

# 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:

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

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,  $\alpha$  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  $\lim_{C \rightarrow \infty} k(C) = k_{max}$ , 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  $\bar{N} = 0$ ,

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

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

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

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  $\bar{N} = 0$ ,  $\bar{C} = C_0$ .

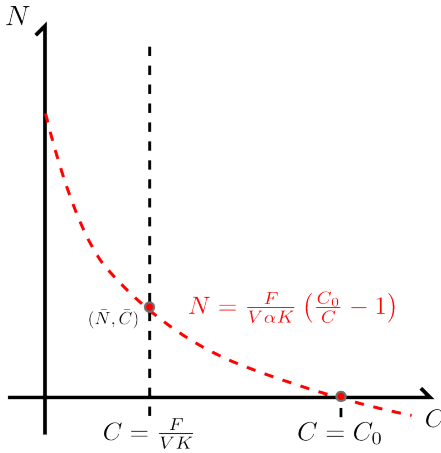


Figure 1: The  $\dot{C} = 0$  nullcline (dashed red) intersecting with the  $\dot{N} = 0$  nullcline (dashed black). The trivial and non-trivial steady-states  $(0, C_0)$  and  $(\bar{N}, \bar{C})$  are shown as red dots.

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  $\alpha$  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  $i = 1, \dots, n$ , where  $n$  is the number of observations.

After we obtain estimates of these parameters for both the killer yeast  $L$  and sensitive yeast  $S$ , ( $\alpha_L$ ,  $\alpha_S$  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

$$\frac{dL}{dt} = K_L CL - \frac{FL}{V}, \quad (6)$$

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

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

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

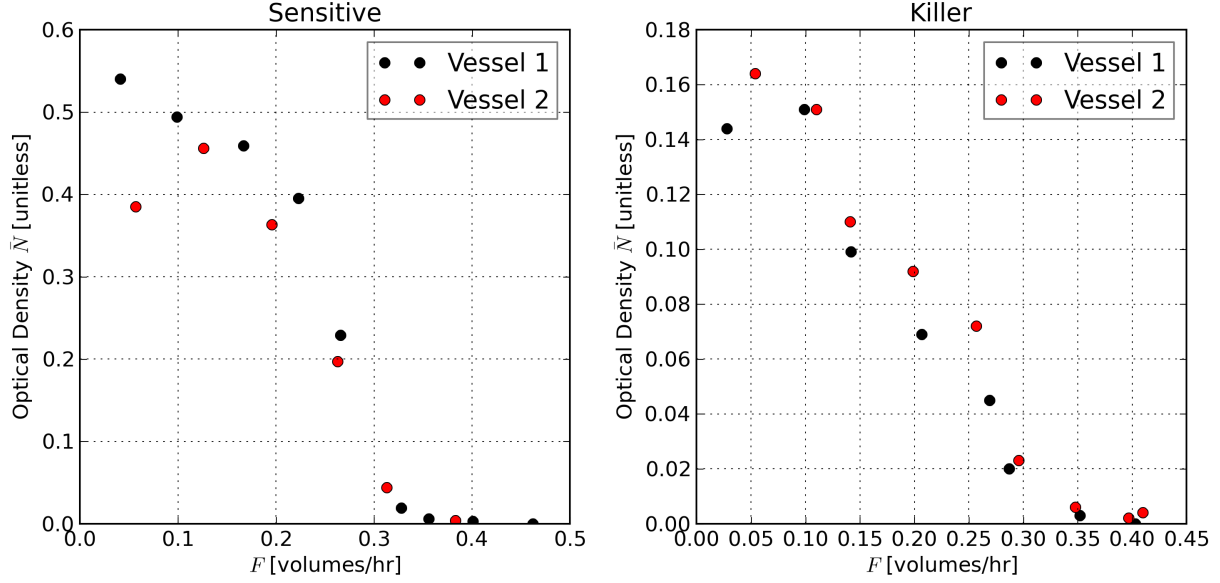
## 2 Sensitive Run

### 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 :

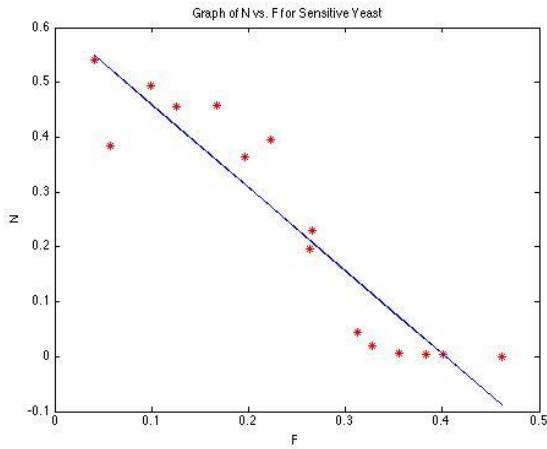
Volumes/Hr	0.0571	0.126	0.196	0.263	0.313	0.383
Optical Density at Steady State	0.385	0.456	0.363	0.197	0.044	0.004



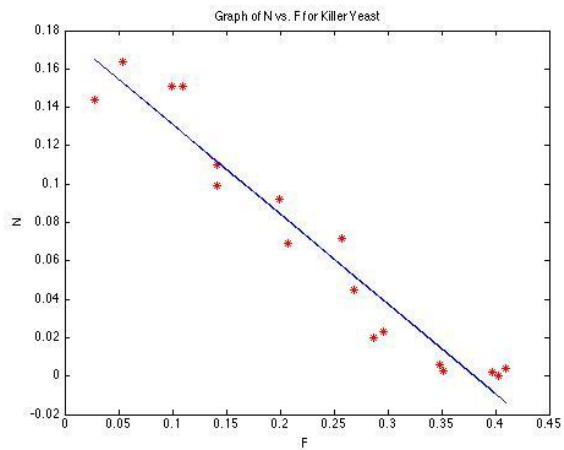
The data provided does not include the volume of the chamber,  $V$ . In order to solve Eq. (5), this quantity is needed. Here we have dimensional analysis of the problem:

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

Here's the best fit lines:



	Estimates	SE	CI
$\alpha_L$	0.1124	0.0053	(0.0969, 0.1279)
$K_L$	19.0288	0.6367	(17.1526, 20.905)



	Estimates	SE	CI
$\alpha_S$	0.0325	0.0024	(0.0255, 0.0399)
$K_S$	20.1818	1.0802	(16.9281, 23.4356)

Here's the dynamics solution:

