

The Structure of Water

Water is unusual

As discussed in more detail below, water² molecules form strong intermolecular interactions with one another. These interactions are actually very complex and are not fully understood, and, as a result, computer simulations of water are only accurate for narrow sets of conditions. Because biological systems depend heavily upon the structure and properties of water, our incomplete understanding of water behavior is a major nuisance in making accurate theoretical predictions about the structure and behavior of biological molecules. However, the discussion below should be correct in both general outline and most details, because it is based largely on the gross properties of water that can be measured empirically.

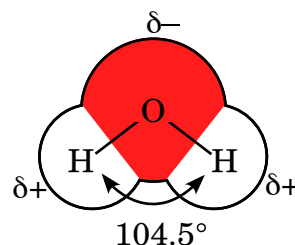
Compared to other molecules of similar size, water has a very high boiling point and a high melting point. Because these physical constants, and especially boiling point, are indirect measures of favorable intermolecular interactions in pure materials, it is clear that water forms much stronger intermolecular interactions than do other molecules of similar size.

Compound	Molecular weight (Da)	Melting point (°C) ³	Boiling point (°C) ³
Methane	16.04	-182.6	-161.4
Ammonia	17.03	-77.7	-33.35
Water	18.02	0	100
Methanol	32.04	-93.9	64.7

Another feature of water is a high heat of vaporization: in other words, a large additional energy input is required to cause the phase transition from liquid to gas (this is why sweating is very efficient as a cooling mechanism: evaporation of the secreted water absorbs large amounts of waste heat). Water also has a high surface tension, and has greater density in liquid form than in solid form. Finally, although water is a good general solvent for many types of compounds, it does not dissolve all types of materials equally well. All of these properties are related to the importance of water to living organisms.

The chemical structure of water

The chemical formula of water is H₂O, familiar to anyone who has taken chemistry. The three dimensional structure of water is represented at right. Notice the **dipole**: the asymmetric separation of partial charges in the molecule. Notice also the



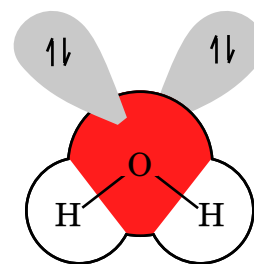
² The name “water” for the molecule H₂O is so widely used as to be considered standard nomenclature. In contrast, the formal IUPAC name for H₂O (oxidane) is so rarely used that its use generally only introduces confusion. While the word “water” actually only applies directly to the liquid phase for H₂O, in biochemistry, the liquid phase is the primary phase for this compound that is generally relevant.

³ Source: *Handbook of Chemistry and Physics*, 63rd Ed, 1982.

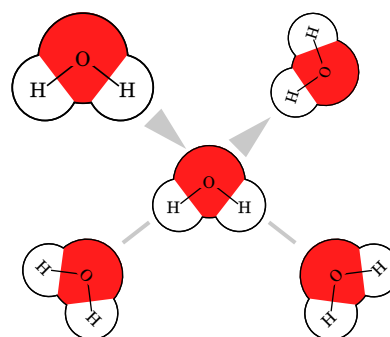
angular or **bent** shape of the molecule.

The oxygen in a water molecule has two lone pairs of electrons.

The lone pairs are capable of forming weak bonds (**hydrogen bonds**) with hydrogens covalently bonded to electronegative atoms on other molecules (especially the hydrogens on other water molecules). Hydrogen bonds are relatively weak (exhibiting typical bond disruption energies of ~20 kJ/mol, compared to 350-450 kJ/mol for covalent bonds), but can be important, because they are typically present in large numbers.



Each water molecule can form up to four hydrogen bonds (with the oxygen accepting two hydrogen bonds, and with each hydrogen acting as an hydrogen bond donor). The arrangement is **roughly** tetrahedral. The H–O–H bond angle does not allow the formation of a perfect tetrahedron. (Note that in actual water, the average number of hydrogen bonds per water molecule is less than four, probably due to geometry constraints and entropic effects.)



