Ex. Tetracycline is an antibiotic prescribed for a range of problems, from ~~ance~~ acne to acute infections. A course is taken orally and the drug moves from the GI-tract through the bloodstream, from which it is removed by the kidneys and excreted in the urine.

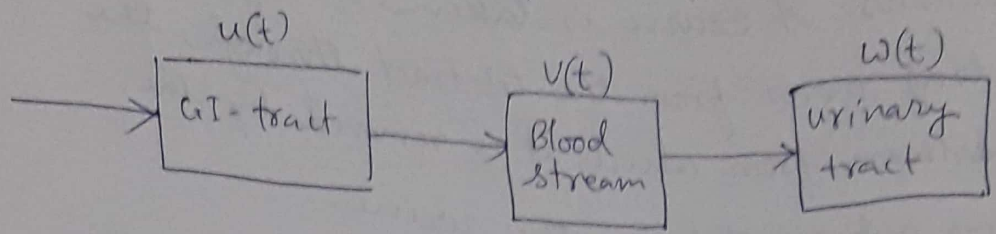
(a) Write word equations to describe the movement of a drug through the body, using three compartments: the GI-tract, the bloodstream and the urinary tract. Note that the urinary tract can be considered as an absorbing compartment, that is, the drug enters but is not removed from the urinary tract.

(b) From the word equations develop the differential equation system that describe this process, definining all variables and parameters as required.

(c) The constants of proportionality associated with the rates at which teracycline (measured in ~~mim~~ miligrams) diffuses from the GI-tract into the bloodstream, and then is removed, are 0·72 $hour^{-1}$ and 0·15 $hour^{-1}$, respectively (Borelli and Columan 1996). Suppose, initially, the amount of tetracycline in the GI-tract is 0·0001 miligram, while there is none in the bloodstream or urinary tract.

Solve this problem analytically and thus establish how the levels of tetracycline change with time in each of the compartments. In case of a single dose establish the maximum level reached by the drug in the bloodstream and how long it take to reach this level with the initial condition as given above.

Solution: Let $u(t)$, $v(t)$ and $w(t)$ are the amount of drug in GI-tract, Bloodstream and urinary tract respectively.



(a) Word Eqns. are

$$\left\{\begin{matrix}\text{rate of change of}\\ \text{drug in GI-tract}\end{matrix}\right\} = -\left\{\begin{matrix}\text{rate of drug}\\ \text{leaves GI-tract}\end{matrix}\right\},$$

$$\left\{\begin{matrix}\text{rate of change of}\\ \text{drug in bloodstream}\end{matrix}\right\} = \left\{\begin{matrix}\text{rate of drug}\\ \text{enters}\\ \text{bloodstream}\end{matrix}\right\} - \left\{\begin{matrix}\text{rate of drug}\\ \text{leaves}\\ \text{bloodstream}\end{matrix}\right\}$$

and

$$\left\{\begin{matrix}\text{rate of change of}\\ \text{drug in urinary tract}\end{matrix}\right\} = \left\{\begin{matrix}\text{rate of drug}\\ \text{enters}\\ \text{urinary tract}\end{matrix}\right\}$$

(b) The word eqns transforms to differential eqns:

$$\frac{du}{dt} = -m_1 u ; \quad u(0) = U_0 \longrightarrow (1)$$

$$\frac{dv}{dt} = m_1 u - m_2 v ; \quad v(0) = 0 \longrightarrow (2)$$

$$\frac{dw}{dt} = m_2 v ; \quad w(0) = 0 \longrightarrow (3)$$

where m_1 & m_2 are rate constants and $m_1 \neq m_2$.

(c) Given that

$m_1 = 0.72\ hr^{-1}$

$m_2 = 0.15\ hr^{-1}$

$u_0 = 0.0001\ mg$

Now, (1) $\Rightarrow$

$$\frac{du}{u} = -m_1\,dt$$

Integrating, we get

$$\log_e u = -m_1 t + \log_e c_1, \quad c_1 \text{ is constant}$$

$$\Rightarrow \quad u = c_1 e^{-m_1 t} \longrightarrow (4)$$

using $u(0) = u_0$ in (4), we get

$$c_1 = u_0$$

$\therefore$ (4) $\Rightarrow$

$$u = u_0 e^{-m_1 t} \longrightarrow (5).$$

$$\Rightarrow \quad u = 0.0001\, e^{-0.72t} \longrightarrow (6).$$

Again, putting the value of u in (2), we get

$$\frac{dv}{dt} = +m_1 u_0 e^{-m_1 t} - m_2 V$$

$$\Rightarrow \quad \frac{dv}{dt} + m_2 V = m_1 u_0 e^{-m_1 t}$$

which is linear.

