Transport Through Neutral Membranes

5

The last chapter discussed some of the general features of solute movement in an infinite medium. Solute particles can be carried along with the flowing solution or they can diffuse. This chapter considers the movement of solute and solvent through membranes, ignoring any electrical forces on the particles.

The movement of electrically neutral particles through aqueous pores in membranes has many applications in physiology. They range from the flow of nutrients through capillary walls, to the regulation of the amount of fluid in the interstitial space between cells, to the initial stages of the operation of the kidney.

Sections 5.1–5.4 are a qualitative introduction to the flow of water through membranes as a result of hydrostatic pressure differences or osmotic pressure differences. The reader who is not interested in the more advanced material can read just this part of the chapter, culminating in the clinical examples of Sect. 5.4.

Sections 5.5 and 5.6 present phenomenological transport equations that are simple linear relationships between the flow of water and solute particles and the pressure and concentration differences that cause the flows. These relationships are valid for any type of membrane as long as a linear relationship adequately describes the flow and the proportionality constants are regarded as experimentally determined quantities. These equations are applied to the artificial kidney in Sect. 5.7.

Section 5.8 presents a simple model for countercurrent transport, which is important in artificial organs, the kidney, and in conserving heat loss from the extremities.

The last section, Sect. 5.9, provides a more advanced treatment of one particular membrane model: a membrane pierced by pores in which electrical forces can be neglected and in which Poiseuille flow takes place. The model leads to expressions for the phenomenological coefficients that can be compared to experimental data, though that is not done here. The last part of the section uses this model to calculate the forces on a membrane when there are osmotic effects.

5.1 Membranes

All cells are surrounded by a membrane 7–10 nm thick. Furthermore, virtually all the physical substructures within the cell are also bounded by membranes. Membranes separate two regions of space; they allow some substances to pass through but not others. The membrane is said to be *permeable* to a substance that can pass through it; it is *semipermeable* when only certain substances can get through. A substance that can pass through is said to be *permeant*.

Simple models for a semipermeable membrane are shown in Fig. 5.1. Figure 5.1a shows a pore that pierces the membrane. A narrower pore, in which the transported particles move single-file, is shown in Fig. 5.1b. Another simple model is shown in Fig. 5.1c: there are no pores, but water and small solute molecules actually "dissolve" in the membrane and diffuse through. The examples in Fig. 5.1 shows water molecules (open circles), solute molecules (small solid circles), and a large protein molecule that cannot pass through the membrane.

In Fig. 5.1a and b the motion of the water molecules is quite different from that of the small solute molecules. Each water molecule is in contact with neighboring water molecules so that when the water molecules move, they flow together. The result is the familiar bulk flow that occurs in a pipe. The solute molecules, on the other hand, are so dilute that they seldom collide with one another. Each solute molecule's motion is *independent of other solute molecules*.

The motion of each solute molecule is *not* independent of the motion of the surrounding water molecules. If the water is at rest, the movement of the solute molecules is diffusion; if the water is moving, this diffusion is superimposed on a flow of the solute molecules with the moving fluid (solvent drag).

In Fig. 5.1c, both the water and solute molecules dissolve into the bilayer lipid membrane. They are very dilute within the membrane, so that both kinds of molecules diffuse. The water molecules are not in contact with each other, but are

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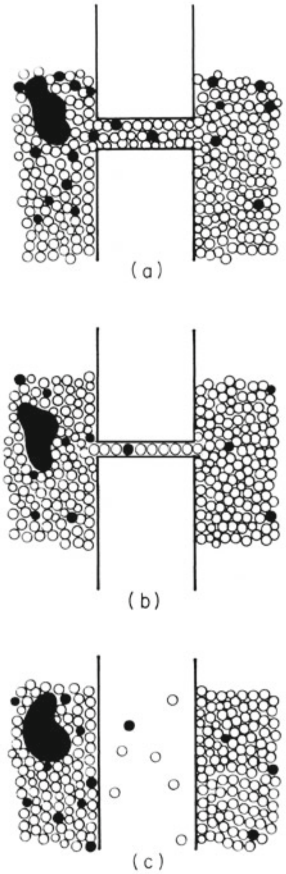

Fig. 5.1 Simple models for a semipermeable membrane. **a** A "large" pore. **b** A single-file pore such as an aquaporin channel. **c** Small molecules dissolve in the membrane and diffuse through

in some sort of interstices within the membrane structure, walking randomly in response to thermal agitation of the membrane.

It has long been known that the rate of water transport through cell membranes was too large to be explained by diffusion as in Fig. 5.1c, although such diffusion does take place. The pores that allow transport are more like those shown in Fig. 5.1a and b. Pores like the one in Fig. 5.1b, called *aquaporins*, were first discovered by Peter Agre in 1993 (Parisi et al. 2007).[1] Other mechanisms for water flow are associated with ion transport and are not discussed here (Zeuthen 2010).

5.2 Osmotic Pressure in an Ideal Gas

The selective permeability of a membrane gives rise to some striking effects. The flow of water that occurs because solutes are present that cannot get through the membrane is called *osmosis*. This phenomenon seems strange when it is first encountered, and explanations are often fraught with misconceptions (Kramer and Myers 2012). Osmosis is important in a variety of clinical problems that are described in Sect. 5.4. We begin by finding the conditions under which no flow takes place and the direction of flow when it does occur. Later, in Sect. 5.5, we consider the rate of flow in response to a given pressure difference.

It is easiest to understand osmotic pressure by considering the special case of two ideal gases and a membrane that is permeable to one but not the other. This case is simple because the gas molecules do not interact with one another. Then, in Sect. 5.3, we will examine the phenomenon when the substances are liquids.

Suppose a box with total volume V^* contains N_1^* molecules of gas species 1. If the box is at temperature T, the ideal-gas law relates the pressure, temperature, and the number of molecules:

$$p_1 V^* = N_1^* k_B T. \tag{5.1}$$

This has been written the way physicists like to write it, in terms of the number of molecules N_1^*. Chemists write it in terms of the number of moles n_1^*:

$$p_1 V^* = n_1^* RT.$$

The only difference is that the gas constant R is per mole while the Boltzmann constant k_B is per molecule. Since 1 mole contains N_A molecules, where N_A is Avogadro's number, $N_1^* = N_A n_1^*$ and $R = N_A k_B$. Numerical values are

$$\begin{aligned} N_A &= 6.022 \times 10^{23}\ \text{mol}^{-1}, \\ k_B &= 1.3806 \times 10^{-23}\ \text{J K}^{-1}, \\ R &= 8.3145\ \text{J mol}^{-1}\ \text{K}^{-1}, \\ R &= 0.08206\ \text{atm l mol}^{-1}\ \text{K}^{-1}. \end{aligned}$$

The concentration is the number of molecules or moles per unit volume. We denote *molecular* concentration by capital letter C and *molar* concentration by lowercase c:

$$\begin{aligned} C_1 &= \frac{N_1^*}{V^*}\ \text{m}^{-3} \text{ or molecules m}^{-3}, \\ c_1 &= \frac{n_1^*}{V^*}\ \text{m}^{-3} \text{ or mol m}^{-3}. \end{aligned}$$

Chemists often express concentrations in moles per liter.

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[1] Some aquaporins are permeable only to water, and not to any other small molecules or ions, even hydrogen ions (Preston et al. 1992). Aquaporins are formed by proteins that span the cell membrane. Their structure has been determined by x-ray crystallography (Murata et al. 2000). Their selectivity arises from a narrowing of the channel to about 0.3 nm, about the size of a single water molecule. Aquaporins allow water to cross cell membranes at a much higher rate than it could diffuse through. Genetically defective aquaporins may be responsible for some clinical diseases, such as nephrogenic diabetes insipidus and congenital cataracts (Agre et al. 2002).

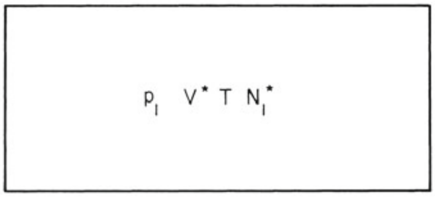

Fig. 5.2 An ideal gas fills a box of volume V^*

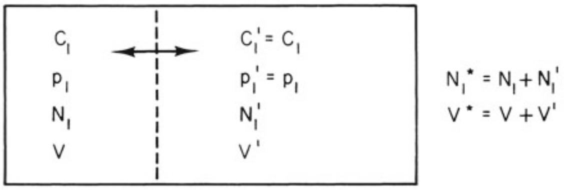

Fig. 5.3 The introduction of a semipermeable membrane does not change the pressure or concentration of the gas

If we were to imagine volume V^* divided into two subvolumes of volume V and V', the average concentration of molecules in each subvolume would remain unchanged. The pressure in each subvolume would still be p_1, and the temperature would be T. We can write

$$p_1 V = N_1 k_B T, \quad p_1 V' = N_1' k_B T.$$

Dividing both sides of each equation by the appropriate volume gives

$$p_1 = C_1 k_B T, \qquad p_1 = p_1' = C_1' k_B T. \tag{5.2}$$

Now place a membrane along the surface separating the subvolumes. The membrane has small holes so that the molecules can pass through, as shown in Fig. 5.3. This does nothing to change the fact that at equilibrium $p_1 = p_1'$. When the pressures are the same on both sides of the membrane, no molecules pass through on average. If the pressure is greater on one side than the other, molecules pass through to bring the pressures into equilibrium, as we saw in Chap. 3. Equations 5.2 say nothing about how frequently a molecule that strikes the membrane passes through. It could take hours or days for equilibrium to be attained if we started away from equilibrium and the molecules do not pass through very often.

Next, keeping V fixed, introduce species 2 on the left as in Fig. 5.4. Suppose that species 2 cannot pass through the membrane. Bombardment of the membrane by the new molecules causes an additional force on the left side of the membrane. The total pressure in volume V is now the sum of the partial pressures p_1 due to species 1 and p_2 due to the second species:

$$p = p_1 + p_2,$$

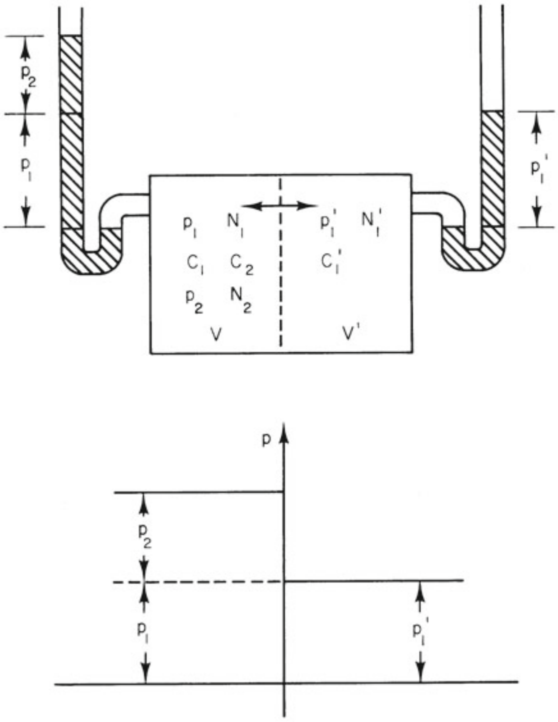

Fig. 5.4 Species 2, which cannot pass through the membrane, has been introduced in V. The pressure in V is higher than in V' by the partial pressure p_2

$$\begin{aligned} p_1 V &= N_1 k_B T, \\ p_2 V &= N_2 k_B T. \end{aligned} \tag{5.3}$$

The ideal-gas law is still obeyed in terms of the total number of molecules in V, $N = N_1 + N_2$: $pV = p_1 V + p_2 V = N_1 k_B T + N_2 k_B T = (N_1 + N_2) k_B T = N k_B T$.

In an ideal gas the presence of the second species does not change the partial pressure p_1. The total pressure on the walls and the membrane is increased by p_2 so the membrane is bowed towards the right, but the total pressure is simply the sum of the two partial pressures. The ratio p_1/p is the fraction of the pressure due to collisions of molecules of the first kind with the membrane.

Suppose now that the pressure in V' is raised, either by compressing the gas or by introducing more molecules of type 1, so that instead of $p_1' = p_1$, we have $p_1' = p$. The partial pressure of species 1 is higher in V' than in V. Since these molecules can pass through the membrane, they will flow from V' to V. An identical flow could have been caused without having species 2, simply by raising the pressure in V'. Not every molecule striking the membrane will pass through, but some fraction of all collisions with the membrane will result in a molecule passing through. The fraction will depend on the details of the membrane structure. The number going through will be proportional to the number of collisions on one side minus the number of collisions on the other and hence to the difference of partial pressures. If $p_1 > p_1'$, species 1 will flow from V to V'. If $p_1 < p_1'$, the flow will be in the other direction. The details of the membrane will determine how rapid this flow is. *The movement of any species of gas molecule that can pass through the membrane will be from the region of higher partial pressure to lower partial pressure.*

Suppose we start out with only species 1 on each side of the membrane and equal pressures on both sides so that $p = p_1 = p' = p_1'$. There are three ways to make p_1 less than p_1', thereby causing movement from right to left. One is simply to let the gas on the left expand into a larger volume, which lowers $p = p_1$. (Or we could have compressed the gas on the right, raising $p' = p_1'$.) The other two ways involve introducing on the left a species 2 that cannot pass through the membrane. The second way would be to keep the total pressure and volume on the left the same, but remove one molecule of species 1 for every molecule of species 2 that is introduced. The third way would be to increase the volume on the left as each molecule of species 2 is introduced, so that $p = p_1 + p_2$ remains the same.

The total partial pressure of all species that cannot pass through the membrane is called the *osmotic pressure* in region V and is usually denoted by π. If the subscript 2 denotes all impermeant species,

$$\pi_2 = C_2 k_B T. \tag{5.4}$$

The flow through the membrane because of an increase in the osmotic pressure or a decrease in the total pressure is identical. In each case the flow is determined by the difference across the membrane of p_1, the total partial pressure of all the species that can pass through.

