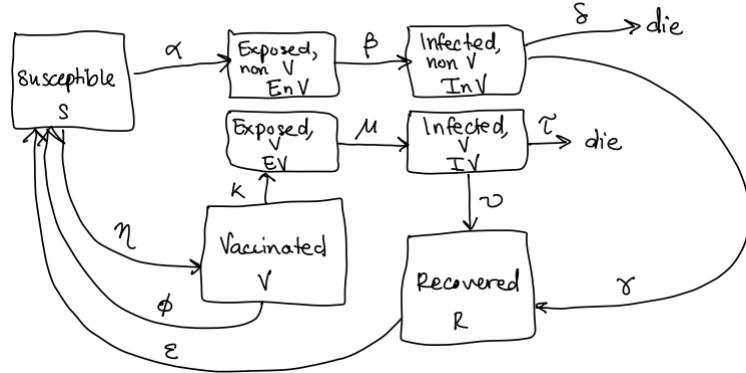


# Math biology

compartment model: SIR

S to I have rate  $\alpha$  (different variances have different  $\alpha$ )



$P_{\Delta t}$  p of moving out of S

discrete:

$$S(t + \Delta t) = S(t) - P_{\Delta t}S(t); S(t + \Delta t) - S(t) = -P_{\Delta t}S(t)$$

$$S_{n+1} = (1 - P_{\Delta t})S_n; S_{n+1} = (1 - P_{\Delta t})^n S_0$$

continuous:

$$dS/dt = -\omega S(t); S(t) = S_0 e^{-\omega t}$$

D,C model in here are close to each other. sometimes they are not.

## Discrete time model

$X_n$  is the population size of time step n.

general form(recursive model):  $X_{n+1} = f(X_n)$

$\{x_0, x_1, \dots\}$  called orbit

### Discrete logistic model

time-homogenous discrete dynamical system:

we will talk about  $x_{n+1} = f(x_n)$ . it is time-homogenous, because  $f(x)$  is the same regardless of time.

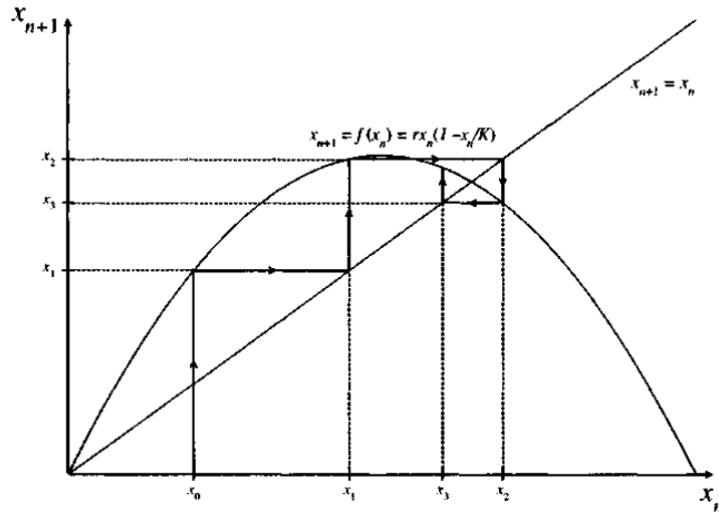
$x_n$  is governed without any randomness(stochastics) or noise allowed.

$x_{n+1} = x_n + k(N - x_n)x_n$ , N is the carrying capacity, k reproductive rate.

$$x_{n+1} = (1 + kN)[1 - \frac{x_n}{(1+kN)/kN}]x_n. 1 + kN = r; (1 + kN)/kN = K.$$

$x_{n+1} = r(1 - x_n/K)x_n$ . let  $r=2.8$ ,  $K=1$ , state space  $S = [0, 1]$ .

Plot  $x_n, x_{n+1}$ :

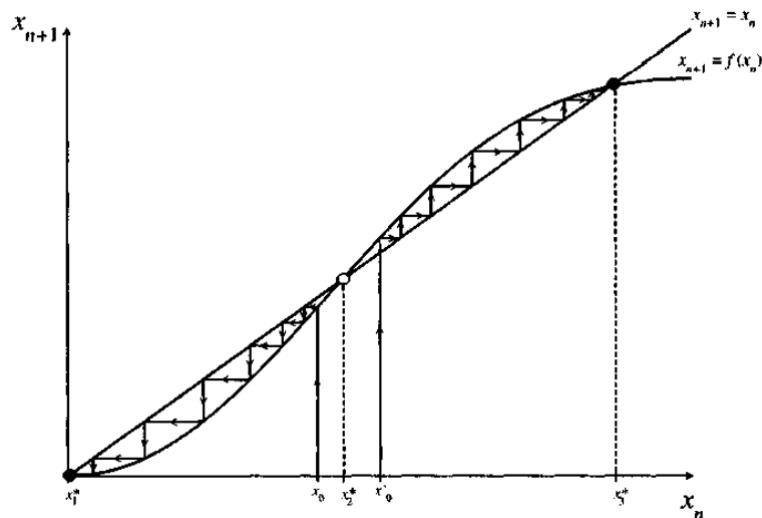


$f(x^*) = x^*$ ,  $x^*$  is a fixed point.  $x = 0$  is a trivial fix point.

if  $x_0 \in S$ ,  $|x_0 - x_1^*| = x_0 < \delta$ , then we "drift away" from  $x_1^* = 0$  toward  $x_2^*$ .

if  $x_0 \in S$ ,  $|x_0 - x_2^*| < \eta$ , then we stay closed to non trivial fix point.

for model with three fix points:



we can see there are stable fixed points and unstable fixed points.

observe that slope of  $f(x_n)$  at stable fix points  $< 1$ . at unstable fix points  $> 1$ .

linear stability analysis.

$$x_n = x^* + y_n; x^* + y_{n+1} = f(x^* + y_n)$$

$$x^* + y_{n+1} = f(x^*) + f'(x^*)y_n + R_2(y_n)$$

$$y_{n+1} \approx y_n f'(x^*) = \lambda y_n$$

$$y_n = \lambda^n y_0$$

**Theorem 2.1.** Let  $x^*$  be a fixed point of  $x_{n+1} = f(x_n)$ . Then,

- $x^*$  is stable when  $|f'(x^*)| < 1$ ;
- $x^*$  is unstable when  $|f'(x^*)| > 1$ ;
- there is no conclusion about the stability of  $x^*$  when  $|f'(x^*)| = 1$ .

### Analysis of discrete logistic equation

suppose  $\tilde{x}_n = x_n/K$  and  $r \in [0, 4]$  (to make sure  $x \in [0, 1]$ ).

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

if  $f(f(x_0)) = x_0$ , but  $f(x_0) \neq x_0$ , this is a periodic orbit of 2.  $x_0$  is a fixed point of second iterate map of  $f^2$ .

fixed point of logistic equation is  $x^* = 0, \frac{r-1}{r}; r > 1$

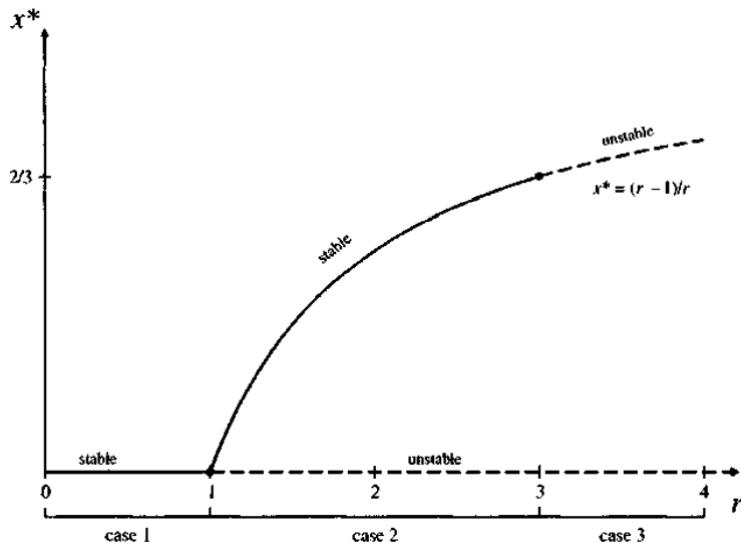
if  $x^*$  is stable fixed point, we need  $f'(x) = r - 2rx < 1$

for trivial fixed point  $x^* = 0, r \in [0, 1)$ , stable.  $r \in (1, 4]$  unstable

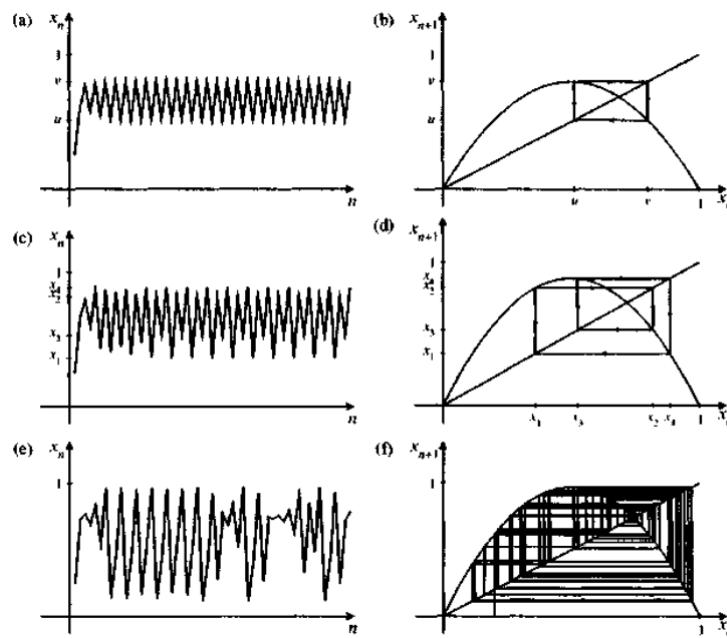
for fixed point  $x^* = \frac{r-1}{r}, r \in (1, 3)$ , stable.  $r \in (3, 4]$  unstable

### bifurcation diagram

observe qualitative change in the behavior of the dynamical system.



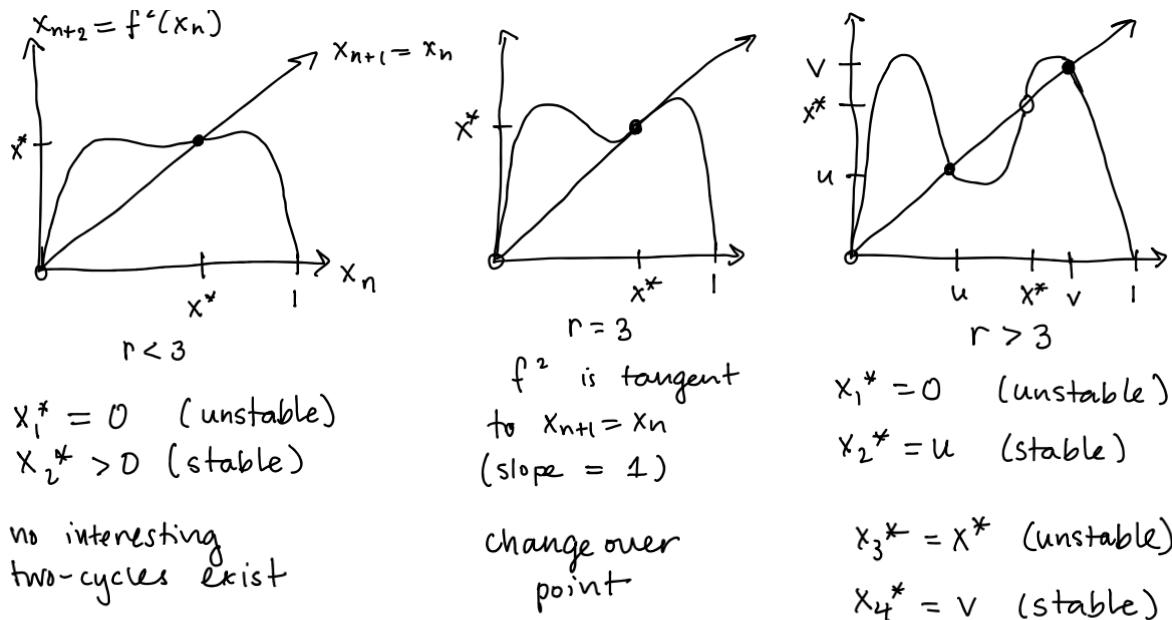
A couple of periodic orbits appear:



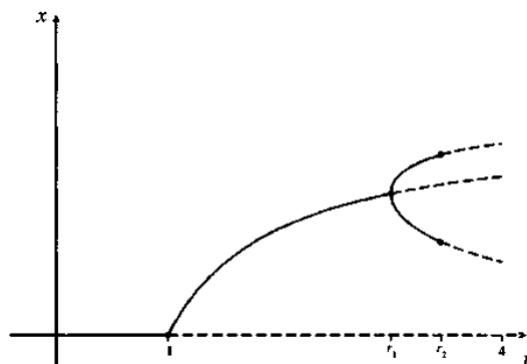
Global (Asymptotic) stability:  $\forall x_0 \in S; f^n(x_0) \rightarrow x^*$ .

draw higher order bifurcation:

$$f^2(x) = r(rx_n(1-x_n))(1-rx_n(1-x_n))$$



$3 < r < 1 + \sqrt{6}$ : 2-cycle stable ;  $r > 1 + \sqrt{6}$  unstable and a 4-cycle arises.



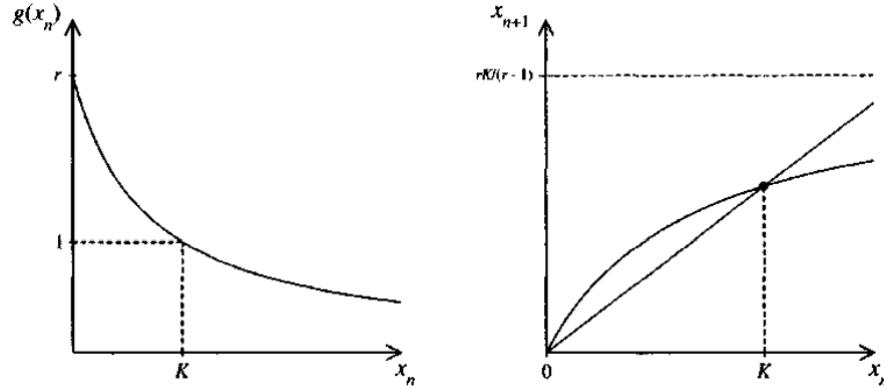
## Alternatives to discrete logistic eqn

### general growth model

$x_{n+1} = g(x_n)x_n$ .  $g(x_n)$ : growth term; if the growth term does not depend on  $x_n$  it is called density-independent. special cases:  $g(x_n) = r$ ;  $g(x_n) = r(1 - x_n)$

### Beverton-Holt model

$$x_{n+1} = f(x_n) = \frac{r}{1+(r-1)x_n/K}x_n = g(x_n)x_n$$



fixed points and stability(derivative = 0):  $x_1^* = 0, f'(0) = r$ ;  $x_2^* = K, f'(K) = 1/r$

$0 < r < 1, x_1^* = 0$  stable;  $x_2^* = K$  unstable     $1 < r, x_1^* = 0$  unstable;  $x_2^* = K$  stable

### Ricker Model

$$x_{n+1} = \exp(r(1 - \frac{x_n}{K}))x_n; r > 0$$

think of this as  $\exp(r)$  constant ;  $\exp(-\frac{rx_n}{K})$  density-dependent mortality factor.

fixed points  $x_1^* = 0, x_2^* = K$

$$f' = \exp(r(1 - x/K))(1 - \frac{rx}{K})$$

$$f'(0) = e^r; f'(K) = 1 - r$$

$x_0^*$  unstable;  $x_1^*$  is global stable for  $0 < r < 2$ , unstable for  $r > 2$

## Models in population genetics

### some terminologies

two sets of chromosomes. Chromosomes contain genes. Due to mutations, a gene can exist in different forms, or alleles. genotypes is allelic composition: WW,Ww,ww. Individuals with WW or ww are called homozygous; those with Ww are called heterozygous. The trait of genotype is phenotypes. W is called dominant, w is called recessive.

