

# Biophysics I (BPHS 3090)

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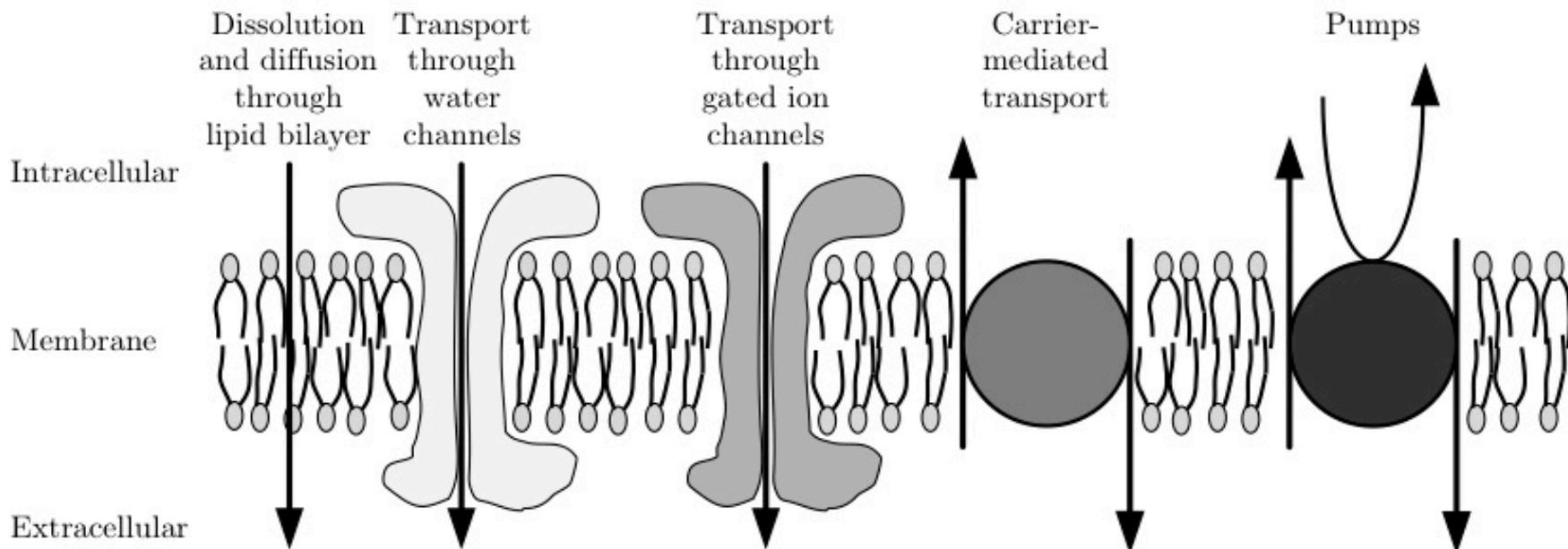
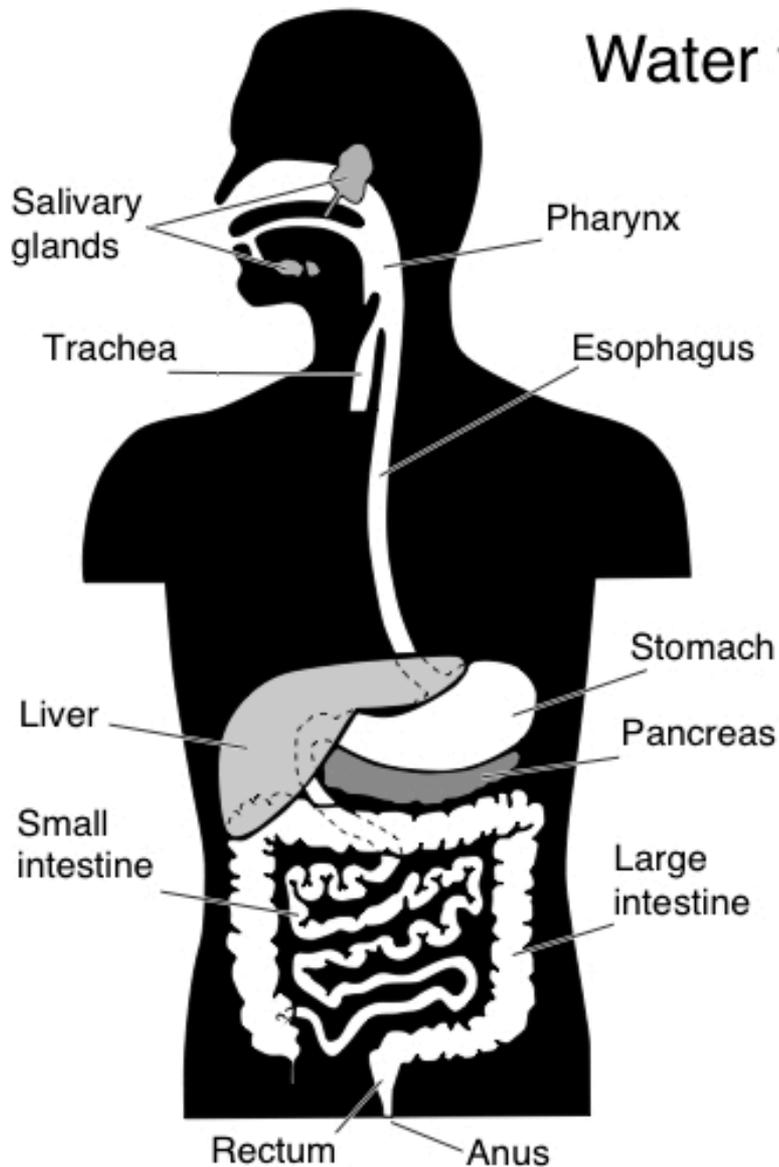


