Contents

$$\frac{dC}{dt} = -\frac{V_{max}}{k_m + C} C, \quad C(0^+) = C_0 \tag{1}$$

Constructed an implicit solution to (1)

$$\frac{1}{V_{max}} \left[(C_0 - C) + k_m \ln \frac{C_0}{C} \right] \tag{2}$$

$$F(C) = t$$

Given a time t – solve (2) for C numerically (Newton's Method).
BUT – we would need to know V_{max} and k_m.
However, we were able to compute the half-life from (2) – very useful!

$$t_{\frac{1}{2}} = \frac{k_m}{V_{max}} \ln 2 + \frac{C_0}{2V_{max}}$$

where $\left[\frac{V_{max}}{k_m} \right] = \frac{1}{T}$
If we could find F^{-1} then $F^{-1}(F(C)) = F^{-1}(t) \Rightarrow C = F^{-1}(t)$.

$$\begin{aligned} F(c) &= \frac{1}{V_{max}} \left[(C_0 - C) + k_m \ln \frac{C_0}{C} \right] \\ &= t \end{aligned} \tag{3}$$

Get a better form of (3).

$$\begin{aligned}
\left[(C_0 - C) + k_m \ln\frac{C_0}{C}\right] &= V_{max} t \\
\frac{C_0 - C}{k_m} + \ln\frac{C_0}{C} &= -\frac{V_{max}}{k_M} t \\
e^{\frac{C_0-C}{k_m} + \ln\frac{C_0}{C}} &= e^{-\frac{V_{max}}{k_M} t} \\
e^{\frac{C_0-C}{k_m}} e^{\ln\frac{C_0}{C}} &= e^{-\frac{V_{max}}{k_M} t} \\
e^{\frac{C_0-C}{k_m}} \frac{C_0}{C} &= e^{-\frac{V_{max}}{k_M} t} \\
e^{\frac{C_0}{k_m}} e^{-\frac{C}{k_m}} \frac{C_0}{C} &= e^{-\frac{V_{max}}{k_M} t} \\
e^{-\frac{C}{k_m}} \frac{1}{C} &= \frac{1}{C_0} e^{-\frac{V_{max}}{k_M} t} e^{\frac{-C_0}{k_m}}
\end{aligned}$$

Does $G = xe^x$ have an inverse G^{-1}?

$$\begin{aligned}
G(x) &= xe^x \\
G(0) &= 0 \\
G'(x) &= e^x + xe^x \\
&= 0 \\
G''(x) &= 2e^x + xe^x \\
G''(0) &= 2 \\
&>0 \text{ (concave up)} \\
G'(-1) &= -\frac{1}{e} \\
\lim_{x \to -\infty} xe^x &= 0
\end{aligned}$$

On $-1 < x < \infty$, $G(x)$ is 1 to 1 $\Longrightarrow G^{-1}$ exists on $-\infty < x < -1$.
Need a name for G^{-1}
. Call $G^{-1}(x) =$ Lambert $W(x)$.

$$\begin{aligned}
G(G^{-1}(x)) &= G(Lambert\ W(x)) \\
&= x \\
G(G^{-1}) &= W(x)e^{W(x)} \\
G(x) &= g(t) \\
&= xe^x \\
x &= G^{-1}(G) \\
&= G^{-1}(g(t))
\end{aligned}$$

becomes $x = W\left(x_0 e^{x_0} e^{-\frac{V_{max}}{k_m}}\right)$

$$C(t) = k_m W\left(\frac{C_0}{k_M} e^{\frac{(C_0 - V_{max})t}{k_M}}\right) \tag{4}$$

Periodic Dosing with non-linear clearance

Key: Each does of size C_0 is given at intervals τ. Decay rate between doses depends on $C(t)$. This is different than the previous periodic dosing with 1st order clearance.
Iterate:

$$\begin{aligned} v_0 &= c_0 \\ u_1 &= k_m LambertW\left(\frac{C_0}{k_M} e^{\frac{C_0 - V_{max} t}{k_M}}\right) \\ v_1 &= u_1 + c_0 \\ u_2 &= k_m LambertW\left(\frac{u_1 + C_0}{k_M} e^{\frac{u_1 + C_0 - V_{max} t}{k_M}}\right) \end{aligned}$$

Do the following limits exist?

$$v_n \to v_\infty$$
$$u_n \to u_\infty$$

Are the limits in the therapeutic window? $MTL < u_\infty < v_\infty < MToL$

Cleanup topics

Enzyme with 2 sites.
We expect that the reaction would be

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} C_1 + S \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} C_2 \to P + E \tag{5}$$

Non-realistic reaction for simplicity!

$$2S + E \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} C_2 \overset{k_p}{\to} E + 2P$$

Epidemiology – model of infectious diseases

Examples:

- AIDS – HIV
- H1N1 flu – Spanish flu (1918-1920)
- Malaria
- Zika
- Hep-C
- SARS
- MERS

- COVID-19

Who models:

- CDC
- WHO
- John Hopkins University - COVID data site

0.3.1 Types of Models

1. Single - individual
   - Viral load $\approx 10^{12}$
   - Effectiveness of specific treatment
2. Spread in an entire population
   - spread of epidemic
3. Agent based models - flow single individuals in (2) – Zika in Miami
   - Spread in localized area

Simple Epidemic Model

Population of fixed size N.
Subdivide population into 2 groups.

1. Susceptible $S(t)$.
   - Health but can contract the disease.
2. Infectives – infected individual $I(t)$
   - Have disease and can spread it on contact

Assumption: Well-mixed population.
Any individual is equally likely to come in contact with any other individuals $\leftarrow$ cannot identify individuals with disease.

SIS model - compartment model

Use modified “Law of Mass Action”. Contact rate $\propto SI$. β = recovery rate, μ = recovery rate per individual $E[time\ sick] = \frac{1}{\mu}$.

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI + \mu I \qquad & S(0) = N - 1 \\ \frac{dI}{dt} &= \beta SI - \mu I \qquad & I(0) = 1 \end{aligned} \tag{6}$$

Look for conservation laws:

$$\begin{aligned} \frac{dS}{dt} + \frac{dI}{dt} &= 0 \\ \frac{d}{dt}(S + I) &= 0 \\ S(t) + I(t) &= S(0) + I(0) \\ I(t) &= N - 1 + 1 - S(t) \\ I(t) &= N - S(t) \end{aligned}$$