Hydrogen Bonding in Water

class – 23 (20.11.24)

LS2103 (Autumn 2024)

IISER Kolkata

Dr. Neelanjana Sengupta

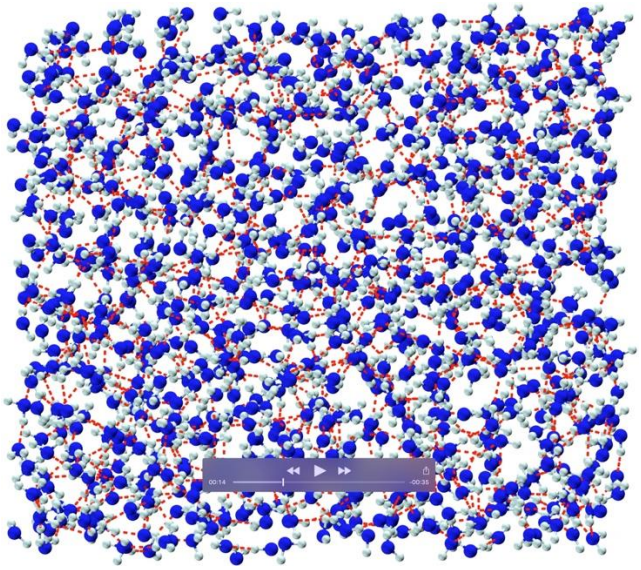
Associate Professor

Dept. of Biological Sciences, IISER Kolkata

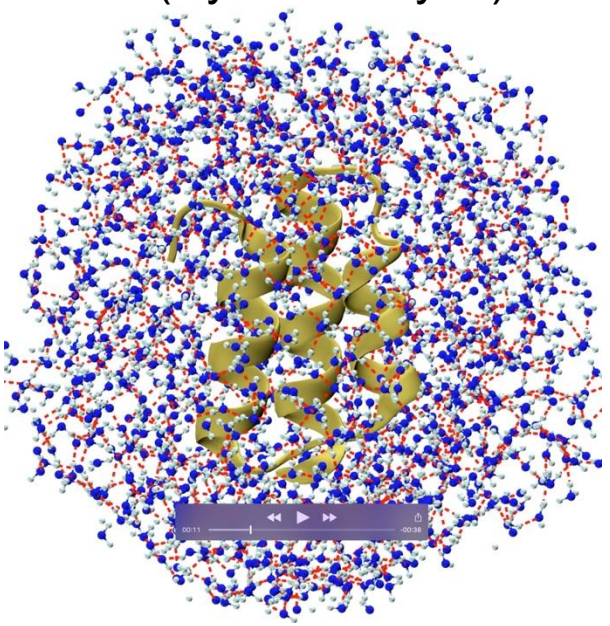
https://www.iiserkol.ac.in/~n.sengupta/

Visualizing the H-bonded network (computer simulations)

Bulk water



Water close to a biomolecule
('hydration layer')



- Protein-water (P-W) H-bonds **compete with** water-water (W-W) H-bonds
- **Lifetimes and energetics** of P-W and W-W H-bonds may differ
- Water helps the protein achieve **functional flexibility**
- Water plays **thermodynamic role** in folding, enzyme-ligand binding, etc

Prob-1. A Raman spectroscopy study showed that breakage of a single H-bond within pure water at room temperature (300 K) is commensurate with an **enthalpy increase of 1.9 kcal mol^{-1}, and an entropy increase of 2.4 k_B**.

a) What is the **free energy cost** of **breaking a single H-bond at room temperature**?

b) Is this a favourable process at room temperature?

c) What is the temperature beyond which this process should be favourable?

a) $\Delta G = \Delta H - T\Delta S$

$\equiv +(1.9) - (300)\left(+2.4 \times \frac{R}{4.1\times10^{3}}\right)$ } WORK IT OUT!