Figure 2.19

# Water transport in digestive system



## Daily traffic

- 800 g food + 1.2 L water ingested daily
  - 1.5 L saliva
  - 2 L gastric secretions
  - 0.5 L bile
  - 1.5 L pancreatic secretions
  - 1.5 L intestinal secretions
- } 7 L digestive fluids

15 pounds of water (10% of body weight)  
secreted and reabsorbed daily

# Low Humidity Stimulates Epidermal DNA Synthesis and Amplifies the Hyperproliferative Response to Barrier Disruption: Implication for Seasonal Exacerbations of Inflammatory Dermatoses

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Although seasonal changes in humidity are thought to exacerbate various skin diseases, whether these flares can be attributed to prolonged exposure to extremes in environmental humidities has not been studied systematically. We recently showed that prolonged exposure to high versus low humidities induced profound changes in epidermal structure and permeability barrier homeostasis. Therefore, we asked here whether comparable extremes in humidity could initiate not only homeostatic, but also potentially pathophysiologic alterations. We showed first that exposure to low humidity increases epidermal DNA synthesis in normal murine epidermis. Moreover, exposure to a low humidity for 48 h further amplifies the DNA synthetic response to barrier disruption, resulting in marked epidermal hyperplasia. Additionally, exposure to a dry environment for 48 h prior to barrier disruption results in dermal mast cell hypertrophy, degranulation, as well as histologic evidence of inflam-

mation. To demonstrate the role of changes in external moisture on these phenomena, we applied either an occlusive, water-impermeable plastic membrane, Petrolatum, or a nonocclusive humectant, both to non-perturbed and to perturbed skin. All three forms of treatment prevented the epidermal hyperplasia and dermal mast cell hypertrophy and degranulation induced by exposure to low humidity. These studies indicate that (i) exposure to changes in environmental humidity alone induces increased keratinocyte proliferation and markers of inflammation, and (ii) that these changes are attributable to changes in stratum corneum moisture content. Finally, these studies provide evidence that changes in environmental humidity contribute to the seasonal exacerbations/amelioration of cutaneous disorders, such as atopic dermatitis and psoriasis, diseases which are characterized by a defective barrier, epidermal hyperplasia, and inflammation. **Key words:** dry environment/humectant/mast cell occlusion. *J Invest Dermatol* 111:873-878, 1998

