Intracellular Water

❤ Intracellular solutions contain more K+ ions
❤ Membranes help create a tendency towards low density water in cells
❤ The effect of intracellular protein on water structuring
❤ The importance of protein carboxylate groups
❤ The importance of protein mobility
❤ Cooperative conversion of the water structuring
❤ Actin, tubulins and the intermediate filaments

"the molecular structure of water is the essence of all life" a
Dr. Albert Szent-Gyorgy, Nobel Prize winner.

Intracellular water is the water inside cells that bathes all the necessary biological molecules including the proteins and nucleic acids. Cells contain differing amounts of water dependent more on their purpose (and hence expressed proteins) rather than their source organism (for example, the % water contents of red blood cells are about 64% whether from man or dog whereas frog heart contains 80% but a frog egg only 49% water) [762]. This water is not solely a medium but a metabolic reactant, product, catalyst, chaperone, messenger and controller (see for example, [1194]). The water is essential for biomolecular recognition [1787] and orchestrates the cell machinery [1785]. The complexity and organization within the cytoplasm is expressed in a comprehensive review of intracellular water [1191] and an interesting current review has considered the versatility and adaptability of intracellular water in engaging in a wide range of cellular biochemistry [1359]. A key feature of intracellular water is its ability to convert between high and low density states [1364] (as exemplified by the ES⇌CS equilibrium). Such changes have been linked to the state of autothixotropy [1898].

An increase in cell size, following cell membrane depolarization, occurs together with a reduction in water's diffusivity, indicating the very different characteristics that intracellular water appears to possess when compared to extracellular water.b Experimentally, this area presents a difficult problem as the properties and functioning of the cell in vivo cannot be easily determined from the sum of its parts in vitro; indeed the commonly practiced in vitro experiments on the homogenized and dilute contents of dead cells may be entirely misleading. For examples, CO_2 production in metabolizing cells may give rise to complex changes in water movement and osmotic pressure changes as neutral CO_2 diffuses readily but ions formed from it on hydration do not [1137] and actively metabolizing cells may be

producing a significant amount of their intracellular water [1139]. Study of the live cell is fraught with difficulty as most procedures may alter the in vivoconditions, although dynamic phase microscopy shows promise [1332]. The structure and hydrogen bonding of intracellular water is clearly central to any theory concerning intracellular cell dynamics with intracellular protein dynamics and internal protein fluctuations both slaved to the water dynamics [1856]. There are two theories concerning intracellular water that have greatly influenced current thinking concerning the complex roles of intracellular water. These are the 'polarized multilayer theory' of Gilbert Ling [634] and the 'gel sol transition' of Gerald Pollack [351, 635]. On this page, the combination of aspartic and glutamic acid ion-pairing with K+ ions, changes in the mobility of key proteins and the natural low density clustering within intracellular water are all shown to contribute towards intracellular metabolic transitions and information transfer. Both prior theories are accommodated within this hypothesis [1093]. [Back to Top ▲]

## Intracellular solutions contain more K+ ions

The different characteristics of the intracellular and extracellular environments manifest themselves particularly in terms of restricted diffusion and a high concentration of chaotropic inorganic ions and kosmotropic other solutes within the cells. Note that both chaotropic inorganic ions and kosmotropic other solutes encourage low density water structuring. The difference in concentration of the ions is particularly apparent between Na+ and K+ (see below); Na+ ions creating more broken hydrogen bonding and preferring a high aqueous density whereas K+ ions prefer a low density aqueous environment. A 1000-fold preference for K+ over Na+ has been found in a halophilic organism without any energy expenditure but with a highly reduced intracellular water mobility [817]. As explained in discussion of the Hofmeister effectand shown by the negative apparent ionic volumes (that is, addition of the ions reduces the volume of the water, see below), the interactions between water and Na+ are stronger than those between water molecules, which in turn are stronger than those between water and K+ ions; all being explained by the differences in surface charge density. The interaction strength is reflected in that the distance between the Na+ ions and water is shorter than between two water molecules which is shorter than between K+ ions and water. Ca2+ ions have even stronger destructive effects, on the hydrogen bonding, than Na+ ions. Clearly, K+ ions are preferred within the intracellular environment.

Comparison of key cellular ions

Ion	Ionic radius	Surface charge density	Molar ionic volume	Intra-cellular	Extra-cellular	Water preference
Ca2+	100 pm	2.11	-28.9 cm3	0.1 µM	2.5 mM	High density

Na+	102 pm	1.00	-6.7 cm3	10 mM	150 mM	High density
K+	138 pm	0.56	+3.5 cm3	159 mM	4 mM	Low density

Although somewhat contentious, it has been reported that the cellular membrane ion-pumps cannot produce these large differences in ionic composition in the absence of other mechanisms, simply as the (ATP) energy required appears to exceed the energy that is available to the cell and the gradients are maintained in the absence of intact membranes and/or the absence of active energy (that is, ATP) production [634, 635]. Also, in contrast to that written in several undergraduate textbooks, many studies show that cells do not need an intact membrane to function [635]. Instead, the intracellular water tends towards a low density structuring due to the kosmotropic character of the majority of the solutes, the confined space within the cell stretching the hydrogen-bonded water and the extensive surface effects of the membranes [1094]. The ions partition according to their preferred aqueous environment; in particular, the K+ ions partition into the cells. Ion pumps must thus be present for other (perhaps fail-safe) purposes, such as speeding up the partition process after metabolically linked changes in ionic concentration. [Back to Top ⋀]

