Biol 398/Math 388 Week 4 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 fd 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.

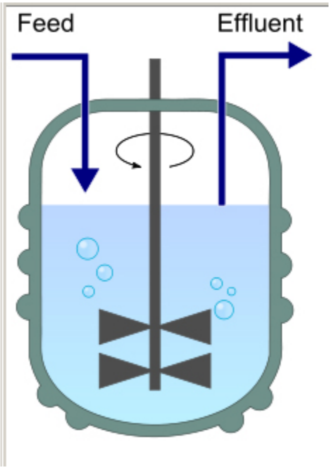

Figure 1. Chemostat cartoon from Wikipedia.

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 $c(t)$ can be determined as follows:

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

Now, the inflow rate is $q*u$ (and this is assumed to be a constant, independent of time). The outflow rate is $q*c(t)$, because the effluent is extracted from the uniform, well-mixed tank contents. Thus, we have

$$\frac{dc}{dt} = qu - qc(t) - \text{consumption rate}$$

For the moment, if we assume no consumption, one can apply Math 245 or Math 123 methods to find a formula for $n(t)$, assuming $n(t=0)=n_0$ is the initial concentration of nutrient in the tank at the start.

$$\begin{aligned}
&\frac{dc}{dt} = qu - qc(t) \\
&\frac{1}{u-c}\frac{dc}{dt} = q \\
&-\ln(u-c) + \ln(u-c_0) = qt \\
&c(t) = u - (u-c_0)e^{-qt}
\end{aligned}$$

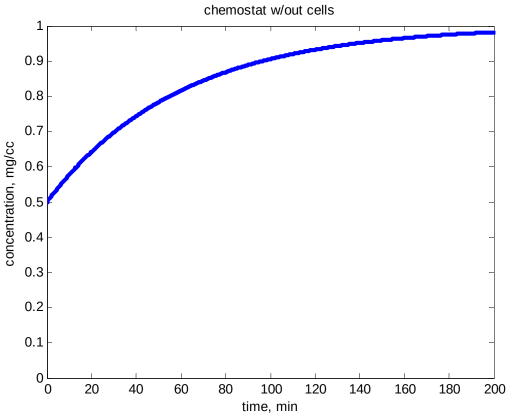

Figure 2. Chemostat equilibrating with only nutrient influx.

To introduce cells, we can take a number of modeling approaches. First, we can assume that the cell population is in stationary phase, meaning the size of the cell colony is constant in time. 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.

$$\frac{dc}{dt} = qu - qn(t) - yV_{\max}\frac{c}{K+c}$$

to capture inflow, outflow, and metabolism of the nutrient. The “new” parameter is y, the concentration of yeast cells in the mixture.

Population dynamics. As discussed in class, the rate of change of the population is a sort of outflow/inflow balance: rate of change = birth rate – death rate. In the Malthus model, each of these rates is a linear function of the population size y(t). The birth rate is b*y(t) and the death rate is d*y(t). The idea is that some fraction of the population reproduce in a time period, and some fraction of the population die in a time period. Thus

$$\frac{dy}{dt} = by - dy = ry,$$

where r is the net growth rate. The solution of this differential equation is $y(t) = y_0 e^{rt}$ which either remains constant if r=0, grows exponentially (without bound) if r>0, or decays toward 0 if r<0.

To tweak this model to include nutrients, one could simply modify the growth rate to capture the consumption of nutrients:

$$\frac{dy}{dt} = yrV_{\max}\frac{c}{K+c},$$

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:

$$\begin{aligned}\frac{dc}{dt} &= qu - qc(t) - yV_{\max}\frac{c}{K+c}\\ \frac{dy}{dt} &= yrV_{\max}\frac{c}{K+c}\end{aligned}$$

The assignment.

(1) Consider the nutrient/cell population model

$$\begin{aligned}\frac{dc}{dt} &= qu - qc(t) - yV_{\max}\frac{c}{K+c}\\ \frac{dy}{dt} &= yrV_{\max}\frac{c}{K+c}\end{aligned}$$

   a. First, make sure you understand which variables are the state variables (dependent variables that determine the concentrations) and which variables are parameters (e.g., rate constants).

   b. Find values of c and y that hold the system in equilibrium: that is, find values of c and y for which constant functions at those values are actually solutions of the differential equation system.

   c. Simulate this system with different values for the constants and the initial concentrations of nutrients and cells. The initial nutrient level can be =0, but the constants and the initial cell population size need to be positive. Can you make any observations about how the system behaves?

(2) What changes if we return a mortality term to the population equation? Repeat b and c for a linear mortality term.

(3) Create a model with two nutrients, both of which are required for the population to grow.