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Math 430 Mathematical Biology – Homework 1

Due: Thursday, February 10, 2022. NAME: Eddie Bakko

(1) [15pts] Recall the simple *growth with harvesting model*

$$x_{n+1} = \lambda x_n - h$$

where x_n is the chicken population after n years, x_0 is the initial population, λ is the growth rate and h is the harvesting rate (chickens per year).

a) Find a formula for the harvesting rate h^* at which the population remains constant.

b Find a formula for the number of years $\bar{n}$ it takes for the population to die out when it is over harvested, i.e. $h > h^*$.

c) Let $\lambda = 1.05$, $x_0 = 100$, $h = 7$. Use Matlab to simulate the run using n between 0 and 30 with x and y plotting ranges in [0,30], [0,300], respectively. Use your formula in b) to verify the $\bar{n}$ at which the population dies out. Label your calculated value $\bar{n}$ as a point on the n versus x_n plot. Include a hardcopy of the plot and one of the Matlab code.

(2) [15pts] Find the (real) general solution of each of the following difference equations.

$$\begin{aligned} 2x_{n+2} - 7x_{n+1} + 3x_n &= 0 \\ x_{n+2} - 4x_{n+1} + 4x_n &= 0 \\ x_{n+2} - \sqrt{3}x_{n+1} + x_n &= 0 \end{aligned}$$

One characteristic polynomial has two real distinct roots, another one real repeated root and the other has a complex roots with a simple polar representation $\lambda = re^{i\theta}$.

(3) [10pts] Read the textbook description of the Red Blood Cell (RBC) population model in Section 1.9, Problem 2:

$$\begin{aligned} R_{n+1} &= (1-f)R_n + M_n &(1) \\ M_{n+1} &= \gamma f R_n &(2) \end{aligned}$$

a) Convert the system above model to a single equation involving only R_{n+1}, R_n, R_{n-1}.

b) Show that the eigenvalues of the difference equation in a) are

$$\lambda_\pm = \frac{(1-f) \pm \sqrt{(1-f)^2 + 4\gamma f}}{2}$$

c) Homeostasis is when the number of red blood cells R_n is roughly constant. This can be achieved when $\lambda_+ = 1$. Show that for this to happen, γ must equal 1.

d) With $\lambda_+ = 1$ in c), show $\lambda_- = -f$ and then write down the general solution for R_n. What does R_n approach as $n \to \infty$.

HOMEWORK 01

Eddie Bakko
Math Bio

#1) Simple Growth With HARVESTING MODEL

$$x_{n+1} = \lambda x_n - h \quad \text{where,}$$

$x_n \equiv$ chicken pop after n years
$x_0 \equiv$ initial population
$\lambda \equiv$ Growth rate
$h \equiv$ harvesting rate (chickens/yr)

(a) We seek a formula for an h^* which keeps the population constant

i.e. $x_{n+1} = x_n$

$$\lambda x_n - h^* = x_n$$

$$h^* = \lambda x_n - x_n$$

$$\boxed{h^* = x_n(\lambda - 1)} \quad ✓$$

Aside: Indeed, for $h = h^*$

$$x_n = \lambda^n x_0 + \frac{(1-\lambda^n)}{(\lambda-1)}h = \lambda^n x_0 + \frac{(1-\lambda^n)}{(\lambda-1)}x_n(\lambda-1)$$

$$= \lambda^n x_0 + x_n - \lambda^n x_n$$

(pop. constant $\Rightarrow x_0 = x_n$) $= x_n$

(b) Find formula for number of years $\bar{n}$ it takes for the population to die out with overharvested $(h > h^*)$. i.e. what n is $x_n = 0$?

We know

$$x_n = \lambda^n x_0 + \frac{(1-\lambda^n)}{(\lambda-1)}h = 0 \Rightarrow -\lambda^n x_0 = \frac{(\lambda^n - 1)}{(\lambda-1)}h$$

$$\Rightarrow \frac{x_0(1-\lambda)+h}{h} = \frac{1}{\lambda^n} \quad ✓$$

$$\Rightarrow \ln(h) - \ln(x_0(1-\lambda)+h) = n\ln\lambda$$

$$\Rightarrow \boxed{\bar{n} = \frac{\ln(h) - \ln(x_0(1-\lambda)+h)}{\ln\lambda}} \quad ✓$$

(c) $\lambda = 1.05$
$x_0 = 100$
$h = 7$

With these values, we see that

$$h^* = 100(1.05-1)$$

$$= 100(.05)$$

$$= 5$$

So $h = 7 > 5 = h^*$

$$\bar{n} = \frac{\ln(7) - \ln(100(1-1.05)+7)}{\ln(1.05)} \approx 25.677 \text{ years} \quad ✓$$

As is shown in the Matlab code.

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#2) Find the (real) gen. soln to each of the following:

(a) $2x_{n+2} - 7x_{n+1} + 3x_n = 0$

yields char. poly $P(\lambda) = 2\lambda^2 - 7\lambda + 3 = 0$

$(2\lambda - 1)(\lambda - 3) = 0$

$\Rightarrow \lambda = 1/2,\ 3 = \lambda_2$ (two distinct real λ) ✓

$\lambda_1 \neq \lambda_2$ real: $\boxed{x_n = c_1 (1/2)^n + c_2 (3)^n}$

(b) $x_{n+2} - 4x_{n+1} + 4x_n = 0$.

yields char. poly $P(\lambda) = \lambda^2 - 4\lambda + 4 = 0$

$(\lambda - 2)^2 = 0$

$\lambda = 2$ (repeated real λ) ✓

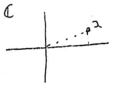
$\lambda_1 = \lambda_2$ real: $\boxed{x_n = (c_1 + c_2 n) 2^n}$

(c) $x_{n+2} - \sqrt{3}\, x_{n+1} + x_n = 0$

15

yields char. poly $P(\lambda) = \lambda^2 - \sqrt{3}\,\lambda + 1 = 0$

By quadratic eqn, $\lambda = \dfrac{\sqrt{3} \pm \sqrt{(\sqrt{3})^2 - 4(1)(1)}}{2}$



$= \frac{\sqrt{3}}{2} \pm \frac{1}{2}\sqrt{-1}$

$= \frac{\sqrt{3}}{2} \pm \frac{1}{2} i$ ✓

$\lambda = \frac{\sqrt{3}}{2} \pm \frac{1}{2} i \Rightarrow r = \sqrt{(\sqrt{3}/2)^2 + (1/2)^2} = \sqrt{3/4 + 1/4} = 1$ ✓

By inspection, $\theta = \pi/6$

Hence, $\lambda = e^{i\pi/6}$

So, $\boxed{x_n = c_1 \cos\left(\frac{n\pi}{6}\right) + c_2 \sin\left(\frac{n\pi}{6}\right)}$ ✓

#3) Red Blood Cell (RBC) population model:

(1) $R_{n+1} = (1-f) R_n + M_n$

(2) $M_{n+1} = \gamma f R_n$

$R_n \equiv$ # of RBCs in circulation on day n

$M_n \equiv$ # of RBCs produced by marrow on day n

$f \equiv$ fraction-o-RBCs removed by spleen

$\gamma \equiv$ production constant (# produces per # lost)

(a) Convert to single eqn:

$M_{n+1} = \gamma f R_n \Rightarrow M_n = \gamma f R_{n-1}$

So, (1) becomes $\boxed{R_{n+1} = \underline{(1-f)} R_n + \gamma f R_{n-1}}$ (3) ✓

(b) We might rewrite (3) as $R_{n+1} + (f+1) R_n - \gamma f R_{n-1} = 0$ which has char poly

$P(\lambda) = \lambda^2 + \underline{(f+1)}\lambda - \gamma f = 0$

By quadratic eqn, $\boxed{\lambda_\pm = \dfrac{(1-f)^{\checkmark} \pm \sqrt{(1-f)^2 + 4\gamma f}}{2}}$ as was to be shown.

eigenvalues

(c) Homeostasis $\equiv R_n$ constant-ish. $\lambda_+ = 1 \Rightarrow$ Homeostasis. Seek to show necessary for $\gamma = 1$.

$\lambda_+ = 1 = \dfrac{(1-f) + \sqrt{(1-f)^2 + 4\gamma f}}{2} \Rightarrow 2 = (1-f) + \sqrt{f^2 + (4\gamma - 2)f + 1}$

$\Rightarrow (f+1)^2 = f^2 + (4\gamma - 2)f + 1$

$\Rightarrow f^2 + 2f + 1 = f^2 + (4\gamma - 2)f + 1$

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w/ polynomial, this is only true if

$2 = 4\gamma - 2$ or $\boxed{\gamma = 1}$ ✓, as was to be shown.

(d) From this, $\lambda_- = \dfrac{(1-f) - \sqrt{(1-f)^2 + 4f}}{2} = \dfrac{(1-f) - \sqrt{f^2 + 2f + 1}}{2} = \dfrac{(1-f) - \sqrt{(f+1)^2}}{2} = \dfrac{(1-f) - (f+1)}{2} = -f$

So, $\lambda_+ = 1 \neq -f = \lambda_-$ (real) yields gen. soln of

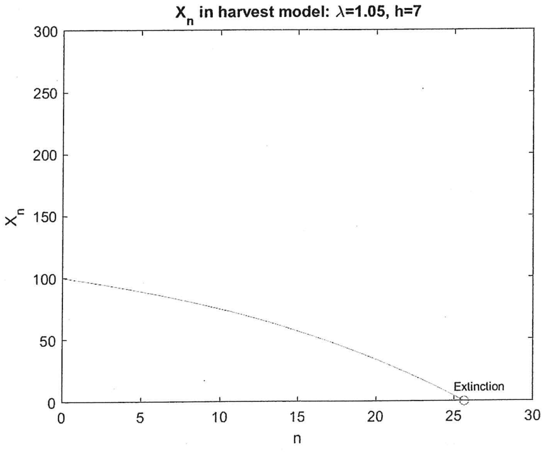
$\boxed{R_n = c_1 + c_2 (-f)^n}$

Clearly, it must be the case that $f < 1$ (otherwise #RBC $= 0 \Rightarrow$ death).

$R_n \nrightarrow c_1 = \text{constant}$

Hence, as $n \to \infty$, $R_n \to c_1$ (stays constant)

i.e. HOMEOSTASIS



✓

Math 430 Mathematical Biology – Homework 2

Due: Thursday, February 24, 2022. NAME: ____________________

1 [10pts] For the following difference equation:

$$x_{n+1} = f(x_n) = \frac{x_n}{x_n - 3}$$

i) Compute the first 3 terms of the orbit using $x_0 = 1$

$$\gamma(x_0) = \{x_0, x_1, x_2, \ldots\}$$

Write out x_0, x_1, x_2 as approximate decimals.

ii) Find all fixed points $\bar{x}$ of the map.

iii) Determine the stability of each fixed point.

2 [10pts] For the following difference equation:

$$x_{n+1} = f(x_n) = -x_n^2(1 - x_n)$$

i) Compute the first 3 terms of the orbit using $x_0 = 1$

$$\gamma(x_0) = \{x_0, x_1, x_2, \ldots\}$$

Write out x_0, x_1, x_2 as approximate decimals.

ii) Find all fixed points $\bar{x}$ of the map.

iii) Determine the stability of each fixed point.

3 [20pts] A frequently encountered model of fish population is given by Ricker's equation (see Greenwell 1984):

$$x_{n+1} = \alpha x_n e^{-\beta x_n}$$

Here x_n is the population in thousands at year n, $\alpha > 0, \beta > 0$.

a) Find the sole positive fixed point $\bar{x} > 0$. For what α is this fixed point positive?

b) Show that $\bar{x}$ is stable only if the growth rate α satisfies:

$$|1 - \ln \alpha| < 1$$

This is equivalent to $\alpha \in (\alpha_1, \alpha_2)$. What are α_k?

c) Modify the posted code cobweb.m to create 3 cobweb figures of the model showing an attraction to a fixed point, an attraction to a period 2 orbit, and an attraction to a period 4 orbit.

d) What is the maximum possible value of x_n? I want the formula involving α and β. Hint: What's the maximum value of $f(x)$ for $x > 0$?

HOMEWORK 2

EDDIE BAKKO
Math Bio

1] $x_{n+1} = f(x_n) = \frac{x_n}{x_n - 3}$

(i) want first 3 terms of orbit using $x_0 = 1$.

$x_0 = 1$

$x_1 = f(1) = \frac{1}{1-3} = -1/2$

$x_2 = f(-1/2) = -1/2/(-1/2 - 3) = 1/7$

$x_3 = f(1/7) = 1/7/(1/7 - 3) = -1/20$

$\gamma(x_0 = 1) = \{1, -1/2, 1/7, -1/20, \dots\}$

$\boxed{\gamma(1) \approx \{1, -0.5, 0.14, -0.05, \dots\}}$ ✓

(ii) Find all fxd pts of the map.

Want $f(\bar{x}) = \bar{x} \longrightarrow \frac{\bar{x}}{\bar{x}-3} = \bar{x}$

$\bar{x} = \bar{x}^2 - 3\bar{x}$

$0 = \bar{x}^2 - 4\bar{x}$

$0 = \bar{x}(\bar{x} - 4) \Rightarrow \boxed{\bar{x}_1 = 0 \ \& \ \bar{x}_2 = 4}$ ✓ 10

(iii) Want Stability of Fxd Pts

Note, $f'(x) = \frac{-3}{(x-3)^2}$ and $|f'(x)| = 3/(x-3)^2$ ✓

Then $|f'(\bar{x}_1)| = |f'(0)| = 3/(0-3)^2 = 3/9 = 1/2 < 1 \Rightarrow$ $\bar{x}_1 = 0$ stable

$|f'(\bar{x}_2)| = |f'(4)| = 3/(4-3)^2 = 3/1 = 3 > 1 \Rightarrow$ $\bar{x}_2 = 4$ unstable ✓

#2] $x_{n+1} = f(x_n) = -x_n^2(1 - x_n)$

(i) Want first 3 terms of orbit using $x_0 = 1$

$x_0 = 1$

$x_1 = f(1) = -(1)^2(1-1) = 0$

$x_2 = f(0) = -(0)^2(1-0) = 0$

$x_3 = f(0) = x_2 = 0$

$\boxed{\gamma(1) = \{1, 0, 0, 0, \dots\}}$ ✓

(ii) Want fxd pts of $f(x_n)$.

Seek $\bar{x} = f(\bar{x}) \longrightarrow$

$\bar{x} = -(\bar{x})^2(1 - \bar{x})$

$\bar{x} = -\bar{x}^2 + \bar{x}^3$

$0 = \bar{x}^3 - \bar{x}^2 - \bar{x}$

$0 = \bar{x}\underbrace{(\bar{x}^2 - \bar{x} - 1)}$

From this, we get that $\bar{x}_1 = 0$ a fxd pt and, by quadratic eqn on (*),

$\boxed{\bar{x}_2 = 1/2 + \sqrt{5}/2 \qquad \bar{x}_3 = 1/2 - \sqrt{5}/2}$ ✓ fxd pts

#2 Continued

(iii) Want to know stability of $\bar{x}_1 = 0$, $\bar{x}_2 = 1/2 + \sqrt{5}/2$, $\bar{x}_3 = 1/2 - \sqrt{5}/2$

Note, $f'(x) = x(3x - 2)$ ✓

Then, $|f'(\bar{x}_1)| = |f'(0)| = |0(0-2)| = 0 < 1 \Rightarrow \boxed{\bar{x}_1 = 0 \text{ stable}}$ ✓ 10

$|f'(\bar{x}_2)| = |f'(\frac{1+\sqrt{5}}{2})| = |(\frac{1+\sqrt{5}}{2})(3(\frac{1+\sqrt{5}}{2}) - 2)| \approx 4.62 > 1 \Rightarrow \boxed{\bar{x}_2 \text{ unstable}}$

$|f'(\bar{x}_3)| = |f'(\frac{1-\sqrt{5}}{2})| = |(\frac{1-\sqrt{5}}{2})(3(\frac{1-\sqrt{5}}{2}) - 2)| \approx 2.38 > 1 \Rightarrow \boxed{\bar{x}_3 \text{ unstable}}$ ✓

#3] Ricker's EqN: $x_{n+1} = \alpha x_n e^{-\beta x_n} = f(x_n)$

with $x_n :=$ pop-o-fish @ year n $\quad \alpha > 0 \quad \beta > 0$

a) Seek sole fxd pt.

$\bar{x} = f(\bar{x}) \longrightarrow \bar{x} = \alpha \bar{x} e^{-\beta \bar{x}}$

$1 = \alpha e^{-\beta \bar{x}}$

$1/\alpha = e^{-\beta \bar{x}}$

$-\ln(\alpha) = \ln(1) - \ln(\alpha) = \ln(1/\alpha) = -\beta \bar{x}$

$\Longrightarrow \boxed{\bar{x} = \frac{\ln(\alpha)}{\beta}}$ ✓, with $\bar{x} \geq 0$ for $\boxed{\alpha \geq 1}$ b/c, for $\alpha > 0$ (by assump), $\ln(\alpha) \geq 0$ iff $\alpha \geq 1$ ✓

b) Seek to show $\bar{x}$ stable only if growth rate, α, satisfies $|1 - \ln \alpha| < 1$

We know $\bar{x}$ stable iff $|f'(\bar{x})| < 1$.

Here, $f'(x) = \alpha e^{-\beta x} - \alpha x \beta e^{-\beta x} = \alpha e^{-\beta x}(1 - \beta x)$

$\longrightarrow |f'(\frac{\ln(\alpha)}{\beta})| = |\alpha e^{-\beta(\frac{\ln(\alpha)}{\beta})}(1 - \beta(\frac{\ln(\alpha)}{\beta}))|$

$= |\alpha e^{-\ln(\alpha)}(1 - \ln(\alpha))|$

$= |\frac{\alpha}{e^{\ln(\alpha)}}(1 - \ln(\alpha)|$

$= |\frac{\alpha}{\alpha}(1 - \ln(\alpha))|$

$= |1 - \ln(\alpha)|$

Hence, $\bar{x}$ stable only if $|1 - \ln(\alpha)| < 1$, as was to be shown. ✓

This is equivalent to $0 < \ln(\alpha) < 2$ or $1 < \alpha < e^2 \Rightarrow \boxed{\alpha \in (1, e^2)}$

continu

QUESTION 3

$f(x) = \alpha x e^{-\beta x}$

$\bar{x} = \frac{\ln(\alpha)}{\beta} > 0$ only if $\alpha > 1$

$f'(x) = \alpha e^{-\beta x}(1-\beta x)$

$f'(\bar{x}) = 1 - \ln \alpha$

Stable if

$-1 < 1 - \ln\alpha < 1$

$-2 < -\ln\alpha < 0$

$2 > \ln\alpha > 0$

$e^2 > \alpha > 1$ $\qquad (1, e^2)$

Maximum $f'(x) = 0$ at $\tilde{x} = \frac{1}{\beta}$

$f(\tilde{x}) = \frac{\alpha}{\beta} e^{-\beta\cdot\beta^{-1}}$

$f(\tilde{x}) = \frac{\alpha}{\beta} e^{-1}$

(c) $T = 1, 2, 4$ orbits.

Math 430 Mathematical Biology – Homework 3

Due: Thursday, March 10, 2022. NAME: ____________________

1) [20] For each of the four linear systems

i) find the general solution,

ii) classify the type of equilibria the origin is (saddle, center, etc)

iii) use pplane8.m to create a phase portrait for $-2 < x < 2$, $-2 < y < 2$

$$\frac{d\vec{x}}{dt} = A\vec{x} = \begin{bmatrix} 3 & 2 \\ 4 & 1 \end{bmatrix}\vec{x} \tag{1}$$

$$\frac{d\vec{x}}{dt} = A\vec{x} = \begin{bmatrix} 0 & 1 \\ -2 & -3 \end{bmatrix}\vec{x} \tag{2}$$

$$\frac{d\vec{x}}{dt} = A\vec{x} = \begin{bmatrix} -4 & -17 \\ 2 & 2 \end{bmatrix}\vec{x} \tag{3}$$

$$\frac{d\vec{x}}{dt} = A\vec{x} = \begin{bmatrix} 1 & 1 \\ -17 & -1 \end{bmatrix}\vec{x} \tag{4}$$

2) [10] For the following two nonlinear systems

i) sketch all the x-nullclines (solid lines)

ii) y-nullclines (dashed lines)

iii) label all fixed point locations.

iv) Then use Figure 5.14 (pg190 text) to categorize the equilibria types.

$$\frac{dx}{dt} = x^2 - y \qquad \frac{dx}{dt} = x(1-x)$$

$$\frac{dy}{dt} = x - 1 \qquad \frac{dy}{dt} = y\left(1 - \frac{y}{x}\right)$$

3) [10] The dimensionless chemostat model is:

$$\frac{dn}{dt} = \alpha_1 \frac{nc}{1+c} - n \tag{5}$$

$$\frac{dc}{dt} = -\frac{nc}{1+c} - c + \alpha_2 \tag{6}$$

i) The coexistence equilibria is physical only if (α_1, α_2) satisfy two inequalities (see posted notes or text for these). These in turn define a region in the (α_1, α_2)-plane. Accurately draw (sketch or shade) this region (along with its bounding curves) only for positive (physical) α_k.

ii) Determine the equality (or equalities) which (α_1, α_2) must satisfy for the extinction state (of bacteria) to be stable. As in i), draw/sketch the region in the (α_1, α_2)-plane where the extinction state is stable.

3ii) When is $P_0=(0,\alpha_2)$ stable extinction.

Following notes, only if

(1) $\quad \text{Tr}\, D\vec{F} = \alpha_1 B - 2 < 0$

(2) $\quad \det D\vec{F} = 1 - \alpha_1 B > 0$

where $B = \alpha_2/(1+\alpha_2)$.

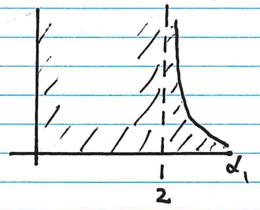
Tr $D\vec{F} < 0$ $\qquad \alpha_2 < \dfrac{2}{\alpha_1 - 2}$ if $\alpha_1 - 2 > 0$

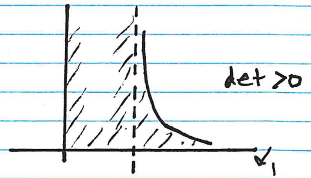
$\qquad \alpha_2 > \dfrac{2}{\alpha_1 - 2}$ if $\alpha_1 - 2 < 0$

det $D\vec{F} > 0$ $\qquad \alpha_2 < \dfrac{1}{\alpha_1 - 1}$ if $\alpha_1 > 1$

$\qquad \alpha_2 > \dfrac{1}{\alpha_1 - 1}$ if $\alpha_1 < 1$

Tr <0

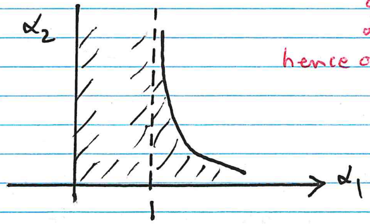




Intersection of these

Simpler need
$\alpha_1 B < 2$ Tr
$\alpha_1 B < 1$ det
hence only $\alpha_1 B < 1$.

P_0 stable.



Math 430 Mathematical Biology – Homework 3

Due: Thursday, March 10, 2022. NAME: ____________

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ii) Determine the equality (or equalities) which (α_1, α_2) must satisfy for the extinction state (of bacteria) to be stable. As in i), draw/sketch the region in the (α_1, α_2)-plane where the extinction state is stable.

Question 1)

System 1: $\frac{d\vec{x}}{dt} = \begin{bmatrix} 3 & 2 \\ 4 & 1 \end{bmatrix} \vec{x}$

(i) Finding general solution.
First, compute

$$\det(A-\lambda I) = \begin{vmatrix} 3-\lambda & 2 \\ 4 & 1-\lambda \end{vmatrix} = (3-4\lambda+\lambda^2) - 8$$
$$= \lambda^2 - 4\lambda - 5$$
$$= (\lambda-5)(\lambda+1)$$

Which yields

$\lambda_1 = 5$ and $\lambda_2 = -1$ ✓

Then, for λ_1, we find eigenvector $\vec{z}_1$

$$\begin{pmatrix} -2 & 2 \\ 4 & -4 \end{pmatrix} \vec{z}_1 = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

$\longrightarrow -2z_{1x} + 2z_{1y} = 0 \Rightarrow z_{1x} = z_{1y} \Rightarrow \vec{z}_1 = \langle 1, 1 \rangle$

Then, for λ_2 we find eigenvector $\vec{z}_2$

$$\begin{pmatrix} 4 & 2 \\ 4 & 2 \end{pmatrix} \vec{z}_2 = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

$\longrightarrow 4z_{2x} + 2z_{2y} = 0 \Rightarrow z_{2x} = -\frac{1}{2} z_{2y} \Rightarrow \vec{z}_2 = \langle 1, -2 \rangle$

So, we conclude with the general solution

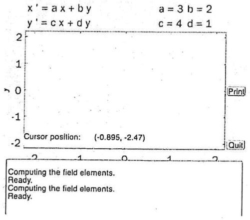
$$\vec{x}(t) = c_1 e^{5t} \begin{pmatrix} 1 \\ 1 \end{pmatrix} + c_2 e^{-t} \begin{pmatrix} 1 \\ -2 \end{pmatrix}$$ ✓

(ii) Classifying equilibria
As $\lambda_2 < 0 < \lambda_1$ (i.e. the eigenvalues have opposite signs), we determine (by page 185 of the text) that the origin has equilibria classification of a saddle. ✓

5

(iii) Phase Portrait

Arrows:



x' = a x + b y   a = 3 b = 2
y' = c x + d y   c = 4 d = 1

Cursor position: (-0.895, -2.47)

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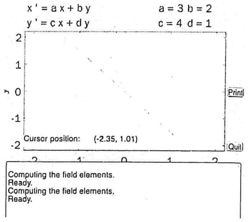
Computing the field elements.
Ready.
Computing the field elements.
Ready.
```

Nullclines:



x' = a x + b y   a = 3 b = 2
y' = c x + d y   c = 4 d = 1

Cursor position: (-2.35, 1.01)

```
Computing the field elements.
Ready.
Computing the field elements.
Ready.
```

System 2: $\frac{d\vec{x}}{dt} = \begin{bmatrix} 0 & 1 \\ -2 & -3 \end{bmatrix} \vec{x}$

(i) Finding general solution.

First, compute

$$\det(A-\lambda I) = \begin{vmatrix} -\lambda & 1 \\ -2 & -3-\lambda \end{vmatrix} = (3\lambda+\lambda^2)+2 = (\lambda+2)(\lambda+1)$$

Which yields

$\lambda_1 = -2$ $\lambda_2 = -1$ ✓

Then, for $\lambda_1 = -2$ we solve for eigenvector $\vec{z}_1$

$\begin{pmatrix} 2 & 1 \\ -2 & -1 \end{pmatrix} \vec{z}_1 = \begin{pmatrix} 0 \\ 0 \end{pmatrix} \Rightarrow 2z_{1x} + z_{1y} = 0 \Rightarrow \vec{z}_1 = \langle 1, -2 \rangle$

Then, for $\lambda_2 = -1$ we solve for eigenvector $\vec{z}_2$

$\begin{pmatrix} 1 & 1 \\ -2 & -2 \end{pmatrix} \vec{z}_2 = \begin{pmatrix} 0 \\ 0 \end{pmatrix} \Rightarrow z_{2x} + z_{2y} = 0 \Rightarrow \vec{z}_2 = \langle 1, -1 \rangle$

So, we conclude the general solution is

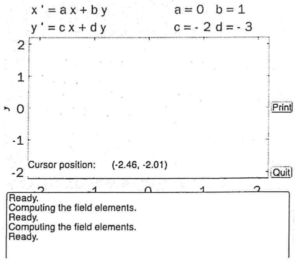
$$\vec{x}(t) = c_1 e^{-2t} \begin{pmatrix} 1 \\ -2 \end{pmatrix} + c_2 e^{-t} \begin{pmatrix} 1 \\ -1 \end{pmatrix}$$ ✓

(ii) Classifying Equilibria
As $\lambda_1 < \lambda_2 < 0$ (i.e. both eigenvalues have negative signs), by page 185 of the book we determine that the origin for this system is a stable node. ✓

5

(iii) Phase Portrait:

Arrows:

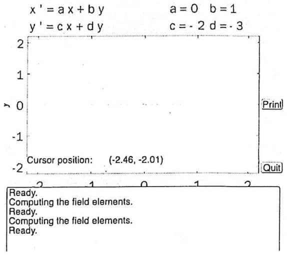


x' = a x + b y   a = 0 b = 1
y' = c x + d y   c = - 2 d = - 3

Cursor position: (-2.46, -2.01)

```
Ready.
Computing the field elements.
Ready.
Computing the field elements.
Ready.
```

Nullclines:



x' = a x + b y   a = 0 b = 1
y' = c x + d y   c = - 2 d = - 3

Cursor position: (-2.46, -2.01)

```
Ready.
Computing the field elements.
Ready.
Computing the field elements.
Ready.
```

System 3: $\frac{dx}{dt} = \begin{bmatrix} -4 & -17 \\ 2 & 2 \end{bmatrix} \vec{x}$

(i) Finding general solution.

First, compute

$$\det(A-\lambda I) = \begin{vmatrix} -4-\lambda & -17 \\ 2 & 2-\lambda \end{vmatrix} = (\lambda^2+2\lambda-8) + 34 = \lambda^2+2\lambda+26$$

Which yields

$$\lambda_\pm = \frac{-2 \pm \sqrt{4-104}}{2} = -1 \pm 5i \quad ✓$$

And therefore

$$\lambda_1 = -1+5i \qquad \lambda_2 = -1-5i$$

Then, for $\lambda_1 = -1+5i$, we can compute (using MATLAB's eig() function)

$$\vec{z} = \langle 17, -3-5i \rangle$$

Therefore,

$$\vec{x}_1(t) = e^{-t}(\cos(5t) + i\sin(5t))\left(\begin{pmatrix} 17 \\ -3 \end{pmatrix} + i\begin{pmatrix} 0 \\ -5 \end{pmatrix}\right)$$

$$= e^{-t}\begin{pmatrix} 17\cos 5t + 17i\sin 5t \\ -3\cos 5t - 3i\sin 5t - 5i\cos 5t - 5\sin 5t \end{pmatrix}$$

$$= e^{-t}\begin{pmatrix} 17\cos 5t \\ -3\cos 5t - 5\sin 5t \end{pmatrix} + e^{-t}i\begin{pmatrix} 17\sin 5t \\ -3\sin 5t - 5\cos 5t \end{pmatrix}$$

So, we conclude the general solution is

$$\vec{x}(t) = e^{-t}\left(c_1\begin{pmatrix} 17\cos 5t \\ -3\cos 5t - 5\sin 5t \end{pmatrix} + c_2\begin{pmatrix} 17\sin 5t \\ -3\sin 5t - 5\cos 5t \end{pmatrix}\right) \quad ✓$$

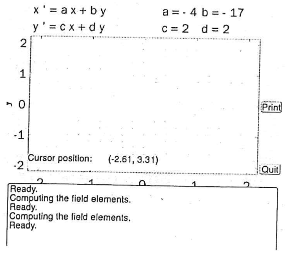
5

(ii) Classifying equilibria.

As the eigenvalues are complex (in the form $\lambda_{1,2} = a \pm ib = -1 \pm 5i$), and they have a negative real part ($a = -1 < 0$), we determine from page 185 of the book that the origin for this system is a stable spiral. ✓

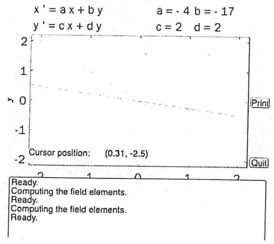
(iii) Phase Portrait:

Arrows:



```
x ' = a x + b y          a = - 4 b = - 17
y ' = c x + d y          c = 2   d = 2
Cursor position:    (-2.61, 3.31)
Ready.
Computing the field elements.
Ready.
Computing the field elements.
Ready.
```

Nullclines:



```
x ' = a x + b y          a = - 4 b = - 17
y ' = c x + d y          c = 2   d = 2
Cursor position:    (0.31, -2.5)
Ready.
Computing the field elements.
Ready.
Computing the field elements.
Ready.
```

System 4: $\frac{dx}{dt} = \begin{bmatrix} 1 & 1 \\ -17 & -1 \end{bmatrix} \vec{x}$

(i) Finding general solution.

First, compute

$$\det(A-\lambda I) = \begin{vmatrix} 1-\lambda & 1 \\ -17 & -1-\lambda \end{vmatrix} = (\lambda^2-1) + 17 = \lambda^2+16$$

Which yields

$$\lambda_\pm = \frac{\pm\sqrt{-4(16)}}{2} = \pm 4i \quad ✓$$

And therefore

$$\lambda_1 = 4i \quad \text{and} \quad \lambda_2 = -4i$$

Then, for $\lambda_1 = 4i$ we can compute (using MATLAB's eig() function)

$$\vec{z} = \langle -1-4i, 17 \rangle$$

Therefore,

$$\vec{x}_1(t) = (\cos(4t) + i\sin(4t))\left(\begin{pmatrix} -1 \\ 17 \end{pmatrix} + i\begin{pmatrix} -4 \\ 0 \end{pmatrix}\right)$$

$$= \begin{pmatrix} -\cos 4t - 4i\cos 4t - i\sin 4t - 4\sin 4t \\ 17\cos 4t + 17i\sin 4t \end{pmatrix}$$

$$= \begin{pmatrix} -\cos 4t - 4\sin 4t \\ 17\cos 4t \end{pmatrix} + i\begin{pmatrix} -4\cos 4t - \sin 4t \\ 17\sin 4t \end{pmatrix}$$

And we conclude the general solution is

$$\vec{x}(t) = c_1\begin{pmatrix} -\cos 4t - 4\sin 4t \\ 17\cos 4t \end{pmatrix} + c_2\begin{pmatrix} -4\cos 4t - \sin 4t \\ 17\sin 4t \end{pmatrix} \quad ✓$$

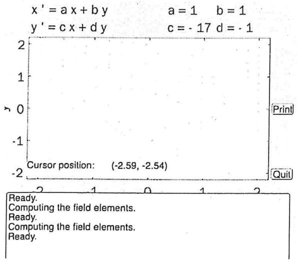
5

(ii) Classifying Equilibria

As λ_1 and λ_2 are complex (i.e. in the form $\lambda_{1,2} = a \pm ib = 0 \pm 4i$), and $a = 0$ (the eigenvalues are pure imaginary), by page 185 of the textbook we determine that the origin for this linear system is a center. ✓

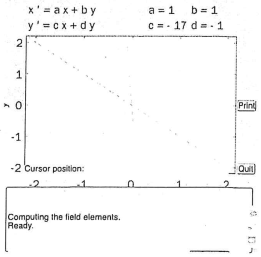
(iii) Phase portrait:

Arrows:



```
x ' = a x + b y          a = 1    b = 1
y ' = c x + d y          c = - 17 d = - 1
Cursor position:    (-2.59, -2.54)
Ready.
Computing the field elements.
Ready.
Computing the field elements.
Ready.
```

Nullclines:



```
x ' = a x + b y          a = 1    b = 1
y ' = c x + d y          c = - 17 d = - 1
Cursor position:
Computing the field elements.
Ready.
```

Question 2)

System 1: $\frac{dx}{dt} = x^2 - y \qquad \frac{dy}{dt} = x - 1$

(i) Find the x-nullclines

The x-nullcline occurs where

$f(x,y) = x^2 - y = 0 \implies y = x^2$

This nullcline is sketched as the solid line on the plot below.

(ii) Find y-nullclines

The y-nullcline occur where

$g(x,y) = x - 1 = 0 \implies x = 1.$

This nullcline is sketched as the dashed line on the plot below.

(iii) Find fixed point locations

Fixed points occur where the x and y nullclines intersect. I.e., where

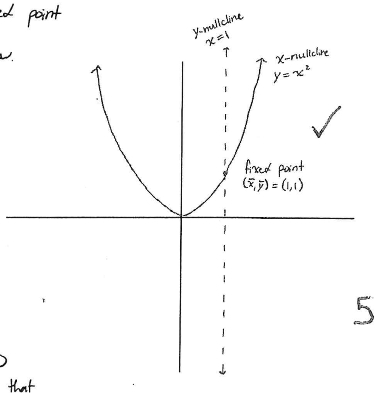
$x = 1$

$y = x^2 = (1)^2 = 1$

So, we conclude the system has a fixed point

$(\bar{x}, \bar{y}) = (1,1)$

This point is indicated on the plot below.



✓

(iv) Classify equilibria

First, we calculate the Jacobian matrix about the fixed point

$$DF(\bar{x},\bar{y}) = DF(1,1) = \begin{bmatrix} 2x & -1 \\ 1 & 0 \end{bmatrix}\Bigg|_{(1,1)}$$

$$= \begin{bmatrix} 2 & -1 \\ 1 & 0 \end{bmatrix} \checkmark$$

Then, we note

$\det(DF(1,1)) = 0 - (-1) = 1 > 0$

$Tr(DF(1,1)) = 2 + 0 = 2 > 0$

$(Tr(DF(1,1)))^2 - 4(\det(DF(1,1))) = (2)^2 - 4(1) = 0$

So, by Page 110 of the text, we determine that the fixed point is $\boxed{\text{stable}}$ ✓ and directly between being a node or a spiral. ✓

5−

System 2: $\frac{dx}{dt} = x(1-x) \qquad \frac{dy}{dt} = y\left(1 - \frac{y}{x}\right)$

(i) Find the x-nullclines

The x-nullclines occur where

$f(x,y) = x(1-x) = 0 \implies x = 0$ and $x = 1$

however, as $\underbrace{x=0 \text{ makes } \frac{dy}{dt} \text{ undefined}}$, the x-nullcline occurs ~~only~~ at $x=1$.

also at $x=0$

(ii) Find the y-nullclines.

The y-nullclines occur where

$g(x,y) = y\left(1 - \frac{y}{x}\right) = 0 \implies y = 0$ and $y = x$

These nullclines are sketched as dashed lines on the plot below.

(iii) Find fixed points

Fixed points occur where the x and y nullclines intersect, i.e. where

$\left.\begin{matrix} x = 1 \\ y = 0 \end{matrix}\right\} \implies P_1 = (\bar{x}_1, \bar{y}_1) = (1,0)$

$\left.\begin{matrix} x = 1 \\ y = x = 1 \end{matrix}\right\} \implies P_2 = (\bar{x}_2, \bar{y}_2) = (1,1)$

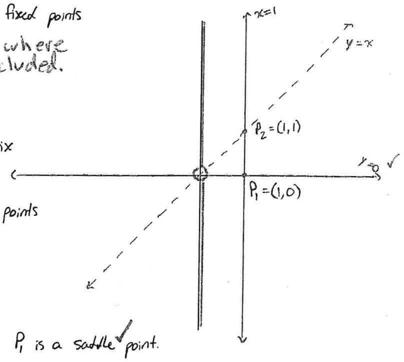
4+

So we conclude the system has two fixed points

$P_1 = (1,0)$ ✓

$P_2 = (1,1)$ ✓

here is where
x=0 excluded.



✓

(iv) Categorize the equilibria

First, we calculate the Jacobian matrix

$$DF(x,y) = \begin{bmatrix} 1-2x & 0 \\ \frac{y^2}{x^2} & 1 - \frac{2y}{x} \end{bmatrix}$$

Then, we see for the two fixed points

$P_1 = (1,0)$:

$$DF(P_1) = \begin{bmatrix} -1 & 0 \\ 0 & 1 \end{bmatrix} \checkmark$$

Which yields

$Tr\,DF(P_1) = 0$

$\det DF(P_1) = -1$

So, by Figure 5.14 we conclude P_1 is a saddle ✓ point.

$P_2 = (1,1)$:

$$DF(P_2) = \begin{bmatrix} -1 & 0 \\ 1 & -1 \end{bmatrix} \checkmark$$

Which yields

$Tr\,DF(P_2) = -2$

$\det DF(P_2) = 1$

$(Tr\,DF(P_2))^2 - 4(\det DF(P_2)) = 0$

So, by figure 5.14 we conclude that at P_2 the system is stable, and directly between a node and a spiral. ✓

Question 3 $\frac{dn}{dt} = \alpha_1 \frac{nc}{1+c} - n$ $\frac{dc}{dt} = \frac{-nc}{1+c} - c + \alpha_2$

(i) First, we find the equilibria of the system.

(1) $n(\alpha_1 \frac{c}{1+c} - 1) = 0$

(2) $\frac{-nc}{1+c} - c + \alpha_2 = 0$

We note the first equilibria is the extinction state, $n = 0$.
Then, plugging this into (2) we find that $c = \alpha_2$.
Hence, our first equilibria is

$$P_0(\bar{n}_0, \bar{c}_0) = (0, \alpha_2)$$

Note that this equilibria is always physical.

Then, we seek to find the equilibria of the coexistence state, i.e. where $n \neq 0$.
So, we know

$$\alpha_1 \frac{c}{1+c} - 1 = 0$$

Which by $\circledast_1$, we find

$$\bar{c}_1 = \frac{1}{\alpha_1 - 1}$$

Then, we use the above in (2), and by $\circledast_2$ find

$$\bar{n}_1 = \alpha_1 \left(\alpha_2 - \frac{1}{\alpha_1 - 1}\right)$$

Therefore, we determine the second point of equilibria

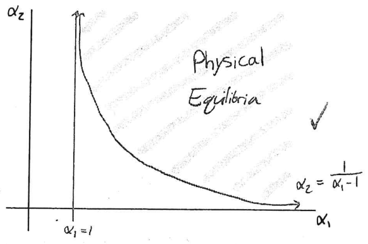
$$P_1(\bar{n}_1, \bar{c}_1) = \left(\alpha_1\left(\alpha_2 - \frac{1}{\alpha_1 - 1}\right), \frac{1}{\alpha_1 - 1}\right)$$

Now, we determine that $P_1(\bar{n}_1, \bar{c}_1)$ is physical if

1) $\frac{1}{\alpha_1 - 1} > 0 \implies \alpha_1 > 1$ ✓

2) $\alpha_2 > \frac{1}{\alpha_1 - 1}$ ✓

This region of physical equilibria can be depicted as:



✓

$\circledast_1$

$$\alpha_1 \frac{\bar{c}_1}{1+\bar{c}_1} - 1 = 0$$
$$\equiv \alpha_1 \frac{\bar{c}_1}{1+\bar{c}_1} = 1$$
$$\equiv \frac{1+\bar{c}_1}{\bar{c}_1} = \alpha_1$$
$$\equiv \frac{1}{\bar{c}_1} + 1 = \alpha_1$$
$$\equiv \frac{1}{\bar{c}_1} = \alpha_1 - 1$$
$$\equiv \bar{c}_1 = \frac{1}{\alpha_1 - 1}$$

$\circledast_2$

$$\frac{-1}{\alpha_1}\bar{n}_1 - \frac{1}{\alpha_1 - 1} + \alpha_2 = 0$$
$$\equiv \frac{-1}{\alpha_1}\bar{n}_1 = -\alpha_2 + \frac{1}{\alpha_1 - 1}$$
$$\equiv \bar{n}_1 = \alpha_1\left(\alpha_2 - \frac{1}{\alpha_1 - 1}\right)$$

5

(ii) We first compute the partial derivatives to find the Jacobian matrix.

$$\frac{\partial f}{\partial n} = \frac{\partial}{\partial n}\left[n\left(\alpha_1 \frac{c}{1+c} - 1\right)\right] = \alpha_1 \frac{c}{1+c} - 1$$

$$\frac{\partial f}{\partial c} = \frac{\partial}{\partial c}\left[n\left(\alpha_1 \frac{c}{1+c} - 1\right)\right] = n \frac{\partial}{\partial c}\left[\alpha_1 \frac{c}{1+c}\right] = \frac{\alpha_1 n}{(1+c)^2}$$

$$\frac{\partial g}{\partial n} = \frac{d}{dn}\left(-\frac{nc}{1+c} - c + \alpha_2\right] = \frac{-c}{1+c}$$

$$\frac{\partial g}{\partial c} = \frac{d}{dc}\left[\frac{-nc}{1+c} - c + \alpha_2\right] = \frac{d}{\partial c}\left[\frac{-nc}{1+c} - c\right] = \frac{-n(1+c) - (-nc)}{(1+c)^2} - 1 = \frac{-n}{(1+c)^2} - 1$$

Then, the Jacobian Matrix is

$$DF = \begin{bmatrix} \alpha_1 \frac{c}{1+c} - 1 & \frac{\alpha_1 n}{(1+c)^2} \\ \frac{-c}{1+c} & \frac{-n}{(1+c)^2} - 1 \end{bmatrix}$$

So, for the extinction state $P_0 = (0, \alpha_2)$ ✓

$$DF(P_0) = \begin{bmatrix} a_1 \frac{\alpha_2}{1+\alpha_2} - 1 & 0 \\ \frac{-\alpha_2}{1+\alpha_2} & -1 \end{bmatrix}$$

For simplicity, define

$$A = \frac{\alpha_2}{1+\alpha_2}$$ ✓

Then,

$$DF(P_0) = \begin{bmatrix} \alpha_1 A - 1 & 0 \\ -A & -1 \end{bmatrix}$$ ✓

In order for the system to be stable at the extinction state P_0, we need

$$\mathrm{Tr}\, DF(P_0) < 0$$
$$\det DF(P_0) > 0$$

Or,

$$\mathrm{Tr}\, DF(P_0) = \alpha_1 A - 1 \overset{\times}{\boxed{+0}} < 0$$
$$\det DF(P_0) = 1 - \alpha_1 A > 0$$ ✓

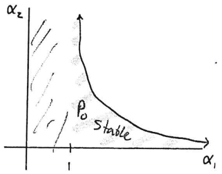
Then,

$$\alpha_1 A - 1 < 0$$
$$\equiv \alpha_1 A < 1$$
$$\equiv \alpha_1 \frac{\alpha_2}{1+\alpha_2} < 1$$
$$\equiv \alpha_1 \alpha_2 < 1 + \alpha_2$$
$$\equiv \alpha_2(\alpha_1 - 1) < 1$$
$$\equiv \alpha_2 < \frac{1}{(\alpha_1 - 1)}$$ ✗

$$1 - \alpha_1 A > 0$$
$$\equiv 1 - \alpha_1 \frac{\alpha_2}{1+\alpha_2} > 0$$
$$\equiv \alpha_1 \frac{\alpha_2}{1+\alpha_2} < 1$$
$$\equiv \alpha_1 \alpha_2 < 1 + \alpha_2$$
$$\equiv \alpha_2(\alpha_1 - 1) < 1$$
$$\equiv \alpha_2 < \frac{1}{\alpha_1 - 1}$$ ✓

So, the region for which the extinction state of the bacteria is stable is
$\alpha_2 < \frac{1}{\alpha_1 - 1}$

which can be reflected as

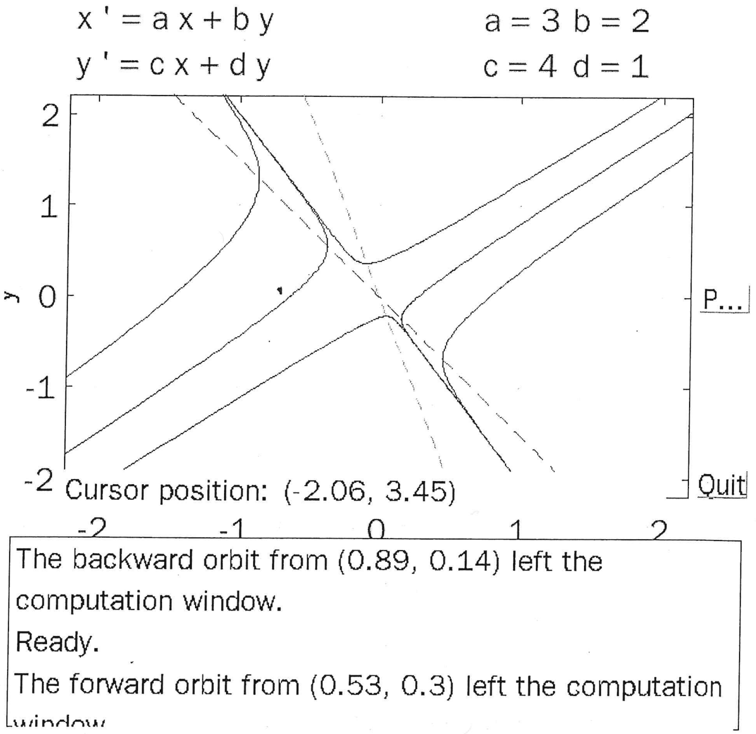


5^-

Between this plot and the plot from (i), we see that the regions where the equilibria are physical and the extinction state is stable do not overlap, so a stable extinction state is not possible.

Eli Quist - M430 HW3 Phase Portraits (Question 1 Part 3)

System 1



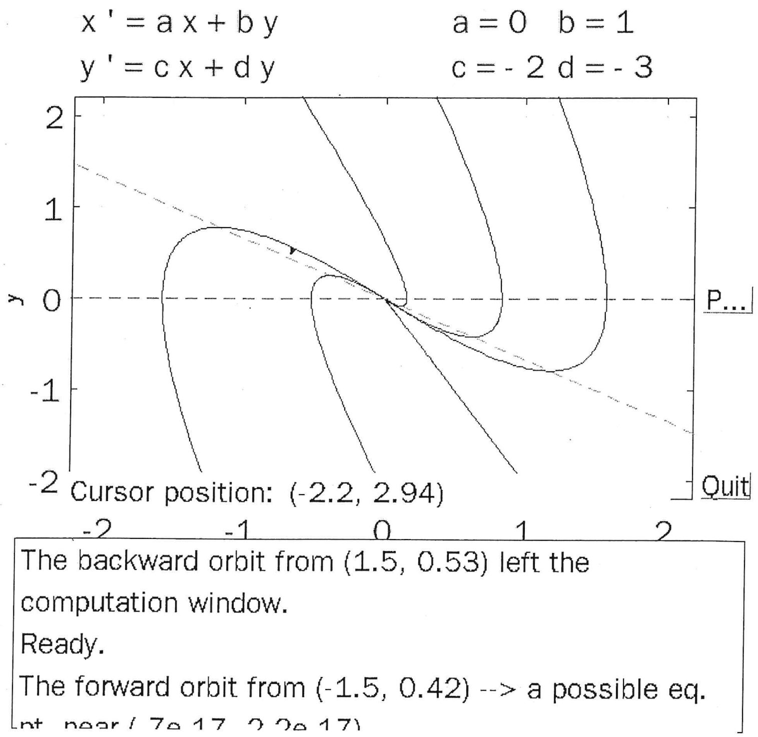
x ' = a x + b y
y ' = c x + d y

a = 3 b = 2
c = 4 d = 1

Cursor position: (-2.06, 3.45)

The backward orbit from (0.89, 0.14) left the computation window.
Ready.
The forward orbit from (0.53, 0.3) left the computation window

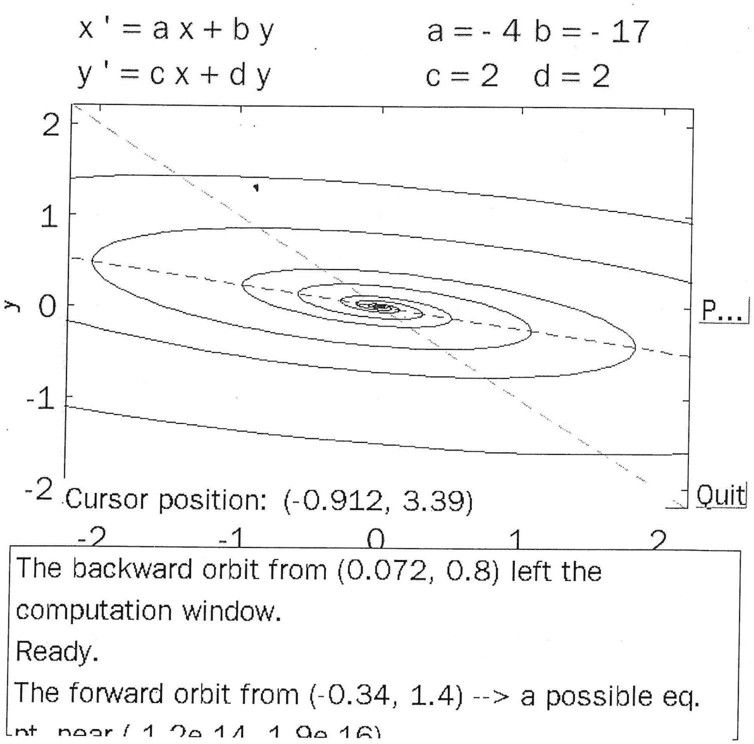
System 2


x ' = a x + b y   a = 0   b = 1
y ' = c x + d y   c = - 2 d = - 3

Cursor position: (-2.2, 2.94)

```
The backward orbit from (1.5, 0.53) left the
computation window.
Ready.
The forward orbit from (-1.5, 0.42) --> a possible eq.
```

System 3


x ' = a x + b y   a = - 4 b = - 17
y ' = c x + d y   c = 2   d = 2

Cursor position: (-0.912, 3.39)

```
The backward orbit from (0.072, 0.8) left the
computation window.
Ready.
The forward orbit from (-0.34, 1.4) --> a possible eq.
```

Math 430 Mathematical Biology – Homework 3

Due: Thursday, March 10, 2022. NAME: ____________________

1) [20] For each of the four linear systems

i) find the general solution,

ii) classify the type of equilibria the origin is (saddle, center, etc)

iii) use pplane8.m to create a phase portrait for $-2 < x < 2$, $-2 < y < 2$

$$\frac{d\vec{x}}{dt} = A\vec{x} = \begin{bmatrix} 3 & 2 \\ 4 & 1 \end{bmatrix}\vec{x} \quad (1)$$

$$\frac{d\vec{x}}{dt} = A\vec{x} = \begin{bmatrix} 0 & 1 \\ -2 & -3 \end{bmatrix}\vec{x} \quad (2)$$

$$\frac{d\vec{x}}{dt} = A\vec{x} = \begin{bmatrix} -4 & -17 \\ 2 & 2 \end{bmatrix}\vec{x} \quad (3)$$

$$\frac{d\vec{x}}{dt} = A\vec{x} = \begin{bmatrix} 1 & 1 \\ -17 & -1 \end{bmatrix}\vec{x} \quad (4)$$

2) [10] For the following two nonlinear systems

i) sketch all the x-nullclines (solid lines)

ii) y-nullclines (dashed lines)

iii) label all fixed point locations.

iv) Then use Figure 5.14 (pg190 text) to categorize the equilibria types.

$$\frac{dx}{dt} = x^2 - y \qquad \frac{dx}{dt} = x(1-x)$$
$$\frac{dy}{dt} = x - 1 \qquad \frac{dy}{dt} = y\left(1 - \frac{y}{x}\right)$$

3) [10] The dimensionless chemostat model is:

$$\frac{dn}{dt} = \alpha_1 \frac{nc}{1+c} - n \quad (5)$$

$$\frac{dc}{dt} = -\frac{nc}{1+c} - c + \alpha_2 \quad (6)$$

i) The coexistence equilibria is physical only if (α_1, α_2) satisfy two inequalities (see posted notes or text for these). These in turn define a region in the (α_1, α_2)-plane. Accurately draw (sketch or shade) this region (along with its bounding curves) only for positive (physical) α_k.

ii) Determine the equality (or equalities) which (α_1, α_2) must satisfy for the extinction state (of bacteria) to be stable. As in i), draw/sketch the region in the (α_1, α_2)-plane where the extinction state is stable.

Math 430 Mathematical Biology
Midterm - Takehome (max=50)
Due Thursday March 24, 2022.

Name: ____________________

Instructions : The following guidelines must be observed:

a) You may use the textbook, notes on the course website, or your own classroom notes

b) You must work alone and may not talk to fellow classmates. You may ask me clarifying questions.

c) Merely stating an answer is insufficient. You must show your work.

d) This test (with your name on it) must be stapled to your work.

e) You may use matlab and/or a calculator.

f) Make sure your work is legible and in the proper order.

---

1. [10pts] Recall the simple *growth with harvesting model*

$$x_{n+1} = \lambda x_n - h$$

where x_n is the chicken population after n years, x_0 is the initial population, λ is the growth rate and h is the harvesting rate (chickens per year). The units are in hundreds of chickens so that x_n=5 means 500 chickens. The solution derived in class was:

$$x_n = \lambda^n x_0 - \left(\frac{\lambda^n - 1}{\lambda - 1}\right) h \qquad 0 = \lambda^{10} x_0 - \left(\frac{\lambda^{10} - 1}{\lambda - 1}\right) h$$

Suppose $x_0 = 10$, $\lambda = 5$ and the population becomes extinct after $n = 10$ years. At what rate h were the chickens harvested? $h = 40$

2. [10pts] Find the general solution of the following difference equation:

$$2x_{n+2} - 3x_{n+1} + x_n = 0$$

What does x_n approach as $n \to \infty$

3. [10pts] Define a map by:

$$x_{n+1} = f(x_n) = -\alpha x_n \ln x_n \quad (1)$$

For $\alpha > 0$, $f(x) > 0$ on $x \in (0, 1)$.

a) Draw an accurate sketch of $y = x$ and $y = f(x)$ for $0 < x \leq 1$ labelling the positive fixed point $\bar{x}$. You may use the fact that $\lim_{x \to 0+} f(x) = 0$.

b) Find a formula for the positive fixed point $\bar{x}$ of (1) in terms of α.

c) Compute and then <u>simplify</u> $f'(\bar{x})$ (it really simplifies!).

d) Given your result in c), for what α is the fixed point stable, i.e. $|f'(\bar{x})| < 1$.

Math 430 Mathematical Biology – Homework 4

Due: Thursday, April 7, 2022. NAME: ____________________

1) [10] Capasso and Serio (1978) considered the following SIR epidemic model with emigration of the susceptible S:

$$\frac{dS}{dt} = -g(I)S - \lambda S \tag{1}$$

$$\frac{dI}{dt} = g(I)S - \beta I \tag{2}$$

$$\frac{dR}{dt} = \lambda S + \beta I \tag{3}$$

where $g(I) = \alpha I e^{-I}$. The parameters α, β, λ are all **positive**. The function $g(I)$ is meant to take into account "psychological" effects. In particular, when the number of infectives I is large the number of interactions $g(I)S$ is smaller since the susceptibles S notice the infected people and actively try to stay away from them.

a) Is the total population $N = S + I + R$ conserved?

b) Show the (S, I) system has no positive (physical $S > 0, I > 0$) equilibria.

c) Show the $(S, I) = (0, 0)$ extinction state is stable.

d) Create a pplane9 (phase plane) diagram showing that S, I both die out and hence all people recover. Include the nullclines and at least one trajectory illustrating the aforementioned dynamic. You may use $\alpha = \beta = \lambda = 1$ as parameter values.

2) [5] Nondimensionalize the SIR model

$$\frac{dS}{dt} = -\alpha S I \tag{4}$$

$$\frac{dI}{dt} = \alpha S I - \beta I \tag{5}$$

$$\frac{dR}{dt} = \beta I \tag{6}$$

In particular, scale the dependent and independent variables :

$$S = sS^* \quad , \quad I = iI^* \quad , \quad R = rR^* \quad , \quad t = \tau t^* \quad ,$$

and show that for a certain choice of the constants S^*, I^*, R^* and t^* the resulting system for lower case s, i, r, τ contains no parameters.

The new dimensionless system should look like:

$$\frac{ds}{d\tau} = -si \tag{7}$$

$$\frac{di}{d\tau} = si - i \tag{8}$$

$$\frac{dr}{d\tau} = i \tag{9}$$

State the constants S^*, I^*, R^* and t^* formulae in terms of α and β.

3) [5] Use Law of Mass Action to write out the (molar) concentration differential equations for the following reactions.

$$X + 2Y \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} Y + Z$$

1) [10] Capasso and Serio (1978) considered the following SIR epidemic model with emigration of the susceptible S:

$$\frac{dS}{dt} = -g(I)S - \lambda S \quad (1)$$

$$\frac{dI}{dt} = g(I)S - \beta I \quad (2)$$

$$\frac{dR}{dt} = \lambda S + \beta I \quad (3)$$

where $g(I) = \alpha I e^{-I}$. The parameters α, β, λ are all **positive**. The function $g(I)$ is meant to take into account "psychological" effects. In particular, when the number of infectives I is large the number of interactions $g(I)S$ is smaller since the susceptibles S notice the infected people and actively try to stay away from them.

a) Is the total population $N = S + I + R$ conserved?

First, we note that $N = S + I + R$. Then, consider the rate of change of the population,

$$\frac{dN}{dt} = \frac{d}{dt}(S + I + R)$$
$$= \frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt}$$
$$= -g(I)S - \lambda S + g(I)S - \beta I + \lambda S + \beta I$$
$$= -\cancel{g(I)S} \cancel{-\lambda S} + \cancel{g(I)S} \cancel{-\beta I} + \cancel{\lambda S} + \cancel{\beta I}$$
$$= 0.$$

✓

As the rate of change of the total population, $\frac{dN}{dt}$, is zero, we know the total population does not change over time. Therefore, we conclude that the total population is conserved.

b) Show the (S, I) system has no positive (physical $S > 0, I > 0$) equilibria.

Recall, an equilibria occurs when $\frac{dS}{dt}$ or $\frac{dI}{dt}$ equal zero. First, consider

$$\frac{dS}{dt} = S(-g(I) - \lambda)$$

This equals zero when,

Case 1: $S = 0$.

By definition, physical equilibria occur when $S > 0$, so this case is not valid.

Case 2: $-g(I) - \lambda = 0$.

As $I > 0$ (due to hypothesis of physicality), $g(I) = \alpha I e^{-I} > 0$, and then it follows that $-g(I) < 0$. By hypothesis, $\lambda > 0$, and therefore $-\lambda < 0$. So, it becomes clear that $-g(I) - \lambda < 0$, and therefore $-g(I) - \lambda \neq 0$.

As neither case holds, we see that

$$\frac{dS}{dt} \neq 0$$

✓

for $S, I > 0$, and therefore the (S,I) system has no physical equilibria.

c) Show the $(S, I) = (0, 0)$ extinction state is stable.

$$\frac{dS}{dt} = f(S,I) = -g(I)S - \lambda S$$

$$\frac{dI}{dt} = g(S,I) = g(I)S - \beta I$$

$g(I) = \alpha I e^{-I}$

First, we calculate the Jacobian,

$$DF = \begin{bmatrix} f_S & f_I \\ g_S & g_I \end{bmatrix}$$

$$\frac{\partial f}{\partial S} = -g(I) - \lambda = -\alpha I e^{-I} - \lambda$$

$$\frac{\partial g}{\partial S} = g(I) - \beta = \alpha I e^{-I}$$

$$\frac{\partial f}{\partial I} = -S \frac{\partial g(I)}{\partial I} = S\alpha e^{-I}(I-1)$$

$$\frac{\partial g}{\partial I} = S\alpha e^{-I}(I-1) - \beta$$

And therefore,

$$DF = \begin{bmatrix} -\alpha I e^{-I} - \lambda & S\alpha e^{-I}(I-1) \\ \alpha I e^{-I} & S\alpha e^{-I}(I-1) - \beta \end{bmatrix}$$

Then, consider the extinction state

$$DF(0,0) = \begin{bmatrix} -\lambda & 0 \\ 0 & -\beta \end{bmatrix}$$

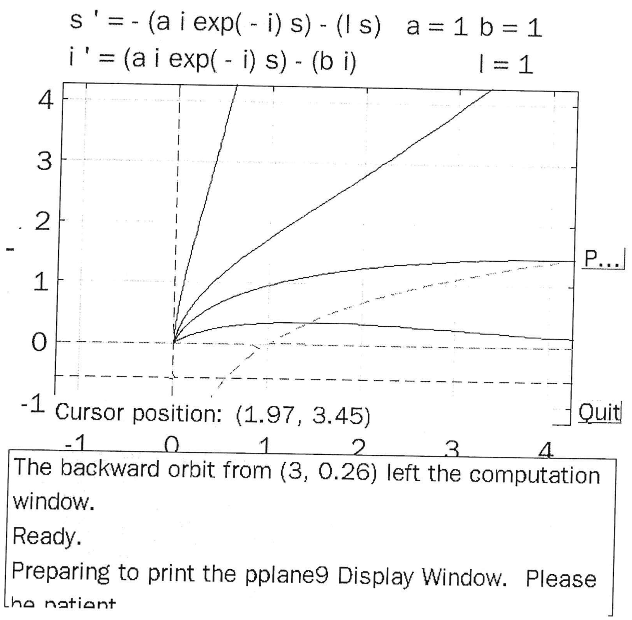
✓

So, it follows that

$$\det DF(0,0) = \beta\lambda > 0$$
$$\operatorname{Tr} DF(0,0) = -\lambda - \beta < 0.$$

As $\det DF(0,0) > 0$ and $\operatorname{Tr} DF(0,0) < 0$, by Page 190 of the textbook we conclude that $(S,I) = (0,0)$ is stable. ✓

d) Create a pplane9 (phase plane) diagram showing that S, I both die out and hence all people recover. Include the nullclines and at least one trajectory illustrating the aforementioned dynamic. You may use $\alpha = \beta = \lambda = 1$ as parameter values.



Cursor position: (1.97, 3.45)

The backward orbit from (3, 0.26) left the computation window.
Ready.
Preparing to print the pplane9 Display Window. Please be patient

10

As all trajectories travel to (0,0), we know eventually $S = I = 0$. Then, as $N = S + I + R$,

$$N = (0) + (0) + R \implies R = N.$$

So, we conclude that the entire population, N, will eventually end up in the "Recovered" group.

---

2) [5] Nondimensionalize the SIR model

$$\frac{dS}{dt} = -\alpha SI \qquad (4)$$
$$\frac{dI}{dt} = \alpha SI - \beta I \qquad (5)$$
$$\frac{dR}{dt} = \beta I \qquad (6)$$

In particular, scale the dependent and independent variables :

$$S = sS^* \quad , \quad I = iI^* \quad , \quad R = rR^* \quad , \quad t = \tau t^* \quad ;$$

and show that for a certain choice of the constants S^*, I^*, R^* and t^* the resulting system for lower case s, i, r, τ contains no parameters.

First, we scale the system, and simplify each

(4a) $\frac{S^*}{t^*}\frac{ds}{d\tau} = -\alpha s S^* i I^*$

(4b) $\frac{ds}{d\tau} = -s i t^* I^* \alpha$

(5a) $\frac{I^*}{t^*}\frac{di}{d\tau} = \alpha s S^* i I^* - \beta i I^*$

(5b) $\frac{di}{d\tau} = s i \alpha S^* t^* - i \beta t^*$

(6a) $\frac{R^*}{t^*}\frac{dr}{d\tau} = \beta i I^*$

(6b) $\frac{dr}{d\tau} = i\,\frac{\beta I^* t^*}{R^*}$

Then, from (4b), (5b), and (6b), to make the system dimensionless we generate a system of equations setting the parameters and scaling constants equal to 1.

(4c) $t^* I^* \alpha = 1$

(5c.1) $\alpha S^* t^* = 1$

(5c.2) $\beta t^* = 1$

(6c) $\frac{\beta I^* t^*}{R^*} = 1$

Starting with (5c.2), we let $t^* = 1/\beta$. Then, using (5c.1) we see

$$\alpha S^* t^* = \alpha S^*\left(\frac{1}{\beta}\right) = 1 \implies S^* = \frac{\beta}{\alpha}$$

Similarly, using (4c), it can be shown $I^* = \frac{\beta}{\alpha}$, and then using (6c) that $R^* = \beta/\alpha$ also.

So, in summary, we have chosen the constants

$t^* = 1/\beta$ $\qquad$ $I^* = \beta/\alpha$

$S^* = \beta/\alpha$ $\qquad$ $R^* = \beta/\alpha$

Then, we want to show that this choice of constants makes the system for s, i, r, and τ contain no parameters.

First, consider (4b)

$$\frac{ds}{d\tau} = -si\,t^* I^* \alpha = -si\left(\frac{1}{\cancel{\beta}}\right)\left(\frac{\cancel{\beta}}{\cancel{\alpha}}\right)\cancel{\alpha} = -si$$

Then, consider (5b)

$$\frac{di}{d\tau} = si\,\alpha S^* t^* - i\beta t^* = si\cdot\cancel{\alpha}\left(\frac{\cancel{\beta}}{\cancel{\alpha}}\right)\left(\frac{1}{\cancel{\beta}}\right) - i\cdot\cancel{\beta}\left(\frac{1}{\cancel{\beta}}\right) = si - i = i(s-1)$$

Finally, consider (6b)

$$\frac{dr}{d\tau} = i\,\frac{\beta I^* t^*}{R^*} = i\,\frac{\cancel{\beta}\left(\frac{\cancel{\beta}}{\cancel{\alpha}}\right)\left(\frac{1}{\cancel{\beta}}\right)}{\left(\frac{\cancel{\beta}}{\cancel{\alpha}}\right)} = i$$

In summary, for $t^* = 1/\beta$, $\underbrace{S^* = \alpha/\beta,\ I^* = \alpha/\beta,\ R^* = \alpha/\beta}_{\text{you flipped them here. See } \circledast}$, we see

$$\frac{ds}{d\tau} = -si$$

$$\frac{di}{d\tau} = i(s-1)$$

$$\frac{dr}{d\tau} = i$$

✓ 5

And therefore, for constants chosen as above, the system for s, i, r, τ contains no parameters.

3) [5] Use Law of Mass Action to write out the (molar) concentration differential equations for the following reactions.

$$X + 2Y \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} Y + Z$$

Using the general formula (as discussed in class), we compute the molar concentration differential equations as

$$\frac{dX}{dt} = -k_1 XY^2 + k_{-1} YZ$$

$$\frac{dY}{dt} = -k_1 XY^2 + k_{-1} YZ$$

$$\frac{dZ}{dt} = k_1 XY^2 - k_{-1} YZ$$

✓ 5

Math 430 Mathematical Biology – Homework 5

Due: Tuesday, April 26, 2022. NAME: ____________________

1) [5] Use Law of Mass Action to write out the (molar) concentration differential equations for the following reactions.

$$3X + Y \underset{k_2}{\overset{k_1}{\rightleftarrows}} X + Z$$

$$X + Y \xrightarrow{k_3} Z$$

2) [10] Let S=substrate, B=buffer and C=complex. A slightly different form of buffering is given by the reaction equations:

$$2S + B \underset{k_-}{\overset{k_+}{\rightleftarrows}} C$$

Using the Law of Mass Action the differential equations governing the molar concentrations is given by:

$$\frac{dS}{dt} = -2k_+BS^2 + 2k_-C \quad , \quad S(0) = S_0 \qquad (1)$$

$$\frac{dB}{dt} = -k_+BS^2 + k_-C \quad , \quad B(0) = B_0 \qquad (2)$$

$$\frac{dC}{dt} = k_+BS^2 - k_-C \quad , \quad C(0) = C_0 \qquad (3)$$

a) Find the function $f(S, B)$ such that the above system can be reduced to

$$S' = 2f(B, S)$$
$$B' = f(B, S)$$

b) Find the function $g(S)$ such that $f = 0$ only if

$$B = g(S) = \frac{\bar{V}}{K_E + S^2}$$

for certain parameters $\bar{V}$ and K_E (write these out in terms of the original model parameters : k_-, k_+, S_0, B_0)

c) Use Matlab or any other plotting program to make a phase plane portrait like that done in my lecture notes for the regular buffering problem. It should be in the (S,B)-plane, be first quadrant only, have an accurate plot of $f = 0$ and several trajectories. Use the parameter values $k_+ = k_- = S_0 = B_0 = 1$ and S values in $[0, 2]$

3) [10] A variation of Michaelis-Menten kinetics is n-site cooperativity where n substrate molecules S must bind in order for the product P to be made. The reaction equations are:

$$nS + E \underset{k_2}{\overset{k_1}{\rightleftarrows}} C \xrightarrow{k_2} P + E$$

The subsequent dimensional differential equations for the reaction are

$$\begin{aligned}
\frac{dS}{dt} &= f_1 = -nk_1S^nE + nk_{-1}C \quad , \quad S(0) = S_0 \\
\frac{dE}{dt} &= f_2 = -k_1S^nE + (k_{-1} + k_2)C \quad , \quad E(0) = E_0 \\
\frac{dC}{dt} &= -f_2 = k_1S^nE - (k_{-1} + k_2)C \quad , \quad C(0) = 0 \\
\frac{dP}{dt} &= k_2C
\end{aligned}$$

a) Without nondimensionalizing the equations, use conservation of receptors to find the quasi-steady state approximation of the production rate

$$\frac{dP}{dt} = V(S)$$

that only depends on S (and not E, C). This is the ubiquitous "Hille" function.

b) According to the fast-subsystem analysis (in class and notes), the complex concentration very quickly rises from 0 to a maximum value C_{max}. Find a formula for C_{max}

First order linear difference eqn population model

a_n = # females in nth generation
p_n = # progeny in nth generation

f = # progeny per female
m = fractional mortality of progeny
r = fraction of females in total population

Given there definitions

(1) $$p_{n+1} = f\, a_n$$

and

(2) $$a_{n+1} = r\, \underbrace{(1-m)\, p_{n+1}}_{\text{progeny that survived generation.}}$$

Combining (1)-(2)

$$\boxed{\begin{array}{c} a_{n+1} = \lambda\, a_n \\ \lambda \equiv fr(1-m) \end{array}}$$

Linear first order solution

$$x_{n+1} = \lambda\, x_n \qquad n = 0, 1, 2, \ldots$$

Here x_0 is the initial condition

$$x_1 = \lambda x_0$$

$$x_2 = \lambda x_1 = \lambda^2 x_0$$

$$x_3 = \lambda x_2 = \lambda^3 x_0$$

By induction

$$\boxed{x_n = \lambda^n x_0}$$

Solution also works if $\lambda \in \mathbb{C}$ is complex.

$$|\lambda| < 1 \quad \Rightarrow \quad x_n \to 0$$

$$|\lambda| > 1 \quad \Rightarrow \quad x_n \to \infty$$

when $|\lambda| = 1$, x_n is constant or period 2.

Ex Let x_n = number of bacteria after n days

$$x_{n+1} = \lambda x_n$$

what is the doubling time?

$$x_n = \lambda^n x_0$$

In how many days n does $x_n = 2x_0$

$$2 = \lambda^n$$

$$\boxed{n = \frac{\ln 2}{\ln \lambda}}$$

Ex Conversion of time units

x_n = # bact after n days

X_N = # bact after N weeks

If we model x_n as before $x_{n+1} = \lambda x_n$

$$X_1 = x_7$$

$$X_2 = x_{14}$$

$$X_3 = x_{21}$$

Clearly

$$X_{N+1} = \lambda^7 X_N$$

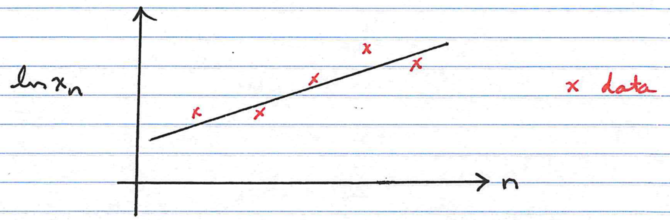
Ex Experimental Data

$$x_{n+1} = \lambda x_n$$

$$x_n = \lambda^n x_0$$

From which we derive

$$(1) \quad \underset{\overset{\uparrow}{\text{plot}}}{\ln x_n} = n \underset{\overset{\uparrow}{\text{don't know}}}{\ln \lambda} + \underset{\overset{\uparrow}{\text{know}}}{\ln x_0}$$



Choose slope $\ln\lambda$ to best match data.

Generally done with linear regression.

Harvesting Model

(1) $$\boxed{x_{n+1} = \lambda x_n - h} \qquad \lambda > 1, \; h \geq 0$$

where

x_n = number of chicken at year n

h = number of chickens harvested per year

To solve (1) we translate x_n into a form we know how to solve

(2) $$x_n = y_n + \bar{x}$$

Substitute (2) into (1)

$$y_{n+1} + \bar{x} = \lambda (y_n + \bar{x}) - h$$

Rearrange terms

$$y_{n+1} = \lambda y_n + \underbrace{(\lambda - 1)\bar{x} - h}_{\text{choose } \bar{x} \text{ so this vanishes}}$$

Thus, for

(3) $$\bar{x} = \frac{h}{(\lambda - 1)}$$

we have

(4) $$y_{n+1} = \lambda y_n$$

This we know how to solve: $y_n = \lambda^n y_0$.

Hence

$$x_n = \lambda^n y_0 + \bar{x}$$

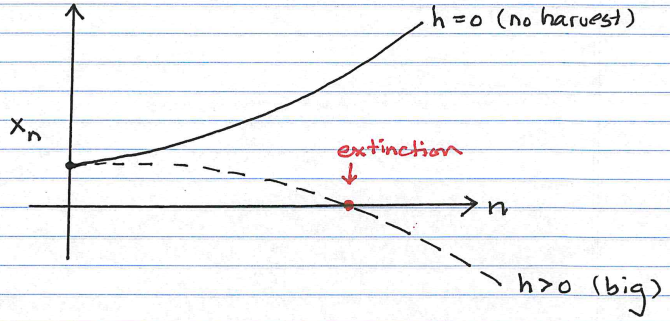
$$x_n = \lambda^n (x_0 - \bar{x}) + \bar{x}$$

Collecting terms and using (3)

$$\boxed{x_n = \lambda^n x_0 - \left(\frac{\lambda^n - 1}{\lambda - 1}\right) h}$$

regular growth

loss to harvesting



QUESTION ONE : For what h does population remain constant?

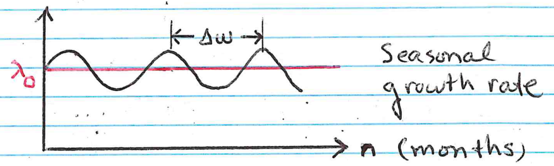
QUESTION TWO : At what year does population become extinct?

Seasonal Growth Rates and Harvesting

$$x_{n+1} = \lambda_n x_n - h$$

growth rate varies with time n.
As an example

$$\lambda_n = \lambda_0 + \alpha \sin(\omega n)$$



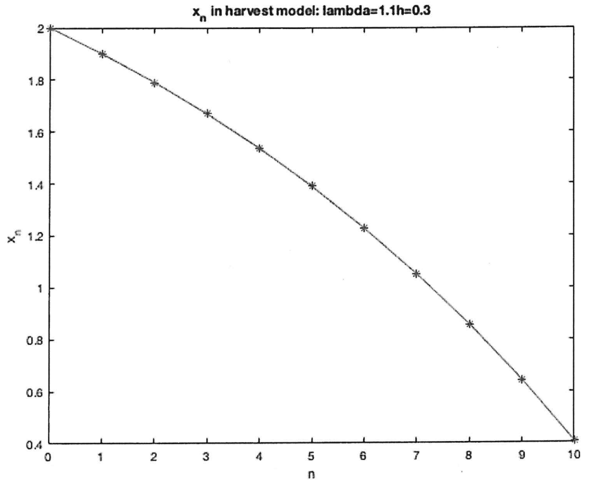
Here $\omega = \frac{2\pi}{12}$

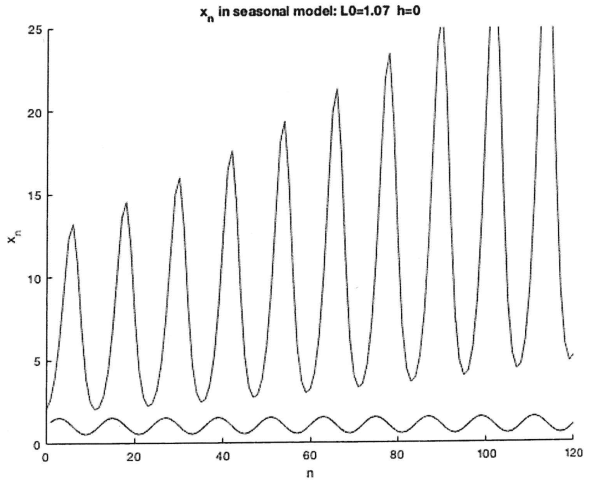
gives an annual oscillation frequency Δω = 12

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%      Harvesting model
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%
%     X(n+1)= lambda X(n) - h
%
% with initial condition X(0)=X0
% has exact solution:
%
%   X(n)=lambda^n X0 -(lambda^n-1)/(lambda-1) h
%
% First calculate X(n) without the formula above.
%
clear X;
lambda=1.1;
X(1)=2;
%h=0.20;
h=0.30;
N=10;
for n=1:N
    X(n+1)=lambda*X(n)-h;
end;
figure(4)
plot(0:N,X)
%
% Now compute Y=X using formula above
%
m=0:N;
Y=lambda.^m*X(1) -(lambda.^m-1)./(lambda-1)*h;
hold on
plot(m,Y,'r*')
title(['x_n in harvest model:
 lambda=',num2str(lambda),'h=',num2str(h)])
xlabel('n')
ylabel('x_n')
hold off

%
%
%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%      Harvesting model with Seasonal Variation
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%
%     Seasonal variation of growth rate. Suppose
%     n=time (in months) since start growth rate at
%     time n is L(n):
%
%     L = L0+alpha*sin(omega*n)
%
%     X(n+1)= L(n) X(n) - h
%
```

```
%     with initial condition X(1)=X0.
%
%
clear X;
N=120;
L0=1.07;
alpha=0.5;
omega=2*pi./12;
L=L0+alpha*sin(omega*(1:N));
%
%
X(1)=2;
h=0.000;
%h=0.035;
for n=1:N
    X(n+1)=L(n)*X(n)-h;
end;
%
figure(5)
clf
hold on
plot(0:N,X,'r-')
plot(1:N,L,'b-')
title(['x_n in seasonal model: L0=',num2str(L0),'  h=',num2str(h)])
xlabel('n')
ylabel('x_n')
axis([0,N,0,25])
hold off
```



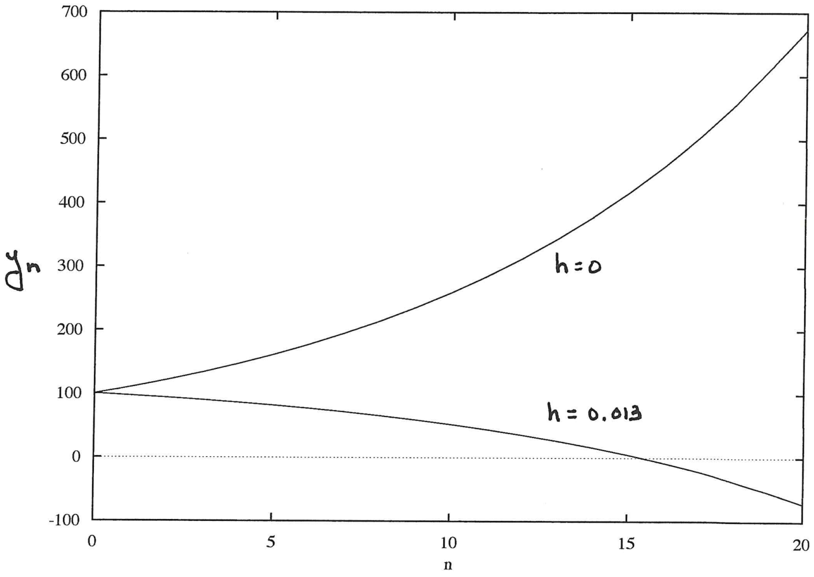


xppaut code for difference (discrete) eqns

$$x_{n+1} = c_1 x_n$$
$$y_{n+1} = c_2 y_n - h$$

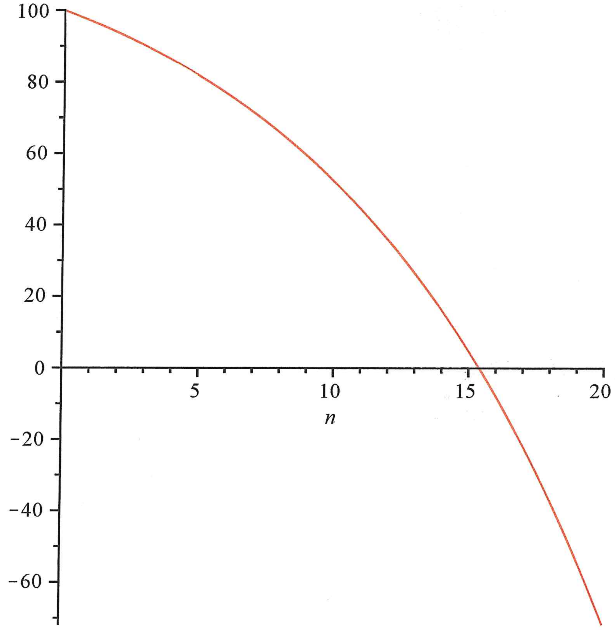
```
#
#
#
par c1=1.1,c2=1.1,h=13
init x=100,y=100
#
#
x(t+1)=c1*x
y(t+1)=c2*y-h
#
#
@ total=20,method=discrete,nout=1
done
```

xppaut output "Graph. Stuff.... postscript"



Maple Code for x_n (notes)

```
> restart;
> x0:=100;lambda:=1.1;h:=13;
                              x0 := 100
                              λ := 1.1
                              h := 13                              (1)
> xn:=lambda^n*x0-h*(lambda^n-1)/(lambda-1);
          xn := -30.0000000 1.1^n + 130.0000000                    (2)
> plot(xn,n=0..20);
```



Nonlinear Density Dependent Models

(1) $$x_{n+1} = x_n\, g(x_n) = f(x_n)$$

where here

$$g(x) = \text{growth rate at density } x$$

Remarks

a) If $g(x) = r$, $r > 0$ constant then the model in (1) is the linear model

$$x_{n+1} = r\, x_n$$

b) If at some time n we have $g(x_n) = 1$ then

$$x_{n+1} = x_n$$

$$x_{n+2} = x_{n+1}\, g(x_{n+1}) = x_n$$

$$x_{n+3} = x_{n+2}\, g(x_{n+2}) = x_n$$

In other words, if $g(x_n) = 1$ then

$$x_N = x_n \qquad \forall N \geq n$$

Note "$\forall$" means for all.

