Membrane Transport II (Osmosis)
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OBJECTIVES:

1. Be able to define and calculate osmolarity.
2. Describe osmosis across a semipermeable membrane and the volume changes that will occur as a result.
3. Be able to calculate osmotic pressure and understand the factors that contribute to it.
4. Understand the role of reflection coefficient in determining effective osmotic pressure.
5. Understand how a difference in effective osmotic pressure drives osmotic water flow.
6. Compare osmosis to diffusion of water.

Suggested Reading:

Physiology, L.S. Costanzo, Saunders, pp 12-15

Most water flow across cell membranes occurs by osmosis, not by diffusion. Osmosis is the topic of today's lecture, but first we will clarify the concepts of osmolarity and osmotic pressure.

I. OSMOLARITY

Osmolarity is the concentration of osmotically active particles in a single solution. To calculate osmolarity, one must know the concentration of the solute and whether that solute dissociates in solution. For example, urea does not dissociate in solution; one mole of urea is one mole in solution. However, in solution NaCl dissociates into two particles (or nearly two particles) and CaCl₂ dissociates into three particles (or nearly three). The symbol "g" gives the number of particles in solution for a given solute. "g" also takes into account whether there is complete dissociation or not; for example, "g" for NaCl is not 2.0, but is slightly less than 2.0 (e.g., 1.85) because in solution some of the Na⁺ and Cl⁻ interact with each other. Thus, g for urea is 1.0; g for NaCl is slightly less than 2.0 as explained; g for CaCl₂ is slightly less than 3.0. The units of "g" are osmoles/mole. The units of osmolarity are osmoles/L or mosmoles/L.

\[
\text{Osmolarity} = g \times C
\]
If two solutions have the same calculated osmolarity, they are called **isosmotic**. If two solutions have different calculated osmolarities, the solution with the higher osmolarity is **hyperosmotic** and the solution with the lower osmolarity is **hyposmotic**.

Osmolarity is calculated for one solution. There is no membrane separating one solution from another and no water flow (that's osmotic pressure and osmosis... coming up!).

**II. OSMOTIC PRESSURE AND OSMOSIS**

A. **Example of osmosis**

**Osmosis** is the flow of water across a semipermeable membrane due to a difference in solute concentration. This difference in solute concentration creates an osmotic pressure difference and the osmotic pressure difference is the driving force for water flow. The figure below illustrates the concept of osmosis. In both A and B, there is a semipermeable membrane separating two solutions, one containing solute (the circles), the other containing only water. The membrane is impermeable to the solute, but permeable to water.

- **In A**, the two solutions are open to the atmosphere. The solute in Solution 1 creates an osmotic pressure, which produces a reduction in hydrostatic pressure in Solution 1 (the higher the osmotic pressure, the lower the hydrostatic pressure). As a result, there is a hydrostatic pressure gradient established between Solution 2 and Solution 1, with the greater hydrostatic pressure in Solution 2. Water flows from 2 to 1, driven by this hydrostatic pressure gradient. With time, the volume in 1 increases and the volume in 2 decreases.

- **In B**, the two solutions are closed and pressure is applied with a piston to stop the flow of water from 2 to 1. The pressure required to stop water flow is the osmotic pressure of Solution 1. This pressure can be measured experimentally.
B. Calculating osmotic pressure

The osmotic pressure ($\pi$) of Solution 1 in the above example is determined by two factors: the concentration of osmotically active particles in the solution and whether the membrane is impermeable to the solute (i.e., whether the solute remains in Solution 1). Effective osmotic pressure is calculated by the **van't Hoff equation**, which converts solute concentration into pressure, taking into account whether the solute remains in the original compartment:

$$\pi = g \cdot C \cdot \sigma \cdot RT$$

where $\pi$ is osmotic pressure (or effective osmotic pressure), $g$ is number of solute particles per mole in solution, $C$ is concentration of solute, $RT$ is gas constant x absolute temperature, and $\sigma$ is a new term called reflection coefficient.

C. Reflection coefficient

The **reflection coefficient ($\sigma$)** is a dimensionless (no units) number that describes the ease with which the solute crosses the membrane. (Yes, reflection coefficient is related to permeability, in case you were wondering.) Values for reflection coefficient vary between 1.0 and zero as follows:
• $\sigma = 1.0$ means the membrane is impermeable to the solute and the solute stays in the original compartment. Referring to the figure above, solute would remain in Solution 1. In this case, the solute exerts its full osmotic effect, the osmotic pressure is maximal, and water flow is maximal. Examples of solutes with $\sigma = 1.0$ are proteins, which are impermeable across cell membranes and capillaries.

• $\sigma = 0$ means that the membrane is freely permeable to the solute and the solute can diffuse down its concentration gradient from the original compartment. Recalling diffusion for a moment, this means that eventually, the solute concentration will be the same in both compartments. In this case, there will be no effective osmotic pressure and no water flow. Notice that, in the van't Hoff equation, when $\sigma = 0$ the effective osmotic pressure also equals zero. An example of a solute with $\sigma = 0$ (or close to 0) is urea.

• $\sigma =$ between 0 and 1.0. Most solutes fall in between — they are neither completely impermeable nor freely permeable. Thus, effective osmotic pressure and water flow fall somewhere between their maximal possible values and zero. Notice in the van't Hoff equation, when $\sigma$ is between 0 and 1.0, that effective osmotic pressure is less than maximal, but greater than zero. There are many examples of solutes with $\sigma$ between 0 and 1: mannitol, glucose, NaCl, KCl, CaCl$_2$. In general, the larger the solute, the higher the value of $\sigma$.

