A PHYSIOLOGICAL FLOW PROBLEM

(After Lin and Segel, Chapter 8)

How is water and salt expelled from the body, e.g. in kidneys ?

J. Diamond (1967): Salt is expelled from the body in a non-direct way by means of so-called *secondary channels,* which are consistently found in fluid secreting tissue.

• At the inner end of the secondary channels chemical pumps enter salt into the channel leading to a local high salt concentration and a gradient towards the opening of the channels

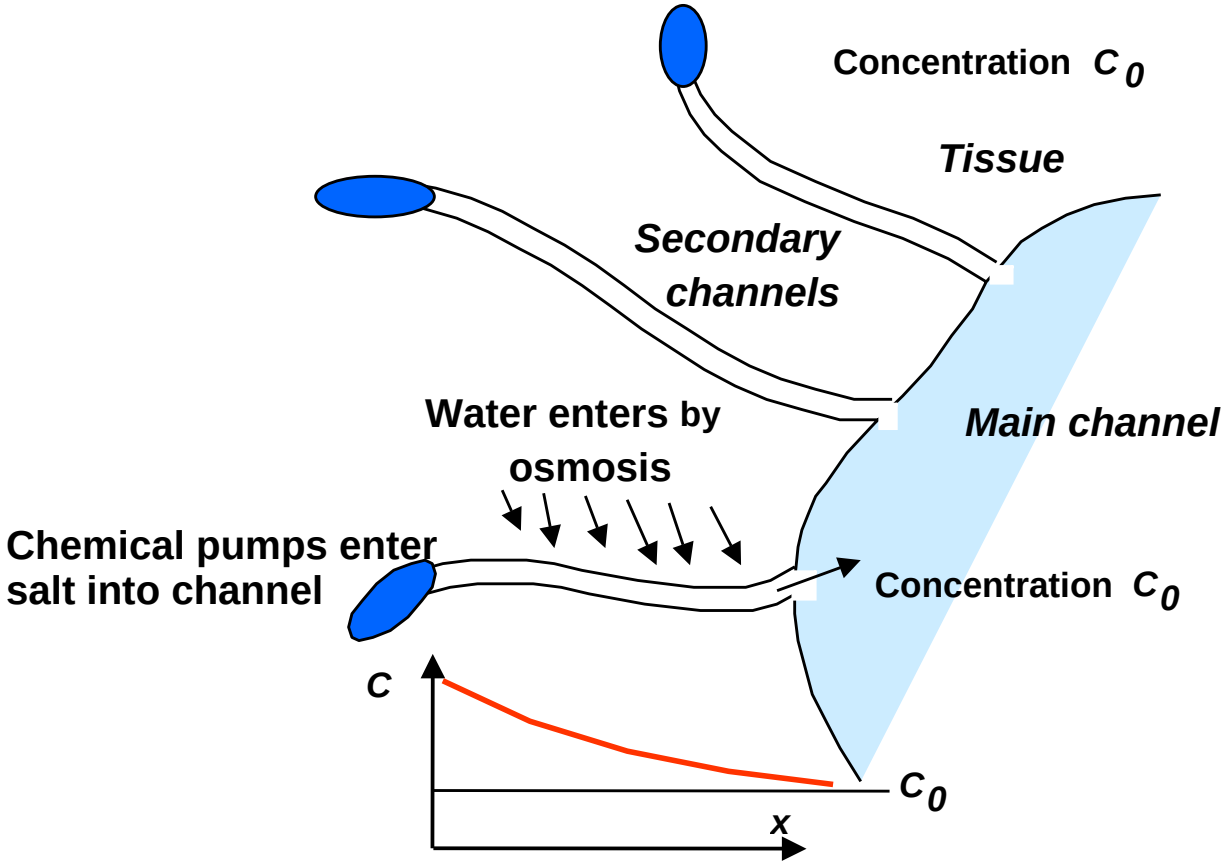
• ***Water*** enters the channel by *osmosis* through the walls

• ***Salt*** is moving in the channel by *diffusion* and *convection*

• At the outer end of the channel, the concentration is about C_0.

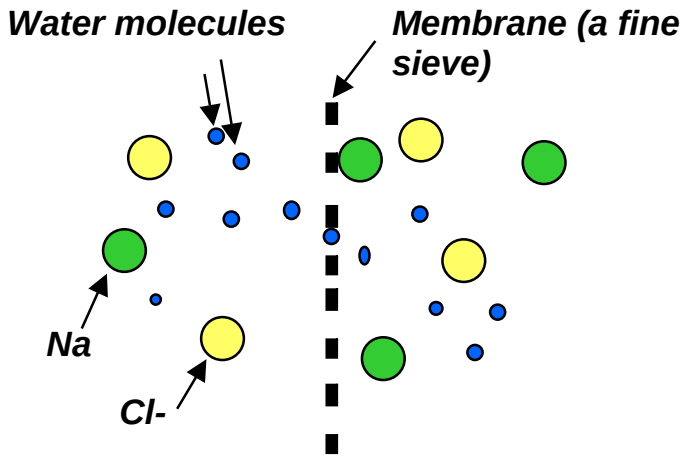
What determines the amount of salt coming out of the secondary channel under stationary (time independent) conditions?