The description in the previous paragraphs of partial pressure is easy to visualize, and for the case given it is correct. It is more general, however, to express the condition for equilibrium in terms of the chemical potential, μ. Recall that in Chap. 3 we derived the pressure in terms of volume changes of a system and the chemical potential in terms of the number of particles in the system. Suppose that the membrane separating the two sides is actually a semipermeable piston that is free to move. Equality of the total pressure on both sides of the piston means that the piston will not move and the two systems will not exchange volume. Equality of the chemical potential of a species that can get through the membrane means that the two systems will not exchange particles. It is better, therefore, to say *the flow of any species that can pass through the membrane will be from the region of higher chemical potential to the region of lower chemical potential for that species. If the chemical potentials are the same, there will be no flow.*

The mixture of two ideal gases is a special case of the ideal solution that was described in Sect. 3.18. The chemical potential of species 1 that can pass through the membrane is given by Eq. 3.77:

$$\begin{aligned}
\Delta\mu_1 &= \overline{V}_1(\Delta p - k_B T \Delta C_2),\\
\mu_1 - \mu_1' &= \overline{V}_1\left[p - p' - k_B T(C_2 - 0)\right],\\
\mu_1 - \mu_1' &= \overline{V}_1(p_1 + p_2 - p_1' - k_B T C_2).
\end{aligned}$$

Since $p_2 = k_B T C_2$, the chemical potential is the same on both sides of the membrane when $p_1 = p_1'$.

5.3 Osmotic Pressure in a Liquid

Imagine now that the two volumes are filled with a solvent, such as water. If the pressure of the water is the same in both regions there is no movement of water through the membrane, nor is there exchange of volume if the membrane piston is free to move. Increasing the pressure on one side of the fixed membrane causes water to move through the membrane from the side with higher pressure to the side with lower pressure. There is no flow when $\Delta p = 0$. If there is a solute in the water that can pass freely through the membrane along with the water, the situation is unchanged.

Now let us add some solute on the left that cannot pass through the membrane. We will keep the volume on the left fixed. To add the solute in such a way that the pressure does not change, we must remove some water molecules as we add it.

We saw in Chap. 3 that replacing some water molecules with solute increases the entropy of the solution.[2] This means that the Gibbs free energy and the chemical potential are decreased. Water moves from the region on the right, where the chemical potential is higher, to the region on the left, where it is lower. The chemical potential of the water on the left can be increased by increasing the total pressure on the left.

The chemical potential contains terms proportional to the pressure and the concentration of the impermeant solute. It

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[2] This, recall, is because the water molecules are indistinguishable. A simple model (Fig. 3.15) shows why this happens. Suppose that three water molecules occupy three identical energy levels, and that these are the only three levels available. Because the molecules are indistinguishable, there is only one microstate and the entropy is zero. If one molecule of water is replaced by one solute molecule, there are then three separate microstates, corresponding to the solute molecule being in any one of the three. The entropy is $k_B \ln(3)$.

was shown in Sect. 3.18 that for an ideal solution[3]

$$\Delta\mu_w = \frac{\Delta p - k_B T \Delta C_s}{C_w}.$$

The osmotic pressure is the excess pressure that we must apply on the left to prevent the movement of water through the membrane. There is no movement of water when $p = p' + \pi$. It is more convenient to write all the unprimed quantities on the left: $p - \pi = p'$. The quantity $p - \pi$ will occur so often in what follows that it is worth a special name. We will define the *driving pressure*

$$p_d \equiv p - \pi. \tag{5.5}$$

As far as we know, it has not been used by other authors. It is a monotonic function of the chemical potential. In an ideal solution it is $C_w \mu_w$. Except in an ideal gas, it is *not* the same as the partial pressure (a concept that is not normally used in a liquid). On the right there is no solute and $p'_d = p'$. *There is no movement when the driving pressure is the same on both sides*,

$$p_d = p'_d, \tag{5.6a}$$

or the chemical potential of the water is the same on both sides,

$$\mu_w = \mu'_w. \tag{5.6b}$$

The water passes through the membrane in the direction from higher p_d to lower p_d (or from higher chemical potential to lower chemical potential). Either the total pressure or the osmotic pressure can be manipulated to change p_d (and μ_w). An increase of total pressure has the same effect as a decrease of osmotic pressure.

Increasing the concentration of the solute increases the osmotic pressure. The fact that $p_d = p - \pi = C_w \mu_w$ means that for ideal solutions obeying Eq. 3.77,

$$\pi = C k_B T = cRT. \tag{5.7}$$

In many cases this is confirmed by experiment, particularly in dilute solutions. This is known as the *van't Hoff* law for osmotic pressure.

An *osmole* is the equivalent of a mole of solute particles. The term *osmolality* is used to refer to the number of osmoles per kilogram of *solvent*, while *osmolarity* refers to the number of osmoles per liter of *solution*. The reason for introducing the osmole is that not all impermeant solutes are ideal; their osmotic effects are slightly less than Ck_BT. The osmole takes this correction into account.

5.4 Some Clinical Examples

As blood flows through capillaries, oxygen and nutrients leave the blood and go to the cells. Waste products leave the cells and enter the blood. Diffusion is the main process that accomplishes this transfer. The capillaries are about the diameter of a red cell; the red cells therefore squeeze through the capillary in single file. They move in plasma, which consists of water, electrolytes, small molecules such as glucose and dissolved oxygen or carbon dioxide, and large protein molecules. All but the large protein molecules can pass through the capillary wall.

Outside the capillaries is the interstitial fluid, which bathes the cells. The concentration of protein molecules in the interstitial fluid is much less than it is in the capillaries. Osmosis is an important factor determining the pressure in the interstitial fluid and therefore its volume. The following values (in units[4] of torr) are typical for the osmotic pressure inside and outside the capillary:[5]

Inside capillary	$\pi_i = 28$ torr
Outside capillary, interstitial fluid	$\pi_o = 5$ torr

Measurements of the total pressure in the interstitial fluid are difficult, but the value seems to be about −6 torr. It is maintained below atmospheric pressure (taken here to be 0 torr) by the rigidity of the tissues. The driving pressure of water and small molecules outside is therefore

$$p_{do} = p_o - \pi_o = -6 - 5 = -11 \text{ torr}.$$

The total pressure within the capillary drops from the arterial end to the venous end, causing blood to flow along the capillary. A typical value at the arterial end is 25 torr; at the venous end, it is 10 torr. If the drop is linear along the capillary, the total pressures versus position is as plotted in Fig. 5.5a.[6] Subtracting from this the osmotic pressure of the large molecules gives the curve for the driving pressure inside, p_{di}, which is also plotted in Fig. 5.5a. Figure 5.5b shows the total and driving pressures in the interstitial fluid. Figure 5.5c compares the driving pressure inside and outside. The driving pressure is larger inside in the first half of the capillary and larger outside in the second half of the capillary. The result is an outward flow of plasma through the capillary wall in the first half and an inward flow in the second half. There is a very slight excess of outward flow. This fluid returns to the circulation via the lymphatic system.

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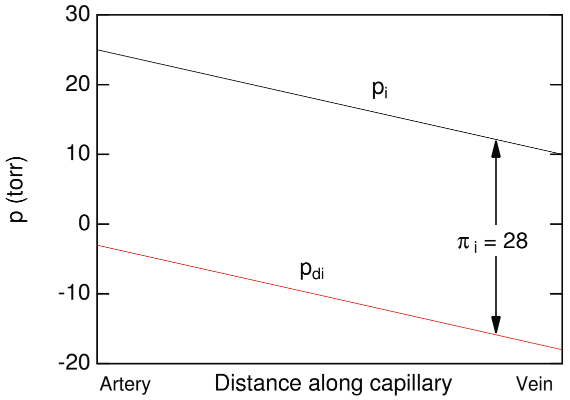
[3] An ideal solution can be defined in several equivalent ways. One is that it is a solution that obeys Eq. 3.77. Another is that when the separated components are mixed, there is no change of total volume and no heat is evolved or absorbed. See Hildebrand and Scott (1964, Chap. 2).

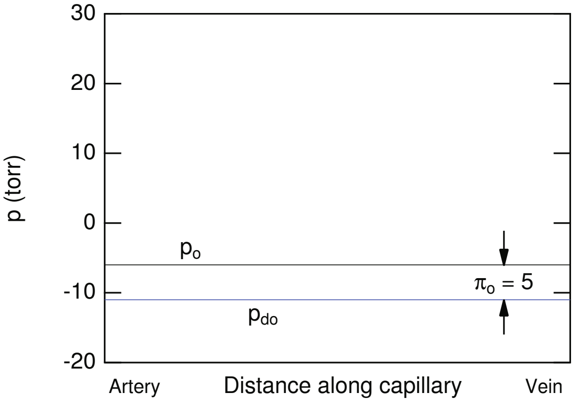
[4] 1 torr = 1 mmHg = 133.3 Pa = 0.019 34 lb in.$^{-2}$.

[5] A short account of the pressures used here is found in Hall (2011, Chap. 16). A more detailed discussion is in Guyton et al. (1975).

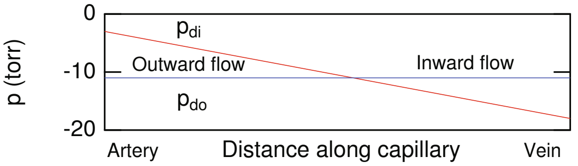
[6] This simple discussion uses pressures that compensate for the fact that the surface area of the capillary is larger at the venous end than at the arterial end.



(a) inside capillary



(b) interstitial fluid outside capillary



(c) comparison of p_d inside and outside

Fig. 5.5 Pressures inside and outside the capillary. **a** Inside. **b** Outside. **c** Comparison of the water driving pressure inside and outside

There are three ways that the balance of Fig. 5.5 can be disturbed, each of which can give rise to *edema*, a collection of fluid in the tissue. The first is a higher average pressure along the capillary. The second is a reduction in osmotic pressure because of a lower protein concentration in the blood (hypoproteinemia). The third is an increased permeability of the capillary wall to large molecules, which effectively reduces the osmotic pressure. Each is discussed below.

5.4.1 Edema Due to Heart Failure

A patient in right heart failure exhibits an abnormal collection of interstitial fluid in the lower part of the body (the legs for a walking patient; the back and buttocks for a patient in bed). This can be understood in terms of the mechanism discussed above. The right heart pumps blood from the veins through the lungs. If it can no longer handle this load, the venous blood is not removed rapidly enough, and the pressure in the veins and the venous end of the capillaries rises. There is a corresponding rise in p_d along the capillary. More fluid flows from the capillary to the interstitial space. The interstitial pressure rises until the net flow is again zero.

The same process can occur in left heart failure in which the pressure in the pulmonary veins builds up. The patient then has pulmonary edema and may literally drown.

5.4.2 Nephrotic Syndrome, Liver Disease, and Ascites

Patients can develop an abnormally low amount of protein in the blood serum, *hypoproteinemia*, which reduces the osmotic pressure of the blood. This can happen, for example, in *nephrotic syndrome*. The nephrons (the basic functioning units in the kidney) become permeable to protein, which is then lost in the urine. The lowering of the osmotic pressure in the blood means that the p_d rises. Therefore, there is a net movement of water into the interstitial fluid. Edema can result from hypoproteinemia from other causes, such as liver disease and malnutrition.

A patient with liver disease may suffer a collection of fluid in the abdomen. The veins of the abdomen flow through the liver before returning to the heart. This allows nutrients absorbed from the gut to be processed immediately and efficiently by the liver. Liver disease may not only decrease the plasma protein concentration, but the vessels going through the liver may become blocked, thereby raising the capillary pressure throughout the abdomen and especially in the liver. A migration of fluid out of the capillaries results. The surface of the liver "weeps" fluid into the abdomen. The excess abdominal fluid is called *ascites*.

5.4.3 Edema of Inflammatory Reaction

Whenever tissue is injured, whether it is a burn, an infection, an insect bite, or a laceration, a common sequence of events initially occurs that cause edema. They include the following:

1. *Vasodilation*. Capillaries and small blood vessels dilate, and the rate of blood flow is increased. This is responsible for the redness and warmth associated with the inflammatory process.
2. *Fluid exudation*. Plasma, including plasma proteins, leaks from the capillaries because of increased permeability of the capillary wall.

3. *Cellular migration*. The capillary walls become porous enough so that white blood cells of the immune system move out of the capillaries at the site of injury.

5.4.4 Headaches in Renal Dialysis

Dialysis is used to remove urea from the plasma of patients whose kidneys do not function. Urea is in the interstitial brain fluid and the cerebrospinal fluid in the same concentration as in the plasma; however, the permeability of the capillary–brain membrane is low, so equilibration takes several hours (Patton et al. 1989, Chap. 64). Water, oxygen, and nutrients cross from the capillary to the brain at a much faster rate than urea. As the plasma urea concentration drops, there is a temporary osmotic pressure difference resulting from the urea within the brain. The driving pressure of water is higher in the plasma, and water flows to the brain interstitial fluid. Cerebral edema results, which can cause severe headaches.

The converse of this effect is to inject into the blood urea or mannitol, another molecule that does not readily cross the blood–brain barrier. This lowers the driving pressure of water within the blood, and water flows from the brain into the blood. Although the effects do not last long, this technique is sometimes used as an emergency treatment for cerebral edema (Fishman 1975; White and Likavec 1992).

5.4.5 Osmotic Diuresis

The functional unit of the kidney is the *nephron*. Water and many solutes pass into the nephron from the blood at the glomerulus. As the urine flows through the rest of the nephron, a series of complicated processes cause a net reabsorption of most of the water and varying amounts of the solutes. Some medium-weight molecules such as mannitol are not reabsorbed at all. If they are present in the nephron—for example, from intravenous administration—the driving pressure of water is lowered and less water is reabsorbed than would be normally. The result is an increase in urine volume and a dehydration of the patient called osmotic diuresis (Gennari and Kassirer 1974; Hall 2011). Similar diuretic action takes place in a diabetic patient who “spills” glucose into the urine.