Its I.F. $= e^{\int m_2\,dt}$

$= e^{m_2 t}$

Scanned with CamScanner

& its solⁿ is

$$V e^{m_1 t} = \int m_1 u_0 e^{-m_1 t} \cdot e^{m_2 t} \, dt + c_2 \text{ (const)}$$

$$= \int m_1 u_0 e^{(m_2 - m_1)t} \, dt + c_2$$

$$\Rightarrow V e^{m_2 t} = m_1 u_0 \frac{e^{(m_2 - m_1)t}}{m_2 - m_1} + c_2 \rightarrow (7)$$

using $V(0) = 0$ in (7), we get

$$0 = m_1 u_0 \frac{1}{m_2 - m_1} + c_2$$

$$\Rightarrow c_2 = \frac{-m_1 u_0}{m_2 - m_1}$$

Putting this value of c_2 in (7), we get

$$V \cdot e^{m_2 t} = m_1 u_0 \frac{e^{(m_2 - m_1)t}}{m_2 - m_1} - \frac{m_1 u_0}{m_2 - m_1}$$

$$\Rightarrow V = m_1 u_0 \frac{e^{-m_1 t}}{m_2 - m_1} - m_1 u_0 \frac{e^{-m_2 t}}{m_2 - m_1}$$

$$\Rightarrow V = \frac{m_1 u_0}{m_2 - m_1} \left[e^{-m_1 t} - e^{-m_2 t} \right] \rightarrow (8)$$

Putting the valuesⁿ of m_1, m_2 & u_0 in (8), we get

$$V = \frac{0.0001 \times 0.72}{0.15 - 0.72} \left(e^{-0.72t} - e^{-0.15t} \right)$$

$$= -0.00012 \left(e^{-0.72t} - e^{-0.15t} \right)$$

$$= 0.00012 \left(e^{-0.15t} - e^{-0.72t} \right) \rightarrow (9)$$

Now, putting the value of v from (8) in (3), we get

$$\frac{dw}{dt} = m_2 \frac{m_1 u_0}{m_2 - m_1}\left(e^{-m_1 t} - e^{-m_2 t}\right)$$

⇒ Integrating we get –

$$w(t) = \frac{m_1 m_2 u_0}{m_2 - m_1}\left(\frac{e^{-m_1 t}}{-m_1} - \frac{e^{-m_2 t}}{-m_2}\right) + C_3$$

$$\Rightarrow w(t) = \frac{m_1 m_2 u_0}{m_2 - m_1}\left(\frac{e^{-m_2 t}}{m_2} - \frac{e^{-m_1 t}}{m_1}\right) + C_3 \rightarrow (10)$$

using $w(0) = 0$, in (10), we get –

$$C_3 = -\frac{m_1 m_2 u_0}{m_2 - m_1}\left(\frac{1}{m_2} - \frac{1}{m_1}\right)$$

$$= -\frac{m_1 m_2 u_0}{m_2 - m_1} \times \frac{m_2 - m_1}{m_1 m_2} = u_0$$

$$\Rightarrow C_3 = u_0$$

Putting $C_3 = u_0$ in (10), we get –

$$w(t) = \frac{m_1 m_2 u_0}{m_2 - m_1}\left(\frac{e^{-m_2 t}}{m_2} - \frac{e^{-m_1 t}}{m_1}\right) + u_0 \rightarrow (11)$$

Putting the value of m_1, m_2 & u_0 in (11), we get –

$$w(t) = \frac{0{\cdot}72 \times 0{\cdot}15 \times 0{\cdot}0001}{0{\cdot}15 - 0{\cdot}72}\left(\frac{e^{-0{\cdot}15t}}{0{\cdot}15} - \frac{e^{-0{\cdot}72t}}{0{\cdot}72}\right) + 0{\cdot}0001$$

$$\Rightarrow w(t) = 0{\cdot}0002\left(\frac{e^{-0{\cdot}15t}}{0{\cdot}15} - \frac{e^{-0{\cdot}72t}}{0{\cdot}72}\right) + 0{\cdot}0001$$