QUALITATIVE MODEL



PHYSICAL MECHANISMS

OSMOSIS:



Salt ions are too large to pass through the membrane!

If the ion concentrations on each side of the membrane are C_1 and C_2, then the amount of water passing through the membrane per area and time units is

$$J = P(C_2 - C_1)$$

The constant *P* is called the ***permeability*****.**

$$J = P(C_2 - C_1)$$

Units:

$$[J] = \frac{Volume}{Area \times Time} = \frac{\mathrm{m}^3}{\mathrm{m}^2\mathrm{s}} = \frac{\mathrm{m}}{\mathrm{s}}$$

$$[C] = \frac{\#\text{ions}}{\text{Volume}} = \frac{\text{osmol}}{\mathrm{m}^3}, \ (1 \text{ osmol} = \text{Avogadro's number of ions})$$

$$[P] = \frac{\mathrm{m/s}}{\mathrm{osmol/m}^3} = \frac{\mathrm{m}^4}{\mathrm{osmol}\times\mathrm{s}}$$

(Note since the concentration of ions is about twice the concentration of salt, we may just as well think of *C* as the salt concentration)

DIFFUSION

Motion of salt in an otherwise stationary solution is due to concentration differences:

$$F = -D\frac{\partial C}{\partial x}$$

F is called the ***flux*** of salt (in the *x*-direction).

$\partial C / \partial x$ is the concentration gradient.

D is called the ***diffusion coefficient***.

Flux (in general a vector!) is the *amount passing through an imaginary surface in the fluid per time and area unit.* Units:

$$[F] = \frac{amount}{area \times time} = \frac{\text{osmol}}{\text{m}^2\text{s}}$$

