Osmolarity and partitioning of fluids

Ben R Waterhouse

Andrew D Farmery

Abstract

This article first outlines definitions and descriptions of key terms that will be used in the discussions that follow including osmolarity, osmolality, osmotic and oncotic pressure. The physicochemical properties of water, ions and organic molecules are discussed in terms of their biological roles. Similarly, the interactions of amphipathic molecules and their three-dimensional structures in aqueous and non-aqueous environments are then explored. The movement of solutes and solvents across semipermeable membranes is considered and an assessment is made of the contribution of such mechanisms to normal physiology. Firstly, simple diffusion is described, followed by comparisons with facilitated diffusion and energy-dependent active transport focusing on the differences in kinetics and rate-limiting factors arising as a result. The mechanisms underlying Gibbs—Donnan equilibria are discussed, with particular emphasis as to how they arise across a selectively permeable membrane by way of a worked example. The equilibrium of forces influencing fluid movements across the capillary endothelium, known as Starling forces, is then described. Comparisons are made between the classic model as first proposed by Starling in 1896 and the modified glycocalyx model, which has developed over the past 25 years. Finally, the impact of these differences on our understanding of trans-capillary fluid flux is discussed.

Keywords Active transport; diffusion; Gibbs—Donnan equilibrium; glycocalyx; ion channels; Michaelis—Menten; osmolality; osmolarity; Starling forces

Royal College of Anaesthetists CPD Matrix: 1A01.

Learning objectives

After reading this article, you should be able to:

- define terms relating to fluid composition, compare and contrast passive and active forms of solute transport, understand the factors that affect and limit the rate of molecular transport
- understand how a Gibbs—Donnan equilibrium is reached across a selectively permeable membrane
- compare the classical and modified model of Starling forces across capillary endothelia and understand the implications of the differences between them

Properties of fluids

Key definitions

Osmolarity: the osmolarity, or osmotic concentration, of a solution is dependent on the number of particles present per unit volume regardless of their nature and is measured in osmoles/litre of solution. Due to the low concentrations of solutes in physiological fluids, quoting osmolarity in milliosmoles/litre (mOsm/litre) is often more appropriate, for example plasma osmolarity has a normal range of 285—295 mOsm/litre. The relationship between the molarity of a solution and its osmolarity depends on the number of particles derived from each molecule. For example glucose remains intact in solution and so a 5 mmol/litre solution will have an osmolarity of 5 mOsm/litre. Conversely, ionic compounds such as sodium chloride will dissociate in aqueous solution though technically an ionic solid, NaCl can be conceptually considered as molecules each containing one Na^+ and one Cl^- ion. Therefore a 100 mmol/litre NaCl solution will produce an osmolarity of 200 mOsm/litre. Conforming to this pattern, each conceptual molecule of calcium chloride will dissociate to give three moieties in solution and so 100 mmol/litre $CaCl_2$ will dissociate produce a 300 mOsm/litre solution and so on. This of course becomes more complex when multiple solutes are present or when solutes do not fully dissociate, as is the case in blood plasma. The freezing point of water containing solute is depressed proportionally to the number of particles. Thus osmolarity can be measured by an osmometer using this principle of freezing point depression.

Osmolality is defined as the number of osmoles per kilogramme of solvent (Osm/kg). For biological solutions, which are primarily water, this is not appreciably different from the osmolarity.

Osmotic pressure is the pressure required to prevent the diffusion of water from a weak solution to a strong one via a semipermeable membrane. A fluid of high osmolarity exerts substantial pressure while the osmotic pressure of pure water is zero. The osmotic pressure of a solution can be calculated using Equation 1.

$$\pi - \mathrm{R}\cdot T\cdot C \qquad (1)$$

Equation 1: calculating osmotic pressure, where π is osmotic pressure, R is the ideal gas constant (0.0826 litre atm/K/mol), T is the absolute temperature (K), and C is the concentration of the solution (mOsm/litre). For example, for a 1 osmolar solution at 0°C the osmotic pressure exerted is 22.4 atmospheres. From this logic, we can define an ‘osmole’ is that quantity of solute which when dissolved in 22.4 litres of water, generates an osmotic pressure of 1 atmosphere.

Oncotic pressure: the oncotic, or colloid osmotic, pressure arises when apertures between cells allow the passage of water and small solutes but not macromolecular particles, for example proteins. Large molecules such as gelatin, starch and proteins

---

Ben R Waterhouse BA BM BCh is an Academic Foundation Doctor in North Bristol NHS Trust, UK. Conflicts of interest: none declared.

Andrew D Farmery BSc MA MD FRCA is a Fellow and Tutor in Medicine and Physiology at Wadham College, Oxford, UK.
Conflicts of interest: none declared.

tend to form viscid, glue-like solutions. These solutions are described as colloids.

