Remarks on Protein – Water – Systems

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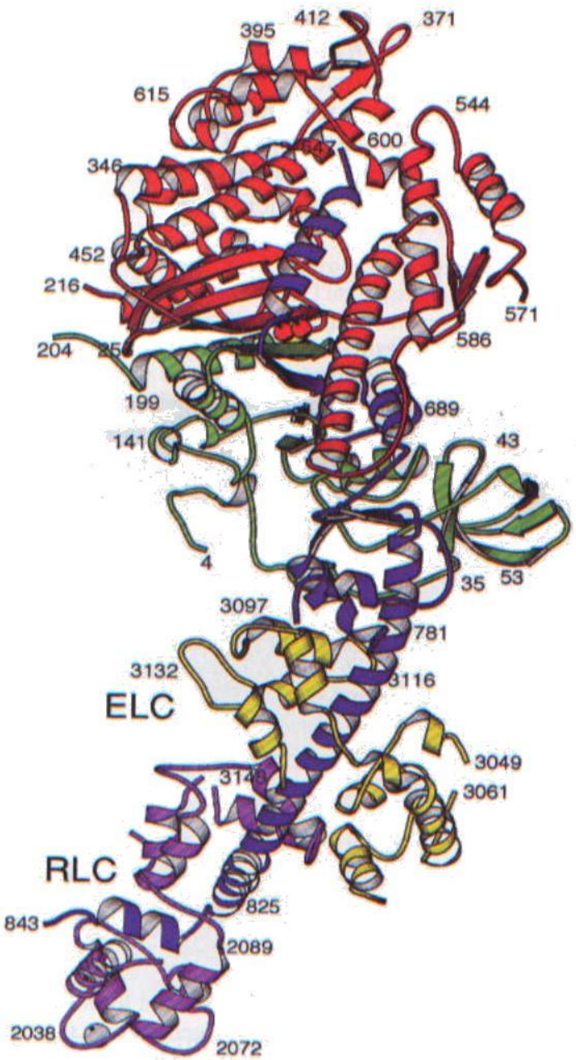
Types (Water, Proteins), Classification ? Atomic Structure ? Bioactivity ?

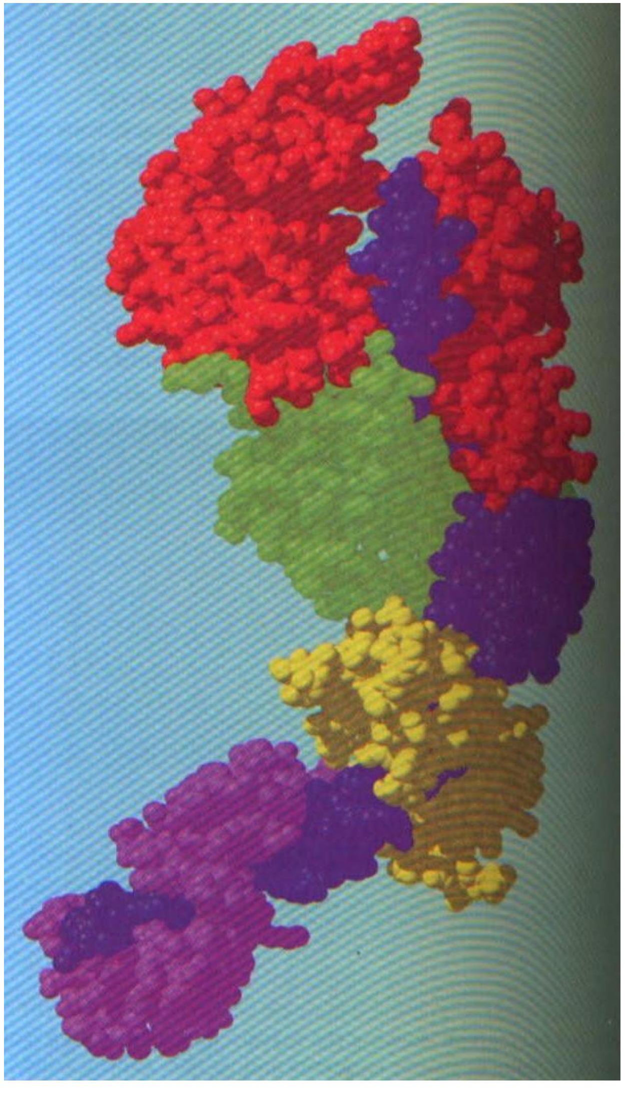
Molecular Information
/--Experiment (Spectroscopy),Simulation
/
/ Lumped Phenomenological Model
/
/ Thermodynamic Formalism
Operations, Variables
/ Equations of State, Process Equations
/
/ Predictions, Forecast of Behaviour
/
/ Comparison with Experiment
/ Highthroughput Techniques
/________/

