Biophysics I (BPHS 4080)

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Website: http://www.yorku.ca/cberge/4080W2018.html

Water flow through semipermeable membrane
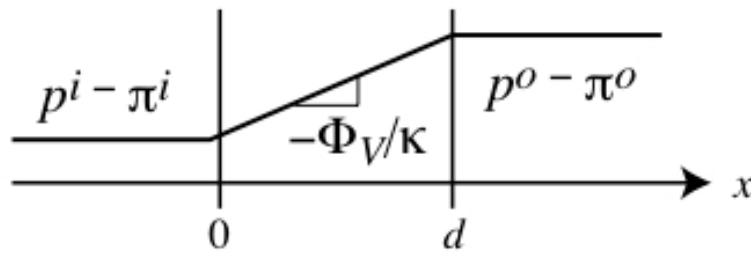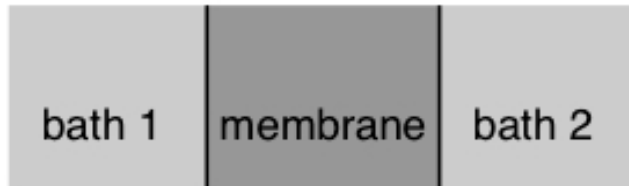
$$\Phi_V = \mathcal{L}_V\Big[\,(\,p^i - \pi^i\,) - (\,p^o - \pi^o\,)\,\Big]$$
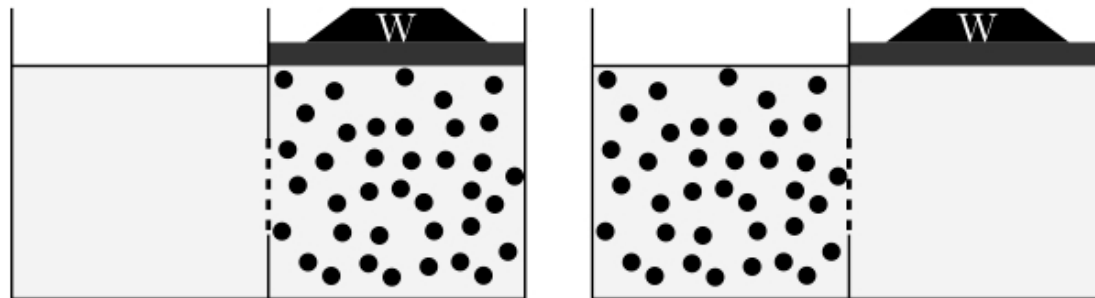
Kinetic Volume Changes in Cell Volume

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

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)

$\Phi_V(t)$

C^i_Σ

C^o_Σ
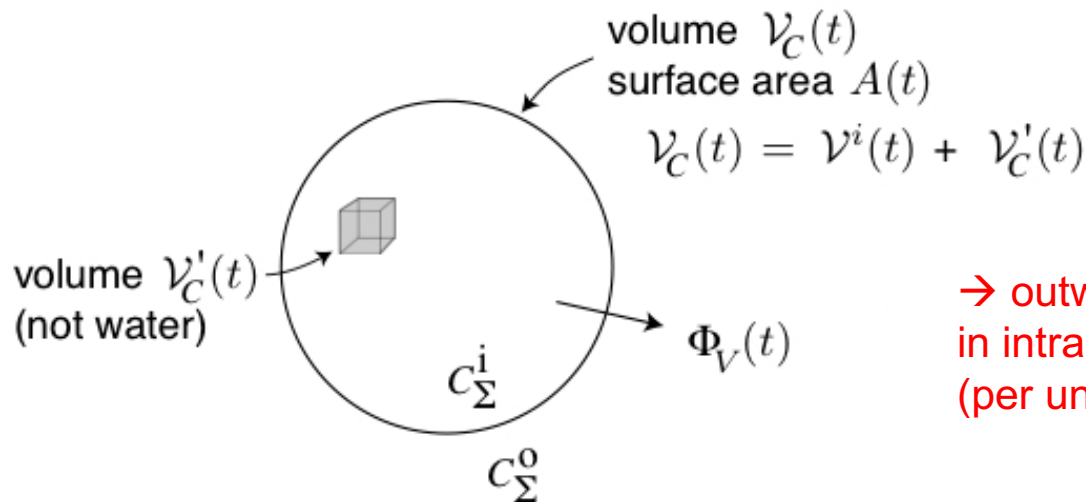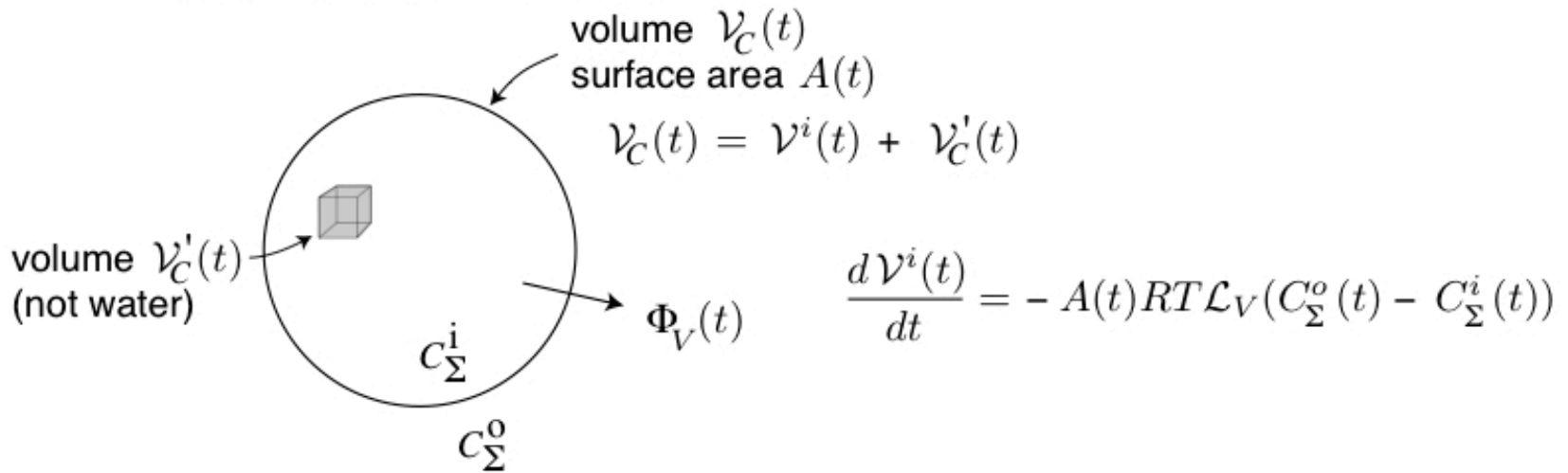
→ outward flux must equal reduction
in intracellular water volume
(per unit area of membrane)

