Math 636 - Mathematical Modeling

Continuous Models
Competition Model

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Outline

Review

Review

- Examined data from Gause on cultures of yeast
- ***ODE models*** are readily solved
- Monocultures of yeast fit to well the ***continuous logistic growth model***
- ***Qualitative analysis*** is performed
  - ***Equilibria*** are found (***extinction*** and ***carrying capacity***)
  - Model is ***linearized*** and ***stability*** is determined
- Created ***phase portraits***, showing model behavior for a 1D model
- Remains to study mixed culture with the ***two species competing*** for same resource

Monoculture Yeast Experiments

Monoculture Yeast Experiments with best fitting ***logistic models***

Below is a table combining two experimental studies of *S. cerevisiae*

Time (hr)	0	1.5	9	10	18	18	23
Volume	0.37	1.63	6.2	8.87	10.66	10.97	12.5
Time (hr)	25.5	27	34	38	42	45.5	47
Volume	12.6	12.9	13.27	12.77	12.87	12.9	12.7

Logistic model: $\frac{dP}{dt} = 0.25864\,P\left(1 - \frac{P}{12.7421}\right), \qquad P_0 = 1.2343.$

Below is a table combining two experimental studies of *S. kephir*

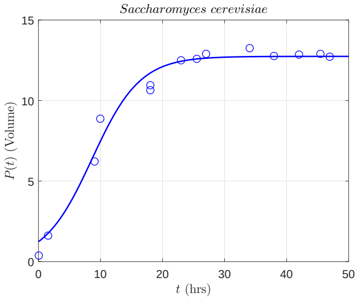
Time (hr)	9	10	23	25.5	42	45.5	66	87	111	135
Volume	1.27	1	1.7	2.33	2.73	4.56	4.87	5.67	5.8	5.83

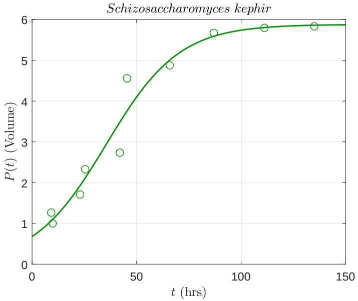
Logistic model: $\frac{dP}{dt} = 0.057442\,P\left(1 - \frac{P}{5.8802}\right), \qquad P_0 = 0.67807.$

These models show that *S. cerevisiae* grows much faster than *S. kephir*

Graph of Data and Logistic Model

The graphs of the data with the best fitting models are shown below.





From the timescales, ***S. cerevisiae*** grows significantly faster, which is also reflected in the parameter r in the models.

Mixed Culture Yeast Experiments

Mixed Culture Yeast Experiments: Two yeast species are competing for the same resource.

Time (hr)	0	1.5	9	10	18	18	23
Vol (*S. cerevisiae*)	0.375	0.92	3.08	3.99	4.69	5.78	6.15
Vol (*S. kephir*)	0.29	0.37	0.63	0.98	1.47	1.22	1.46
Time (hr)	25.5	27	38	42	45.5	47	
Vol (*S. cerevisiae*)	9.91	9.47	10.57	7.27	9.88	8.3	
Vol (*S. kephir*)	1.11	1.225	1.1	1.71	0.96	1.84	

- Both species show the initial ***Malthusian growth*** at low densities with ***S. cerevisiae*** growing faster.
- The limited nutrient causes the populations to level off.
- Monocultures reached ***carrying capacity*** because of ***intraspecies competition***.
- Two species adds the addition element of ***interspecies competition***, affecting the long term outcome.

Two Species Competition Model 1

Two Species Competition Model: Let $X(t)$ be the density of one species of yeast and $Y(t)$ be the density of another species of yeast.

- Assume each species follows the ***logistic growth model*** for interactions within the species.
  - Model has a ***Malthusian growth term***.
  - Model has a term for ***intraspecies competition***.
- The differential equation for each species has a loss term for ***interspecies competition***.
- Assume ***interspecies competition*** is represented by the product of the two species.

