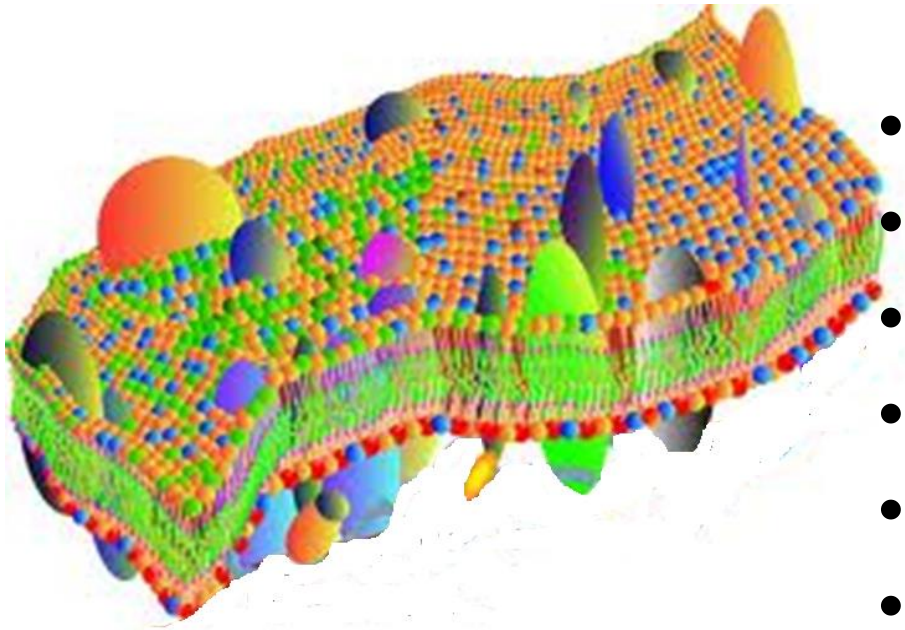
Membranas, proteínas – será que modelos estatísticos tem algo a dizer?

Vera Bohomoletz Henriques

BioLat group

Instituto de Física USP

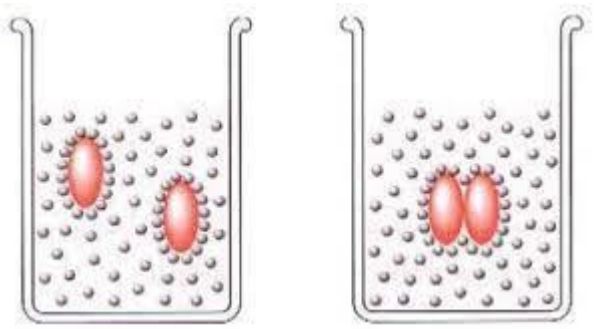
29 de março de 2022

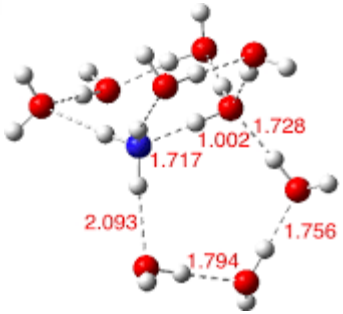


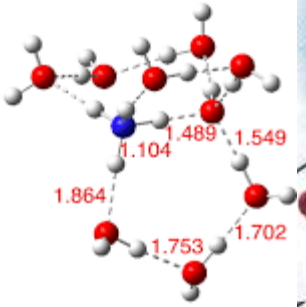
- Lipídeos
- Proteínas
- Açúcares
- Colesterol
- Água
- Íons...

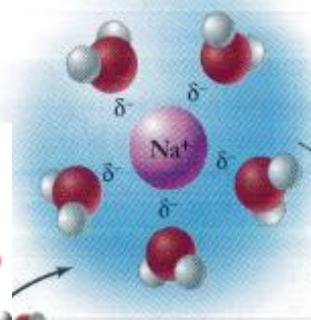
- organização depende das interações entre muitas partículas e da temperatura
- como obter informação das interações a partir do experimento?
- como prever propriedades macroscópicas a partir das interações?