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

Primary osmotic responses of cells

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

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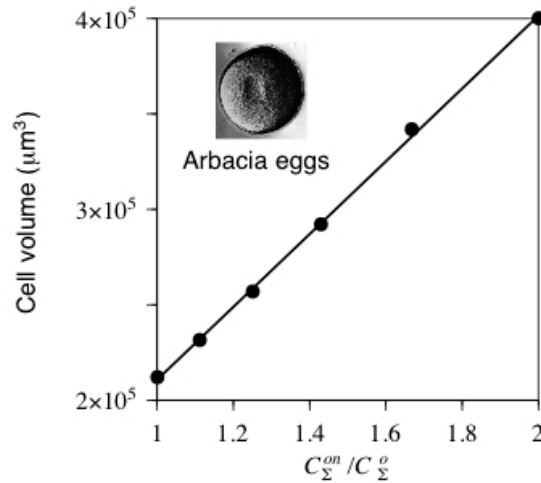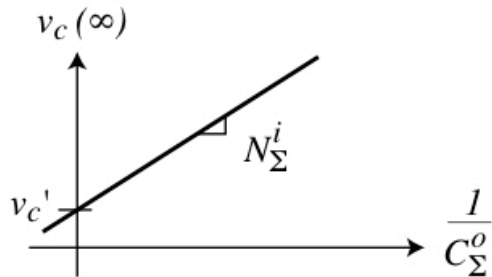
volume $\mathcal{V}_C'(t)$
(not water)

$\Phi_V(t)$

C_Σ^i

C_Σ^o

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

Equilibrium Solution

$$v_c(\infty) = v_c' + \frac{N_\Sigma^i}{C_\Sigma^o} \quad \rightarrow \quad \text{perfect osmometer}$$

$v_c(\infty)$

N_Σ^i

v_c'

$\dfrac{1}{C_\Sigma^o}$

Cell volume (μm^3)