If two species compete for a single resource, then
1. **Competitive Exclusion** - one species out competes the other and becomes the only survivor
2. **Coexistence** - both species coexist around a stable equilibrium

Two Species Competition Model

Two Species Competition Model: The system of ordinary differential equations (ODEs) for $X(t)$ and $Y(t)$:

$$\frac{dX}{dt} = a_1X - a_2X^2 - a_3XY = f_1(X,Y)$$
$$\frac{dY}{dt} = b_1Y - b_2Y^2 - b_3YX = f_2(X,Y)$$

- First terms with a_1 and b_1 represent the exponential or **Malthusian growth** at low densities
- The terms a_2 and b_2 represent **intraspecies competition** from crowding by the same species
- The terms a_3 and b_3 represent **interspecies competition** from the second species

Unlike the ***logistic growth model***, this system of ODEs does not have an analytic solution, so we must turn to other analyses.

Competition Model – Analysis

Competition Model: Analysis always begins finding ***equilibria***, which requires:

$$\frac{dX}{dt} = 0 \qquad \text{and} \qquad \frac{dY}{dt} = 0,$$

in the model system of ODEs.

Thus,

$$\begin{aligned} a_1X_e - a_2X_e^2 - a_3X_eY_e &= 0, \\ b_1Y_e - b_2Y_e^2 - b_3X_eY_e &= 0. \end{aligned}$$

Factoring gives:

$$\begin{aligned} X_e(a_1 - a_2X_e - a_3Y_e) &= 0, \\ Y_e(b_1 - b_2Y_e - b_3X_e) &= 0. \end{aligned}$$

Competition Model – Analysis

The *equilibria* of the *competition model* satisfy:

$$\begin{aligned} X_e(a_1 - a_2 X_e - a_3 Y_e) &= 0, \\ Y_e(b_1 - b_2 Y_e - b_3 X_e) &= 0. \end{aligned}$$

This system of equations must be solved simultaneously. The first equation gives: $X_e = 0 \quad \text{or} \quad a_1 - a_2 X_e - a_3 Y_e = 0.$

If $X_e = 0$, then from the second equation we have either the *extinction equilibrium*,

$$(X_e, Y_e) = (0, 0)$$

or the *competitive exclusion equilibrium* (with Y winning):

$$(X_e, Y_e) = \left(0, \frac{b_1}{b_2}\right),$$

where Y_e is at *carrying capacity*.

Competition Model – Analysis

Continuing the *equilibria* of the *competition model*: If $a_1 - a_2X_e - a_3Y_e = 0$ from the first equation, then from the second equation we have either the *competitive exclusion equilibrium* (with X winning):

$$(X_e, Y_e) = \left(\frac{a_1}{a_2}, 0\right),$$

where X_e is at *carrying capacity* or the **nonzero equilibrium**:

$$(X_e, Y_e) = \left(\frac{a_1b_2 - a_3b_1}{a_2b_2 - a_3b_3}, \frac{a_2b_1 - a_1b_3}{a_2b_2 - a_3b_3}\right).$$

If $X_e > 0$ and $Y_e > 0$, then we obtain the *cooperative equilibrium* with neither species going extinct.

Note: This last *equilibrium* could have a negative X_e or Y_e, depending on the values of the parameters.

Maple Equilibrium

Maple can readily be used to find ***equilibria***:

```
> eq1 := Xe·(a1 - a2·Xe - a3·Ye) = 0;
  eq2 := Ye·(b1 - b2·Ye - b3·Xe) = 0;
```

$$eq1 := Xe\,(-a2\,Xe - a3\,Ye + a1) = 0$$
$$eq2 := Ye\,(-b3\,Xe - b2\,Ye + b1) = 0 \quad \textbf{(1)}$$

```
> solve({eq1, eq2}, {Xe, Ye});
```

$$\{Xe = 0, Ye = 0\}, \left\{Xe = 0, Ye = \frac{b1}{b2}\right\}, \left\{Xe = \frac{a1}{a2}, Ye = 0\right\}, \left\{Xe = \frac{a1\,b2 - a3\,b1}{a2\,b2 - a3\,b3}, Ye = -\frac{a1\,b3 - b1\,a2}{a2\,b2 - a3\,b3}\right\} \quad \textbf{(2)}$$