$$[C] = \frac{amount}{volume} = \frac{\text{osmol}}{\text{m}^3}$$

$$[D] = \frac{\text{m}^2}{\text{s}}$$

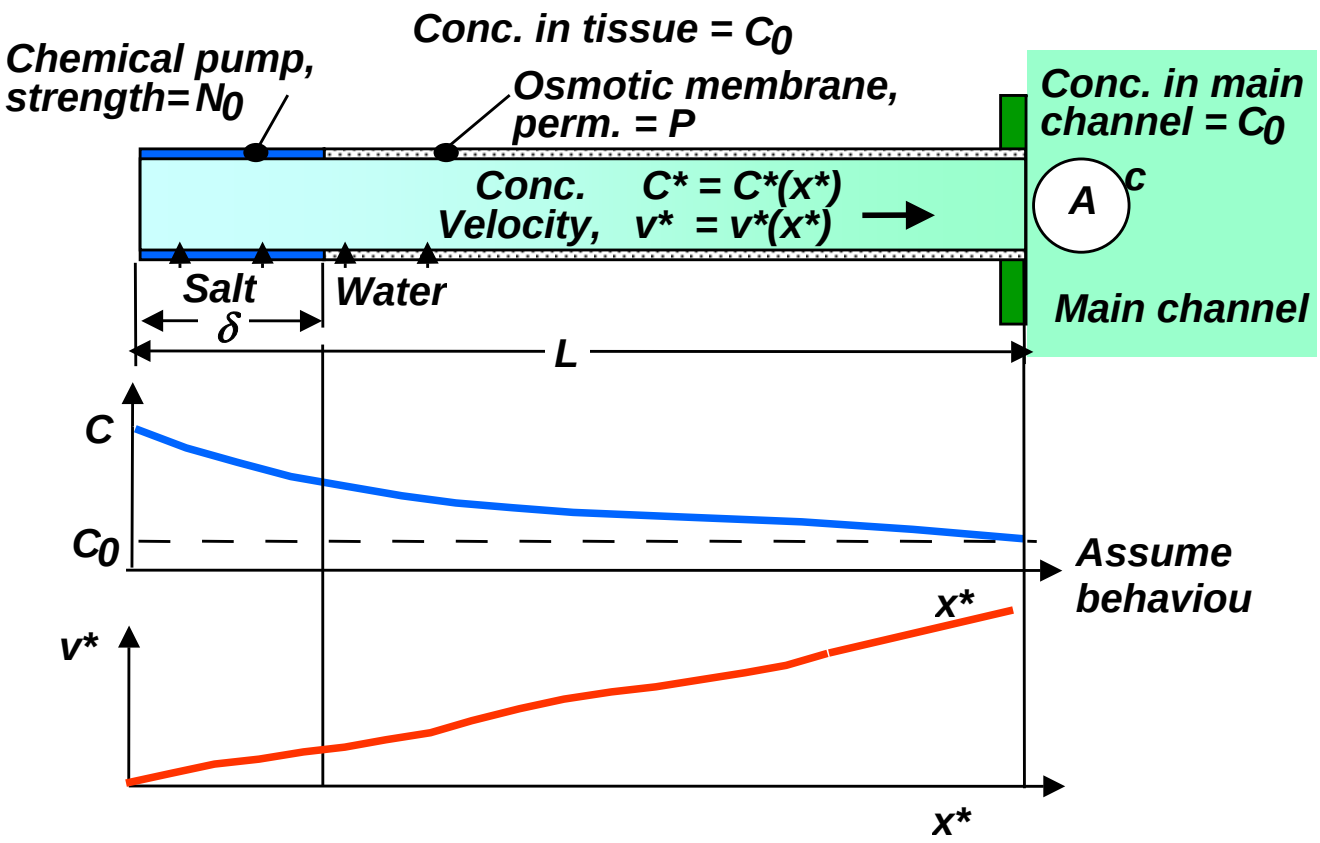
CHEMICAL PUMPS

Enter salt into the solution from the tissue by means of certain chemical mechanisms using energy:

$$[N_0] = \frac{Amount}{Unit\ area\ wall \times time} = \frac{\text{osmol}}{\text{m}^2\text{s}}$$

THE NEXT STEP IS DEFINING THE GEOMETRY:

- The channels are long and narrow. Thus, we consider a 1d model.
- The inner end of the channel is assumed to be closed.



Length: L
Cross sectional area: A
Circumference: c
Active zone for chemical pumps: δ

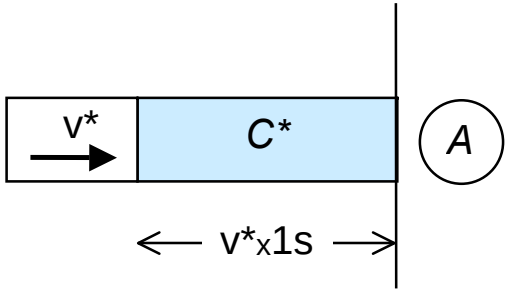
Water entering the channel through osmosis (per area unit):

$$J = P\left[C^*(x^*) - C_0\right]$$

Transport of salt in the channel:

A. Diffusion: $$F_D = -D dC^*/dx^*$$

B. Convection = *Passive transport due to the motion of the fluid*



$$F_c = \frac{v^* \cdot 1s \cdot A \cdot C^*}{A \cdot 1s} = v^* C^*$$

Total flux: $$F^* = F_D + F_c = v^* C^* - D\frac{dC^*}{dx^*}$$

Chemical pumps (do not include the end): $N_0(\delta c)$

The problem presented to us is to determine the *emergent osmolarity* defined by $F^*(L) = v^*(L)Os^*$:

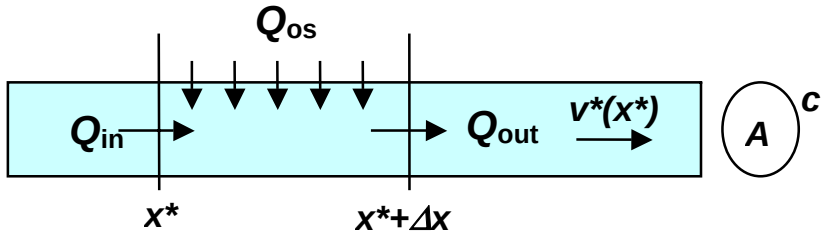
$$Os^* = \frac{F^*(L)}{v^*(L)} = \frac{v^*(L)C^*(L) - D\frac{dC^*}{dx^*}(L)}{v^*(L)}$$

Emergent osmolarity = the *apparent* concentration needed in order to have the same amount of output with the given fluid velocity and *no contribution from diffusion.*

THE EQUATIONS: *CONSERVATION OF WATER AND SALT!*

WATER

(Since the salt concentration is small, the density of water is assumed to be constant)



$$Q_{in} = Av^*(x^*)$$

$$Q_{out} = Av^*(x^*+\Delta x^*)$$

$$Q_{os} = P\left(C^*(x^*+\delta x^*) - C_0\right)\cdot \underbrace{\left(\Delta x^* \cdot c\right)}_{\text{wall area}}$$

$$Q_{out} - Q_{in} = Q_{os}$$

$$Av^*(x^*+\Delta x^*) - Av^*(x^*) = P\left(C^*(x^*+\delta x^*) - C_0\right)$$

$$\Downarrow (\Delta x^* \to 0)$$

$$\boxed{\frac{dv^*}{dx^*} = \frac{Pc}{A}\left(C^*(x^*) - C_0\right)}$$

SALT

We use a conservation argument similar to for water:

$$Q_{out}^{salt} = AF*(x*+\Delta x*)$$
$$Q_{in}^{salt} = AF*(x*)$$
$$Q_{ch.p.}^{salt} = N*(x*)\cdot(c\Delta x*)$$