$\equiv (1.9) - (0.58)\times(2.4)$

$\approx +0.532$ kcal/mol.

c) $\Delta G = 0 \Rightarrow \Delta H = T_{crit.}(\Delta S)$

$T_{critical} = \frac{\Delta H}{\Delta S}$

≈ 395 K.

Read more (advanced): https://doi.org/10.1073/pnas.21333661

Energetics of hydrogen bonds in peptides

Sheh-Yi Sheu*†‡, Dah-Yen Yang†‡§, H. L. Selzle¶, and E. W. Schlag†‡¶

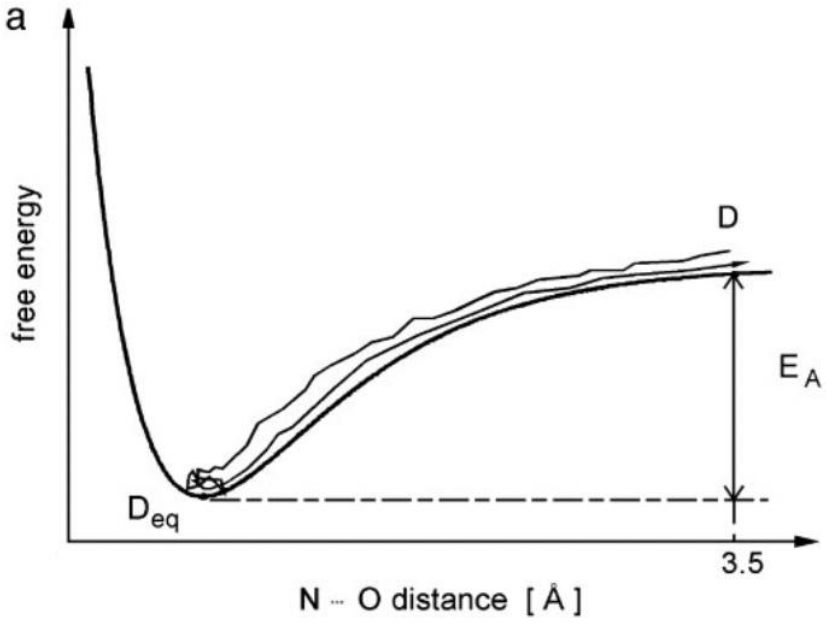
*Department of Life Science, National Yang-Ming University, Taipei 112, Taiwan; §Institute of Atomic and Molecular Science, Academia Sinica, Taipei 106, Taiwan; and ¶Institut für Physikalische und Theoretische Chemie, Technische Universität Muenchen, Lichtenbergstrasse 4, 85748 Garching, Germany

Communicated by A. Welford Castleman, Jr., Pennsylvania State University, University Park, PA, June 3, 2003 (received for review December 8, 2002)

Hydrogen bonds and their relative strengths in proteins are of importance for understanding protein structure and protein motions. The correct strength of such hydrogen bonds is experimentally known to vary greatly from ≈5–6 kcal/mol for the isolated bond to ≈0.5–1.5 kcal/mol for proteins in solution. To estimate these bond strengths, here we suggest a direct novel kinetic procedure. This analyzes the timing of the trajectories of a properly

change in hydrogen bond strengths upon changing the microscopic environment of proteins.

The concept of the hydrogen bond goes back to its discovery by Huggins in 1919 (9, 10). In the gas phase, the strength for a peptide environment has been computed to be ≈4.9 kcal/mol (11–13), in close agreement with the general value of 5–8 kcal/mol first suggested by Pauling in 1936 (14). Measurement

