**BME 303/403**

**Homework 5**

**Due 5/31/18**

**Revised 5-26 to add a third problem**

**1.** The general form for the blood concentration of a drug following a single oral dose is:

C(t) = (fD/Vd) [ka/(ka - ke)] [exp (-ket) - exp (-kat)]

where ka is the absorption rate constant (min-1), ke is the elimination rate constant (min-1), f is the bioavailability (the fraction that is available in the plasma, D is the dose in mg and Vd is the volume of distribution. This is the simplest single compartment model. Let the half-time for elimination, t1/2 be 2 hrs, Vd = 15 liters (i.e. extracellular fluid volume), f = 0.5 and D = 200 mg.

a. Determine ke from the half time for elimination. This is a general problem that does not involve the particular values here. ke is the reciprocal of the elimination time constant, τ,so this problem is really asking you to determine how the rate constant, the half-time and the time constant are related. All are used frequently, so it is useful to know this.

b. What are ke and the time constant for the situation in this problem?

c. Assume that a dose of a drug enters the gut at t=0. Graph the blood concentration vs. time for 10 hours for two cases: ka = 0.8ke and ka = 5 ke. Use the parameters given in the problem statement for f, D, Vd, and ke.

d. For how long is the concentration in blood effective in each of the two cases, where effective is defined as being a concentration above 1 mg/L?

e. Suppose that you did not want fluctuations in the drug concentration, but wanted to insure that the concentration in the blood was 2 mg/L continuously. You don’t need to have the drug reach this level immediately. In order to do this, at what rate would you have to infuse the drug intravenously?

f. How long will it take the drug to reach the minimally effective dose of 1 mg/L?

g. Suppose you do want the concentration to be 2mg/L as soon as possible after t=0. What would you do? (In order to solve this, you will need to assume that distribution is instantaneous.)

2. A new cholesterol medication is known to be eliminated from the plasma by a single process of biotransformation in the liver. The modified drug is then excreted, but after transformation it is ineffective and non-toxic, and is no longer the same molecule, so the transformation in the liver is the key process. In evaluating the drug, the company wanted to know its pharmacokinetic properties, so they collected data on plasma concentration in dogs as a function of time as shown here. Concentration is in mg/L. The initial dose was 500 mg infused rapidly into the bloodstream.

What are your estimates of the volume of distribution, elimination rate constant and time constant, and the clearance?

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| time | C |
| 20 | 42.07 |
| 40 | 32.47 |
| 60 | 23.65 |
| 80 | 15.2 |
| 100 | 12.6 |
| 120 | 10.62 |
| 140 | 8.67 |
| 160 | 7.11 |
| 180 | 5.9 |
| 200 | 4.89 |
| 240 | 3.47 |
| 280 | 2.45 |
| 320 | 1.74 |
| 360 | 1.24 |

3. Secretin is secreted in response to low duodenal pH, and in turn regulates three processes, all of which relate to duodenal pH. Draw a control diagram for secretin. A good starting point is the template provided with homework 4. We have not discussed any of the real transfer functions in this control system, so showing the functions as lines with constant slopes is acceptable