CS 302 : Modeling and Simulation

Drug Concentration

Purvil Mehta (201701073)
Bhargey Mehta (201701074)

Dhirubhai Ambani Institute of Information and Communication Technology
Gandhinagar

January 22, 2020

Contents

1 Introduction

We would be studying the concentration of a drug in the body in this report. We consider three different drug delivering strategies like giving a single drug dose in one instant (impulse), applying a constant drug dosage certain amount of time (impulse train) and applying single drug doses periodically (impulse train). We would be comparing the concentration levels by modeling the whole body as a compartment. We then further refine model by modeling the blood stream as one compartment and the GI-tract as another. The contrast between the two models has been presented in this report.

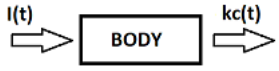
2 Modeling the Problem

We would be following the convention

- C_0 The quantity of the drug dose
- $C(t)$ The drug conc. in the body at time t
- k A rate constant which models excretion
- $D(t)$ The quantity of undissolved drug in the body
- k_1 A rate constant which models the diffusion of the drug
- T the period between drug doses
- τ the time for which a constant drug dose is administered

We used two types of models to solve or model this problem.

2.1 1 - Compartment Model



Each compartment model has three major sections which are inflow, outflow and external parameter. We have assumed some key points over here which will restrict our model to inflow and outflow. Here $I(t)$ is the dose we are applying to body which is the inflow of the compartment and natural excretion of the drug is the outflow of the compartment.

2.1.1 Assumptions

No external factor is affecting the concentration of the drug in the body. For example, no other drug consumed is affecting the behaviour of this drug

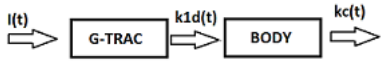
The drug dose administered is instantaneously diffused in the entire body.

The rate of natural excretion is directly proportional to the drug concentration in the body hence the outflow of the drug will be modelled as $kc(t)$ or mathematically,

$$\frac{\mathrm{d}C}{\mathrm{d}t} = I(t) - kC(t)$$

Note that minus sign in $kC(t)$ suggest the decline of the concentration as it is the outflow of the model.

2.2 2 - Compartment Model



We also explore a more realistic model where the drug dose is first dissolved and then affects the concentration in the body.

2.2.1 Assumptions

All the previous assumptions stay true in this model also.

We just relax the assumption that the drug is instantaneously dissolved in the blood stream. Hence we assume that the drug is being dissolved at a rate proportional to the undissolved drug present in the GI-tract which is modelled as another compartment.

We get two coupled differential equations for the system as

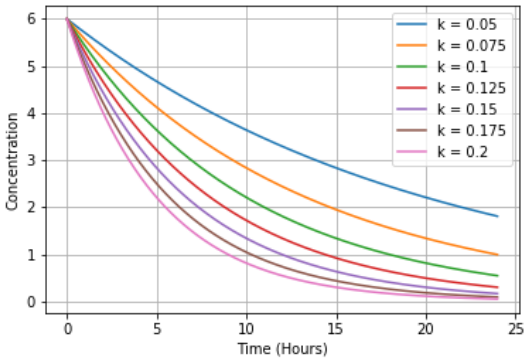
$$\frac{\mathrm{d}D}{\mathrm{d}t} = I(t) - k_1 D(t)$$

$$\frac{\mathrm{d}C}{\mathrm{d}t} = k_1 D(t) - kC(t)$$

3 Drug Administrating Strategies

- Single dose applied as an impulse
- Single dose applied over an interval
- Multiple doses applied as an impulse train
- Multiple doses applied periodically as a rectangular pulse train

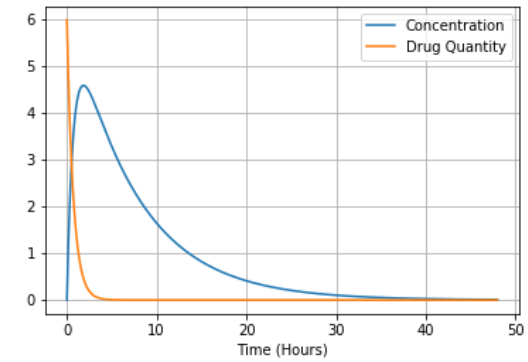
3.1 Single dose applied as an impulse



Solving the equations, we can show that the amount of drug concentration in the body will be equal to

$$C(t) = C_0 e^{-kt}$$

Changing the rate constant k causes the decay to occur faster. Larger the value of k, faster the drug concentration declines. Let $T_{\frac{1}{2}}$ be time for the drug concentration to reach half the initial value C_0. We can show that $T_{\frac{1}{2}} = \frac{\ln 2}{k}$.