Later we find the numerical values of the parameters, so **Maple** easily finds all equilibria:

```
> eq3 := Xe·(0.2586 - 0.02030·Xe - 0.05711·Ye) = 0;
  eq4 := Ye·(0.05744 - 0.009768·Ye - 0.004803·Xe) = 0;
```

$$eq3 := Xe\,(0.2586 - 0.02030\,Xe - 0.05711\,Ye) = 0$$
$$eq4 := Ye\,(0.05744 - 0.009768\,Ye - 0.004803\,Xe) = 0 \quad \textbf{(3)}$$

```
> solve({eq3, eq4}, {Xe, Ye});
```

$$\{Xe = 0., Ye = 0.\}, \{Xe = 0., Ye = 5.880425880\}, \{Xe = 12.73891626, Ye = 0.\}, \{Xe = 9.925065384, Ye = 1.000195635\} \quad \textbf{(4)}$$

Note: The ***positive equilibrium*** is close to the late data points.

SDSU

Nullclines

Equilibrium analysis shows there are always the ***extinction*** and two ***competitive exclusion*** equilibria with the latter going to ***carrying capacity*** for one of the species.

Provided $a_2b_2 - a_3b_3 \neq 0$, there is another equilibrium, and it satisfies: 1. $X_e \leq 0$ and $Y_e > 0$ or 2. $X_e > 0$ and $Y_e \leq 0$ or 3. $X_e > 0$ and $Y_e > 0$.

We concentrate our studies on Case 3, where there exists a ***positive cooperative equilibrium***.

Finding ***equilibia*** can be done **geometrically** using ***nullclines***.

Nullclines are simply curves where

$$\frac{dX}{dt} = 0 \qquad \text{and} \qquad \frac{dY}{dt} = 0.$$

Nullclines

For the ***competition model***, the ***nullclines*** satisfy:

$$\frac{dX}{dt} = X(a_1 - a_2X - a_3Y) = 0 \quad \text{and} \quad \frac{dY}{dt} = Y(b_1 - b_2Y - b_3X) = 0,$$

where the first equation has solutions only flowing in the Y-direction and the second equation has solutions only flowing in the X-direction.

Equilibria occur where the curves intersect.

The ***nullclines*** for the ***competition model*** are only straight lines:

- The $\frac{dX}{dt} = 0$ has $X = 0$ or the Y-axis preventing solutions in X from becoming negative.
- The $\frac{dY}{dt} = 0$ has $Y = 0$ or the X-axis preventing solutions in Y from becoming negative.
- The other ***two nullclines*** are straight lines with negative slopes passing through the positive quadrant, $X > 0$ and $Y > 0$.

Nullclines

Example 1: Consider the ***competition model***:

$$\frac{dX}{dt} = 0.1\,X - 0.01\,X^2 - 0.02\,XY,$$
$$\frac{dY}{dt} = 0.2\,Y - 0.03\,Y^2 - 0.04\,XY.$$

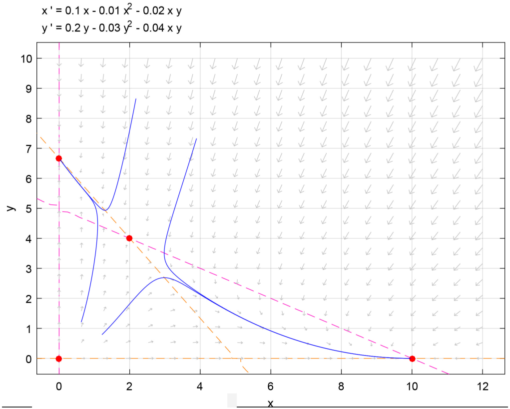
- ***Nullclines*** where $\frac{dX}{dt} = 0$ are
  1. $X = 0$.
  2. $0.1 - 0.01\,X - 0.02\,Y = 0$ or $Y = 5 - 0.2\,X$.
- ***Nullclines*** where $\frac{dY}{dt} = 0$ are
  1. $Y = 0$.
  2. $0.2 - 0.03\,Y - 0.04\,X = 0$ or $Y = \frac{20}{3} - \frac{4}{3}X$.

