FIT3139 Lab
Modelling case-study for week 6

Part 1

Consider the guerilla warfare model discussed in the lectures.

$$\frac{dx}{dt} = -ay$$
$$\frac{dy}{dt} = -bxy$$

for positive constants, a and b, where x is the number of home soldiers and y is the number of enemy soldiers.

- Use phase plane analysis to determine if (and when), it is possible to send a specific number of enemy soldiers y_0, that will guarantee a target level of casualties in the enemy army.
- What factors determine the number of casualties in the winning army.
- Can you use the Euler method to approximate the dynamics, instead of using the `ode45` or `odeint` functions in Matlab or Python respectively [1]?

[1] Consult the slides or attempt this after Monday's lecture

Part 2

Your task for the rest of the lab to construct, simulate and analyse a simple Pharmacokinetic model of drug dosage. You can use any of the tools for modelling we have discussed in the class, or combinations of those as you see fit.

Background

Pharmacokinetics is a branch of pharmacology that studies the effect of substances administered to a living organism. The simplest type of model used in the study of pharmacokinetics is called the *compartment model*. In this model, we are concerned with following the progression of a drug as it enters the intestines (stomach), is absorbed into the blood stream (plasma), and eventually ends up in the urine. As such, we study the amount of drug in three compartments: Intestine, Plasma and Urine.

The purpose of this model is to look at the effect of how a change in the amount of drug (the dose) and the dosing interval affects the amount of drug in the three compartments. We will want to try to stabilize the *plasma concentration* (see glossary below) over a period of about eight days.

Building the Model:

In this model we are interested in the concentrations of drug in each of the three-compartments, as described above. The assumptions to be made in constructing this model are:

1. A specified amount of dosage is delivered *instantaneously* at regular intervals into the intestine compartment.
2. The rate of absorption of the drug is proportional to the amount of drug in intestine.
3. The rate of elimination of the drug is proportional to the amount of drug in plasma
4. Any other parameters that are involved in your model stated without initial values defined (see below) should be treated as variables which you will have to tweak to analyze the problem.

Your task is to build this model (as a script in Python or MATLAB) using the initial values given below, and use it to investigate a number of scenarios by examining plots of Plasma concentration, drug in the intestines, drug in plasma and drug in urine.

Symbol definitions

$$I = \text{amount of drug in intestine in mg/L}$$

$$P = \text{amount of drug in plasma in mg/L}$$

$$U = \text{amount of drug in urine in mg/L}$$

$$k_a = \text{absorption rate constant}$$

$$k_e = \text{elimination rate constant} = \frac{0.693}{t_{\frac{1}{2}}}$$

$$C_p = \text{plasma concentration} = \frac{P}{V_d}$$

Initial values:

- Initial drug in the intestine or plasma or urine = 0 mg/L
- Absorption rate constant (k_a) = 1 /hour
- Volume of distribution (V_d) = 70 L
- Simulation time = 192 hours in 15 minute intervals (Δt = 0.25 hour)

Scenarios to simulate and examine your Model:

1. What is the difference in changing the dosage and the dosing intervals?
2. What settings might you use to reach a certain plasma concentration at the peak of the simulation?
3. What settings stabilize the plasma concentration? Introduce a minimum value (for the drug to have any effect) and maximum value (before the drug becomes toxic) of plasma concentration for a drug and play with parameters of your model which stabilizes the plasma concentration.

Relations of various compartments

1. $\frac{\Delta I}{\Delta t}$ = `pulse`[2](dose, 0, dosing_interval) - $k_a * I$
2. $\frac{\Delta P}{\Delta t} = k_a * I - P * k_e$
3. $\frac{\Delta U}{\Delta t} = P * k_e$

[2] `pulse`(.,.,.) implies a pulse function, which delivers a specified dosage precisely at regular dosing intervals into the intestine compartment. 0 in the argument implies that the specified dosage is "instantaneously" added to the intestines.]

Glossary of terms

In this case study we will use the following terms:

- *Half-life*: The period of time required for the concentration or amount of drug in the body to be reduced to exactly one-half of a given concentration or amount. This is symbolized as $t_{\frac{1}{2}}$, a plausible value is for example 48 hours.
- *Volume of distribution*: The volume, in an organism, throughout which a drug appears to have been distributed; the volume into which a drug appears to have been dissolved after administration to an organism. Symbolized by V_d, measured in liters (L). Calculated by amount of drug in the body divided by the concentration in the plasma.
- *Absorption rate constant:* Symbolized as k_a, the rate at which an orally-dosed drug enters the bloodstream (from intestines).
- *Elimination:* The removal of a drug from the blood stream, usually through the urine.
- *Elimination rate constant:* Symbolized as k_e, the rate at which an orally-dosed drug is removed from the bloodstream.
- *Plasma concentration:* The amount of drug in the plasma divided by the volume of distribution. Concentrations are typically the parameter of **most interest** to pharmacologists