Modeling the Competitive Growth of
Saccharomyces Cerevisiae and *Schizosaccharomyces Kefir*

by

Joshua Francois
Joon Park

BENG 221
10/7/11

Introduction and Background

Yeasts are eukaryotic organisms that serve many practical purposes in today's world. One well known type of yeast, *Saccharomyces cerevisiae*, is especially useful. One such purpose is for biological research. *Saccharomyces cerevisiae* can easily be grown in large quantities, which makes the yeast cells readily available for laboratory experiments.[1] Also, its genome is known, making it a great cell type for genetic engineering.

Saccharomyces cerevisiae is also useful for its ability to produce ethanol. At the end of glycolysis, pyruvate is formed[1]. If oxygen is present in the environment (aerobic conditions), this molecule will be turned into acetyl-CoA and go to the citric acid cycle to eventually make CO_2 and H_2O. If oxygen is not present in the environment (anaerobic conditions), pyruvate is reduced with the help of lactate dehydrogenase to lactate. In yeast cells, pyruvate is not converted to acetyl-CoA. Instead, it is first converted to acetaldehyde and then ethanol with the help of pyruvate decarboxylase and alcohol dehydrogenase, respectively. This process, known as fermentation, is used industrially to make alcoholic beverages, but also alternative fuel.

In both research and industrial uses, the function of yeast cells can be enhanced by having more yeast cells. A factor that can set back the functionality of one type of yeast can possibly be contamination by another type of yeast. When placed in the same environment, two or more yeast species may be in competition for resources.[2] In the case of yeast cells, different species may compete for nutrients. As one species grows, it consumes and therefore can deplete nutrients in the environment. This depletion can then hinder the growth of the other species. Another environmental change that can affect the other species may be the waste products created.

The scenario presented above is a short description of conditions laid out in Georgii Frantsevich Gause's 1932 article "Experimental Studies on the Struggle for Existence." In this article, Gause used the logistic equation to model growth of a mixed population and applied it to two different types of yeast, S*accharomyces cerevisiae and Schizosaccharomyces kefir*. A similar scenario was examined in this project. The numerical solutions were compared with the results found by Gause.

Problem Statement

Write and solve, analytically and numerically, a system of equations that appropriately modeled the growth of the two yeast species, growing in a common environment, given the initial mass of both species.

Analytical Solution

Two functions, y_1 and y_2, were defined such that:

$y_1(t)$ = mass of yeast 1 (Saccharomyces cerevisiae) at time t (in hours), and

$y_2(t)$ = mass of yeast 2 (Schizosaccharomyces kefir) at time t (in hours).

To model the growth of each species of yeast individually, the logistic equation was used:

$$\frac{dy_1}{dt} = b_1 y_1 \left(\frac{K_1 - y_1}{K_1} \right)$$

where b_1 = intrinsic growth rate of the species and K_1 = carrying capacity of the environment.

However, this logistic equation does not take into account the presence of the other species in the environment. In order to model the competitive nature of their growth, a particular term in the equation was further examined:

$$\left(\frac{K_1 - y_1}{K_1}\right)$$

It was observed that this term in the differential equation represents the limiting nature of the environment as the population reaches its capacity. It can be shown that as $y_1 \rightarrow K_1$, $dy_1/dt \rightarrow 0$. Taking the presence of y_2 into account, it is assumed that the presence of y_2 will accelerate this process. To reflect this assumption, the following term is used instead:

$$\left(\frac{K_1 - (y_1 + \alpha y_2)}{K_1}\right)$$

where α = proportionality constant.

Applying this term to the original logistic equation, the following set of differential equations was obtained:

$$\frac{dy_1}{dt} = b_1 y_1 \left(\frac{K_1 - (y_1 + \alpha y_2)}{K_1}\right) \tag{1}$$

$$\frac{dy_2}{dt} = b_2 y_2 \left(\frac{K_2 - (y_2 + \beta y_1)}{K_2}\right) \tag{2}$$