Properties of water

About 70% of the mammalian cell comprises water. Although water molecules do not have true positive or negative charge they do have a polarity. The two hydrogen atoms are bonded to the oxygen by covalent bonds, that is a sharing of an electron pair. However, the greater gross positive charge, or electronegativity, of the oxygen atomic nucleus favours these electrons existing closer to it. As a result there is a higher electron density around it resulting in a partial charge differential between it and the hydrogen atoms (Figure 1).

This uneven charge distribution gives rise to the characteristic properties of water. It allows the formation of hydrogen bonds between neighbouring molecules. This restriction on movement of water molecules gives water a high boiling point relative to its molecular size. As a solvent, water dissolves ions and polar molecules rather than non-polar moieties due to its own polarity.

Properties of organic molecules

The polarity of water molecules contrasts with the non-polar nature of organic molecules, which are made up mainly or entirely of carbon and hydrogen atoms, for example the alkanes and alkenes. In these molecules, the carbon–hydrogen bonds lead to an even distribution of electrons. As a result partial charges do not arise and so the molecules do not interact with each other by formation of hydrogen bonds. For this reason, organic molecules larger than water have much lower boiling points. However, while in their liquid state these act as non-polar solvents, which are able to dissolve other non-polar molecules but not ions or polar molecules. These substances are therefore known as hydrophobic or lipophilic.

Amphipathic molecules: it contain areas of polarity as well as non-polar sections. This allows the polar portion to exist in an aqueous phase while the non-polar portion is in an oil phase. This is the principle that enables detergents to remove non-polar oils and greases from clothing. Figure 2 shows how amphipathic molecules, arrange themselves within the aqueous solutions of the body.

Bi-layered sheets – (Figure 2a) in this configuration the water-soluble heads of the molecules are in the aqueous environment while their hydrophobic tails coalesce internally. This structure is the basis of phospholipid cell membranes; the aqueous intracellular and extracellular fluids are in contact with only the polar regions at the phosphate head. Meanwhile, the non-polar fatty acid tails interact shielded from the surrounding water. An interesting consequence of this structure is that even small ions are very poorly soluble in the non-polar inner portion of the membrane and so are not able to diffuse directly through it. Meanwhile, uncharged moieties such as urea can cross the membrane freely.

Structure and polarity of a water molecule

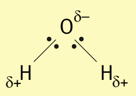

Figure 1

Different configurations of amphipathic molecules

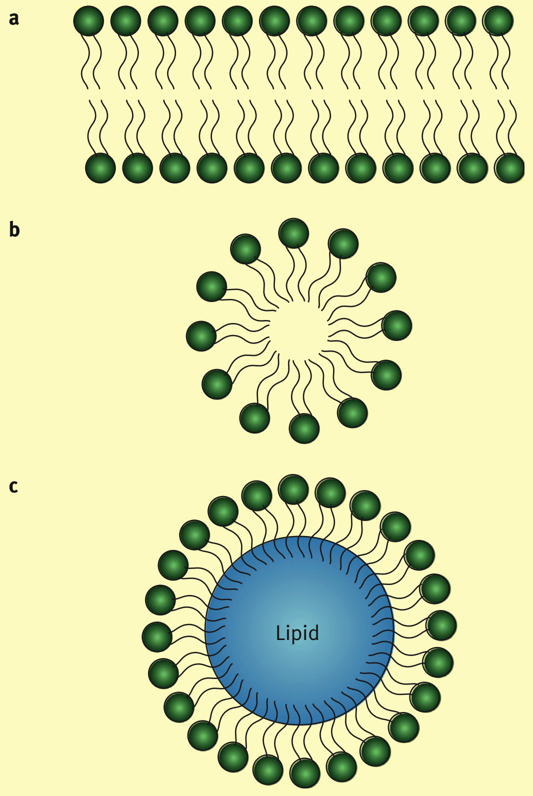

Figure 2 Configurations of (**a**) bilayer, (**b**) micelle and (**c**) chylomicron molecules.

Micelles – (Figure 2b) these are spherical droplets where the molecules have their polar heads facing outwards and their hydrophobic tails pointing towards the centre of the structure. These configurations can be observed to form spontaneously if the membranes of cells suspended in an aqueous solution are manually disrupted.

Chylomicra – (Figure 2c) hydrophobic lipids must be transported in the aqueous plasma in order to be utilized in the appropriate areas of the body. This is achieved by amphipathic bile acids enabling the formation of chylomicra. The non-polar portions of amphipathic molecules are in the lipid phase of the chylomicron and the polar portions are on the outside, forming a protective envelope. In this way, the fat forms an emulsion that is stable in an aqueous environment.

The positions of the polar and non-polar regions of any large molecule determine its shape when placed in an aqueous, a lipid, or a lipid and aqueous environment. Amino acids possessing ionized side-chains are hydrophilic while those possessing aromatic side-chains are hydrophobic. The distribution of amino acid types determines the three-dimensional structure of proteins. The structure of proteins is fundamental to their functions as enzymes or carrier molecules and the functional structure will