4×10^5

3×10^5

2×10^5

Arbacia eggs

1   1.2   1.4   1.6   1.8   2

C_Σ^{on}/C_Σ^o

→ 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

$\Phi_V(t)$

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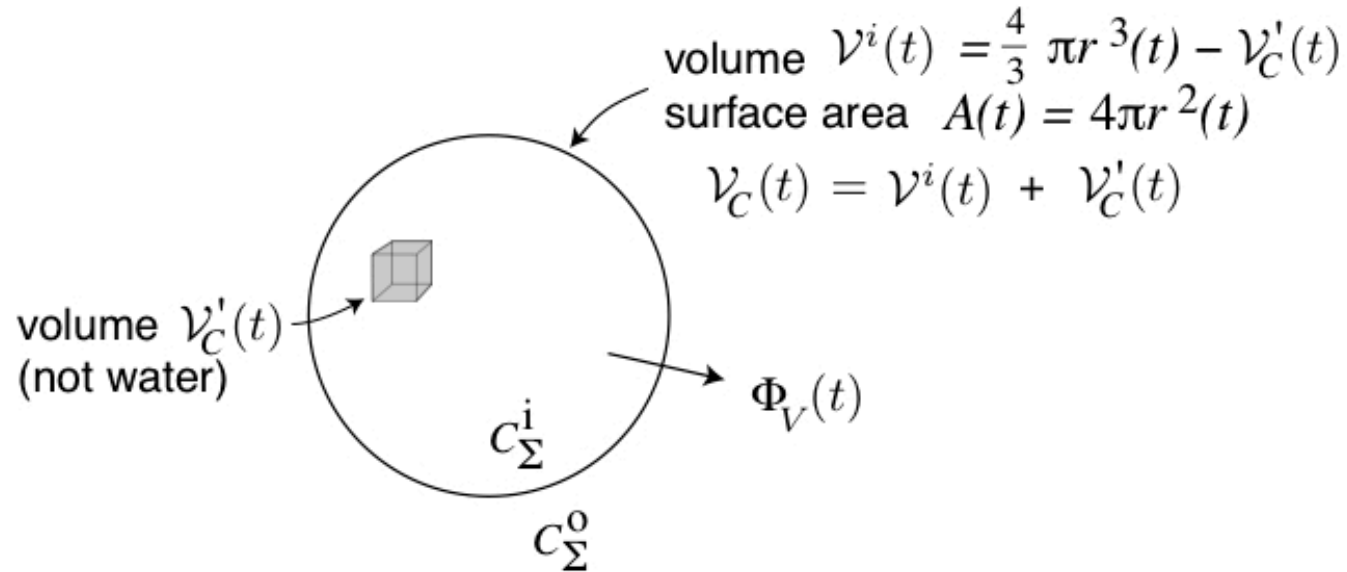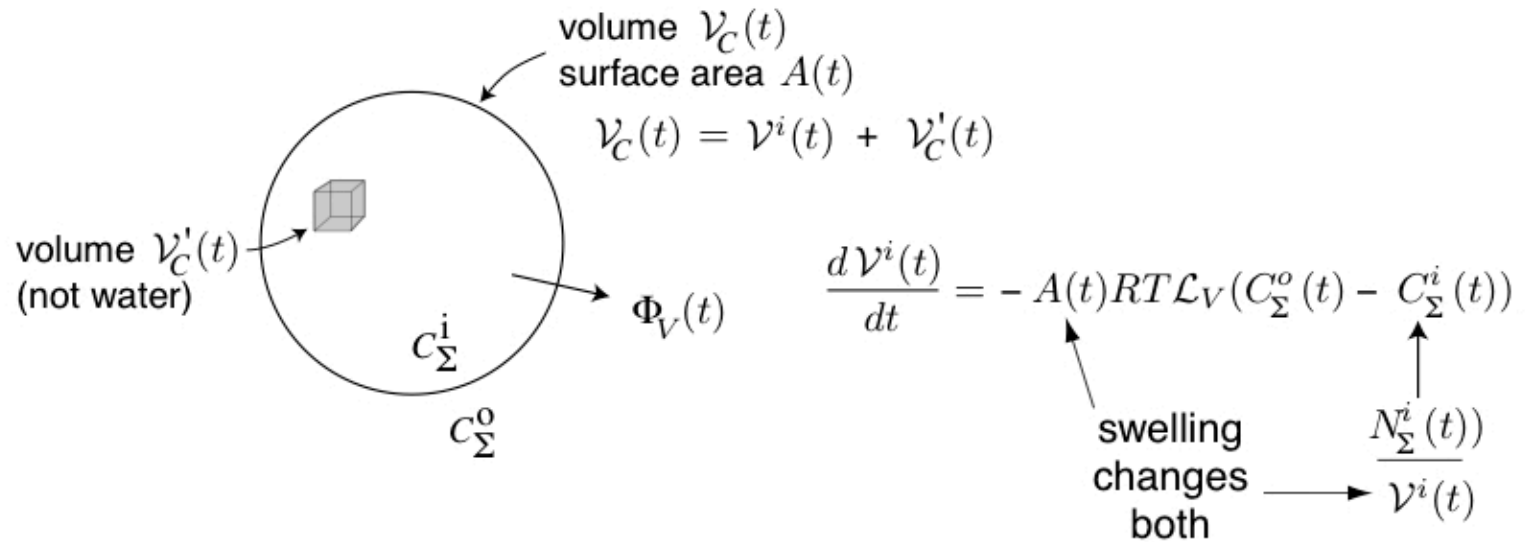
$$\frac{d\mathcal{V}^i(t)}{dt} = 4\pi r^2(t)\, \frac{dr(t)}{dt}$$