The ability of the water molecule to participate in extensive hydrogen bonding networks is responsible for most of the unusual bulk properties of water, including its high melting and boiling points, ΔH of vaporization, and surface tension.

Water as a solvent

Polar and ionic molecules dissolve readily in water. The water molecules interact strongly with these types of molecules, and thereby replace many of the interactions formed by the solute in its solid form. However, water is much less effective as a solvent for non-polar compounds. We will consider water as a solvent for each type of compound.

Ionic solutes

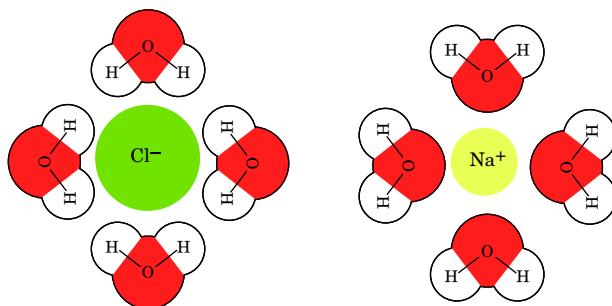
Water has a high dielectric constant; the dielectric constant of a medium is a measure of the ability of the medium to shield charges from one another. The effect of this shielding is a decrease in the force, F , between ions. The force F is given by:

$$F = \frac{kq_1q_2}{\epsilon r^2}$$

where k is a proportionality constant ($8.99 \times 10^9 \text{ J}\cdot\text{m}/\text{C}^2$), q_1 and q_2 are the charges on the ions, ϵ is the dielectric constant of the medium, and r is the distance between ions. A negative value of F corresponds to an attractive force, while a positive value of F corresponds to a repulsive force. Note that the magnitude of F is inversely

proportional to the dielectric constant. Dielectric constants can vary over a wide range, from a value of 1 for vacuum, to about 2 to 4 for non-polar solvents, to a value of 78 for water (25°C).

In addition to the effect of the solvent dielectric constant, water can form favorable interactions with ions. Ions in aqueous solution have several water molecules in close proximity. This associated water forms a **hydration sphere** or **hydration shell**, and acts to shield the charges from one another. These hydration spheres are the result of electrostatic interactions between the water dipole and the charge on the ions in the solution.



Is dissolving ions in water favorable? Generally **yes!** This is easy to observe: salts dissolve in water. Considering this process in thermodynamic terms may clarify why this is true.

Process:



Breaking this down into the thermodynamic factors related to the NaCl and to the solvent:

Thermodynamic Factor	Reasoning
Disrupting NaCl	
$\Delta H^{\circ}_{\text{NaCl}} (+)$	The Na and Cl ions in the crystal are held together by ionic interactions; disrupting these interactions will result in a positive enthalpy.
$\Delta S^{\circ}_{\text{NaCl}} (+)$	Disruption of the crystal lattice will result in a large positive entropy change.
Rearranging H₂O	
$\Delta H^{\circ}_{\text{water}} (+)$	Dissolving NaCl will require disruption of hydrogen bonds between water molecules.
$\Delta S^{\circ}_{\text{water}} (-)$	Hydration shells have more ordered water molecules than bulk water.

Hydration	
$\Delta H^\circ_{shell} (-)$	The formation of the shell will result in favorable interactions.
ΔS°_{shell}	These interactions have little further effect on entropy.
Net effects	
$\Delta H^\circ_{overall} (+)$	The observed value is +7.7 kJ/mol
$\Delta S^\circ_{overall} (+)$	+56.6 joules•(mol ⁻¹ •K ⁻¹) calculated from solubility and ΔH° .
$\Delta G^\circ_{overall} (-)$	Calculated from the known solubility: -9.1 kJ/mol

Although the process of dissolving a solid ionic compound in water results in a negative ΔS° for the water (because the hydration shell is more ordered than the surrounding bulk water), this is compensated by a much larger positive ΔS° for the ions going from the organized solid phase to the more disordered solution. The sign and magnitude of the ΔH° depends on the relative strengths of the interactions present in the solid to those with the solvent. The overall ΔG° for dissolving ionic solids in water is significantly negative.

