Cold Denaturation in Proteins.

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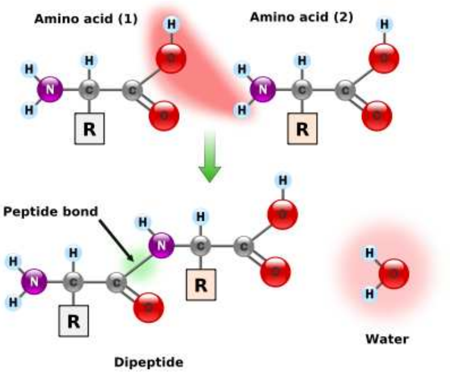
CompPhys07
Leipzig, Nov. 2007

Plan

1. Introduction.
2. The Problem.
3. Model.
4. Results 1. : Two-states phase diagram.
5. Results 2 : Four-states phase diagram.
6. Conclusion.

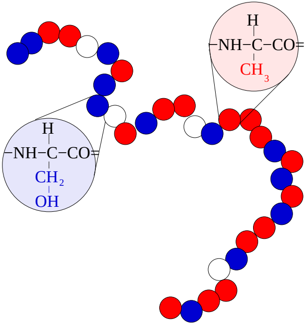
Biochemistry

Amino-acids and Bond between amino acids.



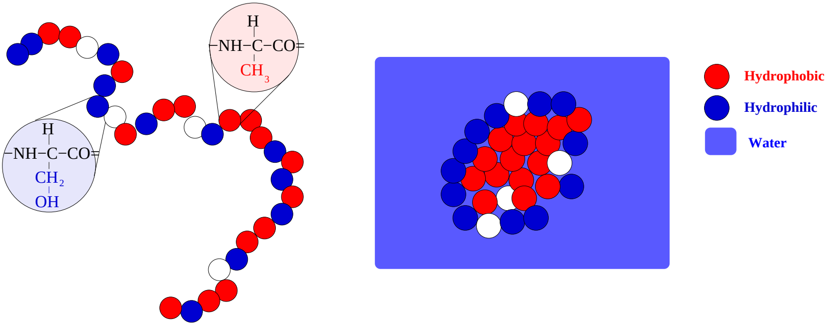
Biochemistry

Proteins are large and linear chains made of amino acids



Biochemistry

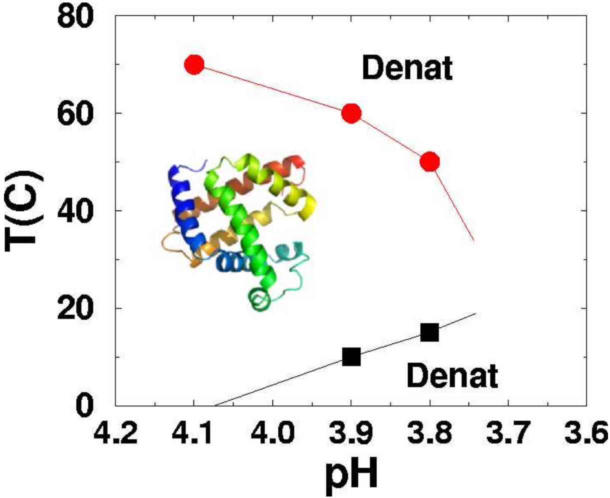
Put into water proteins fold in a unique compact structure



Main folding force is the **Temperature Dependent** Hydrophobic Effect[a].

[a] Kauzmann 1959, Balwin 1987, Pratt-Pohorille 2002

Warm and Cold Denaturations[1].



[1]Privalov, 1989

Statistical Physics approach.

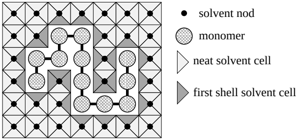
$$\mathcal{H}_{\text{mic}} = E_{\text{intr}}^{(m)} + E_{\text{solv}}^{(mm')} \qquad \begin{cases} m : \text{protein conformation} \\ m' : \text{water configuration} \end{cases}$$

$$\Rightarrow Z(T) = \sum_{m=1}^{\Omega} \sum_{m'=1}^{\Omega'(m)} \exp\left(- \frac{E_{\text{intr}}^{(m)} + E_{\text{solv}}^{(mm')}}{T} \right)$$

