Water and Protein Folding (Second Part)

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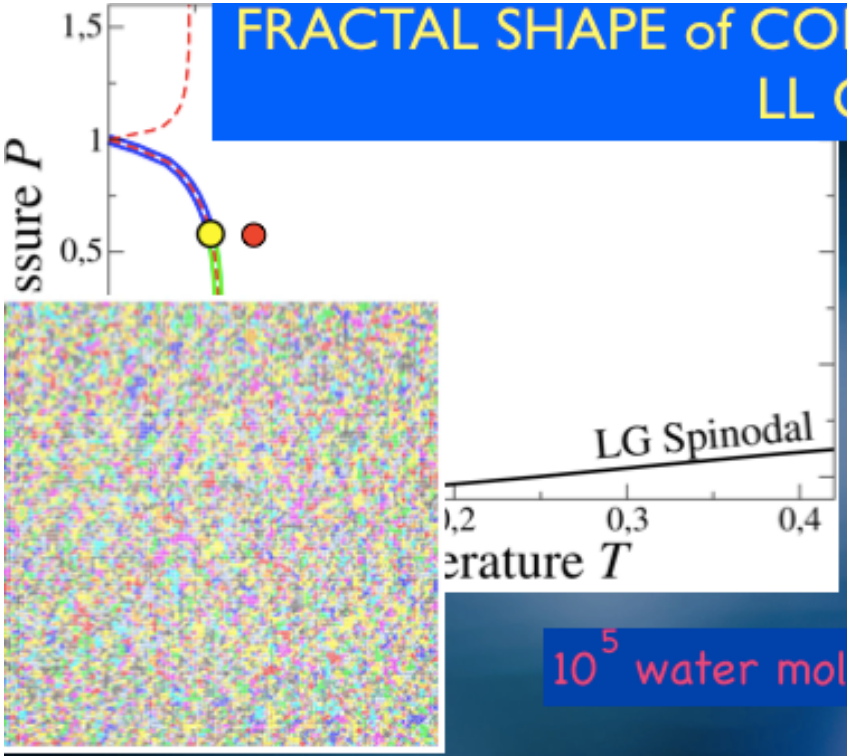
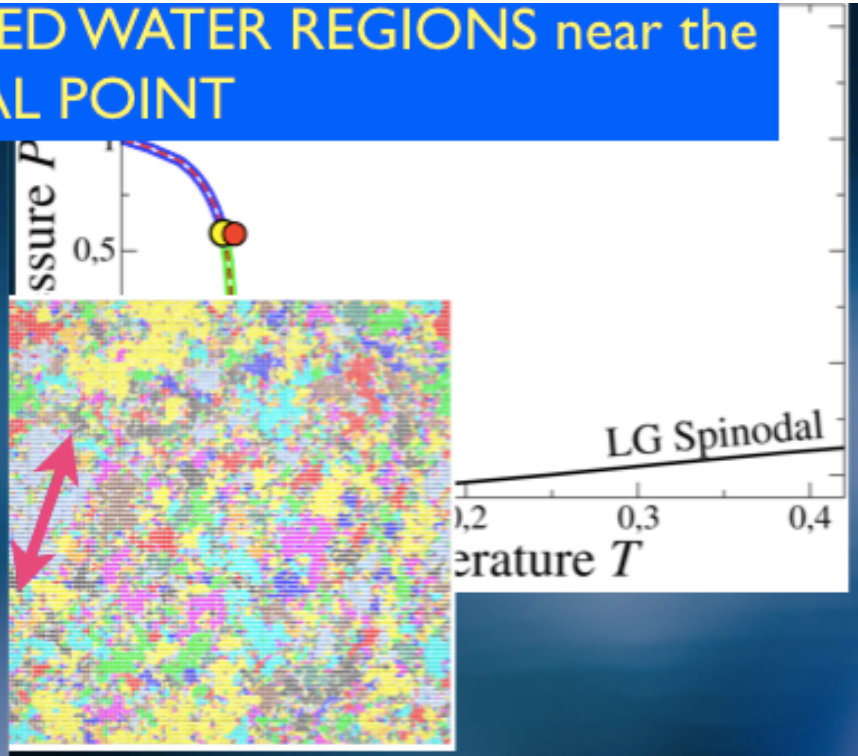
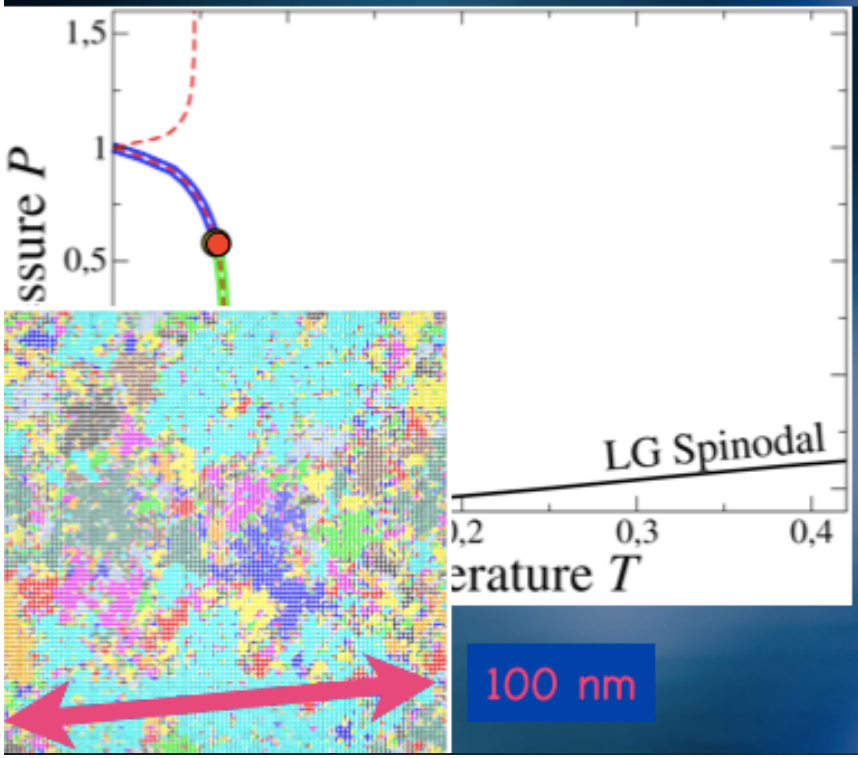
FRACTAL SHAPE of CORRELATED WATER REGIONS near the LL CRITICAL POINT

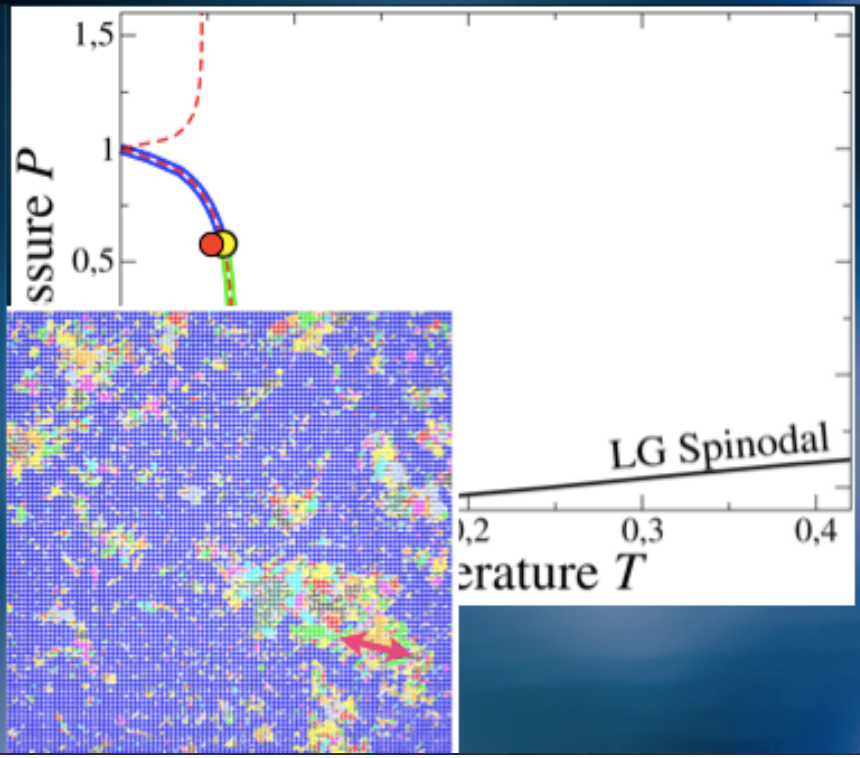


10^5 water molecules





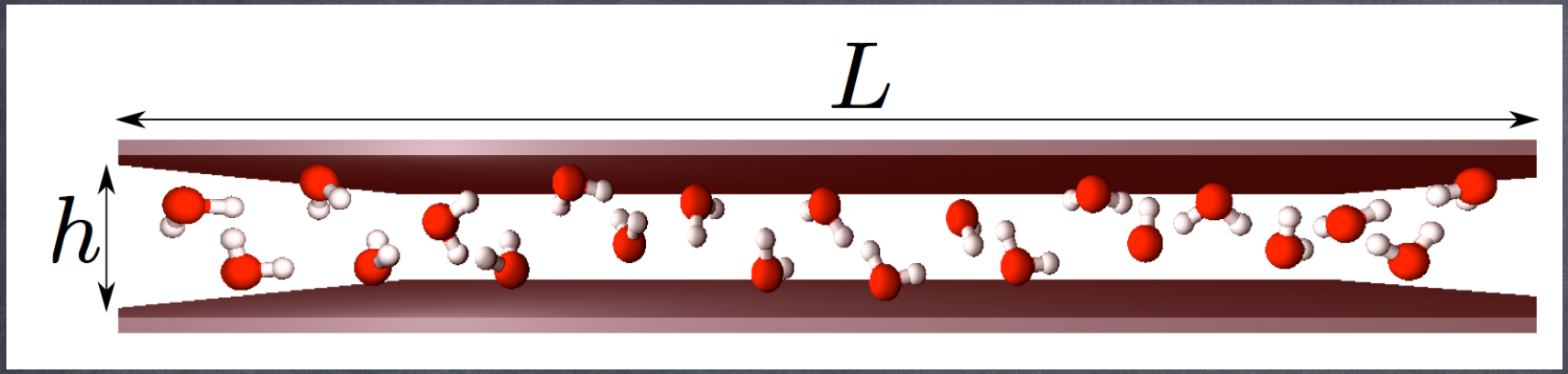
100 nm



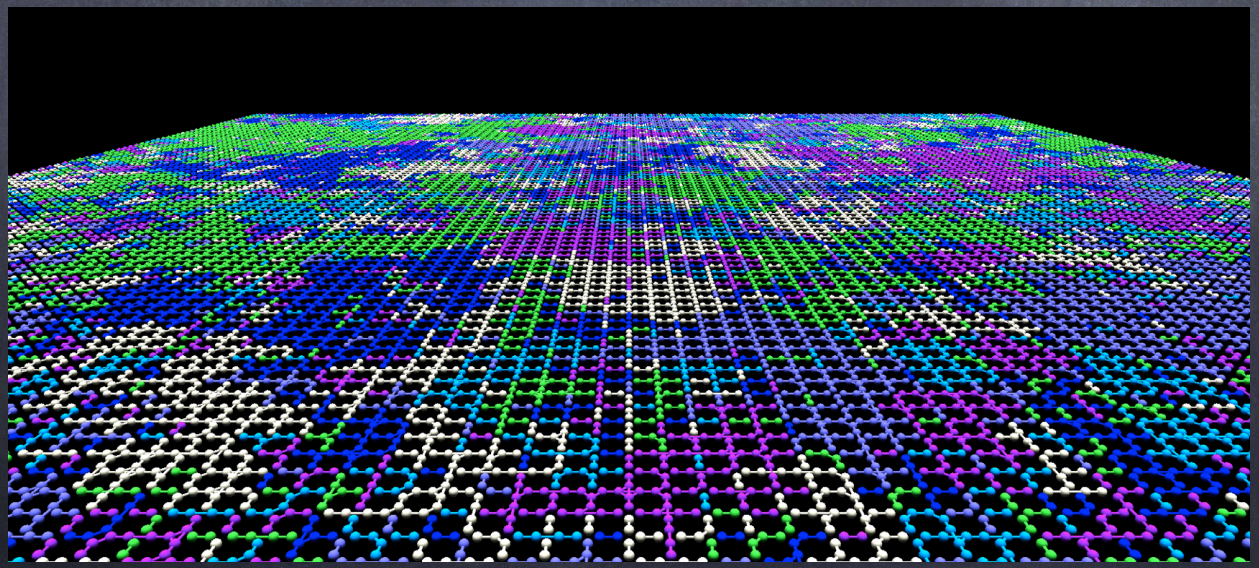
3D bulk water

Unpublished Results not shown here

Water confined between hydrophobic walls



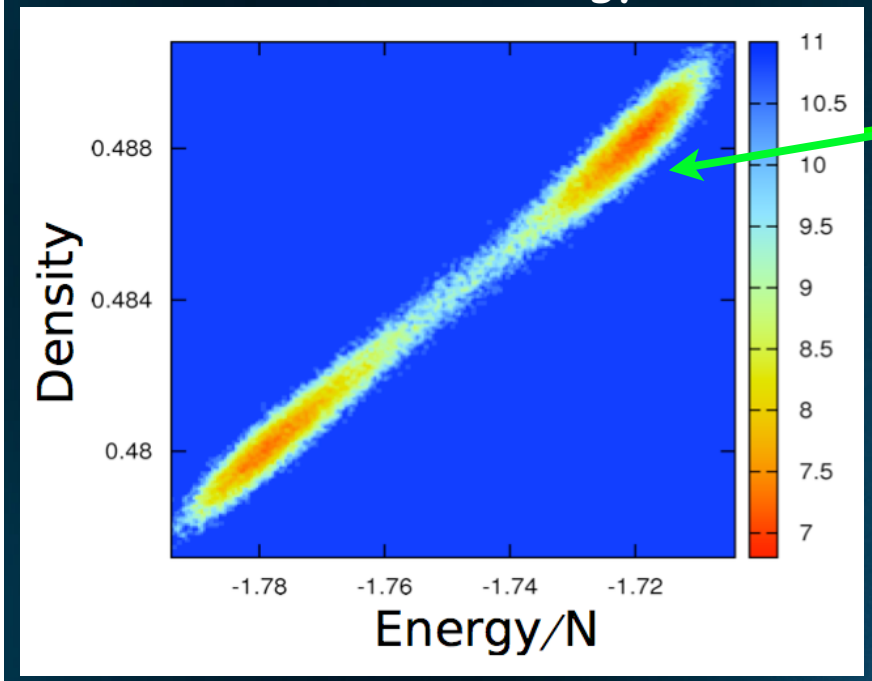
No crystallization for h = 0.5 nm [Zangi, Mark PRL (2003)]



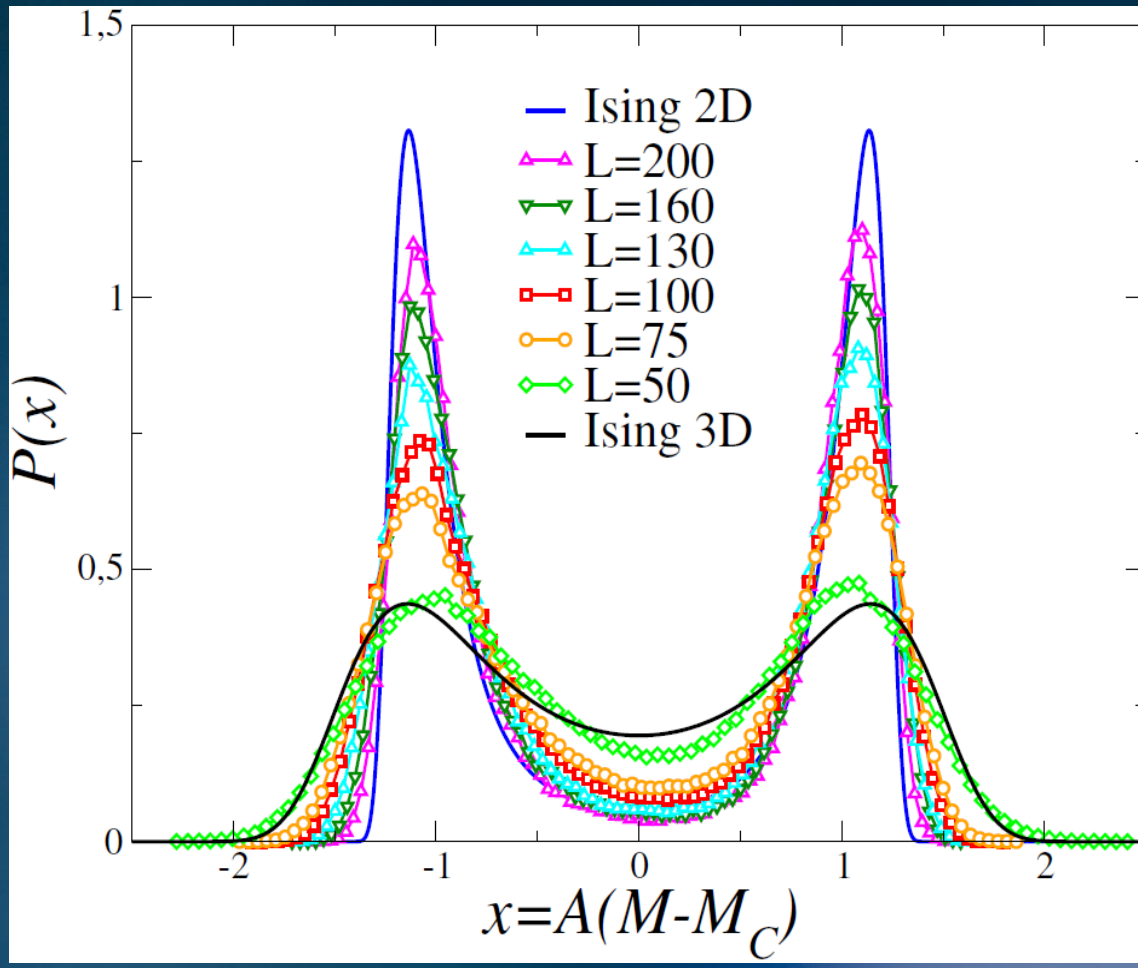
The Critical Point Analysis (Universality Class) in a monolayer

