INTRODUCTION TO BIOMATHEMATICS P

also MATHEMATICAL BIOLOGY

The subject is not as hierarchical as many areas of mathematics and there is some flexibility over what is included. It is an <u>interdisciplinary</u> science.

Classical areas:

- population biology
- epidemiology
- population interactions of several species
- population genetics

[•] mathematical physiology

[•] DNA modelling

Mathematical background

- linear algebra
- ODE & PDE
- difference equations

[•] vector calculus

[•] probabilities & statistics.

Biomathematics as a mathematics discipline

- comparatevely new – last 20 & 30 years.
- increased number of advertised positions in academia, medicine and industry around the world
- new subareas emerge as subject becomes so large, such as • <u>biofluid mechanics</u>
  - theoretical ecology
  - cancer ~~models~~ growth models.
  - cardiomathematics

- The mathematical descriptions of biological phenomena are not biological explanations

- The principal use of any theory is its predictions, this is why mathematical models are important. However only experiments can confirm how closely the model relates to the real biology.

| understanding the process | → | mathematical model | → | predictions |
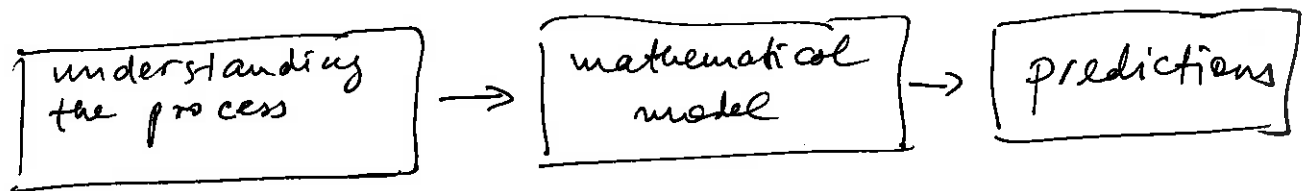
- The model can not take into account every single process - it captures the essence of the process that dominates the interactions. With more data avalable, more sophisticated models are possible. From mathematical point of view the art of good modelling relies on

(i) sound understanding and appreciation of the biological problem

(ii) a realistic mathematical representation of the important biological phenomena

(iii) finding useful solutions, preferably quantitative

(iv) biological interpretation of the mathematical results in terms of insights & predictions.

The mathematics is dictated by the biology and not vice-versa.

We will be using <u>Dynamic Models</u>

- Dynamic models are simplified representations of some real-world entity, in equations or computer code

- They mimic some essential features of the study system while leaving out inessentials.

- The models are called <u>dynamic</u> because they describe how system properties change over <u>time</u> ; e.g

  - gene expression level
  - abundance of an endangered species
  - mercury level in different organs within an individual, ...

- Allow for making <u>forecasts</u> that can not be made strictly by extrapolating from data

| The modeling process : |

1. Conceptual model - represents our ideas about how the system works

2. Diagram with boxes or arrows

3. Equations are developed for the rates of each process and are combined to form a mathematical model consisting of dynamic equations for each <u>state</u> variable.

Compartment models — ~~based~~ based on conservation of mass:

example: Enzyme Kinetics

Enzyme mediated biochemical reaction

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} SE$$

$$SE \xrightarrow{k_2} P + E$$
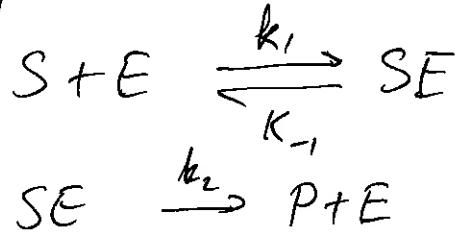
S = substrate   (sucrose) $C_{12}H_{22}O_{11}$ table sugar
E = enzyme   (invertase)
P = reaction product

$C_6H_{12}O_6$

(Hydrolysis of sucrose into glucose & fructose)
                                              $\underbrace{\qquad\qquad}_{P}$

Only assumption: Law of Mass Action — the rate of chemical reaction is proportional to the product of concentration of reactants
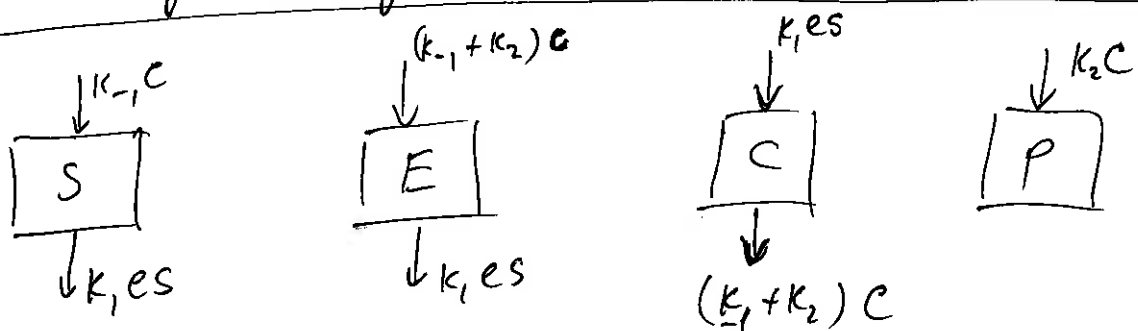
K_1, K_{-1} — constants of proportionality

$s, e, c, p \longrightarrow$ concentrations of S, E, SE, P

- S and E combine to form SE at rate $\boxed{K_1 s e}$
- SE separate to S+E at rate $K_{-1} c$
  SE $——\shortmid—$ S + P $—\shortmid—$ $K_2 c$

we have 4 state variables s, e, c, p

$$\boxed{\text{rate of change} = \text{inflow rate} - \text{outflow rate}}$$

$\downarrow K_{-1}c$ $(k_{-1}+k_2)c \downarrow$ $K_1 es \downarrow$ $\downarrow K_2c$

| S | | E | | C | | P |

$\downarrow k_1 es$ $\downarrow k_1 es$ $\downarrow (K_{-1}+k_2)c$

We can write now equations

$$\frac{ds}{dt} = K_{-1}c - K_1 es$$

$$\frac{de}{dt} = (K_{-1} + K_2)c - K_1 es$$

$$\frac{dc}{dt} = K_1 es - (K_{-1} + K_2)c$$

$$\frac{dp}{dt} = K_2 c$$

Non linear system of 4 ODE s.

Initial data:

$$s(0) = s_0$$
$$e(0) = e_0$$
$$c(0) = p(0) = 0$$

- Our interest is in the rate of product formation, we do not need the eqn. for p: the rate of product formation is $\boxed{K_2 c(t)}$

- We can further simplify by nothing that

$$\frac{de}{dt} + \frac{dc}{dt} = 0 \implies c(t) + e(t) = c(0) + e(0) = e_0$$

$$\implies \boxed{e(t) = e_0 - c(t)}$$

This makes sense because e and c are the unbound and bound forms of the enzyme which is not created or destroyed in this reaction scheme, whereas substrate is irreversibly converted to product.

- We can substitute $e_0 - c$ for e into the equations for s and c, leaving us with a system of only two equations

$$\frac{ds}{dt} = K_{-1} c - K_1 (e_0 - c) s$$

$$\frac{dc}{dt} = K_1 (e_0 - c) s - (K_{-1} + K_2) c$$

we can not solve these (except numerically using computer) but we can get the information that we want by a simple approximation

Enzymes are in a very low concentration,
e_0 is small $e(t) = e_0 - c(t) \geq 0 \Rightarrow c(t) \leq e_0$

$\Rightarrow c(t)$ is also small

We introduce new variable:

$$v = \frac{c}{e_0} \qquad \Rightarrow c = e_0 v$$

$$\frac{dv}{dt} = \frac{1}{e_0} \frac{dc}{dt} = K_1 \left(\frac{e_0}{e_0} - \frac{c}{e_0} \right) s - (K_{-1} + K_2) \frac{c}{e_0}$$

$$\boxed{\frac{dv}{dt} = K_1 (1 - v) s - (K_{-1} + K_2) v}$$

The other equation becomes

$$\frac{ds}{dt} = K_{-1} e_0 v - K_1 (e_0 - e_0 v) s = \underset{\text{small.}}{e_0} \left[K_{-1} v - K_1 (1 - v) s \right]$$

$\Rightarrow s$ changes much more slowly because e_0 is small $\Rightarrow$ we can proceed as if s were constant $\boxed{s \approx \text{const.}}$
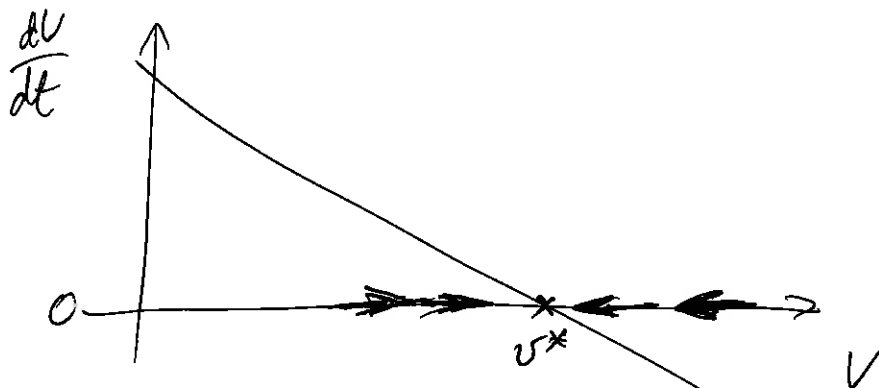
This brings us down to the single eqn:

$$\frac{dv}{dt} = k_1 S - (k_{-1} + k_2 + k_1 S) v$$

Observations:

$$\frac{dv}{dt} > 0 \quad \text{at} \quad v = 0$$

$v(t)$ approaches value v^* at which $\frac{dv}{dt} = 0$

$$k_1 S = (k_1 S + k_{-1} + k_2) v^* = (k_1 S + k_{-1} + k_2) \frac{c^*}{e_0}$$

$$c^* = \frac{k_1 e_0 S}{k_1 S + k_{-1} + k_2} = \frac{e_0 S}{K + S} \quad ; \quad K = \frac{k_{-1} + k_2}{k_1}$$

c^* is called stable equilibrium point: the system tends towards it and then stays there.

We need rate of product formation

$$\left(\frac{dp}{dt}\right)_* = k_2 c^* = \frac{k_2 e_0 S}{K + S} = \frac{V_{max} S}{K + S} \quad \text{where} \quad \boxed{k_2 e_0 \equiv V_{max}}$$

Michaelis - Menten equation.

We have some additional information:
the c - equation describes how enzyme
moves between bound and unbound states —
it reaches equilibrium value, that depends
on S (the amount of substrate)

Physics Models

Based on the physical laws of Mechanics.
The variables are normally positions
and velocities, accelerations, forces, etc.
Equations come from Newton's laws of
motion.

Example: DNA molecule

Simple model: A chain of coupled disks

U_n and φ_n are longitudinal
and angular displacements
of the n-th disk

M and I are the mass and
the moment of inertia of the
disk, ~~k and k~~

k — elasticity constant of spring

K — torsional rigidity of
the chain

$$M \ddot{u}_n = K \left(u_{n+1} - 2u_n + u_{n-1} \right) \qquad \text{liner approx.}$$

↑ acceleration of nth node

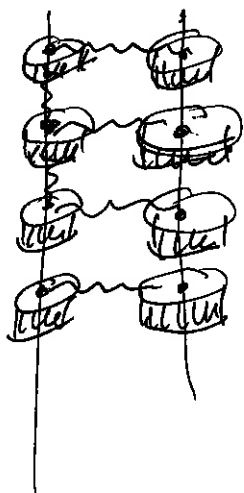$\underbrace{\hphantom{K(u_{n+1}-2u_n+u_{n-1})}}$ Force acting on n-th disk due to (elasticity)

~~This is a linear approximation~~

$$I \ddot{\varphi}_n = K \left(\varphi_{n+1} - 2\varphi_n + \varphi_{n-1} \right)$$

torque

↑ angular acceleration

These two equations give the linear approximation of one of the DNA strands. But DNA has two strands, which have a planar representation — in the next approximation:

Each Disk represents a base of DNA

Actually the real DNA molecule is by far more complex. It is a double ~~Each~~ helix with a turn of about $36°$ per base.
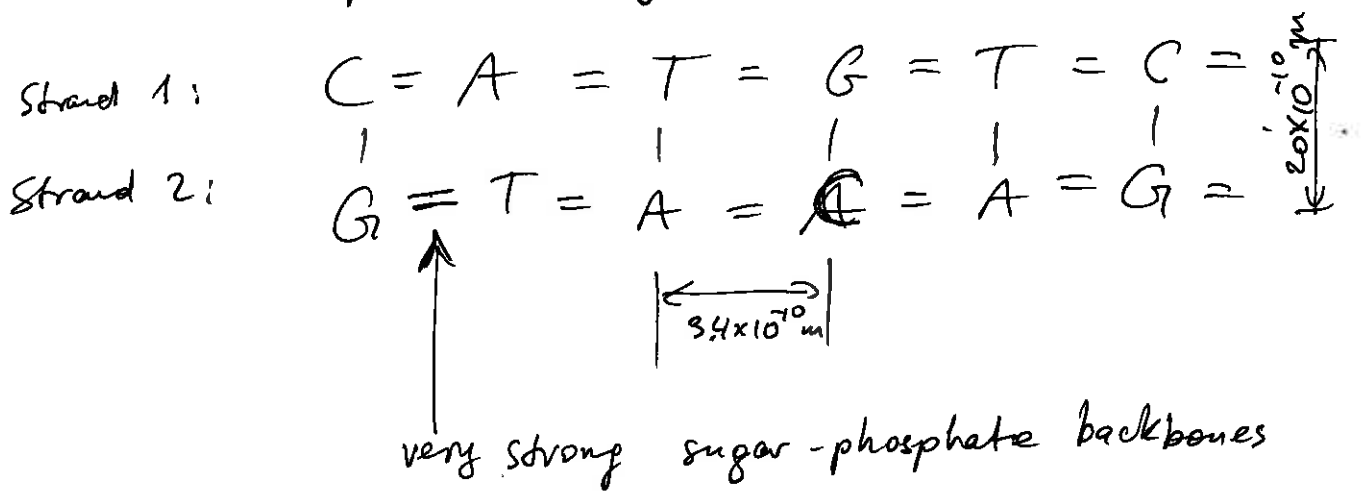
The Watson – Crick Model of DNA

1953

DNA composed of 4 bases (or nucleotides)
A T, C G which pair according to the rules

A – T , C – G

Two complementary strands

Strand 1: $C = A = T = G = T = C =$
Strand 2: $G = T = A = C = A = G =$

$\leftarrow$ 3.4×10^{-10} m $\rightarrow$

2.0×10^{-10} m

very strong sugar - phosphate backbones

Each cell contains 10^{10} base pairs ≈ 3.4 m of DNA in each cell of our body! Actually it is between 1 – 2 meters and not in one piece.