$$\sum_{m'=1}^{\Omega'(m)} \exp\left(- \frac{E_{\text{solv}}^{(mm')}}{T} \right) = z_{\text{solv}}^{(m)}(T) = \exp\left(- \frac{F_{\text{solv}}^{(m)}(T)}{T} \right)$$

$$\Rightarrow \boxed{Z(T) = \sum_{m=1}^{\Omega} \exp\left(- \frac{\mathcal{H}_{\text{eff}}^{(m)}(T)}{T} \right)} \quad \text{with} \quad \boxed{\mathcal{H}_{\text{eff}}^{(m)}(T) = E_{\text{intr}}^{(m)} + F_{\text{solv}}^{(m)}(T)}$$

Effective hamiltonian.



$\Delta_{ij}^{(m)} = 1$ if i and j are first neighbors.
B_{ij} : coupling between i and j
$n_i^{(m)}$: number of cells arround i
$f_i(T)$: free energy of this solvent cell.
$n_s^{(m)}$: total number of solvent cells
$f_s(B_s, T)$: free energy of neat solvent

$$\boxed{\mathcal{H}_{\text{eff}}^{(m)} = \underbrace{\sum_{i>j+1} B_{ij}\ \Delta_{ij}^{(m)}}_{\text{previous works}} + \underbrace{\sum_i n_i^{(m)} f_i(T) + 2 n_s^{(m)} f_s(B_s, T)}_{\text{Collet 2001;2005}}}$$

More complicated form than the usual : $\mathcal{H}_{\text{eff}}^{(m)} = \sum_{i>j+1} B_{ij}\ \Delta_{ij}^{(m)}$!

Constant of the model.

$$\text{total lattice links} \ : \ \sum_i \sum_j \frac{1}{2} \Delta_{ij}^{(m)} + \sum_i n_i^{(m)} + n_s^{(m)} = K_1$$

$$\text{links of monomer } i \ : \ \sum \Delta_{ij}^{(m)} + n_i^{(m)} = 4$$

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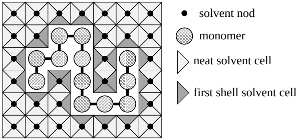

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$$\begin{cases} n_i^{(m)} = 4 - \sum_j \Delta_{ij}^{(m)} \\ n_s^{(m)} = \frac{1}{2} \sum_i \sum_j \Delta_{ij}^{(m)} + K_1 - 4N \end{cases}$$

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Effective Couplings.

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- which forms for $f_i(T)$ and $f_s(B_s, T)$?

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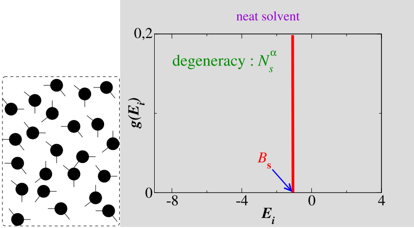
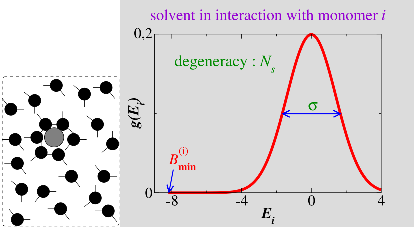
Solvation Model





$$\boxed{f_s(B_s,T) = B_s - \alpha T \ln N_s}$$

Small $B_s \Rightarrow$ bad solvent

Large $B_s \Rightarrow$ good solvent

$$n(B_i) = \frac{2N_s \exp\left(-\frac{B_i^2}{2\sigma^2}\right)}{\sigma\sqrt{2\pi}\;\mathrm{erfc}\left(\frac{B_i^{\mathrm{min}}}{\sigma\sqrt{2}}\right)}$$

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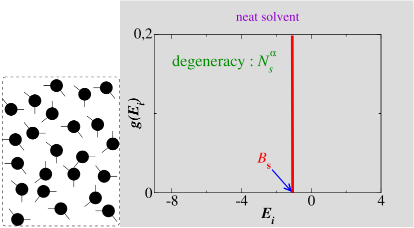

