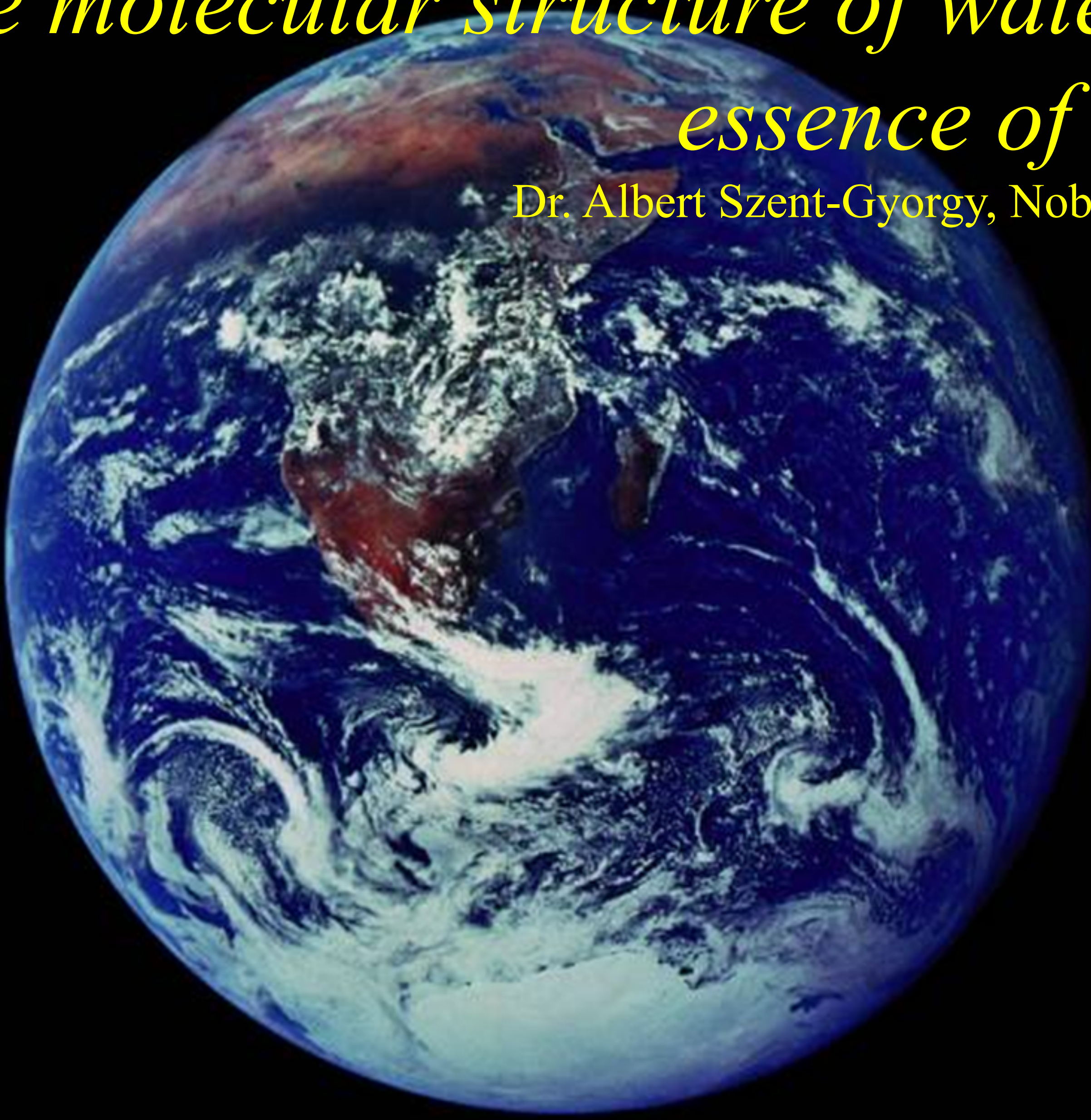
„the molecular structure of water is the essence of all life"

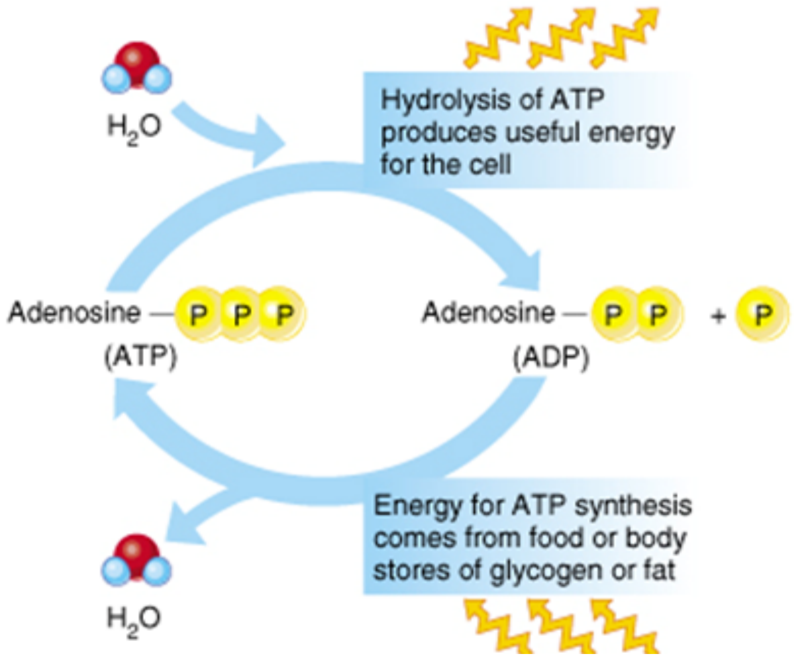
Dr. Albert Szent-Gyorgy, Nobel Prize winner

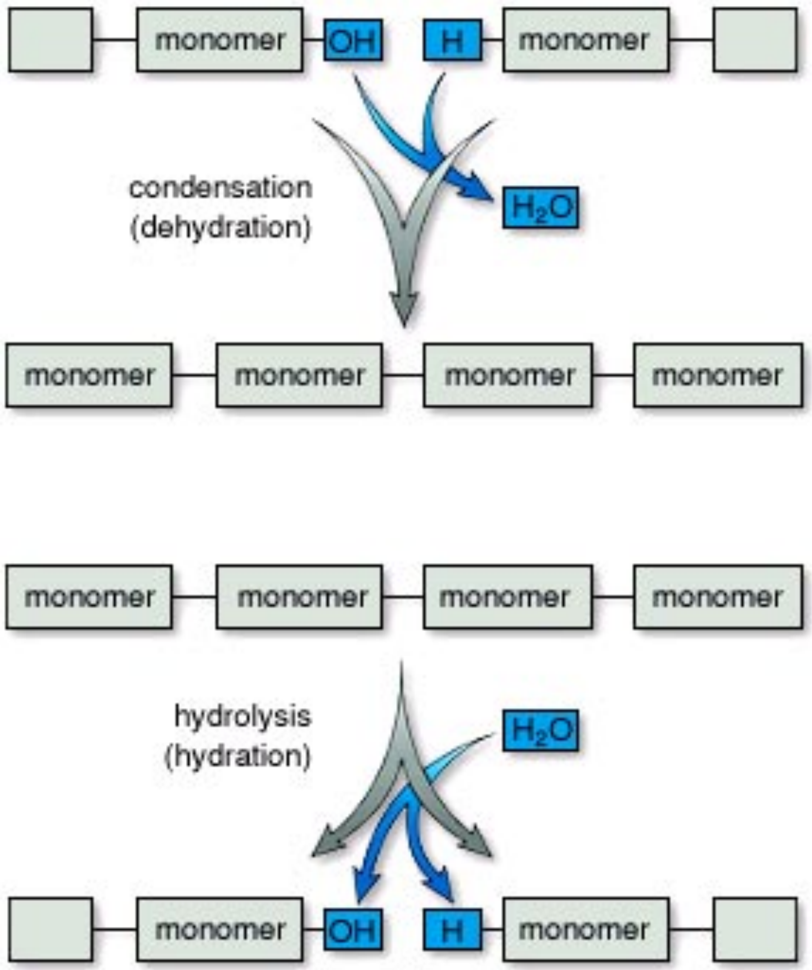


Water as a reactant

$$C_6H_{12}O_6 + 6O_2 \Rightarrow 6H_2O + 6CO_2 + \text{energy}$$

$$ATP + H_2O \Rightarrow ADP + H_3PO_4 + \text{energy}$$



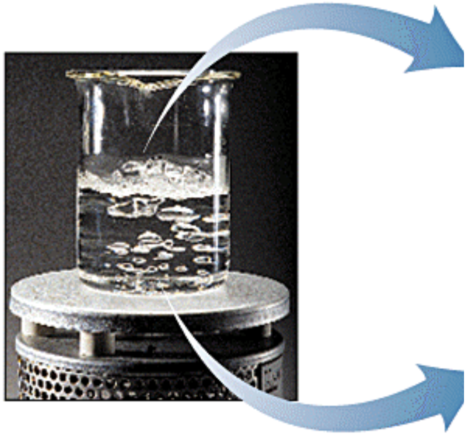


Polimerization, condensation, hydrolysis

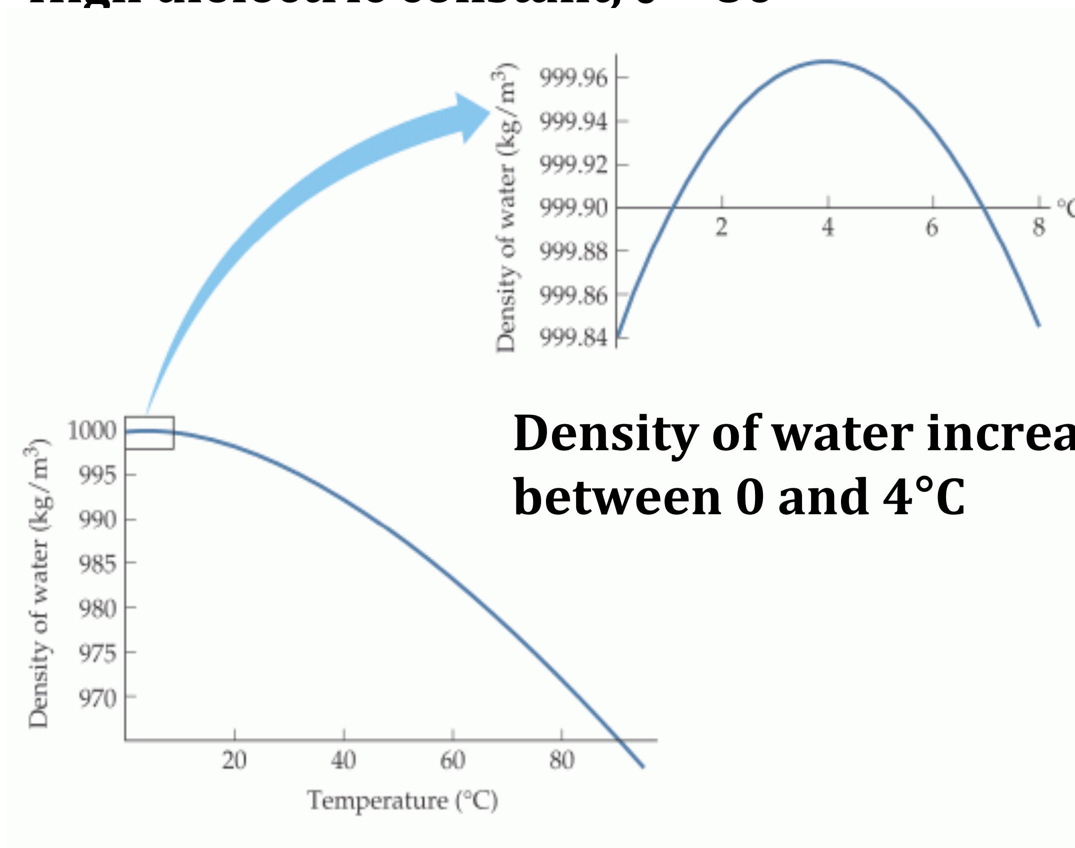
Selected properties of water

- **High boiling point**
- **High viscosity (0.89 cP, at 25°C)**
- **High surface tension (72.75 mJ/m^2, at 20°C)**
- **A low thermal expansivity (0.00021/°C at 20°C)**
- **High specific heat capacity (C_V =4.18 J g^{-1} K^{-1} at 25°C)**
- **The dielectric constant is high (78.4 at 25°C)**
- **Conductivity of protons is anomalously high**

Water is an anomalous liquid



Boiling: 100°C (expected -80°C)
Melting: 0°C (expected -95°C)
High dielectric constant, ε = 80

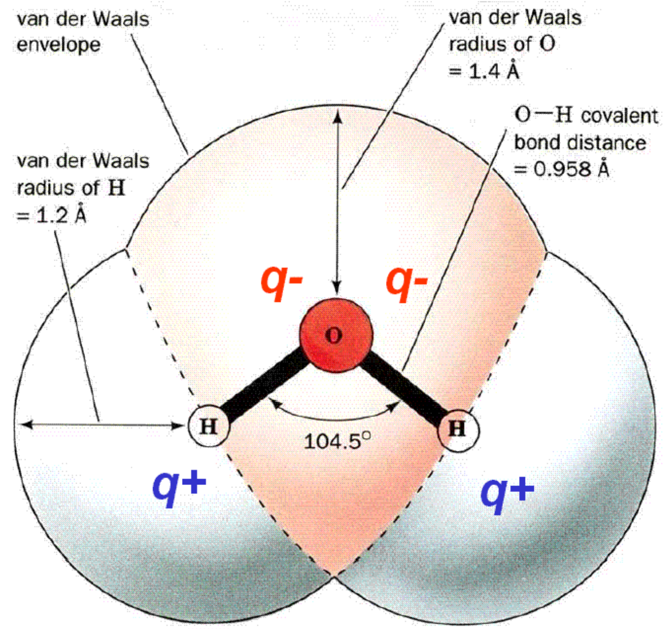


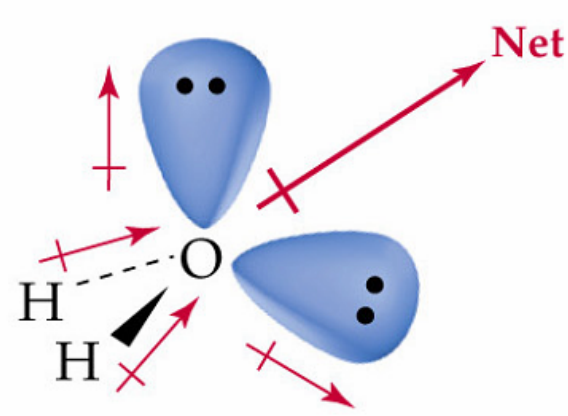
Density of water increases between 0 and 4°C

These anomalies can be explained by the presence of interactions holding together the water molecules.

The water molecule

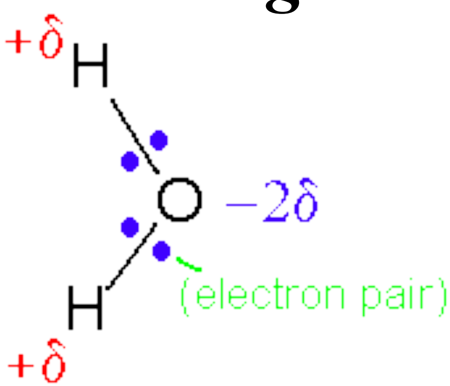
Oxygen is electronegative it draws the electrons in the bonds it shares with the hydrogen atoms towards it.

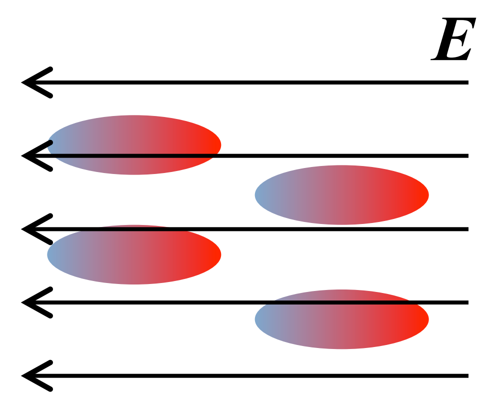




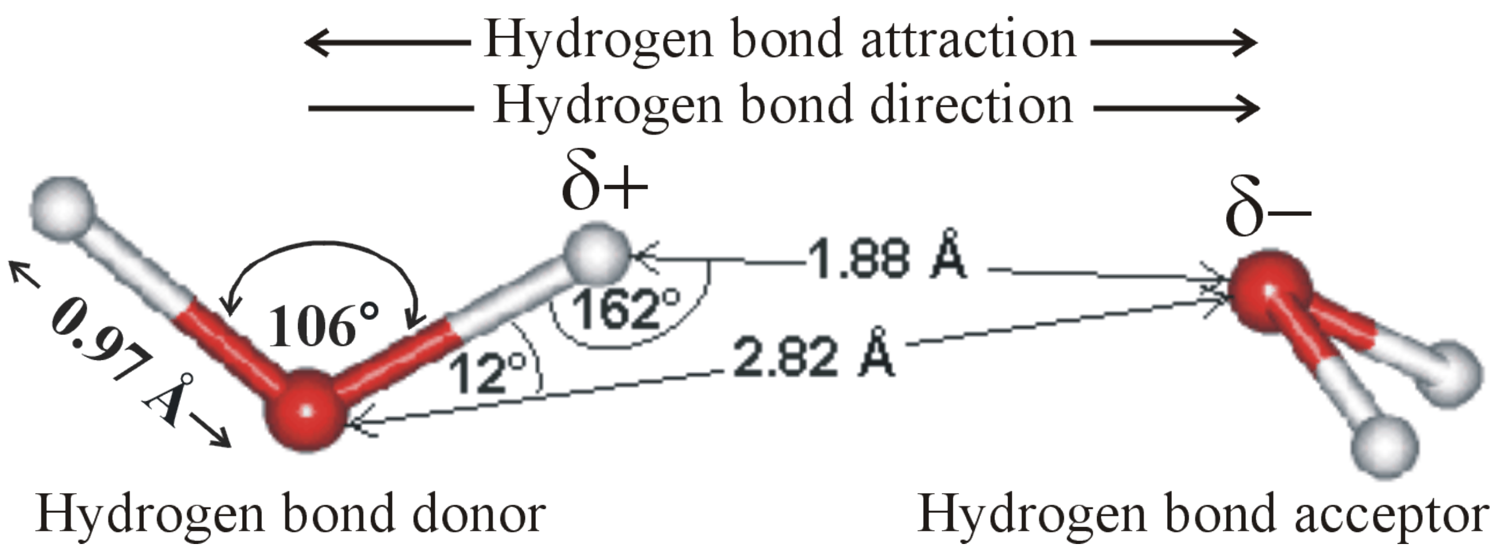
Dipole moment = 1.85 Debye
= 6x10^{-30} Cm

Water has large dielectric constant

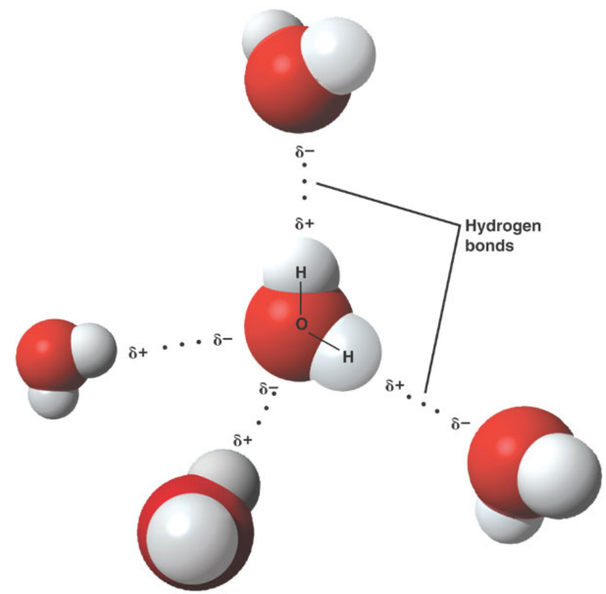




Hydrogen bonds

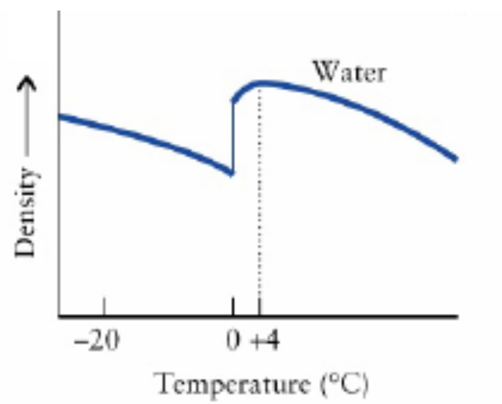


Each water molecule acts as both an H donor and an H acceptor, allowing clusters of molecules to form.

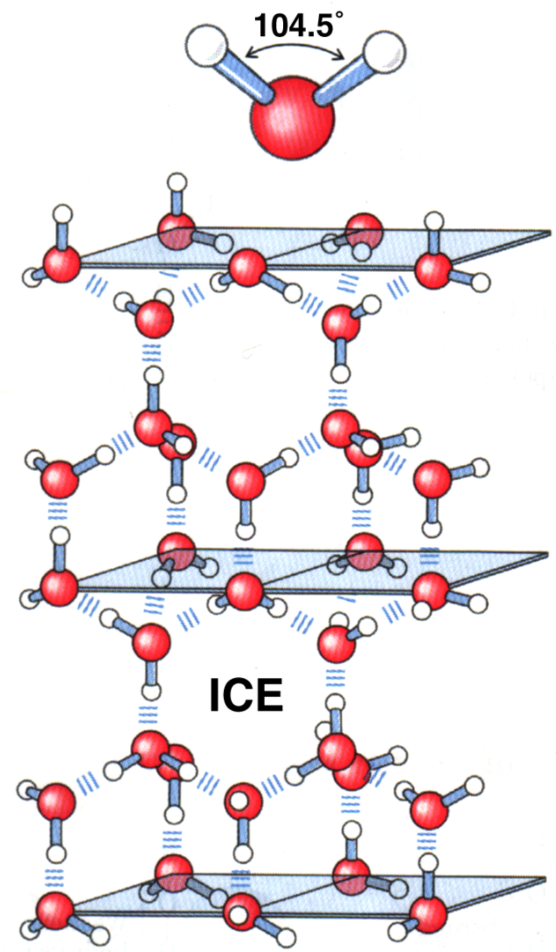


Solid phase - ice

- H-bonding network
- 4 neighbors per molecule
- lower density than liquid water



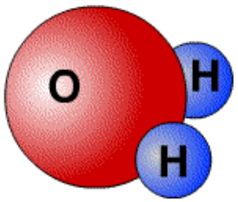
Solid Ice vs. Solid Benzene



Only 42% of the volume is filled by the van der Waals volumes of the atoms, compared to 74% for spherical close packing.

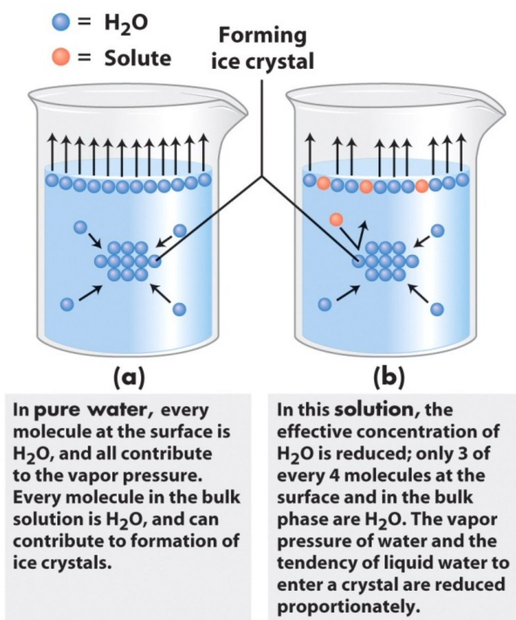
Liquid phase - water

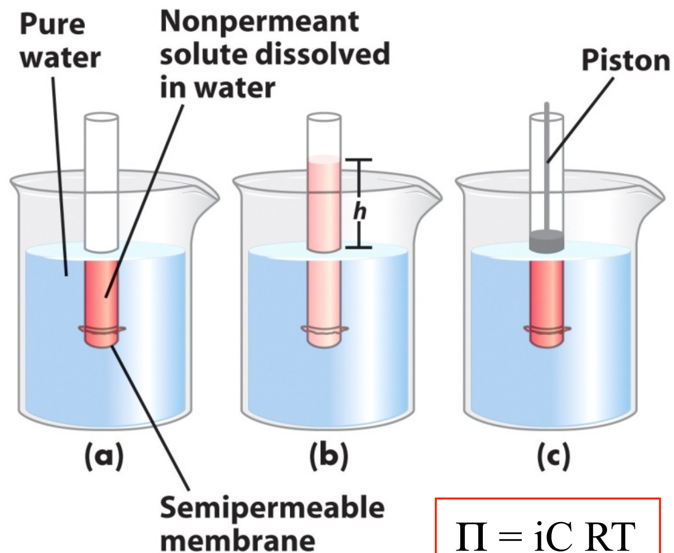
- The number of nearest neighbors in water is 4.4 (4 in ice).
- Hydrogen bonds half life = 10^{-11} - 10^{-15} sec.
- ***Cooperativity in hydrogen bond formation*.**



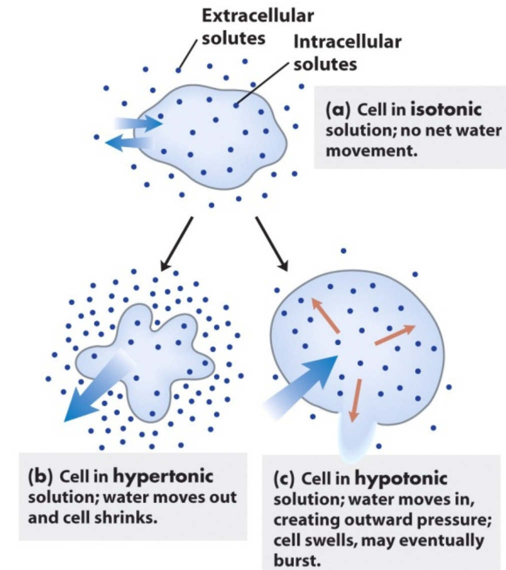
The H-bonding propensity of the water together with the tetrahedral geometry, leads to ***a higher entropy in the bulk phase***.

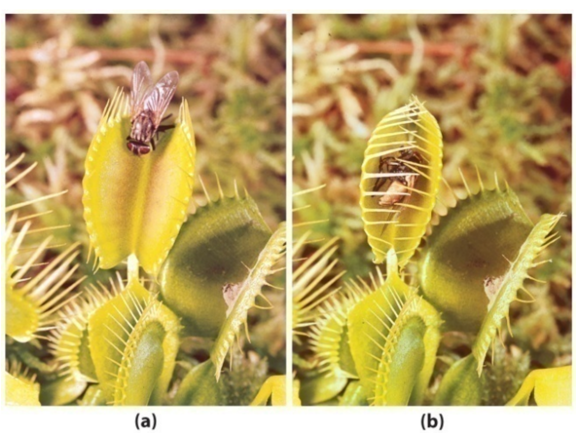
Solutes affect the Colligative Properties of aqueous solutions (vapor pressure, boiling point, freezing point, and osmotic pressure)



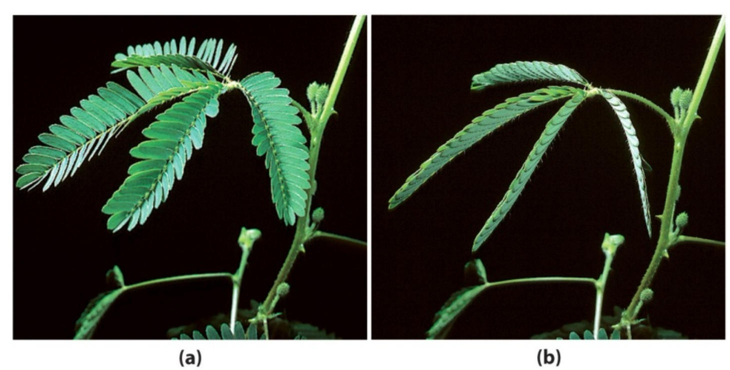


$$\Pi = iC\,RT$$





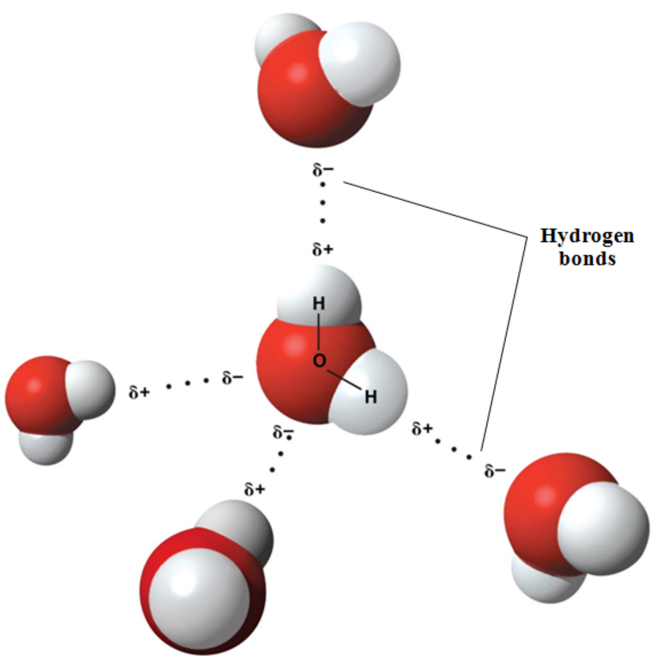
Venus flytrap

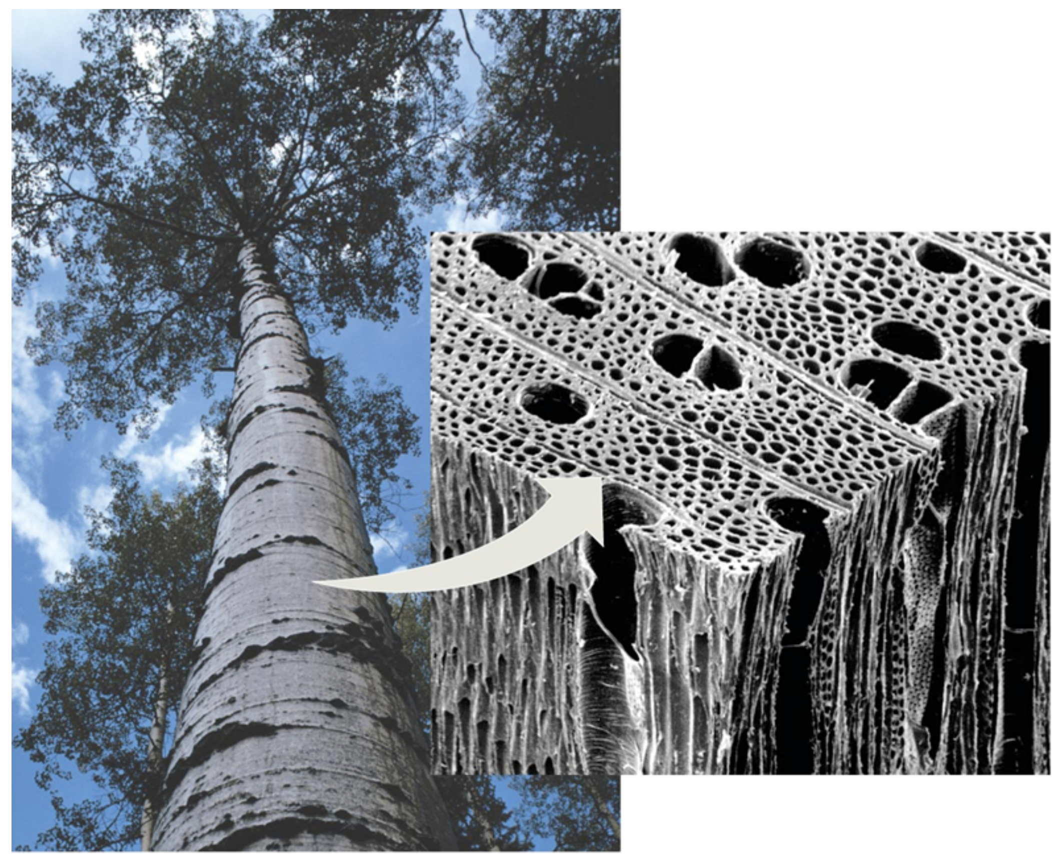


Mimosa pudica

Cohesion

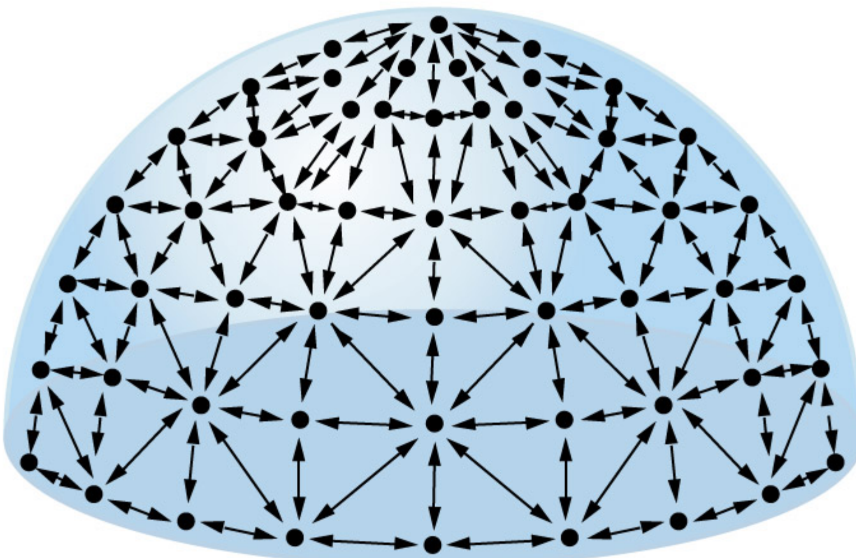
- Collectively, hydrogen bonds hold water molecules together, a phenomenon called cohesion.
- Cohesion helps the transport of water against gravity in plants.
- Adhesion of water to plant cell walls also helps to counter gravity.



