# Killer Yeast Vs. Sensitive Yeast

Evan Cummings Intizor Aliyorov
Malachi J. Cryder
MATH 445 - Statistical, Dynamical, and Computational Modeling

December 2, 2013

## 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 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, $\alpha$ 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 $\lim_{C\to\infty} = k_{max}$, 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 $k(k_n) = k_{max}/2$. The quantitative measurement for fitness is a measurement of optical density at steady state (equilibrium) at a given flow rate ($F$) in volumes/hr.

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

$$\begin{aligned}\frac{d\rho}{dt} &= k(C)\rho - \frac{F\rho}{V},\\ \frac{dC}{dt} &= -\alpha k(C)\rho - \frac{FC}{V} + \frac{FC_0}{V},\end{aligned}$$

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

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 $\dot{\rho} = 0$,

$$\begin{aligned}
k(\bar{C}) = \frac{k_{max}\bar{C}}{k_n + \bar{C}} &= \frac{F}{V} \\
k_{max}\bar{C} &= \frac{F}{V}(k_n + \bar{C}) \\
k_{max}\bar{C} - \frac{F}{V}\bar{C} &= \frac{F}{V}k_n \\
\bar{C}\left(k_{max} - \frac{F}{V}\right) &= \frac{F}{V}k_n \\
\bar{C} &= \frac{Fk_n}{V\left(k_{max} - \frac{F}{V}\right)} \\
\bar{C} &= \frac{Fk_n}{Vk_{max} - F}. \qquad (1)
\end{aligned}$$

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

$$\begin{aligned}
\alpha k(\bar{C})\bar{\rho} + \frac{F\bar{C}}{V} &= \frac{FC_0}{V} \\
\alpha\left[\frac{k_{max}\bar{C}}{k_n + \bar{C}}\right]\bar{\rho} + \frac{F\bar{C}}{V} &= \frac{FC_0}{V} \\
\alpha k_{max}\bar{C}\bar{\rho} + \frac{F\bar{C}}{V}(k_n + \bar{C}) &= \frac{FC_0}{V}(k_n + \bar{C}) \\
\alpha k_{max}\bar{C}\bar{\rho} + \frac{F\bar{C}}{V}(k_n + \bar{C}) &= \frac{FC_0}{V}(k_n + \bar{C}) \\
\alpha k_{max}\bar{C}\bar{\rho} + \frac{F\bar{C}k_n}{V} + \frac{F\bar{C}^2}{V} &= \frac{FC_0k_n}{V} + \frac{FC_0\bar{C}}{V} \\
\alpha k_{max}\bar{C}\bar{\rho} &= \frac{FC_0k_n}{V} + \frac{FC_0\bar{C}}{V} - \frac{F\bar{C}k_n}{V} - \frac{F\bar{C}^2}{V} \\
\bar{\rho} &= \frac{FC_0k_n}{V(\alpha k_{max}\bar{C})} + \frac{FC_0\bar{C}}{V(\alpha k_{max}\bar{C})} - \frac{F\bar{C}k_n}{V(\alpha k_{max}\bar{C})} - \frac{F\bar{C}^2}{V(\alpha k_{max}\bar{C})} \\
\bar{\rho} &= \frac{FC_0k_n}{V\alpha k_{max}\bar{C}} + \frac{FC_0}{V\alpha k_{max}} - \frac{Fk_n}{V\alpha k_{max}} - \frac{F\bar{C}}{V\alpha k_{max}} \\
\bar{\rho} &= \frac{F}{V\alpha k_{max}}\left(\frac{C_0k_n}{\bar{C}} + C_0 - k_n - \bar{C}\right). \qquad (2)
\end{aligned}$$

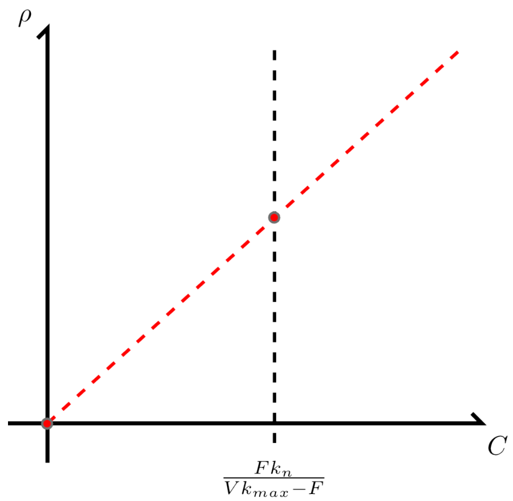



Figure 1: The $\dot{C} = 0$ nullcline (red) intersecting with the $\dot{\rho} = 0$ nullcline (black). The trivial steady-state $(0, 0)$ and non-trivial steady-state $(\bar{\rho}, \bar{C})$ are shown as red dots.