The total volume however of DNA is still rather small and can be packed in individual cells with plenty of space left over

One gene encodes one entire protein and a typical lenth of a gene is 500 – 600 bp (basic pairs)
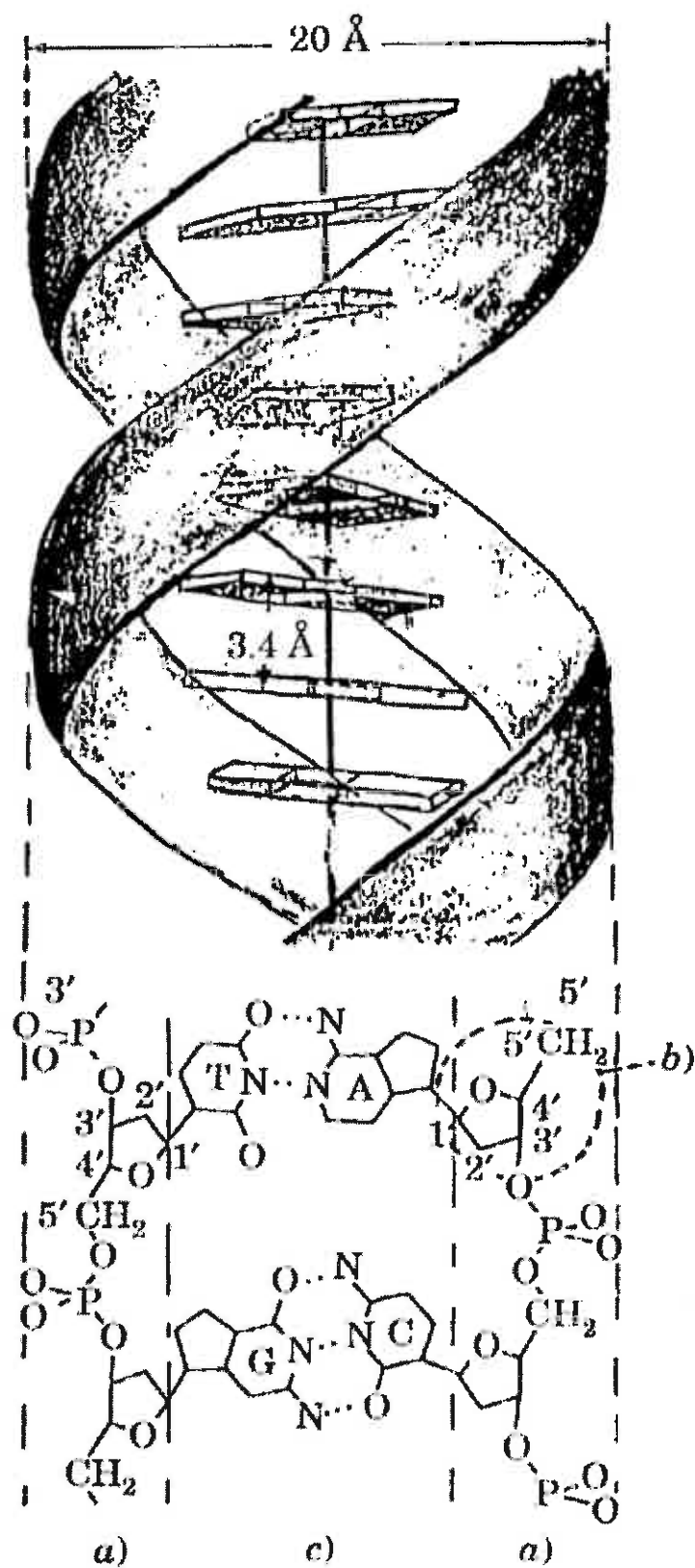
One bp $\Rightarrow$ 60 atoms.

Fig. 1. – Schematic drawing of the double helix (B form), the sugar-phosphate backb
represented as a ribbon, with detailed chemical structure shown in a) and b) (sugar n
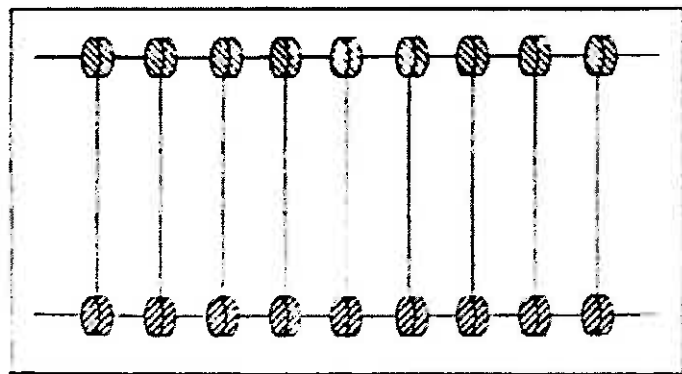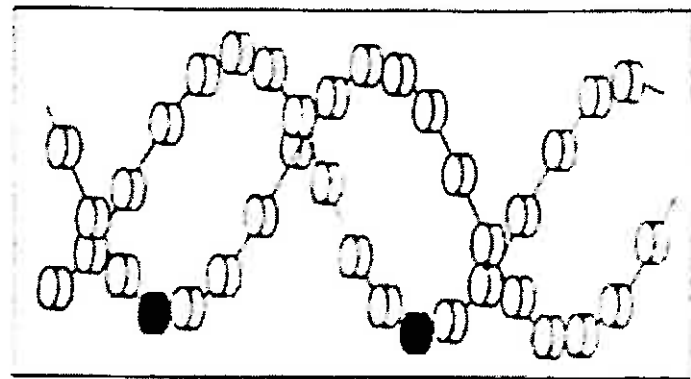The bases are sketched as rectangular plates, with detailed chemical structures shown

Fig. 10.

Fig. 9.

Fig. 9. – Abstract representation of planar models of DNA. Each base is consider... interact only with first neighbours on its chain (stacking interactions, modell... harmonic potential), and on the pairing base at the same site on the other chain (p... forces due to H-bonds, modelled by non-harmonic potentials). The abstract model c... considered planar, which explains the name; in actual DNA, the geometry of the bac... is at the origin of the double-helix structure, with a turn of about 36° per base

Fig. 10. – Abstract representation of helicoidal models of DNA. In addition to stacki... pairing interactions indicated in fig. 9, these consider also interaction between bas... opposite chains which are half-pitch of the helix away in the sequence, and the... nearby in three-space due to helical geometry; two bases connected by such an helic... interaction are indicated. In real DNA, these interaction are mediated by water fila... joining the concerned bases.

Another ~~to our~~ mechanical model : DNA is
smoothed or averaged to yeal a model as
an elastic line.

- DNA is big enough to be seen with
various microscopy techniques
- DNA quite often occurs into closed
loops (150 bp or less), mini-circles,
as well as thousands of bp
- DNA is rather stiff; it has a well-defined
shape.

Optimization Models

Biologists also use optimization models,
in which the modeler assumes that the
study organizms are trying to achieve some
particular goal.
- For example; an animal will gather food
in the habitat that gives it the best chance
of getting enough food to survive, without
itself being eaten by predators
- Optimization of drug usage : effect / damage.

Usage of dynamical models

Why do we need dynamical models?

1. Scientific renderstanding of the underlying
process or phenomenon
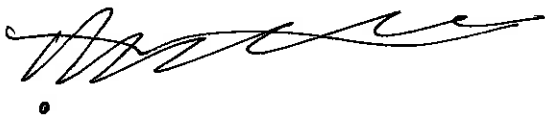
2. Using scientific understanding to manage the world

- Forecasting disease or pest outbreaks
- Designing man-made systems, for example biological pest control, bioengineering

- Managing existing systems such as agriculture or fisheries

- Optimizing medical treatments or improving athletic performances

3. There are experiments that you would rather not do:
- Endangered species management by trial & error
- Clinical experiments on humans
- Experiments with toxic substances, radiological experiments, dosymetry and radiation protection.
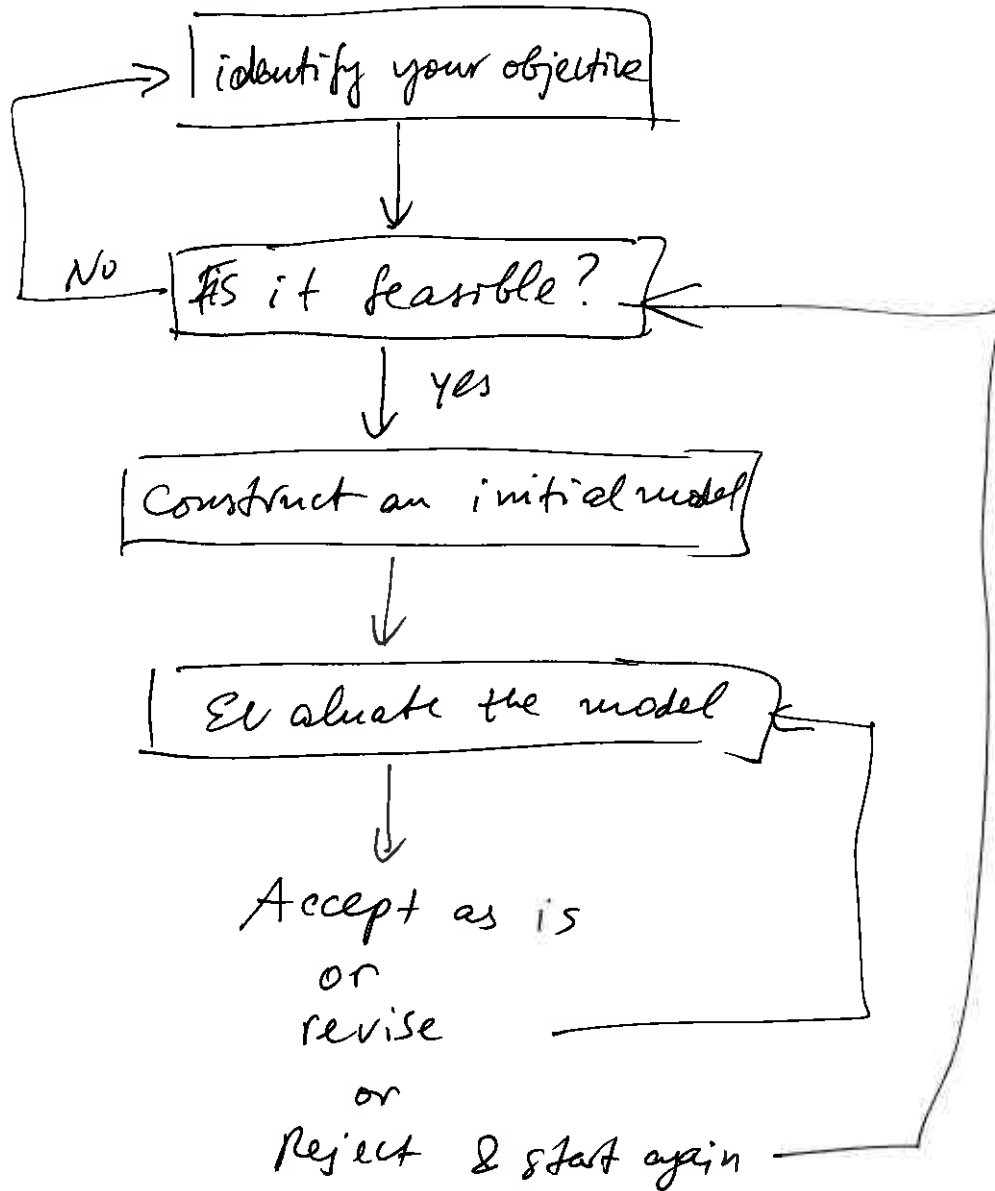
Theoretical versus Practical Models

Practical	Theoretical
• Main goals are management, design & prediction	• Main goals are theoretical understanding and theory development
• Numerical accuracy is desirable, even at the expence of simplicity	• Numerical accuracy is not essential; the model should be as simple as possible.
• Processes and details can be ignored only if they are numerically unimportant	• Processes and details can be ignored if they are conceptually irrelevant to the theoretical issues
• Assumptions are quantitative representations of system processes	• Assumptions may be qualitative representations of hypotheses about the system, adopted conditionally in order to work out their consequences
• System and question specific	• Applies to a range of similar systems