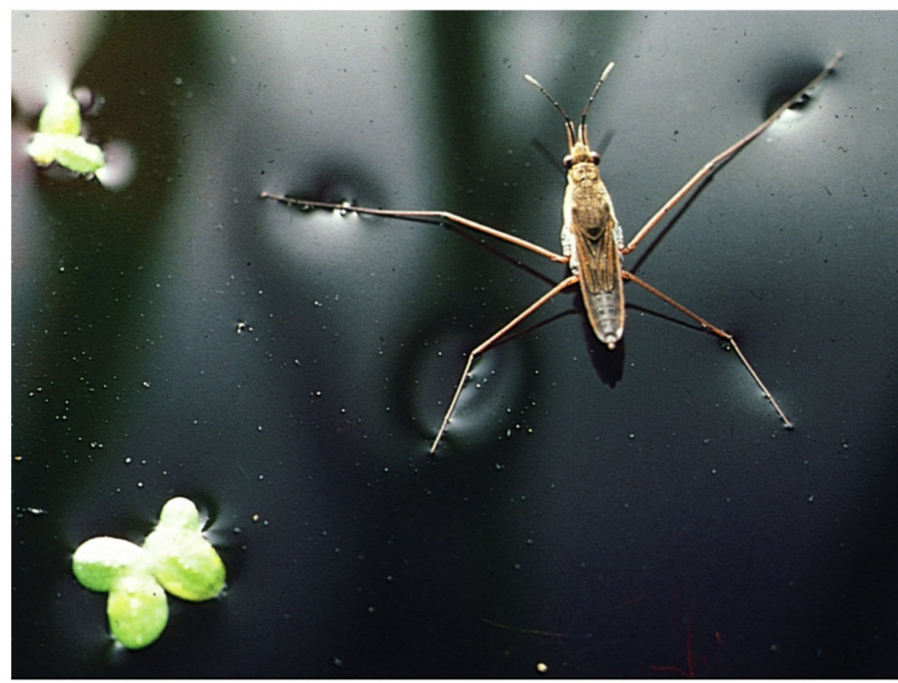


Surface tension

- Surface tension is a measure of how hard it is to break the surface of a liquid
- Surface tension is related to cohesion



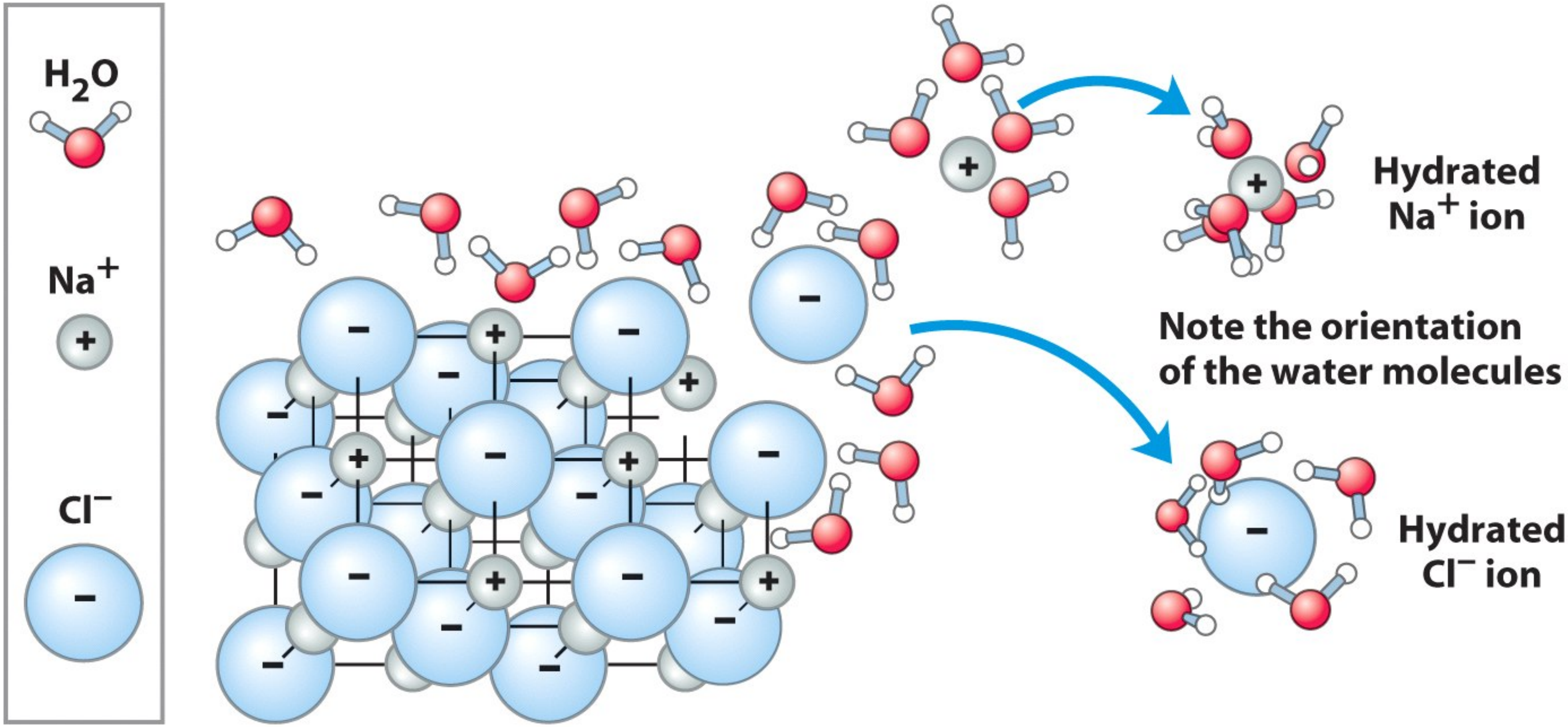
(b) Surface tension created by hydrogen bonds holds a drop of water in a hemispheric shape.



Network of hydrogen bonds

- *At any given time, most of the molecules in liquid water are engaged in hydrogen bonding, but the lifetime of each hydrogen bond is just 1 to 20 picoseconds (1 ps = 10^{-12} s).*
- *Upon breakage of one hydrogen bond, another hydrogen bond forms, with the same partner or a new one, within 0.1 ps.*
- *The apt phrase "flickering clusters" has been applied to the short-lived groups of water molecules interlinked by hydrogen bonds in liquid water.*
- *The sum of all the hydrogen bonds between H_2O molecules confers great internal cohesion on liquid water.*

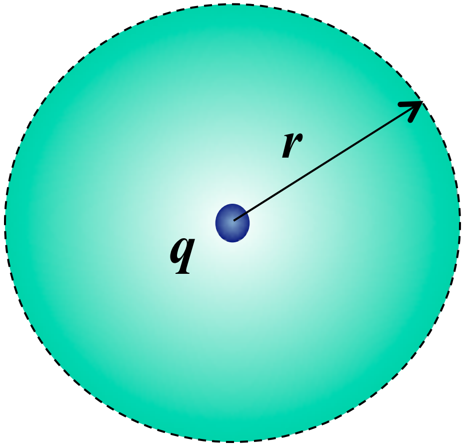
Water's Polarity Can Disrupt Electrostatic Solute-Solute Interactions

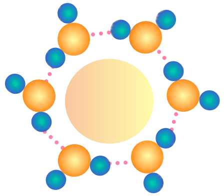


Entropy increases as crystalline substances dissolve

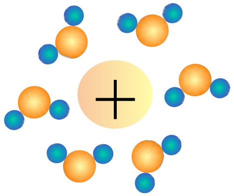
Ions can make or break water structure

$$\Psi_{ion} = \frac{q}{4\pi\varepsilon_0 \varepsilon r}$$

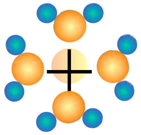




Hydrophobic hydration



Structure-breaking ionic hydration



Structure-creating ionic hydration

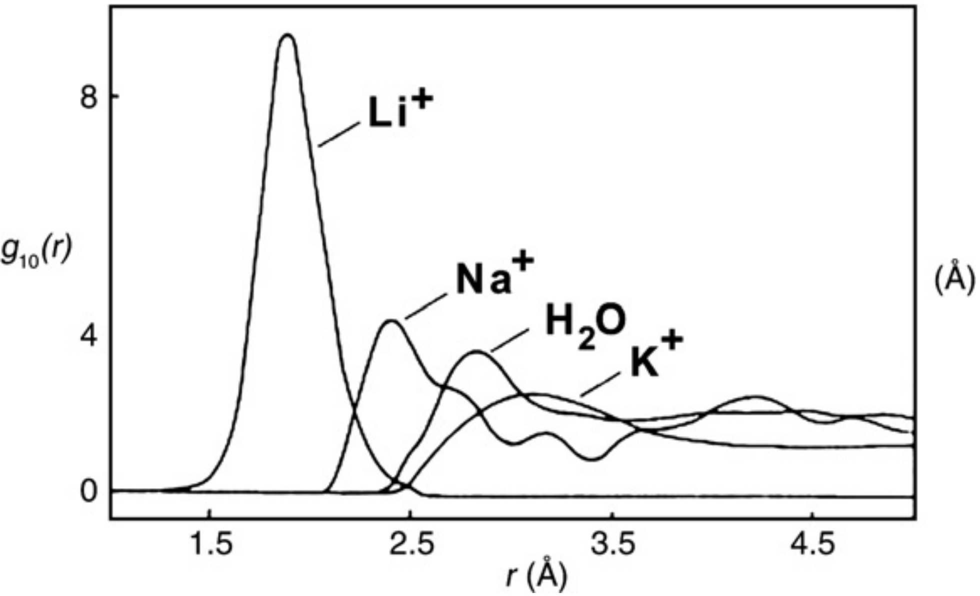
Types of ions

- Structure-breaking ion '**chaotrope**' (disorder-maker) (Na^+)
- structure-forming ion '**kosmotrope**' (order-maker) (K^+)
- Kosmotropes shift the local equilibrium to the right.
- Chaotropes shift it to the left.

more dense (condensed) water ↔ less dense water

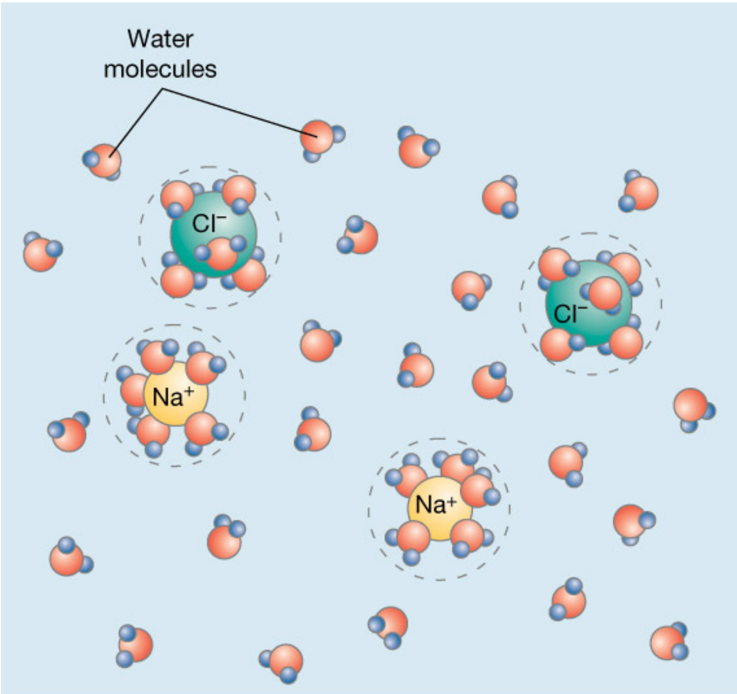
Ion	Surface charge density	Intra-cellular	Extra-cellular	Water preference
Ca^{2+}	2.11	0.1 μM	2.5 mM	High density
Na^+	1.00	10 mM	150 mM	High density
K^+	0.56	159 mM	4 mM	Low density

Small ions perturb water over only a short distance, e.g., ~5 Å.



The radial distribution functions $g_{10}(r)$ for Li^+, Na^+, water, and K^+ in liquid water.

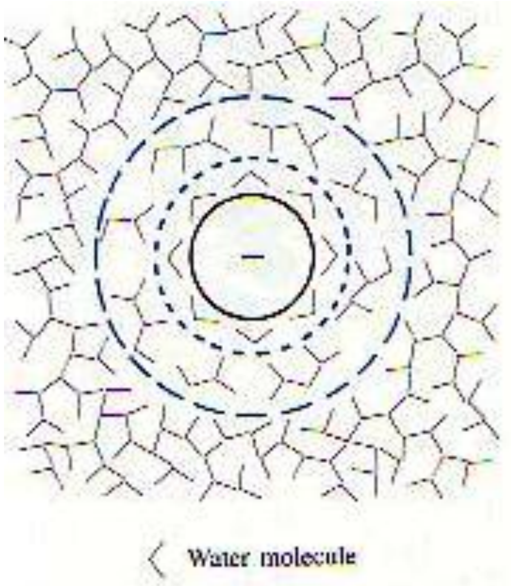
- These curves measure the distance from the monovalent cation to the nearest solvent oxygen.
- The curve labeled "H_2O" measures the oxygen–oxygen distance in liquid water.



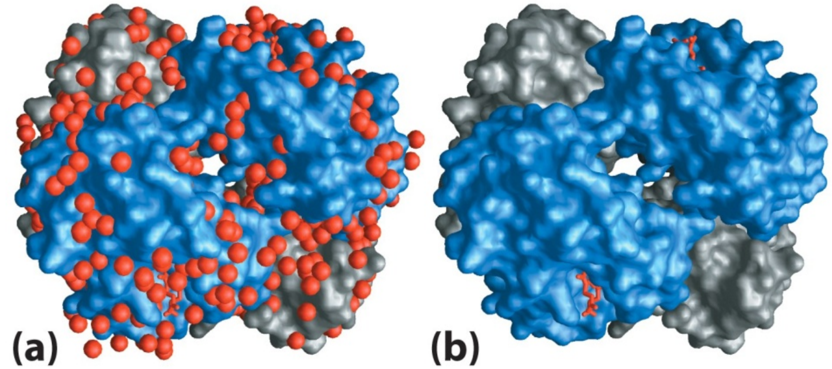
Sodium chloride in solution

‘Bound water’ in biological systems

- *Intracellular water very close to any membrane or organelle (sometimes called* ***vicinal water****)*
- *Organized very differently from* ***bulk water***
- *This structured water plays a significant role in governing the shape (and thus biological activity) of large folded biopolymers.*

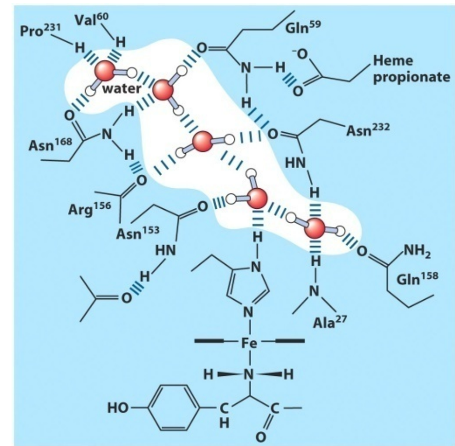


Water binding in hemoglobin

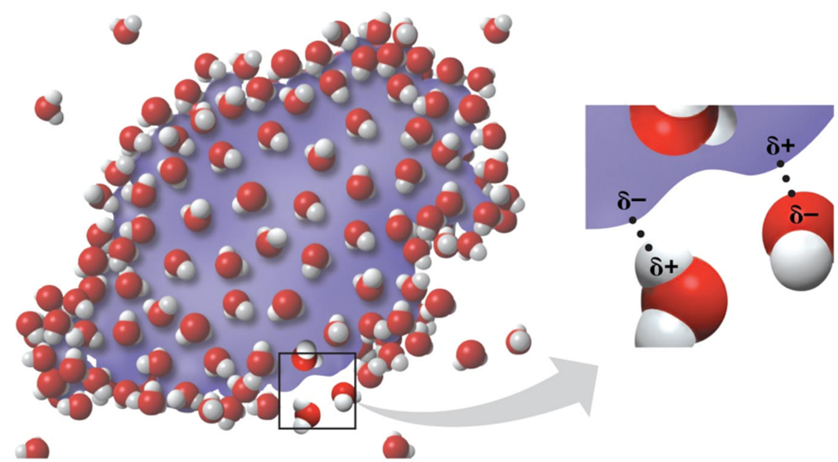


The crystal structure of hemoglobin, shown
(a) with bound water molecules (red spheres) and
(b) without the water molecules

Water chain in cytochrome f



The density of bound water is 10% higher and it has a 15% greater heat capacity suggesting much reduced molecular motion.

