

# Bioinformatics III

## Analysis and prediction of 3D macromolecule structures

Lecture 10  
Non-covalent interactions in  
proteins

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2022

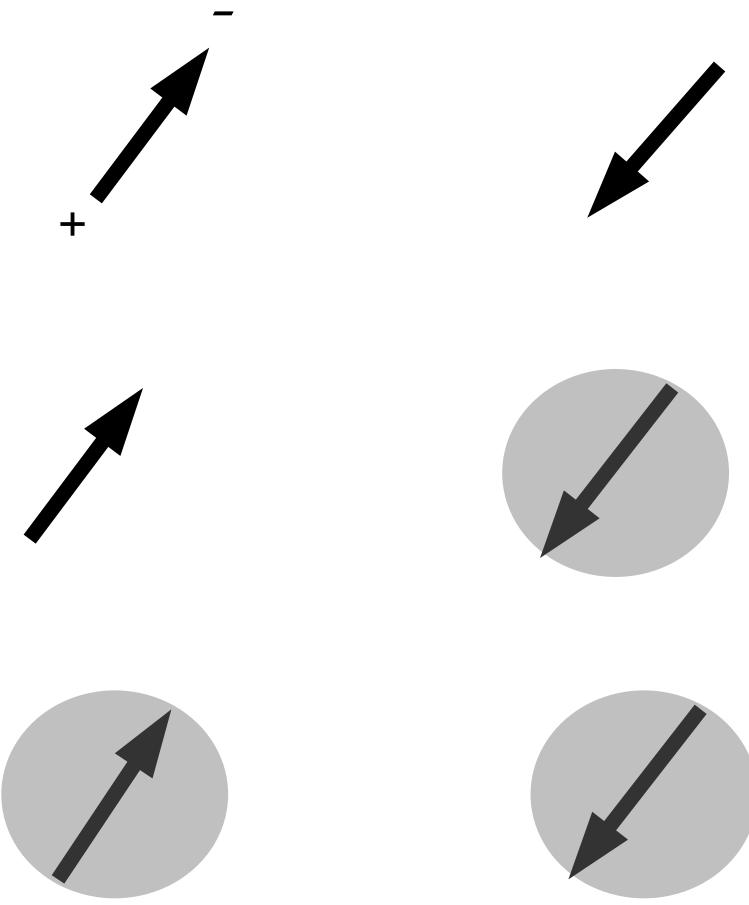
# Non-covalent interactions

- Van der Waals forces
- Hydrogen bonds
- Hydrophobic interactions
- Electrostatic interactions
- (Ion- $\pi$  electron interactions)

# Van der Waals interactions

- Attraction forces:
  - dipole – dipole interaction
  - dipole – induced dipole interaction
  - interaction of two induced dipoles
- Repulsion forces
  - electron orbital interactions (Pauli principle)
- Bond energy: 0.4—2.0 kJ/mol (0.1—0.5 kcal/mol)

# Van der Waals interaction (2)



Keesom interaction:

$$U = -\frac{C_{Keesom}}{r^6}$$

Debye interaction:

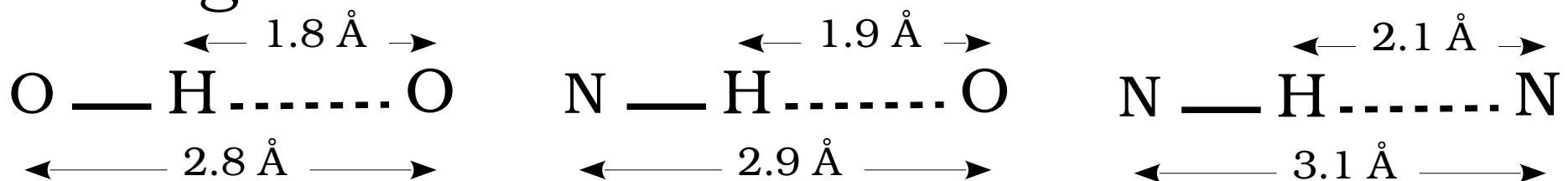
$$U = -\frac{C_{Debye}}{r^6}$$

London dispersion forces:

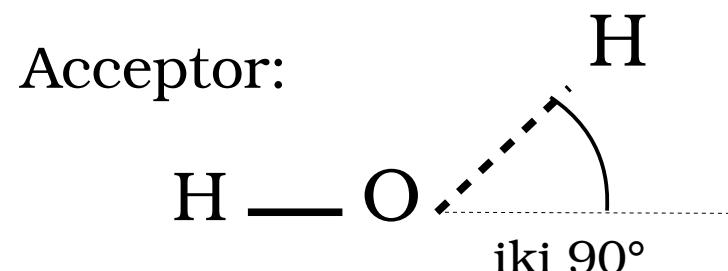
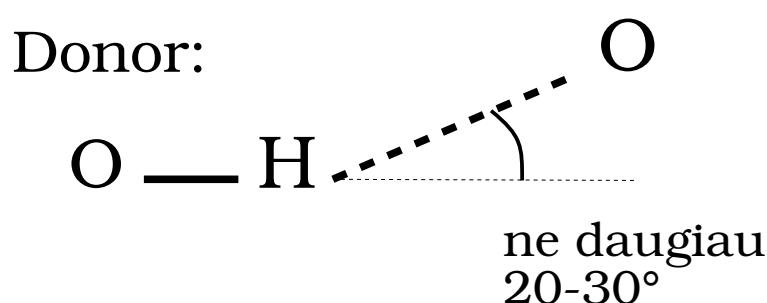
$$U = -\frac{C_{London}}{r^6}$$

# Hydrogen bonds

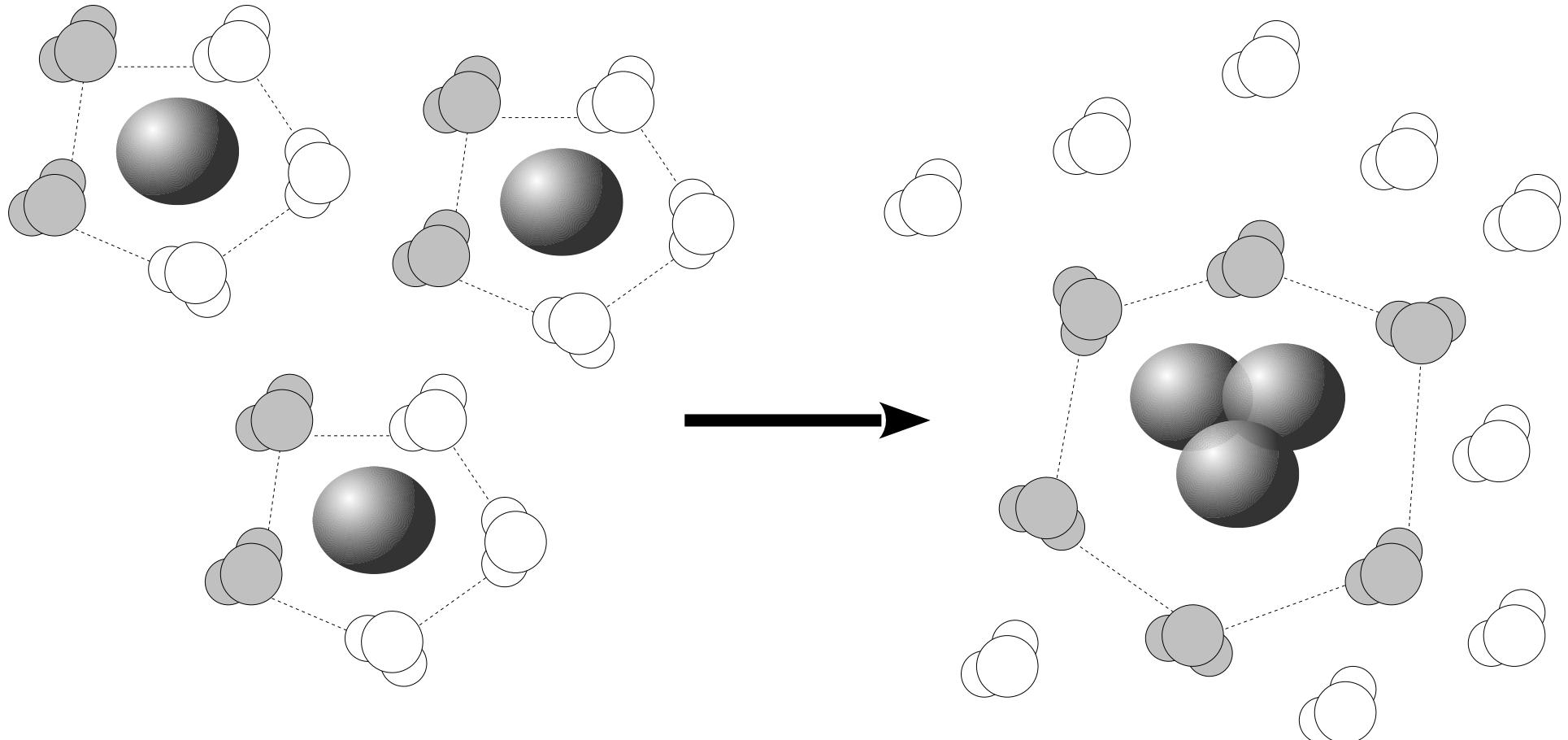
- Bind energy 20 – 40 kJ/mol (5 – 10 kcal/mol)
- Length 2.8 – 3.1 Å