4.Proteins (Example): Myosin from Chicken Muscle



Secondary Structure

Voet&Voet
Biochemistry
Wiley,N.Y.
1995

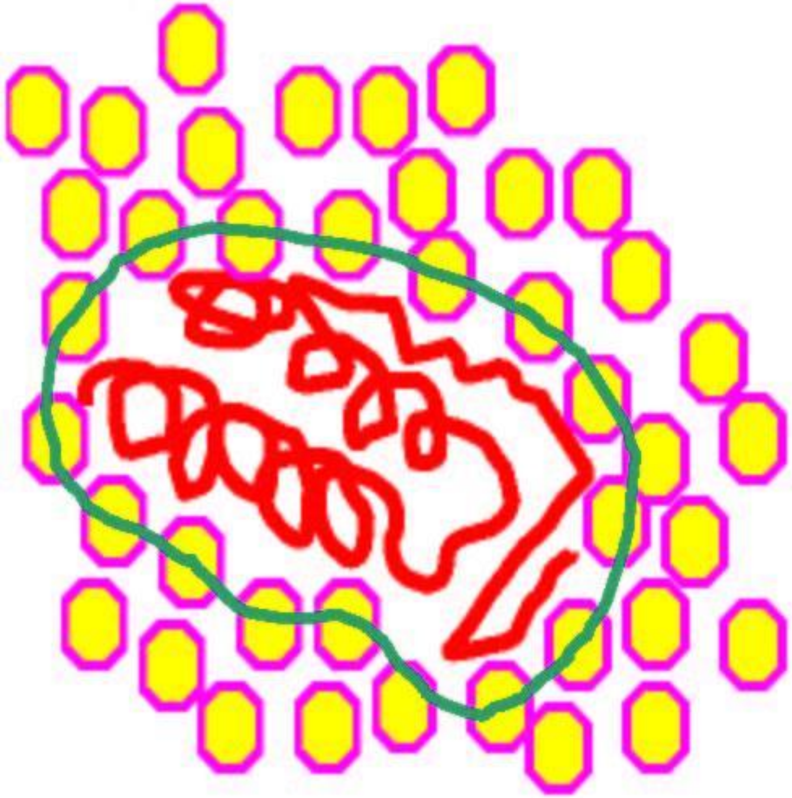


Tertiary Structure (X-Ray)

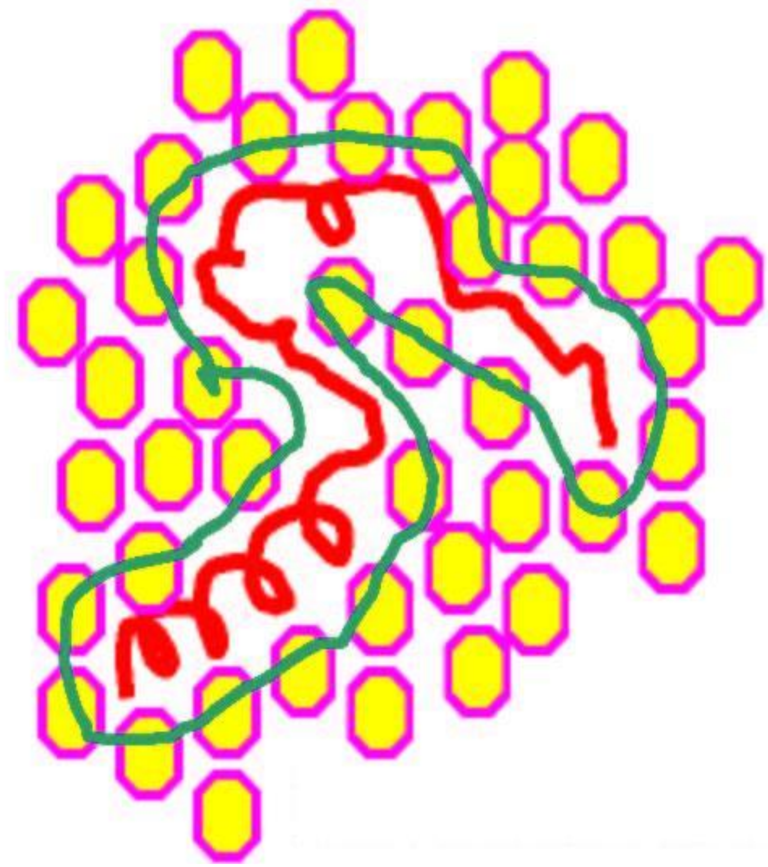
Protein(P) - Water(W) Interactions (E4)

