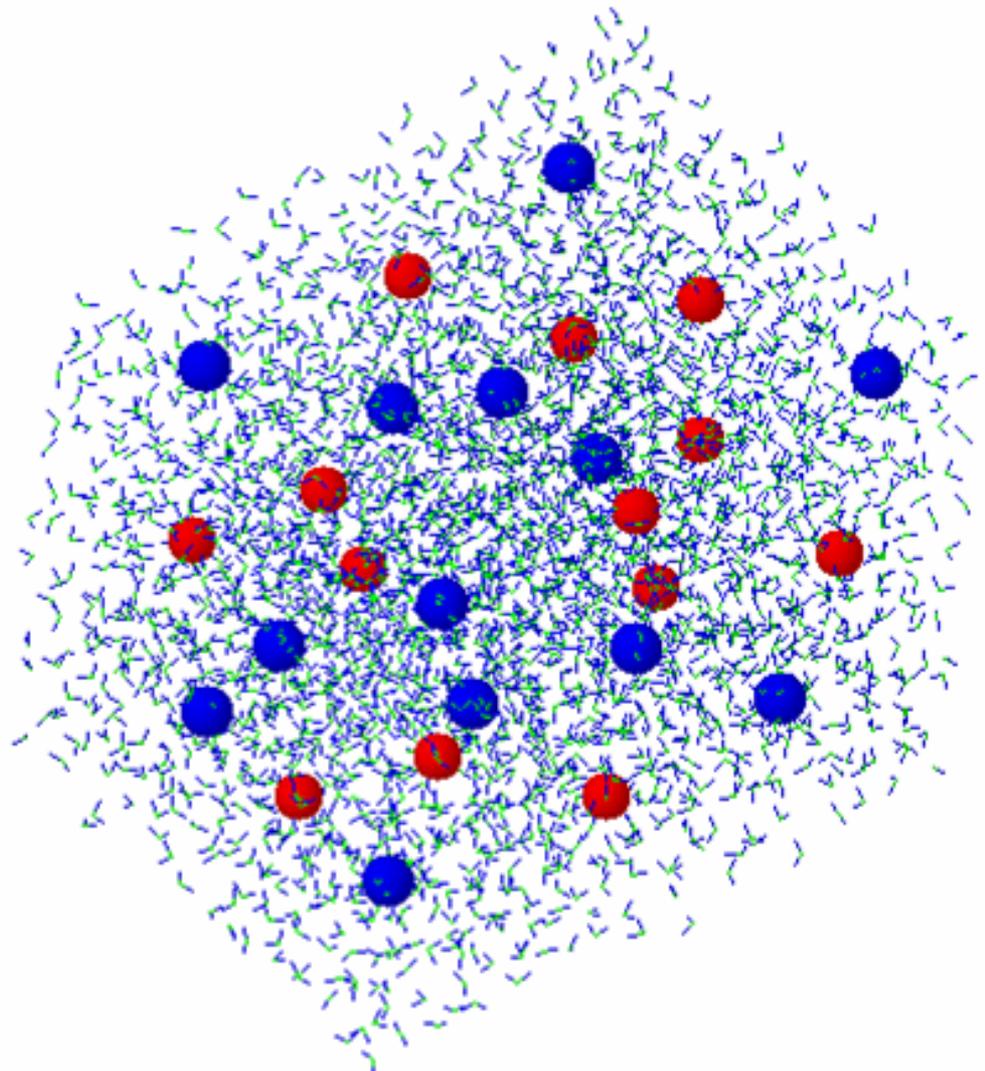
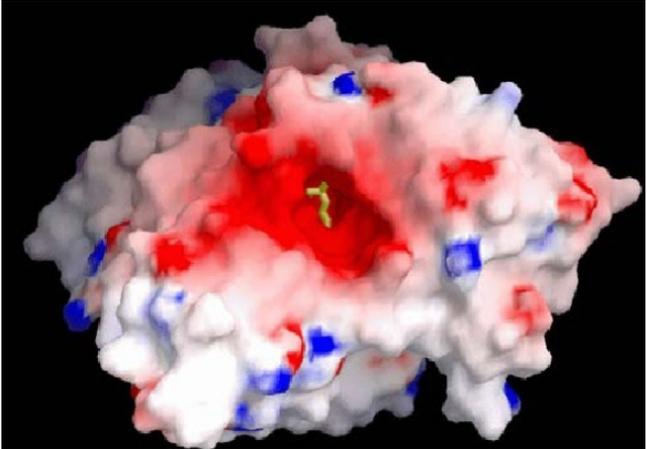
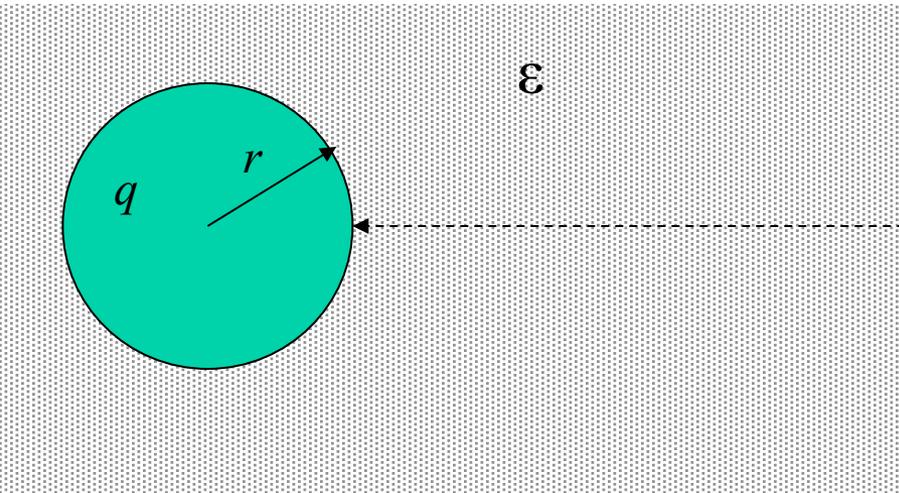


# Molecular Forces in Biological Systems

- *Electrostatic Interactions;*
- *Shielding of charged objects in solution*



# Electrostatic self-energy, effects of size and dielectric constant



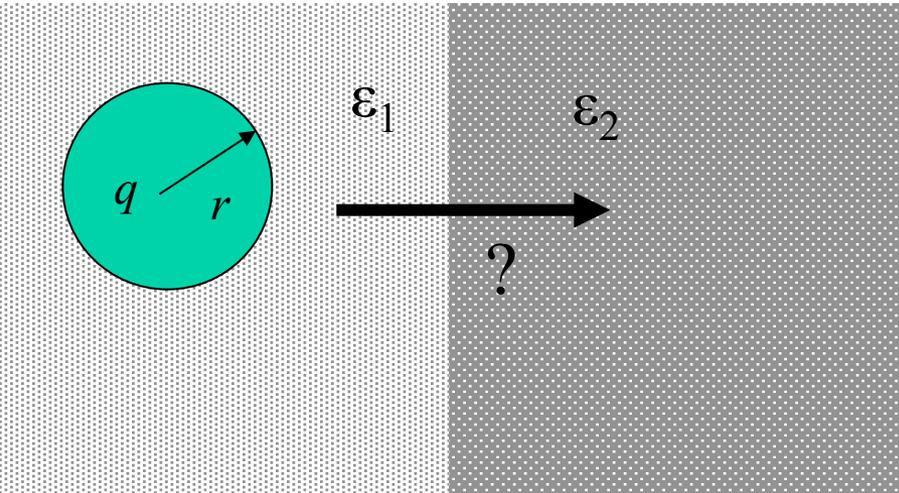
$$\delta U_{el} = \frac{q\delta q}{4\pi\epsilon_0\epsilon r}$$

$\delta q$  brought from infinity

$$U_{el} = \frac{1}{4\pi\epsilon\epsilon_0} \int_0^q q dq = \frac{q^2}{8\pi\epsilon_0\epsilon r}$$

$$\Delta U = \Delta W_{Born} = \frac{q^2}{4\pi\epsilon_0} * \frac{1}{2r} \left( \frac{1}{\epsilon_2} - \frac{1}{\epsilon_1} \right) = \frac{cz^2}{2r} \left( \frac{1}{\epsilon_2} - \frac{1}{\epsilon_1} \right)$$

where  $c = e^2/4\pi\epsilon_0 = 14.4 \text{ eV}\cdot\text{\AA} = 2.3 \cdot 10^{-28} \text{ J}\cdot\text{m}$



For a typical small ion ( $r = 2 - 4\text{\AA}$ ) the energy of transfer between water ( $\epsilon=80$ ) and interior of cellular membrane ( $\epsilon=2$ ) is about 30 - 60 kcal/mol.

**The larger the ion, the easier is to transfer it to low dielectric medium**

# *Biological macromolecules are stabilized by physical interactions:*

*Strong*

*Weak*

*-200 - -800 kJ/mol (-50 - -200 kcal/mol)*

*Covalent bonds*

*-40 - -400 kJ/mol (-10 - -100 kcal/mol)*

*Ionic interactions*

*Ion-dipole interactions*

*Hydrogen bonds*

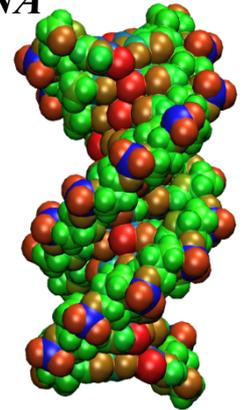
*Van der Waals interactions*

*Hydrophobic effect*

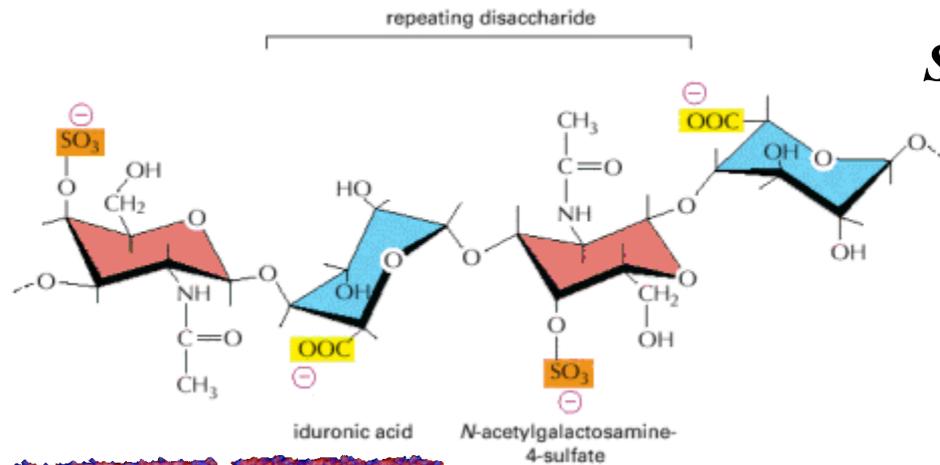
# Why care about electrostatics?

- Longest-range biologicaly relevant interactions.
- A lot of biological molecules are charged. Amino acids: Asp<sup>-</sup>, Glu<sup>-</sup>, Lys<sup>+</sup> Arg<sup>+</sup>, His<sup>+</sup>; DNA: phosphates<sup>-</sup> in backbone, lipids, salt ions, etc.

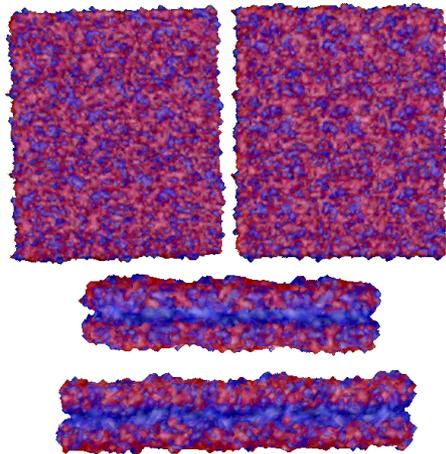
dsDNA



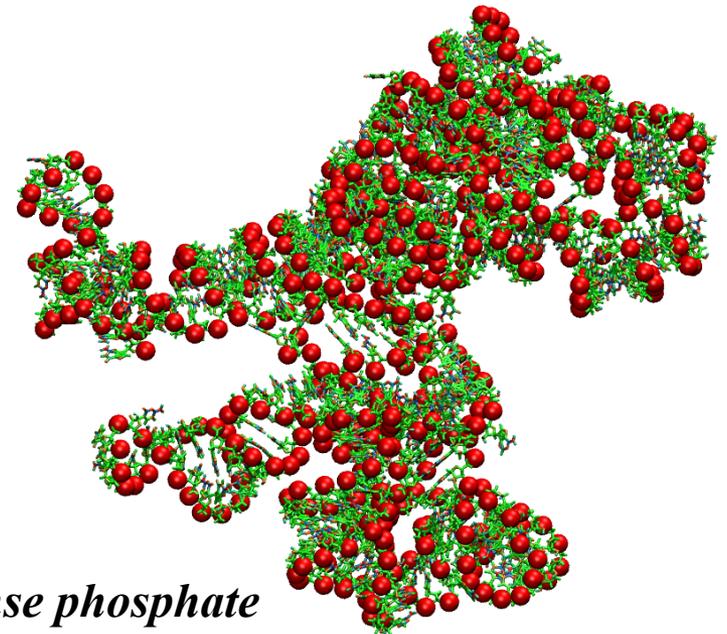
Sugars



Membranes



tRNA (dense phosphate packing)



# *Electrostatic field*



$$V(r) = \frac{q_A}{4\pi\epsilon\epsilon_0 r}$$

$$\vec{E}(r) = \frac{q_A}{4\pi\epsilon\epsilon_0 r^2} \frac{\vec{r}}{|r|}$$

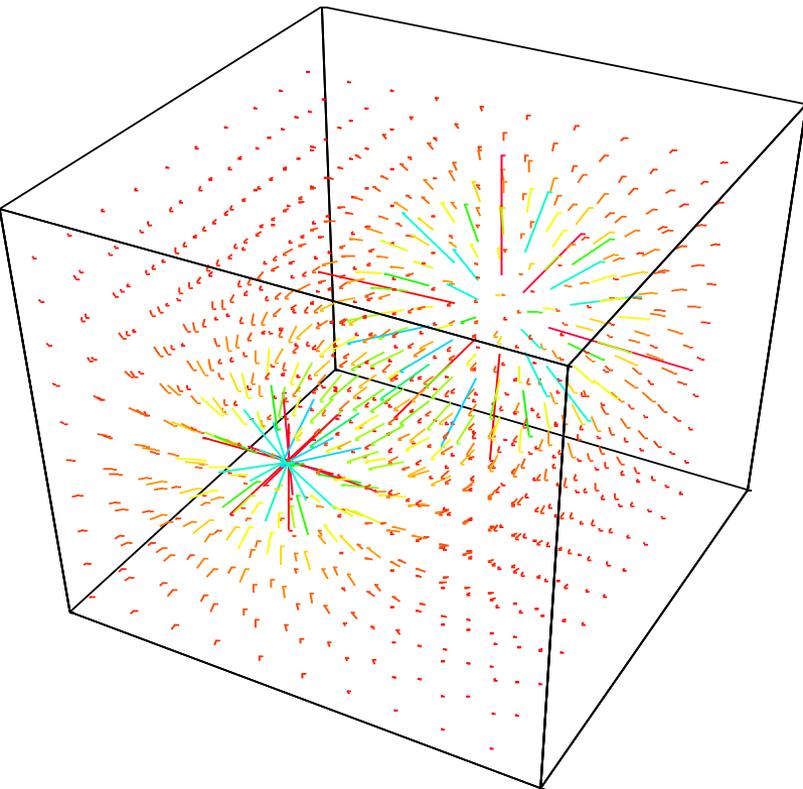
$$\vec{E} = -\nabla V(r) = -\left( \frac{\partial V(r)}{\partial x} \vec{i} + \frac{\partial V(r)}{\partial y} \vec{j} + \frac{\partial V(r)}{\partial z} \vec{k} \right)$$

$$Energy = q_B V(r)$$

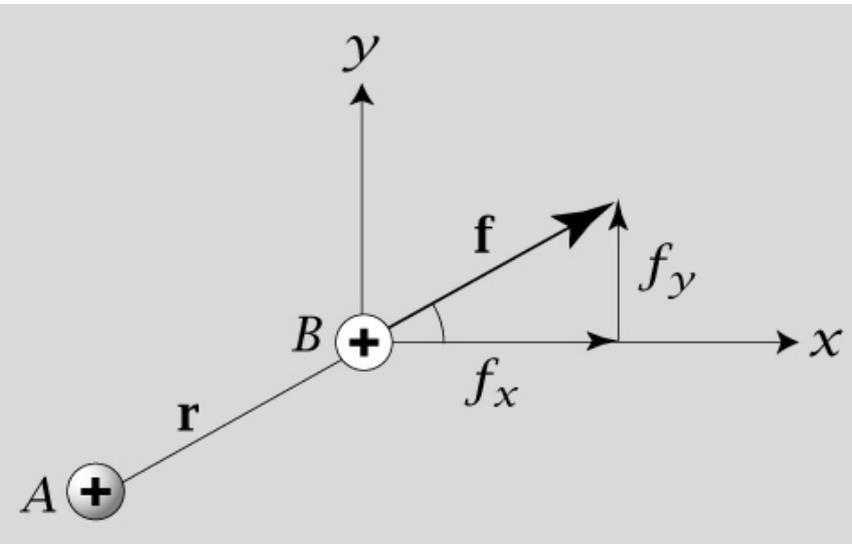
$$\vec{F}(r) = q_B \vec{E}$$

## **Assumptions:**

- homogeneous dielectric medium
- point charges
- no mobile ions
- infinite boundaries

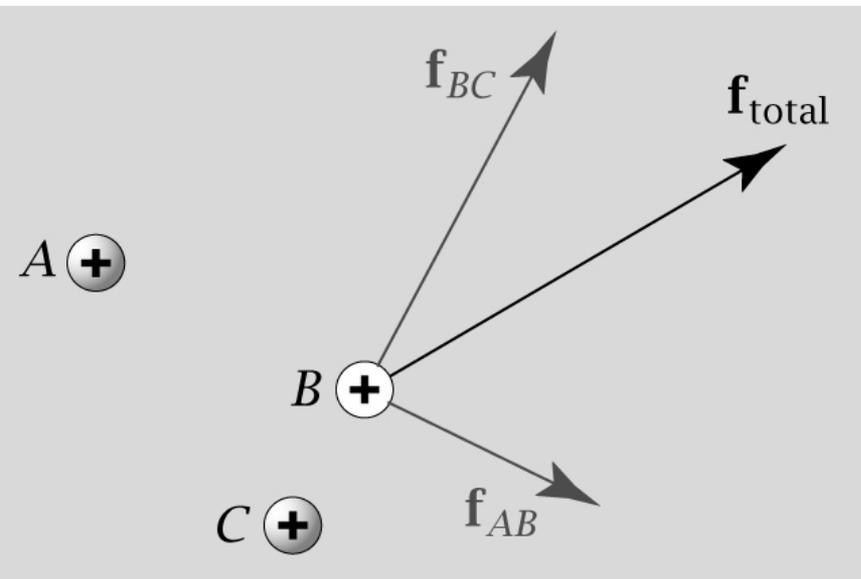


# *Electrostatic force*



$$\vec{F}(r) = \frac{q_A q_B}{4\pi\epsilon\epsilon_0 r^2} \frac{\vec{r}}{|r|}$$

*Force on charge B due to charge A.*



## *Superposition*

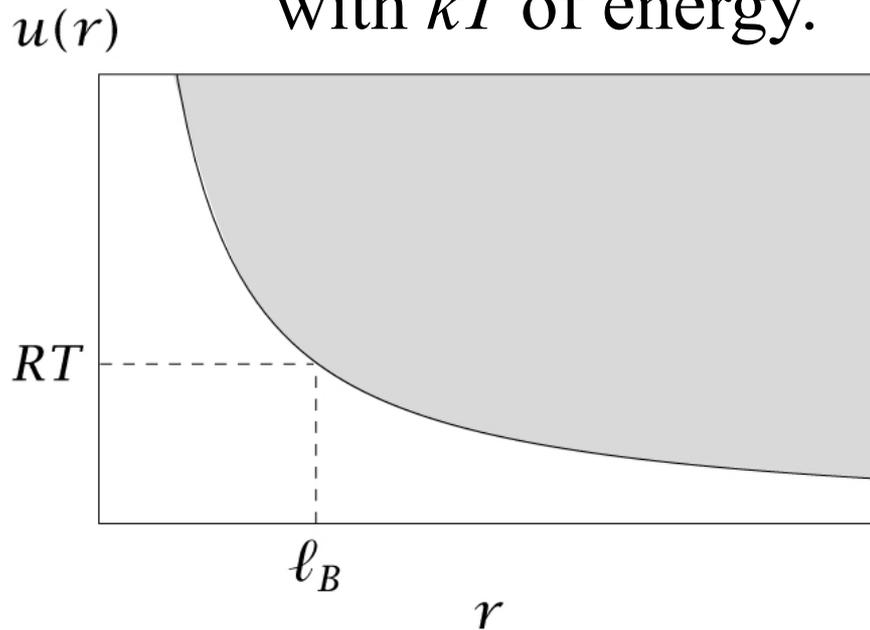
$$U = \frac{q_{\text{ref}}}{4\pi\epsilon_0\epsilon} \sum_i \frac{q_i}{\|\mathbf{x}_i - \mathbf{x}_{\text{ref}}\|}$$

$$\mathbf{F} = \frac{q_{\text{ref}}}{4\pi\epsilon_0\epsilon} \sum_i \frac{q_i}{\|\mathbf{x}_i - \mathbf{x}_{\text{ref}}\|^2} \frac{\mathbf{x}_i - \mathbf{x}_{\text{ref}}}{\|\mathbf{x}_i - \mathbf{x}_{\text{ref}}\|}$$

A mean field theory replaces the interaction between elements in the system by the interaction of a single element with an effective field, which is the sum of the external field and the internal field.

# *Bjerrum length.*

The distance at which two unit charges interact with  $kT$  of energy.



$$k_B T = \frac{e^2}{4\pi D \epsilon_0 l_B}$$
$$l_B = \frac{e^2}{4\pi D \epsilon_0 k_B T}$$

Approximately 7 Å for water  
( $\epsilon = 80$ ) at 298 °K.

*Electrostatic interactions are much stronger than most other non-bonded interactions; e.g., gravitational.*

$$U_{\text{grav}} = -\frac{Gm_p^2}{r} \approx \frac{1.87 \times 10^{-64}}{r} \text{ J m}$$

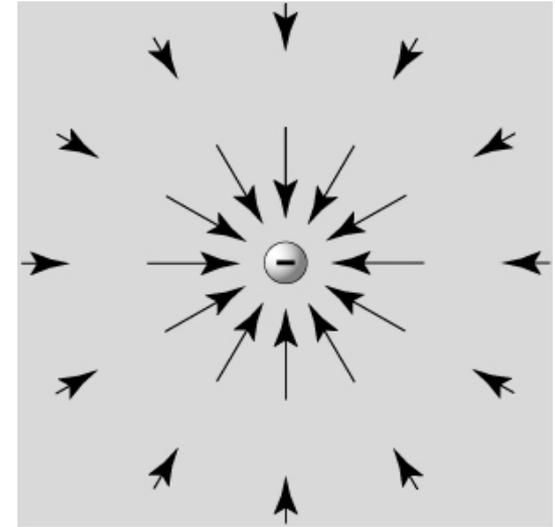
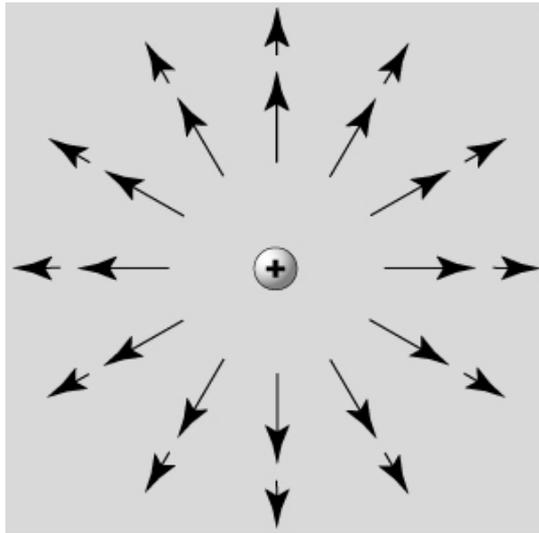
$$U_{\text{elec}} = \frac{e_c^2}{4\pi\epsilon_0 r} \approx \frac{2.30 \times 10^{-28}}{r} \text{ J m}$$

$$\left| \frac{U_{\text{elec}}}{U_{\text{grav}}} \right| \approx 1.23 \times 10^{36}$$

# *Flux of an electric field*

Fluxes arise from

- Sources: positive charges
- Sinks: negative charges



Electric field flux: integral of electric displacement over a surface.

$$\Phi = \int_{\partial\Omega} \underbrace{\varepsilon \mathbf{E}(\mathbf{s})}_{\text{Electric displacement}} \cdot \underbrace{d\mathbf{s}}_{\text{Jacobian; points in surface normal direction}}$$

*Boundary surface of volume  $\Omega$*

# *Gauss' law*

*The integral of field flux through a closed, simple surface is equal to the total charge inside the surface*

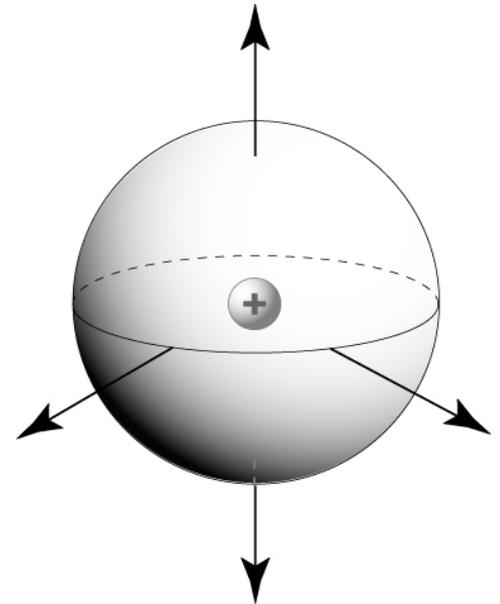
$$\begin{aligned}\Phi &= \oint_{\partial\Omega} \varepsilon \mathbf{E}(\mathbf{s}) \cdot d\mathbf{s} \\ &= \frac{1}{\varepsilon_0} \int_{\Omega} \rho(\mathbf{x}) d\mathbf{x}\end{aligned}$$

This is true for *both* homogeneous and inhomogeneous dielectric media

## *Point charge in a sphere*

- Point charge has spherically-symmetric field
- Field is constant on sphere surface
- Flux is independent of sphere diameter

$$\Phi = \varepsilon E(r) 4\pi r^2 = \varepsilon \frac{q}{4\pi\varepsilon_0\varepsilon r^2} 4\pi r^2 = \frac{q}{\varepsilon_0}$$



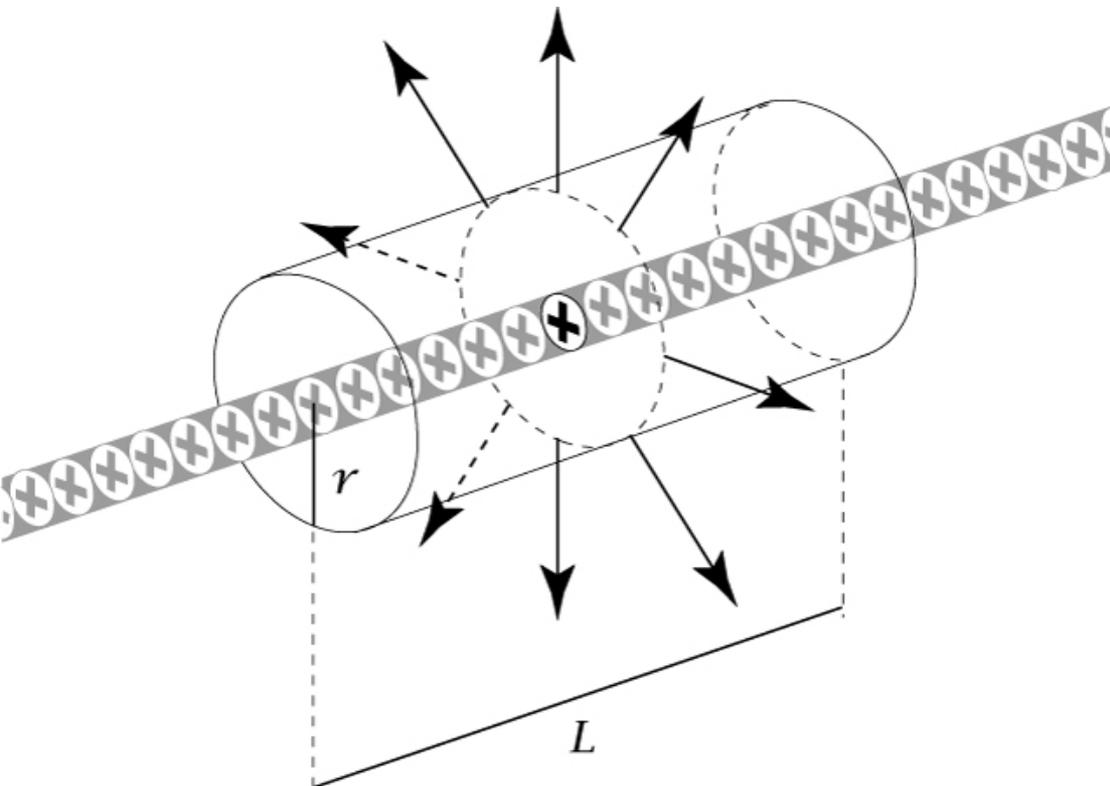
# Field from a line charge

Assumptions:

Homogeneous medium

Line of length  $L$ , where  $L$  is “very big” (radial symmetry)

Linear charge density of  $\lambda$



$$\Phi = \oint_{\partial(\text{cylinder})} \epsilon \mathbf{E}(\mathbf{s}) \cdot d\mathbf{s}$$

$$= \int_0^{2\pi} \int_0^L \epsilon E(r) r dz d\theta$$

$$= 2\pi r L \epsilon E(r)$$

$$\Phi = \int_{\text{cylinder}} \rho(\mathbf{x}) d\mathbf{x} = \frac{q}{\epsilon_0} = \frac{\lambda L}{\epsilon_0}$$

$$2\pi r L \epsilon E(r) = \frac{\lambda L}{\epsilon_0}$$

$$E(r) = \frac{\lambda}{2\pi \epsilon \epsilon_0 r}$$

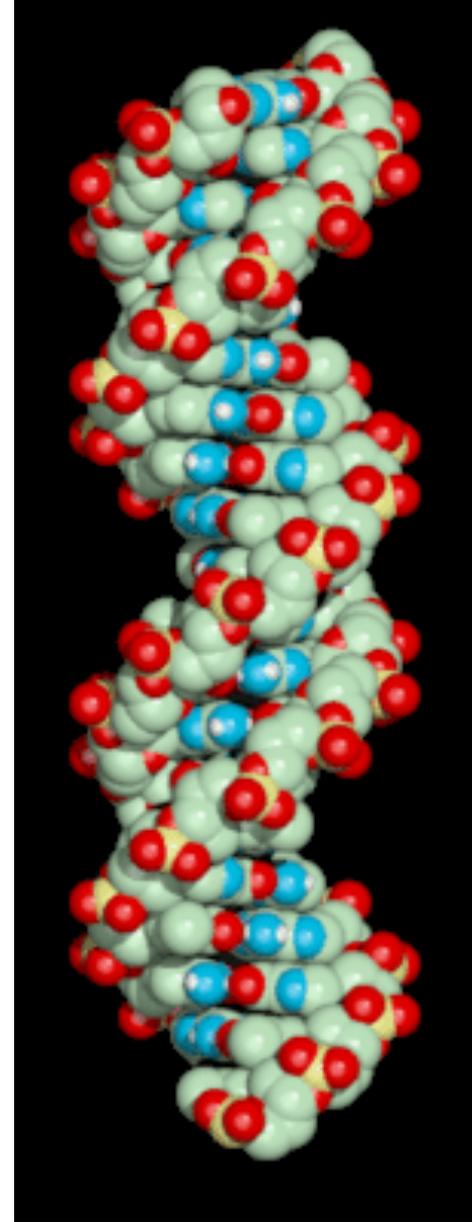
# *Field around DNA*

B-DNA shape:

- 2 phosphates every 3.4 Å
- water dielectric constant of 80

*What is the field 40 Å away from a “very long” B-DNA molecule?*

$$\begin{aligned} E(r) &= \frac{\lambda}{2\pi\epsilon_0\epsilon r} \\ &= \frac{(1.60 \times 10^{-19} \text{ C})}{2\pi(8.854 \times 10^{-12} \text{ C}^2 \text{ J}^{-1} \text{ m}^{-1})(80)(4 \times 10^{-9} \text{ m})} \\ &= 5.29 \times 10^7 \text{ V m}^{-1} \end{aligned}$$



# *Field from a charged plane*

Assumptions:

Homogeneous medium

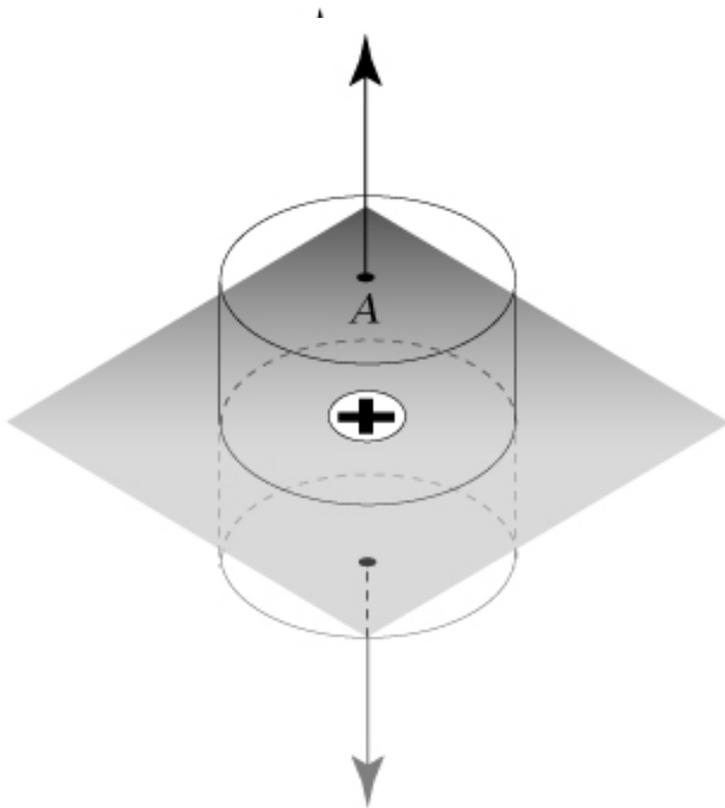
Surface of area  $A$ ,

Surface charge density of  $\sigma$

$$\Phi = \oint_{\partial(\text{pillbox})} \epsilon \mathbf{E}(\mathbf{s}) \cdot d\mathbf{s}$$

$$= 2 \int_0^{2\pi} \int_0^z \epsilon E(r) r dz d\theta$$

$$= 4\pi R^2 \epsilon E(r) = 2A\epsilon E(r)$$



$$\Phi = \int_{\text{pillbox}} \rho(\mathbf{x}) d\mathbf{x} = \frac{q}{\epsilon_0} = \frac{\sigma A}{\epsilon_0}$$

$$2A\epsilon E(r) = \frac{\sigma A}{\epsilon_0}$$

$$E(r) = \frac{\sigma}{2\epsilon\epsilon_0}$$

*What is the field at distance  $r$  from the source?*

# Field around a membrane

POPS membrane

- -1 e charge per lipid
- 1 lipid per 55 Å<sup>2</sup>

*What is the field 20 Å away from the membrane (in water)?*

*Bigger than DNA!*

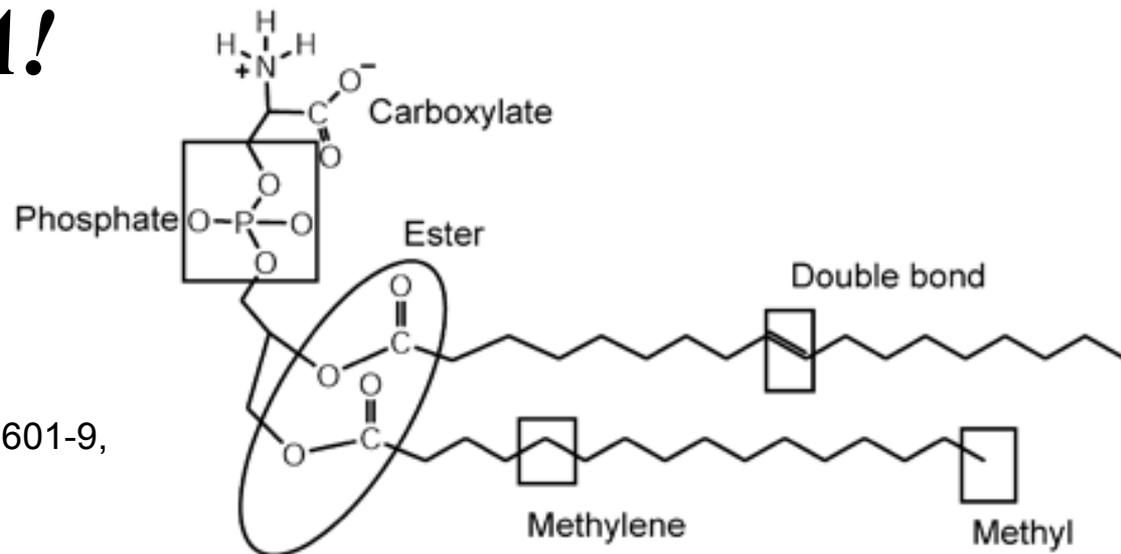
$$\sigma = \left( \frac{1 \text{ e}}{55 \text{ \AA}^2} \right) \left( \frac{1.60 \times 10^{-19} \text{ C}}{e} \right) \left( \frac{\text{\AA}^2}{10^{-20} \text{ m}} \right)$$

$$= 0.29 \text{ C m}^{-2}$$

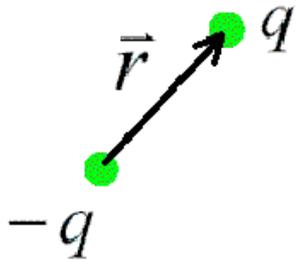
$$E(z) = \frac{\sigma}{2\epsilon_0\epsilon}$$

$$= \frac{(0.29 \text{ C m}^{-2})}{2(8.854 \times 10^{-12} \text{ C}^2 \text{ J}^{-1} \text{ m}^{-1})(2)}$$

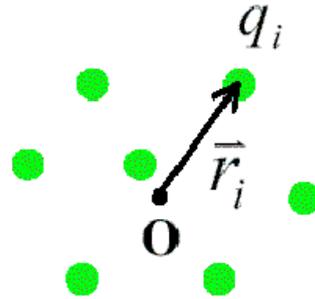
$$= 8.19 \times 10^9 \text{ V m}^{-1}$$



# Electric dipole moment



$$\vec{p} = q\vec{r}$$



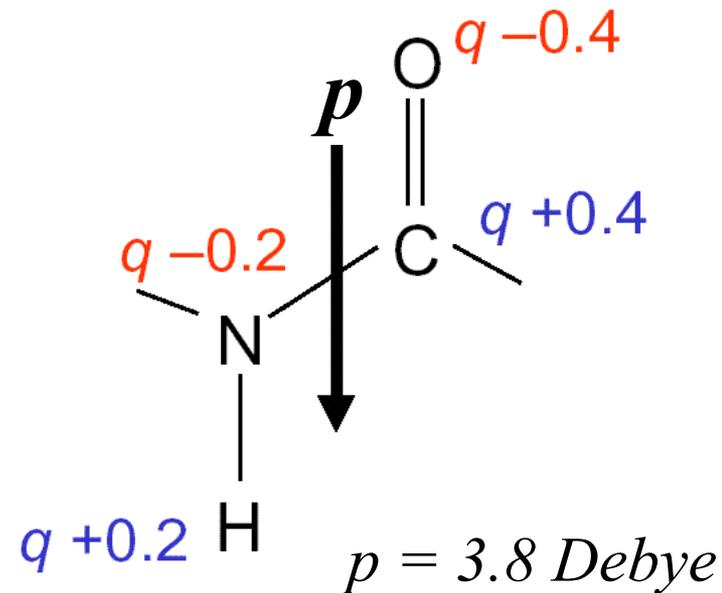
$$\vec{p} = \sum_i q_i \vec{r}_i$$

Interaction energy of a dipole with a field

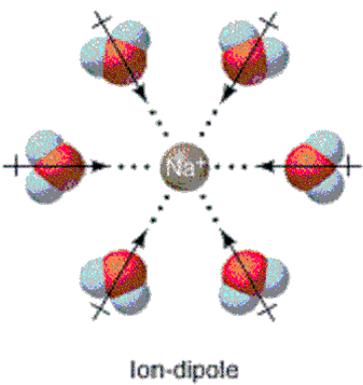
$$U = -\vec{p} \cdot \vec{E}$$

Molecule	Dipole moment
Water	1.9
Ethanol	1.7
Acetic acid (neutral)	1.7
Acetone	2.88
Acetamide	3.8

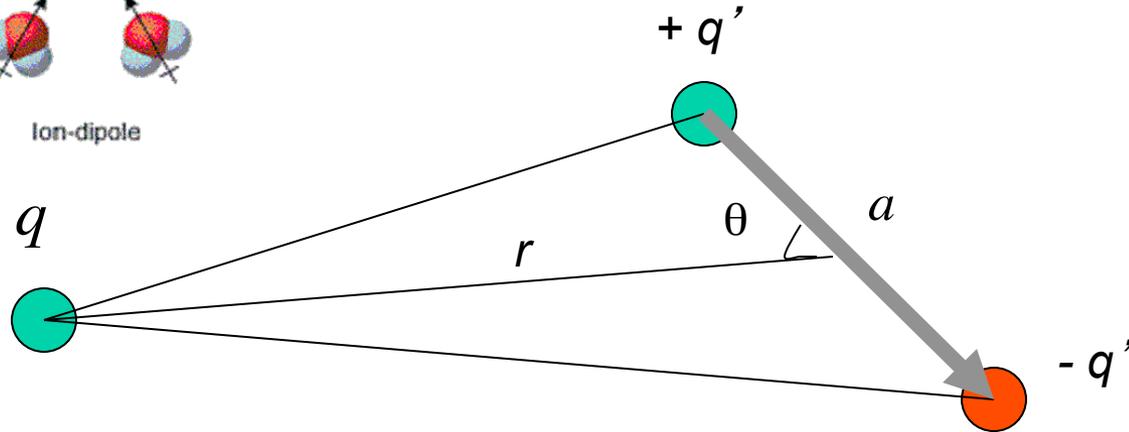
1 Debye = 0.2 electron-Angstroms  
 =  $3.3 \times 10^{-23}$  Cm



# Charge-Dipole and Dipole-Dipole interactions



charge - dipole

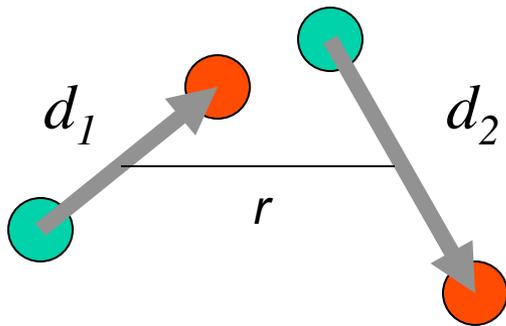


static

$$U = -\frac{qd \cos \theta}{4\pi\epsilon_0\epsilon r^2}$$

with Brownian tumbling

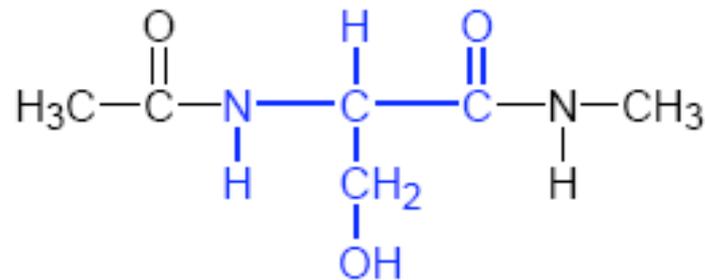
$$U = -\frac{q^2 d^2}{(4\pi\epsilon_0\epsilon)^2 3kTr^4}$$



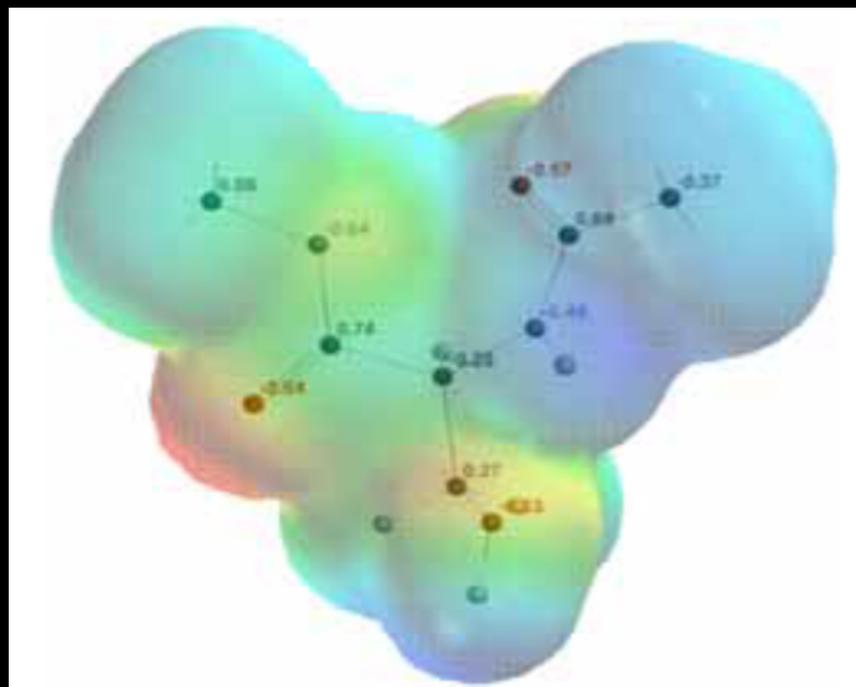
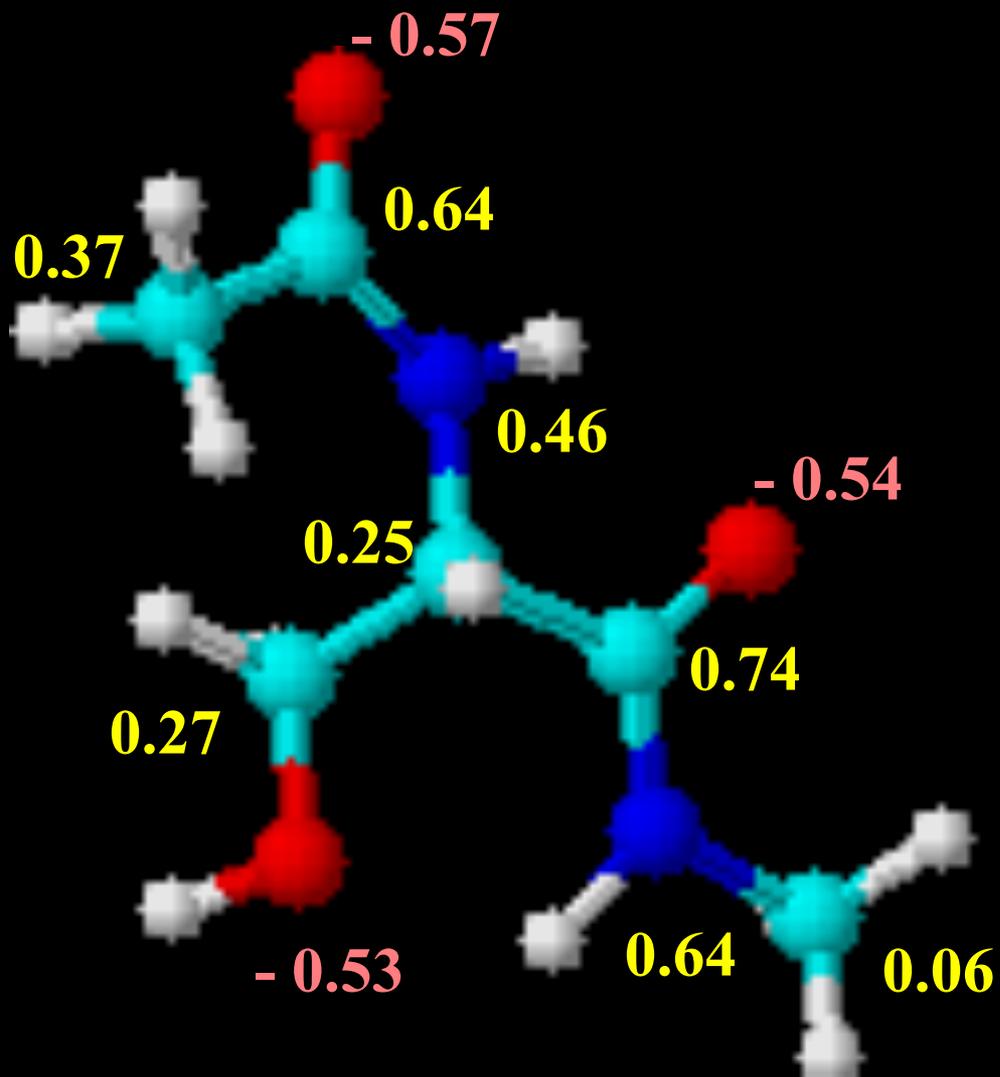
static  $U = \frac{d_1 d_2 K}{4\pi\epsilon_0\epsilon r^3}$   $K$  – orientation factor dependent on angles

with Brownian motion  $U = -2 \frac{d_1^2 d_2^2}{3kT(4\pi\epsilon_0\epsilon)^2 r^6}$