An orbit of $x_{n+1} = f(x_n)$

$$\gamma(x_0) = \{ x_0 , x_1 , x_2 , x_3 , \dots \}$$

$$\gamma(x_0) = \{ x_0 , f(x_0), f^2(x_0), f^3(x_0), \dots \}$$

gives discrete time series for population given an initial density x_0.

EXAMPLE $f(x) = x(1-x)$ $x_0 = \frac{1}{2}$

$$x_1 = f(x_0) = \frac{1}{2}\left(1-\frac{1}{2}\right) = \frac{1}{4}$$

$$x_2 = f(x_1) = \frac{1}{4}\left(1-\frac{1}{4}\right) = \frac{3}{16}$$

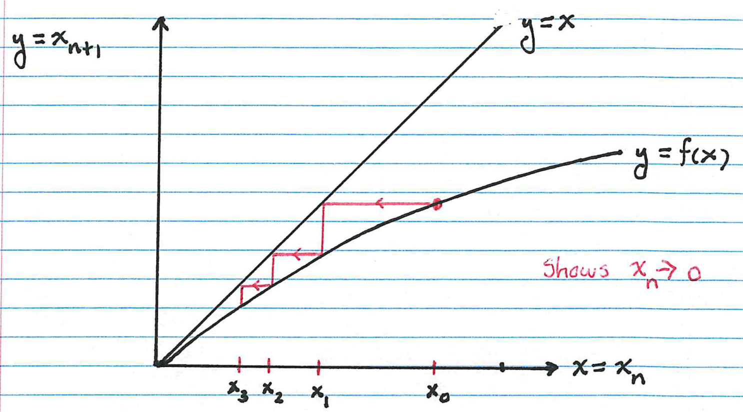
$$x_3 = f(x_2) = \frac{3}{16}\left(1-\frac{3}{16}\right) = \frac{39}{256}$$

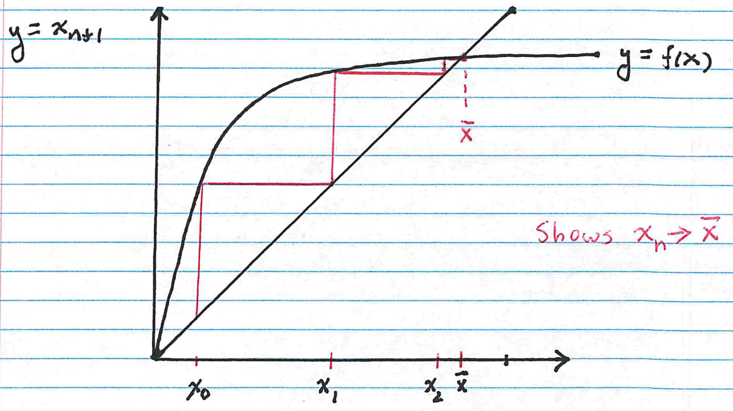
Hence

$$\gamma(x_0) = \left\{ \frac{1}{2}, \frac{1}{4}, \frac{3}{16}, \frac{39}{256}, \dots \right\}$$

Cobwebs $x_{n+1} = f(x_n)$

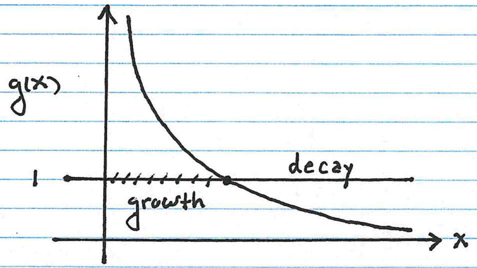
Is a graphical method for finding orbits.

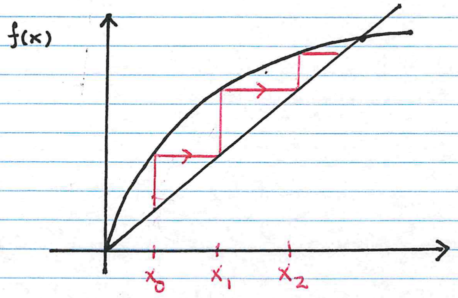




EXAMPLE Varley, Gradwell, Hassel (1975)

$$\boxed{g(x) = \lambda x^{-b} \qquad 0<b<1}$$

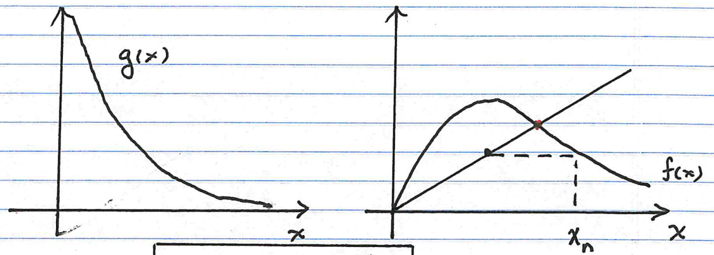




$$f(x) = x\,g(x)$$

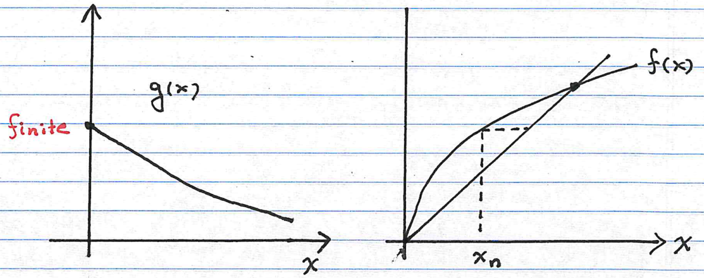
$$f(x) = \lambda x^{1-b}$$

Ex May 1975



$$\boxed{g(x) = e^{r(1-x/K)}}$$

Ex Hassel 1973



$$g(x) = \lambda(1+ax)^{-b}$$

Fixed points and Linear stability

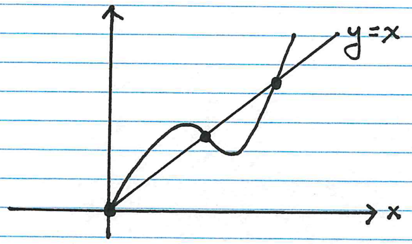
(1) $x_{n+1} = f(x_n)$

A fixed point of (1) is a value $\bar{x}$ such that

(2) $\bar{x} = f(\bar{x})$

For these values $x_n = \bar{x}$ for all n if $x_0 = \bar{x}$

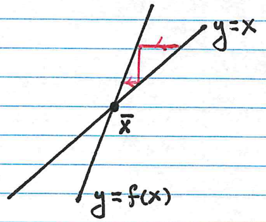
EX



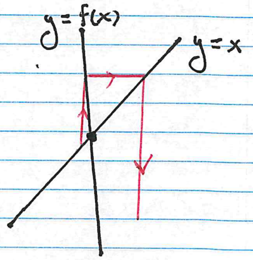
Has 3 fixed points

Linear stability

A fixed point $\bar{x}$ is linearly stable if $x_n \to \bar{x}$ for all x_0 sufficiently close to $\bar{x}$



$\bar{x}$ lin. stable



$\bar{x}$ unstable

Linear Stability

Let $\bar{x}$ be a fixed point of

(1) $x_{n+1} = f(x_n)$

Then

$|f'(\bar{x})| < 1 \Rightarrow \bar{x}$ stable

$|f'(\bar{x})| > 1 \Rightarrow \bar{x}$ unstable

Proof Sketch using Talyor series. Define

(2) $x_n = \bar{x} + \Delta x_n$ ← $|\Delta x_n|$ = distance from $\bar{x}$

Substitute (2) into (1)

$$x_{n+1} = f(x_n)$$

$$\bar{x} + \Delta x_{n+1} = f(\bar{x} + \Delta x_n)$$

$f(\bar{x}) = \bar{x}$ $$\cancel{\bar{x}} + \Delta x_{n+1} = f(\cancel{\bar{x}}) + f'(\bar{x})\Delta x_n + \overset{\text{(smaller)}}{\tfrac{1}{2} f''(\bar{x})\Delta x_n^2} + \cdots$$

$$\boxed{\Delta x_{n+1} \cong f'(\bar{x})\Delta x_n}$$

Looks like $\Delta x_{n+1} = \lambda \Delta x_n$ which decays only if $|\lambda| < 1$

$|f'(\bar{x})| < 1 \Rightarrow \Delta x_n \to 0$

$|f'(\bar{x})| > 1 \Rightarrow \Delta x_n \to \infty$

EXAMPLE

Find any positive fixed point(s) and stability of the difference equation (map)

$$x_{n+1} = x_n \ln x_n^2$$

$$x_{n+1} = f(x_n)$$

Here $f(x) = x \ln x^2$ and $\bar{x}$ is a fixed point if

$$\bar{x} = \bar{x} \ln \bar{x}^2$$

$$1 = \ln \bar{x}^2$$

$$e = \bar{x}^2$$

$$\boxed{e^{1/2} = \bar{x}}$$

To find the stability we need to compute $f'(\bar{x})$

$$f'(x) = \ln x^2 + x \cdot \left(\frac{1}{x^2} \cdot 2x\right)$$

$$f'(x) = \ln x^2 + 2$$

Hence

$$f'(\bar{x}) = \ln \bar{x}^2 + 2 = \ln e + 2 = 3$$

Since $|f'(\bar{x})| = 3 > 1$ we conclude $\bar{x} = e^{1/2}$ unstable

Logistic Model Analysis

$$(1) \qquad x_{n+1} = f(x_n) = r x_n (1 - x_n)$$

Solution behavior

$0 < r < 1$	extinction
$1 < r < 3$	stable fixed point
$3 < r < 1 + \sqrt{6}$	period 2 solutions

To prove requires considerable work

Fixed Point existence and stability

$$(2) \qquad \bar{x} = f(\bar{x})$$

$$\bar{x} = r\bar{x}(1 - \bar{x})$$

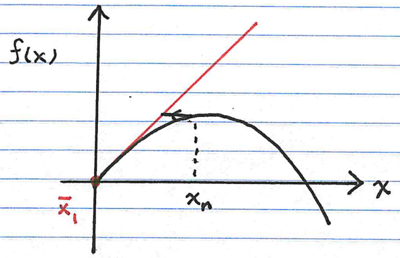
Solving (2) yields two fixed points

$$\bar{x}_1 = 0$$

$$\bar{x}_2 = 1 - \frac{1}{r} > 0 \qquad (\text{only if } r > 1)$$

For $\bar{x}_1$ we use a cobweb argument.

"Global Stability"



Graph of $f = rx(1-x)$ for $r \in (0,1)$

Cobweb implies

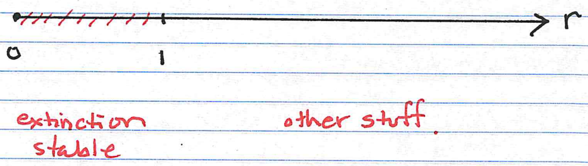
$$x_n \to 0$$

Can also check linear stability of $\bar{x}_1 = 0$

$$|f'(\bar{x}_1)| < 1$$

Explicitly this condition can be shown to be

$$|r| < 1$$



Like wise we can consider other fixed point

$$\bar{x}_2 = 1 - \frac{1}{r} > 0 \qquad (r > 1)$$

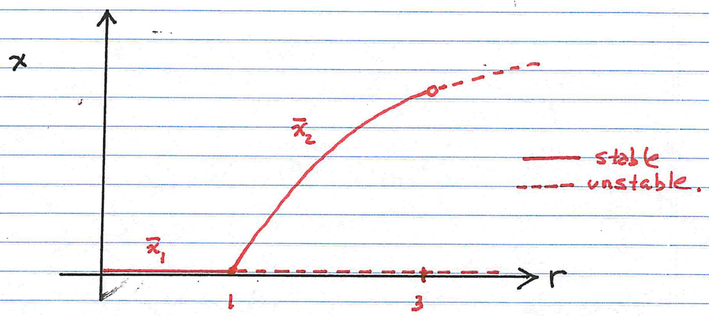
For this fixed point we have stability if

$$|f'(\bar{x}_2)| < 1$$

$$|2 - r| < 1$$

$$r \in (1, 3)$$

Bifurcation diagram $\quad \bar{x}_1 = 0 \; , \; \bar{x}_2 = 1 - \frac{1}{r}$



Note that fixed point $\bar{x}_2$ unstable for all $r > 3$

Period Doubling

(1) $$x_{n+1} = f(x_n)$$

Consider fixed points of the second iterate map. That is, consider roots x of

(2) $$x = f(f(x))$$

The orbit associated with x is

(3) $$\{x,\ f(x),\ x,\ f(x),\ x,\ f(x),\ \ldots\}$$ period 2

This will be period 2 so long as $x \neq f(x)$

The latter corresponds to x not being a fixed point. Recall $\bar{x} = f(\bar{x})$ for a fixed point in which case

$$\bar{x} = f(f(\bar{x})) = f(\bar{x})$$ ✓

whence (3) would be

$$\{\bar{x},\ \bar{x},\ \bar{x},\ \bar{x},\ \bar{x},\ \bar{x},\ \ldots\}$$ period 1

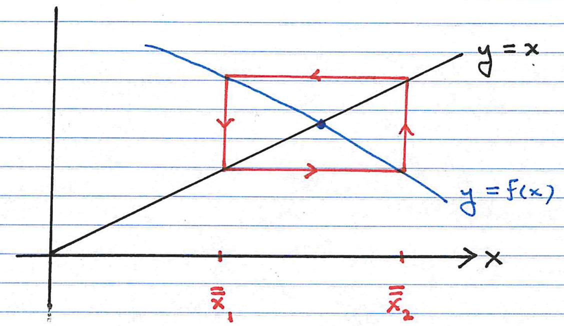
As in the text we shall use double overbar to denote true period two x values:

$$\bar{\bar{x}}_{1,2} = f(f(\bar{\bar{x}}_{1,2}))$$

So the orbit in (3) is

$$\{\bar{\bar{x}}_1,\ \bar{\bar{x}}_2,\ \bar{\bar{x}}_1,\ \bar{\bar{x}}_2,\ \bar{\bar{x}}_1,\ \bar{\bar{x}}_2,\ \ldots\}$$

A typical period two cobweb looks like



Stability $g(x) \equiv f(f(x))$

A period two cycle is stable only if the fixed point of g(x) is:

(5) $$|g'(\bar{\bar{x}})| < 1$$ stable

Since

$$g'(x) = f'(f(x))\, f'(x)$$

and $\bar{\bar{x}}_2 = f(\bar{\bar{x}}_1)$ the stability condition (5) is:

$$\boxed{\left| f'(\bar{\bar{x}}_1)\, f'(\bar{\bar{x}}_2) \right| < 1}$$ stable period 2

Logistic Difference Eqn (Period 2)

$$x_{n+1} = f(x_n) \qquad\qquad f(x) = rx(1-x)$$

We already know two fixed points

(1) $$\bar{x}_1 = 0 \qquad\qquad \bar{x}_2 = 1 - \frac{1}{r}$$

To find period two orbits we need to find all the real roots of

$$x = f(f(x))$$

$$x = r\, f(x)\,(1 - f(x))$$

$$x = r^2 x(1-x)(1-rx(1-x))$$

In summary we need the roots of the quartic

(2) $$\boxed{P(x) = r^2 x(1-x)(1-rx(1-x)) - x}$$

All is not lost. Two roots of (2) must be the fixed points $\bar{x}_k$. Long division yields (not shown)

quadratic

$$P(x) = x(x-\bar{x}_2)\,Q(x)$$

Roots of the quadratic $Q(x)$ can be found

(3) $$\boxed{\bar{\bar{x}}_\pm = \frac{r+1 \pm \sqrt{r^2-2r-3}}{2r}}$$

The condition that $\bar{\bar{x}}$ is stable is

(4) $$\boxed{|f'(\bar{\bar{x}}_+)\,f'(\bar{\bar{x}}_-)| < 1}$$

After a huge amount of calculations eqn (4) simplifies to:

(5) $$|4 + 2r - r^2| < 1$$

We find a range of r for stability by setting the quadratic in (5) equal to ± 1

$$4 + 2r - r^2 = +1 \quad \Rightarrow \quad r = 3$$

$$4 + 2r - r^2 = -1 \quad \Rightarrow \quad r = 1 + \sqrt{6}$$

Conclude period 2 orbit stable only if

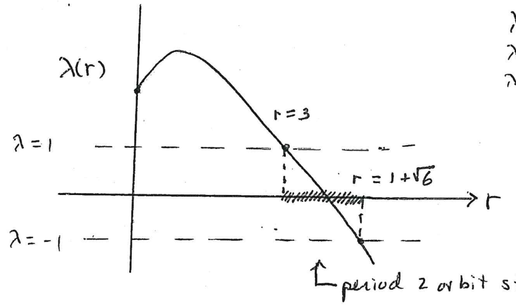
$$3 < r < 1 + \sqrt{6} \simeq 3.45$$

Calculations reveal

$$\lambda = r^2(1-2a)(1-2b) = f'(a)f'(b)$$

$$\lambda = 4 + 2r - r^2$$

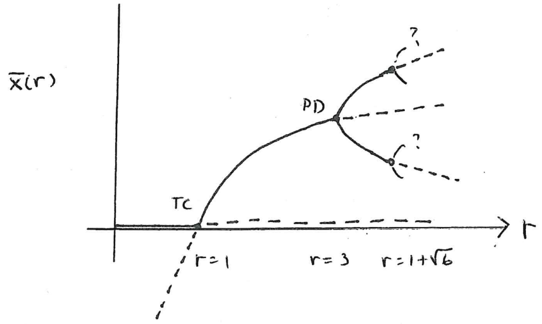
The requirement that $|\lambda| < 1$ can be found graphically:



$\lambda(0) = 4$
$\lambda'(1) = 0$
$\lambda(1) = 5$

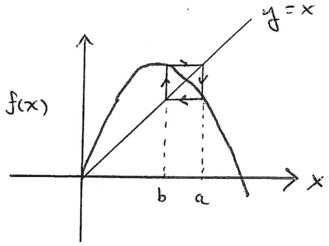
period 2 orbit stable.

Bifurcation diagram



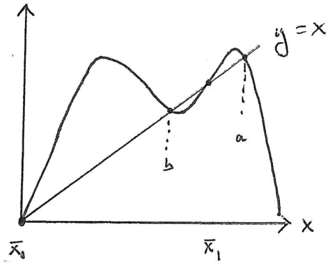
Period 2 orbit Cobweb

$a > b$



$r > 3$

Second-iterate map



Stability of (sole) periodic orbit

Sufficient to show that $\bar{x} = a, b$ are stable fixed points of $f^2(x)$

$$\frac{d}{dx} f(f(x)) = f'(f(x))\, f'(x)$$

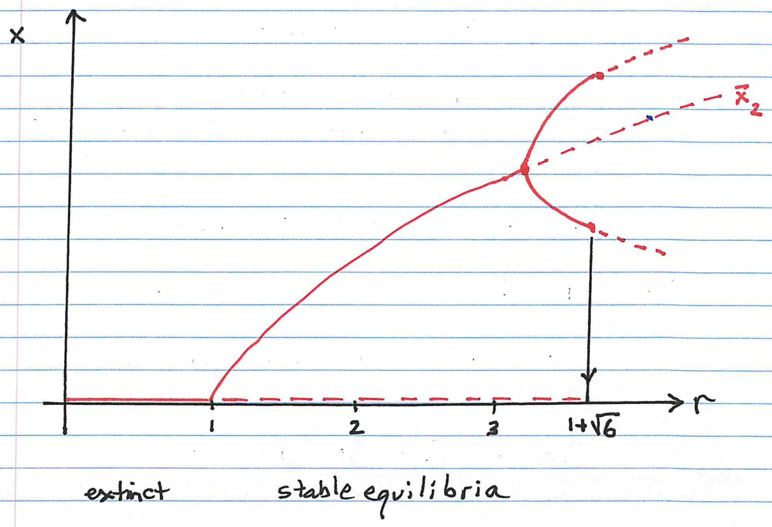
Multiplier

$$\lambda = \frac{d}{dx} f(f(x))\Big|_{x=a} = f'(f(a))\, f'(a) = f'(a)\, f'(b)$$

Logistic model Bifurcation diagram

Plot fixed points $\bar{x}_1$, $\bar{x}_2$ and period 2 $\bar{\bar{x}}_\pm$.

By convention solid line means stable,
dashed line means unstable



Plant Propagation

Consider plants that produce seeds each August. Seeds can germinate only one or two years later.

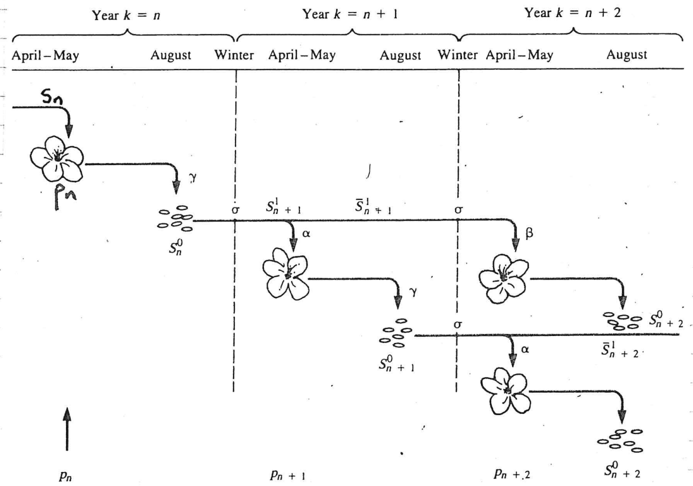


Figure 1.2 Annual plants produce γ seeds per plant each summer. The seeds can remain in the ground for up to two years before they germinate in the springtime. Fractions α of the one-year-old and β of the two-year-old seeds give rise to a new plant generation. Over the winter seeds age, and a certain proportion of them die. The model for this system is discussed in Section 1.2.

γ = # seeds per plant in August

α = fraction of 1-yr old seeds germinate

β = fraction of 2-yr old seeds germinate

σ = fraction of seeds survive winter.

Variable Defns (year n)

P_n = number of plants (May)

S_n^1 = number of 1yr old seeds before April germ.

$\bar{S}_n^1$ = number of 1yr old seeds left in May after germ.

S_n^2 = number of 2yr old seeds before April germ.

$\bar{S}_n^2$ = number of 2yr old seeds left in May after germ

S_n^0 = number new seeds produced in August

Parameter Defns

γ = # seeds per plant in August

α = fraction of 1yr old seeds that germinate

β = fraction of 2yr old seeds that germinate

σ = fraction of seeds that survive winter.

Relation between variables (at year n)

(1) $$p_n = \alpha S_n^1 + \beta S_n^2$$

These plants will produce seeds in August.

(2) $$\bar{S}_n^1 = (1-\alpha) S_n^1$$

(3) $$\bar{S}_n^2 = (1-\beta) S_n^2$$

Seeds produced by plants in August

(4) $$S_n^0 = \gamma p_n$$

Winter mortality

(5) $$S_{n+1}^1 = \sigma S_n^0$$

(6) $$S_{n+1}^2 = \sigma \bar{S}_n^1$$

Simplify system

$$p_{n+1} = \alpha \underline{S_{n+1}^1} + \beta S_{n+1}^2$$

use (4)-(5)

$$p_{n+1} = \underline{\alpha\gamma\sigma p_n} + \beta S_{n+1}^2$$

use (2), (6)

(7) $$p_{n+1} = \alpha\underline{\gamma\sigma p_n} + \beta\sigma(1-\alpha) S_n^1$$

Eqns (7) and (5) can then be written as a system of two first order difference equations

$$\boxed{\begin{aligned} p_{n+1} &= \alpha\gamma\sigma p_n + \beta\sigma(1-\alpha) S_n^1 \\ S_{n+1}^1 &= \underline{\gamma\sigma p_n} \end{aligned}}$$

system of 1st order diff. eqns

Given we know initial values p_0, S_0^1 then (p_n, S_n^1) can be found

To determine fate of population is easier to eliminate S_n^1 noting

(4), (5) $$S_n^1 = \gamma\sigma p_{n-1}$$

hence

$$\boxed{p_{n+1} = \alpha\gamma\sigma p_n + \beta\sigma^2(1-\alpha)\gamma p_{n-1}}$$

Second order difference eqn.

Need to know math for solving this.

Plant model as a system

$$\boxed{\begin{aligned} p_{n+1} &= \alpha\gamma\sigma\, p_n + \beta\sigma(1-\alpha)\, s_n^1 \\ s_{n+1}^1 &= \gamma\sigma\, p_n \end{aligned}}$$

is equivalent to the system

(1) $$X_{n+1} = A X_n \qquad X_n \in \mathbb{R}^2,\ A \in \mathbb{R}^{2\times 2}$$

$$X_n = \begin{pmatrix} p_n \\ s_n^1 \end{pmatrix} \qquad A = \begin{bmatrix} \alpha\gamma\sigma & \beta\sigma(1-\alpha) \\ \gamma\sigma & 0 \end{bmatrix}$$

Plant model as 2nd order difference equation

$$\boxed{p_{n+1} - \alpha\gamma\sigma p_n - \beta\sigma^2(1-\alpha)\gamma\, p_{n-1} = 0}$$

is equivalent to

(2) $$a x_{n+1} + b x_n + c x_{n-1} = 0$$

$$a = 1$$

$$b = -\alpha\gamma\sigma$$

$$c = \beta\sigma^2(1-\alpha)\gamma$$

$$x_n = p_n$$

Mathematics of second order difference equations

Second Order Difference Equations

(1) $$\boxed{a x_{n+1} + b x_n + c x_{n-1} = 0}$$

Seek solutions of the form

(2) $$x_n = \lambda^n \qquad \lambda \in \mathbb{C} \text{ (complex)}$$

Substitute (2) into (1) and simplify

$$a\lambda^{n+1} + b\lambda^n + c\lambda^{n-1} = 0$$

$$\lambda^{n-1}\underbrace{(a\lambda^2 + b\lambda + c)}_{\text{must vanish}} = 0$$

Hence $x_n = \lambda^n$ is a solution only if λ is a root of the characteristic polynomial

$$\boxed{P(\lambda) \doteq a\lambda^2 + b\lambda + c}$$

Solutions depend on whether roots of $P(\lambda)$ are real, equal, complex.

General Solutions (without proof)

Categorized by roots λ_k of $P(\lambda)$

$\lambda_1 \neq \lambda_2$ real	$x_n = c_1\lambda_1^n + c_2\lambda_2^n$
$\lambda_1 = \lambda_2$ real	$x_n = (c_1 + c_2 n)\lambda_1^n$
$\lambda = re^{i\theta}$ complex	$x_n = c_1 r^n\cos(n\theta) + c_2 r^n\sin(n\theta)$

Conversion in complex case

Complex roots of $P(\lambda)$ can be written

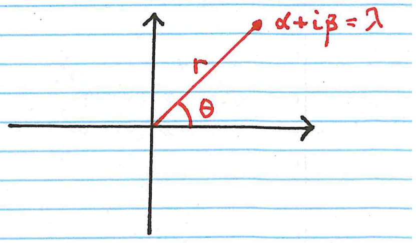
(1) $$\lambda = \alpha + i\beta \qquad \alpha, \beta \in \mathbb{R}$$

To convert λ to polar note

(2) $$\lambda = re^{i\theta} = r\cos\theta + i r\sin\theta$$

Compare (1) and (2)

$$\underbrace{\boxed{\begin{aligned} r\cos\theta &= \alpha \\ r\sin\theta &= \beta \end{aligned}}}_{\text{solve for } (r,\theta)}$$



More on complex solutions

$$L(z_n) = a z_{n+2} + b z_{n+1} + c z_n = 0$$

Solutions may be complex even if a, b, c real

$$z_n = x_n + i y_n$$

where x_n, y_n are both real. From (1) it is easy to see

$$L(z_n) = L(x_n) + i L(y_n) = 0$$

which is true only if both $L(x_n) = 0$ and $L(y_n) = 0$.

Thus, real and complex parts of z_n are each solutions of the difference eqn.

$$z_n = (\alpha + i\beta)^n$$

$$z_n = (re^{i\theta})^n$$

$$z_n = r^n e^{in\theta}$$

$$z_n = r^n(\underset{\uparrow\, x_n}{\cos(n\theta)} + i\,\underset{\uparrow\, y_n}{\sin(n\theta)})$$

Hence general solution is

$$x_n = c_1 r^n \cos(n\theta) + c_2 r^n \sin(n\theta)$$

EXAMPLE $\boxed{x_{n+2} - 5x_{n+1} + 6x_n = 0}$

Let $x_n = \lambda^n$ ultimately yields chacteristic eqn

$$\lambda^2 - 5\lambda + 6 = 0$$

which has two real roots:

$$\lambda_1 = 2 \qquad \lambda_2 = 3$$

General solution of difference eqn is:

(1) $$x_n = c_1 2^n + c_2 3^n$$

where c_k are arbitrary constants.

If one also stipulates initial conditions these constants can be found. For instance

(2) $$x_{n+1} - 5x_n + 6x_{n-1} = 0 \qquad x_0 = 1 \qquad x_1 = 2$$

Use gen. soln (1) to find c_k

n=0 $\quad x_0 = c_1 2^0 + c_2 3^0 = 1$

n=1 $\quad x_1 = c_1 2^1 + c_2 3^1 = 2$

Solving these ⇒ $c_1 = 1$, $c_2 = 0$.

$$x_n = 2^n$$

EXAMPLE $x_{n+2} - 6x_{n+1} + 9x_n = 0$ (repeated)

$$\lambda^2 - 6\lambda + 9 = 0$$

Hence $\lambda = 3$ repeated yields a gen. soln.

$$x_n = (c_1 + c_2 n)3^n$$

EXAMPLE $x_{n+2} - x_{n+1} + x_n = 0$ (complex)

$$\lambda^2 - \lambda + 1 = 0$$

has complex roots $\lambda = \frac{1}{2} \pm \frac{\sqrt{3}}{2} i$

$$\lambda = re^{i\theta} = \underset{\uparrow}{r\cos\theta} + \overset{\downarrow}{ir\sin\theta} = \underset{\uparrow}{\frac{1}{2}} + \overset{\downarrow}{\frac{\sqrt{3}}{2}} i$$

hence

$$r\cos\theta = 1/2$$
$$r\sin\theta = \sqrt{3}/2$$

whose soln: $r = 1$, $\theta = \pi/3$

$$= c_1 (1)^n \cos\left(\frac{n\pi}{3}\right) + c_2 (1)^n \sin\left(\frac{n\pi}{3}\right)$$

Asymptotic Behavior

$$a x_{n+1} + b x_n + c x_{n-1} = 0$$

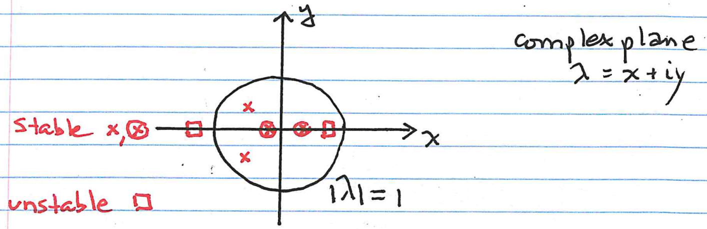
The general solution is $(\lambda_1 \neq \lambda_2)$

$$x_n = c_1 \lambda_1^n + c_2 \lambda_2^n$$

Even when λ_k are complex, very simple conditions determine the large n asymptotic behavior of x_n.

stable $|\lambda_1| < 1$ and $|\lambda_2| < 1$ $\Rightarrow$ $|x_n| \to 0$

unstable $|\lambda_k| > 1$ for some k $\Rightarrow$ $|x_n| \to \infty$



Systems of Difference Equations

(1) $x_{n+1} = a_{11} x_n + a_{12} y_n$

(2) $y_{n+1} = a_{21} x_n + a_{22} y_n$

Can be re-expressed in vector form

(3) $$\mathbf{X}_{n+1} = A \mathbf{X}_n$$

where

$$\mathbf{X}_n = \begin{pmatrix} x_n \\ y_n \end{pmatrix} \qquad A = \begin{bmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{bmatrix} \in \mathbb{R}^{2\times 2}$$

An example of the solution of (3)

Suppose $\lambda_i, \vec{\xi}_i$ are eigenvalue/vector pairs of A

$$A\vec{\xi}_i = \lambda_i \vec{\xi}_i \qquad i = 1,2$$

General solution of (3) is

$$\mathbf{X}_n = c_1 \lambda_1^n \vec{\xi}_1 + c_2 \lambda_2^n \vec{\xi}_2 \qquad \lambda_1 \neq \lambda_2$$

Proof:

$$\begin{aligned} A\mathbf{X}_n &= c_1 \lambda_1^n \overset{\frown}{A\vec{\xi}_1} + c_2 \lambda_2^n \overset{\frown}{A\vec{\xi}_2} \\ &= c_1 \lambda_1^n \cdot \lambda_1 \vec{\xi}_1 + c_2 \lambda_2^n \cdot \lambda_2 \vec{\xi}_2 \\ &= c_1 \lambda_1^{n+1} \vec{\xi}_1 + c_2 \lambda_2^{n+1} \vec{\xi}_2 = \mathbf{X}_{n+1} \qquad \square \end{aligned}$$

EXAMPLE $\mathbf{X}_{n+1} = A\mathbf{X}_n \qquad A = \begin{bmatrix} -10 & -4 \\ 24 & 10 \end{bmatrix}$

First find eigenvalues of A. Characteristic Polynomial

$$P(\lambda) = \det(A - \lambda I) = \lambda^2 - 4$$

Roots of $P(\lambda)$ are eigenvalues of A

$$\lambda_1 = 2 \qquad \lambda_2 = -2$$

Now find eigenvectors for λ_1 and λ_2

$$A - \lambda_1 I = \begin{bmatrix} -12 & -4 \\ 24 & 8 \end{bmatrix} \sim \begin{bmatrix} 3 & 1 \\ 0 & 0 \end{bmatrix} \qquad \vec{\xi}_1 = \begin{pmatrix} 1 \\ -3 \end{pmatrix}$$

$$A - \lambda_2 I = \begin{bmatrix} -8 & -4 \\ 24 & 12 \end{bmatrix} \sim \begin{bmatrix} 2 & 1 \\ 0 & 0 \end{bmatrix} \qquad \vec{\xi}_2 = \begin{pmatrix} 1 \\ -2 \end{pmatrix}$$

Given we now know $\lambda_i, \vec{\xi}_i$ we have

$$\mathbf{X}_n = c_1 2^n \begin{pmatrix} 1 \\ -3 \end{pmatrix} + c_2 (-2)^n \begin{pmatrix} 1 \\ -2 \end{pmatrix} \qquad \square$$

Remarks

General solutions when λ_i are repeated or complex are not shown here.

Analysis of Plant Model

Plant model revisited

Recall the plant population p_n at year n satisfies the second order difference equation

(1)
$$\boxed{\begin{aligned} p_{n+1} - \alpha\gamma\sigma\, p_n - \beta\sigma^2(1-\alpha)\gamma\, p_{n-1} &= 0 \\ p_{n+1} - a\, p_n - b\, p_{n-1} &= 0 \end{aligned}}$$

where

α = fraction of 1-yr old seeds that germinate

β = fraction of 2-yr old seeds that germinate

σ = fraction of seeds that survive winter

γ = number of seeds per plant in August

Wish to answer the simple question:

do the plants thrive (survive) ?

To answer we note the solution to (1) is

(2)
$$\boxed{\begin{aligned} p_n &= c_1\lambda_-^n + c_2\lambda_+^n \\ \lambda_\pm &= \tfrac{1}{2}\left(a \pm \sqrt{a^2+4b}\,\right) \end{aligned}}$$

Note: Both eigenvalues $\lambda_\pm$ are real. Does not preclude oscillations if $\lambda_- < 0$ though.