**T**he main function of the skin is to generate the epidermal permeability barrier at the level of the stratum corneum (SC), which allows life in a terrestrial environment. Acute barrier disruption by organic solvents, detergents, or tape stripping elicits a homeostatic repair response in the epidermis, which rapidly restores normal barrier function (Elias and Feingold, 1992). Repeated perturbations of the barrier induce cutaneous pathology, including epidermal hyperplasia and cutaneous inflammation (Denda *et al.*, 1996).

Seasonal changes effect the condition of normal skin and may trigger various cutaneous disorders (Wilkinson and Rycroft, 1992; Sauer and Hall, 1996). In common dermatoses, such as atopic dermatitis or psoriasis, a decline in barrier function often parallels increased severity of clinical symptomatology (Grice, 1980; Pinnagoda *et al.*, 1989). These conditions all tend to worsen during the winter season, when humidity is lower (Wilkinson and Rycroft, 1992; Sauer and Hall, 1996). Abundant indirect evidence suggests that decreased humidity precipitates these

disorders (Rycroft and Smith, 1980), whereas in contrast, increased skin hydration appears to ameliorate these conditions (Chernosky, 1976; Rawlings *et al.*, 1994). The mechanism(s) by which alterations in relative humidity might influence cutaneous function and induce cutaneous pathology are poorly understood. We recently showed that prolonged exposure of normal murine skin to a dry environment produced an increase in SC weight and thickness, with a commensurate reduction in basal transepidermal water loss (TEWL) (Denda *et al.*, 1998).

Yet, whether exposure to a dry environment alone can also induce pathophysiologic changes is not yet known. In order to determine the possibility that changes in environmental humidity might initiate and/or aggravate cutaneous pathophysiology, we examined the effects of alterations in environmental humidities on epidermal DNA synthesis, epidermal hyperplasia, and mast cell number and degranulation in both normal hairless mice and mice with experimentally induced barrier defects. Our results show first, that changes in environmental humidity alone can modulate epidermal proliferation; and second, that a low humidity, when superimposed on a defective barrier, provokes further pathophysiologic changes. Together, these studies provide strong support for the hypothesis that seasonal exacerbations/aggravation of cutaneous dermatoses are attributable to decreased humidity.

## MATERIALS AND METHODS

**Animals** Hairless mice, 7-10 wk old (HR-1, Hoshino, Japan), were used. Before experiments, animals were caged separately for at least 4 d. These cages

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Abbreviation: TEWL, transepidermal water loss.