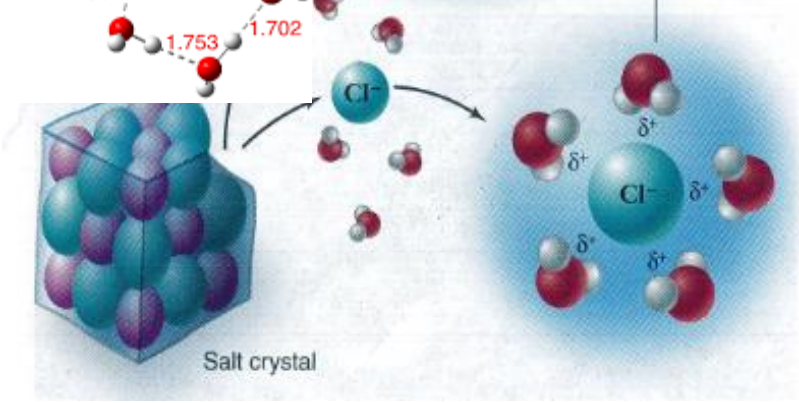
Moléculas polares e apolares

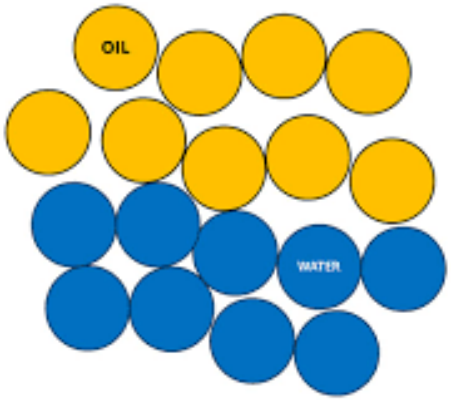




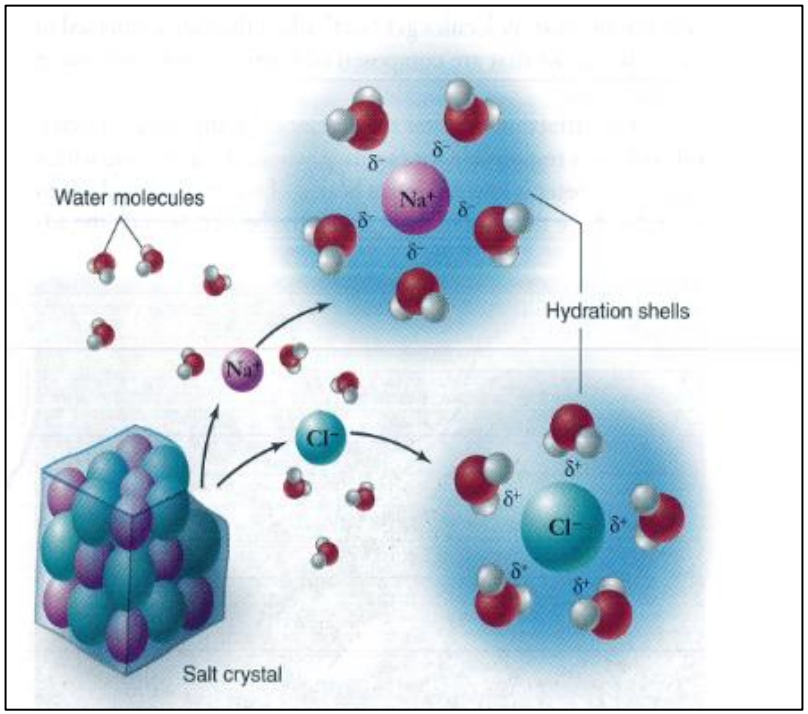


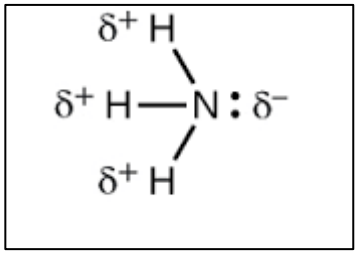


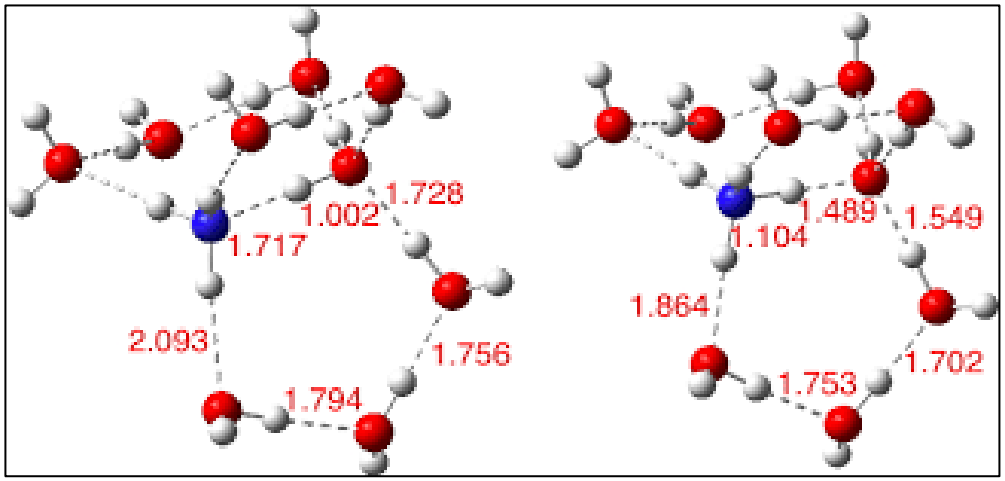




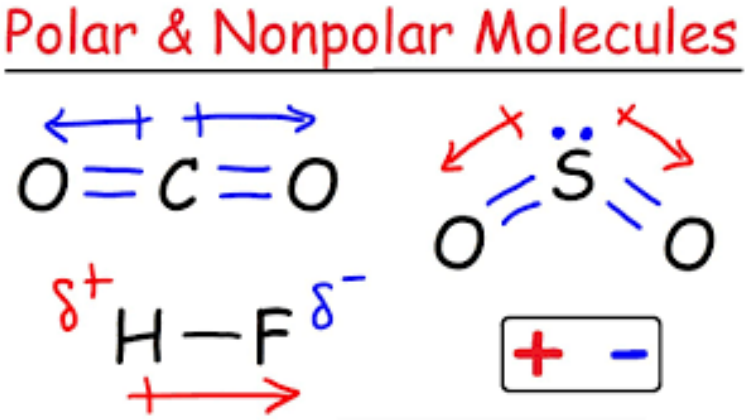
Moléculas polares em água

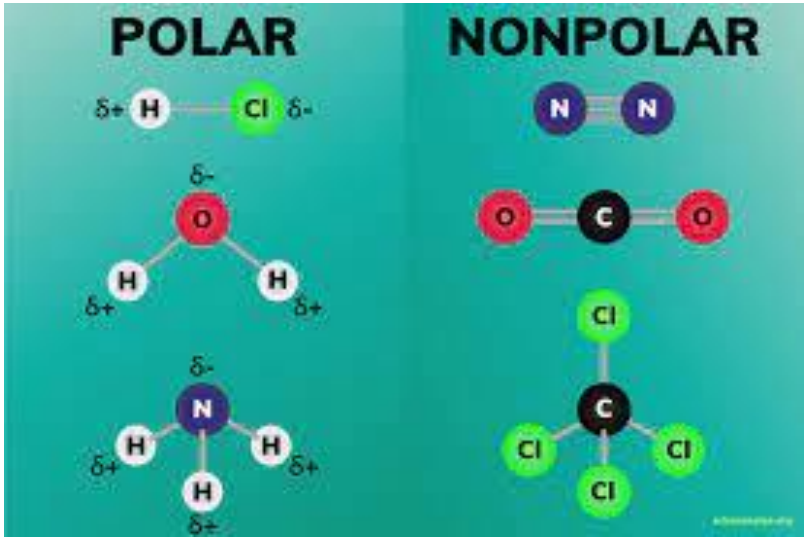


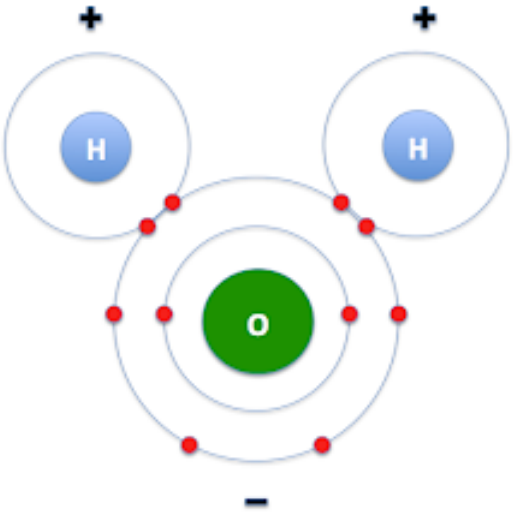




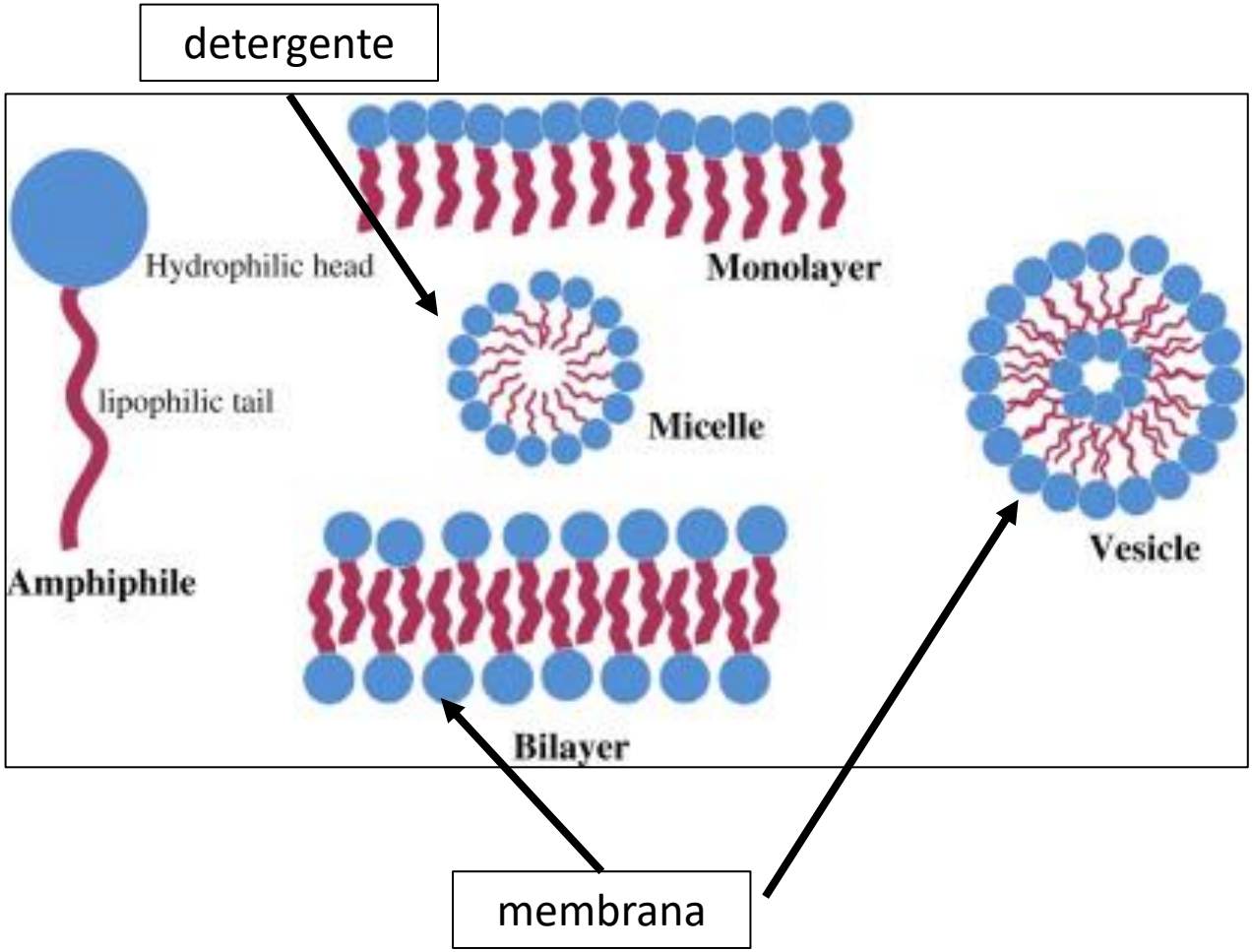
Moléculas polares e apolares na água



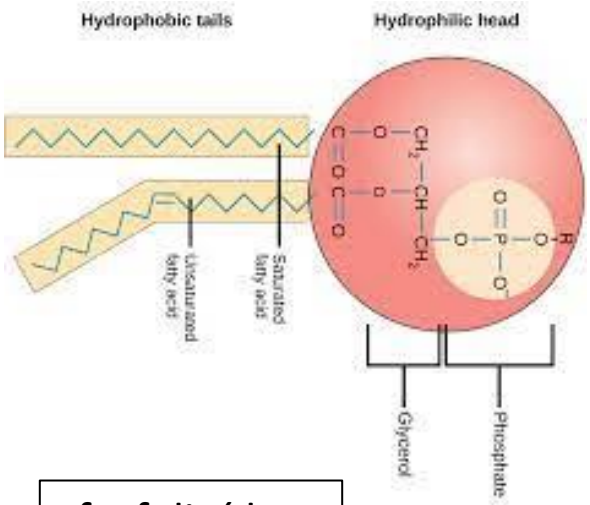




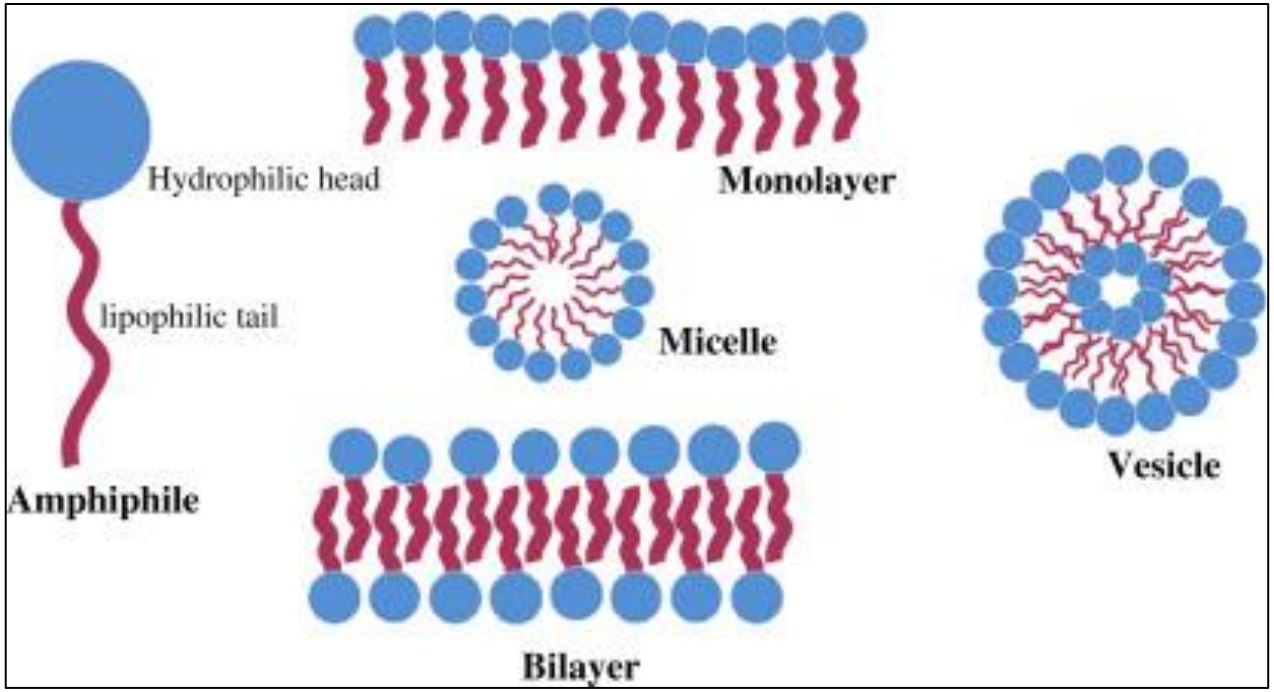
Moléculas biológicas são anfifílicas



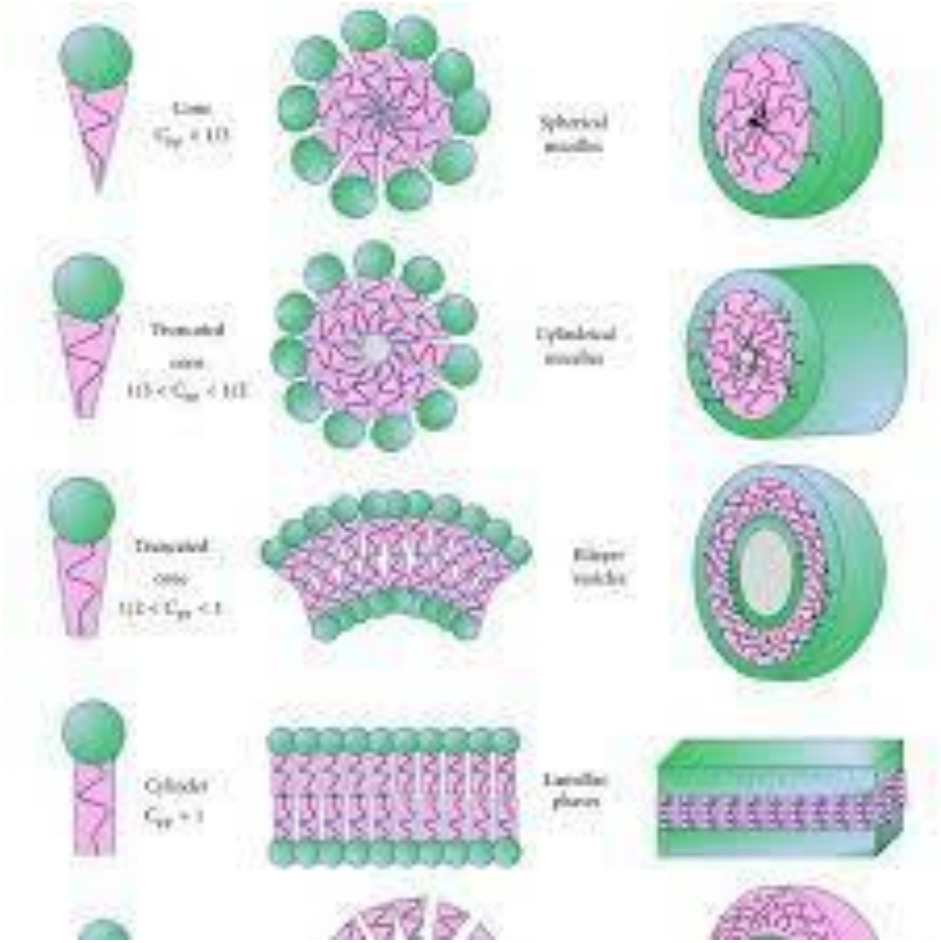
Moléculas biológicas são anfifílicas



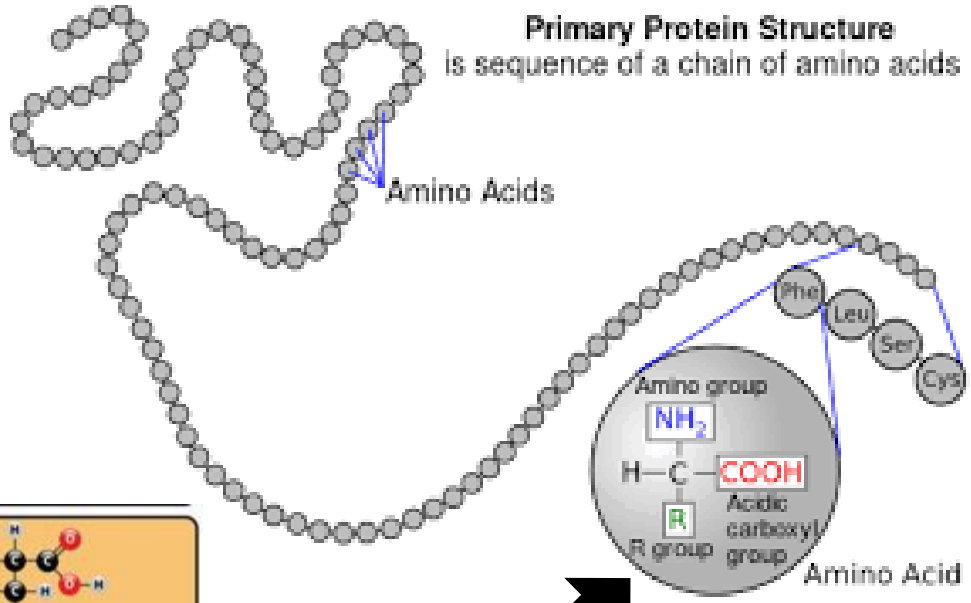
fosfolipídeo

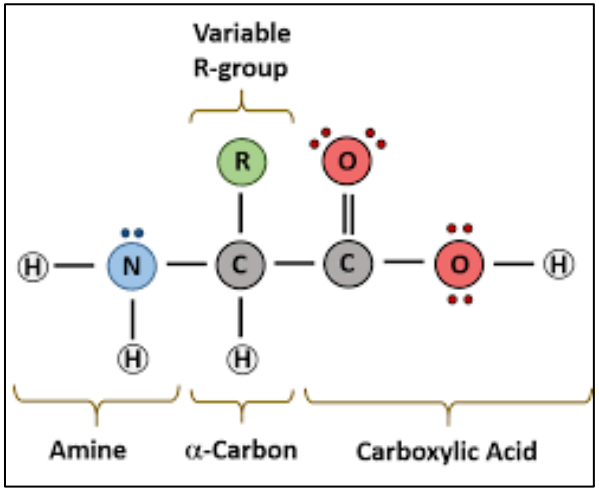


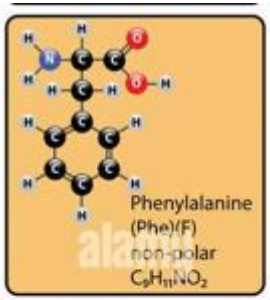
Moléculas anfifílicas formam estruturas em água

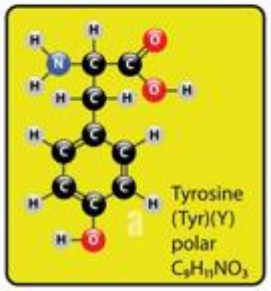


polaridade e organização: proteína



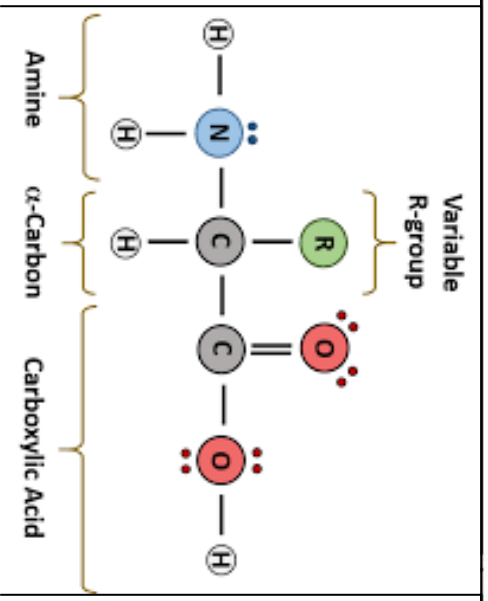


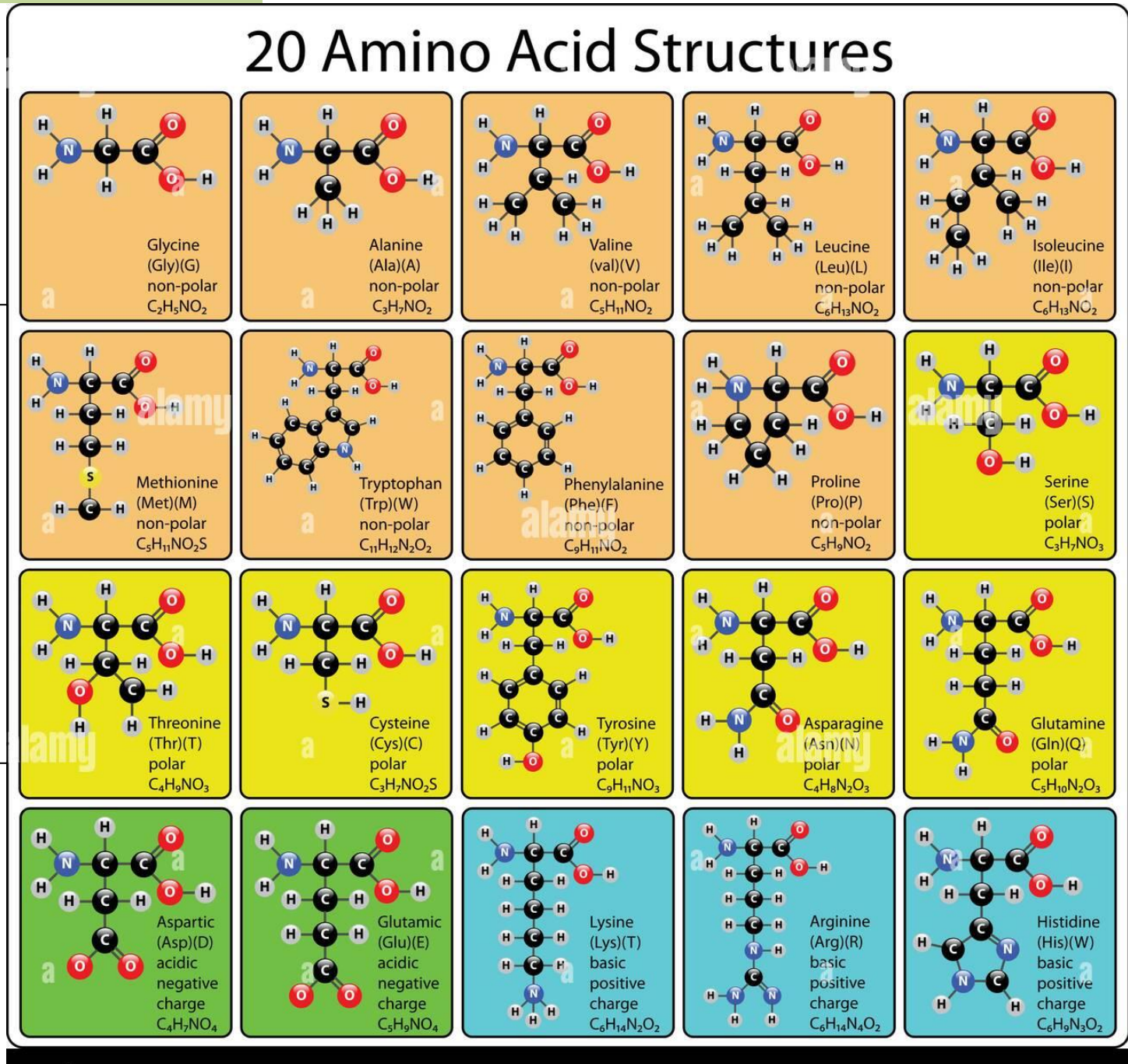




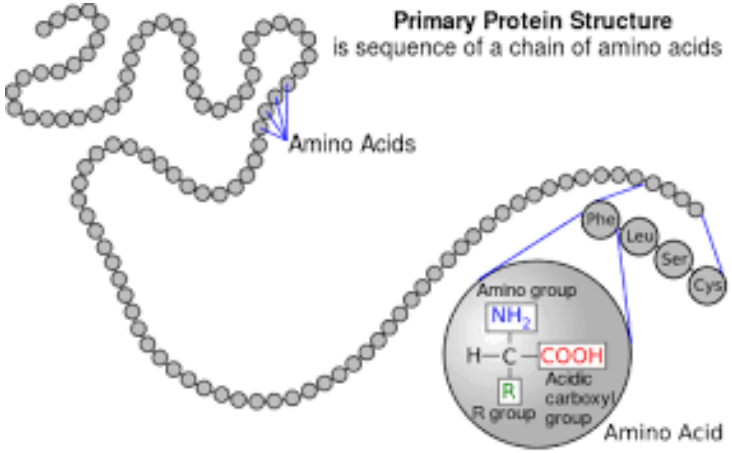
Exemplos de grupos R

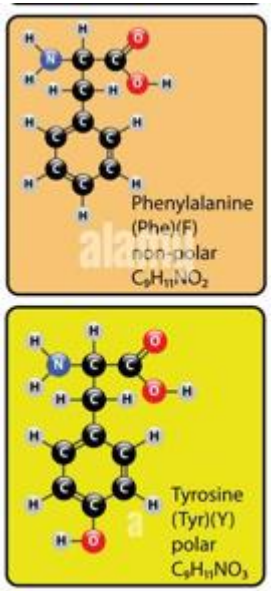
polaridade e organização: membrana

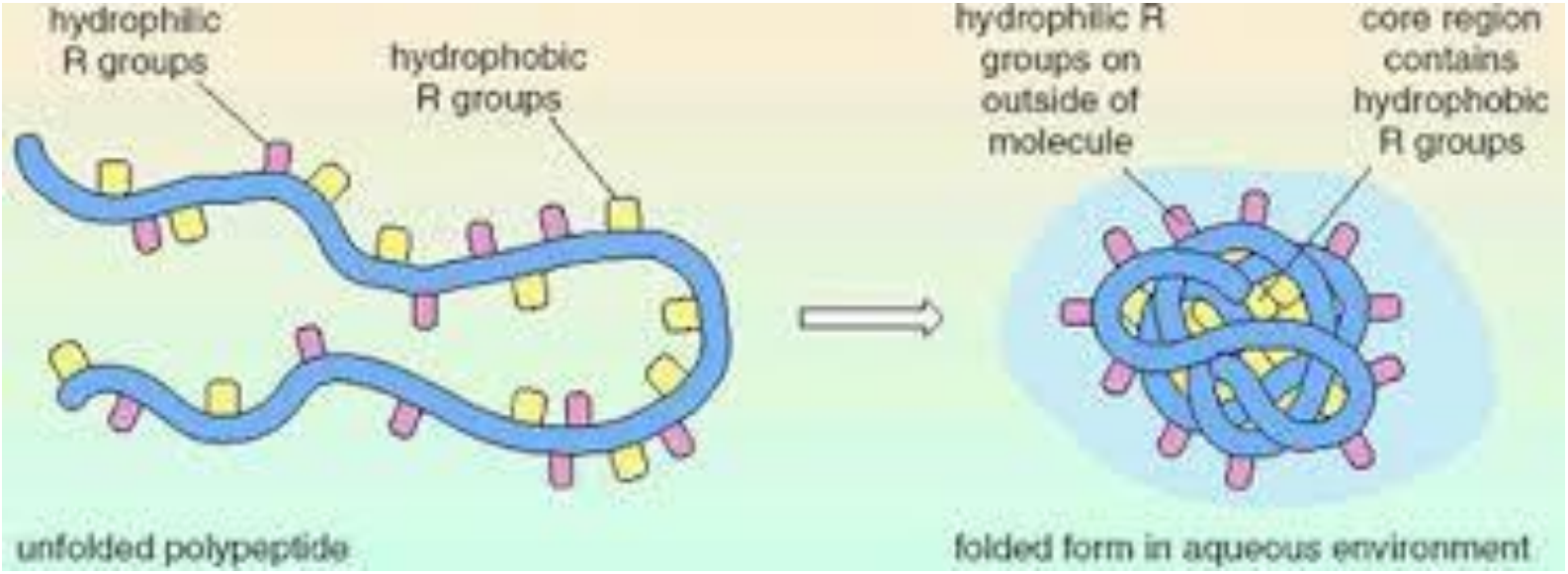




polaridade e organização: membrana







técnicas experimentais

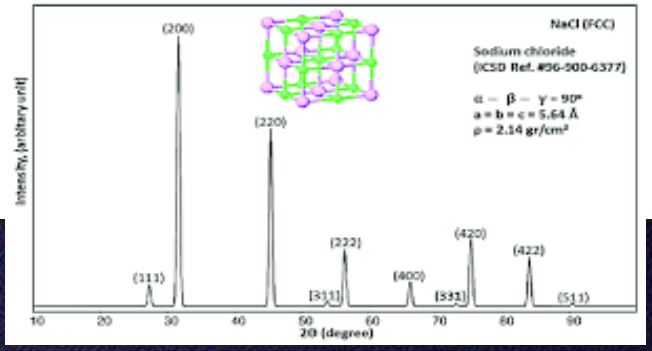
organização molecular

e

estrutura espacial

forma

espalhamento e estrutura



como?

X-ray tube

10,000-40,000 volts

Crystalline solid

Lead screen

Spot from incident beam

Spots from diffracted X-rays

Photographic plate

espalhamento e estrutura

VOLUME 7, NUMBER 6 JUNE 1973

Structure Factor and Radial Distribution Function for Liquid Argon at 85 °K†

J. L. Yarnell, M. J. Katz, and R. G. Wenzel
Los Alamos Scientific Laboratory, University of California, Los Alamos, New Mexico 87544

S. H. Koenig
IBM Thomas J. Watson Research Center, Yorktown Heights, New York 10598

(Received 29 January 1973)

The structure factor $S(Q)$ for liquid argon at 85 °K has been determined in a neutron scattering experiment to an accuracy of ≈0.01. The problem of obtaining $S(Q)$ from the results of neutron scattering measurements, made as a function of scattering angle using a detector with an energy-dependent efficiency, is considered in detail. Smooth curves for $S(Q)$ and its Fourier transform, the radial distribution function $g(r)$, were obtained from the experimental data by an iterative procedure suggested by Verlet and carried out by Schiff, and are tabulated for convenience. The experimental results are in excellent agreement with the predictions of computer simulations based on either the Lennard-Jones two-body interaction, or on the Barker, Fisher, and Watts potential with corrections for three-body and quantum effects included.