Outline of the modelling process

```
        ┌──────────────────────────┐
    ──→ │ identify your objective  │
   ↑     └──────────────────────────┘
   │                 │
   │                 ↓
  No     ┌──────────────────────┐
  ┌──────│   Is it feasible?    │←─────────┐
  │       └──────────────────────┘          │
  │                 │ yes                    │
  │                 ↓                        │
  │       ┌──────────────────────────┐      │
  │       │ Construct an initial model│      │
  │       └──────────────────────────┘      │
  │                 │                        │
  │                 ↓                        │
  │       ┌──────────────────────┐          │
  │       │  Evaluate the model  │←─┐       │
  │       └──────────────────────┘  │       │
  │                 │               │       │
  │                 ↓               │       │
        Accept as is               │       │
           or                      │       │
        revise ──────────────────┘       │
           or                             │
        Reject & start again ─────────────┘
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CONTINUOUS Population models
for single species

$\boxed{N}$ $\underline{N(t)}$

$$\frac{dN}{dt} = births - deaths + migration$$
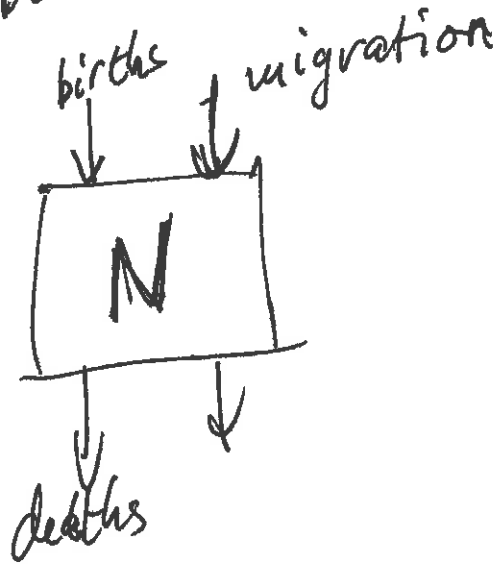
$$\frac{dN}{dt} = rN - dN = (r-d)N$$

$$N(t) = N_0 e^{+(r-d)t}$$

$$N_0 = N(0)$$

$r > d$ — exponential growth
$r < d$ — exponential decay

Malthus 1798

Logistic growth model
Verhulst 1838

$$\frac{dN}{dt} = \underbrace{r\left(1 - \frac{N}{K}\right)}_{\text{effective birth rate}} \cdot N$$

r, K — positive constants

K — carrying capacity of the environment

Equilibrium states (constant solutions)

$$\underline{N^* = 0} \qquad \underline{N^\theta = K}$$

$N \to 0$.

$$\frac{dN}{dt} = rN - \frac{r\cancel{N^2}}{\cancel{K}} \approx rN$$
small

$$\underline{N = N_0 e^{rt}} , \quad - \text{grows exponentially}$$

$N^* = 0$ is $\underline{\text{unstable}}$ solution

$$N^* = K$$

$$N = N^* + (n) = K + n \quad \text{where} \quad |n| \ll 1$$

$$\frac{dN}{dt} = \frac{dK}{dt} + \frac{dn}{dt} = 0 + \frac{dn}{dt} = \frac{dn}{dt}$$

$$\|$$

$$r\left(1 - \frac{N}{K}\right) \cdot N = r\frac{K-N}{K} \cdot N = r\frac{(-n)}{K}(K+n) =$$

$$= -rn - \frac{n^2}{K} = -rn$$

$$\frac{dn}{dt} = -rn \quad \Rightarrow \quad n = n_0 e^{-rt} \to 0$$

$$N(t) = K + n_0 e^{-rt} \to K \quad \text{stable.}$$

$\frac{1}{r}$ timescale

K - site of the population at equilibrium

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right) , \int \frac{dN}{N\left(1 - \frac{N}{K}\right)} = \int r \, dt$$

$$\underbrace{}_{?}$$

$$\|$$
$$rt$$

$$\frac{1}{N\left(1-\frac{N}{K}\right)} = \frac{A}{N} + \frac{B}{1-\frac{N}{K}} = \frac{A\left(1-\frac{N}{K}\right) + BN}{N\left(1-\frac{N}{K}\right)}$$

$$1 = A\left(1-\frac{N}{K}\right) + BN$$

$$N=0 \implies A=1.$$

$$N=K \implies B=1/K$$

$$\int \frac{dN}{N\left(1-\frac{N}{K}\right)} = \int \frac{dN}{N} + \frac{1}{K} \cdot \int \frac{d(N/K)}{1-\frac{N}{K}} = \ln N - \ln\left(1-\frac{N}{K}\right)$$

$$\boxed{x = \frac{N}{K} \qquad \int \frac{dx}{1-x} = -\int \frac{d(1-x)}{1-x} = -\ln(1-x)}$$

$$= \ln \frac{N}{1-\frac{N}{K}} + const.$$

$$\ln \frac{N}{1-\frac{N}{K}} = rt + c \qquad\qquad e^{rt+c} = e^{rt} e^{c}$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad \overset{\shortparallel}{C'}$$

$$\frac{N}{1-\frac{N}{K}} = Ce^{rt}$$

$$N = \left(1-\frac{N}{K}\right) c e^{rt}$$

$$N + \frac{N}{k} C e^{rt} = c e^{rt}$$

$$N\left(1 + \frac{C}{k} e^{rt}\right) = c e^{rt} \quad , \quad \begin{array}{l} t = 0 \\ \underline{\underline{N = N_0 = u(0)}} \end{array}$$

$$N_0 \left(1 + \frac{C}{k}\right) = C$$

$$N_0 = C - \frac{N_0}{k} C = \left(1 - \frac{N_0}{k}\right) C$$

$$\boxed{C = \frac{N_0}{1 - \frac{N_0}{k}}}$$

$$\underline{\underline{N}} \left(1 + \frac{N_0}{k} \cdot \frac{e^{rt}}{\boxed{1 - \frac{N_0}{k}}}\right) = \frac{N_0}{\boxed{1 - \frac{N_0}{k}}} e^{rt} \qquad \left[. 1 - \frac{N_0}{k} \right.$$

$$N\left(1 - \frac{N_0}{K} + \frac{N_0}{K}e^{rt}\right) = N_0 e^{rt}$$

$$\boxed{N = N_0 \frac{e^{rt}}{1 + \frac{N_0}{K}(e^{rt}-1)}}$$

$$\frac{\cdot e^{-rt}}{\cdot e^{-rt}}$$

$$N = N_0 \frac{1}{e^{-rt} + \frac{N_0}{K}(1 - e^{-rt})} \xrightarrow{t \to \infty}$$

$$\Rightarrow N_0 \frac{1}{\frac{N_0}{K}} = \boxed{K}$$

1925 Pearl.