# *Partial Charges*

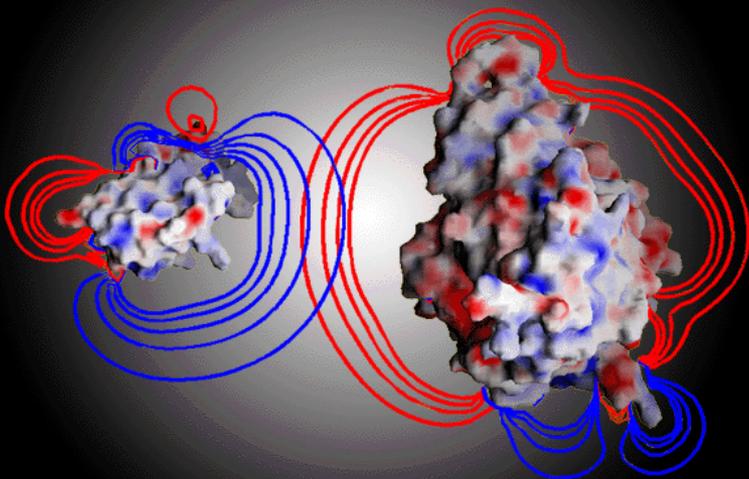


N-Acetyl-N'-Methylserinyl amide



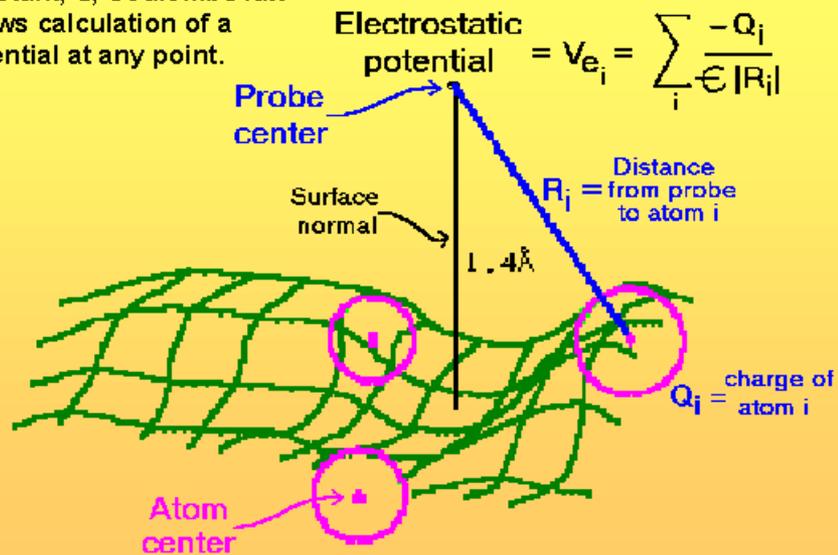
# Electrostatics of macromolecules

## Electrostatically Accelerated Protein-Protein Association



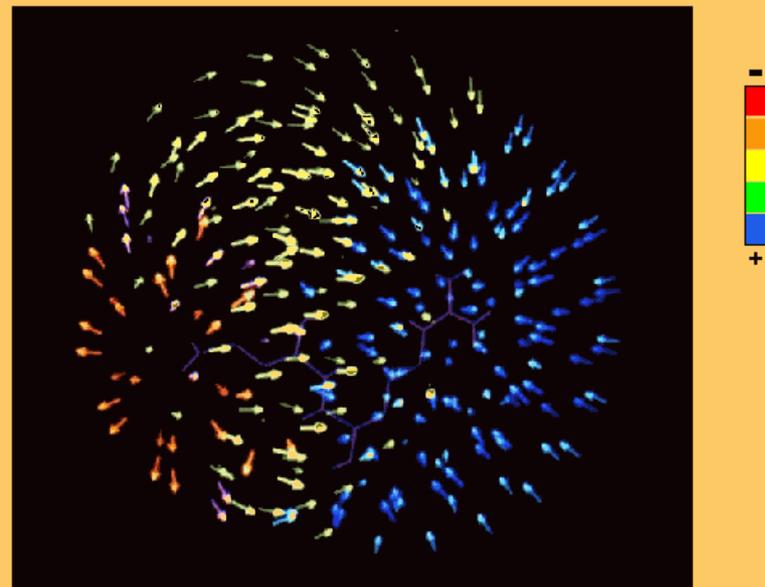
McCammon Group - UCSD

With point charges and a constant dielectric constant,  $\epsilon$ , Coulombs law allows calculation of a potential at any point.



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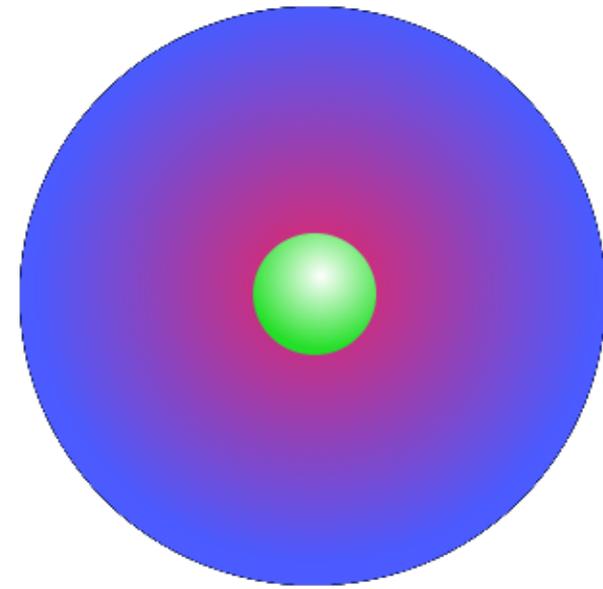
## Potential gradients around the Glu-Arg dipeptide



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# *A continuum dielectric medium*

- Reduces the strength of electrostatic interactions relative to a vacuum.
- It has no atomic detail.



An *isotropic* dielectric continuum exhibits the same response in all directions

□ the dielectric tensor can be reduced to a scalar

□ for a homogeneous isotropic Coulomb's law takes a very simple, scaled form

$$-\nabla \cdot [\epsilon(r) \nabla \varphi(r)] = \frac{\rho(r)}{\epsilon_0}$$

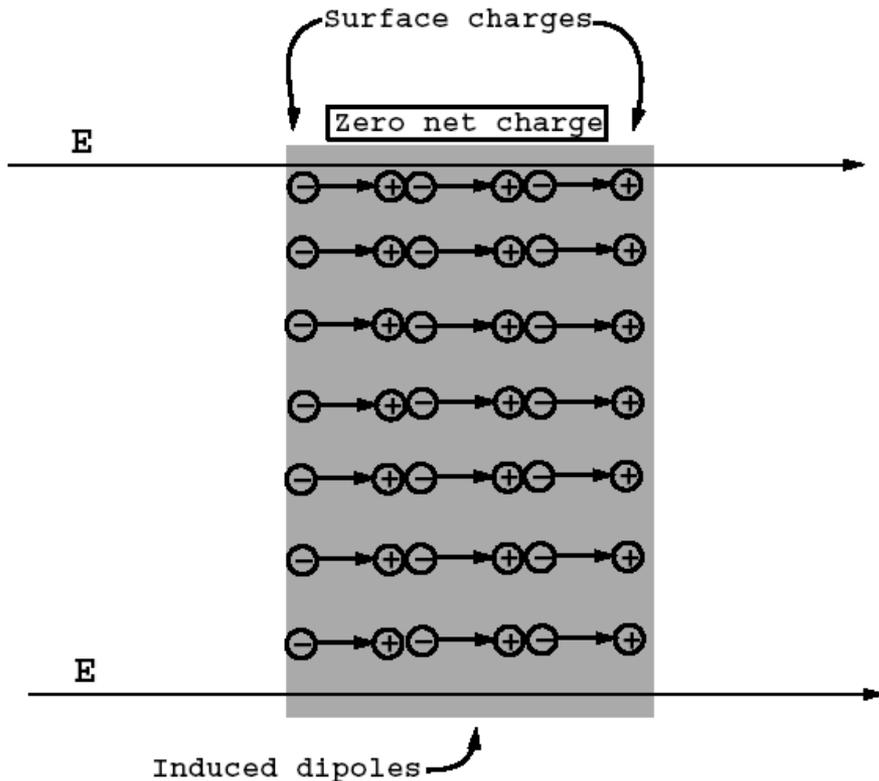
$$-\nabla \cdot \nabla V(r) = \frac{\rho(r)}{\epsilon_0 \epsilon}$$

$$u(r) = \frac{q_1 q_2}{4\pi \epsilon \epsilon_0 r}$$

# Dielectric Boundaries

- Boundary can be modeled as a step–function change in dielectric constant.
- The relevant form of the Poisson equation is:

$$-\nabla \cdot [\epsilon(r) \nabla \varphi(r)] = \frac{\rho(r)}{\epsilon_0}$$



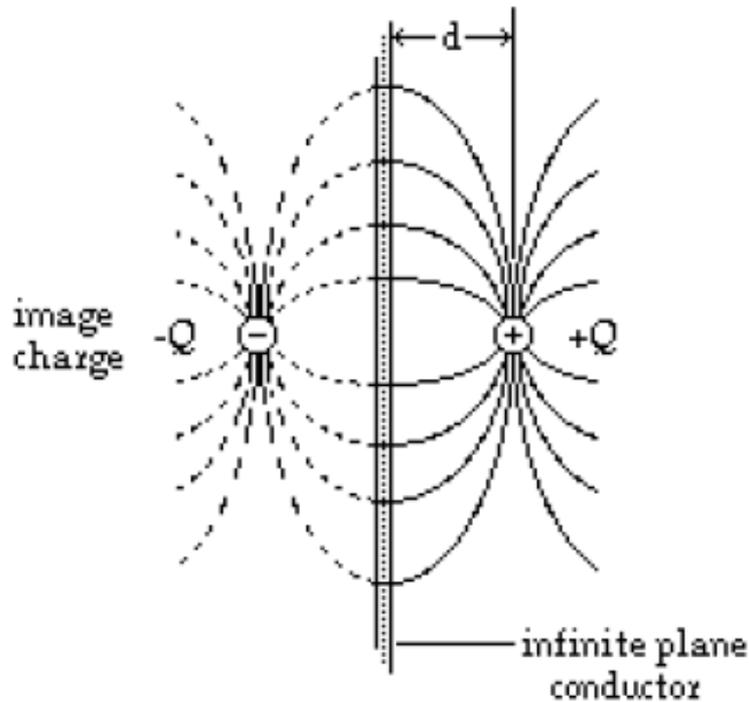
- The dielectric discontinuity can serve as a source of  $\mathbf{E}$ -field lines even if there are no source charges there ( $\rho = 0$ ).

# *Image Charges & Forces*

When a charge approaches a dielectric discontinuity:

$$q_{image} = -\left(\frac{\epsilon_2 - \epsilon_1}{\epsilon_2 + \epsilon_1}\right)Q = kQ$$

(charge is in medium with  $\epsilon_1$ )



$$\text{Force} = kQ^2/(4\pi\epsilon_0\epsilon_1(2d)^2)$$

$k < 0$  when  $\epsilon_1 < \epsilon_2$  (charge in low dielectric)  $\rightarrow$  image charge of opposite sign, *force is attractive*.

$k > 0$  when  $\epsilon_1 > \epsilon_2$  (charge in high dielectric)  $\rightarrow$  image charge of same sign, *force is repulsive*.

# Induced dipole

$$\vec{p} = \alpha \epsilon_0 \vec{E}_A$$

$\alpha$  – polarizability of the molecule

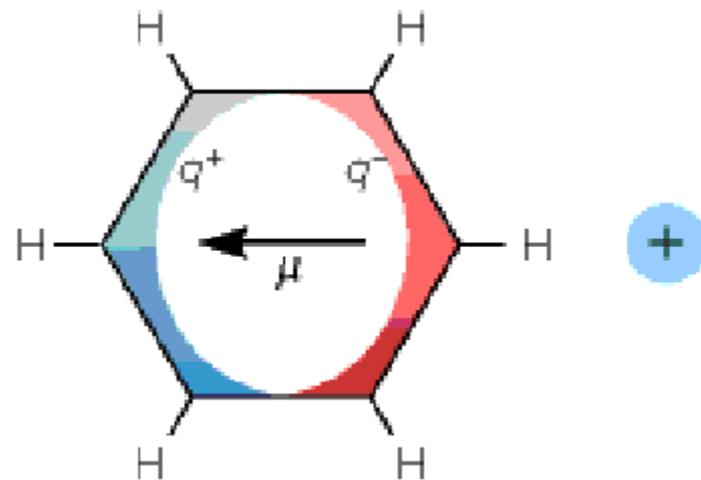


Ion-induced dipole

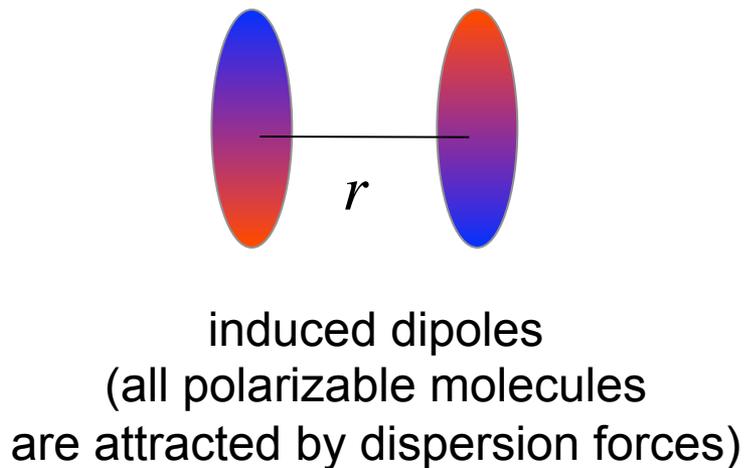
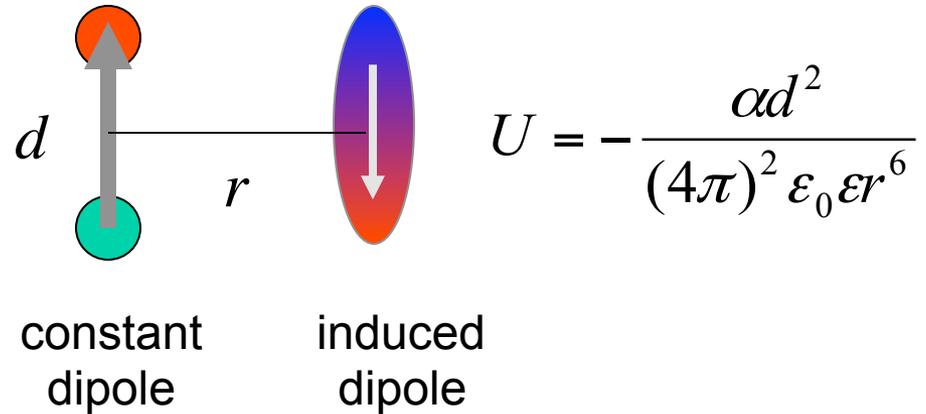
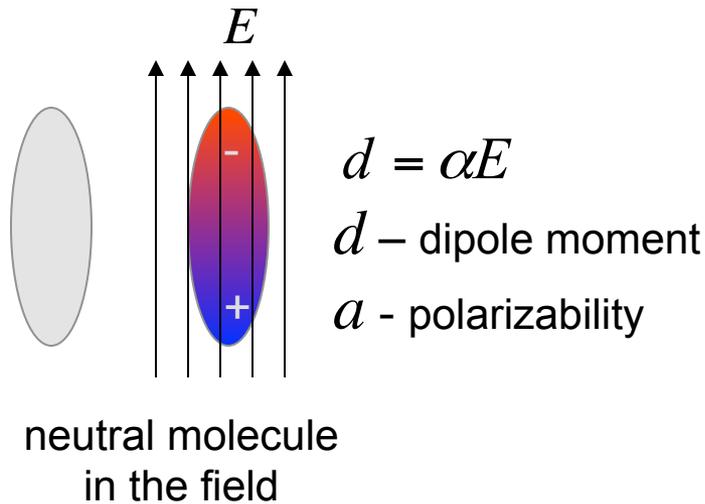
Interaction energy between the induced dipole and the inducing field

