MCB 137, Homework 2 solution

Problem 1:

(a) Reproduce the theophylline model (see attached .mmd file).

Choose *kgm* = 1.58 hr^{-1} so that the plasma theophylline concentration peaks at 2 hr after oral ingestion.

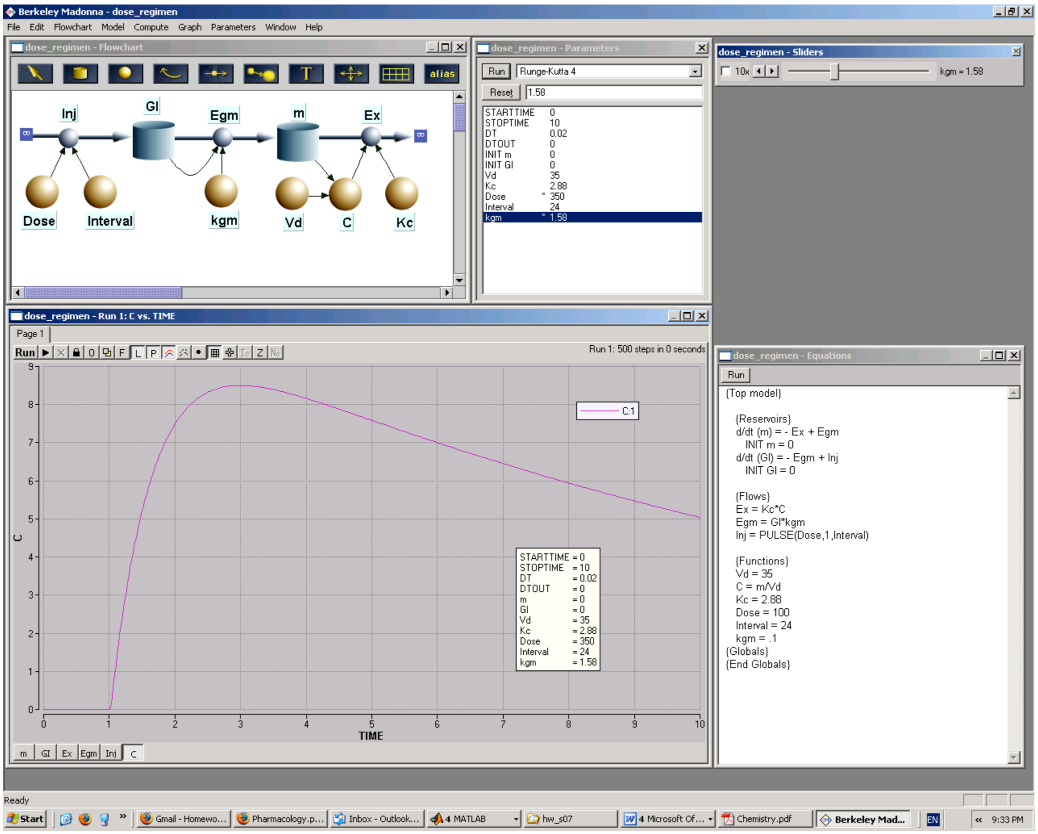

Figure 1: Theophylline oral ingestion model. The lower left figure shows the plasma theophylline peaks at 2hr after oral ingestion when *kgm* = 1.58 hr^{-1}.

(b) Run the model on 1 Dose/day basis.