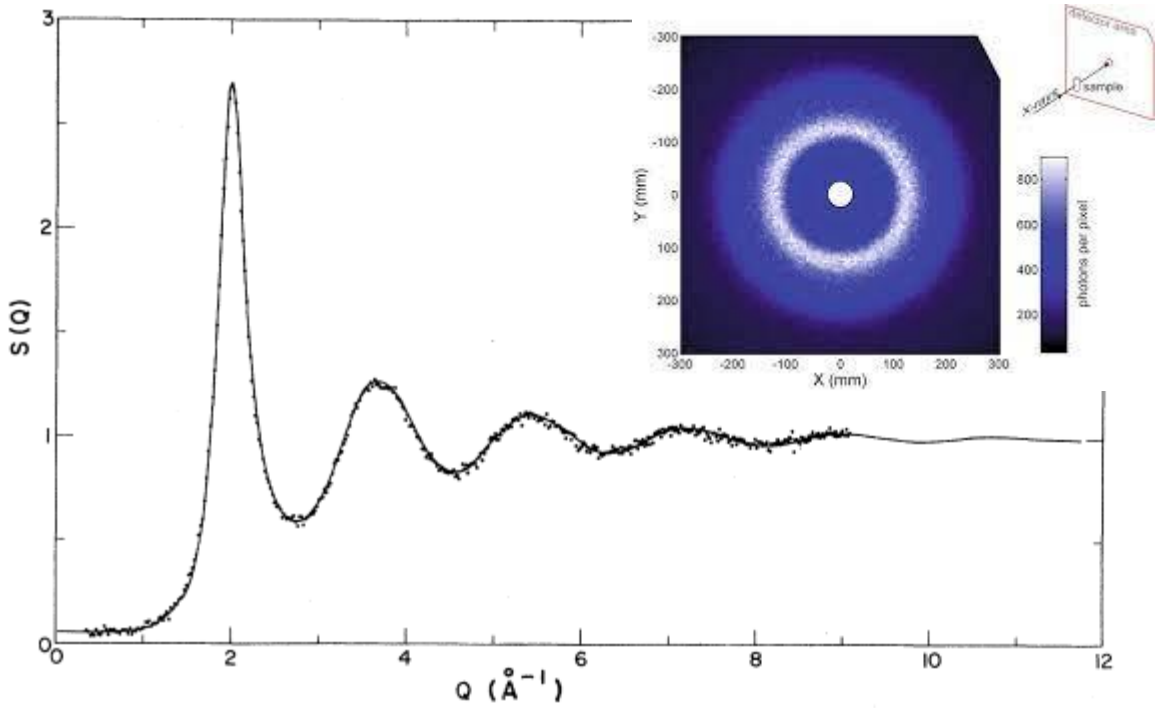
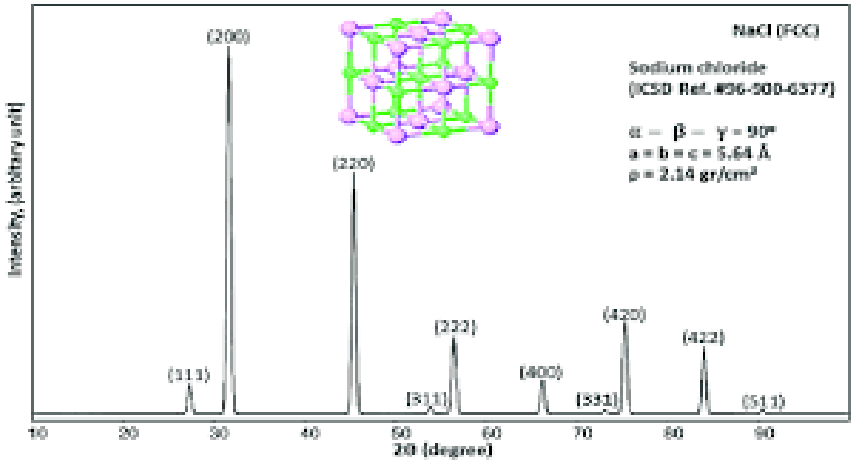
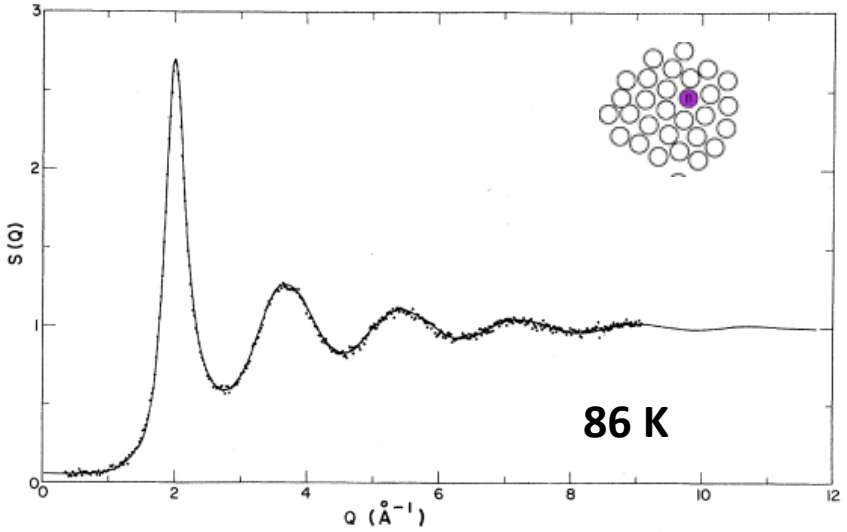


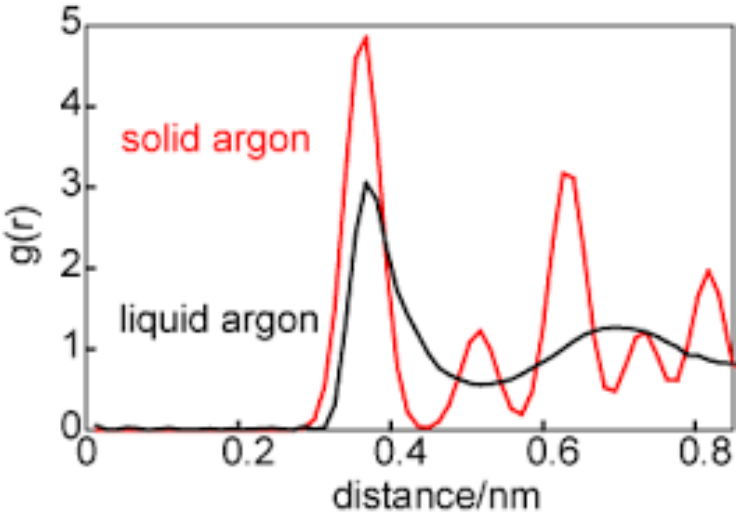
FIG. 3. Fully corrected experimental values of the liquid structure factor $S(Q)$ for ^{36}Ar at 85 °K. The solid line is a smoothed and extended $S(Q)$ obtained from the experimental data by an iterative procedure described in the text. The small dip in the experimental data near the top of the second peak ($Q = 3.75$ Å^{-1}) is apparently statistical in origin.

sólido x líquido





Qual o efeito da temperatura em cada caso?

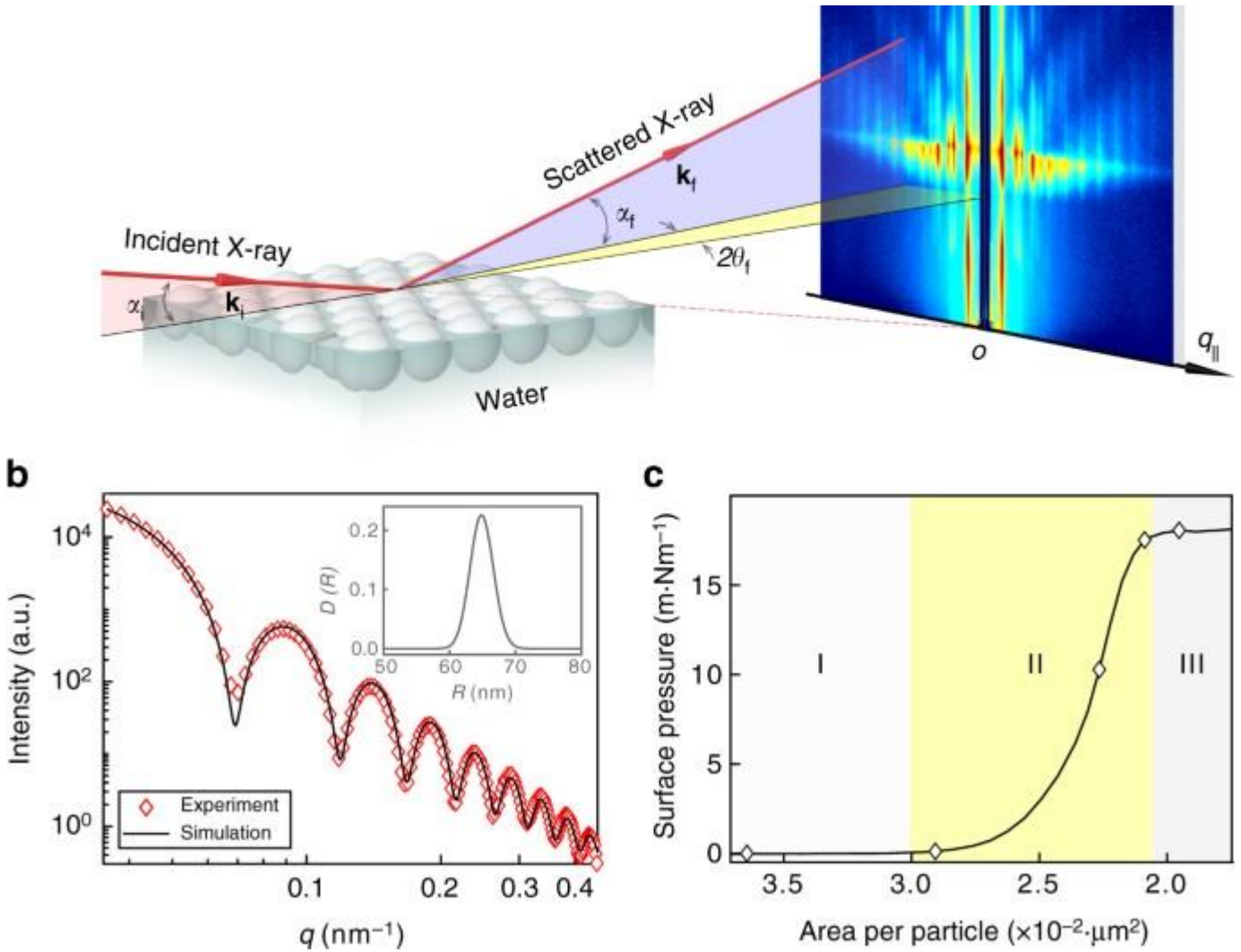


espalhamento e estrutura

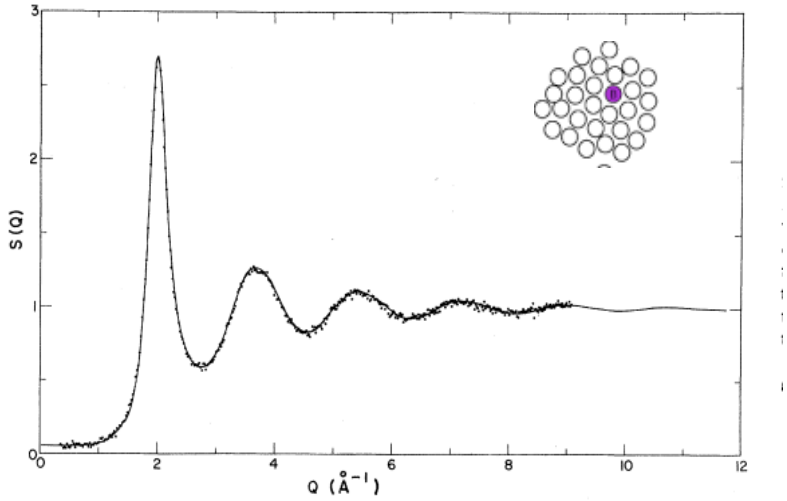
In situ X-ray scattering observation of two-dimensional interfacial colloidal crystallization

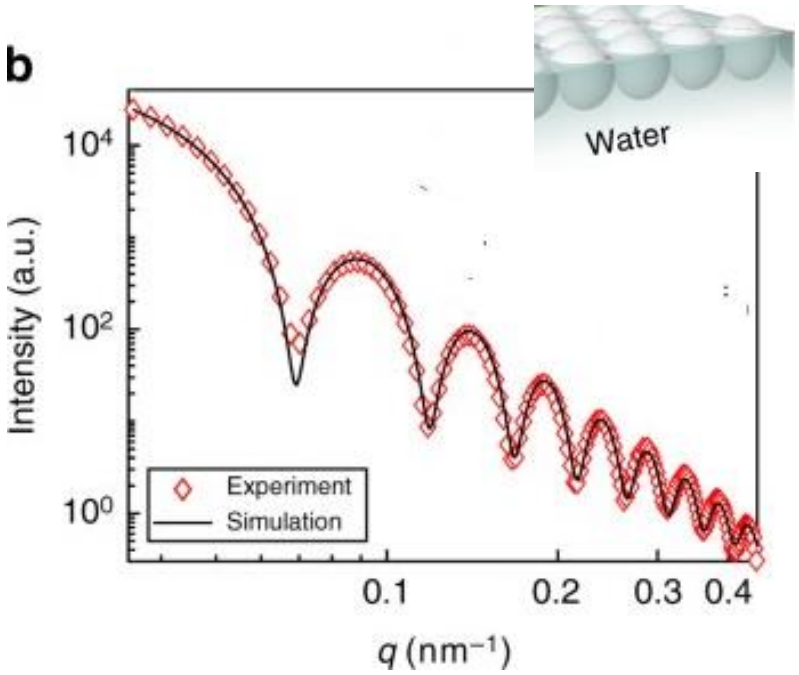
Longlong Wu, Xiao Wang, Geng Wang & Gang Chen

Nature Communications **9**, Article number: 1335 (2018) | Cite this article



líquido x colóide





por que a diferença?

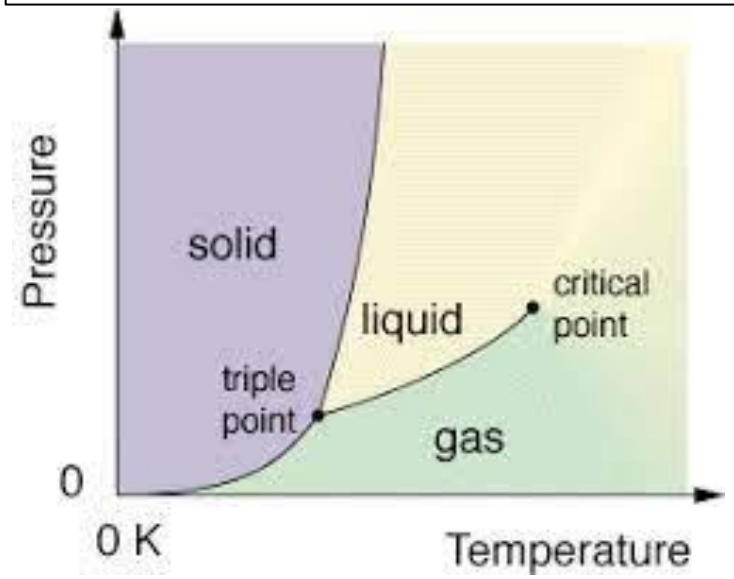
técnicas experimentais

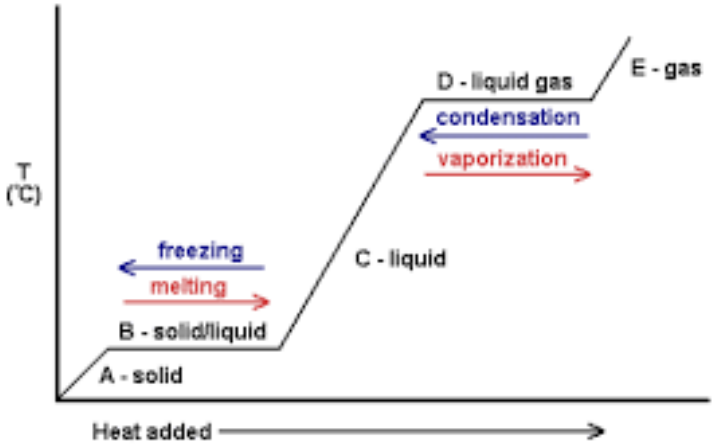
mudança de fase

e

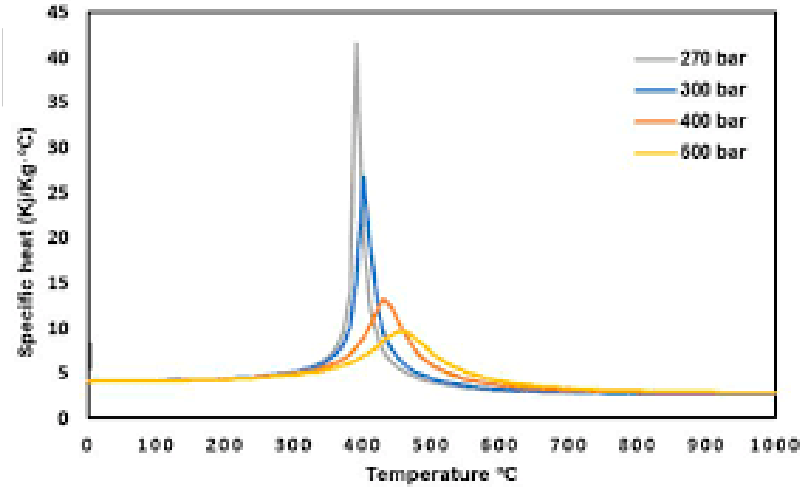
calor específico

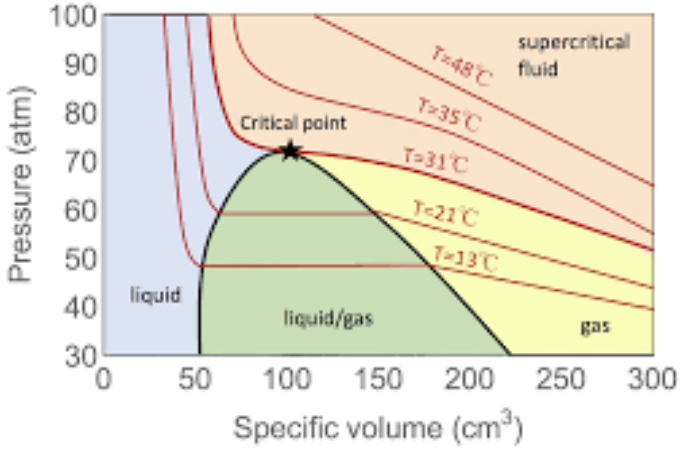
transição de fases e experimentos





Qual a relação entre estas 4 representações?





transição de fase e calor específico

ISSN 0965-545X, Polymer Science, Ser. A, 2010, Vol. 52, No. 11, pp. 1220–1227. © Pleiades Publishing, Ltd., 2010.
Original Russian Text © V.Ya. Grinberg, N.V. Grinberg, T.V. Burova, A.S. Dubovik, D.R. Tur, V.S. Papkov, 2010, published in Vysokomolekulyarnye Soedineniya, Ser. A, 2010, Vol. 52, No. 11, pp. 2025–2033.

Phase Separation in Aqueous Solutions of Polyethylaminophosphazene Hydrochloride during Heating[1]

V. Ya. Grinberg[a], N. V. Grinberg[b], T. V. Bu

[a] *Emanuel Institute of Biochemical Physics, Russian*
[b] *Nesmeyanov Institute of Organoelement Compounds, Ru*
e-mail: g

Abstract—It is shown that aqueous solutions of separation during heating. This phenomenon is s to the composition of the system with the use of and the enthalpy of phase separation of the syster system features a lower critical solution tempera phase separation is 12.8 ± 0.6 J/g of the polymer the analysis of DSC data on the phase separation on the basis of calorimetric parameters couple Through this approach, the main contribution to is related to a change in the energy state of a poly of its dehydration.