Equilibria occur at intersections of a ***nullcline*** with $\frac{dX}{dt} = 0$ and one with $\frac{dY}{dt} = 0$.

The *4* ***equilibria*** are $(0,0)$, $\left(0, \frac{20}{3}\right)$, $(10,0)$, and $(2,4)$.

Nullclines

The figure below was generated with `pplane8` and shows that **Example 1** exhibits ***competitive exclusion*** with all solutions going to either the ***carrying capacity equilibria***, $(X_e, Y_e) = \left(0, \frac{20}{3}\right)$ or $(X_e, Y_e) = (10, 0)$.



Nullclines

Example 2: Consider the ***competition model***:

$$\frac{dX}{dt} = 0.1\,X - 0.02\,X^2 - 0.01\,XY,$$
$$\frac{dY}{dt} = 0.2\,Y - 0.04\,Y^2 - 0.03\,XY.$$

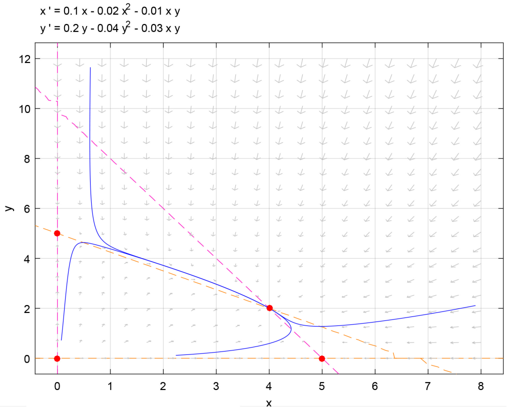
- ***Nullclines*** where $\frac{dX}{dt} = 0$ are
  1. $X = 0.$
  2. $0.1 - 0.02\,X - 0.01\,Y = 0$ or $Y = 10 - 2\,X.$
- ***Nullclines*** where $\frac{dY}{dt} = 0$ are
  1. $Y = 0.$
  2. $0.2 - 0.04\,Y - 0.03\,X = 0$ or $Y = 5 - 0.75\,X.$

Equilibria occur at intersections of a ***nullcline*** with $\frac{dX}{dt} = 0$ and one with $\frac{dY}{dt} = 0$.

The ***4 equilibria*** are $(0,0)$, $(0,5)$, $(5,0)$, and $(4,2)$.

Nullclines

The figure below was generated with `pplane8` and shows that **Example 2** exhibits ***cooperation*** with all solutions going toward the ***nonzero equilibrium***, $(X_e, Y_e) = (2, 4)$.



Fitting the Competition Model 1

Fitting the Competition Model: Need to find the parameters for model with the ***mixed culture data***.

- The examples above show the ***competition model*** has varying behavior depending on the parameters of the specific system.
- Unlike the monocultures, which only required curve fitting, this system of **ODEs** doesn't have an exact solution.
- Must fit data using an ***numerical ODE solver***.
- The ***yeast competition model*** has **6** unknown parameters and **2** unknown initial conditions.
- Need to use known information to reduce the number of parameters to be fit numerically.

Fitting the Competition Model 2

- In the absence of the other yeast species and assuming the same experimental conditions, the ***competition model*** should match the ***monoculture logistic models***.
- This assumption implies that the rate constants, a_1, a_2, b_1, and b_2, come from fitting the logistic growth data.
- Thus, we have:

$$a_1 = 0.25864, \quad a_2 = 0.020298, \quad b_1 = 0.057442, \quad b_2 = 0.0097687.$$

- Thus, the parameter search reduces to the initial conditions and a_3 and b_3, which is only **4** parameters.

Fitting the Competition Model

- Since the ***system of ODEs*** does not have an exact solution, we employ a **MatLab ODE solver**.
- **MatLab** has a Runge-Kutta-Fehlberg **ODE solver**.
- This solver fairly accurately solves the model system in the range of parameters of interest.
- We need the solution at the times the data are recorded; however, there is a quirk that the `ODE23` solver is unable to handle two data points recorded at the same time.
- This requires adjustments in the sum of square errors program to account for the repeated data point.