Order Parameter and Scaling Behavior

Gibbs Free Energy



Using the mixed-field approach we define the order parameter as $M=\rho+sE$



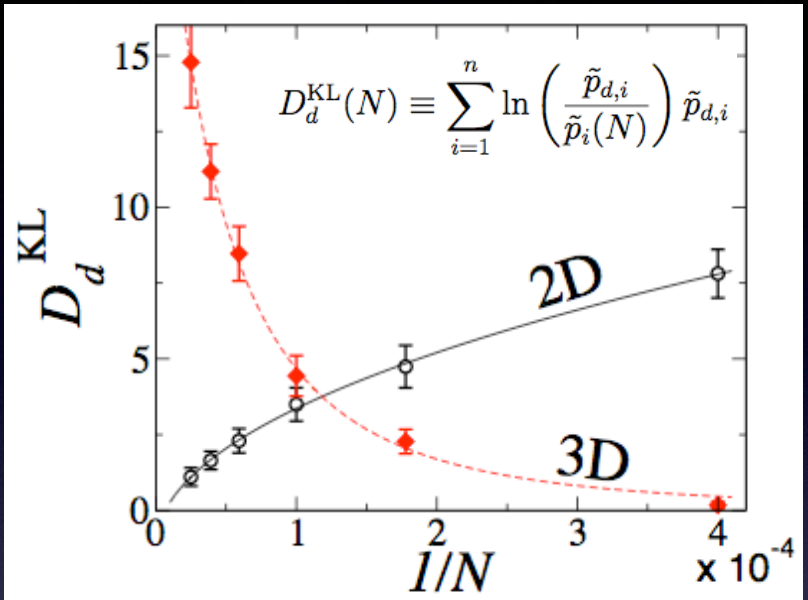
In the thermodynamic limit the probability distribution of The order parameter at the critical point approaches the 2D-Ising model critical distribution

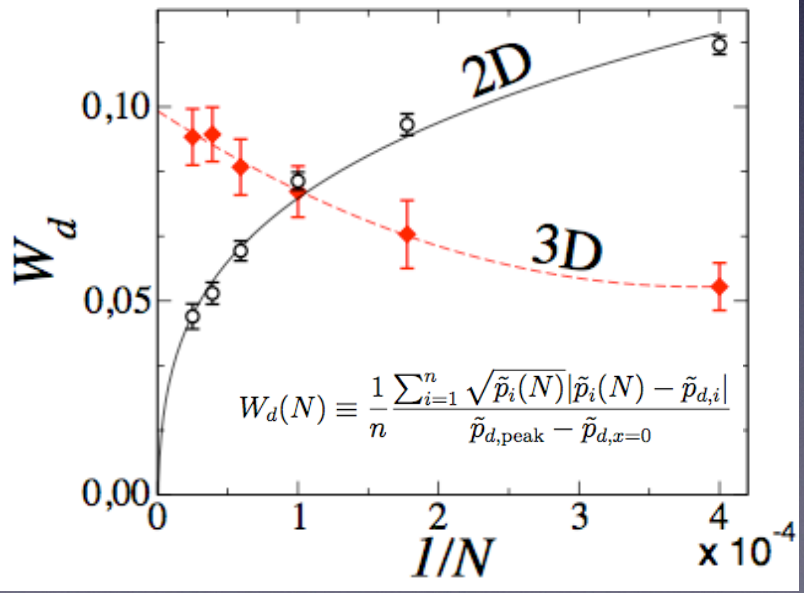
Valentino Bianco & G.F.,
Scientific Reports 4, 4440 (2014).

How fluctuations change with increasing confinement ?

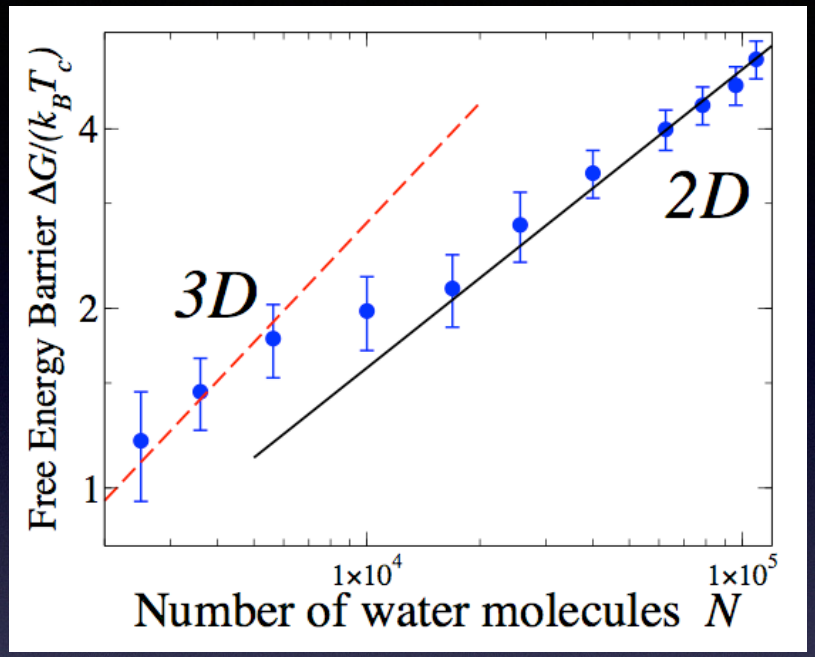
Increasing confinement: increasing fluctuations (2D-3D Crossover)

Kullback-Leibler deviation





Liu-Panagiotopoulos-Debenedetti deviation



Crossover at L/h=50 !!

In water stronger confinement could lead to bulk-like behavior for the fluctuations

Valentino Bianco & G.F., Scientific Reports 4, 4440 (2014).

Increasing confinement: increasing fluctuations (2D-3D Crossover)

For LIQUID-GAS CRITICAL POINT of LJ system the crossover is observed for (*Liu* et al 2010)

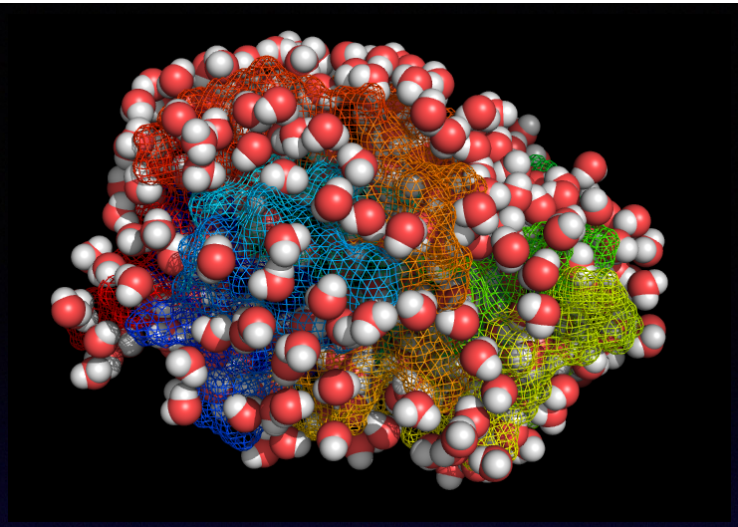
L/h ~ 5

While at the LLCP the crossover occurs at L=25 nm

L/h = 50!!!

The high cooperative behavior of HB enhances the spreading of critical fluctuations along the network.

Valentino Bianco & G.F.,
Scientific Reports 4, 4440 (2014).



Dynamic Crossovers on hydrated proteins?

Hydrogen bonds dynamics on Hydrated Protein

Hydrogen bonds dynamics on Hydrated Protein

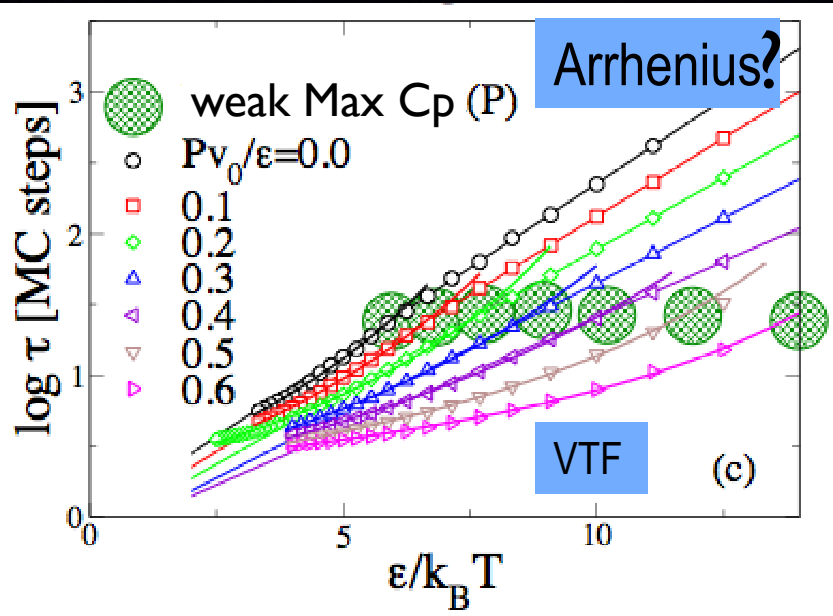
- Protein at low hydration: water monolayer
- Protein (lysozyme) acts as an immobile surface
- Microscopic effect of surface is to force the water molecules out of place with respect to crystal configurations: inhibition of crystallization
- We focus on H bonds dynamics. Is not relevant if H-bond is with surface, but is relevant that we can form a H-bond network (percolation of water molecules): hydration ≈ 0.5 g H_2O/g dry protein

$\tau^{VTF} = \tau_0^{VTF} \exp[T_1/(T - T_0)]$

Dynamic Crossover

$\tau = \tau_0 \exp[\frac{E_A}{k_B T}]$?

Liquid-liquid Critical Point



PRL 100, 105701 (2008) PHYSICAL REVIEW LETTERS week ending 14 MARCH 2008

Predictions of Dynamic Behavior under Pressure for Two Scenarios to Explain Water Anomalies

Pradeep Kumar,[1] Giancarlo Franzese,[2] and H. Eugene Stanley[1]

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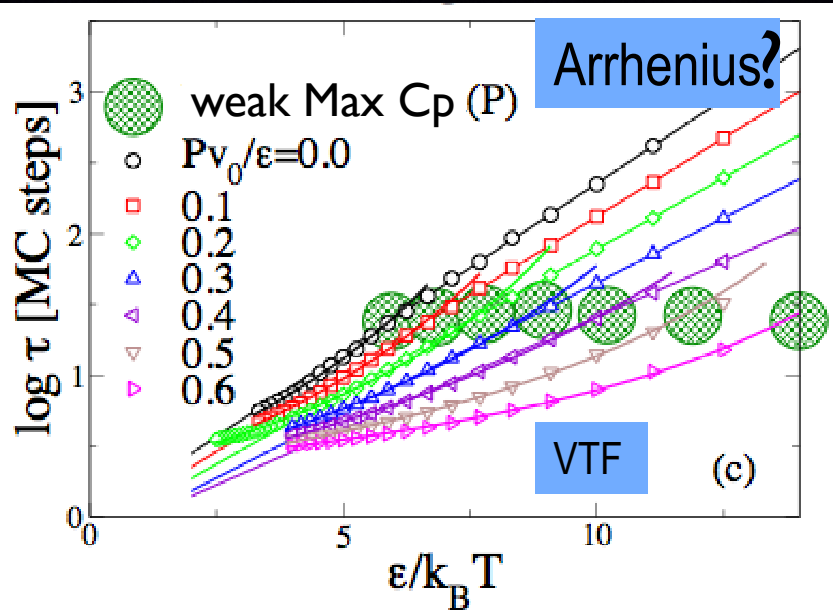
Singularity-Free interpretation



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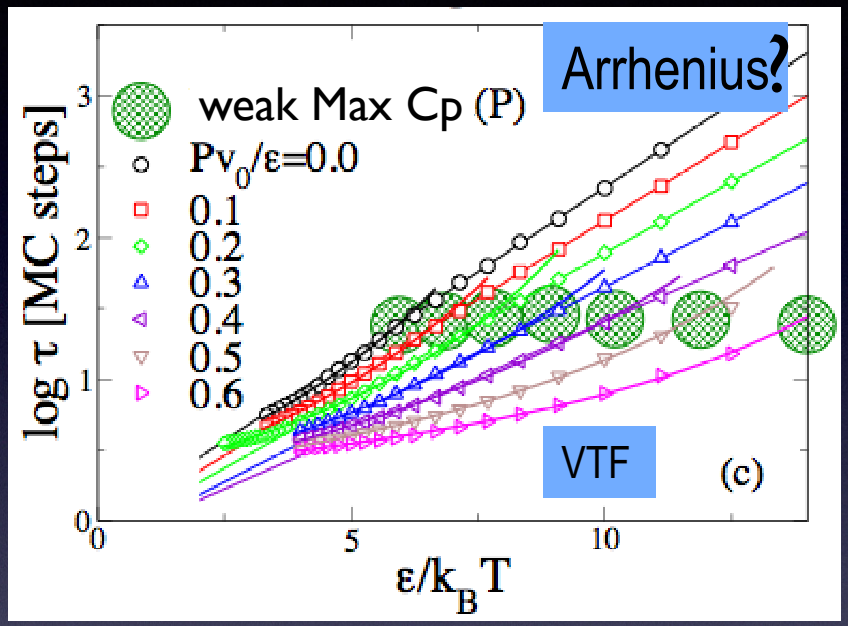

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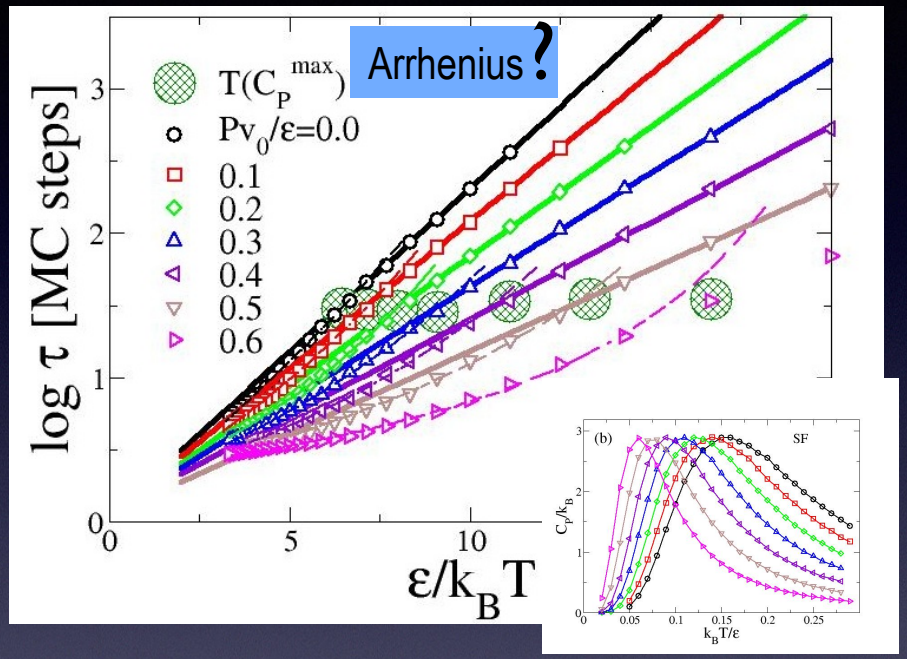

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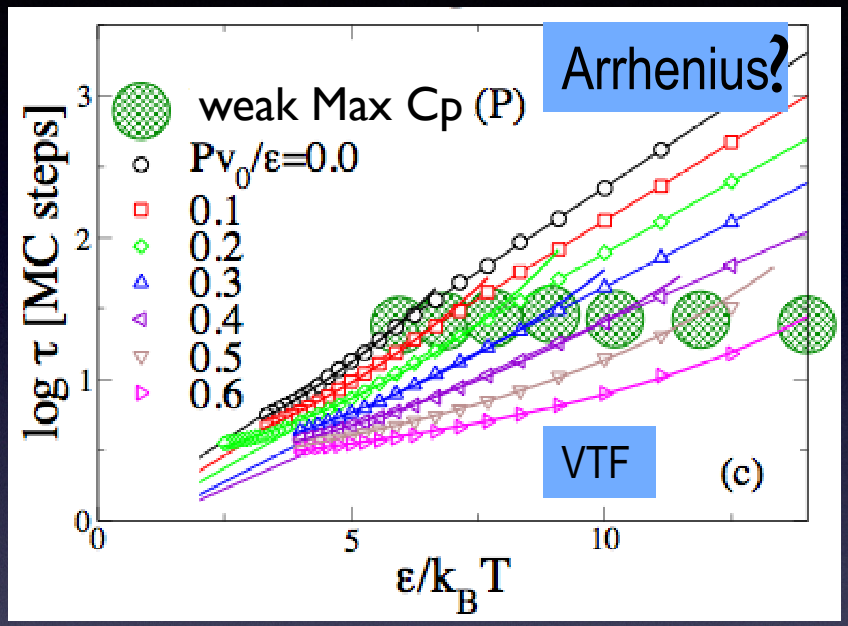

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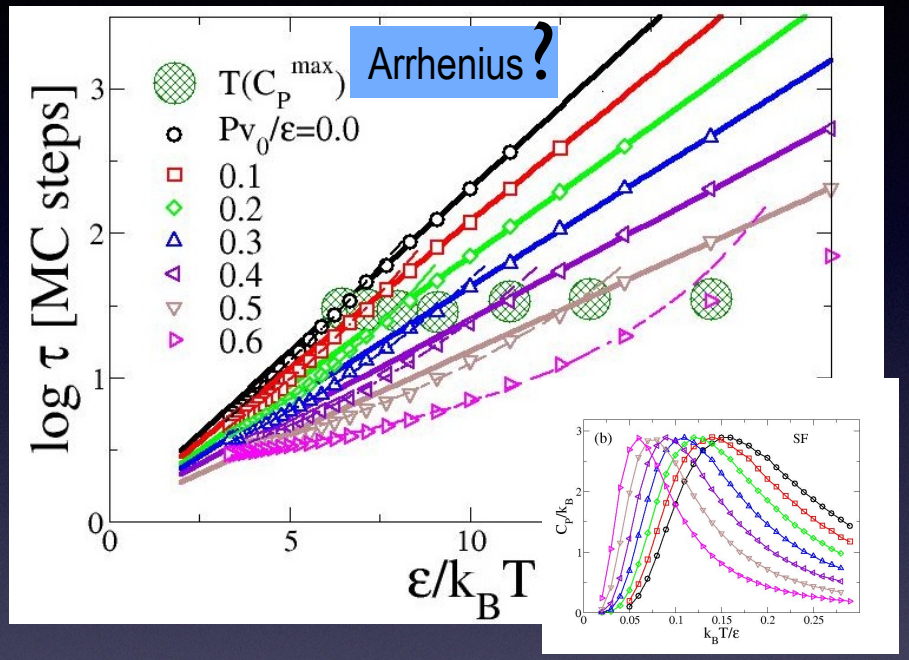

Weak Crossover in BOTH scenarios !