Membranes help create a tendency towards low density water in cells
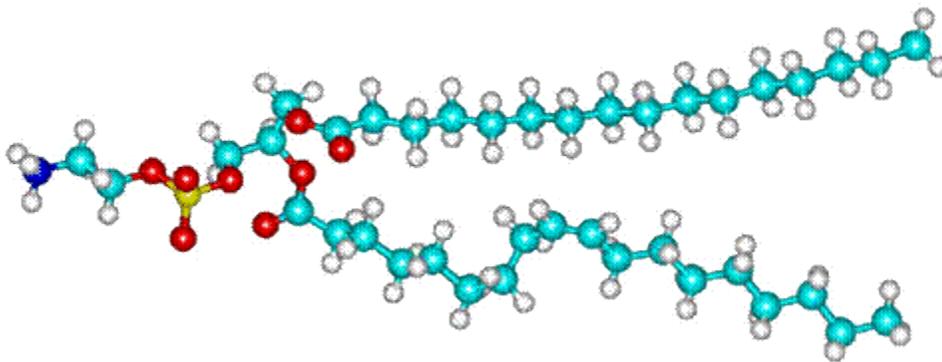
Membrane lipids contain hydrophilic kosmotropic groups such as the phosphatidylethanolamine, shown opposite, which encourages the lower density water structuring inside cells. This is particularly relevant as there is extensive membrane interfacial water within cells, e.g.liver cells contain ~100000 µm2membrane surface area. The aqueous interface next to the membranes forms a functional unit linking the membrane to the water-soluble proteins of the cytosol, facilitating the rapid exchange of structural, dynamic and physiological information [1553]. [Back to Top ⋀]

The effect of intracellular protein on water structuring

The degree of density lowering inside cells is determined by the solutes, their concentration and the conformations and state of motion of the proteins; mobile proteins creating more disorder in the clustering compared with more static proteins. Many intracellular proteins are globular, so retaining rotational entropy notwithstanding the crowded environment. Water has conflicting effects in the mixed environments around proteins. Weak H-bonding between the protein and water molecules allows greater flexibility. Strong H-bonding endows the protein with greater stability and solubility. There is an ordered structure in first shell around the protein, with both hydrophobic clathrate-like and H-bonded water molecules each helping the other to optimize water's H-bonding network. Changes in the proteins' conformations may result in water influx into the cell or efflux from the cell [949] as well as density changes. Protein carboxylate groups are generally surrounded by strongly hydrogen-bonded water whereas the water surrounding basic chaotropic groups (arginine, histidine and lysine) tends towards a clathrate structuring. Clathrate formation over hydrophobic areas maximizes non-bonded interactions without loss of H-bonds whereas carboxylate groups usually only fit a collapsed water structure creating a reactive fluid zone. The diffusional movement of the proteins will cause changes in the water structuring outside the first hydration shell.
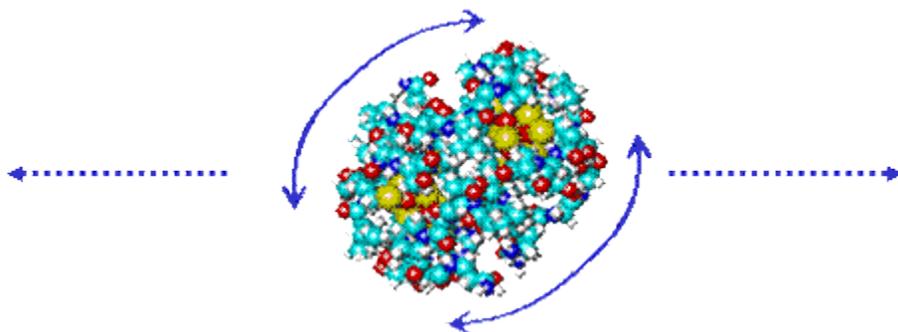
Translational diffusion involves breaking water-water links at a distance from surface whereas rotational diffusion involves breaking close water-water and protein-water links [640]. The surface area for translation and rotation is the same but the velocity differential is constant for all radial distances (r) for translation but varies with r2 with rotation.

At the breaking surface, half the H-bonds are ruptured, therefore creating a zone of higher density water (as explained elsewhere). Protein rotation thus creates a relatively close and surrounding high-density water zone with many broken hydrogen bonds, and as shown by some NMR studies. The volume of this interfacial region of perturbed water around the proteins is comparable to the volumes of the proteins. [Back to Top ▲]
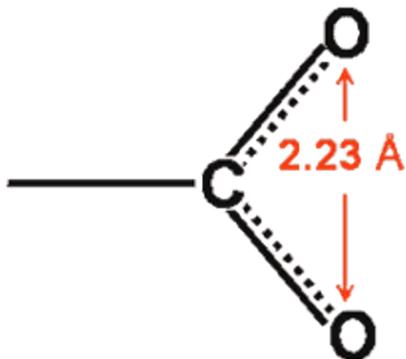
The importance of protein carboxylate groups

The side-chain carboxylate groups (that is, aspartic and glutamic acids) in proteins possess high dipole moments and contain two oxygen atoms that are nearer (~2.23 Å) than occurs between water molecules in bulk liquid water (~2.82 Å). These carboxylate oxygen atoms preferably hydrogen bond ~4 [1169] to ~6 [1781] water molecules which accounts for about 40% of the hydration free energy with the remainder mostly derived from outer aqueous shells [1781 a].f This hydrogen bonding causes a localized high density water clustering due to the closeness of the water molecules as they gather around the carboxylate groups [1063]. Binding of water to the two oxygen atoms is anticooperative and instantaneously the oxygen atoms and C-O bonds are non-identical [1587].