P: Conformational Changes, Unfolding

W: Adsorption, Intrusion, Coating of (P): Stabilization



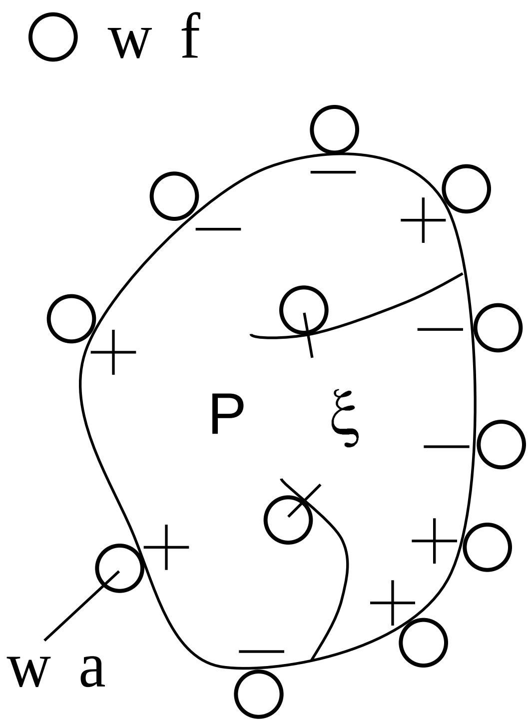
Ref.:Randolph
Private Communication



Native State (N):
compact, surface area small

Unfolded State (D):
expanded, surface area high

Hydration Process of Proteins (E4)
Water Intrusion



Water:

$$T, p, \mu_w^f = \mu_w^a = \mu$$

Stimulus: Chemical potential of water: $\mu = \mu \;\; p, T, \ldots$

Response: Adsorption of water on P

AI: $n = n \;\; \mu, T = \mathrm{const} \;\; = n_0 + H_0 \;\; t \;\; \mu - \mu_0 \;\; + O \;\; 2$

Number of Adsorption sites: ξ ... Internal variable!

a) $\xi = \xi_E = \mathrm{const}$ ... equilibrium : $\xi = \xi_E \left(n, T = \mathrm{const} \right)$

b) $\xi \neq \xi_E$ ... variable ... non-equilibrium:

$$A = A \left(n, T = \mathrm{const}, \xi \right) \neq 0$$

Affinity: Measure for non-equ. deviation.

Hydration Process of Proteins (Water Intrusion)

Thermostatics 1

Free energy of (P, w)-system:

$$F = F(n, \xi, T) = -S\,dT + \mu\,dn - A\,d\xi \quad , \qquad T = \text{const}$$

$$\mu = \left(\frac{\partial F}{\partial n}\right)_{T,\xi} = \mu(n, \xi, T) \text{ ...AI}$$

$$-A = \left(\frac{\partial F}{\partial \xi}\right)_{T,n} = -A(n, \xi, T) \text{ ...IEOS}$$

External & internal or full equilibrium: $F \to \text{Min}$, $T = \text{const}$, $n = \text{const}$

$$A(n, \xi, T) = 0 \to \xi_E = \xi_E(n, T) = \text{const}$$

External equilibrium only (restricted equilibrium), $T = \text{const}$:

$A \neq 0 \qquad \xi$ ... arbitrary value

Hydration Process of Proteins (System: P, w(a))