We make a few observations

$$\sqrt{a^2+4b} > a > 0$$

Consequently

$$\lambda_+ = \frac{1}{2}\left(a+\sqrt{a^2+4b}\right) > a > 0$$

$$\lambda_- = \frac{1}{2}\left(a-\sqrt{a^2+4b}\right) < 0$$

Summarize

$$\boxed{\lambda_- < 0 < \lambda_+} \qquad |\lambda_+| > |\lambda_-|$$

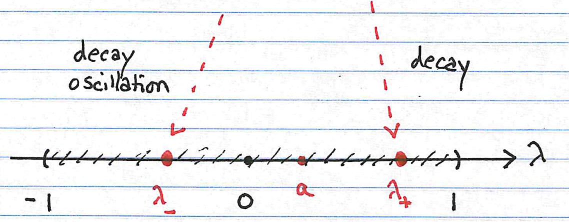
Thus the term λ_-^n in (2) does oscillate.

A necessary condition for the plant population to survive is

$$\boxed{\lambda_+ > 1}$$

Were this not true $p_n \to 0$ as $n \to \infty$

$$p_n = c_1 \lambda_-^n + c_2 \lambda_+^n$$



Necessary Condition $\lambda_+ > 1$

We will first determine when $\lambda_+ < 1 \Rightarrow p_n \to 0$.
Same as

$$a + \sqrt{a^2+4b} < 2$$

$$\sqrt{a^2+4b} < 2-a$$

$$a^2 + 4b < (2-a)^2$$

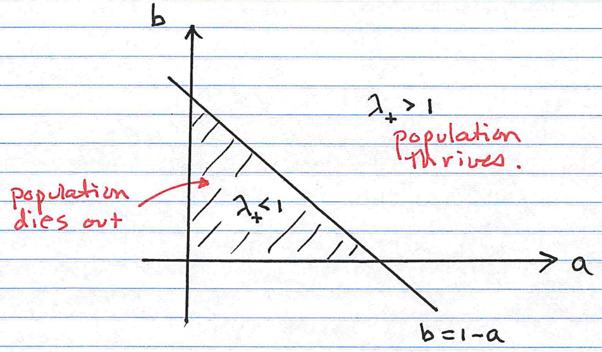
$$\cancel{a^2} + 4b < 4 - 4a + \cancel{a^2}$$

$$4b < 4-4a$$

Conclude $\lambda_+ < 1$ only if

$$b < 1-a$$

*For all other (a,b) positive $\lambda_+ > 1$



Survival $\lambda_+ > 1$

Given the definitions for (a, b)

$$a = \alpha \gamma \sigma$$

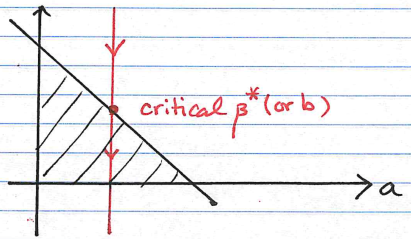
$$b = \beta \sigma^2 (1-\alpha) \gamma$$

the condition $b > 1 - a$ is equivalent to

$$(3) \qquad \boxed{\gamma > \frac{1}{\alpha\sigma + \beta\sigma^2(1-\alpha)}}$$

Decreasing β (2nd yr seeds)

Note only b of (a,b) contains "β".
Decreasing β in (a,b)-plane with other parameters fixed



The change in behavior at β^* is called a bifurcation

Approximations

Condition (3) is hard to understand.
But, when

$$(4) \qquad \varepsilon \equiv \frac{\beta}{\alpha} \ll 1$$

is small, an approximation can be derived.
Using (4) in (3)

$$\gamma > \frac{1}{\alpha\sigma\left(1 + \underset{\uparrow}{\varepsilon}\,\sigma(1-\alpha)\right)}$$

$$\gamma > \frac{1}{\alpha\sigma} f(\underset{\uparrow}{\varepsilon})$$

which has a Taylor Series approximation

$$\gamma > \frac{1}{\alpha\sigma}\left(\underbrace{f(0)}_{\substack{\uparrow \\ 1}} + \underbrace{\varepsilon f'(0)}_{\substack{\uparrow \\ \text{small}}} + \underbrace{O(\varepsilon^2)}_{\substack{\uparrow \\ \text{smaller}}} \right)$$

The first term yields

$$\boxed{\gamma > \frac{1}{\alpha\sigma} \quad \text{if} \quad \beta \ll \alpha}$$

Problem 2: A Schematic Model of Red Blood Cell Production

The following problem[5] deals with the number of red blood cells (RBCs) circulating in the blood. Here we will present it as a discrete problem to be modeled by difference equations, though a different approach is clearly possible.

In the circulatory system, the red blood cells (RBCs) are constantly being destroyed and replaced. Since these cells carry oxygen throughout the body, their number must be maintained at some fixed level. Assume that the spleen filters out and destroys a certain fraction of the cells daily and that the bone marrow produces a number proportional to the number lost on the previous day. What would be the cell count on the *n*th day?

To approach this problem, consider defining the following quantities:

R_n = number of RBCs in circulation on day n,
M_n = number of RBCs produced by marrow on day n,
f = fraction RBCs removed by spleen,
γ = production constant (number produced per number lost).

It follows that equations for R_n and M_n are

$$\begin{aligned} R_{n+1} &= (1-f)R_n + M_n, \\ M_{n+1} &= \gamma f R_n. \end{aligned} \tag{47}$$

Problem 16 discusses this model. By solving the equations it can be shown that the only way to maintain a nearly constant cell count is to assume that $\gamma = 1$. Moreover, it transpires that the delayed response of the marrow leads to some fluctuations in the red cell population.

As in problem 2, we apply a discrete approach to a physiological situation in which a somewhat more accurate description might be that of an underlying continuous process with a time delay. (Aside from practice at formulating the equations of a discrete model, this will provide a further example of difference equations analysis.)

Growth of Microorganisms

$N(t)$ = bacteria density at time t

K = reproduction rate per unit time

The meaning of $\mathbb{K}$ is the number of new bacteria that spawn from one bacteria in one unit of time

(1) $N(t+\Delta t) - N(t) = \mathbb{K} N(t) \Delta t$

hence

(2) $$\frac{N(t+\Delta t) - N(t)}{\Delta t} = \mathbb{K} N(t)$$

Let $\Delta t \to 0$ in (2) to arrive at

(1) $$\boxed{\frac{dN}{dt} = \mathbb{K} N}$$ Malthusian Growth.

When $\mathbb{K}$ is constant and the initial condition is $N(0) = N_0$ the solution of (1) is

(2) $$N(t) = N_0 e^{\mathbb{K}t}$$

Many alternate assumptions can be made about the reproduction rate.

Notes on units

Throughout we will use the square bracket notation $[\mathbb{X}]$ to denote the units of $\mathbb{X}$

Additionally we shall let

L = unit of length

M = unit of mass

T = unit of time

Examples

v = velocity	$[v] = LT^{-1}$
g = gravity constant	$[g] = LT^{-2}$
F = force	$[F] = MLT^{-2}$
E = energy	$[E] = ML^2T^{-2}$

EXAMPLE Microorganism where N is bacteria density

$$\frac{dN}{dt} = KN \qquad [N] = \frac{\#}{L^3} \qquad [K] = T^{-1}$$

where # is "number of bacteria". Now suppose the bacteria are confined to a vat of volume V and let $n = NV$. Then

$$\frac{dn}{dt} = \mathbb{K} n \qquad [n] = \#$$

n = total number of bacteria.

Doubling time and experimental correspondence

$$\frac{dn}{dt} = \mathbb{K} n \qquad n(0) = n_0$$

has the solution

(1) $$n(t) = n_0 e^{+\mathbb{K} t}$$

The time τ it take for population doubling:

$$2n_0 = n_0 e^{+\mathbb{K}\tau}$$

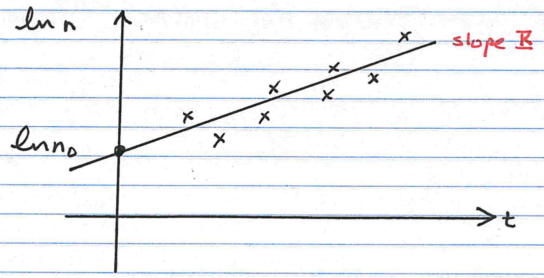
solving for τ

(2) $$\tau = \frac{\ln 2}{\mathbb{K}}$$

To find $\mathbb{K}$ from raw data first note taking log of (1) yields

(3) $$\ln n = \ln n_0 + \underbrace{\mathbb{K}}_{\text{slope}} t$$

Measure many (t, n) pairs and find slope that best fits



Nutrient Dependent Growth

Reasonable to assume bacteria growth rate depends on the nutrient concentration C

C = nutrient concentration

$$[C] = M L^{-3}$$

Simplest assumption:

(1) $$\boxed{\mathbb{K}(C) = \kappa C}$$

Next we introduce yield $\mathbb{Y} = \alpha^{-1}$ where

α = mass of nutrient consumed in producing one new bacteria

$$[\alpha] = M/\#$$

So defined such that

(2) $$\boxed{\frac{dC}{dt} = -\alpha \frac{dN}{dt}}$$

In (2) the units of both sides must match:

$$\frac{M}{\cancel{T}\cancel{L^3}} = [\alpha]\frac{\#}{\cancel{T}\cancel{L^3}}$$

hence

$$[\alpha] = \frac{M}{\#} \qquad \frac{\text{mass}}{\text{bacteria}}$$

Given assumptions (1)-(2) we have

$$(3) \quad \frac{dN}{dt} = B(C)N = \kappa C N$$

$$(4) \quad \frac{dC}{dt} = -\alpha \frac{dN}{dt} = -\alpha \kappa C N$$

are two coupled ODE's for C and N.

We reduce the order of the system by first integrating (4)

$$\frac{dC}{dt} = -\alpha \frac{dN}{dt}$$

$$(5) \quad \boxed{C(t) = C_0 - \alpha N(t)} \qquad C(0) = C_0$$

Consequently (3) becomes

$$(6) \quad \boxed{\frac{dN}{dt} = \kappa \underbrace{(C_0 - \alpha N)}_{\text{same as density dependent growth.}} N}$$

The separable 1rst order ODE (6) can be solved via partial fractions, i.e integ. in N:

$$\frac{dN}{N(C_0 - \alpha N)} = \left(\frac{A}{N} + \frac{B}{C_0 - \alpha N} \right) dN$$

Solution of: $\boxed{\frac{dN}{dt} = \kappa (C_0 - \alpha N) N \qquad N(0) = N_0}$

$$(1) \quad \frac{dN}{N(C_0 - \alpha N)} = \left(\frac{1}{C_0} \frac{1}{N} + \frac{\alpha}{C_0} \frac{1}{C_0 - \alpha N} \right) dN = \kappa \, dt$$

Integrate over $[N_0, N]$

$$(2) \quad \ln N - \ln(\alpha N - C_0) \Big|_{N_0}^{N,} = \underbrace{\kappa C_0}_{r} t$$

$$(3) \quad \ln \left(\frac{N_0 (N\alpha - C_0)}{N (N_0 \alpha - C_0)} \right) = -rt$$

where $r = \kappa C_0$. Solve (3) for $N(t)$

$$(4) \quad N(t) = \frac{N_0 B}{N_0 + (B - N_0) e^{-rt}}$$

where

$r = \kappa C_0$ growth parameter

$B = C_0 / \alpha$ carrying capacity $N' = 0$

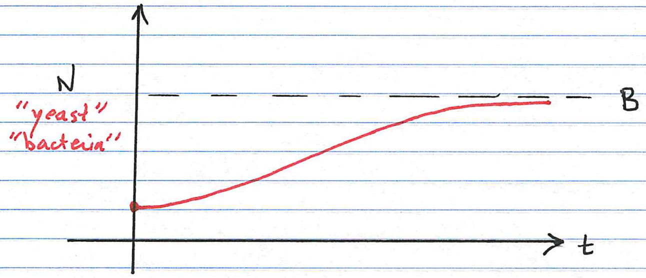
Population Density

$$\boxed{N(t) = \frac{N_0 B}{N_0 + (B - N_0)e^{-rt}}}$$

where $N_0 = N(0)$ and

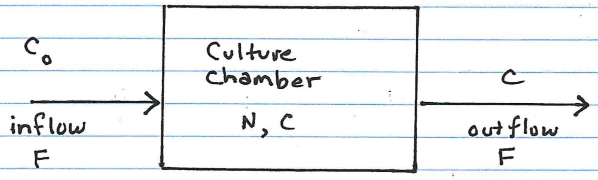
$r = K C_0$ = growth parameter

$B = C_0/\alpha$ = carrying capacity



* More realistic since population remains bounded

Chemostat Model



Bacteria of density N are in a culture chamber having nutrient concentration C. Nutrient of fixed concentration C_0 flows into the chamber at a constant flow rate F. The bacteria nutrient mix is pumped out at the same rate. Thus the volume $\mathcal{V}$ in the chamber is fixed.

$N(t)$ =	bacteria concentration	$\# L^{-3}$
$C(t)$ =	nutrient concentration	$M L^{-3}$
C_0 =	reservoir concentration	$M L^{-3}$
F =	flow rate	$L^3 T^{-1}$
$\mathcal{V}$ =	volume	L^3
Y =	$\frac{1}{\alpha}$ yield constant	$\# M^{-1}$

Conservation of Bacteria

$$\frac{dN}{dt} = \text{reproduction} - \text{outflow}$$

Given $\mathbb{K}$ is the reproduction rate

$$(1) \quad \frac{dN}{dt} = \mathbb{K} N - \frac{FN}{V}$$

Division by V is required for units to match:

$$\left[\frac{FN}{V}\right] = \frac{L^3}{T} \cdot \frac{1}{L^3} \cdot \frac{\#}{L^3} = \frac{\#}{T \cdot L^3}$$

which matches the other terms in (1)

Conservation of Nutrient

$$\frac{dc}{dt} = -\begin{array}{c}\text{bacteria}\\\text{consumption}\end{array} - \text{outflow} + \text{inflow}$$

Given the same unit considerations

$$(2) \quad \frac{dc}{dt} = -\alpha \mathbb{K} N - \frac{FC}{V} + \frac{FC_0}{V}$$

Again note the units

$$\left[\frac{FC}{V}\right] = \frac{L^3}{T} \cdot \frac{1}{L^3} \cdot \frac{M}{L^3} = \frac{M}{L^3 \pi}$$

Summary

One generally assumes the bacteria growth rate depends on the nutrient concentration

$$\mathbb{K} = \mathbb{K}(C)$$

for some function $\mathbb{K}$.

$$\boxed{\begin{aligned} \frac{dN}{dt} &= \mathbb{K}(C)N - \frac{FN}{V} \\ \frac{dc}{dt} &= -\alpha \mathbb{K}(C)N - \frac{FC}{V} + \frac{FC_0}{V} \end{aligned}}$$

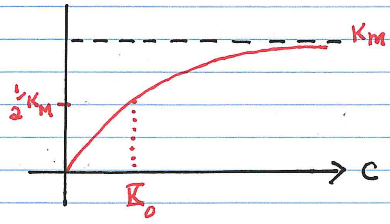
Two coupled nonlinear differential equations.

Michaelis Menten Kinetics

$$\boxed{\mathbb{K}(C) = \frac{K_M C}{\mathbb{K}_0 + C}}$$

Common assumed form. Derivation later

This reproduct rate has a saturation:



Graph of $\mathbb{K}(C)$. Saturates at maximal rate of $\mathbb{K}_M$.

Dimensional Analysis

Is a process by which dependent and independent variables are scaled by constants of like units in a manner which simplifies the model equations. Here

$$(1)\qquad n = \frac{N}{N^*} \qquad c = \frac{C}{C^*} \qquad \tau = \frac{t}{t^*}$$

Here N^*, C^* and t^* are constants having units of $[N]$, $[C]$, $[t]$. We get to chose these constants. And note that (n, c, τ) are now <u>dimensionless</u>!

Substitute (1) into the model equations:

$$\frac{d(nN^*)}{d(\tau t^*)} = \left(\frac{K_M C^* c}{K_0 + C^* c}\right)(nN^*) - \frac{F}{V}(nN^*)$$

$$\underbrace{\frac{dn}{d\tau}}_{\text{isolate}} \cdot \frac{N^*}{t^*} = \frac{K_M \; N^* \overset{\downarrow}{c}}{K_0/C^* + c} \cdot \overset{\downarrow}{n} - \left(\frac{FN^*}{V}\right)\overset{\downarrow}{n}$$

Ultimately for N-equation we get the dimensionless form

$$\frac{dn}{d\tau} = (K_M t^*)\frac{\overset{\downarrow}{c}\overset{\downarrow}{n}}{K_0/C^* + \underset{\uparrow}{c}} - \left(\frac{Ft^*}{V}\right)\overset{\downarrow}{n}$$

Non-arrowed terms are constants.

Pre-dimensionless scaled equations:

$$(2)\qquad \frac{dn}{d\tau} = (K_M t^*)\left(\frac{c}{\underset{\underset{\textcircled{2}}{\uparrow}}{K_0/C^*} + c}\right)n - \left(\frac{Ft^*}{\underset{\underset{\textcircled{1}}{\uparrow}}{V}}\right)n$$

$$(3)\qquad \frac{dc}{d\tau} = \left(\frac{\alpha t^* K_M N^*}{\underset{\underset{\textcircled{3}}{\uparrow}}{C^*}}\right)\left(\frac{c}{K_0/C^* + c}\right) - \left(\frac{Ft^*}{V}\right)c + \left(\frac{t^* F C_0}{V C^*}\right)$$

Pick t^* so term ① equals one

$$(4)\qquad t^* = \frac{V}{F}$$

Pick C^* so term ② equals one

$$(5)\qquad C^* = K_0$$

Pick N^* so term ③ equals one

$$(6)\qquad N^* = \frac{K_0}{\alpha t^* K_M}$$

With these choices (2)-(3) <u>greatly</u> simplify!

$$\boxed{\begin{aligned} \frac{dn}{d\tau} &= \alpha_1 \frac{nc}{1+c} - n \\ \frac{dc}{d\tau} &= -\frac{nc}{1+c} - c + \alpha_2 \end{aligned}}$$

Dimensionless Model

Has only two parameters

$$\alpha_1 = \frac{VK_M}{F}$$

$$\alpha_2 = \frac{C_0}{K_0}$$

Much better than original dimensional model

$$F, V, \alpha, C_0, K_M, K_0$$

six parameters!!

Planar Differential Systems

$$(1) \qquad \boxed{\begin{aligned} x' &= f(x,y) \\ y' &= g(x,y) \end{aligned}}$$

Some systems like (1) can be solved explicitly. For instance the linear system

$$(2) \qquad x' = -y$$

$$(3) \qquad y' = x$$

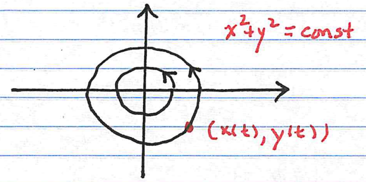
can be shown to have the general soln (Math 274)

$$(4) \qquad \vec{x}(t) = c_1 \begin{pmatrix} \sin t \\ -\cos t \end{pmatrix} + c_2 \begin{pmatrix} \cos t \\ \sin t \end{pmatrix}$$

Such explicit formulae are not always informative but do illustrate solutions (or trajectories) are curves in the (x,y)-plane. We often resort to "qualitate" techniques to get a better idea of what these trajectories look like. For (2)-(3) note:

$$\frac{d}{dt}(x^2+y^2) = 2xx' + 2yy' = -2xy + 2xy = 0$$

says its trajectories are circles

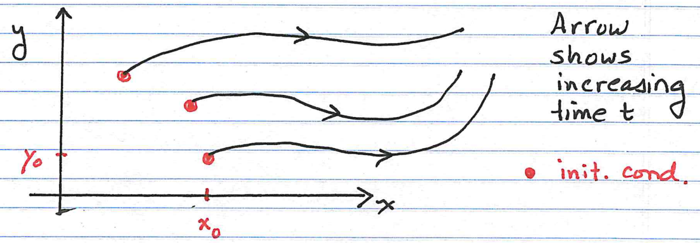


concentric circles for diff init cond.

Again lets recall our general planar problem

$$(1) \qquad \boxed{\begin{aligned} x' &= f(x,y) \\ y' &= g(x,y) \end{aligned}}$$

Each initial condition pair generates its own unique trajectory (or solution). Potentially it might look like



If we pose (1) as a vector equation we can say more

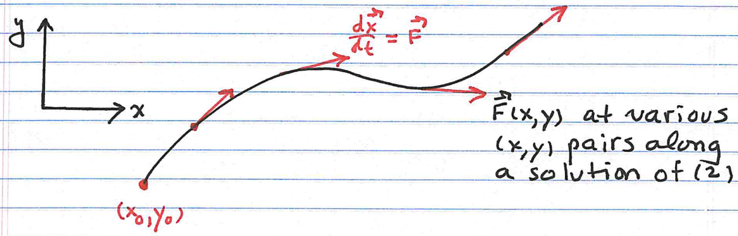
$$(2) \qquad \frac{d\vec{x}}{dt} = \vec{F}(x,y)$$

is equalent to

$$\frac{d}{dt}\begin{pmatrix} x(t) \\ y(t) \end{pmatrix} = \begin{pmatrix} f(x,y) \\ g(x,y) \end{pmatrix} = \vec{F}(x,y)$$

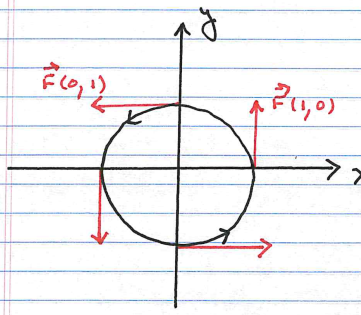
In (2), $\vec{F}(x,y)$ is a known vector field which can be drawn independent of knowing the solution $\vec{x}(t)$.

More importantly (2) states that solutions $\vec{x}(t)$ are everywhere tangent to the vector field $\vec{F}(x,y)$



EXAMPLE

$$x' = -y \qquad \vec{F}(x,y) = \begin{pmatrix} -y \\ x \end{pmatrix}$$
$$y' = +x$$



(x, y)	$\vec{F}(x,y)$	
(1, 0)	(0, 1)	↑
(0, 1)	(-1, 0)	←
(-1, 0)	(0, -1)	↓
(0, -1)	(1, 0)	→

$\vec{F}(x,y)$ is the direction field for the system

Equilibria and Nullclines

Recall the system

(1) $x' = f(x,y)$

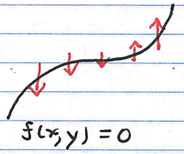
(2) $y' = g(x,y)$

Drawing $\vec{F}(x,y)$ can result in a cluttered mess in the (x,y) phase plane. Typically one uses only a limited selection of $\vec{F}(x,y)$ to infer the direction (or flow) of the solution.

For example, where is the flow horizontal? where is it vertical?

Consider $f(x,y)=0$ This is a curve(s) called the x-nullcline. For (x,y) on this curve

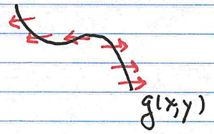
$$\vec{F} = \begin{pmatrix} 0 \\ g(x,y) \end{pmatrix}$$



and $\vec{F}$ is vertical.

Consider $g(x,y)=0$ This is a curve(s) called the y-nullcline. For (x,y) on this curve

$$\vec{F} = \begin{pmatrix} f(x,y) \\ 0 \end{pmatrix}$$



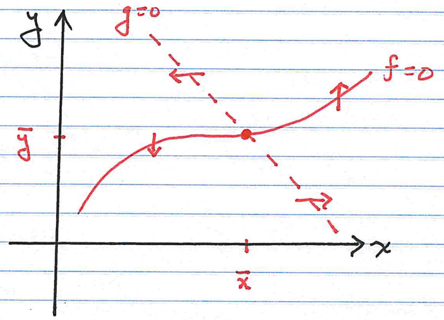
and $\vec{F}$ is horizontal

Lastly consider equilibria. At equilibria both f and g vanish.

We shall use overbar notation to denote these special points

(1) $$\boxed{\begin{aligned} f(\bar{x},\bar{y}) &= 0 \\ g(\bar{x},\bar{y}) &= 0 \end{aligned}}$$

Equilibria occur at the intersection of the x and y nullclines



To find equilibria you must find all solutions to the algebraic problem (1) above. Generally these are two nonlinear equations and may have no soln, one solution or many solutions.

Equilibria summary

Found by solving the coupled algebraic sys:

$$f(\bar{x},\bar{y})=0$$

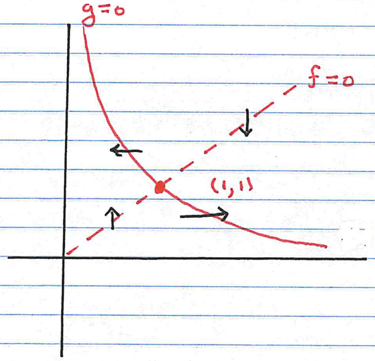
$$g(\bar{x},\bar{y})=0$$

They occur where nullclines intersect and if the initial condition is $(\bar{x},\bar{y})$ the solution is $x(t)=\bar{x}$, $y(t)=\bar{y}$ for all time t.

$$\boxed{\begin{array}{l} x'=f(x,y)\,,\ x(0)=\bar{x}\\ y'=g(x,y)\,,\ y(0)=\bar{y}\end{array}} \Rightarrow \begin{array}{l} x(t)=\bar{x}\\ y(t)=\bar{y}\end{array}$$

EXAMPLE

$$\boxed{\begin{array}{l} x'=x-y\\ y'=1-xy\end{array}}$$



x-nullcline

$$f=0 \Rightarrow y=x$$

y-nullcline

$$g=0 \Rightarrow y=\frac{1}{x}$$

Equilibria

$$x-y=0$$
$$1-xy=0$$

yields $x^2=1$ or $x=\pm 1$ hence

$$(1,1) \qquad (-1,-1)$$

Linear System Review – Planar

$$(1) \qquad \frac{d\vec{x}}{dt}=A\vec{x} \qquad \vec{x}=\begin{pmatrix} x(t)\\ y(t)\end{pmatrix}$$

Eigenvalues and eigenvectors of the matrix A determine the general solution of (1) Letting

$$(2) \qquad \vec{x}(t)=e^{\lambda t}\vec{\xi} \qquad \vec{\xi} \text{ const. vector}$$

we find (2) is a solution of (1) only if

$$(3) \qquad A\vec{\xi}=\lambda\vec{\xi}$$

Moreover, for $\vec{\xi}\neq 0$ we need $(A-\lambda I)$ not invertible, or, its determinant must vanish

$$(4) \qquad P(\lambda)=\det(A-\lambda I) \qquad I=\begin{bmatrix}1&0\\0&1\end{bmatrix}$$

For $A\in\mathbb{R}^{2\times 2}$ this characteristic polynomial is a quadratic with two roots called eigenvalues. The vectors $\vec{\xi}$ in (3) are not unique and are called eigenvectors

Summary

$$\vec{x}(t)=e^{\lambda t}\vec{\xi}$$

$$\det(A-\lambda I)=0$$

$$A\vec{\xi}=\lambda\vec{\xi}$$

Real Distinct eigenvalues $\lambda_1 \neq \lambda_2 \in \mathbb{R}$

The general solution of (1) is

$$\vec{x} = c_1 e^{\lambda_1 t}\underset{\uparrow}{\vec{\xi}_1} + c_2 e^{\lambda_2 t}\underset{\uparrow}{\vec{\xi}_2}$$

eigenvectors for λ_1, λ_2

EXAMPLE

$$\frac{d\vec{x}}{dt} = \begin{bmatrix} 6 & -3 \\ 2 & 1 \end{bmatrix}\vec{x} = A\vec{x}$$

$$P(\lambda) = \det(A - \lambda I) = (\lambda - 3)(\lambda - 4)$$

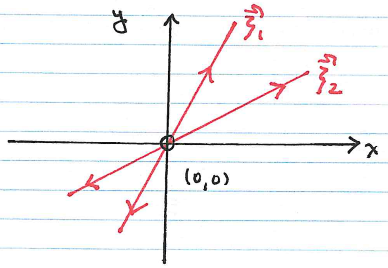
after some calculations.

$\lambda_1 = 3$ $\quad (A - \lambda_1 I)\vec{\xi} = \begin{bmatrix} 3 & -3 \\ 2 & -2 \end{bmatrix}\vec{\xi} = \vec{0} \quad \vec{\xi}_1 = \begin{pmatrix} 1 \\ 1 \end{pmatrix}$

$\lambda_2 = 4$ $\quad (A - \lambda_2 I)\vec{\xi} = \begin{bmatrix} 2 & -3 \\ * & * \end{bmatrix}\vec{\xi} = \vec{0} \quad \vec{\xi}_2 = \begin{pmatrix} 3 \\ 2 \end{pmatrix}$

General solution

$$\vec{x}(t) = c_1 e^{3t}\begin{pmatrix} 1 \\ 1 \end{pmatrix} + c_2 e^{4t}\begin{pmatrix} 3 \\ 2 \end{pmatrix} \qquad \text{grows.}$$



Unstable Node

EXAMPLE (Saddle) $\lambda_2 < 0 < \lambda_1$

$$\frac{d\vec{x}}{dt} = \begin{bmatrix} 0 & 1 \\ 1 & 0 \end{bmatrix}\vec{x} = A\vec{x}$$

Here the characteristic polynomial is

$$P(\lambda) = \lambda^2 - 1 \qquad \lambda = \pm 1$$

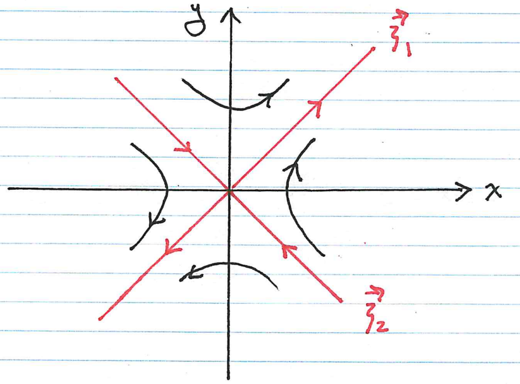
It is easily verified we have eigenvectors:

$\lambda_1 = +1$ $\quad (A - \lambda_1 I)\vec{\xi} = \begin{bmatrix} -1 & 1 \\ * & * \end{bmatrix}\vec{\xi} \quad \vec{\xi}_1 = \begin{pmatrix} 1 \\ 1 \end{pmatrix}$

$\lambda_2 = -1$ $\quad (A - \lambda_2 I)\vec{\xi} = \begin{bmatrix} 1 & 1 \\ * & * \end{bmatrix}\vec{\xi} \quad \vec{\xi}_2 = \begin{pmatrix} 1 \\ -1 \end{pmatrix}$

General Solution

$$\vec{x}(t) = c_1 \overbrace{e^{\lambda_1 t}}^{\text{grows}}\vec{\xi}_1 + c_2 \overbrace{e^{\lambda_2 t}}^{\text{decays}}\vec{\xi}_2$$



Complex eigenvalues $\lambda = \alpha + i\beta \in \mathbb{C}$

Eigenvalues and eigenvectors are both complex. The complex solution is

$$\vec{x}(t) = e^{\lambda t}\vec{\xi} = \vec{x}_r(t) + i\,\vec{x}_i(t)$$

Each of the real and imaginary parts of $\vec{x}$ are independent solutions to

$$\frac{d\vec{x}}{dt} = A\vec{x}$$

After computing $\vec{\xi} = \vec{a} + i\vec{b}$ and expanding

$$\vec{x} = e^{(\alpha+i\beta)t}(\vec{a} + i\vec{b})$$

and using $e^{i\beta t} = \cos\beta t + i\sin\beta t$, two real independent solutions are

$$\vec{x}_1(t) = e^{\alpha t}(\cos\beta t\,\vec{a} - \sin\beta t\,\vec{b})$$

$$\vec{x}_2(t) = e^{\alpha t}(\sin\beta t\,\vec{a} + \cos\beta t\,\vec{b})$$

Note even though solns always oscillate

$\alpha > 0$	$\vec{x}_K$ grow
$\alpha < 0$	$\vec{x}_K \to 0$
$\alpha = 0$	$\vec{x}_K$ periodic

Here β is the frequency.

EXAMPLE Simple Purely imaginary case $\lambda = i\beta$

$$\vec{x}\,' = A\vec{x} = \begin{bmatrix} 0 & -8 \\ 2 & 0 \end{bmatrix}\vec{x}$$

Characteristic Polynomial

$$P(\lambda) = \lambda^2 + 16 \qquad \lambda = 4i$$

Eigenvector

$$(A - \lambda I) = \begin{bmatrix} -4i & -8 \\ 2 & -4i \end{bmatrix} \qquad \vec{\xi} = \begin{pmatrix} 2i \\ 1 \end{pmatrix}$$

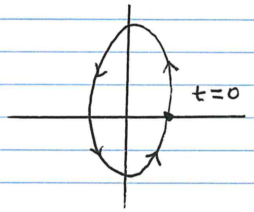
General solution

$$\vec{x}(t) = c_1\begin{pmatrix} -2\sin 4t \\ \cos 4t \end{pmatrix} + c_2\underbrace{\begin{pmatrix} 2\cos 4t \\ \sin(4t) \end{pmatrix}}_{\vec{x}_2(t)}$$

To see what these trajectories, look at $\vec{x}_2(t)$

$$\vec{x}_2 = \begin{pmatrix} x(t) \\ y(t) \end{pmatrix} = \begin{pmatrix} 2\cos 4t \\ \sin 4t \end{pmatrix} \Rightarrow \left(\frac{x}{2}\right)^2 + y^2 = 1$$

is on ellipse



EXAMPLE Complex = Spiral

$$\frac{d\vec{x}}{dt} = \begin{bmatrix} 1 & 1 \\ -1 & 1 \end{bmatrix} \vec{x} = A\vec{x}$$

Characteristic Polynomial

$$P(\lambda) = \lambda^2 - 2\lambda + 2 = 0 \Rightarrow \lambda = \overset{\alpha + i\beta}{1 + i}$$

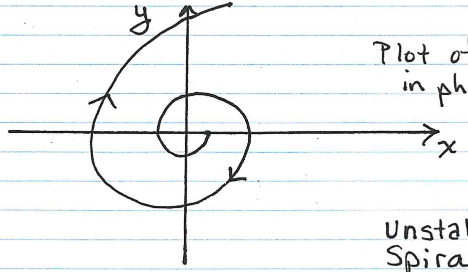
with associated eigenvector

$$\vec{\xi} = \begin{pmatrix} 1 \\ i \end{pmatrix} = \begin{pmatrix} 1 \\ 0 \end{pmatrix} + i \begin{pmatrix} 0 \\ 1 \end{pmatrix} = \vec{a} + i\vec{b}$$

Ultimately $\vec{x} = e^t(\cos t + i \sin t)(\vec{a} + i\vec{b})$ yields the general solution

$$\vec{x}(t) = c_1 \vec{x}_1(t) + c_2 \vec{x}_2(t) = c_1 \underbrace{\begin{pmatrix} e^t \cos t \\ -e^t \sin t \end{pmatrix}}_{\vec{x}_1(t)} + c_2 \underbrace{\begin{pmatrix} e^t \sin t \\ e^t \cos t \end{pmatrix}}_{\vec{x}_2(t)}$$

Notice $\|\vec{x}_1(t)\| = e^t$ so $\vec{x}_1(t) \to \infty$ as $t \to \infty$ but it does so by spiraling outward. Same with $\vec{x}_2$



Plot of $\vec{x}_1(t)$ in phase plane.

Unstable Spiral

EXAMPLE Purely Imaginary $\lambda = i\beta$

$$\vec{x}' = A\vec{x} \qquad A = \begin{bmatrix} -2 & -4 \\ 10 & 2 \end{bmatrix}$$

Characteristic Polynomial (after calculations)

$$P(\lambda) = \lambda^2 + 36 = 0 \qquad \lambda = 6i \qquad (\alpha = 0)$$

Eigenvector

$$(A - \lambda I) = \begin{bmatrix} -2-6i & -4 \\ * & * \end{bmatrix} \qquad \vec{\xi} = \begin{pmatrix} 2 \\ -1-3i \end{pmatrix}$$

General solution

$$\vec{x}(t) = c_1 \underbrace{\begin{pmatrix} 2\cos 6t \\ -\cos 6t + 3\sin 6t \end{pmatrix}}_{\vec{x}_1(t)} + c_2 \begin{pmatrix} 2\sin 6t \\ -\sin 6t - 3\cos 6t \end{pmatrix}$$

Are ellipses with different axes. From $\vec{x}_1(t)$

$$\left(\frac{x}{2}\right)^2 + \left(\frac{x}{6} + \frac{y}{3}\right)^2 = 1$$

$$\cos^2 + \sin^2 = 1$$

Has axes:

$$x = 0 \qquad x + 2y = 0$$

Linearization about equilibria

A useful tool in the study of ODE models is the process of linearization. Typically one wants to know if some given equilibria is stable or not.

Let $(\bar{x}, \bar{y})$ be an equilibria of

$$(1) \qquad \dot{x} = f(x,y)$$

$$(2) \qquad \dot{y} = g(x,y)$$

Then

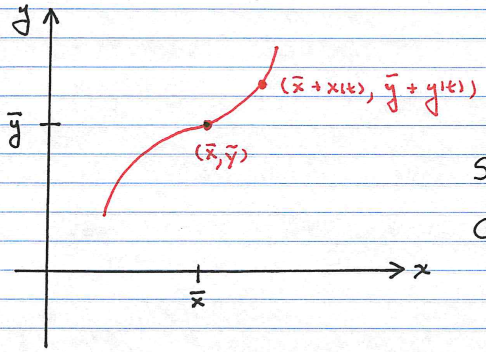
$$(3) \qquad f(\bar{x}, \bar{y}) = 0$$

$$(4) \qquad g(\bar{x}, \bar{y}) = 0$$

Let $(X(t), Y(t))$ be solution trajectories near the equilibria

$$(5) \qquad X(t) = \bar{x} + x(t)$$

$$(6) \qquad Y(t) = \bar{y} + y(t)$$



Small x, y

Close to $(\bar{x}, \bar{y})$!

Start with

$$(1) \qquad X' = f(X, Y)$$

$$(2) \qquad Y' = g(X, Y)$$

where

$$X(t) = \bar{x} + x(t)$$
$$Y(t) = \bar{y} + y(t)$$

Then since $(\bar{x}, \bar{y})$ are constant

$$(3) \qquad x' = f(\bar{x}+x, \bar{y}+y)$$

$$(4) \qquad y' = g(\bar{x}+x, \bar{y}+y)$$

A Taylor series (linear approx) of (3)-(4) is:

$$x' = \cancelto{0}{f(\bar{x},\bar{y})} + f_x(\bar{x},\bar{y})\,x + f_y(\bar{x},\bar{y})\,y + \text{smaller}$$

$$y' = \cancelto{0}{g(\bar{x},\bar{y})} + g_x(\bar{x},\bar{y})\,x + g_y(\bar{x},\bar{y})\,y + \text{smaller}$$

Noting first terms vanish since $(\bar{x}, \bar{y})$ an equilibria and neglecting the smaller terms yields the linearized system:

$$\begin{pmatrix} x \\ y \end{pmatrix}' = \underbrace{\begin{bmatrix} f_x(\bar{x},\bar{y}) & f_y(\bar{x},\bar{y}) \\ g_x(\bar{x},\bar{y}) & g_y(\bar{x},\bar{y}) \end{bmatrix}}_{\text{called the Jacobian matrix } DF(\bar{x},\bar{y})} \begin{pmatrix} x \\ y \end{pmatrix}$$

Summary of Linearization

$$\begin{aligned} X' &= f(X, Y) \\ Y' &= g(X, Y) \end{aligned}$$ original system

Find equilibria

$$\begin{aligned} 0 &= f(\bar{x}, \bar{y}) \\ 0 &= g(\bar{x}, \bar{y}) \end{aligned}$$ equilibria eqns

There may be more than one equilibria satisfying the two eqns above.

$$\begin{aligned} X(t) &= \bar{x} + x(t) \\ Y(t) &= \bar{y} + y(t) \end{aligned}$$

Linearized system in vector form $\vec{x} = (x, y)$

(1) $$\frac{d\vec{x}}{dt} = A\vec{x}$$ $A = D\vec{F}(\bar{x}, \bar{y})$ Jacobian

where the Jacobian

$$A = D\vec{F}(\bar{x}, \bar{y}) = \begin{bmatrix} f_x(\bar{x}, \bar{y}) & f_y(\bar{x}, \bar{y}) \\ g_x(\bar{x}, \bar{y}) & g_y(\bar{x}, \bar{y}) \end{bmatrix}$$

Given how $\vec{x}(t)$ is defined, the system (1) describes the flow/solution only near the equilibria.

