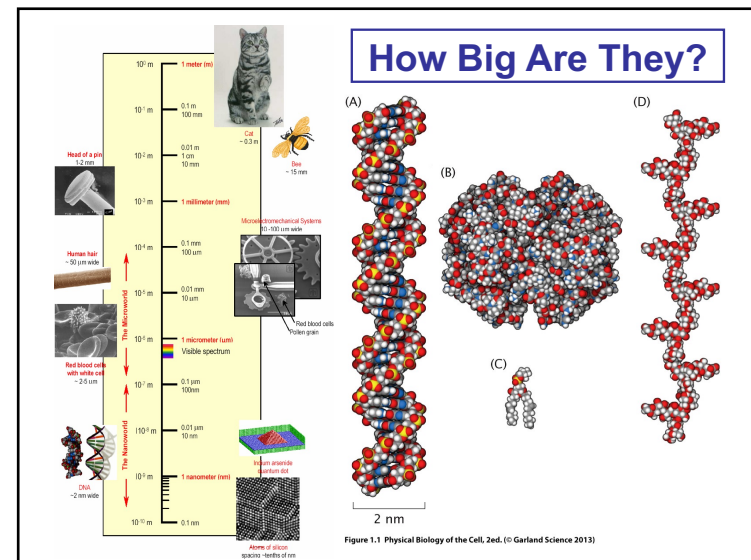


## Formation of Biological Structures

**Szabolcs Osváth**  
Semmelweis University

1



2

## “Plenty of Room at the Bottom”

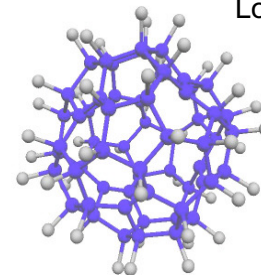
" The principles of physics, as far as I can see, do not speak against the possibility of maneuvering things atom by atom. It is not an attempt to violate any laws; it is something, in principle, that can be done; but in practice, it has not been done because we are too big."

Richard Feynman, 1959

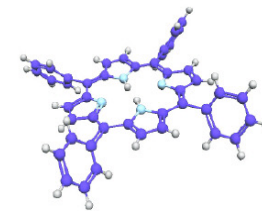
3

## Wave – Particle Duality

Louis De Broglie:  $\lambda = h/p$



fluorofullerene  
 $C_{60}F_{48}$   
1632 Da

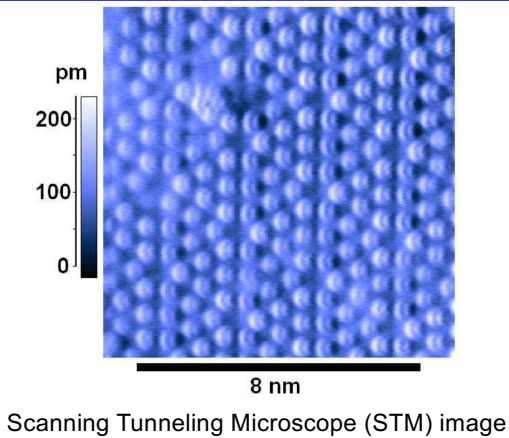


tetraphenylporphyrin  $C_{44}H_{30}N_4$

L Hackermuller, S Uttenthaler, K Hornberger, E Reiger, B Brezger, A Zeilinger, M Arndt; Phys. Rev. Lett. 91 (2003) 90408

4

## Wave – Particle Duality

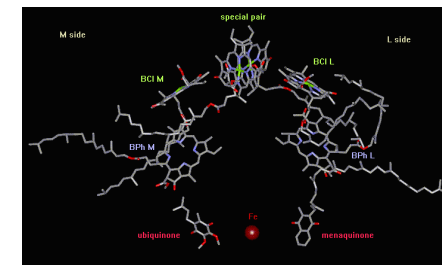


5

## Structure – Function Relationship

From the molecular level to ecosystems, there is a strong relationship between structure and function of biological systems.

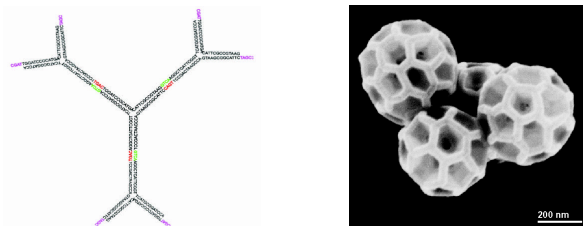
Hartmut Michel, Johann Deisenhofer, Robert Huber  
1982 – 3D structure of the bacterial photosynthetic reaction center  
1988 – Nobel prize



6

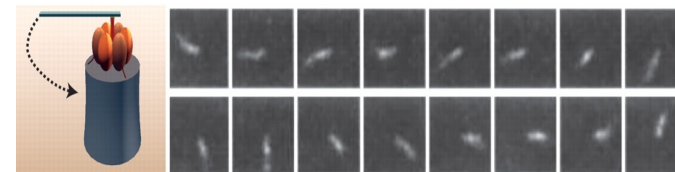
## Self Assembly

Molecular recognition  
(e.g. self assembly of DNA molecules into „balls”).



