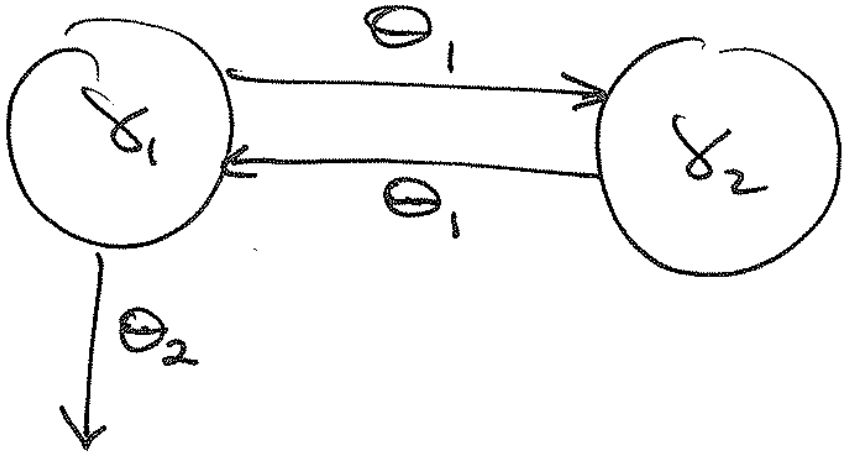
STAT 8230 — Applied Nonlinear Regression
Homework 5 – Due Thursday, Nov. 10

Homework Guidelines:

- Homework is due by 4:30 on the due date specified above. You may turn it in at the beginning of class or place it in my mailbox in the Statistics Building. **No late homeworks will be accepted without permission granted prior to the due date.**
- Use only standard (8.5×11 inch) paper and use only one side of each sheet.
- Homework should show enough detail so that the reader can clearly understand the procedures of the solutions.
- Problems should appear in the order that they were assigned.

Assignment:

1. Consider the two compartment model with diagram:



   a. Find the system transfer matrix **A** for this model, as well as the eigenvalues and eigenvectors of **A** (this can be done without too much trouble by hand, but it is ok if you want to use a symbolic math program like Maple for these computations).

   b. Assume the initial concentrations in compartments 1 and 2 are 100% and 0%, respectively. Use your results from part (a) to find $\gamma_2(t)$, the concentration in compartment 2 at time t.

   c. The file hwk5-1data.dat on the course website contains data on concentrations of a chemical in the blood taken over time. Fit the compartment

model pictured above to these data with and without dead time. Summarize your two fitted models both numerically and graphically (depict the fitted models versus the data). Is dead time useful here? Justify your answer appropriately.

2. The data in Table A4.8 on p.315 of Bates and Watts (also attached to this file) consist of blood plasma concentrations of the drug Haloperidol taken repeatedly from a single subject over time. For this problem use all of the data except the first observation (at time .17 hours). You may assume that initially there is a bolus injection into compartment 1 with dose D=30,000 ng and that the initial concentration in all other compartments is 0.

   a. Using the lipoproteins case study of section 5.4 of our text as a general guide, fit a parsimonious compartment model (assuming spherical error variance-covariance structure) that fits these data well. Produce graphical and statistical evidence to support your choice of model and summarize your fitted model appropriately.

   b. Form a point estimate and 95% confidence interval for V_i, the initial volume of distribution in the blood serum (compartment 1).

   c. The gnls() function in S-PLUS does not work with my compmodel() function, so it is difficult to implement the matrix exponential approach to fitting a compartment model with non-spherical error variance-covariance structure (i.e., in gnls()). Based on your final model from part (a), does it appear the errors are homoscedastic? If not, refit the model with a heteroscedastic error variance structure of the form

$$\text{var}(e_i) = \frac{\sigma^2}{\text{time}_i}.$$

   (*Hint:* although this is hard using gnls(), you should be able to do it using nls(). Remember the discussion of generalized nonlinear least squares and its relationship to ordinary nonlinear least squares on pp.144–45 of our class notes.) Use graphical means and model selection criteria to determine whether this heteroscedastic error variance structure fits the data significantly better than the homoscedastic one. Do the regression parameter estimates change much once heteroscedasticity is accounted for? How about their standard errors?