It can be shown that this set of differential equations is difficult to solve using the methods covered in class. In order to simplify the equations, the following assumptions were made:

$$y_1 >> y_2,$$
$$\alpha \approx 1,$$
$$\beta \approx 1.$$

The first assumption would be valid if y_1 represents the yeast species of interest and y_2 represents contamination. The assumptions regarding α and ß were based on experimental values determined by Gause. Then, equations (1) and (2) simplify to:

$$\frac{dy_1}{dt} = b_1 y_1 \left(\frac{K_1 - y_1}{K_1}\right) \tag{3}$$

$$\frac{dy_2}{dt} = b_2 y_2 \left(\frac{K_2 - \beta y_1}{K_2}\right) \tag{4}$$

Now, (3) can be solved analytically, in the following way:

$$\frac{dy_1}{dt} = b_1 y_1 (\frac{K_1 - y_1}{K_1})$$

$$\int \frac{K_1 dy_1}{y_1 (K_1 - y_1)} = \int b_1 \, dt$$

Using partial fractions,

$$\frac{A}{y_1} + \frac{B}{K_1 - y_1} = \frac{K_1}{y_1(K_1 - y_1)}$$
$$AK_1 - Ay_1 + By_1 = K_1$$
$$AK_1 = K_1 --> A = 1.$$
$$(B - A)y_1 = 0 --> B = 1.$$

Integrating,

$$\int\left(\frac{1}{y_1} + \frac{1}{K_1 - y_1}\right)dy_1 = \int b_1\, dt$$
$$\ln(y_1) - \ln(K_1 - y_1) = b_1 t + C'$$
$$\ln\left(\frac{K_1 - y_1}{y_1}\right) = -b_1 t + C$$
$$\frac{K_1 - y_1}{y_1} = e^{-b_1 t + C} = Ae^{-b_1 t}$$
$$y_1 = \frac{K_1}{1 + Ae^{-b_1 t}}$$

Using initial conditions to find A:

$$y_1(0) = y_{10} = \frac{K_1}{1 + A}$$
$$A = \frac{K_1 - y_{10}}{y_{10}}$$
$$y_1 = \frac{K_1}{1 + \left(\frac{K_1 - y_{10}}{y_{10}}\right)e^{-b_1 t}}$$

Final solution for $y_1(t)$ is:

$$y_1 = \frac{K_1 y_{10}}{y_{10} + (K_1 - y_{10})e^{-b_1 t}} \tag{5}$$

Now, the analytical solution for y_1 can be used to find the solution for y_2:

$$\frac{dy_2}{dt} = b_2 y_2\left(\frac{K_2 - \beta y_1}{K_2}\right) = b_2 y_2\left(\frac{K_2 - \beta\dfrac{K_1 y_{10}}{y_{10} + (K_1 - y_{10})e^{-b_1 t}}}{K_2}\right)$$
$$= \left(b_2 - b_2\beta\frac{K_1}{K_2} y_{10}\left(\frac{1}{y_{10} + (K_1 - y_{10})e^{-b_1 t}}\right)\right)y_2$$

Substituting for variables to simplify the equation,

$$M = b_2\beta\frac{K_1}{K_2}y_{10};\ B = y_{10};\ A = K_1 - y_{10};\ \lambda = -b_1$$

$$\int\frac{dy_2}{y_2} = \int b_2dt - M\int\frac{dt}{B + Ae^{\lambda t}}$$

A table of integral was used to integrate the right hand side:[3]

$$\ln(y_2) = b_2t - M\left(\frac{\lambda t - \ln(Ae^{\lambda t} + B}{B\lambda}\right) + C$$

$$= b_2t - \beta\frac{b_2}{b_1}\frac{K_1}{K_2}(b_1t + \ln((K_1 - y_{10})e^{-b_1t} + y_{10}) + C$$

$$N = \beta\frac{b_2}{b_1}\frac{K_1}{K_2}$$

$$y_2 = e^{b_2t}e^{-Nb_1t}e^{-N\ln\left((K_1-y_{10})e^{-b_1t}+y_{10}\right)}e^C$$

$$A = e^C$$

$$y_2 = \frac{Ae^{b_2t}}{\left(e^{b_1t}\left((K_1 - y_{10})e^{-b_1t} + y_{10}\right)\right)^N} = \frac{Ae^{b_2t}}{\left(K_1 + y_{10}(e^{b_1t} - 1)\right)^N}$$