7

## F<sub>1</sub>-ATPase Driven Nickel Propeller



8

## 9

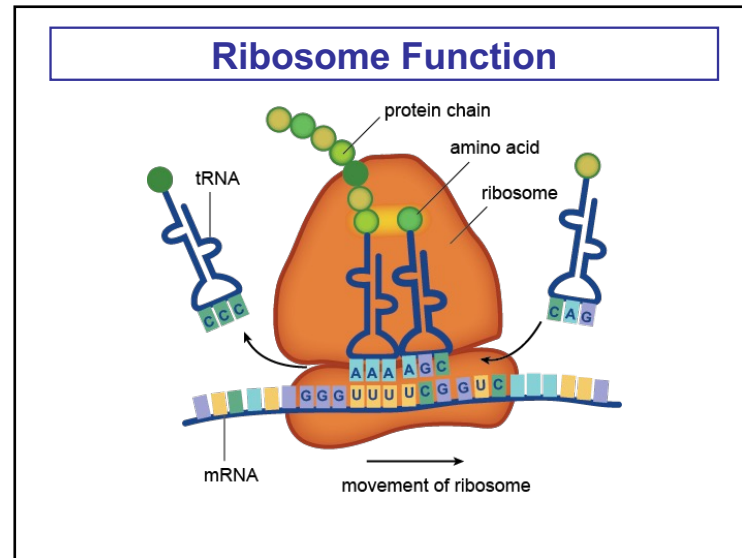


## 12

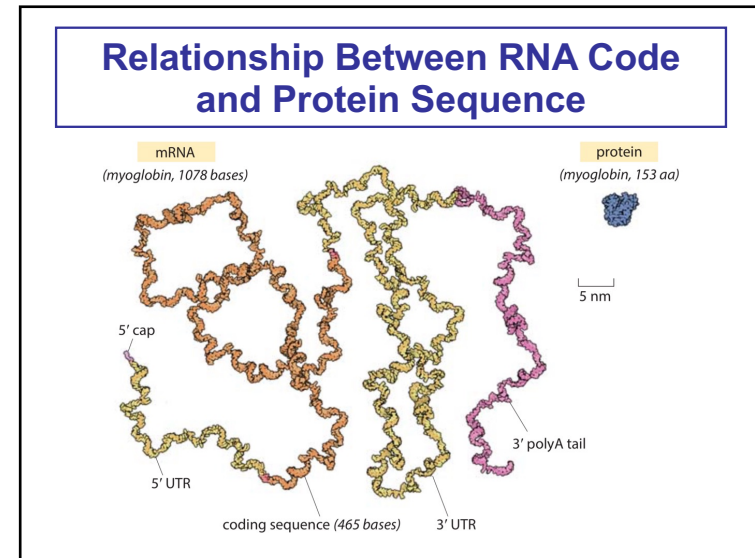
11

Figure 1.2 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

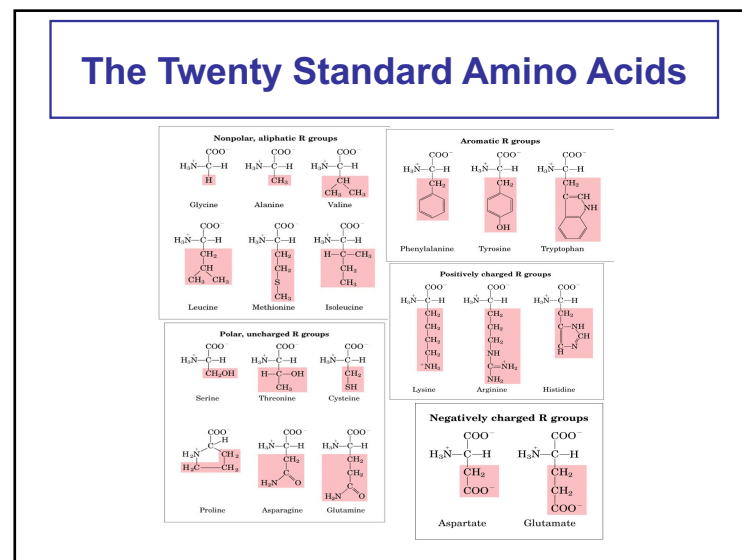
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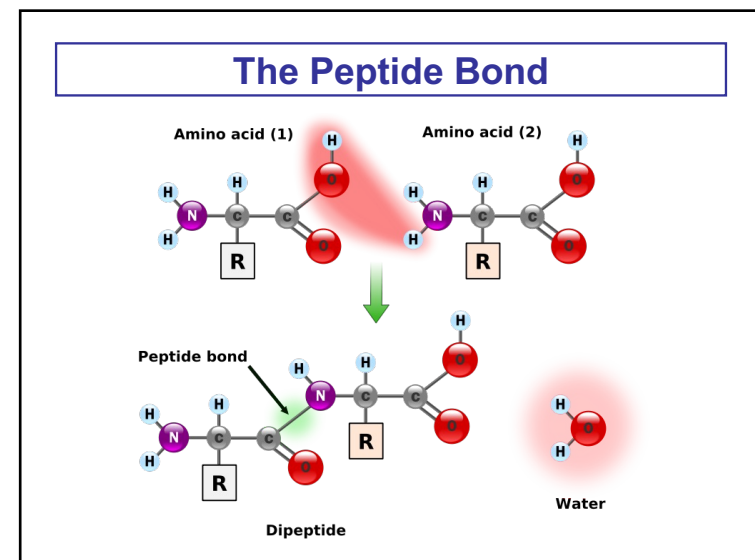
13