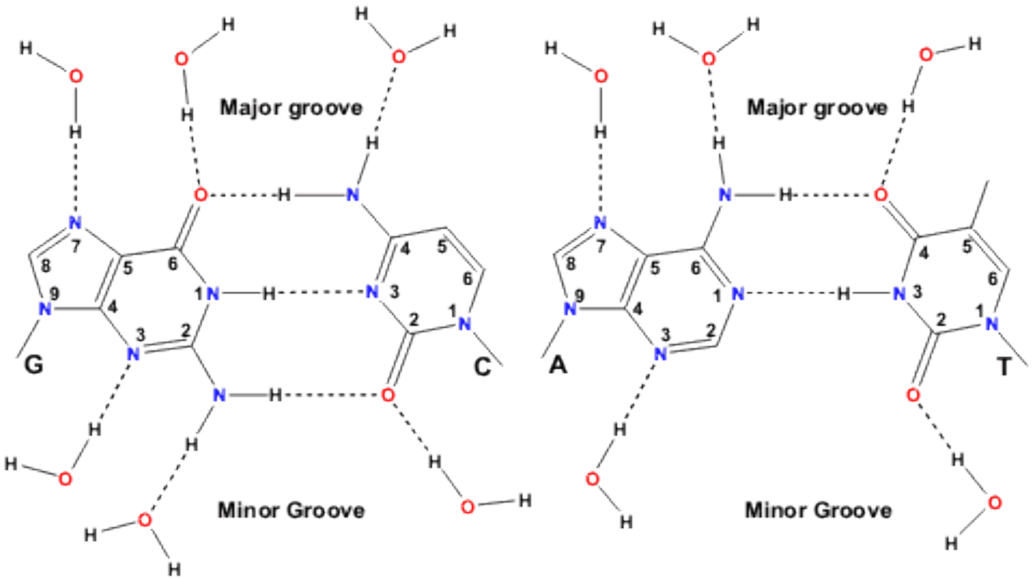


Lysozyme molecule in a aqueous environment.

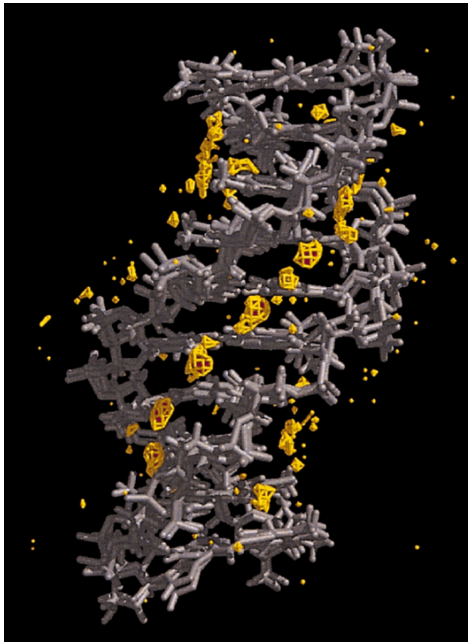
Hydration of DNA

There may be a spine of hydration running down the bottom of the B-DNA minor groove particularly where there is the A=T duplex known to favor B-DNA.

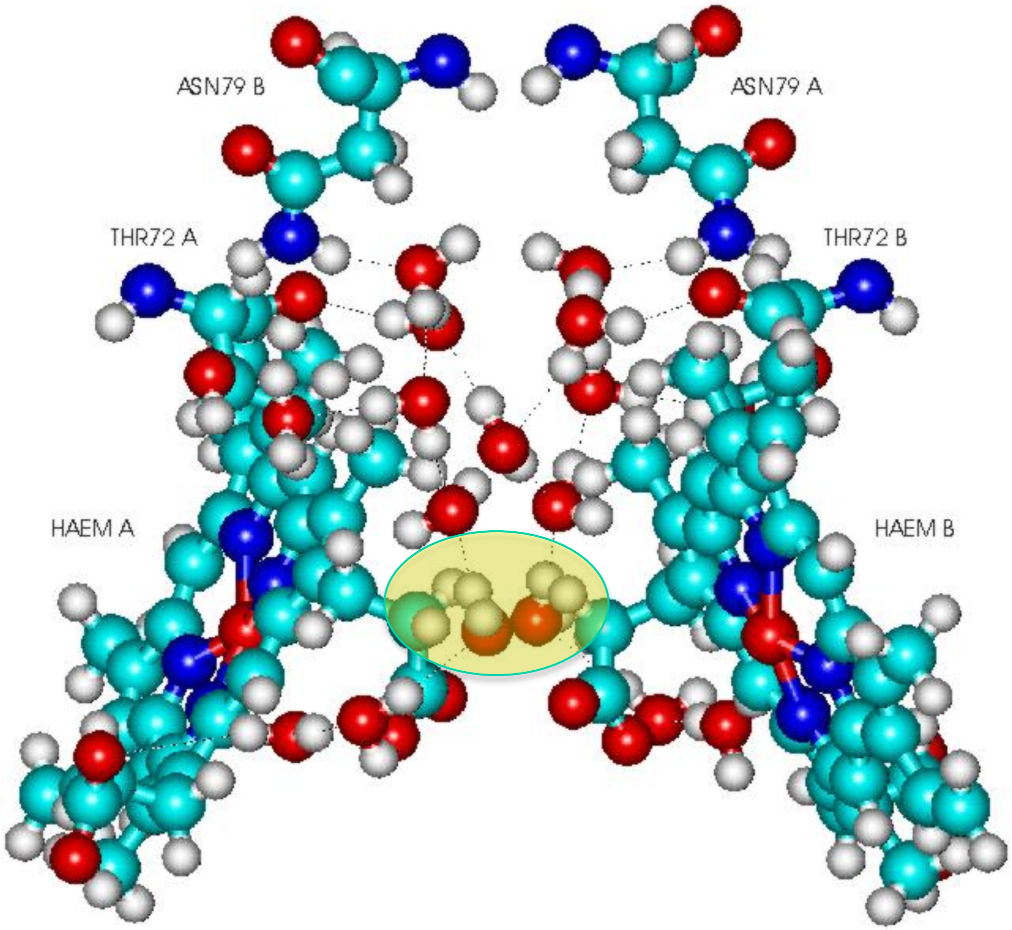
Thus A=T duplex sequences favor water binding in the minor groove and also protein binding there driven by the large entropy release on this low entropy water's release.



Spine of hydration in DNA minor groove



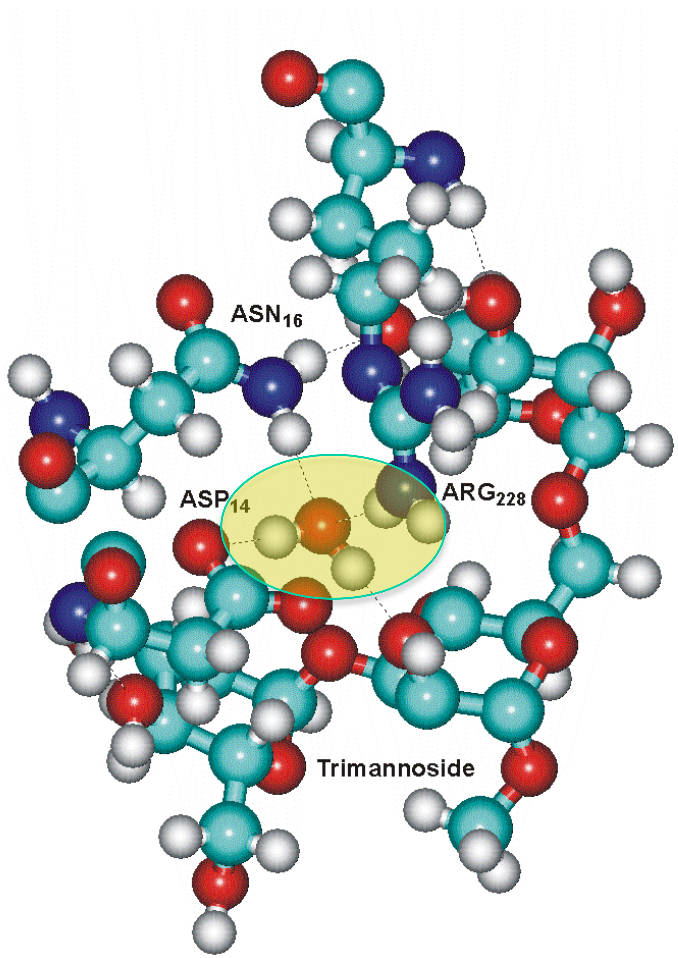
Some surface water is well ordered



Water molecules connecting the haem groups and protein residues of the two identical subunits of *Scapharca inaequivalvis* haemoglobin. On binding oxygen, the water molecules transfer information between the subunits before the water cluster is disrupted .

Royer et al. *Proc. Natl Acad. Sci. USA* **93**, 14526 (1996).

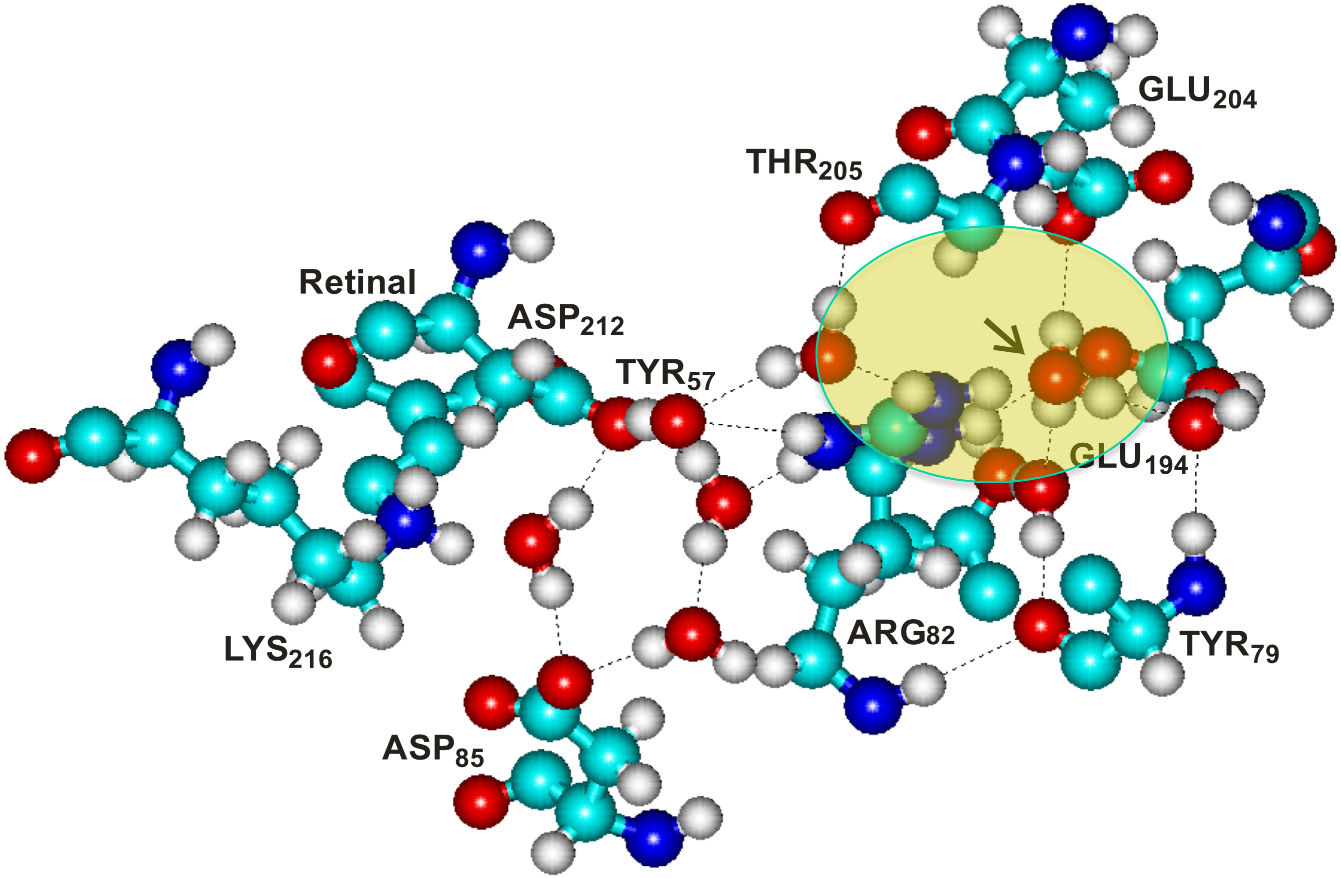
Some water is required for structure



A single water molecule in the ligand-binding site of concanavalin A functions as a link between Asp_{14}, Asn_{16} and Arg_{228} of the protein and the 2'-OH hydroxyl group of the trimannoside ligand.

Li & Lazaridis, *J. Phys. Chem. B* **109**, 662 (2005).

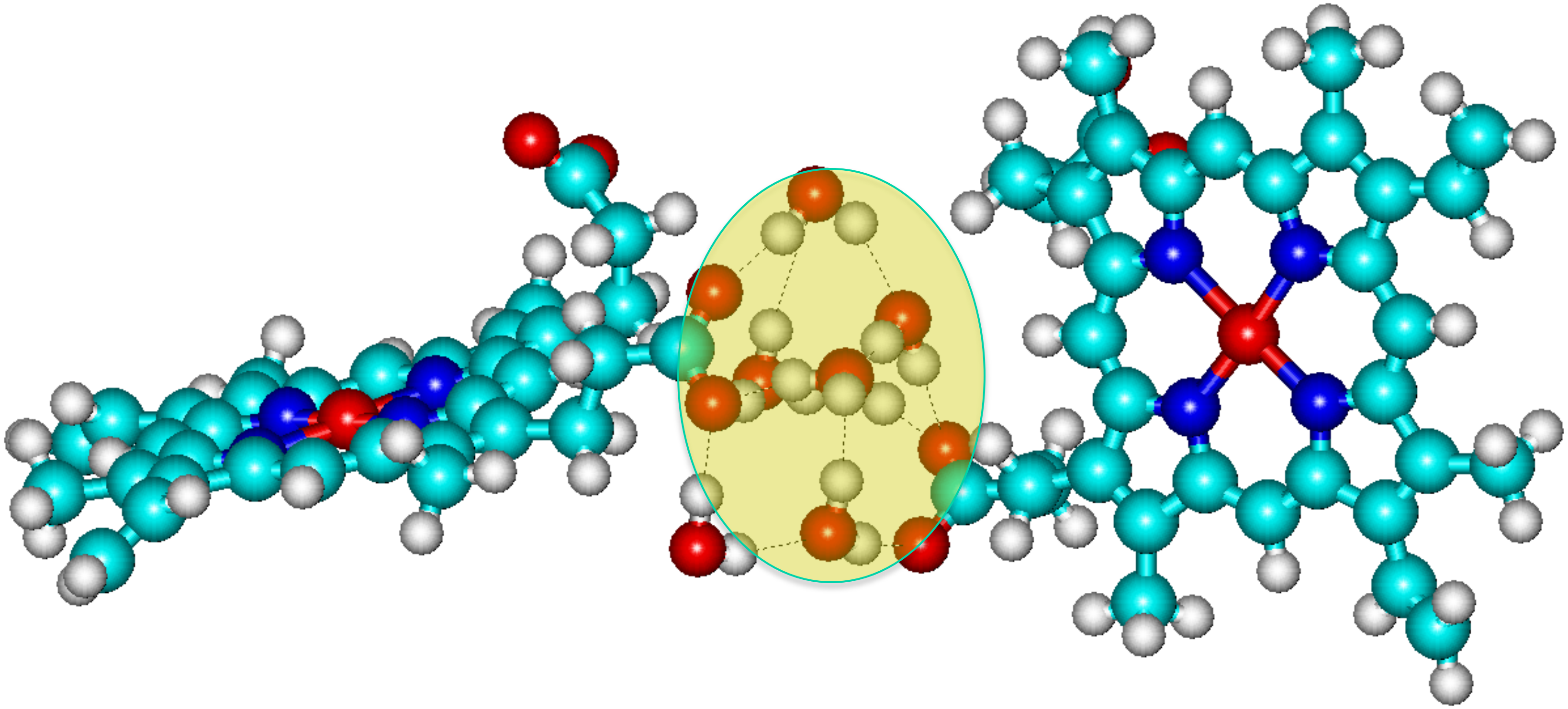
Some water is required for proton transfer



Water molecules in bacteriorhodopsin; photoisomerization of all-trans-retinal (pKa 13) to 13-cis-retinal (pKa 8.45), drives a proton from its Lys_{216}-Schiff base to Asp_{85} releasing the pentagonal hydrogen-bonded ring, flipping the Arg_{82} towards the (arrowed) protonated water molecule, releasing a proton through a water wire) to the extracellular space. The Schiff base is reprotonated from the cytoplasm through another associated water wire.

