Assignment 2 MATH 2200

Michael Walker, March 2021

a. Part 1 of 1

If a single dose of gentamicin is administered to the body so that the resulting blood drug concentration is $7.5\ mg/liter$, then in two hours the blood drug concentration has decayed to $4\ mg/liter$. Set up and solve a differential equation (initial value problem really) to give $G(T)$, the drug concentration in the blood t hours after the single dose

Solution: $G(T) = 7.5e^{\frac{t}{2}\cdot ln(4/7.5)}$

Constants

$$G_o = 7.5mg/L$$
$$G_1 = 4mg/L$$
$$t_o = 0$$
$$t_1 = 2$$
$$G(t) = Amount\ of\ drug\ in\ system\ at\ time\ t.$$

Use exponential decay model

$$\frac{dG}{dt} = -kG \therefore \frac{1}{G}dG = -kd\cdot t$$
$$\int \frac{1}{G}dG = -k\int dt \therefore ln(G) = -k\cdot t + C. \rightarrow e^{ln(G)} = e^{-k\cdot t+C}$$
$$G = C\cdot e^{-k\cdot t}$$

Find constant C

$$G_o = C\cdot e^{-k\cdot t_0} \rightarrow 7.5 = C\cdot e^{-k(0)} \therefore C = 7.5.$$

Find decay constant K

$$G = G_0 e^{-k\cdot t_0} \wedge G = G_1 = G_0 e^{-k\cdot t_1}$$
$$\rightarrow \frac{G_1}{G_0} = e^{-k\cdot t_1} \rightarrow ln\left(\frac{G_1}{G_0}\right) = ln\left(e^{-k\cdot t_1}\right)$$
$$\therefore k = \frac{-ln(G_1/G_0)}{T_1} = -\frac{1}{2}ln(4/7.5).$$

Solution

$$G = G(t) = C\cdot e^{-k\cdot t} = 7.5e^{\frac{t}{2}\cdot ln(4/7.5)} \blacksquare$$

b. Part 1 of 1

(b) Compute the half-life of gentamicin in the body. (The amount of time it takes for half of the drug to be eliminated).

Solution: $T = \dfrac{2 \cdot ln\left(\frac{1}{2}\right)}{ln(4/7.5)}$

Find half – life T

$$G = G_0 e^{-kT} \rightarrow \frac{1}{2} \cdot G_0 = G_0 e^{-kT} \rightarrow \frac{1}{2} = e^{-kT} \therefore T = -\frac{1}{k} ln\left(\frac{1}{2}\right).$$

$$\therefore T = -\frac{ln\left(\frac{1}{2}\right)}{-\frac{1}{2} ln(4/7.5)} = \frac{2 \cdot ln\left(\frac{1}{2}\right)}{ln(4/7.5)} \blacksquare$$

c. Part 1 of 1

Suppose we have an IV drip set up which administers $30\ mg/liter/day$ (the IV continuously drips gentamicin into the bloodstream so that over $24\ hours$, the total amount which has gone into the body is $30mg$ for every $liter$ of blood).

If we let G be the concentration of gentamicin in the blood we can write.

$$dG/dt = -kG + 1.25$$

Where the time t is measured in hours. Why does this equation have this form ?

In other words, explain why the $-kG$ term and the $+1.25$ term on the right hand side of the equation make sense.

Note: the constant k is the same as in part (a) - you should have computed it in part (a).

Solution

The rate of change in G with respect to t, is proportional to the amount G in the bloodstream, where K is the proportionality. So kG is the rate at which the gentamicin is being removed. The value $1.25\ mg/liter/hour$ of gentamicin is added periodically over 24 hours ■

d. Part 1 of 1

Recall that a quantity has a steady-state value when the quantity is no longer changing. If G is no longer changing, what does that mean for the value of $\frac{dG}{dt}$? Use this observation, and the
formula from part (c) to compute the steady-state value for G (Ie. at which concentration, G, is G not changing?).

Solution:

If $\frac{dG}{dt}$ is no longer changing, then the slope of $\frac{dG}{dt} = 0$

$\therefore G = -\dfrac{1.25}{\frac{1}{2}ln(4/7.5)}$

$$
\begin{aligned}
\frac{dG}{dt} &= -kG + 1.25 \\
0 &= -kG + 1.25 \\
G &= \frac{1.25}{k} \\
\textbf{Substitute k} &= -\frac{1}{2}ln(4/7.5) \\
\rightarrow G &= -\frac{1.25}{\frac{1}{2}ln(4/7.5)} \blacksquare
\end{aligned}
$$

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Solve the differential equation from (c) with initial condition $G(0) = 0$ to obtain a formula for $G(t)$.

Solution: $G(t) = \frac{1.25}{e^{kt}k}\left(e^{kt} - 1\right)$; Such that $k = -\frac{1}{2}ln(4/7.5)$.

