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INTERNATIONAL ATOMIC ENERGY AGENCY
INTERNATIONAL CENTRE FOR THEORETICAL PHYSICS
I.C.T.P., P.O. BOX 586, 34100 TRIESTE, ITALY, CABLE: CENTRATOM TRIESTE

SMR.961 - 10

WORKSHOP ON:
PROTEINS, MEMBRANES and their INTERACTIONS

22 JULY - 2 AUGUST 1996

"Structure and thermodynamics of tethered polymer layers and their ability to prevent protein adsorption"

PART II

Igal SZLEIFER
Purdue University
Department of Chemistry
Chemistry Building
1393 Brown Building
IN 47907-1393 West Lafayette
U.S.A.

Theoretical Studies of PEO tethered layers:

essure isotherms and prevention of protein adsorption

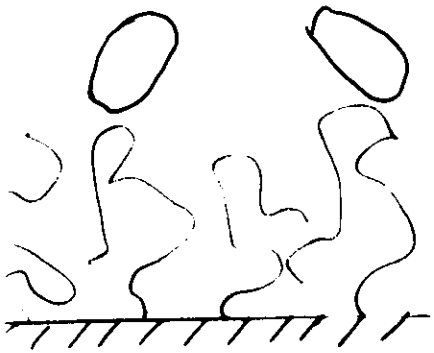
heoretical "ideas".

'S-PEO at water-air interface.
omparison with experimental observations

rotein adsorption on pluronic modified surfaces.

ummary.

Motivation: biocompatible surfaces; surface modified liposomes, ...



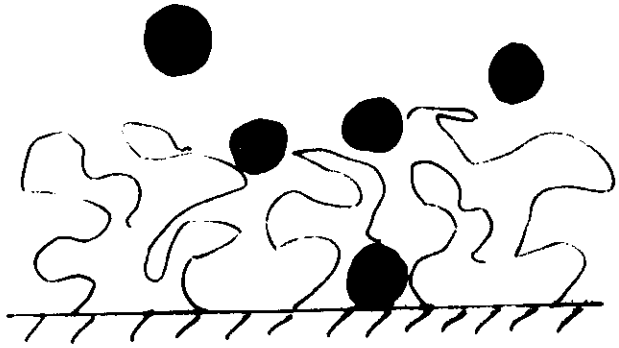
Biocompatible surfaces:

1) Prevention of blood-protein adsorption (no platelet adhesion to surface).

2) Contact lenses: prevent lysozyme adsorption (build up).

Grafted polymers can solve the problem!!

PEO (PEG) $-(CH_2-CH_2-O)_n$ (steric barrier)

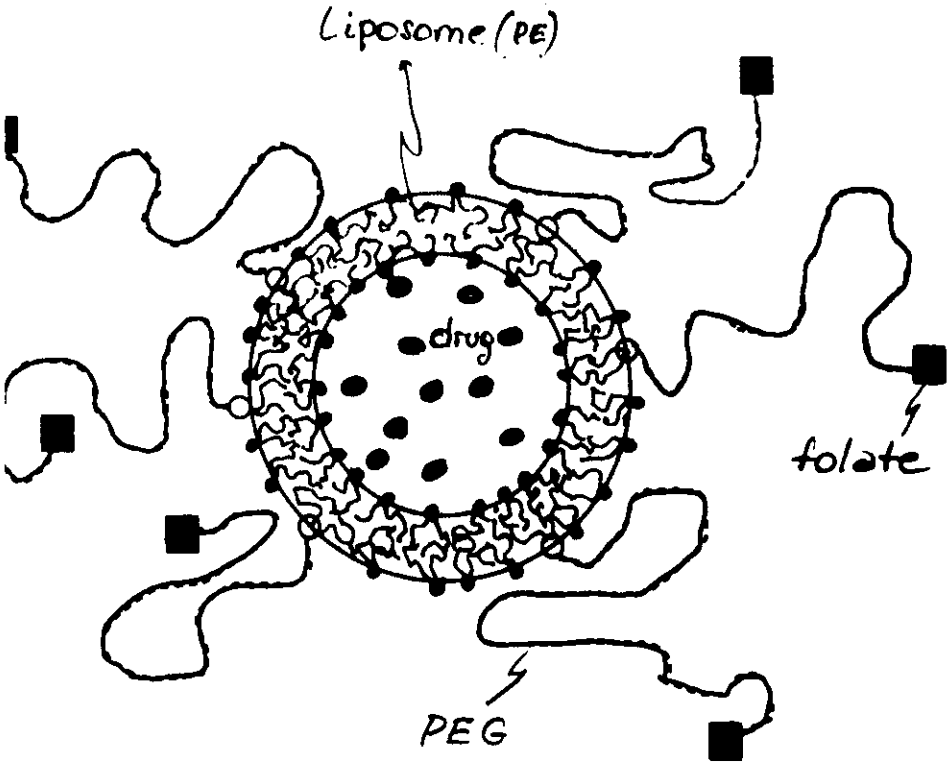


hydrophobic surface

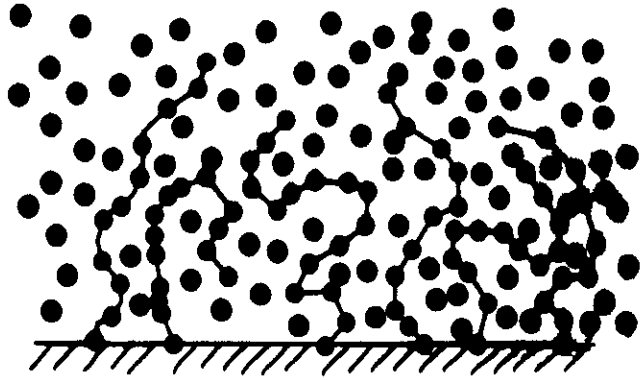
Is this the right picture? nature of PEO, experimental problems.

Drug delivery:

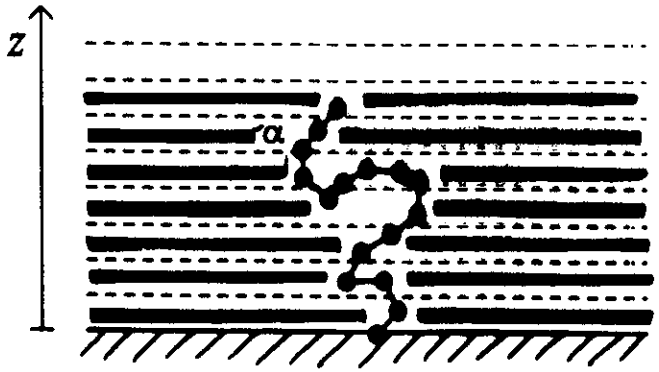
(Prof. P. Law) specific uptake of liposomes by KB cells.



Theoretical Approach: single-chain mean-field theory.



Exact "model" system



"central chain" in the "mean-field" of other molecules.

$P(\alpha)$: probability distribution function of chain conformations.

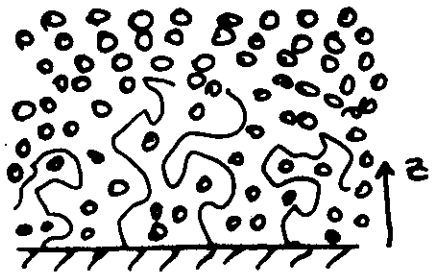
From $P(\alpha)$ any average conformational and thermodynamic property can be calculated.

$P(\alpha)$ is a function of surface coverage, quality of solvent, geometry of surface, etc.

Generalization of single-chain mean-field theory

Polymer-solvent mixture ⇒ packing constraints

$$\frac{N_p}{A} \langle n_p(z) \rangle v_0 + \phi_s(z) = 1 \qquad z \geq 0$$



ee energy density:

$$= \sigma \sum_\alpha P(\alpha) \ln P(\alpha) + \int \phi(z) \ln \phi(z) dz - \beta \int \phi(z) \mu_s dz$$