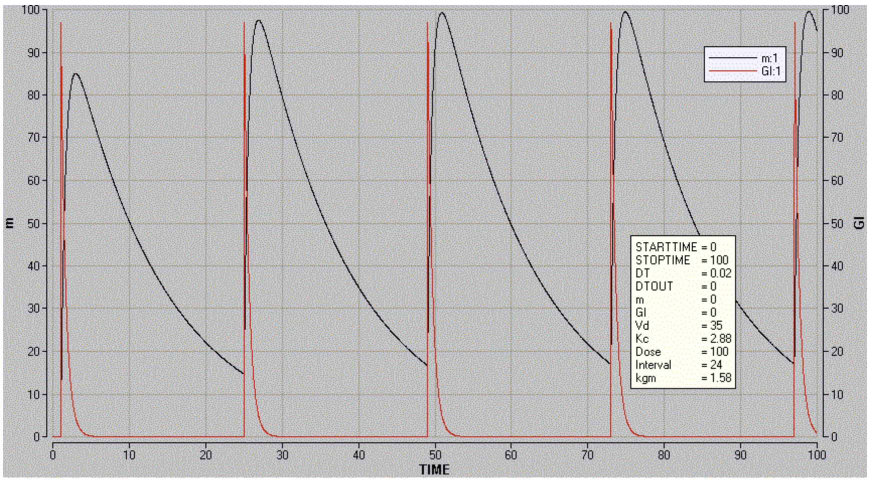

Figure 2: Simulation result for 1Dose/day. Dosage used here is 100 mg.

(c) The theophylline in the GI tract (*GI*) follows a nice exponential decay after the initial pulse input, while the drug in the body fluid (*m*) first undergoes a fast increasing phase and then decays much slower than *GI* does.

The peak value of *GI* does not change for each dose, but the peak value of *m* increases until several doses later (number of doses depending on parameters). The initial increase in the peak value of *m* results from its slow decay rate. The doses accumulate on the residue of the previous ones. But eventually this process comes into equilibrium.

The decaying of *m* is exponential with time constant Vd / Kc, because the exit flow is proportional to *m*, i.e. $Ex = (Vd / Kc) \cdot m$.

* Note that the increase of *m* is also exponential, but not with the time constant Vd / Kc. The inflow to *m* is identically the outflow from *GI*, which is proportional to *GI* with constant *kgm*. Thus the time constant for the increasing phase of *m* is kgm^{-1}.

(d) Safe-but-effective regimen: 350mg * 3 /day. (Answer not unique.)

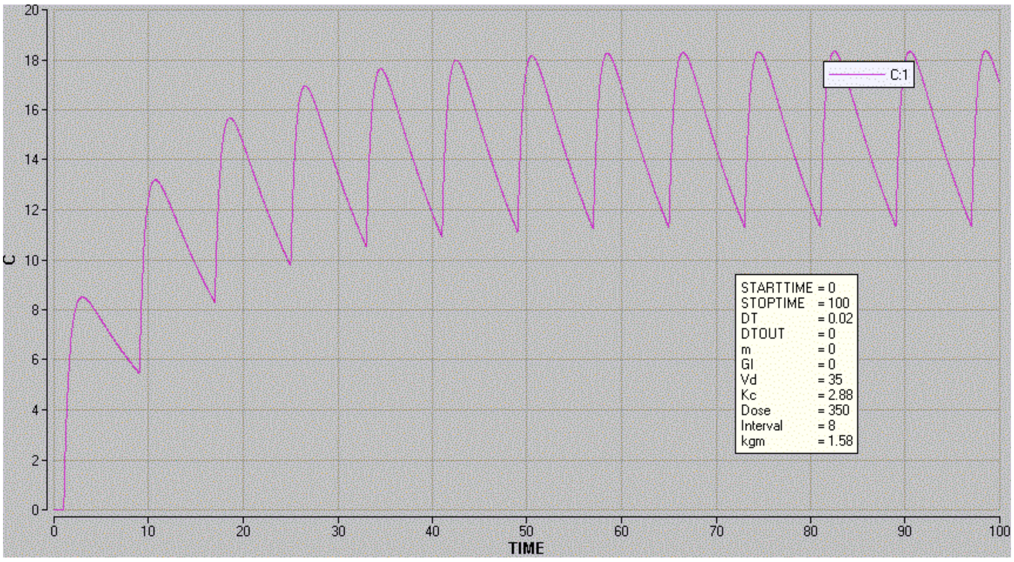

Figure 3: The dosage regimen 350mg/8hr maintains the concentration of theophylline in the body fluid within the safe-but-effective range 10-20mg/L.