Solve DE using integrating factors

$$\frac{dG}{dt} = -kG + 1.25 \rightarrow \left[\frac{dG}{dt} + kG = 1.25\right]$$

Find integrating factor

$$let\ p(t) = k$$
$$q(t) = 1.25$$
$$\rightarrow \mu = e^{\int p(t)dt} = e^{\int k \cdot dt} = e^{kt}$$
$$\mu\frac{dG}{dt} + \mu \cdot p(t)G = \mu \cdot q(t) \rightarrow \frac{d}{dt}[\mu G] = \mu \cdot q(t)$$

Integrate both sides

$$\int \frac{d}{dt}[\mu G] \cdot dt = \int \mu \cdot q(t) \cdot dt$$
$$\therefore e^{kt}G = 1.25\int e^{kt} \cdot dt = \frac{1.25}{k} \cdot e^{kt} + C.$$

Solve constant C

$$e^{k(0)}0 = \frac{1.25}{k} \cdot e^{k(0)} + C. \rightarrow \left[C = -\frac{1.25}{k}\right]$$

Find G(t)

$$e^{kt}G = \frac{1.25}{k} \cdot e^{kt} - \frac{1.25}{k} = \frac{1.25}{k}\left(e^{kt} - 1\right)$$
$$\rightarrow G = \frac{1.25}{e^{kt}k}\left(e^{kt} - 1\right); Such\ that\ k = -\frac{1}{2}ln(4/7.5) \blacksquare$$

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Use the formula for $G(t)$ from (e) to compute $\lim_{t \to \infty} G(t)$. Compare your answer to your answer from part (d). What is the meaning of this quantity in terms of a patient who is hooked up to the IV for very long time ?

Solution: $-\dfrac{1.25}{\frac{1}{2}ln(4/7.5).}$

The meaning of this quantity in terms of a patient who is hooked up to the IV for a very long time. Is the "inflow" of drug is in equilibrium with the "outflow" of the drug.

Note: (I don't know the medical terms).

$$\lim_{t \to \infty} G(t) = \lim_{t - \infty} \frac{1.25}{e^{kt}k}\left(e^{kt} - 1\right) = \frac{1.25}{k} \cdot \lim_{t - \infty} \frac{\left(e^{kt} - 1\right)}{e^{kt}}$$

$$k = -\frac{1}{2} ln(4/7.5).$$

$$Let\ C = \frac{1.25}{k}$$

$$\to C \cdot \lim_{t - \infty} \frac{\left(e^{kt} - 1\right)}{e^{kt}} = C \cdot \lim_{t - \infty} \frac{\left(\frac{e^{kt}}{e^{kt}} - \frac{1}{e^{kt}}\right)}{\frac{e^{kt}}{e^{kt}}} = C \cdot \lim_{t - \infty}\left(1 - \frac{1}{e^{kt}}\right)$$

$$= C \cdot \left[\lim_{t - \infty}(1) - \lim_{t - \infty}\left(\frac{1}{e^{kt}}\right)\right] = C \cdot (1 - 0) = C$$

$$= \frac{1.25}{-\frac{1}{2} ln(4/7.5)} \blacksquare$$

g. Page 1 of 1

How long does it take for the concentration of gentamicin in the blood to reach 95% of the steady-state value?

Solution : $t = \frac{1}{k} \cdot ln\left(\frac{1.25}{0.0625}\right);\ Such\ that\ k = -\frac{1}{2}ln(4/7.5).$

$$let\ k = -\frac{1}{2}ln(4/7.5)$$

Calculate 95% of steady state

$$\rightarrow G = \frac{0.95 \cdot 1.25}{k} = \frac{1.1875}{k}$$

Find t

$$\frac{1.1875}{k} = \frac{1.25}{e^{kt}k}\left(e^{kt} - 1\right) \rightarrow e^{kt}k \cdot \frac{1.1875}{k} = 1.25\left(e^{kt} - 1\right)$$

$$\rightarrow e^{kt} \cdot 1.1875 = 1.25\left(e^{kt} - 1\right)$$

$$= 1.25e^{kt} - 1.25$$

$$\rightarrow 1.1875 = 1.25 - \frac{1.25}{e^{kt}} \rightarrow 1.1875 - 1.25 = -\frac{1.25}{e^{kt}}$$

$$\rightarrow -0.0625 = -\frac{1.25}{e^{kt}} \rightarrow 0.0625 = \frac{1.25}{e^{kt}}$$

$$\rightarrow e^{kt} = \frac{1.25}{0.0625} \rightarrow ln\left(e^{kt}\right) = ln\left(\frac{1.25}{0.0625}\right) \rightarrow kt = ln\left(\frac{1.25}{0.0625}\right)$$

$$\therefore\ t = \frac{1}{k} \cdot ln\left(\frac{1.25}{0.0625}\right);\ Such\ that\ k = -\frac{1}{2}ln(4/7.5)\blacksquare$$

h. Page 1 of 1

Instead of using a continuous drip, suppose the gentamicin is administered 3 times per day (every 8 hours) so that the total amount administered in a day is the same. In other words, the amount given at each dose is $10\ mg/liter$. How much of the original dose is left 8 hours later when the $2nd$ dose is about to be given?
If we call this amount $10r$, what is r?

