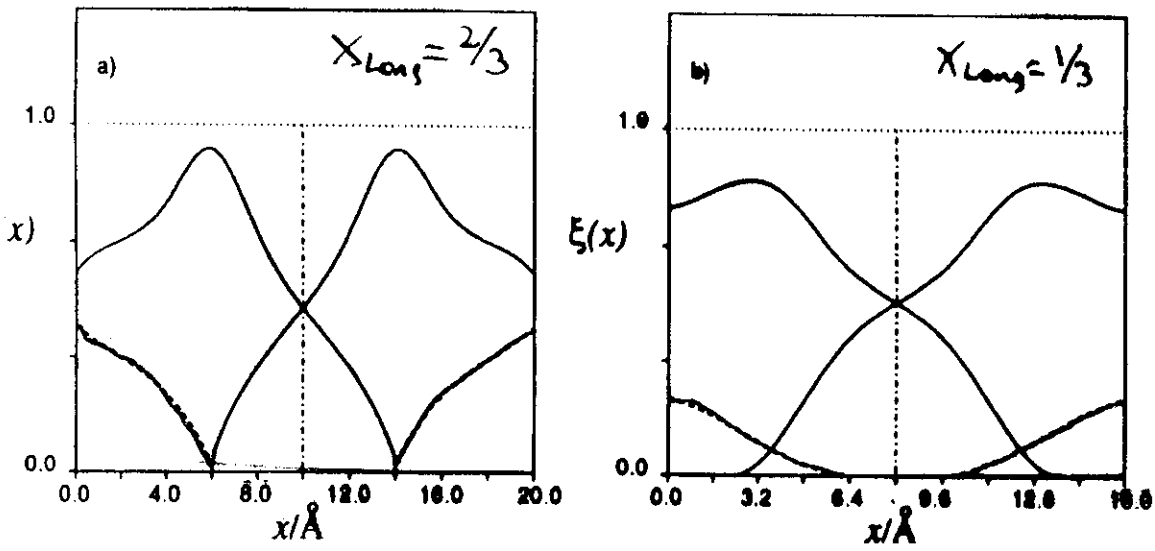


$a = 27\ Å^2$



* only long chains but
* very large effective area

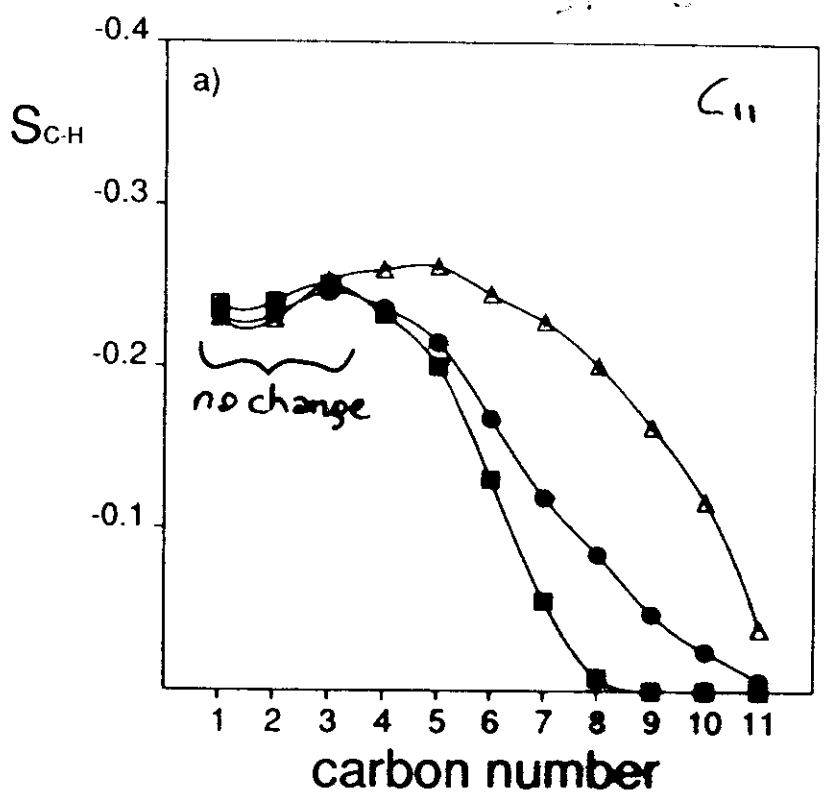
Density Profiles