Garczarek & Gerwert, *Nature* **439**, 109 (2005).

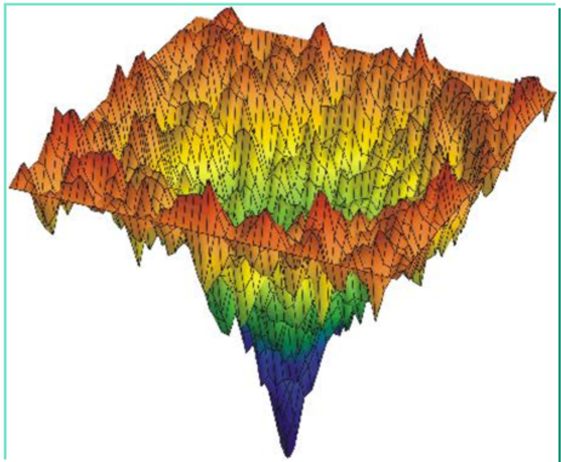
Some water is required for electron transfer



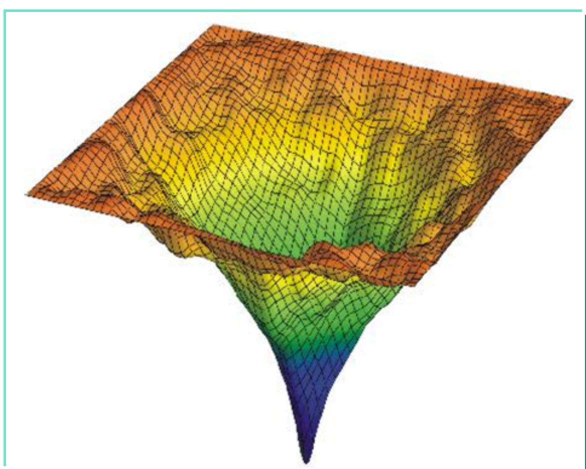
Rapid electron transfer between two molecules of bovine liver cytochrome b5. The electrostatic interactions of the water molecules provide a large donor-to-acceptor coupling that produces a smooth distance dependency for the electron-transfer rate. Only the water cluster and the cytochromes are shown, and the protein residues are hidden.

Lin et al. *Science* **310**, 1311 (2005).

Hydration and the folding of proteins

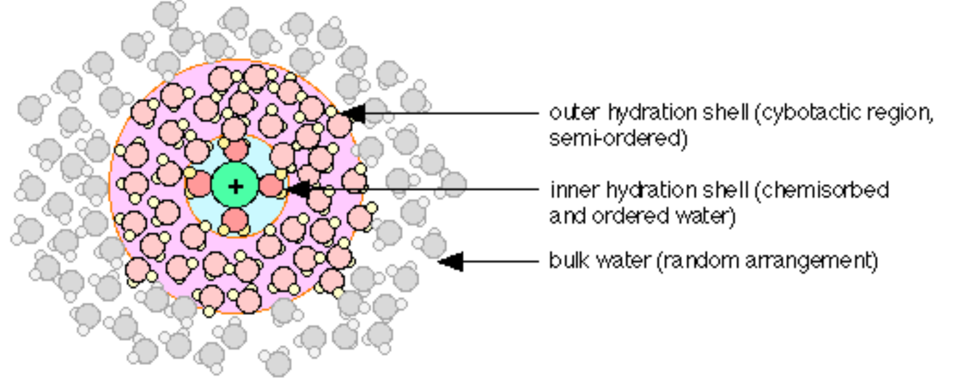


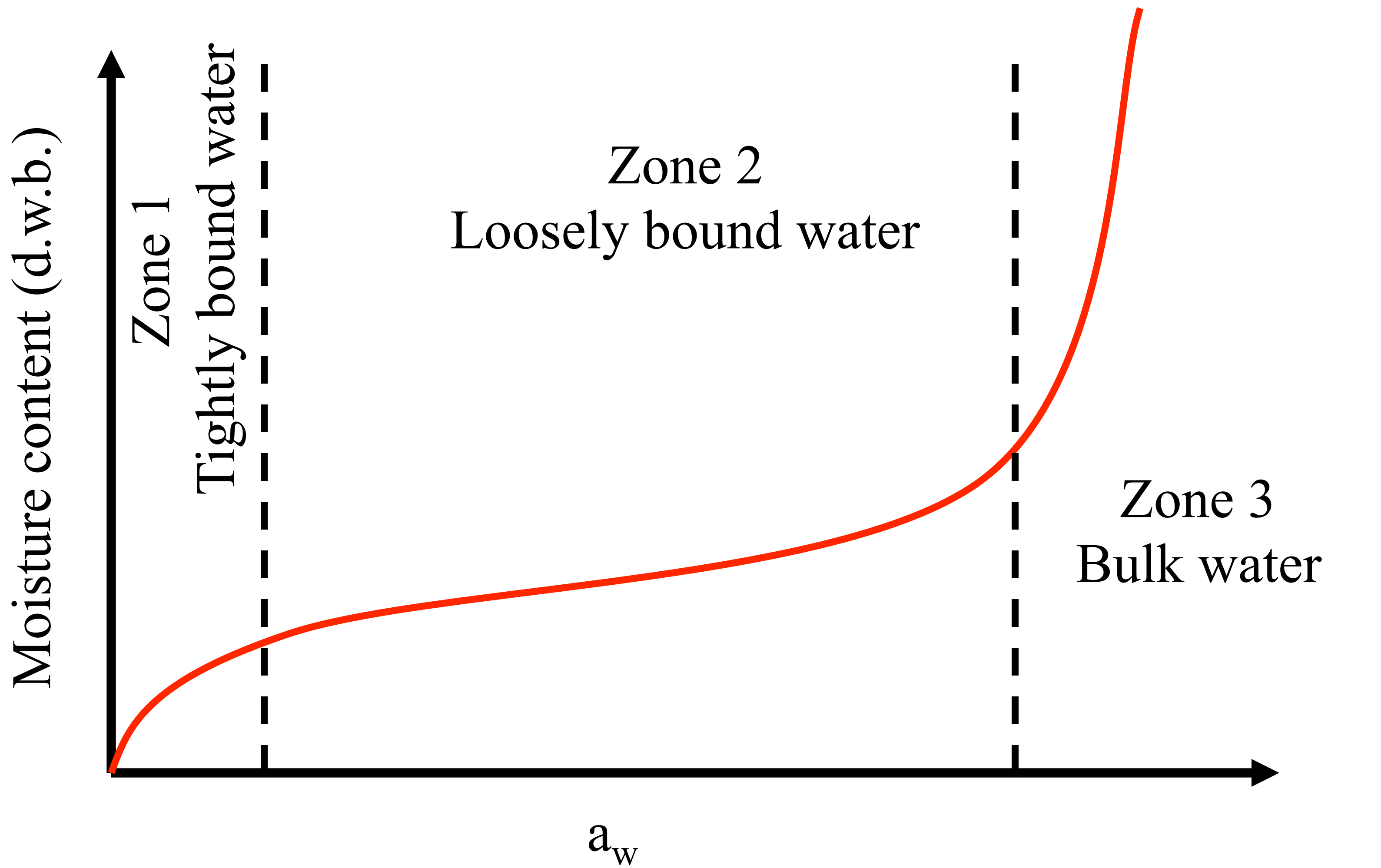
- The folding-energy landscape in the presence of low hydration highlights the numerous barriers to the preferred minimum-energy structure on the folding pathway.
- There are many local minima that might trap the protein in an inactive three-dimensional molecular conformation.



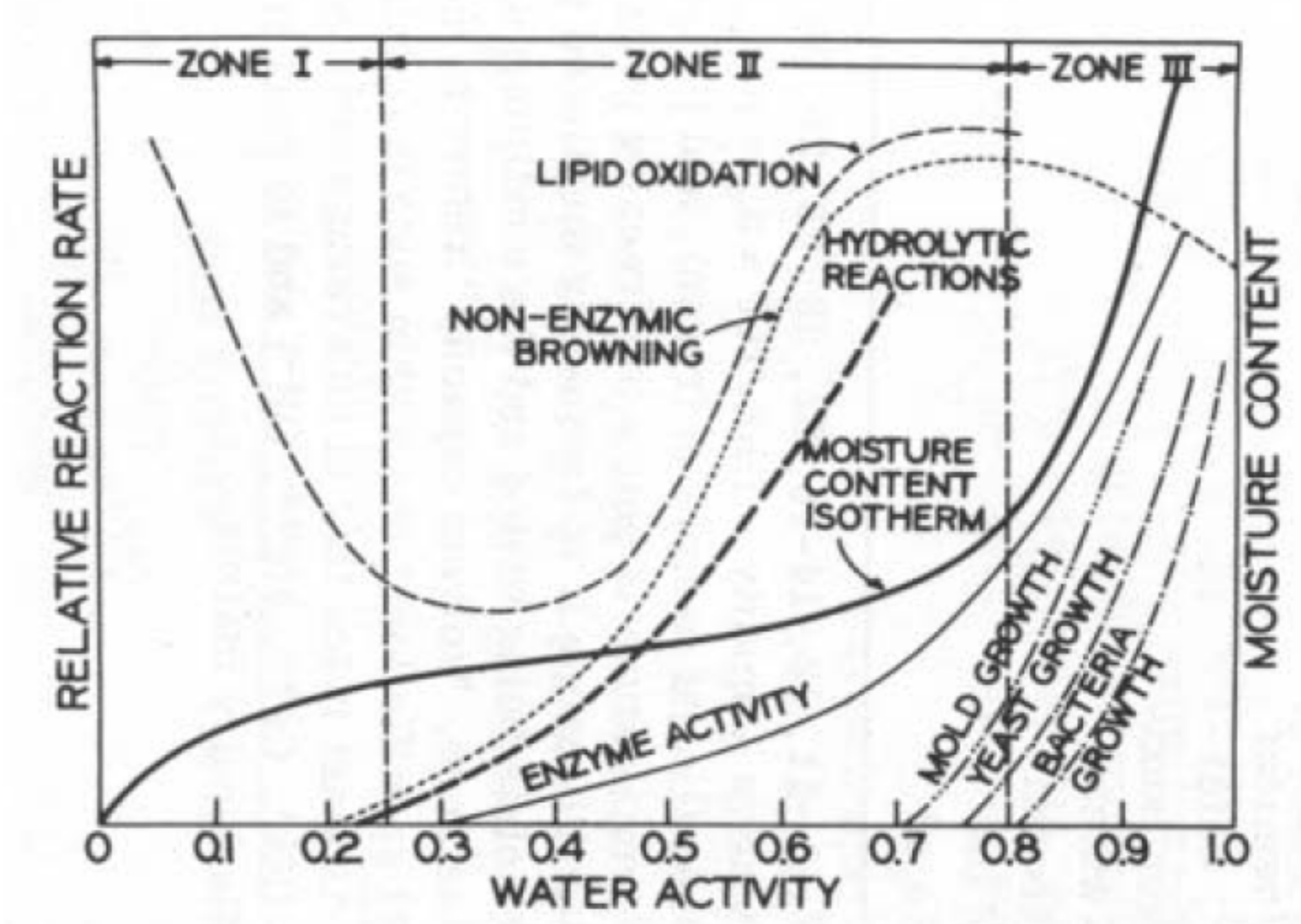
- When a protein is sufficiently hydrated, a smoothed potential-energy landscape is evident.
- This allows proteins to attain their active minimum-energy conformation in a straightforward and rapid manner.

Moisture sorption isotherm

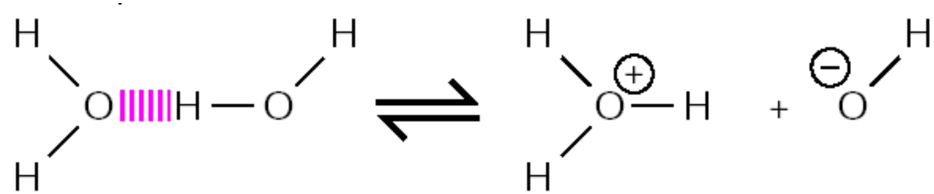




- Activity – “effective concentration”
- Concentration can be related to activity using the activity coefficient γ, where $[a] = \gamma\ (c)$

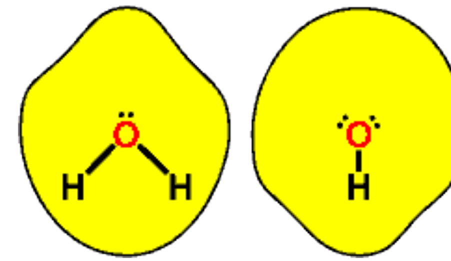


Dissociation - the separation of a water molecule into a hydrogen ion (H^+) and a hydroxide ion (OH^-) .



hydronium ion (water acting as a weak base)

hydroxyl ion (water acting as a weak acid)



$$H_2O + H_2O \leftrightarrow H_3O^+ + OH^-$$

$$K_{eq} = \frac{[H_3O^+][OH^-]}{H_2O}$$

$[H_2O] \sim 55M$ and ionization is very weak, then $[H_2O] \sim$ constant.

For pure water $K_W=[H_3O^+][OH^-] = 10^{-14}$

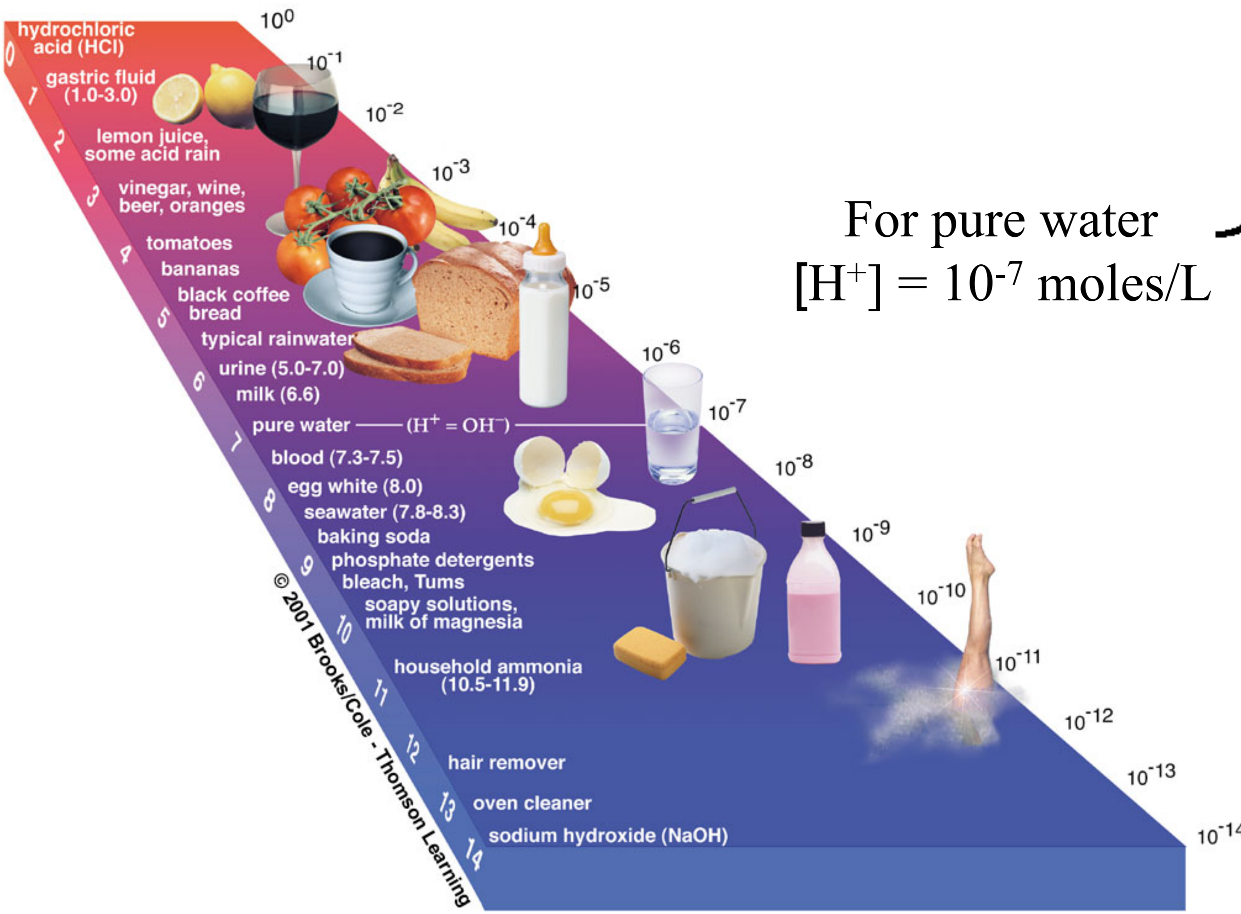
$[H^+] = [H_3O^+] = [OH^-] = 10^{-7}M$
In a neutral solution
$[H_3O^+] = 10^{-7}M$; $[OH^-] = 10^{-7}M$

That is only 1 H^+ for every 560,000,000 water molecules!