$$\boxed{\frac{dN}{dt} = f(N)} = rN\left(1 - \frac{N}{K}\right)$$

$$\frac{dN}{dt} = f(N)$$

$$f(N) = \frac{dN}{dt} ? \quad \text{Linear stability}$$
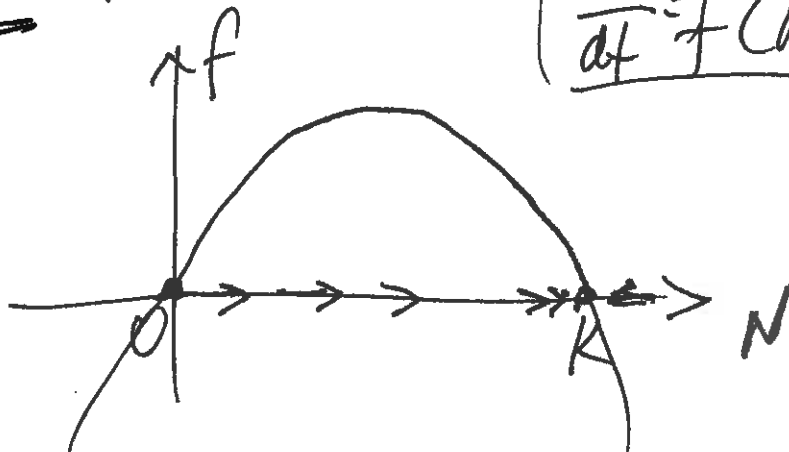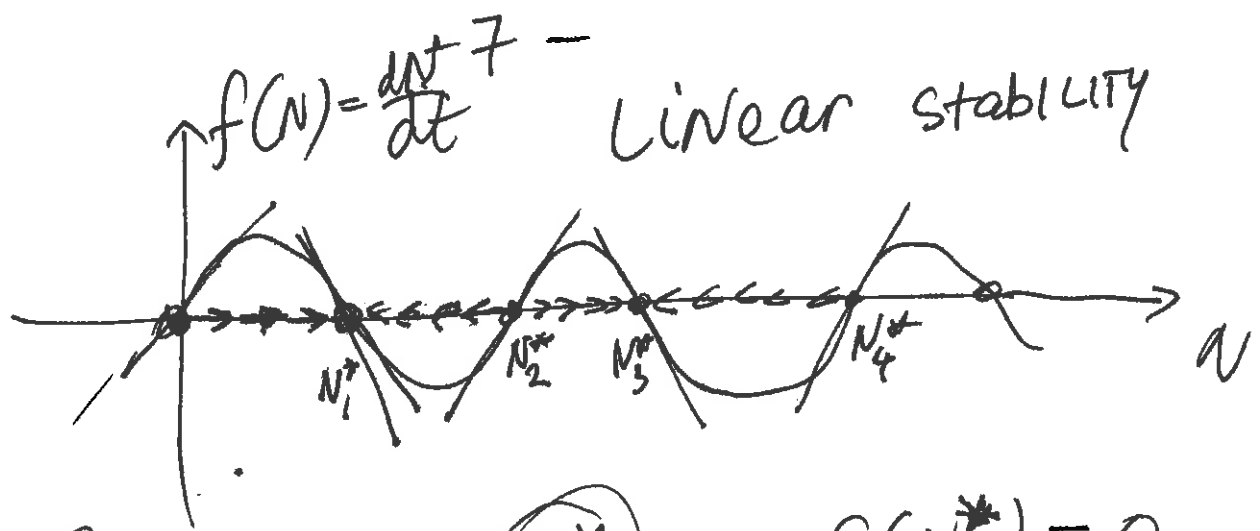
$$f(0) = 0 \rightarrow \boxed{N^*} \qquad f(N^*) = 0$$

$$f(N) = f(N^*) + f'(N^*)(N-N^*) + \tfrac{1}{2}f''(N^*)(N-N^*)^2 + \cdots$$

$$\underbrace{\qquad}_{\text{neglect}}$$

$$n = N - N^* \lll 1$$

$$f(N) = f'(N^*)\, n$$

$$\frac{dn}{dt} = \frac{dN}{dt} - \boxed{\frac{dN^*}{dt}} = 0 \qquad = \frac{dN}{dt}$$

$$\frac{dN}{dt} = f(N) \implies \frac{dn}{dt} \approx \underbrace{f'(N^*)}_{\text{const.}} \cdot n$$

$$h(t) = n_0 e^{f'(N^*) t}$$

$$N = N^* + n_0 e^{f'(N^*) t}$$

$$\text{if} \quad f'(N^*) > 0 \implies N^* \; \text{unstable equilibrium}$$

$$\text{if} \quad f'(N^*) < 0 \implies N^* \; \text{is stable}$$

Insect outbreak Model
Spruce budworm
Ludwig et al. 1978

$$\frac{dN}{dt} = r_B N \left(1 - \frac{N}{K_B}\right) - p(N)$$

$p(N)$ — predation

$$p(N) = \frac{BN^2}{A^2 + N^2}$$

$$\frac{dN/A}{dt/A} = (Ar_B) \frac{N}{A}\left(1 - \frac{N/A}{K_B/A}\right) - \frac{B\, N^2/A^2}{A^2/A^2 + N^2/A^2}$$
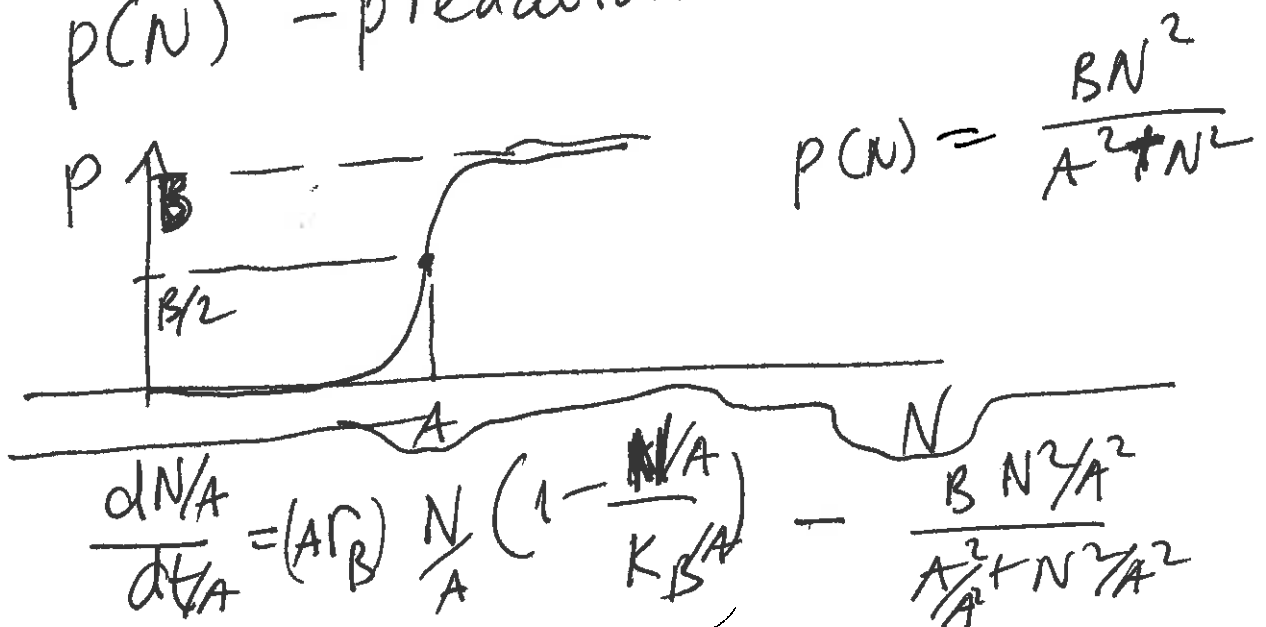
$r_B, \; K_B, \; A, \; B$ — 4 parameters.

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NONDIMENSIONAL TERMS

$$u = \frac{N}{A}, \qquad r = \frac{Ar_B}{B}, \qquad q = \frac{K_B}{A}, \qquad \tau = \frac{Bt}{A}$$

$$\frac{du}{d\left(\frac{t}{A}\right)B} = \left(\frac{Ar_B}{B}\right) u\left(1 - \frac{u}{q}\right) - \frac{Bu^2}{(1+u^2)B}$$

$\boxed{\dfrac{1}{B}}$

$$\boxed{\frac{du}{d\tau} = r\left(1 - \frac{u}{q}\right) - \frac{u^2}{1+u^2}}$$

$u(\tau; r, q)$

$$ma = F_{el}$$

$$m\ddot{x} = -Kx$$

$$\ddot{x} + \frac{K}{m}x = 0 \qquad \frac{K}{m} = \omega_0^2$$

$$\ddot{x} + \omega_0^2 x = 0$$

$$\frac{du}{d\tau} = f(u) = ru\left(1 - \frac{u}{q}\right) - \frac{u^2}{1+u^2}$$

$$f(u^*; q, r) = 0$$

$$ru\left(1 - \frac{u}{q}\right) = \frac{u^2}{1+u^2}$$
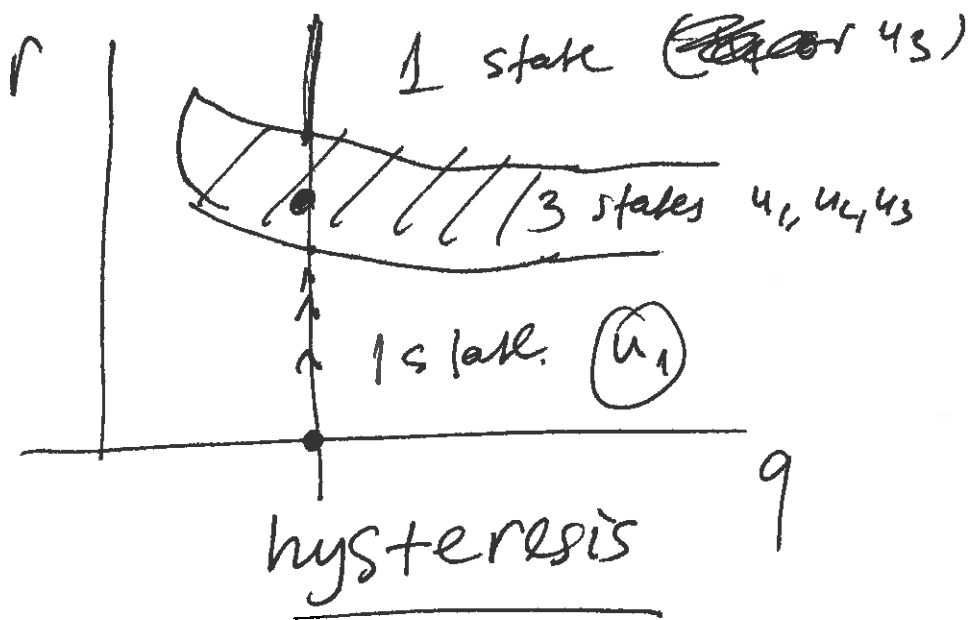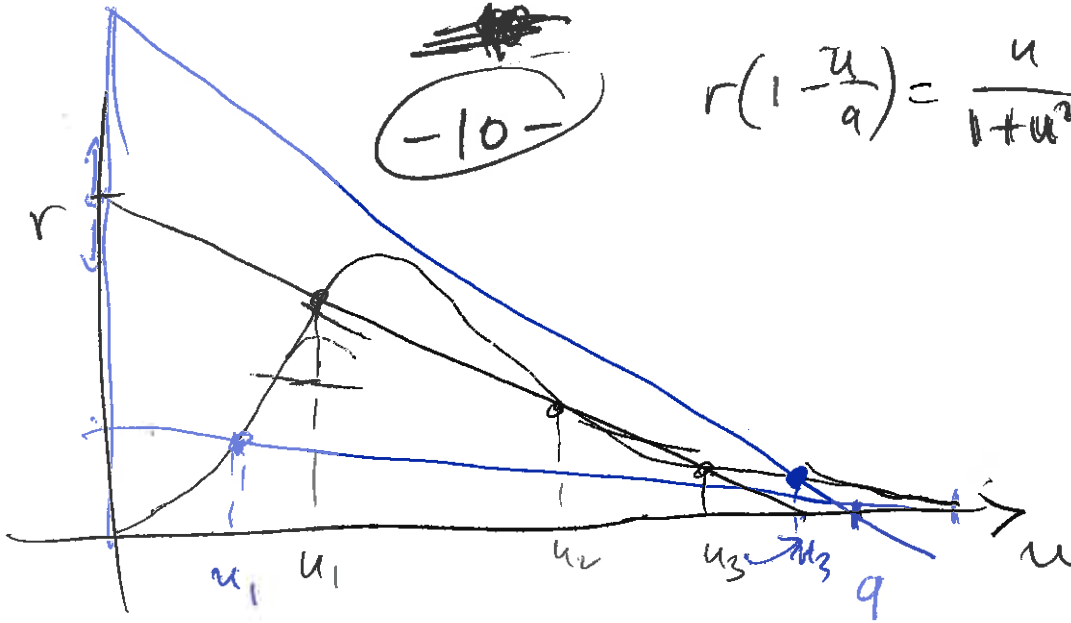
1) $u = 0$ is always a solution

2) $\boxed{r\left(1 - \frac{u}{q}\right) = \frac{u}{1+u^2}}$

$$r(1+u^2)\left(1 - \frac{u}{q}\right) = u \qquad - \text{qubic eqn.}$$

-10-

$$r\left(1 - \frac{u}{q}\right) = \frac{u}{1+u^2}$$

r

u_1 u_1 u_2 u_3 u_3 q u

r

1 state (3 or u_3)

3 states u_1, u_2, u_3

1 state (u_1)

hysteresis q

$u^*(q, r)$

Insect Outbreak Model

$$\frac{dN}{dt} = r_B N\left(1 - \frac{N}{K_B}\right) - p(N)$$

$\underbrace{\phantom{r_B N\left(1 - \frac{N}{K_B}\right)}}$ logistic term $\quad \underbrace{}$ predation term

Spruce Budworm
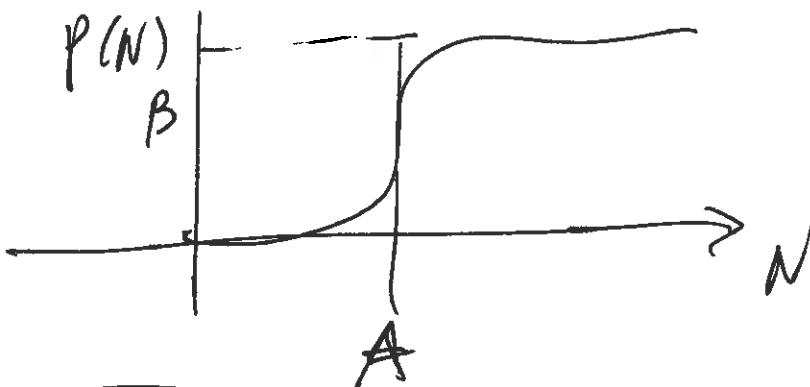
$$p(N) = \frac{BN^2}{A^2 + N^2}$$

$$\boxed{u = \frac{N}{A}} \quad, \quad r = \frac{A r_B}{B} \quad, \quad q = \frac{K_B}{A} \quad, \quad \boxed{\tau = \frac{Bt}{A}}$$

$$\underbrace{\phantom{r = \frac{A r_B}{B} \quad, \quad q = \frac{K_B}{A}}}_{\text{parameters}}$$

$$\frac{du}{d\tau} = ru\left(1 - \frac{u}{q}\right) - \frac{u^2}{1 + u^2} = f(u; q, r)$$

Equilibrium states $\quad \underline{f(u^*; q, r) = 0}$

$$ru\left(1 - \frac{u}{q}\right) = \frac{u^2}{1 + u^2} \quad \Rightarrow \quad \boxed{u = 0}$$

$$r\left(1 - \frac{u}{q}\right) = \frac{u}{1+u^2}$$

$$\underbrace{r(1+u^2)\left(1 - \frac{u}{q}\right) = u}_{\text{cubic eq. for } \textcircled{u}}$$
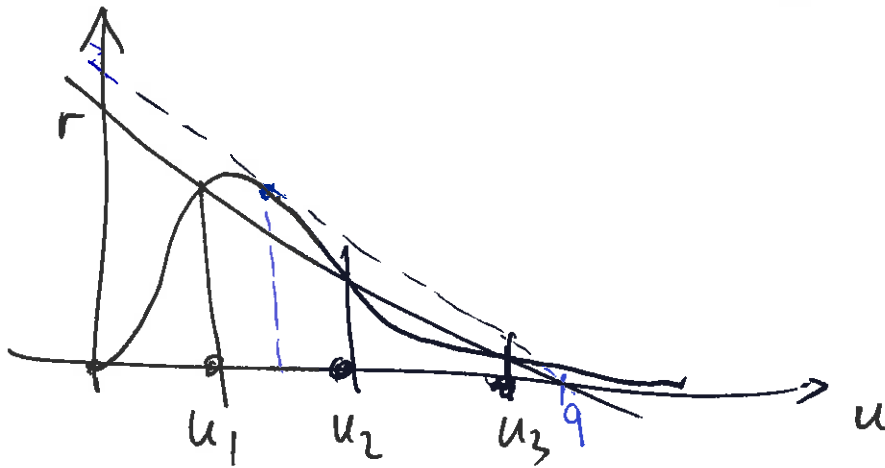
hysteresis - feromagnetic materials
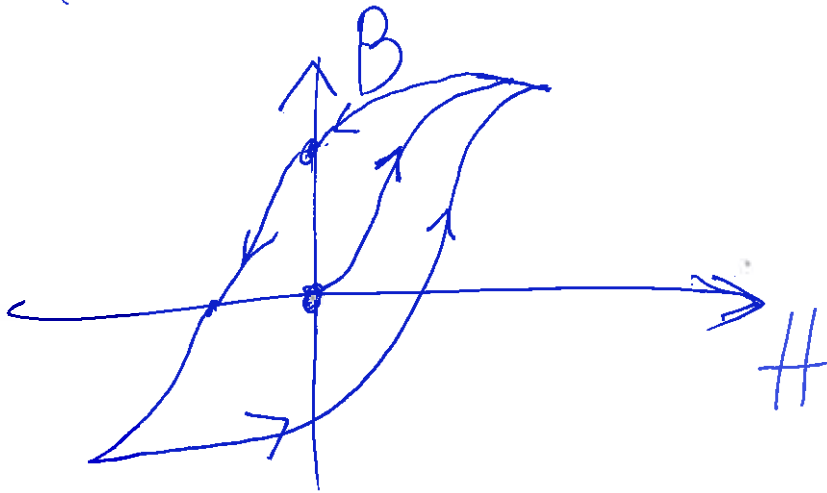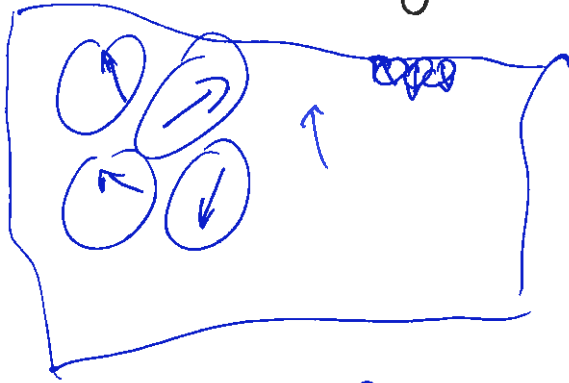
②. For which values of (q, r) we have 1 or 3 real solutions?

$$f(u^k) = 0 \iff \boxed{r\left(1 - \frac{u}{q}\right) = \frac{u}{1+u^2}} \quad (1)$$

$$\text{Slope} = -\frac{r}{q} = \frac{d}{du}\left(\frac{u}{1+u^2}\right) = \frac{1 \cdot (1+u^2) - u(2u)}{(1+u^2)^2}$$

$$-\frac{r}{q} = \frac{1-u^2}{(1+u^2)^2} \qquad \frac{r}{q} = \frac{u^2-1}{(u^2+1)^2} \quad (2)$$

$$r - \left(\frac{r}{q}\right)u = \frac{u}{1+u^2} \implies r = \left(\frac{r}{q}\right)u + \frac{u}{1+u^2}$$

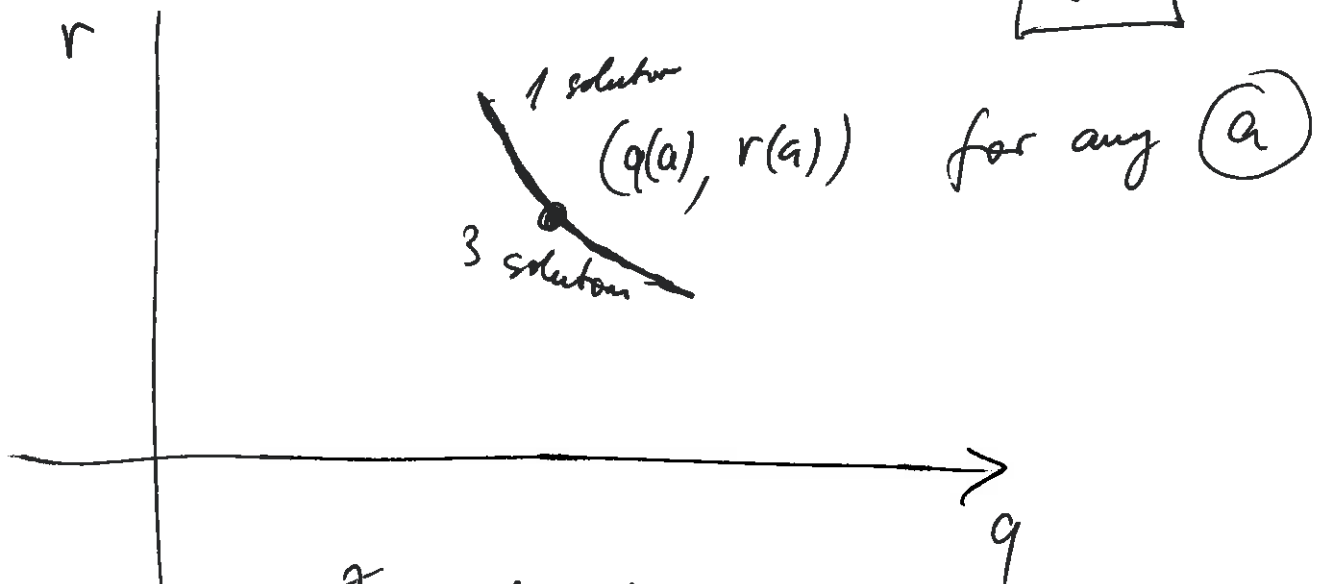$$r = u\frac{u^2-1}{(u^2+1)^2} + \frac{u}{1+u^2} = \frac{u(u^2-1+1+u^2)}{(u^2+1)^2} = \frac{2u^3}{(u^2+1)^2}$$

$$\boxed{r = \frac{2u^3}{(u^2+1)^2}} \qquad q = r\frac{(u^2+1)^2}{u^2-1} = \frac{2u^3}{(u^2+1)^2} \cdot \frac{(u^2+1)^2}{u^2-1}$$

$$q = \frac{2u^3}{u^2-1}$$

$u = a$ is a parameter

$$r(a) = \frac{2a^3}{(a^2+1)^2} > 0 \qquad q(a) = \frac{2a^3}{a^2-1} > 0$$