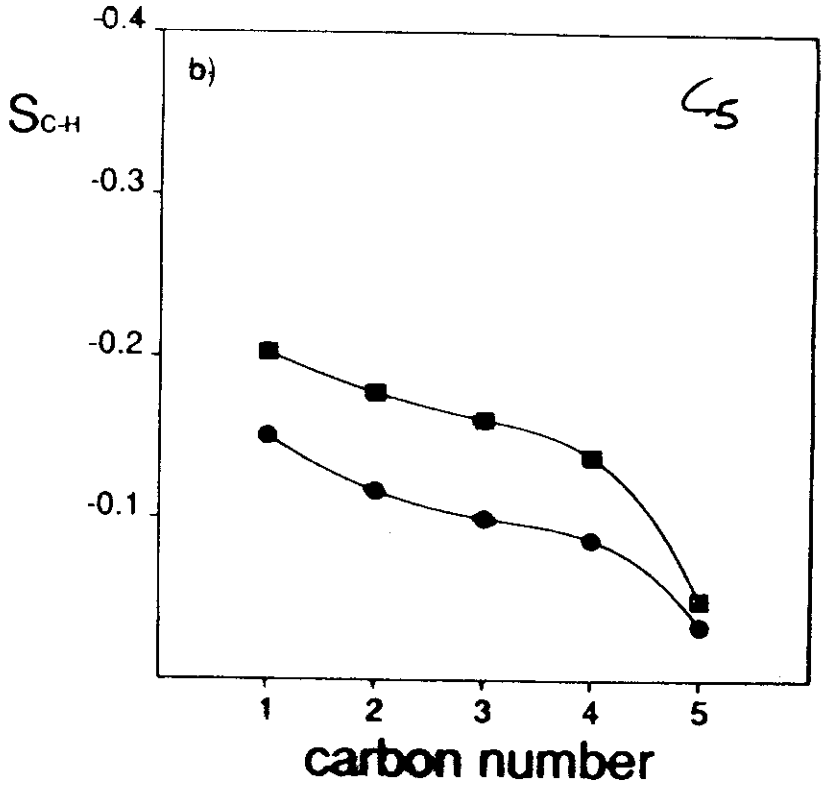


— short chain

Structure in mixed bilayers:
C_{11}/C_5 $a = 27 Å^2$

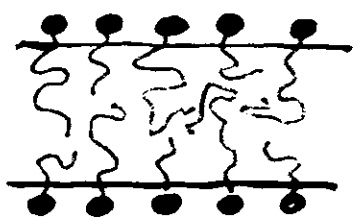
△ $X(long) = 1$
● $X(long) = 2/3$
■ $X(long) = 1/3$