How much of the original dose is left 8 hours later

$$From\ (a):\ G(t) = G_0 e^{-kt} = 10e^{\frac{t}{2}\cdot ln(4/7.5)} \blacksquare$$

How much of the original dose is left 8 hours later

$$G(8) = 10e^{\frac{8}{2}\cdot ln(4/7.5)} = 10e^{4\cdot ln(4/7.5)} \blacksquare$$

If we call this amount 10r, what is r

$$G(8) = G(0)r \rightarrow r = \frac{G(8)}{G(0)}$$

$$\therefore r = \frac{10e^{4\cdot ln(4/7.5)}}{10} = e^{4\cdot ln(4/7.5)} \blacksquare$$

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Explain why the amount after second dose is $10 + 10r$ after the third dose is $10 + 10r + 10r^2$

Explain why after the n^{th} dose is $\sum_{k=0}^{n-1} 10r^k$, before the n^{th}does is $\sum_{k=1}^{n-1} 10r^k$

after the second dose is 10 + 10r

$$\sum_{k=0}^{1} 10r^k = 10 \cdot \sum_{k=0}^{1} [r]^k$$
$$= 10 \cdot \left(r^0 + r^1\right) = 10(1 + r) = 10 + 10r \ \blacksquare$$

after the third dose is $10 + 10r + 10r^2$

$$\sum_{k=0}^{2} 10r^k = 10 \cdot \sum_{k=0}^{2} [r]^k$$
$$= 10 \cdot \left(r^0 + r^1 + r^2\right) = 10\left(1 + r + r^2\right)$$
$$= 10 + 10r + 10r^2 \ \blacksquare$$

after n^{th} dose

$$\sum_{k=0}^{n-1} 10r^k = 10 \cdot \sum_{k=0}^{n-1} [r]^k$$
$$= 10\left(r^0 + r^1 + r^2 + \dots + r^{n-1}\right)$$
$$= 10\left(1 + r^1 + r^2 + \dots + r^{n-1}\right)$$
$$= 10 + 10r + 10r^2 + \dots + 10r^{n-1} \ \blacksquare$$

before the n^{th} dose

$$\sum_{k=1}^{n-1} 10r^k = \sum_{k=0}^{n-1} 10 \cdot [r]^{(k+1)} = \sum_{k=0}^{n-1} 10r \cdot [r]^k = 10r\sum_{k=0}^{n-1} [r]^k$$
$$= 10r\left(r^0 + r^1 + r^2 + \dots + r^{n-1}\right)$$
$$= 10r\left(1 + r + r^2 + \dots + \frac{r^n}{r}\right)$$
$$= 10r\left(1 + r + r^2\right) + \dots + 10r\left(\frac{r^n}{r}\right)$$
$$= 10r + 10r^2 + 10r^3 + \dots + 10r^{n-1} + 10r^n \ \blacksquare$$

i.1. Page 2 of 2

$\therefore$ The expression $\sum_{k=0}^{n-1} 10r^k$ represents the nth immediate dose with no decay r^0, in addition to the previous doses remaining in the blood remaining after having exponentially decayed by the factor r^n. The expression $\sum_{k=1}^{n-1} 10r^k$ representing the amount immediately before the nth dose, represents all of the previous doses after having decayed, but does not introduce an additional term with no decay as opposed to the previous expression.

$\sum_{k=0}^{n-1} 10r^k$ ■

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After a very large number of doses (ie as $n \rightarrow \infty$), compute the amount before and after the n^{th} dose.

Before n$^{\text{th}}$dose

$$a = 10$$

$$r = e^{\frac{8}{2}\cdot ln(4/7.5)} \quad \therefore |r| < 1 \rightarrow convergant\ series.$$

$$\sum_{n=0}^{\infty} 10r^k = \frac{a}{1-r}$$

$$= \frac{10}{1-e^{\frac{8}{2}\cdot ln(4/7.5)}} \blacksquare$$

After n$^{\text{th}}$dose

$$\sum_{k=1}^{\infty} 10r^k = \frac{a}{1-r} - a = \frac{ar}{1-r}$$

$$= \frac{10 \cdot e^{\cdot ln(4/7.5)}}{1-e^{\cdot ln(4/7.5)}} \blacksquare$$