Such hydrogen bonding induces a more negative charge on the carboxyl oxygen atoms, increasing the group's dipole and this leads to an increase in the carboxylate pKa, as is shown below.
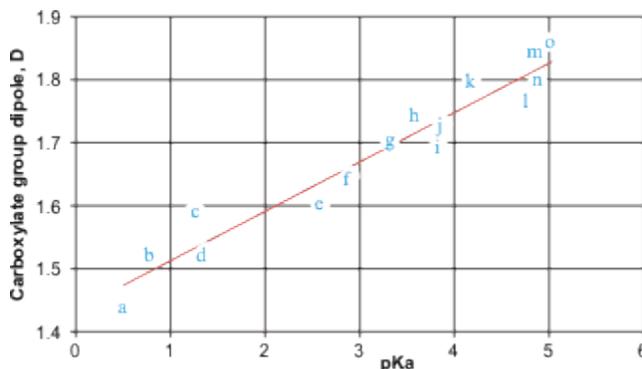

[6]The atomic charges and geometry of various related carboxylate were determined using ab initio molecular dynamics with the 6-31G** basis set. in Hyperchem. The dipoles of the carboxylate groups were calculate in Debye, units. A linear trend can be seen between the carboxylate group dipole and the pKa of the acids: a, trifluoroacetate; b, trichloroacetate; c, dichloroacetate; d, difluoroacetate; e, fluoroacetate; f,

chloroacetate; g, thioglycollate; h, thiolactate; i, glycollate; j, lactate; k, 3-thiopropanoate; l, acetate; m, 2-methylpropanoate; n, propanoate; o, 2,2'-dimethylpropanoate. Most of the acidity constants were obtained from [1142].
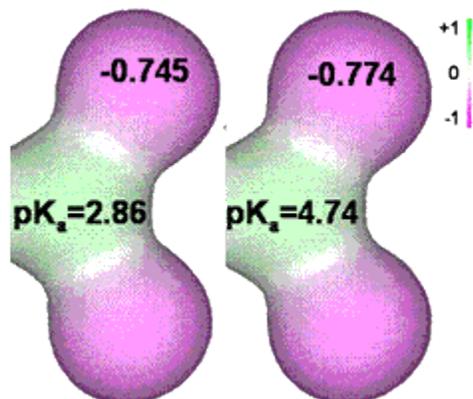

If the charges on the carboxylate oxygen groups are reduced, by neighboring electron-withdrawing substituent groups or imposed negative electric field, the pKais reduced. Note that the charge on the oxygen atoms lies between that on the ionic kosmotrope sulfate (−0.87; with hydrogen-bonds to water) and the ionic chaotrope perchlorate (−0.71; preferring to be surrounded by clathrate water). Thus, only a 5% reduction in the negative charge on the carboxylate oxygen atoms is necessary to switch from kosmotropic to chaotropic behavior. It is found that Na+ ions prefer binding to the weaker carboxylate groups (pKa > 4.5) whereas K+ ions prefer the stronger acids (pKa < 3.5) [634]. [Back to Top ⋀]

The importance of protein mobility
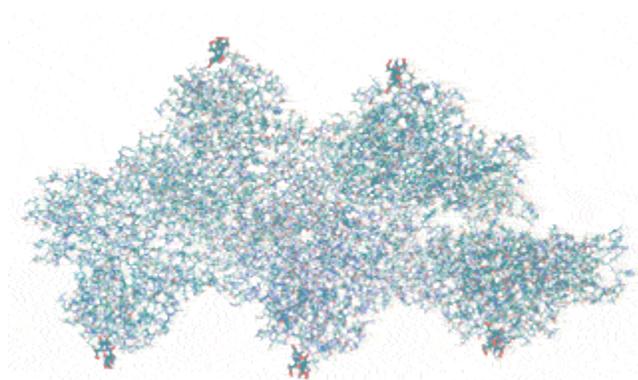
Actin is a highly conserved and widespread eukaryotic protein (42-43 kDa)e responsible for many functions in cells. Non-muscle cells contain 5-10% (of all protein) actin whereas muscle cells contain about 20%. All actin molecules contain a conserved acidic N-terminus with several neighboring aspartic and/or glutamic acids and a post-translation acetylated terminal amino group (for example, N-Ace-Asp-Glu-Asp-Glu in rabbit muscle α-actin). When actin forms a filament structure this highly charged

grouping is placed on the outer exposed edge of the helix, where it may be additionally used as a binding site for other proteins, such as myosin. The positioning of the acidic N-terminal antennae are shown in red in the cartoon below. Tubulin and the intermediate filaments are further structural proteins that form immobile structures with ordered hydration within cells, possessing conserved acidic groupings that serve similar functions.e

