Bioinformatics III

Analysis and prediction of 3D macromolecule structures

Lecture 10
Non-covalent interactions in proteins

Saulius Gražulis
2024

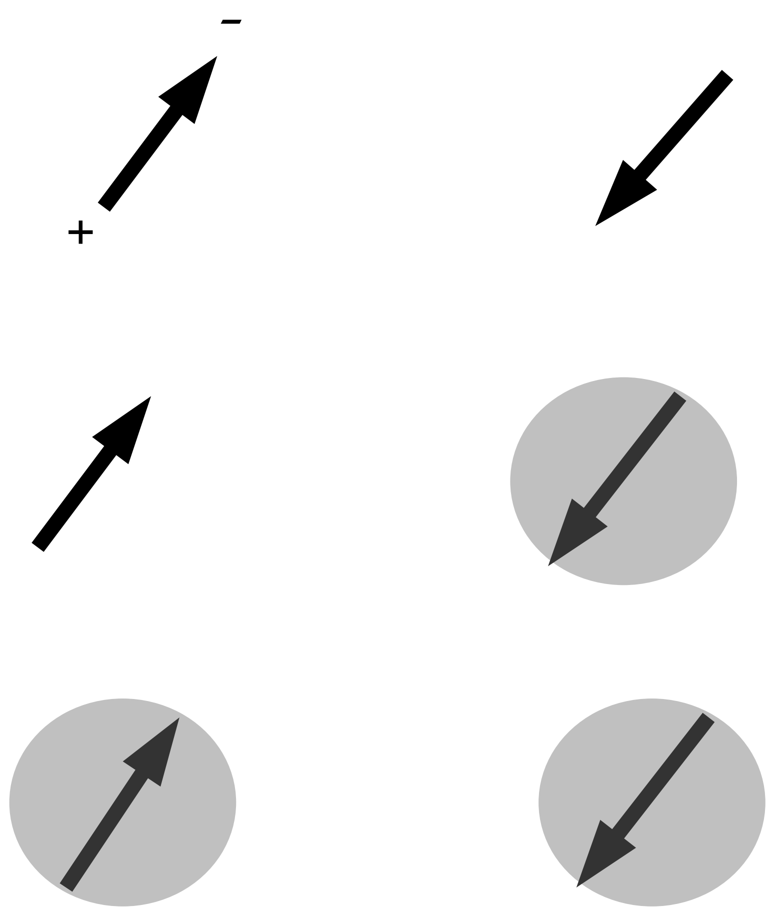
Non-covalent interactions

- Van der Waals forces
- Hydrogen bonds
- Hydrophobic interactions
- Electrostatic interactions
- (Ion-π 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:

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

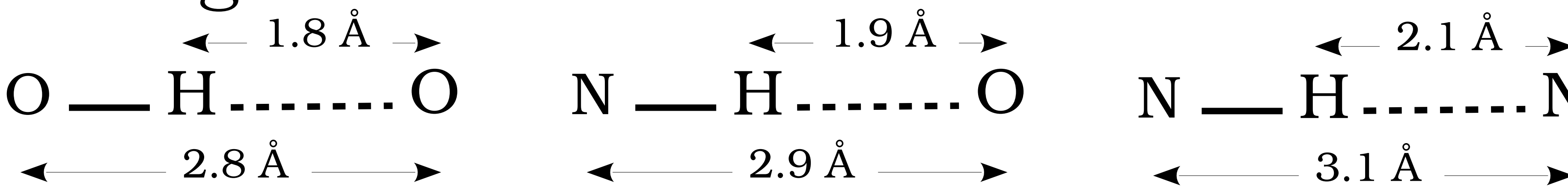
London dispersion forces:

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

V. Adrian Parsegian *Van der Waals forces: a handbook for biologists...*, Cambridge University Press, 2006, psl. 6

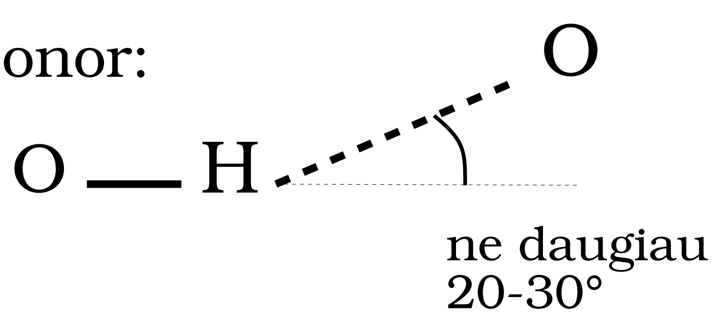
Hydrogen bonds

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

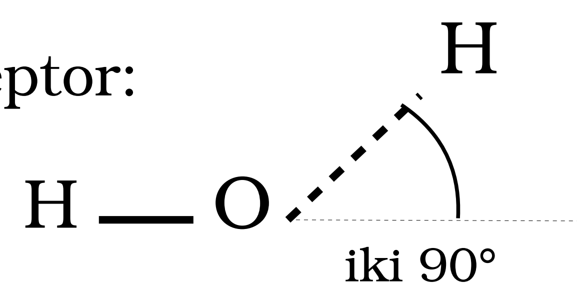


- Directionality:

Donor:

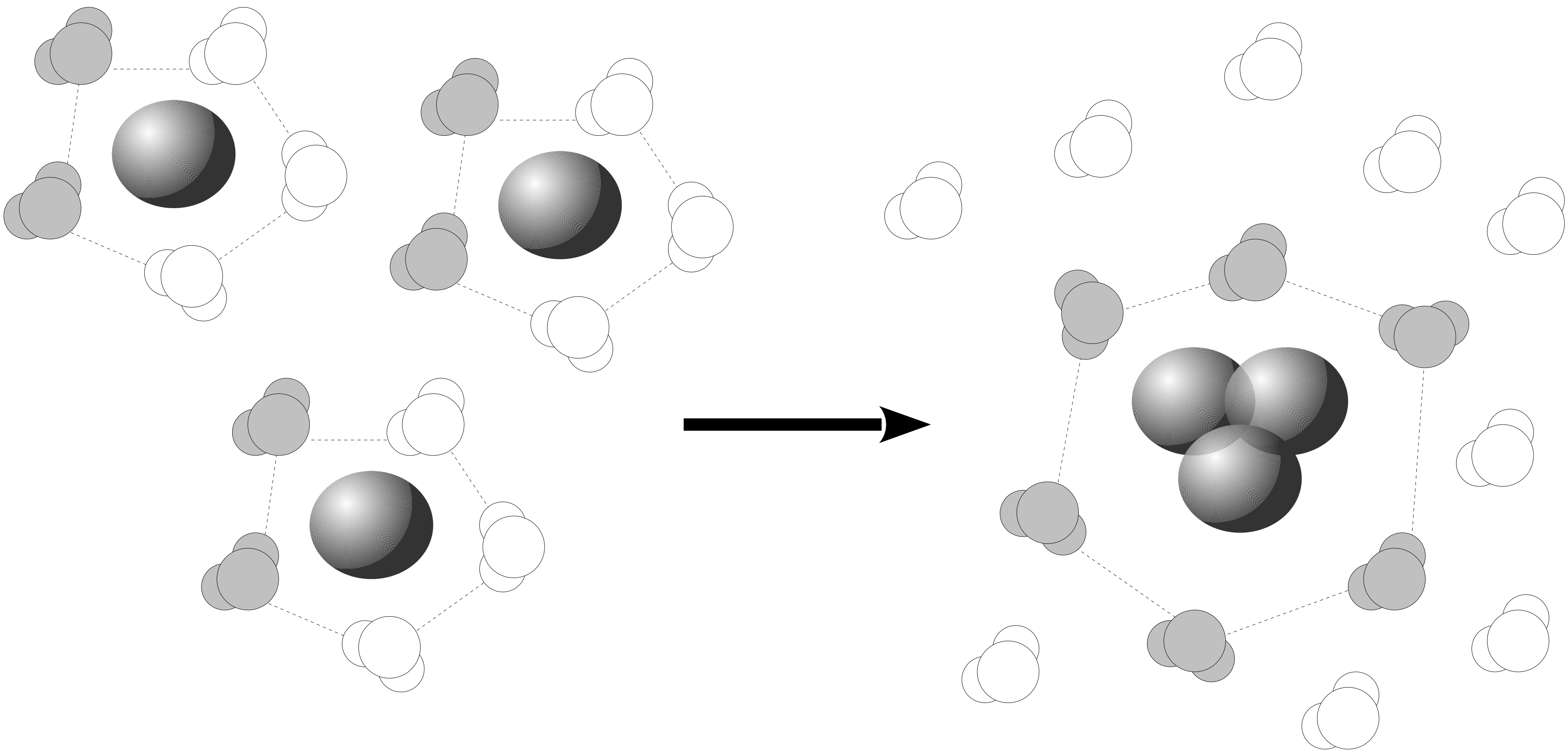


Acceptor:



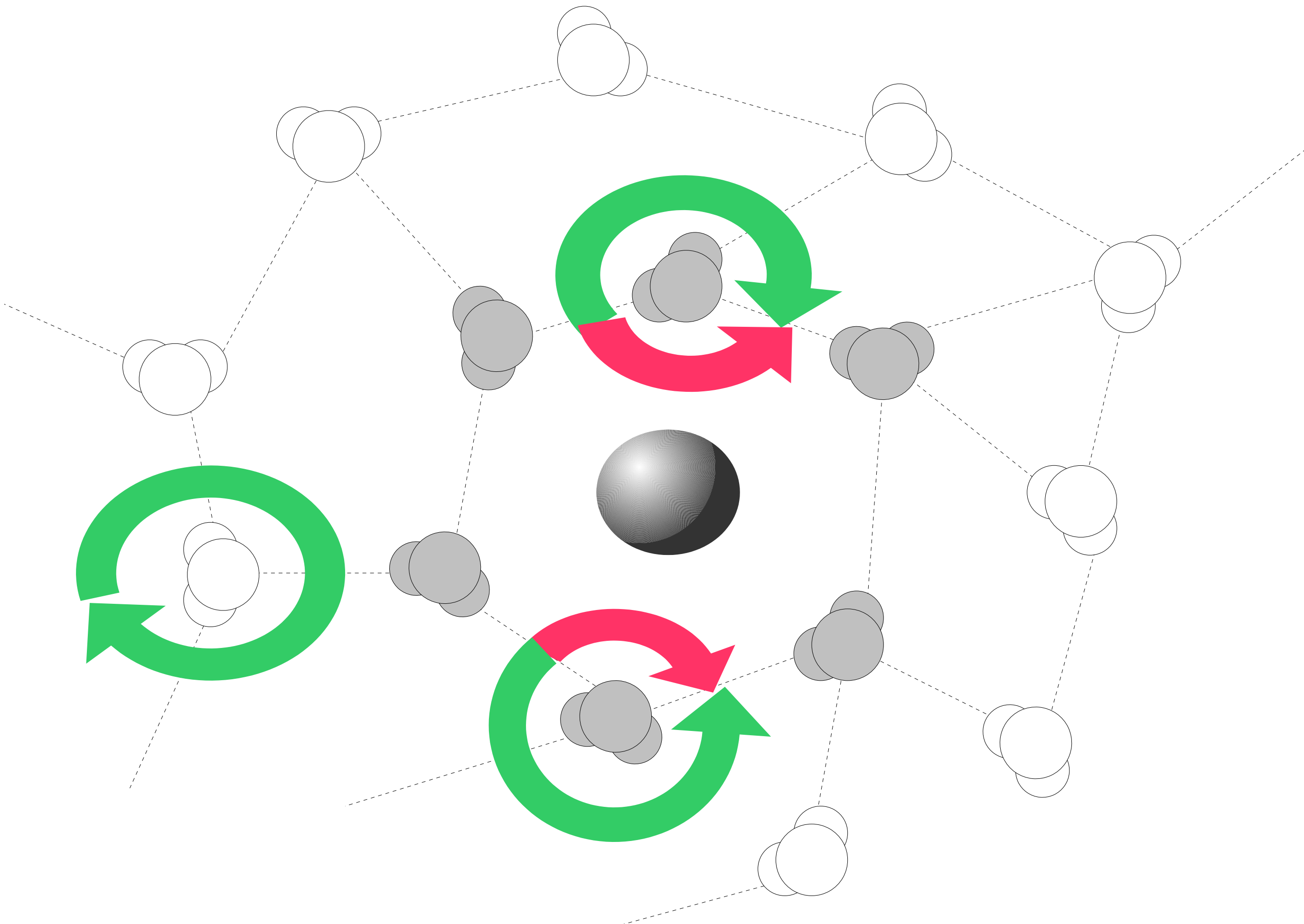
Finkelstein, Ptycin, *Protein physics* (А. В. Финкельштейн, О. Б. Птицын, *Физика белка*, Москва, КДУ, 2005), psl. 41—47