Using initial conditions to find A:

$$y_2(0) = y_{20} = \frac{A}{K_1^N}$$

$$A = y_{20}K_1^N$$

Finally,

$$y_2 = y_{20}e^{b_2t}\left(\frac{K_1}{K_1 + y_{10}(e^{b_1t} - 1)}\right)^N,\ \ N = \beta\frac{b_2}{b_1}\frac{K_1}{K_2} \qquad (6)$$

Numerical Plots (*Note: Matlab code included in Appendix)*

The analytical and numerical solutions to equations (1) and (2) were plotted in Matlab for the purpose of comparing the analytical and numerical solutions. The blue curve represents the solution curve for the growth of species 1 (Saccharomyces cerevisiae or Sce) and the green curve represents the solution for the growth of species 2 (Schizosaccharomyces cerevisiae or Ske). The numerical solutions were obtained by using Euler's approximation method and the ode23 function in Matlab. Different cases with varied initial conditions were considered. The cases were defined as follows:

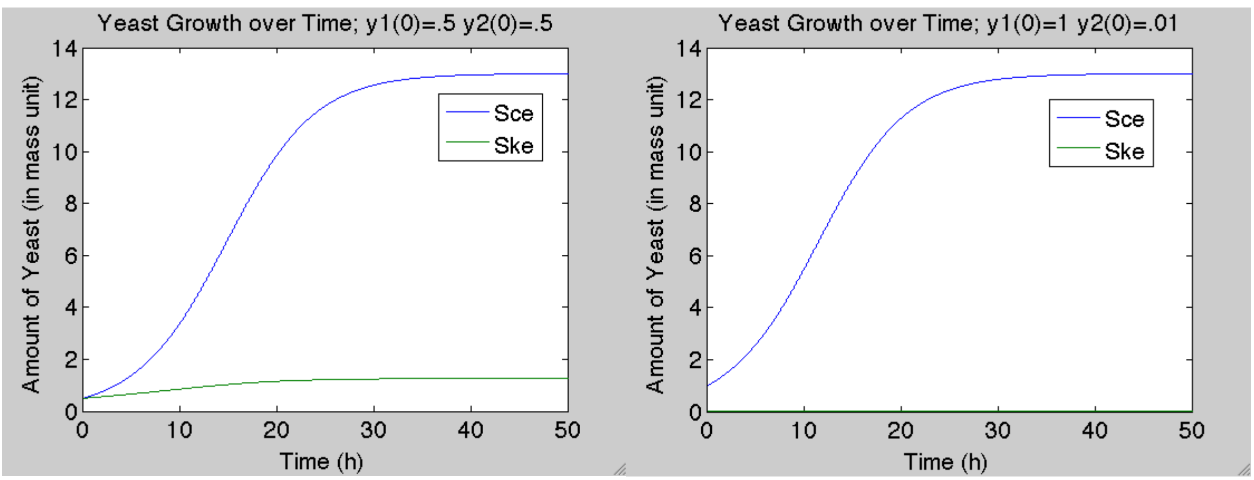
Case 1: y1(0) = y2(0)
Case 2: y1(0) >> y2(0)
Case 3: y1(0) << y2(0)

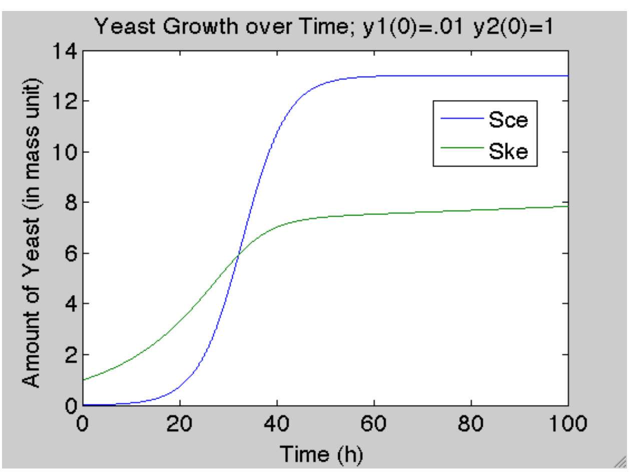
For cases 1 and 2, the solutions were plotted from t = 0 to t = 50 hours. For case 3, the solutions were plotted from t = 0 to t = 100 hours. These time intervals were chosen based on what intervals gave the best view of the yeast growth models in each case. Also, the numerical values for constants were obtained from Gause's article and are as follows:

$$\alpha = 3.15;\ ß = 0.439;\ b_1 = 0.21827;\ b_2 = 0.06069;\ K_1 = 13;\ K_2 = 5.8$$