Application to linearized system (example)

$$\begin{aligned} x' &= f(x, y) = (x-1)y \\ y' &= g(x, y) = xy - x \end{aligned}$$

Can easily verify the system has two equilibria

$P_0 = (0, 0)$ $P_1 = (1, 1)$

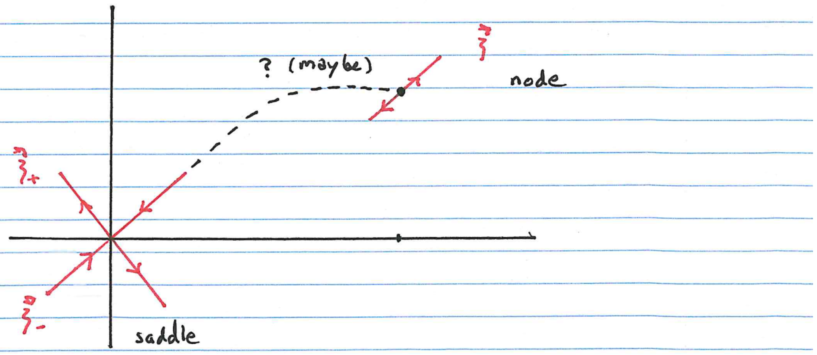
Jacobian at (x, y)

$$DF(x, y) = \begin{bmatrix} y & (x-1) \\ y-1 & x \end{bmatrix} = \begin{bmatrix} f_x & f_y \\ g_x & g_y \end{bmatrix}$$

Jacobian at P_0, P_1 and e-vals:

$$A_0 = DF(P_0) = \begin{bmatrix} 0 & -1 \\ -1 & 0 \end{bmatrix}$$ $\lambda_{\pm} = \pm 1$ saddle

$$A_1 = DF(P_1) = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$ $\lambda = 1$ repeated unstable node



Classification of equilibria

$$\vec{x}\,' = A\vec{x} = \begin{bmatrix} a & b \\ c & d \end{bmatrix} \vec{x} \qquad (1)$$

After some calculations the characteristic polynomial is found

$$P(\lambda) = \det(A - \lambda I)$$

$$P(\lambda) = \lambda^2 - (a+d)\lambda + (ad-bc)$$

or in terms of the trace TrA and determinant of the matrix

$$(2) \qquad \boxed{P(\lambda) = \lambda^2 - \mathrm{Tr}A\,\lambda + \det A}$$

where

$$\mathrm{Tr}A = a + d$$

$$\det A = ad - bc$$

The stability of (1) will then be determined by the sign of the real part of the eigenvalues

$$(3) \qquad \boxed{\lambda_\pm = \frac{1}{2}\left(\mathrm{Tr}A \pm \sqrt{\mathrm{Tr}A^2 - 4\det A}\right)}$$

Again, whether $\lambda_\pm$ are real or complex the real part alone determines stability.
To a large extent the sign of $\mathrm{Tr}A^2 - 4\det A$ matters

Case : $\det A < 0$

$\lambda_- < 0 < \lambda_+$ unstable saddle

Case : $\det A > 0$, $\mathrm{Tr}A^2 - 4\det A > 0$

$\mathrm{Tr}A > 0$ $\lambda_+ > \lambda_- > 0$ unstable node

$\mathrm{Tr}A < 0$ $\lambda_- < \lambda_+ < 0$ stable node

Case : $\det A > 0$, $\mathrm{Tr}A^2 - 4\det A < 0$

$\lambda = \alpha \pm i\beta$ complex $\beta = \frac{1}{2}\sqrt{4\det A - \mathrm{Tr}A^2}$

$\mathrm{Tr}A > 0$ unstable spiral

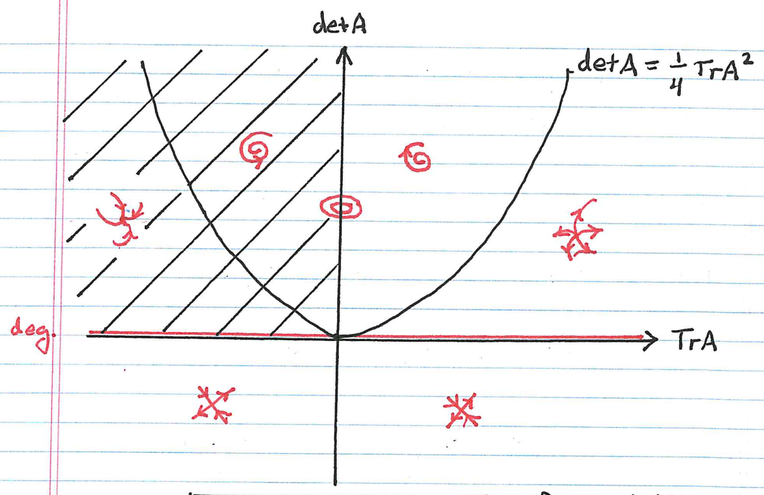
$\mathrm{Tr}A < 0$ stable spiral

Case : $\det A > 0$, $\mathrm{Tr}A = 0$

$\lambda = i\beta$ center

Case : $\det A = 0$

degenerate line of equilibria



$\boxed{\text{Tr}A<0,\ \det A>0}$ for stability. Otherwise $\vec{x}=0$ is unstable.

Applications to nonlinear systems $\vec{x}' = \vec{f}(x,y)$

If we get a linearized system

$$\frac{d\vec{x}}{dt} = A\vec{x} \qquad A = D\vec{F}(\bar{x},\bar{y})$$

where one of the following is true

$$\text{Tr}A = 0 \qquad \det A = 0$$

we can't conclude anything. Such points are "nonhyperbolic" and the linearized system doesn't necessarily well approximate the true system. We exclude all this theory.

Classification using Tr A, det A

Ex $\vec{x}' = A\vec{x}$ $\qquad A = \begin{bmatrix} 1 & 1 \\ 3 & -1 \end{bmatrix}$

$\det A = -4$

$\text{Tr}\,A = 0$

$\det A < 0 \Rightarrow \vec{x}=0$ saddle

Ex $\vec{x}' = A\vec{x}$ $\qquad A = \begin{bmatrix} 3 & -1 \\ -1 & 3 \end{bmatrix}$

$\det A = 8 > 0$

$\text{Tr}\,A = 6$

$\det A - \frac{1}{4}\text{Tr}A^2 = -1 < 0 \Rightarrow$ unstable node

Ex $\vec{x}' = A\vec{x}$ $\qquad A = \begin{bmatrix} 4 & -4 \\ 20 & -4 \end{bmatrix}$

$\det A = 64 > 0$

$\text{Tr}A = 0$

Hence $\vec{x}=0$ a center.

Ex $A = \begin{bmatrix} -13 & -27 \\ -9 & -31 \end{bmatrix}$

$$\left.\begin{aligned} \det A &= 160 > 0 \\ \operatorname{Tr} A &= -44 \\ \det A - \tfrac{1}{4}\operatorname{Tr} A^2 &= -324 \end{aligned}\right\}$$ $\vec{x} = 0$ stable node

Ex $A = \begin{bmatrix} 4 & -6 \\ 2 & -3 \end{bmatrix}$

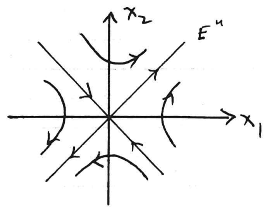
$$\left.\begin{aligned} \det A &= 0 \\ \operatorname{Tr} A &= 1 \end{aligned}\right\}$$ degenerate line of fixed points

Ex $A = \begin{bmatrix} 1 & -2 \\ 3 & -2 \end{bmatrix}$

$$\left.\begin{aligned} \det A &= 4 > 0 \\ \operatorname{Tr} A &= -1 \\ \det A - \tfrac{1}{4}\operatorname{Tr} A^2 &> 0 \end{aligned}\right\}$$ Stable Spiral.

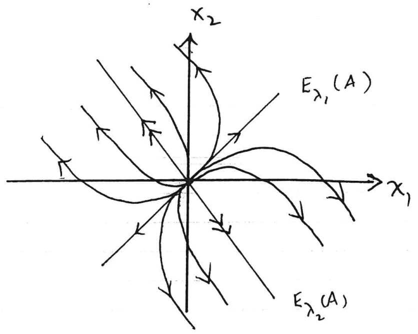
Classification Examples

EX **SADDLE** $A = \begin{bmatrix} 1 & 1 \\ 3 & -1 \end{bmatrix}$ $\lambda_{\pm} = \pm 2$, $\underset{E^u}{\xi_+ = \begin{pmatrix} 1 \\ 1 \end{pmatrix}}$ $\underset{E^s}{\xi_- = \begin{pmatrix} 1 \\ -3 \end{pmatrix}}$



EX **UNSTABLE NODE** $A = \begin{bmatrix} 3 & -1 \\ -1 & 3 \end{bmatrix}$ $\lambda_1 = 2$ $\lambda_2 = 4$

$\xi_1 = \begin{pmatrix} 1 \\ 1 \end{pmatrix}$ $\xi_2 = \begin{pmatrix} 1 \\ -1 \end{pmatrix}$



$$x(t) = c_1 e^{2t} \vec{\xi}_1 + c_2 e^{4t} \vec{\xi}_2$$

$$x(t) \sim c_2 e^{4t} \vec{\xi}_2 \quad \text{as } t \to \infty$$

EX Center $A = \begin{bmatrix} 4 & -4 \\ 20 & -4 \end{bmatrix}$ $\lambda = \pm 2i$; $T = \frac{2\pi}{\omega} = \pi$ period.

$$\xi = \begin{pmatrix} 2 \\ 2-i \end{pmatrix} = \begin{pmatrix} 2 \\ 2 \end{pmatrix} + i \begin{pmatrix} 0 \\ -1 \end{pmatrix}$$

$$\xi = \xi_R + i\,\xi_I .$$

$$x(t) = c_1 u(t) + c_2 v(t)$$

$u(t) = \cos 2t\, \xi_R - \sin 2t\, \xi_I$ $u(0) = \xi_R$ u

$v(t) = \sin 2t\, \xi_R + \cos 2t\, \xi_I$ $v(0) = \xi_I$

Suppose I.C. chosen so that $x(0) = c_1 u(0) = x_0$ with $c_1 = 1$

$x(t) = u(t)$

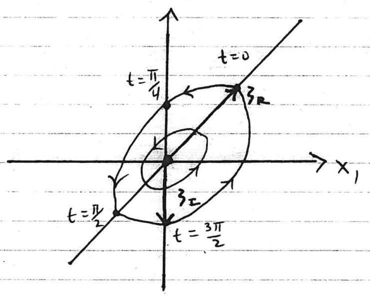
$u(0) = \xi_R$

$u(\pi/4) = -\xi_I$

$u(\frac{\pi}{2}) = -\xi_R$

$u(\frac{3\pi}{4}) = +\xi_I$

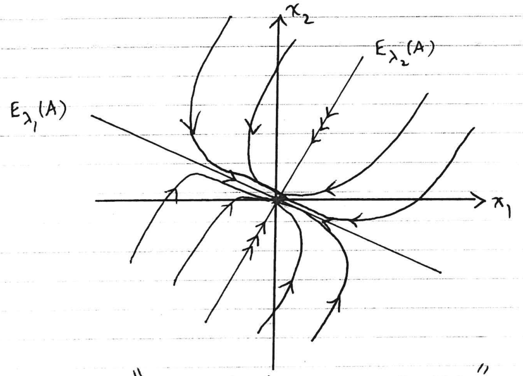
$u(\pi) = \xi_R$



Neutral Stable.

EX STABLE NODE $A = \begin{bmatrix} -13 & -27 \\ -9 & -31 \end{bmatrix}$ $\lambda_1 = -4$ $\xi_1 = (-3, 1)^T$

$\lambda_2 = -40$ $\xi_2 = (1, 1)^T$



$$x(t) = c_1 e^{-4t} \vec{\xi}_1 + c_2 e^{-40t} \vec{\xi}_2$$

E

$E^s(0) = \mathbb{R}^2$

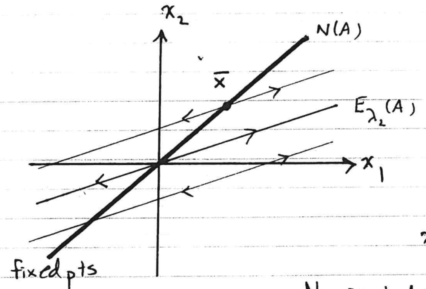
$E^u(0) = \{0\}$

" squashed onto $E_{\lambda_1}(A)$ "

EX DEGENERATE (LINE OF FIXED) $A = \begin{bmatrix} 4 & -6 \\ 2 & -3 \end{bmatrix}$

$\lambda_1 = 0$ $\xi_1 = \begin{pmatrix} 3/2 \\ 1 \end{pmatrix}$

$\lambda_2 = 1$ $\xi_2 = \begin{pmatrix} 2 \\ 1 \end{pmatrix}$



$$x(t) = c_1 \vec{\xi}_1 + c_2 e^t \vec{\xi}_2$$

Non isolated, Neutral stability.

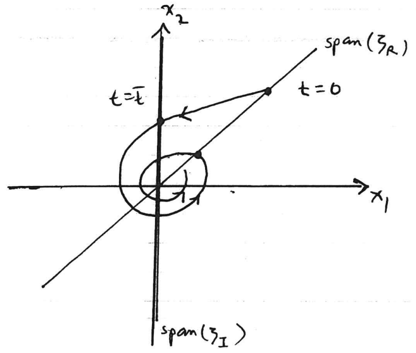
$E^s(\bar{x}) = \{\bar{x}\}$. However, for $\bar{x} = (\bar{x}_1, \bar{x}_2)$

$$E^u(\bar{x}) = \{ (x_1, x_2) : \; x_2 - \bar{x}_2 = \tfrac{1}{2}(x_1 - \bar{x}_1) \}$$

is a straight line. $E^s(\bar{x}) \cup E^u(\bar{x}) \neq \mathbb{R}^2$ in This case

EX STABLE SPIRAL

$$A = \begin{bmatrix} 1 & -2 \\ 3 & -2 \end{bmatrix}$$



$$\lambda_{\pm} = -\frac{1}{2} \pm \frac{\sqrt{15}}{2} i$$

$$\xi = \begin{pmatrix} 4 \\ 3 \end{pmatrix} + i \begin{pmatrix} 0 \\ -\sqrt{15} \end{pmatrix} = \vec{\xi}_R + i \vec{\xi}_i$$

$$\omega = \frac{\sqrt{15}}{2}$$; NOT PERIODIC.

Choose I.C. so that

$$x(t) = u(t) = e^{-\frac{1}{2}t} \left(\cos \omega t \, \vec{\xi}_R - \sin \omega t \, \vec{\xi}_I \right)$$

Then, when $t = \bar{t} = \frac{\pi}{2\omega}$, $x(\bar{t}) = -e^{-\frac{1}{2}\bar{t}} \vec{\xi}_I$

EXAMPLE

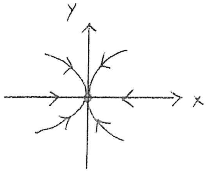
$\dot{x} = ax$
$\dot{y} = -y$

$(\bar{x}, \bar{y}) = (0, 0)$ sole fx pt. if $a \neq 0$.

Solution for $x(0) = x_0$, $y(0) = y_0$ is

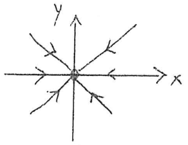
$$x(t) = x_0 e^{at} \qquad y(t) = y_0 e^{-t}$$

$a < -1$



isolated, a.s. NODE

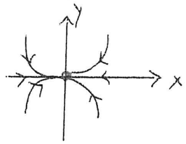
$a = -1$



$\frac{y(t)}{x(t)} = K = \frac{y_0}{x_0}$, $\forall t \in \mathbb{R}$
so long as $x(t) \neq 0$.
isolated, a.s.

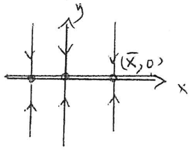
NODE (Star)

$a \in (-1, 0)$



isolated, a.s. NODE

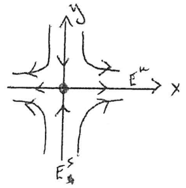
$a = 0$



non isolated. $y = 0$, $x \in \mathbb{R}$ line of fixed pts.

NOT ATTRACTING, IS LIAPUNOV ⇒ Neutral.

$a > 0$



UNSTABLE. SADDLE

(Stable and unstable manifolds)

Chemostat Model Analysis

$$\boxed{\begin{aligned} \frac{dn}{d\tau} &= \alpha_1 \frac{nc}{1+c} - n &&= f(n,c) \\ \frac{dc}{d\tau} &= - \frac{nc}{1+c} - c + \alpha_2 &&= g(n,c) \end{aligned}}$$

where

n = bacterial concentration

c = chemical/nutrient concentration

We aim to prove that when a positive (physical) equilibrium exists the extinction state with $n=0$ is unstable.

- find the equilibria
- determine for what (α_1, α_2) parameter pairs the equilibria are positive/physical.
- Compute the Jacobian
- Use the TrA/detA classification to determine when each equilibria is stable.

Find the equilibria

(1) $$f(n,c) = n\left(\alpha_1 \frac{c}{c+1} - 1\right) = 0$$

(2) $$g(n,c) = -\frac{nc}{c+1} - c + \alpha_2 = 0$$

Extinction state

If $n=0$ in (1)-(2) then $c = \alpha_2$

$$P_0 = (\bar{n}_0, \bar{c}_0) = (0, \alpha_2)$$

is always phsical if $\alpha_2 > 0$.

Coexistence state

Here we assume $n \neq 0$. Then (1) above $\Rightarrow$

(3) $$\alpha_1 \frac{c}{c+1} - 1 = 0$$

Solve this for c

(4) $$c = \frac{1}{\alpha_1 - 1}$$

Substitute (4) into ( ) and solve for n. The algebra is simpler than one might think since (3) implies

$$\frac{c}{c+1} = \frac{1}{\alpha_1}$$

Then $g(n,c) = 0$ becomes

(5) $$-n\left(\frac{1}{\alpha_1}\right) - \frac{1}{\alpha_1 - 1} + \alpha_2 = 0$$

Solve this to get

$$P_1 = (\bar{n}_1, \bar{c}_1) = \left(\alpha_1\left(\alpha_2 - \frac{1}{\alpha_1 - 1}\right), \frac{1}{\alpha_1 - 1}\right)$$

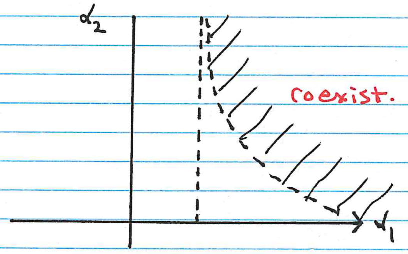
For $\bar{n}_1$ and $\bar{c}_1$ to be positive need $\alpha_1 > 1$ and $\alpha_2 > (\alpha_1 - 1)^{-1}$.

Summary

$P_0 = (0, \alpha_2)$ extinction state always exists

$P_1 = \left(\alpha_1\left(\alpha_2 - \frac{1}{\alpha_1 - 1}\right), \frac{1}{\alpha_1 - 1}\right)$ coexistence only if

$$\boxed{\begin{array}{l} \alpha_1 > 1 \\ \alpha_2 > \dfrac{1}{\alpha_1 - 1} \end{array}}$$



Jacobian (general)

$$\frac{dn}{d\tau} = f(n,c) = \alpha_1 \frac{nc}{1+c} - n$$

$$\frac{dc}{d\tau} = g(n,c) = -\frac{nc}{1+c} - c + \alpha_2$$

Recall Jacobian is

$$D\vec{F} = \begin{bmatrix} \frac{\partial f}{\partial n} & \frac{\partial f}{\partial c} \\ \frac{\partial g}{\partial n} & \frac{\partial g}{\partial c} \end{bmatrix}$$

Explicitly this is a bit of a mess

$$D\vec{F}(n,c) \equiv \begin{bmatrix} \alpha_1 c/(1+c) - 1 & \alpha_1 n/(1+c)^2 \\ -c/(1+c) & -n/(1+c)^2 - 1 \end{bmatrix}$$

Jacobian at P_1 coexistence

To simplify calculations define

$$A = \frac{\bar{n}_1}{(1+\bar{c}_1)^2}$$

After some calculations

$$D\vec{F}(P_1) = \begin{bmatrix} 0 & \alpha_1 A \\ -1/\alpha_1 & -(A+1) \end{bmatrix}$$

Despite the complexity of P_1 we get some simple results

$$\mathrm{Tr}\, D\vec{F} = -(A+1) \qquad < 0 \text{ for stability}$$

$$\det D\vec{F} = A \qquad > 0 \text{ for stability}$$

Then we have

$$\bar{n}_1 > 0 \Leftrightarrow A > 0 \Rightarrow P_1 \text{ stable}$$

In plain language

$$\boxed{P_1 \text{ stable} \Leftrightarrow P_1 \text{ physical}}$$

Jacobian at P_0 extinction

To simplify calculations

$$B = \frac{\alpha_2}{1+\alpha_2} > 0$$

After calculations

$$D\vec{F}(P_0) = \begin{bmatrix} \alpha_1 B - 1 & 0 \\ -B & -1 \end{bmatrix}$$

from which P_0 is stable only if

$$\operatorname{Tr} D\vec{F} = \alpha_1 B - 2 < 0$$

$$\det D\vec{F} = -(\alpha_1 B - 1) > 0$$

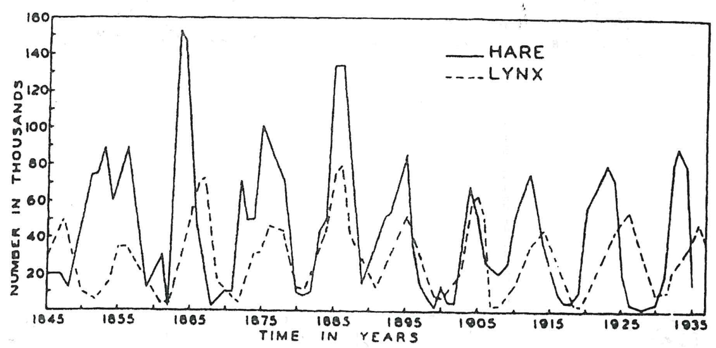
These two inequalities define a region in (α_1, α_2)-plane where P_0 stable. $\Big\}$ part of HW

Can be used to show

P_0 stable only when P_1 not

or that no positive equilibria ⇒ extinction.

Predator Prey (Lotka Volterra) model



Model Equations

$$(1) \quad x' = ax - bxy$$

$$(2) \quad y' = -cy + dxy$$

Here

x = prey $[x] = \#$

y = predators $[y] = \#$

and predation terms proportional to xy

xy = number of possible interactions

Considerations: $b=0, d=0$ in model. Predators die out!

Model analysis

System has two equilibria

$$P_1\,(0,0) \qquad P_2\left(\frac{c}{d}, \frac{a}{b}\right)$$

Jacobian

$$D\vec{F}(P) = \begin{bmatrix} a-by & -bx \\ dy & dx-c \end{bmatrix}$$

Hence

$$D\vec{F}(P_1) = \begin{bmatrix} a & 0 \\ 0 & -c \end{bmatrix} \qquad \det < 0 \qquad \text{saddle}$$

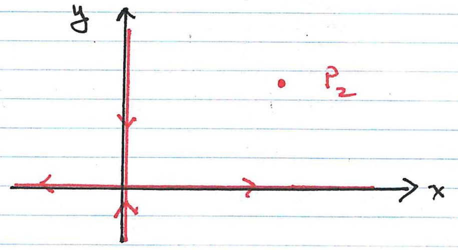
$$D\vec{F}(P_2) = \begin{bmatrix} 0 & -bc/d \\ ad/b & 0 \end{bmatrix} \qquad \begin{matrix} \det > 0 \\ Tr = 0 \end{matrix} \qquad \text{center}$$

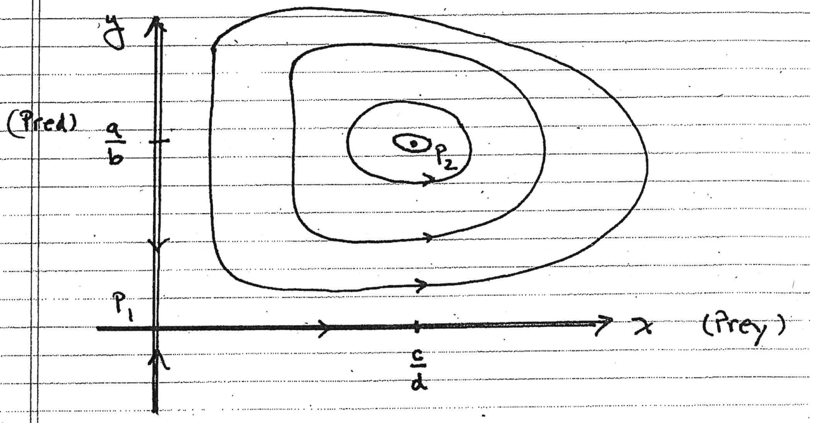
For the saddle

$$\lambda_1 = a > 0 \qquad \vec{\xi}_1 = \begin{pmatrix} 1 \\ 0 \end{pmatrix} \qquad \text{unstable}$$

$$\lambda_2 = -c < 0 \qquad \vec{\xi}_2 = \begin{pmatrix} 0 \\ 1 \end{pmatrix} \qquad \text{stable}$$

In fact $x=0$ and $y=0$ are "invariant".





Neutrally stable concentric periodic ordits

Matlab code for contours of $\phi(x,y)$

```
%
% phase portrait of predator prey system
% as contourplots of phi(x,y)
%
x=linspace(0,3);
y=linspace(0,3);
[X,Y]=meshgrid(x,y);
%
a=1;
b=2;
c=1;
d=1;
phi=-c*log(X)-a*log(Y)+d*X+b*Y;
contour(X,Y,phi)
```

Since $\mathrm{Tr}\,DF(P_2)=0$ it is not "hyperbolic" and linear theory may fail. Here linear theory predicts a center behavior near P_2. The validity of this remains to be shown:

First Integral

A function $\phi(x,y)$ is said to be a first integral if it is constant on trajectories.

A very lucky guess:

(3) $\phi(x,y) \equiv -c\ln x - a\ln y + dx + by$

For the model (1)-(2) and some calculations

$$\frac{d\phi}{dt} = -\frac{c}{x}x' - \frac{a}{y}y' + dx' + by'$$

$$\frac{d\phi}{dt} = -\frac{c}{x}(ax-bxy) - \frac{a}{y}(-cy+dxy) + d(ax-bxy)+b(-cy+dx$$

$$\frac{d\phi}{dt} = 0$$

Thus, level sets of ϕ are trajectories of (1)-(2)

Need software to compute these level sets.

Predator Prey with density dependence

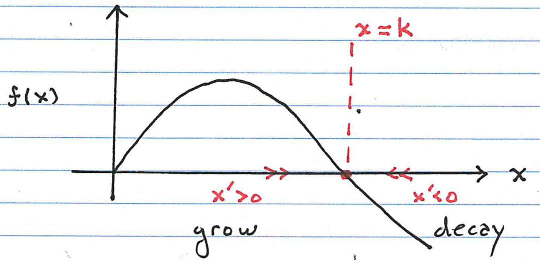
Prey are often more numerous than predators. Hence, they are more subject to density growth rate effects. Predators are not. We examine such effects through a minor change in the previous model.

Model Equations (Logistic Growth Rate)

$$\boxed{\begin{array}{lll} (1) & x' = ax\left(1-\frac{x}{K}\right) - bxy & \text{prey} \\ (2) & y' = -cy + dxy & \text{pred.} \end{array}}$$

In the absense of predation $(y=0)$

$$x' = ax\left(1-\frac{x}{K}\right) = f(x)$$



Then $x(t) \to k$ called carrying capacity

Equilibria

$$0 = ax\left(1-\overset{\downarrow}{\frac{x}{K}}\right) - bxy$$
$$0 = -cy + dxy$$

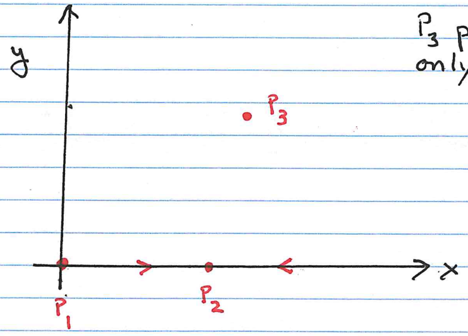
has three solutions (after calculations)

$P_1(0,0)$	both extinct
$P_2(k,0)$	only pred. extinct
$P_3\left(\frac{c}{d}, \frac{a\Delta}{bkd}\right)$	coexistence

where

$$\boxed{\Delta = kd - c}$$

must be positive for a physical coexist P_3



P_3 physical only if $\Delta > 0$

Given P_3 the coexistence value of predators:

$$\text{pred. with density} = \left(\frac{\Delta}{kd}\right) \times \text{pred. no density.}$$

where $\frac{\Delta}{kd} = 1 - \frac{c}{kd} > 0$ smaller!!

```
> restart;
> with(linalg):
> f:=a*x*(1-x/k)-b*x*y:
> g:=-c*y+d*x*y:
```

```
> P:=solve({f=0,g=0},{x,y});
```

$$P := \{x=0, y=0\}, \{x=k, y=0\}, \left\{x=\frac{c}{d}, y=-\frac{a\,(-k\,d+c)}{b\,k\,d}\right\} \tag{1}$$

```
> DF:=map(simplify,jacobian([f,g],[x,y]));
```

$$DF := \begin{bmatrix} \frac{a\,k-2\,a\,x-b\,y\,k}{k} & -b\,x \\ y\,d & -c+d\,x \end{bmatrix} \tag{2}$$

```
> DF1:=subs(P[1],evalm(DF));det(DF1);
```

$$DF1 := \begin{bmatrix} a & 0 \\ 0 & -c \end{bmatrix}$$

$$-a\,c \tag{3}$$

```
> DF2:=subs(P[2],evalm(DF));det(DF2);
```

$$DF2 := \begin{bmatrix} -a & -b\,k \\ 0 & k\,d-c \end{bmatrix}$$

$$-a\,(k\,d-c) \tag{4}$$

```
> DF3:=map(simplify,subs(P[3],evalm(DF)));det(DF3);trace(DF3);
```

$$DF3 := \begin{bmatrix} -\frac{a\,c}{k\,d} & -\frac{b\,c}{d} \\ -\frac{a\,(-k\,d+c)}{b\,k} & 0 \end{bmatrix}$$

$$-\frac{c\,a\,(-k\,d+c)}{d\,k}$$

$$-\frac{a\,c}{k\,d} \tag{5}$$

Jacobians at P_k (calculations omitted here)

$$DF_k = D\vec{F}(P_k)$$

Both extinct

$$DF_1 = \begin{bmatrix} a & 0 \\ 0 & -c \end{bmatrix}$$

$\det DF_1 = -ac < 0$

Saddle always

Pred. extinct

$$DF_2 = \begin{bmatrix} -a & -bk \\ 0 & \Delta \end{bmatrix}$$

$\det DF_2 = -a\Delta < 0$
when P_3 phsical ($\Delta > 0$)
Saddle.

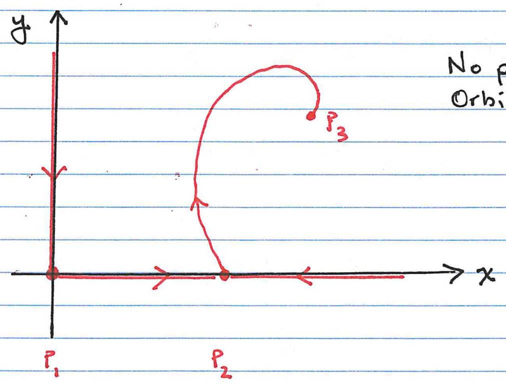
Coexistence

$$DF_3 = \begin{bmatrix} -\frac{ac}{kd} & -\frac{bc}{d} \\ \frac{a\Delta}{bk} & 0 \end{bmatrix}$$

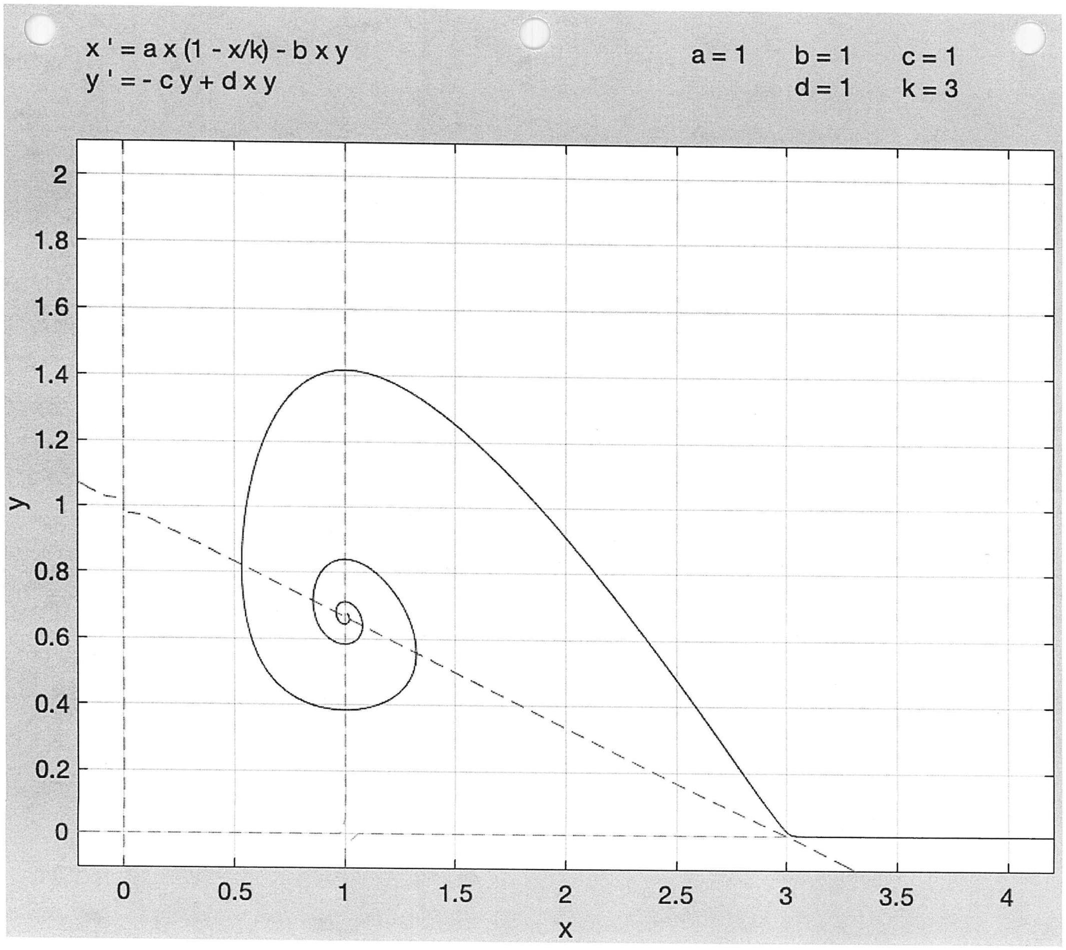
$\det DF_3 = \frac{ac\Delta}{dk}$

$\operatorname{Tr} DF_3 = \frac{-ac}{dk} < 0$

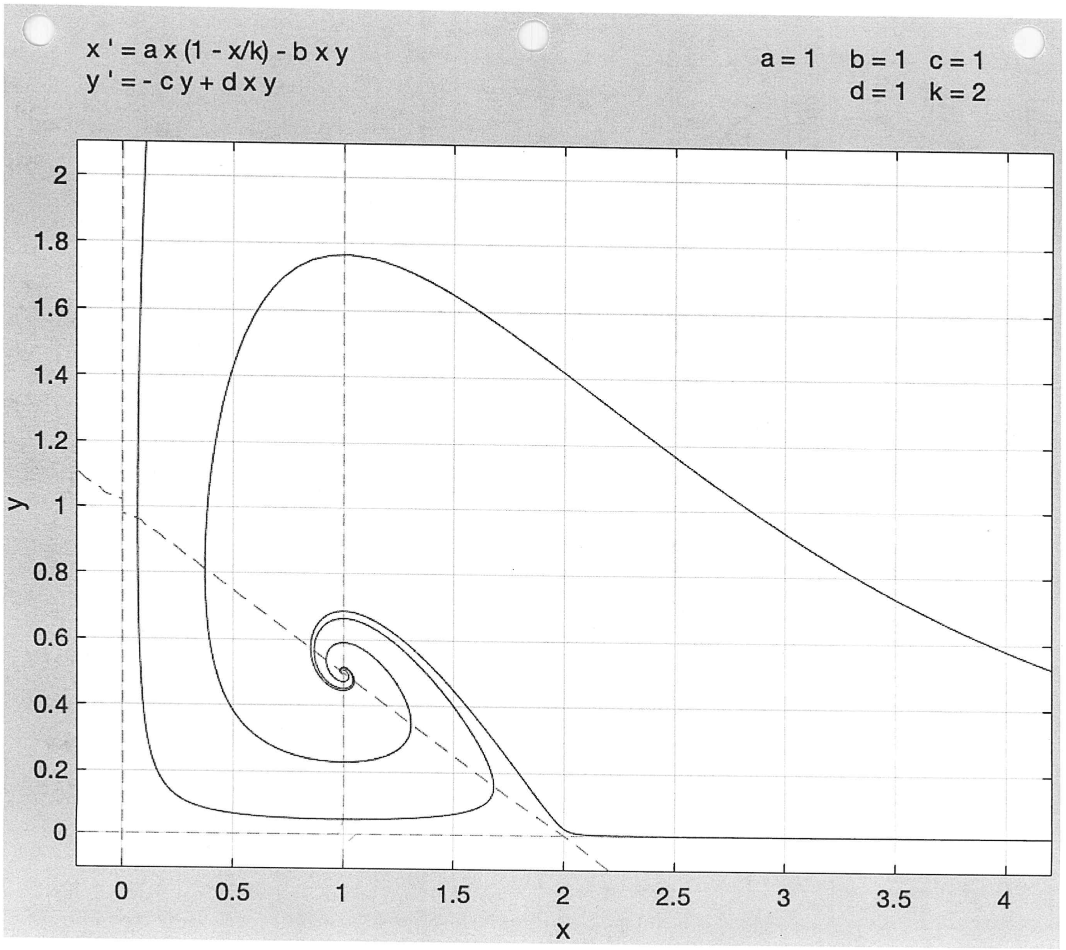
Hence P_3 is stable when physical.



