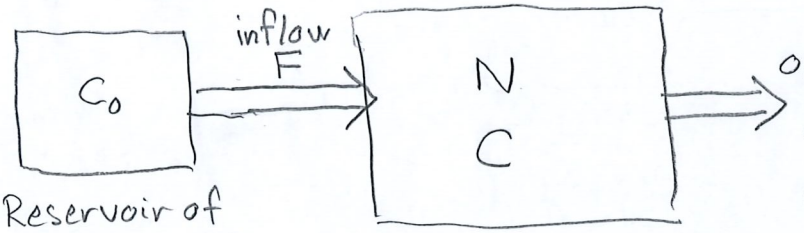
The chemostat

$N(t)$ = bacterial population density

$C(t)$ = nutrient concentration



Reservoir of stock nutrient ($C = C_0$ constant)

Bacterial culture chamber (volume V)

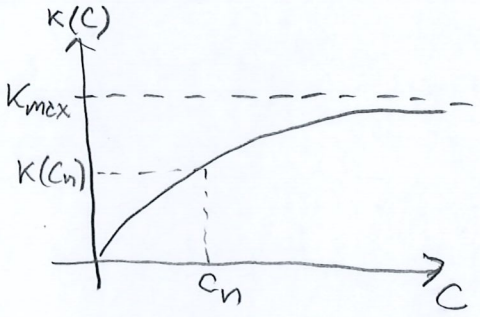
Goal: choose C_0, F, V such that $N(t) \to 0$; $t \to \infty$ (normal growth in chamber)

$N \cdot V$ = number of bacteria in chamber [assume well stirred, N same everywhere in chamber]

* increases by $K(C) \cdot NV$, $K(C) = ?$
* decreases by $-FN$ (outflow: $\frac{\text{volume}}{\text{time}} \cdot \frac{\text{bact.}}{\text{volume}} = \frac{\text{bact.}}{\text{time}}$)

For small C, $K(C) \sim$ linear in C reasonable

For very large C, $K(C) \sim$ constant (cannot make use of C above some level)



Michaelis-Menten model

$$K(C) = K_{max} \cdot \frac{C}{C_n + C}$$

[C_n is denoted K_n in the book]

C_n is where $K(C_n) = \frac{K_{max}}{2}$

$$\Rightarrow \frac{d}{dt}(NV) = K_{max} \frac{C}{C_n + C}(NV) - F \cdot N \quad (1)$$

$C \cdot V$ = mass of nutrient in chamber

* increases by FC_0 (inflow)
* decreases by $-FC$ (outflow) and by nutrient used to grow bacteria; if α units of nutrient used for 1 unit of bacteria, we get a term $\alpha \cdot K(C)$

$$\Rightarrow \frac{d}{dt}(CV) = -\alpha K_{max} \frac{C}{C_n + C}(NV) + FC_0 - FC \quad (2)$$

Divide (1) and (2) by $V \Rightarrow$

$$\begin{cases} \frac{dN}{dt} = K_{max} \frac{C}{C_n + C} N - \frac{F}{V} N \\ \frac{dC}{dt} = -\alpha K_{max} \frac{C}{C_n + C} N + \frac{F}{V}(C_0 - C) \end{cases}$$

Dynamical system for chemostat

We have 6 constants $K_{max}, C_n, F, V, \alpha, C_0$. Reduce by introducing dimensionless variables. Define

$$\begin{cases} N^* = N \cdot \frac{\alpha V K_{max}}{C_n F} \\ C^* = C \cdot \frac{1}{C_n} \\ t^* = t \cdot \frac{F}{V} \end{cases} \qquad \frac{V}{F} \sim \text{time}, \; K_{max} \sim \frac{1}{\text{time}}, \; \alpha N \sim C \Rightarrow N^* \text{ dim. less}$$