In both cases is $T(cross.^{W}) \sim T(C_p^{W\,Max})$

Weak Crossover is not a difference between the two scenarios

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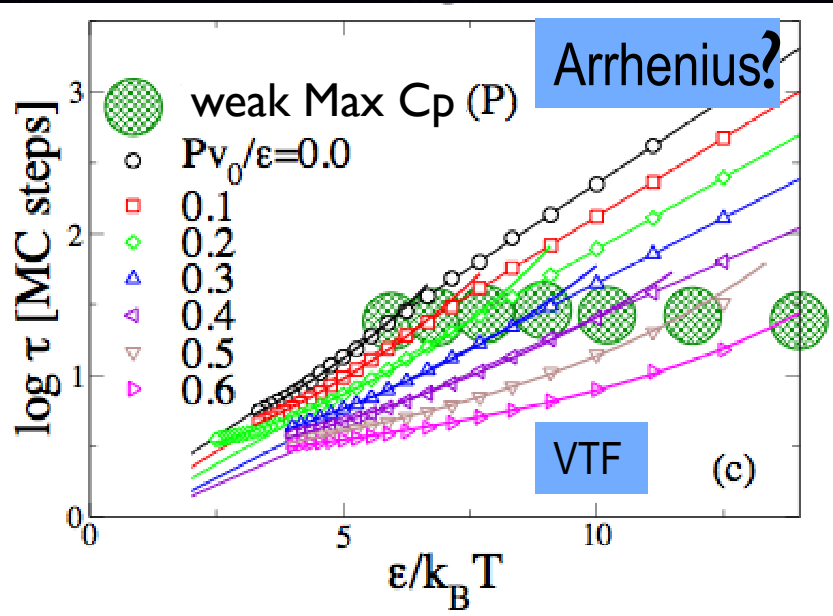

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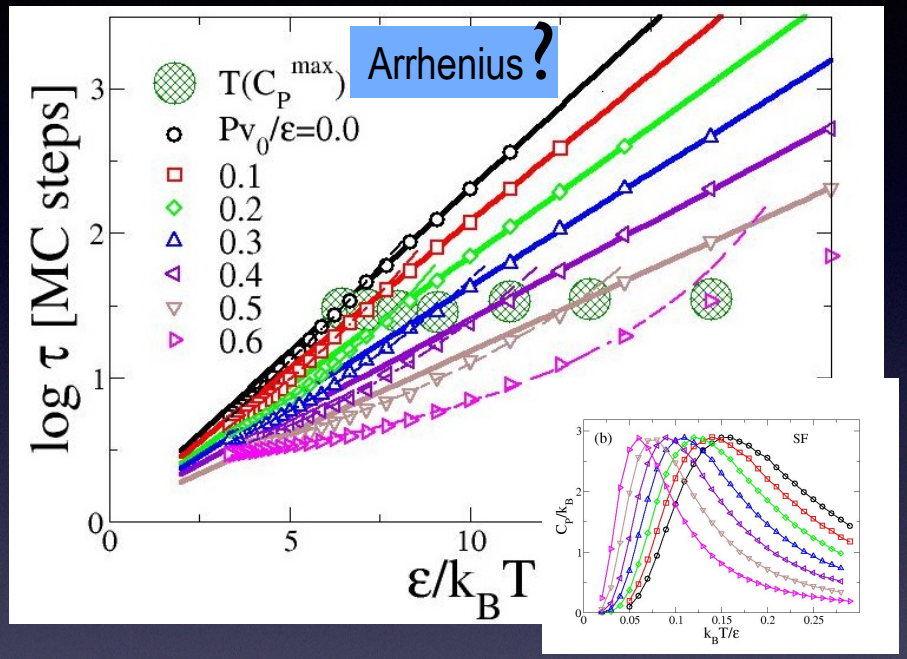

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1st PREDICTION: isochronic log τ (Tcross.) ~ constant

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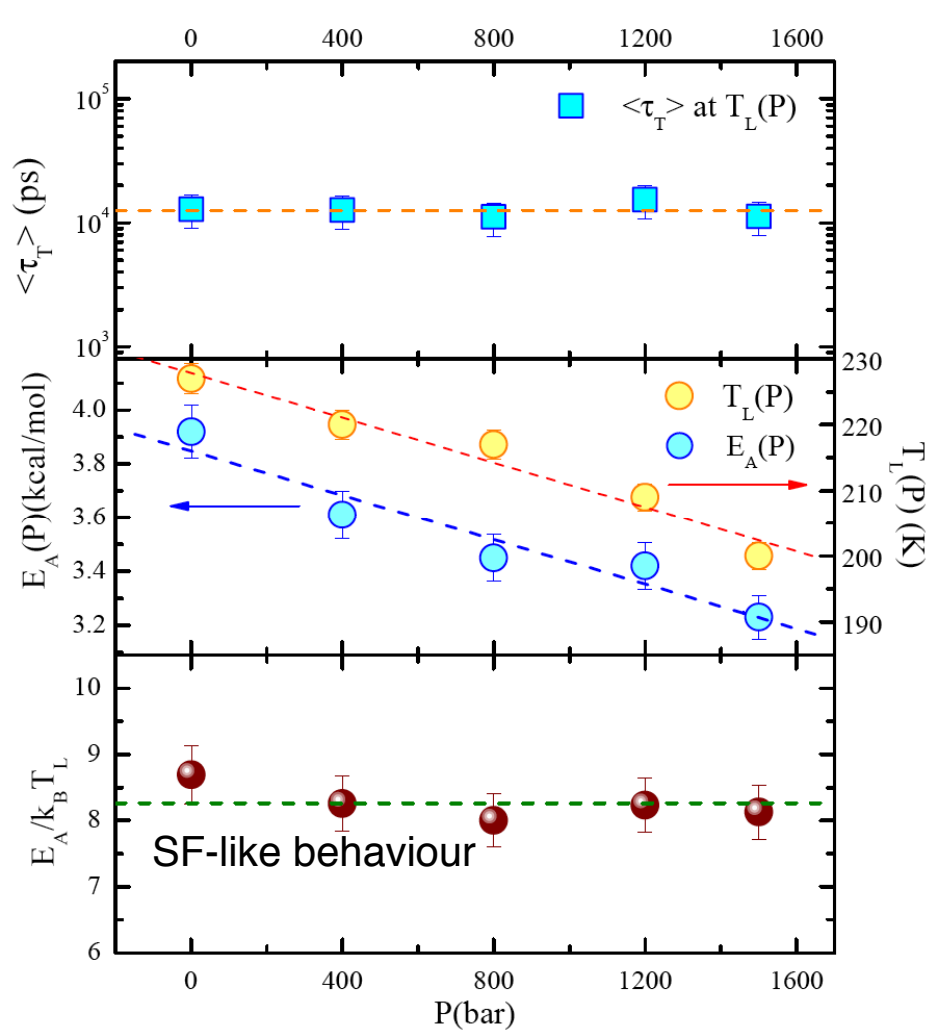
Predictions of Dynamic Behavior under Pressure for Two Scenarios to Explain Water Anomalies

Pradeep Kumar,[1] Giancarlo Franzese,[2] and H. Eugene Stanley[1]

Comparison with Experiments on Lysozyme (QENS)

Lines = Theory
Symbols = Experiment



1st Prediction
(isochronic crossover)

2nd Prediction

3rd Prediction

4th Prediction
(error > 1%)

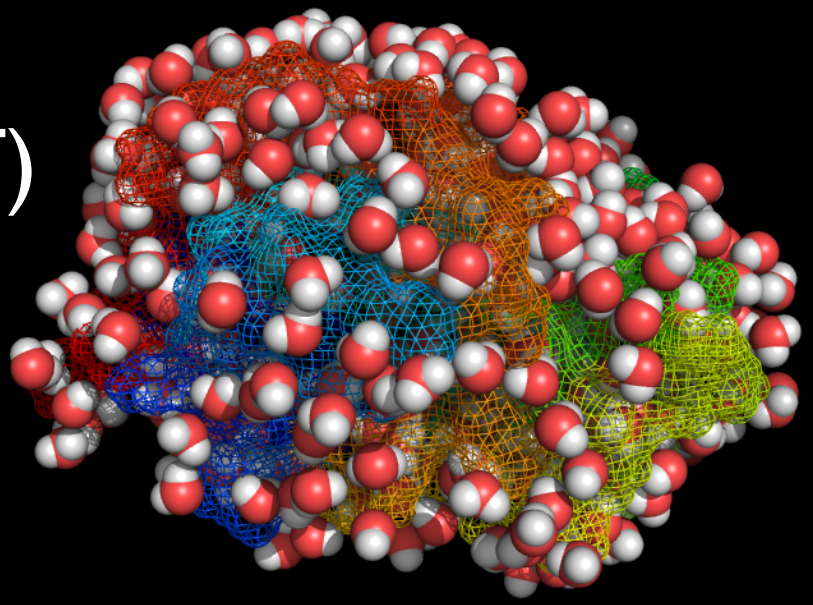
X.-Q. Chu, S.-H. Chen, et al.
J Phys Chem B (2009)

Franzese et al. J. Phys. Cond Mat. 20, 494210 (2008)

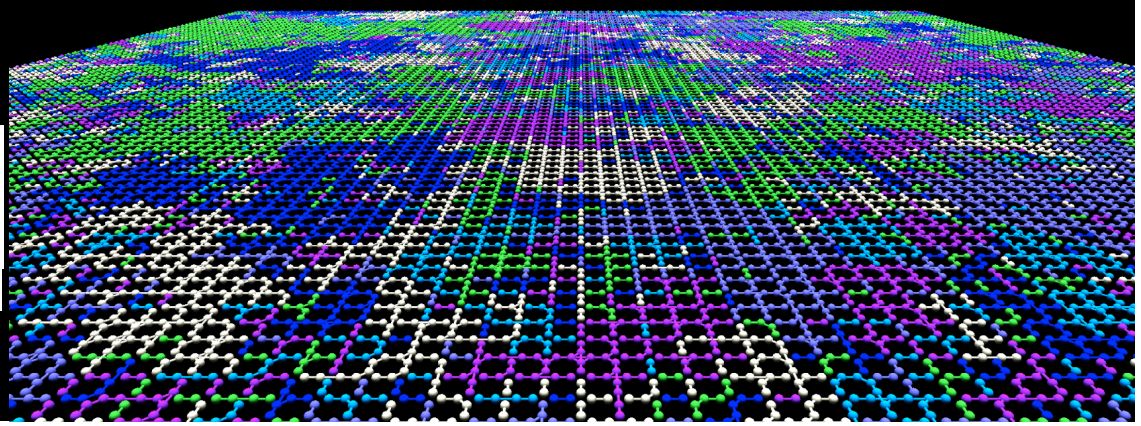
LOWER Hydration
LOWER Temperature

Water hydrating lysozyme
at low hydration (and low T)

hydration=0.3 g_H20/g_pro



forms a water monolayer
with no translational
diffusion but with rotational
diffusion and HB dynamics

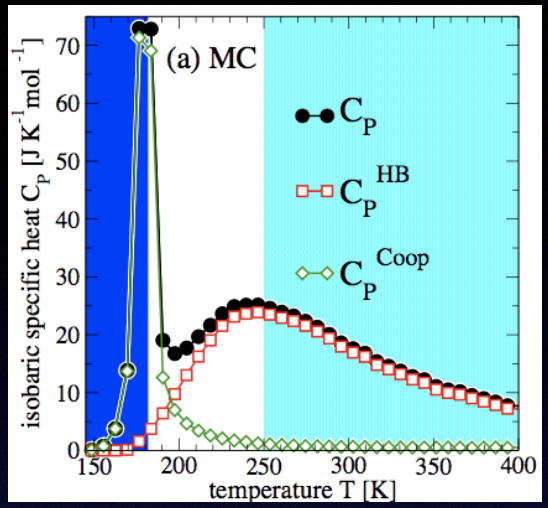


PNAS

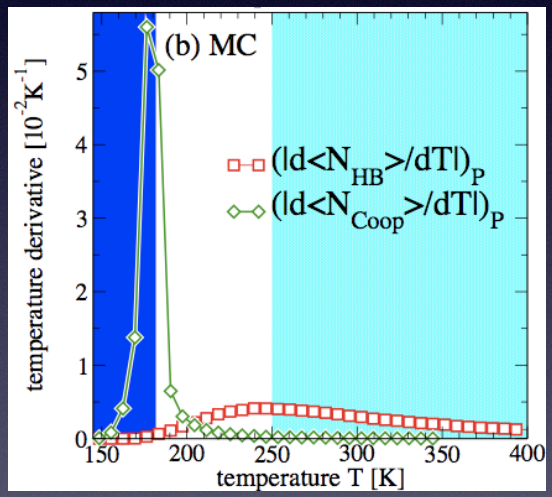
More than one dynamic crossover in protein hydration water

Marco G. Mazza[a,1,2], Kevin Stokely[a], Sara E. Pagnotta[b], Fabio Bruni[c], H. Eugene Stanley[a,2], and Giancarlo Franzese[d,2]

PNAS | December 13, 2011 | vol. 108 | no. 50 | 19877

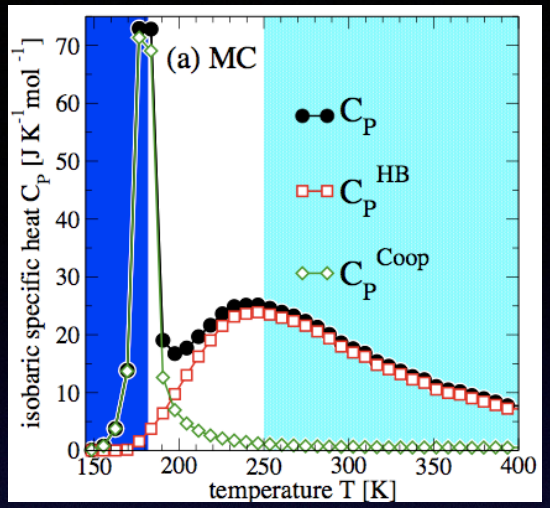


Simul./Theo.:
2 Max in Cp
T≈180 K
T≈250 K



Simul./Theory:
2 Structural changes !!

Mazza, Stokely, Pagnotta, Bruni, Stanley, Franzese PNAS 108, 19873 (2011)



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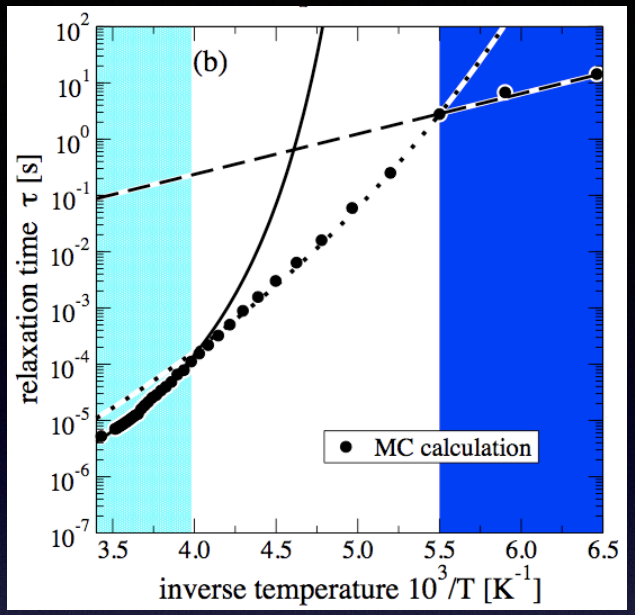
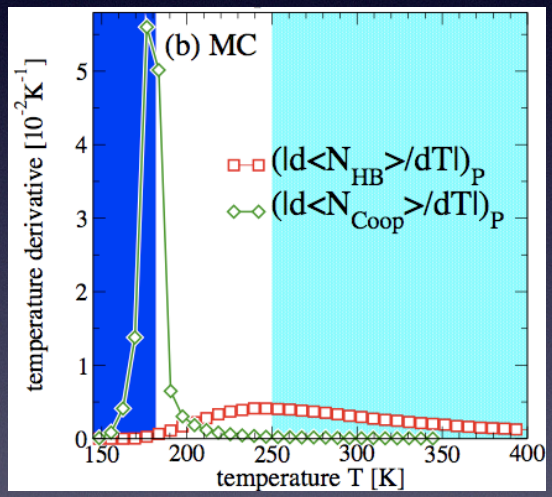


Simulations:
2 Crossovers
in HB
relaxation time



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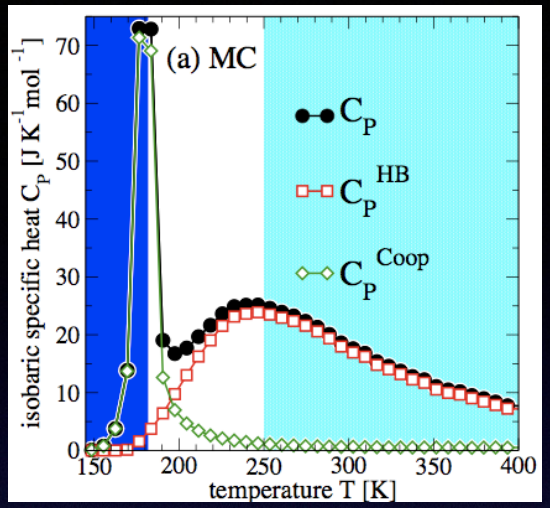

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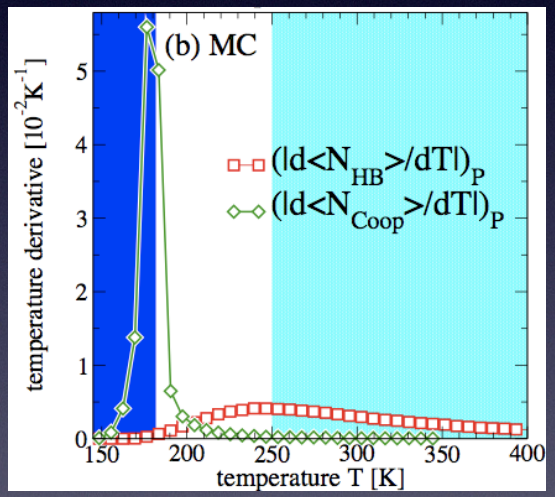