Minimizing subject to constraints:

$$P(\alpha) = \frac{1}{q} e^{-\int \pi(z) n(z,\nu) dz}$$

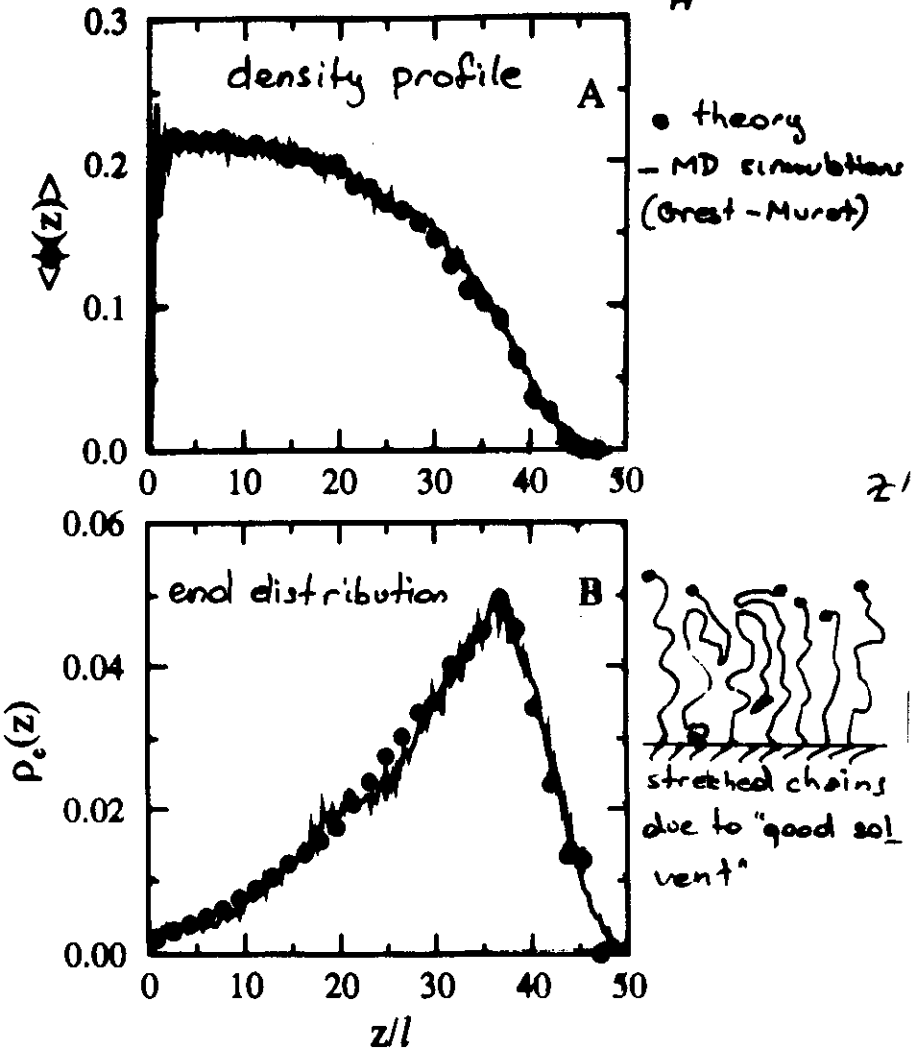
$$\phi(z) = e^{\beta \mu_s - \pi(a)}$$

(z): lateral pressures related to osmotic pressure

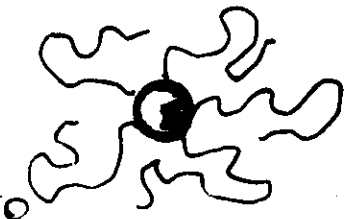
to keep μ_s = const. at all z.

$$\frac{\beta f}{A} = -\sigma \ln q - \int \pi(z) dz$$

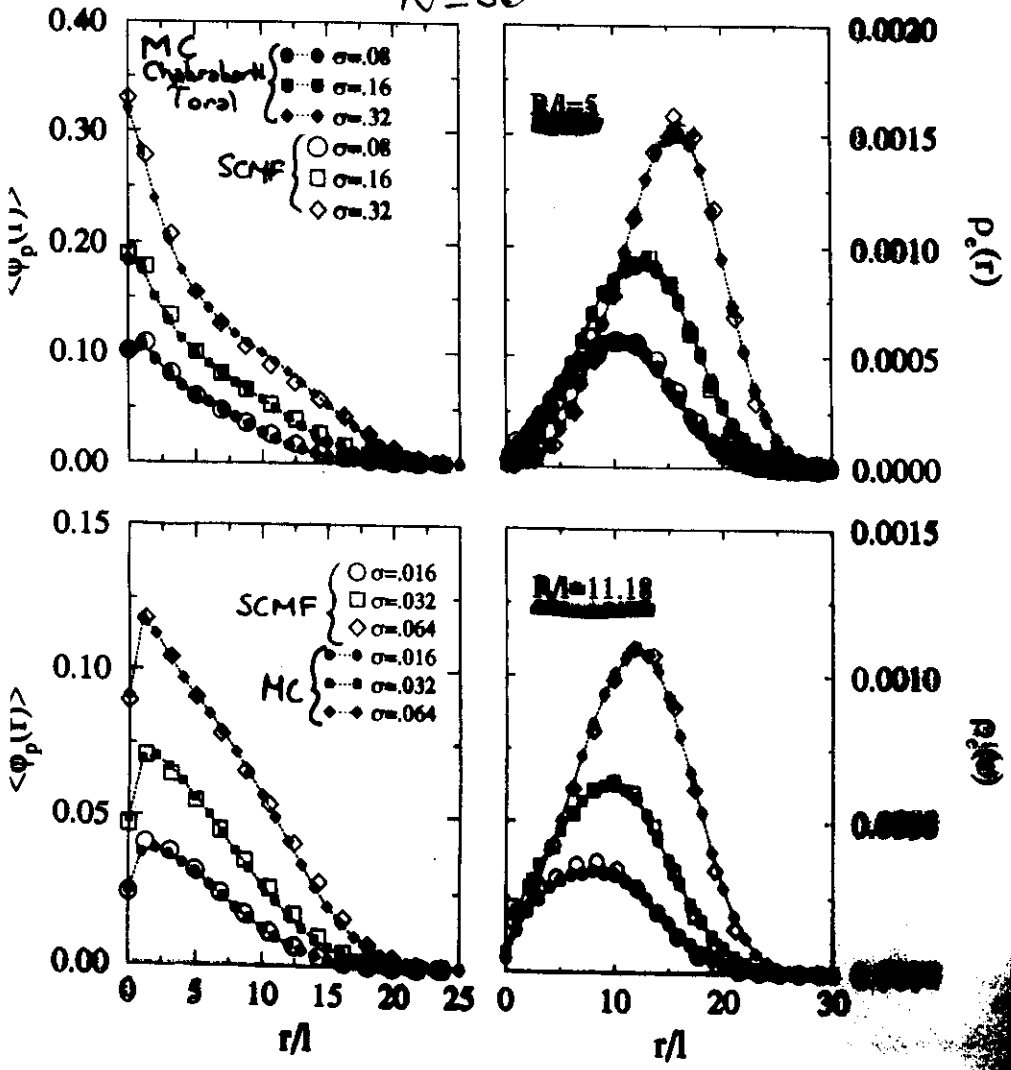
N=100 Good solvent $\sigma = \frac{N_p}{A} = 0.07$



Spherical Surfaces
Good Solvent

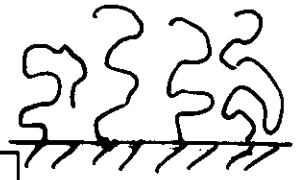


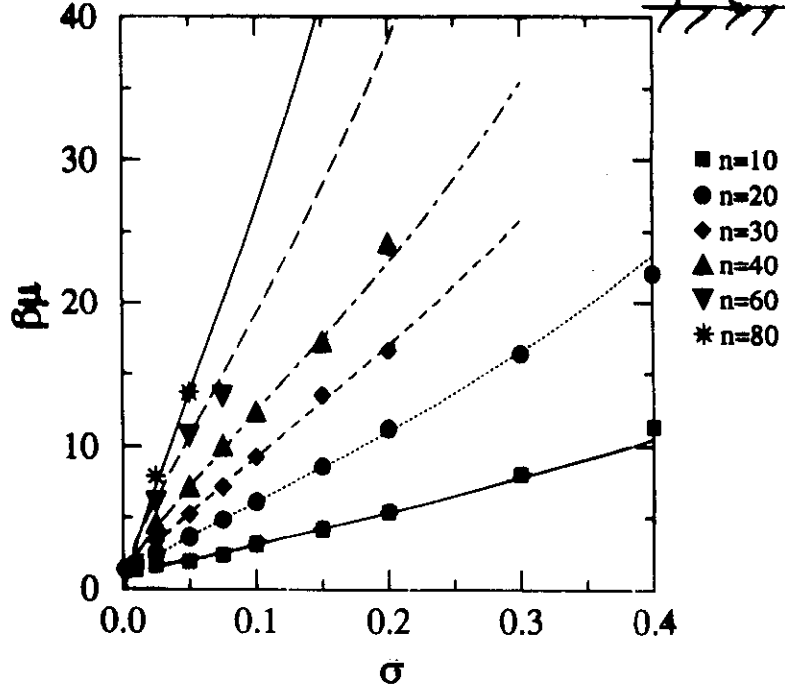
N = 50



Polymer Chemical Potential.