$$\Rightarrow \frac{dN^*}{dt^*} = \frac{\alpha V K_{max}}{C_n F} \cdot \frac{1}{\frac{F}{V}} \cdot \frac{dN}{dt} = \frac{\alpha V^2 K_{max}}{C_n F^2}\left(K_{max} \frac{C_n C^*}{C_n + C_n C^*} \cdot \frac{C_n F N^*}{\alpha V K_{max}} - \frac{F}{V} \cdot \frac{C_n F N^*}{\alpha V K_{max}}\right) =$$

$$= \underbrace{\frac{V K_{max}}{F}}_{\alpha_1} \frac{C^*}{1+C^*} N^* - N^* = \alpha_1 \frac{C^*}{1+C^*} N^* - N^*$$

and $$\frac{dC^*}{dt^*} = \frac{1}{C_n} \cdot \frac{1}{\frac{F}{V}} \frac{dC}{dt} = \frac{V}{C_n F}\left(-\alpha K_{max} \frac{C_n C^*}{C_n + C_n C^*} \cdot \frac{C_n F N^*}{\alpha V K_{max}} + \frac{F}{V}(C_0 - C_n C^*)\right) =$$

$$= -\frac{C^*}{1+C^*} N^* + \underbrace{\frac{C_0}{C_n}}_{\alpha_2} - C^*$$

Gives equations with only 2 constants α_1, α_2. Drop * from notation and write N, C, t (but really N^*, C^*, t^*):

$$\begin{cases} \frac{dN}{dt} = \alpha_1 \frac{C}{1+C} N - N \\ \frac{dC}{dt} = -\frac{C}{1+C} N - C + \alpha_2 \end{cases}$$

chemostat equations

2D non-linear system

Begin analyzing by checking steady states (equilibria) $(\bar{N}, \bar{C})$.

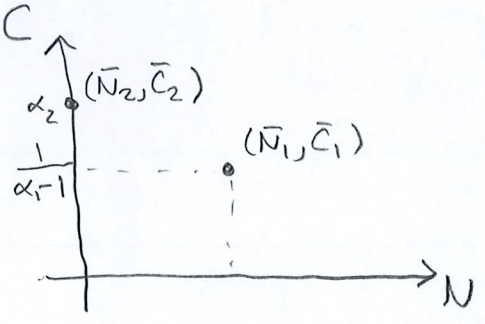
$$\begin{cases} \frac{dN}{dt} = 0 \\ \frac{dC}{dt} = 0 \end{cases} \Rightarrow \begin{cases} \alpha_1 \frac{\bar{C}}{1+\bar{C}} \bar{N} - \bar{N} = 0 \quad (3) \\ -\frac{\bar{C}}{1+\bar{C}} \bar{N} - \bar{C} + \alpha_2 = 0 \quad (4) \end{cases} \Rightarrow \bar{N} = 0 \text{ or } \frac{\alpha_1 \bar{C}}{1+\bar{C}} = 1$$

$\bar{N} = 0$ in (4) $\Rightarrow \bar{C} = \alpha_2$

$\frac{\alpha_1 \bar{C}}{1+\bar{C}} = 1 \Rightarrow \alpha_1 \bar{C} = 1 + \bar{C} \Rightarrow \bar{C} = \frac{1}{\alpha_1 - 1}$, in (4) $\Rightarrow -\frac{\bar{N}}{\alpha_1} - \frac{1}{\alpha_1 - 1} + \alpha_2 = 0 \Rightarrow \bar{N} = \alpha_1\left(\alpha_2 - \frac{1}{\alpha_1 - 1}\right)$

$\Rightarrow$ 2 steady states $(\bar{N}_1, \bar{C}_1) = \underbrace{\left(\alpha_1\left(\alpha_2 - \frac{1}{\alpha_1 - 1}\right), \frac{1}{\alpha_1 - 1}\right)}$ and $(\bar{N}_2, \bar{C}_2) = (0, \alpha_2)$

requires $\alpha_1 > 1$ and $\alpha_2 > \frac{1}{\alpha_1 - 1}$ to exist (we are not interested in $N < 0$ or $C < 0$)



Use linearization to check stability.

$$\begin{cases} \frac{dN}{dt} = F(N,C) = \alpha_1 \frac{C}{1+C} N - N \\ \frac{dC}{dt} = G(N,C) = -\frac{C}{1+C} N - C + \alpha_2 \end{cases}$$

exercise!