Let  $p_n, q_n$  be relative frequency of W,w allele in population at time n.  $\frac{\#W}{\#W + \#w}$

### The Hardy-Weinberg Law

assumption: no mutation; mating is random; no selection pressure; freq is equal for both sexes

Punnett square

			Mother	
	W p <sub>n</sub>		w 1 - p <sub>n</sub>	
	W p <sub>n</sub>	p <sub>n</sub> <sup>2</sup>	p <sub>n</sub> (1 - p <sub>n</sub> )	
Father	w 1 - p <sub>n</sub>	p <sub>n</sub> (1 - p <sub>n</sub> )	(1 - p <sub>n</sub> ) <sup>2</sup>	

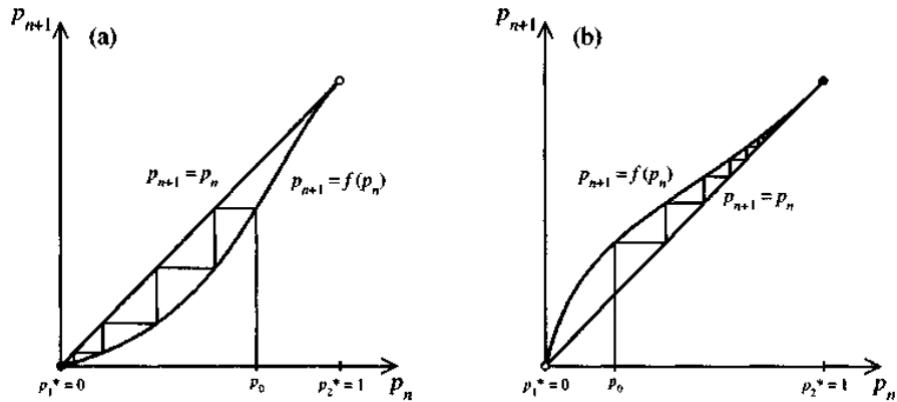
$$p_{n+1} = \frac{p_n^2 + 1/2 * 2 * p_n(1 - p_n)}{p_n^2 + 2 * p_n(1 - p_n) + (1 - p_n)^2} = p_n$$

### selection in a population

$\alpha, \gamma$  be the fraction of white-winged, black-winged moths surviving to produce the next generation.

$$p_{n+1} = \frac{\alpha p_n^2 + 1/2 * \alpha * 2 * p_n(1 - p_n)}{\alpha p_n^2 + 2 * \alpha p_n(1 - p_n) + \gamma(1 - p_n)^2} = \frac{\alpha p_n}{(\gamma - \alpha)p_n^2 - 2(\gamma - \alpha)p_n + \gamma}$$

fixed point  $p_1^* = 0$  all black moths.  $p_2^* = 1$  all white moths



$\alpha < \gamma; p_1^* = 0$  stable ;  $\alpha > \gamma; p_2^* = 1$  stable

### selection in a population with three phenotypes

WW white, Ww grey, ww black;  $\alpha, \beta, \gamma$

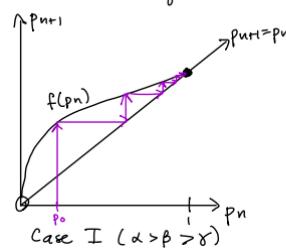
$$p_{n+1} = \frac{\alpha p_n^2 + 1/2 * \beta * 2 * p_n(1 - p_n)}{\alpha p_n^2 + 2 * \beta p_n(1 - p_n) + \gamma(1 - p_n)^2} = \frac{(\alpha - \beta)p_n^2 + \beta p_n}{(\alpha + \gamma - 2\beta)p_n^2 + 2(\beta - \gamma)p_n + \gamma}$$

$p_1^* = 0, p_2^* = 1, p_3^* = \frac{\gamma - \beta}{\alpha + \gamma - 2\beta}; p_3^* \text{ exist when } \beta < \alpha, \gamma || \beta > \alpha, \gamma$

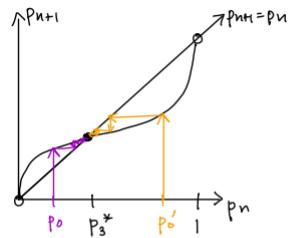
$$f'(p_1^*) = \frac{\beta}{\gamma}; f'(p_2^*) = \frac{\beta}{\alpha}; f'(p_3^*) = \frac{\alpha\beta - 2\alpha\gamma + \beta\gamma}{\alpha\gamma - \beta^2}$$

Case	Model parameter	Fixed points and stability	Long-term behavior	Biological interpretation
I	$\alpha > \beta > \gamma$	0 is unstable 1 is stable	$p \rightarrow 1$	White-winged moths have the selective advantage and black-winged moths have the selective disadvantage; w allele becomes extinct; all moths will have genotype WW (white-winged).
II	$\alpha < \beta < \gamma$	0 is stable 1 is unstable	$p \rightarrow 0$	Black-winged moths have the selective advantage and white-winged moths have the selective disadvantage; W allele becomes extinct; all moths will have genotype ww (black-winged).
III	$\beta > \gamma > \alpha$ or $\beta > \alpha > \gamma$	0 is unstable 1 is unstable $p_3^*$ is stable	$p \rightarrow p_3^*$	Gray-winged moths have the selective advantage; both W and w alleles remain in the population, and their frequencies reach an equilibrium; all genotypes coexist.
IV	$\beta < \gamma < \alpha$ or $\beta < \alpha < \gamma$	0 is stable 1 is stable $p_3^*$ is unstable	$p \rightarrow 0$ or $p \rightarrow 1$	Gray-winged moths have the selective disadvantage; either the W or the w allele becomes extinct; all moths will have either genotype WW or ww (white-winged or black-winged).

let's look at qualitative behavior:



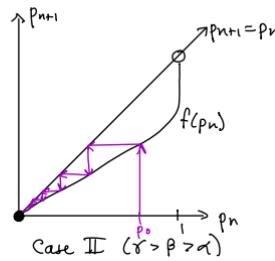
Long term: w goes extinct



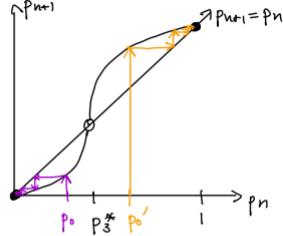
Case II ( $\gamma > \beta > \alpha$ )

Long-term:  $p_3^*$  stable

See de Vries Fig. 2.18



Long term: W goes extinct



Case IV ( $\beta < \alpha, \beta < \gamma$ )

Long term: bistability — one fixed point is approached depending on initial cond.

## Bivariate discrete time system

model  $(x_n, y_n)$  or  $X^n = (x_1^n, \dots, x_d^n)$ .

$$X^{n+1} = f(X^n); f(X^n) = (f_1(X^n), f_2(X^n));$$

Linear stability analysis in 2D. (perturbation analysis)

$$X^{n+1} = \begin{pmatrix} x^* + \delta_n \\ y^* + \epsilon_n \end{pmatrix} = f(X^n), \text{ use Taylor expansion:}$$

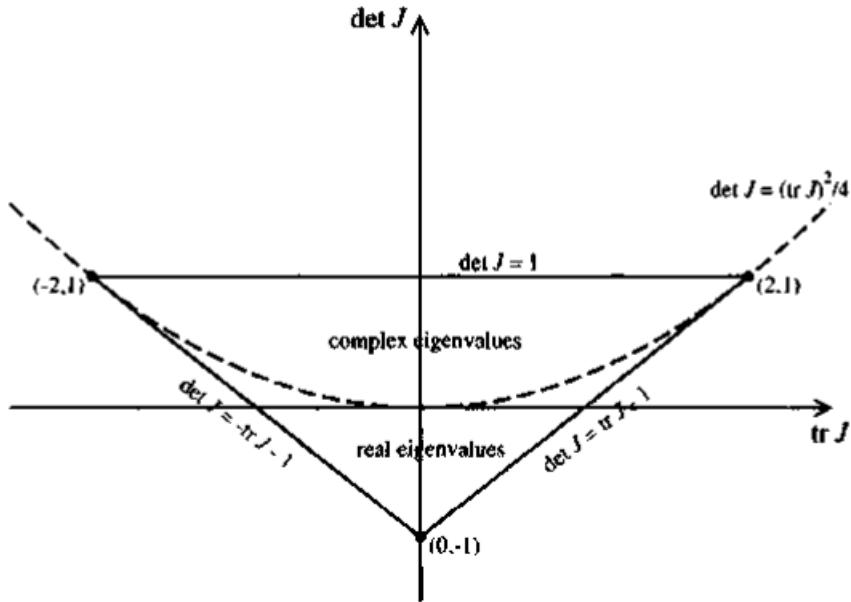
fixed if eigenvalues of Jacobian are both less than 1

thm: for n dimension twice differentiable, a fixed point is stable if all  $\lambda(J(x^*)) < 1$ .

In practice we do not need to cal eval, can use Jury condition:

Jury condition(2D)

$$|tr(J)| < 1 + |J| < 2 \iff \text{specturm less than 1}$$



### Growth of rabbit population

assumptions: time discrete in month, no death, rabbit pair produce a new pair after 2 month.

$a_n$  : month-old pairs;  $b_n$  :  $\geq 2$  month-old pairs.

$$a_{n+1} = b_n; a_0 = 1; b_{n+1} = b_n + a_n; b_0 = 0$$

$$(a^*, b^*) = (0, 0), J = \begin{pmatrix} 0 & 1 \\ 1 & 1 \end{pmatrix}, \lambda = \phi, \phi - 1, \text{not stable.}$$

plot:  $(X_1 \text{ or } X_2, n)$ ; phase plot:  $(X_1, X_2)$

### Host parasite

$H_n$  host population;  $P_n$  parasite population;  $f(H_n, P_n)$  fraction of host pop not parasitized.  
 $1 - f(H_n, P_n)$  fraction of host pop parasitized.

host population grows geometrically in the absence of parasitoids  $k > 1$ .

avg num of eggs laid in a single host that give rise to adult parasitoids is  $c$ .

$$H_{n+1} = kfH_n; P_{n+1} = c(1 - f)H_n;$$

host/parasite encounters is random and independent. # of encounters proportional to  $H_n P_n$  (law of mass action)

avg # encounters  $v = aH_n P_n / H_n = aP_n$ ,  $a$  means search efficiency of parasite.

$p(i)$  the probability host has  $i$  encounters.

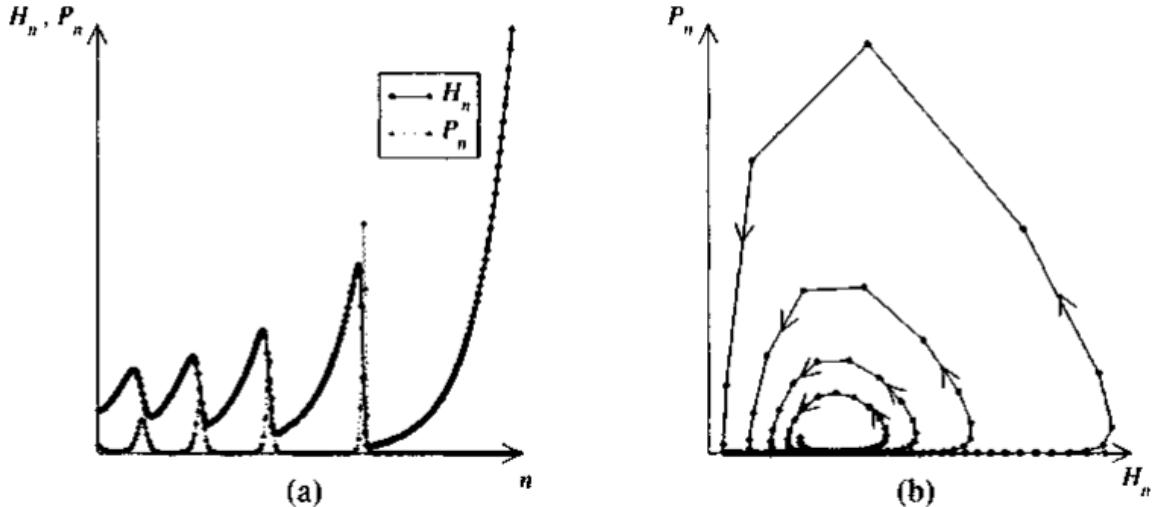
$$p(i) = \frac{v^i e^{-v}}{i!}, f = p(0) = e^{-v} = e^{aP_n}$$

Then we have Nicholson and Bailey's model:

$$H_{n+1} = kH_n e^{-aP_n}; P_{n+1} = cH_n (1 - e^{-aP_n})$$

$$(H_1^*, P_1^*) = (0, 0); (H_2^*, P_2^*) = \left(\frac{klnk}{ac(k-1)}, \frac{lnk}{a}\right)$$

$$J = \begin{pmatrix} ke^{ap} & -akhe^{-ap} \\ c(1 - e^{-ap}) & ace^{-ap} \end{pmatrix}, J_2 = \begin{pmatrix} 1 & -\frac{klnk}{c(k-1)} \\ \frac{c(k-1)}{k} & \frac{lnk}{k-1} \end{pmatrix}, \text{unstable.}$$



Beddington model add carrying capacity, and it has a stable fixed point.

## ODE

$$\vec{\gamma}: R \rightarrow R^d, \gamma \text{ is a curve or } \gamma(t). \vec{\gamma}(t)' = \begin{pmatrix} \gamma'_1(t) \\ \gamma'_2(t) \\ \dots \end{pmatrix}$$

ODE is an equation of form:  $\vec{\gamma}'(t) = \vec{f}(t, \gamma(t))$ ;  $\vec{f}(t, x) : R \setminus \text{cross} R^d \rightarrow R^d$

(the variable does not need to be t, it can be any variable or variables (a vector of variables). In biology usual is with respect to t)

no separate time dependence ODE are called autonomous or time-homogeneous:

$$\vec{\gamma}'(t) = \vec{f}(\gamma(t))$$

with  $\vec{x}(t_0) = \vec{x}_0$ , we say  $x(t)$  is the trajectory with IC(if  $t_0 = 0$ , is the trajectory starting at  $\vec{x}_0$ )

Lipschitz in spatial variable or satisfies a Lipschitz condition means  $\exists L$ , s.t.

$$\forall (t, \vec{x}), (t, \vec{y}) \in \text{dom}(f), \|\vec{f}(t, \vec{x}) - \vec{f}(t, \vec{y})\|_2 \leq M \|\vec{x} - \vec{y}\|_2$$

$$\text{IVP: } \begin{cases} \gamma'(t) = f(t, \gamma(t)) \\ \gamma(t_0) = x_0 \end{cases}; \text{ solution to IVP is a differentiable curve.}$$

Thm: consider initial value problem(IVP): suppose  $\vec{f}$  satisfies a Lipschitz condition then  $\exists!$  solution to the IVP on some open interval I which contains  $t_0$ .