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 (ΔG_t) can be split into:
  - glycine transfer energy ΔG_t^{Gly}
  - side chain transfer energy (hydrophobicity) Δg_t:

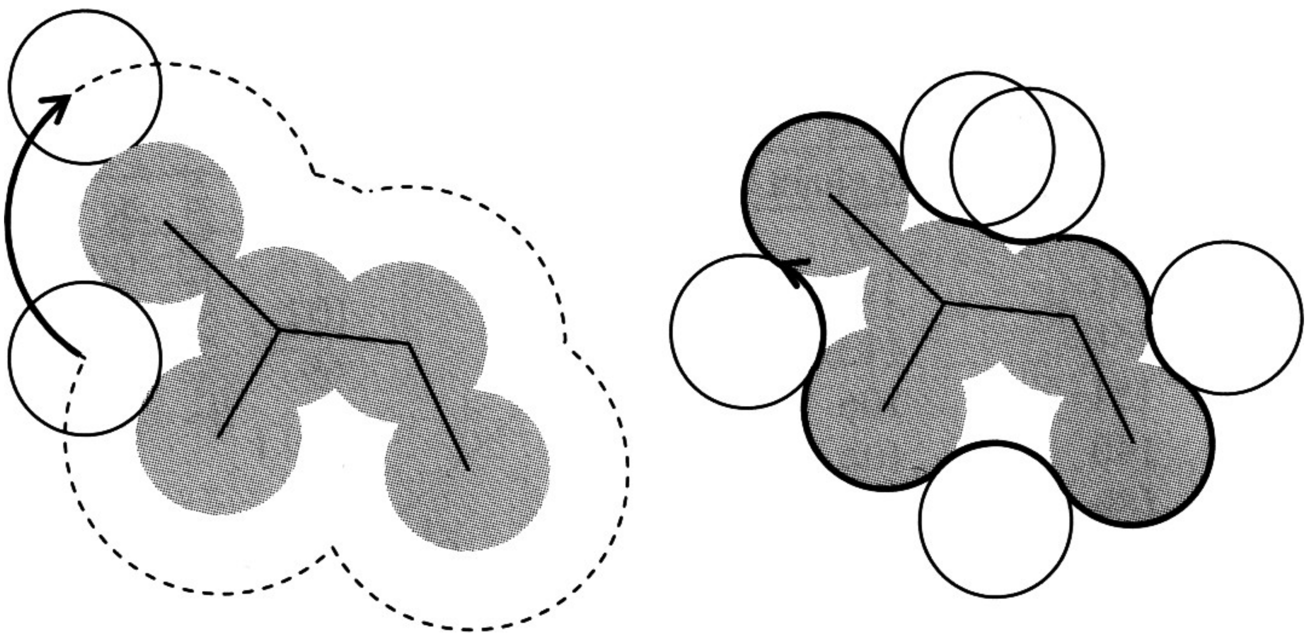
$$\Delta G_t = \Delta G_t^{Gly} + \Delta g_t$$

A. Karshikoff *Non-covalent interactions in proteins;*
Y. Nozaki, C. Tanford *J. Biol. Chem.* 1971 p. 2211

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)