DOI: 10.1134/S0965545X10110167

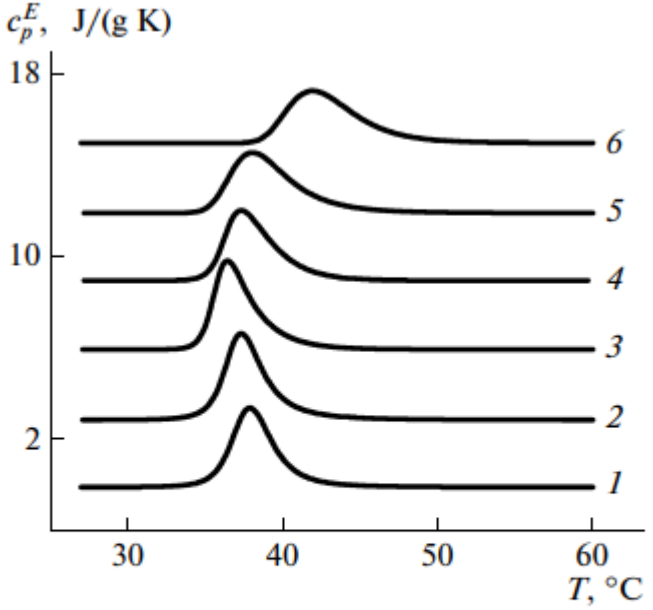


Fig. 3. Excess-heat-capacity curves for the PEAP · HCl–H_2O system of various compositions: w_2 = (*1*) 0.00025, (*2*) 0.0005, (*3*) 0.001, (*4*) 0.002, (*5*) 0.004, and (*6*) 0.01 at pH 3.5 (0.1 M citrate buffer). For the sake of clarity, the curves are arbitrarily shifted along the ordinate axis.

transição de fase e calor específico

PHYSICS REPORTS (Review Section of Physics Letters) 98, No. 2 (1983) 57–143. North-Holland Publishing Company

EQUILIBRIUM CRITICAL PHENOMENA IN BINARY LIQUID MIXTURES

A. KUMAR,* H.R. KRISHNAMURTHY and E.S.R. GOPAL

Department of Physics, Indian Institute of Science, Bangalore-560012, India

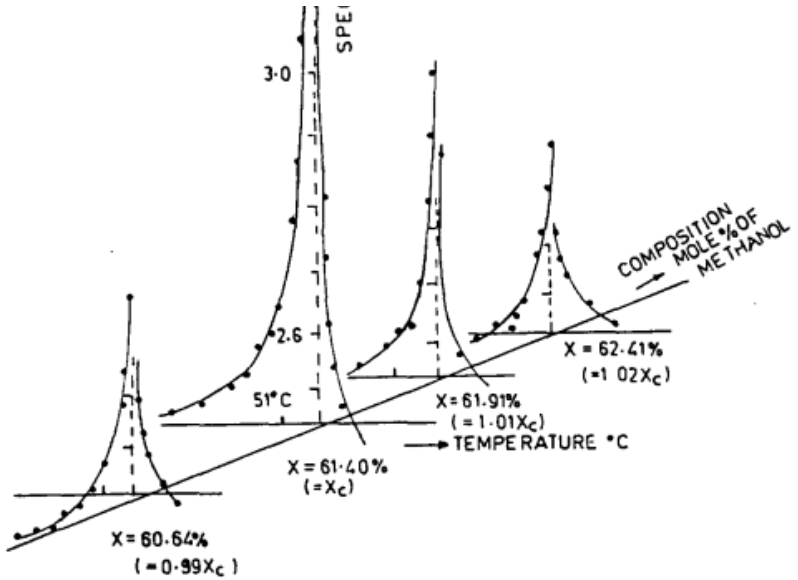
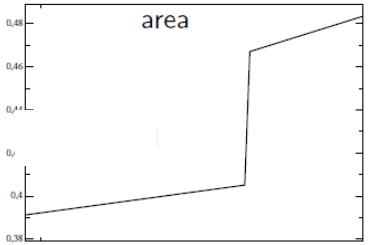


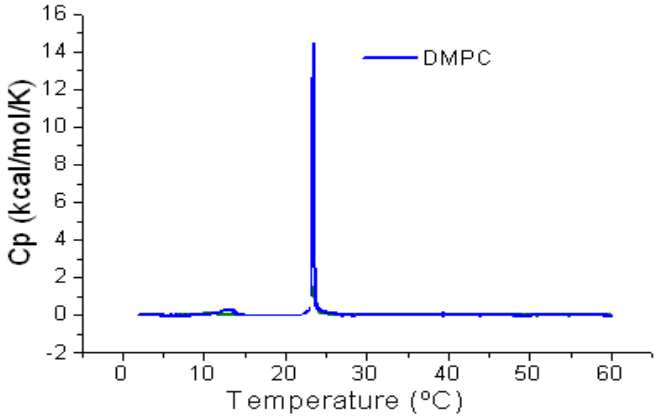
Fig. 4.1. Specific heat of methanol + n. heptane in the critical region (after Viswanathan et al. 1973). Note the sharpness of the specific heat peak at T_c and X_c.

transição ordem-desordem em membranas: experimento e modelagem

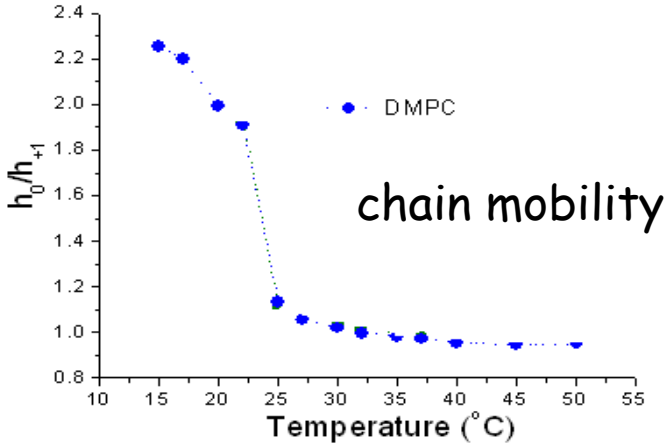
area por lipidio

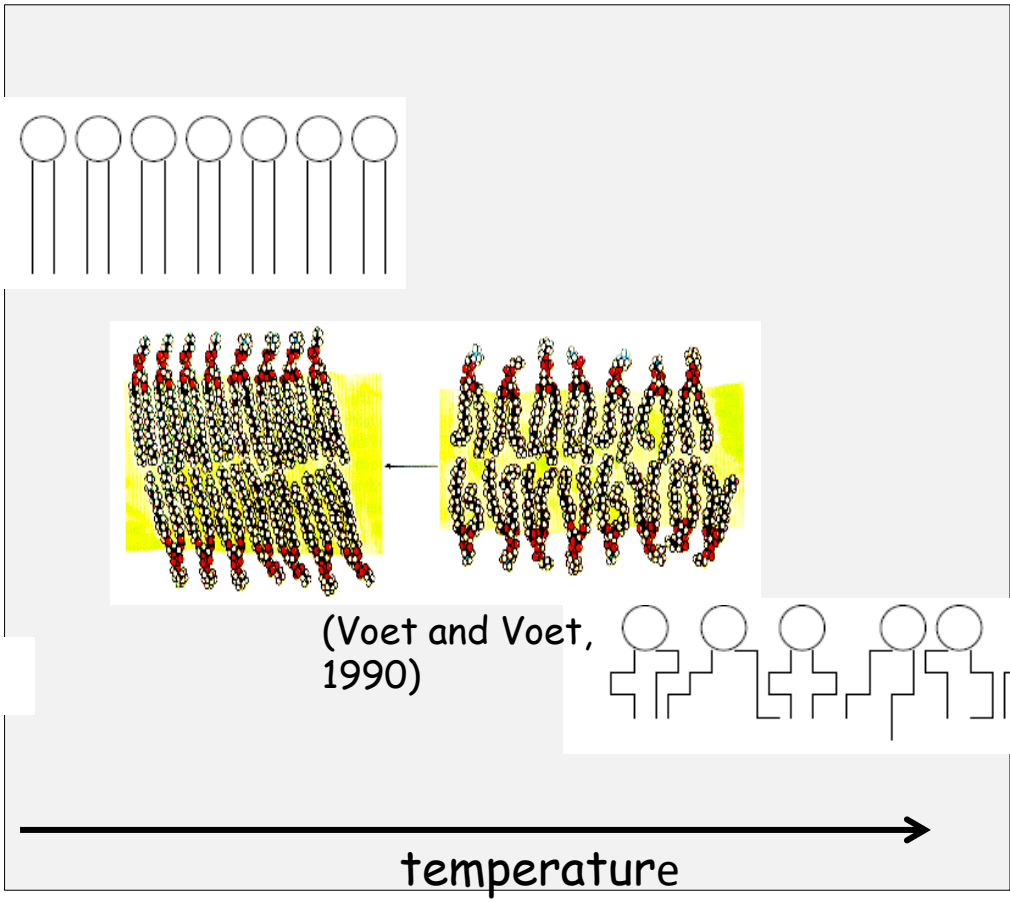


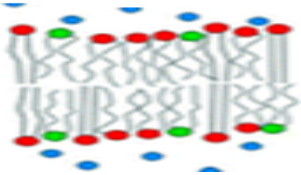
calor específico



electronic paramagnetic resonance

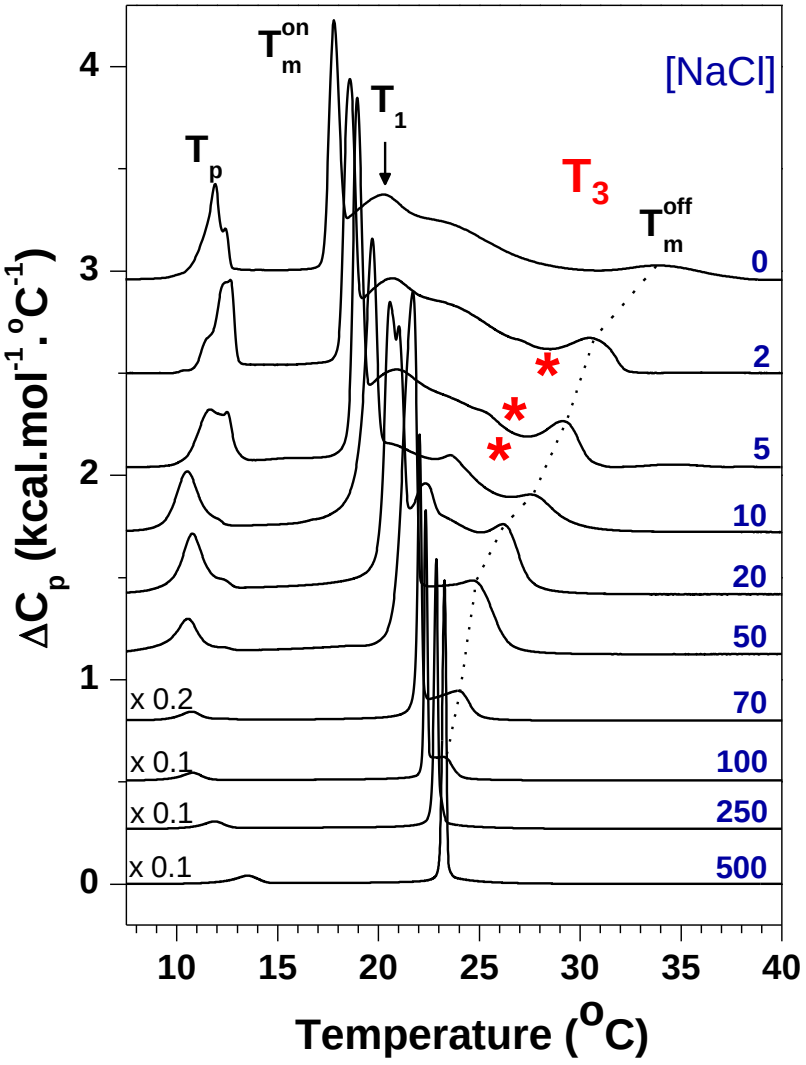




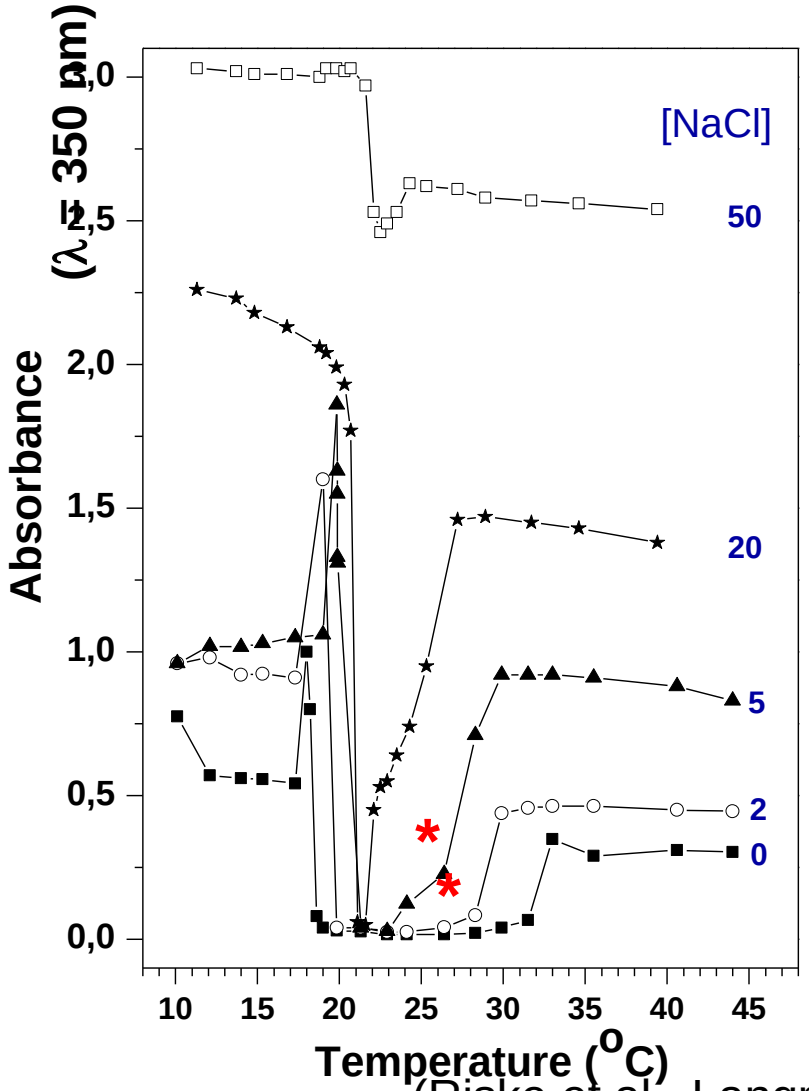


Papel da carga!

calorimetry



light absorption



(Riske et al., Langmuir 2009)

transição de fase e calor específico

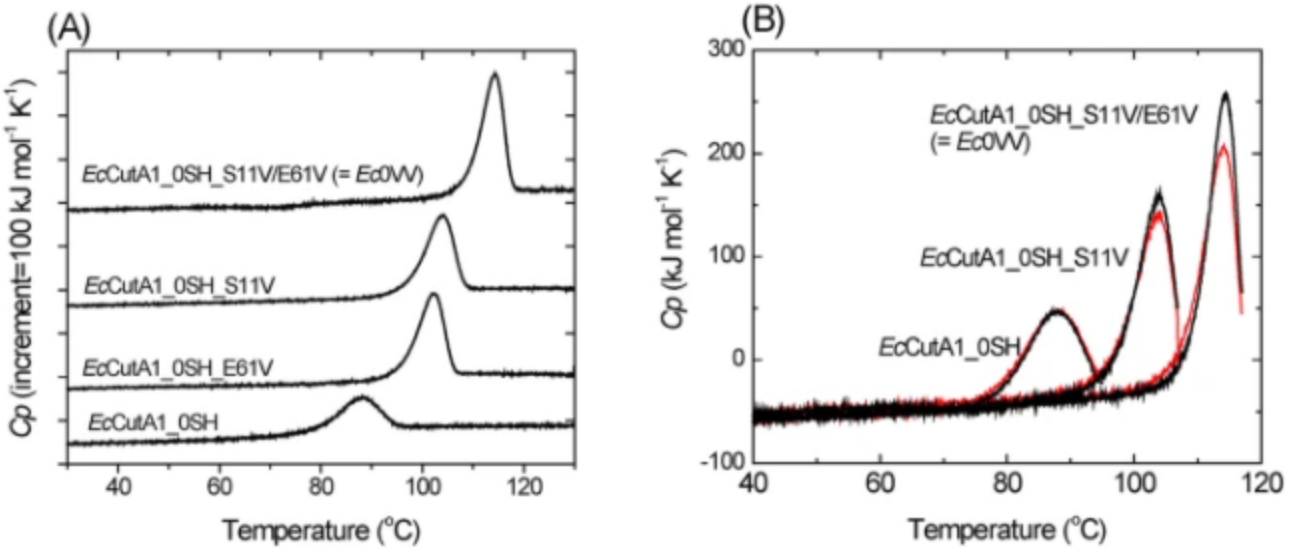
Open Access | Published: 26 October 2015

Thermodynamics of protein denaturation at temperatures over 100 °C: CutA1 mutant proteins substituted with hydrophobic and charged residues

Yoshinori Matsuura, Michiyo Tak
Naoki Kunishima & Katsuhide Yu

Scientific Reports **5**, Article numl

Figure 1



DSC curves of hydrophobic *Ec*CutA1 mutants with no SH group at pH 9.0.
(**A**)Typical DSC curves of four mutants: *Ec*CutA1_0SH, *Ec*CutA1_0SH_S11V, *Ec*CutA1_0SH_E61V and *Ec*CutA1_0SH_S11V/E61V. Scan rates were 60 °C/h. (**B**)Reversibility of heat denaturation of *Ec*CutA1_0SH, *Ec*CutA1_0SH_S11V and *Ec*CutA1_0SH_S11V/E61V. The red curves of three proteins are the second runs of DSC, just after the cooling step of the first run (the black curves). Scan rates of both

teoria

experimento

e

modelo estatístico

teoria

comportamento universal em transições de fase

e

modelo estatístico

experimento e "universalidade"

termodinâmica dos gases

O caso mais antigo:

$$pV = \frac{m}{2}RT \quad hidrogênio$$

$$pV = \frac{m}{32}RT \quad oxigênio$$

$$pV = \frac{m}{28}RT \quad nitrogênio$$

comportamento **universal**
independe de detalhes moleculares ou intermoleculares

invenção do mol

universalidade

$$pV = nRT$$

"universalidade" e modelo estatístico

termodinâmica dos gases

Gás ideal

- moléculas sem volume
- moléculas não interagem (sem choques!)
- distribuição aleatória de velocidades

$$pV = nRT$$

se

$$E_{cin} = \frac{3}{2} nRT$$

experimento e "universalidade"

transição líquido-gás

Temperatura crítica

$-229^o C \quad Ne$

$+16.6C \quad Xe$

$-147^o C \quad N_2$

$-82.3^o C \quad CH_4$

.....