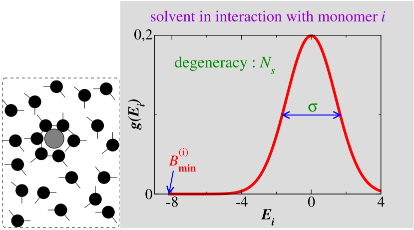

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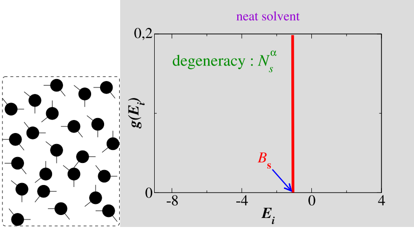

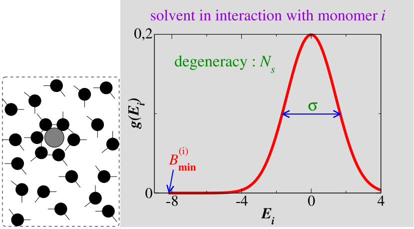

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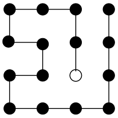
The Chain and the Statistical averages.

The chain.

16-mers
in 2D lattice

802 075 conformations
116 579 extended conformations
69 more maximally compact conf



Nat

Statistical average $\langle X(T)\rangle = \sum_{m=1}^{\Omega} X^{(m)}(T) P_{eq}^{(m)}(T)$ with
$P_{\mathrm{eq}}^{(m)}(T) = \frac{1}{Z(T)} \exp\left(-\frac{\mathcal{H}_{\mathrm{eff}}^{(m)}}{T}\right)$.

Compactness:	$\langle N_c(B_s, T)\rangle$	where	$N_c^{(m)} = \frac{1}{9}\sum_{i>j}^{N} \Delta_{ij}^{(m)}$
Order parameter:	$\langle Q(B_s, T)\rangle$	where	$Q^{(m)} = \frac{1}{9}\sum_{i>j}^{N} \Delta_{ij}^{(m)} \Delta_{ij}^{\mathrm{Nat}}$
Chain entropy, S_{ch}:	$-\langle \ln P_{\mathrm{eq}}^{(m)}(B_s, T)\rangle$		

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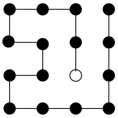

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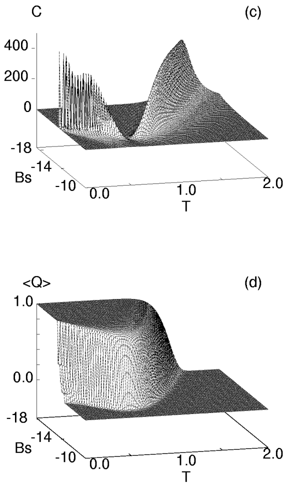

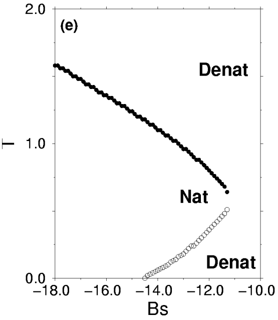

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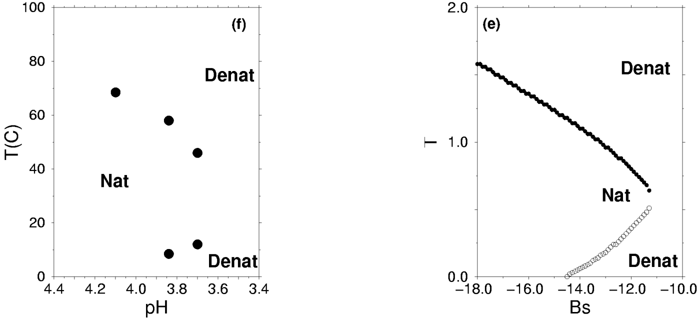
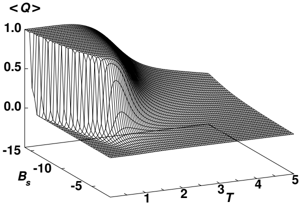
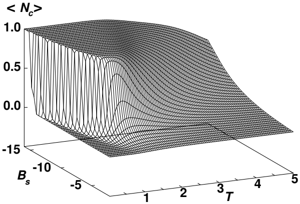
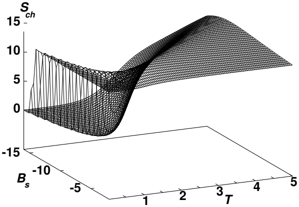


Results 2 : Four-states phase diagram.