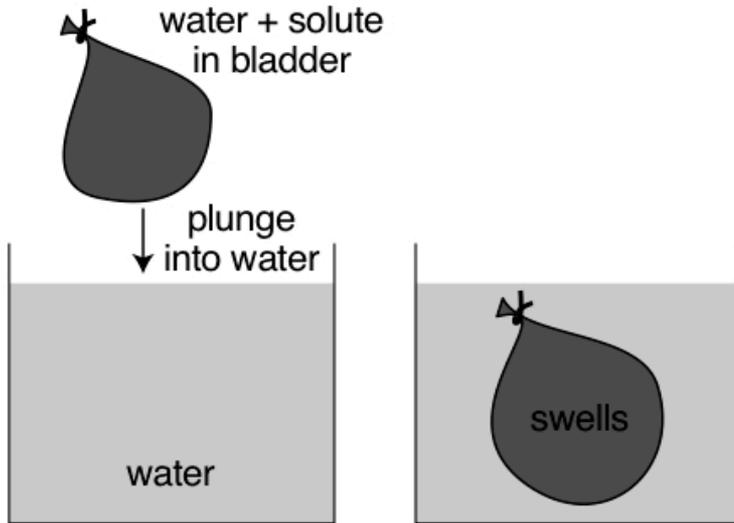
On a drizzly day toward the end of the week, Luce walked them in the woods, making water the topic of her ramble. It's what makes life so rampant around here, she said... All the moons from spring to early fall, everything plumps with water. Think jungle, and then go a degree onward in the direction of a deep green world so wet you could wring it out like a dishrag if you could get a good grip on either end of it. Giant hemlocks and sycamores and tulip trees. Rhododendrons. Moss and ferns. Understory too thick to see more than twenty feet into the woods, until killing frosts reveal the bones of the place. A steamy greenhouse of plants and creatures. Flip any rock or dead log, and myriad beings go crawling down individual vectors toward the darkness they crave. Sit in a yellow sunbeam, and the damp air around you thickens with myriad beings dancing up into the daylight they love. Life likes the wet and rewards it. Archaic forms incompatible with the modern world persist here. Hellbenders, deep in the creek beds. Panthers, high on the ridges. Even dead blighted chestnuts resurrect themselves out of the black forest floor, refusing to accept the terms of their extinction. Hope incarnate. All, Luce explained, due to moisture.

- Charles Frazier  
(Nightwoods)

# Osmosis Observations

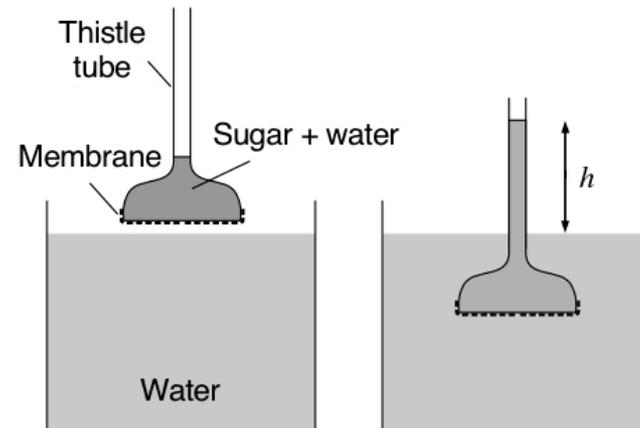
Henri Dutrochet (early 1800s)

- first described phenomenon and called it osmosis
- developed first osmometer: animal bladder filled with test solution, plunge into water, swells, turgid
- pressure greater for solutions with more solute