If x is one dimensional scalar equation:  $x'(t) = \dot{x}(t) = f(t, x(t))$

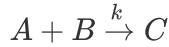
Consider first order(1st derivative in time only) linear, with constant coefficients ODE(planar system):

$$\dot{x}(t) = A \begin{pmatrix} x_1(t) \\ x_2(t) \end{pmatrix}$$

if A is diagonal it is called decoupled system.

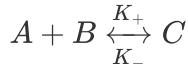
## reaction kinetics, scalar ODE example

**irreversible process:**



law of mass:  $\dot{[C]} = k[A][B]$ , change of concentration of C is proportional to concentration of AB.

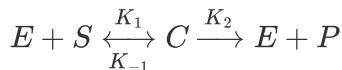
**reversible process:**



$$\begin{cases} \dot{c} = k_+ab - k_-c \\ \dot{a} = k_-c - k_+ab \quad k_+ab \text{ is added to } c; k_-c \text{ is break down of } c. \\ \dot{b} = k_-c - k_+ab \end{cases}$$

### Michaelis-Menten Kinetics

for enzymatic reaction:



$$\begin{cases} \dot{s} = -k_1se + k_{-1}c \\ \dot{e} = -k_1se + k_{-1}c + k_2c \\ \dot{c} = k_1se - k_{-1}c - k_2c \\ \dot{p} = k_2c \end{cases}$$

## stability

for autonomous ODE  $\dot{\vec{x}}(t) = \vec{f}(\vec{x}(t))$ ,  $x^*$  is a fixed point if  $\dot{x} = f(x^*) = 0$ .

$x^*$  is stable: If  $\|x_0 - x^*\| < \delta$ , the trajectory  $x(t)$  with IC  $x_0$  satisfies  $\|x(t) - x^*\| < \epsilon$

If in addition to the prev,  $\lim_{t \rightarrow \infty} \|x(t) - x^*\| = 0$ , then  $x^*$  is asymptotically stable.

two ways to find stable points. 1, phase line(phase plane) analysis: check  $f(x) > 0 | f(x) < 0$  for  $x$  around  $x^*$ .

2, vector field

## 2D system Linear system

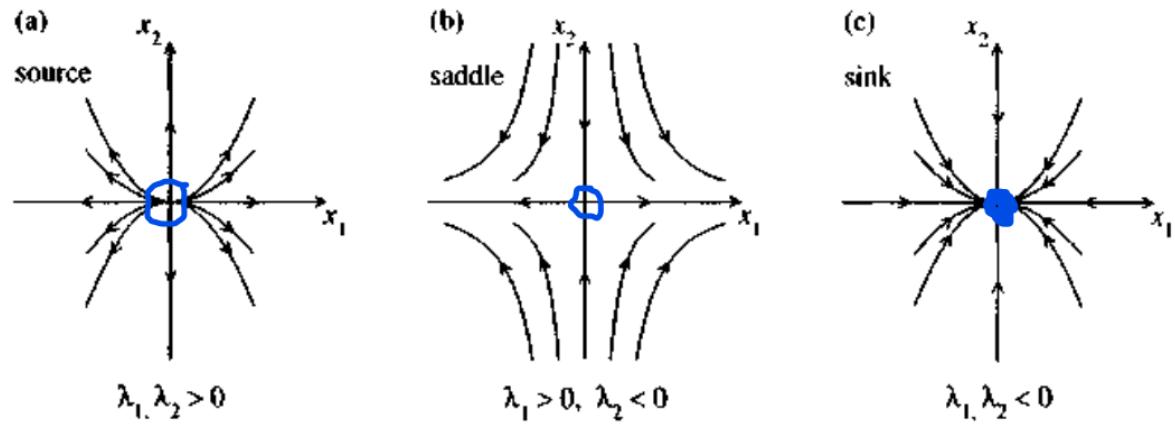
**decoupled planar system:**

$\dot{x}(t) = Ax$ , A is diagonal.  $(0, 0)$  is a unique fixed point, examine its trajectory near 0:

$$\begin{pmatrix} x_1(t) \\ x_2(t) \end{pmatrix} = \begin{pmatrix} e^{a_{11}t} & 0 \\ 0 & e^{a_{22}t} \end{pmatrix} \begin{pmatrix} x_1(0) \\ x_2(0) \end{pmatrix}, \|x(t)\|^2 = (e^{a_{11}t}x_1(0))^2 + (e^{a_{22}t}x_2(0))^2 \text{ if we are around } (0, 0)$$

grow if  $a_{11}|a_{22} > 0$ , origin is a source; decay if  $a_{11}, a_{22} < 0$ , origin is a sink; otherwise, origin is a saddle

## phase portrait



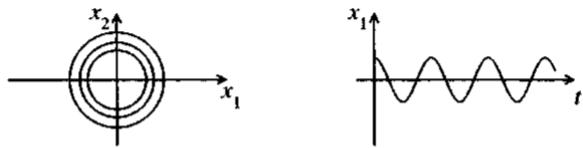
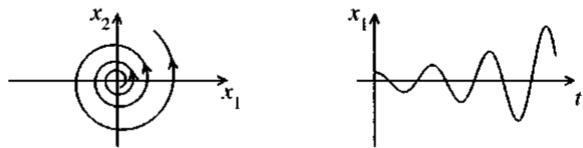
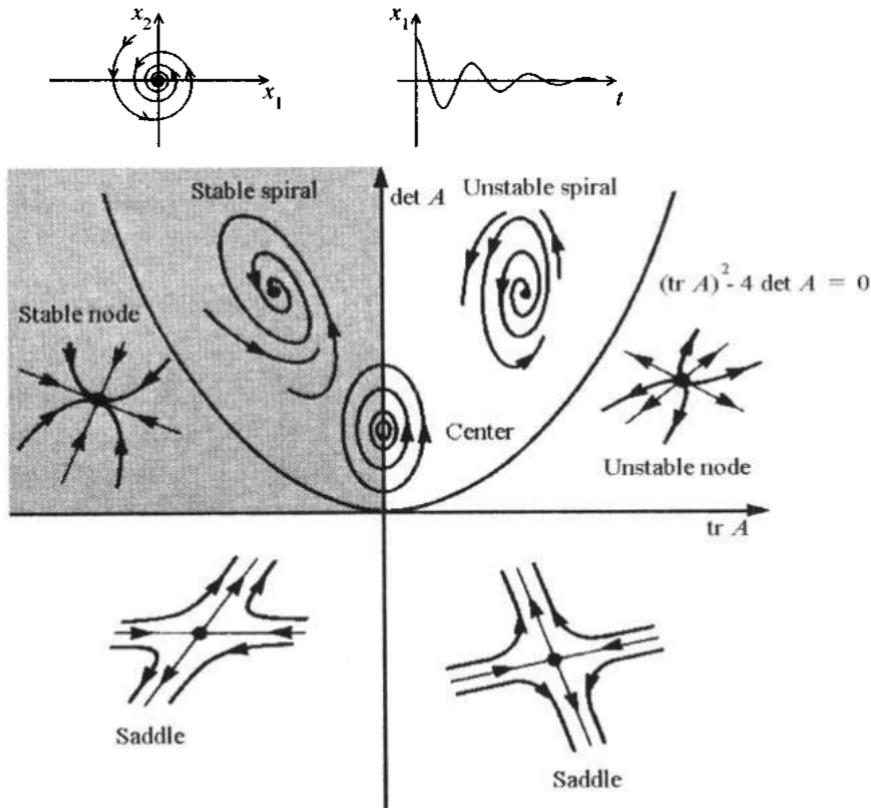
when  $A$  is not diag, the axis directions are eigenvectors. the trajectory is the combination of evect.

$$x(t) = c_1 e^{\lambda_1 t} v_1 + \dots + c_n e^{\lambda_n t} v_n$$

If the evalue are complex, we need to separate real and imaginary:

$$x_1(t) = e^{at} [\vec{c} \cos(bt) - \vec{d} \sin(bt)] + i e^{at} [\vec{c} \sin(bt) - \vec{d} \cos(bt)] = c_1 e^{at} \begin{pmatrix} \cos(bt + \phi) \\ -\sin(bt + \phi) \end{pmatrix}$$

If  $a=0$ , orgin is a center, is stable but not asymptotically stable; If  $a<0$ , origin is a stable spiral or spiral sink; If  $a>0$ , origin is an unstable spiral or spiral source;

(a)  $\alpha = 0$ , center(b)  $\alpha > 0$ , unstable spiral(c)  $\alpha < 0$ , stable spiral**Figure 3.10.** The zoo for the general linear system, (3.18). This is a me

For 2 by 2 linear system the following are equivalent:

$(0, 0)$  is asymptotically stable; all eigenvalues have negative real parts;  $|A| > 0$ ;  $\text{tr} A < 0$ .

## Nonlinear ODEs

Consider the autonomous system:

$$\dot{\vec{x}} = \vec{f}(\vec{x}).$$

do Taylor expansion around fixed point  $x^*$ :

$$f(y) = Df(x^*)(y - x^*)$$

def: a fixed point  $x^*$  is called hyperbolic if all eigenvalues of Jacobian have nonzero real part (not pure imaginary).

thm(Hartman-Grobman): in a small neighborhood of a hyperbolic  $x^*$ , then the the linearized system is equivalent to the original nonlinear system.

**Example that the condition of HG thm does not hold:**

Ex Consider the nonlinear system (2D)

$$\begin{aligned}\dot{x} &= -y + \underbrace{ax(x^2 + y^2)}_{\text{nonlinear terms}} \\ \dot{y} &= x + \underbrace{ay(x^2 + y^2)}_{\text{nonlinear terms}}\end{aligned}$$

Note that by inspection  $\vec{0} = [0, 0]^T$  is a fixed point.

Let's find the Jacobian at the origin.

$$\text{Here, } \det(A - \lambda I) = \lambda^2 + 1 = 0 \quad (\text{tr}(A) = 0, \det(A) = 1)$$

$$\Rightarrow \lambda = \pm i$$

So,  $\vec{x}^*$  is not a hyperbolic fixed point because  $\text{Re}(\lambda) = 0$ .

Then we cannot use the conclusions from the linear setting to approximate the nonlinear behavior near  $\vec{0}$ .

If we did, we'd classify the origin as a center.

(In particular, the linearization predicts a center no matter the value of  $a$  in the equations.)

So, if H-G thm applied, we'd expect periodic motion in closed trajectories around  $\vec{0}$ .

To actually analyze the behavior of the nonlinear system, we change to polar coordinates (motivated by recalling the relationship  $x^2 + y^2 = r^2$ , and  $x^2 + y^2$  appears in the eqns)

let  $x = r \cos \theta$ ,  $y = r \sin \theta$ , and so  $x^2 + y^2 = r^2$ .

Differentiating the third relation gives

$$\frac{d}{dt}(x^2 + y^2 = r^2) = \cancel{2x\dot{x}} + \cancel{2y\dot{y}} = \cancel{2r\dot{r}}.$$

Using the original equations for  $\dot{x} + \dot{y}$  + substituting:

$$\begin{aligned} r\dot{r} &= x(-y + a(x^2 + y^2)) + y(x + ay(x^2 + y^2)) \\ &= \cancel{x(-y + axr^2)} + \cancel{y(x + a yr^2)} \\ &= ar^2(x^2 + y^2) \\ &= ar^4. \end{aligned}$$

$$\Rightarrow \dot{r} = ar^3, \quad r > 0.$$

Now, let's look at the angular coordinate  $\theta = \arctan(\frac{y}{x})$ .

You can check that

$$\dot{\theta} = \frac{x\dot{y} - y\dot{x}}{r^2}$$

and substituting the expressions for  $\dot{x}$  and  $\dot{y}$ , we find  $\dot{\theta} = 1$ .

Thus, in polar coordinates the system is simpler to analyze:

$$\begin{cases} \dot{r} = ar^3, & r > 0 \\ \dot{\theta} = 1 \end{cases}$$

The system is decoupled — all trajectories rotate around  $\vec{O}$  with constant angular velocity.

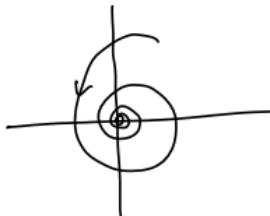
The system is decoupled — all trajectories rotate around  $\vec{O}$  with constant angular velocity.

The qualitative behavior depends on  $a$ :

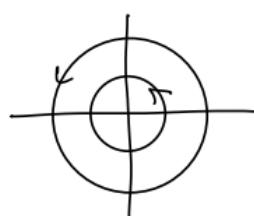
$$\begin{array}{l} a < 0 \\ \dot{r}(t) < 0 \\ r(t) \rightarrow 0 \end{array}$$

$$\begin{array}{l} a = 0 \\ \dot{r}(t) = 0 \\ \vec{O} \text{ is a center} \end{array}$$

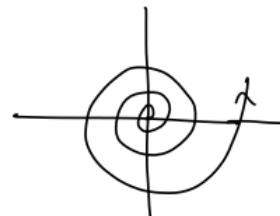
$$\begin{array}{l} a > 0 \\ \dot{r}(t) > 0 \\ r(t) \rightarrow \infty \end{array}$$



stable spiral



radius depends  
on IC



unstable spiral

What have we learned? Centers are delicate: A small perturbation of the linear system can transform the center into a stable or unstable spiral.

Conversely, stable and unstable nodes (sinks and sources) and saddles can be altered by small nonlinearities, but their stability does not change.