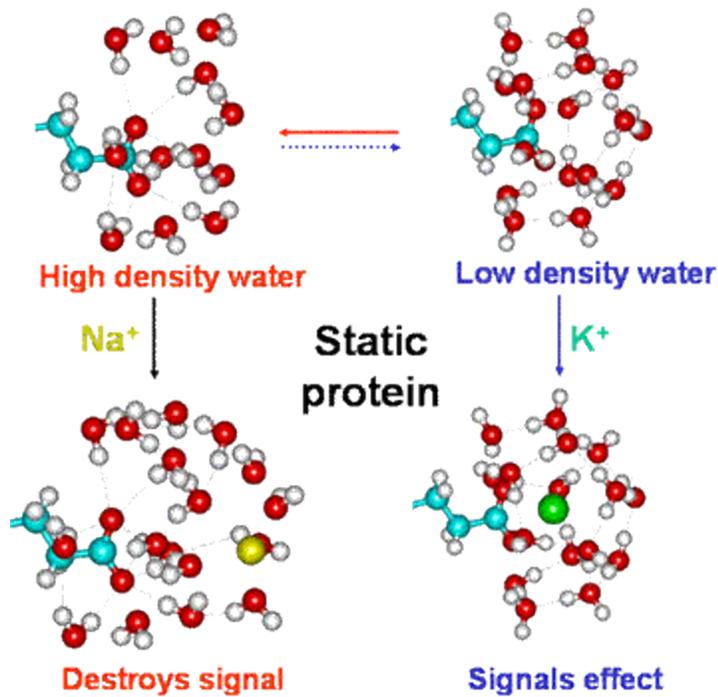Rotating G-actin ← α-helix ⇌ (ATP / ADP+Pi) β-turn → Static F-actin
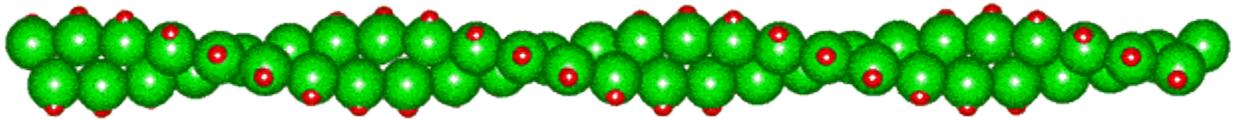
Actin is converted between a freely rotating molecule (G-actin; about 4 - 6 nm diameter) and a static right-handed double helical protein filament (F-actin; up to several microns in length) by ATP; a process involving the conversion of an α-helix to a β-turn in one of the structural domains [636]. Each molecule of the freely rotating G-actin can influence a large volume of water within its effective radius of gyration, causing a reduction in the intracellular low density aqueous clustering. Filamentous actin (F-actin) is a much more ordered structure so creating more order in its surrounding water. Protein fibers trap water, which has decreased entropy. In order to attempt to keep the water activity constant, therefore, the water has to form bonds with a more negative enthalpy. This results in stronger bonds, causing greater structuring and lower density. Also, enclosure of water involves capillary action forming 'stretched' confined water that is much more highly structured (hence lower density) than the bulk water.


Isobutyrate

Polyacrylate
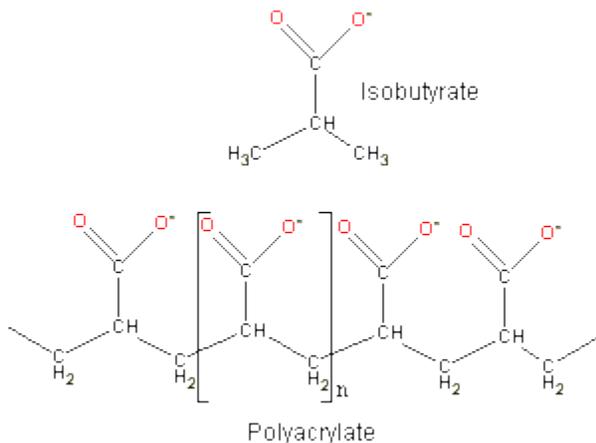
As overlapping fields from nearby groups enhance counter ion association, F-actin's extensive negatively charged N-terminus will cause the partitioning of cations into its vicinity, in a similar manner to that well known from immobilized enzyme studies. This partitioning effect was originally shown by Kern [638] who established that the activity of Na+ with isobutyric acid is >0.9 whereas similarly with polyacrylate it is <0.32, thus proving the greater partitioning of cations within the microenvironment of the multiply-charged polymer.

Na+ and K+ ions behave differently when close to the carboxylate groups; K+ ions have a preference for forming ion pairs whereas Na+ ions form solvent separated pairings [637, 2035]. This is due to the Na+ ions holding on to their water strongly with the inner shell polarized water molecules being ideally situated for forming strong hydrogen bonds to the carboxylate oxygen atoms. The K+ ions prefer an inner shell clathrate water structuring that is reinforced its direct ion pairing to the carboxylate group. Also, Na+ ions cannot take part in clathrate structuring whereas K+ prefers this environment [641]. As the distance between the neighboring amino acid carboxylate groups (about 7.3 Å) is about the same as the diameter of clathrate water clusters (about 7.6 Å), extensive ion pairing of the adjacent carboxylate groups may be accommodated by neighboring clathrate clustering. K+ RCO2- pairs move from solvent separated to ion pair with reduction in the pKa. K+ ions prefer strong acids (that is, low pKa) whereas Na+ prefers weak acids (that is, higher pKa). Direct ion pair association discourages aqueous hydrogen bonding to the carboxylate oxygen atoms but encourages clathrate formation surrounding the ion-paired carboxylate group.