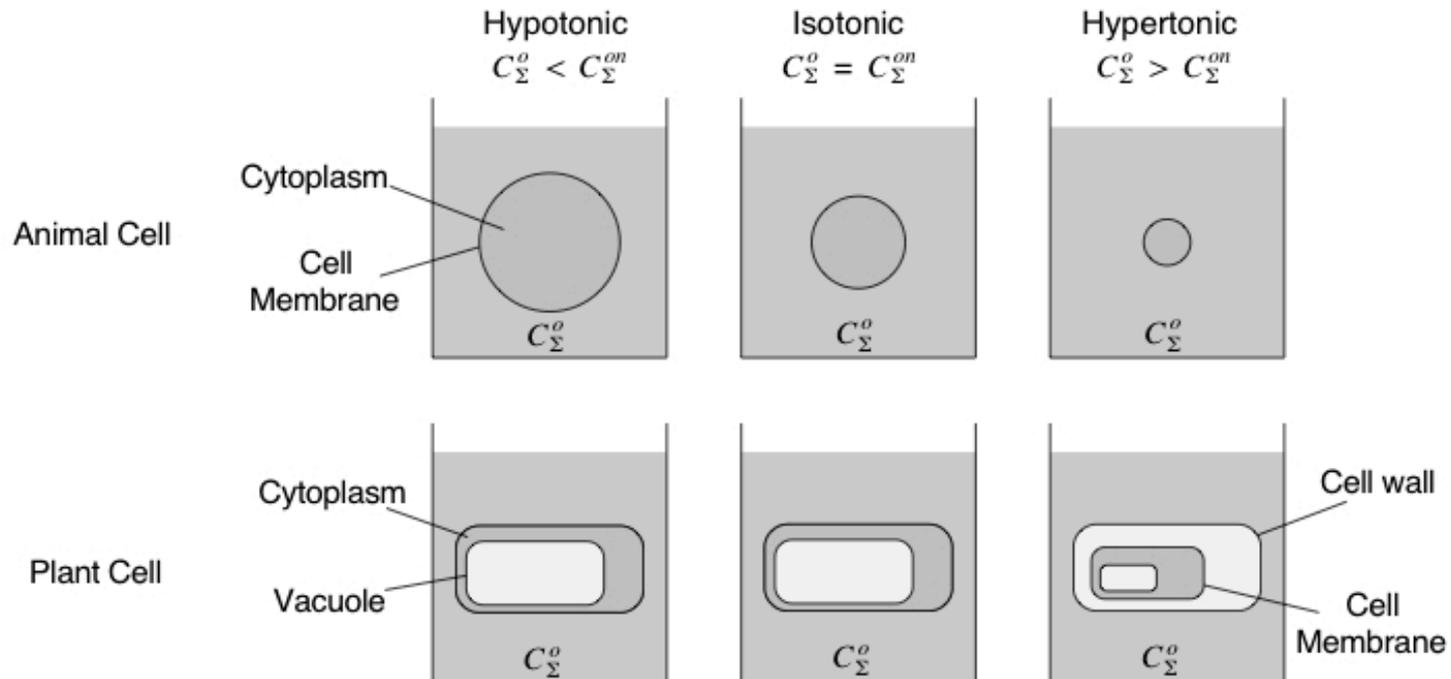
Wilhelm Pfeffer (mid 1800s)

- osmosis can be stopped with hydraulic pressure
- thistle tube + animal bladder (or artificial membrane by late 1800s)
  - water flows in direction to equalize sugar concentration
  - hydraulic pressure develops
  - flow stops when osmotic pressure = hydraulic pressure
- pressure proportional to concentration of solute
- pressure increases slightly with temperature



Hugo de Vries (late 1800s)

- studied osmosis in cells
- animal cell can shrink or swell depending on concentration
- isotonic (same "tension" as in cell's normal environment)
- plasmolysis – plant cell membrane separates from cell wall
- except for salts, plasmolysis occurs at same MOLAR concentration (does not depend on chemical properties of solute)
  - colligative property (freezing point depression, boiling point elevation)
- salts are different: ratios of small integers



Henricus van't Hoff (1886)

- formulated mathematical law
- count number of particles in volume  $V$
- measure temperature  $T$
- osmotic pressure = pressure produced by gas with same number of particles, same volume, and same pressure

van't Hoff's Law

$$\underbrace{\pi(x,t)}_{\substack{\text{osmotic} \\ \text{pressure}}} = \underbrace{R}_{\substack{\text{molar gas} \\ \text{constant} \\ 8.314 \text{ J}/(\text{mol}\cdot\text{K})}} \underbrace{T}_{\substack{\text{absolute} \\ \text{temperature}}} \underbrace{\sum_n C_n(x,t)}_{\substack{\text{total solute} \\ \text{concentration}}}$$

- salts are different

Svante Arrhenius (1884)