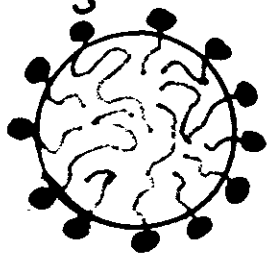


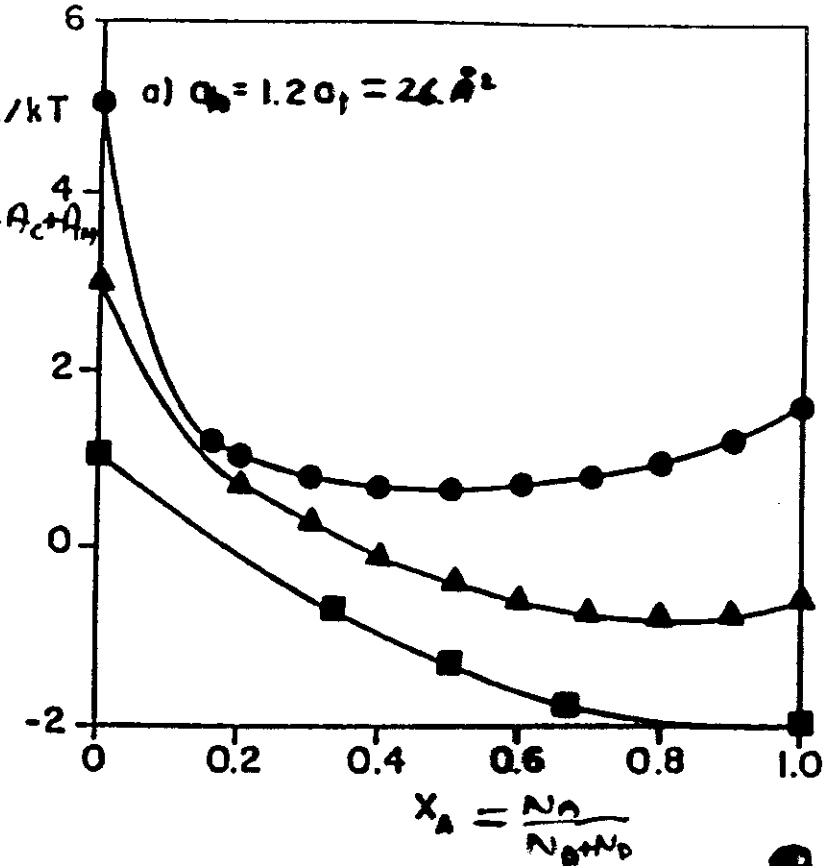


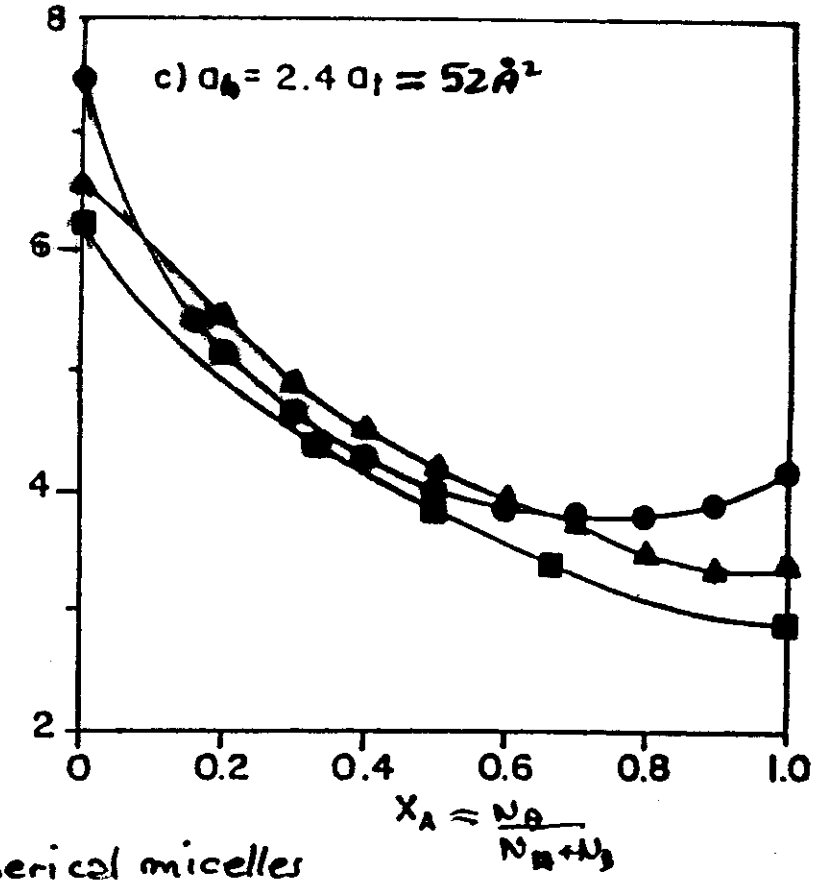
Mixed Aggregates

$A = -(CH_2)_{10}-CH_3$ $B = -(CH)_4-CH_3$





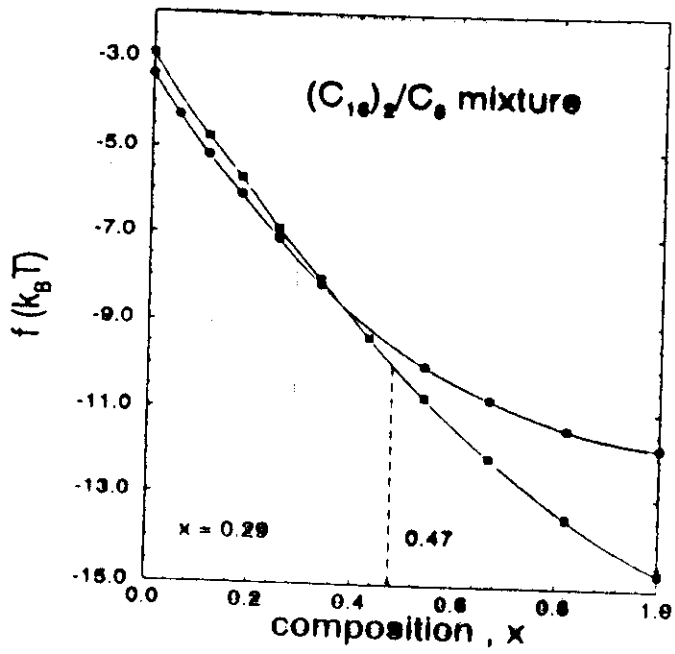




- spherical micelles
- cylindrical aggregate
- bilayer

exp obs: Charvolin, Meli

Phase transition (bilayer → micelle) in mixed aggregates (Fatal; Andelman, Ben-Shaul).



pure C_8 = cylinder
pure $(C_{16})_2$ = bilayer

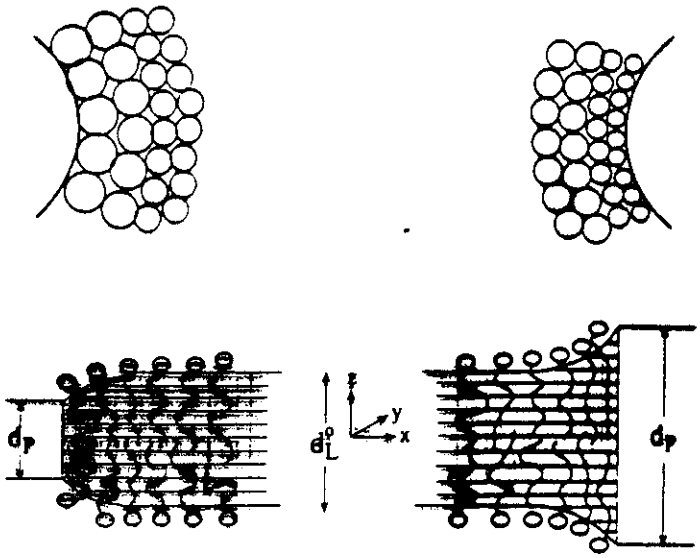