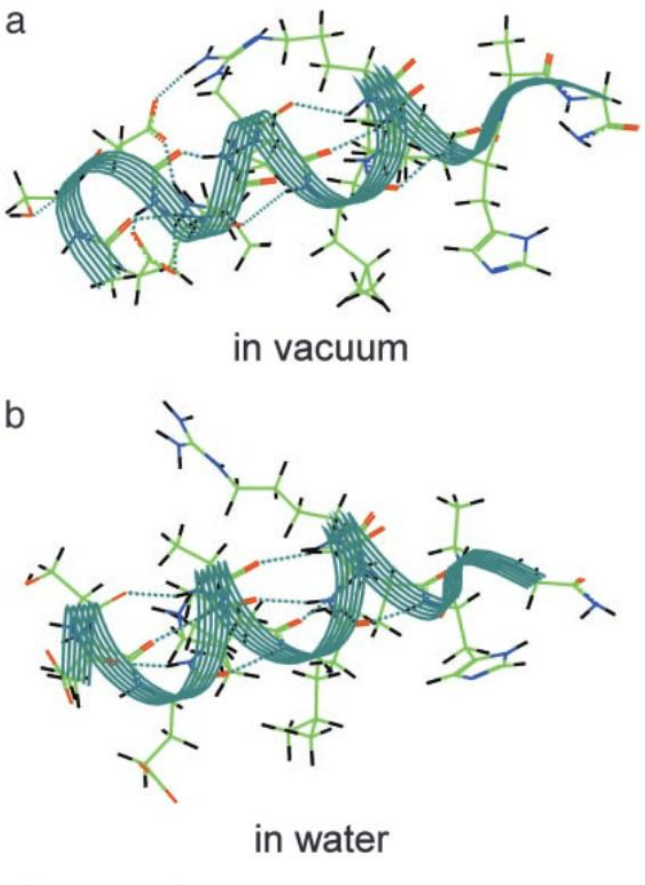


(activation energy for H-Bond breakage)

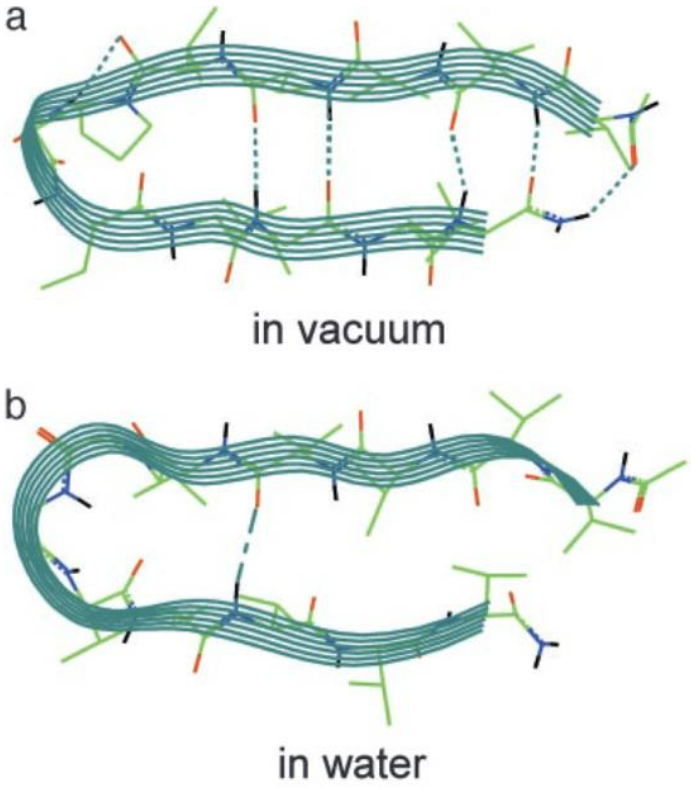
(donor – acceptor distance)

What happens when proteins are shifted from "*gas phase*" to water?