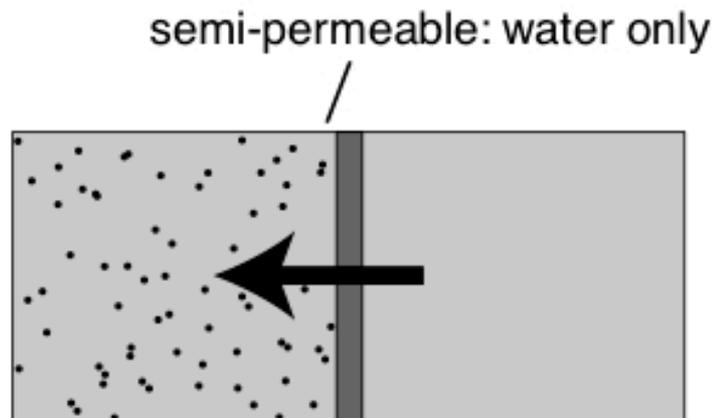
- PhD (age 25): dissolution of salts into ions
- $\text{NaCl} \rightarrow \text{Na}^+ + \text{Cl}^-$  ( $\therefore$  conducts electricity)
- count ions as separate particles  
→ van't Hoff's law works for salts as well

$$\underbrace{\pi(x,t)}_{\substack{\text{osmotic} \\ \text{pressure}}} = R T \sum_n C_n(x,t) = R T \underbrace{C_\Sigma(x,t)}_{\substack{\text{osmolarity} \\ [\text{osmol}/\text{m}^3]}}$$

[ Pa = N/m<sup>2</sup> ]

## Controversy

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



- 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

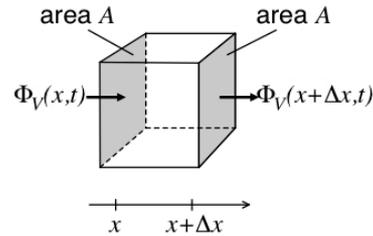
$$\underbrace{\Phi_V(x,t)}_{\text{solvent flux}} = - \underbrace{\kappa}_{\substack{\text{hydraulic} \\ \text{permeability}}} \underbrace{\frac{\partial p(x,t)}{\partial x}}_{\text{hydraulic pressure gradient}}$$

- 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

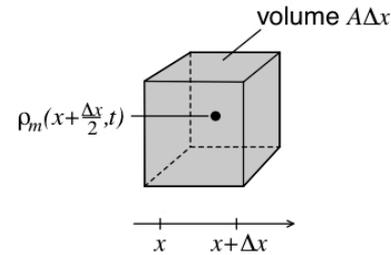
$$\phi_n \left[ \frac{\text{mol}}{\text{m}^2\text{s}} \right] \quad \Phi_V \left[ \frac{\text{m}^3}{\text{m}^2\text{s}} = \frac{\text{m}}{\text{s}} \right] \quad p \left[ \text{Pa} = \frac{\text{N}}{\text{m}^2} \right]$$

# Hydraulic Pressure

## Continuity Equation for Solvent Flow



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



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

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

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

↑  
equal if solvent is neither created nor destroyed

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

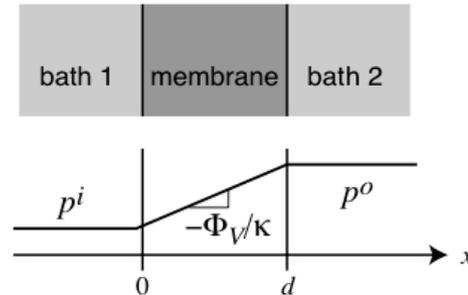
Take limit as  $\Delta x \rightarrow 0$  and  $\Delta t \rightarrow 0$

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

Hydraulic Pressure  
(thin membrane, steady-state)

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

Water flow through thin membrane  
(hydraulic)



