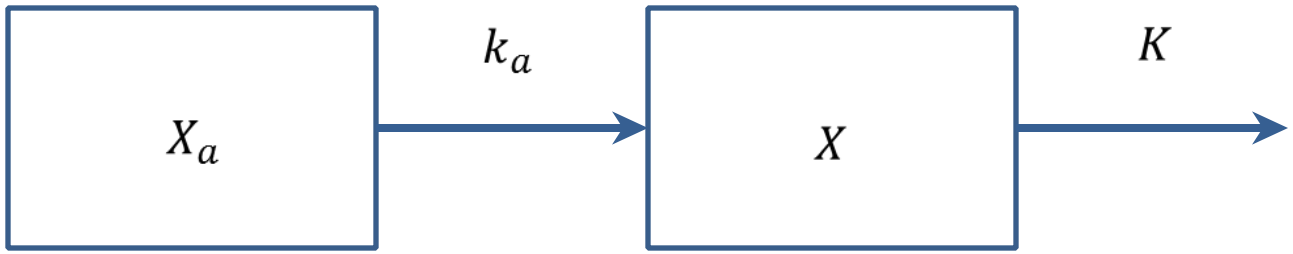
Project #1: Drug Kinetics in Genetically Modified Mice

Model

Initial dose: $X_a(0) = X_0 \cdot F$, where F is the fraction of drug absorbed.



Absorption compartment: total drug amount

Blood (plasma) compartment: total drug amount

Here k_a is absorption rate constant and K is drug elimination rate constant.

Differential equation model describing drug kinetics has the following solution:

$$X(t) = \frac{k_a F X_0}{(k_a - K)} (\exp(-Kt) - \exp(-k_a t)).$$

One can measure the concentration of drug in blood (plasma):

$$C(t) = \frac{X(t)}{V} = \frac{F}{V} \cdot X_0 \cdot \frac{k_a}{(k_a - K)} (\exp(-Kt) - \exp(-k_a t)).$$

Here V is effective distribution volume (not known).

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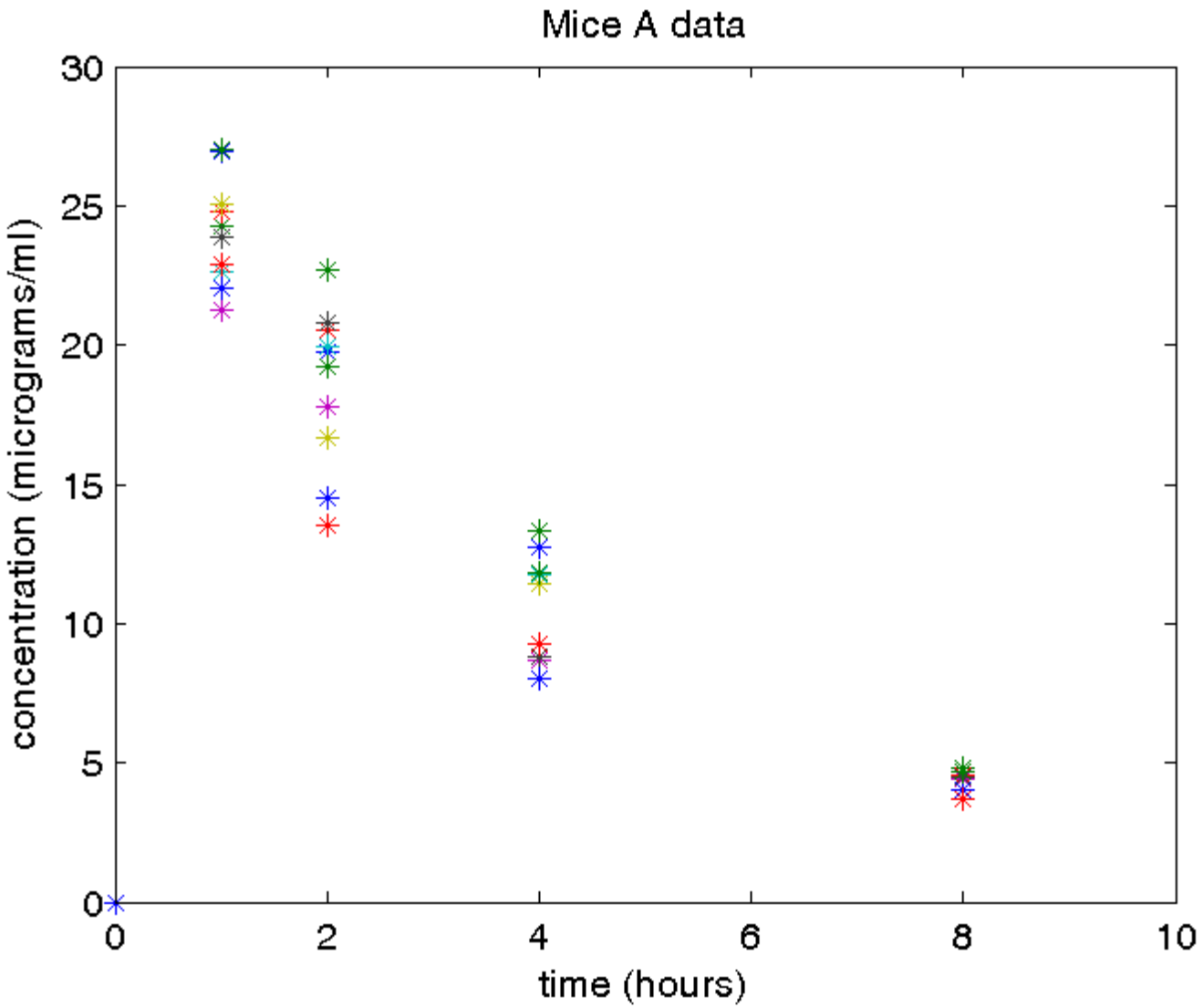
Need to estimate: k_a, K, F/V.