$$\mu = \left(\frac{\partial f}{\partial N_p}\right)_{N_s, a, T}$$



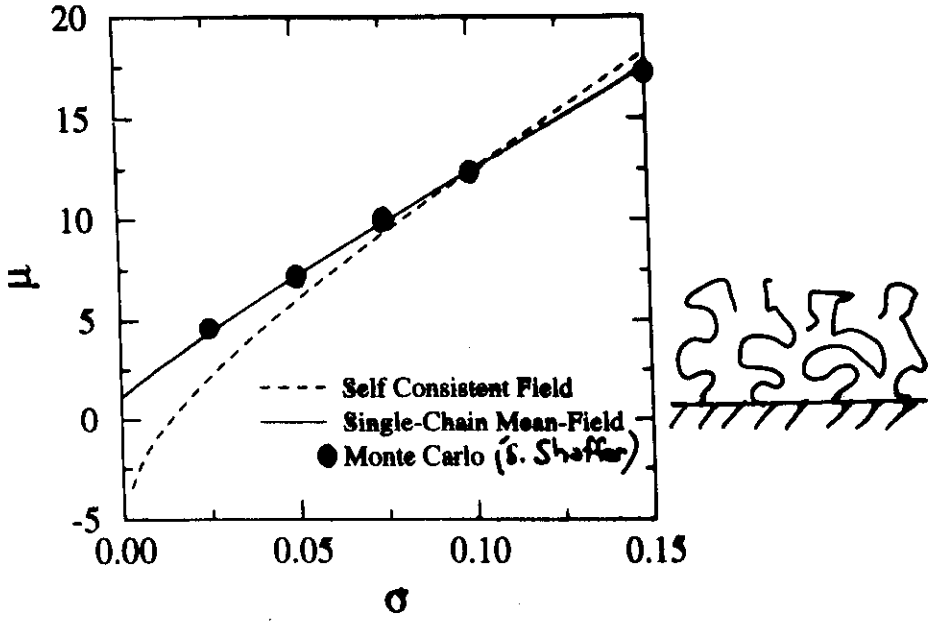


symbols: MC simulations (S. Shaffer)

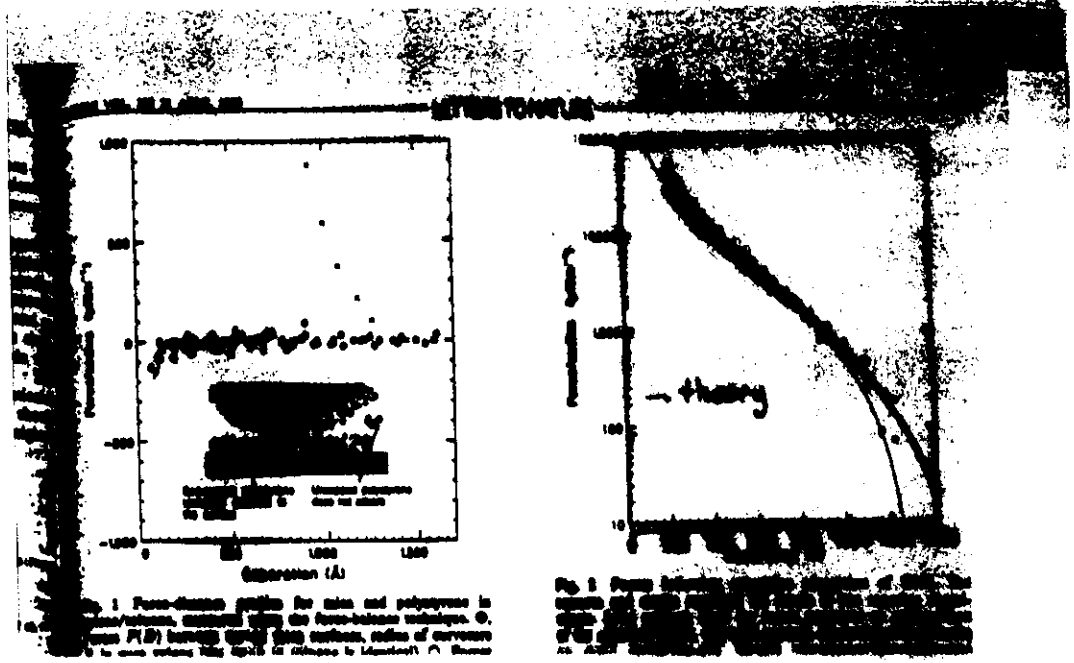
lines: SCMF theory

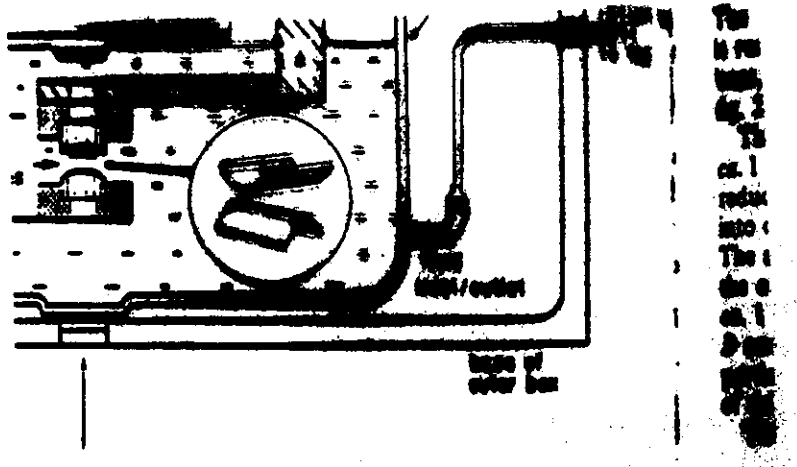
(Lattice chains fluctuation bond model)

$\mu = \left(\frac{\partial f}{\partial N_p}\right)$ chemical potential; $n = 40$



SCF theory is for a RW in the "field" of the repulsive interactions $\Rightarrow$ cost of stretching the chains at low and intermediate surface coverages not properly taken into account !!





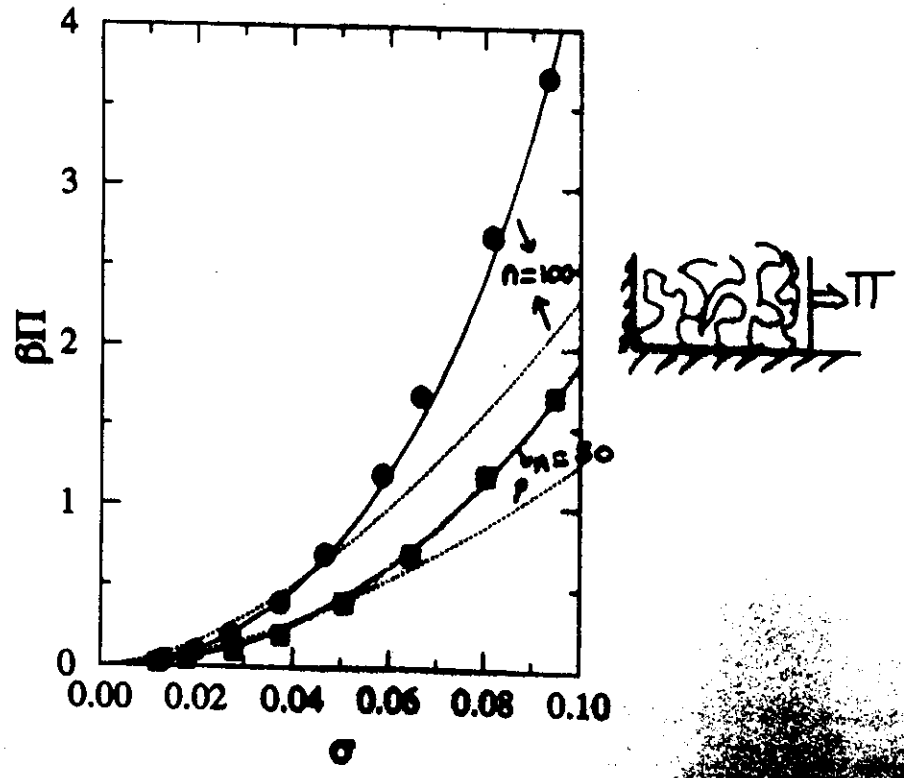
Pressure isotherms $\Pi = \left(\frac{\partial A}{\partial a}\right)$

Good solvent regime

■ ● MD simulations (Grest)