- Directionality:

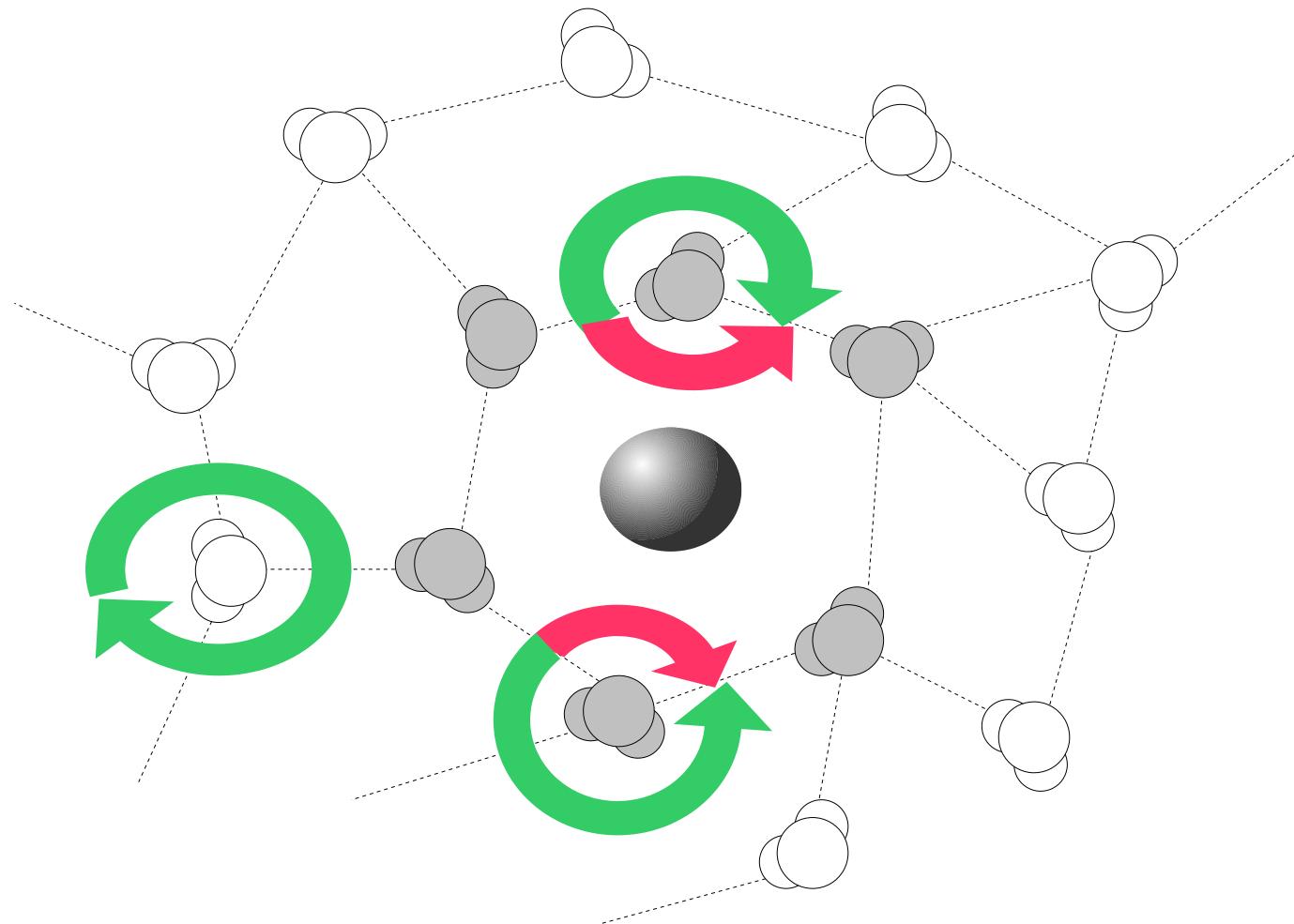


# Hydrophobic interaction *a la* Karshikoff



Andrey Karshikoff *Non-covalent interactions in proteins*, Imperial College Press, 2006, p. 99

# Hydrophobic interaction *a la* Finkelštein



А. В. Финкельштейн, О. Б. Птицын, *Физика белка*,  