**General interaction model for two populations:**

$$\begin{cases} \dot{x} = \alpha x + \beta xy \\ \dot{y} = \gamma y + \delta xy \end{cases}$$

$\alpha$	$\beta$	$\gamma$	$\delta$				
+	+	+	-	Predator ( $x$ ) – prey ( $y$ ) models			
+	+	-	-				
-	+	+	-				
-	+	-	-				
+	+	+	+	Mutualism or symbiosis models			
+	+	-	+				
-	+	-	+				
+	-	+	-	Competition models			
+	-	-	-				
-	-	-	-				

$$x\text{-nullcline} = \{(x, y) | \dot{x} = 0\}, y\text{-nullcline} = \{(x, y) | \dot{y} = 0\}$$

$$x\text{-nullcline} = \{x = 0, y = -\frac{\alpha}{\beta}\}, y\text{-nullcline} = \{y = 0, x = -\frac{\gamma}{\delta}\}$$

fixed point is  $P_1^* = (0, 0)$ ;  $P_2^* = (-\frac{\alpha}{\beta}, -\frac{\gamma}{\delta})$

$$Df(x, y) = \begin{pmatrix} \alpha + \beta y & \beta x \\ \delta y & \gamma + \delta x \end{pmatrix}$$

$$\sigma(D(0, 0)) = \alpha, \gamma$$

$$\sigma(D(-\frac{\alpha}{\beta}, -\frac{\gamma}{\delta})) = \sqrt{\alpha\gamma}, -\sqrt{\alpha\gamma}$$

### **predator-prey (-+-)**

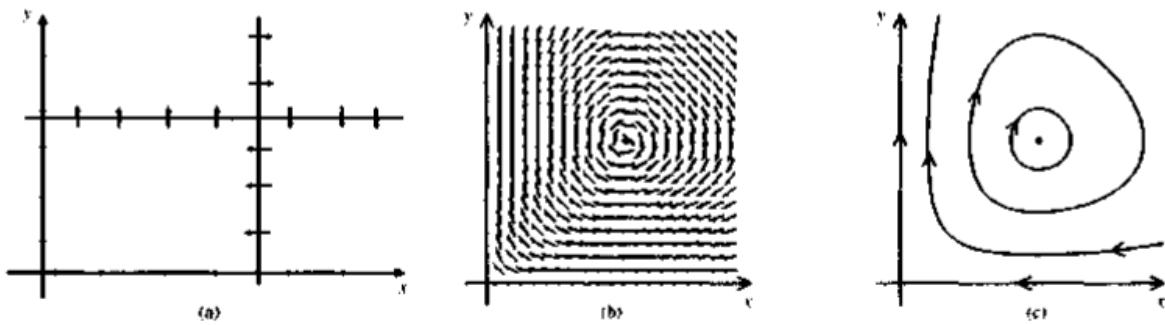
For  $(0, 0)$  it is a saddle. For nontrivial fixed point, eigenvalue are pure imaginary. HG thm does not hold. the fixed point is positive at least(meaning that it have biological meaning).

Analysis for nontrivial point.  $\text{derivative } yx = \text{derivative } yt / \text{derivative } xt$ :

$$\text{separation of variable: } \int \frac{\alpha + \beta y}{y} dy = \int \frac{\gamma + \delta x}{x} dx$$

sequence of closed curves:

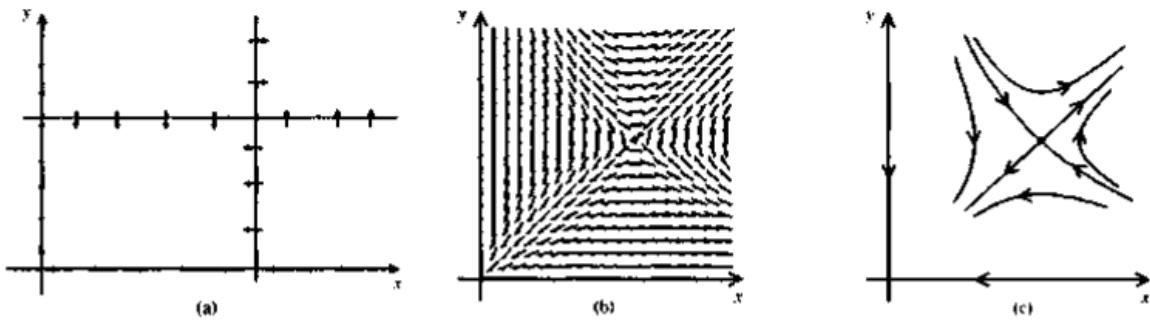
$$h(x, y) = \alpha \ln y + \beta y - \gamma \ln x - \delta x = C_1; P_2^* \text{ is a nonlinear center}$$



**Figure 3.11.** (a) Nullclines; (b) direction field; and (c) phase portrait for the two-species model, (3.8), with sign pattern  $(- + + -)$  (predator-prey).

### **mutualism (-+-)**

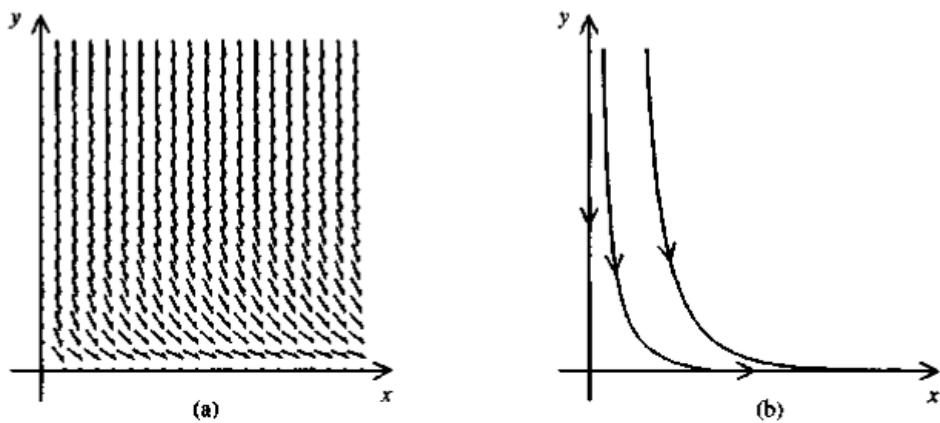
For  $(0, 0)$ , it is stable, a sink. For nontrivial fixed point, it is a saddle.



**Figure 3.12.** (a) Nullclines; (b) direction field; and (c) phase portrait for the two-species model, (3.8), with sign pattern  $(- + - +)$  (mutualism).

### **Competition model (+---**

For  $(0, 0)$  it is a saddle. For nontrivial fixed point, it has no biology meaning.



**Figure 3.13.** (a) *Direction field* and (b) *phase portrait* for the two-species model, (3.8), with sign pattern  $(+ - -)$  (competition).

### Analysis of the Epidemic model

$S(t)$ ,  $I(t)$ ,  $R(t)$ ,  $\beta$ ,  $\alpha$ ,  $\gamma$ : susceptible, infected, Recovered, transmission coefficient, recovery rate of infection, rate of return to S.

$$\begin{cases} \dot{S} = -\beta IS \\ \dot{I} = \beta IS - \alpha I \\ \dot{R} = \alpha I - \gamma R \end{cases} \quad \begin{cases} \dot{S} = -\beta IS + \gamma R \\ \dot{I} = \beta IS - \alpha I \\ \dot{R} = \alpha I - \gamma R \end{cases} \quad \text{turns to 2D if } \gamma = 0$$

assume, no birth, death, exposed category, no vaccines.

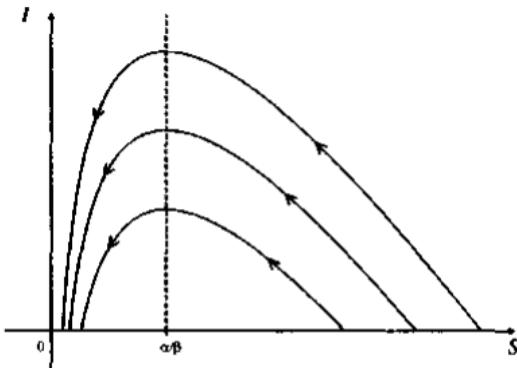
consider 2D:

stable point  $\{(S, 0) | S \geq 0\}$

$$Df(S, I) = \begin{pmatrix} -\beta I & -\beta S \\ \beta I & \beta S - \alpha \end{pmatrix}, \sigma(D(\tilde{S}, 0)) = 0, \beta \tilde{S} - \alpha$$

when  $\tilde{S} < \frac{\alpha}{\beta}$ , stable; when  $\tilde{S} > \frac{\alpha}{\beta}$  unstable.

$$I(S) = -S + \frac{\alpha}{\beta} \ln S + C_1$$



**Figure 3.14.** *Phase portrait of the epidemic model*, (3.11).

$\frac{\alpha}{\beta}$ : critical susceptible population size needed to sustain an epidemic

## Nondimensionalization

eliminate units + reduce # of free parameters

helps us compare large/small quantities

reduce complexity to analyze

example 1: Logistic growth:

let  $\tilde{N} = N/K; \tilde{t} = rt$ , we have:  $\frac{d\tilde{N}}{d\tilde{t}} = \tilde{N}(1 - \tilde{N})$

example 2: 2-species interaction

let  $\tilde{x} = \frac{\delta}{\alpha}x, \tilde{y} = \frac{\beta}{\alpha}y, \tilde{t} = \alpha t, \mu = \frac{\gamma}{\alpha}$  we have:

$$\begin{cases} \dot{x} = x + xy \\ \dot{y} = \mu y + xy \end{cases}$$

## More about global info. Index theory on phase portraits.

### Index theory

consider a closed curve  $C$  in phase plane. not necessary a trajectory. Assume  $C$  does not intersect itself, does not pass through fixed points.

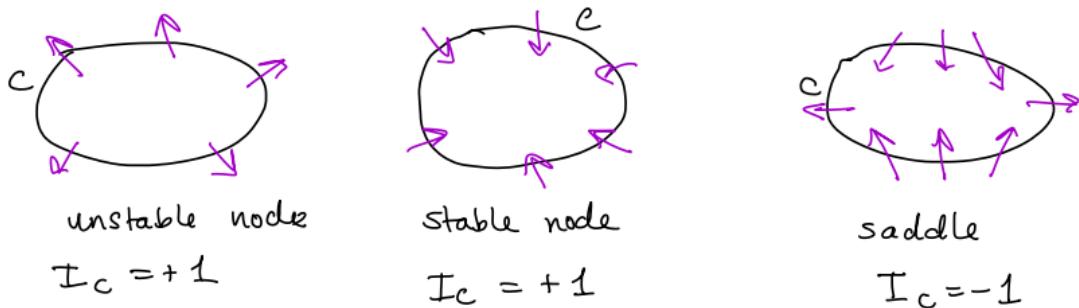
consider any point  $x$  on  $C$  and  $\dot{x}, \phi = \tan^{-1}(y/x)$ .

def: index of curve: net # of CCW revolutions made by vector field as  $x$  moves once CCW around  $C$ .  $I_C$ .

If  $C$  does not enclose any fixed point  $I_C = 0$ , If  $C$  is a trajectory,  $I_C = +/ - 1$ .

def: index of fixed point.  $x^*$  is an isolated fixed point, index of  $x^*$  is  $I_{C^*}$ , where  $C$  is any closed curve that encloses  $x^*$  but not other fixed points.

ex: unstable node,  $I_C = 1$ ; stable node,  $I_C = 1$ ; saddle,  $I_C = -1$



Thm, any closed orbit in the phase plane must enclose fixed points whose indices sum to 1. Always at least one fixed point inside any closed orbit in phase plane. saddle can not be in an orbit.

### long-term behavior

def: A trajectory  $x(t)$  is periodic if  $\exists k > 0, x(t) = x(t + K)$ , the smallest K is called period.

limit cycle is isolated closed trajectory. If all neighboring trajectory toward LC, LC is stable or attracting. otherwise is unstable (or rarely half-stable).



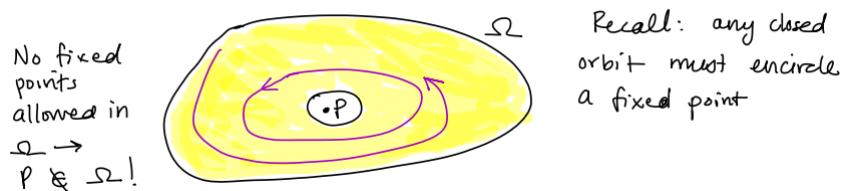
Ex: stable limit cycle in biology: self-sustained oscillations. heart beat, daily temp, chemical reactions.

If LC is stable:  $\exists$  preferred oscillation with period amplitude. perturb  $\rightarrow$  preferred cycle.

LC can not appear in linear system. Because, if  $x(t)$  is a periodic solution for linear system, then  $cx(t)$  is another, so perturbation moves your solution onto a new closed orbit. And LC is not isolated, it is determined by the IC. LC oscillations should be determined by the structure of nonlinear dynamic sys.

### Find Limit cycle(Poincare-Bendixson):

suppose  $\Omega \subseteq \mathbb{R}^2$  is compact and contains no fixed points,  $\dot{x} = f(x)$ ,  $f$  is continuously diff in an open set  $D \supseteq \Omega$ . If there exist a trajectory  $C$  remains confined in  $\Omega$  for all time, then  $C$  is either a closed orbit or approaching a LC as  $t \rightarrow \infty$



We need to locate a trapping region  $R$  to confine the  $C$ . And vector field points inward everywhere on the boundary  $\partial R$ .

### Ex1:

$$\begin{cases} \dot{r} = r(1 - r^2) + \mu r \cos \theta \\ \dot{\theta} = 1 \end{cases}$$

If  $\mu = 0$ ,  $r = 0$  is an unstable fixed point,  $r = 1$  is a stable cycle.

If  $\mu > 0$ ,

Now for  $\mu > 0$ , let's create our trapping region:

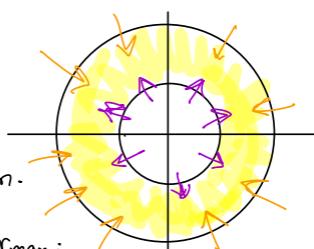
two concentric circles

Outer circle:  $\dot{r} < 0$

Inner circle:  $\dot{r} > 0$

The yellow highlight = trapping region.

To find the inner + outer radii  $r_{min}, r_{max}$ :



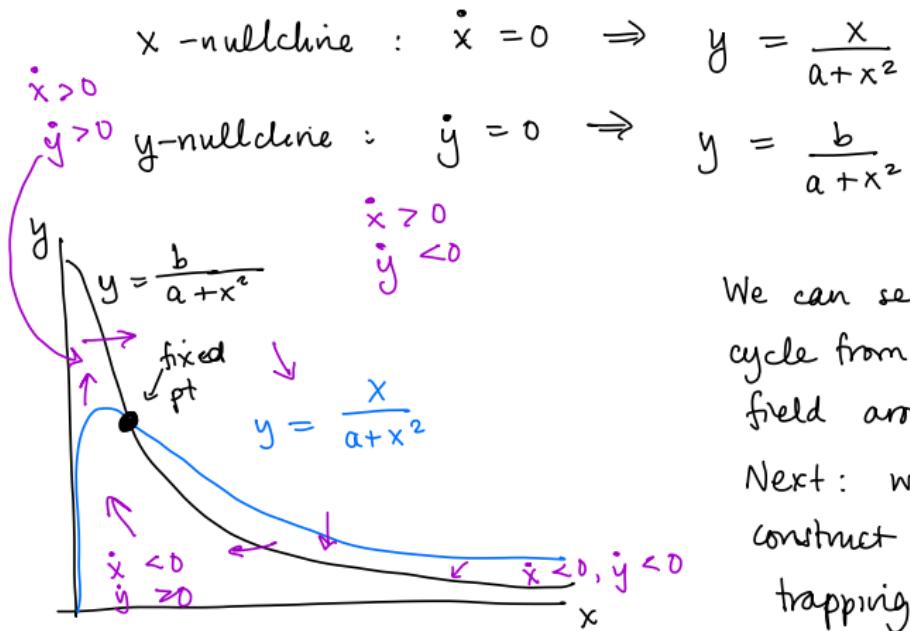
find values of  $\mu, r$  s.t.

$$r_{min}(1 - r_{min}^2) + \mu r_{min} \cos \theta > 0; r_{max}(1 - r_{max}^2) + \mu r_{max} \cos \theta < 0$$

Let  $r_{min} = 0.999\sqrt{1 - \mu}$ ;  $r_{max} = 1.0001\sqrt{1 + \mu}$ . By P-B thm, there is a periodic orbit in the annular region  $\{r_{min} \leq r \leq r_{max}\}$

## Ex2: Selkov's model of glycolysis: break down of sugar

$$\begin{cases} \dot{x} = -x + ay + x^2y \\ \dot{y} = b - ay - x^2y \end{cases} \quad x: \text{concentration of ADP}; y: \text{concentration of fructose-6-phosphate}$$



We can see a potential cycle from the vector field arrows.