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

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)
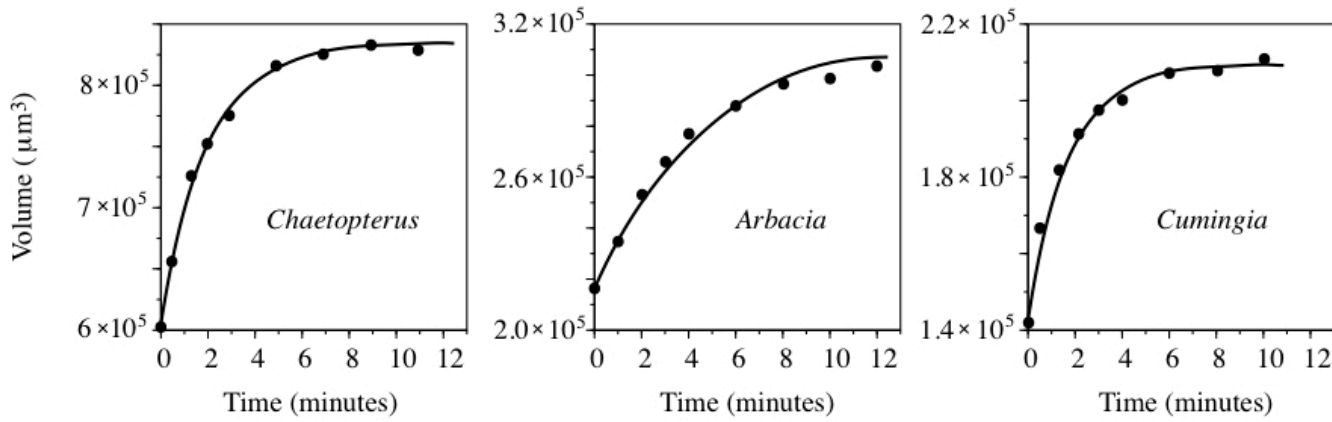
C^i_Σ

C^o_Σ
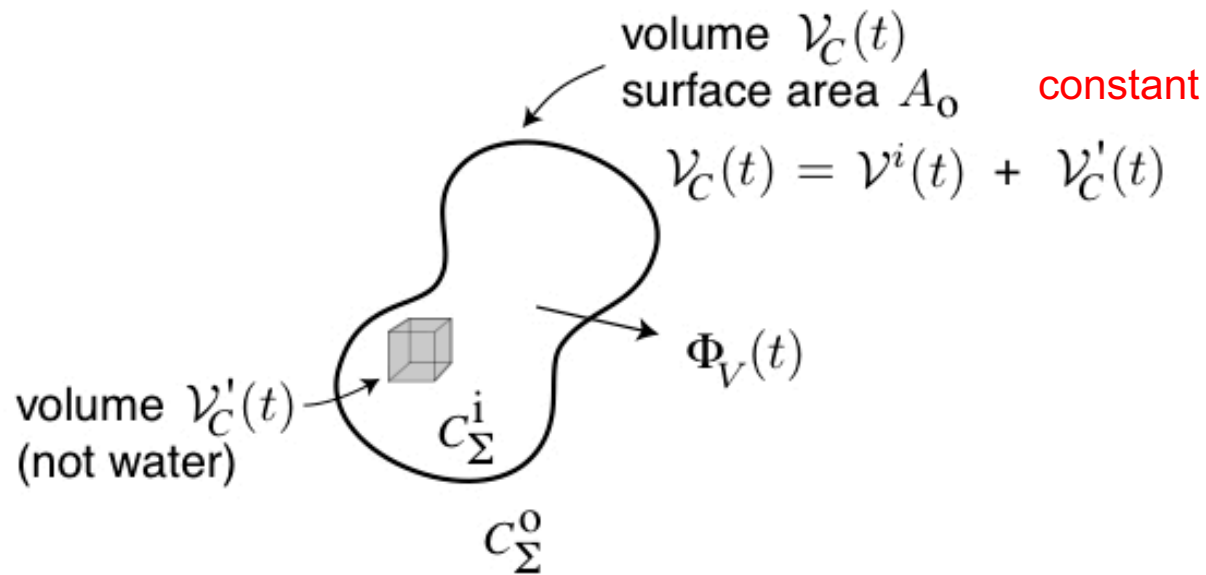
$$\frac{d\mathcal{V}^i(t)}{dt} = A_o \ RT\mathcal{L}_V \left(\frac{N^i_\Sigma}{\mathcal{V}^i(t)} - C^o_\Sigma(t) \right)$$