— single chain mean field theory

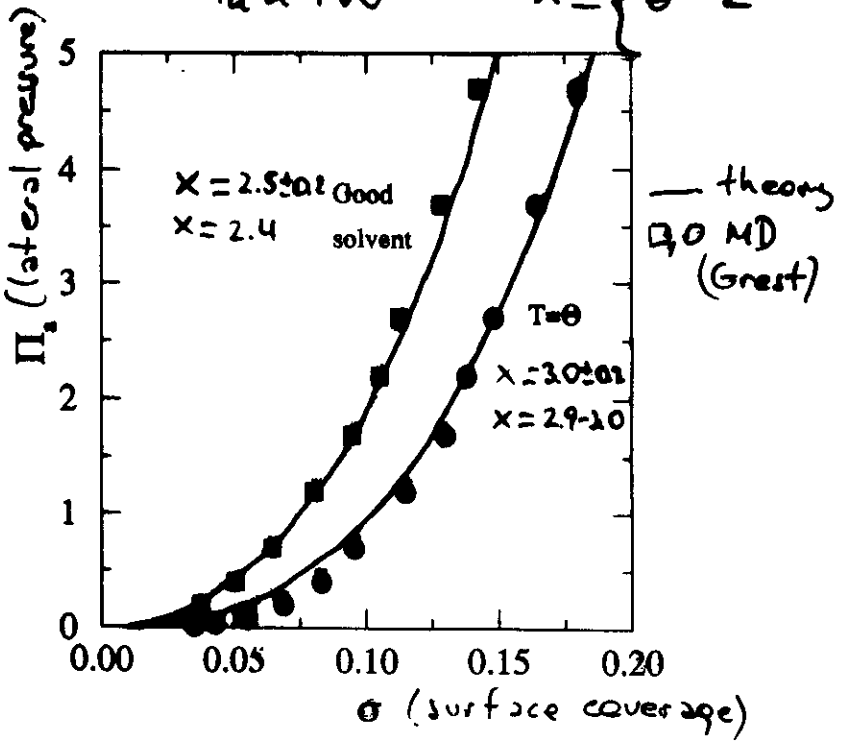
..... analytical SCF theory

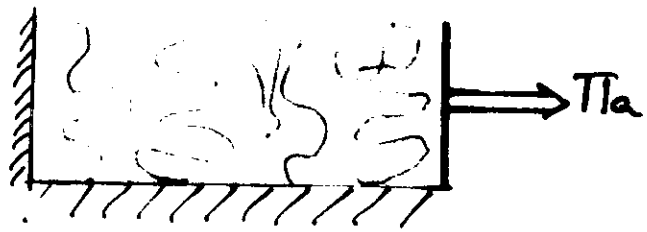


$\Pi_a = \left(\frac{\partial f}{\partial a}\right)_{N_0, N_c, T}$

N = 50

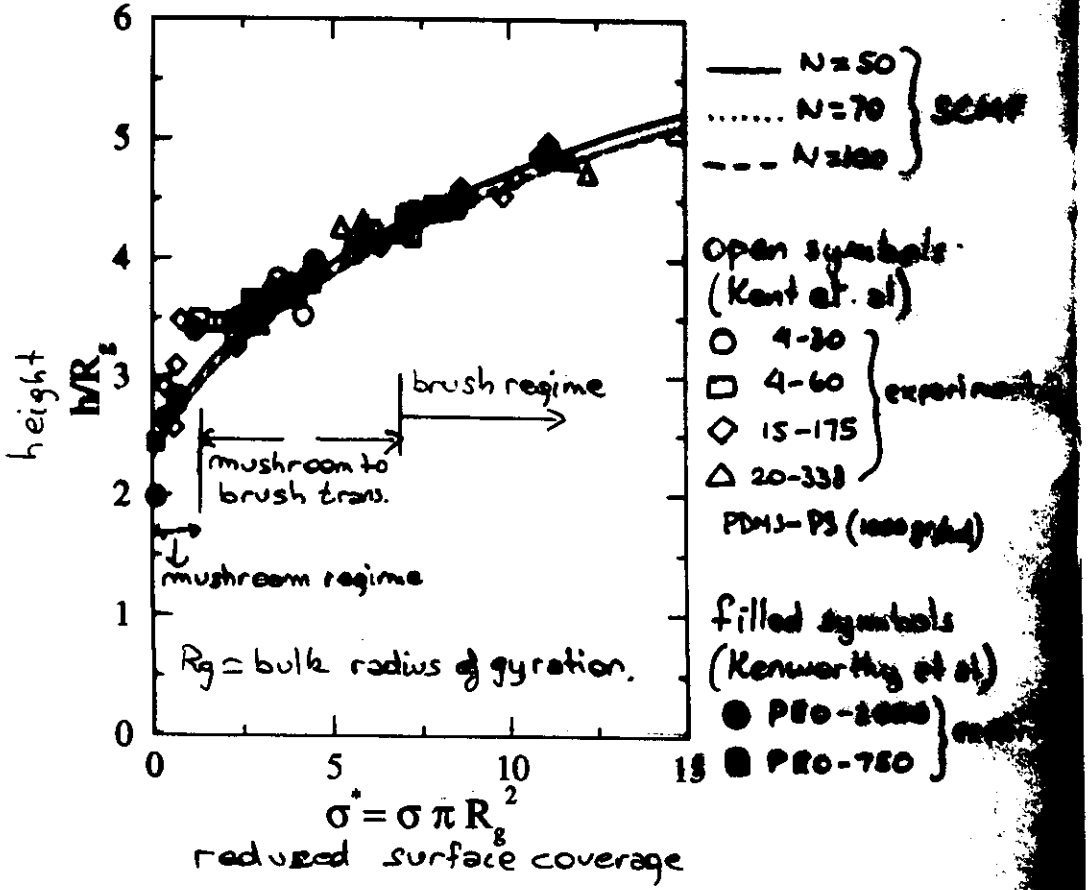
$\Pi_a \propto N\sigma^x$ $\quad x =$ { good: SCF 5/3, scaling 11/6; θ: SCF 2, scaling 2 }

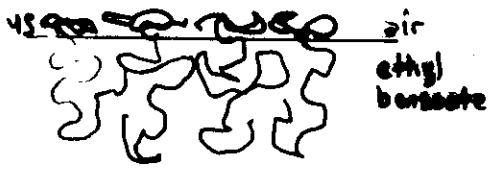


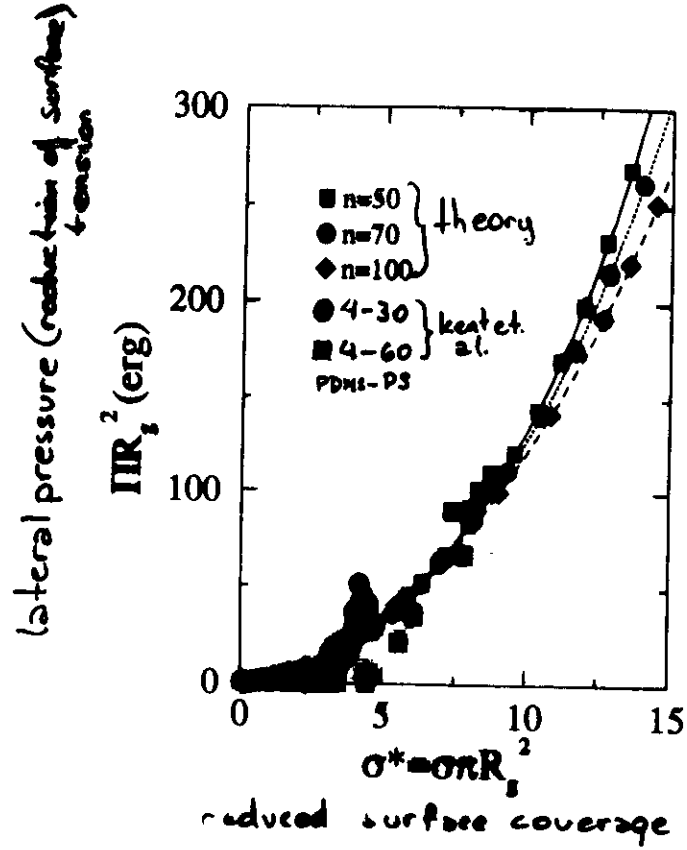


We find virial description better than scaling.

Height of polymer layer







Why ΠR_g^2 vs σ^*

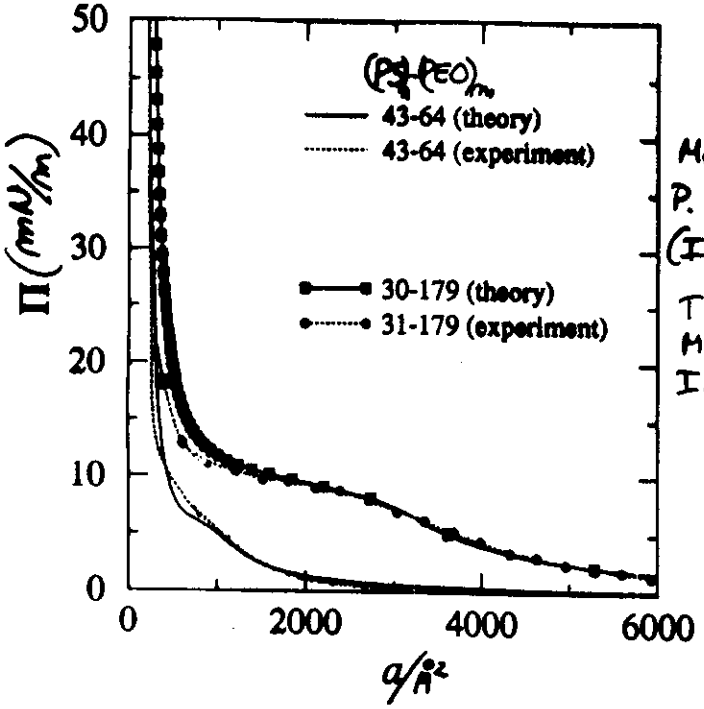
Very low σ we expect $\Pi = A_2 \sigma^2$

$A_2 \propto R_g^2$ (like hard disks, Flory) then

$$\Pi R_g^2 \propto (\sigma R_g^2)^2$$

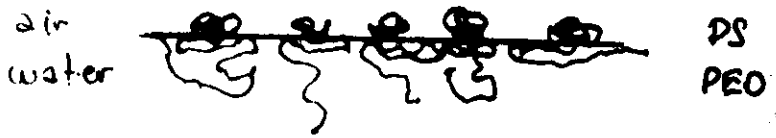
What about the structure?

