Systems Biology, Homework # 5
Metabolic Networks
Due Monday March 28thth 11:59 pm

1. **Carefully read through section 5.3.2 in the text on the Martinov model of the methionine cycle before Monday March 14th!** We will review the section in class Monday and spend a little time working on it, using the code provided on canvas (`methionine_model.m`). You will start to work on the problems in class and then finish them up for homework.

   (a) Define the pathway flux as the rate at which methionine is cycled through the pathway. (This is equal to the rate of consumption V_D.) Determine (via numerical approximation) the flux control coefficients for each of the enzymes in the pathway using parameter values as in Figure 5.10 (for which the system is monostable). Find the coefficients for MATI, MATIII, MET, GNMT by considering changes in V_{max} and the coefficient for D by considering changes in α_d. Note that the relative sensitivity of a reaction's rate to an enzyme abundance is equivalent to the relative sensitivity to the corresponding $V_{\max}$, because enzyme abundance is proportional to $V_{\max}$. Verify that these five control coefficients (one for each reaction in the network) sum to one.

   (b) The system's bistability is caused by the activity of MATIII and GNMT, both of which show nonlinear dependence on AdoMet levels. When methionine levels rise, flux through GNMT and MATIII increases dramatically, while flux through the methylation reactions (lumped into reaction MET) shows only a modest increase. Verify this conclusion by comparing the reactions fluxes (MATI to MATIII, GNMT to MET) in the two steady states displayed in Figure 5.11B.

   (c) Bistability depends on a balance between the flux through MATI and MATIII. Verify that bistability is lost when this balance is upset, as follows. Consider the case when [MET] = 51 μM, as in Figure 5.11B. With the other parameter values as in Figure 5.10, verify that bistability is lost when $V_{\max}^{\mathrm{MATIII}}$ is perturbed by 15% (up or down) from its nominal value.