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

$\Phi_V(t)$

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

swelling
changes
both

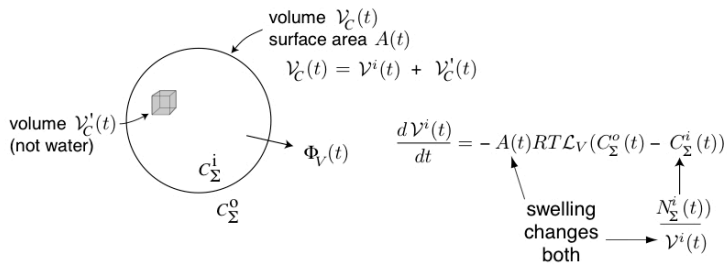$$\frac{N_\Sigma^i(t))}{\mathcal{V}^i(t)}$$

Simple cases

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

Figure 4.28

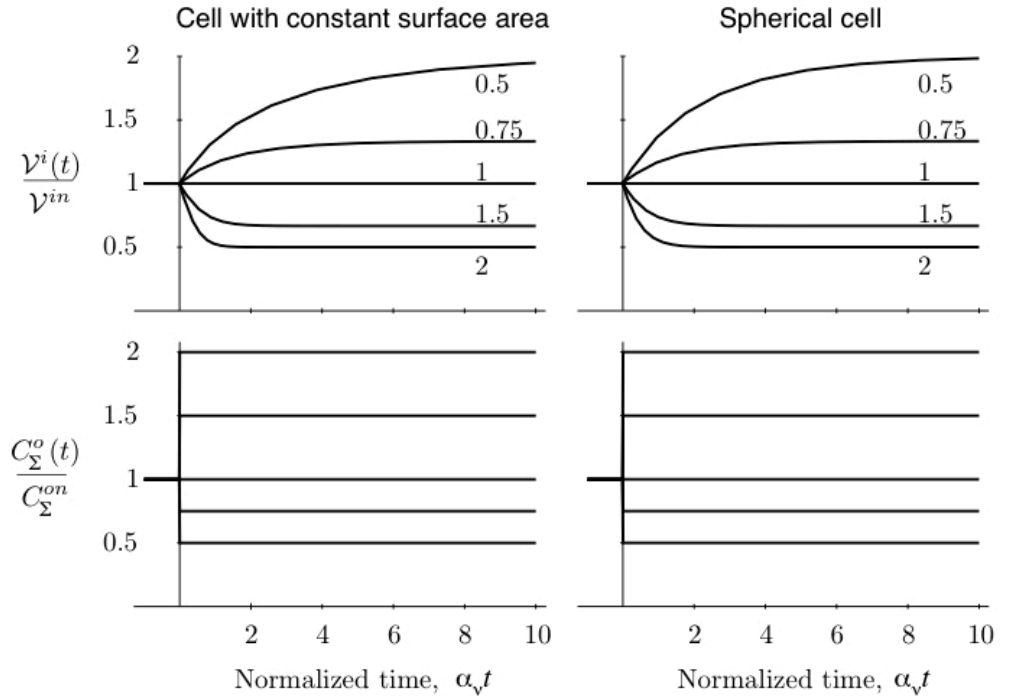Extracellular medium was changed at $t = 0$ from 100% seawater to 60% seawater

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_Σ^i

C_Σ^o

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

swelling changes both

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

Simple cases

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

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

$$\frac{C_\Sigma^o(t)}{C_\Sigma^{on}}$$

Normalized time, $\alpha_v t$ Normalized time, $\alpha_v t$

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

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
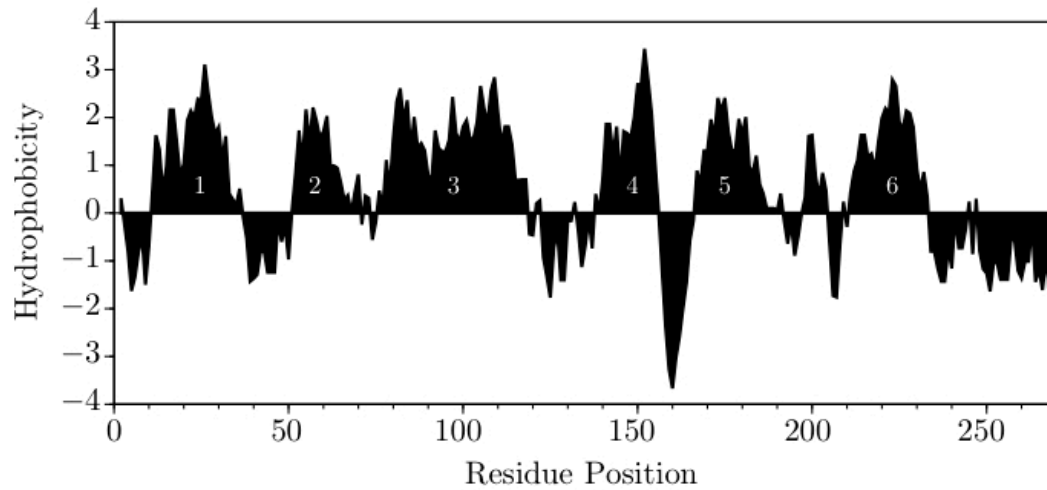
→ 2003 Nobel Prize (Agre & MacKinnon)