Pressure - Area Isotherms
PS-PEO at water-air interface

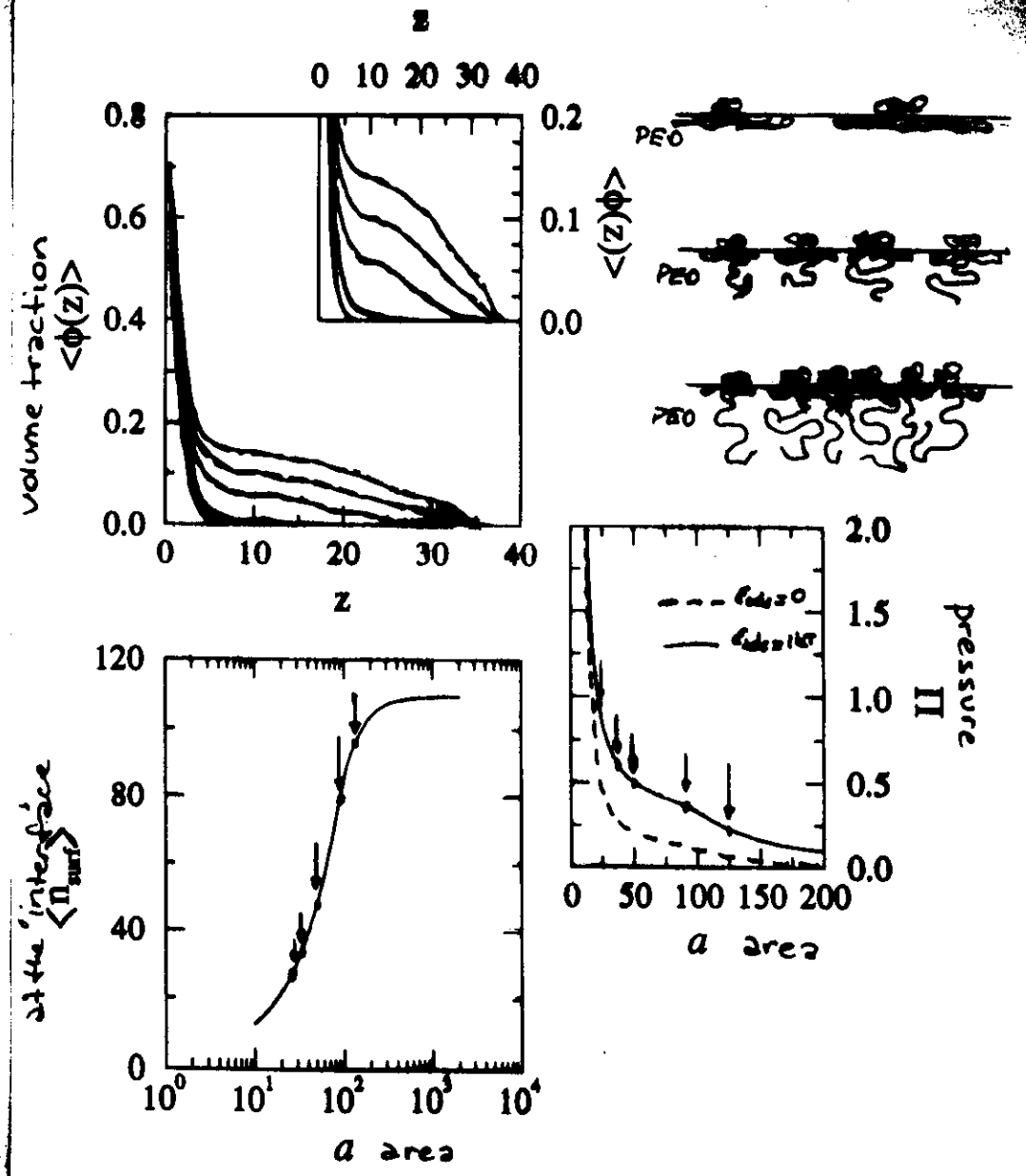


What is the origin of the "plateau".

Preferential adsorption of EO (CH_2-CH_2-O) to water-air interface.



Structure of PEO Layer: $N_{EO} = 44$



Grafted Polymers in contact with protein solution

$$\frac{f}{a} = \sigma f_g + \int_0^\infty \rho_s(z) f_s(z)\,dz + \int_0^\infty \rho_p(z) f_p(z)\,dz$$

$\beta f_g = \sum_\alpha P(\alpha) \ln P(\alpha)$ (polymer)

$\beta f_s = \ln \rho_s(z) - c$ (solvent)

$\beta f_p = \ln \rho(z) + \int \beta_p(z,\Omega)\left[\ln \frac{\beta_p(z,\Omega)}{4\pi} + \phi_w(z,\Omega)\right] d\Omega$ (protein)

Minimization subject to packing constraint:

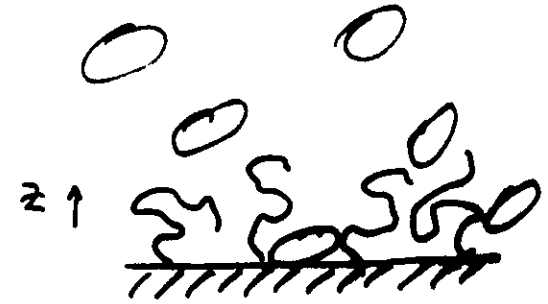
$$\sigma \langle n_g(z) \rangle + \int_\Omega \langle n_p(z) \rangle + \rho_s(z) = 1$$

gives:

$$\rho_p(z) = e^{\beta\mu_p} \beta_p(z)$$

$$P_p(z,\Omega) = \frac{1}{Z_p(\Omega)} e^{-\int \pi(z') n_p(z',\Omega) dz' - \beta \varepsilon_{p-w}(z,\Omega)}$$

(constant μ_p for all α has been taken into account!)



$$P_g(\alpha) = \frac{1}{q} e^{-\int \pi(z) n_g(z,\alpha) dz}$$ (grafted po

$$\rho_s(z) = e^{-\pi(z) n_s + \beta\mu_s}$$ (solvent)

$\pi(z)$ Lagrange multipliers physical significan

lateral pressures!! (osmotic pressure).

How do we find $\pi(z)$? insert $P_p(z,\Omega)$, $P_g(\alpha)$ and $\rho_s(z)$ into const. eq.

Input: set of conformations (α) and prot.; solve and protein μ, and $U_{p-w}(z)$.

