Cellular Electrodynamics
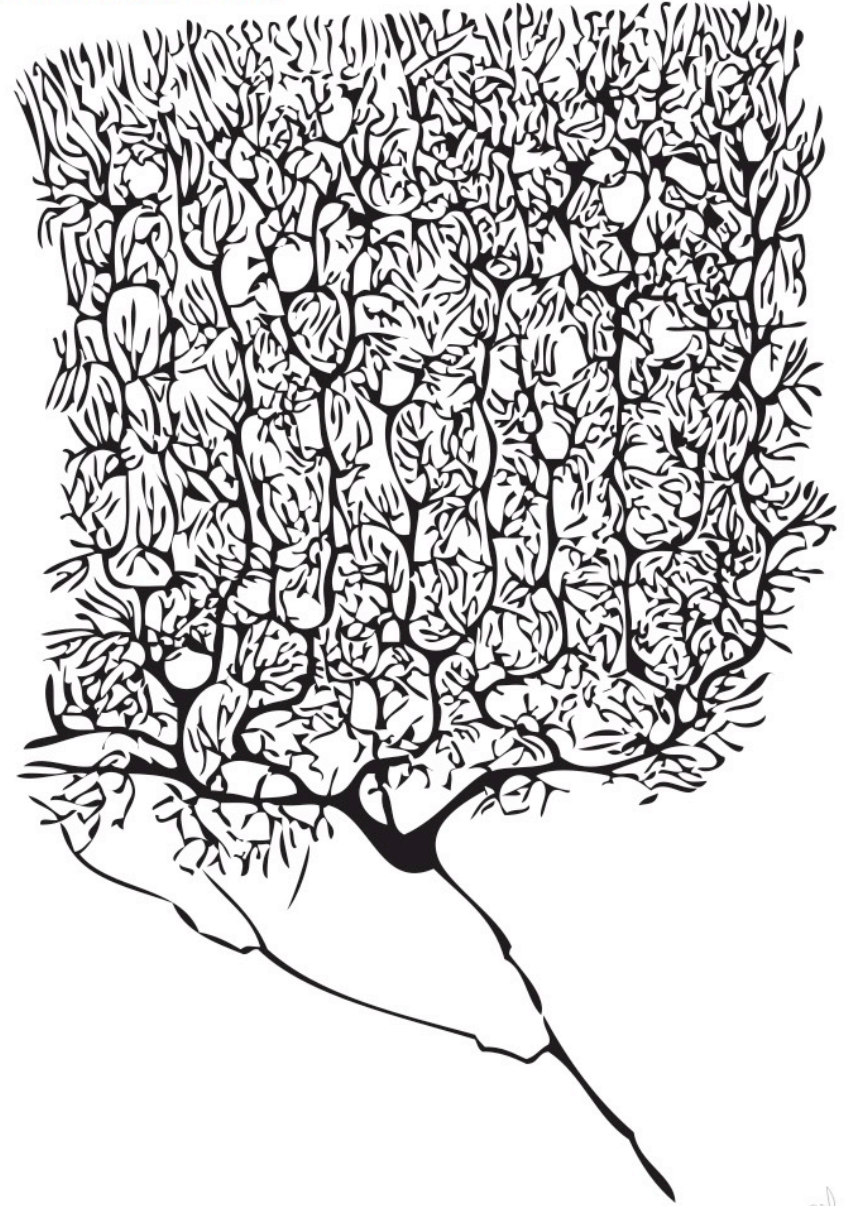
Santiago Ramón y Cajal (1852-1934)

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Website:

http://www.yorku.ca/cberge/4080W2020.html

York University
Winter 2020
BPHS 4080   Lecture 4

Svante Arrhenius (1884)

- PhD (age 25): dissolution of salts into ions
- $NaCl \rightarrow Na^+ + Cl^-$ ($\therefore$ conducts electricity)
- count ions as separate particles
  - $\rightarrow$ van't Hoff's law works for salts as well

$$\pi(x,t) = R\,T \sum_n C_n(x,t) = R\,T\,C_\Sigma(x,t)$$

osmotic pressure

$[\,Pa = N/m^2\,]$

osmolarity

$[\,osmol/m^3\,]$
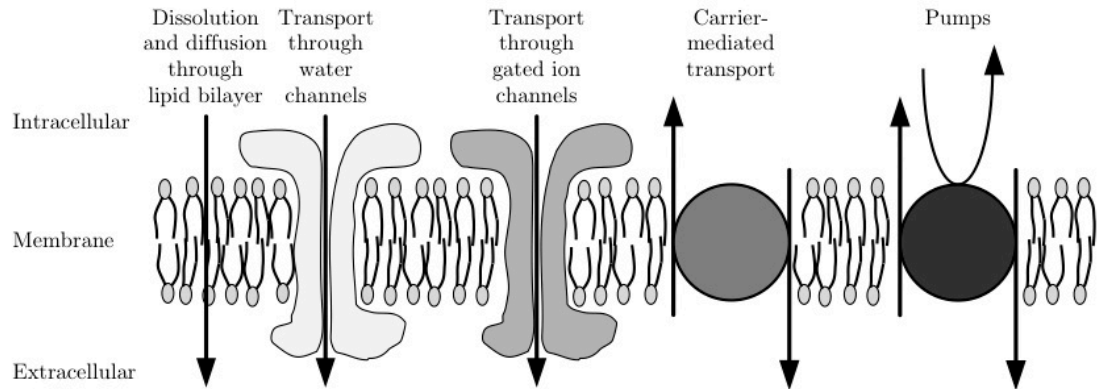
Figure 2.19

$\rightarrow$ Notion of a *semi-permeable membrane*

Controversy
- no question that van't Hoff's law is true
- but why?

semi-permeable: water only
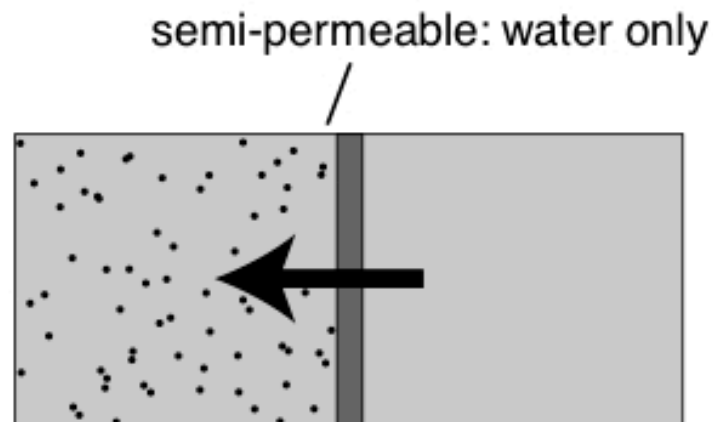
- why should water go TOWARD the solute?
- large osmotic pressure ATTRACTS water!

Hydraulic Pressure

Macroscopic laws of solvent transport: hydraulic case

Darcy's Law: flow through porous medium

hydraulic
permeability
|

$$\Phi_V(x,t) = - \kappa \, \frac{\partial p(x,t)}{\partial x}$$

solvent
flux

hydraulic
pressure
gradient

- analogous to Fick's law for diffusion, Ohm's law for electrical current, Fourier's law for heat flow
- units for solvent flux different from units for solute flux

$$\phi_n \left[\frac{mol}{m^2 s} \right] \qquad \Phi_V \left[\frac{m^3}{m^2 s} = \frac{m}{s} \right] \qquad p \left[Pa = \frac{N}{m^2} \right]$$