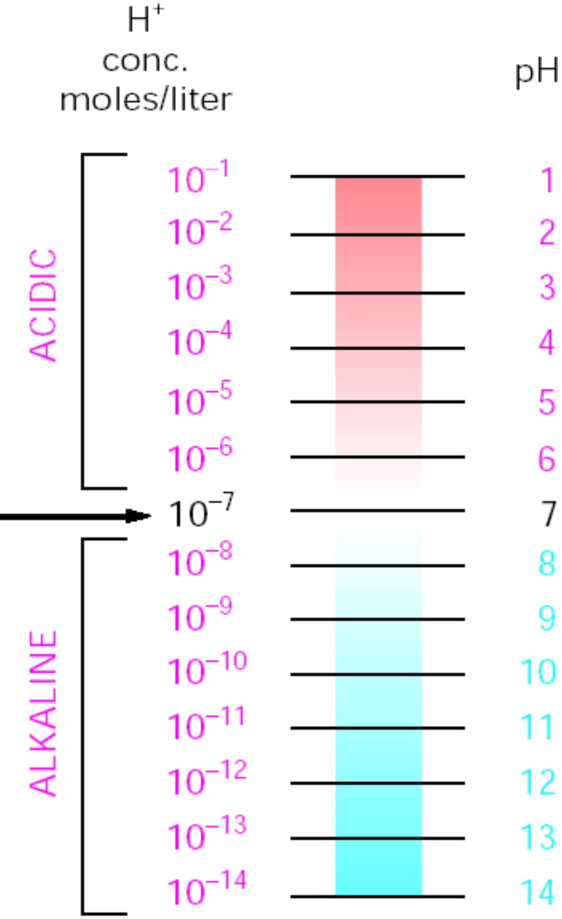
Acid-base chemistry is centered on water

The acidity of a solution is defined by the concentration of H^+ ions.

$$pH = -\log_{10}[H^+]$$

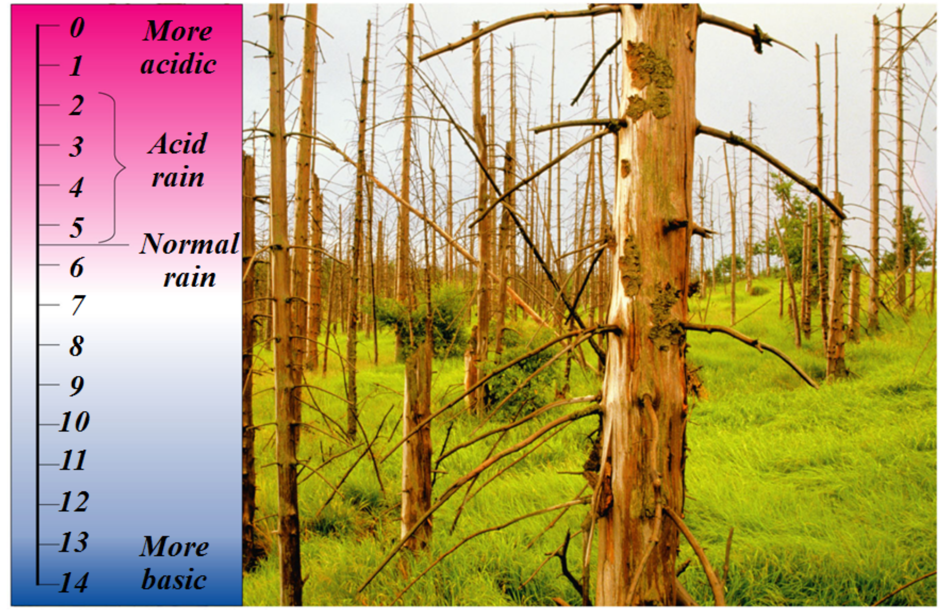


For pure water
$[H^+] = 10^{-7}$ moles/L



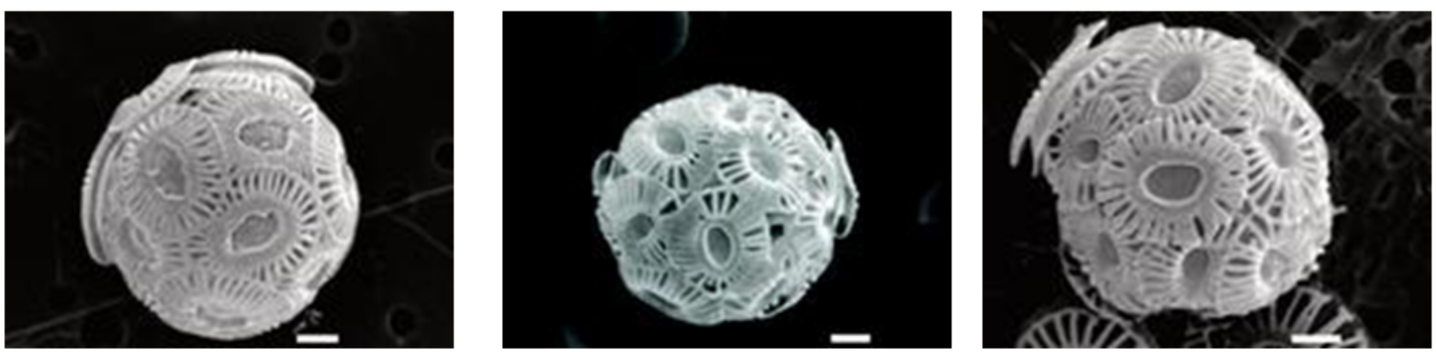
For biological systems, the proton concentration is one of the most important parameters.

The Acid Precipitation



- Acid precipitation refers to rain, snow, or fog with a pH lower than 5.6
- Acid precipitation is caused mainly by the mixing of different pollutants with water in the air
- Acid precipitation can damage life in lakes and streams
- Effects of acid precipitation on soil chemistry are contributing to the decline of forests

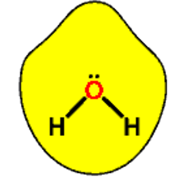
Ocean acidification impacts shell formation of planktonic organisms

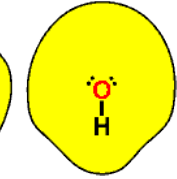


Healthy shell of coccolithophorid

Increasing acidity interferes with proper shell formation

Definition of pK_a



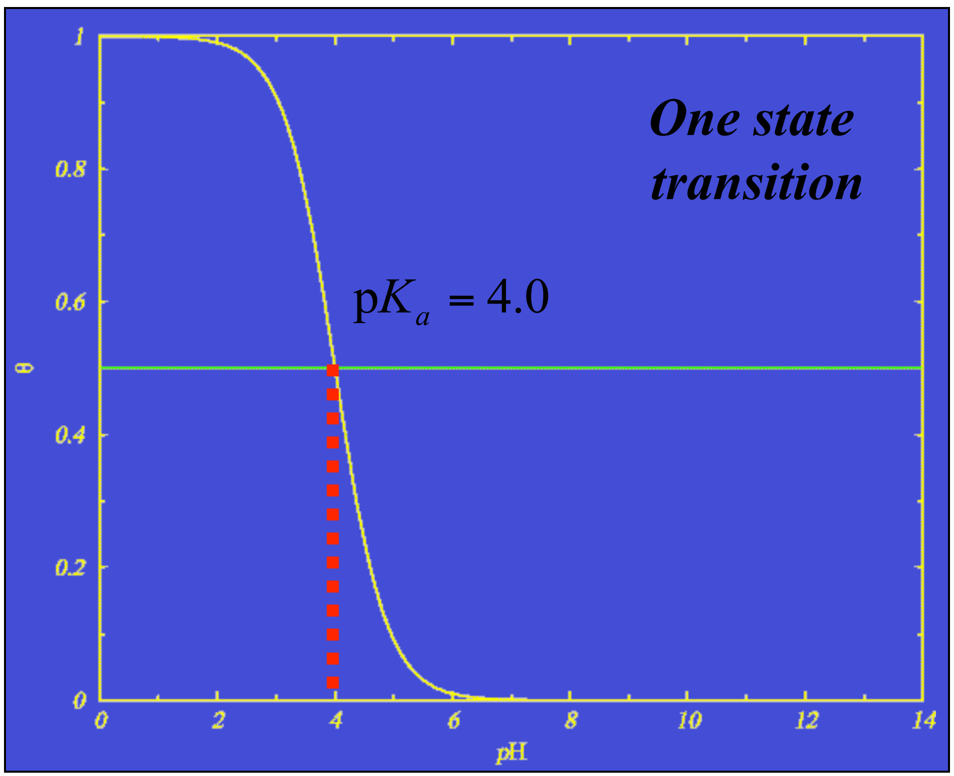


The pK_a of a titrating site is defined as the pH for which the site is 50% occupied,

$$HA + H_2O \Leftrightarrow A^- + H_3O^+$$

$$K_a = \frac{a_{A^-} a_{H_3O^+}}{a_{HA}} = \frac{a_{A^-}}{a_{HA}} a_{H_3O^+} = \frac{1-\theta}{\theta} a_{H_3O^+}$$

Deprotonation reaction



θ is degree of protonation or occupancy: number of bound protons as a function of pH

Titration curve:

$$\theta(\mathrm{p}H) = \frac{1}{1 + e^{-\ln 10(\mathrm{p}K_a - \mathrm{p}H)}}$$

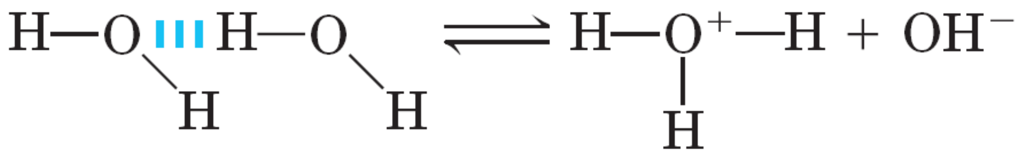
$$pH = pK_a + 1 \quad f_{A^-} = \frac{10}{11} \approx 90\%$$

$$pH = pK_a - 1 \quad f_{A^-} \approx 9\%$$

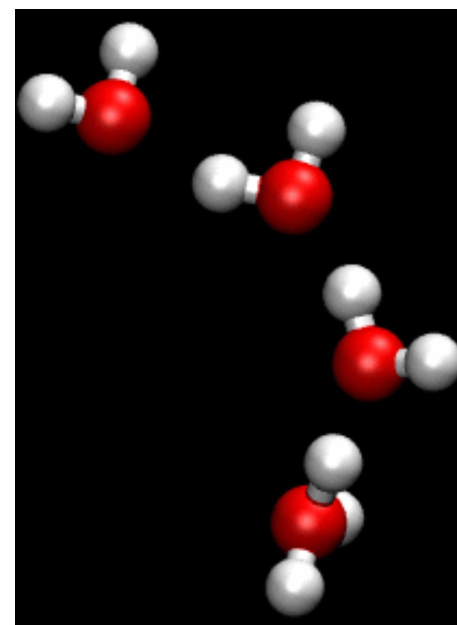
$$pH = pK_a - 2 \quad f_{A^-} \approx 0.9\%$$

The Grotthuss mechanism – proton hopping

Proton has abnormally high mobility in water and other dissociating fluids because it does not diffuse all the way, protons are re-distributed by binding and dissociation.

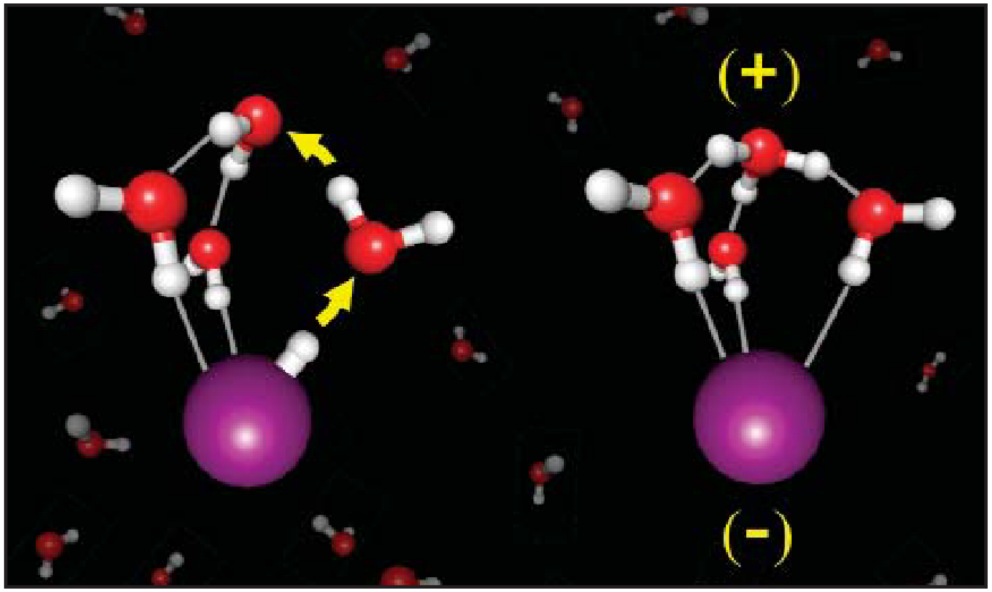


Cation	Mobility $cm^2\ V^{-1}\ s^{-1}$ in water
$NH4^+$	0.763×10^{-3}
Na^+	0.519×10^{-3}
K^+	0.762×10^{-3}
H^+	3.62×10^{-3}



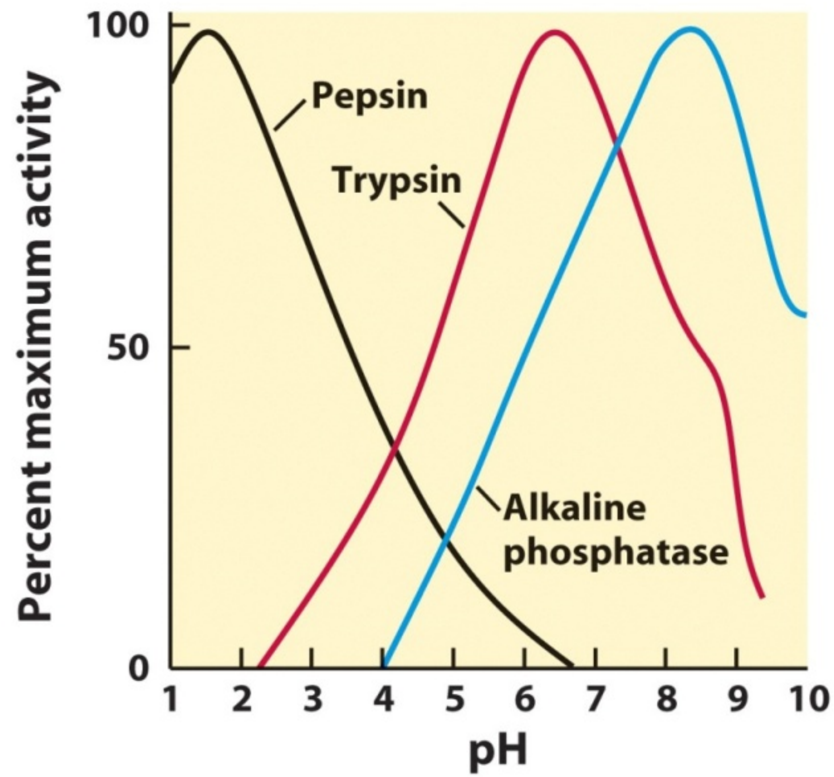
T. Grotthuss, 1806

Hydrogen bonding is critical for acid dissociation



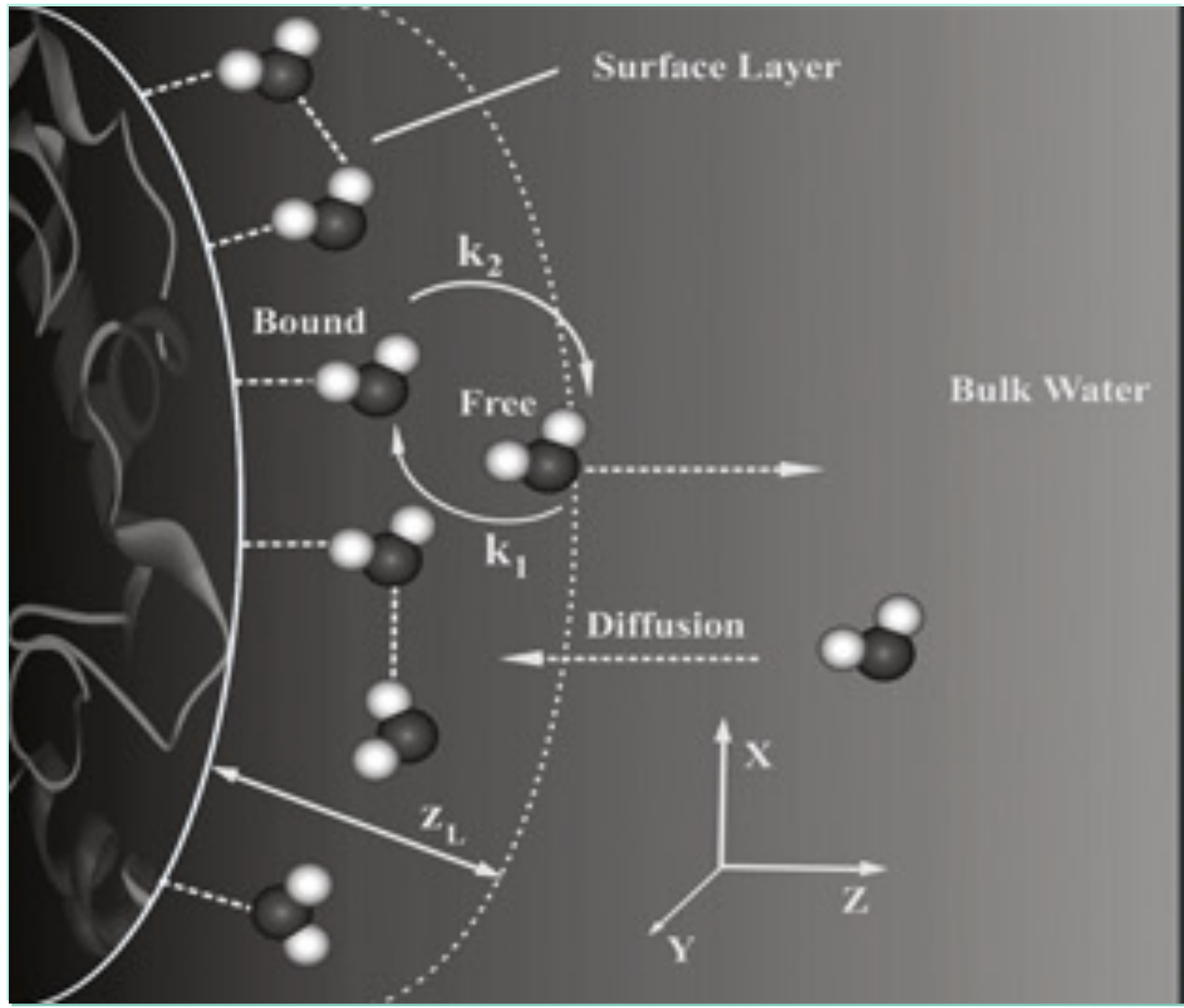
Dissociation of hydrogen bromide in a cluster of four water molecules. The water network is an integral part of the charge separation process, leading to the solvent-separated ion-pair shown on the right. The reaction path shown here is highly schematic; HCl dissociation appears to involve a sequence of several discrete steps (*4*).