By letting $\Delta x*$ tend to 0:

$$A\frac{dF*}{dx*} = \begin{cases} N_0 c, & x* \le \delta \\ 0, & x* > \delta \end{cases}$$

The previous simple equation may be solved immediately:

$x^* \le \delta$:

$$A\frac{dF^*}{dx^*} = N_0 c \quad \Rightarrow \quad F^* = \frac{N_0 c}{A} x^* \quad (\text{Since } F^*(0) = 0)$$

$x^* > \delta$:

$$A\frac{dF^*}{dx^*} = 0 \quad \Rightarrow \quad F^* = \frac{N_0 c}{A} \delta \quad (\text{Since } F^* \text{ is continuous})$$

Together, with the expression for the salt flux, this gives the following differential equation for C^*:

$$C^* v^* - D\frac{dC^*}{dx^*} = \begin{cases} \dfrac{cN_0}{A} x^*, & 0 \le x^* \le \delta \\ \dfrac{cN_0}{A} \delta, & \delta \le x^* \le L \end{cases}$$

BOUNDARY CONDITIONS AND MATCHING

CONDITIONS AT $x^*=\delta$:

Closed end channel:

$$v^*(0) = 0$$

$$F^*(0) = 0$$

In fact,

$$\frac{dC^*}{dx^*}(0) = 0 \quad \left(\text{Since } F^*(0) = C^*(0)v^*(0) - D\frac{dC^*}{dx^*}(0) \right)$$

At the right end we assume that $C^*(L) = C_0$.

Finally, *matching* conditions at $x^*=\delta$:

$$F^*(\delta+) = F^*(\delta-)$$
$$v^*(\delta+) = v^*(\delta-)$$
$$C^*(\delta+) = C^*(\delta-)$$
$$\frac{dC^*}{dx^*}(\delta+) = \frac{dC^*}{dx^*}(\delta-) \quad \left(\text{Since } F^* = C^* v^* - D\frac{dC^*}{dx^*} \right)$$

(Not all conditions are needed in the final formulation)

FINAL FORMULATION

Differential equations:

$$\frac{dv^*}{dx^*} = \frac{Pc}{A}\left(C^*(x^*) - C_0\right), \quad 0 \le x^* \le \delta$$

$$C^* v^* - D\frac{dC^*}{dx^*} = \begin{cases} \dfrac{cN_0}{A}\, x^*, & 0 \le x^* \le \delta \\ \dfrac{cN_0}{A}\, \delta, & \delta \le x^* \le L \end{cases}$$

Boundary conditions:

$$v^*(0) = 0, \quad C^*(L) = C_0$$

$$v^*, C^* \ \text{ continuous for } x^* = \delta$$

Determine:

$$Os^* = \frac{F^*(L)}{v^*(L)} = \frac{cN_0\delta}{Av^*(L)}$$

SCALING

Parameter	Unit	Min. value	Typical value	Max. value
r	cm	10^{-6}	5×10^{-6}	10^{-4}
L	cm	4×10^{-4}	10^{-2}	2×10^{-2}
δ	cm	4×10^{-5}	10^{-3}	2×10^{-3}
D	cm^2/s	10^{-6}	10^{-5}	5×10^{-5}
N_0	$mOsm/cm^2s$	10^{-10}	10^{-7}	10^{-5}
P	cm^4/s mOsm	10^{-6}	2×10^{-5}	2×10^{-4}
C_0	$mOsm/cm^3$	-	3×10^{-1}	

(Table from Lin & Segel, p. 264)

Length scale: δ

Concentration scale: C_0

Velocity scale: $$U = \frac{cN_0\delta}{C_0 A}$$

Derivation of the velocity scale:

$$\underbrace{\frac{cN_0\delta}{A}A}_{\text{Salt out per time unit}} = C_0 A U \Rightarrow U = \frac{cN_0\delta}{AC_0}$$

$$\boxed{\begin{aligned} x^* &= \delta x \\ C^* &= C_0 C \\ v^* &= Uv = \frac{cN_0\delta}{AC_0} v \end{aligned}}$$

SCALED EQUATIONS

$$\varepsilon \frac{dv}{dx} = C - 1, \quad 0 \le x \le \lambda$$

$$Cv - \eta \frac{dC}{dx} = \begin{cases} x & 0 \le x \le 1 \\ 1 & 1 \le x \le \lambda \end{cases}$$

$$v(0) = 0, \quad C(\lambda) = 1$$

$v, C, dC/dx$ continuous at $x = 1$.

$$\varepsilon = \frac{N_0}{PC_0^2}, \quad \eta = \frac{AC_0 D}{N_0 \delta^2 c}, \quad \lambda = \frac{L}{\delta}$$

$$\text{Determine } Os = \frac{1}{v(\lambda)}$$

Turns out to be impossible to solve analytically!