Non-ionic, polar solutes

Polar solutes can be defined in a number of ways. The definition of “polar” that we will use is an operational one: **a polar material is a material that can form favorable interactions with water molecules.** Although most definitions of “polar” refer to the dipole moment of a molecule, not all molecules with significant dipoles are especially water-soluble. The data in the table below illustrate this lack of correlation between dipole moment and water solubility for some molecules widely used in organic chemistry.

Compound	Water solubility ⁴	Dipole moment	Dielectric constant
Water	Miscible	1.85 (gas phase)	80.37 (20°C) 78.54 (25°C)
Methanol	Miscible	1.70 (gas phase)	33.62 (20°C) 32.63 (25°C)
Chloromethane	5.90 g/L	1.87 (gas phase)	12.60 (-20°C)
Fluoromethane	2.39 g/L	1.85 (gas phase)	
Methylamine	519.20 g/L	1.31 (gas phase)	9.40 (25°C)
Dichloromethane	19.38 g/L	1.60 (gas phase)	9.08 (20°C)
1-Butanol	74.60 g/L	1.66 (gas phase)	17.80 (20°C) 17.10 (25°C)
1-Octanol	0.54 g/L	1.65 (benzene)	10.30 (20°C)
Hexane	0.013 g/L	0 (gas phase)	1.89 (20°C)

⁴ **Sources:** Dielectric constants: *Handbook of Chemistry and Physics*, 63rd Ed, 1982; other properties *Chemical Properties Handbook*, Yaws, C.L. Ed., McGraw Hill, 1999. The dielectric constants are for liquid phase; fluoromethane is not a liquid at normal temperature and pressure, and therefore its dielectric constant is not directly comparable to that of the other compounds.

Non-ionic but water-soluble materials (polar molecules by the operational definition) generally dissolve because they can form many hydrogen bonds with water molecules. These hydrogen bonding interactions are more varied than in the solid form of the solute, and therefore the overall entropy of the system increases significantly. As with ionic materials, the enthalpy change of solvation may be positive or negative depending on the relative strength of the intermolecular solute-solute and solute-solvent interactions.

Non-polar solutes

In contrast to ionic and polar compounds, non-polar solutes are difficult to dissolve in water. Water cannot form favorable interactions with non-polar compounds because these compounds cannot act as hydrogen bond donors or acceptors. As a result, water molecules tend therefore to form a cage around the non-polar solute molecule that resembles the crystal lattice found in ice. This **ordered** structure is called a **clathrate**.

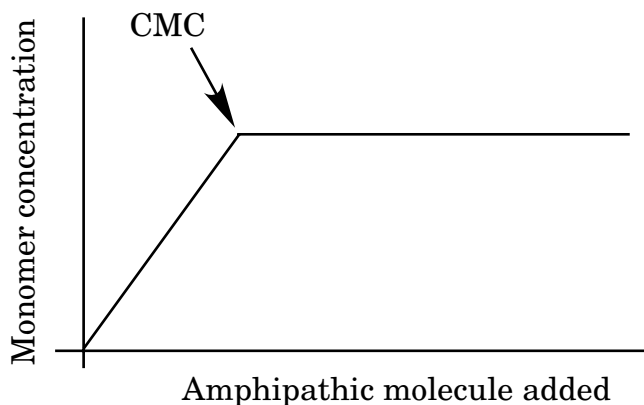
Clathrate formation is associated with a strong decrease in entropy of the solvent. Clathrates and hydration spheres are **not** equivalent. Although both are associated with some decrease in entropy for the water molecules, clathrates are somewhat more ordered structures than hydration spheres. In addition, unlike hydration spheres, clathrates do not involve any favorable interactions between the solvent and the solute; in interacting with non-polar solutes, water molecules must first disrupt their hydrogen bonds to other water molecules, which results in a $+\Delta H^\circ$ that is not countered by any $-\Delta H^\circ$ for bond formation. Finally, because most hydrophobic molecules are much larger than most ions, each non-polar molecule involves larger numbers of water molecules in the clathrate formation.

Surface area increases as r^2 , while volume increases as r^3 . Because the water molecules interact with the surface of the non-polar solutes, placing many hydrophobic molecules into close proximity decreases the number of water molecules affected by the clathrate formation. This increase in solvent entropy (due to the release of water molecules from the clathrate structure) as well as the enthalpic effect associated with the greater number of hydrogen bonds formed by the released water are the major causes of the **hydrophobic effect**. (A less important, but still significant, advantage to the aggregation of the non-polar molecules results from their ability to form more favorable van der Waals interactions with one another than they do with water. Thus, the formation of non-polar aggregates is usually associated with a $-\Delta H^\circ$ term that acts as an additional driving force.

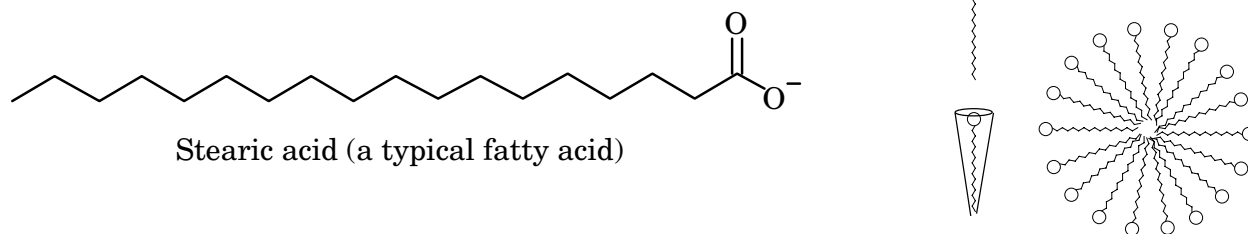
Amphipathic molecules

Molecules that have a polar group on one end, and a non-polar tail are called amphipathic or amphiphilic molecules (“amphi” means “both”; “amphipathic” literally means “hates both”). Most amphipathic molecules are slightly water-soluble. At low concentrations, they simply dissolve in water. As the concentration rises, however, the hydrophobic effect begins to become more important, as the unfavorable entropic term for forming amphipathic aggregates becomes less than the entropic cost of forming clathrates. Because the formation of these aggregates is

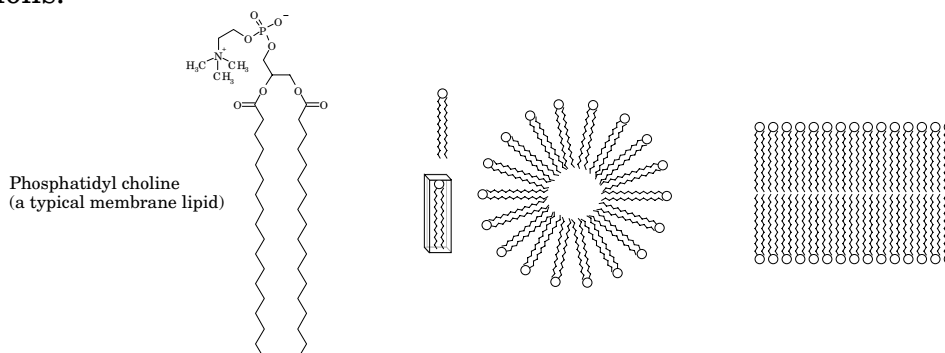
a cooperative phenomenon, the concentration of free monomer only rises until it reaches the **critical micellar concentration (CMC)**, after which, all additional monomers become part of the aggregates.



Fatty acids, which are carboxylic acids with long linear acyl chains, are molecules which have an essentially conical geometry. This results in the formation of essentially spherical aggregates known as **micelles** in aqueous solution. Most **detergents** are either fatty acids or molecules of generally similar structure comprised of a polar group at one end and a long non-polar tail. Detergents allow non-polar molecules to enter the micelle spheres, and therefore become dispersed through the aqueous phase.

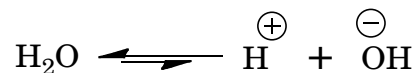


More complex amphipathic molecules, such as phospholipids, have an essentially rectangular solid geometry. This makes formation of spherical micelles less likely, because the molecular geometry precludes formation of a spherical structure without a large void in the center. As a result, these compounds tend to form planar bilayer structures; the geometric constraints of these molecule result in formation of stable biological membranes. Membrane structure will be discussed more fully in later sections.



Ionization of water

Water will spontaneously ionize to release free protons and free hydroxyl ions.



It should be noted that, in aqueous media, free H^+ do not typically exist. Instead, the dissociated proton is shared between many other water molecules to form transient H_3O^+ and related species. For simplicity, in the following discussion the symbol H^+ will be used to reflect the shared ion. Aqueous solutions do contain free hydroxyl ions, although these ions, as with all ions in aqueous solution, have a hydration shell.

It is possible to write the equilibrium equation for dissociation of water as:

$$K = \frac{[\text{H}^+][\text{OH}^-]}{[\text{H}_2\text{O}]}$$

However, in aqueous solution, the concentration of H_2O is so high that it is not significantly altered by the extremely small amount of dissociation that occurs. The effectively constant water concentration is generally included in the equilibrium K term to simplify the calculations.

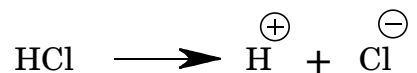
$$K_w = [\text{H}^+][\text{OH}^-] = 10^{-14} \text{ M}^2$$

In pure water, therefore, $[\text{H}^+] = [\text{OH}^-] = 10^{-7} \text{ M}$

To simplify discussion another term was introduced to describe small concentrations of hydrogen ions: **pH**, which is defined as the negative log of the hydrogen ion concentration. Neutral is defined as pH 7.0, because this is the pH for water with no additional ions present. Because pH is a log function, a change of one pH unit (*e.g.*, from pH 7 to pH 6) corresponds to a 10-fold change in hydrogen ion concentration.

Strong acids

Some compounds essentially completely ionize in aqueous solution.



What is the pH of a 1 M HCl solution? $\rightarrow [\text{H}^+] = 1 \text{ M}; -\log[1] = 0$

What is the pH of a 0.1 M HCl solution? $\rightarrow [\text{H}^+] = 0.1 \text{ M}; -\log[0.1] = 1$

What is the pH of a 10^{-8} M HCl solution? $\rightarrow -\log[10^{-8}] = 8$ **No! this is a trick question!** The approximate concentration of hydrogen ions corresponds to 10^{-7} M (from water) + 10^{-8} M from HCl = 1.1×10^{-7} . The pH is therefore about 6.96 (this situation can be solved more exactly, but the actual value will be close to this).

Remember: if an *acid* is added to a solution, *the pH will decrease*. If a *base* is added to a solution, *the pH will increase*. A more general principle can therefore be stated as follows: in performing any calculation, consider the final result to determine whether the answer is logically consistent with the problem.

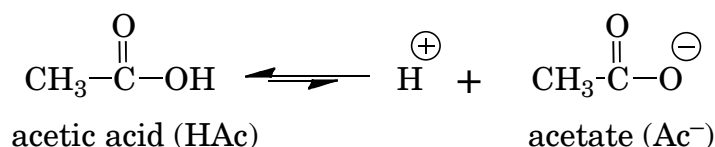
Strong bases

A base is a compound that can abstract protons from another compound (note that this is based on the Brønsted-Lowry definition of acids and bases, which is the definition widely used in biochemistry). One type of base is any compound that will dissociate to release free OH⁻ (e.g., NaOH). Other strong bases include the conjugate bases of weak acids, and compounds such as ammonia that can also accept protons.

In aqueous solution, **pOH = 14–pH**. The term pOH is much more rarely used, and in most cases, the pH is the parameter of interest. In biochemistry, this is in large part because physiological systems rarely reach pH values above 8, while some organs and organelles have significantly acidic pH.

Weak acids

Unlike strong acids, some compounds capable of releasing protons do not completely ionize in aqueous solution. For example, acetic acid also dissociates to yield a free proton and acetate ion (the conjugate base of acetic acid):



Again, this process reaches equilibrium, with the dissociation constant given by:

$$K_a = \frac{[\text{H}^+][\text{Ac}^-]}{[\text{HAc}]}$$

For acetic acid, $K_a = 1.75 \times 10^{-5}$ M; this indicates that only a small proportion of the acetic acid will dissociate.

As with hydrogen ion concentrations, this dissociation constant value is somewhat clumsy to deal with, and therefore, as with pH, it is frequently worth using the negative log of the K_a : $\text{p}K_a = 4.75$. By contrast, HCl has a $\text{p}K_a$ of -7. This illustrates a general principle: **a higher $\text{p}K_a$ corresponds to a higher affinity for protons**.

To determine the pH, the equilibrium equation can be rearranged to solve for hydrogen ion concentration:

$$[\text{H}^+] = K_a \frac{[\text{HAc}]}{[\text{Ac}^-]}$$

Taking the negative log of both sides gives:

$$\text{pH} = \text{pK}_a - \log \frac{[\text{HAc}]}{[\text{Ac}^-]}$$

This is the same as:

$$\text{pH} = \text{pK}_a + \log \frac{[\text{Ac}^-]}{[\text{HAc}]}$$

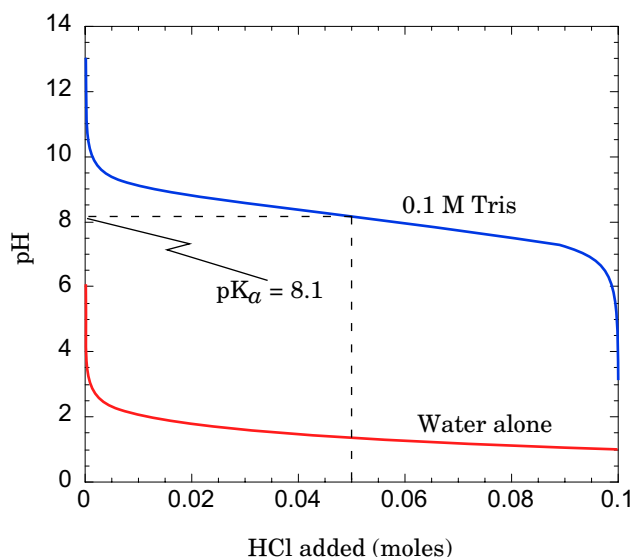
which is the classic **Henderson-Hasselbalch equation**.

For acetic acid (and for all weak acids), when $[\text{Ac}^-] = [\text{HAc}]$ the solution pH is equal to the pK_a . The Henderson-Hasselbalch equation can be used to solve for the relative amounts of acid and conjugate base present at any pH. (**Note: the Henderson-Hasselbalch equation is an approximation; real solutions deviate significantly from Henderson-Hasselbalch behavior.**)

Buffers

Solutions containing mixtures of weak acids and their conjugate bases resist changes in pH due to the addition of either hydrogen ions or hydroxide ions. These solutions are **buffers**. Buffers are critical for maintenance of pH control both in experiments *in vitro* and in physiological systems (although physiological systems also use active mechanisms to control pH).

Weak acids have the ability to act as buffers. Because the conjugate base of a weak acid has a relatively high affinity for hydrogen ions, it will absorb any hydrogen ions added to a solution; alternatively, if the pH decreases, the weak acid can release hydrogen ions. Adding HCl to water causes a rapid drop in pH to a final pH of 1. On the other hand, in the presence of Tris base (a commonly used buffer compound), the decrease in pH is markedly attenuated, with the final pH being 2 pH units higher. In the titration shown below for 0.1 M Tris, the solution pH changes from a high value to a low value upon addition of the strong acid HCl. The inflection point at 0.5 equivalents of strong acid corresponds to the pK_a of the protonated form of Tris. As is apparent in the plot, between about 0.05 and 0.95 equivalents (corresponding to ± 1 pH around the pK_a), the system resists change in pH. (Note that, to a very good approximation, all of the added protons can be assumed to become bound by the conjugate base; the pH change then results from the altered ratio of conjugate base to weak acid.)