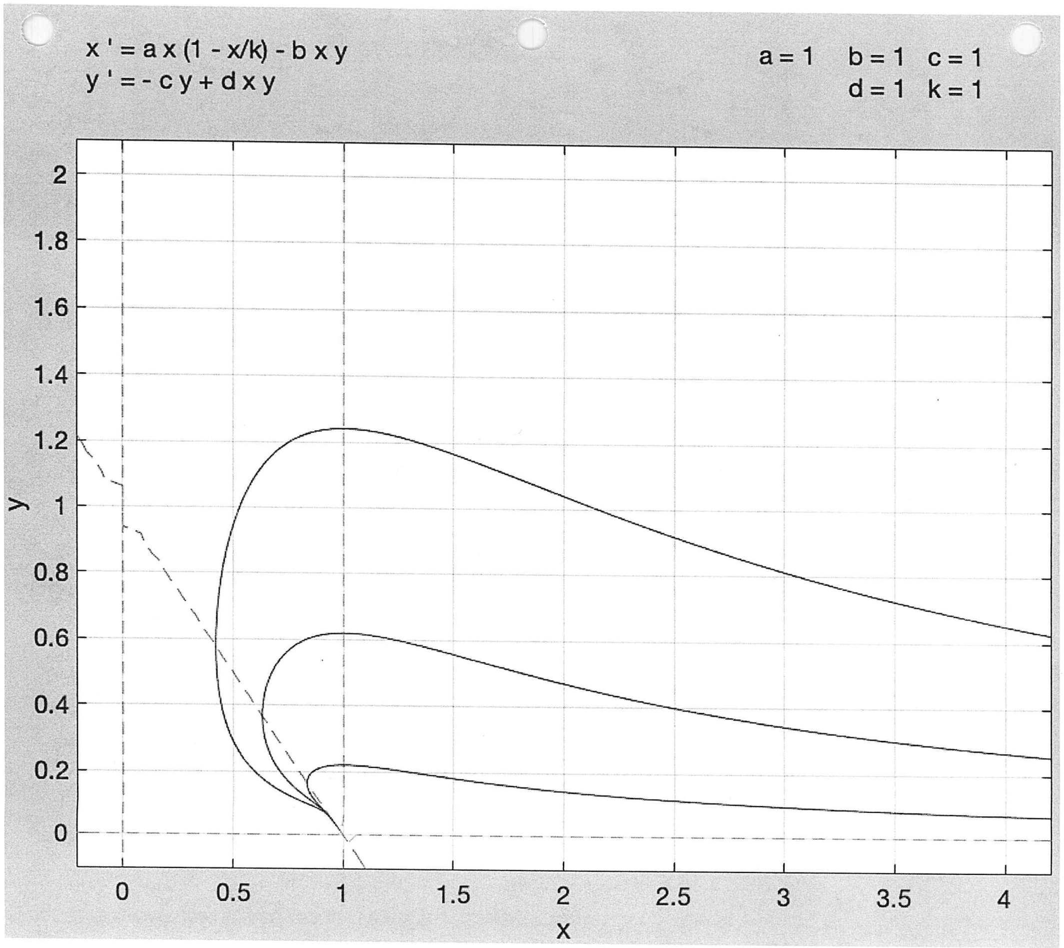
No periodic Orbits.



x ' = a x (1 - x/k) - b x y
y ' = - c y + d x y
a = 1 b = 1 c = 1
d = 1 k = 3
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
y
0
0.5
1
1.5
2
2.5
3
3.5
4
x



x ' = a x (1 - x/k) - b x y
y ' = - c y + d x y
a = 1 b = 1 c = 1
d = 1 k = 2
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
y
0
0.5
1
1.5
2
2.5
3
3.5
4
x


x ' = a x (1 - x/k) - b x y
y ' = - c y + d x y
a = 1   b = 1   c = 1
d = 1   k = 1
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
y
0
0.5
1
1.5
2
2.5
3
3.5
4
x

Competition Models

Two species (or more) competing for the same resources

Though they share the same habitat, their carrying capacities K_i differ.

$$\boxed{\begin{aligned} \frac{dN_1}{dt} &= r_1 N_1 (K_1 - a_{11} N_1 - a_{12} N_2) \\ \frac{dN_2}{dt} &= r_2 N_2 (K_2 - \underbrace{a_{21} N_1 - a_{22} N_2}) \end{aligned}}$$

Note the density dependence weighted average growth rate (underbrace above)

Rather than analyze model directly (8 parameters) we nondimensionalize.

$$x = \frac{N_1}{N_1^*} \qquad y = \frac{N_2}{N_2^*} \qquad \tau = \frac{t}{t^*}$$

Excluding lengthy calculations we use

$$N_1^* = \frac{K_1}{a_{11}} \qquad N_2^* = \frac{K_2}{a_{22}} \qquad t^* = \frac{1}{r_1 K_1}$$

Nondimensionalization of Competition Model

$$(1) \quad \frac{dN_1}{dt} = r_1 N_1 (K_1 - a_{11} N_1 - a_{12} N_2)$$

$$(2) \quad \frac{dN_2}{dt} = r_2 N_2 (K_2 - a_{21} N_1 - a_{22} N_2)$$

Has 8 parameters. Goal is to scale depent and independent variables so new variables are dimension free and new system has fewer parameters.

$$x = \frac{N_1}{N_1^*} \qquad y = \frac{N_2}{N_2^*} \qquad \tau = \frac{t}{t^*}$$

At this point, N_1^* N_2^* and t^* are unknown. We get to pick these.

$$(3) \quad N_1 = x N_1^* \qquad N_2 = y N_2^* \qquad t = \tau t^*$$

First we nondimensionalize (1) using (3)

$$\frac{\cancel{N_1^*}}{t^*} \frac{dx}{d\tau} = r_1 \cancel{N_1^*} x (K_1 - a_{11} N_1^* x - a_{12} N_2^* y)$$

$$\left\| \quad \frac{dx}{d\tau} = (r_1 K_1 t^*) \, x \left(1 - \frac{a_{11} N_1^*}{K_1} x - \frac{a_{12} N_2^*}{K_2} y \right) \quad \right\|$$

↑ choose t^* so this equals 1

↑ choose N_1^* so this equals 1

↑ define new parameter b

Hence

$$\boxed{\frac{dx}{d\tau} = x(1-x-by)}$$

where

(4) $t^* = \dfrac{1}{r_1 K_1}$ $\qquad N_1^* = \dfrac{K_1}{a_{11}}$

and

(5) $b = \dfrac{a_{12} N_2^*}{K_1}$

where N_2^* has yet to be determined.

Next we nondimensionalize (2) keeping in mind t^* and N_1^* are now known in (4). In a similar fashion we get

$$\left\| \frac{dy}{dt} = \underbrace{(r_2 K_2 t^*)}_{\substack{\text{become}\\ \text{parameter}\\ \eta}} y\left(1 - \underbrace{\frac{a_{21} N_1^*}{K_2}}_{\substack{\text{becomes}\\ \text{parameter}\\ c}} x - \underbrace{\frac{a_{22} N_2^*}{K_2}}_{\substack{\text{choose } N_2^*\\ \text{so this}\\ \text{equals } 1}} y\right) \right\|$$

So in particular

(6) $N_2^* = \dfrac{K_2}{a_{22}}$

Summary

If we choose

$N_1^* = \dfrac{K_1}{a_{11}}$ $\qquad N_2^* = \dfrac{K_2}{a_{22}}$ $\qquad t^* = \dfrac{1}{r_1 K_1}$

and define the parameters

$b = \dfrac{a_{12} K_2}{a_{22} K_1}$ $\qquad c = \dfrac{a_{21} K_1}{a_{11} K_2}$ $\qquad \eta = \dfrac{r_2 K_2}{r_1 K_1}$

we obtain the dimensionless system

$$\boxed{\begin{aligned} \frac{dx}{d\tau} &= x(1-x-by) \\ \frac{dy}{dt} &= \eta y(1-cx-y) \end{aligned}}$$

ONLY 3 PARAMETERS!

Dimensionless Model

$$\dot{x} = f(x,y) = x(1-x-by)$$
$$\dot{y} = g(x,y) = \eta y(1-cx-y)$$

where

$$b = \frac{a_{12}K_2}{a_{22}K_1} \qquad c = \frac{a_{21}K_1}{a_{11}K_2} \qquad \eta = \frac{r_2K_2}{r_1K_1}$$

The dimensionless model has only 3 params!

Equilibria

Solving $f = g = 0$ we find four possible equilibria

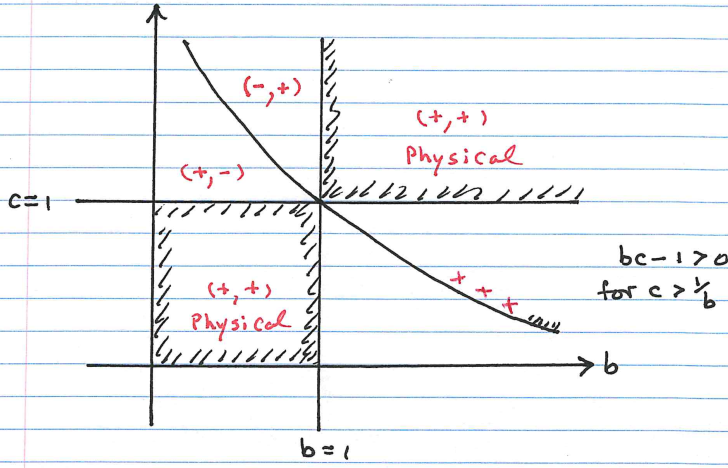
$P_0 = (0, 0)$	both die
$P_x = (1, 0)$	x survives
$P_y = (0, 1)$	y survives
$P_1 = \left(\frac{b-1}{bc-1}, \frac{c-1}{bc-1}\right)$	possible coexistence.

Existence of positive interior P_1

The coexistence state P_1 is positive (physical) if both coefficients of P_1 are positive:

$$P_1 = \left(\frac{b-1}{bc-1}, \frac{c-1}{bc-1}\right)$$

Plot $b=1$, $c=1$ and $c=\frac{1}{b}$



Shows sign of components of P_1 in (b,c)-plane.

$$\boxed{P_1 \text{ physical only in shaded regions}}$$

Stability Conditions

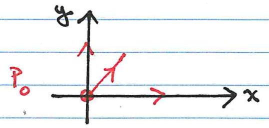
Must evaluate Jacobian at each equilibria.

$$DF(x,y) = \begin{bmatrix} 1-2x-by & -xb \\ -\eta y c & \eta-\eta c x-2\eta y \end{bmatrix}$$

Total Extinction P_0

$$DF(P_0) = \begin{bmatrix} 1 & 0 \\ 0 & \eta \end{bmatrix}$$

$\lambda = 1, \eta$ unstable node with axes as trajectories

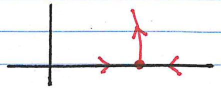


Species x survives P_x

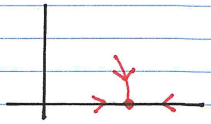
$$DF(P_x) = \begin{bmatrix} -1 & -b \\ 0 & \eta(1-c) \end{bmatrix}$$

$\lambda = -1, \eta(1-c)$

$c < 1$ P_x saddle



$c > 1$ P_x stable



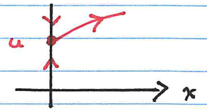
Species y survives P_y

$$DF(P_y) = \begin{bmatrix} 1-b & 0 \\ -\eta c & -\eta \end{bmatrix}$$

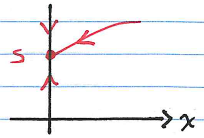
$\lambda = 1-b, -\eta$

From the eigenvalues we conclude

$b < 1$ P_y saddle



$b > 1$ P_y stable

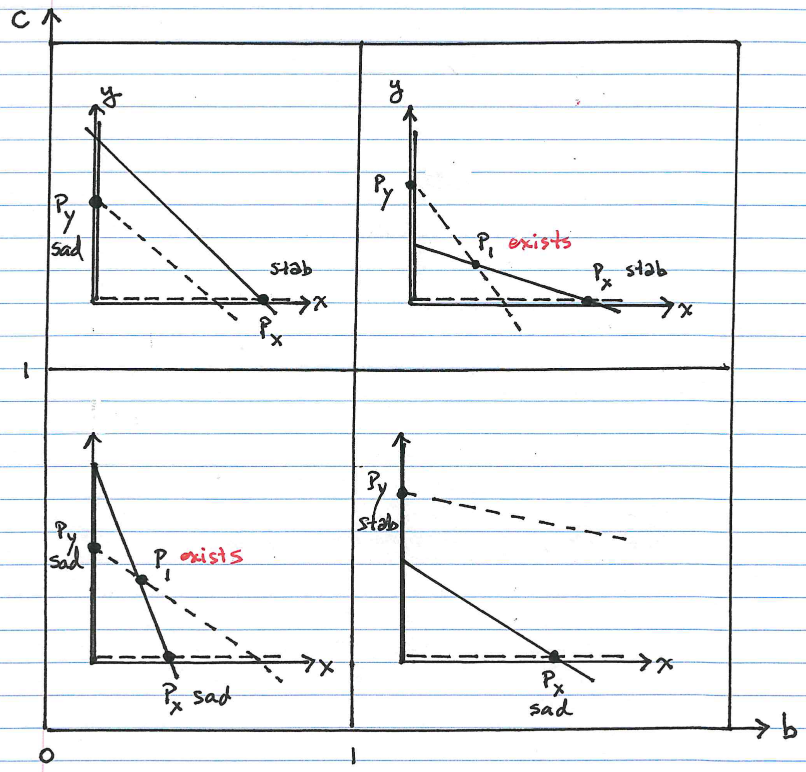


Nullclines and Equilibria Existence

$$\dot{x} = 0 \quad \Leftrightarrow \quad x = 0, \; y = \tfrac{1}{b}(1-x)$$

$$\dot{y} = 0 \quad \Leftrightarrow \quad y = 0, \; y = 1 - cx$$

Below are nullclines of system for (b, c)-pairs



To completely understand what happens for all (b, c) need to examine stability of P_1 when it exists.

Coexistence Equilibria P_1

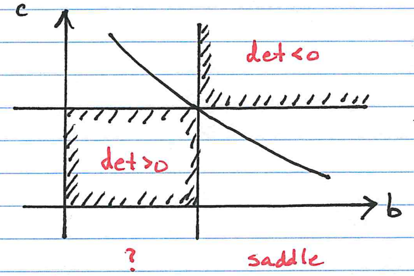
One can calculate the Jacobian at P_1 :

$$DF(P_1) = \frac{1}{(1-bc)} \begin{bmatrix} b-1 & b(b-1) \\ \eta c(c-1) & \eta(c-1) \end{bmatrix}$$

After some calculations

$$\det DF(P_1) = \frac{\eta(b-1)(c-1)}{1-bc}$$

the sign of which can be deduced in the (b, c)-plane



P_1 exists only in shaded regions

So, for $b>1$, $c>1$ we know P_1 exists and is a saddle.

To ascertain the stability when $b<1$, $c<1$ we need to examine the Trace of $DF(P_1)$.

Stability of coexistence $(b,c)\in(0,1)^2$

For

$$0<b<1 \qquad 0<c<1$$

we found $\det DF > 0$ so that equilibria P_1 is not a saddle. Therefore, its stability depends entirely on

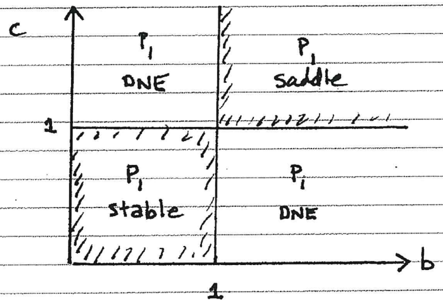
$$\mathrm{Tr}\,DF(P_1) = \frac{(b-1)+\eta(c-1)}{1-bc}$$

For the parameter range being discussed the numerator is negative while the denominator is positive. Hence

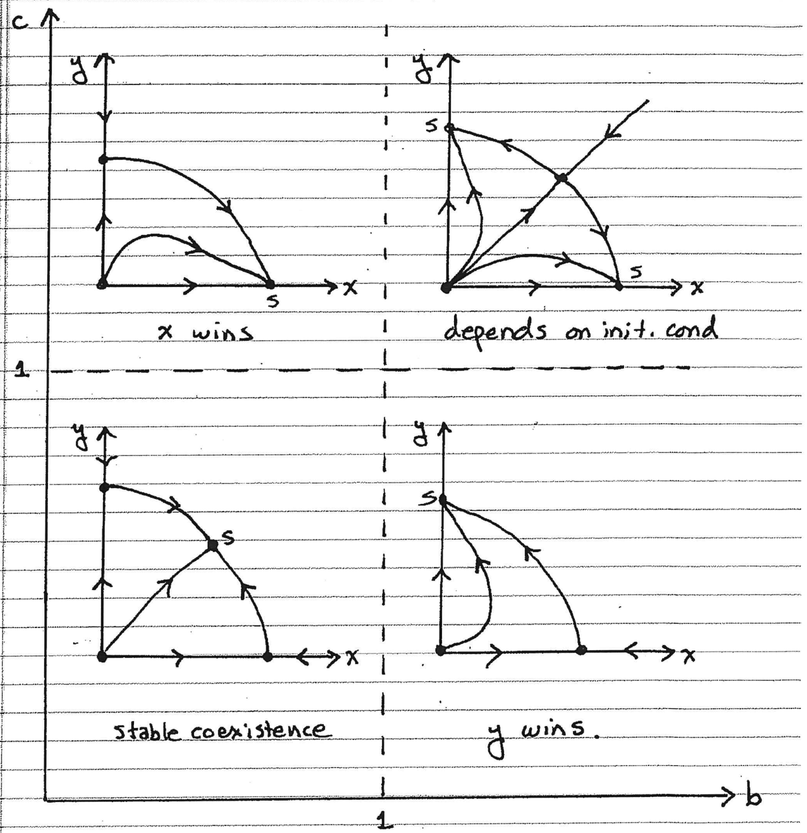
$$\mathrm{Tr}\,DF(P_1) < 0 \qquad \forall\eta$$

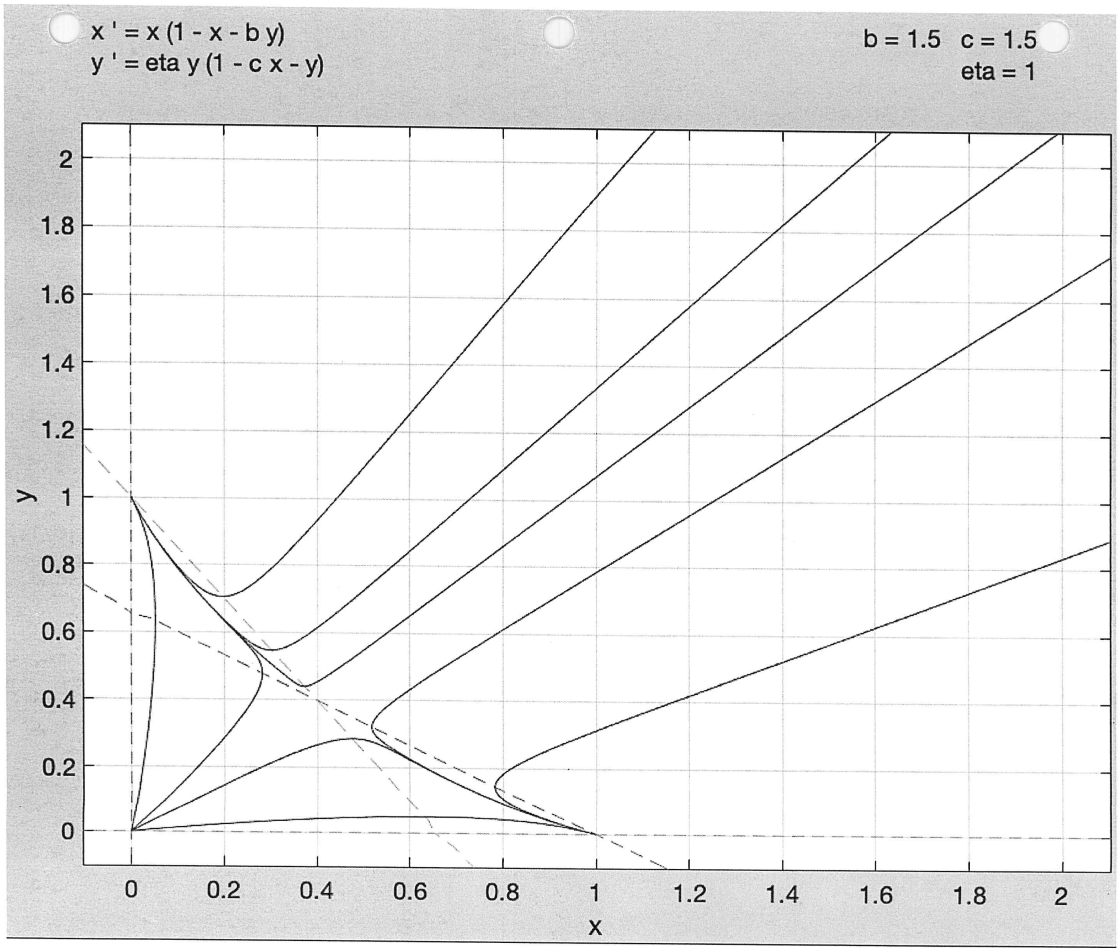
P_1 stable

Summary of P_1 existence and stability:



Conclusion of Phase Portraits




x ' = x (1 - x - b y)
y ' = eta y (1 - c x - y)
b = 1.5   c = 1.5
eta = 1
y
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
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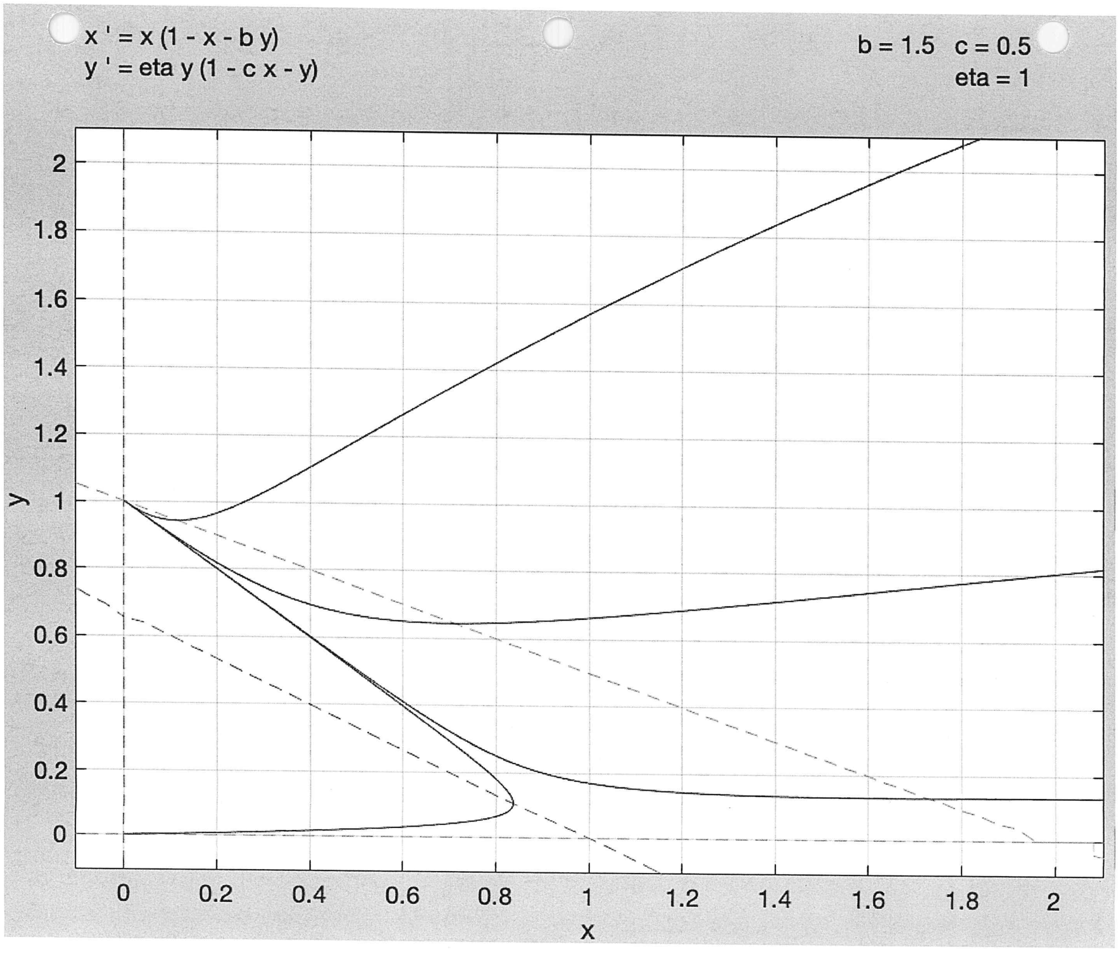
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
x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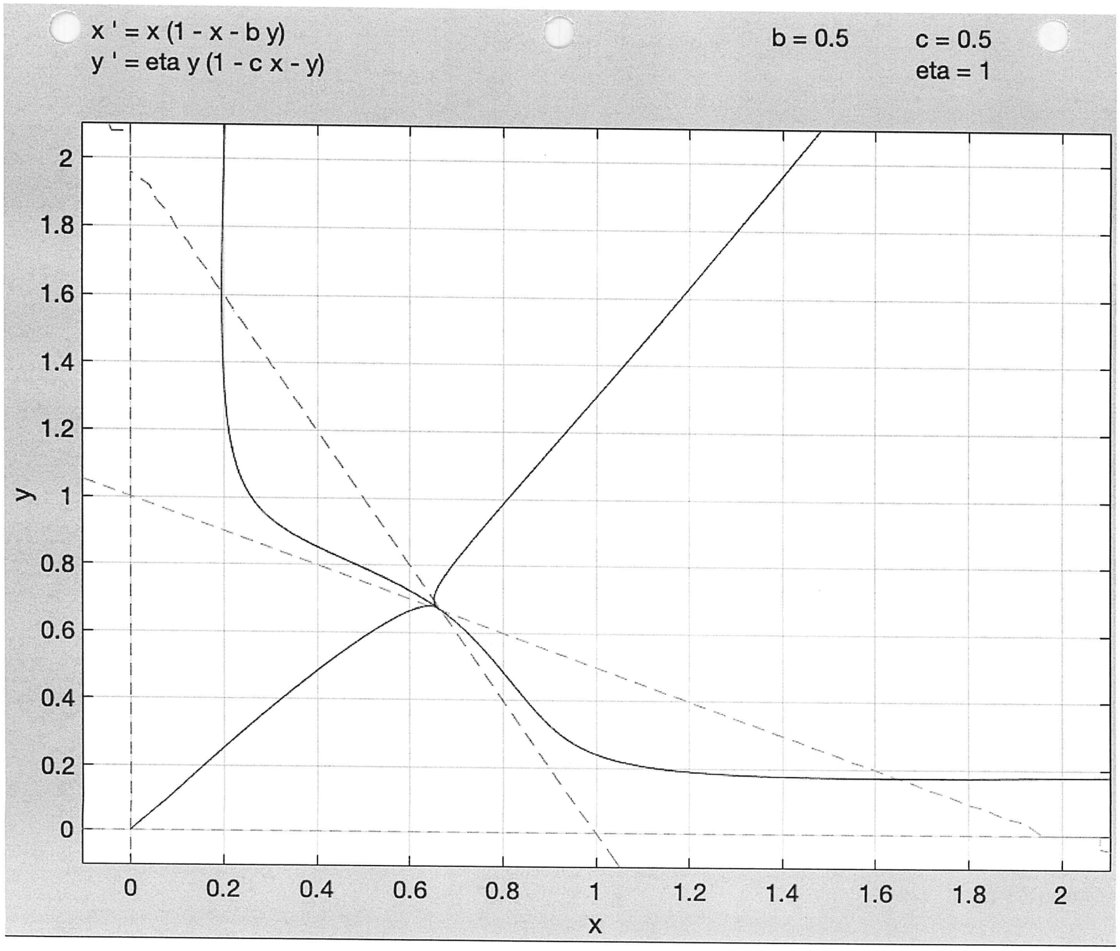
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
x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0.4
0.2
0
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
x

Law of Mass Action – simple

Rate of change of concentration is proportional to the product of reactants

$$A + B \xrightarrow{k} C$$

results in system

$$A' = -kAB$$

$$B' = -kAB$$

$$C' = +kAB$$

where k is the reaction rate.

Remarks

(1) Concentration usually in molarity M

$[A] = 1M$ ⇔ liter contains $N_a = 6.02 \times 10^{23}$ molecules

Mass action law only works for molarity. Once differential eqns have been found they can be converted to gm/liter use the gram molecular weights.

(2) AB proportional to total number of reactions (collisions) at any given instant

Arrhenius Theory

$$k = \alpha e^{-E_a/RT}$$

Reaction rate is proportional to the exponential term where

E_a = activation energy for reaction $[E_a]$ = J/mole

T = temperature $[T]$ = Kelvin

R = Gas constant = 8.314 J/mole/K

In some cases $\alpha = \alpha_0 T^n$ for $n \in (-1, 1)$.

Note that $T \uparrow$ implies rate $k \uparrow$

EXAMPE Stoichiometric coefficients

(1) $A + 2B \xrightarrow{k} C$

Number of possible collisions is $[A][B]^2$ so (1) should be thought of as

(2) $A + B + B \xrightarrow{k} C$

having "three" reactants. L.O.M.A. then ⇒

$$\frac{dc}{dt} = +kAB^2$$

Here "2" in eqn (1) is a stoichiometric coeff.

Law of Mass Action – general

(1) $A + mB \xrightarrow{k} nB + pC$

(2) $kAB^m = -\frac{dA}{dt} = \frac{1}{p}\frac{dC}{dt} = \frac{1}{(n-m)}\frac{dB}{dt}$

The stoichiometric coefficients reflect the fact for every molecule of A

p molecules of C produced

(m-n) net loss of molecules of B

EXAMPLE Reaction equations for

$A + 2B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B + C$ reversible Rx

$A + C \xrightarrow{k_2} B$ irreversible Rx

Is a set of three chem. Rx eqns

$$A' = -k_1AB^2 + k_{-1}BC - k_2AC$$
$$B' = -k_1AB^2 - k_{-1}BC + k_2AC$$
$$C' = k_1AB^2 - k_{-1}BC - k_2AC$$

EXAMPLE Autocatalytic / Stoichiometry

$A + 3B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B + C + D$

$A + D \xrightarrow{k_2} B$

$B + 2C \xrightarrow{k_3} A$

Reaction equations for A, B, C, D

$$A' = -k_1AB^3 + k_{-1}BCD - k_2AD + k_3BC^2$$
$$B' = -2k_1AB^3 + 2k_{-1}BCD + k_2AD - k_3BC^2$$
$$C' = k_1AB^3 - k_{-1}BCD - 2k_3BC^2$$
$$D' = k_1AB^3 - k_{-1}BCD - k_2AD$$

Reaction equations autocatalytic since A is ultimately involved in is' own creation.

$$\boxed{\text{Buffering} \qquad S + B \underset{k_-}{\overset{k_+}{\rightleftarrows}} C}$$

S = Substrate (Ca^{2+})

B = Buffer (Protein)

C = complex (Protein - Ca^{2+} complex)

Law of Mass Action

$$\begin{aligned} &(1) \quad S' = -k_+ SB + k_- C && S(0) = S_0 \\ &(2) \quad B' = -k_+ SB + k_- C && B(0) = B_0 \\ &(3) \quad C' = k_+ SB - k_- C && C(0) = C_0 \end{aligned}$$

Conservation of receptors

$$(B + C)' = 0$$

$$(4) \quad B + C = N = B_0 + C_0 \qquad \text{\# receptor sites}$$

Use (4) to simplify (1) - (3)

$$\begin{aligned} S' &= f(B, S) \\ B' &= f(B, S) \end{aligned}$$

where

$$\boxed{f(B, S) = -k_+ SB + k_-(N - B)}$$

The sign of f determines trajectory direction.

Sign of f(S, B)

$$f(S,B) < 0$$

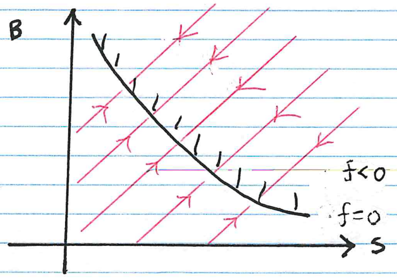
$$-k_+ SB + k_-(N-B) < 0$$

$$-(k_+ S + k_-)B + k_- N < 0$$

solving for B

$$\boxed{f < 0 \iff B < g(S) = \frac{K_E N}{K_E + S}}$$

where the equilibrium constant $K_E = \frac{k_-}{k_+}$



physical region (shaded)
for $C(0) = 0$

Notes

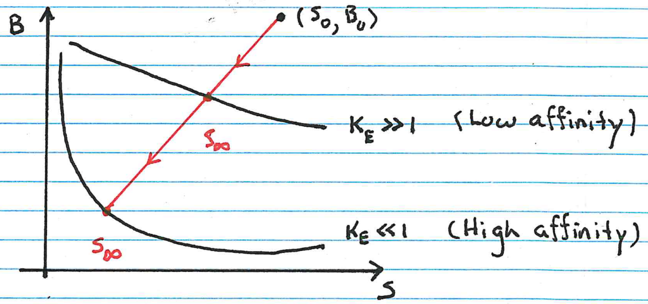
- $f = 0$ is a line of fixed points
- $f < 0$ is physical region since $\frac{dS}{dt} < 0$ there.
- $f = 0$ is a "stable invariant manifold"

Low and High affinity binding

Trajectories in the SB-plane have slope one and approach the curve

$$\boxed{B = g(S) = \frac{K_E N}{K_E + S} \qquad K_E = \frac{k_-}{k_+}}$$

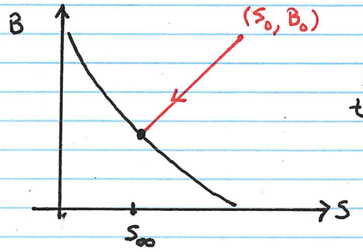
Consider the two cases $K_E \gg 1$ and $K_E \ll 1$



In the high affinity case the asymptotic value S_∞ of S is smaller meaning more substrate molecules are bound.

$K_E \gg 1$	Low Affinity	larger S_∞
$K_E \ll 1$	High Affinity	smaller S_∞

Asymptotic behavior



$$\lim_{t\to\infty} S(t) = S_\infty$$

S_∞ can be found as the intersection of the two curves

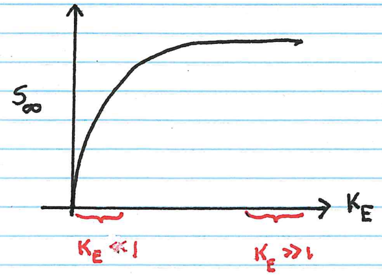
$$B = S + \Delta \qquad \Delta = B_0 - S_0$$

$$B = g(S)$$

Results in a quadratic eqn for S

$$(1) \qquad \boxed{S + \Delta = \frac{K_E N}{K_E + S}}$$

Solving and plotting S_∞ versus K_E one gets



Michaelis-Menten Kinetics

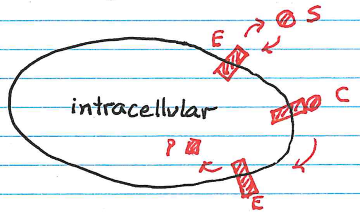
$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} C \xrightarrow{k_2} P + E$$

where

S = substrate (small)
E = enzyme (large)
C = complex
P = product

Can model cell nutrient uptake via membrane proteins E. Typically

$$E_0 \ll S_0$$



Law of Mass Action

$$
\begin{array}{lll}
(1) & \dot{S} = k_{-1} C - k_1 SE & S(0) = S_0 \\
(2) & \dot{E} = (k_{-1} + k_2) C - k_1 SE & E(0) = E_0 \\
(3) & \dot{C} = -\dot{E} & C(0) = 0 \\
(4) & \dot{P} = k_2 C & P(0) = 0
\end{array}
$$

Conservation of receptors: $E + C = E_0$

Nondimensionalization

$$s = S/S^* \quad e = E/E^* \quad c = C/C^* \quad p = P/P^* \quad \tau = t/t^*$$

For the following choices

$$S^* = S_0 \quad E^* = C^* = E_0 \quad P^* = \frac{k_2}{k_1} \quad t^* = \frac{1}{k_1 E_0}$$

one can derive the dimensionless eqns for the dimensionless variables (s, e, c, p, τ)

$$
\left\|
\begin{array}{lll}
(1) & s' = K_1 c - se & s(0) = 1 \\
(2) & \varepsilon e' = K_2 c - se & e(0) = 1 \\
(3) & \varepsilon c' = -K_2 c + se & c(0) = 0 \\
(4) & p' = c & p(0) = 0
\end{array}
\right\|
$$

where

$$\varepsilon = \frac{E_0}{S_0} \ll 1$$

and

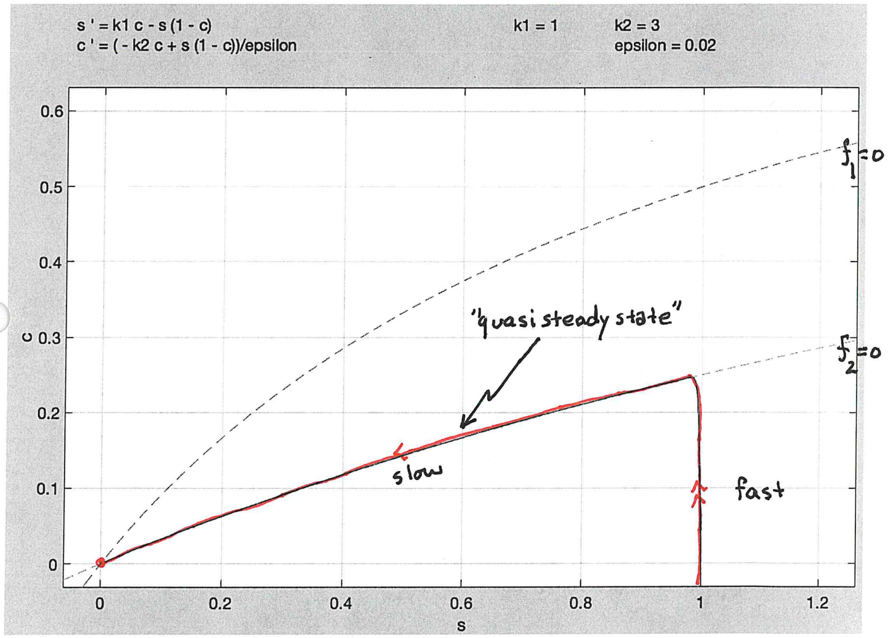
$$K_1 = \frac{k_{-1}}{k_1 S_0} \qquad K_2 = \frac{k_{-1} + k_2}{k_1 S_0}$$

Notice that for positive K_1, k_{-1} and k_2

$$K_2 > K_1 \qquad \text{physicality condition}$$

Typical Numerical solution

$K_2 > K_1$ $\qquad$ $\varepsilon \ll 1$



s and c nullclines shown

FAST-SLOW TIME APPROXIMATIONS

Using conservation of receptors

$$e + c = 1$$

in (1)-(3) we get a planar system

$$(5) \quad \boxed{\begin{aligned} \frac{ds}{d\tau} &= f_1(s,c) = K_1 c - s(1-c) \\ \varepsilon \frac{dc}{d\tau} &= f_2(s,c) = -K_2 c + s(1-c) \end{aligned}}$$

along with initial conditions:

$$s(0) = 1 \qquad c(0) = 0$$

These equations are exact.

Nullclines/Equilibrium

Are easy to define

$$f_1 = 0 \quad \Leftrightarrow \quad c = H_1(s) = \frac{s}{K_1 + s}$$

$$f_2 = 0 \quad \Leftrightarrow \quad c = H_2(s) = \frac{s}{K_2 + s}$$

From these it is easy to show (0,0) is the sole equilibrium.

To understand the solutions of system (5) we introduce fast and slow times.

τ slow time

$t = \frac{\tau}{\varepsilon}$ fast time

Since $\varepsilon \ll 1$, only a small change in the slow time τ is needed to make the fast time change by order 1 or $O(1)$. For instance, $\varepsilon = 10^{-3}$ and $\tau = 2\times10^{-3}$ yields $t = 2$.

