10/06/2022

The nephron: loop of Henle

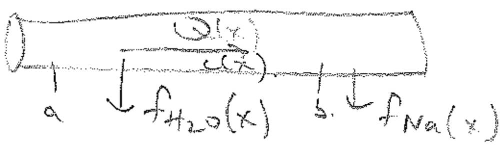
Function of kidney is to regulate composition of blood plasma (part of blood left when cells removed). Goal of this chapter: model regulation of Na^+ concentration in the plasma.

Basic unit of kidney: the nephron. Kidney has 10^6 nephrons connected in parallel.

Details in book: the summary – that the changes in Na^+ concentration occur in the loop of Henle, which will be our modelling focus.

Dynamics of transport

Consider steady flow through a tube



f = flux per unit length

Q = flow rate

Mass balance of water

$$Q(a) - Q(b) = \int_a^b f_{H_2O}(x)\,dx.$$

Now differentiate wrt b

$$-Q'(b) = f_{H_2O}(b).$$

Since b is arbitrary, get

$$0 = Q' + f \quad \text{or} \quad \boxed{0 = \frac{dQ}{dx} + f_{H_2O}}$$

If $f=0$, Q is constant

Now consider transport of Na^+. Mass balance between a and b gives $c(a)Q(a) - c(b)Q(b) = \int_a^b f_{Na}(x)\,dx$ and so the argument is the same with cQ replacing Q.

The resulting ODE is

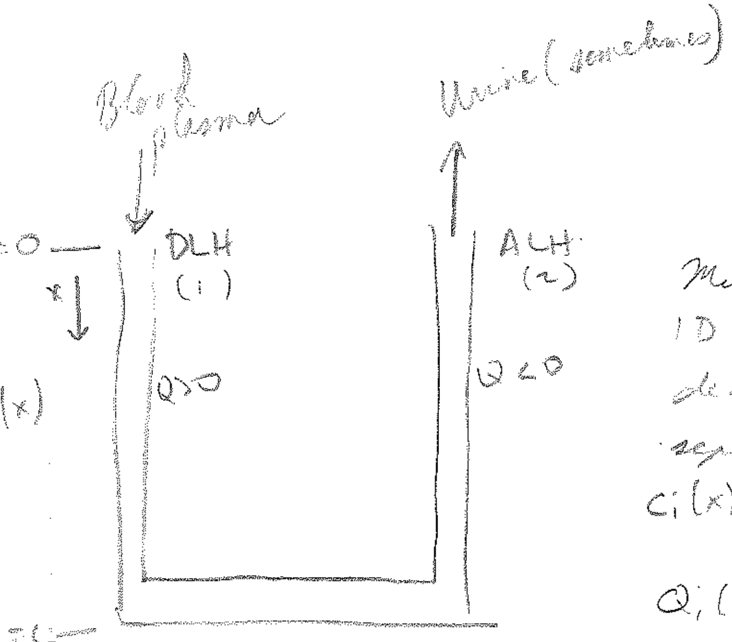
$$\boxed{0 = \frac{d}{dx}(cQ) + f_{Na}.}$$

When $f_{Na} = 0$, cQ is constant.

We will apply these equations to the different tubules in the kidney.

The loop of Henle

Is a subunit in the kidney: the job of the loop is to remove Na^+ and water from the tubular fluid that enters it. The fluid leaving Henle's loop eventually becomes urine.



Model of loop of Henle
1D model where we consider the descending and ascending loop separately.

$c_i(x)$ = concentration (Na+) in tube i
$i = 1, 2$

$Q_i(x)$ = water flow rate

Let $c(x)$ = external sodium concentration

Physiological assumptions + model

1) The descending limb is permeable to water but not Na+. Permeability is large enough to equilibrate internal + external concentrations:

$$c_1(x) = c(x)$$
$$0 = \frac{d}{dx}(c_1 Q_1)$$
$$\frac{dQ_1}{dx} + f_{H_2O}(x) = 0$$

2) Na^+ is pumped out of ascending limb at fixed rate f^*_{Na}. Assume ascending limb impermeable to water.