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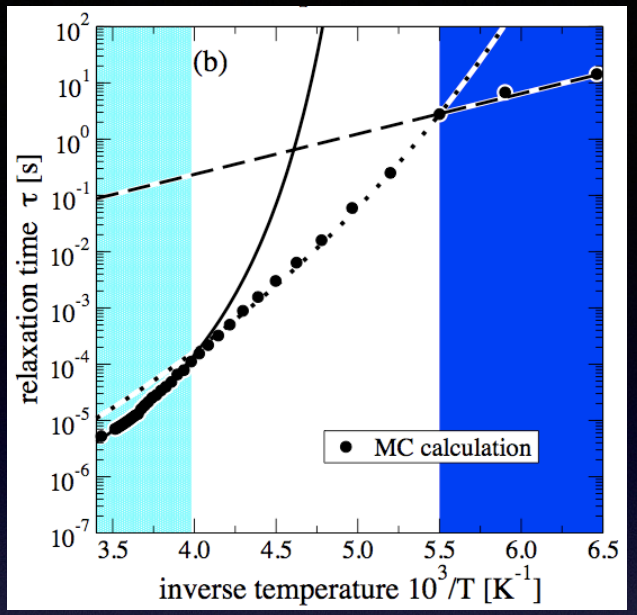

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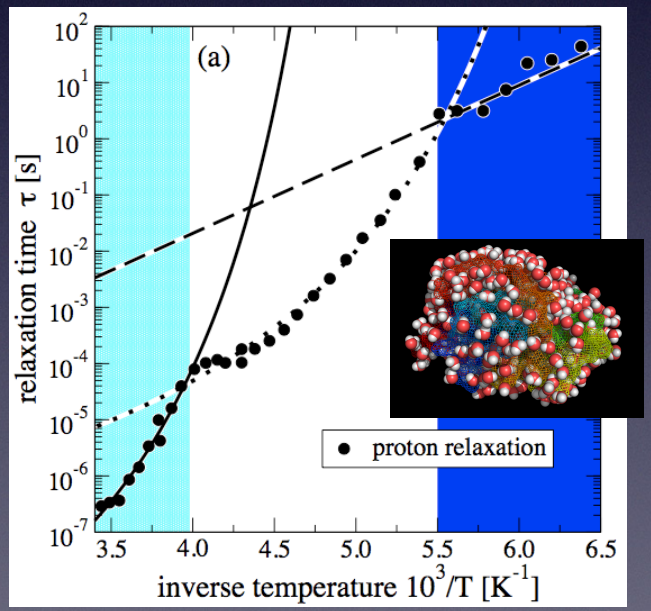

Exper.(DS) :
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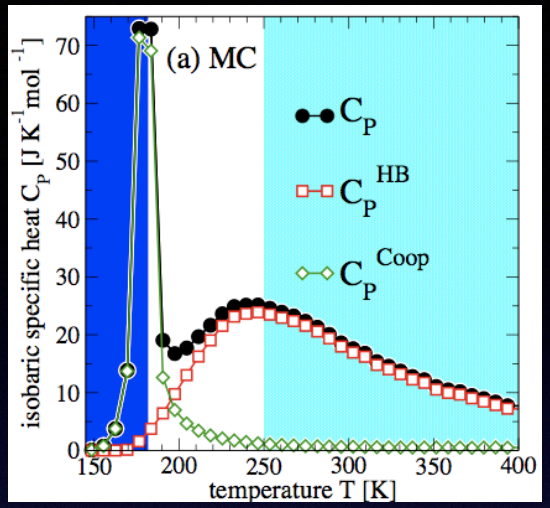
Mazza, Stokely, Pagnotta, Bruni, Stanley, Franzese PNAS 108, 19873 (2011)



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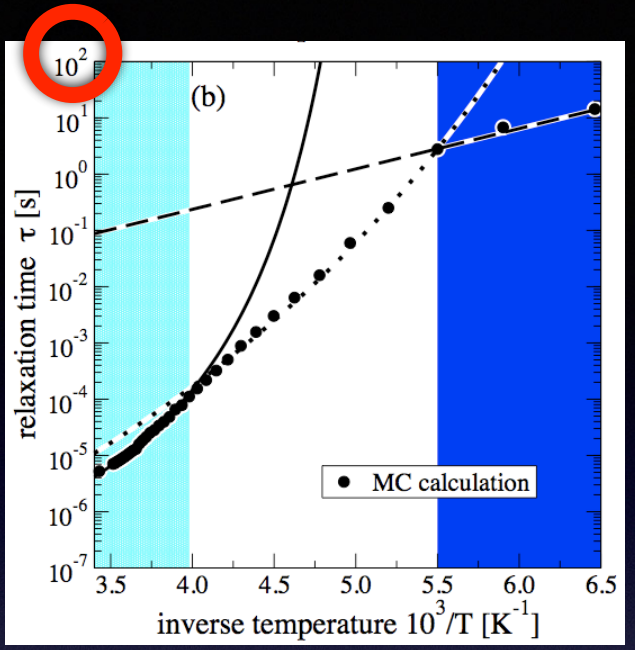

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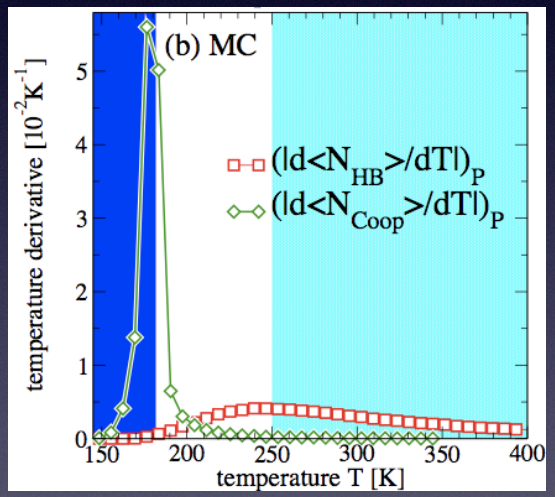

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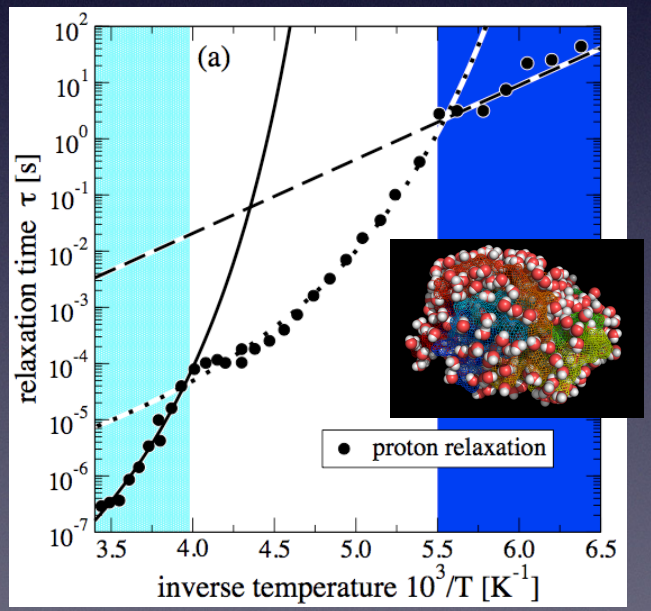

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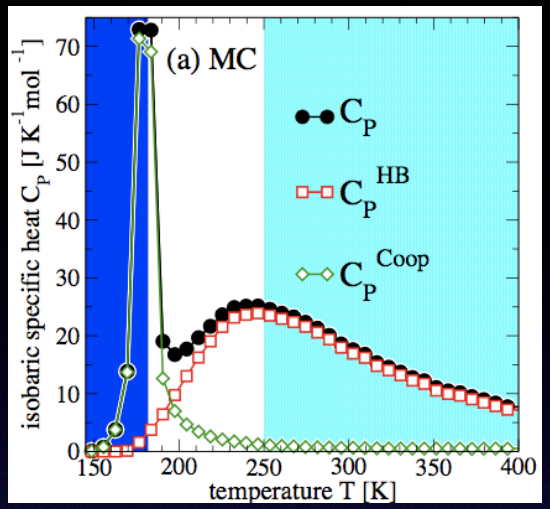

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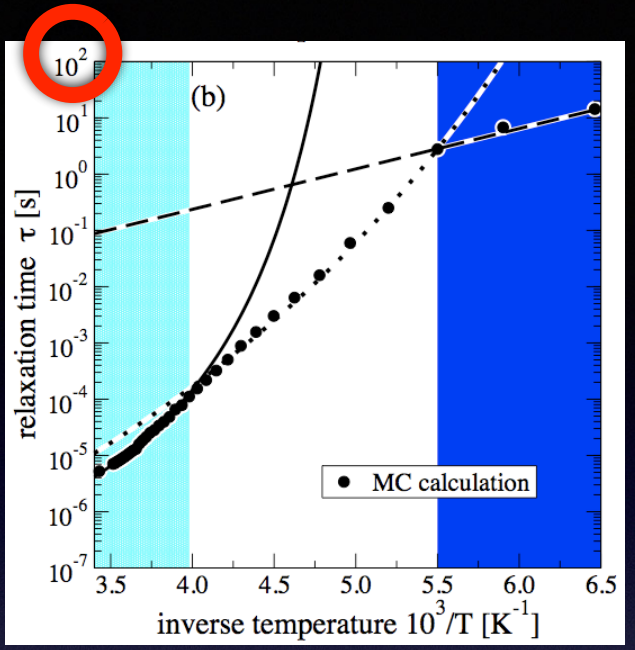

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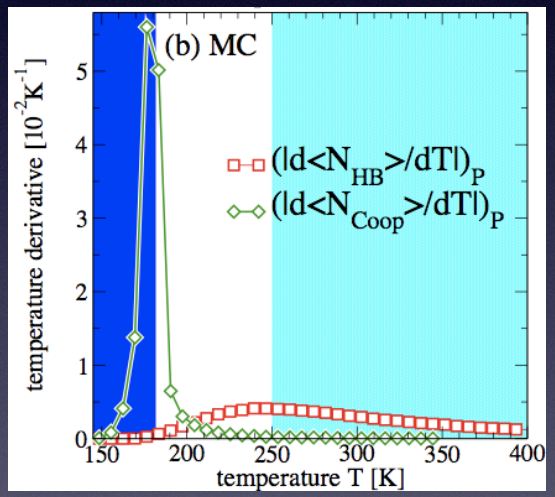

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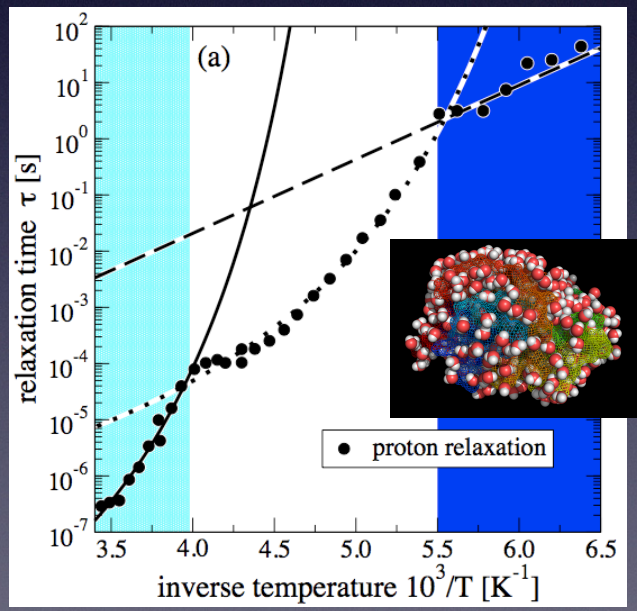

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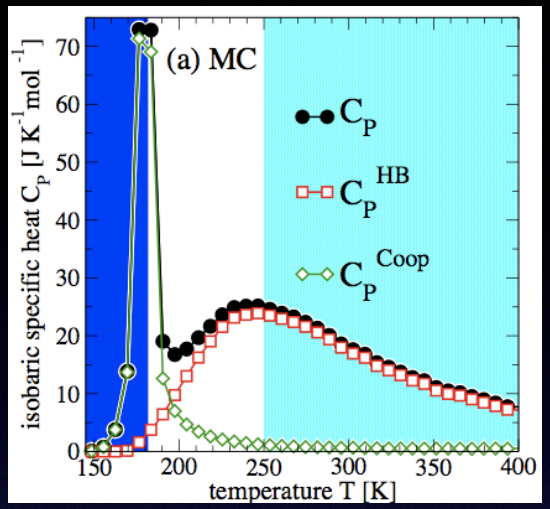
(1 atm)

2nd crossover at the Widom line due to LLCP!

Mazza, Stokely, Pagnotta, Bruni, Stanley, Franzese PNAS 108, 19873 (2011)



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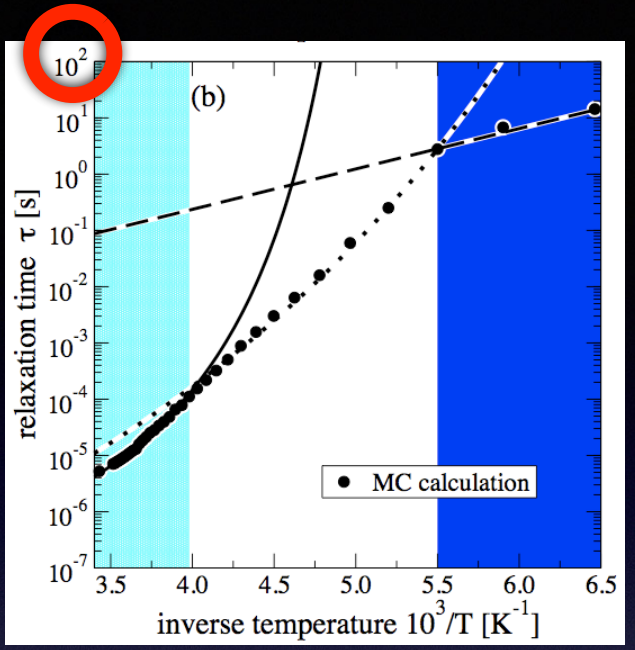
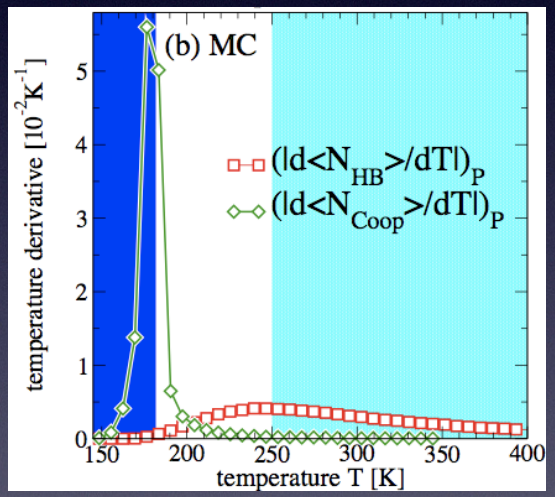
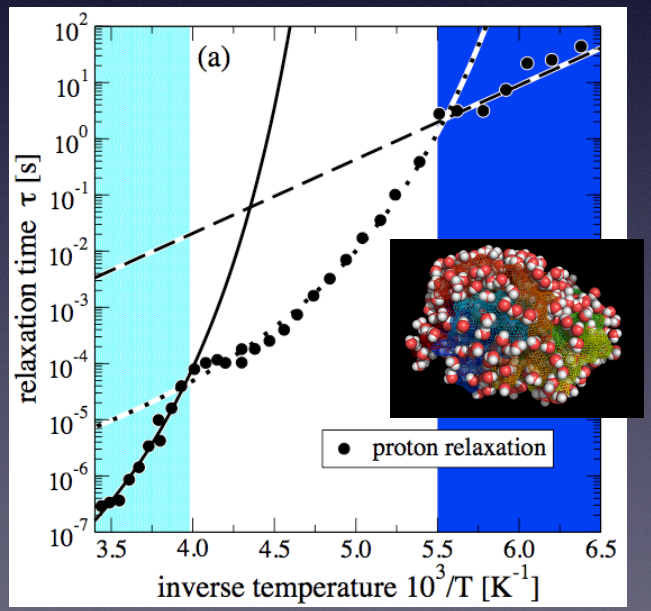
T≈250 K



Simulations:
2 Crossovers
in HB
relaxation time



Simul./Theory:
2 Structural
changes !!



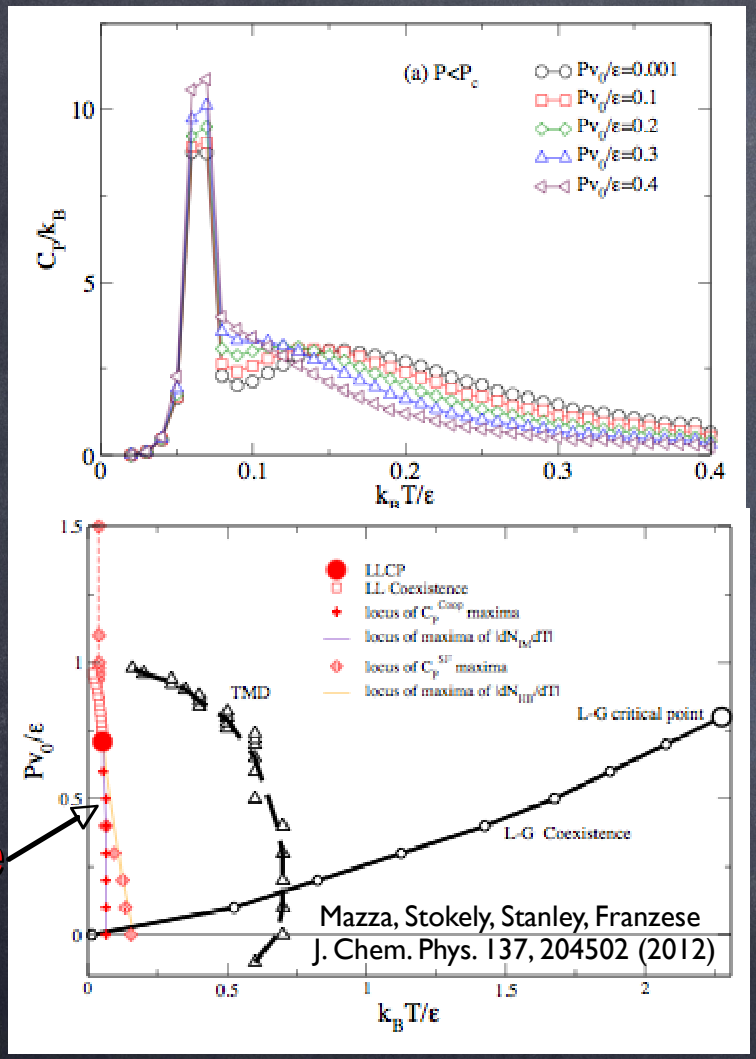
Exper.(DS) :
2 Crossovers
T≈180 K
T≈250 K
(1 atm)

2nd crossover at the Widom line due to LLCP!