Fitting the Competition Model

Outline of Program

- Load the data from the experiments.
- Simulate the ***competition model*** with a reasonable set of parameters and initial conditions, recording the model values at the times matching the experimental times.
- Compute the ***sum of square errors*** between the experimental data and the simulated data.
- Use the **MatLab** program `fminsearch` to find the ***least sum of square errors*** by changing the unknown parameters a_3 and b_3 and initial conditions $X(0)$ and $Y(0)$.
- ***Complications*** are introduced in the program to manage the repeated data at $t = 18$.

MatLab Code for Fitting the Competition Model 1

The primary ***MatLab*** script is the following:

```
load yeast
global A1 A2 B1 B2;
A1 = 0.25864; A2 = 0.020298;
B1 = 0.057442; B2 = 0.0097687;
p = [0.4 0.63 0.057 0.0048];
p1 = fminsearch(@leastcomp2,p,[],tdmix,scdmix,skdmix)
```

This script downloads the data, sets up **Global variables** from the ***monoculture logistic models***, gives a good initial guess for the parameters, and calls the `fminsearch` routine.

MatLab Code for Fitting the Competition Model

Primary ***MatLab*** program computes the ***sum of square errors***:

```
1  function J = leastcomp2(p,tdata,xdata,ydata)
2  global A1 A2 B1 B2
3  [td,M] = reduct(tdata);
4  n1 = length(td);
5  [t,y] = ...
       ode23(@compet,td,[p(1),p(2)],[],A1,A2,p(3),B1,B2,p(4));
6  xd = [xdata(1:M),xdata(M+2:n1+1)];
7  yd = [ydata(1:M),ydata(M+2:n1+1)];
8  errx = y(:,1)-xd(1:n1)';
9  erry = y(:,2)-yd(1:n1)';
10 J = errx'*errx + erry'*erry;
11 J = J + (y(M,1)-xdata(M+1))^2 + ...
       (y(M,2)-ydata(M+1))^2;
12 end
```

Data sets with unique values for each time would remove lines 3, 4, 6, 7, and 11 and simplify lines 8 and 9.

MatLab Code for Fitting the Competition Model

The ***MatLab*** function for the ***competition model*** is:

```
function dydt = compet(t,y,a1,a2,a3,b1,b2,b3)
% Competition Model for Two Species
tmp1 = a1*y(1) - a2*y(1)^2 - a3*y(1)*y(2);
tmp2 = b1*y(2) - b2*y(2)^2 - b3*y(1)*y(2);
dydt = [tmp1; tmp2];
end
```

This ***system of ODEs*** is inserted into the **MatLab** Runge-Kutta-Fehlberg ODE solver with the appropriate parameters.

The `ODE23` solver finds the simulated solution at the times corresponding to the experimental data, which are used for the ***sum of square errors***.

MatLab Code for Fitting the Competition Model

MatLab function that sorts data and finds the repeated time:

```
function [td,i] = reduct(tdata)
% Data reduction - Repeat t-values
% Finds index and removes time for ODE23
n = length(tdata);
temp = sort(tdata);
td = [temp(1)]; i = [];
for k = 1:n-1
    if (temp(k)==temp(k+1))
        i = [i,k];
    else
        td = [td,temp(k+1)];
    end
end
end
```

The code is substantially simpler without this quirk!

Competition Model with Best Parameters 1

The ***MatLab*** code above gives the best fitting ***interspecies competition parameters*** for the ***competition model*** are:

$$a_3 = 0.057011 \quad \text{and} \quad b_3 = 0.0047576$$

and initial conditions:

$$X(0) = 0.41095 \quad \text{and} \quad Y(0) = 0.62578.$$

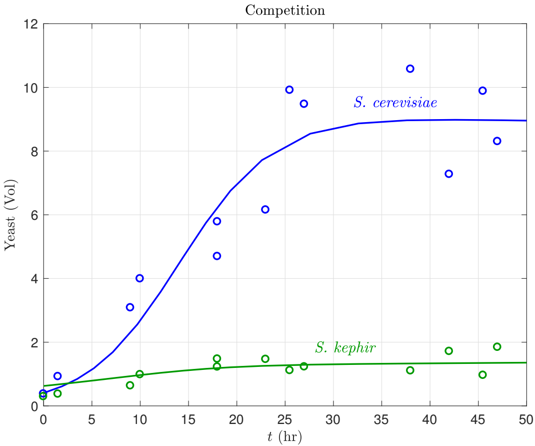
The ***least sum of square errors*** is **19.312**.