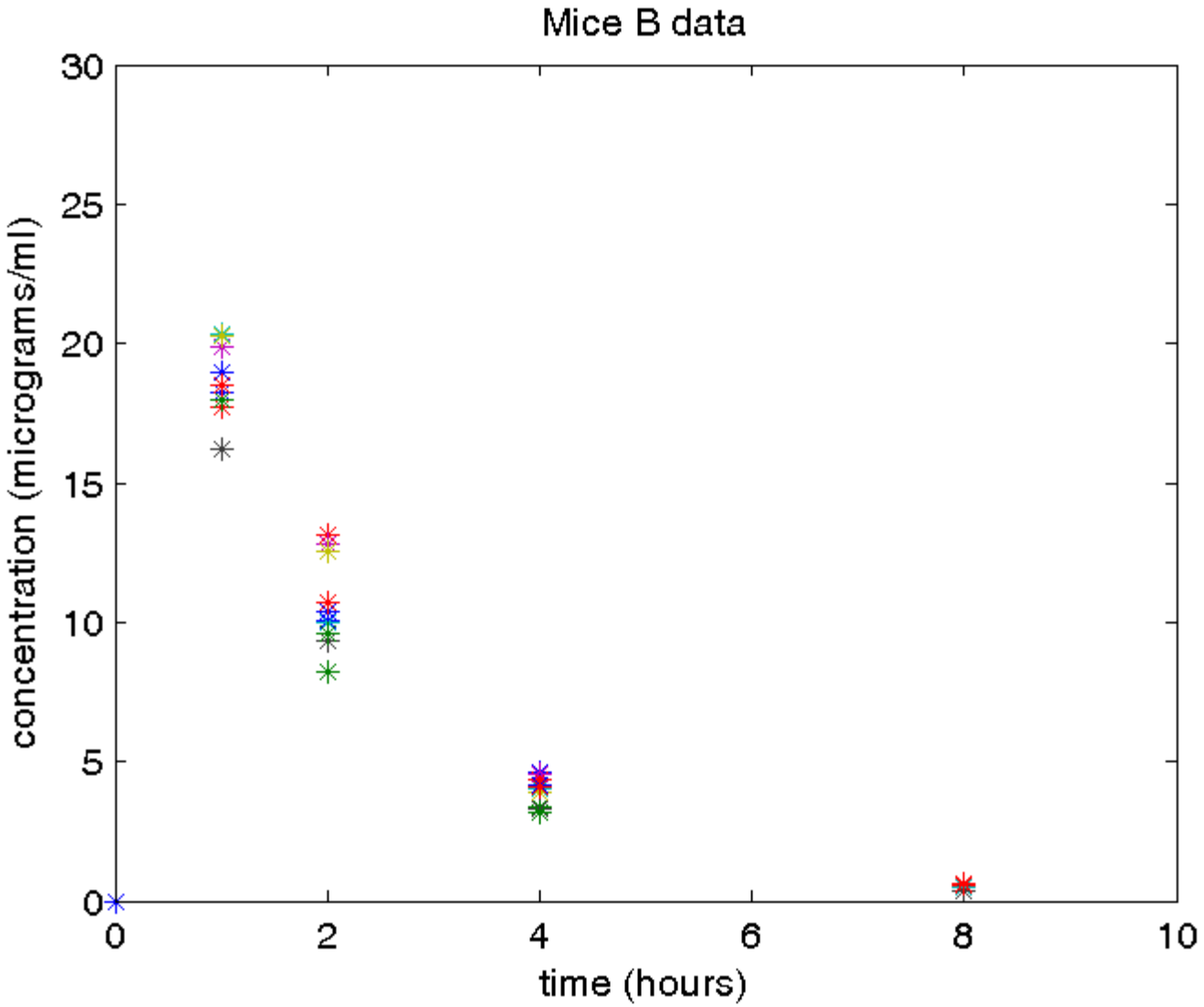
Data: Mice A

	drug concentration in plasma: microgram/ml							
	t=1h	t=2h	t=4h	t=8h			initial dose: micrograms	
mouse1a	26.97792	19.75837	12.76016	4.434793			31.43448	
mouse2a	24.24753	22.72409	13.30686	4.812059			33.26047	
mouse3a	24.77666	20.56166	11.41168	4.557679			30.97779	
mouse4a	22.64532	19.94236	11.72876	4.045205			32.06939	
mouse5a	21.28494	17.78286	8.705149	4.453663			31.45377	
mouse6a	25.03974	16.68711	11.45587	4.022986			29.39312	
mouse7a	23.85169	20.79003	8.796537	4.48717			30.58774	
mouse8a	22.04373	14.48006	8.041883	4.058295			28.42543	
mouse9a	27.03642	19.25051	11.79822	4.692525			31.77679	
mouse10a	22.88891	13.54645	9.237231	3.70474			27.70586	

Data: Mice B

	drug concentration in plasma: microgram/ml								
	t=1h	t=2h	t=4h	t=8h			initial dose: micrograms		
mouse1b	18.22752	10.02384	4.593106	0.496992			29.49211		
mouse2b	17.73821	8.203042	3.365571	0.493685			27.14271		
mouse3b	17.71877	13.10216	4.383508	0.568575			29.95828		
mouse4b	20.32763	10.00664	4.03902	0.482287			28.87867		
mouse5b	19.88525	12.80134	4.552165	0.612637			34.35556		
mouse6b	20.26879	12.57416	3.916291	0.6134			32.27693		
mouse7b	16.21579	9.327095	3.296307	0.374859			25.00623		
mouse8b	18.93819	10.35912	4.153664	0.625798			30.88265		
mouse9b	17.99845	9.563525	3.148519	0.620605			27.20372		
mouse10b	18.51092	10.74009	4.077918	0.593429			29.48989		


Mice A data
concentration (micrograms/ml)
time (hours)
0
5
10
15
20
25
30
0
2
4
6
8
10


Mice B data
concentration (micrograms/ml)
time (hours)
0
5
10
15
20
25
30
0
2
4
6
8
10