$$U = -\int_0^E \vec{p} \cdot d\vec{E} = -\int_0^E \alpha \epsilon_0 \vec{E} d\vec{E} = -\frac{1}{2} \alpha \epsilon_0 E^2$$

Induced dipoles: dependent upon polarizability of molecule, how easily electrons can shuffle around to react to a charge



# Induced dipoles and Van der Waals (dispersion) forces



$$U = - \frac{I_1 I_2 \alpha_1 \alpha_2}{(I_1 + I_2) 3n^4 r^6}$$

$I_{1,2}$  – ionization energies

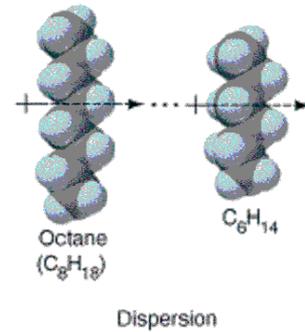
$\alpha_{1,2}$  – polarizabilities

$n$  – refractive index of the medium

*Large planar assemblies of dipoles are capable of generating long-range interactions*

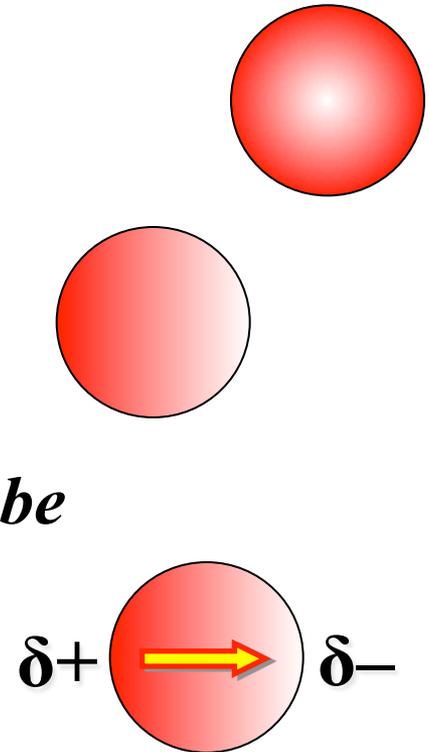
# *van der Waals interactions*

- ✚ this is a general term for the favorable interactions that occur between uncharged atoms
- ✚ van der Waals forces include:
  - permanent dipole-permanent dipole interactions
  - permanent dipole-induced dipole interactions
  - dispersion interactions
- ✚ **all have energies that depend on  $1/\text{distance}^6$**
- ✚ we consider London dispersion interactions here:
  - these are common to all atoms
  - even atoms that have no permanent dipoles (e.g. Ar)



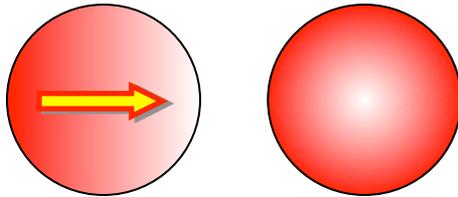
# *London dispersion interactions*

- + also known as ‘temporary dipole-induced dipole’ interactions*
- + consider an argon atom*
- + on average, its electron distribution will be spherically symmetrical:*
- + but at any instant, it will not be perfectly symmetric, e.g.:*
- + when the distribution is like this, there will be an electronic dipole:*

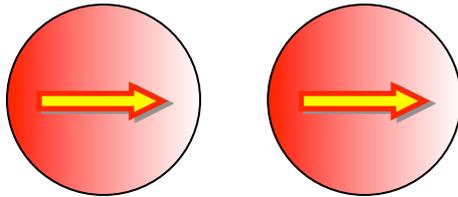


# *London dispersion interactions*

✚ *now consider a second atom adjacent to the first:*



✚ *it will be polarized by the first atom:*



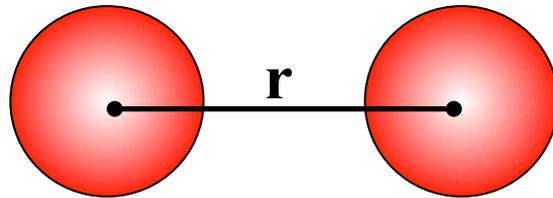
✚ *this will lead to a favorable dipole-dipole interaction between the two atoms*

✚ *the interaction occurs because the electron distributions become correlated*

# London dispersion interactions

✚ *London J Chem Soc 33, 8-26 (1937)*

✚ *the magnitude of this effect depends on the distance between the two atoms:*



*(negative energy → favorable)*

$$E_{\text{dispersion}} \propto -1 / r^6$$

✚ *it also depends on the atoms' polarizabilities ( $a$ ):*

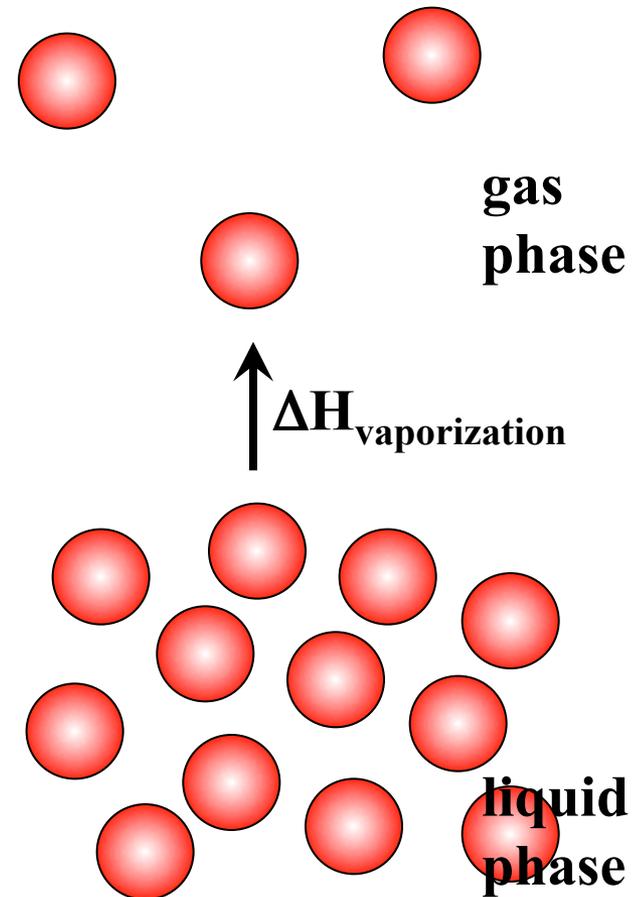
$$E_{\text{dispersion}} \propto a_{\text{atom1}} \times a_{\text{atom2}}$$

✚  *$a$  describes how much an electron distribution can fluctuate or respond to an applied electric field*

# London dispersion interactions

✚ *a (of atoms and molecules) generally increases with more electrons:*

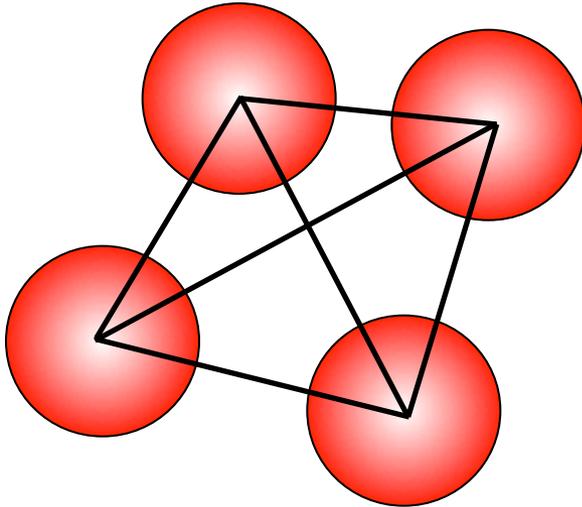
	relative polarizability	boiling point	
He	0.20	4	stronger dispersion interactions  so more energy required to do this:
Ne	0.39	27	
Ar	1.63	87	
Kr	2.46	120	
Xe	4.00	165	



# London dispersion interactions

✚ *the dispersion interaction between many atoms is usually approximated as a sum of London terms:*

$$\text{✚ } E_{\text{dispersion}} = \sum E_{\text{London}}(r_{ij})$$

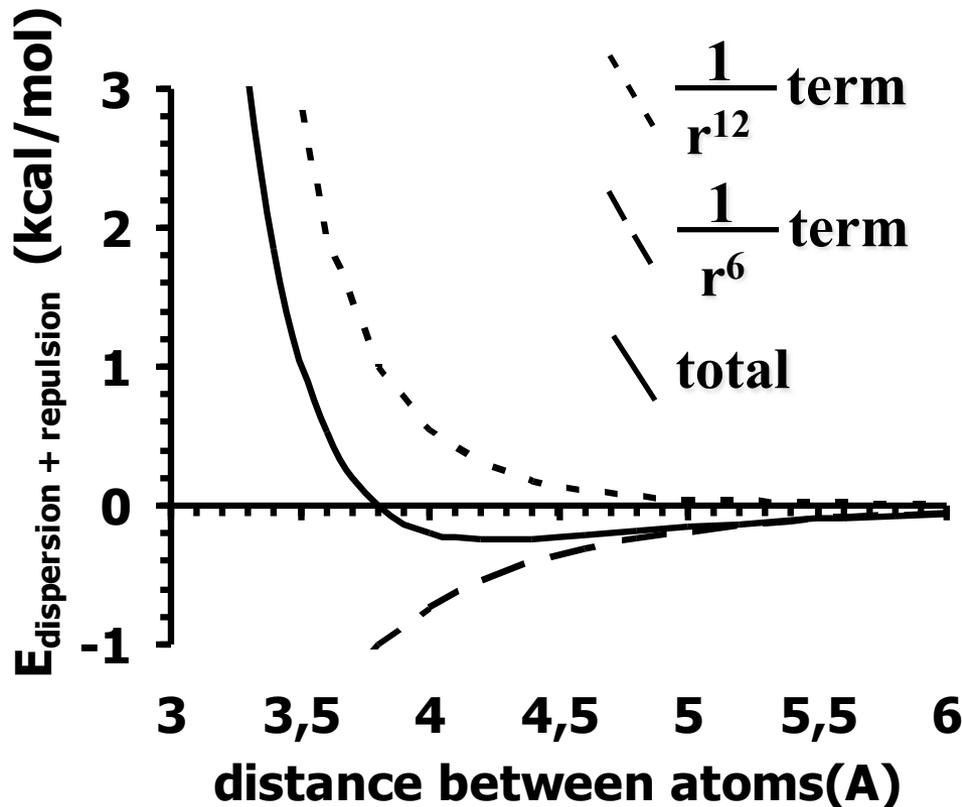


for N atoms, the total energy will be a sum of  $N(N-1)/2$  terms

✚ this is the pairwise additivity assumption

# London dispersion + sterics

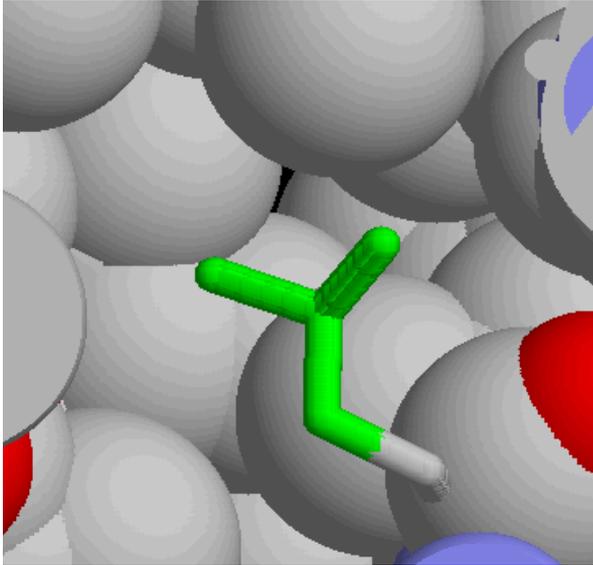
- ✚ *we can now consider the sum of the two types of interactions that we've seen so far*
- ✚ *consider approach of two uncharged atoms (e.g. Ar)*



unfavorable electron overlap dominates at short distance

favorable dispersion interaction dominates at 'long' distance

# Dispersion interactions & protein stability

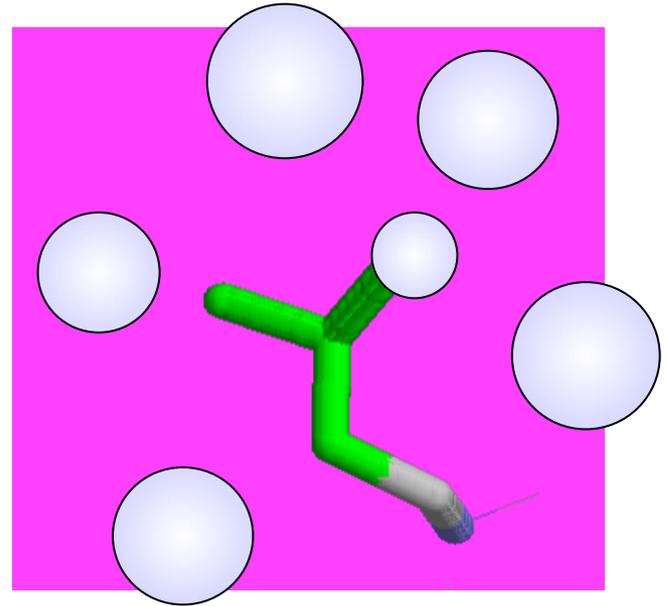


so favorable interactions with close-packed atoms in the folded state

---

are partly balanced by:

---



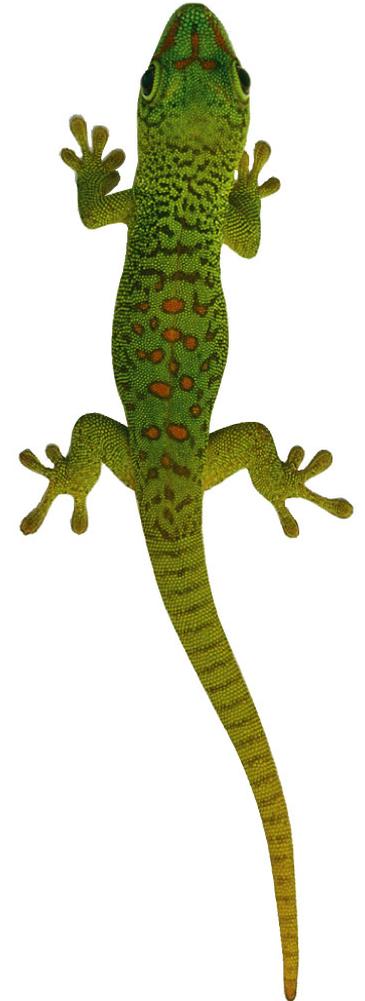
favorable interactions with water molecules in the unfolded state

- ✚ the density of atoms is higher in a protein's folded state than in water (proteins are very tightly packed) so dispersion interactions will stabilize proteins

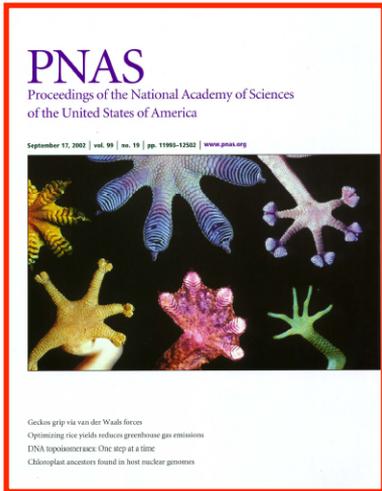
# Dispersion interactions in nature

500,000,000 (approximately)

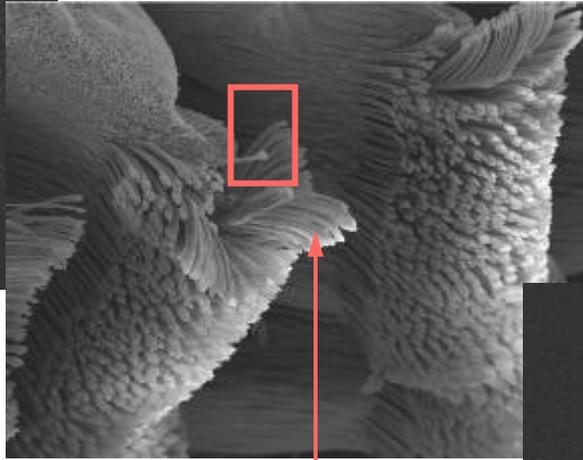
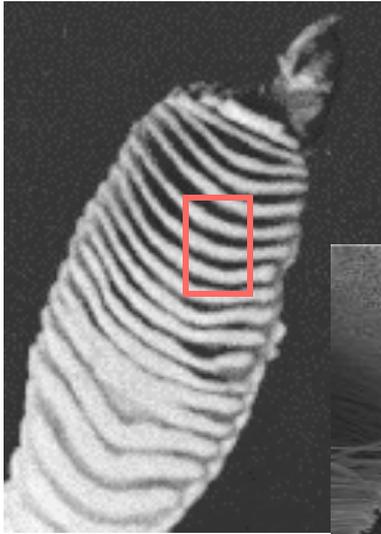
Photo: M. Moffet



Geckos get a grip  
using Van-der-Waals-  
forces

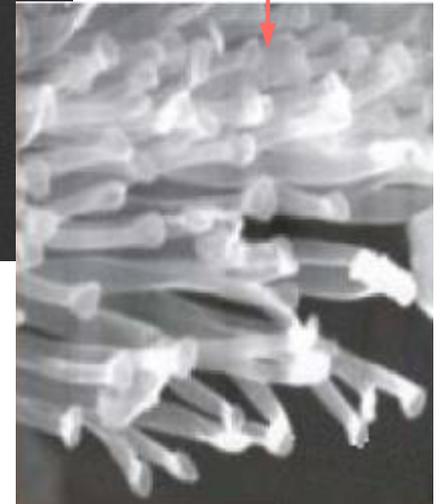
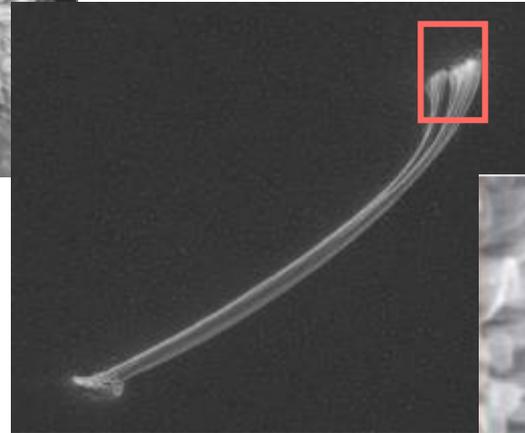


*Autumn et al. PNAS 99, 12252-12256 (2002)*

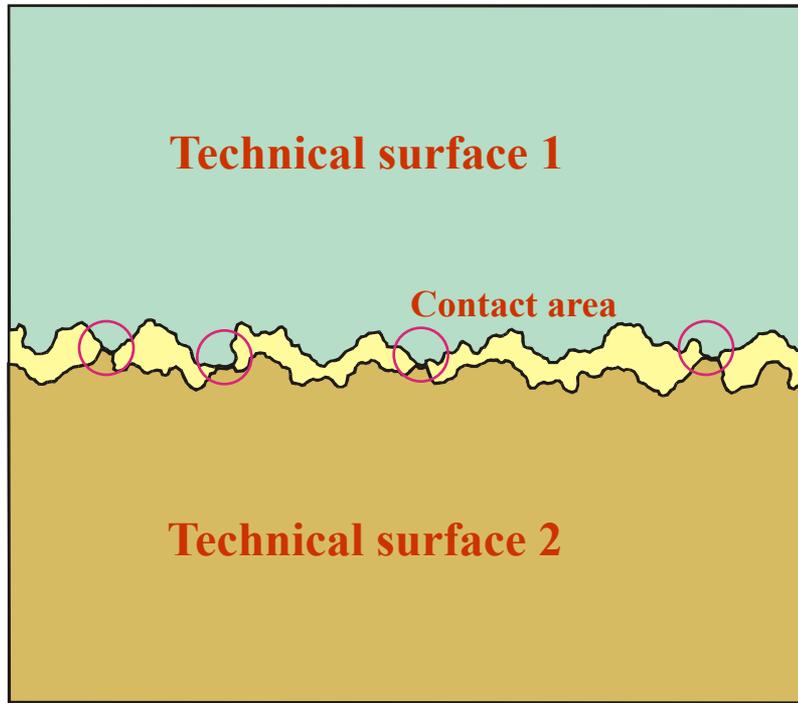


The Gecko toe has 500000 microhairs (setae)

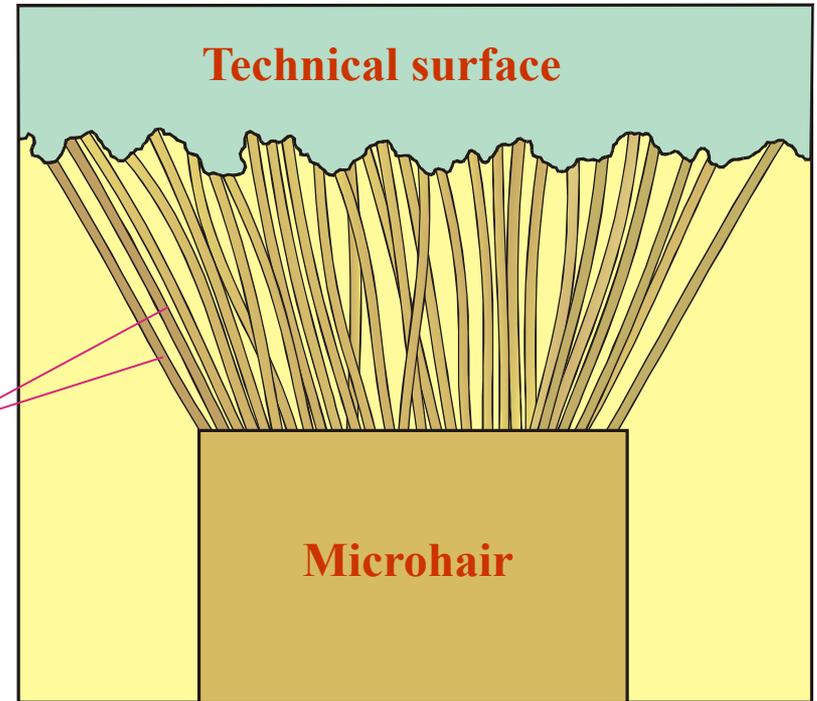
The seta has 1000 nanohairs



*Nanostructure of the Gecko toe*



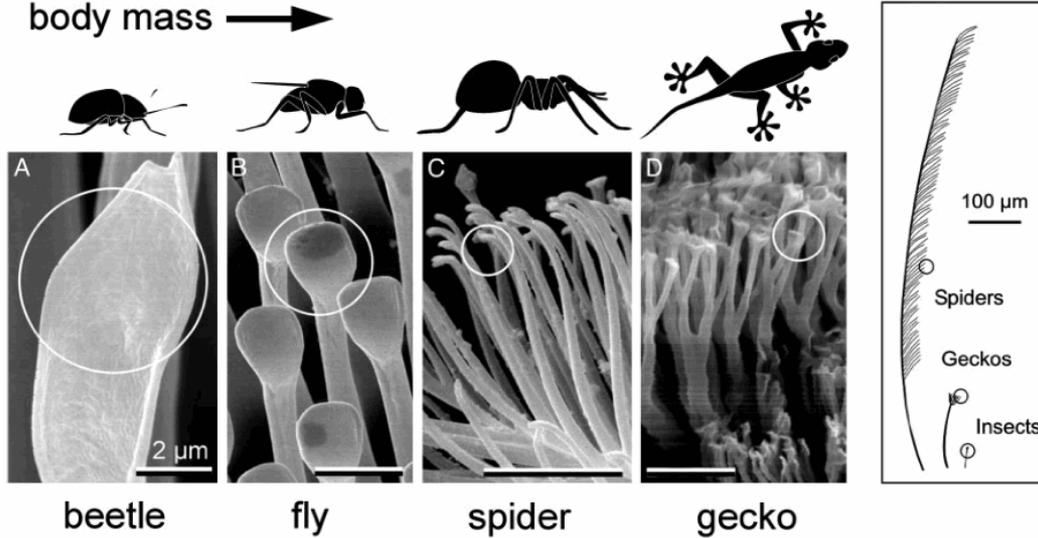
The Gecko effect through  
Adhesion effect through  
Van-der-Waals-forces



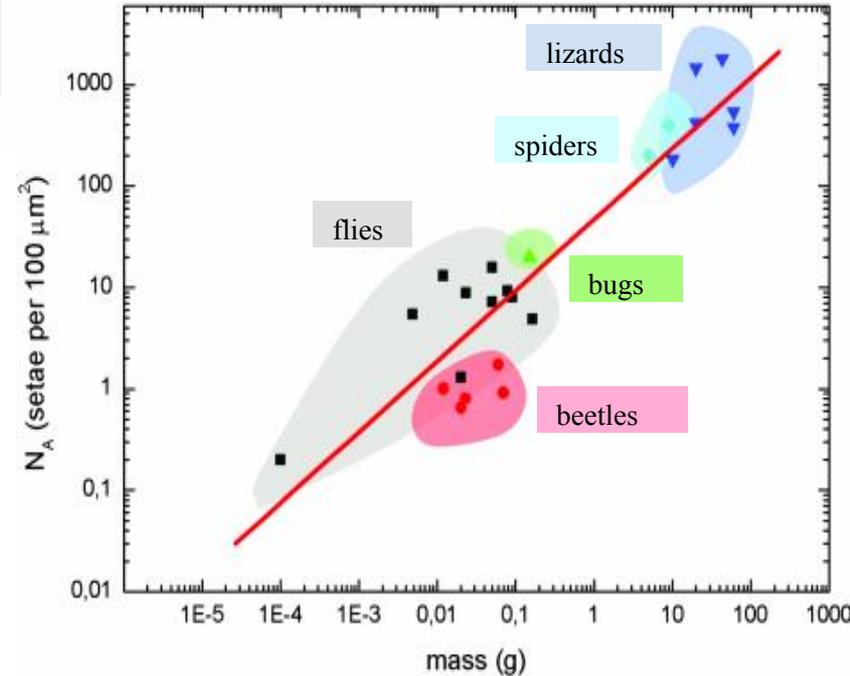
~~Small contact area~~  
~~large contact area~~  
~~large adhesion force~~

If all of a gecko's setae were stuck to a surface at the same time it would be able to support **140 kg!**

body mass →



(“From micro to nano contacts in biological attachment devices,” Arzt et al., PNAS 100(19) 2003))

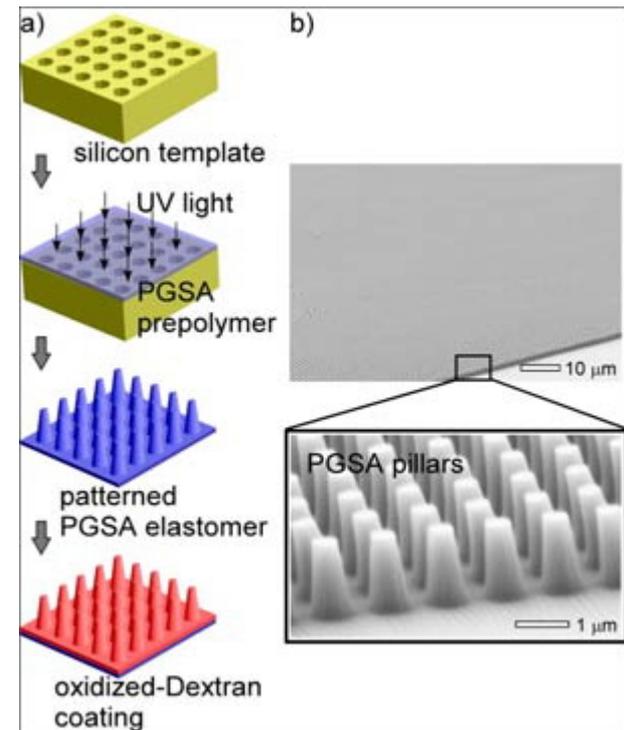


**Small insects:** Compliant pads (to shape themselves to rough surfaces) + sweat

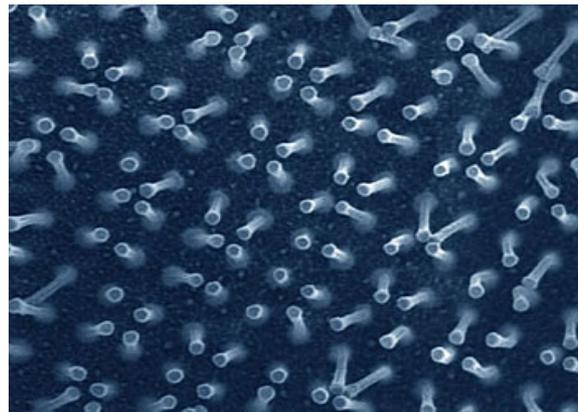
**Medium insects:** Multiple pads per leg + sweat

**Spiders and lizards:** Lots of pads (hair) per foot - but dry / no secretions

# Stanford University's Sticky Bot



# Gecko-Tape



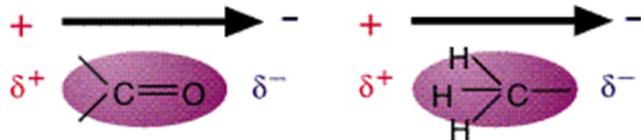
# Electrostatic Steering

<i>System</i>	<i>Potential dependence on distance</i>	<i>Energy [kJ/mol]</i>
<i>ion-ion</i>	$r^{-1}$	<b>250</b>
<i>ion-dipole</i>	$r^{-2}$	<b>15</b>
<i>dipol – dipol</i>	$r^{-3}$	<b>2</b>
<i>London</i>	$r^{-6}$	<b>1</b>