α-Helix

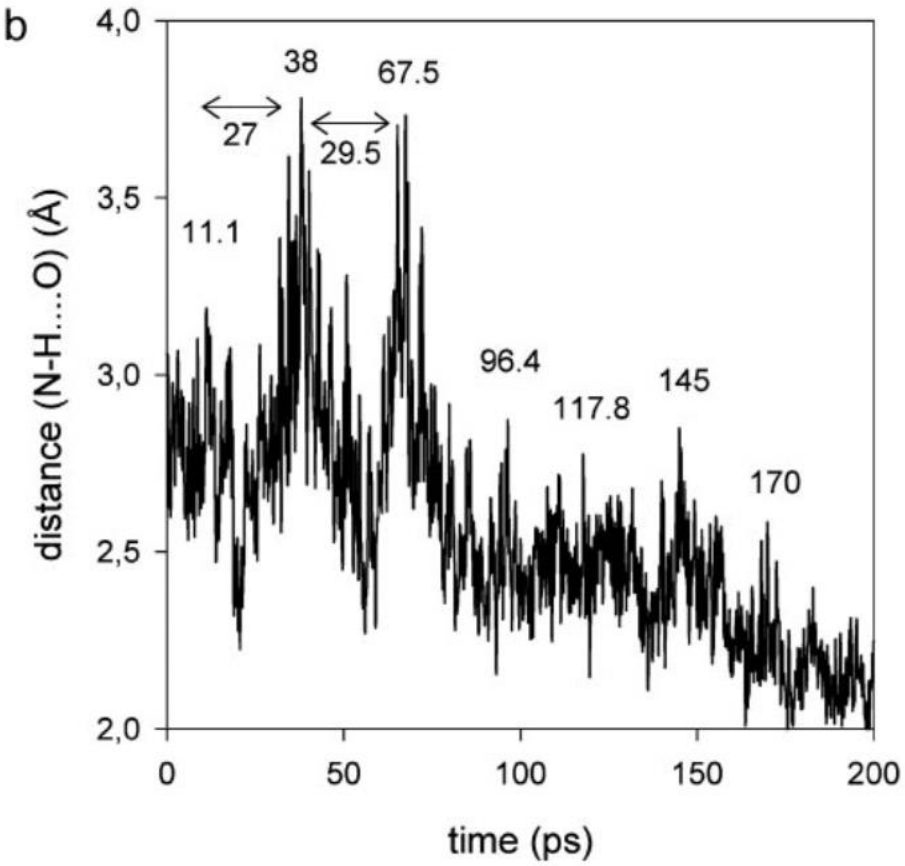


β-Sheet

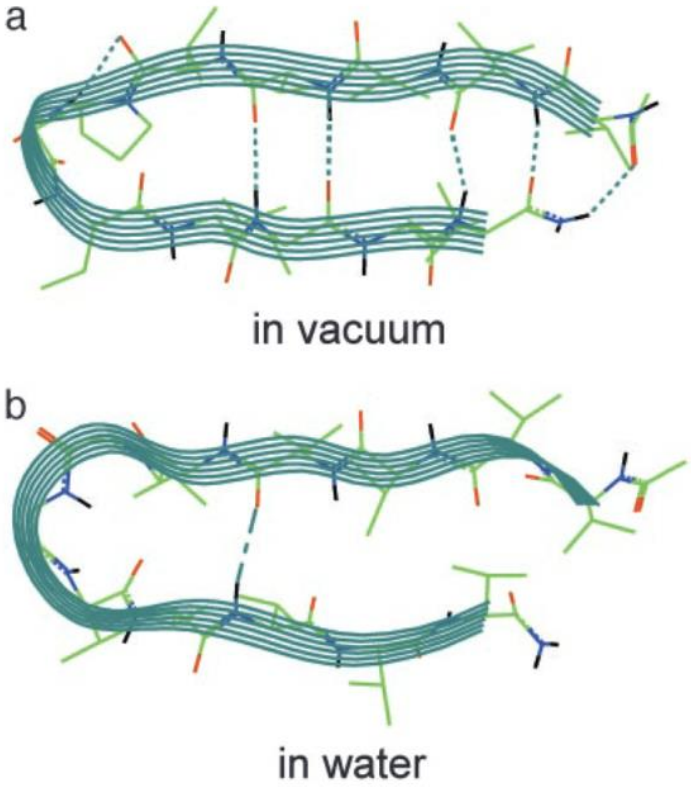


- H-bond rupture, decrease in "lifetimes"
- water H-bonds compete with internal protein H-bonds

What happens when proteins are shifted from "*gas phase*" to water?