Problem 2:

(a) Reproduce the aspirin model

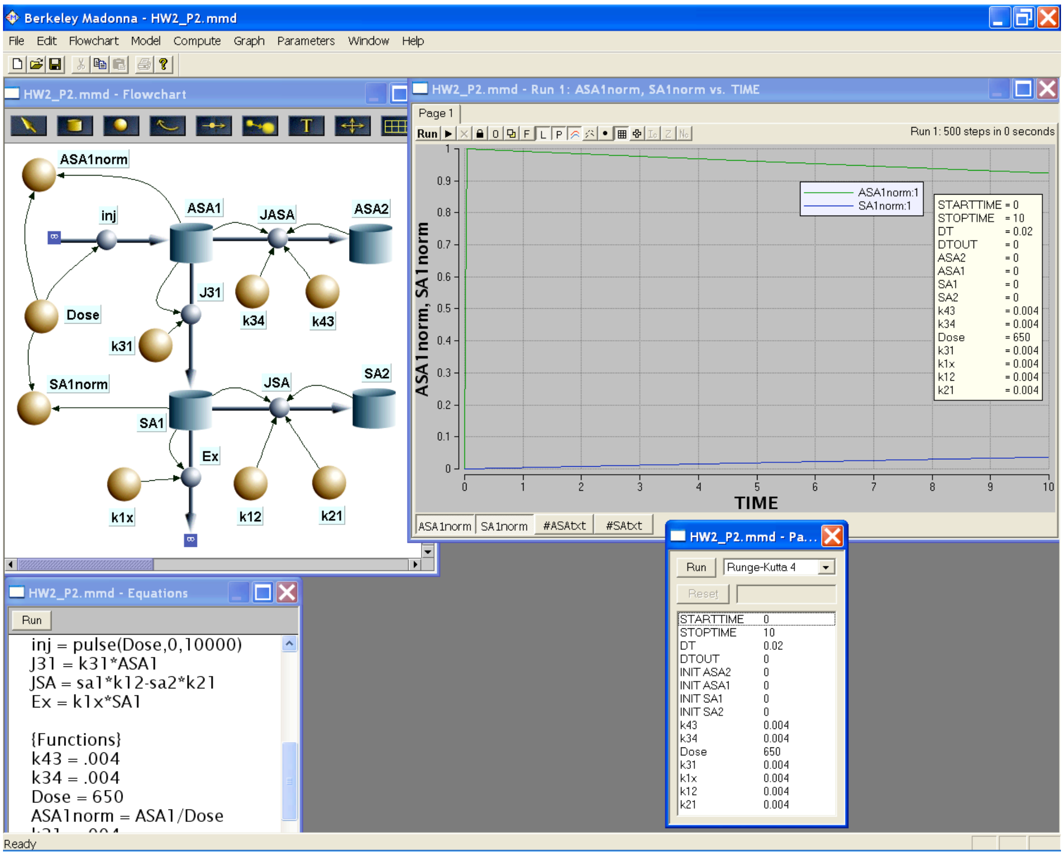

Figure 4: The aspirin injection model.

(b) Curve fitting. Choose SA1norm and ASA1norm as variables to fit the datasets. Choose all the k's as parameters to fit. Set the ranges of the parameters to be positive. The fitting parameters are