5.4.6 Osmotic Fragility of Red Cells

Red blood cells (erythrocytes) are normally disk-shaped, with the center thinner than the rim. In the disease called *hereditary spherocytosis* the red cells are more rounded. If a red cell is placed in a solution that has a higher driving pressure than that inside the cell, water moves in and the cell swells until it bursts. Since cell membranes (as distinct from the lining of capillaries) are nearly impermeable to sodium, sodium is osmotically active for this purpose. The osmotic fragility test consists of placing red cells in solutions with different sodium concentrations and determining what fraction of the cells burst. A patient with hereditary spherocytosis has cells that will be destroyed at a lower external p_d (higher sodium concentration) than normal, because the membrane is more permeable to the sodium.

5.5 Volume Transport Through a Membrane

In this section and the next we develop phenomenological equations to describe flow of fluid and flow of solute through a membrane. These are linear approximations to the dependence of the flows on pressure and solute concentration differences. Three parameters are introduced that are widely used in physiology: the filtration coefficient (or hydraulic permeability), the solute permeability, and the solute reflection coefficient.

The volume fluence rate or volume flow per unit area per second through a membrane is J_v.

$$J_v = \frac{\begin{pmatrix}\text{total volume per second}\\ \text{through membrane area } S\end{pmatrix}}{S} = \frac{i_v}{S}\ \mathrm{m\ s^{-1}}. \qquad (5.8)$$

Consider pure water. The fluence rate depends on the pressure difference across the membrane. When the pressure difference is zero there is no flow. The direction of flow, and therefore the sign of the fluence rate, depends on which side of the membrane has the higher pressure. The simplest relationship that has this property is a linear one:[7]

$$J_v = L_p \Delta p. \qquad (5.9)$$

The proportionality constant is called the *filtration coefficient* or *hydraulic permeability*. It depends on the details of the membrane structure, such as the properties of the pores. The SI units for L_p are m $\mathrm{s^{-1}\ Pa^{-1}}$, $\mathrm{m^3\ N^{-1}\ s^{-1}}$, or $\mathrm{m^2\ s\ kg^{-1}}$. Often in the literature, however, values of L_p are reported in units of cm $\mathrm{s^{-1}\ atm^{-1}}$. Since $1\ \mathrm{atm} = 1.01 \times 10^5$ Pa, the conversion is

$$1\ \mathrm{cm\ s^{-1}\ atm^{-1}} = 0.99 \times 10^{-7}\ \mathrm{m\ s^{-1}\ Pa^{-1}}. \qquad (5.10)$$

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[7] The traditional sign convention has been followed here. There would be a minus sign in the equation if Δp were defined to be $p(x + \Delta x) - p(x)$. However, it is usually defined as $p - p'$. The flow is from the region of higher pressure to the region of lower pressure.

If a solute is present to which the membrane is completely impermeable, only water will flow, and the flow will depend on Δp_d:

$$\begin{aligned}\Delta p_d &= p_d - p'_d = p - \pi - (p' - \pi')\\ &= p - p' - (\pi - \pi')\\ &= \Delta p - \Delta\pi\end{aligned}$$

so

$$J_v = L_p(\Delta p - \Delta\pi). \tag{5.11}$$

Figure 5.6 shows the pressure relations on each side of the membrane for no flow and for flow in either direction.

It is important to note that the quantity in parentheses is a property of the solutions on either side of the membrane. The permeability depends on the transport mechanism.

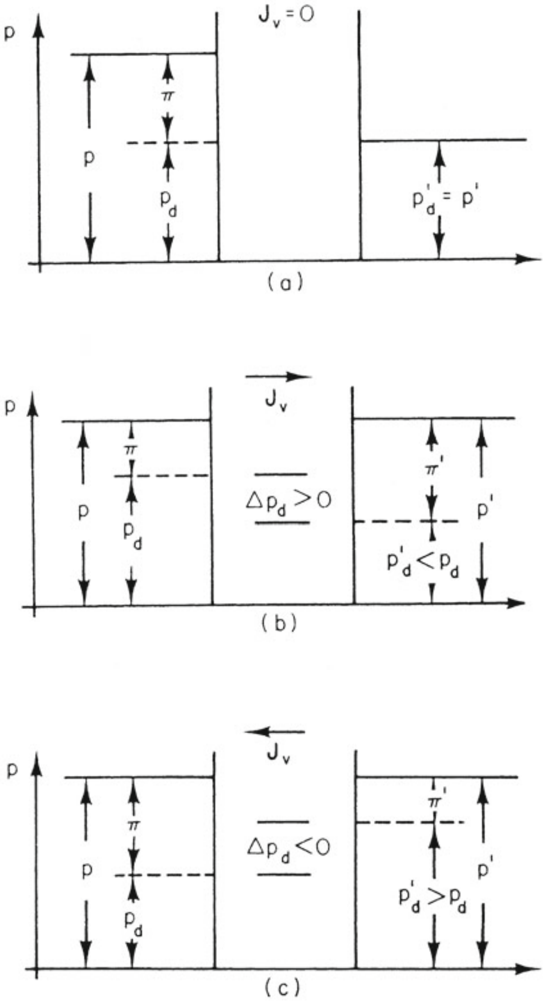


Fig. 5.6 Different flow possibilities for a completely impermeant solute. **a** $\Delta p_d = 0$, so there is no flow even though $p > p'$. **b** Flow to the right even though $p = p'$. **c** Flow to the left even though $p = p'$

When the solute is partially permeant, the volume fluence rate in the linear approximation still depends on both Δp and $\Delta\pi$, but the proportionality constants may be different. Since the solute does not reduce the flow as much as in Eq. 5.11, it is customary to write the two constants as L_p and σL_p:

$$J_v = L_p(\Delta p - \sigma\Delta\pi). \tag{5.12}$$

Parameter L_p is determined by measuring J_v and Δp when $\Delta\pi = 0$, while σ is determined from measurements of Δp and $\Delta\pi$ when $J_v = 0$.

Parameter σ is called the *reflection coefficient*. It has different values for different solutes. When $\sigma = 0$ there is no reflection, and the solute particles pass through like water. When $\sigma = 1$ all the solute particles are reflected and Eq. 5.12 is the same as Eq. 5.11.

We can imagine that part of the solute moves freely with the water and part is reflected. (Later, we will consider a model for partial reflection in which a solute particle of radius $a < R_p$ can enter the pore, but its center cannot be closer to the wall than its radius.) We can write

$$p = p_d + \sigma\pi, \tag{5.13}$$

and we can further break this down to a driving pressure for the water p_{dw} and one for the permeant solute:

$$p = \underbrace{p_{dw}\ \mathrlap{\overbrace{}^{\substack{\text{osmotic pressure}\\ \text{of all solute molecules}}}}+(1-\sigma)\pi}_{\substack{\text{driving pressure}\\ \text{for permeant}\\ \text{molecules}}}\quad\underbrace{+\sigma\pi}_{\substack{\text{osmotic pressure}\\ \text{of impermeant}\\ \text{molecules}}}. \tag{5.14}$$

With this substitution the flow equation becomes

$$J_v = L_p\left[\Delta p_{dw} + (1-\sigma)\Delta\pi\right]. \tag{5.15}$$

Figure 5.7 shows the pressure relationships across the membrane.

In the approximation that van't Hoff's law holds, $\pi = k_B T C = RTc$ and Eq. 5.12 can be written as

$$J_v = L_p(\Delta p - \sigma k_B T\,\Delta C), \tag{5.16}$$

$$J_v = L_p(\Delta p - \sigma RT\,\Delta c). \tag{5.17}$$

In Eq. 5.16 the concentration is in molecules m^{-3}; in Eq. 5.17 it is mol m^{-3}. In both cases the units of $k_B T\,\Delta C$ and $RT\,\Delta c$ are pascals.

As an example of volume flow, consider *ultrafiltration*. Ultrafiltration is the process whereby water and small molecules are forced through a membrane by a hydrostatic

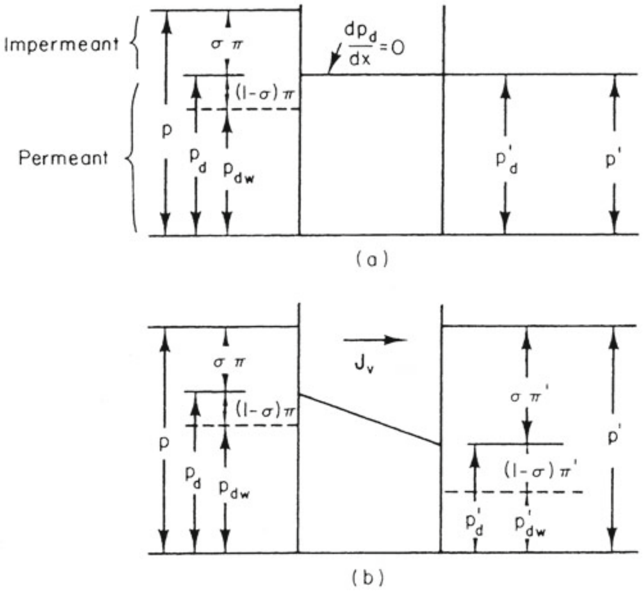


Fig. 5.7 Pressure relationships on each side of the membrane when $\sigma = \frac{2}{3}$. **a** There is no bulk flow. **b** There is flow to the right

pressure difference while larger constituents are left behind. An interesting clinical application of ultrafiltration has been proposed. A severely edematous patient (for any of the reasons mentioned in the previous section) must have the extra water removed from the body. This is usually accomplished with diuretics, drugs that increase the renal excretion of water. Some patients may not respond to these drugs, and in other cases, particularly pulmonary edema, the response may not be fast enough. In the latter case, phlebotomy (bloodletting) is sometimes used to reduce the body water rapidly. This has obvious disadvantages, for example, the removal of blood cells. Silverstein et al. (1974) used ultrafiltration to remove water and sodium from the plasma while leaving the other constituents behind. Ultrafiltration is sometimes called reverse osmosis. The name is unfortunate, because it suggests some mysterious process unrelated to the principles of this section. Ultrafiltration is often used by campers for purifying water and has been suggested for desalinization of sea water.

5.6 Solute Transport Through a Membrane

Solute can pass through the membrane in two ways: it can be carried along with flowing water (solvent drag), and it can diffuse.

If there is no reflection ($\sigma = 0$) and the solute concentration is the same on both sides of the membrane so there is no diffusion, the flux density or fluence rate is caused by solvent drag and is simply the solute concentration (particles per unit volume) times the volume fluence rate (Sect. 4.2):

$$J_s = C_s J_v.$$

If the solute particles are completely reflected ($\sigma = 1$) then $J_s = 0$.

In the intermediate case with coefficient σ,

$$J_s = (1-\sigma) C_s J_v.$$

This is consistent with the idea expressed by Eq. 5.14 that a fraction $(1-\sigma)$ of the solute particles can enter the membrane. In that case, C_s is the outside solute concentration on both sides of the membrane, and $C_s(1-\sigma)$ is the solute concentration inside the membrane. We will develop a detailed model for transport in a right-cylindrical pore in Sect. 5.9. We anticipate that discussion and present a simple justification of the factor $1-\sigma$. In bulk solution the concentration C_s is obtained by imagining a certain volume of solution, counting the number of solute particles whose centers lie within the volume, and taking the ratio. In a cylindrical pore of radius R_p and length ΔZ, the volume of fluid is $\pi R_p^2 \Delta Z$. The centers of solute particles of radius a cannot be within distance a of the pore wall. The number of solute particles within the pore is therefore $C_s \pi \left(R_p - a\right)^2 \Delta Z$. The concentration in the pore is the number of particles divided by the pore volume:

$$\begin{aligned} C_{s,\,\text{inside}} &= \frac{C_s \pi \left(R_p - a\right)^2 \Delta Z}{\pi R_p^2 \Delta Z} \\ &= C_s \left(1 - \frac{a}{R_p}\right)^2 = C_s \left(1 - \sigma\right). \end{aligned}$$

This correction is called the *steric factor*. Solvent flow within a distance a of the walls contributes to J_v but not to solvent drag. This model will be extended to a volume flow with a parabolic velocity profile in Sect. 5.9.4.

If $J_v = 0$ there will be no solvent drag but there will be diffusion. The solute flux will be proportional to the concentration gradient and therefore to the concentration difference across the membrane: $J_s \propto \Delta C_s$. The proportionality constant depends on properties of the membrane. If the membrane is pierced by pores, for example, it depends on pore size, membrane thickness, number of pores per unit area, and the diffusion constant. The dependence will be derived later in this chapter. It is customary to write the proportionality constant as ωRT: $J_s = \omega RT \Delta C_s$. The factor ω is called the *membrane permeability* or *solute permeability*.

In the linear approximation the fluence rate resulting from both processes is the sum of these two terms:

$$J_s = (1-\sigma)\overline{C}_s J_v + \omega RT\, \Delta C_s. \tag{5.18}$$

Here an average value $\overline{C}_s$ has been written for the solvent drag term, because the concentration on each side of the membrane is not necessarily the same. The way that this average is taken will become clearer in the discussion of the pore model described in Sect. 5.9.

The solute equation has been written for both fluence rate and concentration in terms of particles. In terms of molar fluence rate and concentration, it is exactly the same:

$$J_s(\text{molar}) = (1-\sigma)\overline{c}_s J_v + \omega RT\,\Delta c_s. \tag{5.19}$$

Either way, the diffusion proportionality constant is ωRT. It does not change because C_s and J_s(particles) are both written in terms of particles, and c_s and J_s(molar) are both written in terms of moles. Referring to Eq. 5.18, the solvent drag term has units of (particles m^{-3}) (m s^{-1}) = particles m^{-2} s^{-1}. Therefore the factor ωRT has units of m s^{-1}. Since the units of RT are joules or N m (per mole), the units of ω are

$$\frac{\text{mol m s}^{-1}}{\text{N m}} = \text{mol N}^{-1}\,\text{s}^{-1}. \tag{5.20}$$

Further interpretation of ω will be made for specific models.