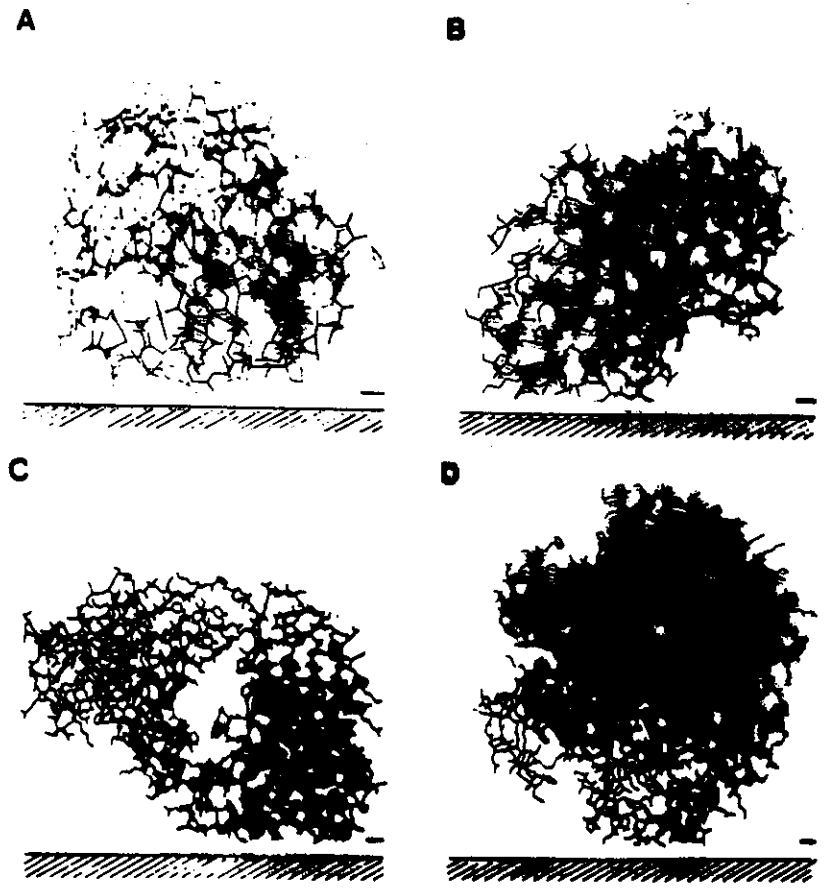
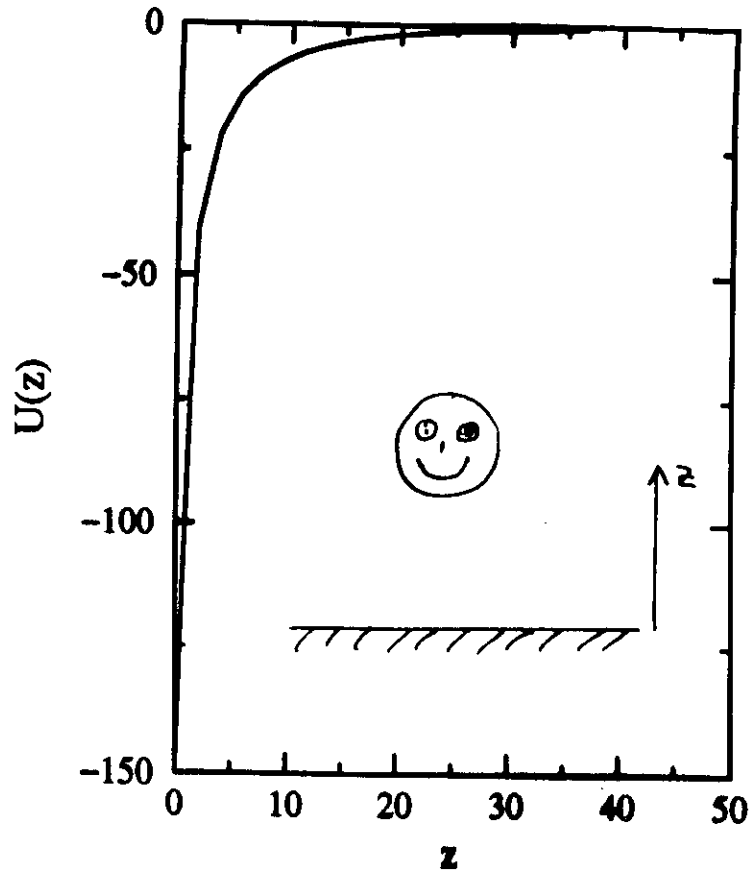
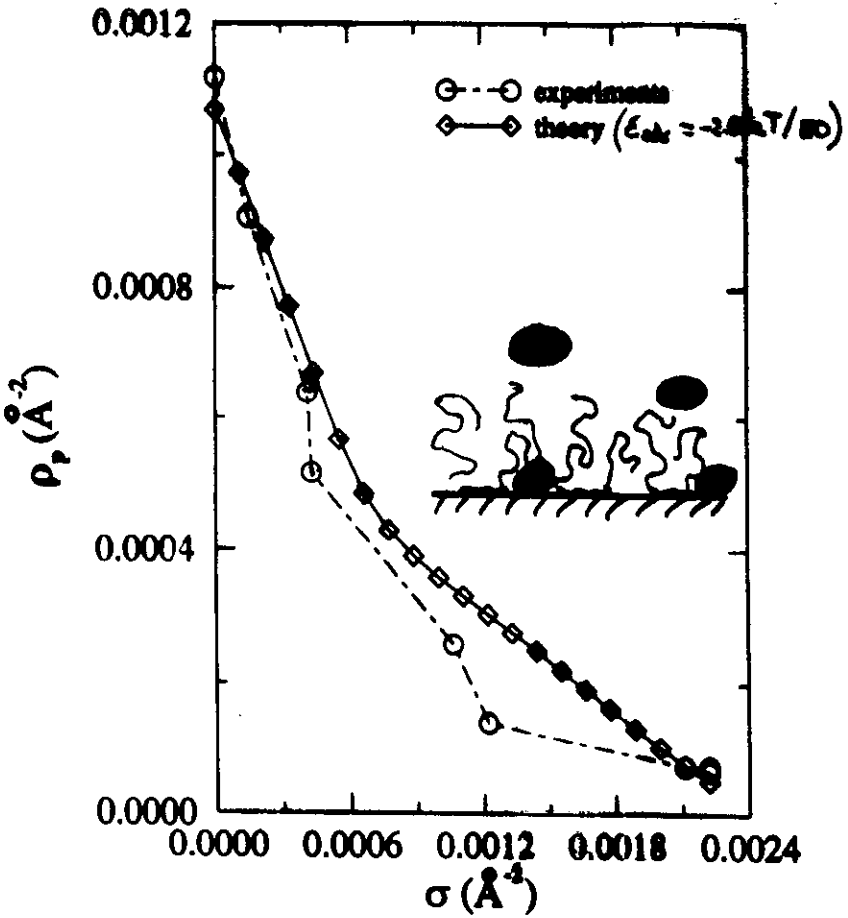


Figure 6. Structures of the four proteins on the polyethylene surface with orientations having the lowest solvation energies. Bar = 2 Å. (A) Lysozyme; (B) trypsin; (C) immunoglobulin F_{ab}; (D) hemoglobin.

Bare protein-surface potential
Lysozyme (Lee and Park)



Lysozyme adsorption on Pluronic F127 modified surface

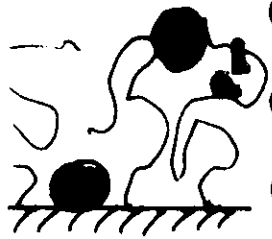


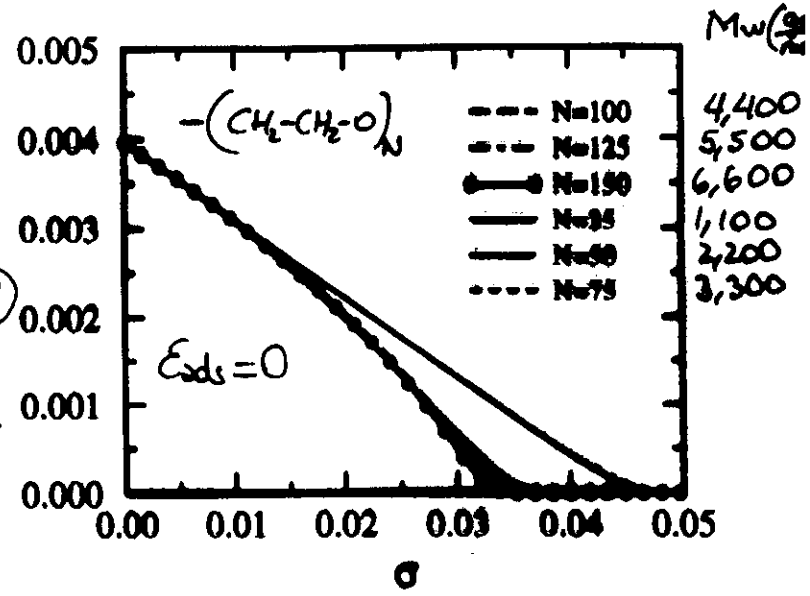
Experimental work : Prof. Kinam Park (Purdue Univ.)

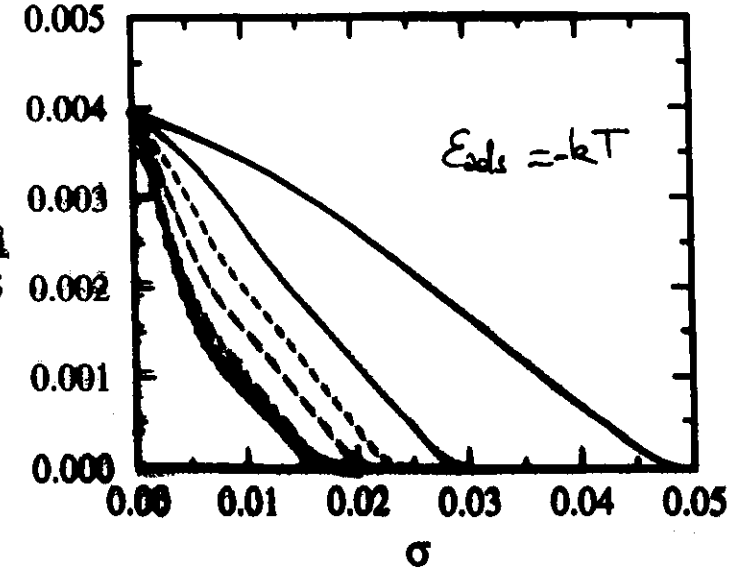
Pluronic F127: $(EO)_{99}-(PO)_{67}-(EO)_{99}$