Mazza, Stokely, Pagnotta, Bruni, Stanley, Franzese PNAS 108, 19873 (2011)
compare with QENS for Rutile (TiO2) at low hydration [Chu, Ehlers, Mamontov, et al. PRE 2011]
and with EINS for low-hydr. perdeut. C-phycocyanin [S. Combet & J.-M. Zanotti PCCP 2012]

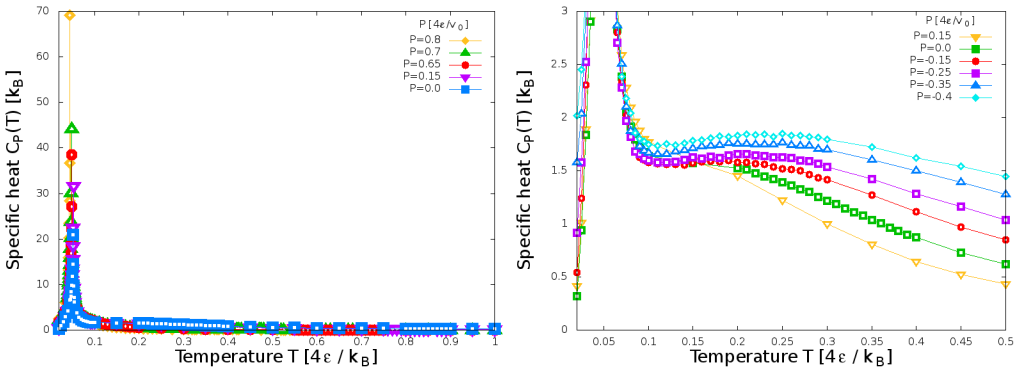
The Weak Crossover is NOT a "smoking gun" for the Critical Point (but the Strong Crossover is !)

At higher P/hydration



W line

Specific heat at higher hydration (h)



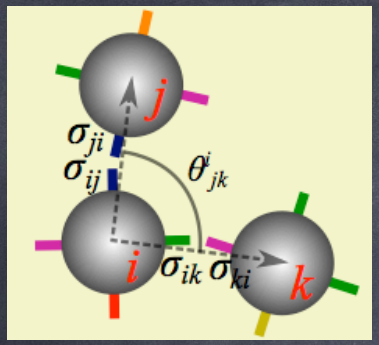
PREDICTION: at higher P or h intermediate non-Arrhenius regime disappears

Open question:

how hydration, T and P are related in exper. ?

What about polymorphism and the stability with respect to the crystal homogeneous nucleation?

Including explicit 3-body interaction?



J_3/J_5

Ratio of 3-body / 5-body interaction is the relevant parameter

Polymorphism + Critical Point + Hexatic (2D) !!

Solid

$$g_\alpha(r) \sim \text{constant}$$

$$g_{\vec{G}} \sim r^{-\eta}$$

Hexatic

$$g_\alpha(r) \sim r^{-\eta}$$

$$g_{\vec{G}} \sim \exp(-r/\xi)$$

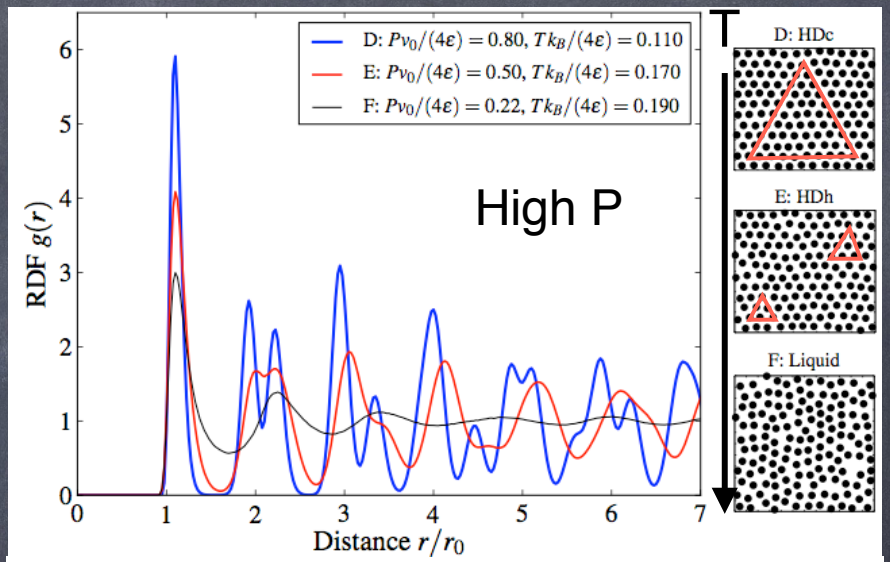
Liquid

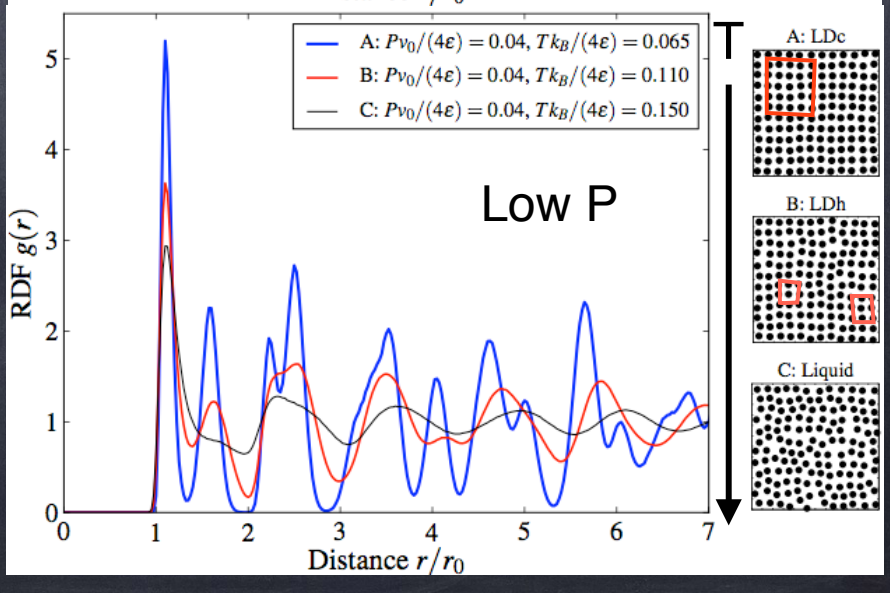
$$g_\alpha(r) \sim \exp(-r/\xi)$$

$$g_{\vec{G}} \sim \exp(-r/\xi)$$

g_α = core. func. for orientational o.p.

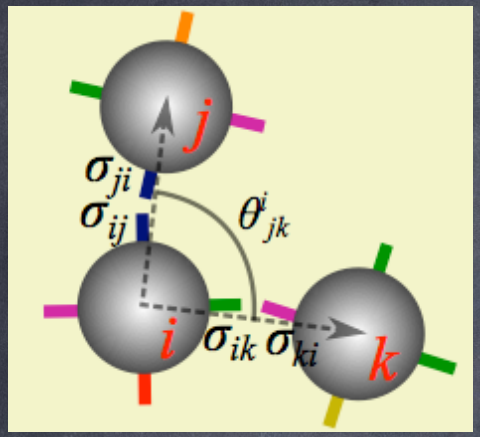
g_G = core. func. for translational o.p.





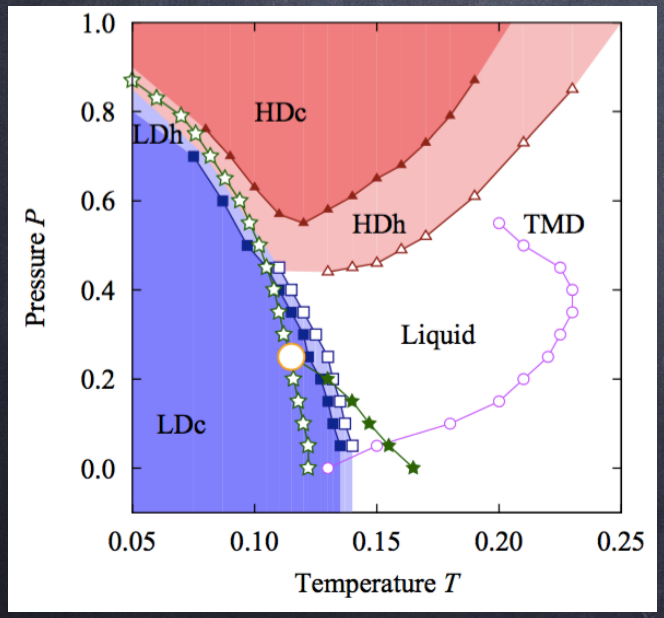
Oriol Vilanova, G.F. arXiv:1102.2864

Increasing explicit 3-body interaction?

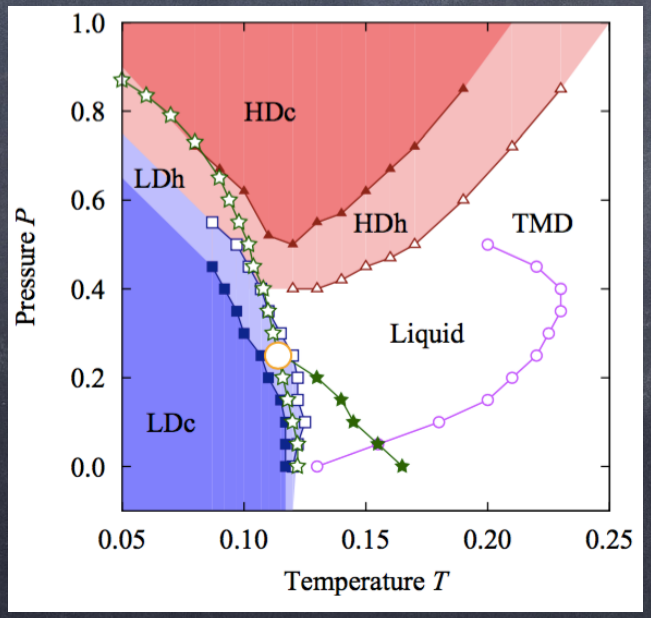


LLCP is above the limit of stability of crystal for decreasing 3-body interaction !!

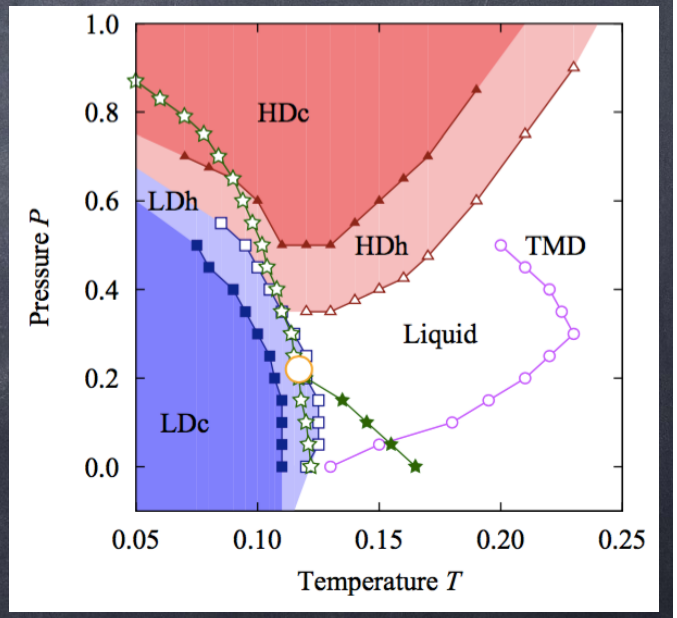
J_3/J_5 =1.3



J_3/J_5 =1.0



J_3/J_5=0.8



OBS: mW model has only 3-body, hence promotes crystallization

Oriol Vilanova, G.F. arXiv:1102.2864

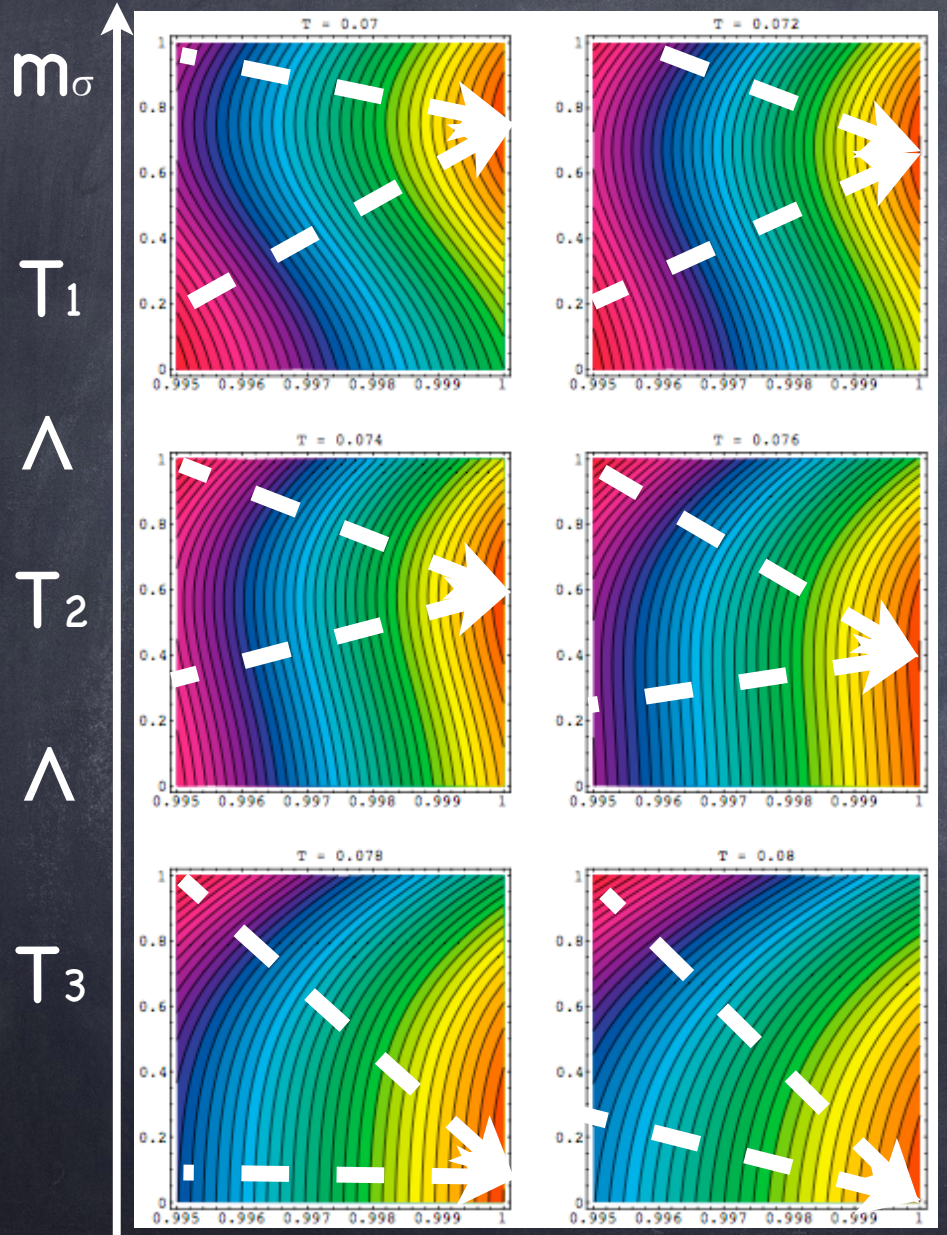
Analytic calculations

- Gibbs molar free energy in terms of density order parameter (m) + tetrahedral order parameter (m_σ)

G. Franzese and H.E. Stanley JPCM 14, 2201 (2002)

c.f.r. H. Tanaka's talk on Two-State Model (EPL 2000)
c.f.r. M. Anisimov's Two-State Model (PRL 2006)

Free energy at Low P: no phase transition



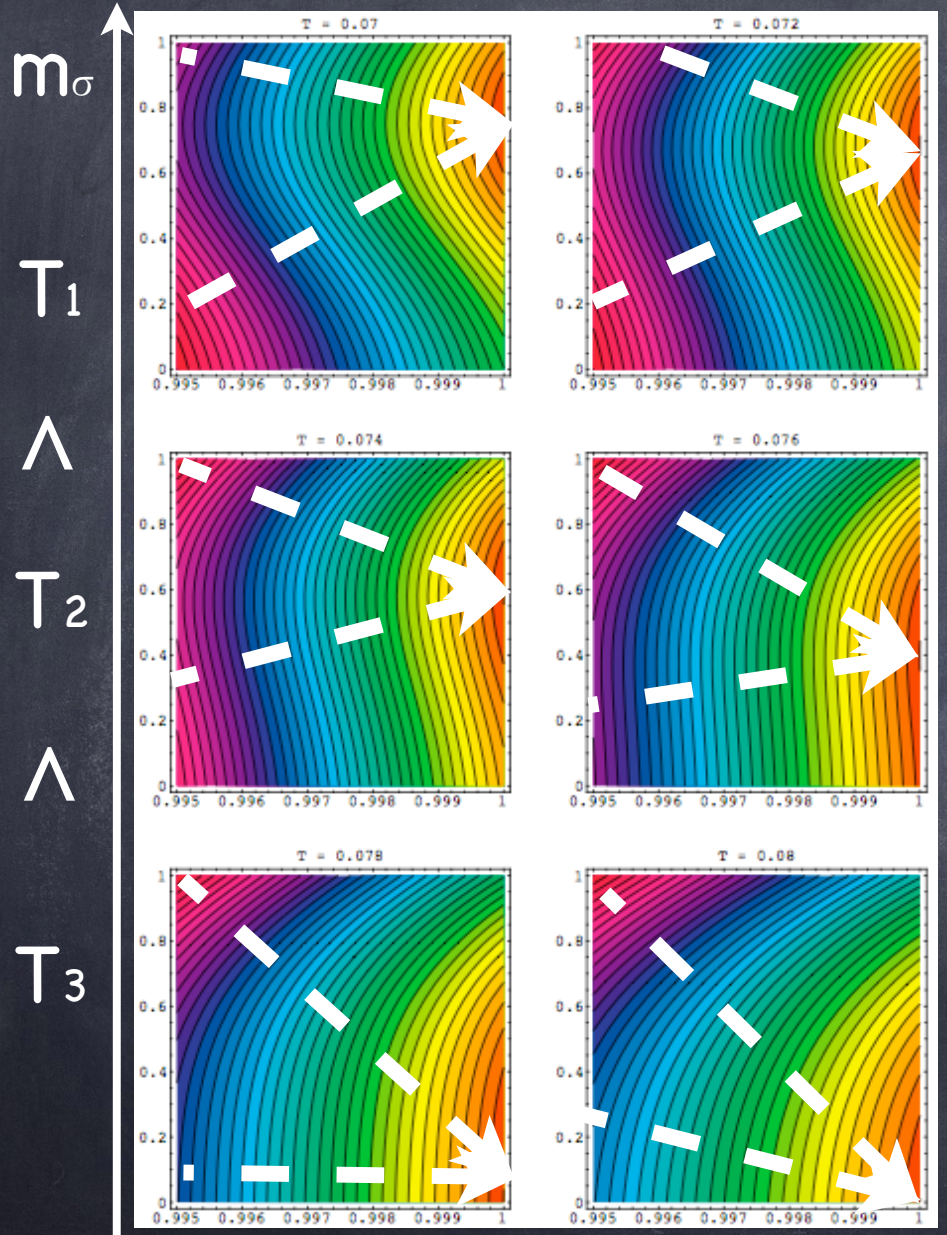
LDL-like

Continuous change of density: Widom line = Max correlation length

HDL-like

KINK as in Zhang et al. "nanoconfined water in MCM-41" PNAS (2012)