Next: we'll try to construct a trapping region.

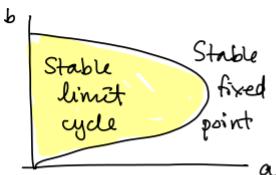
build a 5 edges trapezoid region.

$x = 0; y = 0; y = b/a, x = \text{large enough } x \text{ s.t. } dx, dy < 0; -\dot{y} > \dot{x} \text{ if } x > b$

As for the inner cycle, we need to prove fixed point is unstable, so that the orbit will not become a spiral.

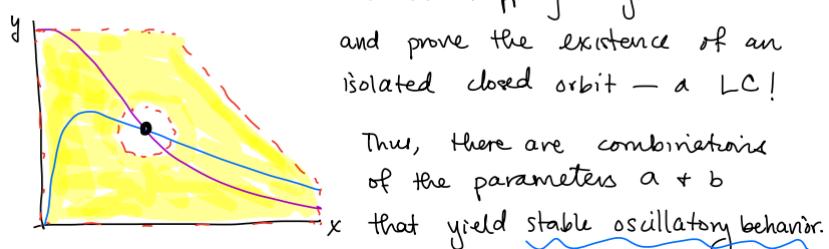
$x^* = (b, \frac{b}{a+b^2})$ , some combos that yield stable oscillatory behavior.

We can then look at regions in parameter space:



Thus, there are parameter combinations  $(a, b)$  where the fixed point is repelling (unstable node or source), and we can create the desired trapping region:

and prove the existence of an isolated closed orbit — a LC!



Thus, there are combinations of the parameters  $a + b$  that yield stable oscillatory behavior.

## Ruling out closed orbits

### Index theory

no fixed point, no closed orbit

## Gradient function

Ex:  $\begin{cases} \dot{x} = xe^{-x} \\ \dot{y} = 1 + x + y^2 \end{cases}$  nullclines do not intersect, so no fixed point, so no closed orbits.

An ODE is a gradient system, if we can write:  $\dot{x} = -\text{grad}V(x)$ .  $V$  is called the potential function.

Thm: in gradient system we can not find closed orbits.

Ex:  $\begin{cases} \dot{x} = \sin y \\ \dot{y} = x \cos y \end{cases}; V(x, y) = -x \sin y$ , it's a gradient system, there do not exist closed orbits.

## Show a fixed point is globally asymptotically stable(GAS)

Asymptotic stable: in a  $N_\delta(x^*)$ ,  $x(t, x_0) \rightarrow x^*$ .

GAS:  $x(t, x_0) \rightarrow x^*$ . No matter where you start. (surely no LC).

positive definite function: for a  $V : N_0 \rightarrow \mathbb{R}$ , at  $x^*$ , if  $V(x) \geq 0$  and  $V(x) = 0$  iff  $x = x^*$ . similar for negative definite function.

Lyapunov function: if on  $N_0$ ,  $V$  is positive definite at  $x^*$ , and  $\dot{V} = \text{derivative}tV(x(t))$  is negative definite at  $x^*$ .

Thm: If we can construct a global lyapunov function at  $x^*$ , then  $x^*$  is GAS

Ex:  $\begin{cases} \dot{x} = -x + 4y \\ \dot{y} = -x - y^3 \end{cases}; x^* = (0, 0); V(x, y) = x^2 + ay^2, a > 0$ ; when  $a = 4$ ,  $V$  satisfy the lyapunov function condition.

## Relaxation oscillations

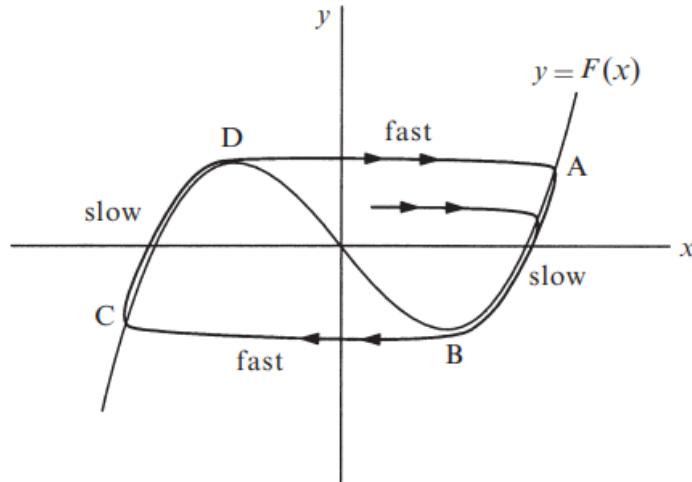
### Time-scale separation

What is the shape and period of closed orbit

Pol equation(Pol)  $\ddot{x} + \mu(x^2 - 1)\dot{x} + x = 0; \mu \gg 1$

$\ddot{x} + \mu(x^2 - 1)\dot{x} + x = \text{derivative}t(\dot{x} + \mu(1/3x^3 - x)); F(x) = 1/3x^3 - x; w = \dot{x} + \mu F(x); y = \frac{w}{\mu}$

$\begin{cases} \dot{x} = \mu(y - F(x)) \\ \dot{y} = -\frac{1}{\mu}x \end{cases}$ ; x-nullcline  $y = F(x)$ ; y-nullcline  $x = 0$

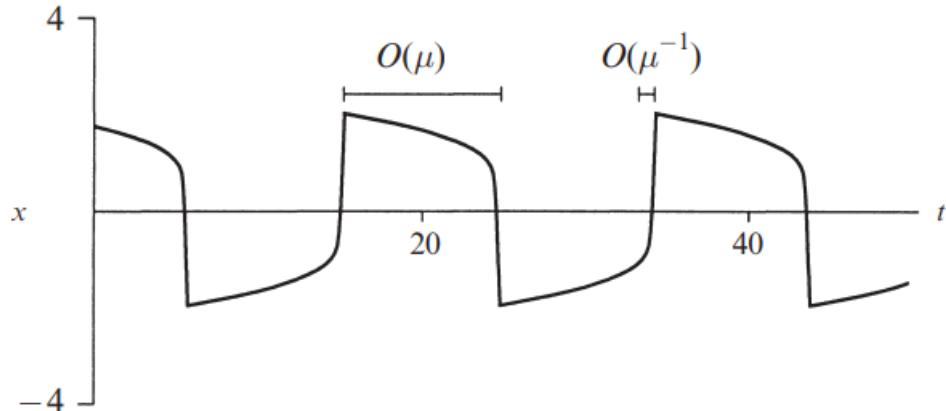


Suppose  $y - F(x) \sim O(1)$  then  $|\dot{x}| \sim O(\mu) \gg 1, |\dot{y}| \sim O(\mu^{-1}) \ll 1$

When  $y$  close to the trajectory  $y - F(x) \sim O(\frac{1}{\mu^2})$ ;  $|\dot{x}| \sim |\dot{y}| \sim O(\frac{1}{\mu})$

Relaxation oscillations: limit cycle consists of an extremely slow buildup followed by a sudden discharge, followed by another slow buildup. Strongly nonlinear

Has two widely separated time scales,  $\Delta_1 t \sim O(\mu)$ ,  $\Delta_2 t \sim O(\mu^{-1})$



## Bifurcation

describe the ways in which oscillations can be turned on or off. The qualitative change in the dynamics for different parameter values:

emergence/disappearance of fixed points; change in stability; limit cycles

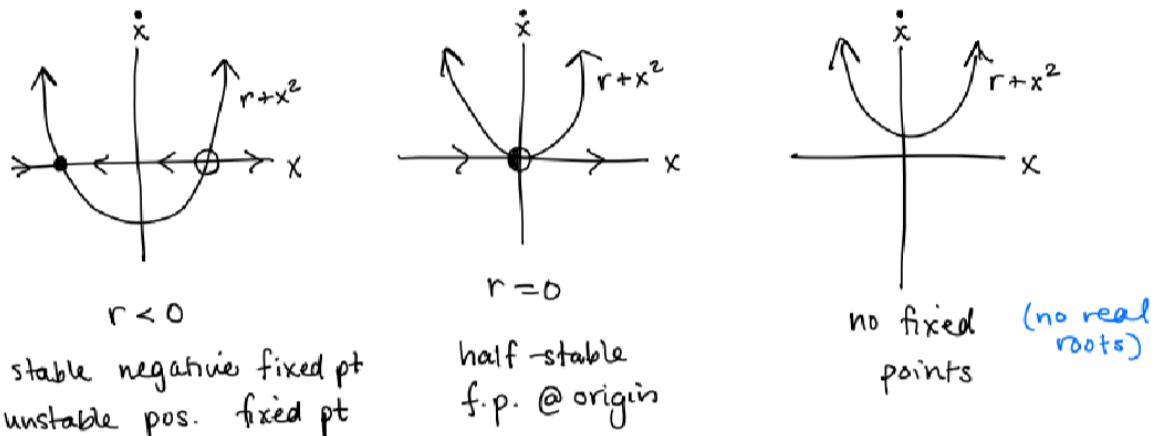
Only consider 1D

### Saddle node bifurcation

creation/destruction of fixed points

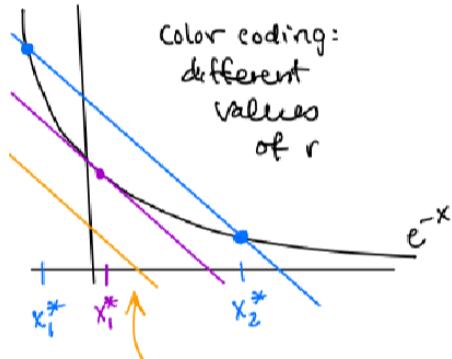
Ex1:  $\dot{x} = r + x^2$

Fixed points:  $\dot{x} = 0 \Rightarrow x^2 = -r \Rightarrow 3$  cases:  $r$  neg,  $r=0$ ,  $r$  pos



Ex2:  $\dot{x} = r - x - e^{-x}$

To find fixed points:  $\dot{x} = 0 \Rightarrow r - x^* - e^{-x^*} \Rightarrow r - x^* = e^{-x^*}$   
for values  $x^*$  that are fixed pts



no fixed pts b/c no intersections!

So we see as  $r$  is decreased,  
we go from 2 fixed points,  
to 1 (they join)  
to none (they disappear).

Let's investigate further by  
Taylor expanding  $e^{-x}$ :

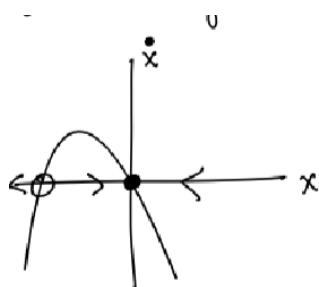
Or using taylor expanding:

$$\dot{x} = r - 1 - \frac{x^2}{2} + o(x^2)$$

### transcritical bifurcation

stability changes.

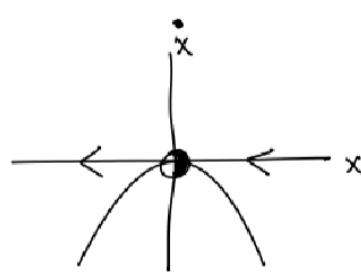
$$\dot{x} = rx - x^2$$



$$r < 0$$

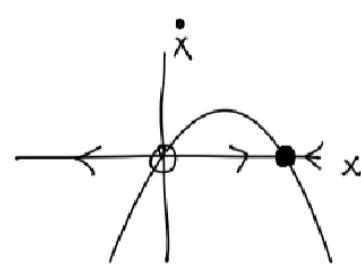
$x_1^* < 0$  unstable

$x_2^* = 0$  stable



$$r = 0$$

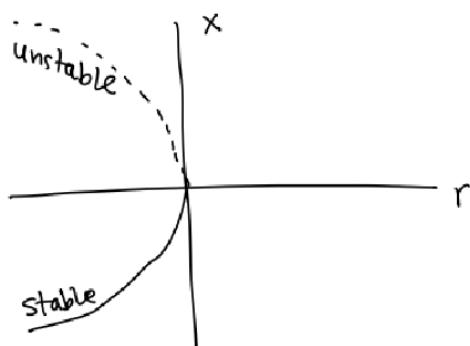
$x^* = 0$  only  
fixed point  
half stable



$$r > 0$$

$x_1^* > 0$  stable

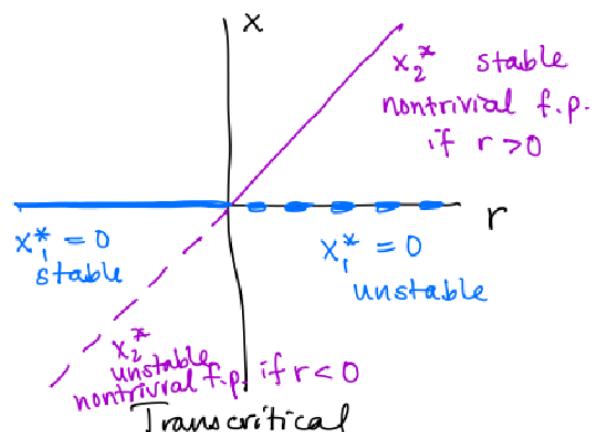
$x_2^* = 0$  unstable



Saddle-node

Two fixed points are  $x^* = \pm\sqrt{r}$

$$\dot{x} = r + x^2$$



$$\dot{x} = rx - x^2 = x(r-x)$$

Ex:

$\dot{x} = x(1-x) - a(1-e^{-bx})$  has a transcritical bifurcation.

$$x_1^* = 0; \dot{x} \simeq (1-ab)x + \frac{ab^2x^2}{2}$$

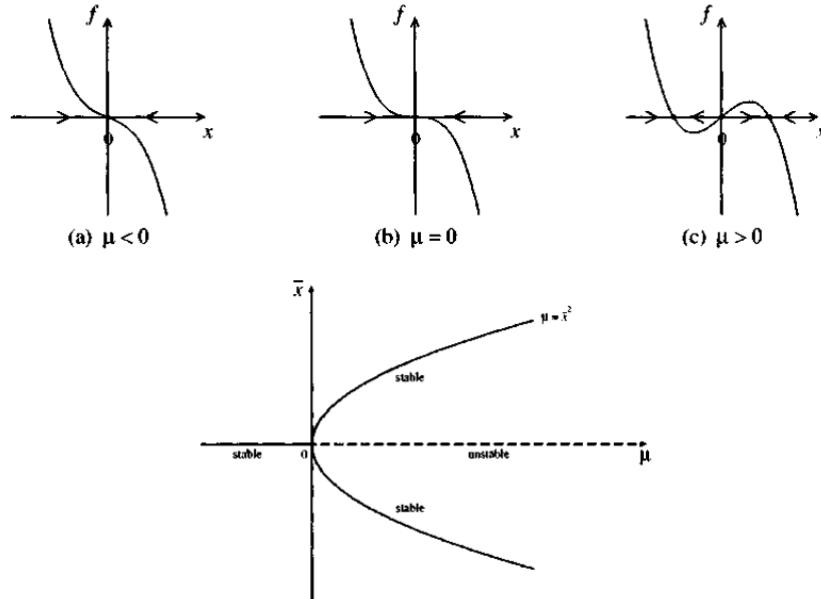
### Pitchfork Bifurcation

supercritical/subcritical; happens to problem that have a symmetry(even/odd functions)

a fixed point trifurcate -- two new symmetric f p (both stable/unstable) + original f p changes stability.