By placing Eq. (1) inside Eq. (2), we can find the intersection of the null-clines:

$$\begin{aligned}\bar{\rho}(\bar{C}) &= \frac{F}{V\alpha k_{max}}\left(\frac{C_0 k_n}{\bar{C}} + C_0 - k_n - \bar{C}\right)\\ &= \frac{F}{V\alpha k_{max}}\left(\frac{C_0 k_n}{\frac{Fk_n}{Vk_{max}-F}} + C_0 - k_n - \frac{Fk_n}{Vk_{max}-F}\right)\\ &= \frac{F}{V\alpha k_{max}}\left(\frac{C_0(Vk_{max}-F)}{F} + C_0 - k_n - \frac{Fk_n}{Vk_{max}-F}\right).\end{aligned}$$

The unknowns in this are $\alpha$, $k_{max}$, and $k_n$. First, assume $\alpha = 1$. With this assumption we can then minimize the difference between the equilibrium solution for $\rho$ 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 $\bar{C}$, which we can then plug into equations (1) and (2) to get $k_{max}$ and $k_n$.

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

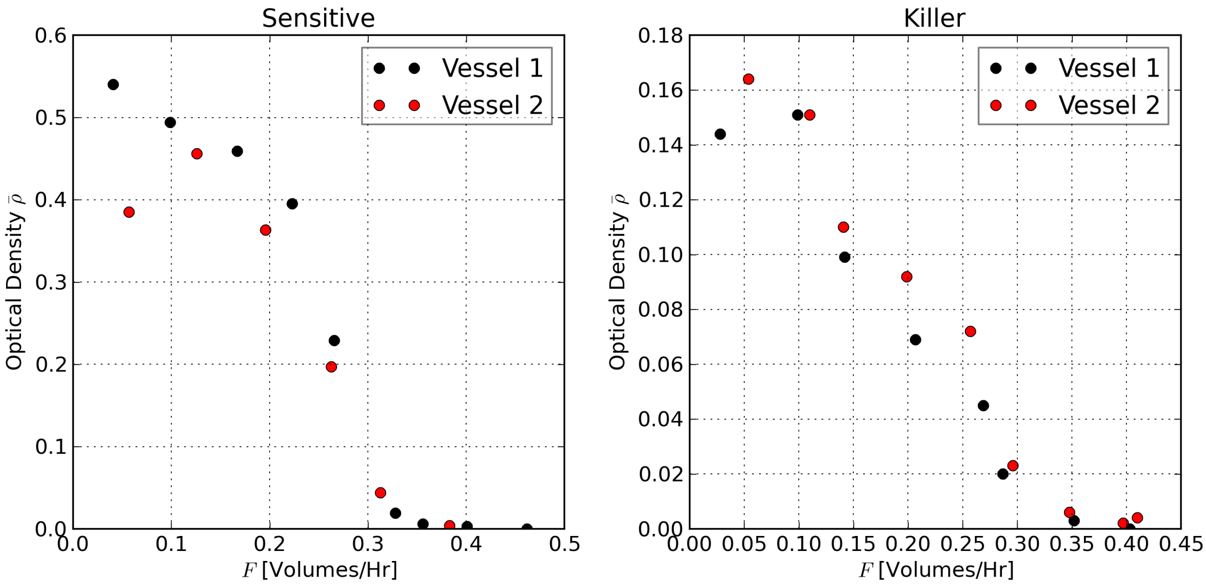
## Vessel One :

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 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 |



Sensitive
Killer
Vessel 1
Vessel 2
Optical Density $\bar{\rho}$
$F$ [Volumes/Hr]