In principle, the Henderson-Hasselbalch equation can be used to calculate the pH of a buffer given the ratio of weak acid and conjugate base, or to calculate the amount of weak acid and conjugate base that must be added to a solution to obtain a desired pH. Because, in most cases, real solutions deviate from ideal behavior, most biochemists obtain the desired pH by titrating a solution while directly measuring pH using a pH meter. The Henderson-Hasselbalch allows an *estimate* of the amount of strong acid or strong base that must be added to obtain the correct pH, which tends to make buffer preparation less tedious.

The Henderson-Hasselbalch equation is of considerable use in understanding the **approximate** behavior of a buffer, in choosing suitable buffer conditions to achieve the necessary resistance to pH changes required for a successful experiment, and in predicting the approximate changes in pH that will occur when hydrogen ions are removed from or added to a solution.

Buffer Problems

Because an understanding of buffers is important for an understanding of biochemistry, and because buffers are necessary in the vast majority of biochemical experiments, it is highly useful to be able to use the Henderson-Hasselbalch equation appropriately. Two types of calculations are typical:

1. Choosing and preparing a buffer from a given set of available starting materials.
2. Determining the approximate behavior of the buffer as a result of perturbations.

For example:

Consider a reaction that is optimally effective at a pH of 8.0. The compounds listed in the table below are available. Which would be the most effective buffer? How could 1 liter of a 50 mM buffer be prepared?

Common Name	Chemical Name	pK _a
MES	2-(<i>N</i> -morpholino) ethanesulfonic acid	6.15
PIPES	piperazine- <i>N,N'</i> -bis(2-ethanesulfonic acid)	6.76
HEPES	4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid	7.55
Bicine	2-(<i>bis</i> (2-hydroxyethyl)amino)acetic acid	8.35

Step 1: choose a buffer: HEPES and Bicine have the pK_a values closest to the desired pH of 8.0. Bicine has a pK_a slightly closer to this value than the pK_a of HEPES; Bicine is most likely to be the best of these buffers for this experiment.

Step 2: buffer calculations: Calculating the concentrations of the protonated and deprotonated forms of the buffer requires the Henderson-Hasselbalch equation and the fact that the total concentration of all buffer species is (in this case) 0.05 M (50 mM).

$\text{pH} = \text{pK}_a + \log \frac{[\text{Bicine}^-]}{[\text{Bicine} \bullet \text{H}]}$; substituting the relevant terms yields:
 $8.0 = 8.35 + \log \frac{[\text{Bicine}^-]}{[\text{Bicine} \bullet \text{H}]}$; which means that: $10^{-0.35} = \frac{[\text{Bicine}^-]}{[\text{Bicine} \bullet \text{H}]}$, and therefore
 $0.447 = \frac{[\text{Bicine}^-]}{[\text{Bicine} \bullet \text{H}]}$. Because $[\text{Bicine}^-] + [\text{Bicine} \bullet \text{H}] = 0.05 \text{ M}$, $[\text{Bicine}^-] = \underline{0.0154 \text{ M}}$,
 and $[\text{Bicine} \bullet \text{H}] = \underline{0.0346 \text{ M}}$. (The extra significant figure is necessary to avoid some problems later.)

(Reality check: the pH is *below* the pK_a , and therefore, the concentration of the protonated species should be *higher* than the concentration of the deprotonated species.)

(A 50 mM buffer with HEPES instead of bicine would have $[\text{HEPES}^-] = 0.037 \text{ M}$ and $[\text{HEPES} \bullet \text{H}] = 0.013 \text{ M}$; note that for HEPES, the protonated species has a lower concentration than the deprotonated species, because the pH is above the pK_a .)

Step 3: buffer preparation: The method required to prepare the buffer depends on the starting material available. In general, the stock bottles available would contain either the free acid ($\text{Bicine} \bullet \text{H}$) or the conjugate base (Bicine^-) with an appropriate counter ion such as sodium.

If $\text{Bicine} \bullet \text{H}$ is available, add 0.050 moles of the $\text{Bicine} \bullet \text{H}$ to water, add 0.015 moles of a strong base (such as NaOH), and add enough water to yield a final volume of 1 liter. Note that the 0.015 moles of NaOH will deprotonate the required 0.015 moles of $\text{Bicine} \bullet \text{H}$ to generate the 0.015 moles of Bicine^- required.