Free energy at Low P: no phase transition



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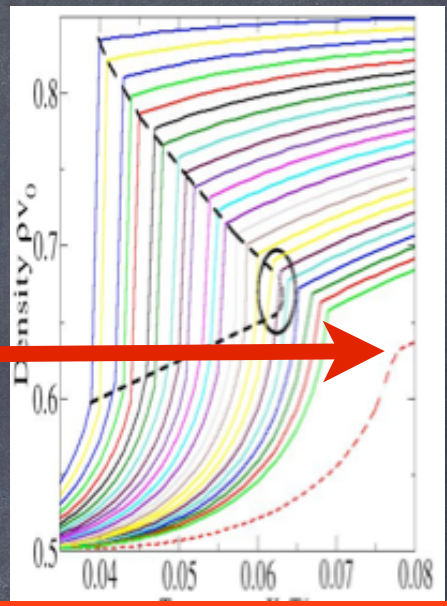

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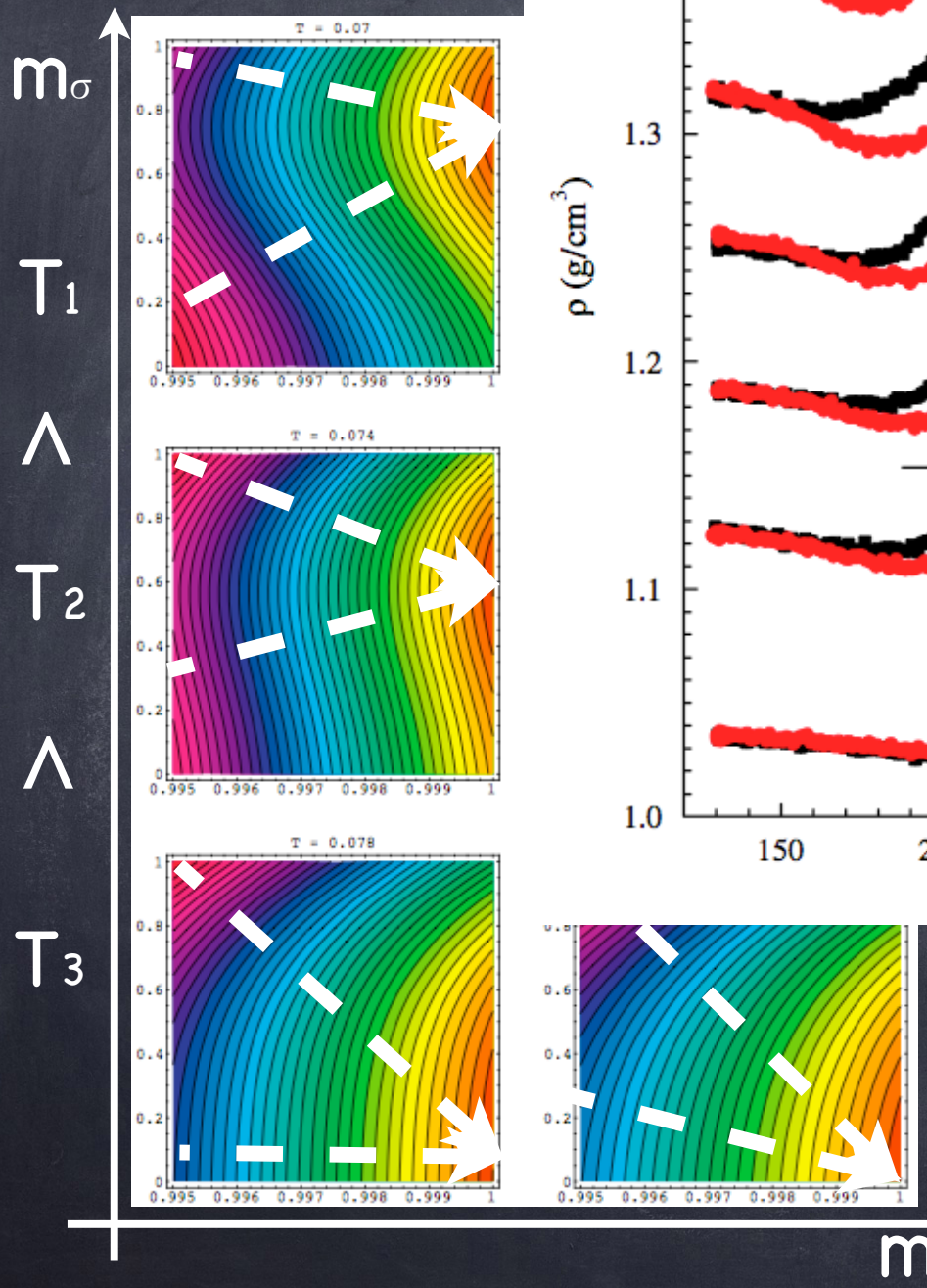
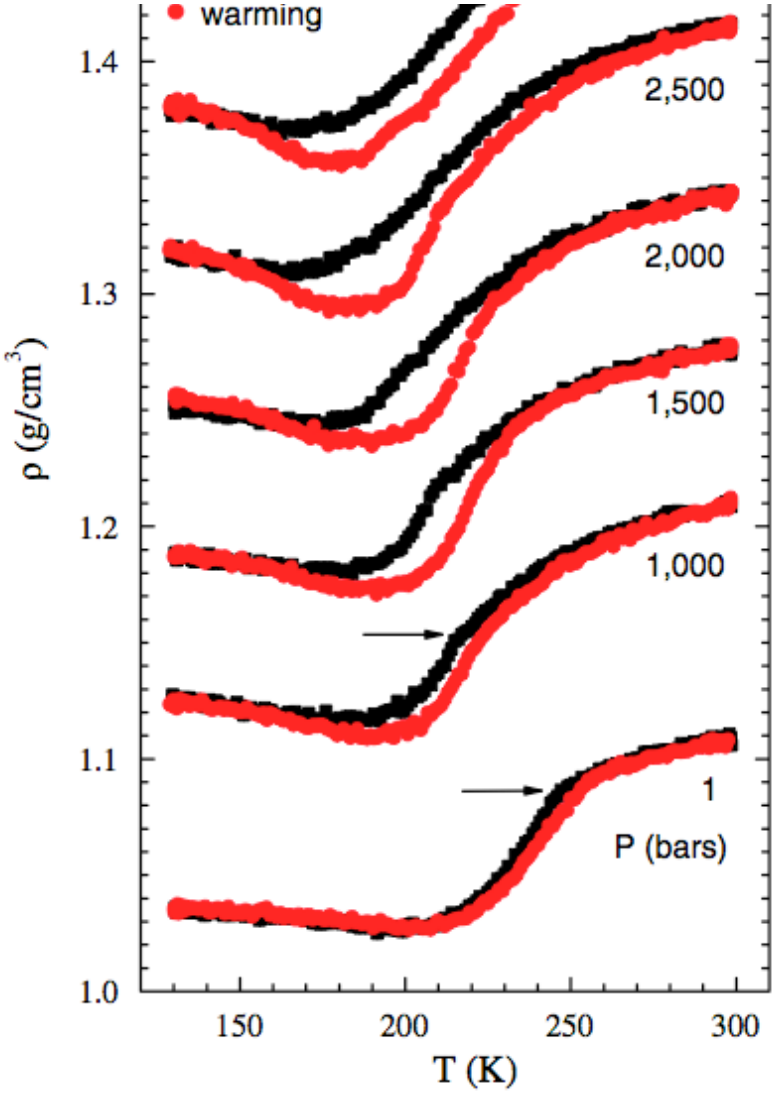
HDL-like

Free ene

e transition

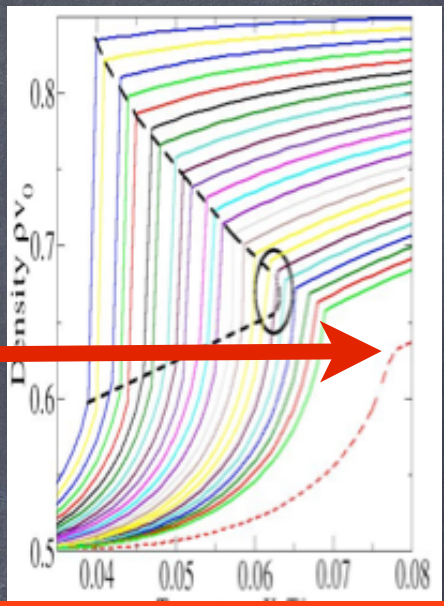


HDL-like



nge

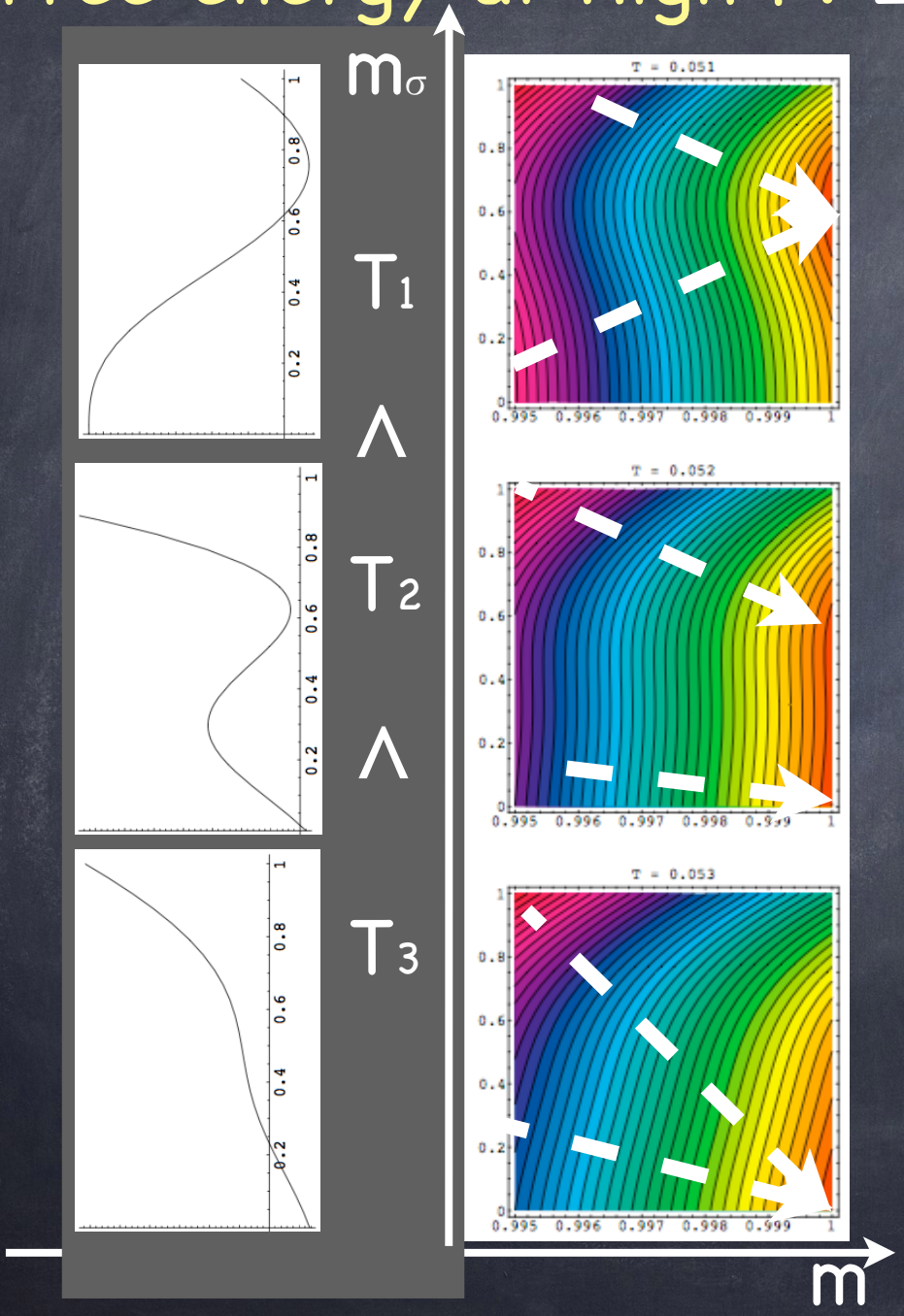
on



KINK as in Zhang et al. "nanoconfined water in MCM-41" PNAS (2012)

Free energy at High P: Liq-Liq 1st or. transition

Stockly et al.



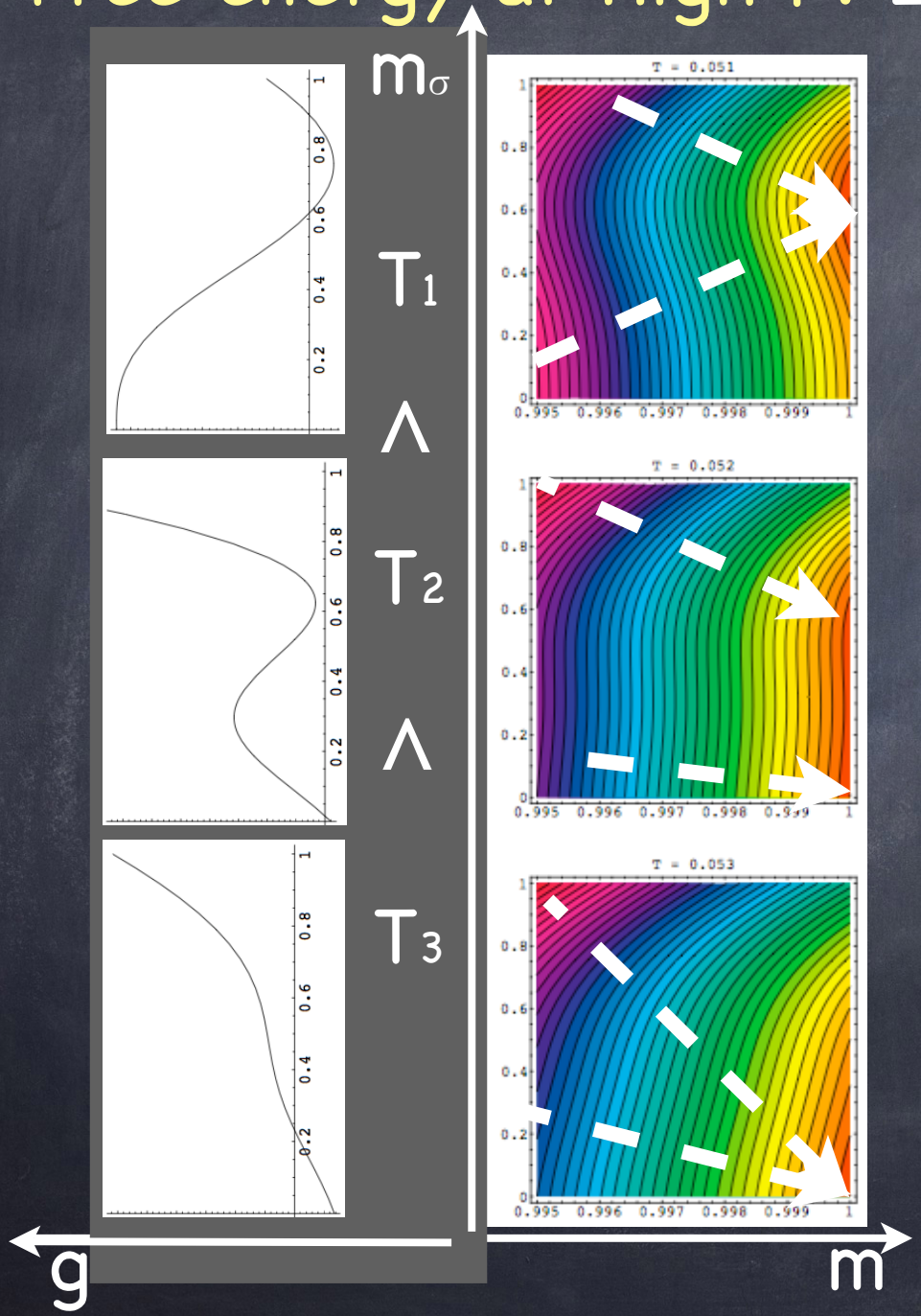
Bonding Order
= Low Density Liquid (LDL)

LDL-HDL
coexistence

Bonding Disorder
= High Density Liquid (HDL)

Free energy at High P: Liq-Liq 1st or. transition

Stockly et al.



