Biol 398/Math 388 Week 11 Assignment:

A simple chemostat model of nutrients and population growth

Background. The chemostat is an idealization of a reactor for growing populations of cells like yeast. Nutrients are fed continuously at a fixed flow rate and concentration, and effluent is extracted at a fixed flow rate. A slight subtlety in the extraction part is that what is extracted is at a fixed flow rate, to keep the volume constant, but the effluent has a concentration that depends on the reaction. An illustration of the chemostat is given below.

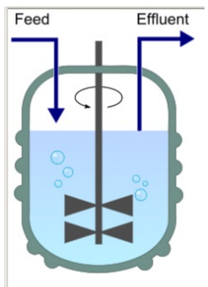

Figure 1. Chemostat cartoon from Wikipedia.

The basic assumption of the chemostat is that the contents are sufficiently well mixed that the concentration of the mixture is uniform throughout the container. Under this assumption, we do not need to consider spatial effects or non-uniformity of nutrients and cells: all cells have equal access to nutrient. If the volumetric inflow rate is Q (vol/time), then the **dilution rate** is $q = Q/V$ in units of (1/time), where the volume of the mixture in the tank is V (and that's constant: the effluent outflow rate is assumed the same as the inflow dilution rate). The **feed concentration** is u (in concentration units, mass or molar). Then the concentration of the nutrient $y(t)$ can be determined as follows:

Rate of change of nutrient = inflow rate – outflow rate – rate consumed in the tank.

Modeling the conservation of (bio and nutrient) mass. Now, the inflow rate is qu (and this is assumed to be a constant, independent of time). The outflow rate is $qy(t)$, because the effluent is extracted from the uniform, well-mixed tank contents. Thus, we have

$$\frac{dy}{dt} = qu - qy(t) - \text{consumption rate}$$

The model of consumption we consider is called Monod, Michaelis-Menten, or Briggs-Haldane, depending on the context, and it adds a third term to the mass balance equation due to cell population consumption of the nutrient.

$$\frac{dy}{dt} = qu - qy(t) - Er\frac{y}{K+y}x(t)$$

to capture inflow, outflow, and metabolism of the nutrient. Here we introduce x, the concentration of yeast cells in the mixture, and the parameter e denotes a unit conversion rate between biomass (the units of x) and nutrient concentration.

We model the population of cells with its own differential equation, coupled with the nutrient by

$$\frac{dx}{dt} = -qx + r\frac{y}{K+y}x,$$

so that the net growth rate depends on the nutrient level. This model leads to a coupled pair of differential equations, because the consumption model depends on the size of the population:

$$\frac{dx}{dt} = -qx + r\frac{y}{K+y}x$$
$$\frac{dy}{dt} = qu - qy - Er\frac{y}{K+y}x$$

Among the interesting things to consider is the equilibrium, or steady state. By equilibrium, we mean a state that would remain constant in time if we reached it. Since constant functions have 0 derivative, steady states can be found by setting the right hand side of the DE system to 0:

$$\frac{dx}{dt} = 0 = -qx + r\frac{y}{K+y}x$$
$$\frac{dy}{dt} = 0 = qu - qy - Er\frac{y}{K+y}x$$

Looking at the second equation, we see that x=0 works (but that's not interesting, as the cell population would be extinct). If x is not 0, then we must have

$$q = r\frac{y}{K+y}, \quad or$$
$$y = \frac{qK}{r-q}$$

as part of the equilibrium condition. Plugging the first part of this into the first equation, we get that

$$qu - qy = Eqx$$
$$x = (u-y)/E$$

Two important things to note are that the steady state nutrient concentration is independent of the feed rate *u*, while the cell population depends linearly on *u*.

Your assignment. Use the MATLAB files `chemostat_script.m` and `chemostat_dynamics.m` to simulate a chemostat and compare the computations to a steady state outcome.

(1) Use the parameter values q = 0.10 (1/hr), u = 5 (g/L), E=1.5, r=0.8 (1/hr), K = 8 (g). Using the formulae above, what are the steady states of cell biomass and nutrient mass?
(2) Assuming a 2 L chemostat, what are the steady state ***concentrations*** of cells and nutrient?
(3) Simulate the system dynamics using the MATLAB files and the parameters of (1).
    a. Do the graphs show the system going to steady state?
    b. Do the steady states match your (1) calculations?
    c. Be sure to save the graphs and upload them to your journal.
    d. BONUS: can you get two y-axes, with the second one to the right of the picture like in the journal articles you've read?

Shared assignment. Discuss amongst yourselves whether or not the Tai *et al* (2007) journal club paper gives you enough information to perform such a simulation. What parameters are explicitly given? Can you back any others out from the data tables? To what in the model do the quantities in Table 1 correspond?