D. Osmotic pressure difference drives water flow

For osmosis to occur (water flow due to an osmotic pressure difference), what we really care about is the effective osmotic pressure difference between two
solutions separated by a membrane. In practice, if you're given two solutions, calculate the effective osmotic pressure of each one (units of pressure in mm Hg or atm), then take the difference to determine the driving force for water flow. Follow these rules to determine the direction of water flow:

- If the two solutions have the same effective osmotic pressure, they are isotonic and no water flows between them.

- If the two solutions have different effective osmotic pressures, the one with the higher pressure is called hypertonic and the one with the lower pressure is called hypotonic. Very important: water flows from the hypotonic solution into the hypertonic solution, from lower effective osmotic pressure to higher effective osmotic pressure.

Consider the following example, based on the figure below that illustrates the difference between osmolarity and osmotic pressure and the importance of the reflection coeffi

![Diagram](image)

\[
g = 1 \text{ for all solutes} \\
\sigma_{\text{albumin}} = 1.0 \\
\sigma_{\text{globulin}} = 1.0 \\
\sigma_{\text{urea}} = 0
\]

In A, the two solutions are isosmotic, since their calculated osmolarities are equal. They also are isotonic because their calculated effective osmotic pressures are equal (same \( \sigma \) for albumin and globulin). In B, the two solutions are also isosmotic, but they are not isotonic: the urea solution is hypotonic and the
albumin solution is hypertonic; thus water would flow from right to left, from hypotonic to hypertonic.

III. OSMOSIS VS DIFFUSION OF WATER

Osmosis of water should be distinguished from diffusion of water (with osmosis being much more important across biological membranes). Diffusion of water obeys Fick's Law of diffusion and depends on the concentration difference of water and the surface area for diffusion. Surface area for diffusion is proportional to the area of water-filled pores in the membrane \((r^2)\). Osmosis of water depends on an osmotic pressure difference (see above). Water flow due to a pressure difference (rather than a concentration difference) is based on Poiseuille's law which states that flow is proportional to \(r^4\) of the water-filled pores. Thus, osmosis of water is much faster than diffusion of water because of its fourth power relationship with pore radius!

\[
\text{Flow} = \frac{\pi r^4 \Delta P}{8 \eta \Delta x}
\]

III. PRACTICE PROBLEMS

1. Red blood cells are placed in 150 mM NaCl and no change in their cell volume is observed. It can be concluded that:
   A. 150 mM NaCl is hypertonic
   B. 150 mM NaCl is hypotonic
   C. ICF has an effective osmotic pressure of 300 mOsM.
   D. NaCl acts as if it were an undissociated molecule
   E. NaCl has a higher permeability than water in red blood cells.

2. Red blood cells are placed in 300 mM solution of a nonelectrolyte with a reflection coefficient of 0.4 and the cells swell. It may be concluded that:
   A. a 300 mM solution of this substance is isotonic.
   B. the solution has approximately the effective osmotic pressure of 60 mM NaCl.
C. this substance will remain in the extracellular fluid compartment.
D. the solution is isosmotic with 60 mM NaCl.
E. the effective osmotic pressure of this solution is 150 mOsM.

3. Solutions 1 and 2 contain different concentrations of the same solute. After a brief time, the volume of Solution 1 decreases, and the volume of Solution 2 increases. Which of the following statements explains or describes these initial volume changes?

A. Initially, the effective osmotic pressure of Solution 1 is greater than the effective osmotic pressure of Solution 2.
B. The observed volume changes would have been greater if the reflection coefficient of the solute is 1.0 rather than 0.5.
C. The observed volume changes would have been greater if the solute concentration of Solution 1 was doubled.
D. The reflection coefficient of the solute is zero.

4. Which of the following pairs of solutions is both isosmotic and isotonic. Assume that NaCl is completely dissociated (i.e., g = 2) and the following values for σ.

<table>
<thead>
<tr>
<th>Substance</th>
<th>σ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>1.0</td>
</tr>
<tr>
<td>Sucrose</td>
<td>0.6</td>
</tr>
<tr>
<td>NaCl</td>
<td>0.5</td>
</tr>
<tr>
<td>Urea</td>
<td>0</td>
</tr>
<tr>
<td>Water</td>
<td>0</td>
</tr>
</tbody>
</table>

A. 100 mM protein; 100 mM sucrose
B. 100 mM sucrose; 100 mM NaCl
C. 100 mM urea; 50 mM NaCl
D. 100 mM urea; water
E. None of the above

**ANSWERS**
1. C. (Since no volume change occurred, 150 mM NaCl must be isotonic with respect to the ICF. That is it must be in osmotic equilibrium with it. Since the osmotic pressure of the NaCl is approximately $2 \times 150 = 300$ mOsM, this must also be the osmotic pressure of the ICF.)

2. B. (Since the substance is a nonelectrolyte its osmotic pressure is $1 \text{mOsmole/mmole} \times 300 \text{mM} = 300$ mOsM. However, its effective osmotic pressure with respect to red blood cell membranes is: $\sigma \times 300 = 0.4 \times 300 = 120$ mOsM. That is it has the same effect as a substance with $\sigma = 1$, but at an osmotic pressure of 120 mOsM. Such a substance would be NaCl at 60 mM, since it would also have an osmotic pressure of $2 \times 60 = 120$ mOsM. This is a hypotonic solution. That is why a 300 mOsm solution of this substance causes the cells to swell. The solution is clearly not isosmotic with respect to 60 mM NaCl. The latter has far fewer dissolved particles than the solution in question.)

3. B. Since water flowed into Solution 2 (its volume increased), the initial effective osmotic pressure of Solution 2 must have been greater than that of Solution 1. The higher the reflection coefficient, the greater the effective osmotic pressure difference and the greater the water flow. If the solute concentration of Solution was doubled, the initial effective osmotic pressure difference would have been decreased. If the reflection coefficient was zero, there would have been no water flow.

4. E.