Aquaporin

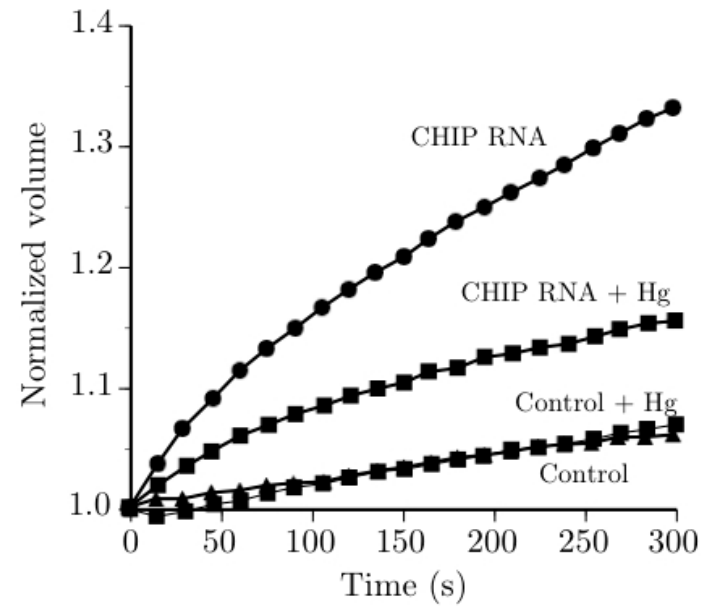

Figure 4.31

CHIP =
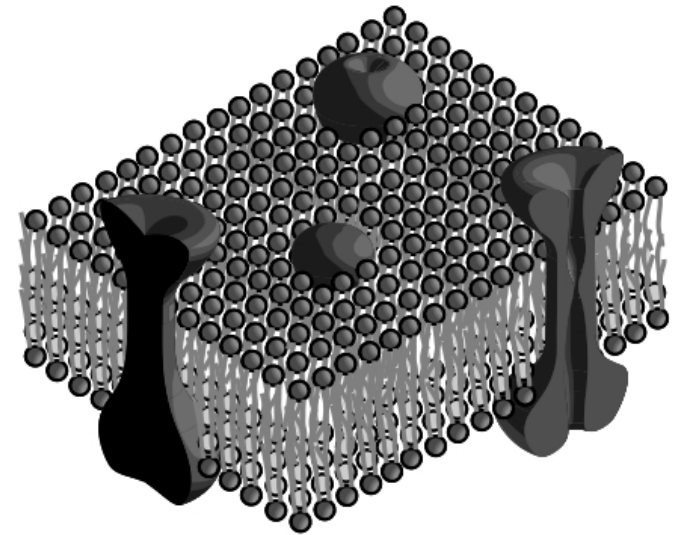