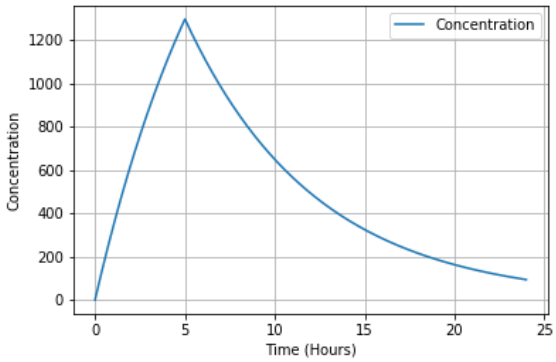


In the two compartment model, the drug in the GI tract follows the exponential decay pattern. Simulating the drug concentration in the blood stream, we see that till the drug is being dissolved, the concentration of the drug in body increases. Hence once the drug in the GI-tract gets decayed completely the concentration in the blood stream peaks.

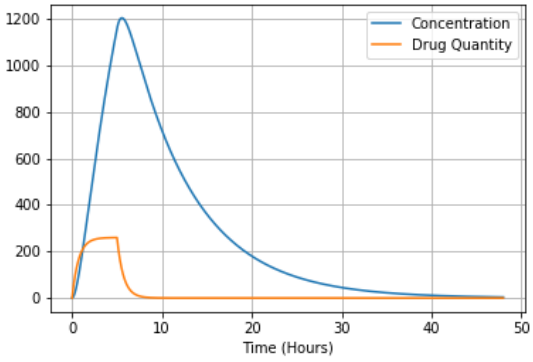
3.2 Single dose applied over an interval

When the drug is applied over an interval over certain amount of time, the different model shows different results. In 1 - compartment model, when dose is applied to the certain time interval, the result shows two type of tendency. The concentration of the drug increases first till the time we applied the drug to the body and then decreases exponentially as we saw in the previous strategy. Solving the equation, we get

$$C(t) = \begin{cases} \frac{C_0}{k}(1 - e^{-kt}) & 0 < t < T \\ \frac{C_0}{k}(e^{kT} - 1)e^{-kt} & T < t < \infty \end{cases}$$



In 2-Compartment model,when we apply drug for certain amount of time, it is clear from the figure that as the drug quantity increases, the concentration of the drug in the body increases. Again the concentration in the blood peaks when the drug quantity in the GI-tract decays completely like in the previous section.



3.3 Multiple doses applied as an impulse train

Solving the equation we get

$$C(t) = C_0 \left[\frac{e^{(n+1)kT} - 1}{e^{kT} - 1} \right] e^{-kt}$$

where $n = \lfloor \frac{t}{T} \rfloor$ Putting the appropriate limits i.e. $n \to \infty$ on $t = nT^+$ to get the minimum and $t = (n+1)T^-$ we get the maximum and minimum drug concentration in the body when the system saturates which is

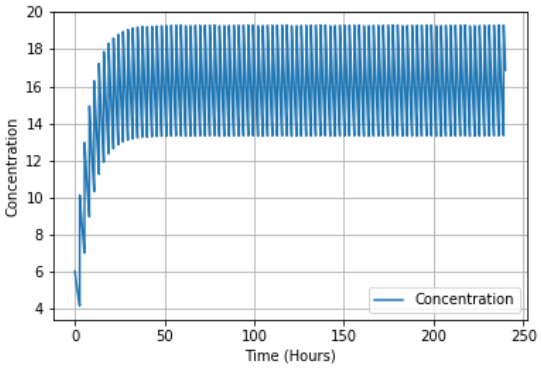
$C_{max} = C_0 \frac{e^{kT}}{e^{kT}-1}$ and $C_{min} = C_0 \frac{1}{e^{kT}-1}$ which follows the intuition that $C_{max} - C_{min} = C_0$ in saturation.