The Gause ***mixed culture data*** are best fit by the ***competition model***:

$$\frac{dX}{dt} = 0.25864\,X - 0.020298\,X^2 - 0.057011\,XY,$$
$$\frac{dY}{dt} = 0.057442\,Y - 0.0097687\,Y^2 - 0.0047576\,XY.$$

Competition Model with Best Parameters 2

The best fitting ***competition model*** is readily simulated and compared to the Gause ***mixed culture data***:



Competition Model Analysis

Competition Model Analysis:

$$\frac{dX}{dt} = f_1(X,Y) = 0.25864\,X - 0.020298\,X^2 - 0.057011\,XY,$$

$$\frac{dY}{dt} = f_2(X,Y) = 0.057442\,Y - 0.0097687\,Y^2 - 0.0047576\,XY,$$

$$X(0) = 0.41095 \quad \text{and} \quad Y(0) = 0.62578.$$

- Begin by finding all ***equilibria***.
- Draw the ***nullclines*** and study behavior.
- Linearize at each of the ***equilibria***.
- Interpret the results and simulate long term behavior.

Equilibria for Competition Model

Equilibria for Competition Model: Let the equilibria for *S. cerevisiae* and *S. kephir* be X_e and Y_e, respectively

$$\begin{aligned} X_e(0.25864 - 0.020298X_e - 0.057011Y_e) &= 0 \\ Y_e(0.057442 - 0.0097687Y_e - 0.0047576X_e) &= 0 \end{aligned}$$

- Must solve the above equations simultaneously, giving 4 equilibria
- **Extinction equilibrium**, $(X_e, Y_e) = (0, 0)$
- **Carrying capacity equilibria**, $(X_e, Y_e) = (12.742, 0)$ and $(X_e, Y_e) = (0, 5.8802)$
- **Coexistence equilibrium**, $(X_e, Y_e) = (10.257, 0.88482)$

Linearization of Competition Model

Linearization of Competition Model: With equilibria X_e and Y_e, let $u = X - X_e$ and $v = Y - Y_e$

$$\begin{pmatrix} \dot{u} \\ \dot{v} \end{pmatrix} = \begin{pmatrix} \frac{\partial f_1(X_e,Y_e)}{\partial u} & \frac{\partial f_1(X_e,Y_e)}{\partial v} \\ \frac{\partial f_2(X_e,Y_e)}{\partial u} & \frac{\partial f_2(X_e,Y_e)}{\partial v} \end{pmatrix} \begin{pmatrix} u \\ v \end{pmatrix}$$

so the linear system is

$$\begin{pmatrix} \dot{u} \\ \dot{v} \end{pmatrix} = \begin{pmatrix} a_1 - 2a_2 X_e - a_3 Y_e & a_3 X_e \\ b_3 Y_e & b_1 - 2b_2 Y_e - b_3 X_e \end{pmatrix} \begin{pmatrix} u \\ v \end{pmatrix},$$

where

$$a_1 = 0.25864 \qquad a_2 = 0.020298 \qquad a_3 = 0.057011$$

$$b_1 = 0.057442 \qquad b_2 = 0.0097687 \qquad b_3 = 0.0047576$$

Local Stability of Competition Model

Local Stability of Competition Model: At the equilibrium, $(X_e, Y_e) = (0, 0)$

$$\begin{pmatrix} \dot{u} \\ \dot{v} \end{pmatrix} = \begin{pmatrix} 0.25864 & 0 \\ 0 & 0.057442 \end{pmatrix} \begin{pmatrix} u \\ v \end{pmatrix},$$

which has eigenvalues $\lambda_1 = 0.25864$ and $\lambda_2 = 0.057442$, so this **equilibrium** is an **Unstable Node**