Hydraulic Pressure
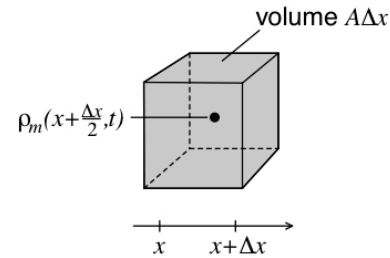
Continuity Equation for Solvent Flow

area A area A

$\Phi_V(x,t)$ →   → $\Phi_V(x+\Delta x,t)$

x $x+\Delta x$
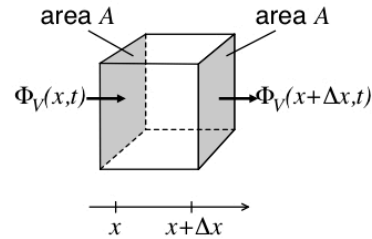
Net mass of solvent entering
through edges during $(t,t+\Delta t)$

volume $A\Delta x$

$\rho_m(x+\frac{\Delta x}{2},t)$

x $x+\Delta x$

Change in mass of solvent
in volume from t to $t+\Delta t$

——— left ———   ———— right ————   — time $t+\Delta t$ —   — time t —

$$\rho_m(x,t+\tfrac{\Delta t}{2})\,\Phi_V(x,t+\tfrac{\Delta t}{2})\,A\,\Delta t - \rho_m(x+\Delta x,t+\tfrac{\Delta t}{2})\Phi_V(x+\Delta x,t+\tfrac{\Delta t}{2})\,A\,\Delta t \;=\; \rho_m(x+\tfrac{\Delta x}{2},t+\Delta t)\,A\,\Delta x - \rho_m(x+\tfrac{\Delta x}{2},t)\,A\,\Delta x$$

↑

equal if solvent is neither created nor destroyed

$$\frac{\rho_m(x,t+\tfrac{\Delta t}{2})\Phi_V(x,t+\tfrac{\Delta t}{2}) - \rho_m(x+\Delta x,t+\tfrac{\Delta t}{2})\Phi_V(x+\Delta x,t+\tfrac{\Delta t}{2})}{\Delta x} \;=\; \frac{\rho_m(x+\tfrac{\Delta x}{2},t+\Delta t) - \rho_m(x+\tfrac{\Delta x}{2},t)}{\Delta t}$$
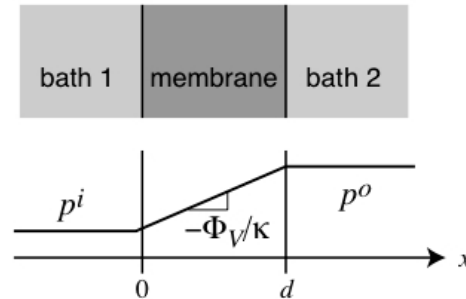
Take limit as $\Delta x \rightarrow 0$ and $\Delta t \rightarrow 0$

$$-\frac{\partial}{\partial x}\Big[\rho_m(x,t)\Phi_V(x,t)\Big] \;=\; \frac{\partial \rho_m(x,t)}{\partial t}$$

Hydraulic Pressure
(thin membrane, steady-state)

Water flow through thin membrane
(hydraulic)

$$\frac{p^o(t) - p^i(t)}{d} = -\frac{\Phi_V(t)}{\kappa}$$

$$\Phi_V(t) = \mathcal{L}_V(p^i(t) - p^o(t)) \ ; \ \ \mathcal{L}_V = \kappa/d$$

hydraulic conductivity

analogous to Fick's law for membranes

$$\phi_n(t) = P_n(c_n^i(t) - c_n^o(t)) \ ; \ \ P_n = \frac{D_n k_n}{d}$$

Hydraulic + Osmotic Pressure (thin membrane)

Side 1 Membrane Side 2

C_Σ^1 $C_\Sigma(x)$ C_Σ^2

p_1 $p(x)$ p_2

Φ_V

0 d x

$$p_1 - p_2 = \pi_1 - \pi_2 = RT(C_\Sigma^1 - C_\Sigma^2)$$

$$\Phi_V = -\kappa \frac{\partial(p - \pi)}{\partial x}$$

(modified version of Darcy's Law)

$$\frac{\partial(\rho_m \Phi_V)}{\partial x} = -\frac{\partial \rho_m}{\partial t}$$
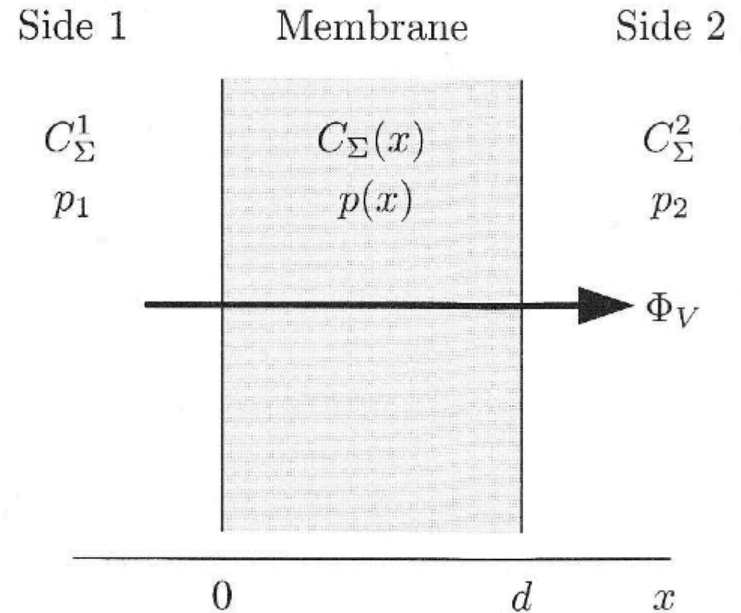
Hydraulic + Osmotic Pressure (thin membrane)

Assume solvent density is independent of t (i.e., the solvent is incompressible)

$$\frac{\partial(\rho_m \Phi_V)}{\partial x} = 0$$

$$\Phi_V = -\kappa \frac{\partial(p - \pi)}{\partial x} \qquad = \text{const.}$$

Since Φ_V is constant, $p - \pi$ must be a linear function of x in the steady state, so that

$$(p(x) - p(x_o)) - (\pi(x) - \pi(x_o)) = -\frac{\Phi_V}{\kappa}(x - x_o), \qquad (4.13)$$

Hydraulic + Osmotic Pressure (membrane)

Water flow through semipermeable membrane
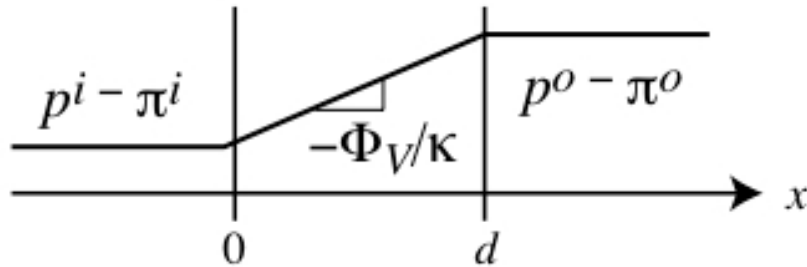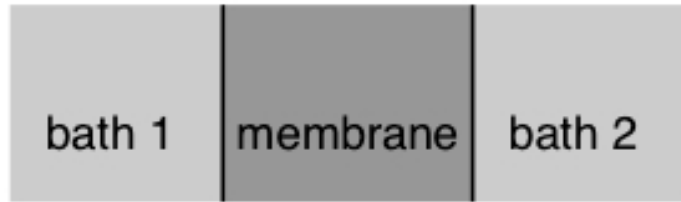
$$\Phi_V = \mathcal{L}_V\left[\left(p^i - \pi^i\right) - \left(p^o - \pi^o\right)\right]$$

Hydraulic + Osmotic Pressure (membrane)