Now to get the bounds on the time interval T, we force the following conditions.

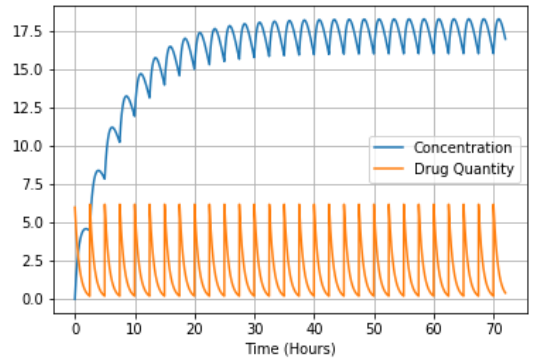
$C_{max} < MTC$ and $C_{min} > MEC$

$$T_{max} = \frac{1}{k} log(\frac{MEC + C_0}{MEC})$$

$$T_{min} = \frac{1}{k} log(\frac{MTC}{MTC - C_0})$$



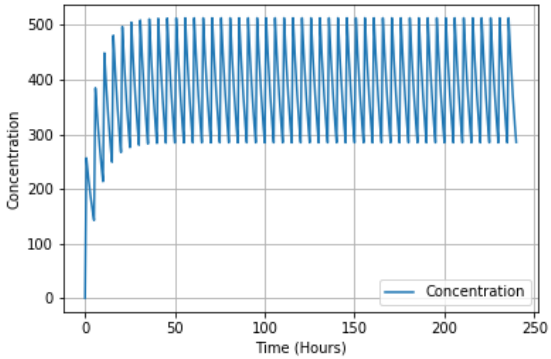
Thus we can keep the concentration between MEC and MTC by choosing a correct T such that $T_{min} < T < T_{max}$. Choosing a value close to T_min causes a concentration nearer to MTC and vice versa for T_{max}



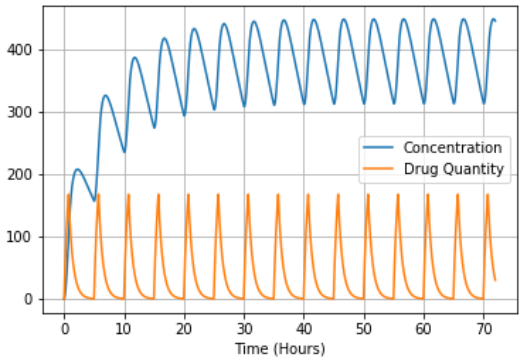
Now the delays in the GI-tract causes the blood concentration to increase less rapidly hence the peak value is just 22.73 units as compared to 24.99 (when $T = T_{min}$) units in the case of the single compartment model. We also observe that the oscillations are not that high $< C_0$ in the case of the 2-compartment model.

3.4 Multiple doses applied over an interval as a rectangular pulse train

When a pulse train of drug is administered we see that the range of τ and T depend on each other. Tweaking one causes the allowable range for the other to change. We find one such combination that results in the drug saturation being in the therapeutic limits. For $T = 300$ minutes and $\tau = 45$ minutes, the concentration fluctuates between 284 to 512 units.



Taking $T = 300$min and $\tau = 45$min in 2-compartment model, the saturated concentration of drug in body remains between 312 to 449.



A similar kind of behaviour is observed here. In this case delay in GI - tract causes the blood concentration to increase less rapidly and thus if we stop giving the dosage to the model, model-1 will reach to the zero concentration more rapidly compare to model-2.

4 Conclusion

We concluded that the peak value of the drug concentration on the drug always remains less in all the strategies in the 2-compartment model.

Also the fluctuations between the maximum saturation concentration and minimum saturation concentration are less in the 2-compartment model.