At the equilibrium, $(X_e, Y_e) = (12.742, 0)$

$$\begin{pmatrix} \dot{u} \\ \dot{v} \end{pmatrix} = \begin{pmatrix} -0.25863 & 0.72643 \\ 0 & -0.0031793 \end{pmatrix} \begin{pmatrix} u \\ v \end{pmatrix},$$

which has eigenvalues $\lambda_1 = -0.25863$ and $\lambda_2 = -0.0031793$, so this **equilibrium** is a **Stable Node**

Local Stability of Competition Model

Local Stability of Competition Model: At the equilibrium, $(X_e, Y_e) = (0, 5.8802)$

$$\begin{pmatrix} \dot{u} \\ \dot{v} \end{pmatrix} = \begin{pmatrix} -0.076596 & 0 \\ 0.027976 & -0.057442 \end{pmatrix} \begin{pmatrix} u \\ v \end{pmatrix},$$

which has eigenvalues $\lambda_1 = -0.076596$ and $\lambda_2 = -0.057442$, so this **equilibrium** is a **Stable Node**

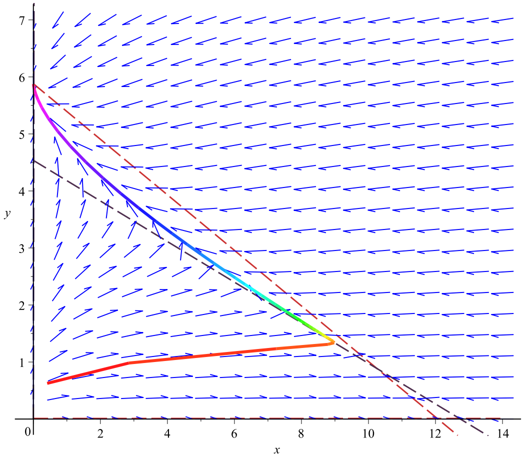
At the equilibrium, $(X_e, Y_e) = (10.257, 0.88482)$

$$\begin{pmatrix} \dot{u} \\ \dot{v} \end{pmatrix} = \begin{pmatrix} -0.20820 & 0.58476 \\ 0.0042096 & -0.0086438 \end{pmatrix} \begin{pmatrix} u \\ v \end{pmatrix},$$

which has eigenvalues $\lambda_1 = -0.21985$ and $\lambda_2 = 0.0030111$, so this **equilibrium** is a **Saddle Node** (weak in the repelling direction)

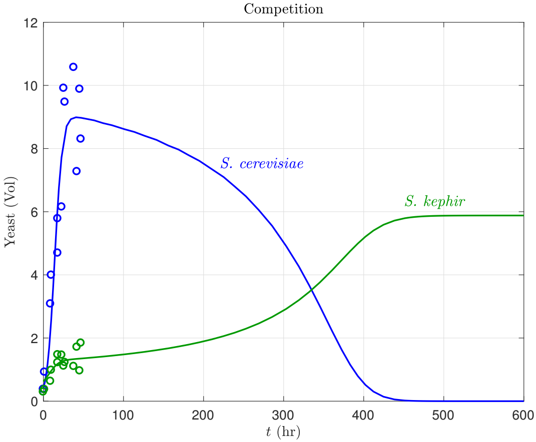
Competition Model

Competition Model Phase Portrait: Plot shows nullclines and solution trajectory



Competition Model

Competition Model Time Series: Plot shows the solution trajectories



Behavior of Yeast Competition Model

Competition Model Summary

- The *local analysis* suggests that the *least squares best fit* to the Gause data would result in the ***competitive exclusion*** of one species over time.
- ***Competitive exclusion*** is very common among similar species.
- The ***phase portrait*** plot with *nullclines* suggests that ***S. kephir*** has a competitive advantage over long time.
- The ***phase portrait*** shows that rapid growth of ***S. cerevisiae*** has solutions moving quickly in the horizontal direction, yet ultimately, the slower growing ***S. kephir*** can dominate the culture.
- The ***eigenvalue*** analysis helps explain the local behavior, including a local attraction of the ***cooperative equilibrium*** before ultimately repelling of this *saddle node*.