Math 463: Introduction to Mathematical Biology
Homework 5 Solutions

8a. Describe Scalings

- $\alpha_1 = \frac{VK_{max}}{F}$: ratio of the maximum growth rate to the flow rate or ratio of the residence time in the growth chamber to ln(2)xdoubling time of the bacteria.

- $\alpha_2 = \frac{C_0}{K_n}$: ratio of the stock nutrient concentration to the half saturation constant.

- $\tau = \frac{V}{F}$: emptying time for the chamber or bacteria residence time in the chamber

- $T = \frac{F}{V}$: flow rate

- $B = \hat{C} = K_n$: nutrient concentration is scaled by the half-saturation constant for bacterial growth.

- $A = \hat{N} = \frac{K_n F}{\alpha K_{max} V}$: ratio of maximum doubling and consumption time to residence time

8b. Interpretation

- The existence condition for c_2 was $\alpha_1 = \frac{VK_{max}}{F} > 1$. This implies that $\frac{V}{F} > \frac{1}{K_{max}}$. This means that the residence time should be greater than ln(2) x the doubling time. Or alternatively, $\frac{F}{V} < K_{max}$ meaning the flow rate should be less than the maximum growth rate.

- The existence condition for n_2 was $\alpha_2 = \frac{C_0}{K_n} > \frac{1}{\alpha_1 - 1} = c_2$, the non-trivial steady state. In dimensional terms this says: $\frac{C_0}{K_n} > \frac{C_2}{K_n}$. Therefore $C_0 > C_2$ which says that the nutrient concentration in the tank cannot exceed the nutrient concentration in the reservoir.

11. The nontrivial steady state for the chemostat model in nondimensional form is given by:

$$n_2 = a_1 \left(a_2 - \frac{1}{a_1 - 1} \right).$$

In order to increase n_2 one could either increase a_1 or increase a_2. Recall that $a_1 = \frac{rV}{F}$ and $a_2 = \frac{C_0}{a}$. We have no control over r and a; therefore to increase n_2 one should increase C_0 (the stock nutrient concentration) and/or decrease the dilution rate by increasing its volume (V) or decreasing the flow rate (F).

12a. Add a third equation for the additional nutrient. The model below assumes that both nutrients are crucial for cellular proliferation (other assumptions are also acceptable)

$$\frac{dN}{dt} = \frac{K_{m1} C_1}{K_{n1} + C_1} \frac{K_{m2} C_2}{K_{n2} + C_2} N - \frac{F}{V} N$$
$$\frac{dC_i}{dt} = -\alpha_i \frac{K_{mi} C_i}{K_{ni} + C_i} N - \frac{F}{V} C_i + \frac{F}{V} C_{i0} \qquad \text{i = 1,2}$$

12b. Add a third equation for the chemical.

$$\frac{dN}{dt} = \frac{K_{max}NC}{K_n + C + \beta S} - \frac{F}{V}N$$
$$\frac{dC}{dt} = -\alpha\frac{K_{max}NC}{K_n + C + \beta S} - \frac{F}{V}C + \frac{F}{V}C_0$$
$$\frac{dS}{dt} = \frac{aN^2}{b + N^2} - \delta S$$

12c. Add a third equation for the additional bacteria population. In the model below competition is indirect in that each population is comsuming the nutrient that the other population also needs (other assumptions are also possible).

$$\frac{dN_i}{dt} = K_i(C)N_i - \frac{F}{V}N_i \qquad \text{i = 1,2}$$
$$\frac{dC_i}{dt} = -\alpha_1 K(C)N_1 - \alpha_2 K(C)N_2 - \frac{F}{V}C + \frac{F}{V}C_0$$

25a. Equations

$$\frac{dN}{dt} = rN - \frac{aNC}{b + C}$$
$$\frac{dC}{dt} = d - \beta\frac{aNC}{b + C} - \mu C$$

25b. Dimensional Analysis

- N has units of $\frac{\#}{volume}$
- C has units of $\frac{mass}{volume}$
- a has units of $\frac{1}{time}$
- b has units of $\frac{mass}{volume}$
- μ has units of $\frac{1}{time}$
- r has units of $\frac{1}{time}$
- β has units of $\frac{mass}{\#}$
- $d = \frac{C_0F}{V}$ has units of $\frac{mass}{volume \times time}$

Nondimensionalize

Using the scalings: $n = \frac{N}{A},\ c = \frac{C}{B},\ \tau = Tt$ with $T = r,\ B = b\ A = \frac{br}{\beta d},\ a_1 = \frac{a}{r},\ a_2 = \frac{\mu}{r},\ a_3 = \frac{d}{br}$; we find

$$\frac{dn}{d\tau} = n - \frac{a_1 nc}{1+c}$$
$$\frac{dc}{d\tau} = a_3 - \frac{nc}{1+c} - a_2 c$$

25c. Steady States and Their Stability

The steady states are: $n = 0, v = \frac{a_3}{a_2}$ and $n = n^* = a_1\left(a_3 - \frac{a_2}{a_1-1}\right), v = v^* = \frac{1}{a_1-1}$. Note that for existence of (n^*, c^*) we must require $a_1 > 1$ and $a_3 > \frac{a_2}{a_1-1}$.

The elimination state, $[0, \frac{a_3}{a_2}]$, is locally stable as long as $\frac{a_1 a_3}{a_2+a_3} > 1$. Note that upon rearranging this expression we find that the elimination state is stable even when the nontrivial steady state exists. The steady state $n = n^* = a_1\left(a_3 - \frac{a_2}{a_1-1}\right), v = v^* = \frac{1}{a_1-1}$ is never stable.

25d. Conclusion: The analysis suggests that the tumor will either be irradicated or will grow unbounded. If $\frac{a_1 a_3}{a_2+a_3} < 1$ or in dimensional terms $\frac{a}{r} < \frac{\mu b}{d}$ the tumor will grow exponentially. This condition implies that the ratio of tumor cell death and growth is less than the ratio of the drug's clearance and infution so it makes since that in this case the tumor should not be controlled. If however $\frac{a_1 a_3}{a_2+a_3} > 1$, tumors of certain sizes will be irradicated. That is if $N_0 < n_c$, the drug is able to control the tumor's growth, but if $N_0 > n_c$ the tumor will overcome the treatment and grow exponentially.

25e. Gompertz Law

$$\frac{dN}{dt} = \gamma N \qquad (1)$$
$$\frac{d\gamma}{dt} = -\alpha\gamma \qquad (2)$$

First integrate equation (2) to get $\gamma = \gamma_0 e^{-\alpha t}$. Then plug into (1) to get $\frac{dN}{dt} = \gamma_0 e^{-\alpha t} N$. Now use the fact that $\gamma = \frac{1}{N}\frac{dN}{dt} = \frac{d}{dt}(\ln N)$. Plug this expression into (2) to get $\frac{d\gamma}{dt} = -\alpha \frac{d}{dt}(\ln N)$. Integrate both sides and you'll see that $\gamma = -\alpha \ln N$. Plug this into (1) and you've shown that

$$\frac{dN}{dt} = \gamma_0 e^{-\alpha t} N = -\alpha N \ln N$$

25f. New Model

$$\frac{dN}{dt} = -\alpha(C)N\log N - \frac{aNC}{b+C}$$
$$\frac{dC}{dt} = d - \beta\frac{aNC}{b+C} - \mu C$$

Any choice for $\alpha(C)$ is expectable. This model is more realistic because unbounded growth is no longer possible.