Москва, КДУ, 2005, psl. 61 ir toliau

# Hydrophobicity

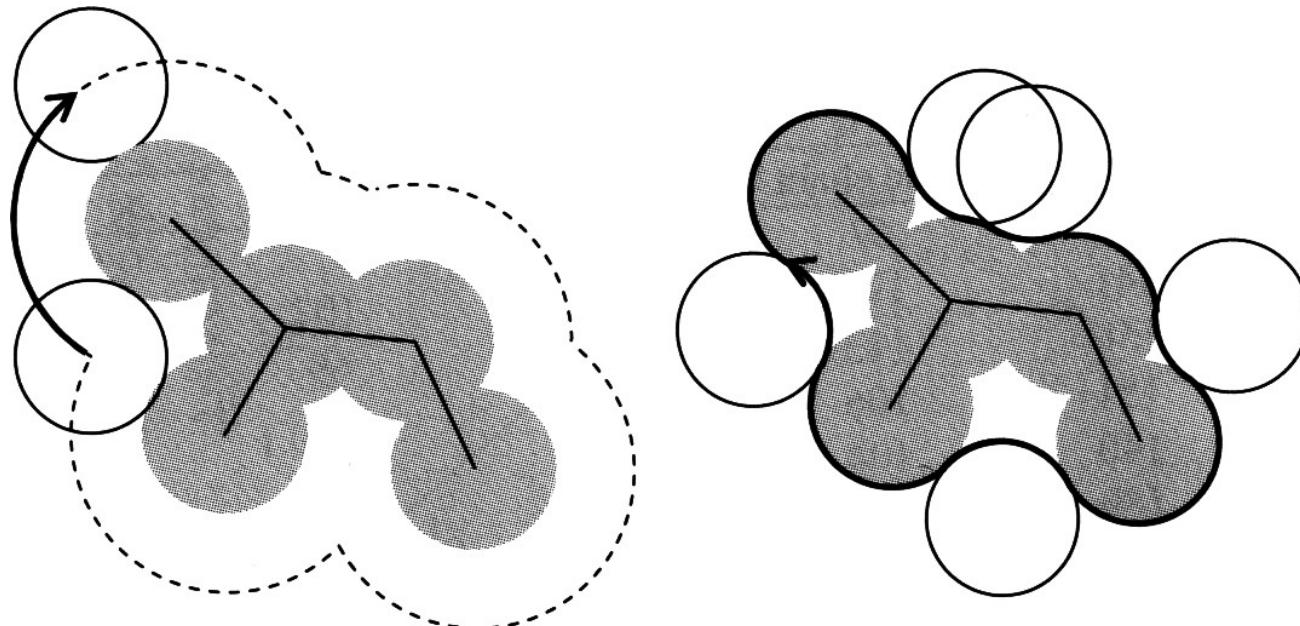
- Hydrophobic transfer energy ( $\Delta G_t$ ) can be split into:
  - glycine transfer energy  $\Delta G_t^{Gly}$
  - side chain transfer energy (hydrophobicity)  $\Delta g_t$ :