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

hydraulic conductivity

analogous to Fick's law for membranes

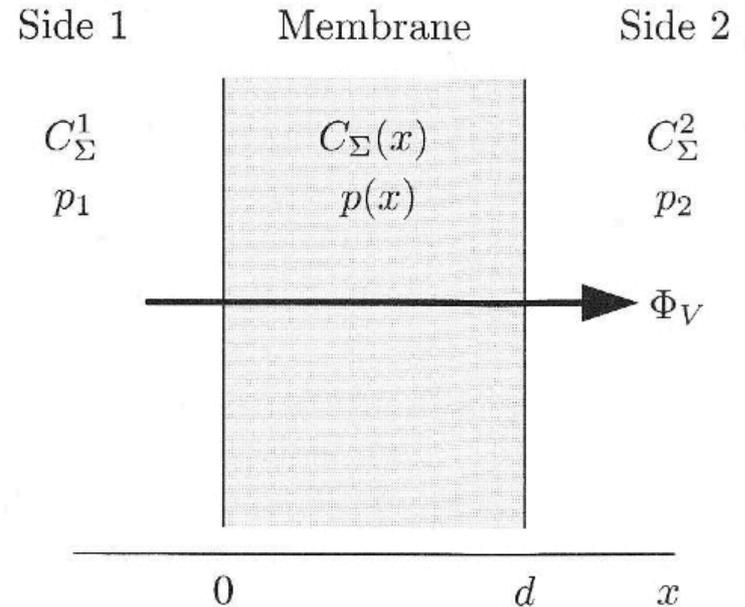
$$\phi_n(t) = P_n ( c_n^i(t) - c_n^o(t) ) ; \quad P_n = \frac{D_n k_n}{d}$$

## Hydraulic + Osmotic Pressure (thin membrane)

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

$$\Phi_V = -K \frac{\partial(p - \pi)}{\partial x} \quad (\text{modified version of Darcy's Law})$$

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



## Hydraulic + Osmotic Pressure (thin membrane)

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

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

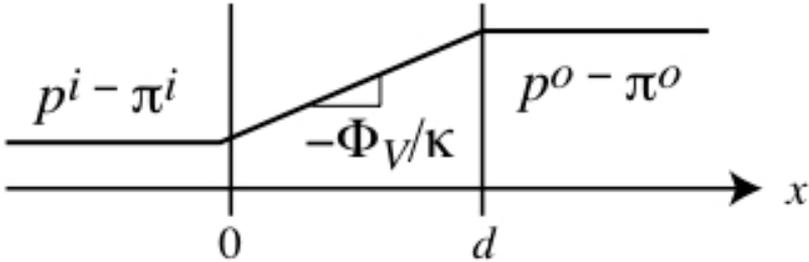
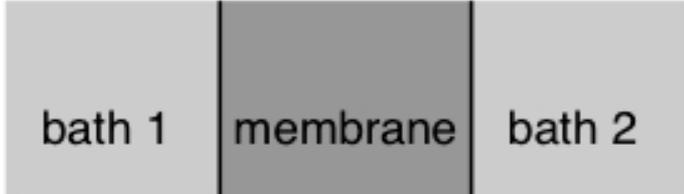
$$\Phi_V = -\kappa \frac{\partial(p - \pi)}{\partial x} = \text{const.}$$

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

$$(p(x) - p(x_0)) - (\pi(x) - \pi(x_0)) = -\frac{\Phi_V}{\kappa}(x - x_0), \quad (4.13)$$

