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 number of yeast in the chamber in units number/volume, C is the concentration of nutrient in the chamber with units mass/volume, C_0 is the concentration of nutrient in the reservoir, F is the in/out 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:

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

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

$$k(C) = \frac{k_{max}C}{k_n + C} \approx \frac{k_{max}C}{k_n} = KC.$$

Also, because the data is collected in density form, we propose solving for density $\rho = N/V$:

$$\frac{d\rho}{dt} = KC\rho - \frac{F\rho}{V}, \tag{1}$$
$$\frac{dC}{dt} = -\alpha KC\rho - \frac{FC}{V} + \frac{FC_0}{V}, \tag{2}$$

with initial conditions $\rho(0) = \rho_i$ and $C(0) = C_i$, and all other constants are identical as before.

The quantitative measurement for fitness is a measurement of optical density at steady state (equilibrium) 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 $(\bar{\rho}, \bar{C})$, i.e. $d\bar{\rho}/dt = 0$ and $d\bar{C}/dt = 0$:

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

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

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

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

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

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

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

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

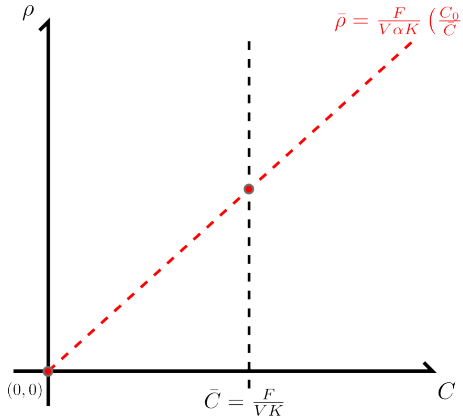

Figure 1: The $\dot{C} = 0$ nullcline (red) intersecting with the $\dot{\rho} = 0$ nullcline (black). The trivial steady-state $(0, 0)$ and non-trivial steady-state $(\bar{\rho}, \bar{C})$ are shown as red dots.

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

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

The unknowns in this equation are α and K. We can then minimize the difference between the equilibrium solution for ρ determined from the differential equations $\dot{\rho}$ and $\dot{C}$ (determined numerically) and the observed optical density $\bar{\rho}$ for a given F to provide an estimate for $\bar{C}$, α, and K.

After we have estimates for the initial conditions, α and K (and hence $\bar{C}$), we can model a "what if" scenario where we put both species of yeast, sensitive and killer, into one chemostat.

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