We have used the same σ in both the solvent drag term and in the preceding section. Although this was made plausible by saying that $1-\sigma$ is the fraction of solute molecules that gets through the membrane, its rigorous proof is more subtle. It has been proved in general using thermodynamic arguments, which can be found in Katchalsky and Curran (1965). It can be proved in detail for specific membrane models.

5.7 Example: The Artificial Kidney

The artificial kidney provides an example of the use of the transport equations to solve an engineering problem. The problem has been extensively considered by chemical engineers, and we will give only a simple description here. Those interested in pursuing the problem further can begin with reviews by Mavroidis (2006) or Lysaght and Moran (2006). The reader should also be aware that this "high-technology" solution to the problem of chronic renal disease is not entirely satisfactory. It is expensive and uncomfortable and leads to degenerative changes in the skeleton and severe atherosclerosis (Lindner et al. 1974). The alternative treatment, a transplant, has its own problems, related primarily to the immunosuppressive therapy. Anyone who is going to be involved in biomedical engineering or in the treatment of patients with chronic disease should read the account by Calland (1972), a physician with chronic renal failure who had both chronic dialysis and several transplants. The distinction between a high-technology treatment and a real conquest of a disease has been underscored by Thomas (1974, pp. 31–36).

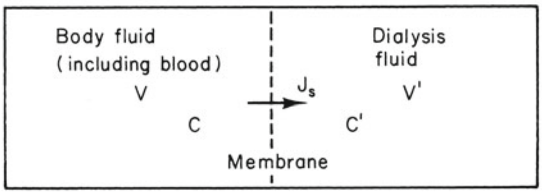


Fig. 5.8 The simplest model of dialysis. All the body fluid is treated as one compartment; transport across the membrane is assumed to take longer than transport from various body compartments to the blood

The simplest model of dialysis is shown in Fig. 5.8. Two compartments, the body fluid and the dialysis fluid, are separated by a membrane that is porous to the small molecules to be removed and impermeable to larger molecules. If such a configuration is maintained long enough, then the concentration of any solute that can pass through the membrane will become the same on both sides. The dialysis fluid is prepared with the desired composition of such small molecules as sodium, potassium, and glucose. Volume V' must be larger than V for effective dialysis to take place; otherwise, the concentration of solutes in the dialysis fluid builds up from the initially prepared values. In early work, V' was up to 100 l (since V is about 40 l). Although the fluid was replaced every two hours or so, it was an excellent medium in which to grow bacteria. Although the bacteria could not get through the membrane, they released exotoxins (or, if they died, endotoxins) which diffused back into the patient and caused fever. Now a continuous flow system has been used in which the solutes are continually metered into flowing dialysis fluid that is then discarded. Because of this, we will assume that there is no buildup of concentration in the dialysis fluid. (Effectively volume V' is infinite.) We will assume that $\Delta p = 0$. (Actually, proteins cause some osmotic pressure difference, which we will ignore.)

Without solvent drag, the solute transport is by diffusion, $J_s = \omega RT(C - C')$, where C is the concentration of solute in the blood and C' is the concentration in the dialysis fluid. If the surface area of the membrane is S, then the rate of change of the number of solute molecules N is

$$\frac{dN}{dt} = -S\omega RT(C - C').$$

If the solute is well mixed in the body fluid compartment, then $N = CV$, and this equation can be written as

$$\frac{dC}{dt} = -\frac{S\omega RT}{V}(C - C').$$

This is the equation for exponential decay. The steady state solution is $C = C'$. The complete solution is (Appendix F)

$$C(t) = \left[C(0) - C'\right]e^{-t/\tau} + C', \tag{5.21}$$

where the time constant is

$$\tau = \frac{V}{S\omega RT}. \tag{5.22}$$

The only things that are adjustable in this equation are the membrane area S and its permeability ω. The size of pores in the membrane is dictated by what solutes are to be retained in the blood. The number of pores per unit area and the thickness of the membrane can be controlled. Typical cellophane membranes have $\omega RT = 5 \times 10^{-6}$ m s^{-1} (with a thickness of 500 µm). The area may be 2 m^2. With a fluid volume $V = 40$ l, this gives

$$\tau = \frac{40 \times 10^{-3}\,\mathrm{m}^3}{\left(2\,\mathrm{m}^2\right)\left(5 \times 10^{-6}\,\mathrm{m\ s}^{-1}\right)} = 4 \times 10^3\,\mathrm{s} = 1.1\,\mathrm{h}.$$

Typically, dialysis requires several hours. This longer period is for two reasons. Some of the larger molecules have smaller permeabilities and therefore longer time constants, and rapid dialysis causes cerebral edema and severe headaches.

The actual apparatus is quite complicated. First, it must be sterile, which requires a sterilized, disposable dialysis membrane. Second, the apparatus causes clots, so the blood must be treated with heparin as it enters the machine, and the heparin must be neutralized with protamine as it returns to the patient.

5.8 Countercurrent Transport

This section considers a problem that demonstrates the principle of *countercurrent* transport. An apparatus (perhaps a dialysis machine or an oxygenator) transports a single solute across a thin membrane of permeability ωRT. On one side of the membrane (the "inside") is a thin layer of solvent that flows along the membrane in the $+x$ direction as shown in Fig. 5.9. On the "outside" is another thin layer of solvent that may be at rest or may flow in either the $+x$ or the $-x$ direction. When it flows in the opposite direction of the fluid inside we have the countercurrent situation.

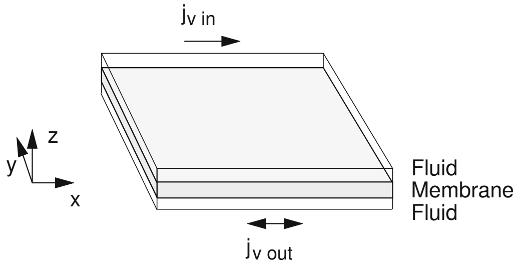
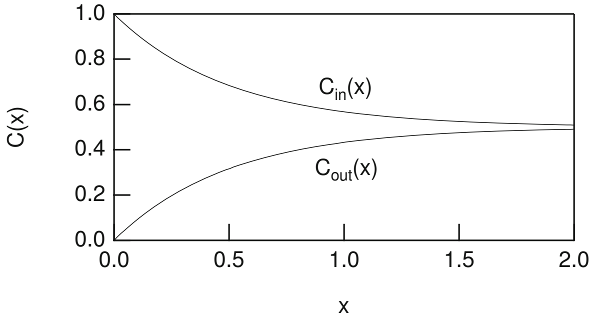


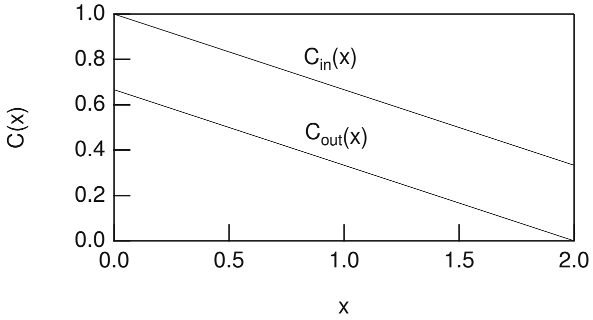
Fig. 5.9 Layers of fluid containing a solute flow parallel to the x axis on either side of a membrane

Suppose that the concentration of solute in the two layers is $C_{\mathrm{in}}(x)$ inside and $C_{\mathrm{out}}(x)$ outside. Solute is transported in the x direction in each fluid layer by pure solvent drag. It diffuses through the membrane from the side with higher concentration to the other. We develop the model below and show that the steady-state concentration profiles are quite different depending on whether the solvent flows are in the same or opposite directions. The results are shown in Fig. 5.10 for the situation in which the value of C_{in} is 1 and the value of C_{out} is 0 where each solvent starts to flow across the membrane. In Fig. 5.10a both layers flow to the right; in Fig. 5.10b they flow in opposite directions. The countercurrent case is more effective in reducing C_{in}. The final value of C_{in} is 0.5 in the first case and 0.33 in the second.

To develop the model, we make the following assumptions. The concentration of solute in each fluid layer is independent of y, z, and t. The thickness of the fluid layer inside is h_{in}. The fluid velocity $j_{v\,\mathrm{in}}$ is everywhere constant. The only important mechanism for solute transport within the fluid is solvent drag. Let the width of the slab in the



(a) Both flows are to the right.



(b) The flows are in opposite directions.

Fig. 5.10 Solute concentration profiles for two different situations where solvent flows parallel to the membrane surface and solute moves through the membrane from inside to outside. **a** Both fluid layers flow to the right. The concentrations rise and falls exponentially, eventually becoming the same on both sides of the membrane. **b** The countercurrent case, in which the solvent flows are in opposite directions. The solvent outside flows from right to left. The concentrations vary linearly

y direction be Y. Inside, the number of particles per second in through the face of the rectangle of area Yh_{in} at x is $C_{\text{in}}(x)\,j_{v\,\text{in}}Yh_{\text{in}}$. The number out through the face at $x+dx$ is $C_{\text{in}}(x+dx)\,j_{v\,\text{in}}Yh_{\text{in}}$. The number through the membrane into the exterior volume is $[C_{\text{in}}(x) - C_{\text{out}}(x)]\,\omega RTYdx$. Combining these we get

$$\frac{dC_{\text{in}}}{dx} = -\frac{\omega RT}{j_{v\,\text{in}}h_{\text{in}}}\left[C_{\text{in}}(x) - C_{\text{out}}(x)\right]. \tag{5.23}$$

A similar expression can be derived for the exterior:

$$\frac{dC_{\text{out}}}{dx} = \frac{\omega RT}{j_{v\,\text{out}}h_{\text{out}}}\left[C_{\text{in}}(x) - C_{\text{out}}(x)\right]. \tag{5.24}$$

Our notation allows j_v to have a different direction (sign). Defining $a = \omega RT/j_v h$ we have the coupled differential equations

$$\begin{aligned} \frac{dC_{\text{in}}}{dx} &= -a_{\text{in}}(C_{\text{in}} - C_{\text{out}}), \\ \frac{dC_{\text{out}}}{dx} &= +a_{\text{out}}(C_{\text{in}} - C_{\text{out}}). \end{aligned} \tag{5.25}$$

We restrict ourselves to the case in which $|a_{\text{in}}| = |a_{\text{out}}| = a$. Changing the direction of j_v changes the sign of a. Assume a is the same on both sides. The equations show that the slope of $C_{\text{in}}(x)$ is minus the slope of $C_{\text{out}}(x)$ if both currents are in the same direction, and the two slopes are the same if the currents are in opposite directions. This can be seen in the solutions in Fig. 5.10.

You can verify that Eqs. 5.26 represent a solution of Eqs. 5.25:

$$\begin{aligned} C_{\text{in}}(x) &= \frac{c_1}{2}\left(1 + e^{-2ax}\right) + \frac{c_2}{2}\left(1 - e^{-2ax}\right), \\ C_{\text{out}}(x) &= \frac{c_1}{2}\left(1 - e^{-2ax}\right) + \frac{c_2}{2}\left(1 + e^{-2ax}\right), \end{aligned} \tag{5.26}$$

where c_1 and c_2 are the values of C_{in} and C_{out} at $x = 0$. Figure 5.10a shows the concentrations for $c_1 = 1$ and $c_2 = 0$ with $a = 1$ and $0 < x < 2$. If the sign of a is changed in the second differential equation, then the fluid outside is flowing in the opposite direction to the fluid inside. Again you can verify that the most general solution is

$$\begin{aligned} C_{\text{in}}(x) &= c_1 + (c_2 - c_1)ax, \\ C_{\text{out}}(x) &= c_2 + (c_2 - c_1)ax. \end{aligned} \tag{5.27}$$

Figure 5.10b is a plot with the constants set so that the concentration inside on the left is 1 and on the outside on the right is zero ($c_1 = 1, c_2 = 2/3, a = 1, 0 < x < 2$). This configuration is called *countercurrent* flow. We can see from the figure that the transport through the membrane is increased because the concentration difference across the membrane is, on average, greater.

The countercurrent principle is found in the renal tubules (Hall 2011, p. 309; Patton et al. 1989, p. 1081), in the villi of the small intestine (Patton et al. 1989, p. 915), and in the lamellae of fish gills (Schmidt-Nielsen 1972, p. 45). The principle is also used to conserve heat in the extremities—such as people's arms and legs, whale flippers, or the leg of a duck. If a vein returning from an extremity runs closely parallel to the artery feeding the extremity, the blood in the artery will be cooled and the blood in the vein warmed. As a result, the temperature of the extremity will be lower and the heat loss to the surroundings will be reduced.

5.9 A Continuum Model for Volume and Solute Transport in a Pore

In this section we develop a model to predict the values of the phenomenological coefficients of Sects. 5.5 and 5.6. The success of the model depends on its ability to predict behavior, particularly as the size of solute particles is varied. This was an important problem in physiology in the 1960s and 1970s. Instead of comparing the model to experiment, we conclude the section by showing what the forces are on the membrane. This is important because there has been a fair amount of confusion in the literature about the forces on a semipermeable membrane. This section is fairly long. It stands alone; you can skip it if you wish.

The model assumes that the membrane has a particularly simple structure.

1. The membrane is pierced by n circular pores per unit area, all having radius R_p and all being right cylinders. The membrane thickness is ΔZ.
2. The pore and the fluid are electrically neutral. No electrical forces are considered.
3. There is complete mixing on both sides of the pore, so that flow within the liquid on either side can be neglected.
4. The system is in the steady state. There is no variation in flux density (fluence rate) or concentration as a function of time.
5. The pores are large enough so that the bulk flow can be calculated by continuum hydrodynamics.

The quantities considered in this section are summarized in Table 5.1.