Analytical Solution

Figures 1-3 show the plots of the analytical solutions (equations 5 and 6) for the competitive yeast growth model for cases 1, 2, and 3, respectively. In each plot, the general shape for species 1 looked the same. The initial conditions dictated where the curve began, but the change in the mass of species 1 first increased. The change in the mass then remained constant. Finally, the change in the mass leveled out and eventually the mass remained constant, at its carrying capacity (K_1).





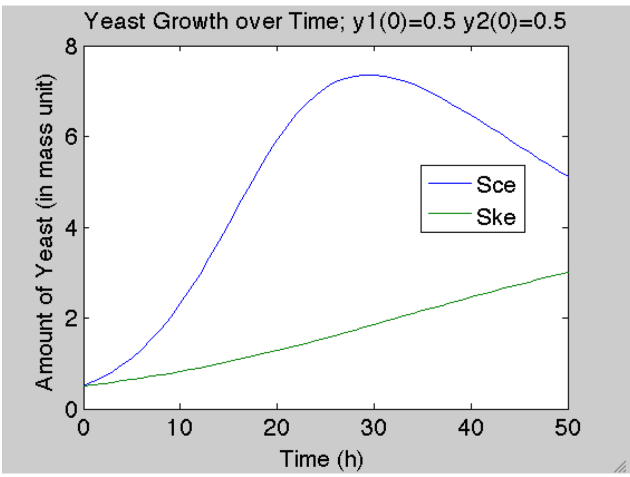
Figures 1 (top left), 2 (top right), and 3 (bottom). Plots of the analytical solution for cases 1, 2, and 3, respectively.

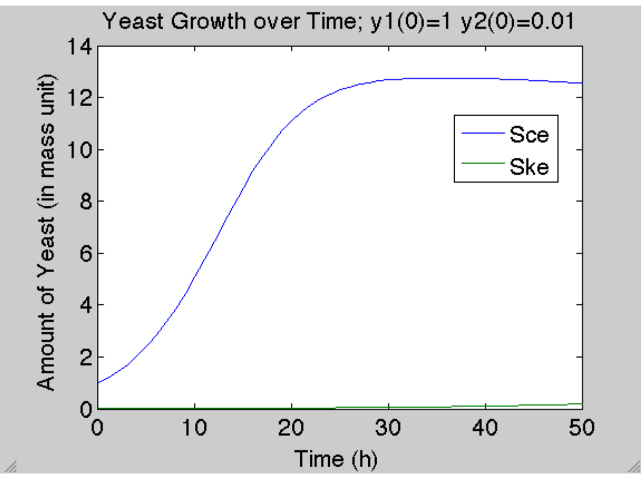
The initial conditions had a greater effect on the growth curve for species 2. For case 1, the mass of species 2 increased slightly before remained relatively constant. For case 2, the mass of species 2 appeared to remain constant at its initial value. In case 3, the curve for species 2 showed more of a resemblance to the curve for species 1. The mass increased, but eventually leveled off to a relatively constant value.

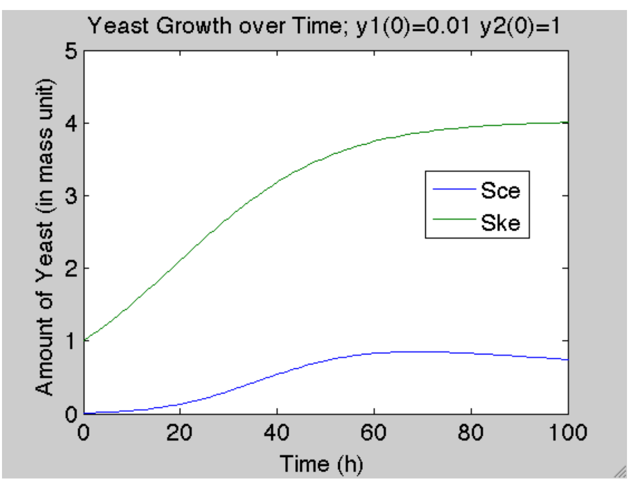
The figures clearly showed the effect of assuming that y1 >> y2. The shapes of the curves for species 1 were generally identical. The final mass of species 1 was greater than that for species 2 in all cases. The curves for species 1 also leveled off at the same value of 13, which was the carrying capacity for the species. This showed that the presence of species 2 did not have any effect on the growth of species 1. In contrast, the presence of species 1 did have an effect of the growth of species 2.