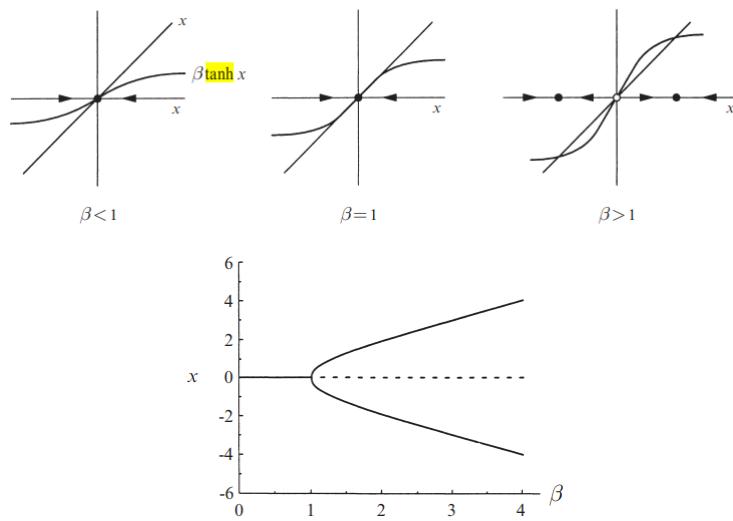
Ex1(supercritical PB):

$$\dot{x} = rx - x^3; x^* = 0, \pm\sqrt{r}$$



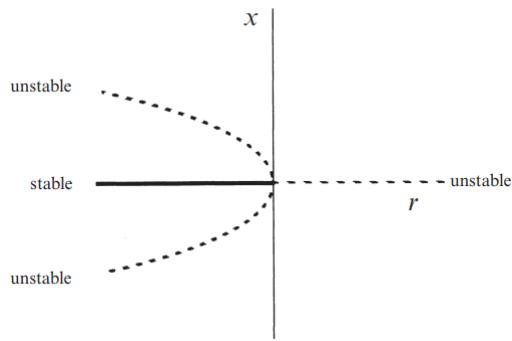
Ex2(supercritical PB):

$$\dot{x} = -x + \beta \tanh(x)$$



Ex3(subcritical PB):

$$\dot{x} = rx + x^3; x^* = 0, \pm\sqrt{-r}$$



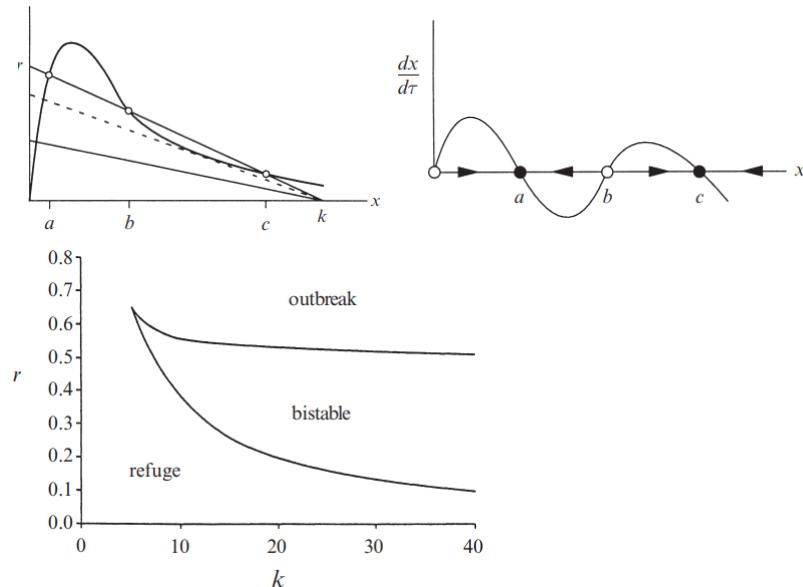
### Spruce Budworm Model

model of insect outbreak

$$\dot{N} = RN\left(1 - \frac{N}{K}\right) - p(N); p(N) = \frac{BN^2}{A^2 + N^2}; N(t) \text{ is the budworm pop}$$

$$\text{after dimensionless: } \textcolor{red}{\text{derivative}} x\tau = rx\left(1 - \frac{x}{k}\right) - \frac{x^2}{1+x^2}$$

$$\text{cal } r\left(1 - \frac{x}{k}\right) = \frac{x}{1+x^2}$$



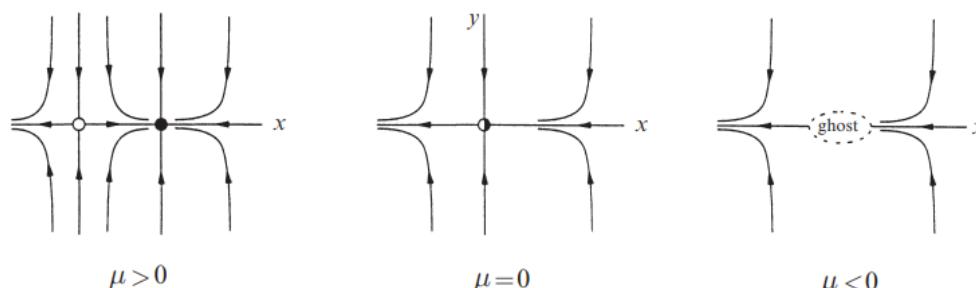
a is called the refuge level of the budworm population, while the larger stable point c is the outbreak level. b is the threshold.

$x^* = 0$  is unstable f p

### 2D bifurcation

**saddle node:**

$$\begin{cases} \dot{x} = \mu - x^2; x_1^* = (\sqrt{\mu}, 0) \text{ sink}, x_1^* = (-\sqrt{\mu}, 0) \text{ saddle} \\ \dot{y} = -y \end{cases}$$

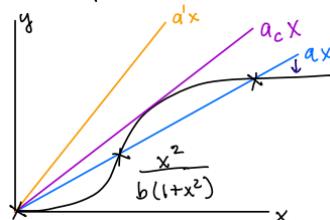


Ex: Griffith's gene regulatory model. Activity of gene stimulated by protein it codes for, which can lead to an autocatalytic feedback loop.

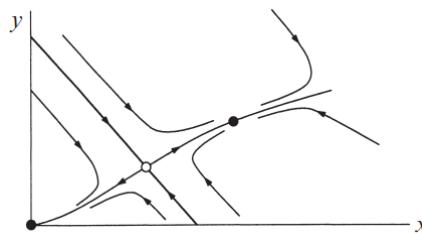
$\begin{cases} \dot{x} = -ax + y \\ \dot{y} = \frac{x^2}{1+x^2} - by \end{cases}$   $a, b$  depreciation rates.  $x$  and  $y$  are proportional to the concentrations of the protein and the mRNA from which it is translated.

$$x_1^* = 0; x_2^* = \frac{1 \pm \sqrt{1-4a^2b^2}}{2ab}; \text{ stability changes when } 2ab > 1. a_c = \frac{1}{2b}$$

phase portrait:



$$J = \begin{pmatrix} -a & 1 \\ \frac{2x}{(1+x^2)^2} & -b \end{pmatrix}; \text{ tr}J = -(a+b) < 0, \text{ so the fixed points can be sink or saddles.}$$



when  $ab < 1/2$ , the system can act like a biochemical switch.  $x_3^*$  is a high activity regime. the middle saddle f p is a threshold. IC below  $x_2^*$ , then gene gets turned off. otherwise, gene is active and sustained by high protein levels

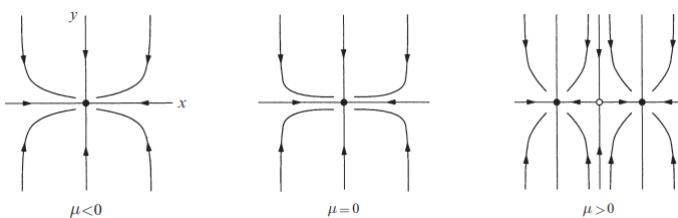
### transcritical bifurcation

$$\text{normal form } \begin{cases} \dot{x} = \mu x - x^2 \\ \dot{y} = -y \end{cases}$$

### pitchfork bifurcation

$$\text{normal form: supercritical, } \begin{cases} \dot{x} = \mu x - x^3 \\ \dot{y} = -y \end{cases}; \text{ subcritical, } \begin{cases} \dot{x} = \mu x + x^3 \\ \dot{y} = -y \end{cases}$$

supercritical portrait graph:



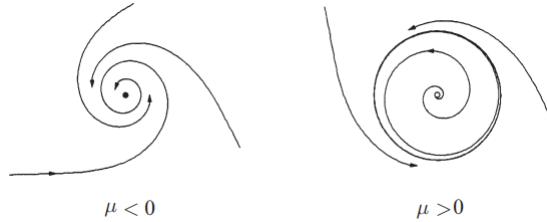
### Hopf bifurcations

planar system involves oscillations and limit cycles

## supercritical Hopf

In many cases the resulting motion is a small-amplitude, sinusoidal, limit cycle oscillation about the former steady state.

Ex:  $\begin{cases} \dot{r} = \mu r - r^3 \\ \dot{\theta} = w + br^2 \end{cases}$   $\mu$  controls the stability of the fixed point at the origin,  $w$  gives the frequency of infinitesimal oscillations, and  $b$  determines the dependence of frequency on amplitude for larger amplitude oscillations.



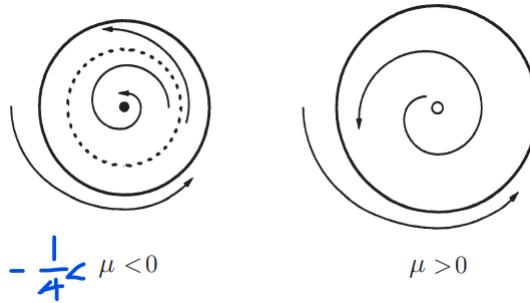
To see how the eigenvalues behave during the bifurcation, we rewrite the system in Cartesian coordinates;  $\begin{cases} \dot{x} = \mu x - \omega y + \text{cubic terms} \\ \dot{y} = \omega x + \mu y + \text{cubic terms} \end{cases}$

$$J(0,0) = \begin{pmatrix} \mu & -\omega \\ \omega & \mu \end{pmatrix}, \sigma(J(0,0)) = \mu \pm i\omega$$

## subcritical Hopf

The subcritical case is always much more dramatic, and potentially dangerous in engineering applications. After the bifurcation, the trajectories must jump to a distant attractor, which may be a fixed point, another limit cycle, infinity, or—in three and higher dimensions—a chaotic attractor.

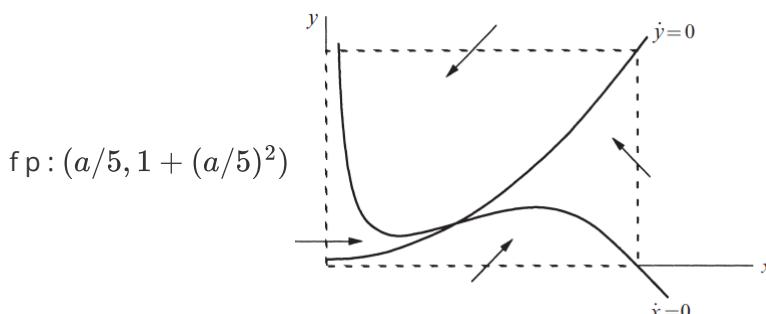
Ex  $\begin{cases} \dot{r} = \mu r + r^3 - r^5 \\ \dot{\theta} = 1 \end{cases}$



## Bio Ex: Chlorine Dioxide-Iodine-Malonic Acid Reaction

$\begin{cases} \dot{x} = a - x - \frac{4xy}{1+x^2} \\ \dot{y} = bx(1 - \frac{y}{1+x^2}) \end{cases}$ ;  $x, y$  are the dimensionless concentrations of  $I^-$ ,  $ClO_2^-$

x-nullcline:  $y = \frac{(a-x)(1+x^2)}{4x}$ ; y-nullcline:  $y = 1 + x^2$



$J(x^*) = \frac{1}{1 + (x^*)^2} \begin{pmatrix} 3x^2 - 5 & -4x \\ 2bx^2 & -bx \end{pmatrix}$ ,  $|J| > 0$ . If  $\text{tr} J > 0$ , need  $b < b_c = 3a/5 - 25/a$ . And  $x^*$  is a repeller. So guarantee a limit cycle. At  $b_c$ , there is a supercritical hopf bifurcation.

## PDE

so far, 1 independent variable(time, space); Now two or more.

Blood flow, fluid dynamics, chemotaxis, swarms/flocks, weather.

consider  $f(x, y)$ , level sets or contour lines of  $f$  are curves in  $(x, y)$  plane where  $f(x, y) = k$

$$\vec{x} = (x, y, f(x, y)); \nabla f(x, y) = \begin{pmatrix} \partial_x f \\ \partial_y f \end{pmatrix}$$

### Ex: age-structured model

$u(t, a)$ : density of potential mothers in a population.  $t$ :time,  $a$ :age

consider changes in pop after a small change in time  $\Delta t$

$u(t + \Delta t, a) - u(t, a) = u(t, a - \Delta a) - u(t, a) - \mu(a)u(t, a)\Delta t$ : add from prev age class; subtract current age class because they move to next age class; dying,  $\mu(a)$  age dependent death rate.

divide both by  $\Delta t$  and take lim,  $\Delta t = \Delta a$ ;

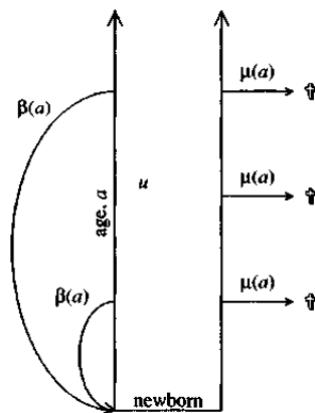
$$\frac{\partial u}{\partial t} = -\frac{\partial u}{\partial a} - \mu(a)u \rightarrow \text{total derivative } \frac{\partial u}{\partial t} = -\mu(a)u$$

$$\frac{\partial u}{\partial t} = \partial_t u = u_t$$

this is a 1st order PDE, we need boundary condition at  $a = 0$ , and IC at  $t = 0$

$u_0(a) = u(0, a)$  is the initial age distribution, non neg function with finite integral taken over all ages.

$u(t, 0) = \int_0^\infty \beta(a)u(t, a)da$  number of newborns at time  $t$ ,  $\beta(a)$  is an age dependent reproduction rate.



### Solution:

def  $\mathcal{L}$  operator,  $\mathcal{L} = -\frac{\partial}{\partial a} - \mu$

$u_t = \mathcal{L}u$ ,  $\mathcal{L}$  is a linear function, we will view  $\mathcal{L}$  as a matrix, we will seek eigenvalues  $\lambda$  and eigenfunctions  $\omega(a)$ .