5.9.1 Volume Transport

The results of Chap. 1 can be used when the pore is filled with pure water or water and a solute for which $\sigma = 0$. From Eq. 1.40 the flux through a single pore is

$$i_v(\text{single pore}) = \frac{\pi R_p^4}{8\eta}\frac{\Delta p}{\Delta x}. \tag{5.28}$$

Table 5.1 Symbols used for porous membrane

Quantity	On left	In pore	On right
Total pressure	p		p'
Solute concentration	C_s	$C(z)$	C_s'
Osmotic pressure	$\pi = k_B T C_s$		$\pi' = k_B T C_s'$
Effectively impermeant part of osmotic pressure	$\sigma\pi$		$\sigma\pi'$
Effectively permeant part of osmotic pressure plus water driving pressure	$(1-\sigma)\pi + p_{dw}$	$p_d(z)$	$(1-\sigma)\pi' + p_{dw}'$

The fluence rate through the membrane is obtained by multiplying i_v by n, the number of pores per unit area. The result is

$$J_v = \frac{n\pi R_p^4}{8\eta}\frac{\Delta p}{\Delta Z}$$

so that

$$L_p = \frac{n\pi R_p^4}{8\eta\,\Delta Z}. \tag{5.29}$$

While L_p can be measured fairly easily using Eq. 5.12, it is much more difficult to measure the microscopic quantities needed to test Eq. 5.29. We will not compare the model to experiment here;[8] we will simply give an example of how calculations are done.

A commercial filter used for ultrafiltration might have the property $L_p \approx 1$ ml min^{-1} m^{-2} torr^{-1}. Since 760 torr $=$ 1×10^5 Pa, the hydraulic permeability in SI units is

$$\begin{aligned} L_p &= \frac{1\ \text{ml}}{1\ \text{torr min m}^2}\,\frac{1\ \text{min}}{60\ \text{s}}\,\frac{10^{-6}\ \text{m}^3}{1\ \text{ml}}\,\frac{760\ \text{torr}}{1\times 10^5\ \text{Pa}} \\ &= 1.27\times 10^{-10}\ \text{m s}^{-1}\ \text{Pa}^{-1}. \end{aligned}$$

The manufacturer's literature[9] can be used to estimate

$$\begin{aligned} R_p &\approx 4.5\ \text{nm}, \\ \Delta Z &\approx 10\ \mu\text{m}.^{10} \end{aligned}$$

The viscosity of water is 0.9×10^{-3} Pa s at 25 °C. This gives us enough information to estimate n and the fraction of the filter surface that is pores. From Eq. 5.29

$$\begin{aligned} n = \frac{8\eta\,\Delta Z\, L_p}{\pi R_p^4} &= \left(\frac{(8)(0.9\times 10^{-3}\ \text{Pa s})(10\times 10^{-6}\ \text{m})}{\pi\left(4.5\times 10^{-9}\right)^4\ \text{m}^4}\right) \\ &\times (1.27\times 10^{-10}\ \text{m s}^{-1}\ \text{Pa}^{-1}) \\ &= 7.1\times 10^{15}\ \text{m}^{-2}. \end{aligned}$$

Since the area of one pore is $\pi R_p^2 = 6.36 \times 10^{-17}$ m^2, the total pore area in 1 m^2 is 0.45 m^2, a number that is not unreasonable.

Next consider the volume flow when the reflection coefficient is not zero. The position within the pore is specified by cylindrical coordinates (r, ϕ, z). The position along the axis of the pore is given by z. The position in a plane perpendicular to the axis of the pore is specified by polar coordinates r and ϕ. Flow of the fluid is described by the vector volume fluence rate $\mathbf{j}_v(r, \phi, z)$. (We use J for fluence rate for the membrane as a whole and j for the fluence rate in bulk solution inside a pore.) It is possible to show rigorously that as long as the pore is a right circular cylinder, $\mathbf{j}_v$ points only along z and is independent of ϕ (the fluid does not flow in a spiral and does not flow into or out of the walls):

$$\mathbf{j}_v(r, \phi, z) = j_v(r, z)\hat{\mathbf{z}}. \tag{5.30}$$

The solution is in a steady state and the flow is not changing with time. Therefore the flux density into a volume at z must be the same as the flux density out at $z + dz$:

$$\frac{\partial j_v}{\partial z} = 0 \tag{5.31}$$

so that j_v is constant along the z axis (although it can be a function of r). This is just what we saw in Chap. 1 for Poiseuille flow; the variation of j_v with r corresponds to the parabolic velocity profile. A value of $j_v(r)$ that is constant in the z direction requires a constant value of $\partial p/\partial z$ inside the pore.

In the pore, the driving pressure is $p_d(z)$. A typical pressure profile is shown in Fig. 5.11. The symbols are defined in Table 5.1. The pressure in the pore has been drawn with constant slope, since $\partial p_d/\partial z$ is constant. Using Eqs. 5.16 and 5.29, we can write

$$J_v = L_p(\Delta p - \sigma k_B T\,\Delta C_s), \tag{5.32}$$

where L_p is given by Eq. 5.29. The value of σ is derived in the next section.

The average value of $j_v(r)$ within the pore will be called $\bar{j}_v$. It is the total flux density through the pore divided by πR_p^2:

$$\bar{j}_v = \frac{i(\text{single pore})}{\pi R_p^2} = \frac{1}{\pi R_p^2}\int_0^{R_p} j_v(r)\,2\pi r\,dr$$

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[8] See the third or earlier editions or, for example, Bean (1969, 1972).

[9] Amicon XM-50.

[10] This value may not be consistent with the value of L_p quoted. The pore length ΔZ is not well known, and L_p is variable, depending on experimental conditions.

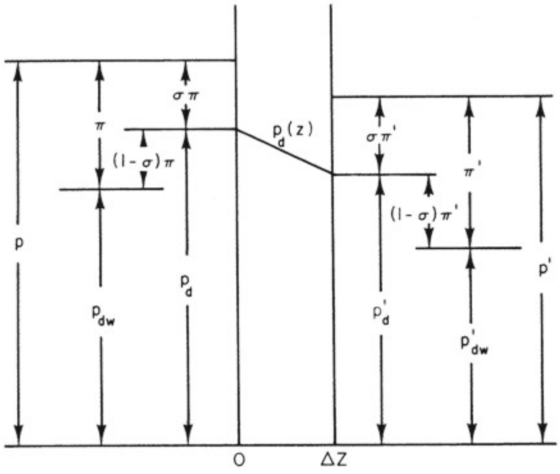

Fig. 5.11 Pressure within a pore and at the boundaries in the steady state

$$= \frac{J_v}{n\,\pi R_p^2} = -\frac{R_p^2}{8\eta}\frac{\partial p_d}{\partial z}. \tag{5.33}$$

5.9.2 Solute Transport

We now consider solute transport in our model pore. The arguments here are very similar to those for combined diffusion and solvent drag that were developed in Sect. 4.12. Those arguments are extended by averaging over the cross section of the pore.

Within the pore, the local solute flux is $\mathbf{j}_s(r, \phi, z)$. Arguments similar to those in the preceding section can be offered to show that $\mathbf{j}_s$ points along the z axis and is independent of ϕ:

$$\mathbf{j}_s(r, \phi, z) = j_s(r, z)\hat{\mathbf{z}}. \tag{5.34}$$

The solute concentration does not depend on ϕ, or else there would be diffusion in the ϕ direction and $\mathbf{j}_s$ would have a ϕ component. So $C = C(r, z)$. The r dependence must be kept because the center of a solute molecule of radius a cannot be within a distance a of the wall. (Recall the discussion of the steric correction on p. 125) Thus $C(r, z) = 0$ if $r > R_p - a$. We write[11]

$$C(r, z) = \begin{cases} 0, & R_p - a < r \\ C(z), & 0 \leqslant r \leqslant R_p - a. \end{cases} \tag{5.35}$$

The solute flux due to solvent drag is $C_s j_v$. For diffusion in one dimension the solute flux along the z axis is $-D(\partial C/\partial z)$. For the cylindrical pore we can combine these and write

$$j_s(r, z) = C(r, z)\,j_v(r, z) - D(r, a, R_p)\frac{\partial C(r, z)}{\partial z}. \tag{5.36}$$

The diffusion constant has been written as a function of r, a, and R_p because in the pore, as distinct from an infinite medium, the constant depends on how close the particle is to the walls. (Remember the relation of D to the viscous drag and the fact that Stokes' law requires modification when the fluid is confined in a tube.)

The preceding section showed that for the steady state j_v is independent of z. A similar argument can be made using the continuity equation for solute particles, implying that j_s is independent of z. Therefore Eq. 5.36 simplifies to

$$D(r, a, R_p)\frac{\partial C(r, z)}{\partial z} - j_v(r)C(r, z) = -j_s(r). \tag{5.37}$$

The easiest way to write $C(r, z)$ in accordance with Eq. 5.35 is

$$C(r, z) = C(z)\Gamma(r),$$

where

$$\Gamma(r) = \begin{cases} 0, & R_p - a < r \\ 1, & 0 \leqslant r < R_p - a. \end{cases} \tag{5.38}$$

With this substitution Eq. 5.37 becomes

$$\Gamma(r)D(r, a, R_p)\frac{dC(z)}{dz} - C(z)\Gamma(r)j_v(r) = -j_s(r).$$

This equation can be multiplied by $2\pi r\,dr$ and integrated from $r = 0$ to $r = R_p$. The result is

$$\left(\int_0^{R_p} \Gamma(r)D(r, a, R_p)2\pi r\,dr\right)\frac{dC(z)}{dz} - \left(\int_0^{R_p} \Gamma(r)\,j_v\,2\pi r\,dr\right)C(z) = -\int_0^{R_p} j_s(r)2\pi r\,dr. \tag{5.39}$$

The physical meaning of this integration can be understood with the aid of Fig. 5.12, which shows a slab of fluid in the pore between z and $z+dz$. Solute does not cross a surface of constant r but moves parallel to the z axis. Diffusion and solvent drag are considered in each shaded area $2\pi r\,dr$. The integration of Eq. 5.39 establishes an average solute fluence rate, since the right-hand side of the equation is the total flux or current of solute particles per second passing through the pore:

$$i_s = \int_0^{R_p} j_s(r)2\pi r\,dr.$$

---

[11] It can be argued that this is the only possible form for $C(r, z)$. See Levitt (1975, p. 535ff.).

As with the volume fluence rate, it is convenient to call the average solute fluence rate $\overline{j}_s$:

$$\overline{j}_s = \frac{i_s}{\pi R_p^2} = \frac{1}{\pi R_p^2}\int_0^{R_p} j_s(r)2\pi r\,dr. \tag{5.40}$$

The first term of Eq. 5.39 is the diffusive flux at z averaged over the entire cross section of the pore. Define an effective diffusion constant

$$D_{\text{eff}} = \frac{1}{\pi R_p^2}\int_0^{R_p} \Gamma(r)D(r,a,R_p)2\pi r\,dr. \tag{5.41}$$

The second term on the left of Eq. 5.39 is the solvent drag flux averaged over the entire cross section of the pore. The integral is

$$\int_0^{R_p} j_v(r)\Gamma(r)2\pi r\,dr = \int_0^{R_p-a} j_v(r)2\pi r\,dr. \tag{5.42}$$

This integral can be evaluated because we know the velocity profile, $j_v(r)$, Eq. 1.39:[12]

$$j_v(r) = \frac{1}{4\eta}\frac{\Delta p}{\Delta z}\left(R_p^2 - r^2\right). \tag{5.43}$$

We have already defined the average volume fluence rate to be

$$\overline{j_v} = \frac{1}{\pi R_p^2}\int_0^{R_p} j_v(r)2\pi r\,dr.$$

The desired quantity differs only in the limits of integration. To calculate it, write

$$\int_0^{R_p-a} j_v(r)2\pi r\,dr = \pi R_p^2\,\overline{j}_v\frac{\displaystyle\int_0^{R_p-a} j_v(r)2\pi r\,dr}{\displaystyle\int_0^{R_p} j_v(r)2\pi r\,dr}.$$

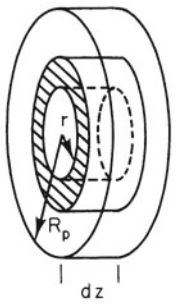

Fig. 5.12 A slab of fluid in a pore between z and $z + dz$, showing how the integration over r is done

The integrals are easily evaluated (see the Problems). The result is

$$\int_0^{R_p} j_v(r)\Gamma(r)2\pi r\,dr = \pi R_p^2\,\overline{j}_v\,f(a/R_p), \tag{5.44a}$$

where the function f is

$$f(\xi) = 1 - 4\xi^2 + 4\xi^3 - \xi^4. \tag{5.44b}$$

When Eqs. 5.40, 5.41, and 5.44a are substituted into Eq. 5.39 and each term is divided by πR_p^2, the result is

$$D_{\text{eff}}\left(\frac{dC}{dz}\right) - j_v f\left(\frac{a}{R_p}\right)C(z) = -\overline{j}_s \tag{5.45a}$$

or

$$\frac{dC}{dz} - \frac{j_v f(a/R_p)}{D_{\text{eff}}}C(z) = -\frac{\overline{j}_s}{D_{\text{eff}}}. \tag{5.45b}$$

This is a differential equation for $C(z)$. The right-hand side is the total solute fluence rate, which is constant. On the left-hand side, C varies along the pore so that the diffusive and solvent-drag fluence rates add up to this constant value. If the constant in front of $C(z)$ is written as

$$\frac{1}{\lambda} = \frac{j_v f(a/R_p)}{D_{\text{eff}}}, \tag{5.46}$$

this is recognized as Eq. 4.58 for drift plus solvent drag in an infinite medium. The results of Sect. 4.13 can be applied here. It is only necessary to determine values for C_0 and C_0'. Recall that in the pore $C(r,z) = C(z)\Gamma(r)$. The function $\Gamma(r)$ takes into account the reflection that occurs because solute particles cannot be closer to the pore wall than their radius. It was also assumed that the solution on either side of the membrane is well stirred. Therefore, $C_0 = C_s$ and $C_0' = C_s'$. Equation 4.70 becomes

$$\overline{j}_s = f\,\overline{j}_v\,\overline{C}_s + D_{\text{eff}}\frac{(C_s - C_s')}{\Delta Z}. \tag{5.47}$$

This is an expression for $\overline{j}_s$, the average solute fluence rate in the pore. To get solute fluence rate in the membrane, it must be multiplied by πR_p^2 and the number of pores per unit area. Since $J_v = n\pi R_p^2\,\overline{j}_v$, we have

$$J_s = f\overline{C}_s\,J_v + \frac{n\pi R_p^2\,D_{\text{eff}}}{\Delta Z}C_s. \tag{5.48}$$

Comparing this with the general phenomenological equation for solute flow, Eq. 5.18,

$$J_s = (1-\sigma)\overline{C}_s J_v + \omega RT\,\Delta C_s$$

we see that

$$1 - \sigma = f,$$

---

[12] This ignores the fact that since the walls affect the force on the solute particles, the solute must distort the velocity profile slightly. This point is discussed below.

$$\omega RT = \frac{n\,\pi R_p^2\,D_{\mathrm{eff}}}{\Delta Z}, \tag{5.49}$$

$$\lambda = \frac{D_{\mathrm{eff}}}{\overline{j}_v(1-\sigma)} = \frac{\omega RT(\Delta Z)}{J_v(1-\sigma)}.$$

The average solute concentration C is obtained from Eq. 4.66 with the substitution of ΔZ for the pore length:

$$\overline{C}_s = \frac{C_s e^x - C_s'}{e^x - 1} - \frac{1}{x}(C_s - C_s').$$

This can be rearranged as

$$\overline{C}_s = \tfrac{1}{2}(C_s + C_s') + G(x)(C_s - C_s') \tag{5.50a}$$

with

$$G(x) = \frac{1}{2}\left(\frac{e^x + 1}{e^x - 1}\right) - \frac{1}{x}, \tag{5.50b}$$

where $x = \Delta Z/\lambda$. This is the same function we saw in Fig. 4.17.