If $\text{Na} \bullet \text{Bicine}$ is available, add 0.050 moles of the $\text{Na} \bullet \text{Bicine}$ to water, add 0.035 moles of a strong acid (such as HCl), and add enough water to yield a final volume of 1 liter. Note that the 0.035 moles of HCl will protonate the required 0.035 moles of $\text{Na} \bullet \text{Bicine}$ to generate the 0.035 moles of $\text{Bicine} \bullet \text{H}$ required. This method will result in the formation of 0.035 moles of NaCl, which may or may not be a desirable addition to the overall buffer.

Step 4: using the buffer for a reaction: Many biochemical reactions release protons into the surrounding solution, or absorb protons from the solution. In the absence of a buffer this would result in a dramatic pH change. The buffer cannot prevent the pH change, but it can limit the magnitude of the change in pH.

First, consider a reaction that **absorbs 0.01 moles of protons**. (This is a very large amount, but then most biochemical reactions are not run in 1 liter volumes; dividing both the moles of protons and the volume by 1000 would result in more reasonable numbers, but the calculations would be the same.)

In the Bicine buffer, the loss of 0.01 moles of protons from the solution would result in release of protons from the buffer species. To a good approximation, this would

result in a decrease in the $[\text{Bicine}\cdot\text{H}] = 0.0346 \text{ moles} - 0.01 \text{ moles} = 0.0246 \text{ moles}$.
The amount of Bicine^- would change also: $0.0154 + 0.01 \text{ moles} = 0.0254 \text{ moles}$.

The final pH would therefore be: $8.35 + \log \frac{[0.0254]}{[0.0246]} = 8.37$

In contrast, the final pH for the HEPES buffer would be 8.73, while in the absence of buffer, the final pH would be 12.

Next, consider a reaction that **releases 0.01 moles of protons**.

In the Bicine buffer, the release of 0.01 moles of protons into the solution would result in binding of protons by the buffer species. To a good approximation, this would result in an increase in the $[\text{Bicine}\cdot\text{H}] = 0.0346 \text{ moles} + 0.01 \text{ moles} = 0.0446 \text{ moles}$. The amount of Bicine^- would change also: $0.0154 - 0.01 \text{ moles} = 0.0054 \text{ moles}$.

The final pH would therefore be: $8.35 + \log \frac{[0.0054]}{[0.0446]} = 7.44$

Note that, in this case, the Bicine buffer is nearing the limit in its capacity to control a pH change. For **the HEPES buffer, the final pH would be 7.62**; because the initial pH = 8.0 conditions meant that there was much more of the deprotonated HEPES than the protonated form, the HEPES buffer is better than the Bicine buffer at resisting changes due to release of protons by the reaction being tested.

Note, also, that in the absence of any buffer the final pH would be 2, so once again the buffer had a significant effect.

Summary

Polar and ionic materials dissolve readily in water as **entropy-driven** processes. Dissolution of some solids can also be enthalpy driven (*e.g.*, MgCl_2 , NaOH), while dissolution of some is enthalpy opposed (*e.g.*, urea).

Non-polar materials do not dissolve readily in water, largely because the presence of these molecules in the water causes a large decrease in entropy of the solvent. The hydrophobic effect can be a powerful driving force in aqueous solutions, because it is an additive function of many interactions. Protein and membrane structure requires the hydrophobic effect; the formation of these structures will be discussed further in future sections.

Water can dissociate to release free hydrogen ions (which are actually transferred to neighboring water molecules) and free hydroxyl ions. In addition, other molecules may release or accept protons. Compounds that dissociate essentially completely are termed strong acids; compounds that have relatively high affinity for their exchangeable protons are termed weak acids.

A solution containing a mixture of a weak acid and its conjugate base is capable of resisting changes in pH and is termed a buffer. Buffer components are important reagents in biochemical experiments, because pH is an important parameter in most biochemical reactions.

The course website contains a lengthy tutorial on pH and buffers.