4.10 pharmacokinetics model

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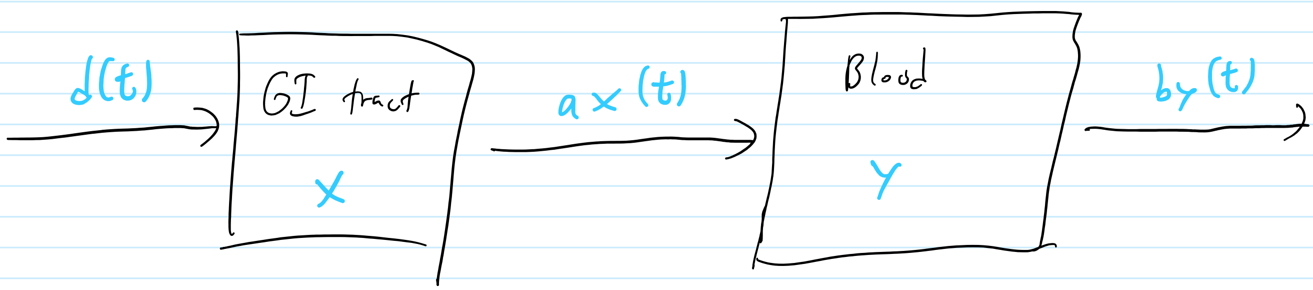
1. Ingest a drug orally and it passes in the gastrointestinal (GI) tract at a rate $d(t)$.

2. The drug passes from GI tract to blood at a rate a, proportional to the GI tract concentration $x(t)$.

3. The drug leaves the blood at rate b, proportional to the blood concentration $y(t)$



$$\begin{cases} \dfrac{dx}{dt} = -ax(t) + d(t) \\[2mm] \dfrac{dy}{dt} = ax(t) - by(t), \qquad a, b > 0, \quad a \neq b. \end{cases}$$

Alternately,

$$\underbrace{\begin{bmatrix} \dot{x}(t) \\ \dot{y}(t) \end{bmatrix}}_{\dot{X}(t)} = \underbrace{\begin{bmatrix} -a & 0 \\ a & -b \end{bmatrix}}_{A} \underbrace{\begin{bmatrix} x(t) \\ y(t) \end{bmatrix}}_{X(t)} + \underbrace{\begin{bmatrix} d(t) \\ 0 \end{bmatrix}}_{G(t)}$$

Then

$$X(t) = e^{At} X_0 + e^{At} \int_0^t e^{-As} G(s)\, ds.$$

Note that the eigenvalues of A are $-a$, $-b$ and are negative, so the homogeneous solution $X_h(t) = e^{At} X \longrightarrow 0$ as $t \to \infty$

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the homogeneous solution $X_h(t) = e^{At} X_0 \longrightarrow 0$ as $t \to \infty$.

Thus, $\lim_{t \to \infty} X(t) = \lim_{t \to \infty} e^{At} \int_0^t e^{-As} G(s)\, ds$.

$$\begin{bmatrix} -\frac{a-b}{a} & 0 \\ 1 & 1 \end{bmatrix}^{-1}$$

Want e^{At}

$$At = \begin{bmatrix} -at & 0 \\ at & -bt \end{bmatrix} = \begin{bmatrix} -\frac{a-b}{a} & 0 \\ 1 & 1 \end{bmatrix} \begin{bmatrix} -at & 0 \\ 0 & -bt \end{bmatrix} \overbrace{\begin{bmatrix} -\frac{a}{a-b} & 0 \\ \frac{a}{a-b} & 1 \end{bmatrix}}$$

Thus,

$$e^{At} = \begin{bmatrix} -\frac{a-b}{a} & 0 \\ 1 & 1 \end{bmatrix} \begin{bmatrix} e^{-at} & 0 \\ 0 & e^{-bt} \end{bmatrix} \begin{bmatrix} -\frac{a}{a-b} & 0 \\ \frac{a}{a-b} & 1 \end{bmatrix}$$

$$= \begin{bmatrix} -\frac{a-b}{a} & 0 \\ 1 & 1 \end{bmatrix} \begin{bmatrix} e^{-at} \cdot \frac{-a}{a-b} & 0 \\ e^{-bt} \cdot \frac{a}{a-b} & e^{-bt} \end{bmatrix}$$

$$= \begin{bmatrix} e^{-at} & 0 \\ \frac{a}{a-b}\left[e^{-bt} - e^{-at}\right] & e^{-bt} \end{bmatrix}$$

Alternately

$$\begin{cases} \dot{x} = -ax + d(t) \\ \dot{y} = ax - by \end{cases}$$

$\leftarrow$ has no dependence on y.

- Can solve for $x(t)$ first, and then solve for $y(t)$

Ex. Let's say $d(t) = 1$, $x(0) = 0 = y(0)$

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$$\begin{cases} \dot{x} = -ax + 1 \\ \dot{y} = ax + by \end{cases}$$

$$\dot{x} + ax = 1$$

Char. eq $\lambda + a = 0$, $\lambda = -a$ $\Rightarrow x_h(t) = Ce^{-at}$ — Hom solution

$x_p = K$, $aK = 1$, $K = \frac{1}{a}$, $x_p(t) = \frac{1}{a}$ — particular solution

$$\Rightarrow x(t) = x_h(t) + x_p(t) = \frac{1}{a} + Ce^{-at}$$

$$x(0) = 0 = \frac{1}{a} + C \Rightarrow C = -\frac{1}{a}$$ IVP

$$\Rightarrow x(t) = \frac{1}{a}\left(1 - e^{-at}\right)$$

Thus, need to solve $\dot{y} = ax + by$

$$\Rightarrow \dot{y} = \left(1 - e^{-at}\right) + by$$

With some techniques, $y(t) = \frac{1}{b} + \frac{e^{-at}}{a-b} - \frac{ae^{-bt}}{b(a-b)}$.

So $\lim_{t\to\infty} x(t) = \frac{1}{a}$, $\lim_{t\to\infty} y(t) = \frac{1}{b}$.

In reality, often something periodic, e.g. if drug taken every 6 hours and released into GI tract over half an hour.

$$d(t) = \begin{cases} 2, & 0 \le t \le \frac{1}{2} \\ 0, & \frac{1}{2} < t < 6 \end{cases}, \quad d(t+6) = d(t).$$