Lastly, system (5) can be expressed with either time using the chain rule.

$$\frac{ds}{d\tau} = \frac{ds}{dt}\frac{dt}{d\tau} = \frac{1}{\varepsilon}\frac{ds}{dt}$$

(SS)	$\frac{ds}{d\tau} = f_1(s,c)$ $\varepsilon\frac{dc}{d\tau} = f_2(s,c)$	$\frac{ds}{dt} = \varepsilon f_1(s,c)$ $\frac{dc}{dt} = f_2(s,c)$	(FS)
	SLOW SUBSYSTEM	FAST SUBSYSTEM	
	τ = slow time	t = fast time	

Quasi Steady State (QSS)

Is a science term where one lets $\varepsilon \to 0$ as an approximation to (1)-(4). This yields from the $\varepsilon e'$ eqn

(5) $$K_2 c - s e = 0$$

Conservation of receptors (dimensionless) is:

(6) $$e + c = 1$$

One may solve the system (5)-(6) for e in terms of s or c in terms of s)

$$\boxed{e = \frac{K_2}{K_2 + s} \qquad c = \frac{s}{K_2 + s}}$$

Next page shows a typical numerical solution of (1)-(4)

$K_1 = 1$ $\quad K_2 = 3$

Leading order Fast Subsystem (FS)

Le

smaller higher order terms

$$s(t) = s_0(t) + \varepsilon s_1(t) + \cdots$$

$$c(t) = c_0(t) + \varepsilon c_1(t) + \cdots$$

in the (FS) yields leading order behavior

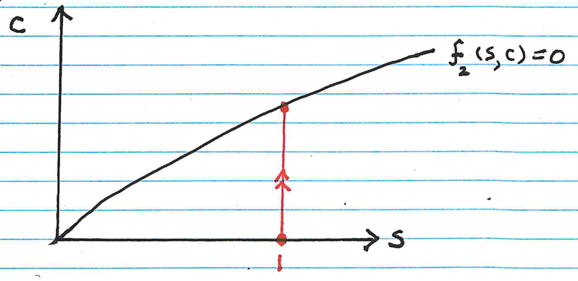
$$\left\| \begin{array}{ll} \dfrac{ds_0}{dt} = 0 & s_0(0) = 1 \\ \dfrac{dc_0}{dt} = f_2(s_0, c_0) & c_0(0) = 0 \end{array} \right\|$$

Solving with initial conditions

$$s_0(t) = 1$$

$$c_0(t) = \frac{1}{\mu}\left(1 - \exp(-\mu t)\right) \qquad \mu \equiv K_2 + 1$$

Note $c_0(t) \to \frac{1}{K_2+1}$ or that $f_2(1, c_0) \to 0$



Leading order Slow Subsystem (SS)

Let

functions of slow time

$$s(\tau) = s_0(\tau) + \varepsilon s_1(\tau) + \cdots$$

$$c(\tau) = c_0(\tau) + \varepsilon c_1(\tau) + \cdots$$

in the (SS) yields leading order behavior

$$(6) \quad \left\| \begin{array}{l} \dfrac{ds_0}{d\tau} = f_1(s_0, c_0) \\ 0 = f_2(s_0, c_0) \end{array} \right\| \quad \text{Differential Algebraic Equations}$$

Recall that $f_2 = 0 \iff c_0 = H_2(s_0) = \dfrac{s_0}{K_2 + s_0}$

$$(7) \quad \frac{ds_0}{d\tau} = F(s_0) = f_1(s_0, H_2(s_0))$$

Explicitly (7) is

$$\frac{ds_0}{d\tau} = (K_1 - K_2) \cdot H_2(s_0) < 0$$

This is separable and its implicit soln is

$$\boxed{s_0 + K_2 \ln(s_0) - 1 = -(K_2 - K_1)t}$$

Equilibria Stability (FS)

$$\frac{ds}{dt} = \varepsilon f_1(s,c)$$
$$\frac{dc}{dt} = f_2(s,c)$$

Sole equilibria is $P=(0,0)$. Nullclines are

$f_1 = 0$ $\qquad c = H_1(s) = \frac{s}{K_1+s}$

$f_2 = 0$ $\qquad c = H_2(s) = \frac{s}{K_2+s}$

Jacobian at $P=(0,0)$

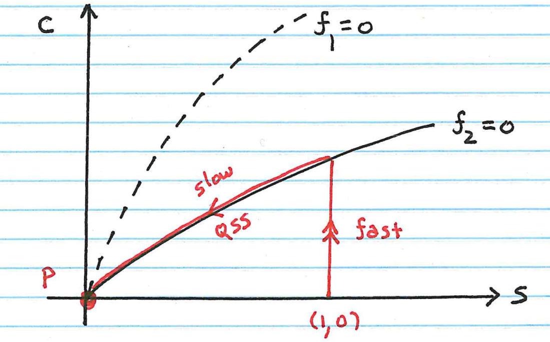
$$D\vec{f}(0,0) = \begin{bmatrix} -\varepsilon & \varepsilon K_1 \\ 1 & -K_2 \end{bmatrix}$$

From this we see

$$\det D\vec{f} = \varepsilon(K_2 - K_1) > 0$$
$$\mathrm{Tr}\, D\vec{f} = -(K_2+\varepsilon) < 0$$

hence P is <u>stable</u>.

Summary of Dynamics



(1) Rapidly achieves QSS

(2) Measurable dynamic more likely to only be motion on slow subsystem manifold $f_2=0$ or

$$c = \frac{s}{K_2+s}$$

(3) Continues until substrate depleted

(4) Since $e+c=1$, $e \to 1$ as $t \to \infty$.

(5) Production <u>rate</u> given by slow subsystem

$$\frac{dp}{dt} = c = \frac{s}{K_2+s}$$

Production Rate

The dimensionless production rate v is

$$v \equiv \frac{dp}{dt} = \frac{s}{s + K_2}$$

This can be converted back to dimensional form

$$(1) \qquad V = \frac{dP}{dt} = \frac{\bar{V} S}{K_m + S}$$

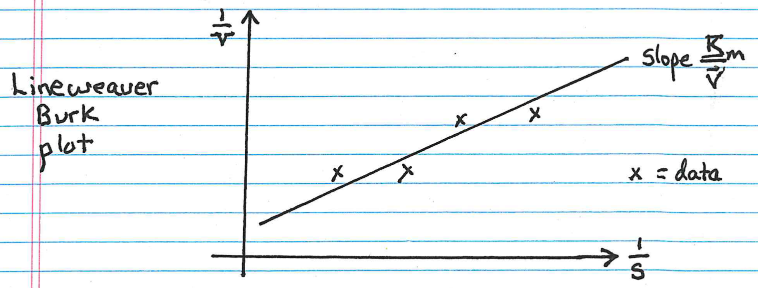
where

$$\bar{V} = k_2 E_0 \qquad K_m = \frac{k_{-1}+k_2}{k_1}$$

Eqn (1) can be re-written

$$\boxed{\frac{1}{V} = \frac{1}{\bar{V}} + \frac{K_m}{\bar{V}} \frac{1}{S}}$$

Measure production rate and S. Use linear regression to find $\bar{V}$ and K_m



Quick Derivation (Michaelis-Menten)

Suppose you know apriori that E and C are 'fast' variables then production rates can be computed directly from the dimensional equations

$$S' = k_{-1} C - k_1 SE$$

$$\left.\begin{aligned} E' &= (k_{-1}+k_2) C - k_1 SE \\ C' &= -(k_{-1}+k_2) C + k_1 SE \end{aligned}\right\} \text{Both zero when in QSS}$$

$$P' = k_2 C$$

Noting that the number of receptors is conserved

$$\boxed{\begin{aligned} (k_{-1}+k_2) C - k_1 SE &= 0 \qquad \text{QSS} \\ E + C &= E_0 \qquad \text{receptors.} \end{aligned}}$$

These are two eqns for (E, C). Solving these we get C and E as functions of S:

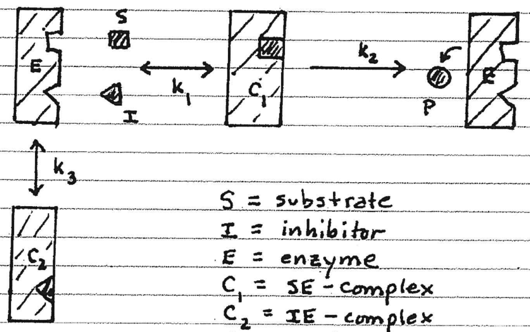
$$C = \frac{SE_0}{K_m + S}$$

so that

$$\frac{dP}{dt} = k_2 C = \frac{\bar{V} S}{S + K_m}$$

as before.

Competetive Inhibition



S = substrate
I = inhibitor
E = enzyme
C_1 = SE - complex
C_2 = IE - complex
P = product

Enzyme has two binding sites but only SE complex can make product P so I acts to inhibit such production.

Law of mass action ($\varepsilon = E_0/S_0 \ll 1$ assumed)

$$\left.\begin{aligned}(1)\quad S' &= -k_1 SE + k_{-1} C_1\\ (2)\quad I' &= -k_3 IE + k_{-3} C_2\end{aligned}\right\}\ \text{slow}$$

$$\left.\begin{aligned}(3)\quad C_1' &= k_1 SE - (k_{-1}+k_2) C_1\\ (4)\quad C_2' &= k_3 IE - k_{-3} C_2\end{aligned}\right\}\ \text{fast}$$

$$(5)\quad E' = -C_1' - C_2' \qquad \text{conserved receptors}$$

$$(6)\quad P' = k_2 C_1 \qquad \text{production rate}$$

Reaction Equations

$$S + E \overset{k_1}{\longleftrightarrow} C_1 \xrightarrow{k_2} E + P$$

$$I + E \overset{k_3}{\longleftrightarrow} C_2$$

With nondimensimalizing we know (3)-(4) will be fast. If E, C_k are scaled by E_0 and S by S_0 the dimensimless forms will be

$$\varepsilon \dot{c}_k = O(1) \qquad \varepsilon = \frac{E_0}{S_0} \ll 1$$

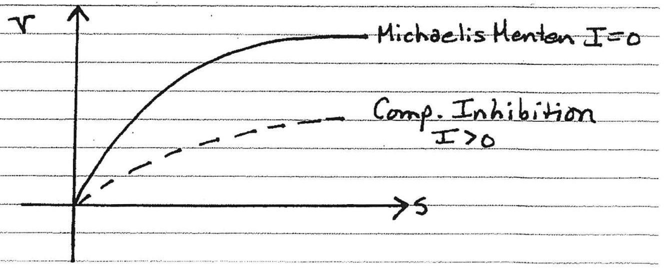
Quasi Steady State

Set $C_1' = C_2' = 0$ and use conservation law (5) to solve for C_1 in terms of slow variables S', I to ultimated get production rate

$$\frac{dP}{dt} = V = \frac{\bar{V} S}{S + K_m(1 + \underset{\uparrow \text{inhibition}}{I/K_i})}$$

where $\bar{V} = k_2 E_0$ maximal rate and

$$K_m = \frac{k_{-1} + k_2}{k_1} \qquad K_i = \frac{k_{-3}}{k_3}$$

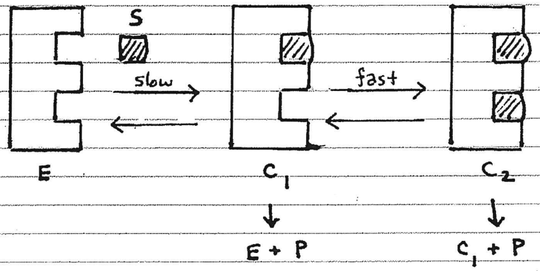


Cooperativity

$$S + E \underset{k_1}{\longleftrightarrow} C_1 \xrightarrow[k_2]{} E + P$$

$$S + C_1 \underset{k_3}{\longleftrightarrow} C_2 \xrightarrow[k_4]{} C_1 + P$$

Cartoon



Indicated rates k_1 and k_3 are, respectively, assumed to be small and large. System favors cooperative C_2 state.

QSS Approximation, conservation receptors, $\varepsilon = \frac{E_0}{S_0} \ll 1$

$$\bar{V} = \frac{dP}{dt} = \frac{(k_2 K_2 + k_4 S') E_0 S'}{K_1 K_2 + K_2 S' + S'^2}$$

where

$$K_1 = \frac{k_{-1} + k_2}{k_1} \qquad K_2 = \frac{k_4 + k_{-3}}{k_3}$$

Large Positive Cooperativity

As indicated we assume (see cartoon) that k_1 is relatively small while k_3 is relatively large:

$$k_1 = \delta \ll 1 \qquad k_3 = \frac{k}{\delta} \gg 1$$

for some constant k. Then V is a function of S

$$V = V(\delta) \qquad \delta \ll 1$$

Since $V \sim V(0)$ we have an approximate production rate

$$(1) \qquad V = \frac{\bar{V} S^2}{K + S^2} \qquad K = K_1 K_2$$

where $\bar{V} = k_4 E_0$. $V(S)$ is a Hille function of Hille coefficient $n = 2$.

n-site Positive Cooperativity

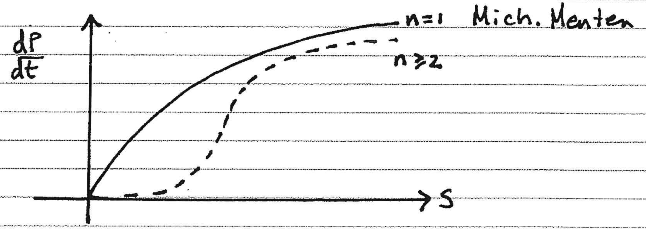
Assume formation of C_1 is slow ($k_1 \ll 1$)
but formation C_k, $k \geqslant 1$ fast.

Here E has n-sites and C_k = complex
of E with k-substrate molecules
attached.

Same analysis

$$\frac{dP}{dt} = V = \frac{\bar{V} S^n}{K + S^n} \qquad \text{Hill eqn, coeff } n$$

where $K = \prod_{j=1}^{n} K_j$



Experimental Correlation

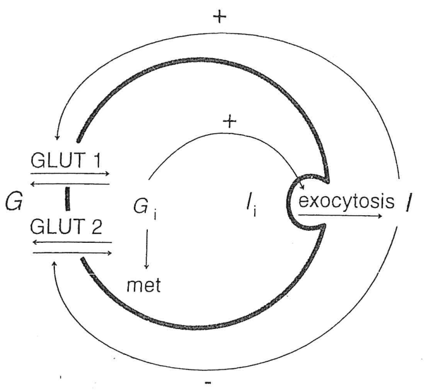
$$n \ln S = n \ln K + \ln\left(\frac{V}{V - \bar{V}}\right)$$

$$n\,\alpha_k = n \ln K + \beta_k$$

Data $\{(\alpha_k, \beta_k)\}$ and linear regression for n, K.

Glucose-dependent insulin secretion

Pancreatic β-cells secrete insulin I via exocytosis at a rate dependent on intra and extracellular glucose.



The following rates and assumptions apply

R_1 = rate of transport into cell through insuline <u>activated</u> GLUT 1 transporters

R_2 = rate of transport into cell through insulin inactived GLUT 2 transporters

R_s = insulin production rate

R_m = intracellular glucose metabolism rate

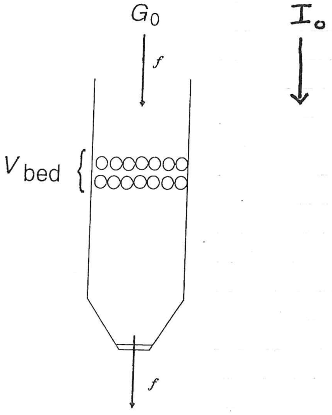
G = extracellular glucose

G_i = intracellular glucose

I = insulin

J = inhibition variable

Experimentally β-cells in a bed (V_{bed}) and glucose of concentration G_0 is continuously flushed through at flow rate f :



Controlled: inflow G_0, I_0

measured: outflow G, I

Nondimensionalized model (Fall et al, pg 87)

(1) $$g' = -R_1 - R_2 - k_0(g - g_0)$$

(2) $$g_i' = R_1 + R_2 - R_m$$

(3) $$i' = R_s - k_0 i$$

(4) $$j' = j_\infty(i) - j \qquad \text{(phenomenological)}$$

where

$$R_1 = \frac{K_1 V_1 (g - g_i)}{(K_1 + g)(K_1 + g_i)} \cdot \frac{i^n}{K_i^n + i^n} \; ⊕$$

$$R_2 = \frac{K_2 V_2 (g j^{m} \overset{⊖}{} - g_i)}{(K_2 + g)(K_2 + g_i)}$$

$$R_m = \frac{V_m g_i}{1 + g_i} \qquad \text{Mich-Menten QSS}$$

$$R_s = \frac{V_s (R_m^4 + L^4)}{K_s^4 + R_m^4 + L^4} \qquad \text{(phenomenological)}$$

The latter assumes insulin secretion rate that grows with glucose metabolism rate. Looks like 4-site cooperativity (were it not for L). Lastly

$$j_\infty(i) = \frac{1}{1 + i}$$

Model Parameters

Table 4.1 Standard Dimensional Parameters

Fixed by experiment	V_m	0.24 mM/min
	K_m	9.8 mM
	V_s	0.034 mM/min
	K_s	0.13 mM/min
	V_{max2}	32.0 mM/min
	K_2	17.0 mM
	V_{max1}	120.0 mM/min
	K_1	1.4 mM
	L	0.01 mM/min
Experimentally variable	k_0	400.0/min
	I_0	0.0 mM
	G_0	8-22 mM
Adjustable in the model	K_I	1×10^{-6} mM
	K_i	4.0×10^{-5} mM
	τ	20.0 min

Table 4.2 Standard Dimensionless Parameters

Dimensionless parameter	Dimensional definition	Standard value	
$\hat{V}_m$	$\tau V_m/K_m$	0.50	
$\hat{V}_s$	$\tau V_s/K_I$	$\boxed{6.8 \times 10^5}$	large
$\hat{K}_s$	$\tau K_s/K_m$	0.27	
$\hat{V}_{max2}$	$\tau V_{max2}/K_m$	65.3	
$\hat{K}_2$	K_2/K_m	1.7	
$\hat{V}_{max1}$	$\tau V_{max1}/K_m$	245.0	
$\hat{K}_2$	K_1/K_m	0.14	
$\hat{L}$	$\tau L/K_m$	0.02	
$\hat{k}_0$	τk_0	$\boxed{8 \times 10^3}$	large
$\hat{G}_0$	G_0/K_m	0.8-2.2	
$\hat{K}_i$	K_i/K_I	40.0	

Fast-slow dynamis,

Since $k_0 \gg 1$ in

$$g' = -R_1 + R_2 - k_0(g - g_0)$$
$$i' = R_S - k_0 i$$

yields (QSS) approximations:

$$0 = -R_1 + R_2 - k_0(g - g_0)$$
$$0 = R_S - k_0 i$$

Using these one can eliminate (g, i) to get a slow subsystem of the form

$$g_i' = F_1(g_i, j)$$
$$j' = F_2(g_i, j)$$

This system has oscillations!

Passive Transport

Transport of S from high to low concentrations through a membrane transporter such as extracellular glucose into cells. No energy input is required.

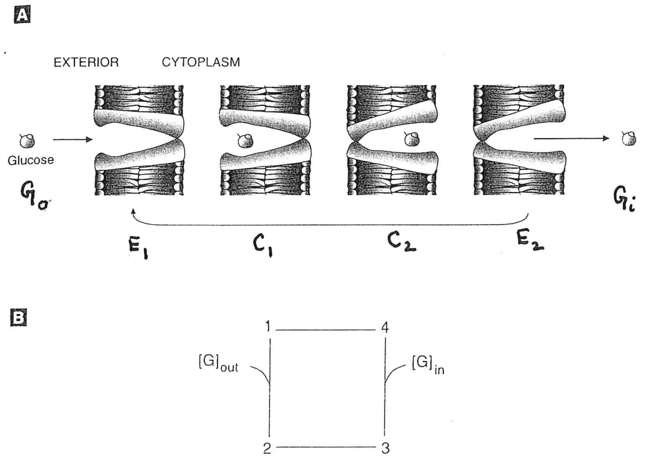


Figure 3.1 (A) Cartoon of four states of a GLUT transporter, showing the empty pore facing the exterior of the cell, glucose bound facing the exterior, glucose bound facing the interior, and the open pore facing the interior of the cell. Adapted from Leinhard et al. (1992). (B) Four-state kinetic diagram of a GLUT transporter based on the cartoon in (A).

E_1 = one unbound conformational state
C_1 = one bound conformational state
C_2 = another bound conformational state
E_2 = another unbound conformational state

(QSS)
$$V = \frac{dG_i}{dt} = \frac{\alpha_0 + \alpha_1 G_0 + \alpha_2 G_i + \alpha_3 G_0 G_i}{\beta_0 + \beta_1 G_0 + \beta_2 G_i + \beta_3 G_0 G_i}$$

SERCA Pumps $[Ca^{2+}]_o > [Ca^{2+}]_i$

pump Ca^{2+} up gradient

Rate of Ca^{2+} accumulation inside cell measured by rate of radioactive $^{45}Ca^{2+}$ uptake at ER (endoplasmic reticulum) Conversion of ATP to ADP generates energy (loss of PO^4 phosphate group)

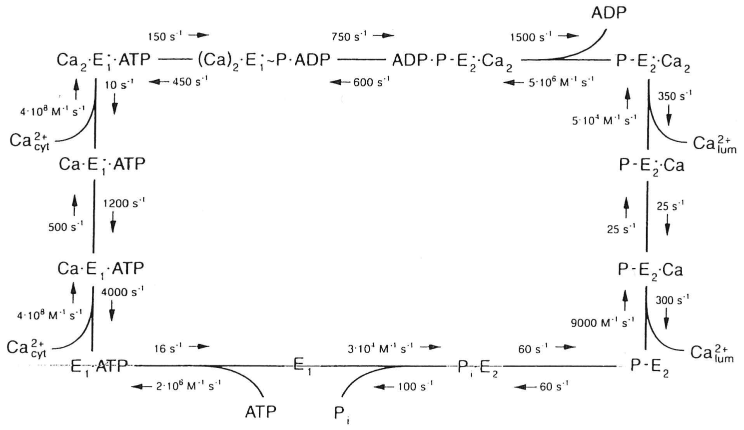


Figure 3.14 A twelve-state model of the SERCA pump. Note the two sequential Ca^{2+} binding steps on the left-hand side. Although the cycle is driven by the hydrolysis of ATP, all of the steps in the diagram contribute to the steady-state rate. Redrawn from Läuger (1991).

Twelve State model well approximated by 2-site cooperativity model hence intracellular production rate (QSS)

$$V = \frac{dCa_i}{dt} = \frac{\bar{V}\,[Ca_i]^2}{\underline{K}^2 + [Ca_i]^2}$$

Chemical Oscillators - Brusselator (1968)

Mostly inorganic chemical species.

$A = [BrO_3^-]$

B = organic species

$X = [HBrO_2]$

$Y = [Br^-]$

where the reactions are

$$A \xrightarrow{k_1} X$$

$$B + X \xrightarrow{k_2} Y + D$$

$$2X + Y \xrightarrow{k_3} 3X$$

$$X \xrightarrow{k_4} E$$

Here D and E are other products.

It is assumed that the concentrations of A, B are artificially maintained at (nearly) constant levels. Resulting nondimensimalized eqns are called the Brusselator

Autocatalysis since X involved in its own production.

$$\boxed{\begin{array}{ll} (1) & \dot{x} = a - (b+1)x + x^2 y \\ (2) & \dot{y} = bx - x^2 y \end{array}}$$

where (x, y) are dimensionless (X, Y).

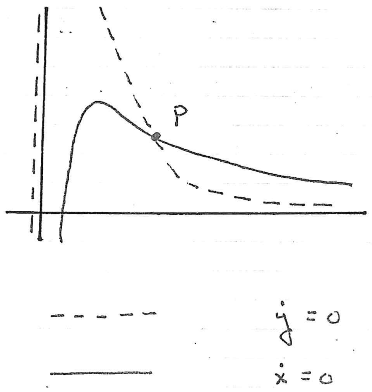
<u>Nullclines, equilibria</u>

$\dot{x} = 0 \qquad y = F(x) = \frac{(b+1)}{x} - \frac{a}{x^2}$

$\dot{y} = 0 \qquad x = 0, \; y = \frac{b}{x}$

Sole equilibria

$$P = \left(a, \frac{b}{a}\right)$$



Jacobian at P

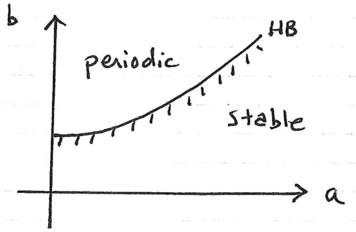
$$DF(P) = \begin{bmatrix} b-1 & a^2 \\ -b & -a^2 \end{bmatrix}$$

from which

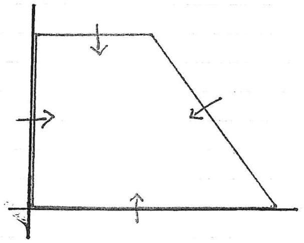
$$\det DF(P) = a^2 > 0$$

$$\mathrm{Tr}\, DF(P) = b - 1 - a^2$$

Hopf bifurcations occur when Tr DF(P)



Hopf points alone only prove small amplitude periodic orbits



Trapping region shape to prove existence given $\mathrm{Tr}\,DF(P) > 0$

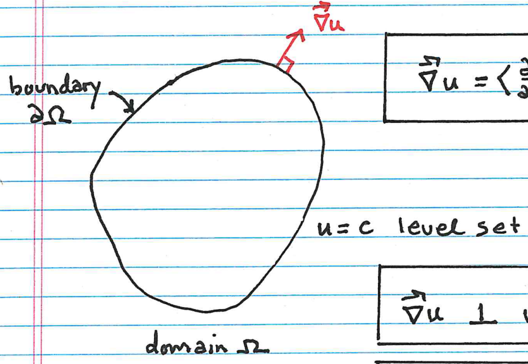
Spatial inhomogeneity

In nature, molecules, microorganisms and even larger species (such as plants) move within their environment. As a consequence their density depends on position x (as well as time). Typically such movement is

- a consequence of random motion
- a consequence of motion triggered by environmental factors such as food concentration, temperature and electric fields (for ions)

Gradients

$u(\vec{x},t)$ = density at $(\vec{x},t)$



$$\boxed{\vec{\nabla}u = \left\langle \frac{\partial u}{\partial x}, \frac{\partial u}{\partial y}, \frac{\partial u}{\partial z} \right\rangle}$$

$$\boxed{\vec{\nabla}u \perp u = \text{const lev. sets}}$$

$$\boxed{\vec{\nabla}u \text{ direction of max increase}}$$

EXAMPLE

The concentration of nutrient particles in a pond is

$$c(x,y,z) = C_0 \exp(-\alpha(x^2+y^2+z^2))$$

$$c(x,y,z) = C_0 \exp(-\alpha r^2)$$

where $r^2 = x^2+y^2+z^2$. An organism at $(1,-1,1)$ moves in the direction in which c is increasing most rapidly. What direction is it?

$$\vec{\nabla} c(P) \qquad P = \langle 1,-1,1 \rangle$$

Generally

$$\frac{\partial c}{\partial x} = -2\alpha x c \quad \frac{\partial c}{\partial y} = -2\alpha y c \quad \frac{\partial c}{\partial z} = -2\alpha z c$$

Hence

$$\vec{\nabla} c(x,y,z) = c(x,y,z) \langle -2\alpha x, -2\alpha y, -2\alpha z \rangle$$

and at $P = \langle 1,-1,1 \rangle$

$$\vec{\nabla} c(P) = c(P) \langle -2\alpha, 2\alpha, -2\alpha \rangle$$

$$\vec{\nabla} c(P) = +2\alpha c(P) \underbrace{\langle -1, 1, -1 \rangle}_{\text{direction parallel}}$$

(non unique answer)

Conservation Laws

Let $u(\vec{x},t)$ be the concentration of something at position $\vec{x} \in \Omega$ and time t. For instance

u = mass density of a fluid (gas)

u = chemical concentration

u = population density of an organism

u = ionic concentration

Then at any given instant

$$M(t) = \int_\Omega u(\vec{x},t)\, d\vec{x}$$

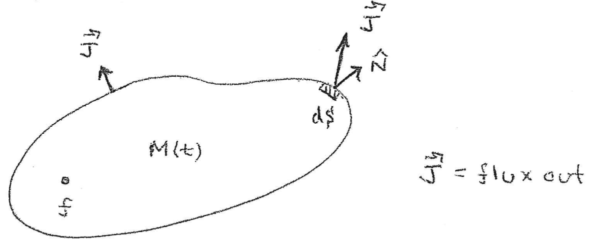
is the total amount at time t. Here M could be total mass, population or net charge

Let

$\vec{J}$ = flux of u at $\vec{x} \in \Omega$

f = internal sources or sinks of u at $\vec{x}$. For instance if u is a chemical concentration $f(\vec{x},t,u)$ is the local production rate <u>per unit volume</u>

If u is conserved the rate of change of M must balance the rate of production and flux out of Ω.



For <u>any domain</u> Ω

$$\frac{d}{dt}\int_{\Omega} u(\vec{x},t)\,d\vec{x} = -\int_{\partial\Omega} \vec{J}\cdot\hat{N}\,ds + \int_{\Omega} f(\vec{x},t,u)\,d\vec{x}$$

where the minus sign indicates a flux out.

Assuming u is sufficiently smooth and applying the Divergence theorem

$$\int_{\Omega} \frac{\partial u}{\partial t}\,d\vec{x} = -\int_{\Omega} \vec{\nabla}\cdot\vec{J}\,d\vec{x} + \int_{\Omega} f(\vec{x},t,u)\,d\vec{x}$$

If the integrands are continuous then since the <u>domain is arbitrary</u> the integrands on each side must match:

$$\text{(i)} \quad \boxed{\frac{\partial u}{\partial t} = -\vec{\nabla}\cdot\vec{J} + f(\vec{x},t,u)}$$

Differential form of conservation law.

Functional forms for $\vec{J}$ and f are assumptions based off "constitutive laws".

A constituitive law is a measured or assumed mathematical relationship between physical quantities.

For instance, the ideal gas law

$$PV = nRT$$

may be viewed as a "constituitive law".

Generally for models there may be many different kinds of fluxes and sources so that (i) becomes

$$u_t = -\sum_{i=1}^{N} \vec{\nabla}\cdot\vec{J}_i + \sum_{j=1}^{M} f_j(\vec{x},t,u)$$

EXAMPLE Diffusion

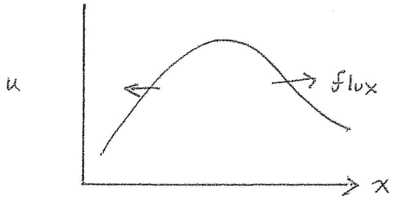
Let u = concentration of a substance

$$(1) \qquad \vec{J} = -D\vec{\nabla}u \qquad \text{Fick's Law}$$

is an assumed law for the flux. Here D is the *diffusivity* of the substance in the medium.

$$\vec{\nabla}u = \text{direction } u \uparrow \text{ most rapidly}$$

Thus flux in (1) indicates substance moves in direction u decreasing most rapidly



In some media D depends on $\vec{x}$.

Large molecules typically have a small D.

Spatial dependence of D on $\vec{x}$ may be due to the medium is not homogeneous (perhaps stratified in some manner)

If one assumes $\vec{J} = -D(\vec{x})\vec{\nabla}u$ in the conservation equation we arrive at

$$(2) \qquad \frac{\partial u}{\partial t} = \vec{\nabla}\cdot(D(\vec{x})\vec{\nabla}u)$$

and when $D > 0$ is constant, eqn (2) becomes the *diffusion eqn*

$$(3) \qquad u_t = D\nabla^2 u \qquad \vec{x} \in \Omega,\ t > 0$$

With sources present

$$(4) \qquad u_t = D\nabla^2 u + f(\vec{x}, t, u)$$

is a *reaction-diffusion equation*

Remarks on units:

Let M, L, T be mass, time and length.

$$[u] = ML^{-3}$$

$$[u_{xx}] = ML^{-5}$$

Thus since $[u_t] = [D][\nabla^2 u]$ we have

$$[D] = L^2T^{-1}$$

$$[\vec{J}] = ML^{-2}T^{-1}$$

EXAMPLE Heat Eqn (Thermal Transport)

$\vec{T}(\vec{x},t)$ = temperature $[T] = {}^\circ$

$u(\vec{x},t)$ = energy density $[u] = J/m^3$

ρ = medium density $[\rho] = kg/m^3$

C = specific heat $[C] = J/(m\text{-}{}^\circ)$

K = thermal conductivity of medium $[K] = J/(m\,sec\,{}^\circ)$

Most generally $\underline{K}$, C and ρ could depend on $\vec{x}$. For example the medium insular properties could vary.

Empirical (Constituitive) laws

$$u(\vec{x},t) \equiv C\rho\, T(\vec{x},t)$$

$$\vec{J}(x,t) = -\underline{K}\,\vec{\nabla} T$$

in which case

$$C\rho\, T_t = \nabla\cdot(\underline{K}\,\vec{\nabla} T) + f$$

If $C, \rho, \underline{K}$ are constant

$$\frac{\partial T}{\partial t} = D\,\nabla^2 T + F(\vec{x},t,T), \quad \vec{x}\in\Omega$$

is a PDE whose solution yields the spatio temperal variations of temperature

$$D = \frac{\underline{K}}{C\rho} \qquad F = \frac{f}{C\rho}$$

EXAMPLE Advection/Diffusion

$\vec{J}_{Diff} = -D(x)\,\vec{\nabla} u$ Diffusion

$\vec{J}_{Adv} = +\,u\,\vec{v}(\vec{x})$ Advection

where D = diffusivity and $\vec{v}(\vec{x})$ is the velocity of the fluid that u is in.

Conservation of u implies

$$u_t = \vec{\nabla}\cdot(D(x)\vec{\nabla} u) - \vec{\nabla}\cdot(\vec{v}\,u) + f$$

Is a reaction-diffusion-advection eqn.

If D, are constant

$$u_t = D\,\nabla^2 u - \vec{v}\cdot\vec{\nabla} u + f$$

which in one dimensional spatial domain becomes

$$u_t = D\,u_{xx} - v\,u_x + f$$

Remark For diffusion the "−" sign is needed for u to move toward lower concentrations

For advection the "+" sign implies u moves along with the fluid flow

Spatial Models

$$\frac{\partial u}{\partial t} = -\underbrace{\sum_i \vec{\nabla}\cdot\vec{J}_i}_{\text{Sum of assumed fluxes of } u} + \underbrace{\sum_j f_j}_{\text{Sum of sources and sinks}} \quad \Big\}\ \text{conservation law}$$

Must be accompanied by Boundary Conditions

Dirichlet	u known on boundary $\partial\Omega$
Neumann (NO FLUX)	$\frac{\partial u}{\partial n} = 0$ on $\partial\Omega$. Normal derivative $\frac{\partial u}{\partial n} = \vec{\nabla} u \cdot \hat{N}$
Mixed	$u + \alpha \frac{\partial u}{\partial n}$ known on $\partial\Omega$.

EXAMPLE Population Models

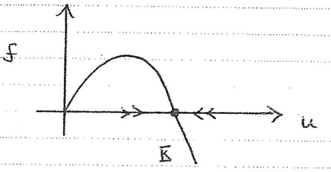
$u(\vec{x},t)$ = population density at $\vec{x} \in \Omega$.

Notion of density works better for bacteria or cells. Could be trees, etc.

Logistic source term

$$f(u) = ru\left(1-\frac{u}{\overline{K}}\right)$$

where $\overline{K}$ = carrying capacity of environment.



Fact $f(u)<0$ for $u>\overline{K}$ meant to reflect death due to overcrowding (competition)

Other source terms

Suppose a substance $c(\vec{x},t)$ is the primary food source.

$$f = f(u,c)$$

may have the generic property $f_c > 0$ to reflect (bacterial) birth rate is higher if c is larger. Perhaps

$$f(u,c) = \kappa \frac{uc}{c+\overline{K}} \qquad \kappa, \overline{K} \in \mathbb{R}$$

Constituitive laws for organism movement

$\vec{J} = -D\vec{\nabla}u$	Diffusive (random)
$\vec{J} = +u\vec{v}$	Advection
$\vec{J} = +\alpha u\vec{\nabla}c$	Chemotaxis
$\vec{J} = +\alpha u\vec{\nabla}T$	Thermotaxis

where $\vec{v}$ = fluid velocity, c = food concentration, T = temperature

Some bacteria are chemotactic. They tend to move toward food.

Slime mold and nematudes are thermotactic

MODEL ONE

$$\frac{\partial u}{\partial t} = D_1\nabla^2 u + f_1(u,c)$$

$$\frac{\partial c}{\partial t} = D_2\nabla^2 c + f_2(u,c)$$

Both organism and food diffuse through homogeneous medium.

$$f_1 > 0 \qquad \frac{\partial f_1}{\partial c} > 0$$

and f_2 reflects a loss of c that u eats.

MODEL TWO (Logistic)

$$\vec{J} = -D\vec{\nabla}u \qquad D \in \mathbb{R}^+ \text{ const.}$$

$$f = ru\left(1-\frac{u}{K}\right)$$

yields in one spatial domain

$$u_t = Du_{xx} + ru\left(1-\frac{u}{K}\right)$$

MODEL THREE (very slow fluid flow)

$$\vec{J}_1 = -D_1\vec{\nabla}u \qquad D \in \mathbb{R}^+ \text{ const}$$

$$\vec{J}_2 = +\alpha u\vec{\nabla}c \qquad \alpha \in \mathbb{R}^+ \text{ const}$$

and certain source terms f_k. Conservation law implies

$$(1) \quad \frac{\partial u}{\partial t} = -\vec{\nabla}\cdot\vec{J}_1 - \vec{\nabla}\cdot\vec{J}_2 + f_1$$

If c merely diffuses we obtain coupled equations for u, c

$$(2) \quad \frac{\partial u}{\partial t} = \underbrace{D_1\nabla^2 u}_{\text{diff}} \underbrace{-\alpha\vec{\nabla}\cdot(u\vec{\nabla}c)}_{\text{chemotaxis}} + f_1$$

$$(3) \quad \frac{\partial c}{\partial t} = D_2\nabla^2 c + f_2$$

For $\Omega \subset \mathbb{R}$ eqn (2) would be

$$u_t = D_1 u_{xx} - \alpha(uc_x)_x + f_1$$

EXAMPLE Electro Diffusion

Charged particles diffuse through a medium having electric field $\vec{E}(\vec{x})$.

$u(\vec{x},t)$ = charge density

Ohmic flux law

$$\vec{J} = z\sigma\vec{E} \qquad z = \text{valence}$$

and σ is conductivity (generally a matrix for anisotropic non homogeneous media)

If the electric field is given by

$$\vec{E} = -\vec{\nabla}\phi$$

where ϕ is the electric potential one obtains

$$\frac{\partial u}{\partial t} = \underbrace{D\nabla^2 u}_{\text{diff}} + \underbrace{z\sigma\nabla^2\phi}_{\text{electric}}$$

The eqn for ϕ is obtained using Maxwell's eqn. Steady state version is

$$0 = D\nabla^2 u + z\sigma\nabla^2\phi$$

$$-\beta u = \nabla^2\phi \qquad (\vec{\nabla}\cdot\vec{E} = 4\pi\rho)$$

for an appropriate constant β

Steady States of PDEs

More generally the steady states $\bar{u}(x)$ of some PDE (system) is a time t independent solution which satisfies all boundary conditions. Stability is a separate condition. By way of example:

$u_t = u_{xx}$	$x \in [0,1]$
$u_x(0,t) = 0$	no flux BC
$u_x(1,t) = 0$	no flux BC
$u(x,0) = f(x)$	initial cond I.C.

Associated problem for steady state $\bar{u}(x)$

$0 = \bar{u}_{xx}$	$x \in [0,1]$
$\bar{u}_x(0) = 0$	no-flux
$\bar{u}_x(1) = 0$	no-flux

This is an ODE problem! The general solution of $\bar{u}_{xx} = 0$ is

$$\bar{u}(x) = Ax + B \qquad A, B \text{ constants}$$

Find A using B.C.

$$\bar{u}'(x) = A$$

$$\bar{u}'(0) = A = 0$$

Hence $$\boxed{\bar{u}(x) = B}$$

This also satisfies the other B.C. $\bar{u}'(1) = 0$. But, we don't know B yet.

Recall that

$$M(t) = \int_0^1 u(x,t)\,dx$$

is the total amount of $u(x,t)$ in the domain $[0,1]$. Since the B.C. are no flux at both endpoints (boundary), $M(t)$ must remain constant. Hence

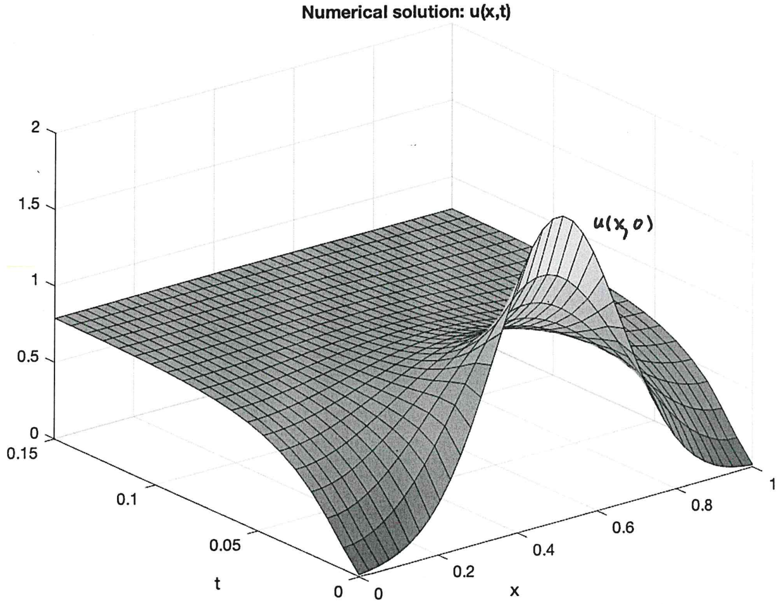
$$M(0) = \int_0^1 \bar{u}(x)\,dx = \int_0^1 u(x,0)\,dx$$

For the initial condition

$$u(x,0) = 2\exp(-(x-\tfrac{1}{2})^2/0.05)$$

we find $\bar{u}(x) = B$ where

$$\boxed{B = \int_0^1 u(x,0)\,dx \simeq 0.79}$$



$u_t = u_{xx}$

$u_x(0,t) = 0$

$u_x(1,t) = 0$

} Both no-flux Boundary Conditions

Ⓐ

```
% Heat equation with Neumann BC on [0,1]
%
function pdex01
m = 0;
x = linspace(0,1,40);
t = linspace(0,0.15,20);
sol = pdepe(m,@pdex1pde,@pdex1ic,@pdex1bc,x,t);
% Extract the first solution component as u.
u = sol(:,:,1);
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% Surface plot of u(x,t)
surf(x,t,u)
title('Numerical solution: u(x,t)')
xlabel('x')
ylabel('t')
% Solution profile u(x,*) at last time.
figure
plot(x,u(end,:))
title('u(x,t) at t = 0.15')
xlabel('x')
ylabel('u(x,0.15)')
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%          Defining the problem (m=0)
%
%   c(x,t,u,u_x) u_t = (f(x,t,u,u_x))_x + s(x,t,u,u_x)
%
function [c,f,s] = pdex1pde(x,t,u,DuDx)
c = 1;
f = 1*DuDx;
s = 0;
%        u(x,0)=u0(x)
%
function u0 = pdex1ic(x)
u0=2*exp(-(x-0.5)^2/(0.05));
%
%       p + q*f = 0           x=xl,xr
%
%  where f is the flux f declared in the PDE above
%
function [pl,ql,pr,qr] = pdex1bc(xl,ul,xr,ur,t)
pl = 0;
ql = 1;
pr = 0;
qr = 1;
```

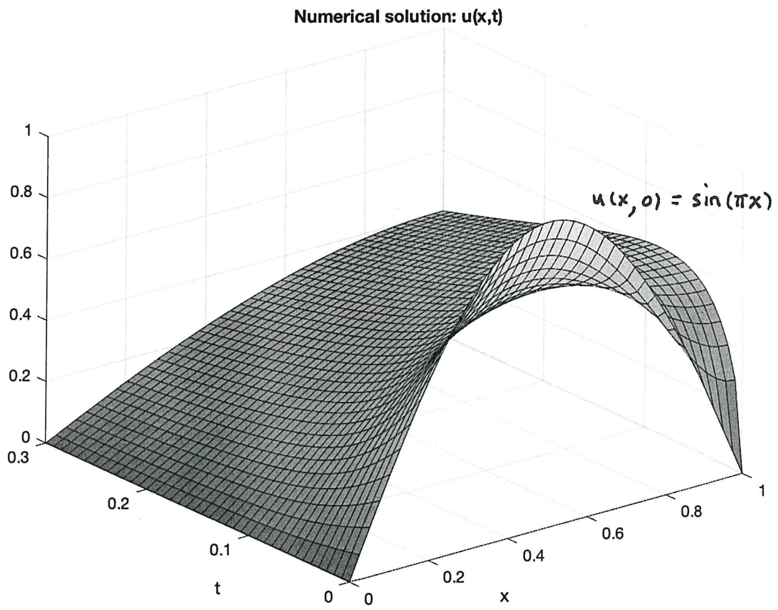
$x \in [0,1]$

$u(x,0) = A \exp(-(x-x_0)^2/\sigma^2)$

$u_x(0,t) = 0$

$u_x(1,t) = 0$

Ⓐ



$u(x,0) = \sin(\pi x)$

$$\boxed{\begin{array}{l} u_t = u_{xx} \\ u(0,t) = 0 \\ u_x(1,t) = 0 \end{array}}$$

Dirichlet B.C.
no-flux B.C.