Typical values of the non-dimensional parameters

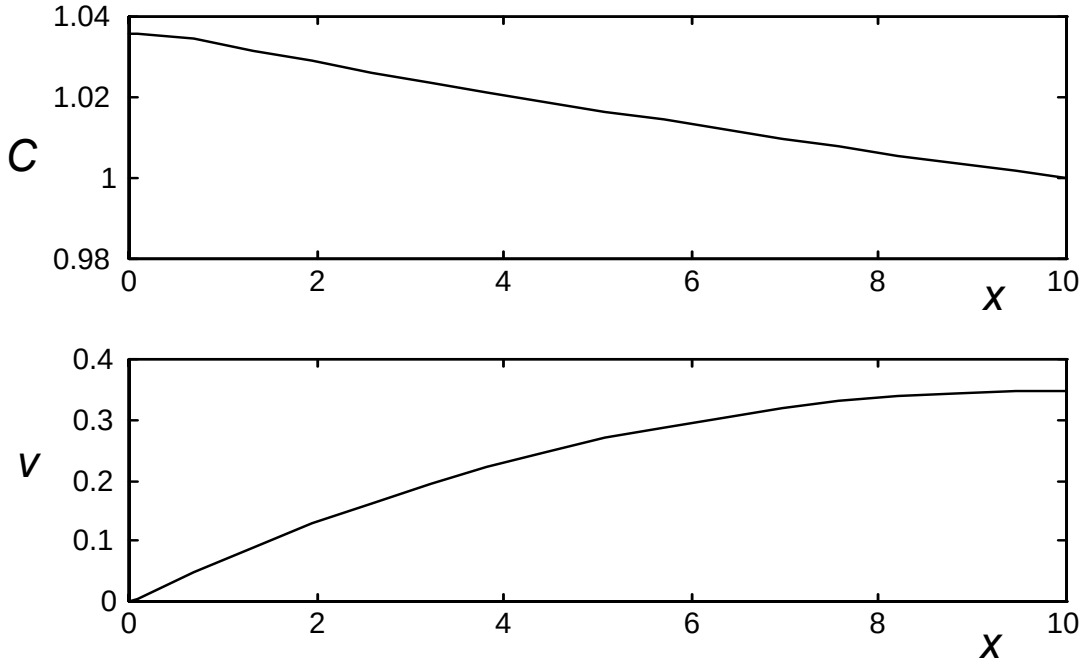
Parameter	Minimum	Typical	Maximum
ε	10^{-5}	$2 \cdot 10^{-2}$	10^{2}
η	$4 \cdot 10^{-3}$	75	10^{10}
λ	10(?)	10	500

SOME NUMERICAL SOLUTIONS

obtained by means of a simple shooting method for

$$\lambda = 10, \quad \kappa = 1, \quad \varepsilon = .5$$

(The parameter κ will be defined below)



(*Note*: *C(0)* = 1.0375)