Bonding Order
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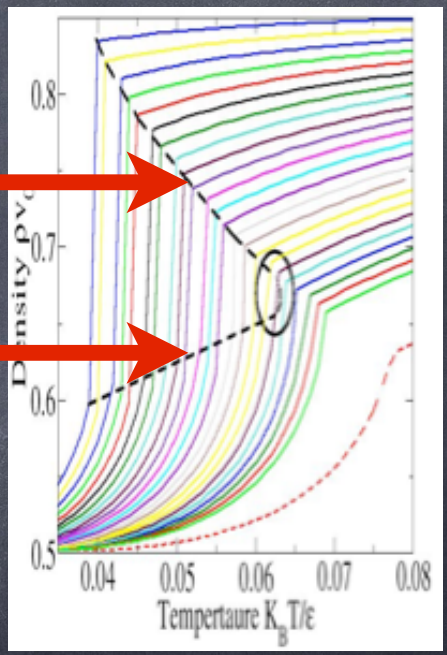
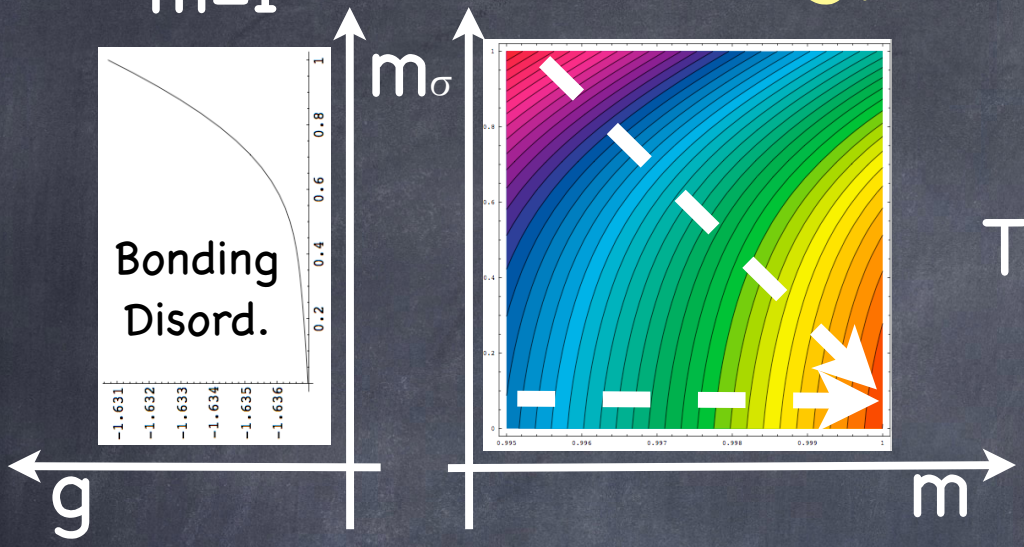
LDL-HDL
coexistence



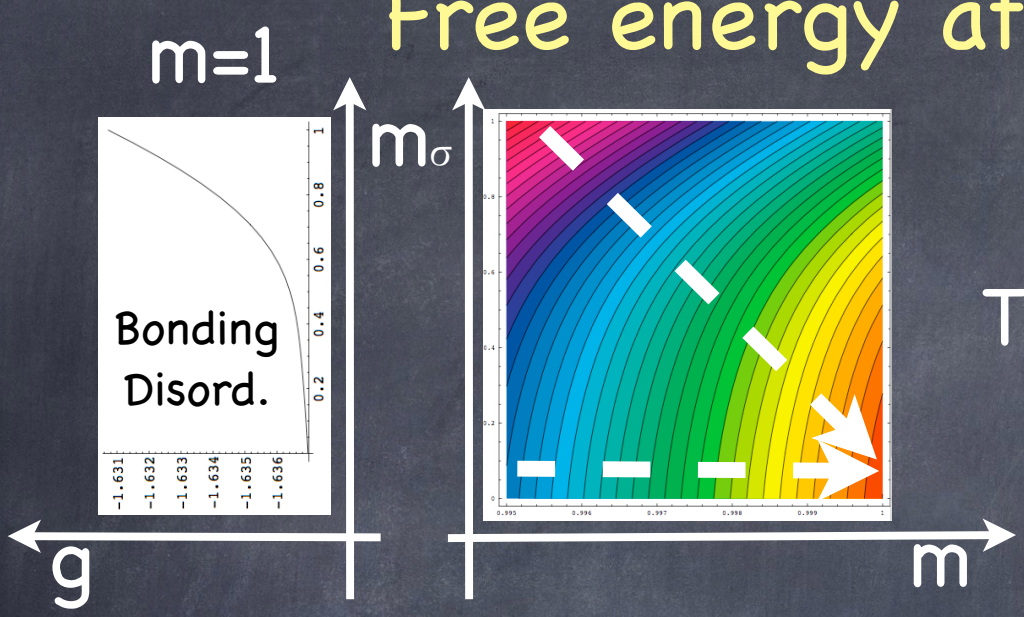
Bonding Disorder
= High Density Liquid (HDL)

Free energy at low T, high P



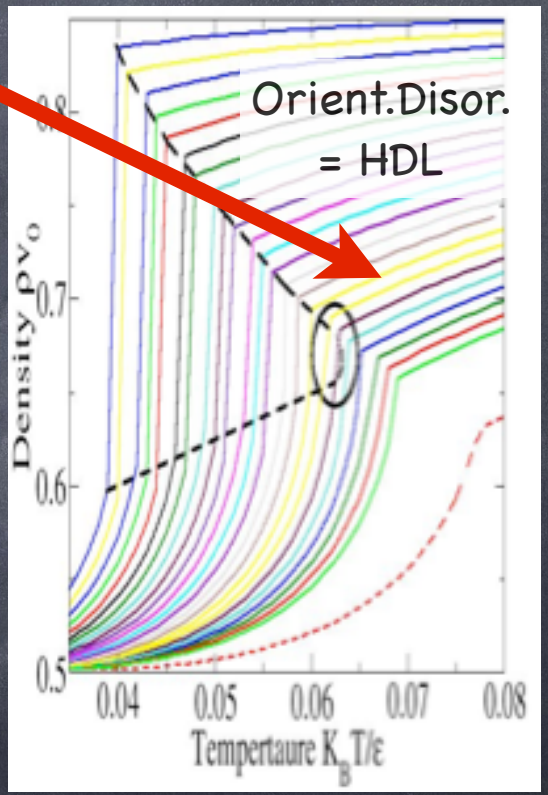
$T > T_{LLCP}$

Free energy at low T, high P

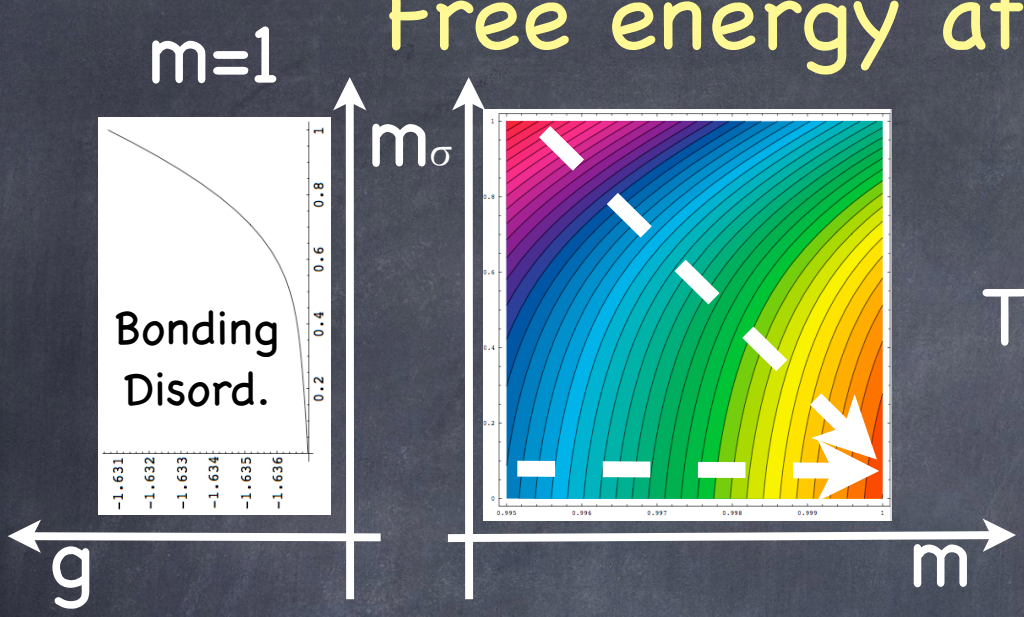


$T > T_{LLCP}$

High Density Liq (HDL)

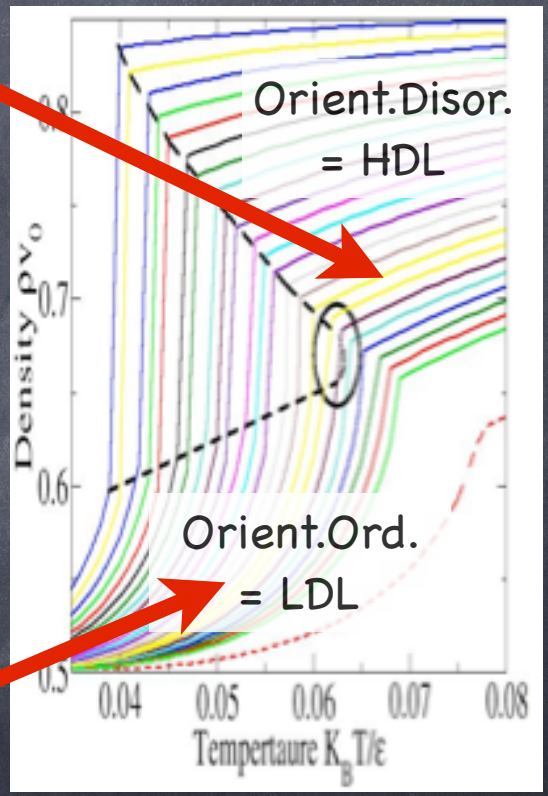


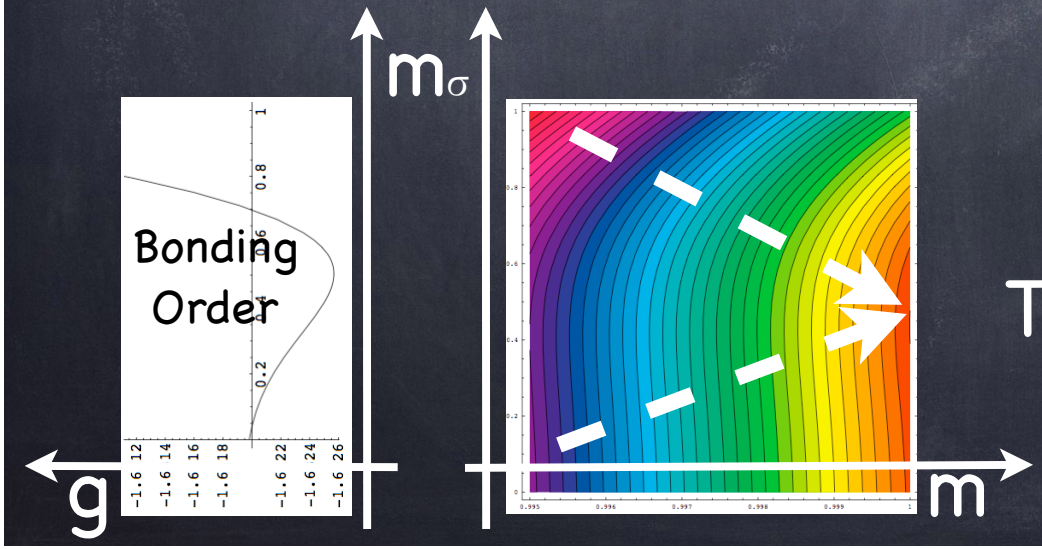
Free energy at low T, high P



$T > T_{LLCP}$

High Density Liq (HDL)

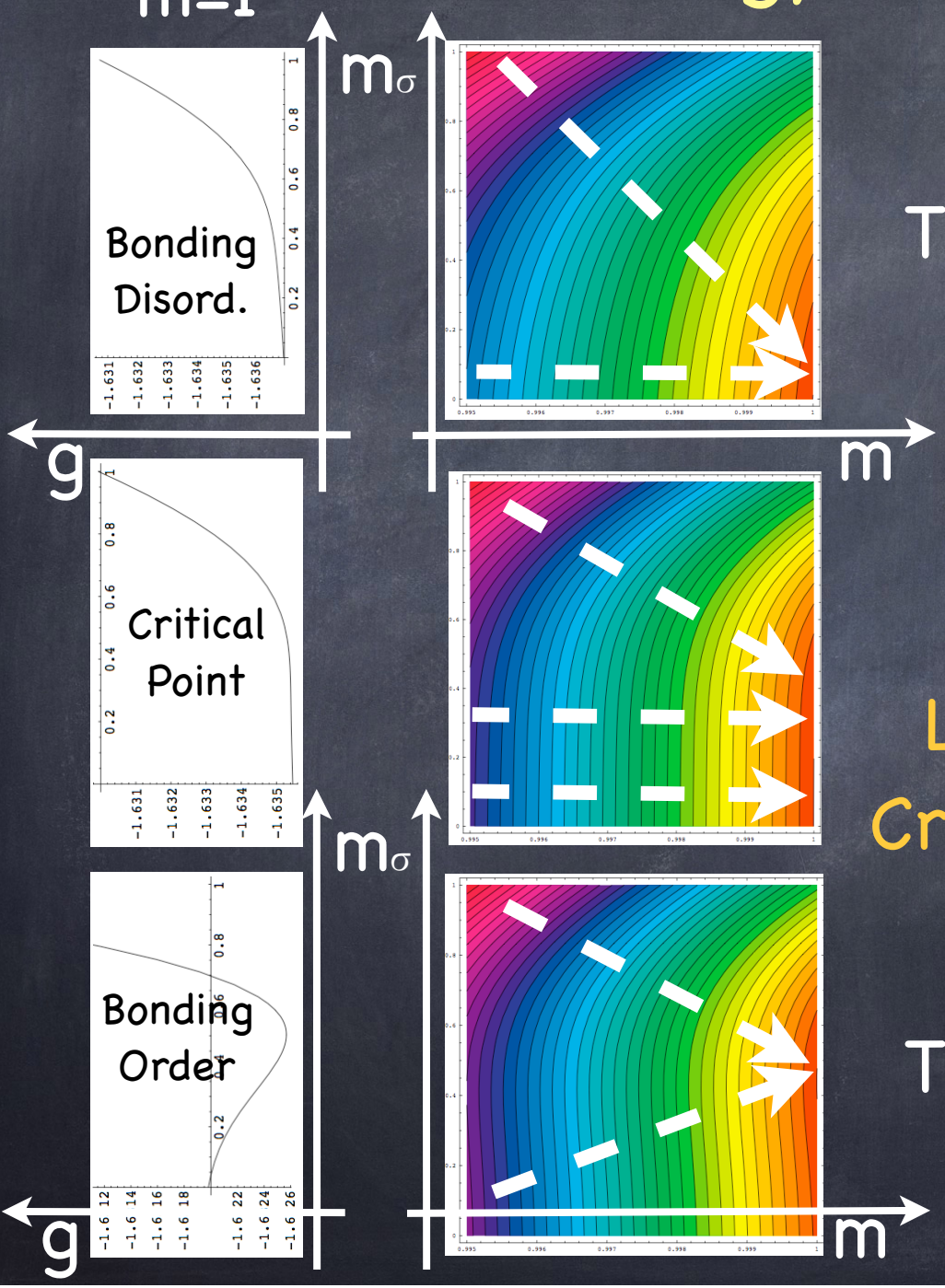




$T < T_{LLCP}$

Low Density Liq (LDL)

Free energy at low T, high P



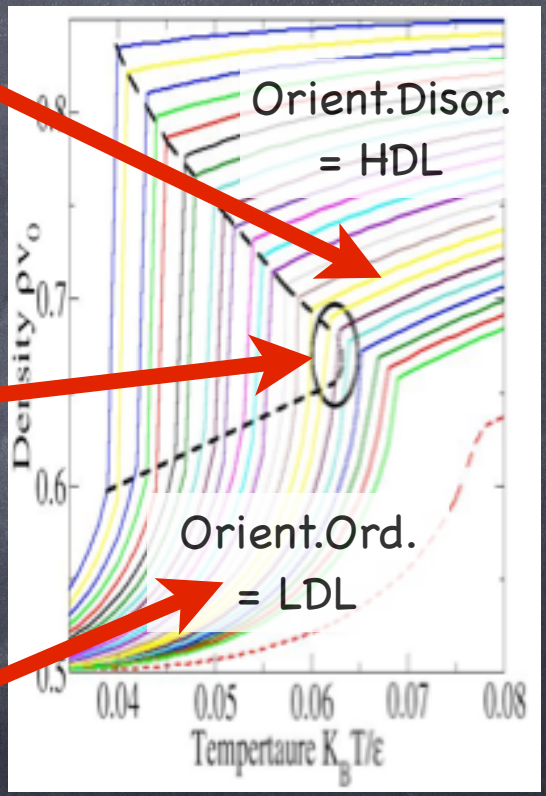
$T > T_{LLCP}$

$\sim T_{LLCP}$

Liq-Liq Crit. Point

$T < T_{LLCP}$

High Density Liq (HDL)



Low Density Liq (LDL)

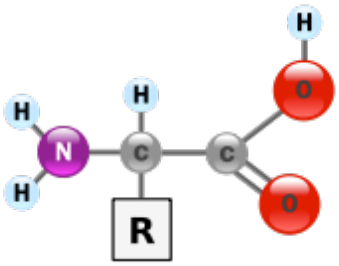
Are the properties of interfacial water relevant for protein stability ?