(B)

```
% Heat equation with Neumann BC on [0,1]
%
function pdex02
m = 0;
x = linspace(0,1,40);
t = linspace(0,0.30,40);
sol = pdepe(m,@pdex1pde,@pdex1ic,@pdex1bc,x,t);
% Extract the first solution component as u.
u = sol(:,:,1);
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% Surface plot of u(x,t)
surf(x,t,u)
title('Numerical solution: u(x,t)')
xlabel('x')
ylabel('t')
% Solution profile u(x,*) at last time.
figure
plot(x,u(end,:))
title('u(x,t) at t = 0.15')
xlabel('x')
ylabel('u(x,0.15)')
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%          Defining the problem (m=0)
%
%   c(x,t,u,u_x) u_t = (f(x,t,u,u_x))_x + s(x,t,u,u_x)
%
function [c,f,s] = pdex1pde(x,t,u,DuDx)
c = 1;
f = 1*DuDx;
s = 0;
%        u(x,0)=u0(x)
%
function u0 = pdex1ic(x)
u0=sin(pi*x);
%
%      p + q*f = 0          x=xl,xr
%
%  where f is the flux f declared in the PDE above
%
function [pl,ql,pr,qr] = pdex1bc(xl,ul,xr,ur,t)
pl = ul;
ql = 0;
pr = 0;
qr = 1;
```

$x \in [0,1]$

$u(x,0) = \sin(\pi x)$

$\}\ u(0,t) = 0$

$\}\ u_x(1,t) = 0$

(B)

EXAMPE Find the steady state of

$u_t = u_{xx}$

$u(0,t) = 0$ Dirichlet

$u_x(1,t) = 0$ Neumann (no-flux)

$u(x,0) = \sin(\pi x)$

Steady state problem

$\bar{u}_{xx} = 0$ $\bar{u}(0) = 0$ $\bar{u}'(1) = 0$

General Soln

$\bar{u}(x) = Ax + B$

Use B.C.

$\bar{u}(0) = B = 0$

$\bar{u}'(1) = A = 0$

Conclude

$\bar{u}(x) = 0$

More on Diffusion

and

Applications

Diffusion

Is a result of random particle motion. which tends to disperse particles throughout the medium. Continuum limits of random walk processes can be used to derive flux formulae. Most common is

$$\vec{J} = -D\vec{\nabla}u \qquad D = \text{diffusivity}$$

Since $\vec{\nabla}u$ is the direction in which concentration u increases most rapidly, particles move <u>down</u> gradient.

$$\vec{J} = -D(x)\vec{\nabla}u \qquad \text{nonhomogeneous isotropic diffusion}$$

$$\vec{J} = -\underline{D}\,\vec{\nabla}u \qquad \underline{D} \in \mathbb{R}^{3\times 3} \text{ yields anisotropic diffusion.}$$

For particles of radius a, viscosity μ

$$D = \frac{kT}{6\pi\mu a} \qquad \text{Einstein formula}$$

Here T = temperature, k = Boltzman· constant

EXAMPLE Reaction Diffusion Equation

$$U + V \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} W \qquad \text{buffering}$$

Law of mass action for source terms.
If buffering sites are immobile then $D_v = D_w = 0$.

Since U allowed to diffuse in cell we arrive at the Rx-Diff system

$$\begin{aligned} u_t &= D_u \nabla^2 u - k_1 uv + k_{-1} w, \qquad x \in \Omega \\ v_t &= -k_1 uv + k_{-1} w \\ w_t &= k_1 uv - k_{-1} w \end{aligned}$$

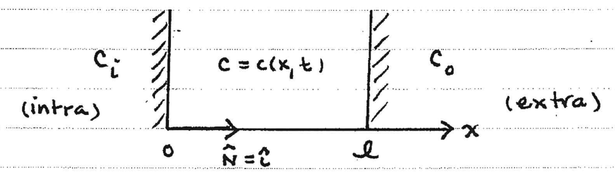
Boundary conditions needed to complete model

$$\vec{u}_t = D\nabla^2\vec{u} + f(\vec{u}) \qquad D = \text{diag}(D_u, 0, 0)$$

A common B.C. for diffusion is "no flux" as in $\vec{J}\cdot\hat{N}|_{\partial\Omega} = 0$ on $\partial\Omega$. For diffusion:

$$\vec{\nabla}u\cdot\hat{N} = \left.\frac{\partial u}{\partial n}\right|_{\partial\Omega} = 0$$

Diffusion thru a membrane (passive)



Diffusion equation for membrane

$$(1) \qquad \frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} \qquad c(0,t) = c_i\,, \quad c(\ell,t) = c_o$$

At equilibrium, $c_t = 0$ implies

$$c(x) = c_i + (c_o - c_i)\left(\frac{x}{\ell}\right)$$

Using $\vec{J} = -D\vec{\nabla}c$, one can compute the steady state flux thru membrane.

$$\boxed{J = \frac{D}{\ell}(c_i - c_o)} \qquad \vec{J} = J\hat{\imath}$$

If $c_i > c_o$ there is a steady flow out.

For cell membranes sometimes called "leaky" channels. Also, no energy is utilized hence passive transport

Facilitated Transport (of Oxygen in Muscle)

$$O_2 + Mb \underset{k_-}{\overset{k_+}{\rightleftarrows}} Mb\,O_2$$

where

		(gmm)
$S = [O_2]$	oxygen	32
$E = [Mb]$	myoglobin	17K
$C = [Mb\,O_2]$	oxymyoglomin	17K

Here E and C are large (intracellular) molecules

Dimensional Reaction Diffusion Equations

$$(1) \qquad S_t = D_s S_{xx} + F \qquad x \in (0,\ell)$$

$$(2) \qquad E_t = D_e E_{xx} + F$$

$$(3) \qquad C_t = D_c C_{xx} - F$$

where ℓ is the membrane thickness.

$$F = k_{-1} C - k_+ S E$$

and the boundary conditions are

$$S(0,t) = S_0' \qquad S(\ell,t) = \beta S_0$$

$$E_x(0,t) = 0 \qquad E_x(\ell,t) = 0$$

$$C_x(0,t) = 0 \qquad C_x(\ell,t) = 0$$

The latter for E, C are "no flux" or Neumann B.C.

Dimensional Analysis

$$\mathcal{S} = s\,\mathcal{S}_0 \qquad E = E_0\, e \qquad \mathcal{C} = E_0\, c$$

$$x = y\,l \qquad t = t_0\,\tau$$

where $t_0 = (k_+ E_0)^{-1}$. Define dimensionless param:

$$\varepsilon = \frac{E_0}{\mathcal{S}_0} \qquad \alpha = \frac{k_-}{k_+ \mathcal{S}_0} \qquad \varepsilon_1 = \frac{D_s}{E_0 k_+ l^2} \qquad \varepsilon_2 = \frac{D_e}{E_0 k_+ l^2}$$

Since $D_e \approx D_c$ (large similar weight molecules)

(4) $s_\tau = \varepsilon_1 s_{yy} + f$ $\qquad s(0,\tau) = 1,\ s(1,\tau) = \beta$

(5) $e_\tau = \varepsilon_2 e_{yy} + \frac{1}{\varepsilon} f$ $\qquad$ Neumann

(6) $c_\tau = \varepsilon_2 c_{yy} - \frac{1}{\varepsilon} f$ $\qquad$ Neumann

and

(7) $f = -se + \alpha c$

Parameter assumptions

(A1) $0 < \varepsilon \ll 1$ $\qquad$ E_0 low relative to $\mathcal{S}_0$

(A2) $\varepsilon_2 \ll \varepsilon_1$ $\qquad$ since large E molecules (move) diffuse more slowly than O_2.

Initial Condition Assumptions

$s(y,0)$ = any fn satisfying B.C. on s

$e(y,0) = 1$ $\qquad$ throughout membrane

$c(y,0) = 0$ $\qquad$ " $\qquad$ "

The latter mimics Michaelis Menten I. Cond.

Conservation of Myoglobin

Total amount of Mb (bound or not) is

$$v = e + c$$

Given (5)-(6), boundary and initial conditions

(8) $v_\tau = \varepsilon_2 v_{yy}$ $\qquad y \in (0,1),\ t > 0$

(9) $v_y(0,t) = v_y(1,t) = 0$ $\qquad \forall t > 0$

(10) $v(y,0) = 1$ $\qquad y \in (0,1)$

The unique solution of (8)-(10) is $v(y,\tau) \equiv 1$

$$e + c = 1 \qquad \forall (y,\tau)$$

Quasi-Steady State

On account $\varepsilon \ll 1$, $\varepsilon_2 \ll 1$ eqn (5) $\Rightarrow$ $f = 0$ at QSS

$$c = \frac{s}{s + \alpha}$$

is dimensionless form of QSS

Dimensional Flux at Equilibrium

$$S_t + C_t = 0$$

Adding (1)-(2) yields

$$D_s S_{xx} + D_e C_{xx} = 0 \qquad x \in (0, \ell)$$

Integrate

(11) $$-J = D_s S_x + D_e C_x$$

where J is the (constant) equilibrium flux.
Integrate (11) over $(0, \ell)$ using B.C.

(12) $$-J\ell = D_s(\beta - 1) S_0 + D_e(C_\ell - C_0)$$

Don't know C_ℓ, C_0 so use QSS approximation in dimensional form

(13) $$C_1 = \left(\frac{E_0}{k_+}\right) \frac{S'}{\underline{K} + S} \qquad \underline{K} \equiv \frac{k_-}{k_+}$$

Since $S_\ell = S(\ell)$, $S_0 = S(0)$ in (13) to get C_ℓ, C_0.

After much algebra (12)-(13) yield flux

$$\boxed{J = \frac{D_s}{\ell} \overbrace{(1 + \mu p)}^{>1} (S_0 - S_\ell) \qquad \text{Facilated Diffusion}}$$

where facilitation factor μp is

$$\mu p = \frac{D_e}{D_s} \frac{\underline{K}}{k_+} \frac{E_0}{(\underline{K} + S_\ell)(\underline{K} + S_0)}$$

Diffusion and Random walks

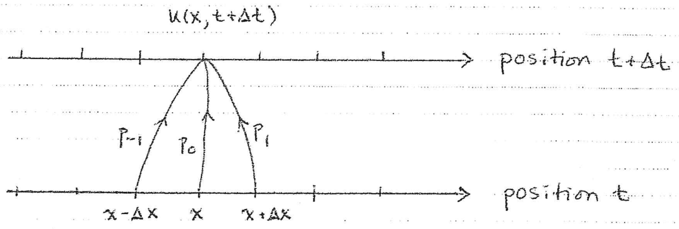
Diffusion can be viewed as the continuum limit of a discrete random walk process.

Let $\underline{X}(t)$ be the random variable for the position of an organism and let $u(x,t)$ be probability density function.

$u(x,t)\Delta x$ = probability organism is located in the interval $(x, x+\Delta x)$ at time t

$$u(x,t)\Delta x = P(x < \underline{X}(t) < x + \Delta x)$$

In a random walk one attributes probabilities to the organisms movement from time t to $t+\Delta t$.



Schematic illustrates a random walk where organism position at x, $t+\Delta t$ could have arisen from organism moving left or right Δx units with probabilties P_1, P_{-1} or remaining stationary with prob p_0.

For such a random walk (assuming independence)

$$u(x, t+\Delta t) = p_{-1}\, u(x-\Delta x, t) + p_0\, u(x,t) + p_1\, u(x+\Delta x, t)$$

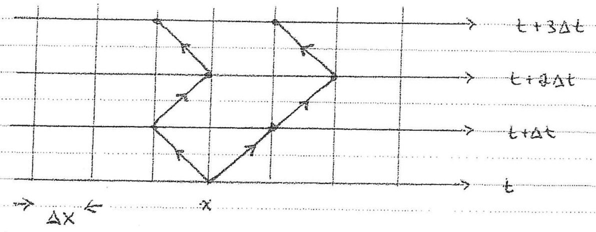
where

$$p_{-1} + p_0 + p_1 = 1$$

As a special case we consider $p = p = \frac{1}{2}$, $p_0 = 0$

$$(1) \qquad u(x, t+\Delta t) = \tfrac{1}{2} u(x-\Delta x, t) + \tfrac{1}{2} u(x+\Delta x, t)$$

Here the organism moves left/right Δx units with equal probability and with certainty moves (doesn't stay a posit. x)



Shows two potential realizations for the random walk.

Continuum Limit ($\Delta x, \Delta t \to 0$)

$$(1) \qquad u(x, t+\Delta t) = \tfrac{1}{2} u(x-\Delta x, t) + \tfrac{1}{2} u(x+\Delta x, t)$$

Seek a PDE that $u(x,t)$ satisfies. Expand each term in a Taylor series about (x,t):

$$u(x, t+\Delta t) = u + u_t \Delta t + \tfrac{1}{2} u_{tt} \Delta t^2 + O(\Delta t^3)$$

$$u(x+\Delta x, t) = u + \Delta x + \tfrac{1}{2} u_{xx} \Delta x^2 + O(\Delta x^3)$$

$$u(x-\Delta x, t) = u - u_x \Delta x + \tfrac{1}{2} u_{xx} \Delta x^2 + O(\Delta x^3)$$

After substituting these into the assumed rule (1) the u terms cancel:

$$(2) \qquad u_t \Delta t + \tfrac{1}{2} u_{tt} \Delta t^2 = \tfrac{1}{2} \Delta x^2 u_{xx} + \text{h.o.t.}$$

where h.o.t. denotes higher order terms. Dividing both sides by Δt and rearranging

$$(3) \qquad u_t = \underset{\substack{\uparrow \\ \text{fix constant}}}{\left(\frac{\Delta x^2}{2\Delta t}\right)} u_{xx} - \tfrac{1}{2} u_{tt} \underset{\substack{\uparrow \\ \text{as } \Delta t \to 0}}{\Delta t} + \text{h.o.t}$$

and we arrive at the <u>diffusion eqn</u> for $u(x,t)$

$$(4) \qquad u_t = D\, u_{xx}$$

where

$$D = \frac{\Delta x^2}{2\Delta t}$$

Earlier we showed that

$$(5) \quad u(x,t) = \frac{1}{\sqrt{4\pi D t}} e^{-x^2/4Dt} \qquad x \in \mathbb{R},\ t > 0$$

was a solution to the diffusion eqn (4). It is readily verified that

$$\int_{\mathbb{R}} u(x,t)\,dx = 1$$

so the fundamental solution in (5) is the probability density function for the random walk. Moreover,

$$P(a < X(t) < b) = \int_a^b u(x,t)\,dx$$

is the probability the organism is in (a,b) at time t.

Connection to concentration

If the "organism" in the preceding discussion is a molecule and Ω contains N such molecules which randomly move (independently) then

$$c(x,t) = N\,u(x,t) = \text{molecular (\#) concentrat.}$$

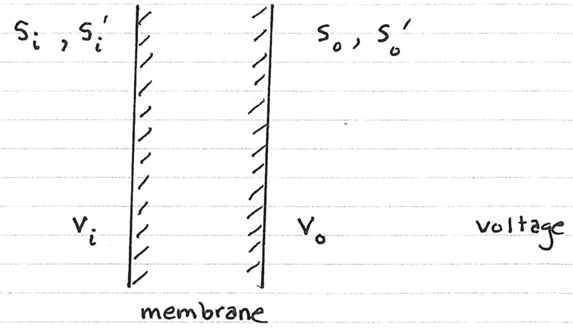
and $c(x,t)$ also satisfies a diffusion equation

$$c_t = D c_{xx}$$

Transmembrane ionic transport

Ionic concentrations inside and outside cells are typically different and as a consequence the electric potential across the membrane is not zero.

Cations (positive) are designated by S.
Anions (negative) are designated by S'.



Remarks

(1) $S = Na^+, K^+, Ca^{2+}$ whereas $S' = Cl^-$

(2) Typically membrane only permeable to S (not S')

(3) If $[S_i] \neq [S_o]$ concentration then this gradient induces a flux of S until the induced potential

$$V = V_i - V_o$$

balances electrodiffusion.

Typical Values (mM)

		intra	extra	
Skeletal Muscle	K^+	150	4.5	→
	Na^+	12	145	←
	Cl^-	4.2	116	←
Squid Axon	K^+	400	20	
	Na^+	50	440	
	Cl^-	40	560	
	Ca^{2+}	0.0003	10	
Generic Mammal	K^+	139	4.5	
	Na^+	15	145	
	Cl^-	20	116	
	Ca^{2+}	< 0.0002	1.8	

Some cells that have electrical behavior:

- muscle
- heart
- neurons
- sensory cells
- endocrine (pancreas, hypothalamus, ..)

Electrodiffusion Summary

1) Planck's Equation for flux of charged particles

$$\vec{J}_\phi = -u \frac{z}{|z|} c \vec{\nabla} \phi$$

where

u = ion mobility
z = ion valence
c = ionic concentration
ϕ = electric potential
$\vec{E} = -\vec{\nabla}\phi$ electric field

2) Einstein Diffusivity

$$D = \frac{uRT}{|z|F} \qquad \frac{RT}{F} = 25.8 \text{mV} \ @ \ 27^\circ C$$

$F = 96485$ Coul/mole, $R = 8.31$ J/mole/°K (Gas Const)

3) Nernst-Planck Electrodiffusion

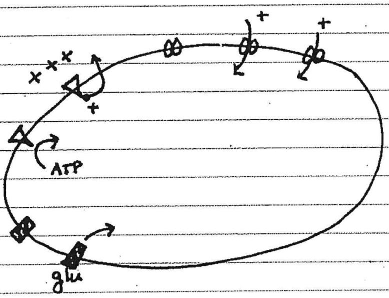
$$\vec{J} = -D \Big(\underset{\substack{\uparrow \\ \text{diffusive} \\ \text{flux}}}{\vec{\nabla} c} + \underset{\substack{\uparrow \\ \text{electro} \\ \text{flux}}}{\frac{zF}{RT} c \vec{\nabla}\phi} \Big)$$

Remark: A low velocity $\vec{v}$ the drag force $\vec{f} = \frac{1}{u}\vec{v}$ where u is the mobility. For a sphere from Nav-Stokes $u = (6\pi\mu a)^{-1}$, μ = viscosity, a = radius. Then

$$D = \frac{kT}{6\pi\mu a} = ukT = \frac{uRT}{|z|F}$$

since $R = N_A k$, $N_A = 6.02 \times 10^{23}$ particles/mole.

Transmembrane transport



membrane is a phospholipid bilayer and is impermeable

●● ion channels (down gradient)

▼ ion pumps (up gradient) - need energy

▮ receptors (non ionic transport)

Cell capacitance

Neutral membrane separates different ionic concentrations (intra, extra cellular). As such, the membrane has a capacitance C typically given in Farads/m^2 of cell surface.

$$C = \frac{k\varepsilon_0}{d}$$

is the capacitance of a plate

k = dielectric constant of media

ε_0 = permitivity of free space

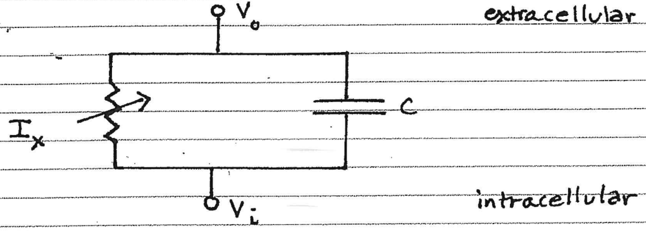
d = plate thickness

Membrane circuit model

For a (plate) capacitor $Q = CV$ where Q is total charge. Thus, capacitive current is

$$I = \frac{dQ}{dt} = C\frac{dV}{dt}$$

Regard whole cell as a circuit



Here I_x is an (sum of) ionic current(s).

Conservation of charge then implies

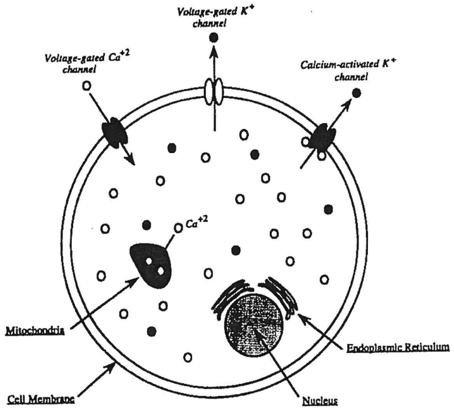
$$\boxed{C\frac{dV}{dt} + I_x = 0}$$

For a given ionic channel (or pump)

$$I_x = g_x(V - V_x)$$

where conductance g_x

Single Cell Models-generic



$$\frac{dv}{dt} = -\sum_X I_X(v,w,\vec{c}) \ , \tag{4}$$

$$\frac{dw}{dt} = \frac{w_\infty(v,\vec{c}) - w}{\tau(v,\vec{c})} \ , \tag{5}$$

$$\frac{d\vec{c}}{dt} = \epsilon \vec{h}(v,w,\vec{c}) \quad , \vec{c} \in \mathbb{R}^K \quad , \tag{6}$$

v = potential across cellular membrane
I_X = membrane ionic current through channels of type X
w = channel activation parameter
$\vec{c}$ = concentrations of agents which regulate the electrical activity

General Single cell model

$$C_m \frac{dV}{dt} = \sum_x I_x(V, \phi, c) + I_a(t)$$

$$\frac{d\phi_i}{dt} = \frac{\phi_{\infty,i}(V) - \phi_i}{\tau_{\phi,i}(V)} \qquad i = 1, 2, \dots N_i$$

$$\frac{dc_j}{dt} = f_j(V, c)$$

where

V = membrane potential
ϕ_i = subunit gating variables
c_j = ionic or chemical concentrations

Broadly

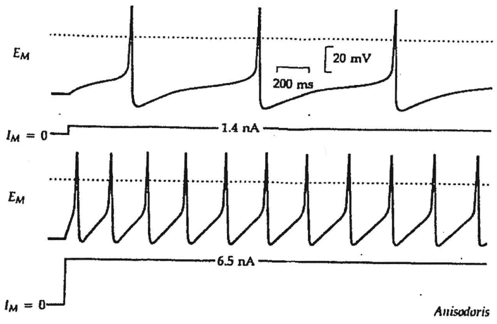
I_x = current thru channel or pump of type X. Ion specific
I_a = experimentally applied current or currents from elsewhere, i.e. coupling, synaptic.
C_m = membrane capacitance

Examples of excitable cells

Cell	Type	Stimulus
Mechanoreceptor	neuron	mechanical
Photoreceptor	neuron	light
Chemoreceptors	neuron	smell
Thermoreceptors	neuron	heat
	neuron	electrical
Muscle		electrical
		mechanical
Pancreas	endocrine	hormone
		electrical
Hippocampal	endocrine	hormone
		electrical

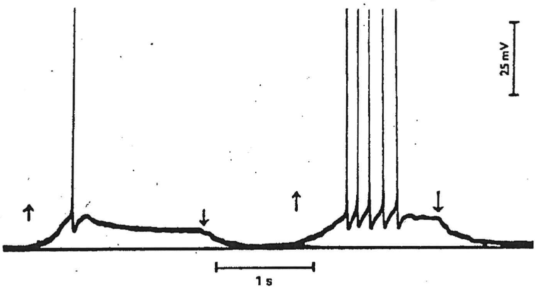
REPETITIVE FIRING OF AN ISOLATED NEURON

(*Anisodoris* neuron, soma electical stimulus) (Seaslug)



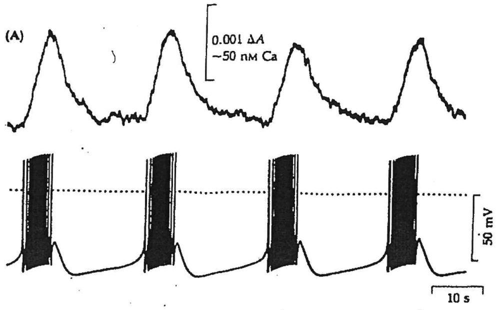
REPETITIVE FIRING OF AN MECHANORECEPTOR NEURON

(*Crayfish* neuron, mechanical (stretching) stimulus)



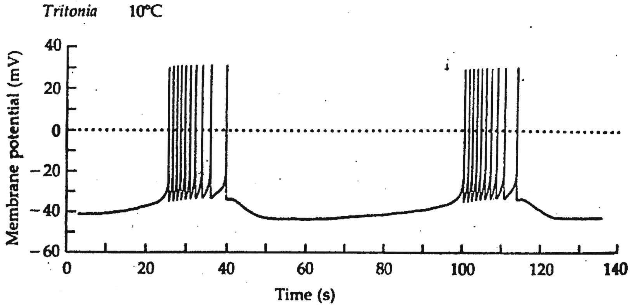
PARABOLIC BURSTING IN A PACEMAKER NEURON

(*Aplysia* neuron, slow calcium oscillations) (snail)



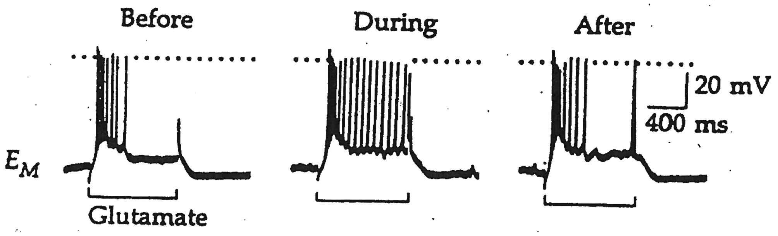
BURSTING IN A PACEMAKER NEURON

(*Tritonia* neuron)



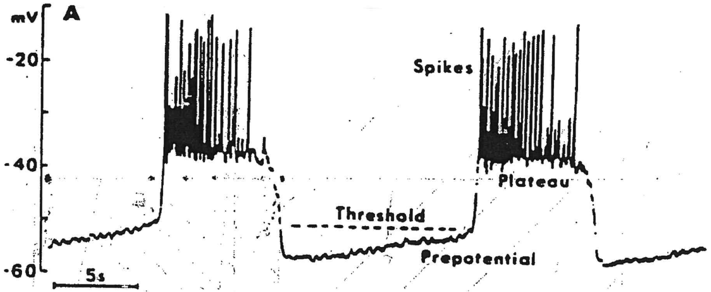
BURSTING INITIATED BY HORMONES

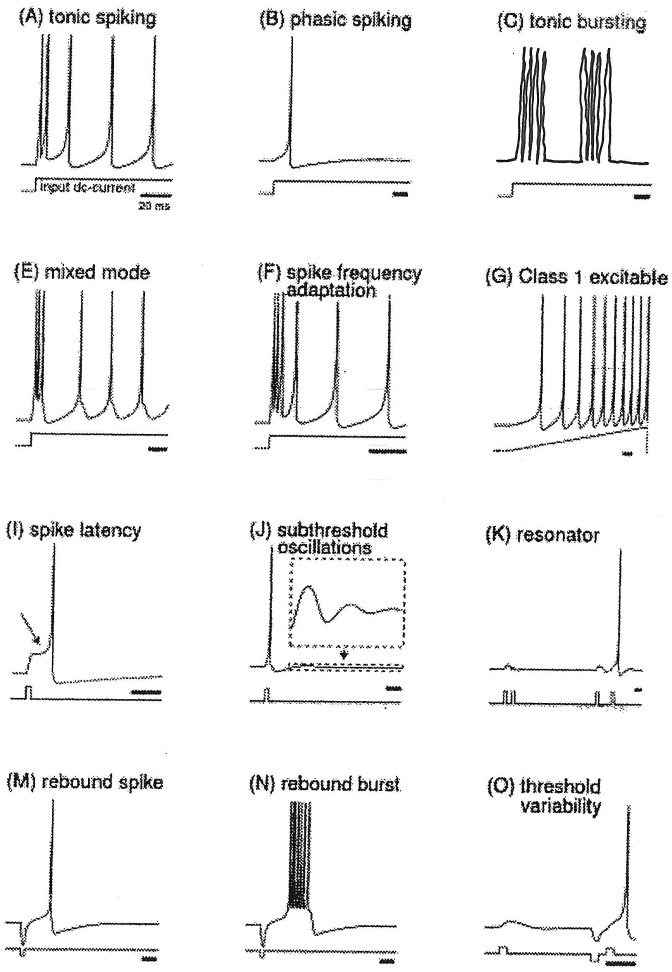
(pyramidal cells in hippocampus, Norepinephrine stimulus)



BURSTING IN PANCREATIC β-CELL

(*mouse* β-cell, glucose stimulus)





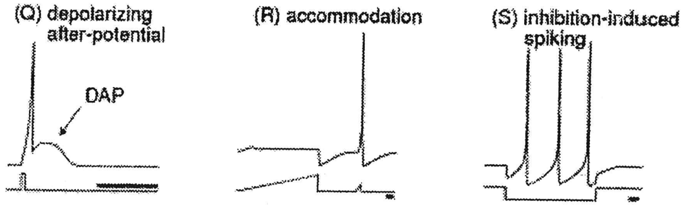


Figure 8.8: Summary of neurocomputational properties exhibited b
see exercise 11. The figure is reproduced, with permission, from w
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Ion pumps versus Ion Channels.

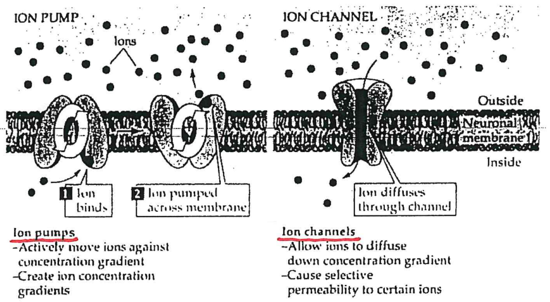
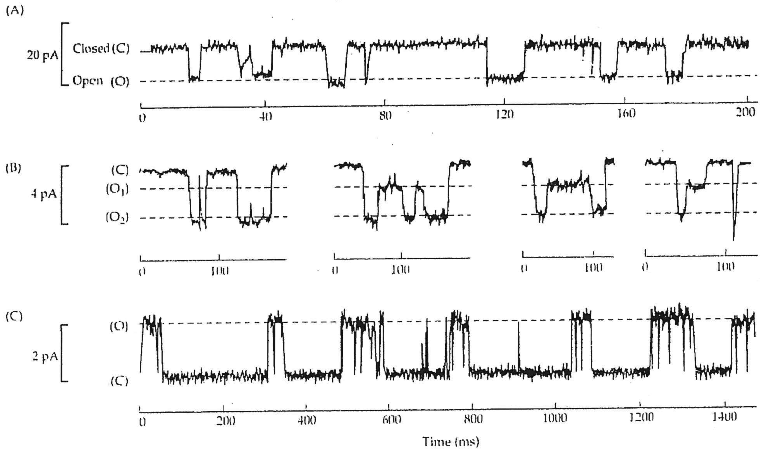
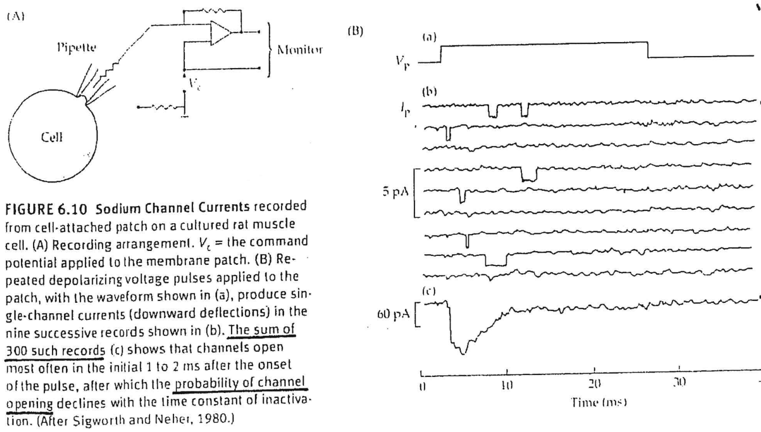


Figure 2.2 Ion pumps and ion channels are responsible for ionic movements across neuronal membranes. Pumps create ion concentration differences by actively transporting ions against their chemical gradients. Channels take advantage of these concentration gradients, allowing selected ions to move, via diffusion, down their chemical gradients.

↓ single channel events





"voltage clamp"

single channel event

probab. open (many chann)

FIGURE 6.10 Sodium Channel Currents recorded from cell-attached patch on a cultured rat muscle cell. (A) Recording arrangement. V_c = the command potential applied to the membrane patch. (B) Repeated depolarizing voltage pulses applied to the patch, with the waveform shown in (a), produce single-channel currents (downward deflections) in the nine successive records shown in (b). The sum of 300 such records (c) shows that channels open most often in the initial 1 to 2 ms after the onset of the pulse, after which the probability of channel opening declines with the time constant of inactivation. (After Sigworth and Neher, 1980.)

Two state K^+ channel

$$C \xrightleftharpoons[\beta]{\alpha} O$$

where C, O are closed and open states. Let

$$n = \text{fraction of open channels}$$

$$1-n = \text{fraction of closed channels}$$

Tacitly assumed number of channels constant.

Law of mass action yields

$$\frac{dn}{dt} = \alpha(V)\underbrace{(1-n)}_{C} - \beta(V)n \tag{1}$$

We assume the rates depend on Voltage. Can rewrite (1) as

$$\frac{dn}{dt} = \frac{n_\infty(V) - n}{\tau_n(V)} \tag{2}$$

for

$$n_\infty(V) = \frac{\alpha}{\alpha+\beta} \qquad \tau_n(V) = \frac{1}{\alpha+\beta}$$

Thus a Nernst current with conductance g_K for ion K^+ might be

$$I_K = \bar{g}_K n\,(V - V_K) \tag{3}$$

where $\bar{g}_K$ is the maximal conductance.

Multiple subunit models

- each unit is closed or open
- all units must be open for ions to flow

Two unit model

$$S_{ij} = \text{state of two units}$$

Here $i,j \in \{0,1\}$, where 0 denotes closed

Assume S_{01} and S_{10} states identical. Hence reaction equations are:

$$S_0 \xrightleftharpoons[\beta]{2\alpha} S_1 \xrightleftharpoons[2\beta]{\alpha} S_2 \qquad S_1 \equiv S_{10} + S_{01}$$

Let

$$x_i = \text{fraction of channels in state } S_i$$

Resulting differential equations

$$\dot{x}_0 = \beta x_1 - 2\alpha x_0$$

$$\dot{x}_1 = -\dot{x}_0 - \dot{x}_2$$

$$\dot{x}_2 = \alpha x_1 - 2\beta x_2$$

and chennels are conserved

$$x_0 + x_1 + x_2 = 1 \tag{1}$$

Using conservation of channels

(2) $\dot{x}_0 = f(x_0, x_2) = \beta(1 - x_0 - x_2) - 2\alpha x_0$

(3) $\dot{x}_2 = g(x_0, x_2) = \alpha(1 - x_0 - x_2) - 2\beta x_2$

Nonhomogeneous, linear, planar system.

If we define n to be solution of

$$\frac{dn}{dt} = \alpha(1-n) - \beta n$$

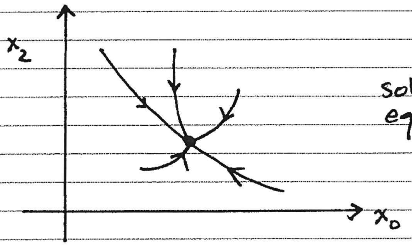
then

$$x_0 = (1-n)^2$$

$$x_1 = 2n(1-n)$$

$$x_2 = n^2$$

solves (1)-(3). Such a solution in (x_0, x_2)-plane



sole stable equilibria.

Linearization about this solution

$$x_0 = (1-n)^2 + y_0$$

$$x_2 = n^2 + y_2$$

yields

$$\dot{y}_0 = -2\alpha y_0 - \beta(y_0 + y_2)$$

$$\dot{y}_2 = -\alpha(y_0 + y_2) - 2\beta y_2$$

which is homogeneous linear system with eigenvalues

$$\lambda_1 = -(\alpha+\beta) \qquad \lambda_2 = -2(\alpha+\beta)$$

Since $\lambda_k < 0$ we conclude

$$\boxed{\begin{aligned} x_0 &= (1-n)^2 \\ x_2 &= n^2 \end{aligned}}$$

Stable
Invariant
Manifold

Remarks

(1) n = "probability" that each unit open

(2) Current model for two subunits

$$I_K = \bar{g}_K n^2 (V - V_K)$$

where $\bar{g}_K$ = maximal conductance.

(3) For k subunits get n^k term

Na^+ multi unit channel model (sketch)

S_{ij} = i open m type subunits and j open h type subunits

Assume 2-m type and 1-h type subunits.

$$\begin{tikzcd}
S_{00} \arrow[r, shift left, "2\alpha"] \arrow[d, shift right, "\gamma"'] & S_{10} \arrow[l, shift left, "\beta"] \arrow[r, shift left, "\alpha"] \arrow[d, shift right, "\gamma"'] & S_{20} \arrow[l, shift left, "2\beta"] \arrow[d, shift right, "\gamma"'] \\
S_{01} \arrow[u, shift right, "\delta"'] \arrow[r, shift left, "2\alpha"] & S_{11} \arrow[u, shift right, "\delta"'] \arrow[l, shift left, "\beta"] \arrow[r, shift left, "2\alpha"] & S_{21} \arrow[u, shift right, "\delta"'] \arrow[l, shift left, "\beta"]
\end{tikzcd}$$

Only S_{21} state allows ions thru

$$\left.\begin{aligned}
&(1) \quad x_{21} = m^2 h \\
&(2) \quad \dot{m} = \alpha(1-m) - \beta m \\
&(3) \quad \dot{h} = \gamma(1-h) - \delta h
\end{aligned}\right\} \text{manifold defined here is stable}$$

Other states

$$\begin{aligned}
x_{00} &= (1-m)^2(1-h) \\
x_{01} &= (1-m)^2 h \\
x_{10} &= 2m(1-m)(1-h) \\
x_{20} &= m^2(1-h) \\
x_{11} &= 2m(1-m)h
\end{aligned}$$

Resulting current I_{Na} given by

$$I_{Na} = \bar{g}_{Na}\, m^2 h\, (V - V_{Na})$$

where m, h satisfy (2)-(3).