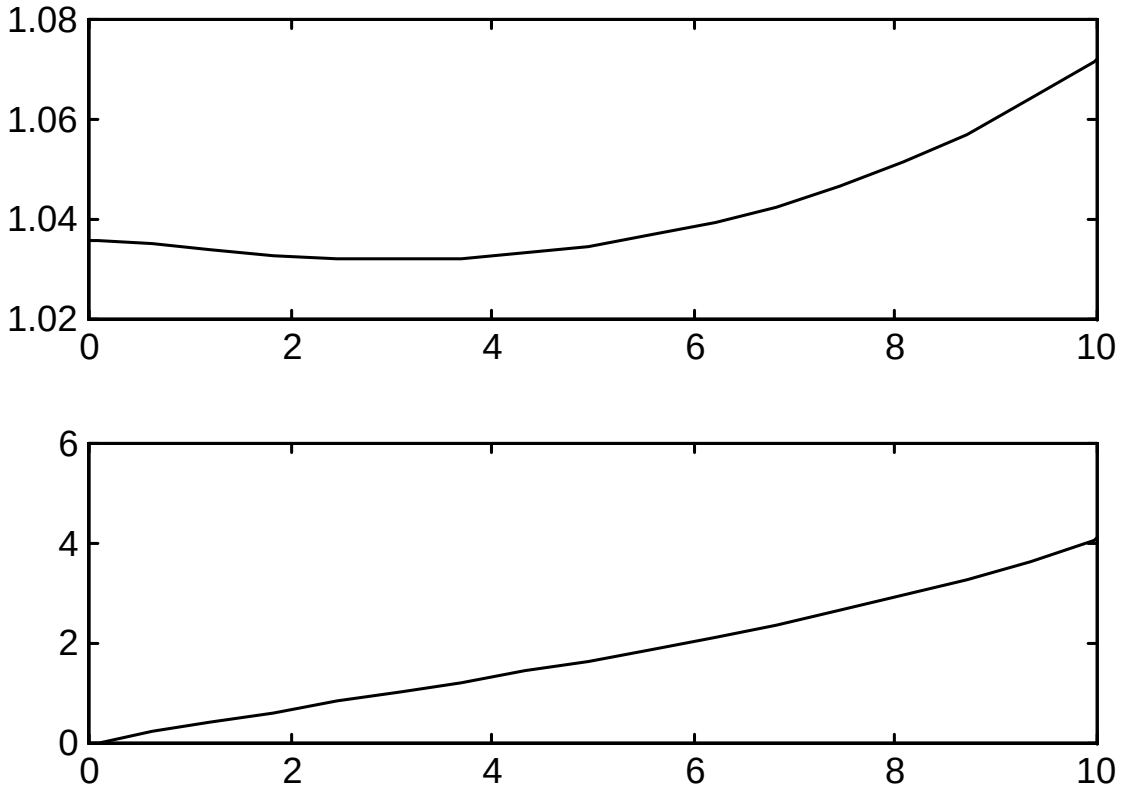
MATLAB CODE:

```
x0 =[0, 1.0355];
xspan = [0,10];
[t,x]=ode23('kidney',xspan,x0);
subplot(2,1,1); plot(t,x(:,2));
subplot(2,1,2); plot(t,x(:,1));

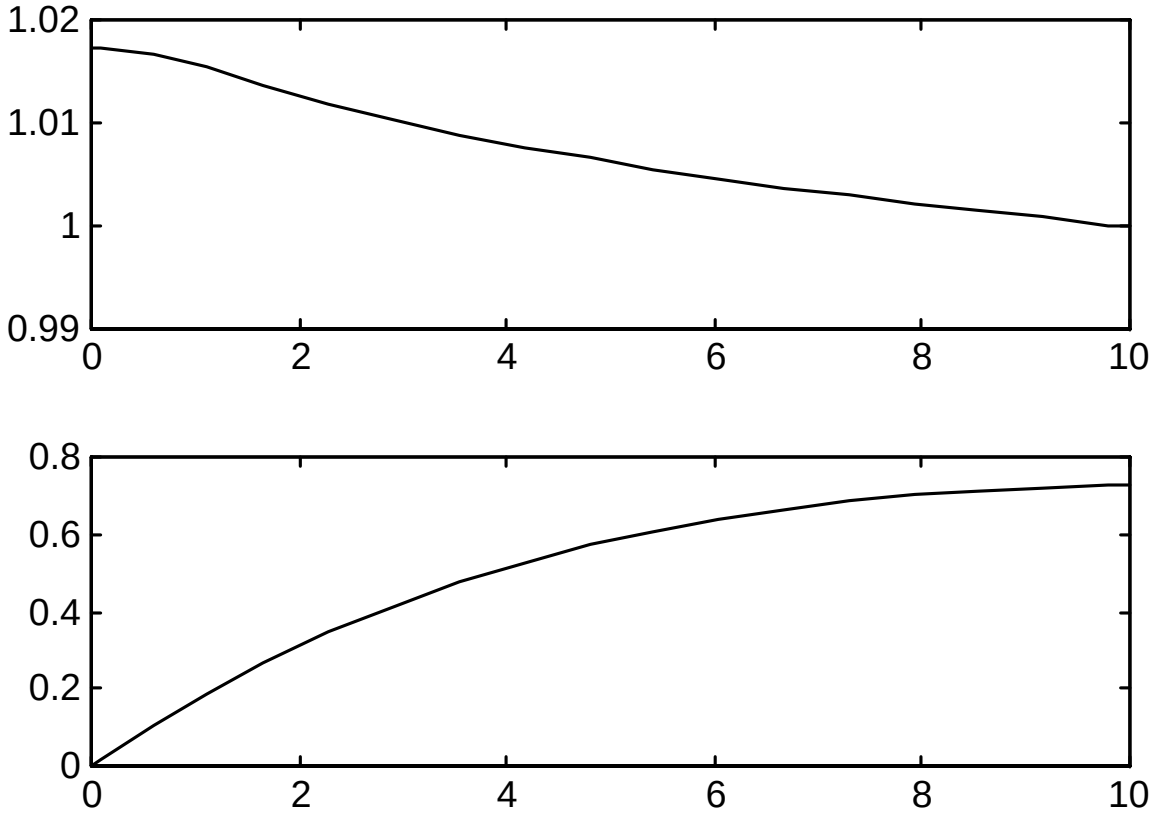

%L&S Eqn. 16a,b, Section 8.3: v=x(1), C = x(2):
function xdot = kidney(t,x)
lambda = 10.;
kappa = 1;
eps = .5;
f = (eps*kappa^2/lambda^2);
xdot(1)=( x(2)-1 )/eps;
xdot(2)=f*x(1)*x(2)-f*min(t,1);
```

$$\lambda = 10, \quad \kappa = 1, \quad \varepsilon = 0.1:$$

$C(0) = 1.0375$:



$C(0)$=1.0173:



A FIRST-TRY PERTURBATION EXPANSION

$$\varepsilon \frac{dv}{dx} = C - 1, \quad 0 \le x \le \lambda$$

$$Cv - \eta \frac{dC}{dx} = \begin{cases} x & 0 \le x \le 1 \\ 1 & 1 \le x \le \lambda \end{cases}$$

$$C = C_0 + \varepsilon C_1 + \varepsilon^2 C_2 + \ldots$$

$$v = v_0 + \varepsilon v_1 + \varepsilon^2 v_2 + \ldots$$

To order ε^0:

$$C_0 - 1 = 0 \Rightarrow C_0 = 1,$$

$$1 v_0 + \eta \frac{dC_0}{dx} = \begin{cases} x \\ 1 \end{cases} \Rightarrow v_0 = \begin{cases} x \\ 1 \end{cases},$$

To order ε^1:

$$C_1 = \frac{dv_0}{dx} = \begin{cases} 1 \\ 0 \end{cases} \Rightarrow C_1 \text{ is discontinuous!}$$

This is against our requirement that C should be continuous.

The problem is that η *tends to be large when* ε *is small!*

We introduce the modified parameter κ and eliminate η:

$$\eta = \frac{\left(\lambda^2 / \kappa^2\right)}{\varepsilon}$$

(The somewhat strange form is basically for making the expressions simpler!)

MODIFIED PERTURBATION EXPANSION

$$C - 1 = \varepsilon \frac{dv}{dx}, \quad 0 \le x \le \lambda$$

$$\varepsilon\kappa^2 Cv - \lambda^2 \frac{dC}{dx} = \varepsilon\kappa^2 \begin{cases} x, & 0 \le x \le 1 \\ 1, & 1 \le x \le \lambda \end{cases}$$

$$\varepsilon << 1, \quad \kappa, \lambda \sim O(1)$$

$$C = C_0 + \varepsilon C_1 + \varepsilon^2 C_2 + \ldots$$

$$v = v_0 + \varepsilon v_1 + \varepsilon^2 v_2 + \ldots$$

To order ε^0:

$$\left.\begin{array}{l} C_0 - 1 = 0 \\ \lambda^2 C_0' = 0 \end{array}\right\} \Rightarrow C_0 = 1,$$

To order ε^1:

$$\boxed{\left.\begin{array}{c} C_1 = v_0' \\ \kappa^2 v_0 C_0 - \lambda^2 C_1' = \kappa^2 \begin{pmatrix} x \\ 1 \end{pmatrix} \end{array}\right\} \Rightarrow \kappa^2 v_0 - \lambda^2 v_0'' = \kappa^2 \begin{pmatrix} x \\ 1 \end{pmatrix}}$$

Solution for $0 \le x \le 1$:

$$v_0 = x - K_1 \sinh\left(\frac{\kappa}{\lambda} x\right)$$

$$C_1 = v_0' = 1 - K_1 \frac{\kappa}{\lambda} \cosh\left(\frac{\kappa}{\lambda} x\right)$$

Solution for $1 \le x \le \lambda$:

$$v_0 = 1 - K_2 \cosh\left(\frac{\kappa}{\lambda} x + \Psi\right)$$

$$C_1 = v_0' = -K_2 \frac{\kappa}{\lambda} \sinh\left(\frac{\kappa}{\lambda} x + \Psi\right)$$

(since $C_1(\lambda) = 0$, $\Psi = -\kappa$)

The constants K_1 and K_2 are determined from the continuity requirements at $x = 1$:

$$K_1 = \frac{\lambda}{\kappa} \frac{\cosh(\kappa/\lambda - \kappa)}{\cosh(\kappa)}$$

$$K_2 = \frac{\lambda}{\kappa} \frac{\sinh(\kappa/\lambda)}{\cosh(\kappa)}$$

The *dimensionless osmolarity* at $x=\lambda$:

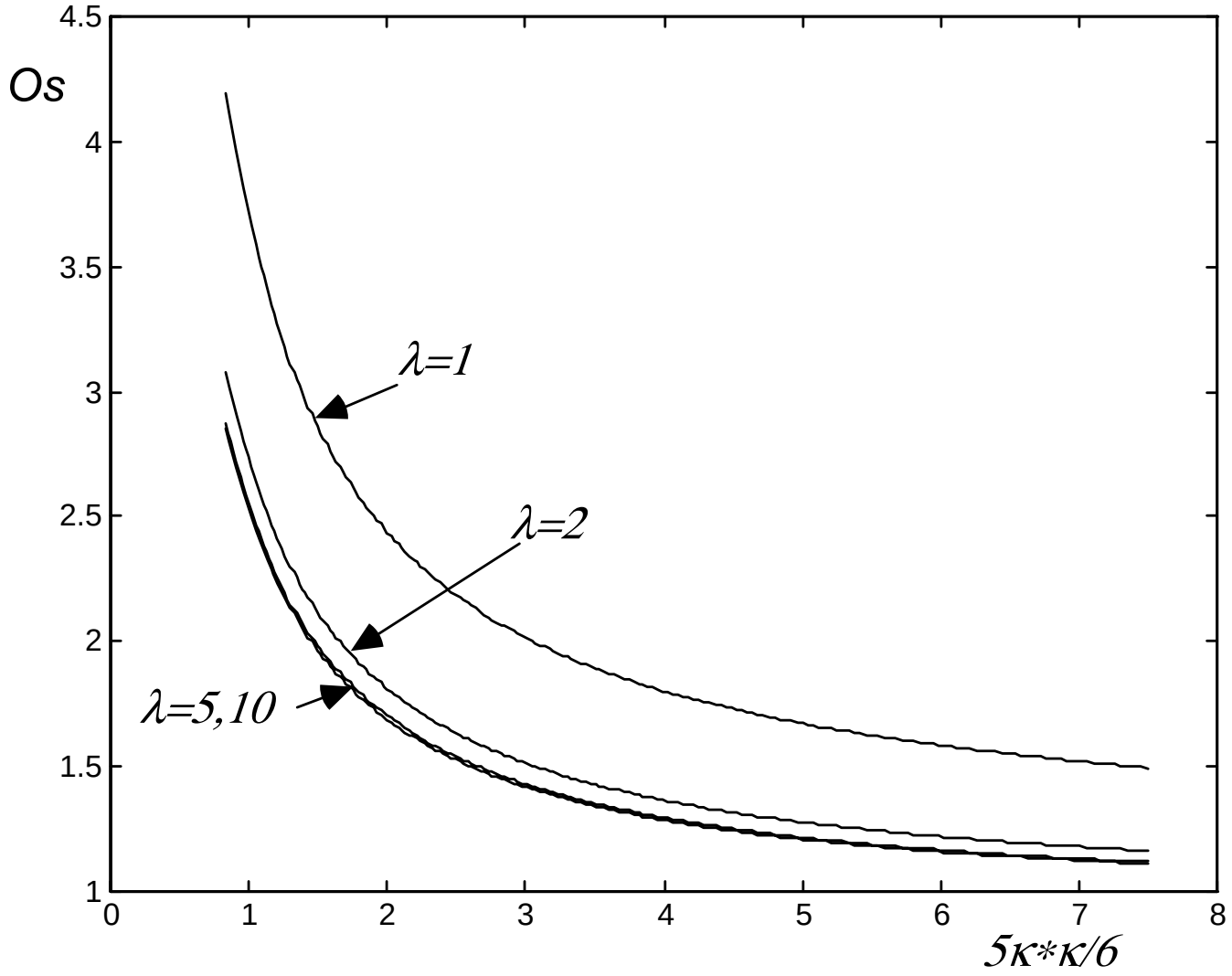
$$\boxed{Os = \frac{1}{v(\lambda)} \approx \frac{1}{v_0(\lambda)} = \frac{1}{1-K_2}}$$

Assume $\kappa/\lambda<1$:

$$Os \approx \frac{1}{1-K_2} \approx \frac{1}{1-\frac{1}{\cosh(\kappa)}} = \frac{\cosh(\kappa)}{\cosh(\kappa)-1}$$

When κ is small compared to 1, then

$$Os \approx \frac{\cosh(\kappa)}{\cosh(\kappa)-1} \approx \frac{1+\kappa^2/2+\ldots}{\kappa^2/2+\ldots} \approx \frac{2}{\kappa^2}$$


Os
4.5
4
3.5
3
2.5
2
1.5
1
0
1
2
3
4
5
6
7
8
λ=1
λ=2
λ=5,10
5κ*κ/6

ALL DIMENSIONLESS PARAMETERS MEAN SOMETHING IMPORTANT AND USEFUL!

$$\frac{\kappa^2}{2} = \frac{cPC_0L^2}{AD2}\frac{\overline{C}-C_0}{\overline{C}-C_0} = \frac{\left(cLP(\overline{C}-C_0)\right)C_0\frac{1}{A}}{D\left(\overline{C}-C_0\right)/(L/2)}$$

Now,

$$\underbrace{\left(cLP(\overline{C}-C_0)\right)C_0\frac{1}{A}}_{\text{water in by osmosis}} \approx F_{conv.}$$

$$F_{diff} \approx -D\left.\frac{dC^*}{dx^*}\right|_{ave} \approx D\frac{\overline{C}-C_0}{L/2}$$

That is,

$$\frac{\kappa^2}{2} \approx \frac{F_{conv.}}{F_{diff.}}$$

Thus,

$$Os = \frac{Os^*}{C_0} = \frac{F^*(L)}{v^*(L)C_0} = \frac{F_{conv.} + F_{diff}}{F_{conv.}} = 1 + \frac{F_{diff}}{F_{conv.}} \approx 1 + \frac{2}{\kappa^2}$$

THE STEPS OF THE ANALYSIS:

- A qualitative idea of the model
- Identify physical mechanisms
- Sort out the geometry
- The mathematical modelling: based on conservation principles!
- Scaling
- Perturbation analysis
- Modified scaling
- Numerical experiments
- Final analysis
- Conclusions