The solute concentration away from the sides of the pore is

$$C(z) = \frac{C_s(e^{\Delta Z/\lambda} - e^{z/\lambda}) + C_s'(e^{z/\lambda} - 1)}{e^{\Delta Z/\lambda} - 1}. \tag{5.51}$$

While the concentration profile is not usually measured experimentally, it is useful to plot it to help us visualize the interrelation of diffusion and solvent drag. Call $\phi = C_s'/C_s$. Equation 5.51 can be rearranged as

$$C(z) = C(0)\left(1 - (1-\phi)\frac{e^{z/\lambda} - 1}{e^{\Delta Z/\lambda} - 1}\right). \tag{5.52}$$

We can see several things from this equation. First, if the concentration is the same at each end of the pore, $\phi = 1$, the second term in the large parentheses vanishes, and the concentration is uniform throughout the pore. If $\phi \neq 1$, then the concentration is that at $z = 0$, plus a factor which may be positive or negative, depending on whether ϕ is less than or greater than 1. The ratio of exponentials occurring in that factor is plotted in Fig. 5.13 for different values of $\Delta Z/\lambda$, the ratio of the pore length to the effective diffusion distance.

These curves determine the shape of the concentration profile along the pore. If the flow is zero, $\lambda = D_{\mathrm{eff}}/\overline{j}_v(1-\sigma)$ is infinite and $\Delta Z/\lambda$ is zero. We then have pure diffusion, and the concentration changes uniformly along the pore, corresponding to the straight line in Fig. 5.13. The plots in Fig. 5.14 show what the concentration profiles are like for diffusion to the left and to the right when the flow is to the right. Compare the shape of the concentration profile on the left in Fig. 5.14 with the curve for $\Delta Z/\lambda = 1$ in Fig. 5.13. When the concentration is higher on the left, we have to take the mirror image of Fig. 5.13; the curve for $\Delta Z/\lambda = -1$ gives the concentration profile in Fig. 5.14 on the right.

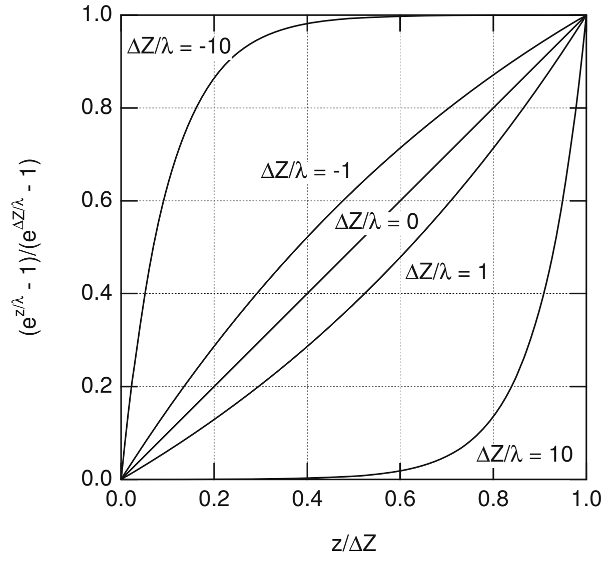

Fig. 5.13 Plot of the factor $(e^{z/\lambda} - 1)/(e^{\Delta Z/\lambda} - 1)$, which appears in Eq. 5.52

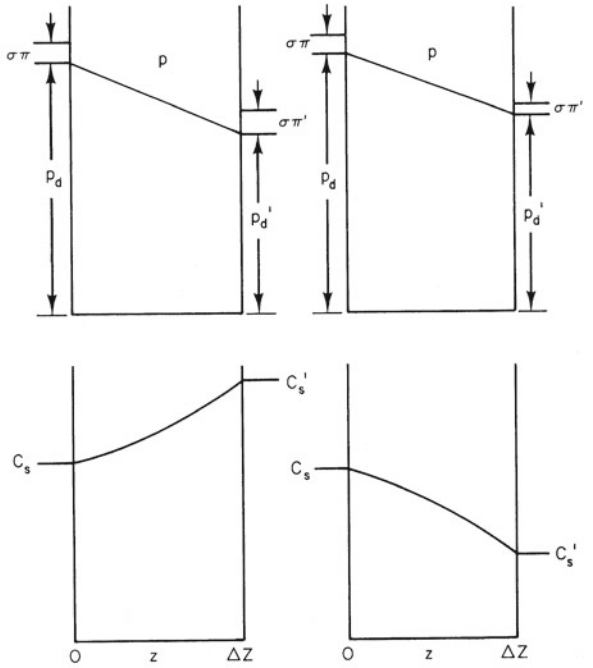

Fig. 5.14 A possible set of values for p, p_d, and C along a pore for diffusion to the left and diffusion to the right. The fluid on each side of the pore is well stirred and of sufficient volume so that concentrations do not change with time

As the pore becomes very long compared to the diffusion length (for example, $|\Delta Z/\lambda| = 10$ or more), the concentration along the pore is nearly that carried into the pore by bulk flow from the left until we get to the far end, where diffusion back up the pore gives a smooth transition to the final concentration on the right.

We can think of the pressure in the pore as being made up of driving pressures due to water and to the solute within the pore:

$$p_d(z) = p_{dw}(z) + p_{ds}(z).$$

Since the effective driving pressure for impermeant solute in the J_v equation is $k_B T \Delta C$, it would be nice to be able to write

$$p_d(z) = p_{dw}(z) + (1-\sigma) k_B T\, C(z).$$

This is consistent with the solvent drag flux at position z in the pore, which was given in Eq. 5.45a by

$$\overline{j}_v\, f\, C(z) = \overline{j}_v (1-\sigma) C(z).$$

The "effective" concentration for solvent drag is $(1-\sigma)C(z)$.

5.9.3 Summary

To summarize, the combination of solvent and a solute with reflection coefficient has a volume flux

$$J_v = L_p(\Delta p - \sigma\, k_B T\, \Delta C_s) \tag{5.53}$$

and a solute flux

$$J_s = (1-\sigma)\overline{C}_s J_v + \omega RT\, \Delta C_s. \tag{5.54}$$

The hydraulic permeability is

$$L_p = \frac{n\, \pi R_p^4}{8\eta \Delta Z}. \tag{5.55}$$

The solute permeability is

$$\omega RT = \frac{n\, \pi R_p^2\, D_{\text{eff}}}{\Delta Z}. \tag{5.56}$$

The characteristic length for diffusion is

$$\lambda = \frac{D_{\text{eff}}}{\overline{j}_v (1-\sigma)} = \frac{\Delta Z\, \omega RT}{J_v (1-\sigma)}. \tag{5.57}$$

The average concentration is

$$\overline{C}_s = \tfrac{1}{2}(C_s + C_s') + G(x)\, \Delta C_s, \tag{5.58}$$

where $G(x)$ is given by Eq. 5.50b. The parameter x is

$$x = \frac{J_v(1-\sigma)}{\omega RT} = \frac{\Delta Z}{\lambda}. \tag{5.59}$$

Notice that the solvent drag term as well as the diffusion term depends on ΔC_s, through the factor $\overline{C}_s$.

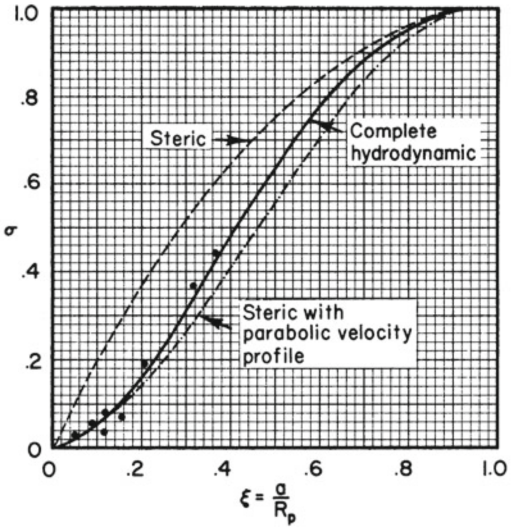

Fig. 5.15 Calculated values of the reflection coefficient are indicated by the lines. Calculations are shown for the simple steric factor, the steric factor weighted by a parabolic velocity profile, Eq. 5.60, and a more detailed calculation, which takes account of the distortion of the velocity profile by the solute particles by Levitt (1975) and by Bean (1972, pp. 29–35). The data points are from Durbin (1960) as reinterpreted by Bean (1972)

5.9.4 Reflection Coefficient

We have referred previously to the fact that the centers of solute particles can occupy only a fraction of the pore volume. A solute particle's center cannot be further from the pore axis than $R_p - a$. The simplest correction is the steric factor, seen on p. 125 . The ratio of effective area to total area approximates $1-\sigma$. If $\xi = a/R_p$, then

$$1-\sigma \approx \frac{\pi (R_p - a)^2}{\pi R_p^2} = 1 - \frac{2a}{R_p} + \frac{a^2}{R_p^2},$$
$$\sigma = 2\xi - \xi^2.$$

A better calculation was seen in the preceding subsection. Accept the fact (quoted from thermodynamic results) that the same σ occurs in the equations for J_v and J_s. We saw that the edges of the pore have less bulk flow than the center, so that the steric effect overestimates how many particles are reflected. From Eq. 5.44b,

$$\sigma = 1 - f = 4\xi^2 - 4\xi^3 + \xi^4. \tag{5.60}$$

These two approximations to σ are plotted in Fig. 5.15, along with the results of a more detailed calculation that takes account of distortions in the velocity profile due to rotation of the solute molecules.

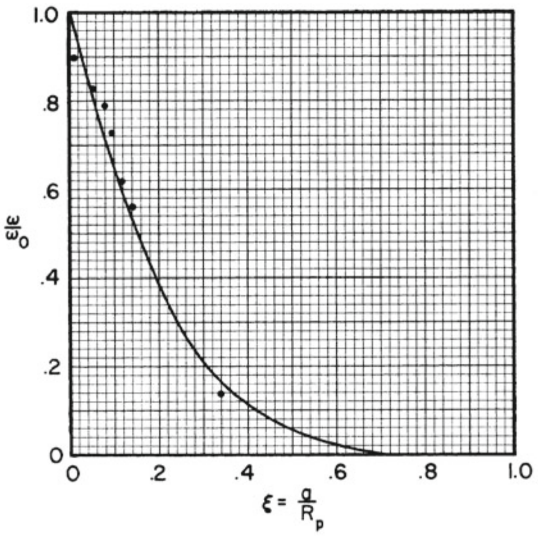

Fig. 5.16 Plot of ω/ω_0 for experimental data by Beck and Schultz (1970) and a calculation by Bean (1972)

5.9.5 The Effect of Pore Walls on Diffusion

The solute permeability is given by

$$\omega RT = \frac{n\pi R_p^2 D_{\text{eff}}}{\Delta Z}.$$

The effective diffusion coefficient takes into account the steric factor as well as the drag on the solute particles by the pore walls. If the pore had an infinitely large diameter, the unrestricted permeability would be

$$\omega_0 RT = \frac{n\pi R_p^2 D}{\Delta Z},$$

where D is the diffusion coefficient for an infinite medium. Figure 5.16 shows some data from Beck and Schultz (1970) and a curve for ω/ω_0 calculated by Bean (1972).[13]

In Europe, filtration rather than dialysis is used to treat kidney patients. There is evidence that some as yet unidentified toxin of medium molecular weight accumulates in the blood. Comparison of $1 - \sigma$ from Fig. 5.15 with ω/ω_0 from Fig. 5.16 shows that solvent drag removes medium-sized molecules more effectively. The fluid and electrolytes lost by the patient must be replaced.