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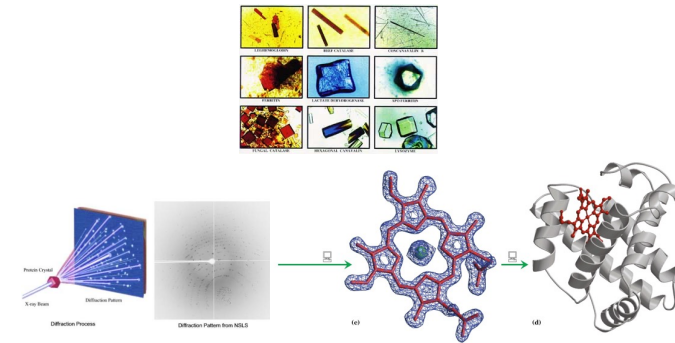
16

## Role of Proteins in Living Systems

- chemical catalysis
- transport
- energy conversion and storage
- coordinated movement
- mechanical skeleton
- immune response
- molecular recognition
- passing information
- gene regulation
- growth and differentiation

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## X-ray Crystallography



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## NMR Structure Determination



NMR structure of the 64 amino acid SH3 domain of the Src protein

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## Interactions Stabilizing the Native State

- short range repulsion
- Van der Waals interaction
- electrostatic interaction
- hydrogen bonding
- hydrophobic interaction
- disulfide bridge

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## Short Range Repulsion

Due to the exchange (Pauli) interaction, at short distances there is a strong repulsion between electrons.

The potential energy of the repulsion increases quickly with decreasing distance ( $\sim 1/r^{12}$ ).

Atoms can be considered hard spheres with a given radius (Van der Waals radius).

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## Van der Waals Interaction

Occurs between any two atoms due to the interaction of induced dipole moments.

Dependence on the distance of the interaction energy:  $\sim 1/r^6$

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## Electrostatic Interaction

Distance dependence of the interaction energy of the Coulomb force:

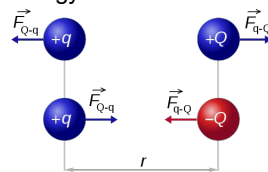
$$E = \frac{q \cdot Q}{4\pi\epsilon_0\epsilon_r\cdot r}$$

The relative dielectric constant inside the protein is approx. 4, and 80 in water.

Salt bridges between ion pairs (Lys, Arg and Glu, Asp).

There is a large hydrate shell around charges in water.

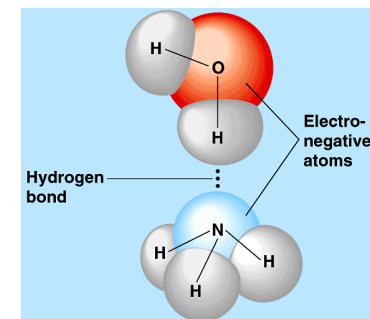
Mobile ions can strongly shield charges.



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## Hydrogen Bonding

Attraction force between a H atom of a more electronegative atom or group (hydrogen bond donor) and another atom bearing a lone pair of electrons (hydrogen bond acceptor).

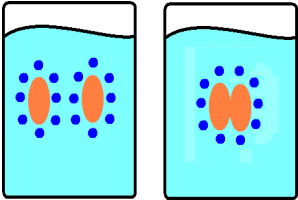


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## Hydrophobic Interaction

observed tendency of nonpolar surfaces to adhere in an aqueous solution and exclude water molecule

entropic effect originating from the disruption of hydrogen bonds of liquid water by the nonpolar solute



25

## Disulfide Bridge

stabilizes the native structure

decreases the conformational entropy of the unfolded protein:

$$\Delta S = -2.1 \text{ J/K} - 1.5 \cdot R \cdot \ln n$$

n is the number of AAs between the two bonded AAs.

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