β-Sheet



- H-bond rupture, decrease in "lifetimes"
- water H-bonds compete with internal protein H-bonds

What happens when proteins are shifted from "*gas phase*" to water?

Table 1. Hydrogen bond energy for α-helix and β-sheet in gas phase and water environment

	Vacuum		Water	
	A	E_a	A	E_a
α-Helix	2.00×10^{14}	5.57	5.49×10^{11}	1.93
β-Hairpin	9.37×10^{12}	4.79	3.53×10^{11}	1.58

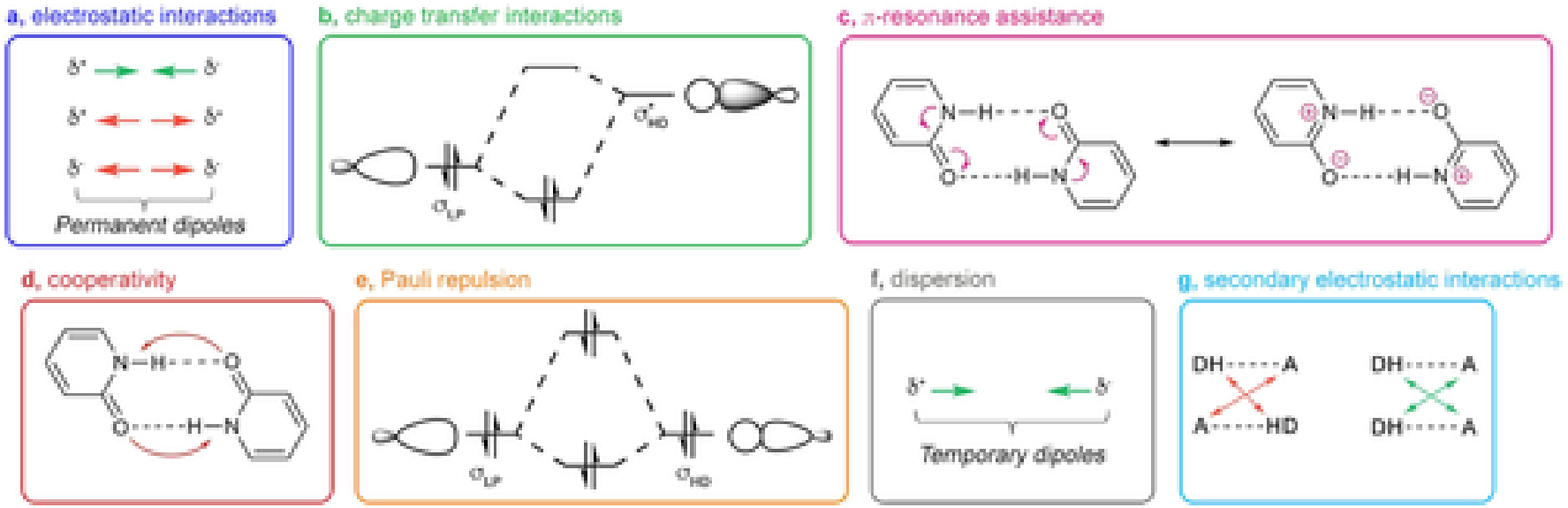
E_a is given in kcal/mol, and A is given in s^{-1}.

Rate of breakage,

$$k = A\, e^{-(\frac{E_a}{RT})}$$

- How does the rate of breakage compare in the two scenarios?