hydrophilic — hydrophobic — hydrophilic

Effect of Molecular Weight

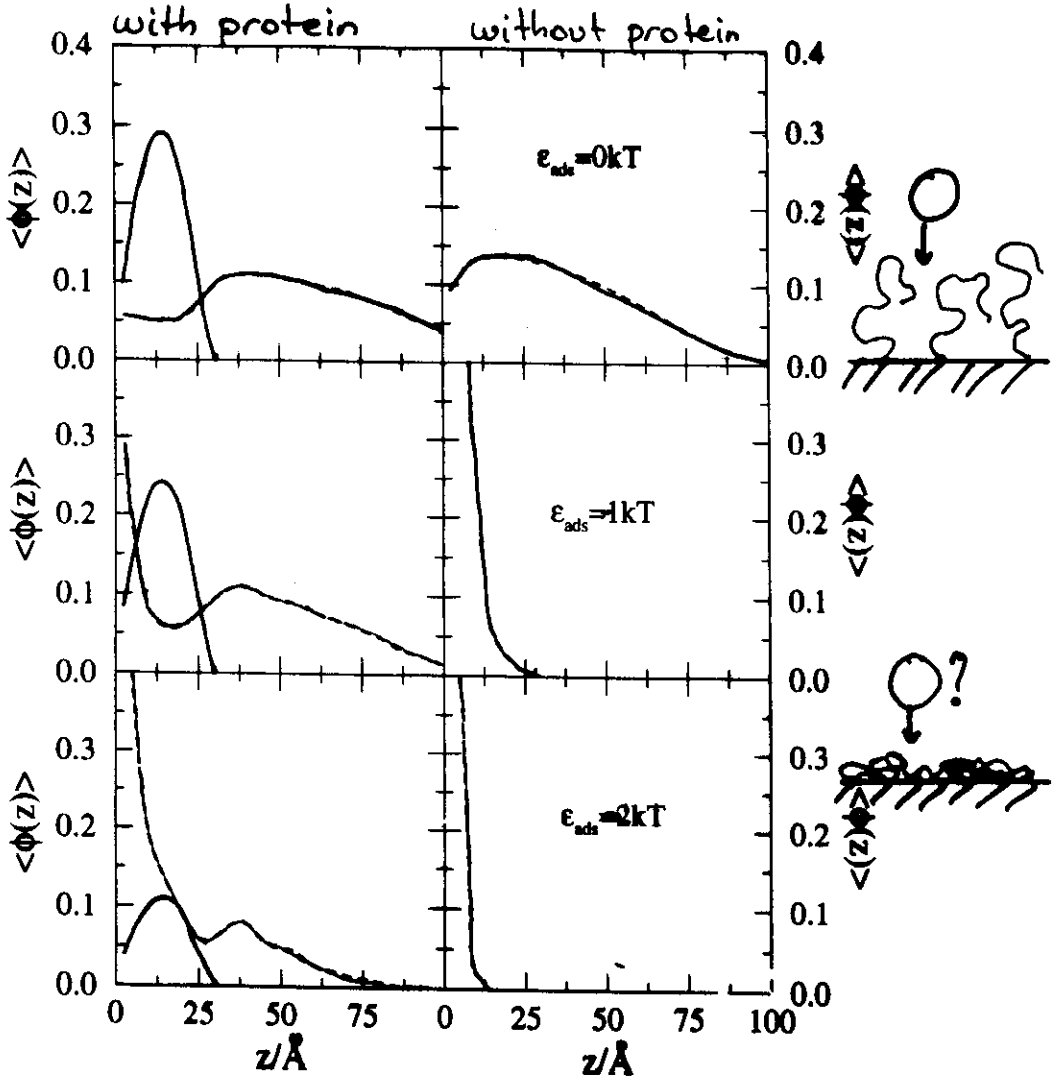




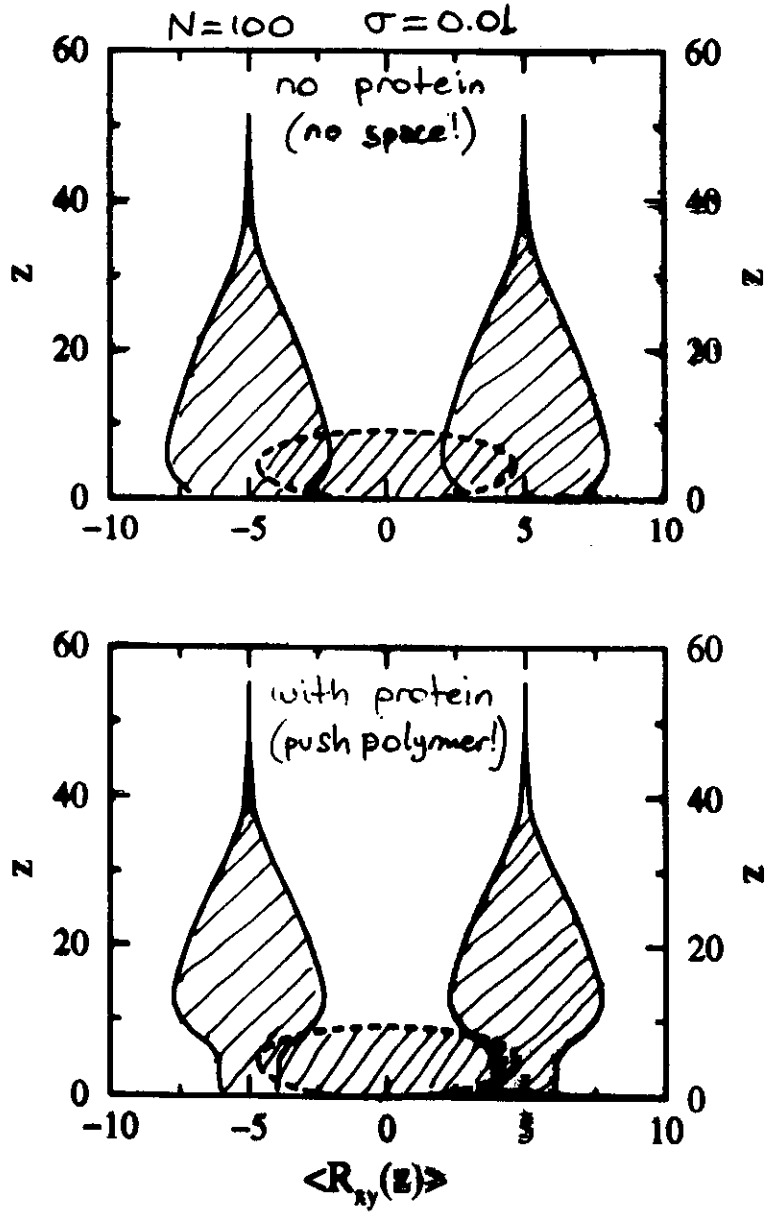


Protein and Pluronic density profiles

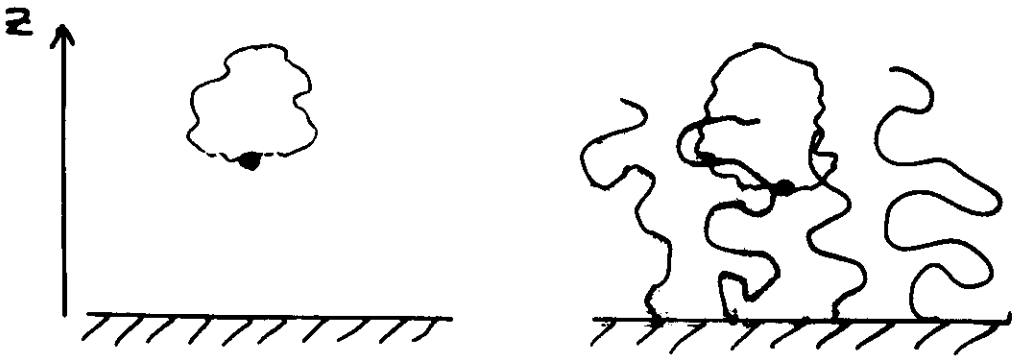
protein "pushes" polymer towards solvent !!



Structure of the polymer layer



Protein adsorption (or lack of it?)



How does $U_{p-s}(z)$ change due to polymer layer?

