Week 9 - Monday, 3/11

More IVP's.

(A) Circadian rhythms.

"Circadian" means "occuring naturally on a 24-hour cycle."

One model (see Tyson et al. (1999), on our web page) says: circadian rhythms are regulated by feedback of two proteins, PER (short for "periodic") and TIM (short for "timeless"), on the "per" and "tim" mRNA that produces them.

Variables:

M = per/tim mRNA

P_1 = PER/TIM monomers (basic protein building blocks)

P_2 = PER/TIM dimers (a dimer is built up from two monomers)

(A more detailed study might have six variables, by not grouping per and tim, or PER and TIM, together. But the above three are enough for us.)

The model says:

(CR)

$$\frac{dM}{dt} = \underbrace{\frac{a}{1+bP_2^2}}_{\text{(i)}} - \underbrace{cM}_{\text{(ii)}}$$

$$\frac{dP_1}{dt} = \underbrace{dM}_{\text{(iii)}} - \underbrace{\frac{eP_1}{f+P_1+gP_2}}_{\text{(iv)}} - \underbrace{hP_1}_{\text{(v)}} - \underbrace{2kP_1^2}_{\text{(vi)}} + \underbrace{2lP_2}_{\text{(vii)}}$$

$$\frac{dP_2}{dt} = \underbrace{-\frac{mP_2}{f+P_1+gP_2}}_{\text{(viii)}} - \underbrace{nP_2}_{\text{(ix)}} + \underbrace{kP_1^2}_{\text{(x)}} - \underbrace{lP_2}_{\text{(xi)}}.$$

Analysis of terms:

(i) P_2 inhibits production of M: (i) tells us that more P_2 means slower growth of M.

(ii) M is degraded/used up at a rate proportional to the amount of M present.

(iii) P_1 is produced at a rate proportional to the amount of M present.

(iv) and (viii) represent phosphorylation: P_1 and P_2 combine with phosphates and are inactivated. Note that the decay implied by the numerators of (iv) and (viii) is tempered by the denominators.

(v) and (ix) represent proteolysis: P_1 and P_2 decay (proteins have half-lives).

(vi) and (x) represent the reaction
monomer + monomer → dimer.
[Note that (vi) cancels twice (x).]

(vii) and (xi) represent the reaction
dimer → monomer + monomer.
[Note that (vii) cancels twice (xi).]

COOL FACTS:

(1) Solutions to (CR) are normally circadian, but

(2) A certain mutation per L of per mRNA changes the "dimerization rate" k in (vi) and (x) above, resulting in M, P_1, P_2 having periods > 24 hours!

(3) Equations (CR) can further be reduced, under certain conditions, by combining P_1 and P_2 into a single protein variable P. See Sage worksheet Circadian.sws (on the Sage Page).

(B) Other phenomena.

Some other things we can model with IVP's (and solve using Euler's method/Sage) are:

(i) Monomers/dimers/trimers: see tutorial, 10/18.
(ii) Fermentation: see Mini Project 3.
(iii) Genetic toggle switch: see HW 7.
(iv) Neurons: see paper by Nelson, on our course page, and section 3.6 in our text.