Note that the association of K+ with proteins' aspartate and glutamate groups is the central theme of Ling's fixed charge hypothesis [634] where evidence for the molecular mechanism for the association includes (1) the low intracellular electrical conductance, (2) the strongly reduced mobility of intracellular K+ ions, (3) the altered X-ray absorption fine edge structure, (4) the widely different activity coefficients of K+ ions in different cells, (5) K+ ion absorption shows one to one stoichiometric absorption to the carboxylate groups and (6) identification of K+ ion absorption sites as aspartate and glutamate side chains.

High density water   **Low density water**

Na⁺   **Static protein**   K⁺

Destroys signal   **Signals effect**

Under conditions when the carboxylate groups possess high pKa, both K+ and Na+ form solvent separated species when partitioned into the carboxylate environment. This gives a preference for Na+ and high-density water. However, rotation of the protein will tend to sweep such ions, and their associated water, away. If the protein stops rotating, Na+ ions tend to destroy any low density structuring around carboxylate groups of the protein. However generally the intracellular Na+ ion concentration is far lower than that of K+ions (see above). At low pKa, K+ ion pairs to carboxylate groups, particularly when partitioned into their microenvironment due to the presence of a number of contiguous acidic amino acids.
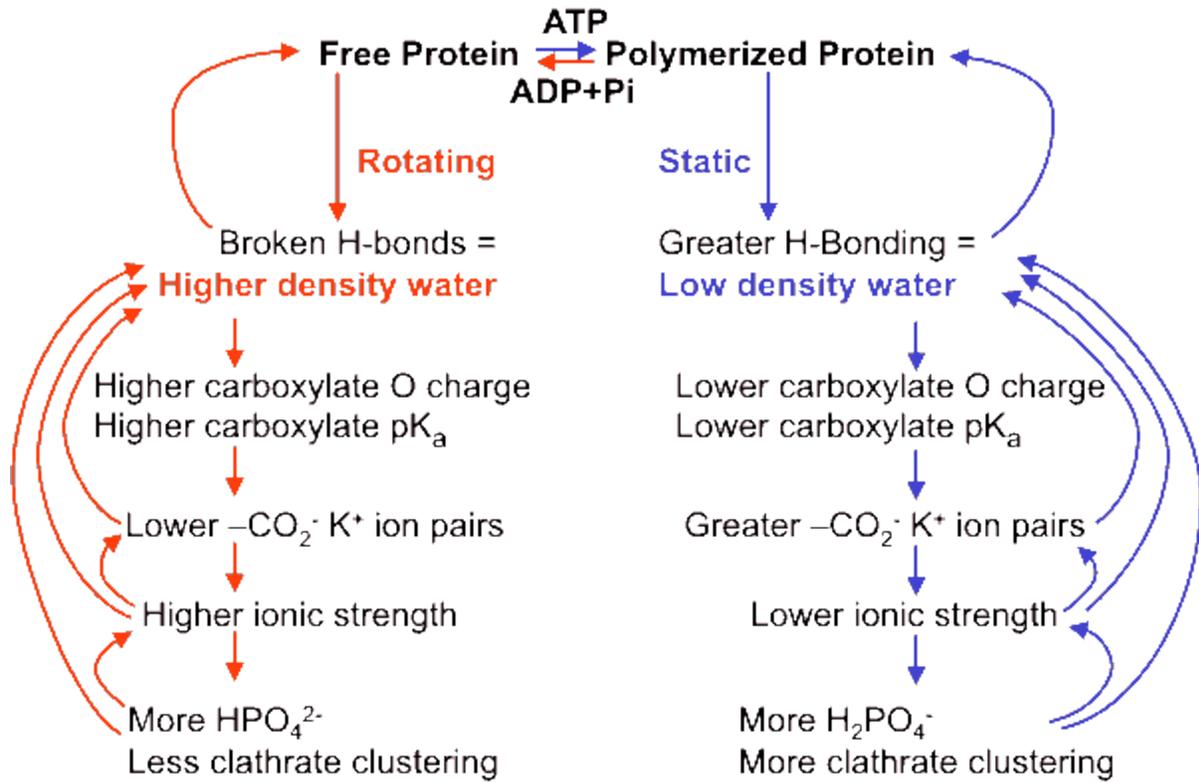
High density water   Low density water
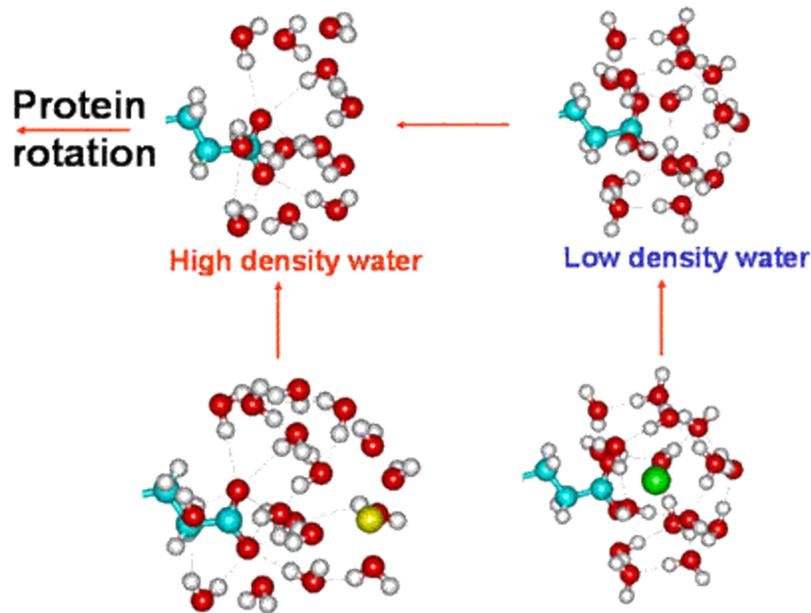
When ion-paired the hydrogen bonding to the carboxylate oxygen atoms is prevented and a surrounding clathrate structuring is preferred. The clathrate clustering can signal their state to other neighboring carboxylate groups (see later).

When the static protein filaments converts to freely diffusing proteins, the ions are swept away due to the multiple contacts with surrounding water molecules and their inability to keep up with the rotating protein at increasing radial distances. This results in the conversion of any localized clathrate water structuring to high-density water involving hydrogen-bonded carboxylate groups. [Back to Top ▲]

Cooperative conversion of the water structuring

Binding of K+ by the carboxylate groups lowers the ionic strength of the intracellular solution. As this ionic strength decreases, the pKa of phosphate groups increases resulting in the conversion of the more kosmotropic intracellular doubly-charged HPO_4^{2-} ions to the singly-charged more chaotropic $H_2PO_4^-$ ions.d All intracellular phosphate entities (about 100 milli-equivalents l-1) will behave similarly, so increasing the tendency towards low-density water. Thus the cooperative effects of the change between static filament formation and freely-diffusional protein can be summarized as below.

ATP

Free Protein ⇌ Polymerized Protein

ADP+Pi

Rotating   **Static**

Broken H-bonds =   Greater H-Bonding =
Higher density water   **Low density water**

Higher carboxylate O charge   Lower carboxylate O charge
Higher carboxylate pK_a Lower carboxylate pK_a

Lower $-CO_2^-$ K^+ ion pairs   Greater $-CO_2^-$ K^+ ion pairs

Higher ionic strength   Lower ionic strength

More HPO_4^{2-} More $H_2PO_4^-$
Less clathrate clustering   More clathrate clustering

Further support for this process is given by F-actin becoming more static in the presence of about 100 mM K+ [642].
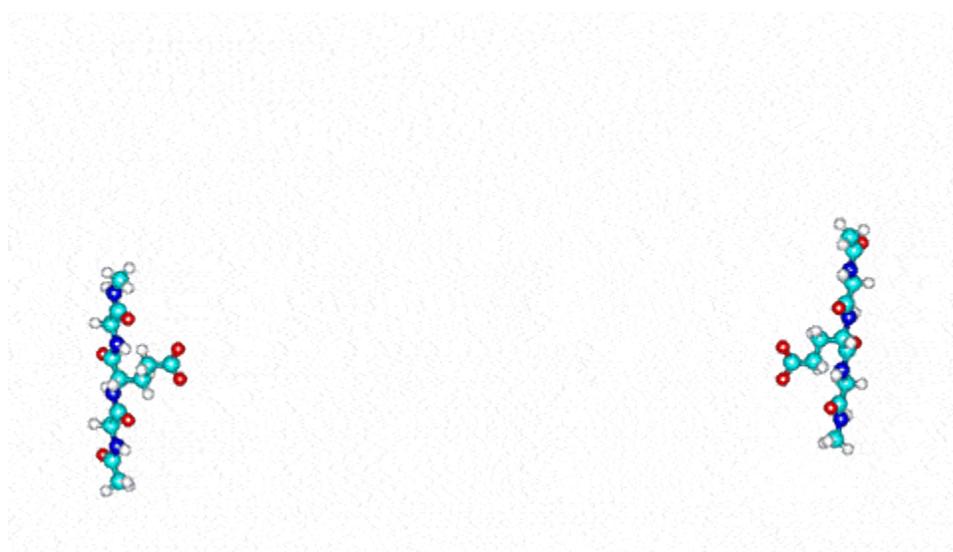
Forward   Backward

Only the oxygen atoms of the water network are shown above.

Formation of K+-carboxylate ion pairs lead to the formation of a surrounding clathrate water structuring that further leads to icosahedral water structuring (so ensuring maximal hydrogen-bond formation) and informing neighboring carboxylate groups. This signaling cooperatively reinforces the tetrahedralityof the water structuring found between these groups. The mechanism is indicated on the right (press the Forward button). Note that the clathrate arrangement allows cluster mobility (like a ball-and-socket joint), enabling the hydrogen bonding to search out cooperative partners. The expected greater rigidity of such structures with lower temperatures has been proven [1466].

The diameter of the cylindrical water cluster appears to be less than 3% different from that invoked to explain the hydrophobic effect between flat hydrophobic surfaces and extending over some tens of nanometers [1316], indicating that the same clustering may be involved in both cases.

The cooperative nature of this signaling offers an explanation for the signal amplification seen in the conduction of impulses along the microtubules and actin [1434],e and perhaps linking to other parts of the cytoskeletone [1307]. The importance of this cannot be overstated as microtubules are implicated in information processing and memory [1307]. The structuring of water may therefore be key to the conscious mind [1337].

Although the clustering (above right) involves a major drop in entropy, this is compensated by a more-negative enthalpy due to the stronger bonding of the fully-tetrahedral hydrogen-bonded structure. The phase transition between ordered and disordered water has been regarded as a mechanism to release energy for biological work rather than the membrane (pump) theory [1960]. It is consistent with Ling's association-induction polarized multilayer model [634],c as can be seen from the net dipoles emanating from the clathrate arrangement, but offers a more realistic explanation. The initial icosahedral size (3 nm diameter) also equals the water domain size proposed by Watterson [546]. Extensive (1.4 nm) long-lived (> 300 ps) aqueous dipole arrangements between biomolecules have been found in molecular dynamics studies [329]. Further support for this model is given by a number of studies concerning different types of intracellular water, such as "normal" bulk and "abnormal" osmotically inactive interfacial water [639]. Also, the water in the extreme halophileHaloarcula marismortui, which contains

particularly large amounts of bound intracellular K+ ions, shows particularly slow translational
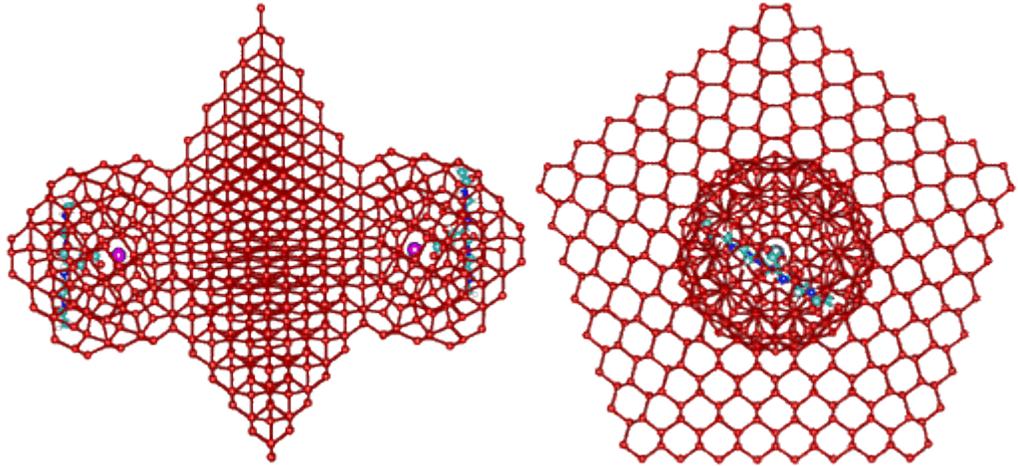
diffusion [1253].

These orthogonal diagrams show the maximum limit of fully tetrahedral water clustering due to the cooperative clustering (see above) from two K+-carboxylate ion pairs. This fully tetrahedral structuring, which resembles a mixture of hexagonal and cubic ice structures but with 5-fold symmetry (such that it cannot be easily frozen), is idealized in the cartoons. An interactive structure is given (Jmol).

Extension of the clathrate network and its associated low density water enables K+ ion binding to all aspartic and glutamic acid groups, not just the key ones within the extensive acidic centers. Thus, the gel-sol transition of Pollack [635] is interpreted as the conversion to low density water clustering (the gel state) due to clathrate clustering around K+-carboxylate ion pairs. The changes in the functional state of the cell and its organisms has been shown to be reflected in the changes in the cell's refractivity [1997]. Certainly, the stiffness of the cytoplasm depends on the structure of the water as shown by changing the H2O water to D2O heavy water when the intracellular relaxation frequency reduces by between two and four orders of magnitude depending on the timescale [1856].

In the presence of raised levels of Na+ and/or Ca2+ ions, as occasionally occurs during some cell functions, these ions will replace some of the bound K+ ions. These newly formed solvent separated Na+ and/or Ca2+ ion pairings destroy the low-density clathrate structures and initiate a cooperative conversion of the associated water towards a denser structuring.

In conclusion the information transfer within the cell involves the following:

Intracellular water favors K+ ions over Na+ ions.

Freely rotating proteins create zones of higher density water, which tend towards a lower density clustering if the rotation is prevented.

Static charge-dense intracellular macromolecular structures prefer K+ ion pairs over freely soluble K+ ions.

Ion paired K+-carboxylate groupings prefers a local clathrate water structuring.

Clathrate water prefers local low density water structuring.

Low density water structuring can reinforce the low density character of neighboring site water structuring.

Na+ and Ca2+ ions can destroy the low density structuring in a cooperative manner. [Back to Top ▲]

Footnotes

a Philosophical, historical and scientific views of water in living systems have been reviewed [1011] [Back]

b   The cytoplasm of cells is described in [892]. Nuclear magnetic resonance signal widths are much broader inside cells, showing that intracellular water is far more structured than extracellular or pure water; for example, see [884]. For a review of the relationship between the intracellular water and the cytoskeleton see [880]). It is noteworthy that the amount of 'free' versus 'bound' water [969], K+ ions and the cytoskeleton are all intimately linked in the differences between normal and cancer cells [1333]. [Back]

c   The polarized multilayer theory relies on the hypothesis that static proteins in the cell change their secondary structure from compact to extended forms, so that the newly formed extensive lengths of polypeptide 'polarize' the water by means of their amide (N-H and C=O) backbone. Although there is support for the presence of polarized multilayers of water [634], there is no experimental support to this explanation for their presence. Indeed, most experimental data is contra-indicative, resulting in only minority support from scientists in this area. [Back]