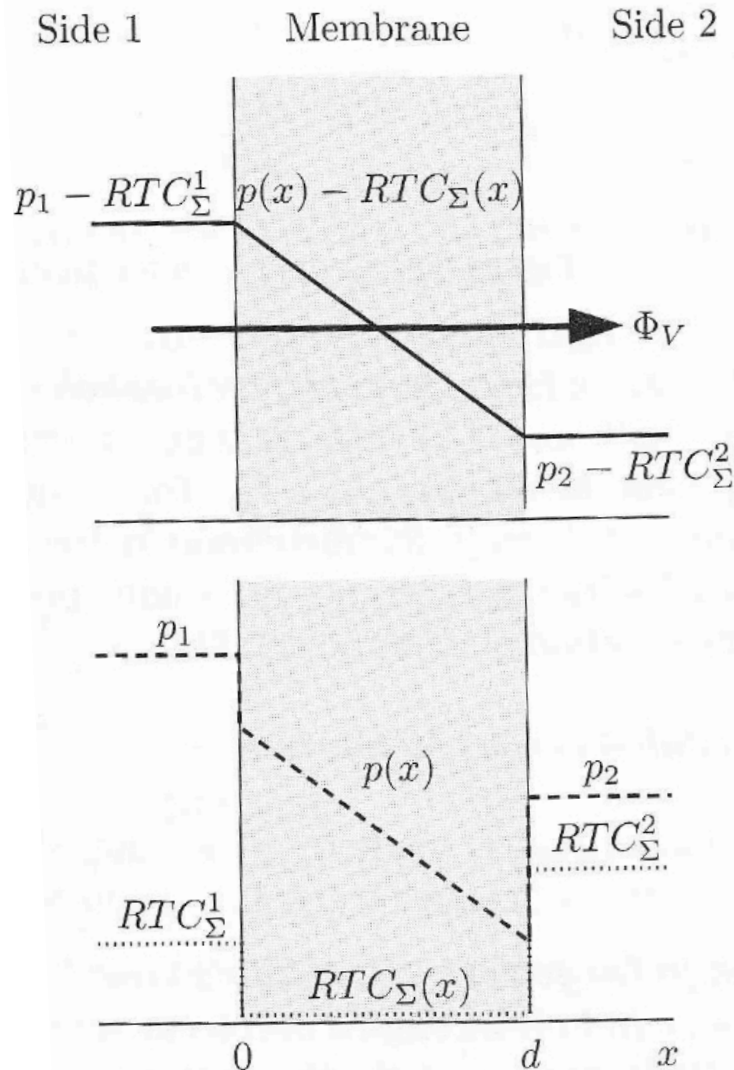**Figure 4.9** Sketch of osmotic and hydraulic pressure through a membrane for steady-state solvent transport. The upper panel shows a plot of the difference of hydraulic and osmotic pressure. This difference is continuous at the interface between the membrane and each bath. The lower panel shows the hydraulic (dashed line) and osmotic pressures (dotted line) individually. Both are discontinuous at each membrane-bath interface.

Exercise

The following figure shows two experiments. In each experiment, two fluid-filled compartments are separated by a semi-permeable membrane that is permeable to water but not to the solute.
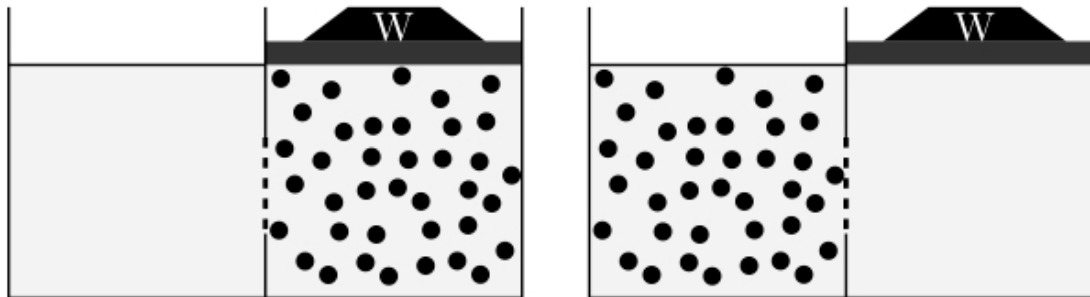
One of the compartments contains a weight W on a piston, the other does not. The only difference between the two experiments is the location of the solute particles indicated by dots in the fluid. Which of the two experiments could be in osmotic equilibrium? Explain.

ANS: Equilibrium is possible for the case on the left, but not the one on the right

Exercise

A membrane separates two solutions subjected to hydraulic pressures p_1 and p_2, as shown in the following figure
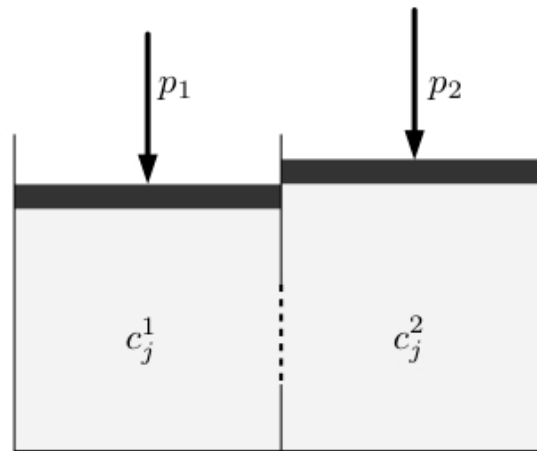
→ The membrane is permeable to water **and** solute j which is the only solute in the solutions. Is thermodynamic equilibrium possible for $c_j{}^1$ not equal to $c_j{}^2$ for some choice of $p_1 - p_2$? Explain.

ANS: Equilibrium is not possible since diffusive equilibrium requires the two concentrations to be equal

Kinetic Volume Changes in Cell Volume

$$\Phi_V = \mathcal{L}_V \left[\left(p^i - \pi^i \right) - \left(p^o - \pi^o \right) \right]$$

assume no hydraulic pressure

Primary osmotic responses of cells

volume $\mathcal{V}_C(t)$
surface area $A(t)$

$$\mathcal{V}_C(t) = \mathcal{V}^i(t) + \mathcal{V}'_C(t)$$

volume $\mathcal{V}'_C(t)$
(not water)

C_Σ^i

C_Σ^o

$\Phi_V(t)$
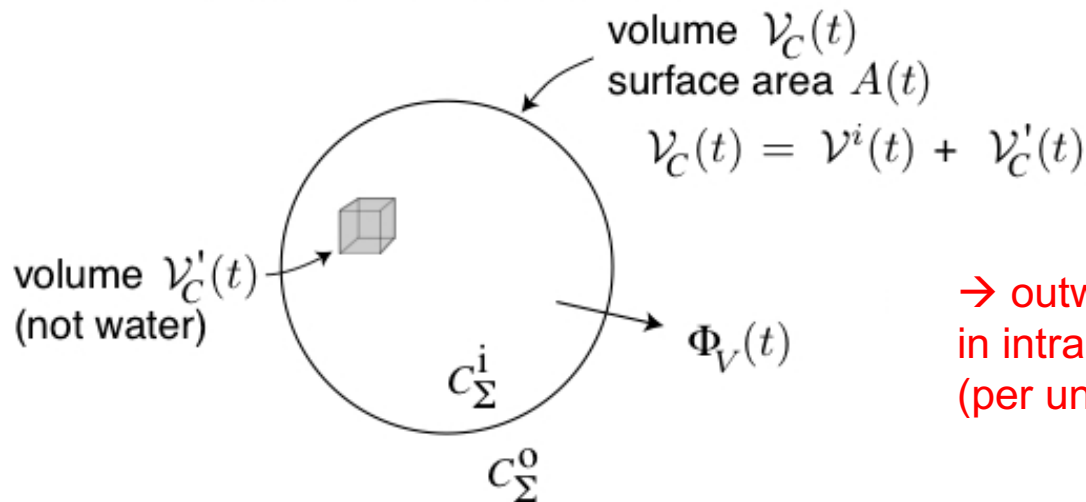
→ outward flux must equal reduction
in intracellular water volume
(per unit area of membrane)

$$\frac{d\mathcal{V}^i(t)}{dt} = - A(t) RT \mathcal{L}_V \left(C_\Sigma^o(t) - C_\Sigma^i(t) \right)$$