PRL 115, 108101 (2015) PHYSICAL REVIEW LETTERS week ending 4 SEPTEMBER 2015

Contribution of Water to Pressure and Cold Denaturation of Proteins

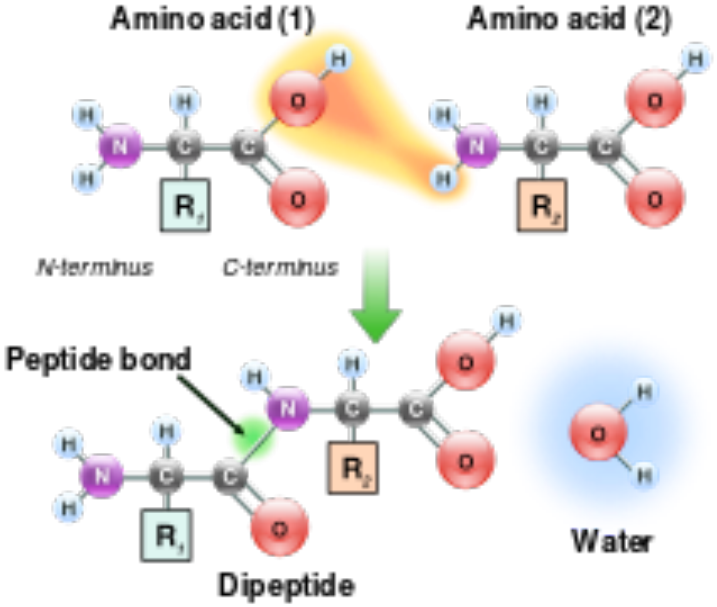
Valentino Bianco and Giancarlo Franzese*

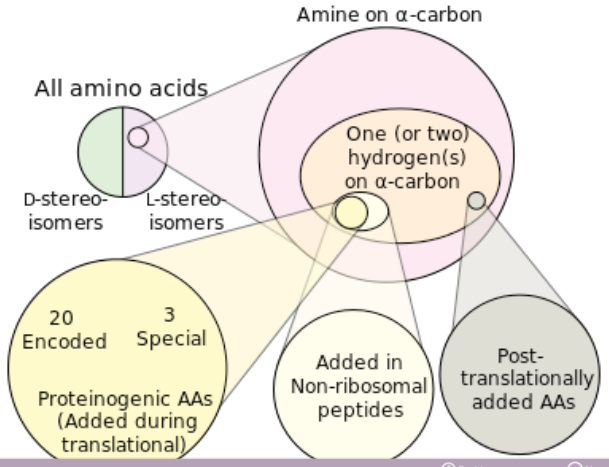
PROTEINS

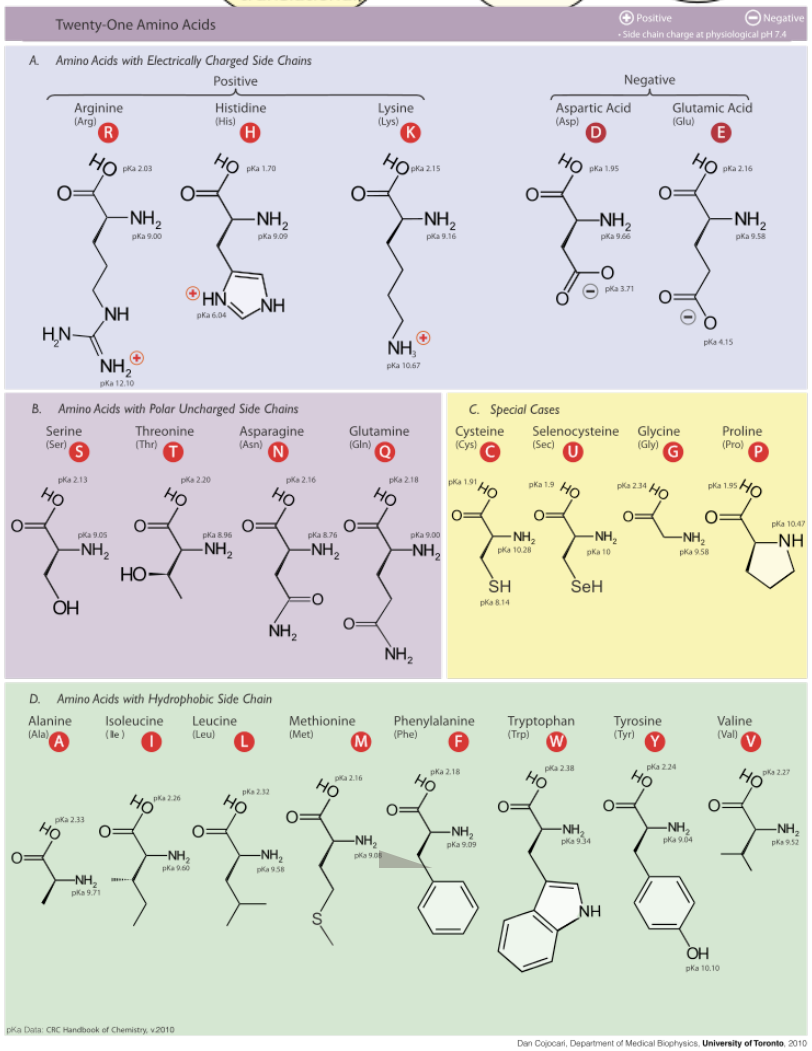


ARE POLYMERS

- Amino acids residues = compounds with amine (NH2) and carboxylic acid (COOH) functional groups, + side-chain (R) specific to each amino acid (of ~500)
- α-amino acids = both the amine and the carboxylic acid groups attached to the first (alpha-) carbon
- 23 Proteinogenic amino acids combine into chains linked by peptide (amide) bonds (with expulsion of water) to form proteins.





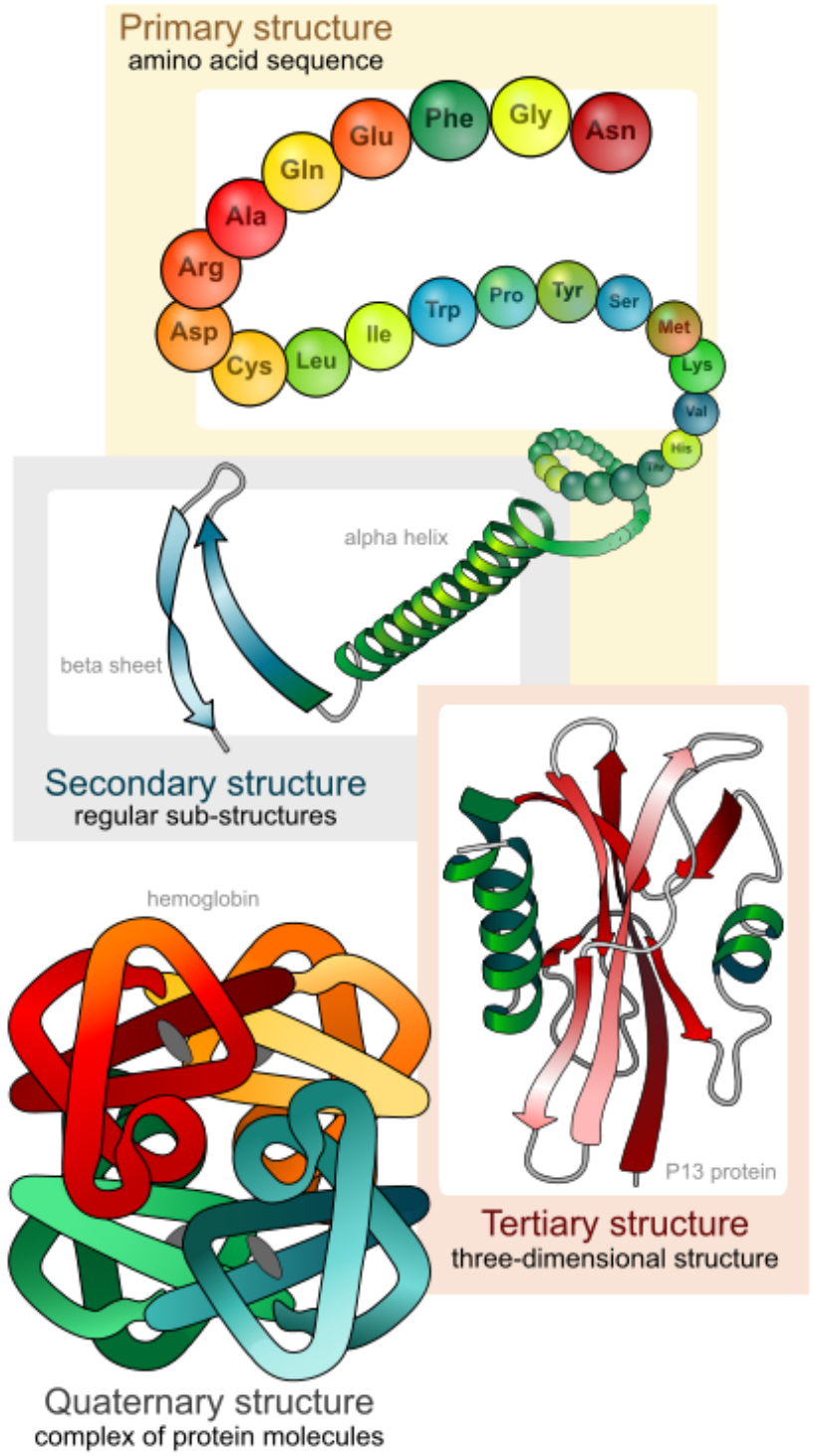


PROTEIN

HIERARCHICAL STRUCTURE

- Proteins = polymers (polypeptides) made of monomer amino acids residues. Peptide = if less than 40 residues. *Primary structure*: the amino acid sequence.
- *Secondary structure*: regularly repeating local structures stabilized by hydrogen bonds: *alpha helix*, *beta sheet* and *turns* (Loops, Multiple turns, Hairpins)
- *Tertiary structure*: Most proteins fold into unique 3-dimensional (*native*) structures generally stabilized by nonlocal interactions (salt bridges, hydrogen bonds, disulfide bonds) and controls the protein's function.
- *Quaternary structure*: a protein complex, made of several protein subunits, that works as a single unit with a function (e.g., molecular chaperones).

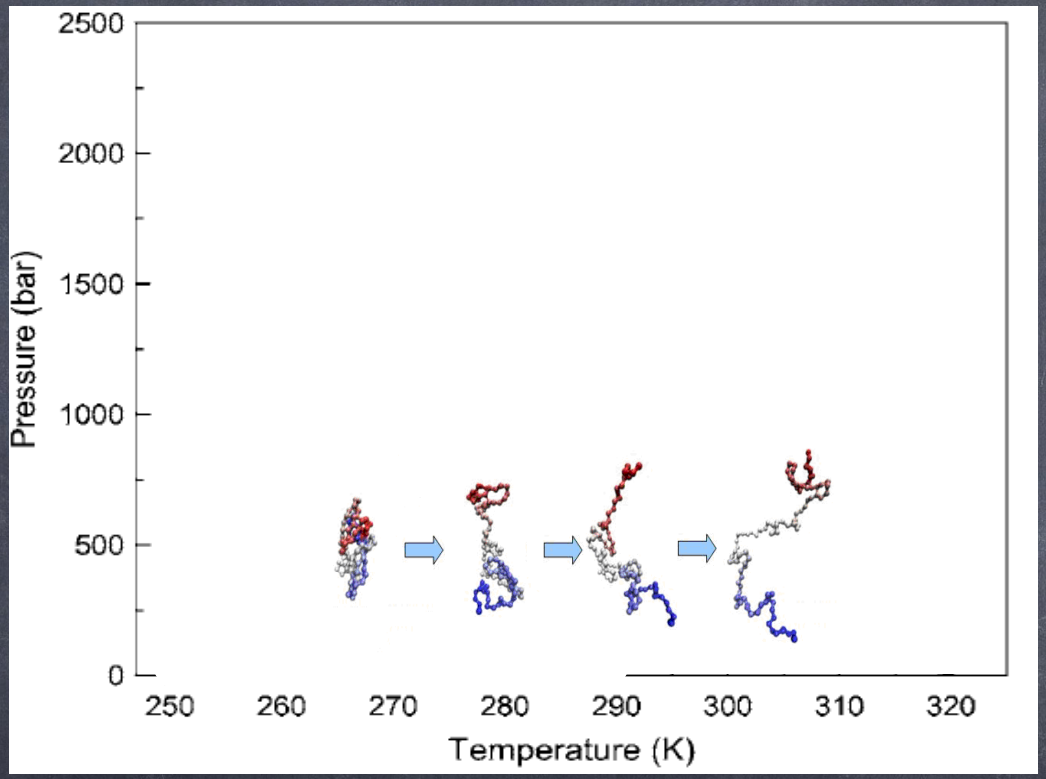
β-hairpin



Protein Denaturation

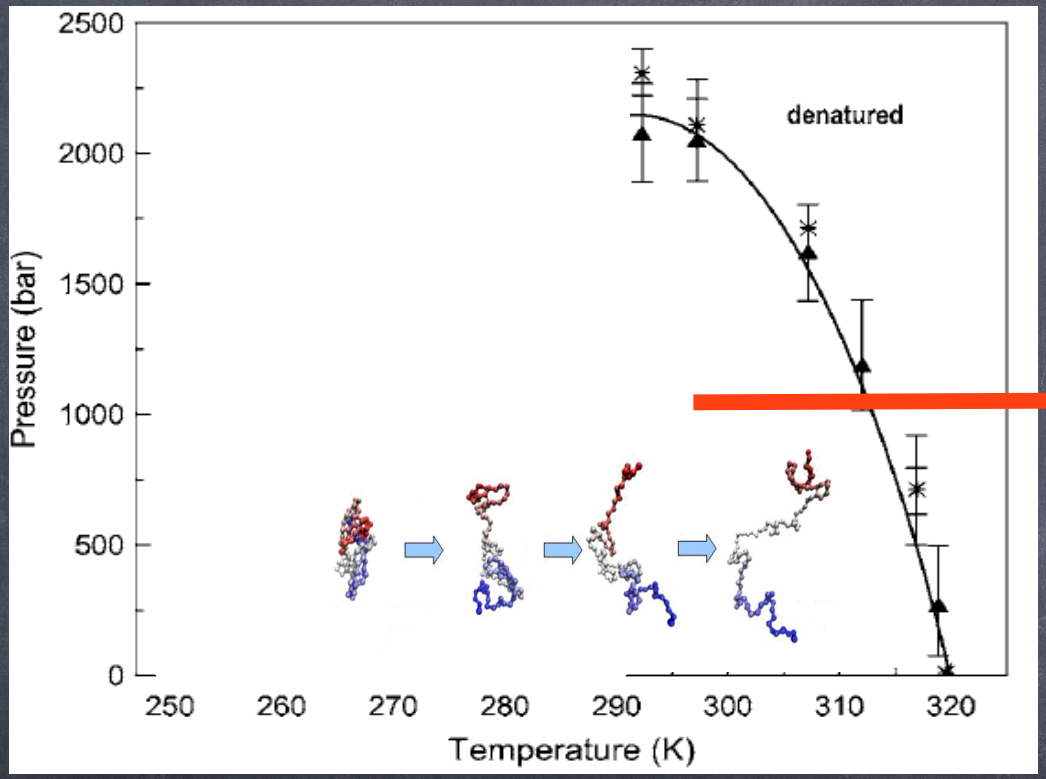
Protein Denaturation

Staphylococcal nuclease



Protein Denaturation

Staphylococcal nuclease



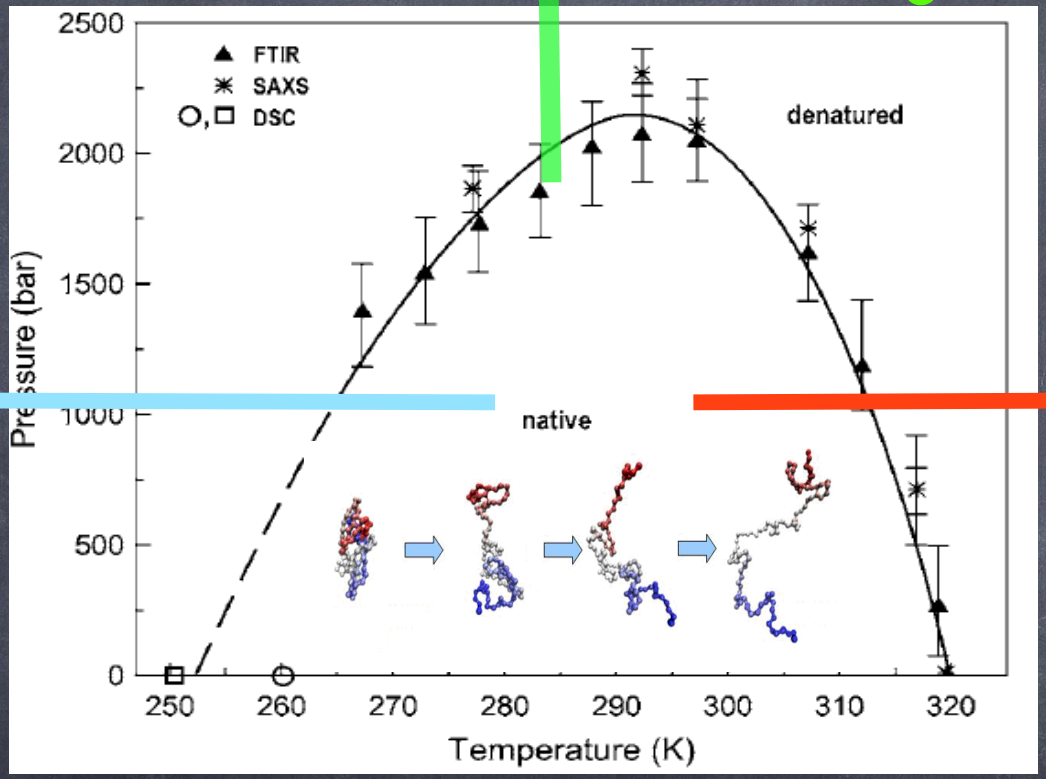
Hot

Thermal energy (melting)

Protein Denaturation

Pressure ?

Staphylococcal nuclease



Cold ?

Hot

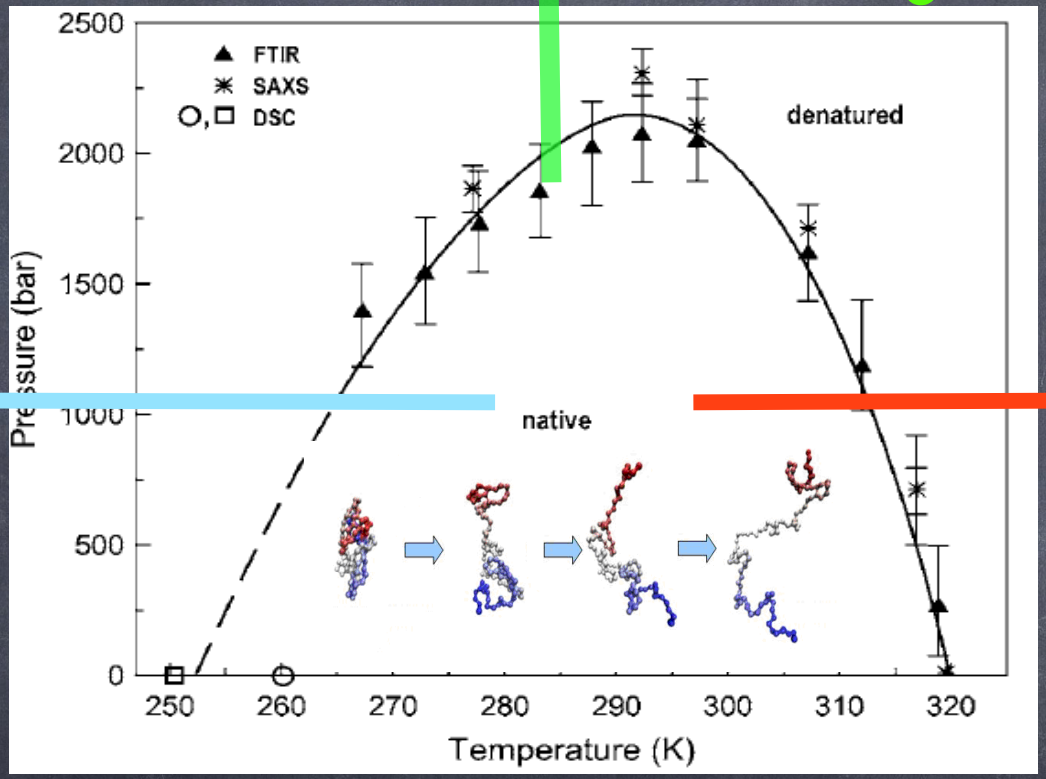
Thermal energy (melting)

R. Ravindra and R. Winter, ChemPhysChem (2003)

Protein Denaturation

Pressure ?

Staphylococcal nuclease



R. Ravindra and R. Winter, ChemPhysChem (2003)

Cold ?

Hot

Thermal energy (melting)

Also under physiological conditions: Yeast Frataxin,

Tc=-7 C ---------- Th=30 C (at 1bar)

Annalisa Pastore et al. JACS (2007)