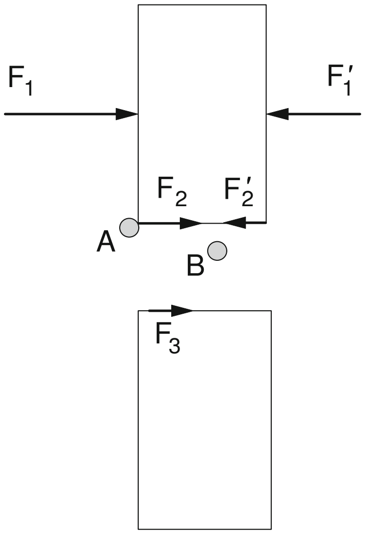

Fig. 5.17 The forces on a membrane with pores. The fluid on the left exerts force $\mathbf{F}_1$ due to the hydrostatic pressure p. A similar force $\mathbf{F}_1'$ is exerted on the right. Solute molecules like A are reflected at the pore edge and exert force $\mathbf{F}_2$. Solute molecule B enters the pore. It contributes to the viscous force of the flowing fluid on the cylindrical walls of the pore, $\mathbf{F}_3$. $\mathbf{F}_3$ is to the right if the fluid flows from left to right through the pore

5.9.6 Net Force on the Membrane

We conclude the section by calculating the force of the fluid on our model membrane. The results give some insight into the nature of osmotic pressure.

A membrane of total area S is pierced by n pores per unit area of radius R_p. The pressures in the fluid on each side of the membrane are p and p'. A solute with reflection coefficient σ has concentration C on the left and C' on the right. We want to calculate the total force exerted by the fluid on the membrane. There are three contributions to this force. These can be understood by referring to Fig. 5.17.

Forces F_1 and F_1' are the forces exerted by the fluid on the walls of the membrane on each side. They are obtained by multiplying the total pressure on each side by the area of the membrane that is not occupied by pores. In a total area S there are nS pores, each of area πR_p^2.

$$F_1 = pS\left(1 - n\pi R_p^2\right)$$

$$F_1' = p'S\left(1 - n\pi R_p^2\right).$$

The net force to the right is

$$F_1 - F_1' = S\left(p - p'\right)\left(1 - n\pi R_p^2\right). \qquad (5.61)$$

Forces F_2 and F_2' are exerted by solute molecules reflected from the pore region, such as molecule A in Fig. 5.17. These

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[13] The steric factor, which Bean includes separately, is built into D_{eff} through the function $\Gamma(r)$.

are the ones that contribute to the osmotic pressure. The net force to the right is therefore the total pore area $Sn\pi R_p^2$ times the impermeant part of the osmotic pressure difference:

$$F_2 - F_2' = Sn\pi R_p^2 \left(\sigma\pi - \sigma\pi'\right). \qquad (5.62)$$

Force F_3 is the viscous drag exerted on the walls of the pores by the water and permeant solute molecules flowing through them. To calculate it we recall that the viscous force per unit area is $-\,\eta\,(\partial v/\partial r)$. The velocity is $v = j_v$. Differentiating Eq. 5.43,we obtain

$$\frac{\partial j_v}{\partial r} = -\frac{1}{4\eta}\frac{\Delta\left(p - \sigma\pi\right)}{\Delta Z}2r.$$

The total force is η times this quantity evaluated at $r = R_p$, times total area of the cylindrical walls of all the pores, which is $(Sn)\left(2\pi R_p \Delta Z\right)$:

$$F_3 = Sn2\pi R_p \Delta Z \eta \left(\frac{1}{4\eta} \frac{(p - p') - \sigma\left(\pi - \pi'\right)}{\Delta Z} 2R_p \right)$$

$$= Sn\pi R_p^2 \left[(p - p') - \sigma\left(\pi - \pi'\right)\right]. \qquad (5.63)$$

The net force on the membrane is the sum of these forces:

$$F_1 - F_1' + F_2 - F_2' + F_3 = S(p - p'). \qquad (5.64)$$

We see that the net force on the membrane is the total pressure difference times the total area of the membrane, regardless of the differences in osmotic pressure on each side. Both solute and solvent exert a force on the nonpore area of the membrane. The solute molecules at the membrane surface whose centers are within the area of a pore may be reflected or may enter the pore. If they are reflected, they contribute to the force when they strike the membrane at the edge of a pore. If they are not reflected, they enter the pore and contribute to the viscous drag on the membrane due to flow through the pore.

Symbols Used In Chapter 5

Symbol	Use	Units	First used page
a	Solute particle radius	m	125
$a, a_{\text{in}}, a_{\text{out}}$	Parameters	m^{-1}	128
c_1, c_2, c_1', c_2'	Solute concentration	(mole) m^{-3}	118
f	Temporary function		131
h	Thickness of fluid layer	m	127
i	Solute current through membrane	s^{-1}	137
i_s	Solute flow	s^{-1}	130
i_v	Volume flow	$\text{m}^3\ \text{s}^{-1}$	123
$j_s, \mathbf{j}_s$	Solute fluence rate in pore	$\text{m}^{-2}\ \text{s}^{-1}$	130
$j_v, \mathbf{j}_v$	Volume fluence rate in pore	m s^{-1}	129
k_B	Boltzmann's constant	J K^{-1}	118
n	Number of moles		118
n	Number of pores per unit area	m^{-2}	125
p_1, etc.	Pressure	Pa	118
p_d	Driving pressure	Pa	121
p	Total pressure	Pa	121
p_{dw}	Driving pressure of water	Pa	121
r	Radius in cylindrical coordinates	m	129
x, y, z	Position	m	127
x	$\Delta Z/\lambda$		133
z	Distance along pore	m	129
$\hat{\mathbf{z}}$	Unit vector in z direction		129
C, C_s, etc.	Particle concentration of the species indicated by the subscript	(particle) m^{-3}	118
D, D_{eff}	Diffusion constant	$\text{m}^2\ \text{s}^{-1}$	130
F	Force	N	134
G	Factor relating solvent drag and diffusion		132
J_s	Solute fluence rate through membrane	$\text{m}^{-2}\ \text{s}^{-1}$	125
J_v	Volume fluence rate through membrane	m s^{-1}	123
L_p	Hydraulic permeability	$\text{m s}^{-1}\ \text{Pa}^{-1}$	123
N_1, etc.	Number of molecules		118
N_A	Avogadro's number		118
R	Gas constant	$\text{J mol}^{-1}\ \text{K}^{-1}$	118
R_p	Pore radius	m	125
S	Surface area	m^2	123
T	Absolute temperature	K	118
V, V', V^*	Volume	m^3	118
X, Y	Distance	m	127
ΔZ	Pore length	m	125
η	Viscosity	Pa s	128
λ	Effective diffusion distance	m	131
μ	Chemical potential	J molecule^{-1}	120
ξ	a/R_p		133
π	Osmotic pressure	Pa	120
$\mathrm{\pi}$	Geometric constant		
σ	Reflection coefficient		124
τ	Time constant	s	127
ω	Solute permeability	$\text{mol N}^{-1}\ \text{s}^{-1}$	125
ω_0	Solute permeability in an infinite medium	$\text{mol N}^{-1}\ \text{s}^{-1}$	134
ϕ	Angle in cylindrical coordinates		129
ϕ	C_s'/C_s		132
Γ	Radial dependence of solute concentration		130

Problems

Section 5.3

Problem 1. Use estimates of the size of a water molecule, the osmolarity of body fluids, and the thickness of a cell membrane to decide if Fig. 5.1 is drawn to scale or if

(a) the size of the water molecules has been exaggerated for clarity
(b) the ratio of the number of solute molecules to the number of solvent molecules has been exaggerated for clarity.

Problem 2. Perform the unit conversions to verify that 8.3145 J mol^{-1} K^{-1} is equivalent to 0.08206 atm l mol^{-1} K^{-1}.

Problem 3. The protein concentration in serum is made up of two main components: albumin (molecular weight 75,000) 4.5 g per 100 ml and globulin (molecular weight 170,000) 2.0 g per 100 ml. Calculate the osmotic pressure due to each constituent. (These results are inaccurate because of electrical effects.)

Problem 4. If the osmotic pressure in human blood is 7.7 atm at 37 °C, what is the solute concentration assuming that $\sigma = 1$? What would be the osmotic pressure at 4 °C?

Problem 5. Sometimes after trauma the brain becomes very swollen and distended with fluid, a condition known as cerebral edema. To reduce swelling, mannitol may be injected into the bloodstream. This reduces the driving force of water in the blood, and fluid flows from the brain into the blood. If 0.01 mol l^{-1} of mannitol is used, what will be the approximate osmotic pressure?

Section 5.4

Problem 6. When a person is given an intravenous fluid, the solute concentration in the fluid must be matched to the solute concentration in the blood to avoid problems arising from a change in the blood's osmotic pressure. One such fluid, called "isotonic saline," can be made by adding salt (NaCl) to distilled water. The osmolarity of the blood is about 0.3 osmole.

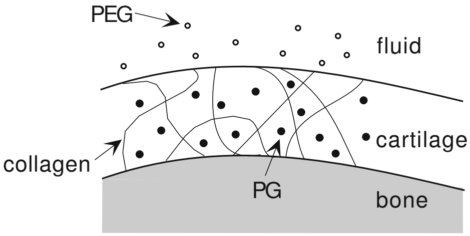
(a) How many grams of NaCl must be added to a liter of water to make isotonic saline? What fraction of the solution's mass is NaCl? (Hint: recall that NaCl dissolves into Na^+ and Cl^-, and both contribute to the osmotic pressure.)

(b) Repeat for dextrose, $C_6H_{12}O_6$, which does not dissociate.

Problem 7. An understanding of osmotic pressure is important in medicine. Consider the case reported by Steinmuller (1998) in the *New England Journal of Medicine*. A 5 % solution of albumin was needed to infuse into a patient with kidney disease (renal insufficiency). No 5 % solution was available, so the hospital pharmacy used 25 % albumin diluted 1:4 with pure water. Injection of the solution into the patient caused renal failure. The albumin in a 25 % albumin solution has an osmolarity of about 36 mosmol. Typically, such a solution also contains about 300 mosmol of other ions (see Problem 6).

(a) Calculate the osmolarity of the solution injected into the patient.
(b) Calculate the osmolarity of the solution if the pharmacy had properly used isotonic saline instead of pure water to perform the 1:4 dilution.

Problem 8. Articular cartilage covers the ends of bones in joints and allows the bones to move smoothly against each other. It contains a network of collagen fibers that can exert a mechanical tensile stress to resist tissue swelling, resulting in a pressure P_c within the cartilage. The collagen fibers do not withstand compression. The cartilage also contains proteoglycan molecules that cause tissue swelling because of their osmotic pressure, π_{PG}. One can determine P_c by placing the cartilage in a polyethylene glycol solution with osmotic pressure π_{PEG}, measuring π_{PG} and π_{PEG}, and using the relationship $P_c = \pi_{\text{PG}} - \pi_{\text{PEG}}$.



Typical data are

π_{PEG} (atm)	π_{PG} (atm)
0.0	4.0
2.5	5.5
5.0	7.0
7.5	8.5
10.0	10.0

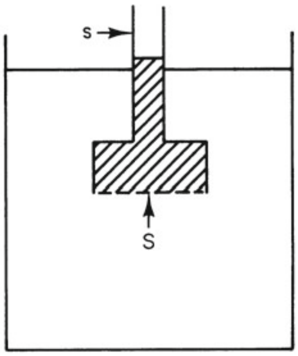
(a) What is the excess pressure P_c exerted by the collagen matrix under normal conditions ($\pi_{\text{PEG}} = 0$)?
(b) At what value of π_{PEG} does the collagen matrix exert no tensile stress (become "limp")?
(c) Plot P_c vs π_{PEG}. Find a linear equation that fits the data.
(d) If the collagen in an arthritic joint can only exert a pressure of 2 atm when $\pi_{\text{PEG}} = 0$, by how much will the tissue swell (by what percent will its volume change?)

In (b) and (d), assume that only the proteoglycans cause osmotic pressure and that their number does not change, but the tissue volume increases as the tissue swells with water. This problem is based on the work of Basser et al. (1998), but the data have been modified.

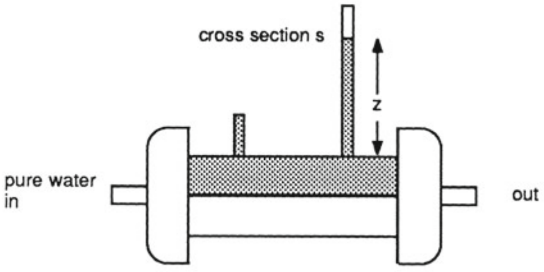
Section 5.5

Problem 9. Suppose that L_p is expressed in $\text{m}^3\ \text{N}^{-1}\ \text{s}^{-1}$ or $\text{m s}^{-1}\ \text{Pa}^{-1}$. Find conversion factors to express it in
(a) ml min^{-1} cm^{-2} torr^{-1}.
(b) ml s^{-1} cm^{-2} $(\text{in. water})^{-1}$.
(c) ml s^{-1} cm^{-2} $(\text{lb in.}^{-2})^{-1}$.

Problem 10. An ideal semipermeable membrane is set up as shown. The membrane surface area is S; the cross-sectional area of the manometer tube is s. At $t = 0$, the height of fluid in the manometer is zero. The density of fluid is ρ. Show that the fluid height rises to a final value with an exponential behavior. Find the final value and the time constant. Ignore dilution of the solute.



Problem 11. Consider the design of a lecture demonstration apparatus to show osmotic pressure that uses a commercially available filter as shown in the drawing. Assuming well-stirred fluid on both sides of the membrane and neglecting the change of solute concentration in the manometer tube as water flows in, one finds that height z increases to the equilibrium value exponentially, with a time constant obtained in the previous problem. What would be the time constant if one used a membrane for which $L_p = 1$ ml min^{-1} m^{-2} torr^{-1}, and the total membrane area is $S = 0.2$ m^2. Suppose that the inner radius of the manometer tube is 1 mm. (One could not use sucrose as a solute, because this particular membrane is permeable to molecules of molecular weight less than 50,000.)



Problem 12. A cell has variable volume V and fixed surface area S. The total hydrostatic pressure p is the same inside and outside the cell, and there is complete and instantaneous mixing. Initially the interior and exterior are both pure water. The initial volume of the cell is V_0. At $t = 0$ the exterior is bathed in a solution containing an impermeant solute of concentration C_0.