$$\Delta G_t = \Delta G_t^{Gly} + \Delta g_t$$

# Hydrophobicity and surface

- Hydrophobic effect is additive (for parts of side chains)
- Hydrophobic effect is proportional to the (accessible) surface area of the side chain

# Solvent accessible surface area (SASA)



# Electrostatic interaction

- Coulomb law
- Debye-Hückel theory
- Born equation
- Poisson-Boltzmann equation

# Coulomb law

$$F = k_0 \frac{q_1 q_2}{r^2}$$

$$k_0 = \frac{1}{4\pi \epsilon_0} = 9 \cdot 10^9 [m/F]$$

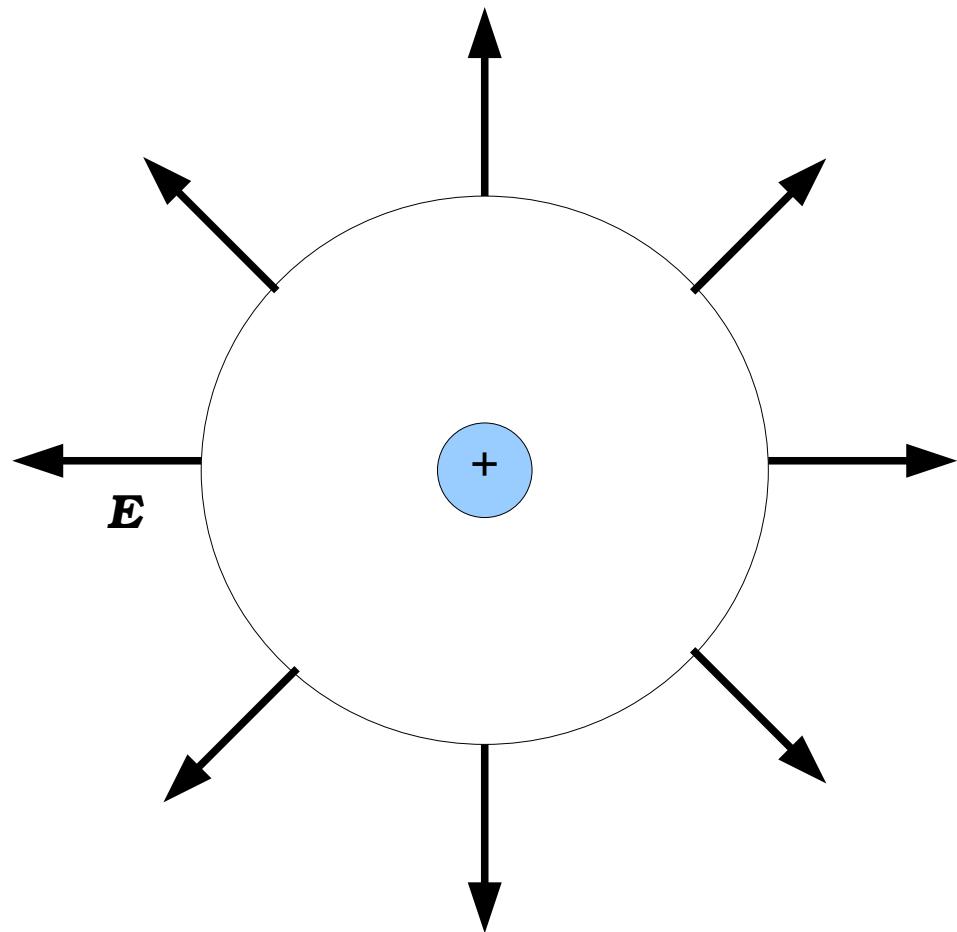
$$\oint_{\delta\Omega} \epsilon \epsilon_0 \vec{E} d\vec{S} = \int_{\Omega} \rho dV$$

$$\operatorname{div} \vec{E} = \rho$$

$$\vec{E} = -\operatorname{grad} \varphi$$

$$\operatorname{div} \operatorname{grad} \varphi = -\rho$$

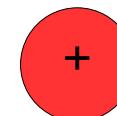
$$\epsilon \epsilon_0 \nabla^2 \varphi = -\rho$$