Numerical Solution Using Euler's Method

Figures 4-6 show the numerical solutions for the model using Euler's approximation method for cases 1, 2, and 3, respectively. In case 1, the mass of species 1 appeared to increase for the first 30 hours then decreased. The mass of species 2 increased more constantly and at a much lower rate than the increase for species 1. Also, the mass of species 2 did not decrease.







Figures 4 (top left), 5 (top right), and 6 (bottom). Plots of the numerical solution using Euler's method for cases 1, 2, and 3, respectively.

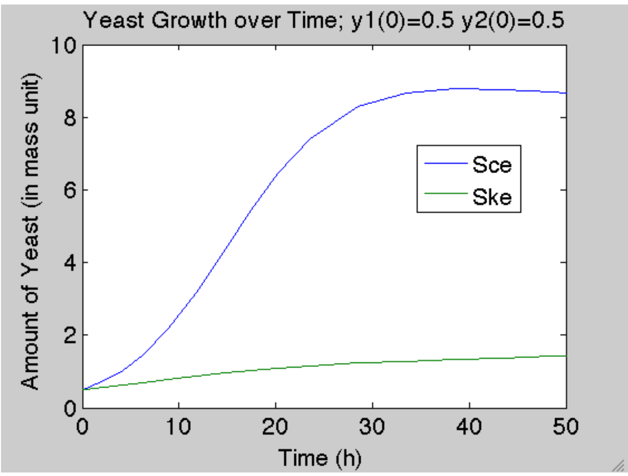
The growth curves for case 2 using the Euler approximation were almost identical to the curves obtained with the analytical for the same case. There was an increase in the mass of species 1, until about 25 hours. After this point, the mass remained relatively constant. The mass of species 2 seemed to remain constant throughout.

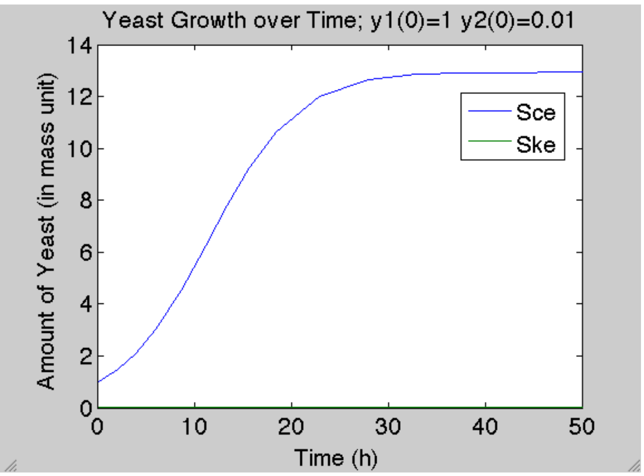
For case 3, the mass of species 1 initially increased, but then began to decrease after about 60 hours. The mass of species 2 increased. Interestingly, in this case the mass of species 2 increased at a higher rate than the mass of species 1. The final mass for species 2 was also greater than the final mass for species 1.

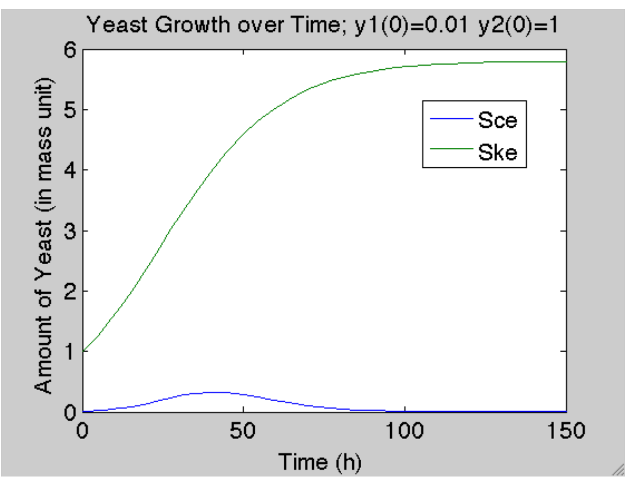
The solutions obtained with Euler's method did not include the assumption that y1>>y2. This was evident from the maximum mass that each species reached. The maximum varied for the three different conditions, showing that the initial amount of each species had an effect on the growth of the other.