Free Energy, Taylor Series

$$F \;\; n,\xi,T \;\; = F_{00} + F_{10} n + F_{01}\xi + \frac{1}{2!} \;\; F_{20} n^2 + 2F_{11} n\xi + F_{02}\xi^2 \;\; + O \;\; 3$$

Thermodynamic Stability (2nd Law): $\left\| \partial^2 F / \partial n \, \partial\xi \right\| > 0 \;\; , \;\; F_{ik} = F_{ik} \;\; T$

$$\rightarrow F_{20} \geq 0 \;\; , \;\; F_{20}F_{02} - F_{11}^2 > 0 \;\; , \;\; F_{02} \geq 0$$

Reference State: $Z_0 \;\; n_0, \mu_0, \xi_0, A_0 = 0, T$

Equations of State:

$$\mu = \;\; \partial F / \partial n \;\; _{\xi,T} \quad : \quad \mu - \mu_0 = F_{20} \;\; n - n_0 \;\; + F_{11} \;\; \xi - \xi_0 \qquad 1$$

$$-A = \;\; \partial F / \partial\xi \;\; _{n,T} \quad : \quad -A = F_{11} \;\; n - n_0 \;\; + F_{02} \;\; \xi - \xi_0 \qquad 2$$

Internal Equilibrium: $A \;\; n, \xi_E T \;\; = 0 \;\; , \;\; \xi_E - \xi_0 = -\frac{F_{11}}{F_{02}} \;\; n - n_0$

$$1 \;\; : \underline{\underline{n - n_0 = H \;\; \mu - \mu_0}} \;\; , \;\; H = \frac{F_{02}}{F_{20}F_{02} - F_{11}^2} > H_0 = \frac{1}{F_{20}}$$

Hydration Process of Proteins (System: P, w(a))

Thermodynamics of Processes

1st Law: $dU = dQ + h\,dn + 0$

2nd Law: $dS = \frac{1}{T} dU - \frac{\mu}{T} dn + \frac{A}{T} d\xi$

$$dS = \frac{Q}{T} + s\,dn + dS_{in}$$

$$\mu = h - Ts \qquad\qquad P_s = \dot{S}_{\dot{m}} = \frac{A}{T}\dot{\xi} \geq 0$$

Eckart-Onsager: $\Delta\;\dot{\xi} = \alpha\;\;n, \xi, T\;\;A + O\;\;A^2$

Equations of State: $\Delta\mu = F_{20}\Delta n + F_{11}\Delta\xi$

$$-A = F_{11}\Delta n + F_{02}\Delta\xi$$

*

$$\Delta\mu\;\;t\;\; = \mu - \mu_0 \rightarrow \Delta n\;\;t\;\; = n - n_0\;\;,\;\;\Delta\xi\;\;t\;\; = \xi - \xi_0\;\;,\;\;A = A\;\;t\;\;\rightarrow 0!$$

Stimulus Adsorption Structure Equilibrium

Hydration Process of Proteins (System: P, w(a))

Stimulus : $\Delta\mu = \mu(p, T, \ldots) - \mu_0$

Adsorption: $\Delta n = n(t) - n_0$

Structure : $\Delta\xi = \xi(t) - \xi_0$ ... adsorption sites

$$\tau_n \Delta\dot{\mu} + \Delta\mu = E(\Delta n + \tau_\mu \Delta\dot{n})$$ (Poynting, Elastic Relax.)

* $$\tau_n^{-1} = \alpha F_{02} > 0\,,\; E = F_{20} - \frac{F_{11}^2}{F_{02}} \geq 0\,,\; \tau_\mu^{-1} = \left(F_{02} - \frac{F_{11}^2}{F_{20}} \right) \alpha > 0$$

$$\tau_n < \tau_\mu$$

Adsorption Process

$$\Delta n(t) = \frac{1}{\tau_\mu E} \int_0^t ds \left[\Delta\mu(s) + \tau_n \Delta\dot{\mu}(s) \right] e^{-(t-s)/\tau_\mu} ds$$

Protein structure / Adsorption sites

$$\Delta\xi(t) = \frac{1}{F_{11}} \left\{ \Delta\mu - \alpha F_{20} \int_0^t ds \left[\Delta\mu(s) + \tau_n \Delta\dot{\mu}(s) \right] \right\} e^{-(t-s)/\tau_\mu} ds$$