The pH optima of some enzymes



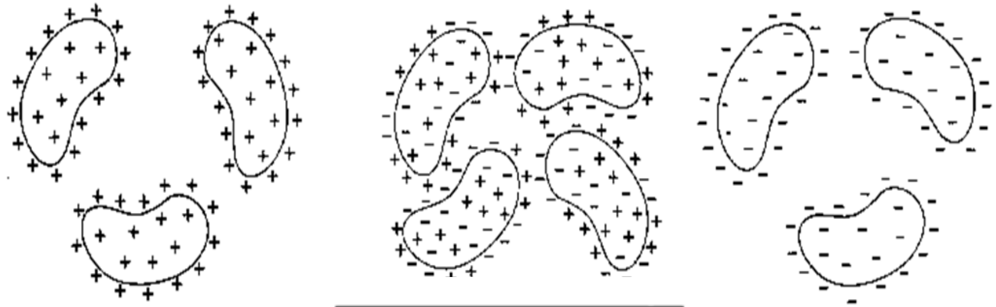
Because of the interfacial potential barrier, the proton equilibration between the surface and the bulk occurs slower (at ~ 0.1–10 ms) than the proton spreading along the surface (at ~ 0.1–10 μs).

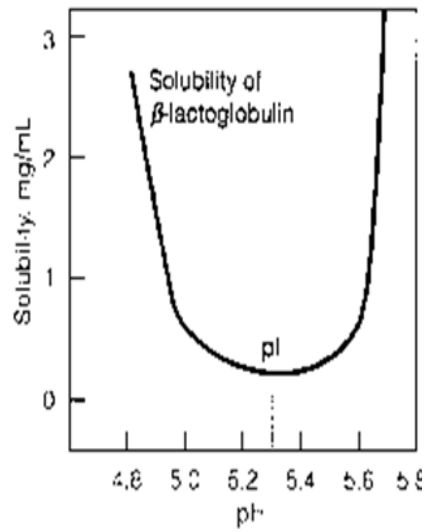
At steady state, the proton activity at the membrane surface might then deviate from the respective activity in the adjoining bulk aqueous phase.

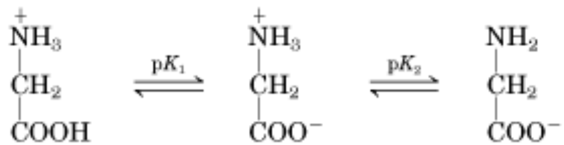


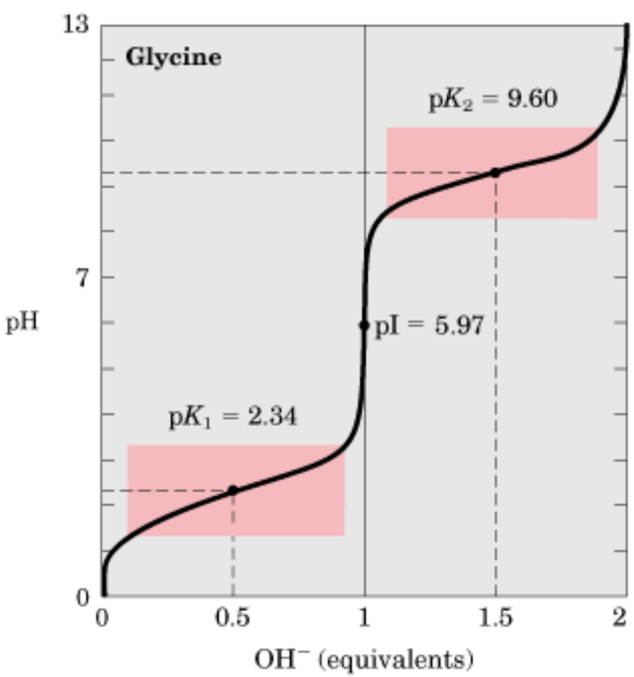
Isoelectric point

pH < pI **pH = pI** **pH > pI**





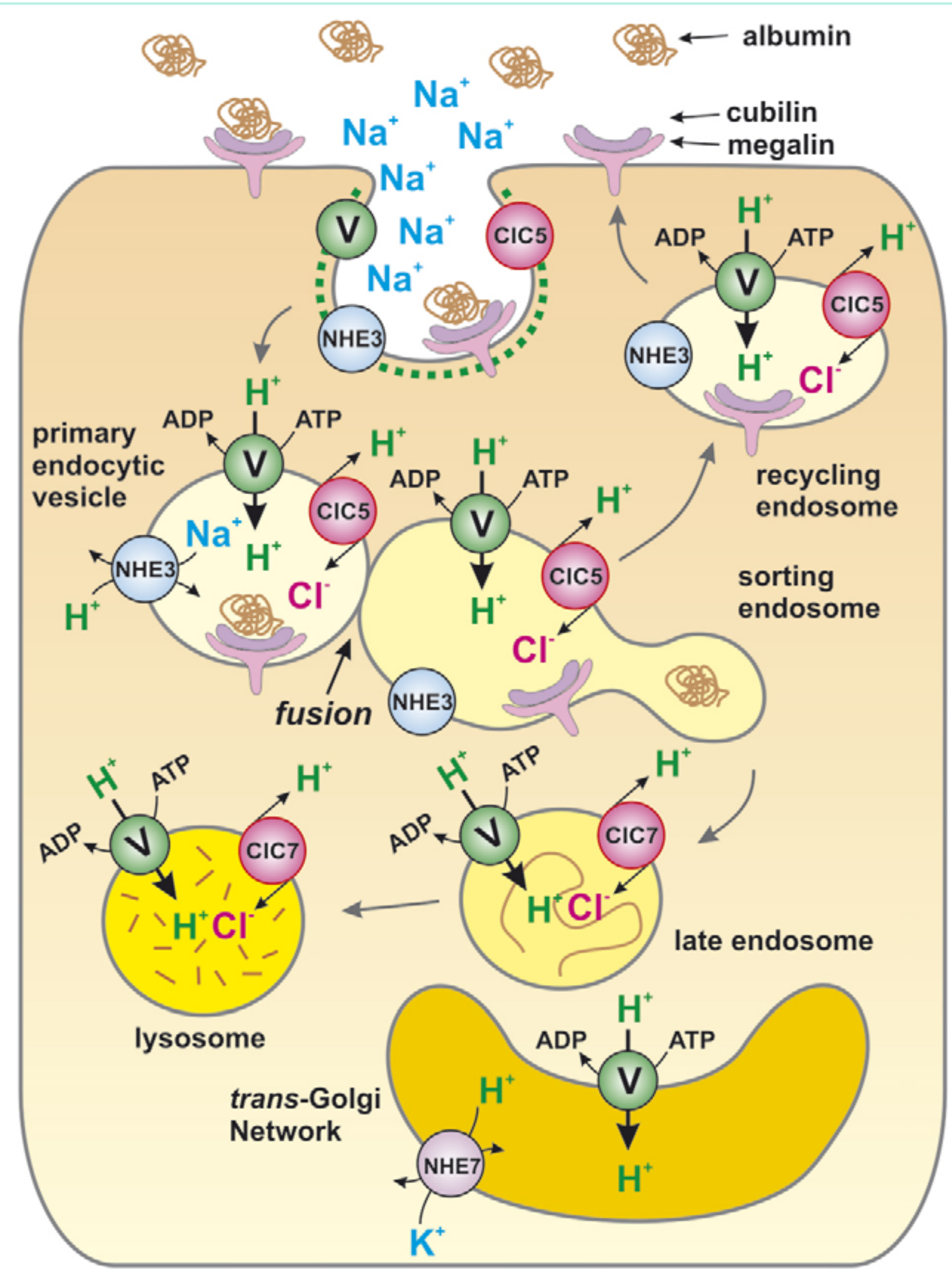




Isoelectric Points of Several Common Proteins

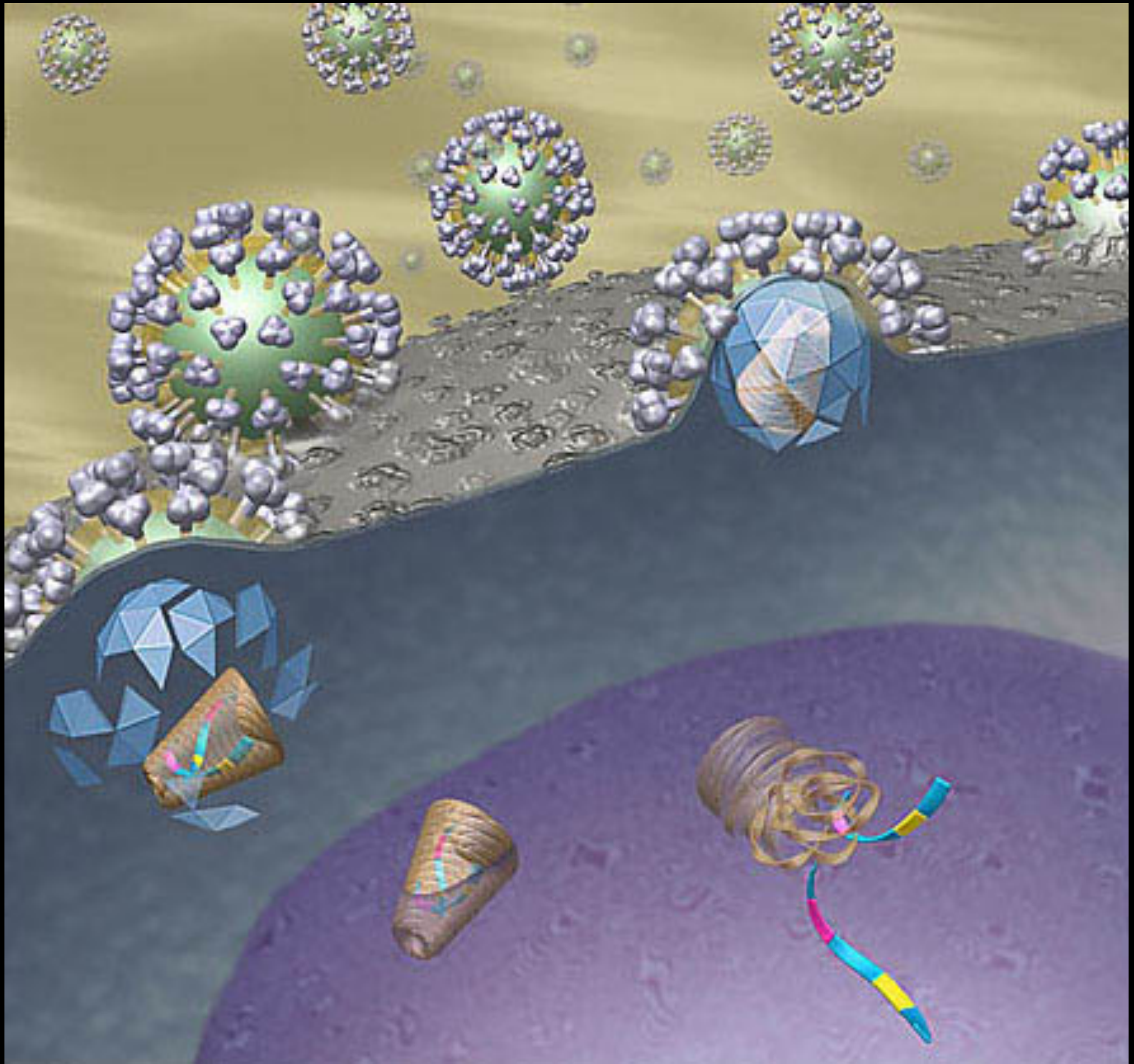
Protein	*pI*
Pepsin	<1.0
Ovalbumin (hen)	4.6
Serum albumin (human)	4.9
Tropomyosin	5.1
Insulin (bovine)	5.4
Fibrinogen (human)	5.8
γ-Globulin (human)	6.6
Collagen	6.6
Myoglobin (horse)	7.0
Hemoglobin (human)	7.1
Ribonuclease A (bovine)	9.4
Cytochrome *c* (horse)	10.6
Histone (bovine)	10.8
Lysozyme (hen)	11.0
Salmine (salmon)	12.1

Endosomal pH and reabsorption of albumin in renal proximal tubules.



Acidification of intracellular compartments is driven by:
-the vacuolar type (V) H^+-ATPase pumps (V-ATPases)
- counterion Cl influx pathways that minimize the generation of a large inside-positive voltage that would otherwise impede V-ATPase function.
- the apical Na+/H+ exchanger isoform 3 (NHE3) - acidification of early/recycling endosomes.

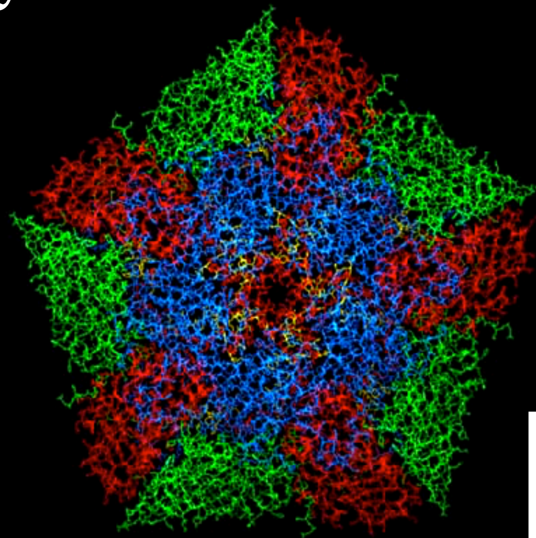
Virus cell entry



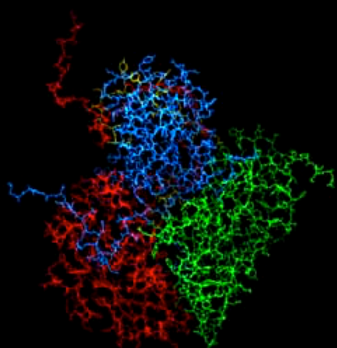
What is the molecular basis for this effect?