$\lambda w(a) = \mathcal{L}w(a)$ , if we know  $\lambda$  then  $w_a = -(\lambda + \mu(a))w$

note that there is no  $t$  in this equation, so we can solve  $w(a) = w_0 \exp(-\int_0^a -\lambda + \mu(s)ds)$

For  $t$  part, we use separation of variables: suppose(very strong assumption, may not work for the other time)  $u(t, a) = g(t)w(a)$ , then we have  $g'(t)w(a) = \lambda g(t)w(a)$ . eigenfunction is non-zero, so  $g(t) = g_0 e^{\lambda t}$

general solution  $u(t, a) = g_0 e^{\lambda t} w_0 \exp(-\int_0^a \lambda + \mu(s)ds)$

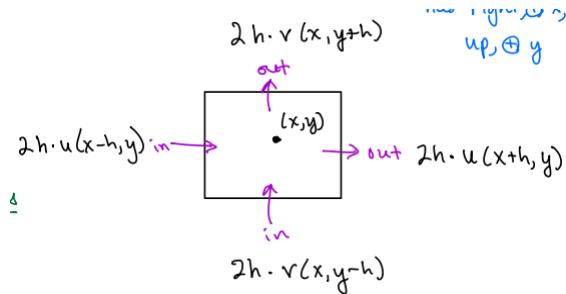
use BC,IC:  $u(t, 0) = \int_0^\infty \beta(a)u(t, a)da; 1 = \int_0^\infty \beta(a) \exp(-\int_0^a \lambda + \mu(s)ds)da$

By some thm, if  $\beta(a) \neq 0$ , there  $\exists \bar{\lambda}$  as the solution

if  $\bar{\lambda} < 0$ ,  $u \rightarrow 0$  as  $t \rightarrow \infty$ ,  $\bar{\lambda} > 0$ ,  $u \rightarrow \infty$  as  $t \rightarrow \infty$

## Ex: 2D concentration flow

$\vec{u} = (u, v)$  is the flow velocity,  $N$  is the # of particles in a tiny square around  $(x, y)$ ,  $c$  concentration.



$$\frac{\partial c}{\partial t} = \frac{\partial N}{\partial t} / (2h)^2 = \frac{1}{2h} (u(x-h, y) + v(x, y-h) - u(x+h, y) - v(x, y+h))$$

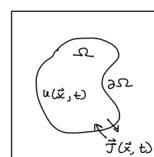
$$\frac{\partial c}{\partial t} = -\left(\frac{\partial u}{\partial x} + \frac{\partial v}{\partial y}\right) = -\nabla \cdot \vec{u} = -\text{div}(u)$$

If we have a flux  $J$  and source/sink  $s$ :  $\frac{\partial c}{\partial t} = -\nabla \cdot \vec{J} + s$

flux is defined as the rate of flow of a property per unit area.

## Reaction-diffusion equations

$t$ : time,  $\vec{x}$  space; to model spread of quantity. Consider population with density  $u(x, t)$  in a rectangular container. Consider flux  $\vec{J}(x, t)$  point direction of general movement at  $(x, t)$ .



consider a test volume  $\Omega$  in the container, consider how  $u$  changes in  $\Omega$ . (movement in boundary  $\partial\Omega$ ; birth/death)

change of  $u$  in  $\Omega$  = flux across  $\partial\Omega$  + birth - death

$$\frac{\partial}{\partial t} \int_{\Omega} u(x, t) dV = - \int_{\partial\Omega} J(x, t) dS + \int_{\Omega} f(u(x, t)) dV$$

$$\text{By Divergence thm: } \int_{\partial\Omega} J(x, t) dS = \int_{\partial\Omega} \nabla \cdot J(u(x, t)) dV$$

$$\int_{\Omega} \frac{\partial u}{\partial t} + \nabla \cdot J - f(u) dV = 0; \text{ equals } \frac{\partial u}{\partial t} + \nabla \cdot J - f(u) = 0$$

Fick's 2nd law, flux is proportional to  $\nabla u$ ;  $J = -D \nabla u$ ;  $D$  is the diffusion coefficient.

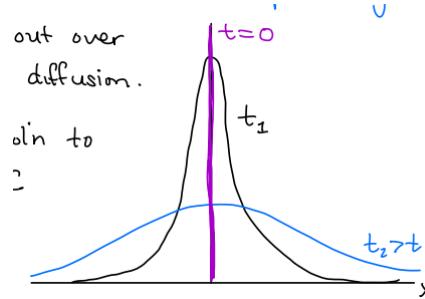
$$\frac{\partial u}{\partial t} = D(\nabla \cdot \nabla u) + f(u) = D\Delta u + f(u); \text{ Laplacian } \Delta u = \frac{\partial^2 u}{\partial x_1^2} + \dots + \frac{\partial^2 u}{\partial x_n^2}$$

If  $f = 0$ , we have heat or diffusion equation.

## IC

for  $g$  is  $g_t = Dg_{xx}$ ;  $g(x, 0) = \delta_0(x)$  (delta function)

The fundamental solution is  $g(x, t) = \frac{1}{2\sqrt{\pi Dt}} e^{-\frac{x^2}{4Dt}}$



The general solution for general IC:  $u_t = Du_{xx}$ ,  $u(x, 0) = f(x)$  is

$$u(x, t) = f * g(\cdot, t)$$

## BC

Dirichet BC: specify the value of  $u$  at a boundary  $u = b(x, t); x \in \partial\Omega$ ; if  $b=0$  it's called homogenous.

Neumann 2nd order BC: specify a spatial derivative of  $u$  at boundary.

$\nabla u \cdot \vec{n} = b(x, t), x \in \partial\Omega$ ,  $\vec{n}$  is the outer normal vector to  $\Omega$  at  $x$ . If  $\frac{\partial u}{\partial x} = 0$  (1D example) then it is called homogeneous.

Robin BC: Dirichet + Neumann:  $\alpha(x, t)u + \beta(x, t)\nabla u \cdot \vec{n} = b(x, t)$

Periodic BC: equal BC at edge of symmetric domin.

## Ex: bacteria indie a thin tube of length $\pi$ , open at both end



Assume if bacteria leave the tube, they are lost. Assume we have homogeneous dirichet BC

$$u(0, t) = u(\pi, t) = 0$$

Diffusion equation:  $u_t = u_{xx}$ ;  $u=0$  is a trivial solution. Assume Separation of variables.

$$u(x, t) = X(x)T(t)$$

$XT' = X''T \rightarrow \frac{T'}{T} = \frac{X''}{X}$ , LHS(function of t) and RHS(function of x) are independent so they must be equal to a constant  $-\lambda < 0$ ; so we have

$$T = T(0)e^{-\lambda t}; X = a \cos(\sqrt{\lambda}x) + b \sin(\sqrt{\lambda}x)$$

plug in BC:  $X(0)T(0) = 0; X(\pi) = 0$ ; we have  $a=0$   $\lambda = k^2; k \in Z/\{0\}$ . In the end we have the general solution is an infinite sum:

$$u(x, t) = \sum_{k=-\infty}^{\infty} c_k e^{-k^2 t} \sin(kx); k \in Z$$

as  $t \rightarrow 0$ ;  $u \rightarrow 0$ , bacteria left the tube.

## Ex: Fisher

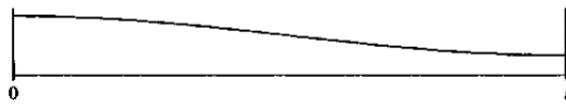
add term to diffusion equation to look at size of habitat needed to support a population.

$u_t = Du_{xx} + ru(1 - u)$ ,  $u$  is the density of the mutant, advantageous gene;  $r$  is the logistic growth term,  $D$  is the diffusion coefficient.

need 2 BC, on interval  $[0, l]$ . Suppose we consider an island, so we have a homogeneous Dirichlet BCs  $u(0, t) = u(l, t) = 0$ ; Suppose no organisms can cross the fence, so we have a homogeneous Neumann BCs(or no flux condition)  $u_x(0, t) = u_x(l, t) = 0$



**Figure 4.7.** A typical solution of (4.19) with homogeneous Dirichlet boundary conditions (island conditions).



**Figure 4.8.** A typical solution of (4.19) with homogeneous Neumann boundary conditions (box conditions).

The Following Are Equivalent:

1, size of habitat needed to support a population

The equivalent question is when is the trivial solution  $u(x, t) = 0$  unstable, So the population will be grow.

2, What is the critical domain size  $l^*$  s.t.  $u = 0$  is stable for  $l < l^*$  and unstable for  $l > l^*$ . 3, What is the critical domain size  $l^*$  s.t. a nontrivial steady state solution exists for  $l > l^*$ .

A steady state solution satisfies  $u_t = 0, 0 = Du_{xx} + ru(1 - u); u_{xx} = -\frac{r}{D}u(1 - u)$ . And this is an ODE. change to planar system:

$$\begin{cases} u_x = v \\ v_x = -\frac{r}{D}u(1 - u) \end{cases}; \text{Dirichlet: } u(0) = u(l) = 0; \text{Neumann: } v(0) = v(l) = 0$$

$$\text{Fixed points } (0, 0), (1, 0). J = \begin{pmatrix} 0 & 1 \\ 2\frac{r}{D}u^* - \frac{r}{D} & 0 \end{pmatrix}$$

$(1, 0)$  is a saddle,  $\sigma(J(1, 0)) = \pm\sqrt{\frac{r}{D}}$ ;  $(0, 0)$ :  $\sigma(J(0, 0)) = \pm\sqrt{\frac{r}{D}}i$  has evaluate with real part equals zero, we need other approach.

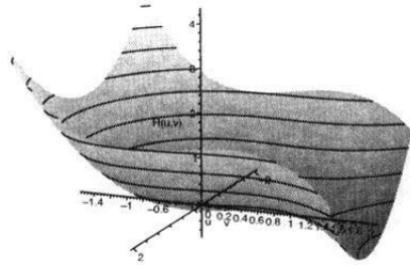
### Hamiltonian function

If  $H$  satisfies  $\frac{\partial H}{\partial v} = \frac{\partial u}{\partial x}; \frac{\partial H}{\partial u} = -\frac{\partial v}{\partial x}$ , then  $\cancel{\text{derivative}}xH(u(x), v(x)) = 0$

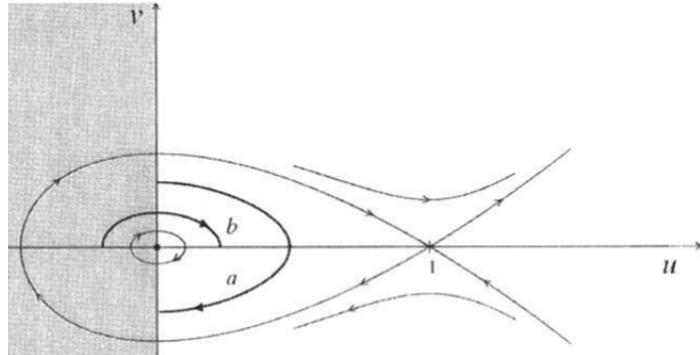
$H$  does not change along solution curves  $(u(x), v(x))$ .

For our problem:  $H(u, v) = \frac{1}{2}v^2 + \frac{r}{D}\frac{u^2}{2} - \frac{r}{D}\frac{u^3}{3} = \text{integral of } \frac{\partial u}{\partial x} + \text{integral of } -\frac{\partial v}{\partial x}$

Thm: If we have  $H$  function, Each bounded solution is either a equilibrium point(or a connection of equilibrium points) or a closed orbit.



In our case, we can say the origin is a center.



We will see from the Phase portrait, to BCs, to relevant solutions, to answer to Q.

curve "a" satisfies Homogeneous Dirichlet BC. curve "b" satisfies Homogeneous Neumann BC(But not biologically relevant).The only Neumann BC satisfied solution is  $u = 0, u = 1$ (fixed points).

For Neumann,  $u(x, t) = 1$  exist for any value of  $l$ , so  $l^* = 0$

For Dirichlet, suppose the solution intersect u axis at  $\bar{u}$ .

When  $\bar{u}$  approach 1, the solution approaches the saddle, the point take longer time to move forward.  $l \rightarrow \infty$  for  $\bar{u} \rightarrow 1$

When  $\bar{u}$  approach 0, general solution nearby are

$$(u(x), v(x)) = c_1(\cos(\sqrt{\frac{r}{D}}x + \phi), \sin(\sqrt{\frac{r}{D}}x + \phi))$$

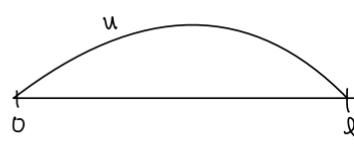
To find the phase shift  $\phi$ , we know that  $(u(0), v(0)) = (0, c_1); (u(l), v(l)) = (0, -c_1)$

plugin we have  $l = \pi\sqrt{\frac{D}{r}}$

$$\text{or } l^* = \pi\sqrt{\frac{D}{r}}.$$

If  $l > l^*$ , we get a solution of the form:

If  $l < l^*$ , the island cannot support the population and each initial population will die out.



linear stability analysis cannot determine  $l = l^*$

### ex: PDE spruce-budworm model

$$u_t = Du_{xx} + ru(1 - u) - \frac{1}{R} \frac{u^2}{\epsilon^2 + u^2} \quad (\text{add a predation term})$$

R: amount of foliage available(assume constant by time scale)(maybe, for foliage make predator hard to find the worm)

$\epsilon$  1/2 rate value, critical population level.

similar to dirichlet BCs in Fisher model, the critical domain size  $l^* = \pi\sqrt{\frac{D}{r}}$

For  $l > l^*$ , stationary solution exist depending on R.

1. small  $R < R_1$ , only one nontrivial solution at the refuge level(stable)
2.  $R_1 < R < R_2$  stable solution at refuge level exist. But when  $l > l_1(R)\sqrt{\frac{D}{r}}$ , then a second solution exists at outbreak level(stable), and unstable third solution exist at threshold level.
3.  $R_2 < R < R_3$ , If  $l > l_2(R)\sqrt{\frac{D}{r}}$ , the solution at the refuge level disappears. Depending on IC, solution to 0, or solution to outbreak level(stable)
4.  $R > R_3$ , solution to stable outbreak level(stable)

use critical domain size to prevent an outbreak:

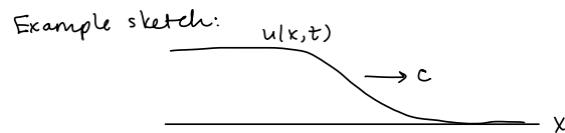
1.  $R > R_3$ , divide forest into regions  $l < l^*$
2.  $R_1 < R < R_3$  can divide into larger regions than  $l^*$ ,  $l < l_1(R)\sqrt{\frac{D}{r}}$

### use Fisher equ to analysis species invading a habitat

seek traveling wave solutions to  $u_t = Du_{xx} + ru(1 - u)$  on  $(-\infty, \infty)$

seek solutions of the form  $u(x, t) = \phi(x - ct)$ , travel with wave speed c,  $x - ct$  is the wave variable.

$\phi$  is the wave profile,  $z = x - ct$



traveling wave ansatz:  $\phi(-\infty) = 1$ ,  $\phi(\infty) = 0$ ;  $\frac{\partial}{\partial t}u(x, t) = -c\phi'$   $\frac{\partial^2}{\partial x^2}u(x, t) = \phi''$

simplify the PDE to 2nd order ODE, then to 1st order planar ODE.