Reescalar por grandezas críticas

$T \rightarrow T/T_c$

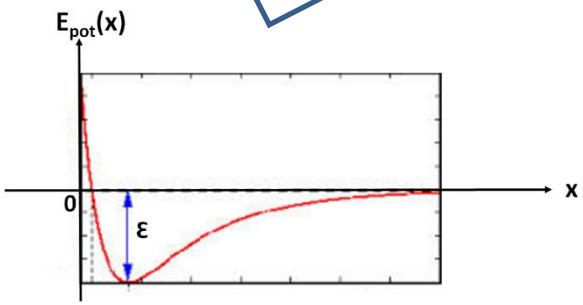
$\rho \rightarrow \rho/\rho_c$

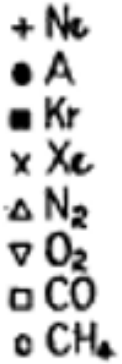
curva universal

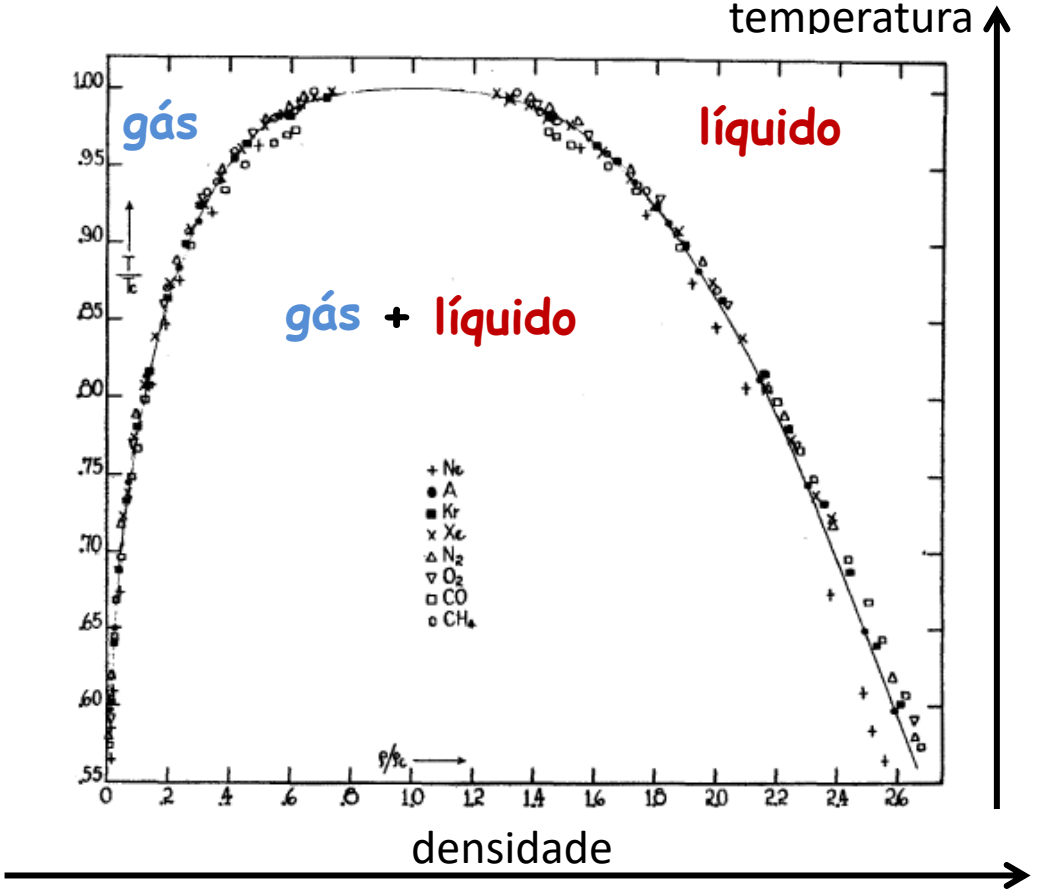
experimento e "universalidade"

transição líquido-gás

comportamento **universal**
independe de detalhes moleculares ou intermoleculares

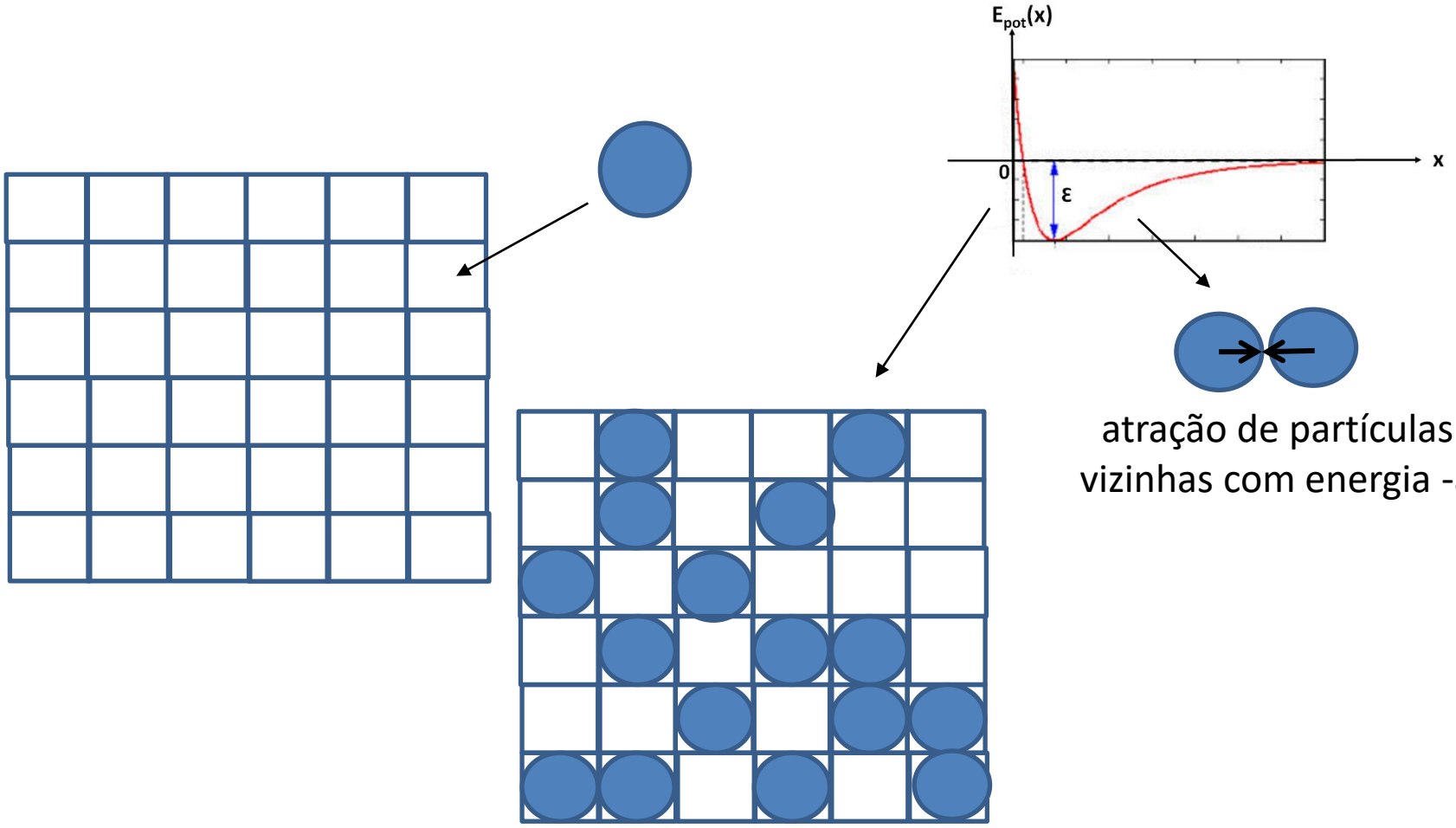






"universalidade" modelo estatístico

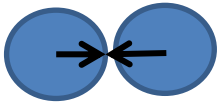
- **discretização do espaço: rede de células**
- **moléculas = ocupam espaço (as células) e se atraem**



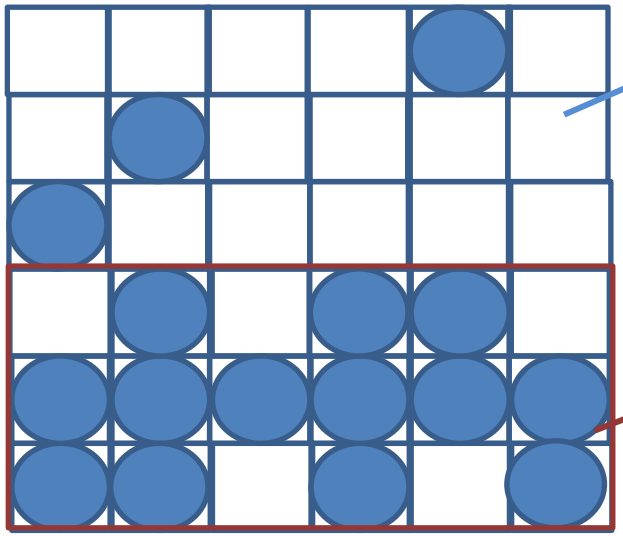
atração de partículas vizinhas com energia $-\varepsilon$

"universalidade"
modelo estatístico

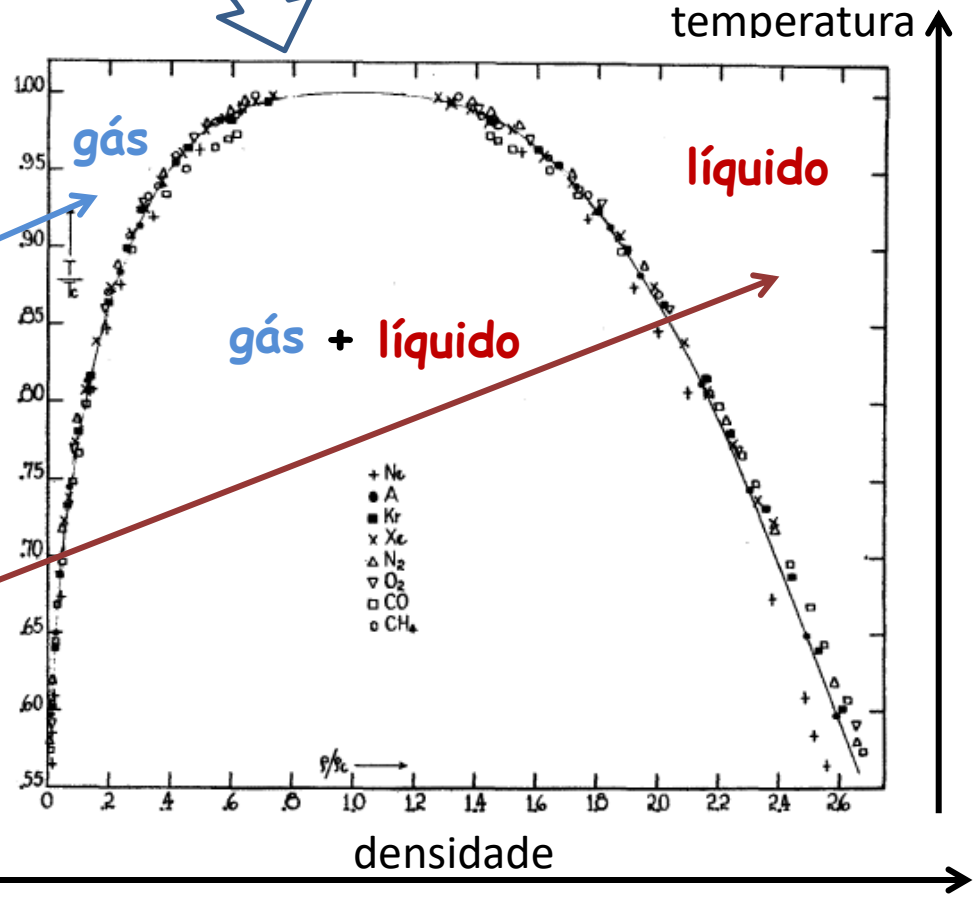
transição líquido-gás



atração de partículas
vizinhas com energia -ε

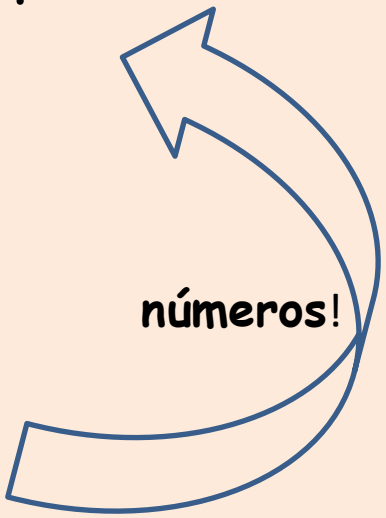


baixas temperaturas



experimento
no laboratório e na simulação

"universalidade" – interpretação do experimento

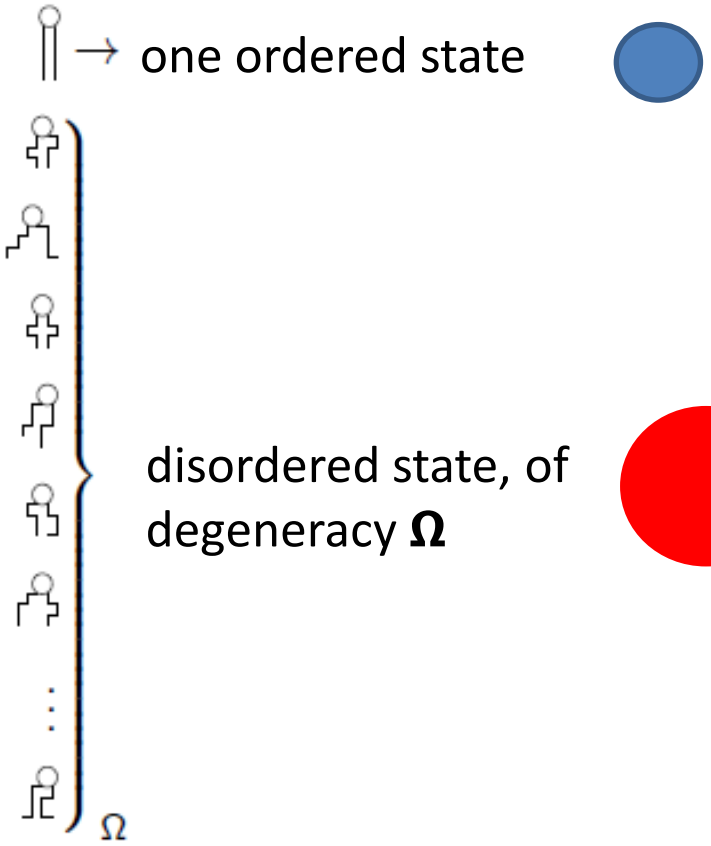


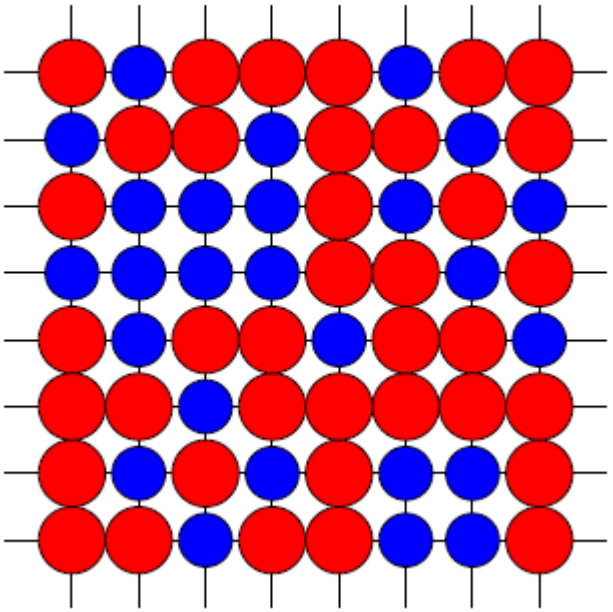
modelo estatístico

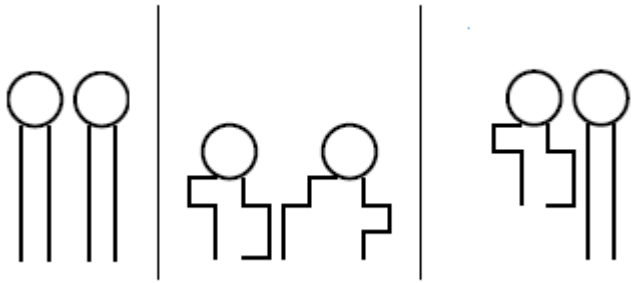
desafio!

"universalidade" e modelo estatístico

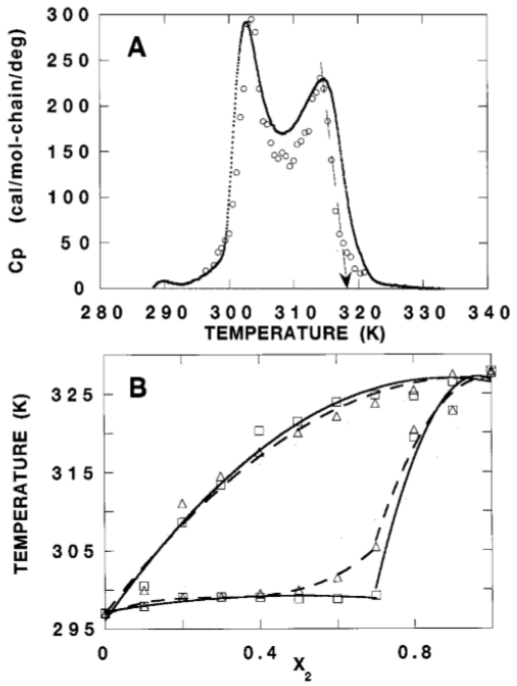
Doniach's two-state model (1980)







Success of Doniach's model



DMPC – DSPC
Sugar, Thomas, Biltonen Bioph J 1999

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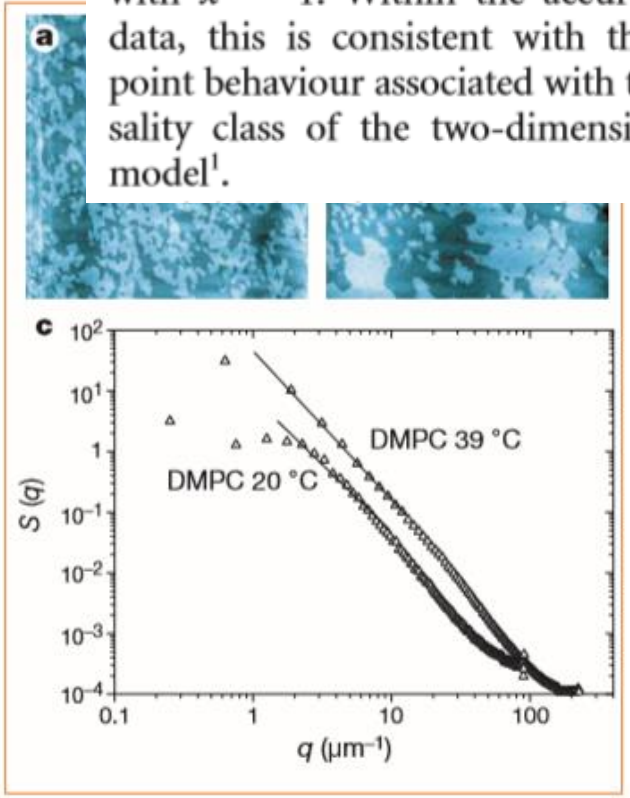


Figure 1 Critical fluctuations in phospholipid monolayers imaged by atomic-force microscopy as a height-difference map. **a,b,**

O Mouritsen

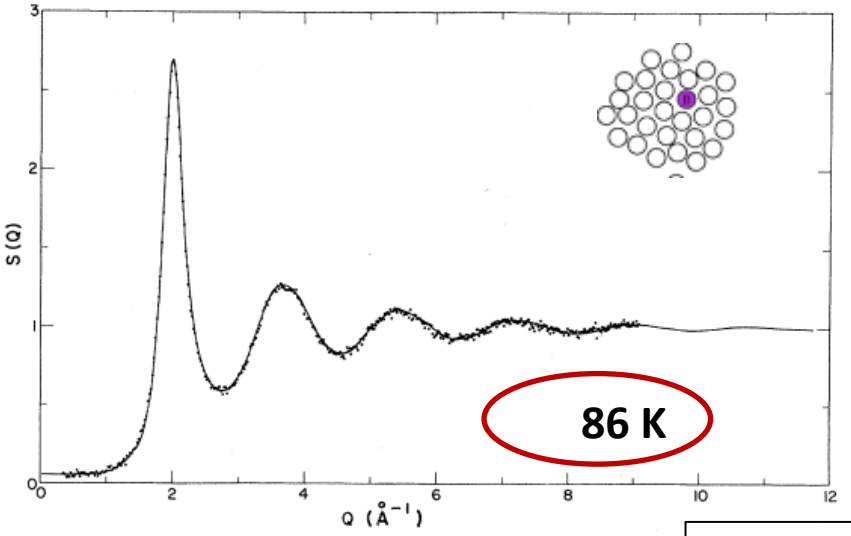
teoria

cálculo da estrutura

e

modelo estatístico

intensidade



ângulo

probabilidade de encontrar duas moléculas a uma dada distância

?