Numerical Solution Using ode23

Figures 7-9 show the numerical solutions for the model using the ode23 function in Matlab for case 1, 2, and 3, respectively. In case 1, the mass of species 1 increased until around 30 hours. It then remained relatively constant. The mass of species 2 increased slightly and at a fairly constant rate.







Figures 7 (top left), 8 (top right), and 9 (bottom). Plots of the numerical solution using ode23 for cases 1, 2, and 3, respectively.

In case 2, the growth curves for both species resembled the curves obtained analytically and with Euler's method with the same initial conditions. In case 3, the mass of species 2 was greater and grew at a faster rate than that of species 1. Species 1 seemed to increase in mass initially but decreased again to a negligible value. Similar to the solution through Euler's method, this was the only case when the mass of species 2 remained higher and grew at a faster rate than that of species 1.

Conclusion

From the results, several conclusions may be drawn. First, the results demonstrated the usefulness and exactness of the analytical solution when accurate assumptions are made. In this case, the assumption that $y_1 >> y_2$ was true only in case 2, and as figures 2, 5 and 8 show, the analytical solution is identical to the numerical solutions. On the other hand, the other two cases demonstrated the importance of the dependence of one parameter on the other. the assumption made in obtaining the analytical solution for y_1 removed the dependence of y_1 on y_2, which made the analytical solution inaccurate for cases 1 and 3. Furthermore, the results exhibit the superior usefulness of the numerical method. Analytical solutions are useful when the problem is reducible to sets of equations that are solvable; however, the types of questions that the analytical methods can answer are limited. On the other hand, numerical methods, as demonstrated above, are more versatile in producing solutions for more complex sets of differential equations.

References

1. Nelson, David L. and Cox, Michael M. *Lehninger Principle of Biochemistry.* 2008. W. H. Freeman and Company.
2. Gause, G.F. *Experimental Studies on The Struggle For Existence*. Journal of Experimental Biology, 1932. 9: p. 389- 402.
3. http://en.wikipedia.org/wiki/List_of_integrals_of_exponential_functions

Appendix

For the plotting of the analytical solution:

```
%
clear all
close all
clc

t = 0:.01:50;

al=3.15;
B=0.439;
b1=0.21827;
b2=0.06069;
K1=13;
K2=5.8;
y10=.5;
y20=.5;
N=B*b2/b1*K1/K2;

y1 = K1*y10./(y10+(K1-y10)*exp(-b1*t));

for i = 1:5001
    y2(i) = y20*exp((b2-N*b1)*(i-1)*(.01))*(K1/((K1-y10)*exp(-b1*(i-1)*(.01)) +
y10))^N;
end

figure(1)
plot(t, y1, t, y2)
set(gca, 'fontsize', 17)
xlabel('Time (h)');
ylabel('Amount of Yeast (in mass unit)');
title('Yeast Growth over Time; y1(0)=.5 y2(0)=.5');
legend('Sce','Ske');

y10=1;
y20=.01;

y1 = K1*y10./(y10+(K1-y10)*exp(-b1*t));

for i = 1:5001
    y2(i) = y20*exp((b2-N*b1)*(i-1)*(.01))*(K1/((K1-y10)*exp(-b1*(i-1)*(.01)) +
```

```
y10))^N;
end

figure(2)
plot(t, y1, t, y2)
set(gca, 'fontsize', 17)
xlabel('Time (h)');
ylabel('Amount of Yeast (in mass unit)');
title('Yeast Growth over Time; y1(0)=1 y2(0)=.01');
legend('Sce','Ske');

y10=0.01;
y20=1;

t = 0:.01:100;

y1 = K1*y10./(y10+(K1-y10)*exp(-b1*t));

for i = 1:10001
    y2(i) = y20*exp((b2-N*b1)*(i-1)*(.01))*(K1/((K1-y10)*exp(-b1*(i-1)*(.01)) +
y10))^N;
end

figure(3)
plot(t, y1, t, y2)
set(gca, 'fontsize', 17)
xlabel('Time (h)');
ylabel('Amount of Yeast (in mass unit)');
title('Yeast Growth over Time; y1(0)=.01 y2(0)=1');
legend('Sce','Ske');
```