Primary osmotic responses of cells

volume $\mathcal{V}_C(t)$
surface area $A(t)$

$$\mathcal{V}_C(t) = \mathcal{V}^i(t) + \mathcal{V}'_C(t)$$
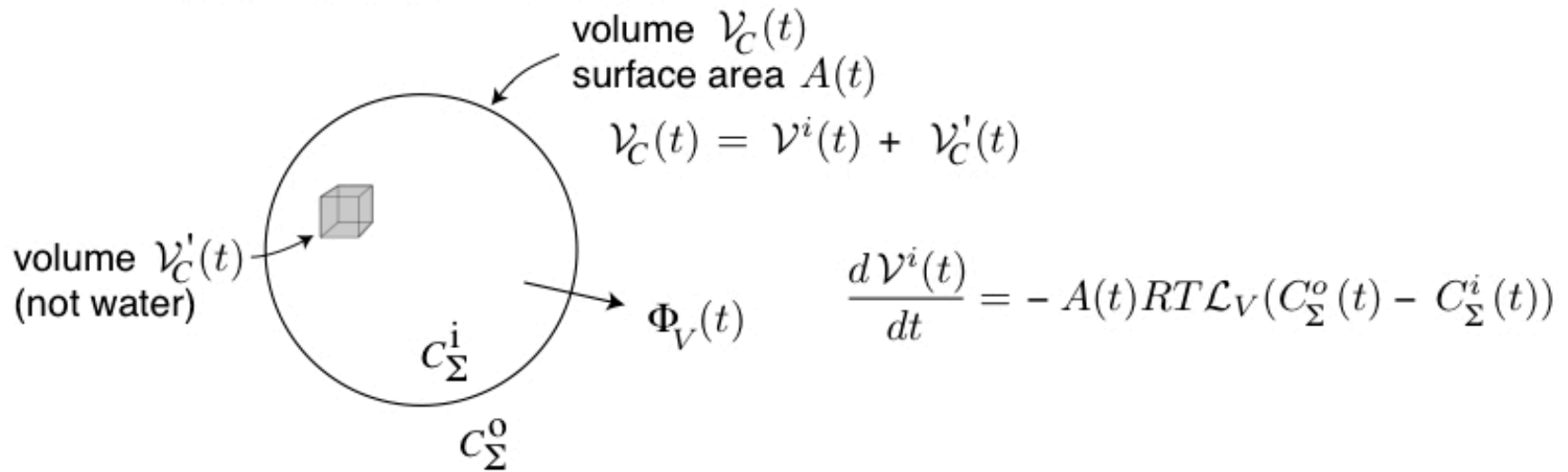
volume $\mathcal{V}'_C(t)$
(not water)

$$\Phi_V(t) \qquad \frac{d\mathcal{V}^i(t)}{dt} = -A(t)RT\mathcal{L}_V(C^o_\Sigma(t) - C^i_\Sigma(t))$$

C^i_Σ

C^o_Σ

Equilibrium Solution

$$v_c(\infty) = v_c' + \frac{N^i_\Sigma}{C^o_\Sigma} \qquad \rightarrow \qquad \text{perfect osmometer}$$

Arbacia eggs

Cell volume (μm^3) vs $C^{on}_\Sigma / C^o_\Sigma$
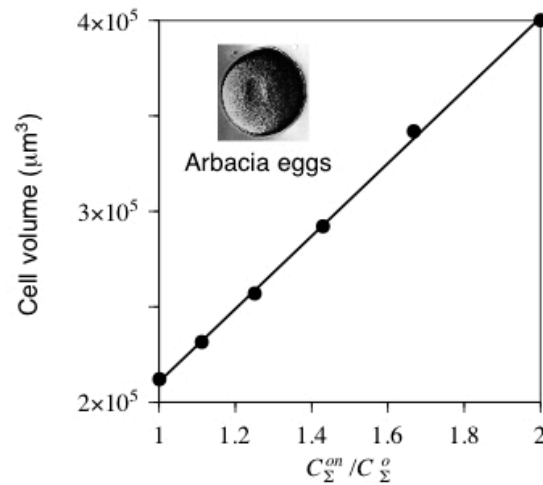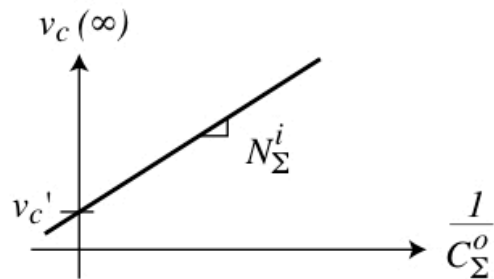
→ Cells can actually behave in this way!

Osmotic Response Dynamics: Egg Cell

volume $\mathcal{V}^i(t) = \frac{4}{3}\pi r^3(t) - \mathcal{V}'_C(t)$

surface area $A(t) = 4\pi r^2(t)$

$$\mathcal{V}_C(t) = \mathcal{V}^i(t) + \mathcal{V}'_C(t)$$

volume $\mathcal{V}'_C(t)$
(not water)

C^i_Σ

C^o_Σ

$\Phi_V(t)$
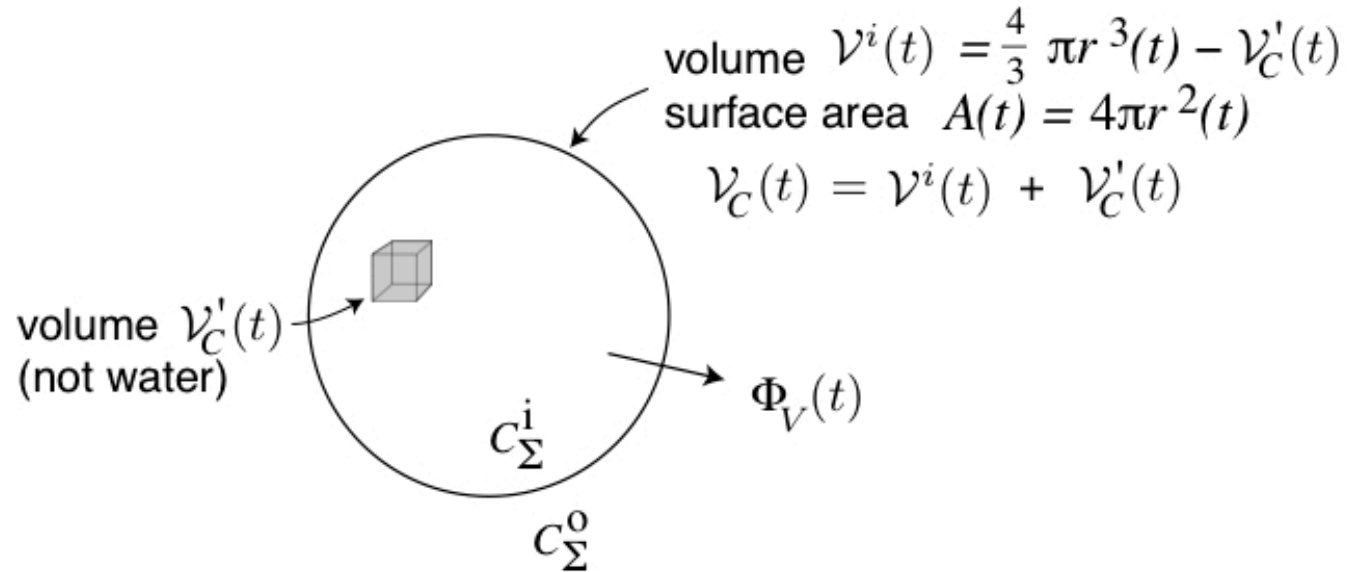
$$\frac{d\mathcal{V}^i(t)}{dt} = 4\pi r^2(t)\,\frac{dr(t)}{dt}$$

$$= 4\pi r^2(t)\,RT\mathcal{L}_V\left[\ \frac{N^i_\Sigma}{\frac{4}{3}\pi r^3(t) - \mathcal{V}'_C}\ -\ C^o_\Sigma(t)\ \right]$$

Osmotic Response Dynamics: RBC

volume $\mathcal{V}_C(t)$
surface area A_o **constant**

$$\mathcal{V}_C(t) = \mathcal{V}^i(t) + \mathcal{V}_C'(t)$$

$\Phi_V(t)$

volume $\mathcal{V}_C'(t)$
(not water)

C_Σ^i

C_Σ^o
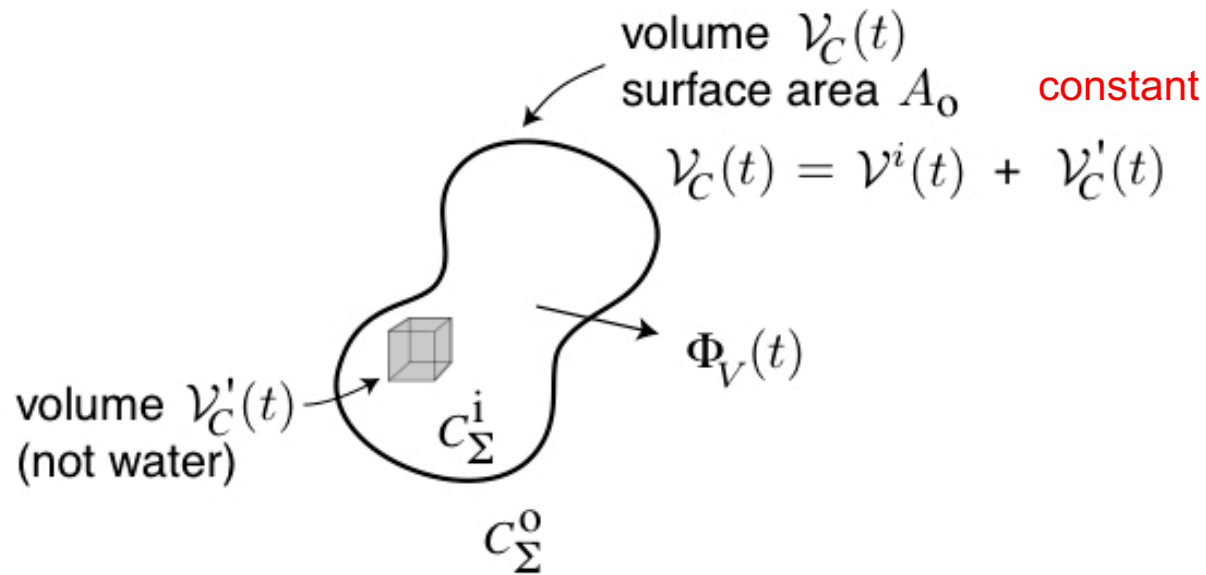
$$\frac{d\mathcal{V}^i(t)}{dt} = A_o\ RT\mathcal{L}_V\left(\frac{N_\Sigma^i}{\mathcal{V}^i(t)} - C_\Sigma^o(t)\right)$$

Primary osmotic responses of cells: Dynamics
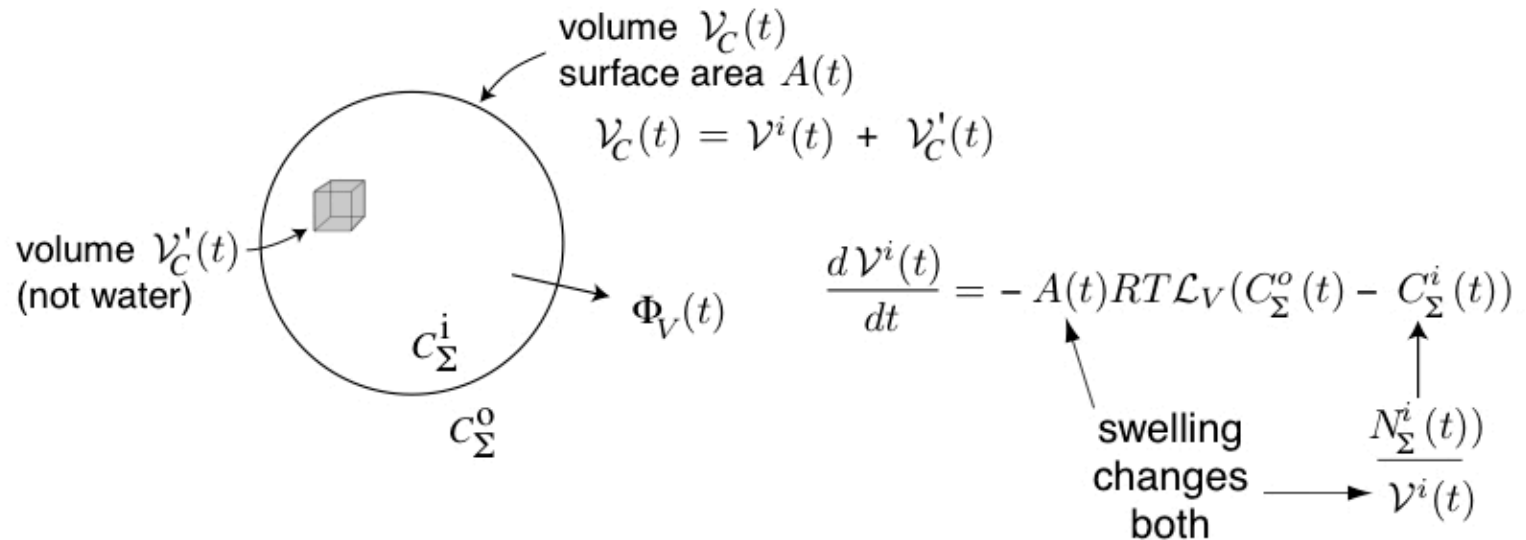
volume $\mathcal{V}_C(t)$
surface area $A(t)$

$$\mathcal{V}_C(t) = \mathcal{V}^i(t) + \mathcal{V}_C'(t)$$

volume $\mathcal{V}_C'(t)$
(not water)

C_Σ^i

C_Σ^o

$\Phi_V(t)$

$$\frac{d\mathcal{V}^i(t)}{dt} = -A(t)RT\mathcal{L}_V(C_\Sigma^o(t) - C_\Sigma^i(t))$$

swelling
changes
both

$$\frac{N_\Sigma^i(t))}{\mathcal{V}^i(t)}$$
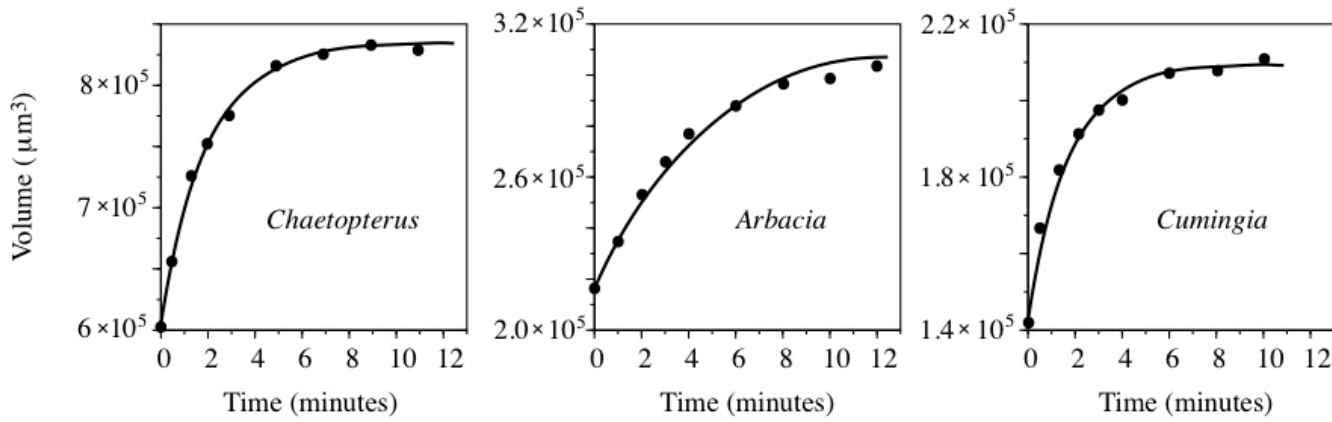
Simple cases

- spherical cell (egg): $A(t) = 4\pi r^2(t);$ $\mathcal{V}^i(t) = \frac{4}{3}\pi r^3(t) - \mathcal{V}_C'(t)$
- cylindrical cell (muscle fiber): $A(t) = 2\pi r(t)L;$ $\mathcal{V}^i(t) = \pi r^2(t)L - \mathcal{V}_C'(t)$
- concave cell (RBC): $A(t) = A_o$

Figure 4.28

Extracellular medium was changed at $t = 0$ from 100% seawater to 60% seawater

Primary osmotic responses of cells: Dynamics

volume $\mathcal{V}_C(t)$
surface area $A(t)$

$\mathcal{V}_C(t) = \mathcal{V}^i(t) + \mathcal{V}'_C(t)$

volume $\mathcal{V}'_C(t)$ (not water)

$\Phi_V(t)$

C^i_Σ

C^o_Σ

$$\frac{d\mathcal{V}^i(t)}{dt} = -A(t)RT\mathcal{L}_V(C^o_\Sigma(t) - C^i_\Sigma(t))$$

swelling changes both

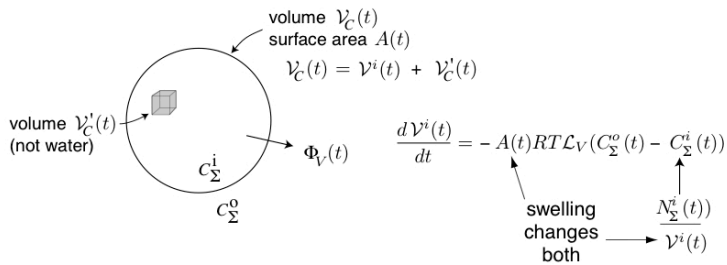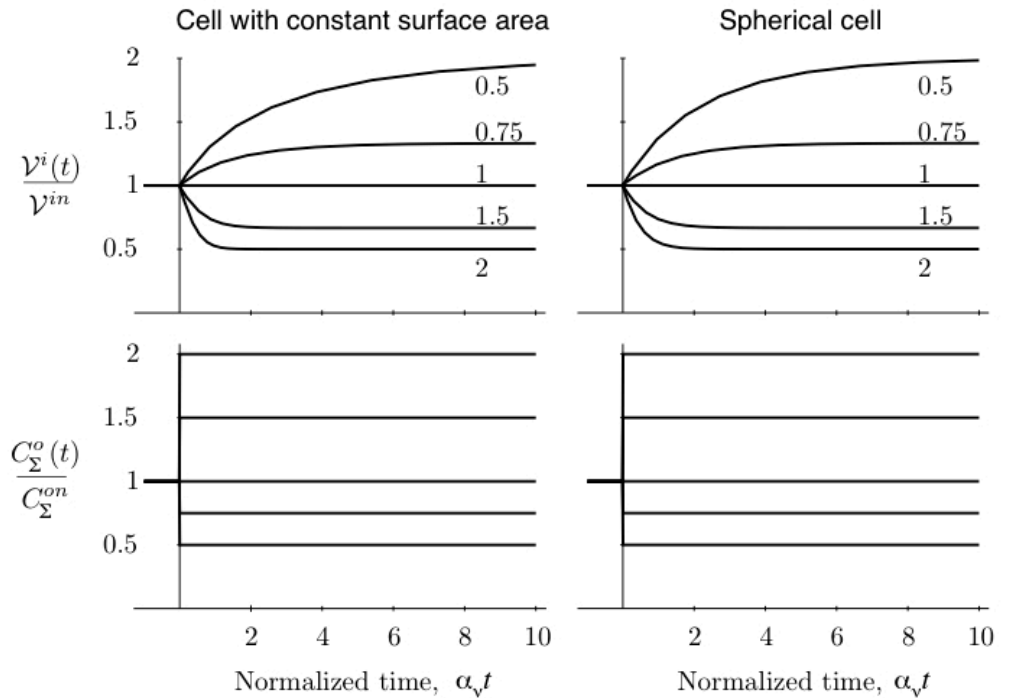$\dfrac{N^i_\Sigma(t))}{\mathcal{V}^i(t)}$

Simple cases

- spherical cell (egg): $A(t) = 4\pi r^2(t);$ $\quad \mathcal{V}^i(t) = \frac{4}{3}\pi r^3(t) - \mathcal{V}'_C(t)$
- cylindrical cell (muscle fiber): $A(t) = 2\pi r(t)L;$ $\quad \mathcal{V}^i(t) = \pi r^2(t)L - \mathcal{V}'_C(t)$
- concave cell (RBC): $A(t) = A_o$

→ Can simulate numerically

Cell with constant surface area

Spherical cell

$\dfrac{\mathcal{V}^i(t)}{\mathcal{V}^{in}}$

$\dfrac{C^o_\Sigma(t)}{C^{'on}_\Sigma}$

Normalized time, $\alpha_v t$

$$\alpha_v = \frac{RT\mathcal{L}_V A^n C^{in}_\Sigma}{\mathcal{V}^{in}}$$

Conclusions from Water Transport Experiments

- Both equilibrium and kinetic responses of simple cells (eggs) consistent with simple model of swelling based on macroscopic laws of osmosis

- However, there are some important issues that don't fit
  - water specialists: $\mathcal{L}_V$ varies by factor of 1000 across cell types (RBC's are very permeant, artificial lipid bilayers are not)
  - Hg compounds: small amounts of Hg $\rightarrow$ large $\Delta\mathcal{L}_V$ (little effect on artificial lipid bilayers)
  - hormonal control: vasopressin
    - antidiuretic hormone, secreted by hypothalamus
    - controls water retention in kidney
    - mechanism is to alter $\mathcal{L}_V$ in water transporting epithelia

Molecular Aspects of Water Channels

Water Channels (Aquaporins)   "the plumbing system for cells"

First sequenced by Preston and Agre (1991)
- CHIP: CHannel-forming Integral Protein
- 807 base pairs in cDNA → 269 amino acids
  (sequence provides 1D structure)
- hydrophobicity: 6 membrane spanning sections
  (20 amino acids organized in alpha helix)
  → suggests 2D structure
- 4 proteins per water channel

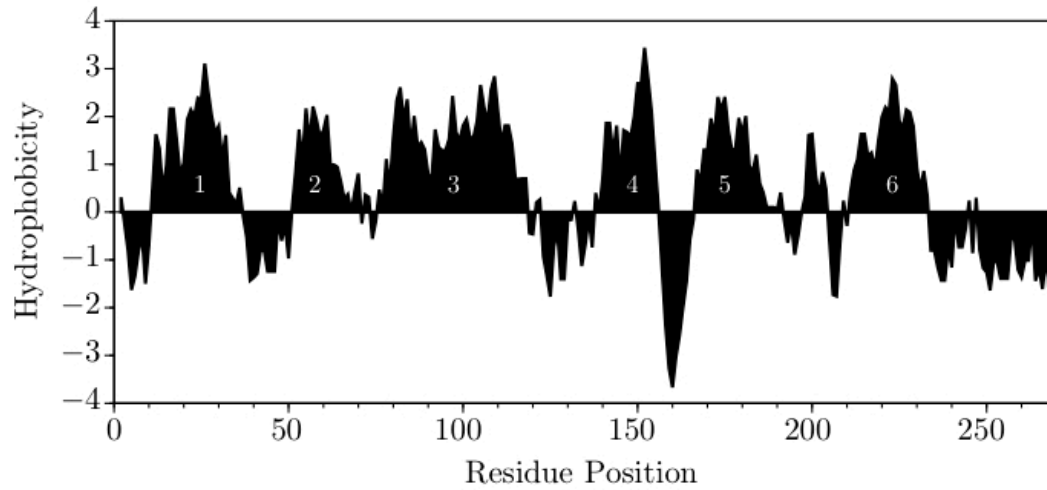→ 2003 Nobel Prize (Agre & MacKinnon)