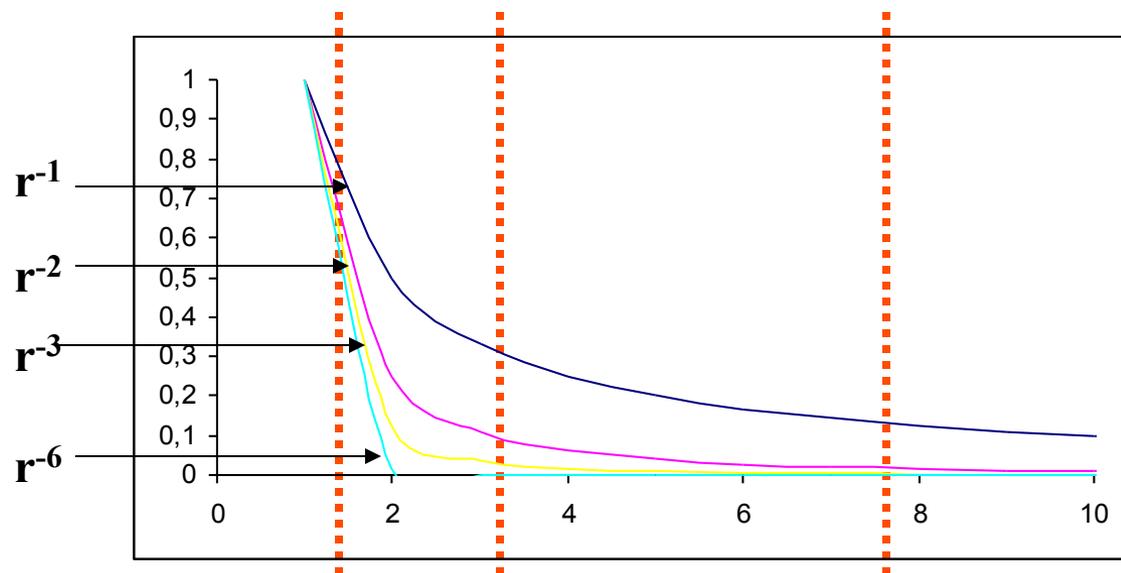
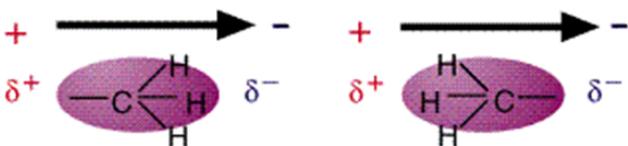
Dipole - dipole interactions



Dipole - induced dipole interactions



Induced dipole - induced dipole interactions



# *Interaction between ions and macromolecules*

## *Non-specific screening effects*

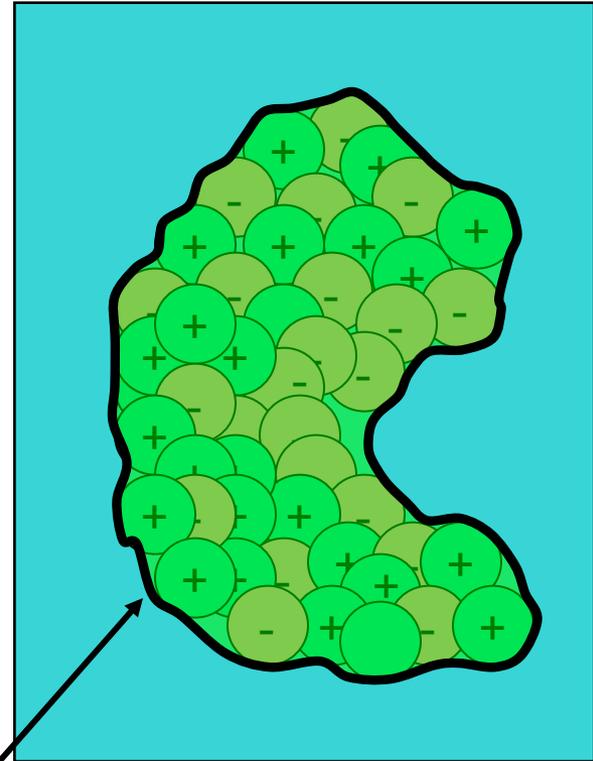
- Depends only on ionic strength (not species)
- Results of damped electrostatic potential
- Described by Debye-Hückel and Poisson-Boltzmann theory for low concentration

## *Site-specific binding*

- Ionic specific (*concentration* of specific ion, not necessarily ionic strength)
- Site geometry, electrostatics, coordination, etc. enables favorable binding
- Influences
  - Co-factors
  - Allosteric activation
  - Folding (RNA)

# *Polar solvation: Poisson equation*

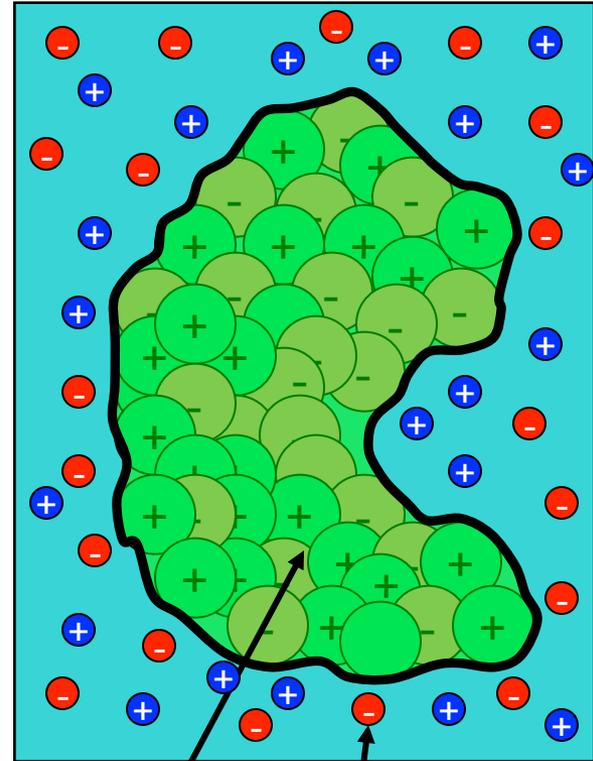
- Poisson equation
  - Classic equation for continuum electrostatics
  - Can be derived from hard sphere dipolar solvent
- Assumptions
  - No dielectric saturation (linear response)
  - No solvent-solvent correlation (local response)



$$\begin{aligned} -\nabla \cdot \varepsilon(\mathbf{x}) \nabla u(\mathbf{x}) &= 4\pi\rho(\mathbf{x}) && \text{for } \mathbf{x} \in \Omega \\ u(\mathbf{x}) &= u_0(\mathbf{x}) && \text{for } \mathbf{x} \in \partial\Omega \end{aligned}$$

# *Polar solvation: Boltzmann equation*

- Mean field model
  - Include “mobile” charges
  - Boltzmann distribution
  - Ignore charge-charge correlations
    - Finite ion size
    - Weak ion-ion electrostatics
    - Low ion correlations
- Missing ion “chemistry”
  - No detailed ion-solvent interactions
  - No ion coordination, etc.

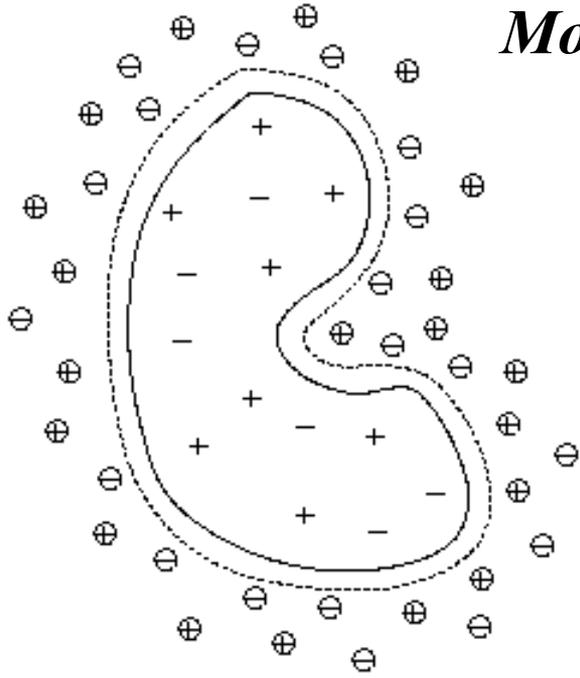


$$\begin{aligned}\rho(\mathbf{x}) &= \rho_f(\mathbf{x}) + \rho_m(\mathbf{x}) \\ &= \rho_f(\mathbf{x}) + \sum_i q_i c_i e^{-q_i u(\mathbf{x}) - V_i(\mathbf{x})}\end{aligned}$$

# Poisson-Boltzmann equation

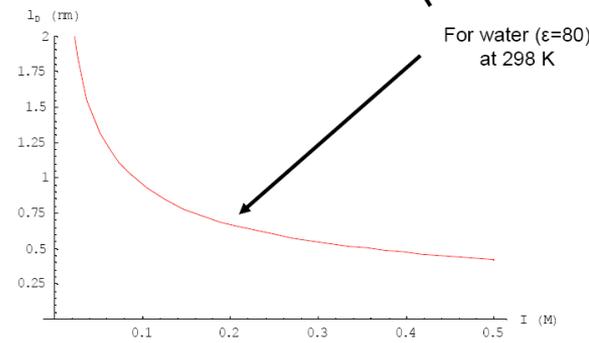
The space – dielectric properties

Mobile charge distribution



$$4\pi\rho(x)$$

$$l_D = \kappa^{-1} = \sqrt{\frac{\epsilon_0 \epsilon k_B T}{2000 N_{av} e^2 I}} = \frac{(0.3 \text{ nm M}^{1/2})}{\sqrt{I}}$$



$$-\nabla \cdot \epsilon(x) \nabla \phi(x) = 4\pi \sum_i q_i \delta(x - x_i) + 4\pi\rho(x)$$

$$\phi(\infty) = 0$$

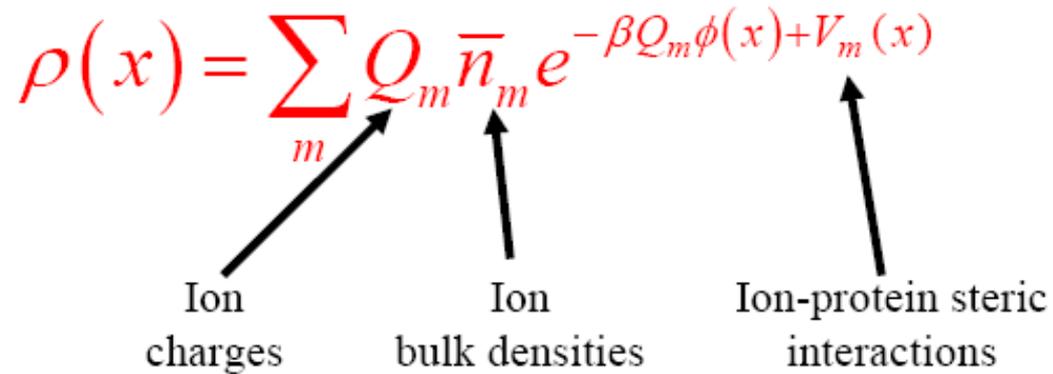
$$\kappa^2 = \frac{\sum_{i=1}^M Q_i^2 N_i}{\epsilon_0 \epsilon k_B T} = \frac{1000 N_{av} e^2 \sum_{i=1}^M z_i^2 c_i}{\epsilon_0 \epsilon k_B T} = \frac{2000 N_{av} e^2 I}{\epsilon_0 \epsilon k_B T}$$

Avogadro's # (6.02 × 10<sup>23</sup> mol<sup>-1</sup>)  
 Electron charge (1.60 × 10<sup>-19</sup> C)  
 Species charge (e)  
 Ionic strength (M)  
 Species concentration (M)

$$I = \frac{1}{2} \sum_{i=1}^M z_i^2 c_i$$

## *Mobile ion charge distribution form:*

- Boltzmann distribution – no explicit ion-ion interaction
- No detailed structure for atom (de)solvation

$$\rho(x) = \sum_m Q_m \bar{n}_m e^{-\beta Q_m \phi(x) + V_m(x)}$$


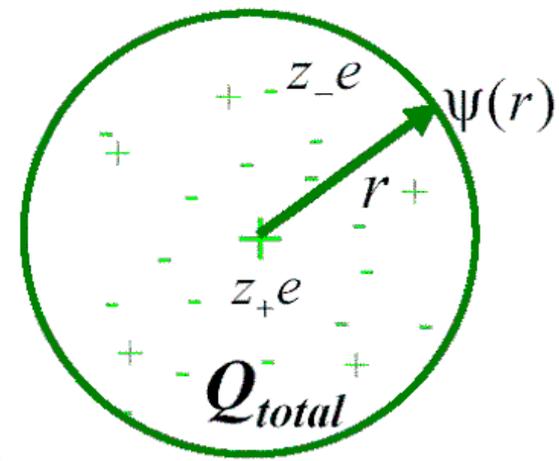
Ion charges      Ion bulk densities      Ion-protein steric interactions

Result: Nonlinear partial differential equation

$$-\nabla \cdot \epsilon(x) \nabla \phi(x) - 4\pi \sum_m Q_m \bar{n}_m e^{-\beta Q_m \phi(x) + V_m(x)} = 4\pi \sum_i q_i \delta(x - x_i)$$
$$\phi(\infty) = 0$$

For not very high ion concentrations  $\kappa a \ll 1$

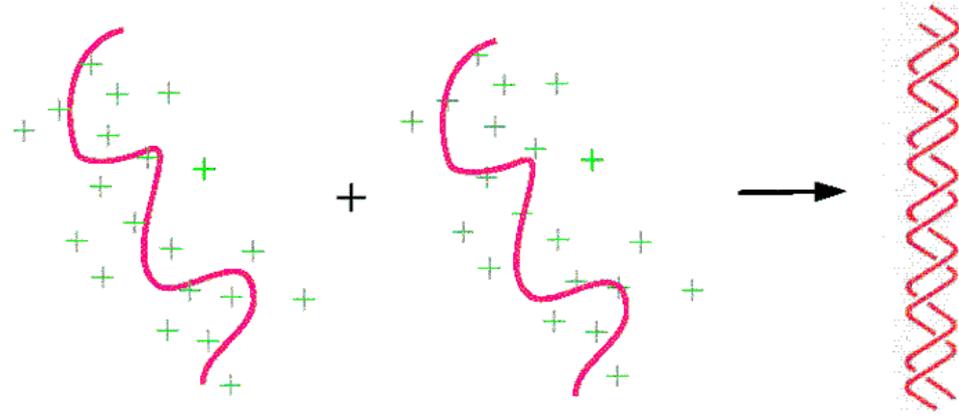
$$V(r) = \frac{z_+ e}{4\pi\epsilon\epsilon_0 r} e^{-\kappa r}$$