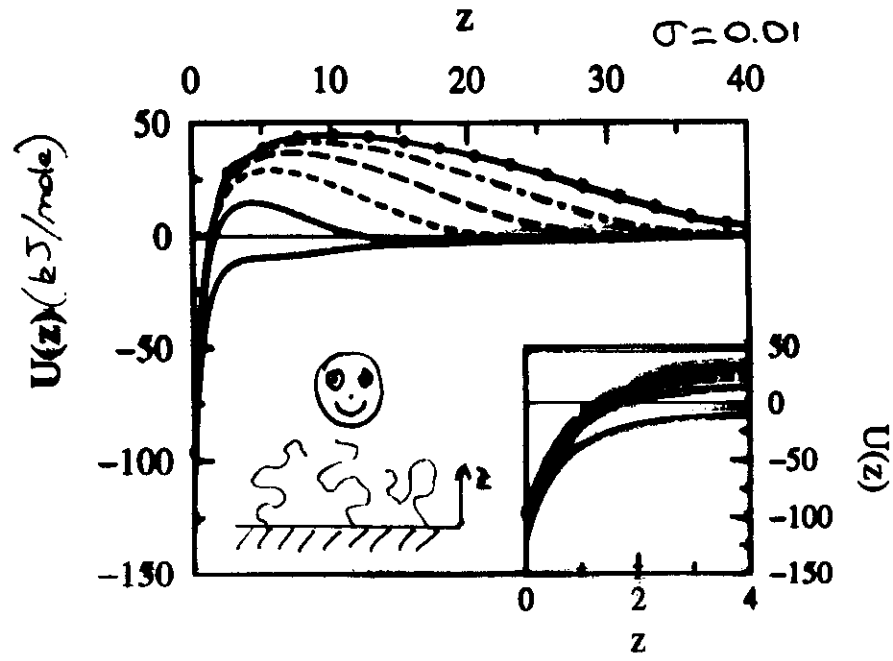
$$U_{p-s}(z) = U_{p-s}^{attr}(z) + U_{p-s}^{rep}(z)$$

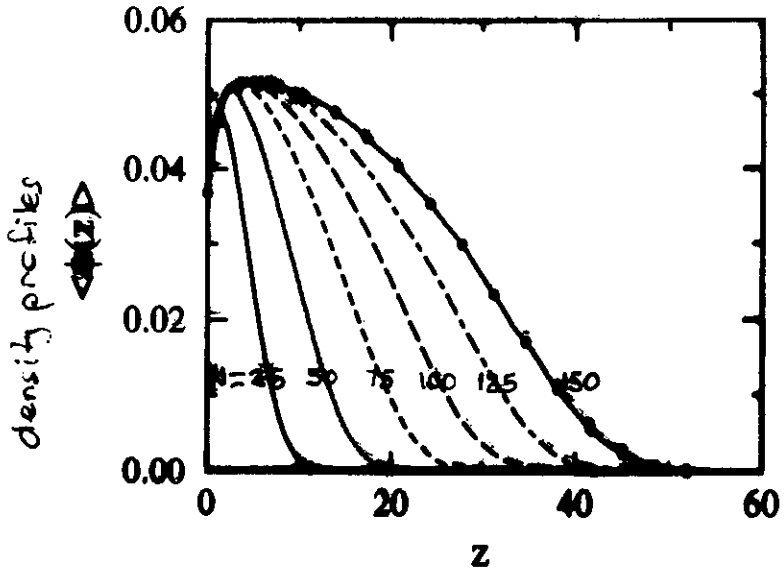
$$U_{p-s}^{rep} = \mu(z) = \int_z^\infty \Pi(z)\, A_{p,s}(z)\, dz$$

"Potential of mean-force": averaged over all possible configurations of the polymer

Note that $\Pi(z)$ is that of the layer with

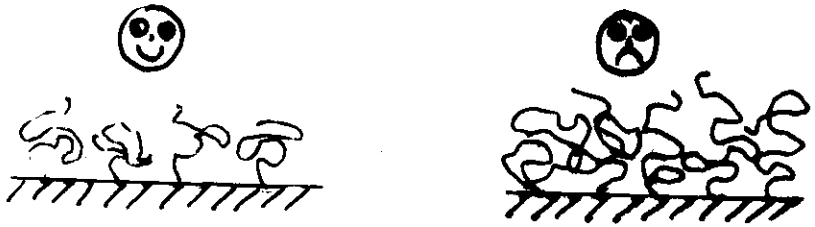
Potential of mean force

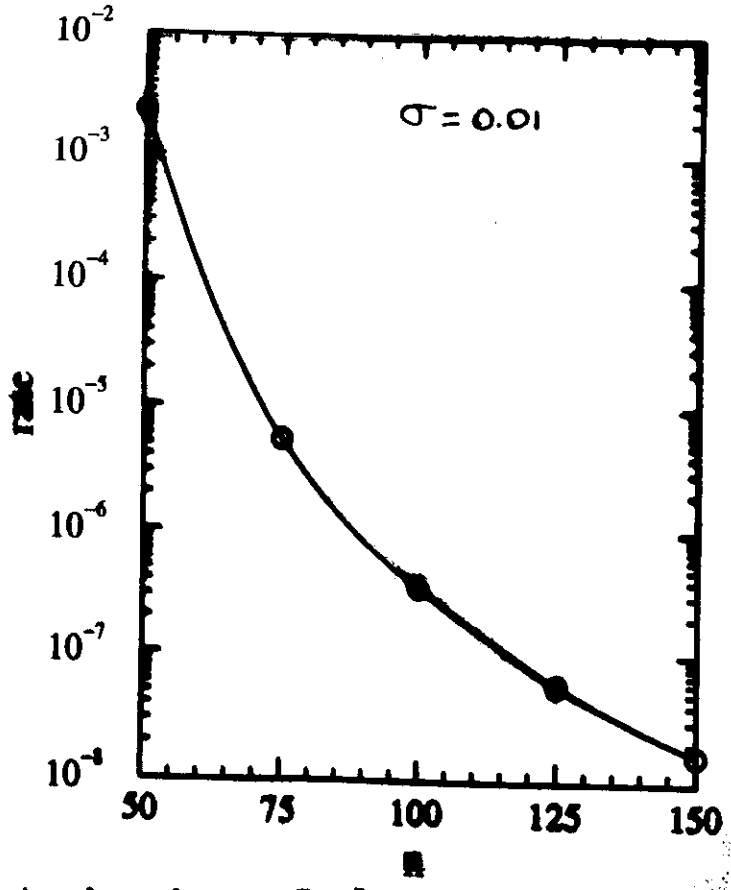




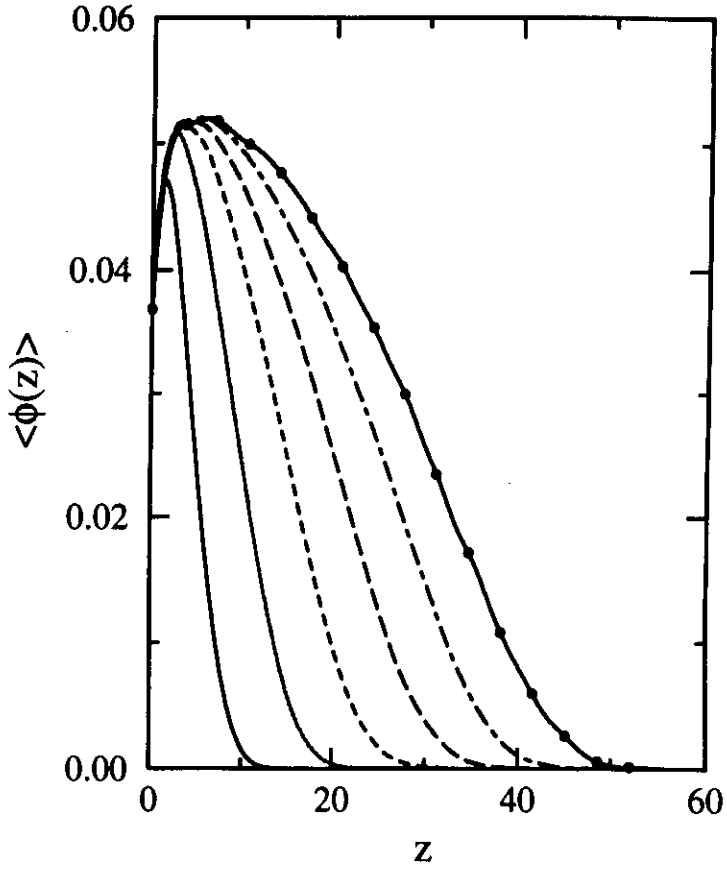
Time scales for adsorption:

TST ⇒ $k = \frac{1}{\tau} \propto e^{-\beta U_{barrier}}$





same equil. adsorption



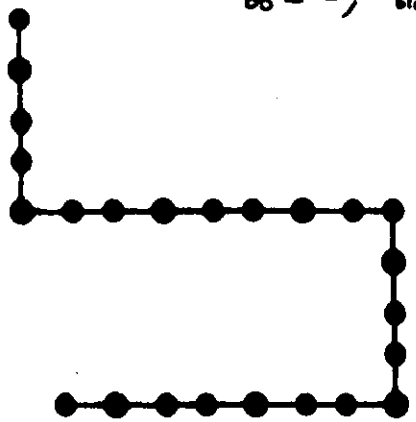
Model Protein:

cubic lattice: $z = 6$

blue segments: "hydrophobic"

black segments: "hydrophilic"

$\varepsilon_{bb} = \varepsilon$; $\varepsilon_{black,black} = \varepsilon_{bb} = 0$



Number of possible configurations $\sim 5^{22} \sim 2 \times 10^{15}$

but only ~ 10 "native structure"

and different (~ 10) "surface native [illegible]