First order phase transition!! many observations: e.g. lipid surfactant; lecithin-bilayer

Andelman, Kozlov, Helfrich:

$$\beta f = k\,(c_1 + c_2 - c_0(x)) + x \ln x + (1-x)\ln(1-x)$$

k = constant (?)

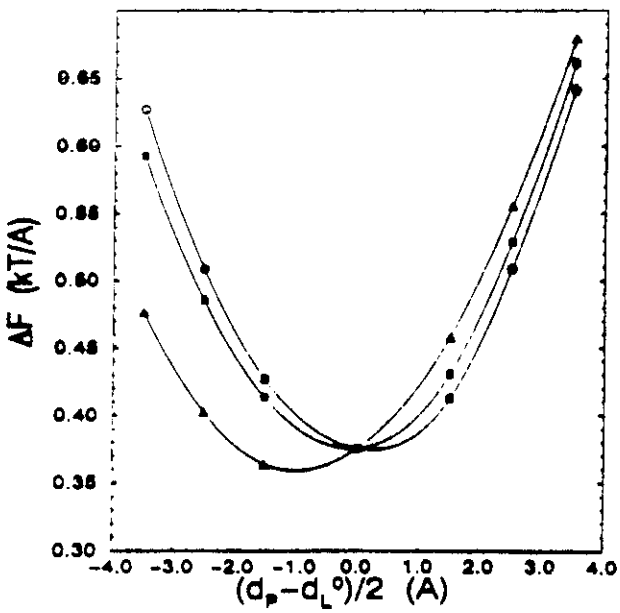
$c_0(x)$ = linear.



Hydrophobic mismatch

(postulated) $d_L(x) = d_L^0 + (d_p - d_L^0)\exp(-x/\xi)$

ξ is determined by minimizing the free energy for each d_p



$H-(CH_2)_{13}-CH_3$

$f_h = 2\gamma a_h + \frac{\kappa}{a}(a - a_h)^2$

$a_h = 20\text{Å}^2$

$a_0 = 32\text{Å}^2$