Killer Yeast Vs. Sensitive Yeast

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Proposal

The differential equation we may use for modeling the growth of yeast is the same as that used for bacterial growth in a chemostat:

$$\frac{dN}{dt} = k(C)N - \frac{FN}{V},$$
$$\frac{dC}{dt} = -\alpha k(C)N - \frac{FC}{V} + \frac{FC_0}{V},$$

with initial conditions $C(0) = C_i$ and $N(0) = N_i$, N is the unitless optical density of yeast in the chamber, C is the unitless optical density of nutrient in the chamber, C_0 is the unitless optical density of nutrient in the reservoir, F is the in/out volume flow rate with units volume/time, V is the volume of the chamber, α is a unitless inverse of the yield constant, and $k(C)$ is the reproduction rate for yeast in units 1/time with possible formula chosen such that $\lim_{C\to\infty} = k_{max}$, and k_{max} represents the maximum possible reproduction rate:

$$k(C) = \frac{k_{max}C}{C_n + C}.$$

where C_n is chosen such that $k(C_n) = k_{max}/2$. Because the concentration in the tank $C(t)$ is related to the concentration in the reservoir by $C(t) \leq C_0$, C_0 may be chosen sufficiently small such that

$$k(C) = \frac{k_{max}C}{C_n + C} \approx \frac{k_{max}C}{C_n} = KC,$$

where K has units 1/time. The equations we need to solve then become

$$\frac{dN}{dt} = KCN - \frac{FN}{V}, \tag{1}$$
$$\frac{dC}{dt} = -\alpha KCN - \frac{FC}{V} + \frac{FC_0}{V}. \tag{2}$$

The quantitative measurement for fitness is a unitless measurement of optical density at steady state (N) at a given flow rate (F) in volumes/hr. In order to find the steady states, we have to

find the intersections of the null-clines at equilibrium points $(\bar{N}, \bar{C})$, i.e. $dN(\bar{N}, \bar{C})/dt = 0$ and $dC(\bar{N}, \bar{C})/dt = 0$:

$$\begin{aligned}\frac{dN(\bar{N}, \bar{C})}{dt} &= K\bar{C}\bar{N} - \frac{F\bar{N}}{V}, \\ &= \bar{N}\left(K\bar{C} - \frac{F}{V}\right) = 0,\end{aligned}$$

which is zero for $\bar{N} = 0$ or $K\bar{C} = F/V$. Solving the other equation gives us the other steady-states:

$$\frac{dC(\bar{N}, \bar{C})}{dt} = -\alpha K\bar{C}\bar{N} - \frac{F\bar{C}}{V} + \frac{FC_0}{V} = 0,$$

which is zero for $\alpha K\bar{C}\bar{N} + \frac{F\bar{C}}{V} = \frac{FC_0}{V}$.

In order to evaluate these null-clines, we need to evaluate the non-trivial cases, here for $\dot{N} = 0$,

$$\begin{aligned}K\bar{C} &= \frac{F}{V} \\ \implies \bar{C} &= \frac{F}{VK}. \end{aligned} \tag{3}$$

Likewise, for $\dot{C} = 0$,

$$\begin{aligned}\alpha K\bar{C}\bar{N} + \frac{F\bar{C}}{V} &= \frac{FC_0}{V} \\ \implies \bar{N} &= \frac{FC_0}{V\alpha K\bar{C}} - \frac{F}{V\alpha K} = \frac{F}{V\alpha K}\left(\frac{C_0}{\bar{C}} - 1\right).\end{aligned} \tag{4}$$

This intersects the $\bar{N} = 0$ nullcline at $\frac{F}{V\alpha K} = 0$ or $\frac{C_0}{\bar{C}} = 1$. However, because F is never 0, we can disregard the first equation, and we know that the only trivial steady-state is located at $\bar{N} = 0$, $\bar{C} = C_0$.

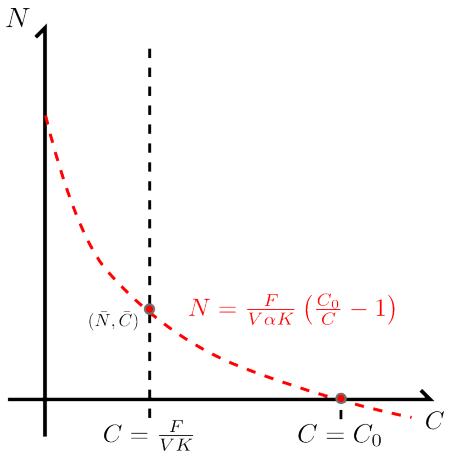


Figure 1: The $\dot{C} = 0$ nullcline (dashed red) intersecting with the $\dot{N} = 0$ nullcline (dashed black). The trivial and non-trivial steady-states $(0, C_0)$ and $(\bar{N}, \bar{C})$ are shown as red dots.

By placing Eq. (3) inside Eq. (4), we can find the non-trivial steady-state, the intersection of null-clines:

$$\begin{aligned}\bar{N}(\bar{C}) &= \frac{FC_0}{V\alpha K\bar{C}} - \frac{F}{V\alpha K} \\ &= \frac{FC_0}{V\alpha K\frac{F}{VK}} - \frac{F}{V\alpha K} \\ &= \frac{C_0}{\alpha} - \frac{F}{V\alpha K} = \frac{1}{\alpha}\left(C_0 - \frac{F}{VK}\right).\end{aligned} \tag{5}$$

The unknown parameters in Eq (5) are α and K. We can find these parameters by fitting Eq (5) to the data by non-linear least squares fitting $\bar{N}_i$ at F_i for $i = 1, \ldots, n$, where n is the number of observations.