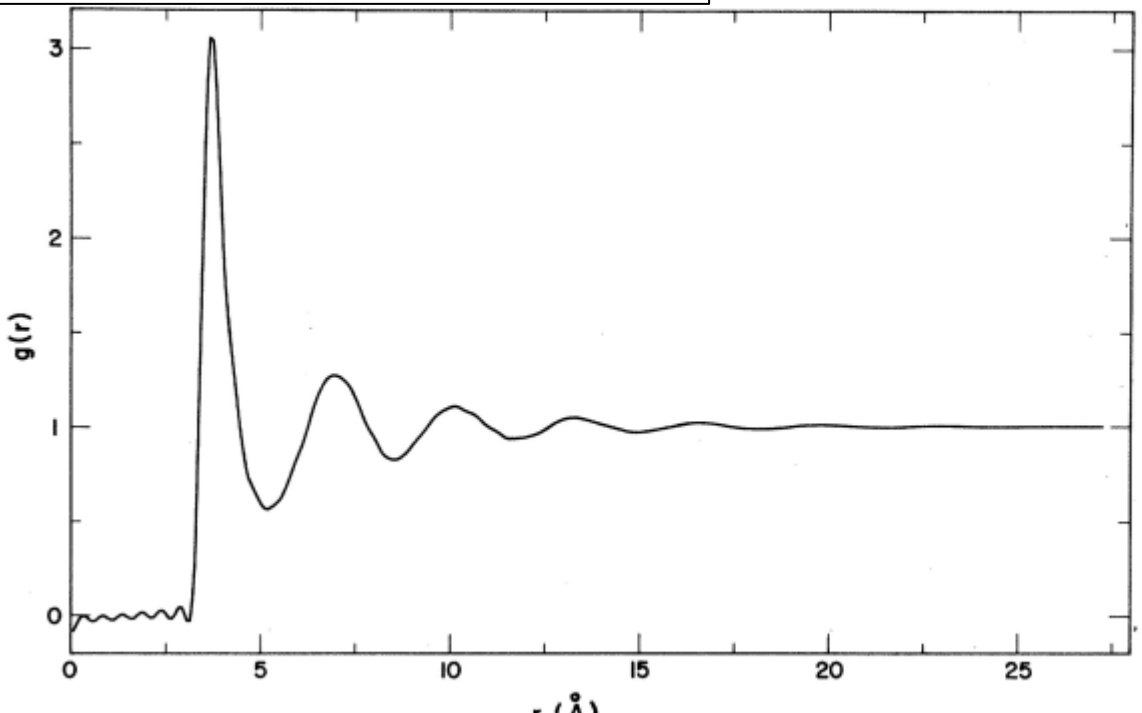


FIG. 4. Radial distribution function $g(r)$ for ^{36}Ar at 85 °K. This curve is the Fourier transform of the smoothed and extended $S(Q)$ shown as a solid line in Fig. 3.

distância entre moléculas

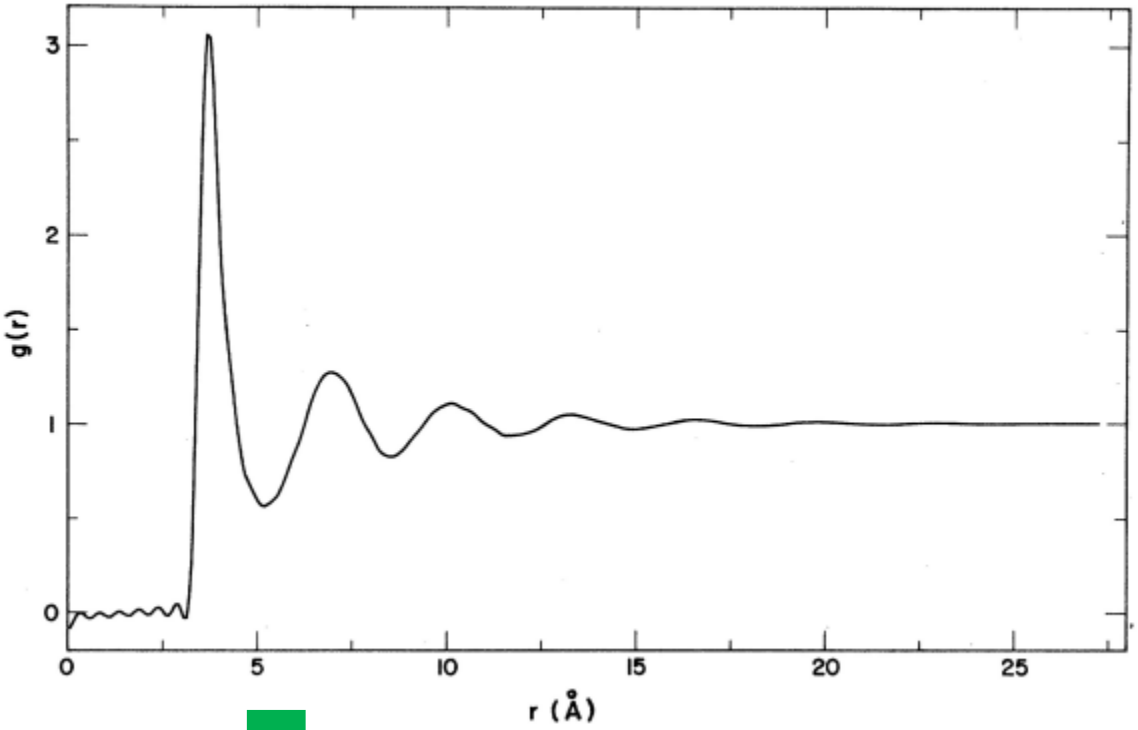
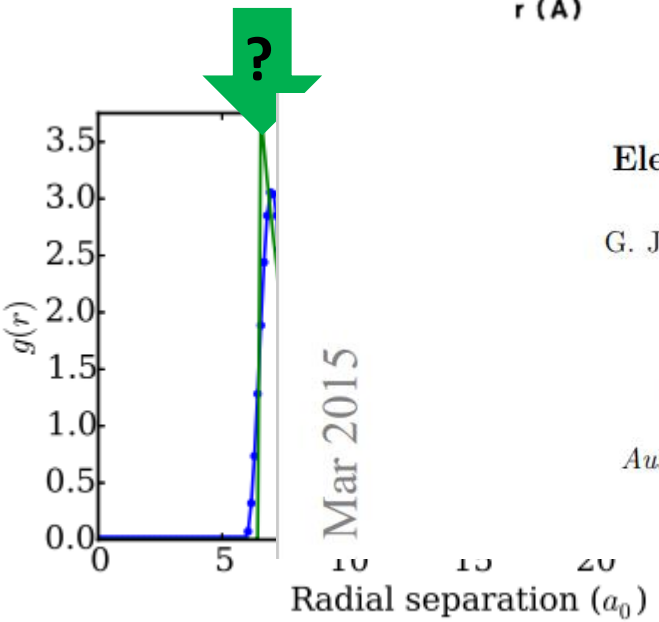


FIG. 4. Radial distribution function $g(r)$ for ^{36}Ar at 85 °K. This curve is the Fourier transform of the smoothed and extended $S(Q)$ shown as a solid line in Fig. 3.

Phys Rev 1973



Mar 2015

Electron scattering and transport in liquid argon

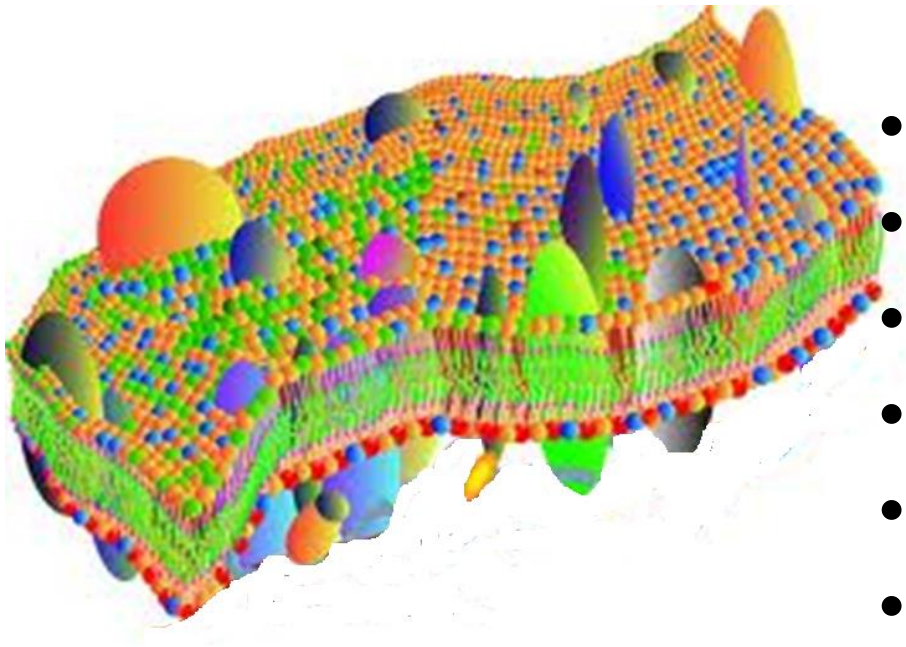
G. J. Boyle,[1] R. P. McEachran,[2] D. G. Cocks,[1] and R. D. White[1]

[1] *College of Science, Technology & Engineering, James Cook University, Townsville 4810, Australia*

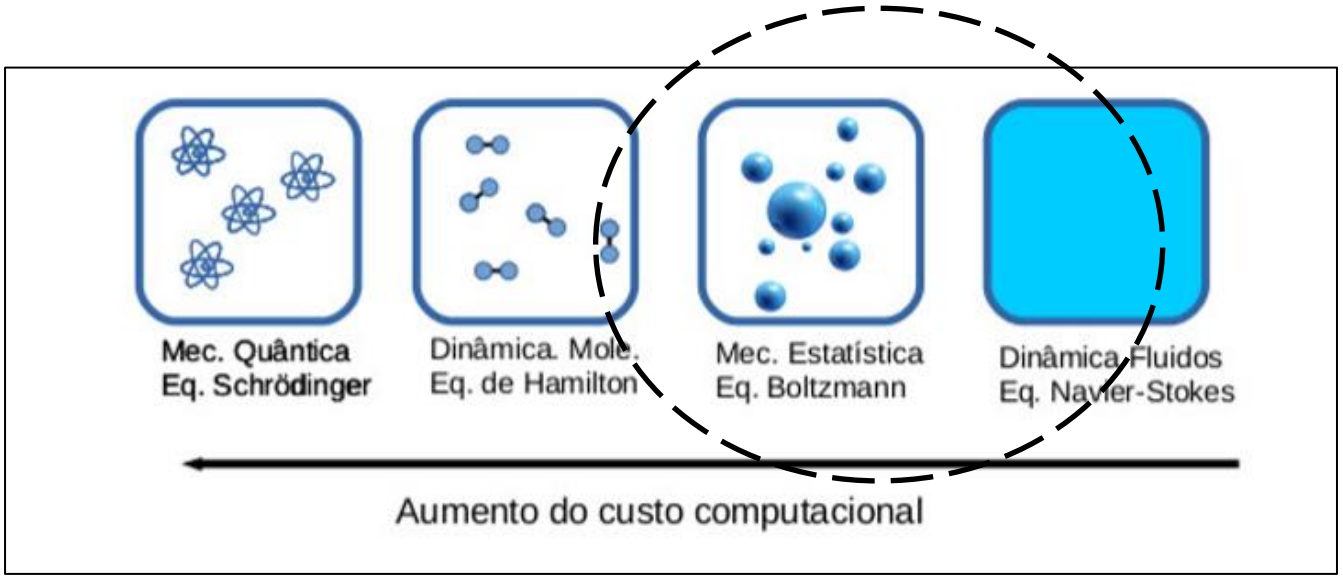
[2] *Research School of Physical Sciences and Engineering, Australian National University, Canberra, ACT 0200, Australia*

Abstract

teoria e estudo de modelos de muitas partículas



- Diferentes lipídeos
- Proteínas
- Açúcares
- Colesterol
- Água
- Íons...



particular

geral

Parte 2

modelos estatísticos estudados pelo *grupoBioLat*

- o caso da membrana lipídica -

Modelos estatísticos estudados pelo *Grupo BioLat*

- água (estrutura e hidratação)
- monocamadas e bicamadas
- membranas carregadas e poros
- cristal líquido nemático
- propriedades de transporte

Laboratório de Biofísica do IFUSP

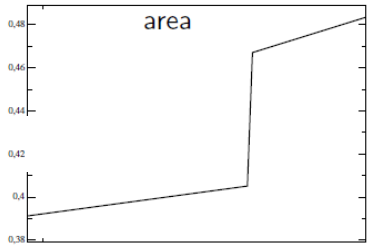
- **estudos de membranas modelo (Figura de vesícula)**

- **<u>técnicas experimentais</u>:** calorimetria, espalhamento de luz dinâmico e estético, raio-x, ressonância paramagnética eletrônica, fluorescência, viscosímetro, eletroforese, ... como função da temperatura

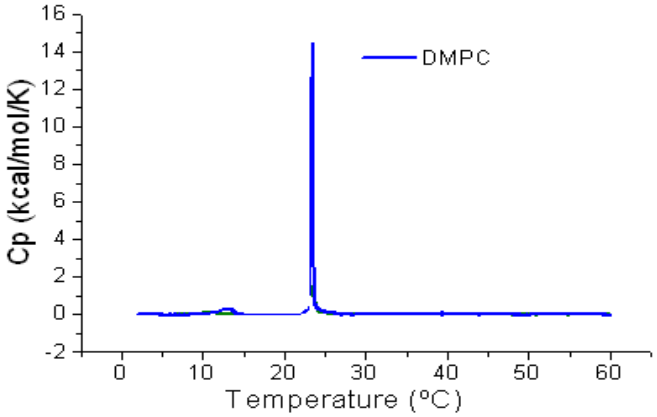
transição ordem-desordem em membranas: **experimento**