d   The chaotropic/kosmotropic nature of these ions has been confirmed by FTIR [1072]. [Back]

e

Actin, tubulins and the intermediate filaments

An analysis of the known actin structures from the UniProt Knowledgebase showed the 32 complete α-actin structures recorded from fish, birds, snakes and mammals all to have the conserved acidic N-terminal structure Acetyl- D/E- D/E- D/E-D/E- T/S/V- T- A- L- V- C- D- N- G- S- G- L- V- K- A- G- F- A- G- D- D- A- P- R- A- V- F- P- S- I- V- G- R- P- R- H- Q- G- V- M- V- G- M- G and the 70 complete β- and γ-actin structures recorded, from a similar range of species, to all have the conserved and closely related N-terminal structures of Acetyl- D/E- D/E- D/E- I/V/T- A/T- A/S- L- V- V/I/C- D/A- N- G- S- G- M/L- C- K- A- G- F- A/G- G/R- D- D/G- A- P- R- A- V/A- F- P- S- I- V- G- R- P- R- H- Q- G- V- M- V- G/R- M- G with even the variations limited to one or a very few molecules.
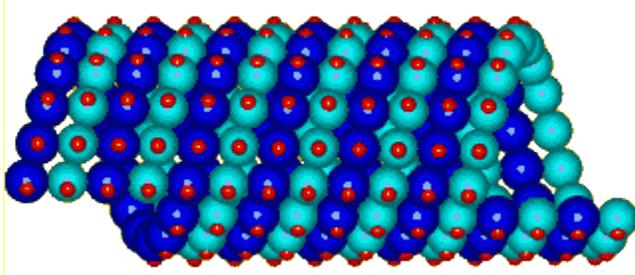
Eukaryotic tubulin is another structural protein that forms immobile structures with ordered hydration within cells [689]. It forms fat hollow and stiff microtubules (~25 nm diameter, containing low density water) making tracks through the intracellular space for the movement of organelles. These tubular structures are built up from pairs of similar subunits (α and β), each of about 450 amino acids [1140]. Tubulins have a GTP binding domain near their N-terminal and two separate β-sheets each surrounded by α-helices. The microtubules are formed from head to tail arrangement of α/ β dimers with the beta-subunit GTP at the open end. Only this GTP is hydrolyzed following polymerization. Outside the molecular core, two exterior antiparallel α-helices lead to highly acidic C-termini, which are thus situated on the outside of the microtubule and away from the tubulin surface [1306]. The α-tubulin structure is highly conserved with C-terminal consensus sequence - A- R- E- D- M- A- A- L- E- K- D- Y- E- E- V- G- V- D- S- V- followed by an extremely variable but highly acidic C- terminus exemplified by the human α- tubulin (type 'ubiquitous') structure - E- G- E- G- E- E- E- G- E- E- COOH. The β- tubulin structure is also highly conserved with C-terminal consensus sequence - A- E- S- N- M- N- D- L- V- S-E- Y- Q- Q- Y- Q- D- A- T- A-

followed by an extremely variable highly acidic C- terminus exemplified by the human β- tubulin (type '4Q') structure - E- E- E- E- D- E- E- Y- A- E- E- E- V- COOH. As with the actins, these examples indicate clearly that very strongly conserved structures exist for tubulins except for at an end (here the C-terminus) where glutamic acid and aspartic acid occur apparently interchangeably and in variable but always very acidic sub-structures. Improper functioning of tubulin has been linked with intracellular water clustering in the origin of cancer [1901].

Intermediate filaments are fibrous, flexible and elastic proteins formed mainly from coiled coils ('ropes', ~11 nm diameter) of multi-stranded acidic α-helices [1141]. There are a number of families of associated proteins such as the nuclear lamins, sarcomere desmins, neuron neurofilaments and epithelial cytokeratins. In addition, the vimentins generally support the organelles and maintain cellular integrity. All these proteins possess α-helical central 'rod' domains (~48 nm long) that contain about 310 amino acids plus more variable end domains. Whilst some acidic groups form salt links across to basic groups in other strands to build up and lengthen the resulting 'elastic rope' structure, there exists an excess of acidic groups on the surface of the filaments. Within the α-helices are acidic bulges (formed from single π-helical loops) containing clusters of three glutamic acids within four residues and creating flexible 'linker' regions. As different strands come together to form the fibrous 'ropes' these acidic clusters are grouped together with contributing acidic clusters from about 20 helices on the surface of the filaments. [Back]
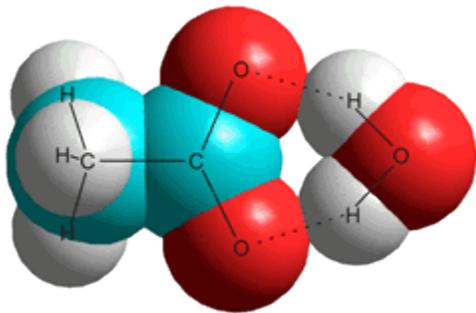
f Time-resolved infrared pump-prime spectroscopy of acetate in D2O suggests the bridge structure (right) as the most stable (single-hydrated) structure [1804], but other water molecules are also involved. [Back]

[Back to Top ⮝]

Source:http://www1.lsbu.ac.uk/water/cell.html