$$\boxed{a > 1}$$

for any $\boxed{a}$

1 solution

$(q(a), r(a))$

3 solutions

$$\frac{dr}{da} = \frac{6a^2(a^2+1)^2 - 2a^3 \cdot 2(a^2+1) \cdot 2a}{(a^2+1)^{4 \; 3}} = \frac{a^2(6a+6-8a^2)}{(1+a^2)^3}$$

$$\frac{dr}{da} = \frac{a^2(6-2a^2)}{(1+a^2)^3} = \frac{2a^2(3-a^2)}{(1+a^2)^3}$$

$$\frac{dq}{da} = \frac{d}{da}\left(\frac{2a^3}{a^2-1}\right) = \frac{6a^2(a^2-1) - 2a^3(2a)}{(a^2-1)^2} = \frac{2a^2(3a^2-3-2a^2)}{(a^2-1)^2}$$

$$\boxed{\frac{dq}{da} = \frac{2a^2(a^2-3)}{(a^2-1)^2}}$$
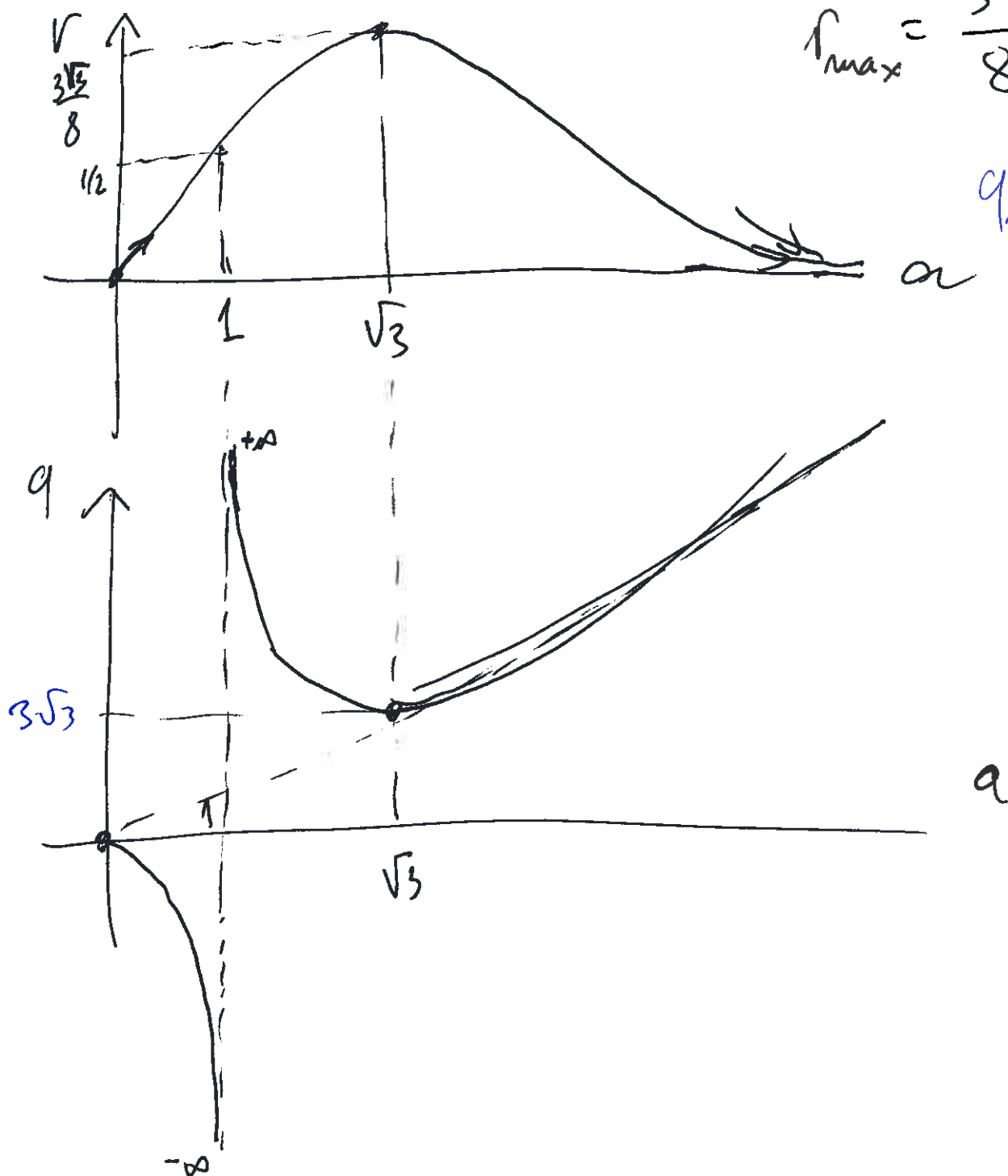
$$\frac{dv}{da} = \frac{2a^2(3-a^2)}{(1+a^2)^3}$$

$$\frac{dq}{da} = \frac{2a^2(a^2-3)}{(a^2-1)^2}$$

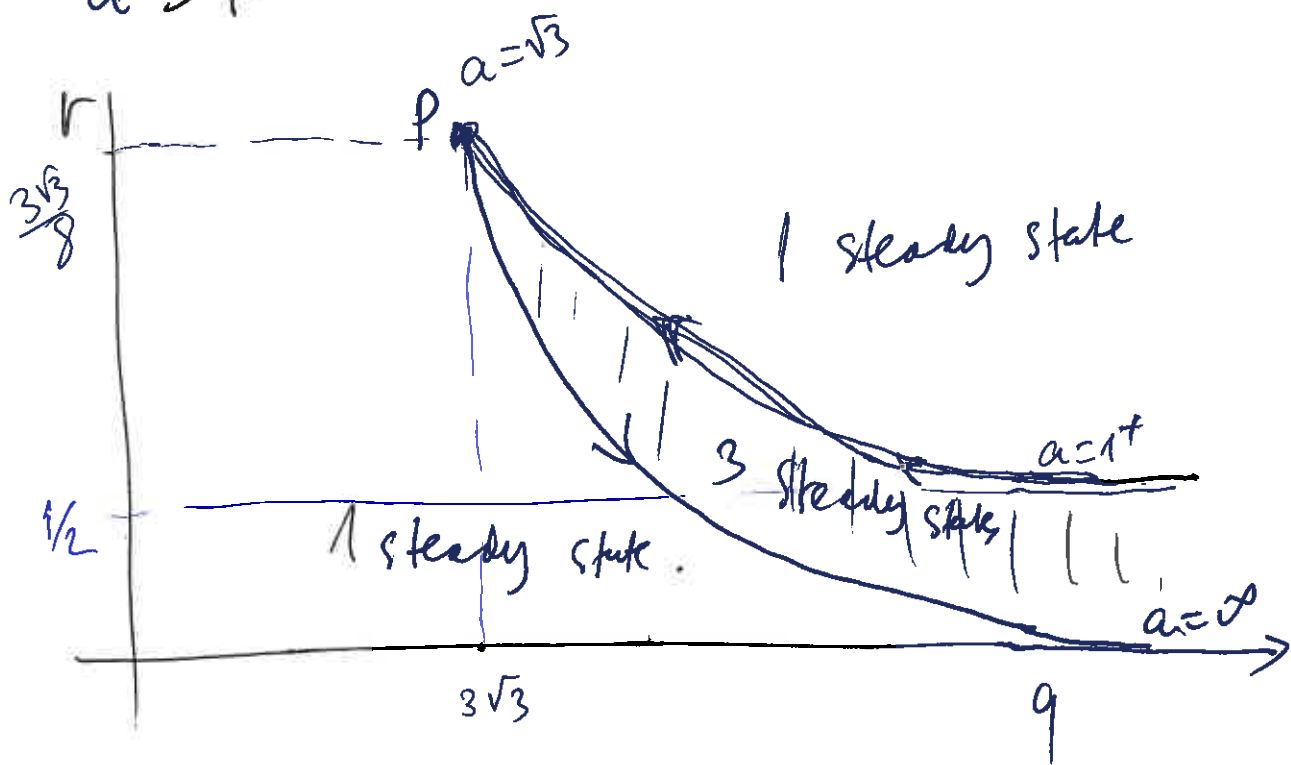$$r(a) = \frac{2a^3}{(a^2+1)^2}$$

$$q(a) = \frac{2a^3}{a^2-1}$$

$$r_{max} = \frac{3\sqrt{3}}{8} \text{ when } a=\sqrt{3}$$

$$q_{min} = \frac{2 \cdot 3\sqrt{3}}{2} = 3\sqrt{3}$$

$a > 1$

$a \rightarrow 1^+$

$a = \sqrt{3}$

r

$\frac{3\sqrt{3}}{8}$

P

1 steady state

3 steady state

$a = 1^+$

$\frac{1}{2}$

1 steady state .

$a = \infty$

$3\sqrt{3}$

9

P – 'cusp point'

Delay Models
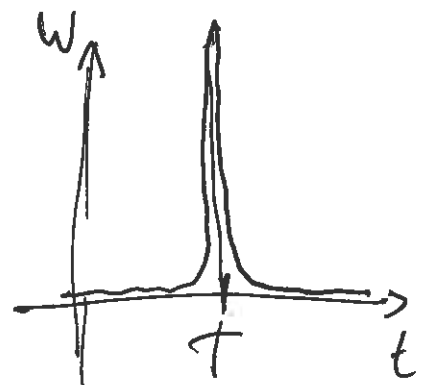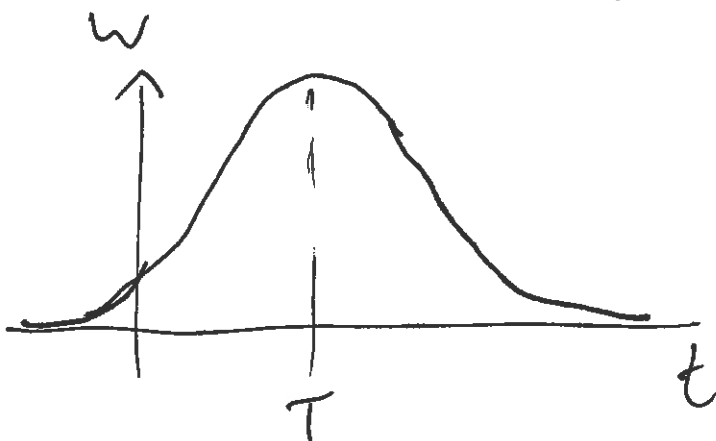
$$\frac{dN(t)}{dt} = f(N(t))$$

$$\frac{dN(t)}{dt} = f(N(t), N(t-T))$$

$$T - \text{'Delay'}$$

$$\frac{dN}{dt} = rN(t)\left[1 - \frac{N(t-T)}{K}\right] \qquad (1)$$

regulatory effect which depends on the population at earlier time $t-T$, rather than t.

$$\frac{dN}{dt} = rN(t)\left[1 - \frac{1}{K}\int_{-\infty}^{t} w(t-t')N(t')dt'\right] \qquad (2)$$

Let $w(t) = \delta(t-T)$.

Then $\displaystyle\int_{-\infty}^{t} w(t-t')\, N(t')\, dt' \implies$

$$\implies \int_{-\infty}^{t} \delta(t-t'-T)\, \underline{\underline{N(t')}}\, dt' = N(t-T)$$

$$t' = t - T$$

Delta function

φ, g defined on $(-\infty, \infty)$

$$(\varphi, g) = \int_{-\infty}^{\infty} f(x) g(x)\, dx \quad - \text{scalar product.}$$

$$(\varphi, \delta) = \varphi(0)$$

$$\int_{-\infty}^{\infty} \varphi(x)\, \delta(x)\, dx = \varphi(0)$$

$$\int_{-\infty}^{\infty} \varphi(x) \delta(x-x_0)\, dx = \varphi(x_0)$$

$$\delta(x) = \begin{cases} 0 & x \neq 0 \\ \infty & x = 0 \end{cases}$$

$$\int_{-\infty}^{\infty} \delta(x)\, dx = 1.$$

$$\delta(x) = \frac{1}{\pi} \lim_{\varepsilon \to 0} \frac{\varepsilon}{x^2 + \varepsilon^2} \qquad \begin{array}{ll} x \neq 0 & \delta(x) = 0 \\ x = 0 & \frac{1}{\varepsilon} \to \infty \end{array}$$

$$\int_{-\infty}^{\infty} \delta(x) = \lim_{\varepsilon \to 0} \frac{1}{\pi} \int_{-\infty}^{\infty} \frac{\varepsilon \, dx}{x^2 + \varepsilon^2} = \frac{1}{\pi} \lim_{\varepsilon \to 0} \int_{-\infty}^{\infty} \frac{d(\frac{x}{\varepsilon})}{1 + (\frac{x}{\varepsilon})^2}$$
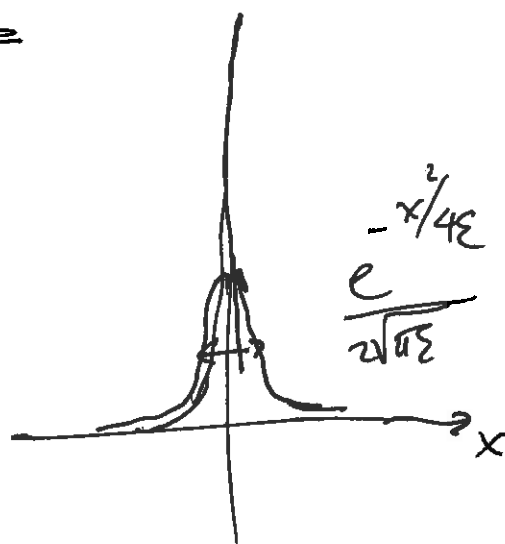
$$= \frac{1}{\pi} \lim_{\varepsilon \to 0} \left(\tan^{-1}\left(\frac{x}{\varepsilon}\right) \Big|_{-\infty}^{\infty} \right) = \frac{1}{\pi} \left(\frac{\pi}{2} - \left(-\frac{\pi}{2}\right) \right) = 1$$

$$\tan \frac{\pi}{2} = \frac{\sin \pi/2}{\cos \pi/2} = \infty$$

$$\tan \left(-\pi/2\right) = \underline{\underline{-\infty}}$$

$$\delta(x) = \lim_{\varepsilon \to 0} \frac{1}{\pi x} \sin\left(\frac{x}{\varepsilon}\right)$$

$$\delta(x) = \lim_{\varepsilon \to 0^+} \frac{1}{\sqrt[2]{\pi \varepsilon}} e^{-\frac{x^2}{4\varepsilon}}$$

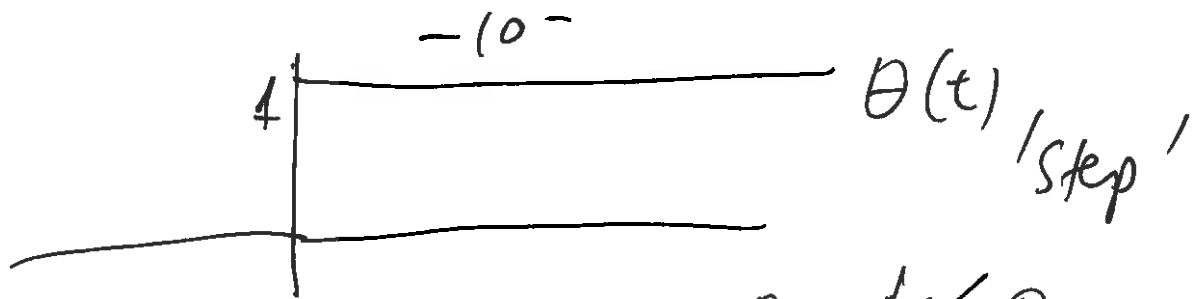$$\frac{e^{-x^2/4\varepsilon}}{\sqrt[2]{\pi \varepsilon}}$$

$$\delta(\alpha x) = \frac{\delta(x)}{|\alpha|}$$

$$\delta(-x) = \delta(x)$$

$$\delta(g(x)) = \frac{\delta(x - x_0)}{|g'(x_0)|} \qquad g(x_0) = 0, \; g'(x_0) \neq 0$$

-10^-

$\theta(t)$ 'step'

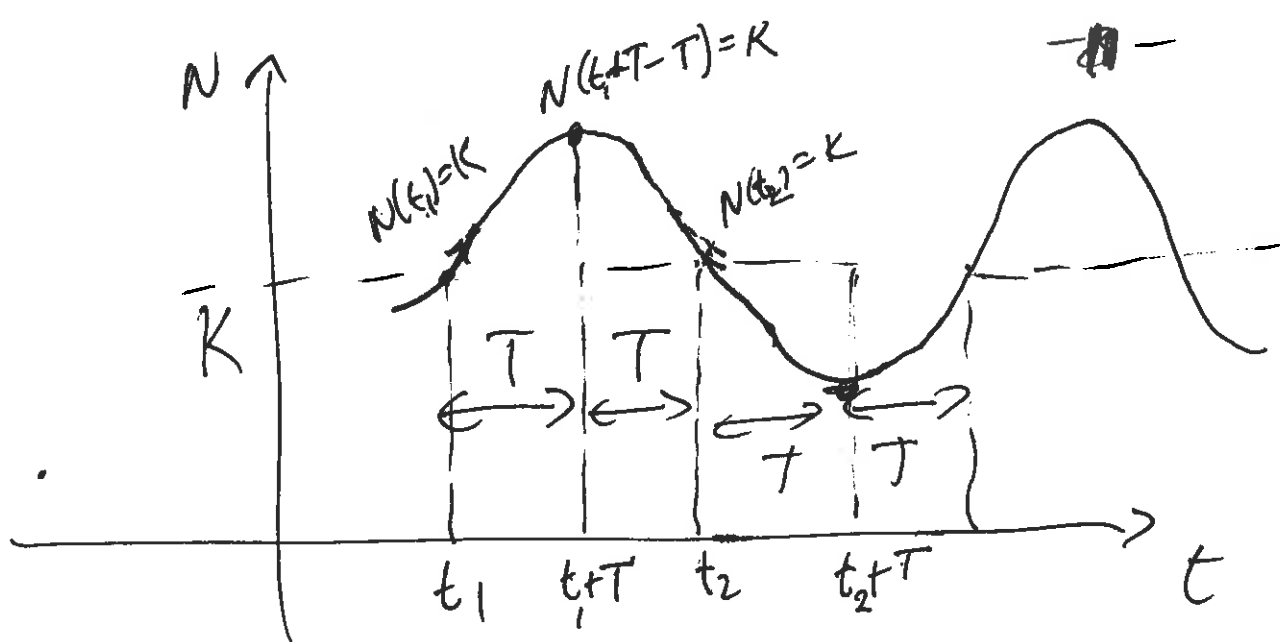$$\theta(t) = \begin{cases} 0 & t < 0 \\ 1 & t > 0 \end{cases}$$

$$\delta(t) = \frac{d\,\theta(t)}{dt}$$

$$\int_{-\infty}^{\infty} \delta(t)\,dt = \int_{-\infty}^{\infty} \frac{d\theta(t)}{dt}\,dt = \theta(\infty) - \theta(-\infty) = 1.$$

$$\underbrace{\theta(\infty)}_{1} \quad \underbrace{\theta(-\infty)}_{0}$$

$$\boxed{x\,\delta(x) = 0} \qquad x^n\,\delta(x) = 0$$

$$\cancel{\int \varphi(x)\,\delta(x-x_0) = \varphi(x_0)}$$

$$\cancel{x_0 = 0} \qquad f(x)\,\delta(x) = f(0)\,\delta(x)$$

$$\frac{dN}{dt} = r N(t) \left(1 - \frac{N(t-\tau)}{K}\right)$$

suppose that $t=t_1 \implies N(t_1) = K$

$\quad$? periodic behaviour?

$\qquad$ Period $= 4T = 4 \times$ Delay ?

Example:

$$\frac{dN}{dt} = -\frac{\pi}{2T} N(t-T) \quad , \quad N(t) = A\cos\frac{\pi t}{2T}$$

$$\frac{dN}{dt} = -A\left(\frac{\pi}{2T}\right)\sin\frac{\pi t}{2T} \overset{?}{=} \underbrace{\left(-\frac{\pi}{2T}\right)A\cos\left(\frac{\pi(t-T)}{2T}\right)}_{-\pi/2\, N(t-T)}$$

$$\sin\frac{\pi t}{2T} = \cos\left(\frac{\pi}{2T} - \frac{\pi t}{2T}\right) = \cos\left(\frac{\pi t}{2T} - \frac{\pi}{2}\right) =$$

$$= \cos\frac{\pi t}{2T}\cos\frac{\pi}{2} + \sin\left(\frac{\pi t}{2T}\right)\sin\left(\frac{\pi}{2}\right) = \sin\frac{\pi t}{2T}$$

Period of the solution t_p

$$\frac{\cancel{\pi}\,(t_p)}{2\,T} = 2\cancel{\pi} \implies \cos \text{ is } 2\pi\text{-periodic}$$

$$\boxed{t_p = 4\,T}$$

stable Limit cycle periodic solutions

Remark: periodic solutions are not possible
for models without delay.

Proof: $\dfrac{dN}{dt} = f(N)$, $\boxed{N(t) = N(t \pm t_p)}$

$$0 < \int_0^{t_p} \left(\frac{dN}{dt}\right)^2 dt = \int_0^{t_p} \underbrace{\left(\frac{dN}{dt}\right)}_{f(N)} \cdot \frac{dN}{dt}\, dt = \int_{N(0)}^{\cancelto{N(t_p)}{N(t+t_p)}} f(N)\, dN$$

$$= \int_{N(0)}^{N(t_p)} f(N)\, dN = 0 \qquad\qquad \text{Contradiction!}$$

Lecture 4
10/10/2011

Models with delay

$$\frac{dN(t)}{dt} = \dot{r} \, N(t) \left(1 - \frac{N(t-T)}{K} \right)$$

T — "delay"

$t_p \sim 4T$
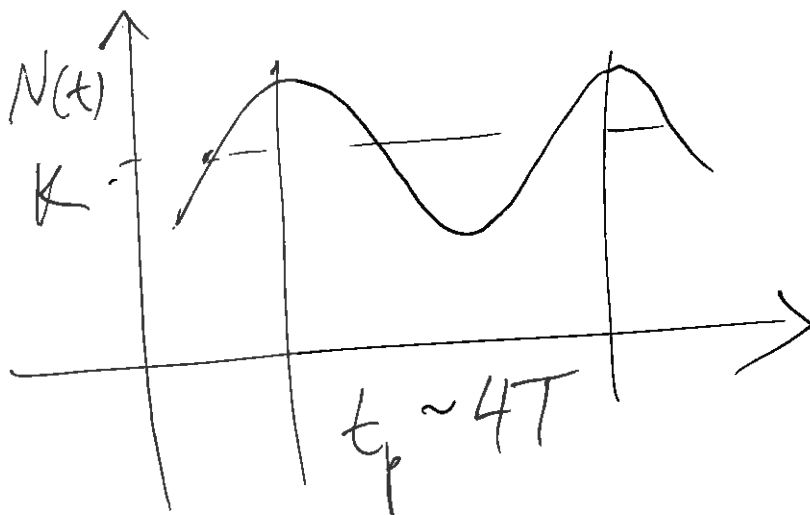
$$u(t) = \frac{N(t)}{K} \qquad \tau = rt$$

$$\frac{dN/K}{d(t\,r)} = \left(\frac{N}{K}\right)\left(1 - \frac{N(t-T)}{K}\right)$$

$$\frac{du}{d\tau} = u(t)\left(1 - \frac{u(t-T)}{K}\right)$$

$$\frac{du}{d\tau} = u(\tau)\left[1 - u(\tau - T^*)\right]^{-2}$$

$$\tau = rt$$
$$T^* = rT$$

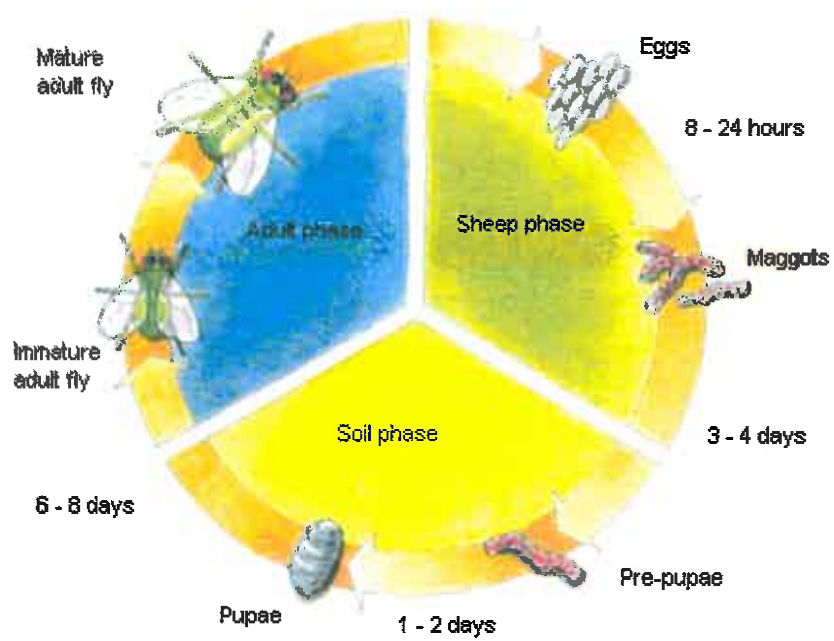| $T^* = rT$	$\dfrac{N_{max}}{N_{min}} = \dfrac{u_{max}}{u_{min}}$	t_p	
1.6	2.56	4.03T	⊛
2.1	42.3	4.54T	
2.5	2930	5.36T	

sheep - blowfly

$t_p = 40$ days

$40 = 4.54 T$

$$\boxed{T \cong 9 \text{ days.}}$$

Models with T=0 ~~connot~~ do not have periodic solutions.

Mature adult fly

Eggs

8 - 24 hours

Adult phase

Sheep phase

Maggots

Immature adult fly

3 - 4 days

Soil phase

6 - 8 days

Pre-pupae

Pupae

1 - 2 days

again approximately 1. If the effect of predation is incorporated into the single equation for the vole population.
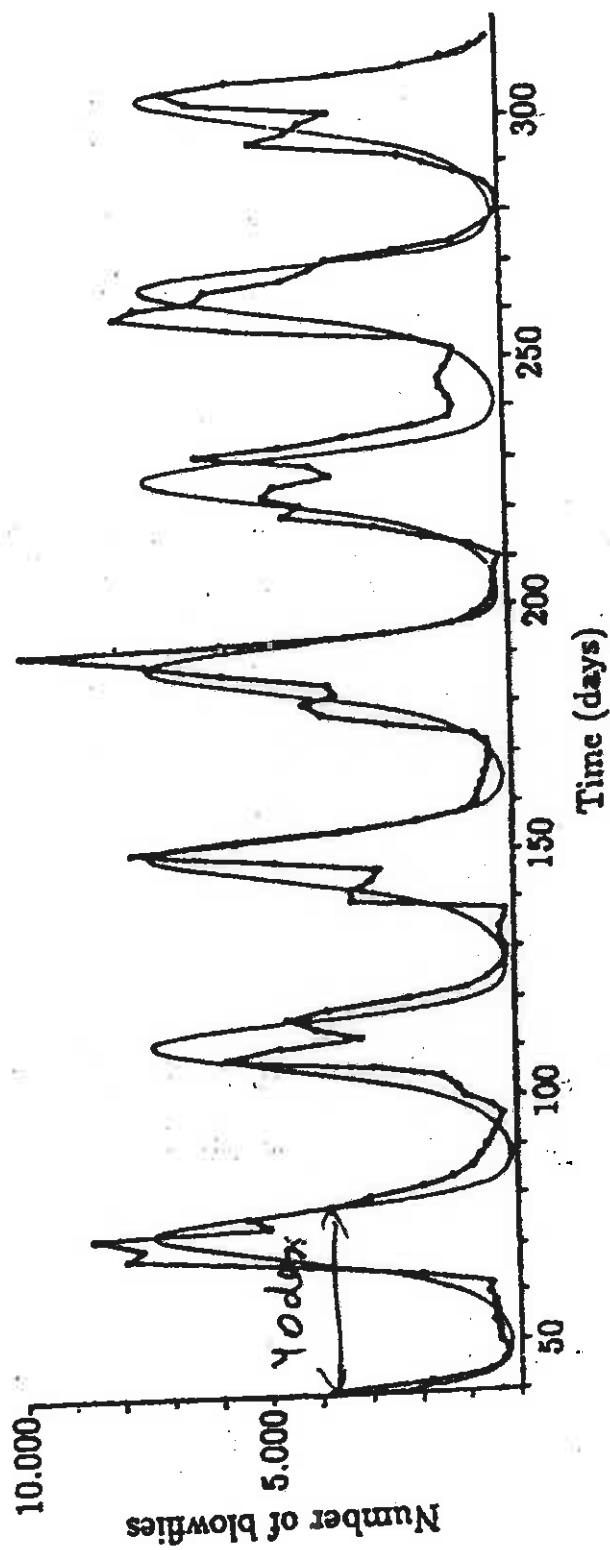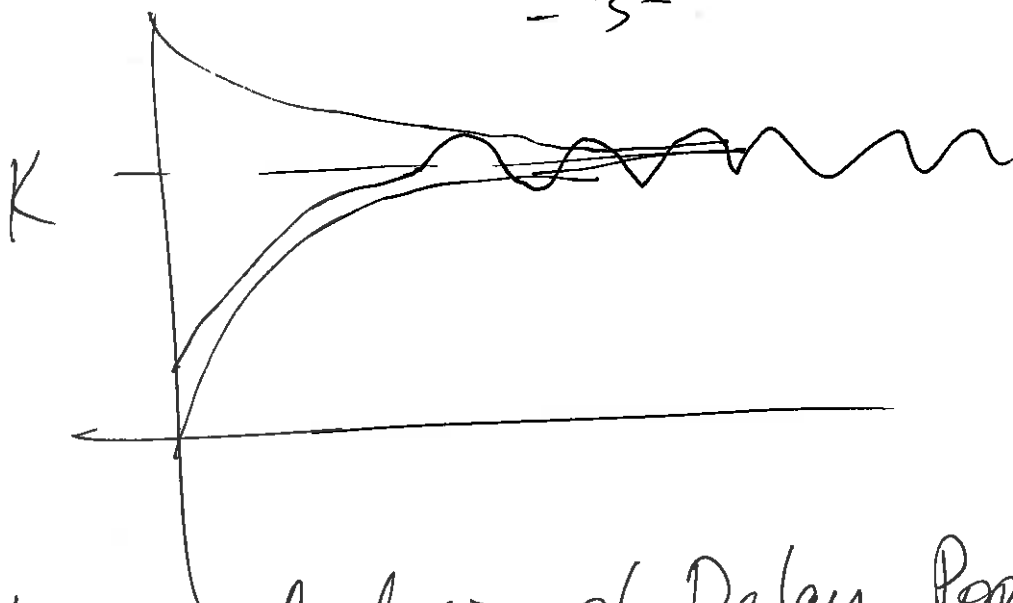

Figure 1.12. Comparison of Nicholson's (1957) experimental data for the population of the Australian sheep-blowfly and the model solution from (1.12) with $rT = 2.1$. (From May 1975).

Linear Analysis of Delay Population Models : Periodic Solutions

Instead of $u = \dfrac{N}{K} \rightarrow \boxed{N}$

$$\frac{dN}{dt} = N(t)\left[1 - N(t-T)\right]$$

Steady states $\qquad N = 0, \qquad N = 1$

Investigate $\qquad N = 1 + n(t), \qquad |n| \ll 1$

$$\frac{dN}{dt} = \frac{dn}{dt}$$

$$\frac{dn}{dt} = \left[1 + n(t)\right]\left[1 - \left(1 + n(t-T)\right)\right]$$

$$\frac{dn}{dt} = \left(1 + n(t)\right)\left(-n(t-T)\right) \approx -n(t-T)$$

$$\underbrace{n^2 \sim 0}$$

$$\boxed{\frac{dn(t)}{dt} = -n(t-T)} \quad \text{Linearised}$$

$$n(t) = c e^{\lambda t} \qquad c, \lambda - \text{constants}$$

$$\frac{dn}{dt} = c \lambda e^{\lambda t}$$

$$n(t-T) = c e^{\lambda(t-T)}$$

$$\frac{dn}{dt} = -n(t-T) \iff \cancel{c}\lambda e^{\lambda t} = -\cancel{c} e^{\lambda(t-T)}$$

$$\lambda \cancel{e^{\lambda t}} = -\cancel{e^{\lambda t}} e^{-\lambda T}$$

$$\circledast \quad \boxed{\lambda = -e^{-\lambda T}} \qquad \begin{array}{c}\text{transcendental eqn.}\\ \text{for } \lambda\end{array}$$

$$z = \frac{1}{\lambda}$$

$$w(z) = 1 \cancel{+} \frac{1}{\lambda} e^{-T/(1/\lambda)}$$

$$w(z) = 1 + z e^{-T/z} = 0$$

$\frac{1}{z}$ is 'essential' singularity for $w(z)$

Picard's theorem $\Rightarrow$ $w(z)$ infinitely many complex roots.

$$\lambda = \mu + i\omega$$

$$\boxed{e^{ix} = \cos x + i \sin x}$$

$$e^{x} = 1 + x + \frac{x^2}{2!} + \frac{x^3}{3!} + \cdots + \frac{x^n}{n!} + \cdots$$

$$i = \sqrt{-1} \quad i^2 = -1 \quad i^3 = -i, \quad i^4 = 1, \quad i^5 = i$$

$$e^{ix} = 1 + ix \cancel{+} \frac{x^2}{2!} - \frac{ix^3}{3!} + \frac{x^4}{4!} + i\frac{x^5}{5!} + \cdots$$

$$= \left(1 - \frac{x^2}{2!} + \frac{x^4}{4!} + \cdots\right) + i\left(x - \frac{x^3}{3!} + \frac{x^5}{5!} + \cdots\right)$$

$$\boxed{e^{ix} = \cos x + i \sin x} \qquad (1)$$

$$e^{-ix} = \cos(-x) + i \sin(-x) = \cos x - i \sin x$$

$$\boxed{e^{-ix} = \cos x - i \sin x} \qquad (2)$$