e modelagem

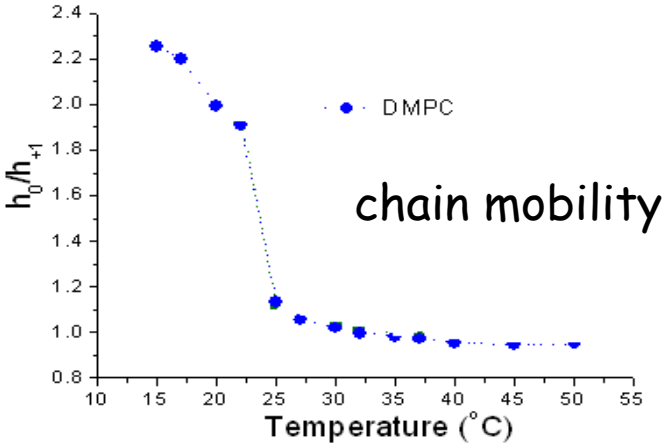
area por lipidio



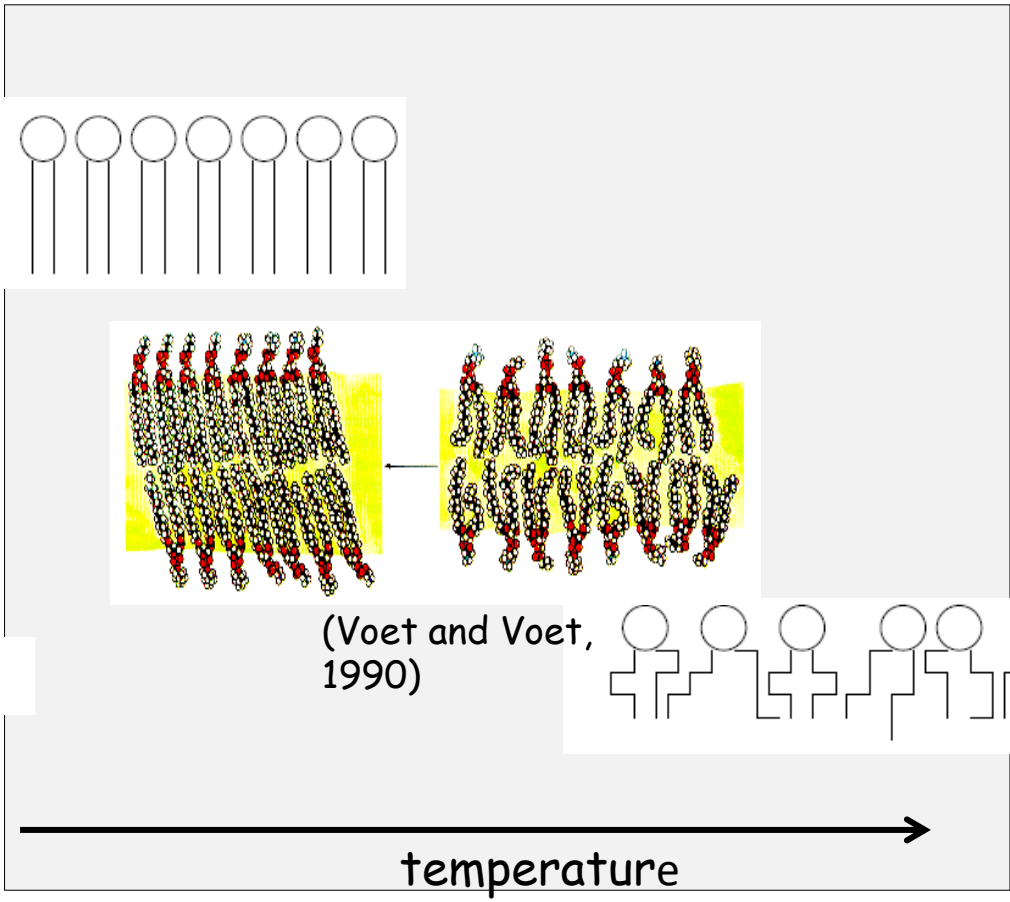
calor específico



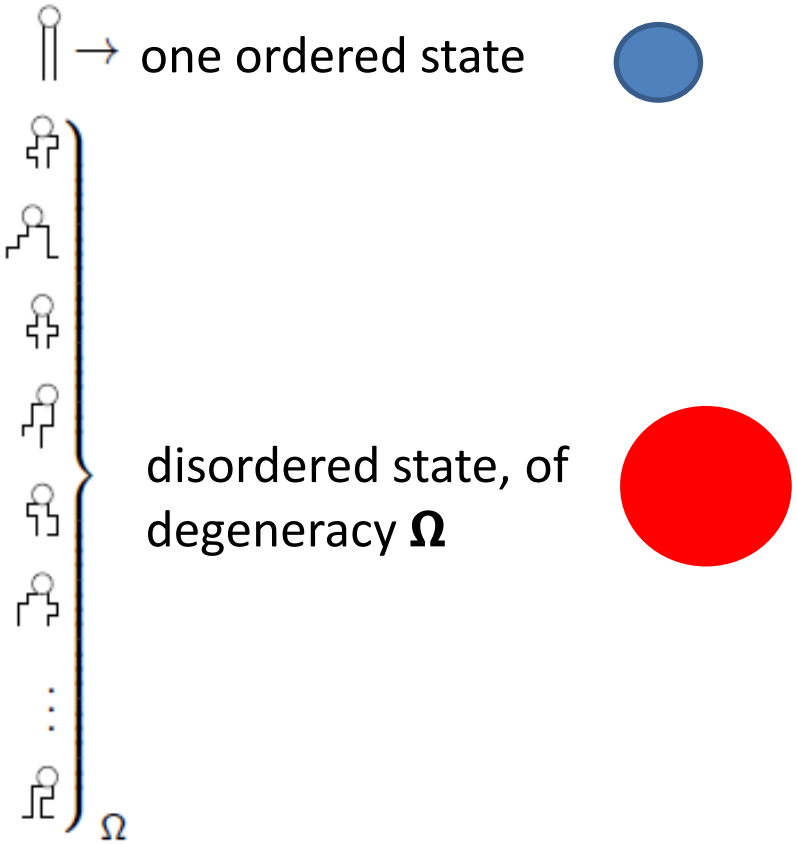
electronic paramagnetic resonance

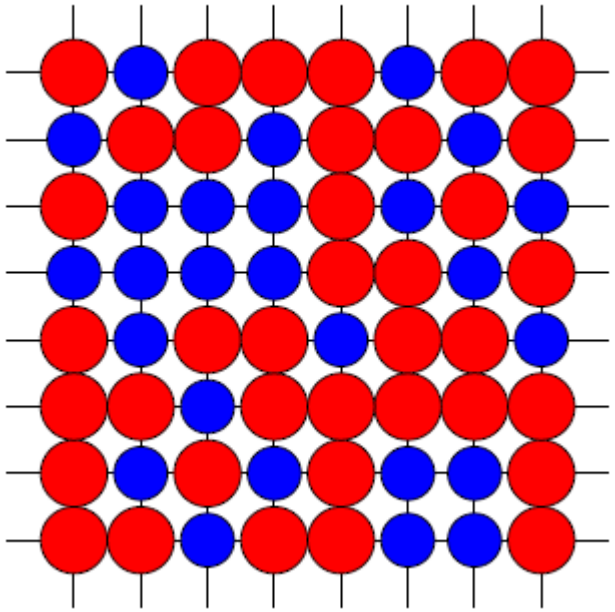


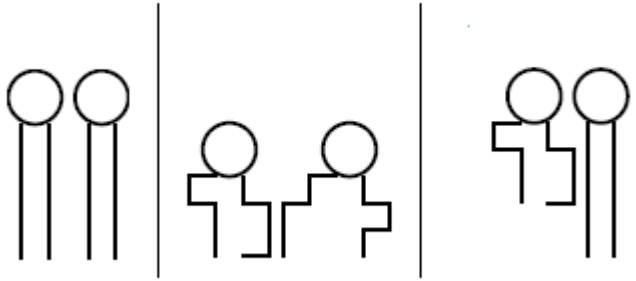
chain mobility



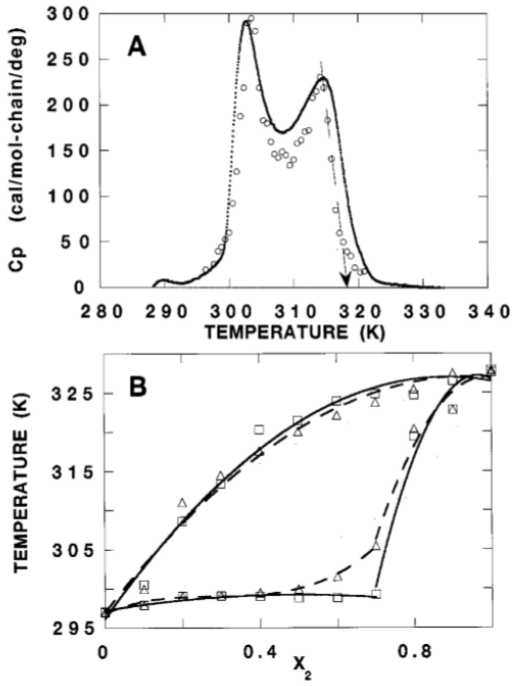
Doniach's two-state model (1980)







Success of Doniach's model



DMPC – DSPC
Sugar, Thomas, Biltonen Bioph J 1999

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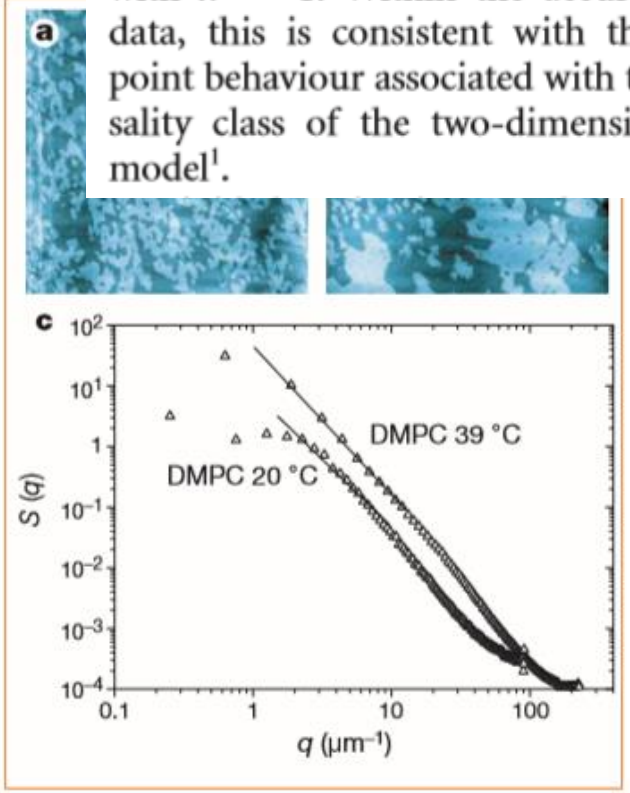
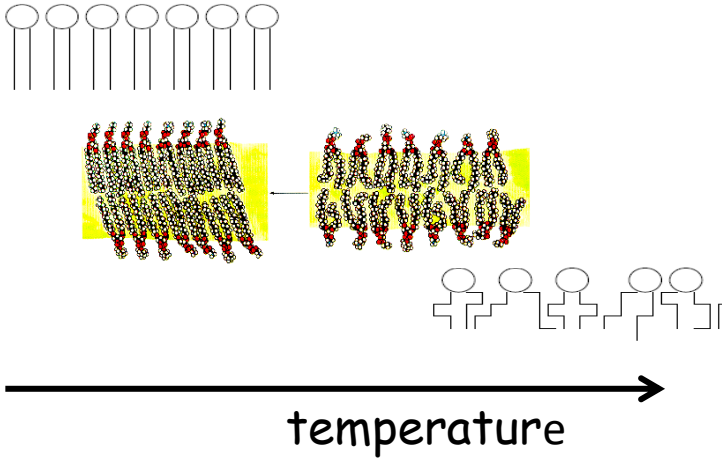
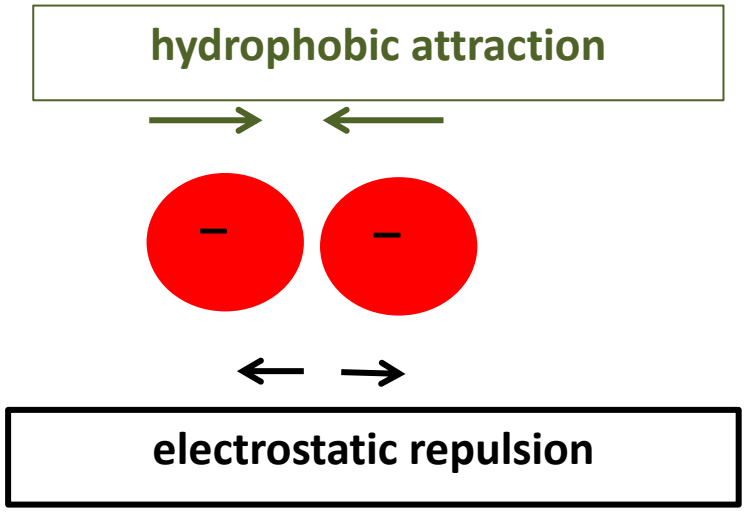


Figure 1 Critical fluctuations in phospholipid monolayers imaged by atomic-force microscopy as a height-difference map. **a,b,**

O Mouritsen

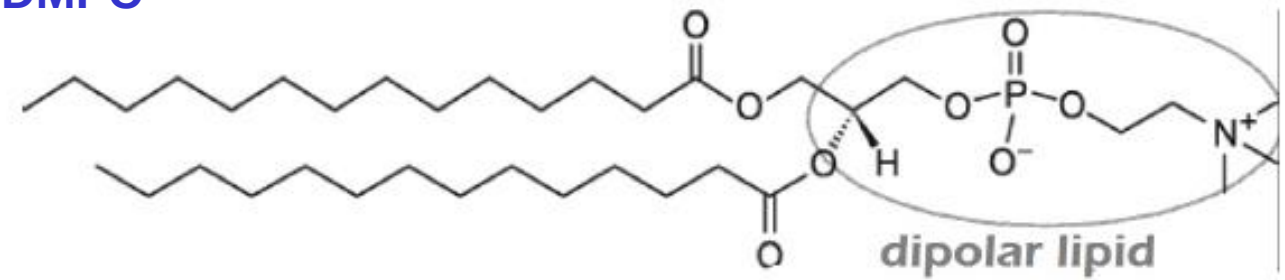
Anionic membrane – competition between electrostatic and hydrophobic interaction

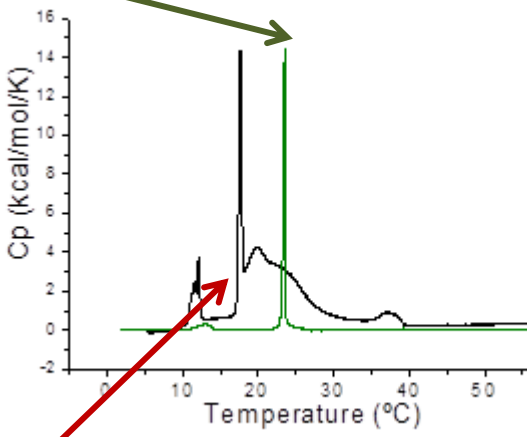




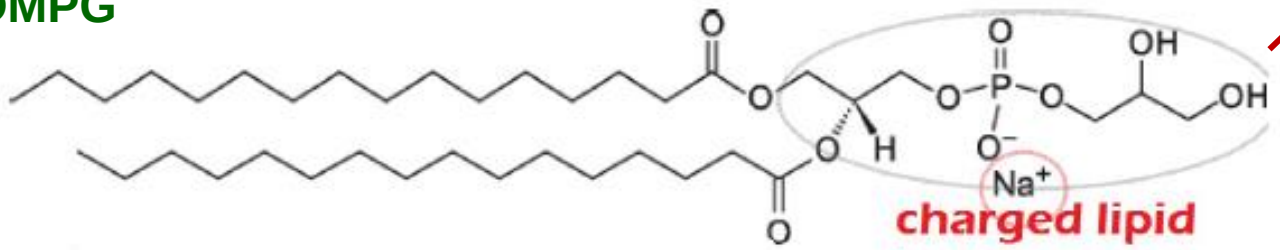
lipídeos ionizáveis (Lab Biofísica)
x
lipídeos neutros

DMPC



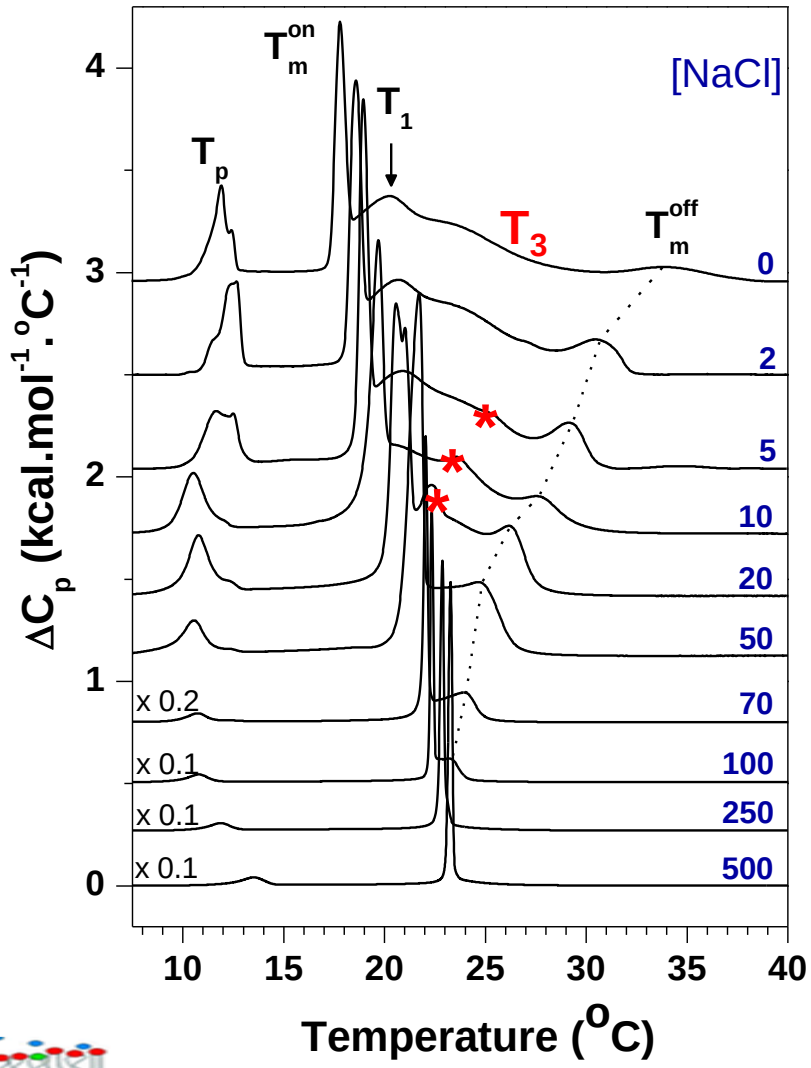


DMPG



Biophysics Lab at IFUSP - experiment

calorimetry



Papel da carga!

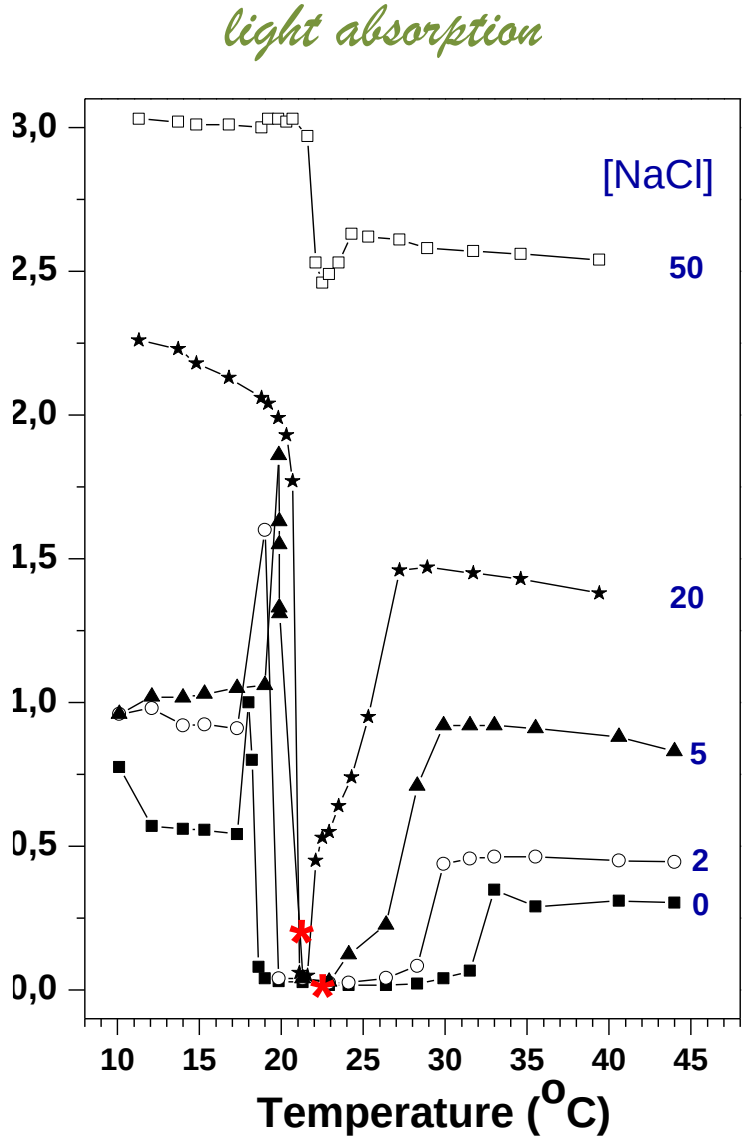
(Riske et al., Langmuir 2009)

Biophysics Lab at IFUSP - experiment

Aumento da transparência

-> mais água na membrana?

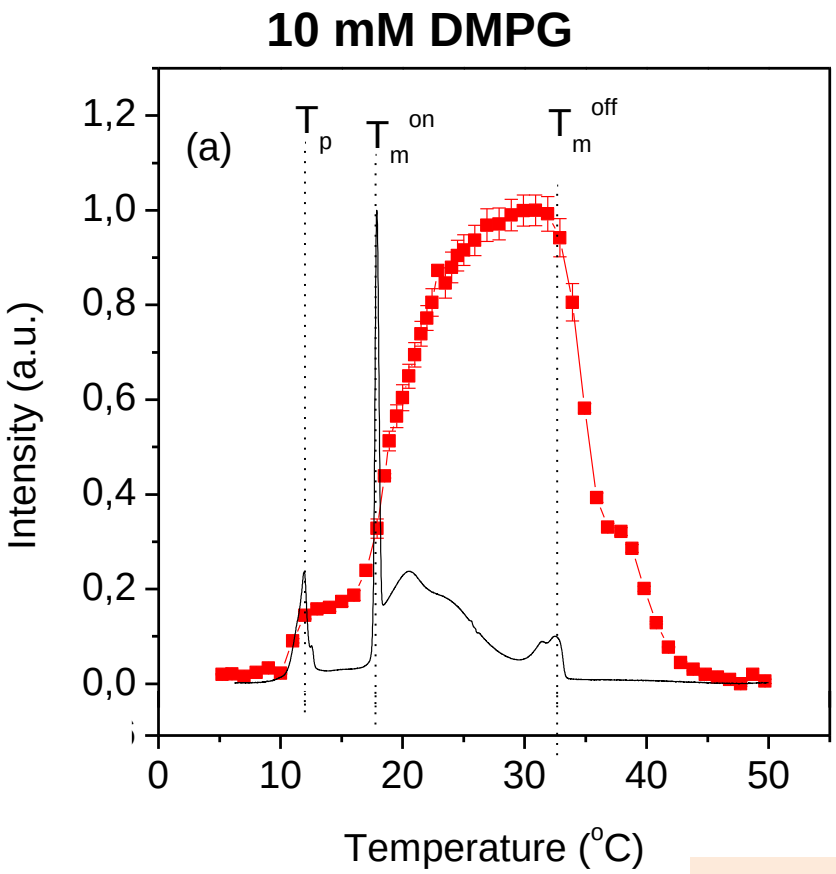
-> como?