$$\frac{dQ_2}{dx} = 0.$$
$$\frac{d}{dx}(c_2 Q_2) + f^*_{Na} = 0.$$

3) at turn of the loop assume continuity of ascending + descending limb

$$c_1(L) = c_2(L)$$
$$Q_1(L) = -Q_2(L)$$

4) Consider the other part of the kidney, called the peritubular capillaries that picks up sodium and water. In our model, rate of sodium pick up from ascending limb $= f^*_{Na}$, while the rate of water pick up from descending limb is $f^{(1)}_{H_2O}$. But the sodium must come through the water! So

$$\boxed{f^*_{Na} = f^{(1)}_{H_2O}(x)\, c(x)}$$

Let us derive an ODE for $c(x)$ from

$$0 = \frac{dQ_1}{dx} + f^{(1)}_{H_2O} = \frac{dQ_1}{dx} + \frac{f^*_{Na}}{c} \longrightarrow c\,\frac{dQ_1}{dx} + f^*_{Na} = 0$$

But we know sodium is conserved in the descending loop

$$\frac{d}{dx}\left(c\,Q_1\right) = 0 \longrightarrow Q_1(x)\,c(x) = Q_1(0)\,c(0)$$

$$\boxed{Q_1(x) = \frac{Q_1(0)\,c(0)}{c(x)}}$$

important for later

So $\quad c(x)\,Q_1(0)\,c(0)\,\frac{d}{dx}\left(\frac{1}{c(x)}\right) + f^*_{Na} = 0.$

$$= \cancel{c(x)}\,Q_1(0)\,c(0)\;-\;\frac{1}{c^{\cancel{2}}(x)}\,\frac{dc}{dx} + f^*_{Na} = 0.$$

$$\boxed{\frac{dc}{dx} = \frac{f^*_{Na}\,c(x)}{Q_1(0)\,c(0)}}$$

<u>Exercise:</u> Solve this for $c(x)$.

$$c(x) = c(0)\exp\left(\frac{f^*_{Na}\,x}{Q_1(0)\,c(0)}\right)$$

So

$$c(L) = c(0)\exp\left(\frac{f^*_{Na}\,L}{Q_1(0)\,c(0)}\right)$$

Note that $f^*_{Na}L$ = rate at which Na^+ is pumped out through ALH.
$Q_1(0)c(0)$ = total rate at which Na^+ enters DLH.

So $\quad \alpha = \dfrac{f^*_{Na}\,L}{Q_1(0)\,c(0)} < 1$

determines concentrating ability of nephron through eqn

$$c(L) = c(0)\exp(\alpha).$$

Now ready to look at ascending limb (Na^+ pumped out).

$$Q_2(x) = Q_2(L) = -Q_1(L) = -\frac{Q_1(0)\,c(0)}{c(L)} = -Q_1(0)\exp(-\alpha)$$

Since Q_2 is constant, the sodium eqn

$$0 = \frac{d}{dx}\left(Q_2 c_2\right) + f^*_{Na}$$

becomes

$$Q_2\,\frac{dc_2}{dx} = -f^*_{Na} \Rightarrow \frac{dc_2}{dx} = \frac{f^*_{Na}\exp(\alpha)}{Q_1(0)}$$

<u>Exercise</u> Solve this ODE $\quad c_2(L) = c_1(L)$

$$\boxed{c_2(x) = c_2(L) + \frac{f^*_{Na}\exp(\alpha)}{Q_1(0)}\,(x-L)}$$

But by continuity

$$c_2(L) = c_1(L) = c(L) = c(0)\exp(\alpha). \text{ So}$$

$$c_2(x) = c(0)\exp(\alpha) + (x-L)\frac{f^*_{Na}\exp(\alpha)}{Q_1(0)}$$

and
$$c_2(0) = c(0)\exp(\alpha) - \frac{Lf^*_{Na}}{Q_1(0)\,c(0)}\exp(\alpha).\,c(0)$$

$$= c(0)\left[\exp(\alpha) - \alpha\exp(\alpha)\right]$$

$$= c(0)\exp(\alpha)(1-\alpha).$$

When $\alpha \neq 0$, $\exp(\alpha)(1-\alpha) < 1$. So $c_2(0) < c(0)$.

Fluid leaving ALH is more dilute than blood plasma

Do we want this and how can we control α? Next time.