(a) Does the cell shrink to zero volume or expand to its maximum volume, which is a sphere of surface area S?

(b) Derive a differential equation for the volume change and integrate it to find how long it takes for the cell to reach zero or maximum volume.

Problem 13. A cell has variable volume V and fixed surface area S. The total hydrostatic pressure p is always the same both inside and outside the cell. There is complete and instantaneous mixing both inside and out. An impermeant solute has an initial concentration $C(0)$ both inside and outside. The initial cell volume is V_0. At $t = 0$ the exterior solute is removed.

(a) Does the cell shrink to zero volume or expand to its maximum volume, which is a sphere of surface area S?

(b) Derive a differential equation for $V(t)$ and find how long it takes for the cell to reach zero or maximum volume.

Section 5.6

Problem 14. Two membranes have permeabilities $\omega_1 RT$ and $\omega_2 RT$. Find the permeability of a two-layered membrane in terms of ω_1 and ω_2.

Problem 15. Solute is carried through a pipe by solvent drag. The radius of the pipe is b. The average flow along the pipe is $\overline{j}_v$ (independent of r because it has been averaged over r). Assume that within the pipe the concentration of solute is independent of radius and can be written as $C(z)$. The solute is carried along purely by solvent drag. Solute concentration outside the pipe is zero. Solute diffuses through the wall of the pipe, which has solute permeability ωRT. In terms of $\overline{j}_v$, b, and ωRT, obtain a differential equation for $C(z)$ and show that C decays exponentially along the pipe. Find the decay constant.

Section 5.7

Problem 16. A kidney machine has a membrane permeability $\omega RT = 0.5 \times 10^{-3}$ cm s^{-1}. If the membrane area is 1 m^2, the volume of body fluid is 40 l, and the volume of dialysate is effectively infinite, what is the time constant? How long will it take to reduce the BUN (blood urea nitrogen) concentration from 120 mg per 100 ml to 20 mg per 100 ml?

Problem 17. Find the pair of coupled differential equations for C and C' for a dialysis machine in which V' is not infinite.

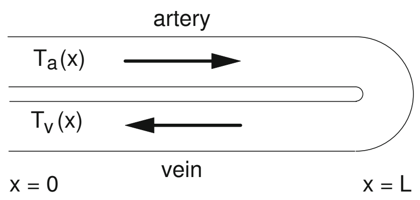
Section 5.8

Problem 18. In the countercurrent model (Eq. 5.25) the total current i through the membrane when its length is X is

$$i = \omega RTY \int_0^X [C_{\text{in}}(x) - C_{\text{out}}(x)]\,dx.$$

Solve this integral for the two cases given by Eqs. 5.26 and 5.27. Show that the current ratio in these two cases is 1.36 when $a = 1$ and $X = 2$.

Problem 19. The countercurrent model applies to the transport of heat as well as particles, with temperature taking the place of concentration. Consider a countercurrent heat exchanger, which represents the arrangement of blood vessels in the flipper of a whale (Schmidt-Nielsen 1972).



The temperatures of the arterial and venous blood are governed by equations similar to Eq. 5.27:

$$T_a = c_1 + (c_2 - c_1)ax,$$
$$T_v = c_2 + (c_2 - c_1)ax.$$

Assume that the arterial blood at $x = 0$ is at the warm temperature of the whale's body, T_w. The arterial blood at $x = L$ enters the capillaries at temperature $T_a(L)$ and is cooled to the temperature of the surrounding ocean water, T_c, by the time it enters the vein at $x = L$.

(a) Determine c_1 and c_2 in terms of T_w, T_c, a, and L.

(b) Plot $T_a(x)$ and $T_v(x)$ for $T_w = 37\,°\text{C}$, $T_c = 7\,°\text{C}$, $a = 1\ \text{mm}^{-1}$ and $L = 3\ \text{mm}$.

(c) The loss of heat from the body to the surroundings is proportional to $\Delta T = T_a(L) - T_c$. Find an expression for ΔT. What does ΔT reduce to if $aL \gg 1$? Interpret these results physically. To minimize heat loss to the ocean should aL be large or small?

(d) The energy the body must supply to heat the returning venous blood is proportional to $\Delta T' = T_w - T_v(0)$. Find an expression for $\Delta T'$.

Section 5.9

Problem 20. Derive Eqs. 5.44a and 5.44b.

Problem 21. Show that Eq. 5.51 gives $C(z) = \text{const}$ when $\lambda = 0$ (pure solvent drag) and gives $dC/dz = \text{const}$ when $\lambda \to \infty$ (pure diffusion).

Problem 22. Obtain expressions for J_s when $\lambda = 0$ and $\lambda \to \infty$.

Problem 23. Show that for very large pores when $\sigma = 0$ the parameter $x = \Delta Z/\lambda = J_v/\omega RT$ depends only on pore radius, solute particle radius, pressure difference and temperature, and not on viscosity, the number of pores per unit area, or the membrane thickness.

Problem 24. When $C_s' = 0$, what are the limiting values of $\overline{C_s}$ as $x \to 0$? As $x \to \infty$? As $x \to -\infty$?

Problem 25. (a) Write J_s in terms of C_s, C_s', J_v and x.

(b) Specialize to the case $C_s' = 0$.

Problem 26. (a) Find the ratio $(1-\sigma)\overline{C_s}J_v/[\omega RT(C_s - C_s')]$ in terms of x, C_s and C_s'.

(b) Specialize to the case $C_s' = 0$ and discuss limiting values for small and large x.

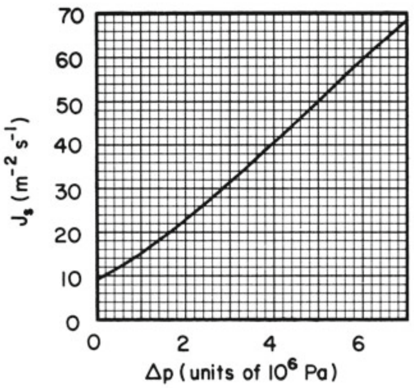
Problem 27. (a) Show that

$$J_s = \omega RT\left(C_s\frac{xe^x}{e^x-1} - C_s'\frac{x}{e^x-1}\right)$$

where $x = J_v(1-\sigma)/\omega RT$.

(b) Discuss the special case $C_s' = 0$ in the limits $x \to 0$ and x→ ∞.

(c) From the data shown, estimate L_p and ωRT. The data are for the transport of radioactive water with a concentration of 10^{15} molecules m^{-3} on one side of the membrane and zero on the other.



Problem 28. Consider the following cases for transport of water through a membrane.

(a) Water flows by bulk flow through the membrane with $\Delta p = 0$. There is an impermeant solute ($\sigma = 1$) on the right with concentration C_{big} and zero concentration on the left. Find the particle fluence rate of water in terms of L_p.

(b) There is no volume flow through the membrane ($J_v = 0$). Some of the water molecules on the left are tagged with radioactive hydrogen (tritium). The concentration of tagged water molecules is C_s on the left and 0 on the right. Find the particle fluence rate of tagged water in terms of L_p and ωRT.

(c) There is volume flow, as in case (a), and there are also tagged water molecules on the left. Find the particle fluence rate of tagged water in terms of L_p and ωRT.

(d) Restate the answers in terms of the parameters of a collection of n pores per unit area of radius R_p and length ΔZ.

(e) Estimate the value of x for part (c) if $R_p = 10^{-8}$ m and $c_{\text{big}} = c_s = 0.1$ mol 1^{-1}.

Problem 29. Construct diagrams analogous to Fig. 5.14a when the total pressure is the same on both sides and $\pi' = 0$ and (b) when $(p - \sigma\pi) < p'$ and $\pi' = 0$.

Problem 30. Consider the case of water permeability shown in Fig. 5.1c. Water and solute molecules move through the membrane in the same way. They "dissolve" from solution into the membrane. Assume that the concentration of water molecules just inside the membrane is proportional to the pressure just outside: $C = \alpha p$. The membrane has thickness ΔZ and the diffusion constant for water in the membrane material is D. Under steady-state conditions, derive an expression for L_p.

Problem 31. Consider the case in which solute moves along a tube by a combination of diffusion and solvent drag. Ignore radial diffusion within the tube, but assume that solute is moving out through the walls so that j_s is changing with position in the tube. In particular, the number of solute particles passing out through the wall in length dz in time dt is $CA2\pi R_p\, dz\, dt$, where A is related to the permeability of the wall. Consider a case in which C does not change with time, but depends only on position along the tube.

(a) Write down the conservation equation for an element of the tube and show that

$$-\frac{\partial j}{\partial z} - \frac{2AC}{R_p} = 0.$$

(b) Combine the results of part (a) with Eq. 5.45a and show that $C(z)$ must satisfy the differential equation

$$\frac{\partial^2 C}{\partial z^2} - \frac{\bar{j}_v f}{D}\frac{\partial C}{\partial z} - \frac{2A}{DR_p}C = 0.$$

Show that this equation will be satisfied if the concentration decreases exponentially along the tube as $C(z) = C_0 e^{-\alpha z}$, where

$$\alpha = \frac{\bar{j}_v f}{2D}\left[-1 + \left(1 + \frac{8AD}{R_p \bar{j}_v^2 f^2}\right)^{1/2}\right].$$

Problem 32. The volume of a water molecule is V_w and the volume of a solute molecule is V_s. Define a new quantity J_w that is the number of water molecules per unit area per second passing through the membrane. What is J_w in terms of J_v and J_s?

References

Agre P, King LS, Yasui M, Guggino WB, Ottersen OP, Fujiyoshi Y, Engel A, Nielsen S (2002) Aquaporin water channels: From atomic structure to clinical medicine. J Physiol 542:3–16

Basser PJ, Schneiderman R, Bank RA, Wachtel E, Maroudas A (1998) Mechanical properties of the collagen network in human articular cartilage as measured by osmotic stress technique. Arch Biochem Biophys 351:207–219

Bean CP (1969) Characterization of cellulose acetate membranes and ultrathin films for reverse osmosis. Research and Development Progress Report No. 465 to the U.S. Department of Interior, Office of Saline Water. Contract No. 14-01-001-1480. Washington, Superintendent of Documents, October 1969.

Bean CP (1972) The physics of porous membranes—neutral pores. In: Eisenman G (ed) Membranes, vol 1. Dekker, New York, pp 1–55

Beck RE, Schultz JS (1970) Hindered diffusion in microporous membranes with known pore geometry. Science 170:1302–1305

Calland CH (1972) Iatrogenic problems in end-stage renal failure. N Engl J Med 287:334–336

Cokelet GR (1972) The rheology of human blood. In: Fung YC et al (eds) Biomechanics, its foundations and objectives. Prentice Hall, Englewood Cliffs (especially p. 77, Fig. 4)

Durbin RP (1960) Osmotic flow of water across permeable cellulose membranes. J Gen Physiol 44:315–326

Fishman RA (1975) Brain edema. N Engl J Med 293:706–711

Gennari FJ, Kassirer JP (1974) Osmotic diuresis. N Engl J Med 291:714–720

Guyton AC, Taylor AE, Granger HJ (1975) Circulatory physiology II. Dynamics and control of the body fluids. Saunders, Philadelphia

Hall JE (2011) Guyton and Hall textbook of medical physiology, 12th edn. Saunders/Elsevier, Philadelphia

Hildebrand JH, Scott RL (1964) The solubility of nonelectrolytes, 3rd edn. Dover, New York

Katchalsky A, Curran PF (1965) Nonequilibrium thermodynamics in biophysics. Harvard University Press, Cambridge

Kramer EM, Myers DR (2012) Five popular misconceptions about osmotic pressure. Am J Phys 80:694–699

Levitt DG (1975) General continuum analysis of transport through pores. I. Proof of Onsager's reciprocity postulate for uniform pore. Biophys J 15:533–551

Lindner A, Charra B, Sherrard DJ, Scribner BH (1974) Accelerated atherosclerosis in prolonged maintenance hemodialysis. N Engl J Med 290:697–701

Lysaght MJ, Moran J (2006) Peritoneal dialysis equipment. In: Bronzino JD (ed) The biomedical engineering handbook, 3rd edn. Vol 3: Tissue engineering and artificial organs. CRC Press, Boca Raton, pp 68-1–68-13

Mavroidis C (2006) Artificial kidney. In Bronzino JD (ed) The biomedical engineering handbook, 3rd edn. Vol 3: Tissue engineering and artificial organs. CRC Press, Boca Raton, pp 67-1–67-24

Murata K, Mitsuoka K, Hirai T, Walz T, Agre P, Heymann JB, Engel A, Fujiyoshi Y (2000) Structural determinants of water permeation through aquaporin-1. Nature 407:599–605

Parisi M, Dorr RA, Ozu M, Toriano R (2007) From membrane pores to aquaporins: 50 years measuring water fluxes. J Biol Phys 33(5–6):331–343

Patton HD, Fuchs AF, Hille B, Scher AM, Steiner RF (eds) (1989) Textbook of physiology, 21st edn. Saunders, Philadelphia

Preston GM, Carroll TP, Guggino WB, Agre P (1992) Appearance of water channels in *Xenopus* oocytes expressing red cell CHIP28 protein. Science 256:385–387

Schmidt-Nielsen K (1972) How animals work. Cambridge University Press, Cambridge

Silverstein ME, Ford CA, Lysaght MJ, Henderson LW (1974). Treatment of severe fluid overload by ultrafiltration. N Engl J Med 291:747–751

Steinmuller DR (1998) A dangerous error in the dilution of 25 percent albumin. N Engl J Med 338:1226–1227

Thomas L (1974) Lives of a cell. Viking, New York

White RJ, Likavec MJ (1992) Current concepts: the diagnosis and initial management of head injury. N Engl J Med 327:1507–1511

Zeuthen T (2010) Water-transporting proteins. J Membrane Biol 234:57–73