$(1) + (2) \implies \qquad e^{ix} + e^{-ix} = 2 \cos x$

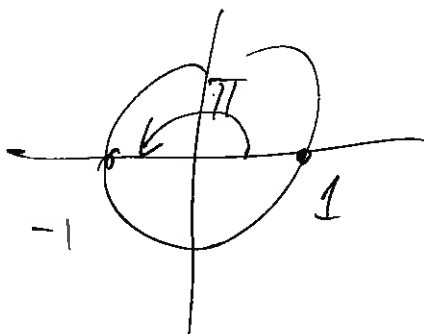$$\boxed{\cos x = \frac{e^{ix} + e^{-ix}}{2}} \qquad \cosh x \equiv \frac{e^{x} + e^{-x}}{2}$$

$(1) - (2) \implies \qquad e^{ix} - e^{-ix} = 2i \sin x$

$$\boxed{\sin x = \frac{e^{ix} - e^{-ix}}{2i}} \qquad \sinh x = \frac{e^{x} - e^{-x}}{2}$$

Take $x = \pi$ $\qquad e^{i\pi} = \underbrace{\cos \pi}_{-1} + \underbrace{i \sin \pi}_{0}$

$$e^{i\pi} = -1$$

$$\boxed{e^{i\pi} + 1 = 0}$$

$$i, \ \pi, \ e, \ 1, \ 0$$

$$\lambda = -e^{-\lambda T} \quad \overline{-6-} \qquad (1.17)$$

$$\lambda = \mu + i\omega$$

$$\mu + i\omega = -e^{-(\mu+i\omega)T} = -e^{-\mu T} e^{-i\omega T}$$

$$\mu + i\omega = -e^{-\mu T}\left[\cos(-\omega T) + i\sin(-\omega T)\right]$$

$$\mu + i\omega = -e^{-\mu T}(\cos\omega T - i\sin\omega T)$$

$$\mu + i\omega = -e^{-\mu T}\cos\omega T + i e^{-\mu T}\sin\omega T$$

$$\left|\begin{array}{l} \mu = -e^{-\mu T}\cos\omega T \\ \omega = e^{-\mu T}\sin\omega T \end{array}\right. \qquad (1.18)$$

$$\mu(T), \quad \cancel{\phi} \quad \omega(T)$$

$$\mu(T_c) = 0,$$

Observation $\omega \to -\omega$, $\quad \underline{\omega > 0}$
$\mu = 0$

$$\left\|\begin{array}{l} 0 = -\cos\omega T_c \\ \omega = \sin\omega T_c \end{array}\right.$$

smallest solution $\omega T_c = \pi/2$

$$\omega = \sin\pi/2 \Rightarrow 1, \quad \underline{\omega = 1} \quad \Rightarrow \quad 1. T_c = \tfrac{\pi}{2}, \quad \boxed{T_c = \tfrac{\pi}{2}}$$

$T_c = \frac{\pi}{2}$ is a bifurcation value.

~~where~~ $0 < T < \frac{\pi}{2}$ condition for stability

Back to physical variables $T^* = rT$

$$0 < rT < \frac{\pi}{2}$$

at the critical point $\mu = 0$

$$\lambda = \mu + i\omega = 0 + i1 = i$$

$$N = 1 + n = 1 + c e^{\lambda t} = 1 + c e^{it} =$$

$$\boxed{N = 1 + c \cos t}$$ take real part.

$$t_p = 2\pi = 4\left(\frac{\pi}{2}\right) = 4T_c .$$

$$\frac{1 + |c| e^{i\gamma} e^{it} \qquad +}{N = 1 + c e^{it} + (c.c.)}$$

$$T_c = \frac{\pi}{2} , \qquad T = \frac{\pi}{2} + \varepsilon \qquad\qquad 0 < \varepsilon \ll 1$$

$$\mu = \mu(T) , \quad \omega = \omega(T)$$
$$\mu = 0 + \delta , \quad \omega = 1 + \sigma \quad , 0 < \delta \ll 1 , \quad |\sigma| \ll 1$$

$$e^x = 1 + x + \frac{x^2}{2!} + \dots \underbrace{\quad}_{neglect} \approx 1 + x \quad , \quad x \ll 1$$

$$\sin x = x - \frac{x^3}{3!} + \frac{x^5}{5!} + \dots \underbrace{\quad}_{neglect} \approx x \quad , \quad x \ll 1.$$

$$\cos x = 1 - \frac{x^2}{2!} + \frac{x^4}{4!} \underbrace{\quad}_{small} \approx 1 \quad , \quad x \ll 1$$

$$\omega = e^{-\mu T} \sin \omega T$$

$$1 + \sigma = e^{-\delta(\frac{\pi}{2} + \varepsilon)} \sin\left[(1+\sigma)\left(\frac{\pi}{2} + \varepsilon\right)\right] \quad , \quad \delta\varepsilon \approx 0$$

$$1 + \sigma = e^{-\delta\frac{\pi}{2}} \sin\left(\frac{\pi}{2} + \sigma\frac{\pi}{2} + \varepsilon + \cancel{\delta\varepsilon}\right)$$

$$1 + \sigma = \left(1 - \delta\frac{\pi}{2}\right)\left[\underset{\underset{1}{\|}}{\sin\frac{\pi}{2}} \underset{\underset{1}{\underbrace{\quad}}}{\cancel{\cos}\left(\sigma\frac{\pi}{2} + \varepsilon\right)} + \underset{\underset{0}{\|}}{\cos\frac{\pi}{2}} \sin\left(\sigma\frac{\pi}{2} + \varepsilon\right)\right]$$

$$1 + \sigma = \cancel{1} - \delta\frac{\pi}{2} \qquad \boxed{\sigma = -\delta\frac{\pi}{2}}$$

$$\mu = -e^{-\mu T} \cos \omega T$$

$$0 + \delta = -e^{-(0+\delta)(\frac{\pi}{2} + \varepsilon)} \cos\left(\frac{\pi}{2} + \sigma\frac{\pi}{2} + \varepsilon\right)$$

$$\delta = -e^{-\delta\frac{\pi}{2}}\left[\underset{\underset{0}{\|}}{\cos\frac{\pi}{2}} \cos\left(\sigma\frac{\pi}{2} + \varepsilon\right) - \underset{\underset{1}{\|}}{\sin\frac{\pi}{2}} \sin\left(\sigma\frac{\pi}{2} + \varepsilon\right)\right]$$

$$\delta = - \left(1 - \delta \frac{\pi}{2}\right)\left[0 - \sin\left(\sigma \frac{\pi}{2} + \varepsilon\right)\right]$$

$$\delta = \left(1 - \delta \frac{\pi}{2}\right)\left(\sigma \frac{\pi}{2} + \varepsilon\right) = \sigma \frac{\pi}{2} + \varepsilon + \cancel{\text{higher order}}.$$

$$\boxed{\delta \approx \varepsilon + \sigma \frac{\pi}{2}}$$

$$\boxed{\sigma = - \delta \frac{\pi}{2}}$$

$$\delta = \varepsilon + \left(- \delta \frac{\pi}{2}\right)\frac{\pi}{2} \quad \Rightarrow \quad \delta\left(1 + \frac{\pi^2}{4}\right) = \varepsilon$$

$$\boxed{\delta = \frac{\varepsilon}{1 + \frac{\pi^2}{4}}} \qquad \boxed{\sigma = - \frac{\varepsilon \pi}{2\left(1 + \frac{\pi^2}{4}\right)}}$$