# Splvation energies

Spherical ion: Born formula

$$\Delta G_{transfer} = 116 \frac{q^2}{r} \left( \frac{1}{\epsilon_2} - \frac{1}{\epsilon_1} \right)$$



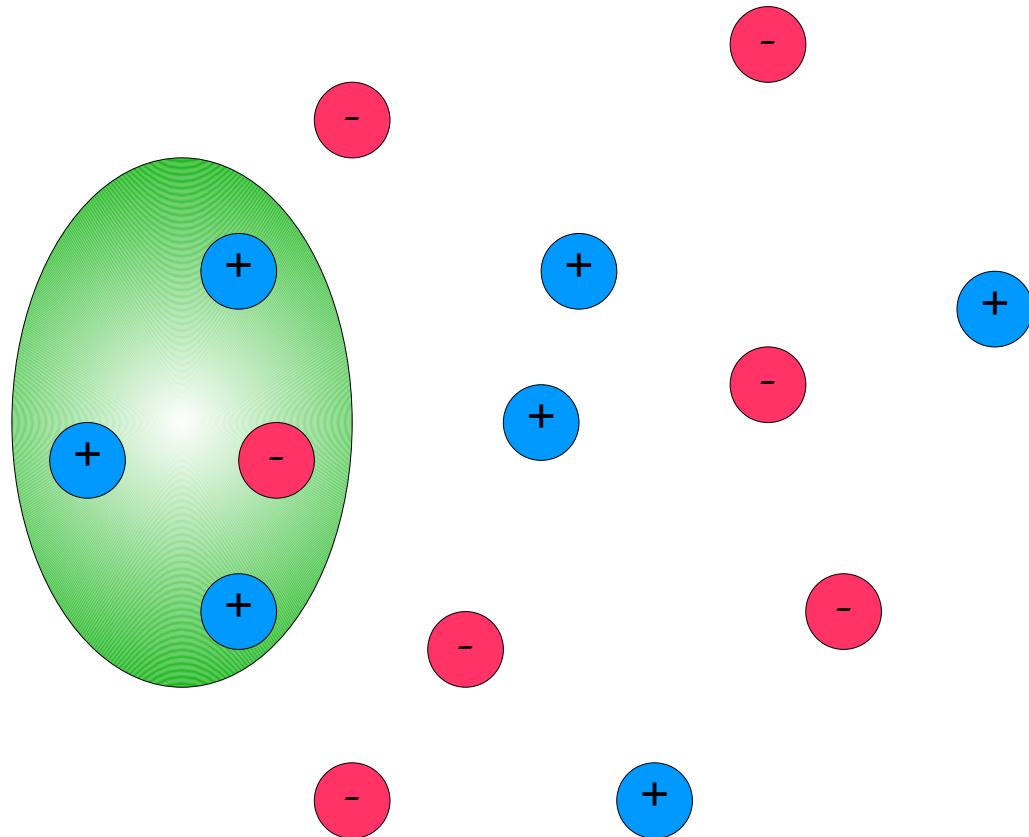
$$\epsilon = 1$$

For a particle of arbitrary shape:  
P-B equation



$$\epsilon = 78$$

# Krūvių pasiskirstymas aplink molekulę



Poisson eqn.:

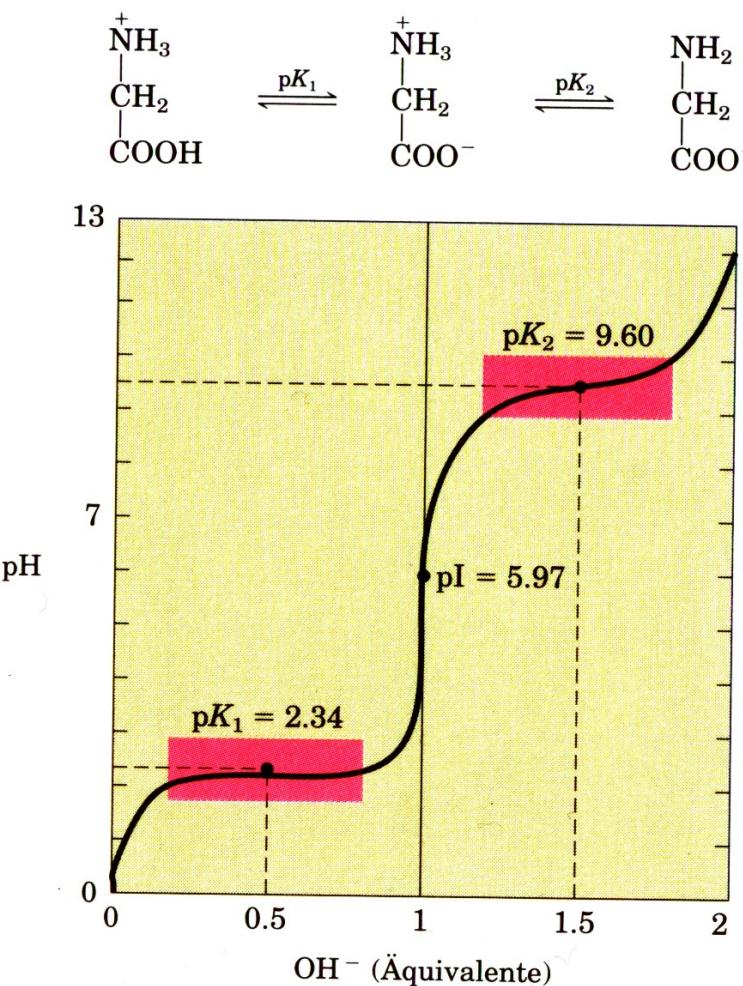
$$\varepsilon_0 \nabla (\varepsilon(\vec{r}) \nabla \varphi) = -\rho$$

Boltzmann distribution:

$$\rho_i = z_i c_i = z_i c_{i0} e^{-\frac{z_i \Phi}{kT}}$$

$$\varepsilon_0 \vec{\nabla} (\varepsilon(\vec{r}) \vec{\nabla} \varphi) = -\rho_p - \sum_i z_i c_{i0} e^{-\frac{z_i \Phi}{kT}}$$

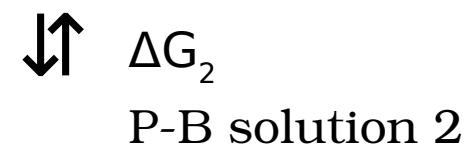
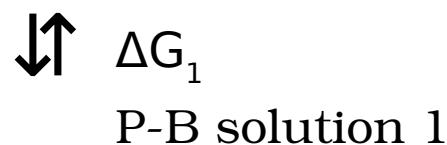
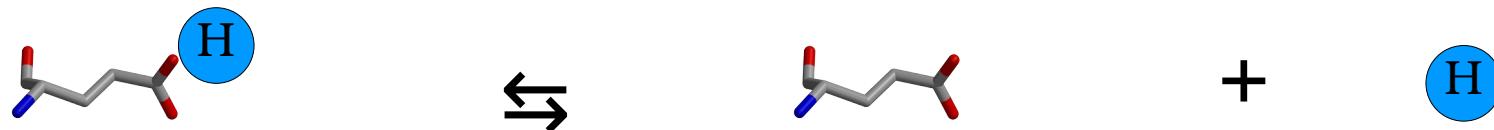
# Ionisation equilibria of proteins



# Local pK values

In aqua:

$$\Delta G = -RT\ln K = 2.3RTpK$$
$$pK = -\lg K$$



$$\Downarrow \Delta G = 0$$