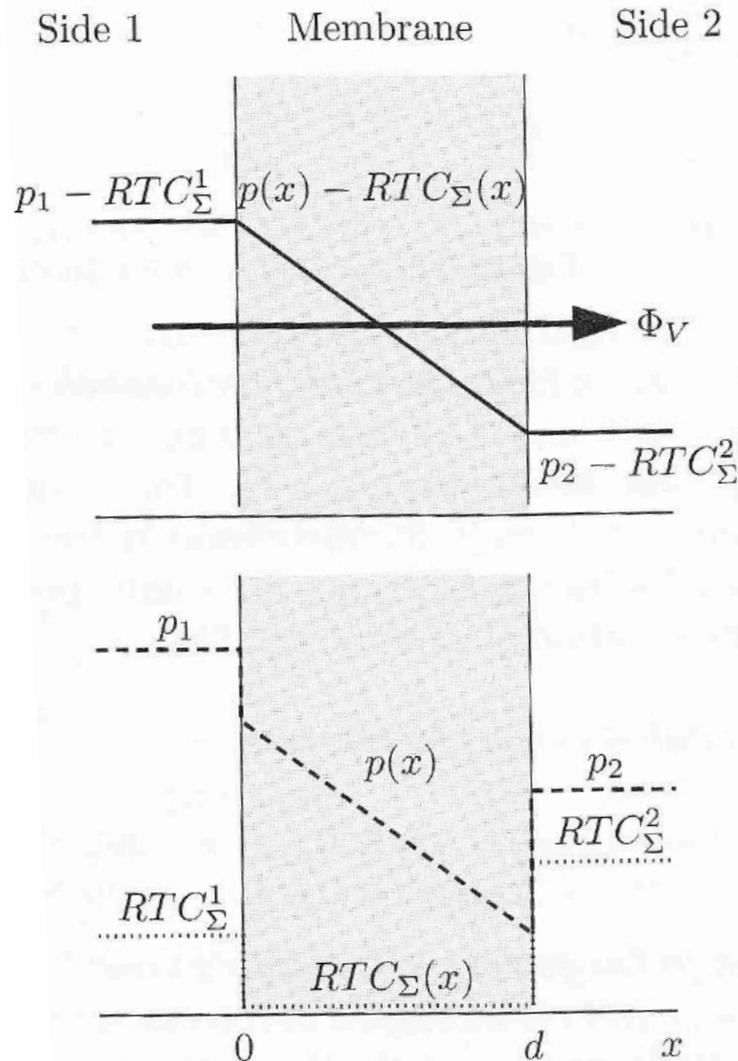
# Hydraulic + Osmotic Pressure (membrane)

Water flow through semipermeable membrane



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

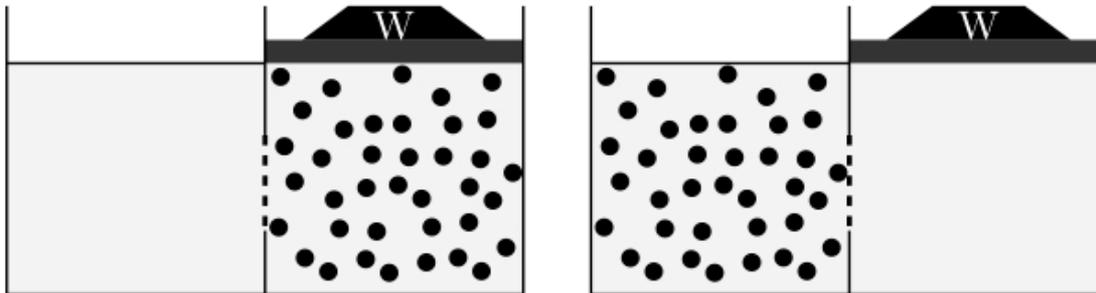
# Hydraulic + Osmotic Pressure (membrane)



**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.

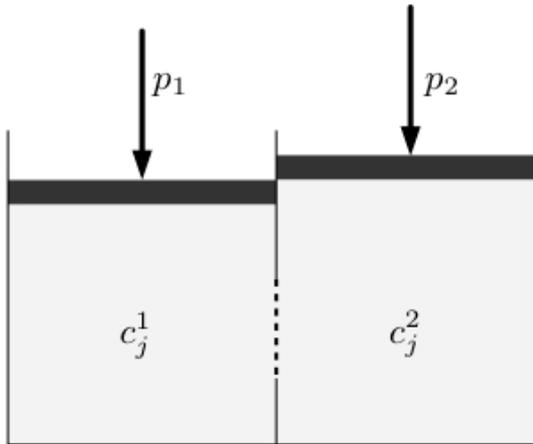


One of the compartments contains a weight  $W$  on a piston, the other does not. The only difference between the two experiments is the location of the solute particles indicated by dots in the fluid. Which of the two experiments could be in osmotic equilibrium? Explain.

**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  $c_j^1 \neq c_j^2$  for some choice of  $p_1 - p_2$ ? Explain.

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