Aquaporin

Figure 4.31
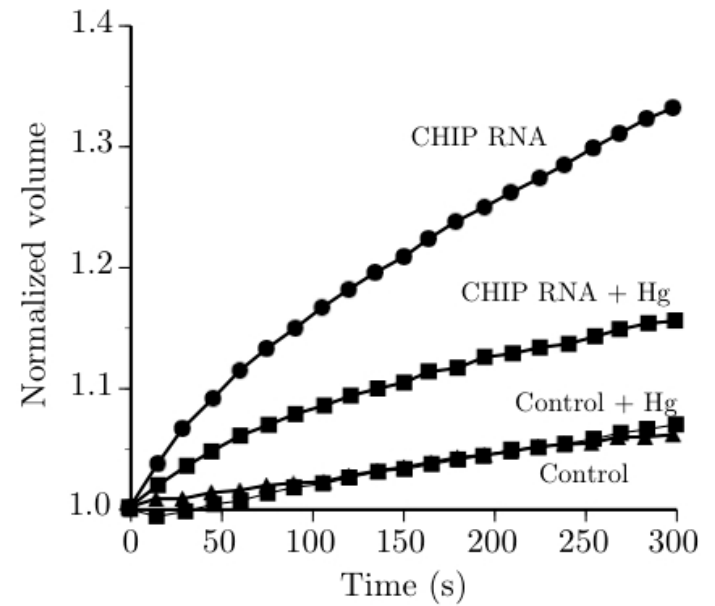
CHIP =
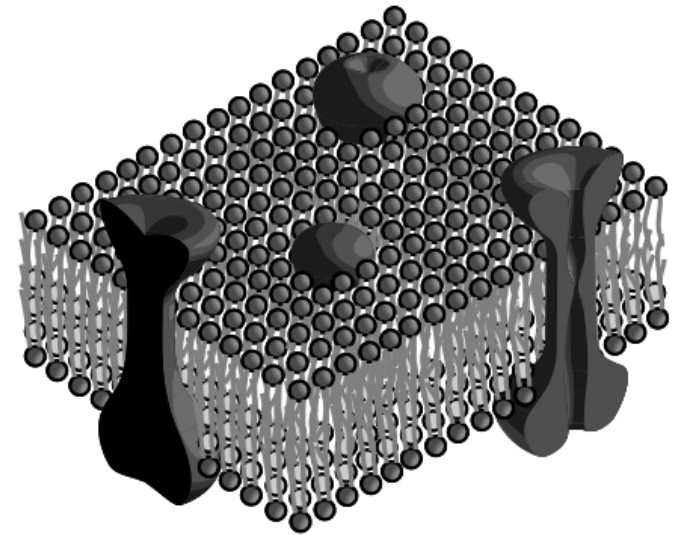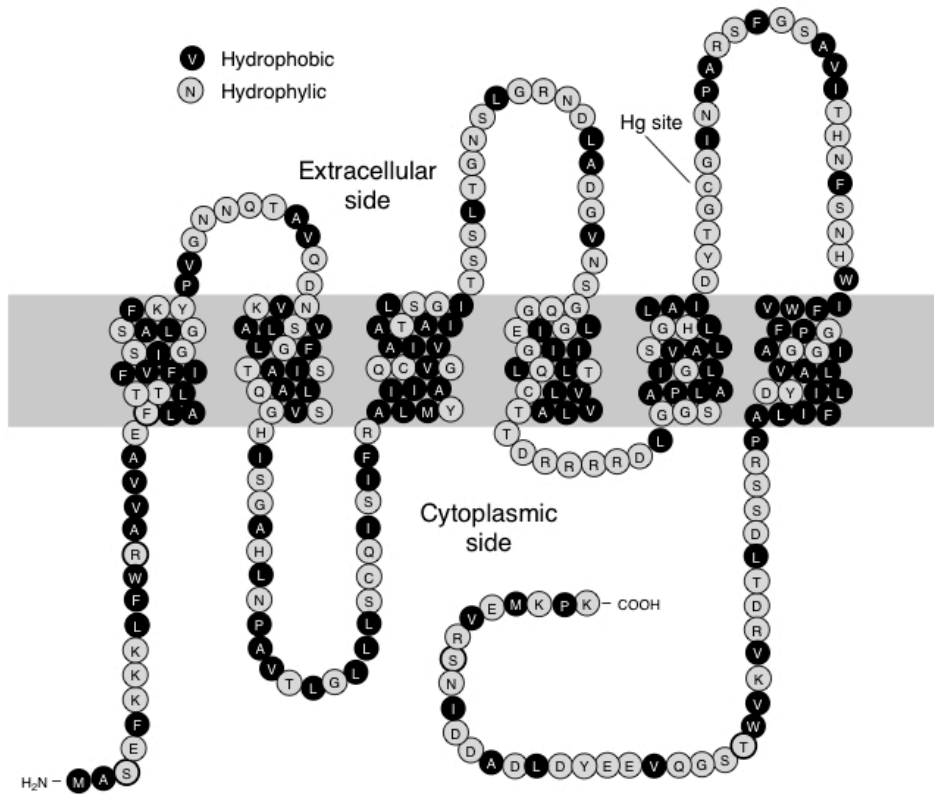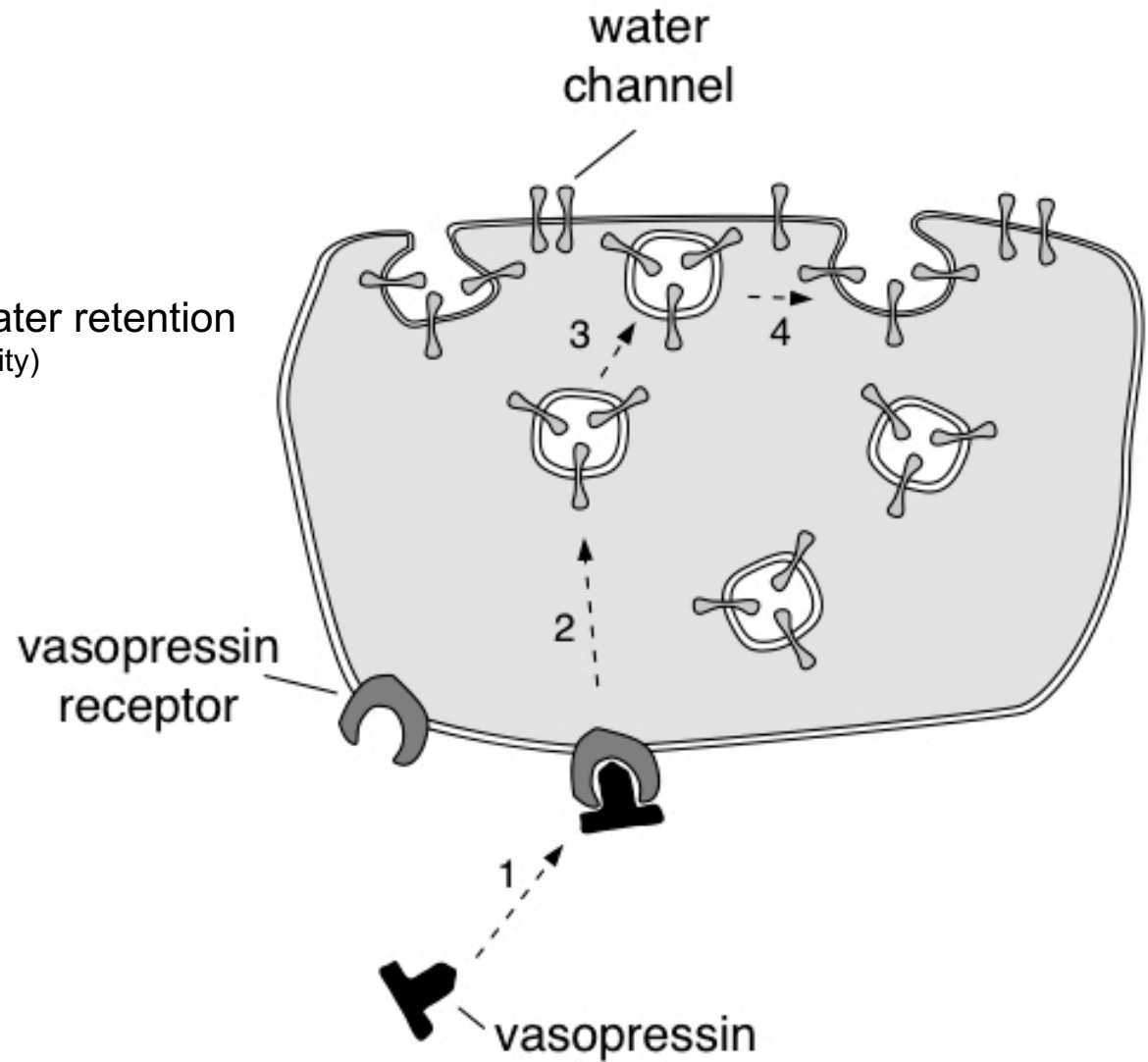channel-forming integral protein

Figure 4.33

Aquaporin

Figure 1.37

Vasopressin

water
channel

→ hormone that regulates water retention
(via affecting the membrane permeability)