Jacobian $J(N,C) = \begin{pmatrix} F'_N & F'_C \\ G'_N & G'_C \end{pmatrix} = \begin{pmatrix} \frac{\alpha_1 C}{1+C} - 1 & \frac{\alpha_1 N}{(1+C)^2} \\ -\frac{C}{1+C} & -\frac{N}{(1+C)^2} - 1 \end{pmatrix}$

At $(\bar N_1, \bar C_1)$, $\frac{\alpha_1 \bar C_1}{1+\bar C_1} = 1$, put $\frac{\bar N_1}{(1+\bar C_1)^2} = a \Rightarrow J(\bar N_1, \bar C_1) = \begin{pmatrix} 0 & \alpha_1 a \\ -\frac{1}{\alpha_1} & -a-1 \end{pmatrix} = J_1$

$\operatorname{Tr} J_1 = -a-1 < 0$, $\det J_1 = a > 0 \Rightarrow (\bar N_1, \bar C_1)$ stable. More precise:

eigenvalues $\det(J_1 - \lambda I) = 0 \Rightarrow \lambda^2 + (a+1)\lambda + a = (\lambda + a)(\lambda + 1) = 0$

$\Rightarrow \lambda_1 = -a < 0$, $\lambda_2 = -1 < 0 \Rightarrow$ stable. Assume $a \neq 1$ for simplicity.

eigenvectors

$\lambda_1 = -a \Rightarrow (J_1 + aI)\bar v_1 = \bar 0$: $\left(\begin{array}{cc|c} a & \alpha_1 a & 0 \\ -\frac{1}{\alpha_1} & -1 & 0 \end{array}\right) \sim \left(\begin{array}{cc|c} 1 & \alpha_1 & 0 \\ 0 & 0 & 0 \end{array}\right) \Rightarrow \bar v_1 = \begin{pmatrix} \alpha_1 \\ -1 \end{pmatrix}$

$\lambda_2 = -1 \Rightarrow (J_1 + I)\bar v_2 = \bar 0$ $\left(\begin{array}{cc|c} 1 & \alpha_1 a & 0 \\ -\frac{1}{\alpha_1} & -a & 0 \end{array}\right) \sim \left(\begin{array}{cc|c} 1 & \alpha_1 a & 0 \\ 0 & 0 & 0 \end{array}\right) \Rightarrow \bar v_2 = \begin{pmatrix} \alpha_1 a \\ -1 \end{pmatrix}$

Solution to linearized system

$$\begin{pmatrix} n(t) \\ c(t) \end{pmatrix} = c_1 e^{-at} \begin{pmatrix} \alpha_1 \\ -1 \end{pmatrix} + c_2 e^{-t} \begin{pmatrix} \alpha_1 a \\ -1 \end{pmatrix} \to \begin{pmatrix} 0 \\ 0 \end{pmatrix}, t \to \infty$$