After we obtain estimates of these parameters for both the killer yeast L and sensitive yeast S, (α_L, α_S and K_L, K_S respectively), we can model a "what if" scenario whereby we place both species of yeast, sensitive and killer, into one chemostat. The population of sensitive yeast S will be negatively impacted by the amount of toxin the killer yeast K can produce, so we add the term $-\beta KL$ to the differential equation describing population S. The differential equations we use to solve this three-species model is

$$\frac{dL}{dt} = K_L CL - \frac{FL}{V}, \tag{6}$$

$$\frac{dS}{dt} = K_S CS - \frac{FS}{V} - \beta SL, \tag{7}$$

$$\frac{dC}{dt} = -\alpha_L K_L CL - \alpha_S K_S CS - \frac{FC}{V} + \frac{FC_0}{V}. \tag{8}$$

The data we are provided with include two sets of two separate runs, along with the concentration of nutrient in the reservoir, $C_0 = 0.02$:

1 K1 Run

Vessel One :

Volumes/Hr	0.028	0.099	0.142	0.207	0.269	0.287	0.352	0.403
Optical Density at Steady State	0.144	0.151	0.099	0.069	0.045	0.02	0.003	0

Vessel Two :

Volumes/Hr	0.054	0.11	0.141	0.199	0.257	0.296	0.348	0.397	0.41
Optical Density at Steady State	0.164	0.151	0.11	0.092	0.072	0.023	0.006	0.002	0.004

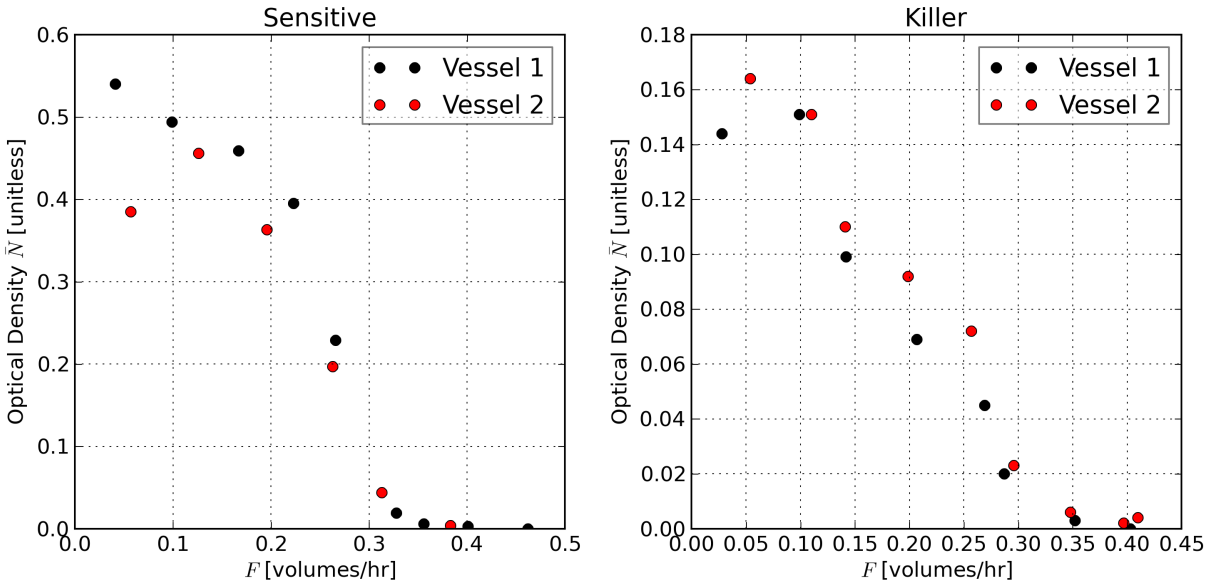
2 Sensitive Run

Vessel One :

Volumes/Hr	0.041	0.099	0.167	0.223	0.266	0.328	0.356	0.401	0.462
Optical Density at Steady State	0.54	0.494	0.459	0.395	0.229	0.019	0.006	0.003	0

Vessel Two :

a	Volumes/Hr	0.0571	0.126	0.196	0.263	0.313	0.383
	Optical Density at Steady State	0.385	0.456	0.363	0.197	0.044	0.004



The data provided does not include the volume of the chamber, V. In order to solve Eq. (5), this quantity is needed. Here we have dimensional analysis of the problem:

$$\begin{aligned}
\frac{dN}{dt} &= KCN - \frac{FN}{V} \\
\equiv \left[\frac{1}{\text{time}}\right] &\equiv \left[\frac{1}{\text{time}} - \frac{\text{volume}}{\text{time}} \cdot \frac{1}{\text{volume}}\right] \equiv \left[\frac{1}{\text{time}}\right], \\
\frac{dC}{dt} &= -\alpha KCN - \frac{FC}{V} + \frac{FC_0}{V} \\
\equiv \left[\frac{1}{\text{time}}\right] &\equiv \left[-\frac{1}{\text{time}} - \frac{\text{volume}}{\text{time}} \cdot \frac{1}{\text{volume}} + \frac{\text{volume}}{\text{time}} \cdot \frac{1}{\text{volume}}\right] \equiv \left[\frac{1}{\text{time}}\right].
\end{aligned}$$