3

4

vasopressin
receptor

2

1

vasopressin

Dissolution and diffusion through lipid bilayer · Transport through water channels · Transport through gated ion channels · Carrier-mediated transport · Pumps
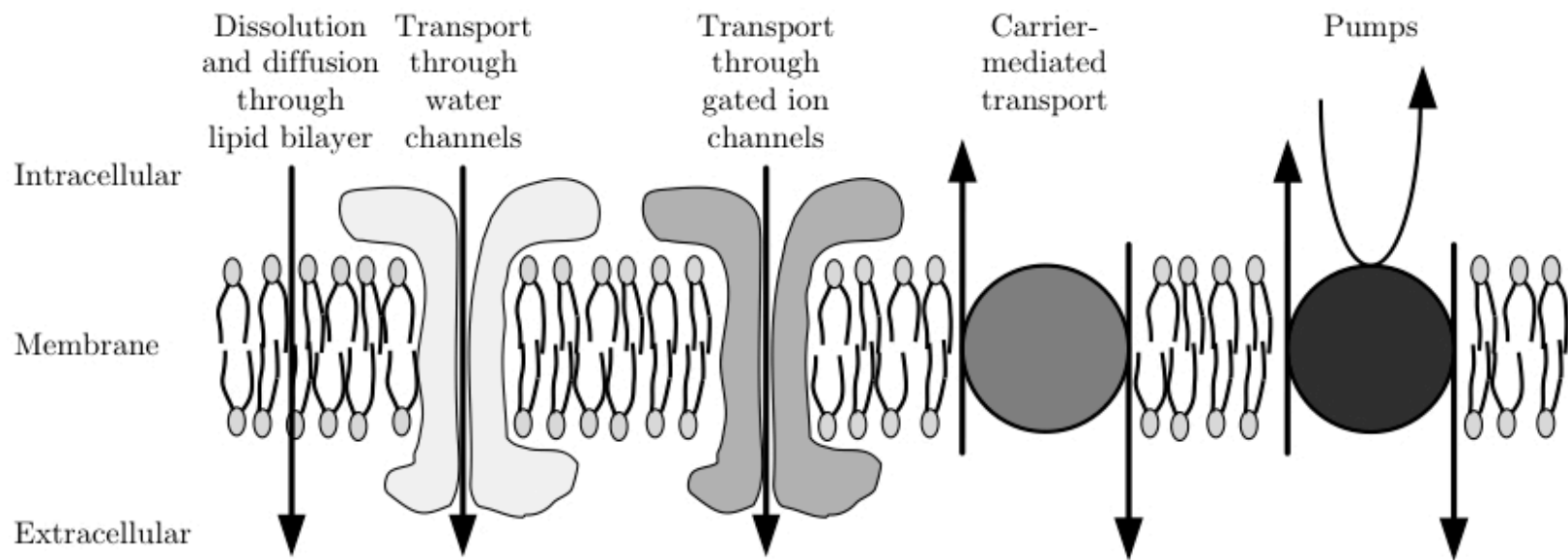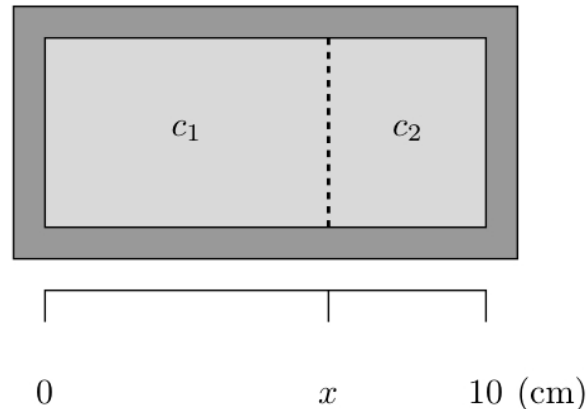
Intracellular

Membrane

Extracellular

Figure 2.19

Exercise

A volume element with constant cross-sectional area A has rigid walls and is divided into two parts by a rigid, semi-permeable membrane that is mounted on frictionless bearings so that the membrane is free to move in the x-direction as shown in the following figure.

The semi-permeable membrane is permeable to water but not to the solutes (glucose or NaCl or $CaCl^2$). At $t = 0$, solute 1 is added to side 1 to give an initial concentration of $c_1(0)$ and solute 2 is added to side 2 to give an initial concentration of $c_2(0)$. Concentrations are specified as the number of milli-moles of glucose or NaCl or $CaCl^2$ per liter of solution. The initial position of the membrane is $x(0)$. For the following values, find the final (equilibrium) values of the membrane position $x(\infty)$, and the concentrations, $c_2(\infty)$ and $c_2(\infty)$:

$$c^1_{glucose}(0) = 0; \ c^2_{glucose}(0) = 10; \ x(0) = 5.$$

$$c^1_{glucose}(0) = 30; \ c^2_{NaCl}(0) = 20; \ x(0) = 4.$$

The semi-permeable membrane is permeable to water but not to the solutes (glucose or NaCl or CaCl²). At $t = 0$, solute 1 is added to side 1 to give an initial concentration of $c_1(0)$ and solute 2 is added to side 2 to give an initial concentration of $c_2(0)$. Concentrations are specified as the number of milli-moles of glucose or NaCl or CaCl² per liter of solution. The initial position of the membrane is $x(0)$. For the following values, find the final (equilibrium) values of the membrane position $x(\infty)$, and the concentrations, $c_1(\infty)$ and $c_2(\infty)$:
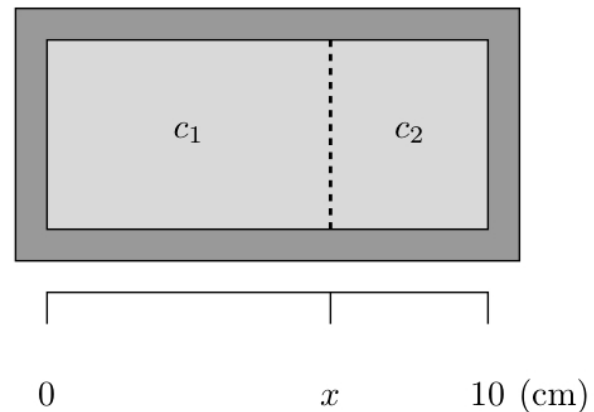
$$c^1_{glucose}(0) = 0; \; c^2_{glucose}(0) = 10; \; x(0) = 5.$$

$$c^1_{glucose}(0) = 30; \; c^2_{NaCl}(0) = 20; \; x(0) = 4.$$

ANS: Keep in mind that the salt will disassociate. So when considering the osmolarity for each case:
➤ first scenario will cause the membrane to move all the way to the left ($c_1(\infty)$ will be undefined and $c_2(\infty)=5$)
➤ second scenario requires for osmotic equilibrium that $c_1(\infty) = 2c_2(\infty)$. Thus $c_1(\infty) = 36$, $c_2(\infty) = 18$, and $x(\infty) = 10/3$.

Exercise

A long and thin cylindrical cell of radius r and length l contains N_Σ^i moles of the impermeant solute S, and is immersed in a bath whose concentration of S is C_Σ^o. The membrane has a hydraulic conductivity $\mathcal{L}_V$. Assume that the membrane of the cell is permeable only to water and that the volume of water in the cell equals the volume of the cell. Also assume that flow of water through the ends of the cylindrical cell is negligible and that, as the cell changes its volume, only the radius changes while the length of the cell is constant. Assume that the hydraulic pressure difference across the membrane is zero.

a) Show that the cell radius r satisfies the differential equation

$$\frac{dr(t)}{dt} + \frac{A}{r^2(t)} = B.$$

b) Find A and B in terms of l, $\mathcal{L}_V$, N_Σ^i, C_Σ^o, R, and T, where R is the molar gas constant and T is absolute temperature.

a. The equation of water volume conservation is

$$-\frac{1}{A(t)}\frac{d\mathcal{V}_c(t)}{dt} = \mathcal{L}_V RT\left(C_\Sigma^o - \frac{N_\Sigma^i}{\mathcal{V}_c(t)}\right).$$

If the surface areas of the circular ends of the cell are ignored, then the surface area of the cell is $A(t) = 2\pi r(t)l$ and its volume is $\mathcal{V}_c(t) = \pi r^2(t)l$. Substitution of these relations into the conservation relation yields

$$
\begin{aligned}
-\frac{1}{2\pi r(t)l}\frac{d(\pi r^2(t)l)}{dt} &= \mathcal{L}_V RT\left(C_\Sigma^o - \frac{N_\Sigma^i}{\pi r^2(t)l}\right),\\
-\frac{dr(t)}{dt} &= \mathcal{L}_V RT\left(C_\Sigma^o - \frac{N_\Sigma^i}{\pi r^2(t)l}\right),\\
\frac{dr(t)}{dt} - \frac{\mathcal{L}_V RT N_\Sigma^i/(\pi l)}{r^2(t)} &= -\mathcal{L}_V RT C_\Sigma^o.
\end{aligned}
$$

The last equation has the form

$$\frac{dr(t)}{dt} + \frac{A}{r^2(t)} = B.$$

b. The constants are

$$
\begin{aligned}
A &= -\frac{\mathcal{L}_V RT N_\Sigma^i}{\pi l},\\
B &= -\mathcal{L}_V RT C_\Sigma^o.
\end{aligned}
$$