For the plotting of the solution using Euler's method:

```
clc
clear all
%
al=3.15;
B=0.439;
b1=-0.21827;
b2=-0.06069;
K1=13;
K2=5.8;
%
y1(1)=.5;
y2(1)=.5;
t=1;
%
% Euler
%
for i=1:50
    y1(i+1)=y1(i)+t*(-b1/K1)*y1(i)*(K1-(y1(i)+al*y2(i)));
    y2(i+1)=y2(i)+t*(-b2/K2)*y2(i)*(K2-(y2(i)+B*y2(i)));
end
%
t1 = 0:1:50;
figure(1)
plot (t1,y1,t1,y2)
set(gca,'fontsize',17)
xlabel('Time (h)');
ylabel('Amount of Yeast (in mass unit)');
title('Yeast Growth over Time; y1(0)=0.5 y2(0)=0.5');
% ylim([0 35]);
% xlim([0 t_end]);
legend('Sce','Ske');
%
```

```
y1(1)=1;
y2(1)=.01;
t=1;
%
% Euler
%
for i=1:50
    y1(i+1)=y1(i)+t*(-b1/K1)*y1(i)*(K1-(y1(i)+al*y2(i)));
    y2(i+1)=y2(i)+t*(-b2/K2)*y2(i)*(K2-(y2(i)+B*y2(i)));
end
%
t1 = 0:1:50;
figure(2)
plot (t1,y1,t1,y2)
set(gca,'fontsize',17)
xlabel('Time (h)');
ylabel('Amount of Yeast (in mass unit)');
title('Yeast Growth over Time; y1(0)=1 y2(0)=0.01');
% ylim([0 35]);
% xlim([0 t_end]);
legend('Sce','Ske');
%
y1(1)=.01;
y2(1)=1;
t=1;
%
% Euler
%
for i=1:100
    y1(i+1)=y1(i)+t*(-b1/K1)*y1(i)*(K1-(y1(i)+al*y2(i)));
    y2(i+1)=y2(i)+t*(-b2/K2)*y2(i)*(K2-(y2(i)+B*y2(i)));
end
%
t1 = 0:1:100;
figure(3)
plot (t1,y1,t1,y2)
set(gca,'fontsize',17)
xlabel('Time (h)');
ylabel('Amount of Yeast (in mass unit)');
title('Yeast Growth over Time; y1(0)=0.01 y2(0)=1');
% ylim([0 35]);
% xlim([0 t_end]);
legend('Sce','Ske');
```

For the plotting of the solution using ode23:

```
function numode()

t_start = 0; %s -- the point when your simulation starts
t_end = 50; %s -- the point when your simulation ends

% ODE Solver
Initials = [.5; .5]; % Your initial values of x and y are stored in a column vector
[t,Q] = ode23(@get_derivs_solver, [t_start; t_end], Initials);

figure (1)
plot(t, [Q(:,1) Q(:,2)]); %Plots each column of Q vs. time
set(gca,'fontsize',17)
xlabel('Time (h)');
ylabel('Amount of Yeast (in mass unit)');
title('Yeast Growth over Time; y1(0)=0.5 y2(0)=0.5');
xlim([0 t_end]);
legend('Sce','Ske');

return
```

```
% Function to Calculate Derivatives
function derivatives = get_derivs_solver(t,Q)

x = Q(1); %unpack - Q(1) is passed from ode23 above - it is the value of the x-
variable
y = Q(2);

al=3.15;
B=0.439;
b1=-0.21827;
b2=-0.06069;
K1=13;
K2=5.8;
%

dxdt = (-b1/K1)*x*(K1-(x+al*y)); % compute the derivatives
dydt = (-b2/K2)*y*(K2-(y+B*x));

derivatives = [dxdt; dydt]; %pass back the derivatives in a column vector
return
```

(The same code was used for all three cases, changing initial conditions each run.)