V. Adrian Parsegian *Van der Waals forces: a handbook for biologists...*, Cambridge University Press, 2006, psl. 108

Electrostatic interaction

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

Coulomb law

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

$$k_0 = \frac{1}{4\pi\varepsilon_0} = 9 \cdot 10^9 [m/F]$$

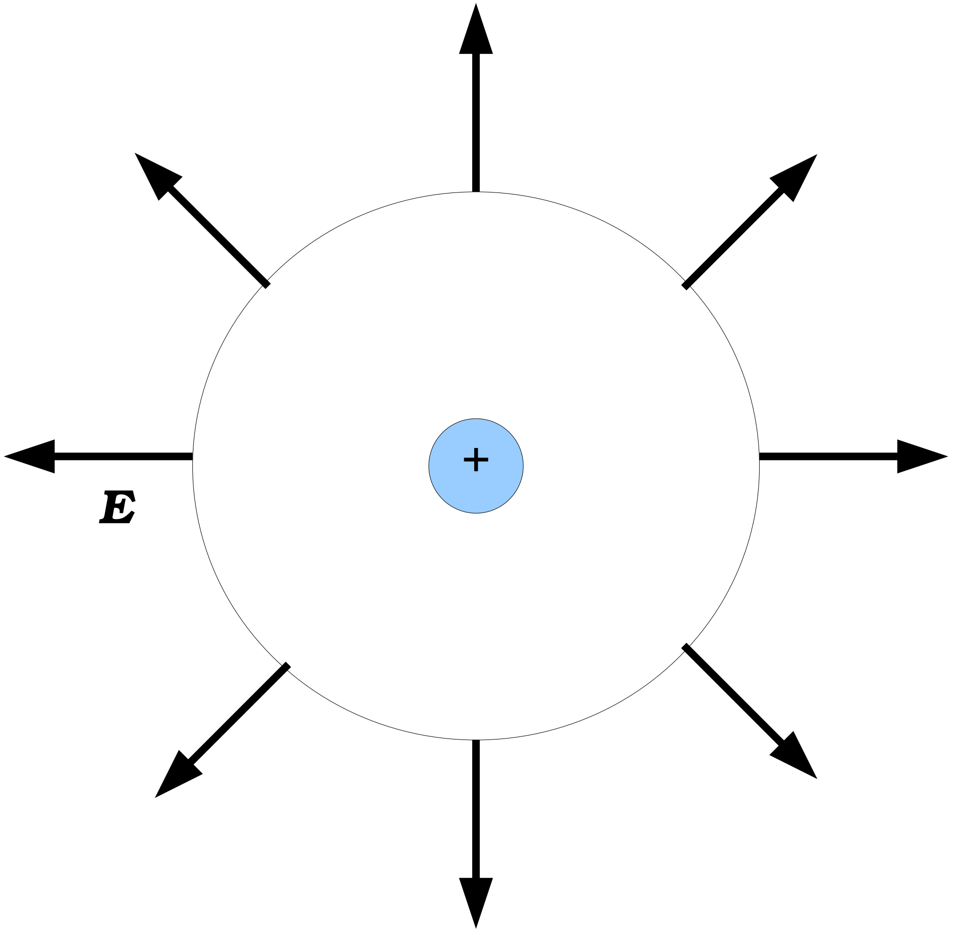
$$\oiint_{\delta\Omega} \varepsilon \varepsilon_0 \vec{E} \, d\vec{S} = \int_{\Omega} \rho \, dV$$