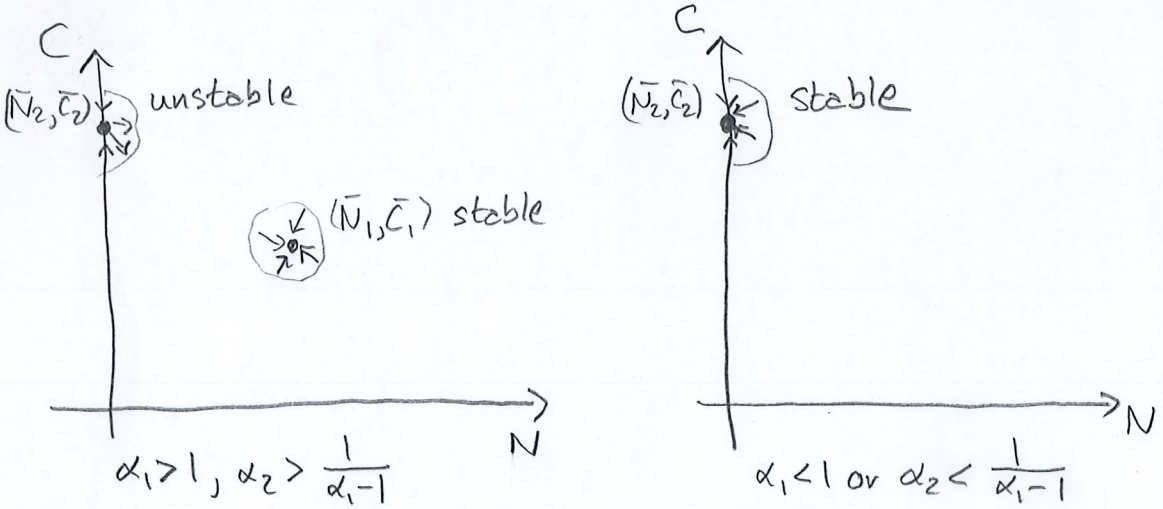
At $(\bar N_2, \bar C_2) = (0, \alpha_2)$ $J(\bar N_2, \bar C_2) = \begin{pmatrix} \frac{\alpha_1 \alpha_2}{1+\alpha_2} - 1 & 0 \\ -\frac{\alpha_2}{1+\alpha_2} & -1 \end{pmatrix} = J_2$

eigenvalues $\lambda_1 = \frac{\alpha_1 \alpha_2}{1+\alpha_2} - 1 = \frac{\alpha_1 \alpha_2 - \alpha_2 - 1}{1+\alpha_2} = \frac{(\alpha_1 - 1)\alpha_2 - 1}{1+\alpha_2} = \frac{(\alpha_1 - 1)\left(\alpha_2 - \frac{1}{\alpha_1 - 1}\right)}{1+\alpha_2}$, $\lambda_2 = -1 < 0$

eigenvectors (exercise) $\bar v_1 = \begin{pmatrix} \alpha_1 \\ -1 \end{pmatrix}$, $\bar v_2 = \begin{pmatrix} 0 \\ 1 \end{pmatrix}$

If $\alpha_1 > 1$ and $\alpha_2 > \frac{1}{\alpha_1 - 1}$ (required for $(\bar N_1, \bar C_1)$ to exist), $\lambda_1 > 0 \Rightarrow$ saddle

If $\alpha_1 < 1$ or $\alpha_2 < \frac{1}{\alpha_1 - 1}$ (cannot have both!), $\lambda_1 < 0 \Rightarrow (\bar N_2, \bar C_2)$ stable but $(\bar N_1, \bar C_1)$ has disappeared



Interpretation of conditions $\alpha_1 > 1$, $\alpha_2 > \frac{1}{\alpha_1 - 1}$, needed to have a stable steady state with $\bar{N} > 0$.

$\alpha_1 = \frac{VK_{max}}{F}$, $\alpha_2 = \frac{c_0}{c_n}$

We can influence V, F and c_0
c_n and K_{max} likely to get values from observations/data.

$\alpha_1 > 1 \Leftrightarrow F < V \cdot K_{max}$

means the flow cannot be too big

$\alpha_2 > \frac{1}{\alpha_1 - 1} \Leftrightarrow \frac{c_0}{c_n} > \frac{1}{\frac{VK_{max}}{F} - 1} \Leftrightarrow \frac{c_n}{c_0} < \frac{VK_{max}}{F} - 1 \Leftrightarrow \left(\frac{c_n}{c_0} + 1\right) F < VK_{max}$

$\Leftrightarrow F < \frac{VK_{max}}{1 + \frac{c_n}{c_0}}$, which is $< VK_{max}$, so an even stricter upper limit on the flow.

It is reasonable that F cannot be too big if a balanced bacteria level should exist.

Next sem.: from local to global picture