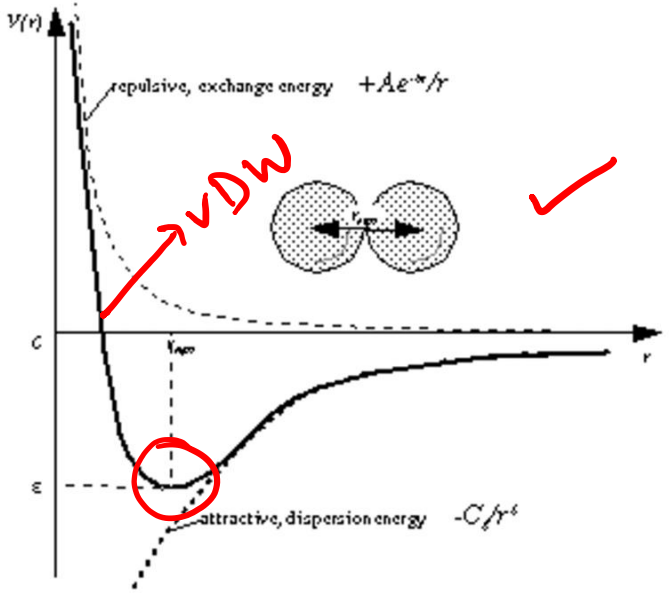
The Energetic Components Underlying Hydrogen Bonds



Read more: https://doi.org/10.1002/asia.201900717

- Some of the non-electrostatic components make up the "van der Waals (vDW) interactions"

- vDW forces are generally weaker than electrostatic forces



Let us assume :

$E_{HB} \approx E_{(g)} + E_{vdW}$

g: electrostatic

Yet, vDW forces are a major contributor to protein-water H-bonding

Read more (advanced): https://doi.org/10.1021/ja029833a

J|A|C|S
ARTICLES
Published on Web 07/11/2003

On the Nonpolar Hydration Free Energy of Proteins: Surface Area and Continuum Solvent Models for the Solute−Solvent Interaction Energy

Ronald M. Levy,* Linda Y. Zhang, Emilio Gallicchio, and Anthony K. Felts

Contribution from the Department of Chemistry and Chemical Biology, Rutgers University, Piscataway, New Jersey 08854

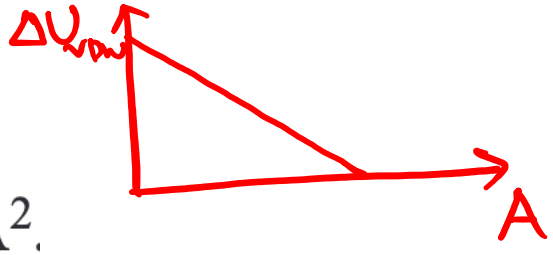
Received December 19, 2002; E-mail: ronlevy@lutece.rutgers.edu

The free energy of solvation is proportional to the protein surface area:

$$\Delta G_{np} = \gamma A + b$$

A **model study*** assumes that *only vDW forces* contribute to protein-water H-bonding in a solvated peptide, ie,

$$\Delta U_{vdW} = \gamma_{vdW} A + b_{vdW}$$



where 'A' is the peptide's 'solvent accessible surface area',

'surface tension' due to vDW, $\gamma_{vdW} = -84$ cal/mol/Å^2,

intercept, $b_{vdW} = 8.97$ cal/mol.

Prob-2. If a protein of SASA of 6.0 nm^2 is submerged in water, estimate:

a) Energetic cost or favorability

$$\Delta U_{vdw} = (6.0 \times 10^2)(-84) + 8.7$$

$$\approx -50.4 \text{ Kcal/mol.}$$

Table 1. Hydrogen bond energy for α-helix and β-sheet in gas phase and water environment

	Vacuum		Water	
	A	E_a	A	E_a
α-Helix	2.00×10^{14}	5.57	5.49×10^{11}	1.93
β-Hairpin	9.37×10^{12}	4.79	3.53×10^{11}	1.58

E_a is given in kcal/mol, and A is given in s^{-1}.

$\langle E_{a(P\text{-}W)} \rangle \approx 3.43$ kcal/mol.

Prob-2. If a protein of SASA of 6.0 nm^2 is submerged in water, estimate:

a) Energetic cost or favorability

b) Assuming that $(E_a)_{P\text{-}W}$ is the average difference of $(E_a)_{in\ vacuum}$ and $(E_a)_{in\ water}$ find the number of P-W H-bonds commensurate with it.
Ignore entropic effects.

c) What are your conclusions about the **model study*?**