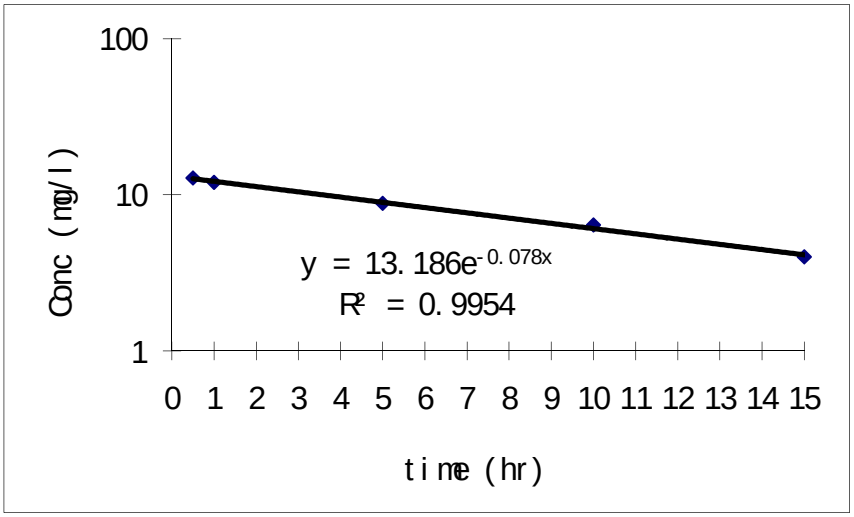
PHA 5127 (Fall, 2008)
Homework #1 (10 points)

Please show your calculations and make sure your numerical answers have units!

Q1. 1000 mg of drug A was administered to a patient as a single i.v. bolus dose. The following plasma concentrations were observed. (4 points)

Time (hrs)	Conc. (mg/l)
0.5	12.8
1	12
5	8.8
10	6.4
15	4

a) Verify the first-order elimination process of this drug. (1 point)



If you plot data points on a semi-log scale, you can see they almost perfectly line up on straight line. Therefore, the elimination process is first-order kinetics.

b) Estimate the elimination rate constant (ke). (0.5 pts; -0.1 pts for no units)

ke = (ln(8.8)-ln(4))/(15-5)=0.08 /hr

c) Estimate the half-life (T1/2) (0.5 pts; -0.1pts for no units)

T1/2 = 0.693/0.08=8.7 hr

d) Estimate the initial plasma concentration (C_0) (0.5 pts; -0.1pts for no units)

C_0=12.8*exp(0.08*0.5)=13 mg/l

e) Estimate the volume of distribution (0.5 pts; -0.1pts for no units)

Vd = D/ C_0 = 1000/13 = 77 L

f) Estimate the $AUC_{0\text{-inf}}$. (1 pts)

$$AUC_{1\to 2} = \frac{C_1 + C_2}{2} * (t_2 - t_1)$$

Time (hrs)	Conc. (mg/l)	AUC(t1-t2) hr*mg/l
0	13	0
0.5	12.8	6.45
1	12	6.2
5	8.8	41.6
10	6.4	38
15	4	26
AUC(0-15) total		118.25

$AUC_{15\text{-inf}}$ = 4/0.08 =50 hr*mg/l
Therefore, $AUC_{0\text{-inf}}$ = $AUC_{0\text{-15}}$ + $AUC_{15\text{-inf}}$ = 118.25 + 50 = 168.25 hr*mg/l

Q2. Mark each of the following statements True or False. (0.5 point each)

T **F** For a zero-order elimination process, change in amount of drug in the body depends on the amount of drug in the body.

T F For a first-order elimination process, the actual amount of drug eliminated per time unit is changing.

T F For a first-order elimination process, Ke and T1/2 do not change with dose.

T F Most lipophilic drugs are able to distribute throughout the body (entire extra- and intracellular space).

T F In a perfusion limited distribution, slower blood flow means slower uptake of drug into tissues.

T **F** In a permeability limited distribution, the degree of drug unionization will not affect the drug uptake.

T F Only free drug is able to interact with receptors and is therefore of pharmacological interest.

T F In general, we can assume free drug in plasma is in equilibrium with free drug in tissue.

T F Volume of Distribution (Vd) is a hypothetical volume which relates the amount of a drug in the body to its plasma concentration.

T **F** Vd can never exceed the total body water volume.

T **F** Drug plasma protein binding and drug tissue binding are the main factors determining how fast a drug gets into tissues.

T F A change in protein binding is especially important if the drug shows a high degree of protein binding.