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

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

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

$$\varepsilon \varepsilon_0 \nabla^2 \varphi = -\rho$$

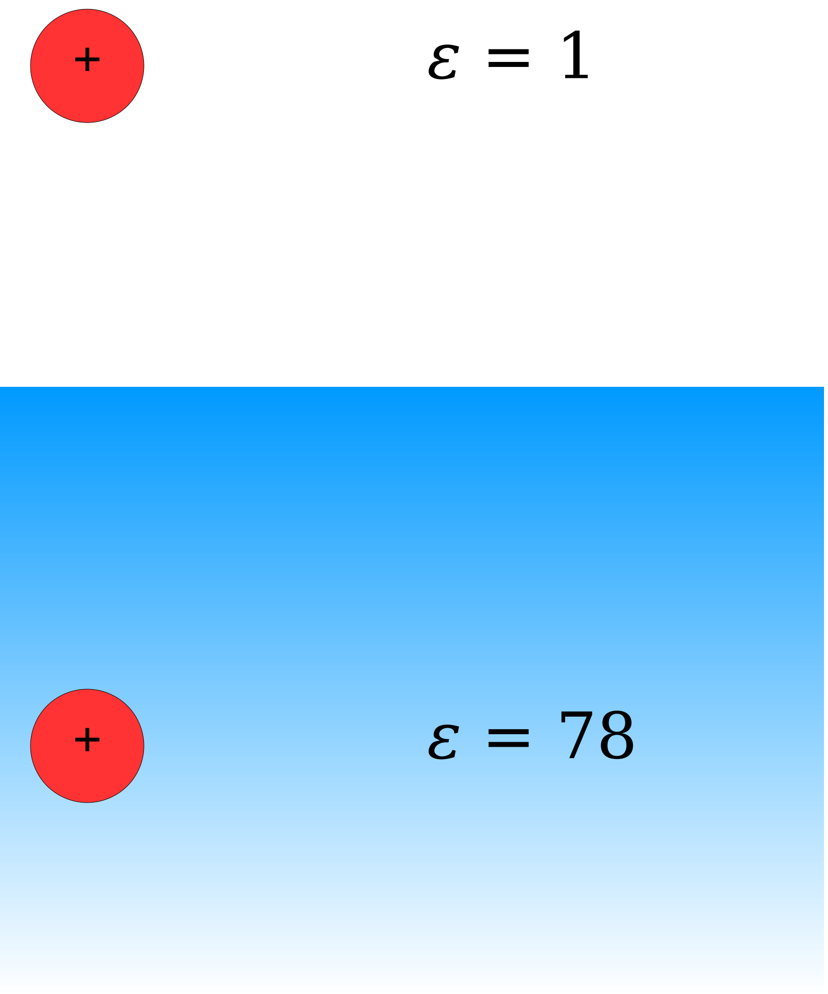


Solvation energies

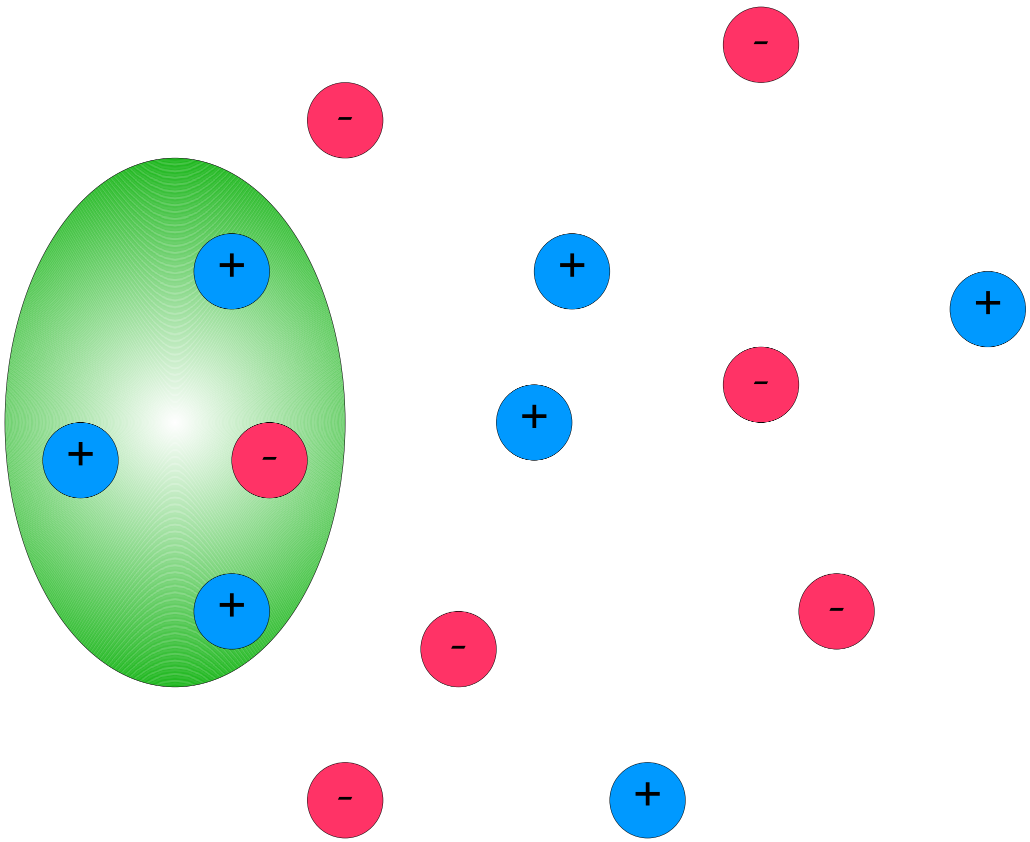
Spherical ion: Born formula

$$\Delta G_{transfer} = 116 \frac{q^2}{r} \left(\frac{1}{\varepsilon_2} - \frac{1}{\varepsilon_1} \right)$$

For a particle of arbitrary shape:
P-B equation



Krūvių pasiskirstymas aplink molekulę



Poisson eqn.:

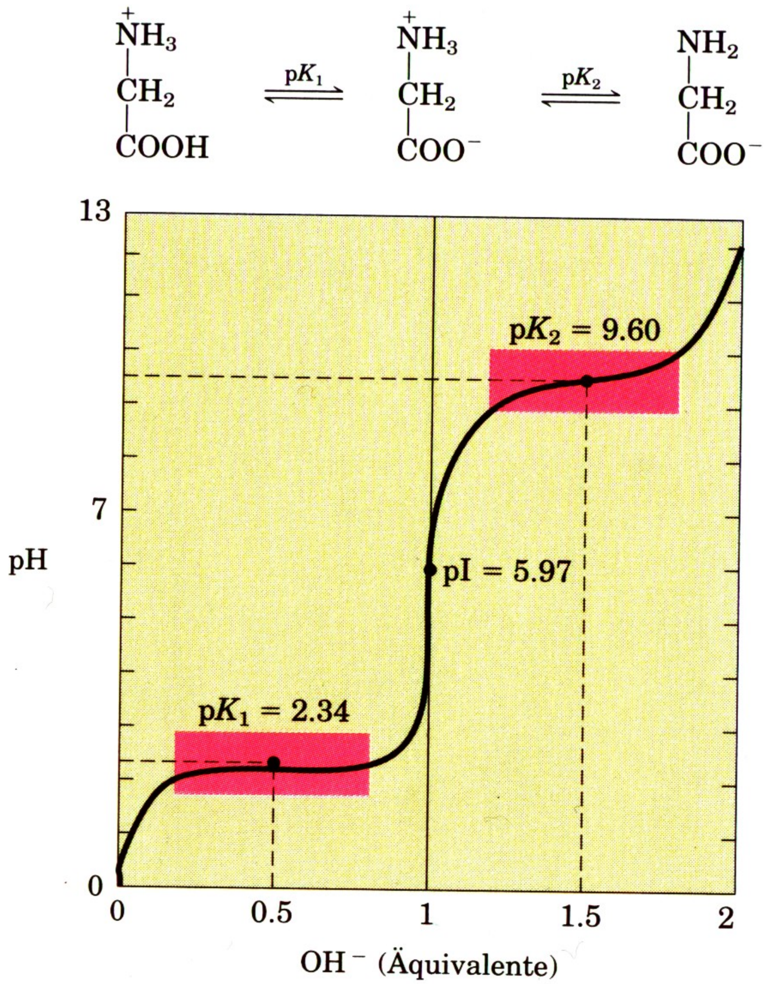
$$\varepsilon_0 \nabla(\varepsilon(\vec{r}) \nabla \varphi) = -\rho$$

Boltzmann distribution:

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

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

Ionisation equilibria of proteins



Lehninger 1998, II edition, p. 131

Local pK values

In aqua:

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

$pK = -\lg K$