(Riske et al., Langmuir 2009)

Biophysics Lab at IFUSP - experiment

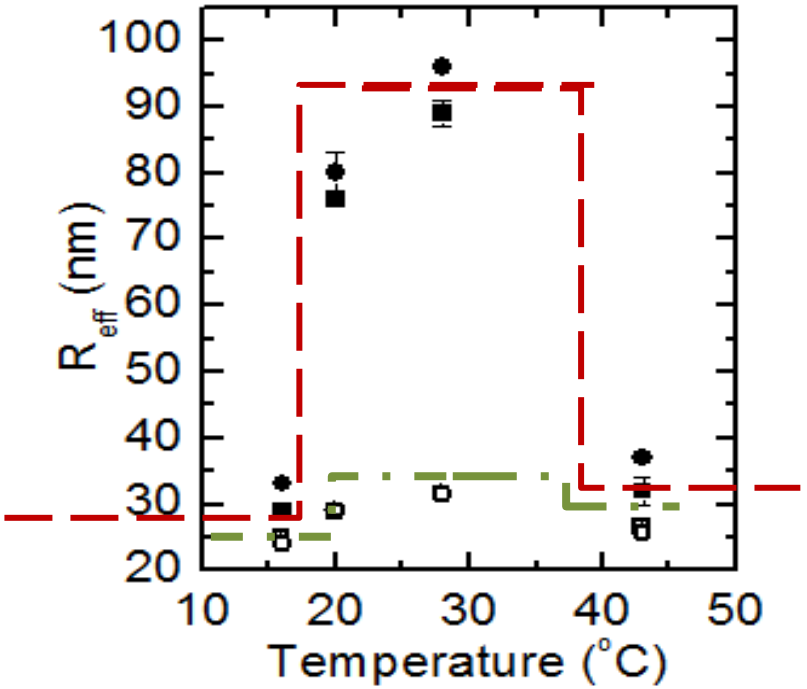
dsc and conductivity



Aumento de íons livres com desordenamento das cadeias?

Biophysics Lab at IFUSP - **experiment**

light scattering – probing vesicle size



Chem Phys Lipids, 2012

static light scattering

raio aumenta 3 vezes!

X

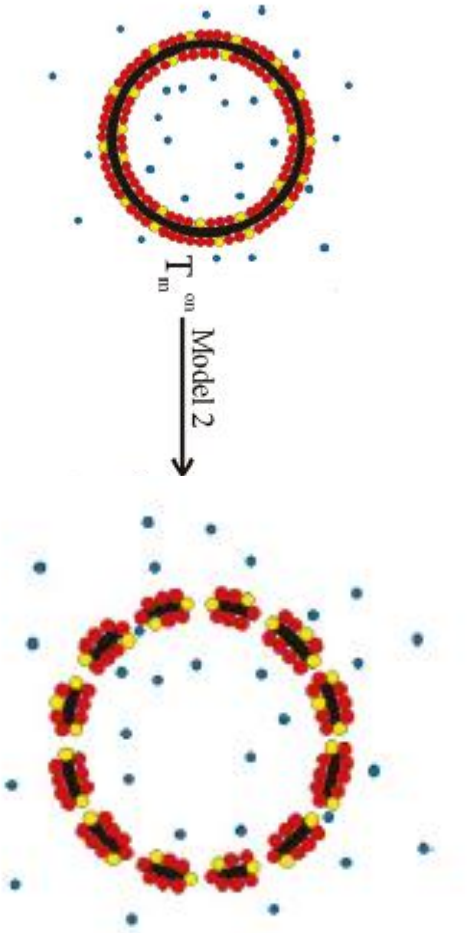
dynamic light scattering

raio aumenta 50%

!!!!???

❖**Como explicar essa discrepância??**

Biophysi cs Lab at IFUSP – experiment and "hand-waving" models



$D=kT/6\pi\eta R$

Os poros podem explicar o "crescimento" da vesícula?

Como entender a discrepância entre DLS e SLS?

questões

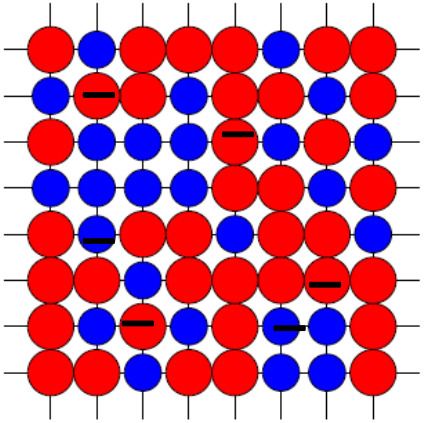
- microsegregação de lipídeo (EXP: EPR)
- microsegregação de carga (T: competição)
- poros e carga (EXP: transparência, condutividade; T: competição)
- poros e fluidez (T: curvatura)
- íons
- água
- .....

BioLat group

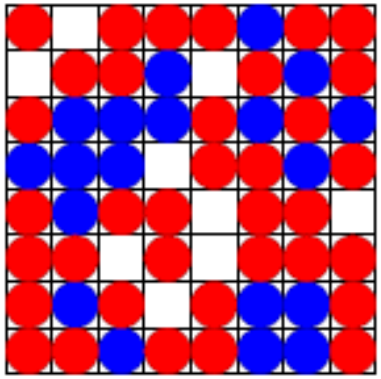
i - introduce lipid density fluctuations

ii- introduce charge

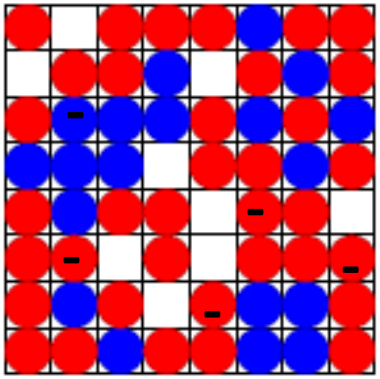
iii- introduce density and charge fluctuations



Phys Rev E 2010

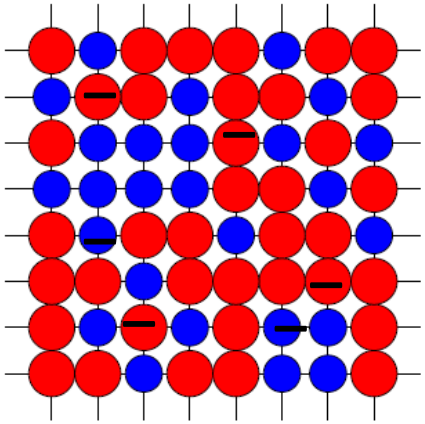


Phys Rev E 2015

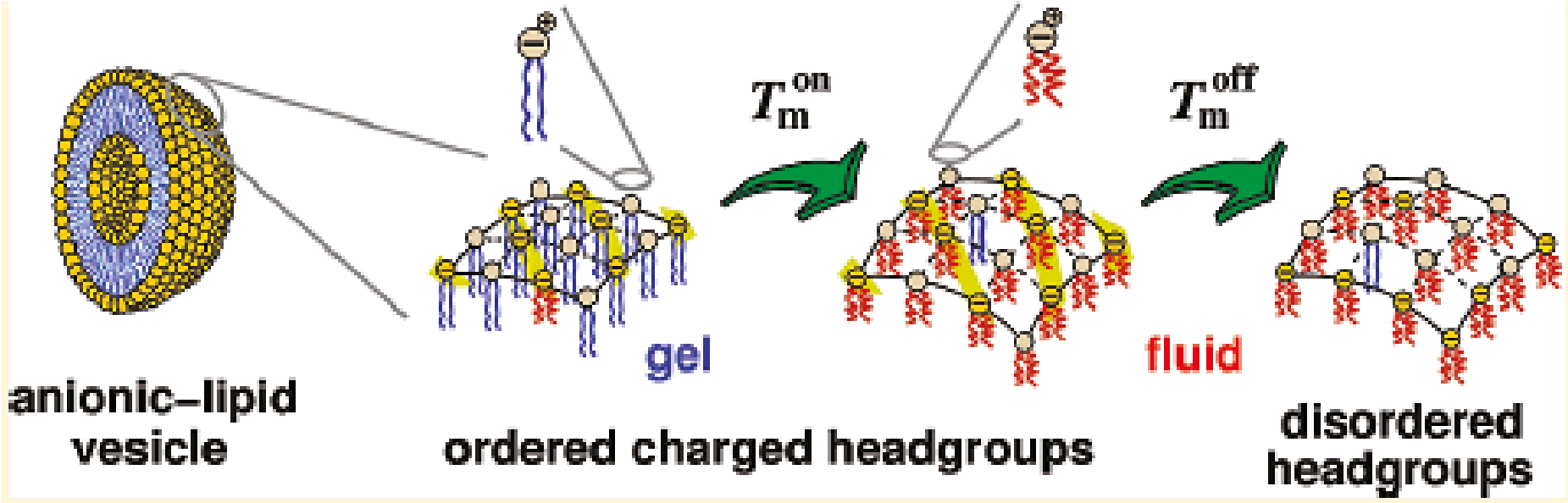


Tese Henrique Guidi
Publicação em preparação

Charge order of ionized lipids

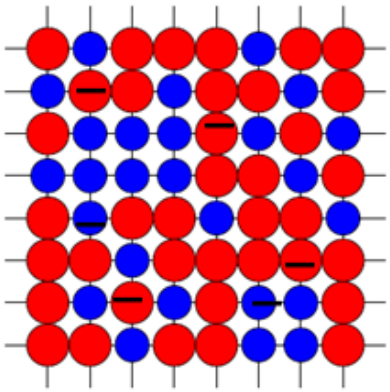


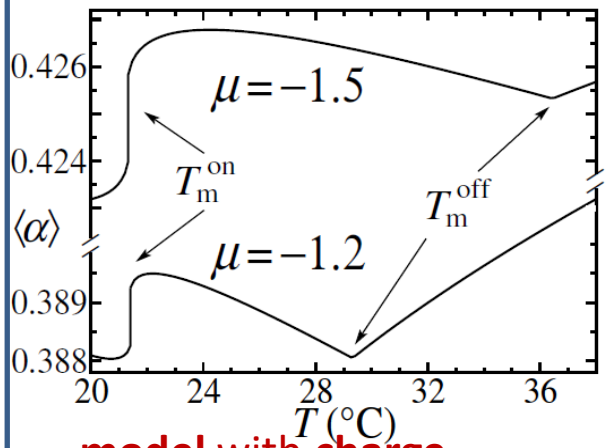
charge fluctuations



experiment vs model: ionization and lipid density

charge AND density fluctuations

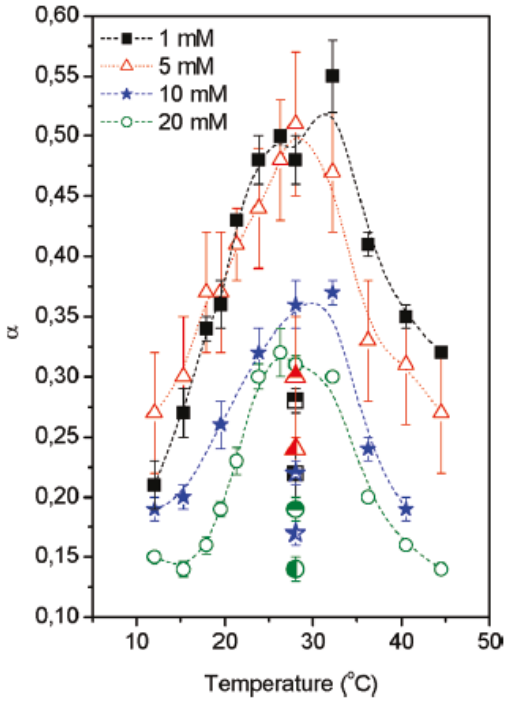




model with **charge** fluctuations

Δα **~ 0.424 -> 0.426**

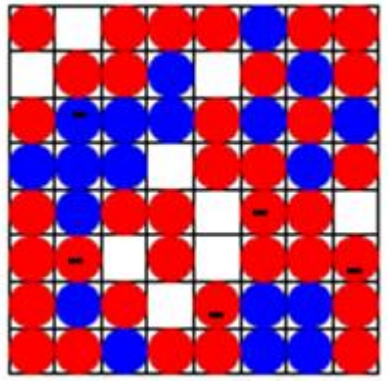
Langmuir 2011



experiment for anionic vesicles

Δα **~ 0.15 -> 0.20/ 0.20->0.28**

Langmuir 2010

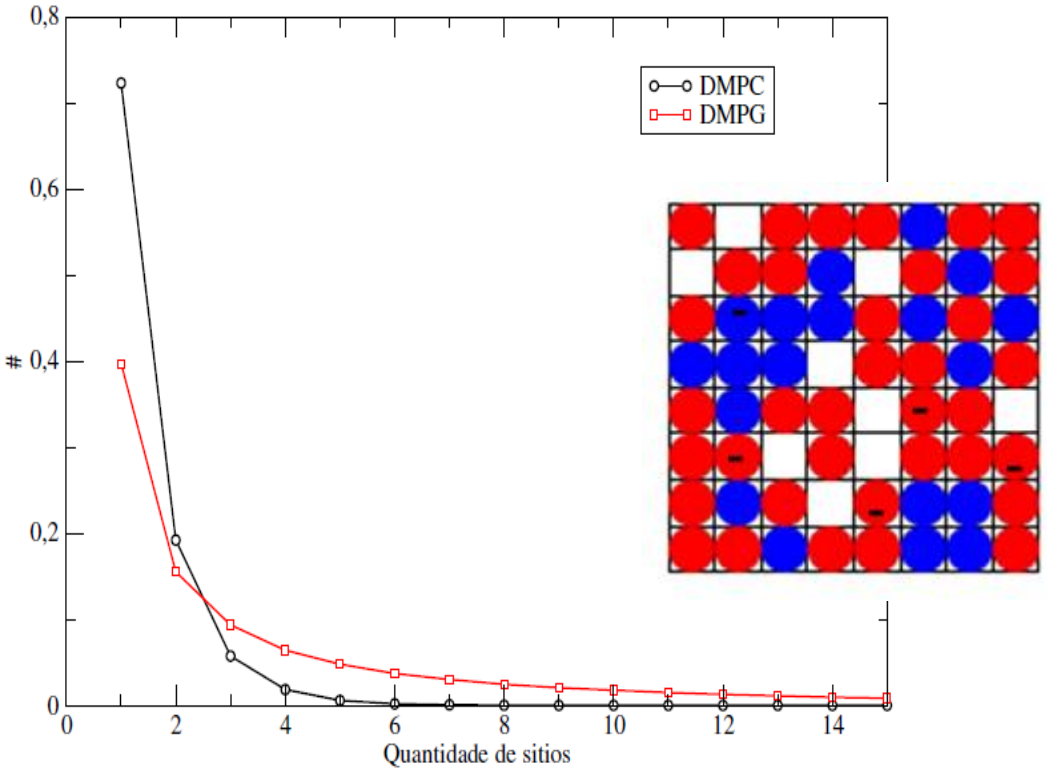


model with **charge and density** fluctuations

Δα **~ 0.18 -> 0.28**

pores form on chain disordering in the presence of charge

charge AND density fluctuations



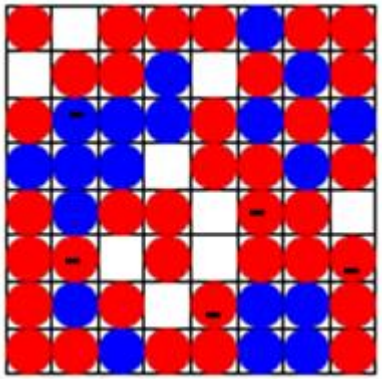
Average pore size for fixed lipid density

~1,4 para membrana neutra

~4,5 para membrana carregada

porous charged vesicle!

charge concentrates on pore rims



Theoretical x experimental model o que aprendemos?

- Pores may explain transparency
- Ionization produces larger pores (condutividade e transparência)
- Correlation between ionized lipid and pore rim
- Discrepancy between DLS e SLS – vesículas porosas ou carregadas não satisfazem Stokes ou Stokes-Einstein (estudos de Boltzmann na rede)

many open questions...

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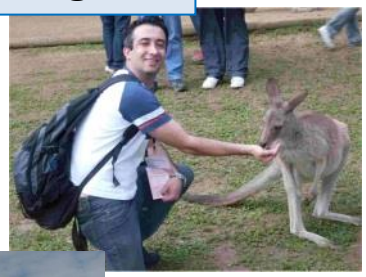
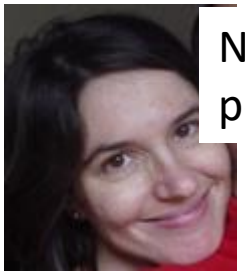
cristais líquidos

grupo de água



Marco Barbosa, UNB - Planaltina

Marcia Barbosa, UFRGS



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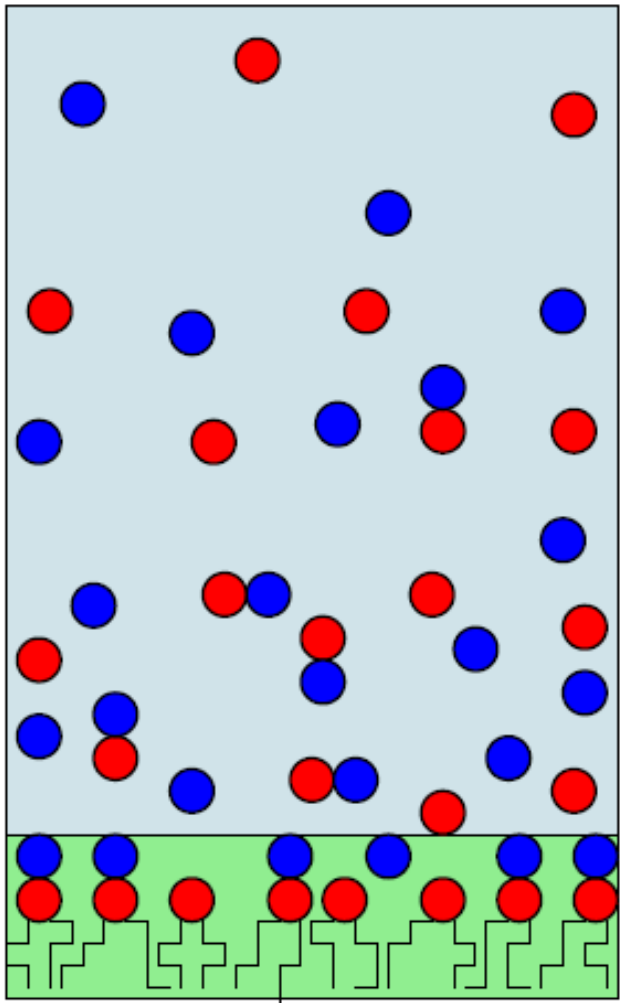
Carlos Fiore, USP

Maurício Girardi e Marcia Szortyka, UFSC

Obrigada!

Is local lipid density a relevant feature? Is there a correlation with charge distribution?



generic positive ion

generic negative ion

IONIC SOLUTION

MEMBRANE/MONOLAYER