k12 = 0.072 min^{-1}

k21 = 0.121 min^{-1}

k1x = 0.0079 min^{-1}

k31 = 0.091 min^{-1}

k34 = 0.048 min^{-1}

k43 = 0.056 min^{-1}

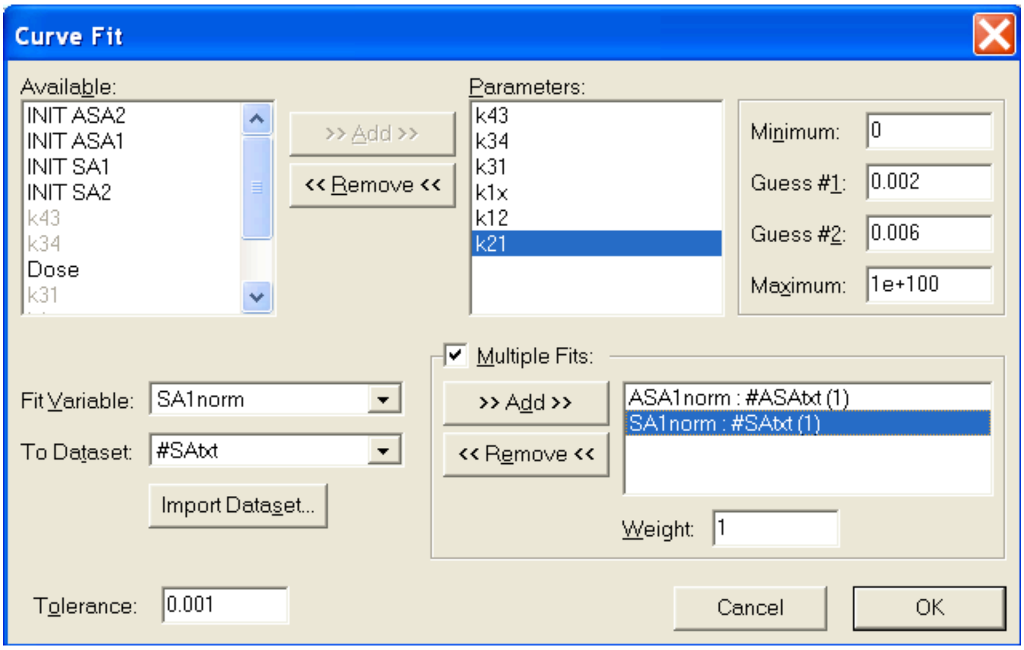

Figure 5: Curve Fit window in Berkeley Madonna (Not required). Choose Minimum values to be 0 for all k's.

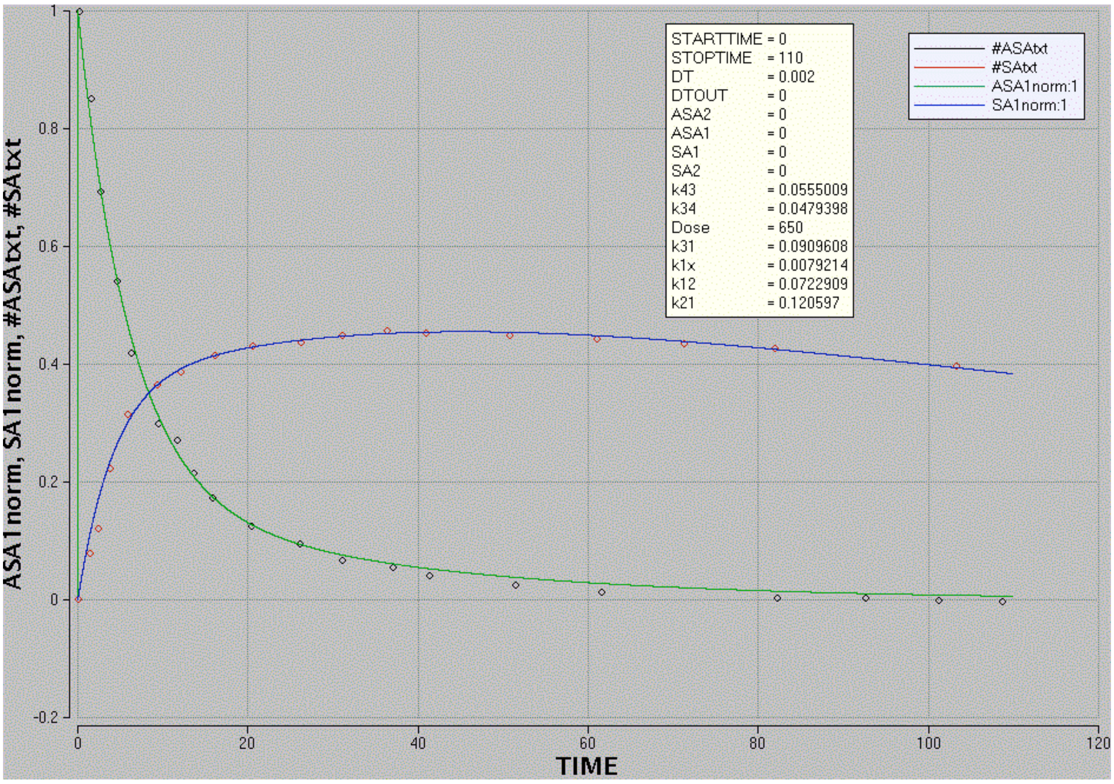

Figure 6: Comparing the data with the fit result.