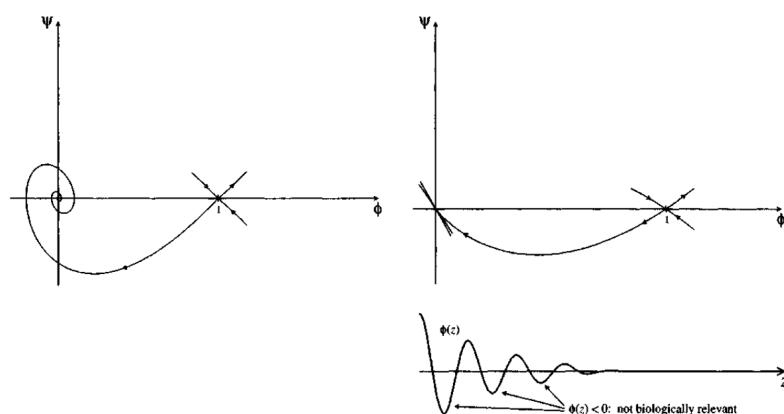
$$\begin{cases} \phi' = \psi \\ \psi' = -\frac{c}{D}\psi - \frac{r}{D}\phi(1 - \phi) \end{cases}$$

$x_1^* = (0, 0)$ ;  $x_2^* = (1, 0)$  are fixed points.

$$J = \begin{pmatrix} 0 & 1 \\ -\frac{r}{D} + 2\frac{r}{D}\phi & -\frac{c}{D} \end{pmatrix}$$

origin is stable spiral for  $2\sqrt{Dr} > c > 0$ ; sink for  $2\sqrt{Dr} < c$ .  $(1, 0)$  is always a saddle.

$(\phi(-\infty), \psi(-\infty)) = (1, 0)$ , so in phase portrait, sink and saddle should be connected.



minimal wave speed  $c^*$  for wave front solution is  $c^* = 2\sqrt{Dr}$ ; that means the minimal speed of an invading species is  $c^*$

solution behave like  $\exp -\frac{c^*}{2D}x, x \rightarrow \infty$

$-\frac{c^*}{2D}$  is the decay rate of the wave front

## Generalized finsher equations

$u_t = Du_{xx} + ru(1-u) - f(u)$ , require  $\exists k > 0$  s.t.  $f(0) = 0, f(K) = 0, f(u) > 0$  for  $0 < u < K, f'(0) > 0, f'(K) < 0$

If we assume that  $f$  satisfies the sub tangential condition  $f'(0)u > f(u); 0 < u < \infty$

The min wave speed is  $c^* = 2\sqrt{Df'(0)}$

the origin changes from spiral to sink at  $c^*$ ,  $c^*$  is a center.

## Keller-Segel model for chemotaxis(1971)

movement of organism toward(away) from a chemical signal. original model cellular slime mold

cells behave individually but they aggregate when food supply is low, form "sluge" to find food.

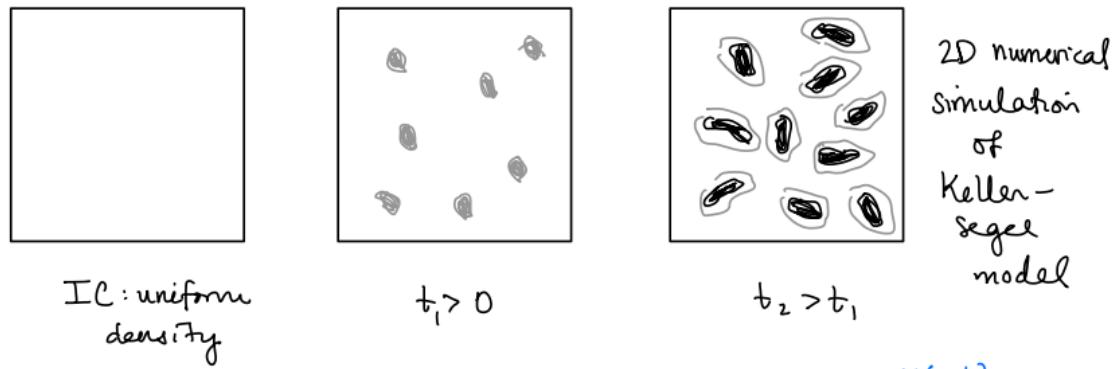
assume: cells initially uniformly distributed. cells both produce and are attracted to chemical signal(CAMP). cells and chemical signal diffuse. cells do not reproduce or die.

$$\begin{cases} \frac{\partial a}{\partial t} = \mu \Delta a - X \text{divergence}(a \nabla c) \\ \frac{\partial c}{\partial t} = D \Delta c + f a - k c \end{cases}$$

diffusion + transport term cells move towards chemical gradient.

diffusion + cell produce chemical - decay of chemical(absence of cells)

a: cell density, c chemical concentration,  $\mu$  rate of cell mobility, D diffusion constant of chemical. X rate of cellular chemotaxis, f rate of chemical secreted by the cells, k rate of chemical decay



For homogeneous equilibria state(time, space derivative is 0), substitute  $a_{eq}, c_{eq}$ ,

$$\begin{aligned} \frac{\partial a_{eq}}{\partial t} &= \mu \Delta a_{eq} - \chi \nabla \cdot (a_{eq} \nabla c_{eq}) \\ \frac{\partial c_{eq}}{\partial t} &= D \Delta c_{eq} + f a_{eq} - k c_{eq} \end{aligned}$$

we have  $a_{eq} = \frac{k}{f} c_{eq}$

Homogenous equilibria related by ratio of rate of chemical decay and secretion

explicitly add a small perturbation  $\Delta c, \Delta a$ . and linear stability analysis.

$$(a, c) = (a_{eq}, \frac{f}{k}a_{eq}) + (\Delta a, \Delta c)$$

$$\frac{\partial a}{\partial t} = \frac{\partial a_{eq}}{\partial t} + \frac{\partial \Delta a}{\partial t} = \mu \frac{\partial^2 \Delta a}{\partial x^2} - X a_{eq} \frac{\partial^2 \Delta c}{\partial x^2} - X \frac{\partial \Delta a}{\partial x} \frac{\partial \Delta c}{\partial x} - X \Delta a \frac{\partial^2 \Delta c}{\partial x^2}$$

$$\frac{\partial a}{\partial t} = D \frac{\partial^2 \Delta c}{\partial x^2} + f \Delta a - k \Delta c$$

Assume a wave solution:  $(\Delta a, \Delta c) = \sin(wx + \phi)(\Delta a(t), \Delta c(t))$

wave number, determine spatial frequency:  $\frac{w}{2\pi}$ ,

$$\begin{pmatrix} (\Delta a)' \\ (\Delta c)' \end{pmatrix} = \begin{pmatrix} -\mu w^2 & X a_{eq} w^2 \\ f & -D w^2 - k \end{pmatrix} \begin{pmatrix} \Delta a \\ \Delta c \end{pmatrix}, \text{ near } \begin{pmatrix} \Delta a \\ \Delta c \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

The system is unstable(perturbation grows, spontaneous patterns aggregation form):

$$|J| < 0; \mu(Dw^2k) < Xa_{eq}f$$

critical condition for aggregation, wave length  $l^* = \frac{2\pi}{w^*} = 2\pi \sqrt{\frac{\mu D}{Xa_{eq}f - \mu k}}$

I spatial length scale of perturbation char distance between aggregation form spontaneously from uniform IC. If  $l > l^*$  perturbation grows,  $l < l^*$  perturbation disappear.

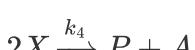
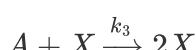
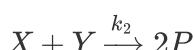
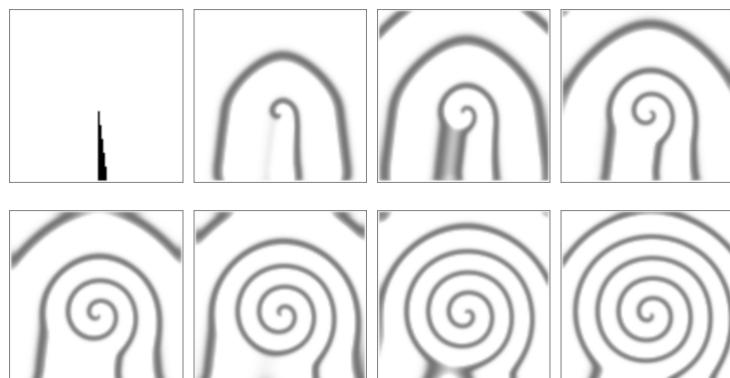
## Belousov-Zhabotinsky

Oscillatory chemical reaction(1950s)

oxidation of malonic acid by an acidified bromide solution

dynamics nonlinear oscillation for a while before chemical equilibrium

cause traveling waves form spirals if spatial symmetry broken by noise



conc of A assumed constant, P is a product, X,Y conc of malonic acid and bromide

nondimensional oregonator model (1974) u,v are conc of (X,Y)

$$\begin{cases} \frac{\partial u}{\partial t} = Lrv + u(1 - u - rv) + \frac{\partial^2 u}{\partial x^2} \\ \frac{\partial v}{\partial t} = -Mv - buv + \frac{\partial^2 v}{\partial x^2} \end{cases}$$

v produce u +( logistic growth + competition term ) + Diffusion term

decay term + competition term(oxidation) + Diffusion term

$$L = \frac{k_1 k_4}{k_2 k_3}, M = \frac{k_1}{k_3}, b = \frac{k_2}{k_4}, r \text{ constant}$$

Homogeneous equilibria:  $(0, 0), (1, 0)$

with realistic parameter,  $L \ll 1, M \ll 1$ , neglect those terms

$$\begin{cases} \frac{\partial u}{\partial t} = u(1 - u - rv) + \frac{\partial^2 u}{\partial x^2} \\ \frac{\partial v}{\partial t} = -buu + \frac{\partial^2 v}{\partial x^2} \end{cases}$$

looking for traveling solution, BC:  $u(-\infty, t) = 0, u(\infty, t) = 1, v(-\infty, t) = 1, v(\infty, t) = 0$

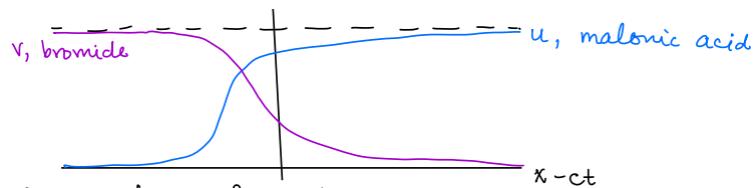
assume wave solutions  $u(x, t) = f(x - ct), v(x, t) = g(x - ct)$ , get an ODEs

$$\begin{cases} -cf' = f(1 - f - rg) + f'' \\ -cg' = -bfg + g'' \end{cases} \text{ BC: } f(\infty) = g(-\infty) = 1, f(-\infty) = g(\infty) = 0$$

change to planar system:

$$\begin{cases} h = f' \\ j = g' \\ h' = ch + f(1 - f - rg) \\ j' = cj + bfg \end{cases} \text{ is the 1st order 4-eqns nonlinear ODE}$$

wave solutions to reduced system



Above is the equation based model. Now

## Agent-based models(game: Sim)

-computational -algorithms

-involve many discrete agents- entities that act individually with set of rules

-too complex to analyze analytically - statistical tools

Ex: flocking/ schooling behavior of birds/fish; cell growth+ morphogenesis

assumptions: agents have internal states define on a list of attributes(people in game sim). agents interact with other agents. agents behave based on a set of rules. agents have associated spatial locations

Human interaction during pandemic:

people has attributes: age, covid cautionsness, living situation, job setting, covid status, underlying health conditions

internal states of attributes: age(young, adult, senior)(very contingent); add up precautions for a score; ...

rules of behaviors: positive infects negative, interact according to function of attributes.

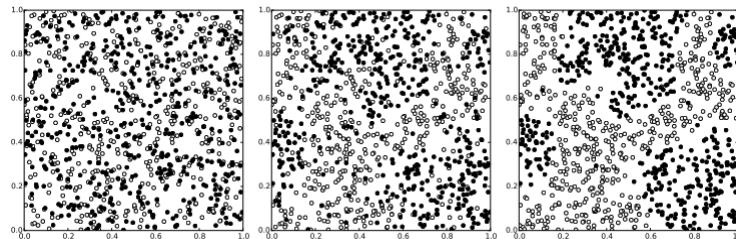
Schelling's segregation model(1971)

model/explain hypothesis: people with different ethnic backgrounds tend to self-segregate geographically.

assume: 2 types of agents in a finite 2D space. iteration, a randomly chosen agent looks at its neighborhood. if % of agents of its type in neighborhood below a threshold, then agent jumps to random location.

Question: how high does threshold have to be for segregation.

N by N grid, equal population



Reynolds Boids model

three rules:

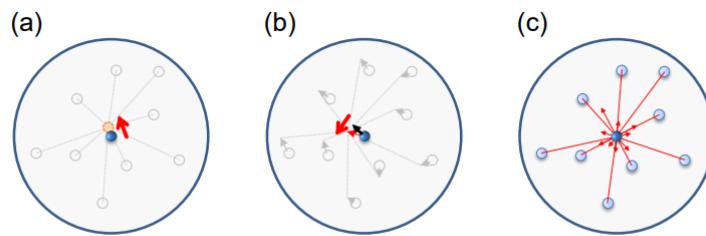


Figure 19.3: Three essential behavioral rules of Boids. (a) Cohesion. (b) Alignment. (c) Separation.

## Parameter estimation

parameter identifiability

Positron emission tomography: image blood flow + metabolism

person injected weakly radioactive tracer

$B(t)$  conc of tracer in blood over time(know); blood delivering radioactivity to tissue

parameter identifiability: inhomogenous tissue(white grey matter)

consider the radioactive signal in a voxel(tiny volume), with 2 tissues:

volume  $\tau$ , volume  $1 - \tau$ ,  $\tau$  unknown

radioactivity in two types  $C(t)$ ,  $D(t)$ , tracer exchange with blood vessel and tissues with ratio  $k_{C1}, k_{C2}, k_{D1}, k_{D2}$

model the exchange:

$$\begin{cases} \text{\color{red}\backslash derivative} C t = -k_{C1} c(t) + k_{C2} B(t) \\ \text{\color{red}\backslash derivative} D t = -k_{D1} D(t) + k_{D2} B(t) \end{cases}$$

measure signal:  $S(t) = \tau C(t) + (1 - \tau) D(t)$

known:  $B(t), S(t)$  by PET

unknown:  $\tau, k$

$\frac{\text{derivative}}{\text{dd}} St = \tau \frac{\text{derivative}}{\text{dd}} Ct + (1 - \tau) \frac{\text{derivative}}{\text{dd}} Dt$ ; do some replacement

$$\frac{\text{dd}[2]S}{\text{dd}t^2} + \theta_a \frac{\text{dd}S}{\text{dd}t} + \theta_b S = \theta_c \frac{\text{dd}B}{\text{dd}t} + \theta_d B$$

known S,B, combination of  $\theta$ , not  $\tau$  and  $k$

info lost by combining C,D into S

## Method of Least square

any data fitting method: optimization problem