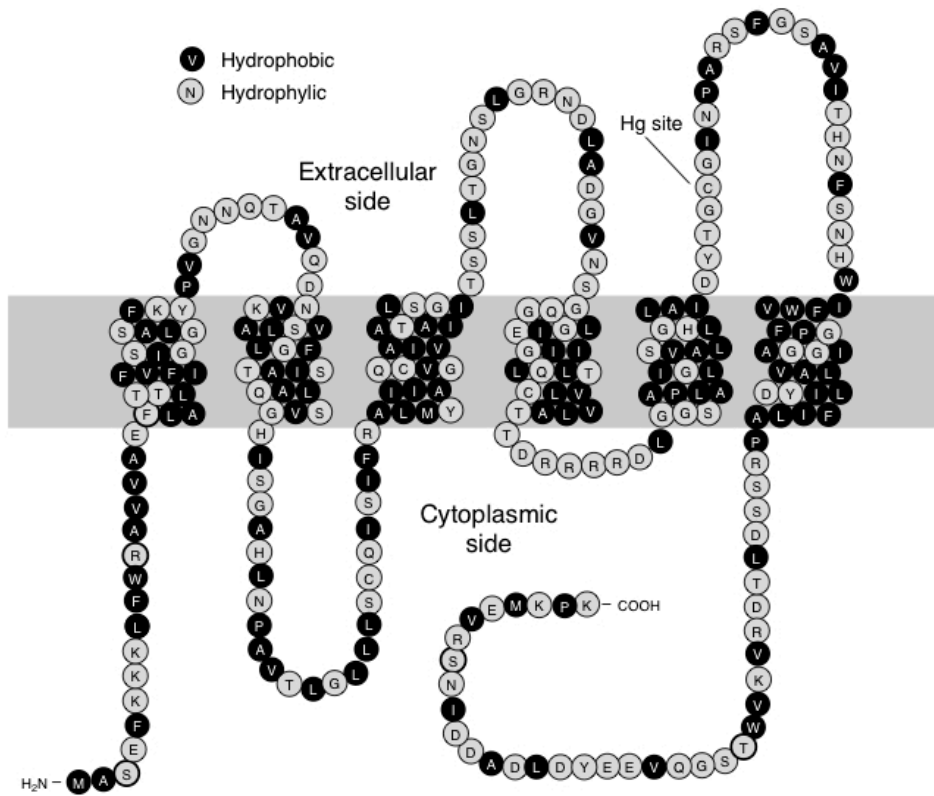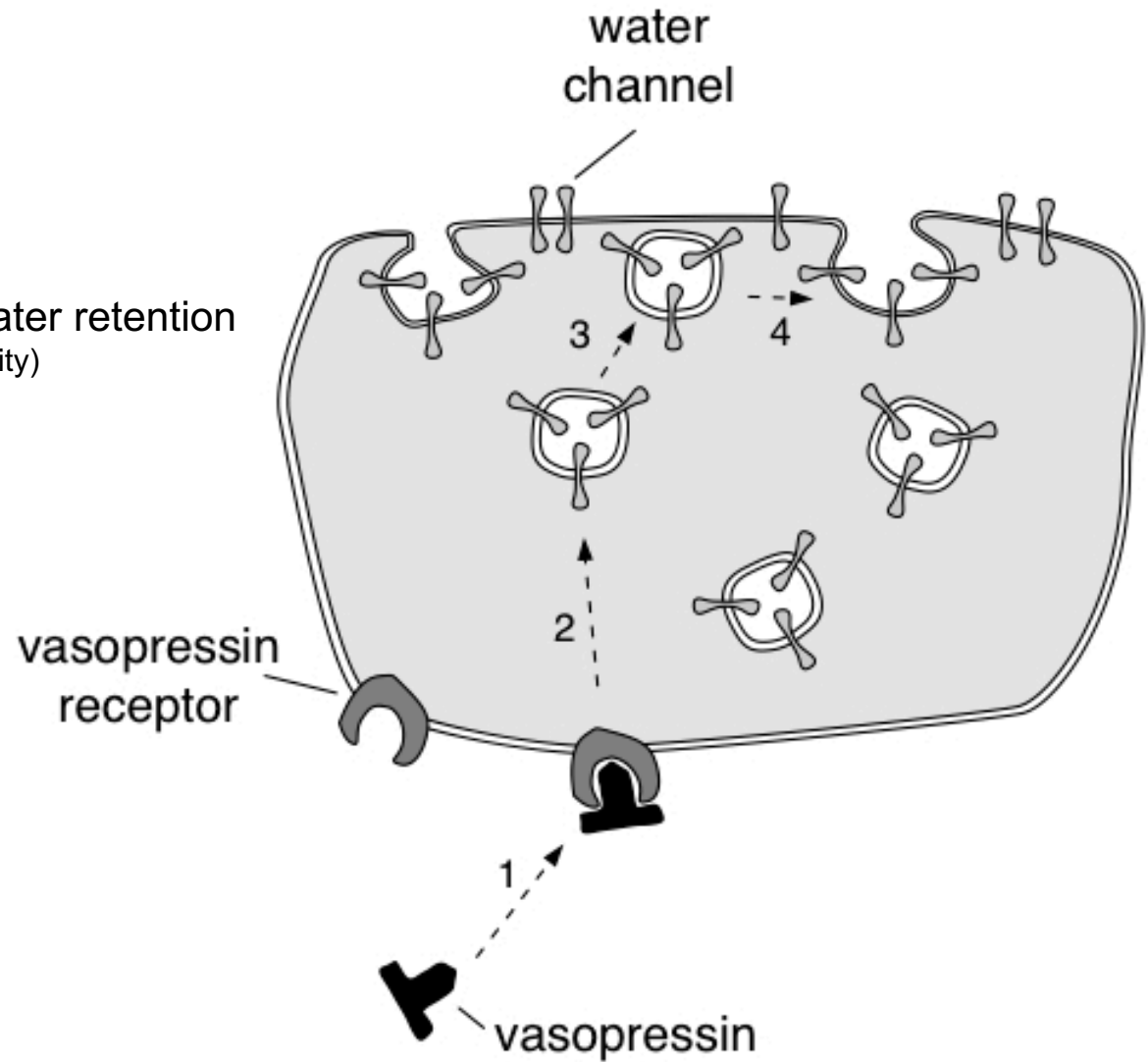channel-forming integral protein