$\alpha = 0.5 \rightarrow 0.9$







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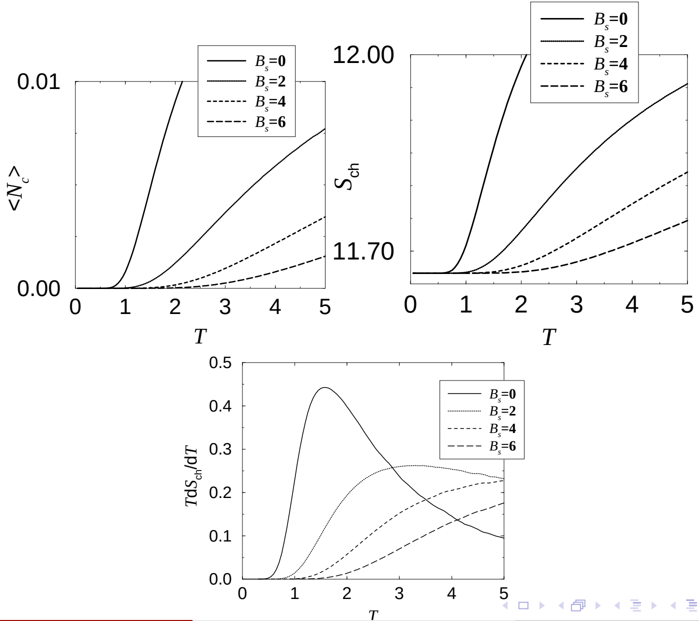

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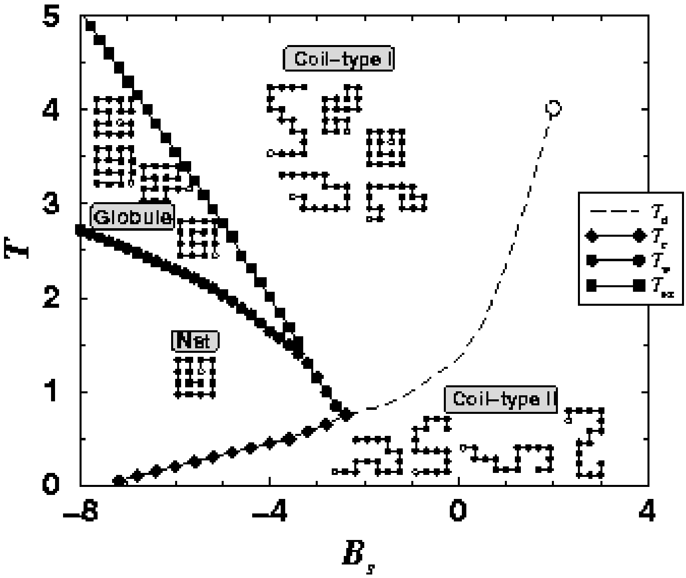

Conclusions.

Calculation of $\mathcal{H}_{\text{eff}}^{(m)}(T)$ also simple than $E_{\text{intr}}^{(m)}$
Cold Denaturation due to hydrophobic effect

Realistic couplings must

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Effective Couplings as function of T.

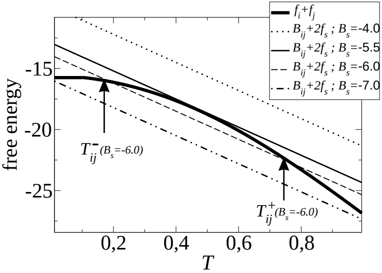

Figure: Curves of the different contributions to the effective coupling between the monomers 1 and 4 as function of the temperature for several values of the solvent quality. The two temperatures for which the coupling vanishes are shown for $B_s = -6.0$.

$B^{\text{eff}}_{ij}(B_s, T) = B_{ij} - f_i(T) - f_j(T) + 2f_s(B_s, T)$ **may be :**

positive at low T
negative at medium T
positive at high T

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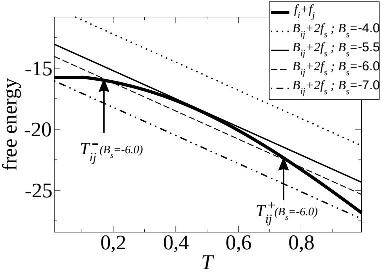

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