Acid sensitivity of Foot-and-Mouth Disease Virus (FMDV)

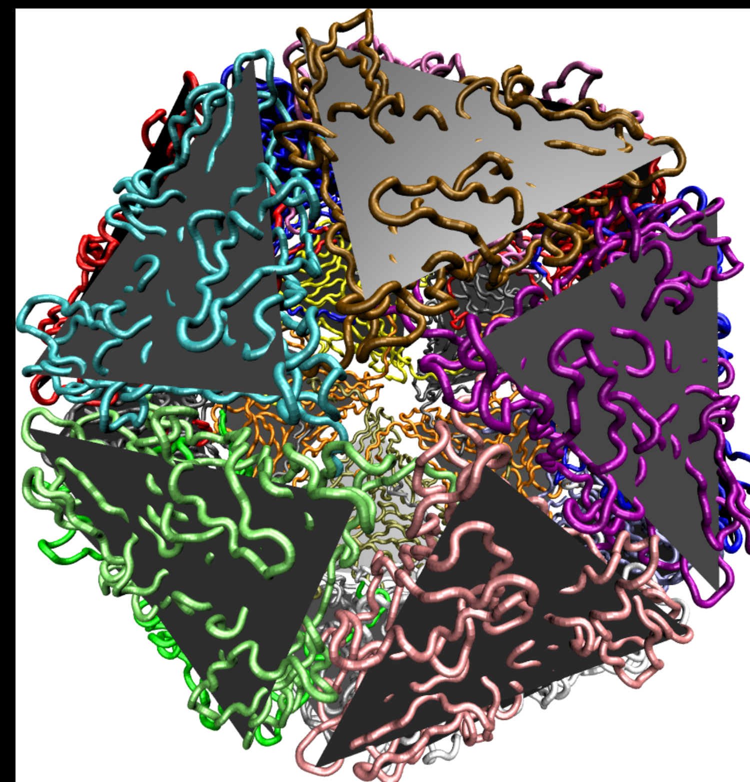
Pentamer



FMDV
Assembly

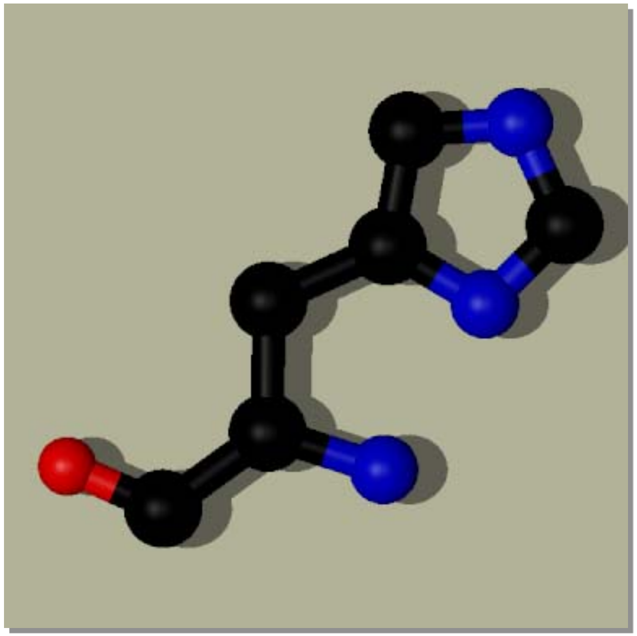


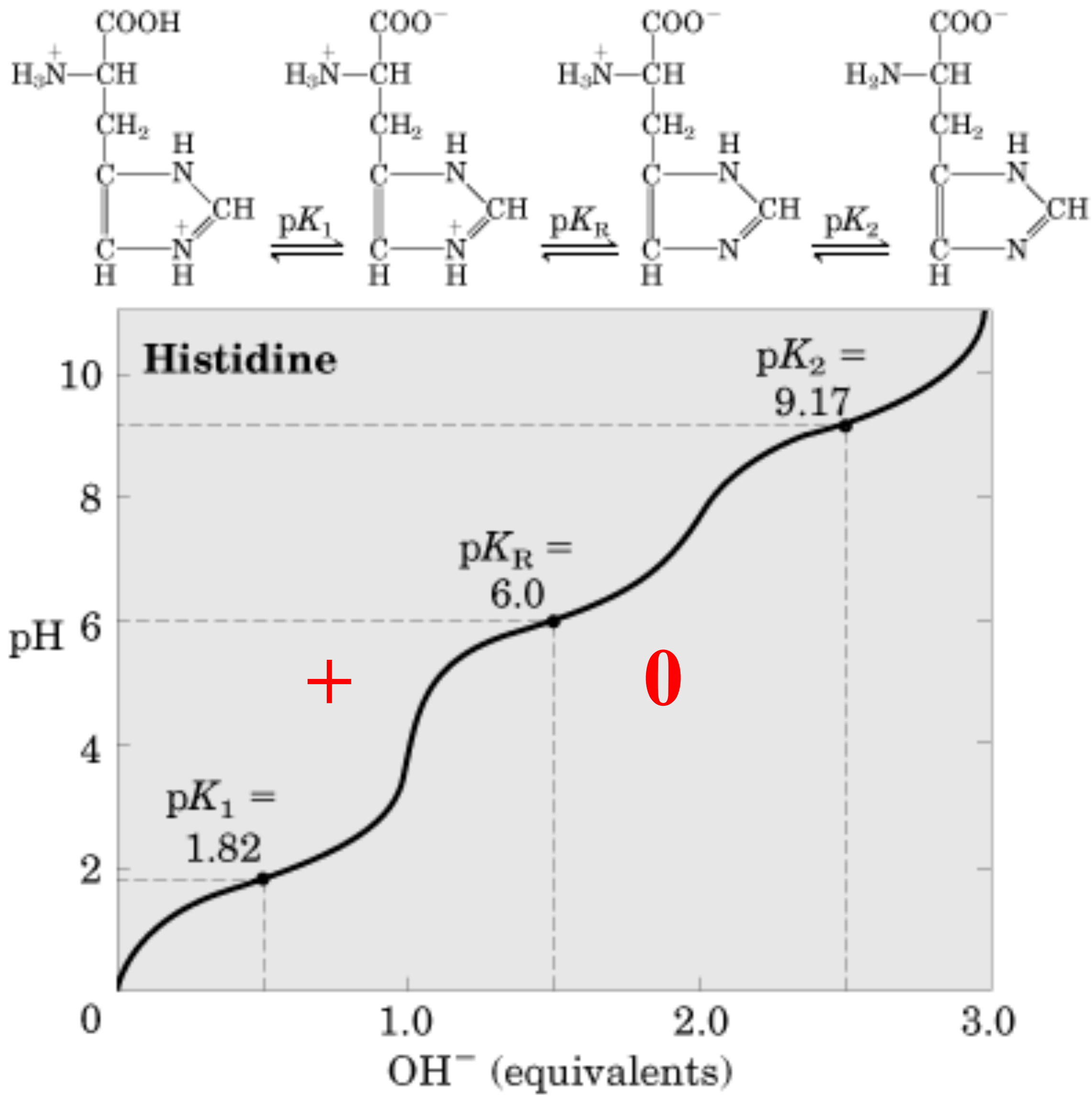
Protomer



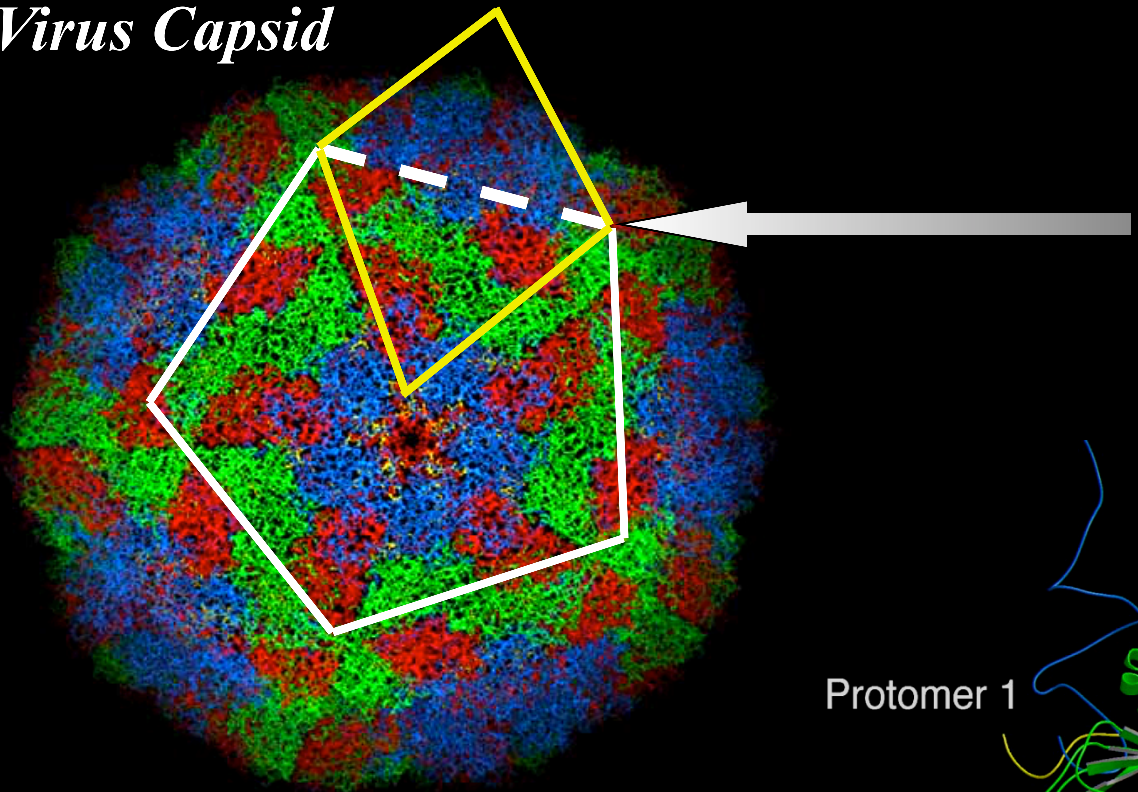
Capsid
(contains RNA genome)

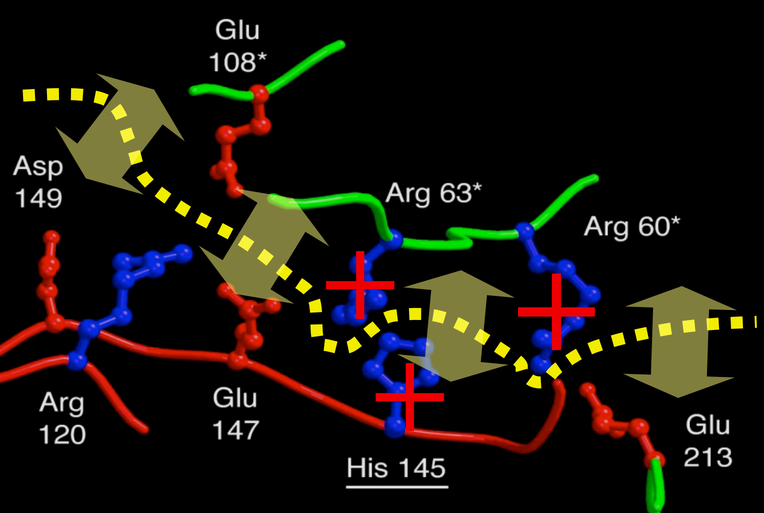
Histidine is a prime suspect



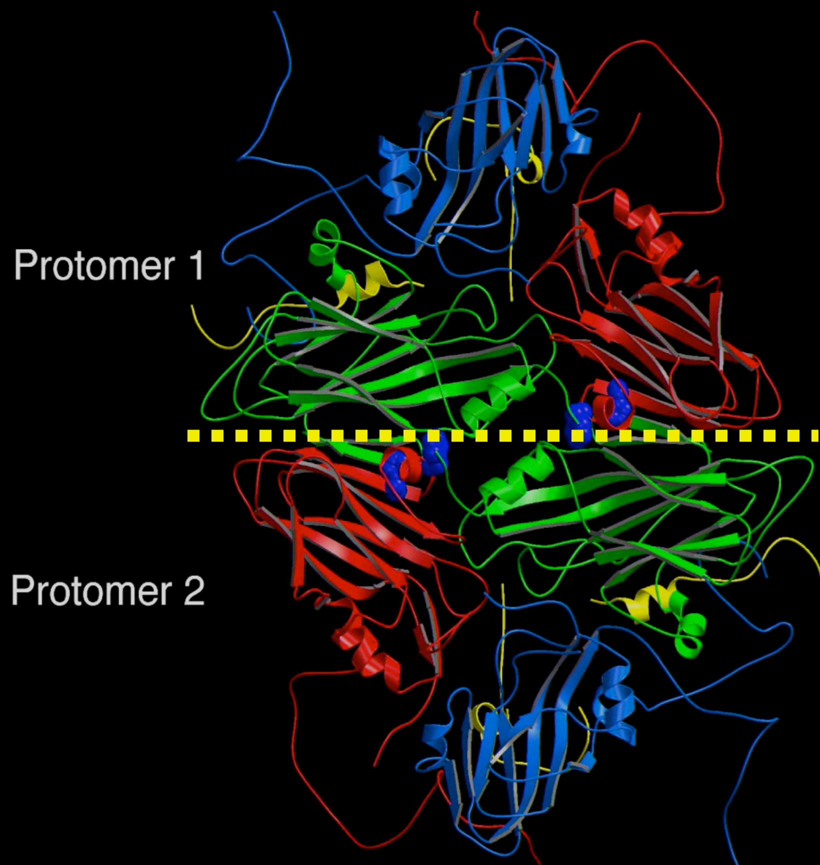


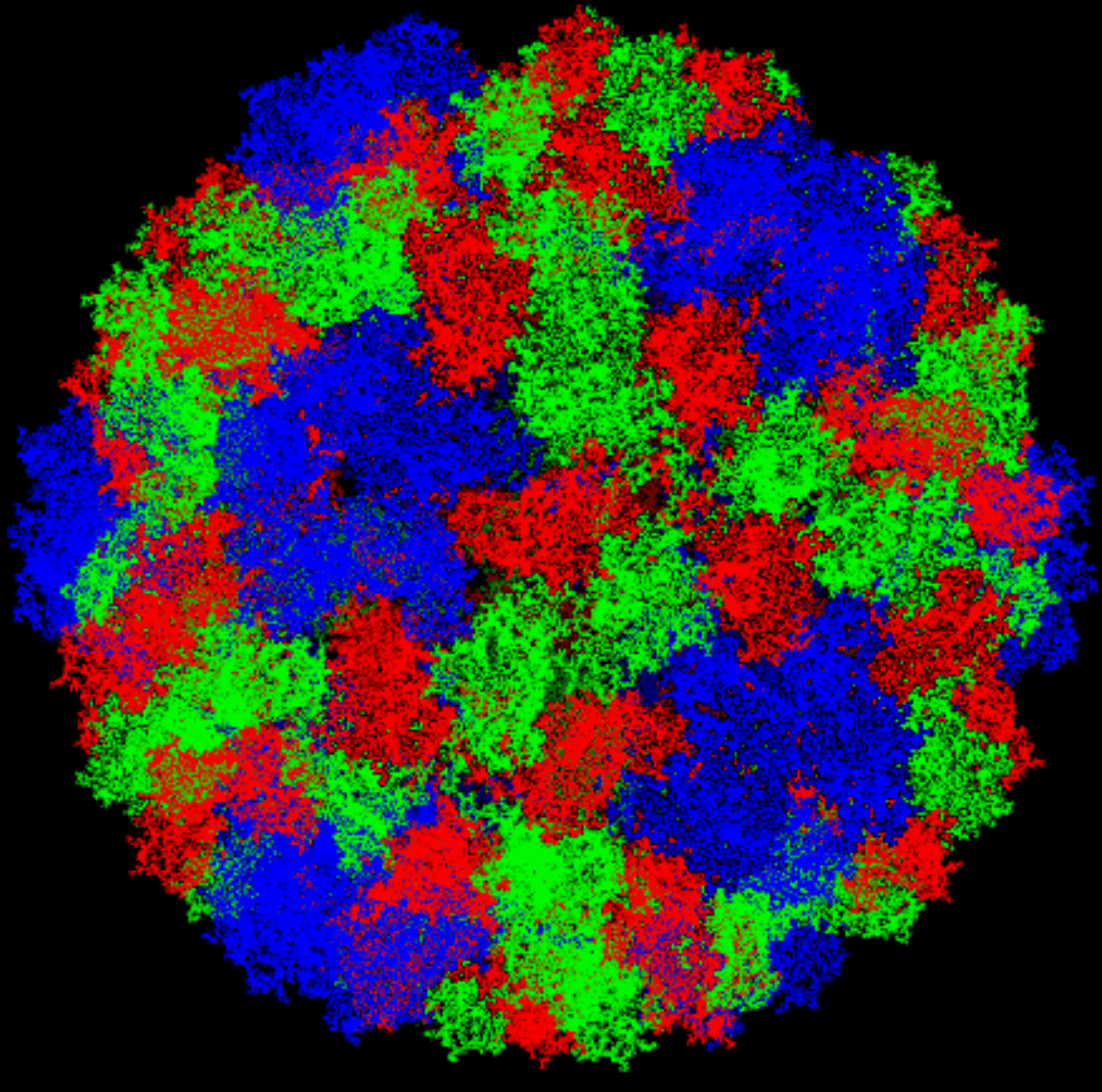
Virus Capsid





pH 3.0





The Grotthus representation

In the cell, protons are in countable quantity:

- just few tens in bacteria or in a mitochondrion
- at pH 7.0, the mean distance between two protons is 250 nm,
- a concentration gradient is not a force field. It is only a probability gradient.