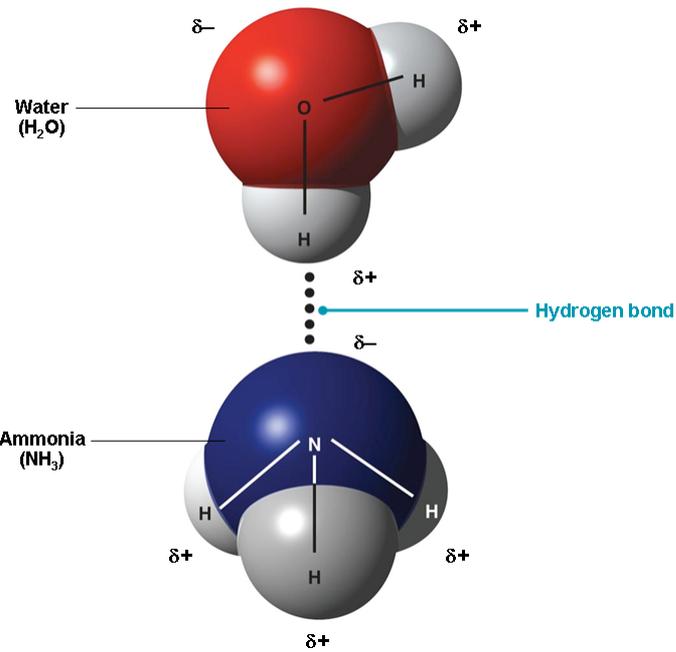
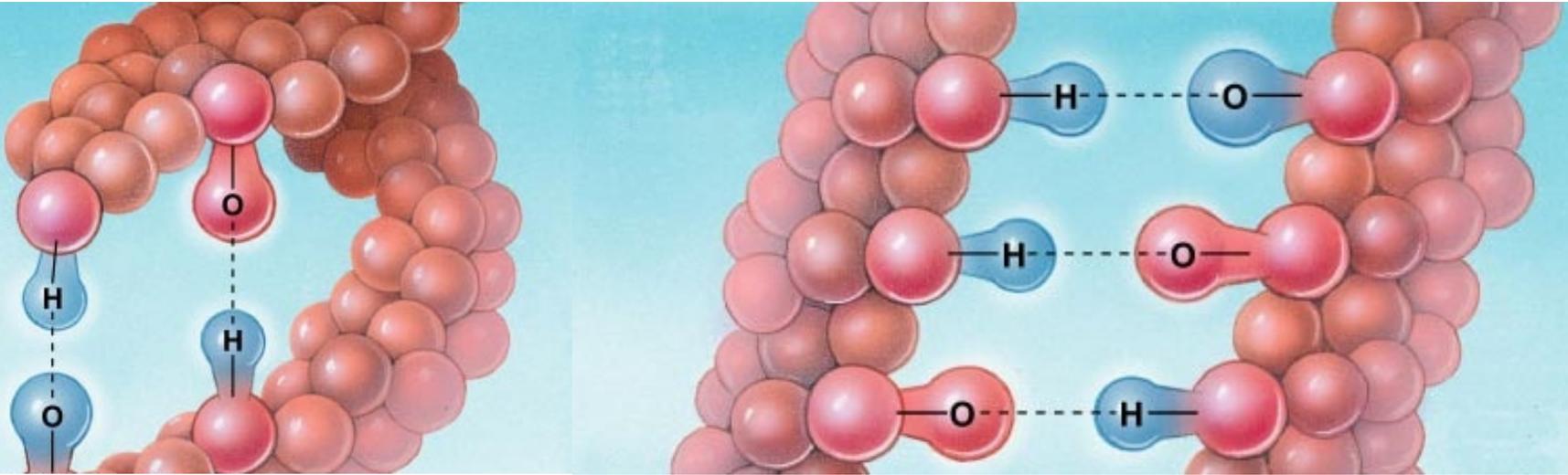
□ Viewed from beyond the counterion cloud, the macroion appears neutral.

□ Macroions will not feel each other until they're nearby

□ Once they are nearby, the detailed surface pattern of charges can be felt by its neighbor, not just overall charge - stereospecificity.



# Hydrogen bonds

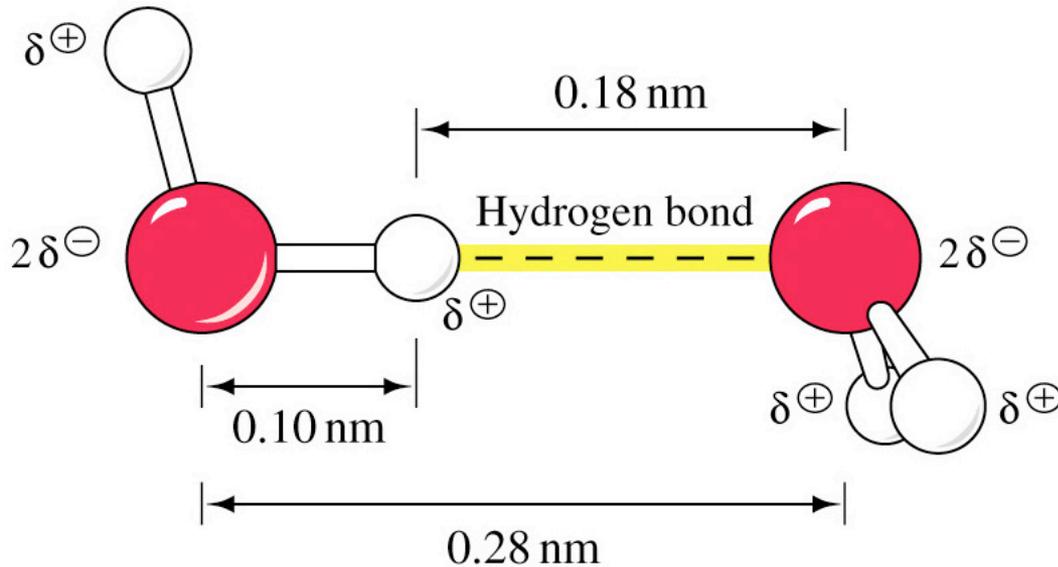


The hydrogen bonds is in the range of **3 - 40** kcal mol<sup>-1</sup>.

The covalent bond between H and O in water is about **492** kJ mol<sup>-1</sup>.

The van der Waals interaction is about **5.5** kJ mol<sup>-1</sup>.

A **hydrogen bond** consists of a hydrogen atom lying between two small, strongly electronegative atoms with lone pairs of electrons (N, O, F).

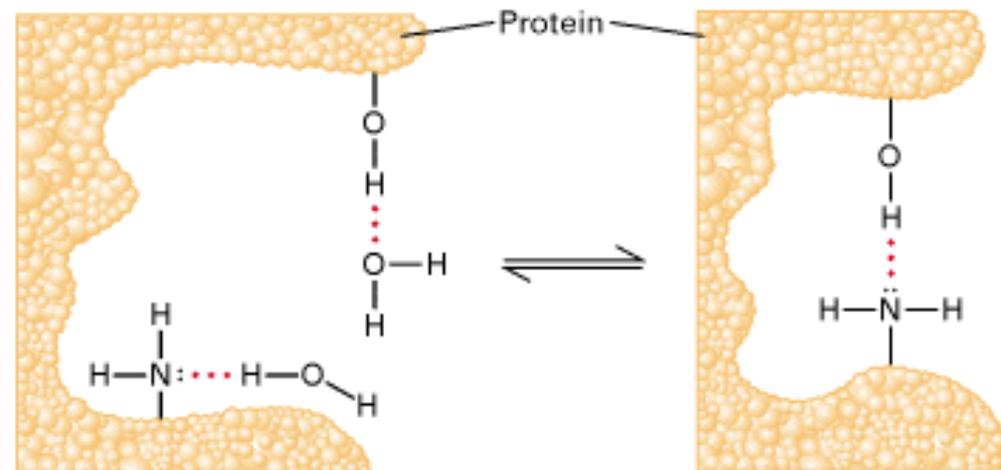


Strength of an H-bond is related to the **D-H---A**

- Distance

- The D-H-A angle.

The hydrogen bond is stronger than typical electrostatic interactions between partial charges, but ***it is easily disassociated by heat or by interaction with other atoms.***



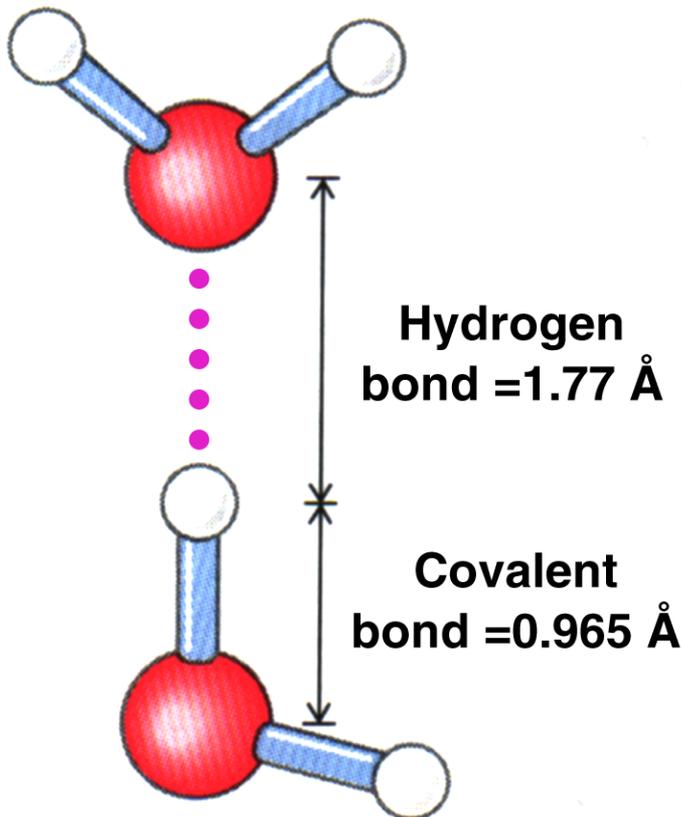
# *Distance*

Van der Waals radius of

H: **1.1 Å**, O **1.5 Å**.

The closest approach should be **2.6 Å**.

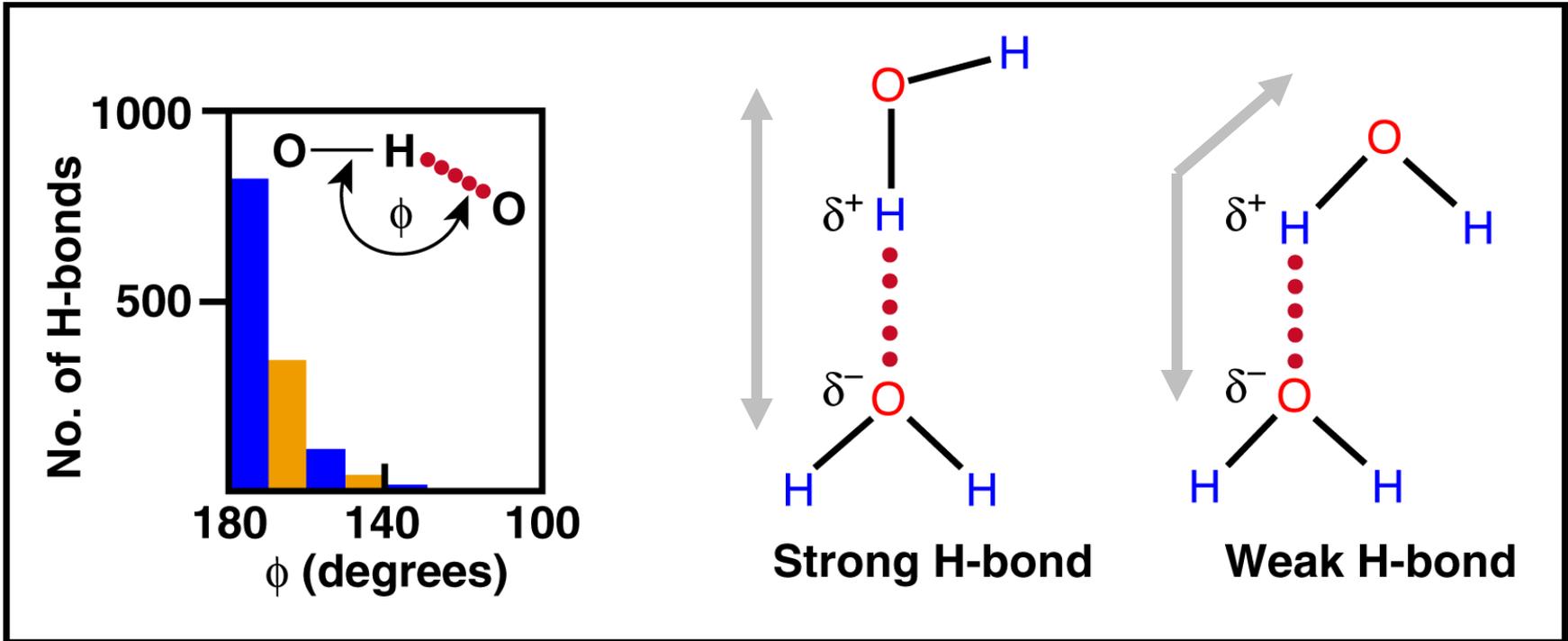
Separation is about 1 Å less! It is **1.76 Å**.



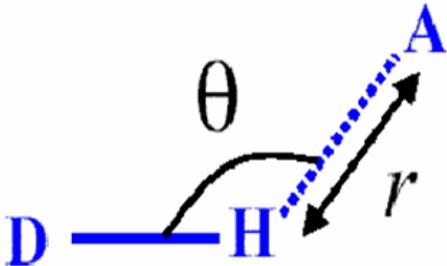
*Intermediate between  
VdW distance and  
typical O-H covalent  
bond of 0.96 Å.*

*The shorter the distance  
between D & A the stronger  
the interaction.*

# Hydrogen bond is directional

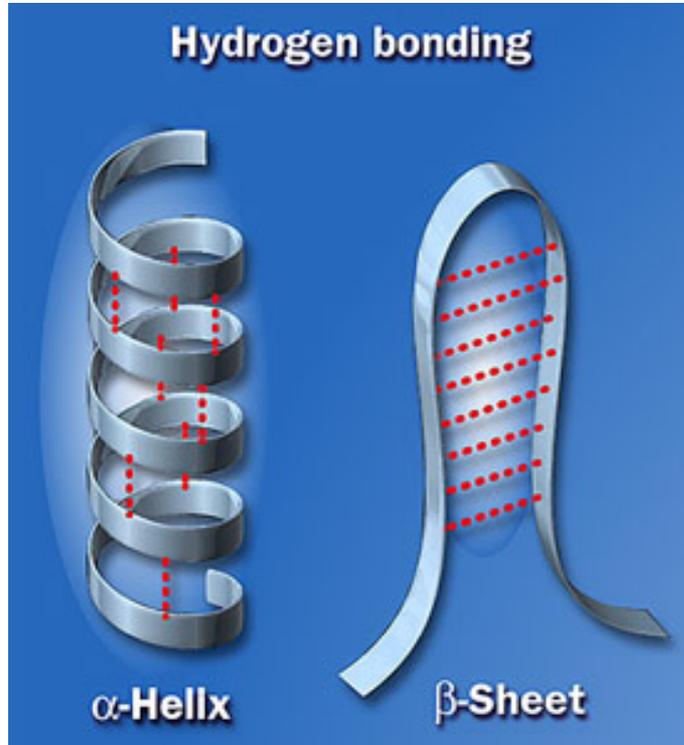


## Hydrogen bond potential energy

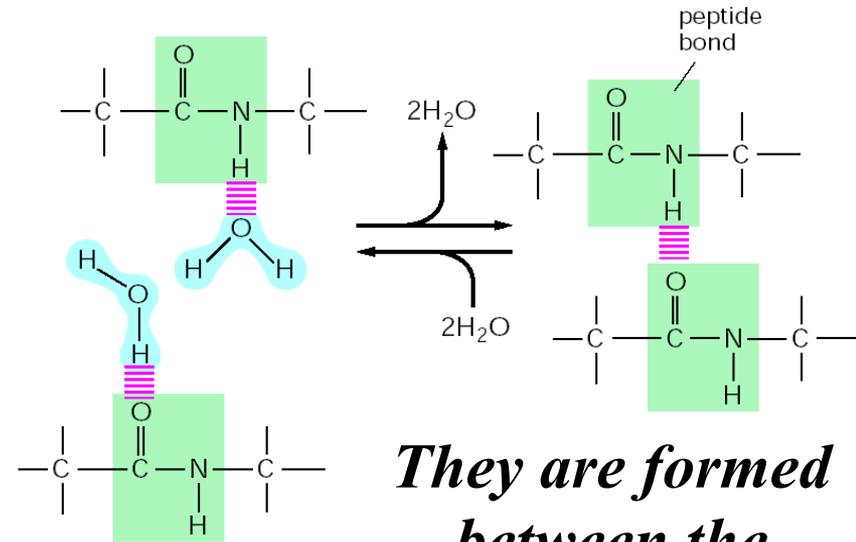


$$U = \left( \frac{A}{r^{12}} - \frac{B}{r^6} \right) \cos \theta + \left( \frac{A'}{r^{12}} - \frac{B'}{r^6} \right) (1 - \cos \theta)$$

*The hydrogen bonds define secondary structure of proteins.*



*Hydrogen bonds define protein binding specificity*



*They are formed between the backbone oxygens*