Figure 4.33

Aquaporin

Figure 1.37

Vasopressin

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

water
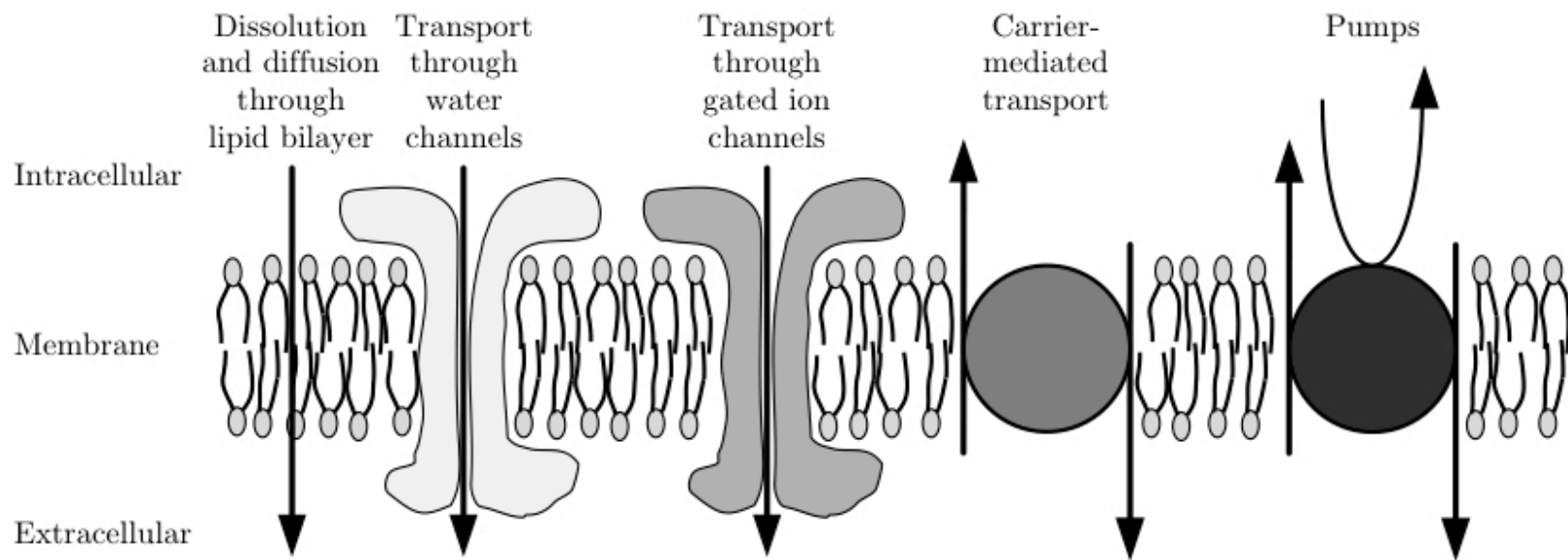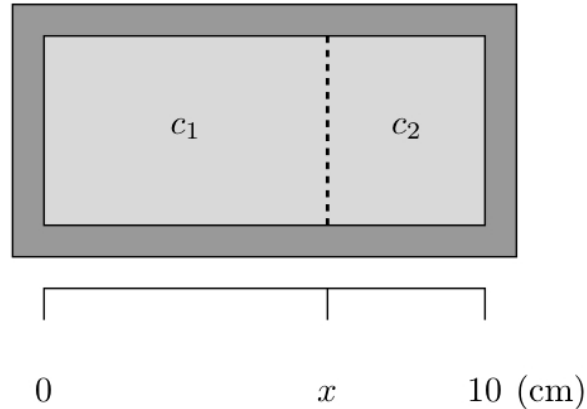channel

3

4

vasopressin
receptor

2

1

vasopressin

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 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, $c_2(\infty)$ and $c_2(\infty)$:

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

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

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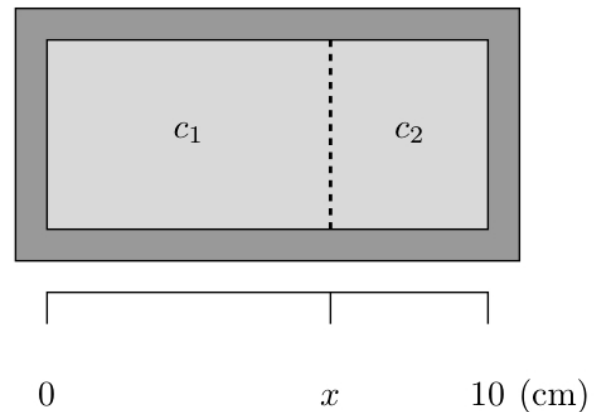
$$c^1_{glucose}(0) = 0;\ c^2_{glucose}(0) = 10;\ x(0) = 5.$$

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

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.

<u>ANS</u>:

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

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

$$-\frac{dr(t)}{dt} = \mathcal{L}_V RT\left(C_\Sigma^o - \frac{N_\Sigma^i}{\pi r^2(t)l}\right),$$

$$\frac{dr(t)}{dt} - \frac{\mathcal{L}_V RT N_\Sigma^i/(\pi l)}{r^2(t)} = -\mathcal{L}_V RT C_\Sigma^o.$$

The last equation has the form

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

b. The constants are

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