$$T = \frac{\pi}{2} + \varepsilon$$

$$\mu = 0 + \frac{\varepsilon}{1 + \frac{\pi^2}{4}} \qquad\qquad \omega = 1 + \sigma = 1 - \frac{\varepsilon \pi}{2\left(1 + \frac{\pi^2}{4}\right)}$$

$$N(t) = 1 + \text{Real}\left[c\, e^{(\mu + i\omega)t}\right] =$$

$$= 1 + \text{Real}\left[c\, e^{\frac{\varepsilon t}{1 + \frac{\pi^2}{4}}}\, e^{it\left(1 - \frac{\varepsilon \pi}{2\left(1 + \frac{\pi^2}{4}\right)}\right)}\right]$$

$$= 1 + c\, e^{\frac{\varepsilon t}{1 + \frac{\pi^2}{4}}} \cos\left[t\left(1 - \frac{\varepsilon \pi}{2\left(1 + \frac{\pi^2}{4}\right)}\right)\right]$$

$$t_p\left(1 - \frac{\varepsilon \pi}{2\left(1 + \frac{\pi^2}{4}\right)}\right) = 2\pi$$

$$t_p = \frac{2\pi}{1 - \frac{\varepsilon\pi}{2\left(1+\frac{\pi^2}{4}\right)}} \longrightarrow 2\pi \quad \text{when } \varepsilon = 0$$

Recall: $T = \frac{\pi}{2} + \varepsilon$

$T = 1.6$

$$\boxed{t_p = 4.03\,T}$$

$\varepsilon = 1.6 - \frac{\pi}{2} = 0.029 \ll 1.$

$$t_p = \frac{2\pi}{1 - \frac{0.029\,\pi}{2\left(1+\frac{\pi^2}{4}\right)}} \approx (4.05)\underbrace{(1.6)}_{T}$$

If $T = 2.1$, $\varepsilon = 0.53$ (not small)

$$t_p = (5.26) \times \underbrace{(2.1)}_{T} = \underline{5.26\,T}$$

Numerically $\qquad t_p = \underline{4.54\,T}$

$f(x+y) = f(x)f(y) \qquad f(x) = e^{x}$

$f'(x+y) = f(x)f(y)$

Liapunov function technique
for necessary conditions for stability

If y_s is a steady state then
$L[y]$ is a Liapunov function if

1) $L[y(t)] > 0$ for all $y(t) \neq y_s$

2) $L[y_s] = 0$

3) $\dfrac{dL[y(t)]}{dt} < 0$ for all $y(t) \neq y_s$

Then y_s is globally asymptotically stable.

~~And t=0~~

$$\boxed{\frac{dy}{dt} = a y(t) + b y(t-\tau)}, \qquad t > 0$$

$$L[y(t)] = y^2(t) + |b| \int_{t-\tau}^{t} y^2(s)\, ds$$

$$\frac{dL}{dt} = 2y(t)\frac{dy}{dt} + |b|\left[y^2(t) - y^2(t-\tau)\right] =$$

$$= 2y(t)\left[a y(t) + b y(t-\tau)\right] + |b|\left[y^2(t) - y^2(t-\tau)\right]$$

$$= 2a y^2(t) + \underline{2by(t)y(t-\tau)} + |b|\left(y^2(t) - y^2(t-\tau)\right)$$

$(?) \quad \underline{2by(t)y(t-\tau)} \leq |b|\left(y^2(t) + y^2(t-\tau)\right)$

$0 \leq y^2(t) \pm 2y(t)y(t-\tau) + y^2(t-\tau)$

$0 \leq \left[y(t) \pm y(t-\tau)\right]^2 \checkmark$

$$\frac{dL}{dt} \leqq 2ay^2(t) + |b| \left(y^2(t) + y^2(t-\tau) \right) + |b| \left(y^2(t) - y^2(t-\tau) \right)$$

$$= 2(a + |b|) y^2(t) \quad < \quad 0$$

$$\text{if} \quad \underline{\underline{a < -|b|}} \qquad y_s = 0 \quad \text{is stable.}$$

Introduction to Biomathematics
Lecture 5

Delay Models in Physiology:
Periodic Dynamic Diseases

CO_2 arterial concentration $C(t)$

T

Volume per breath is given by

Hill function

$$V(t) = V_{max} \frac{c^m(t-T)}{a^m + c^m(t-T)}$$

m, a — constants

p — constant production of CO_2 in the body —

The dynamics of the CO_2 level is modeled by

$$\frac{dc(t)}{dt} = p - b\, c(t)\, V(t)$$

b — constant parameter

$$\frac{dc(t)}{dt} = p - b\, c(t)\, V_{max} \frac{c^m(t-T)}{a^m + c^m(t-T)}$$

• Nondimensional quantities $\quad x(t) = \frac{c(t)}{a}$

1. Continuous Population Models for Single Species
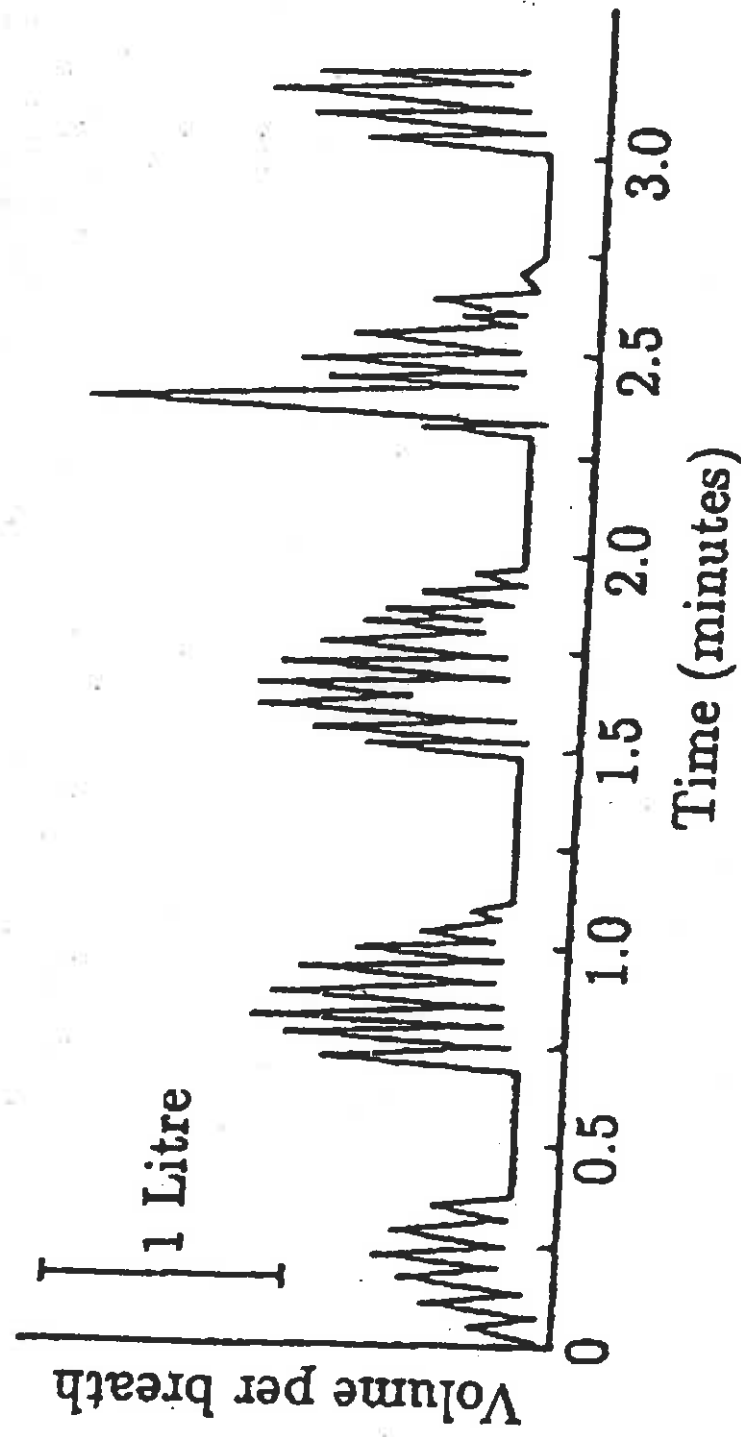
ıre 1.13. A spirogram of the breathing pattern of a 29-year-old man with Cheyne–Stokes respiration. The t_{y_i}
:al waxing and waning of the volume of breath is interspersed with periods of low ventilation levels; this ıs
neic breathing. (Redrawn with permission from Mackey and Glass 1977)

ıth is exceedin.

$$x(t) = \frac{c}{a}$$

$$\frac{d(c/a)}{dt} = \frac{p}{\boxed{a}} - bV_{max}\frac{c(t)}{\boxed{a}} \cdot \frac{\frac{c^m(t-T)}{a^m}}{1 + \frac{c^m(t-T)}{a^m}}$$

$$\frac{dx(t)}{dt} = \frac{p}{a} - bV_{max}\, x(t)\, \frac{x^m(t-T)}{1 + x^m(t-T)} \qquad \bigg|_{\otimes \frac{a}{p}}$$

$$\frac{dx(t)}{d\left(t\frac{p}{a}\right)} = 1 - \boxed{\frac{abV_{max}}{p}}\, x(t)\, \frac{x^m(t-T)}{1 + x^m(t-T)}$$

$$\alpha$$

$$t^* = t\frac{p}{a} \qquad T^* = T\frac{p}{a} \qquad V^*(x) = \frac{x^m}{1 + x^m}$$

$$\frac{dx(t^*)}{dt^*} = 1 - \alpha\, x(t^*)\, V^*\!\left(x(t^* - T^*)\right)$$

Let us 'dprop' the star notations

$$\frac{dx(t)}{dt} = 1 - \alpha\, x(t)\, \frac{x^m(t-T)}{1 + x^m(t-T)} = 1 - \alpha x(t)\, V(t-T)$$

where $V(t) = \dfrac{x^m(t)}{1 + x^m(t)}$

Steady state $\bigodot$ x_o

$$1 - \alpha x_o\, \frac{x_o^m}{1 + x_o^m} = 0, \qquad \frac{1}{\alpha x_o} = \frac{x_o^m}{1 + x_o^m}$$
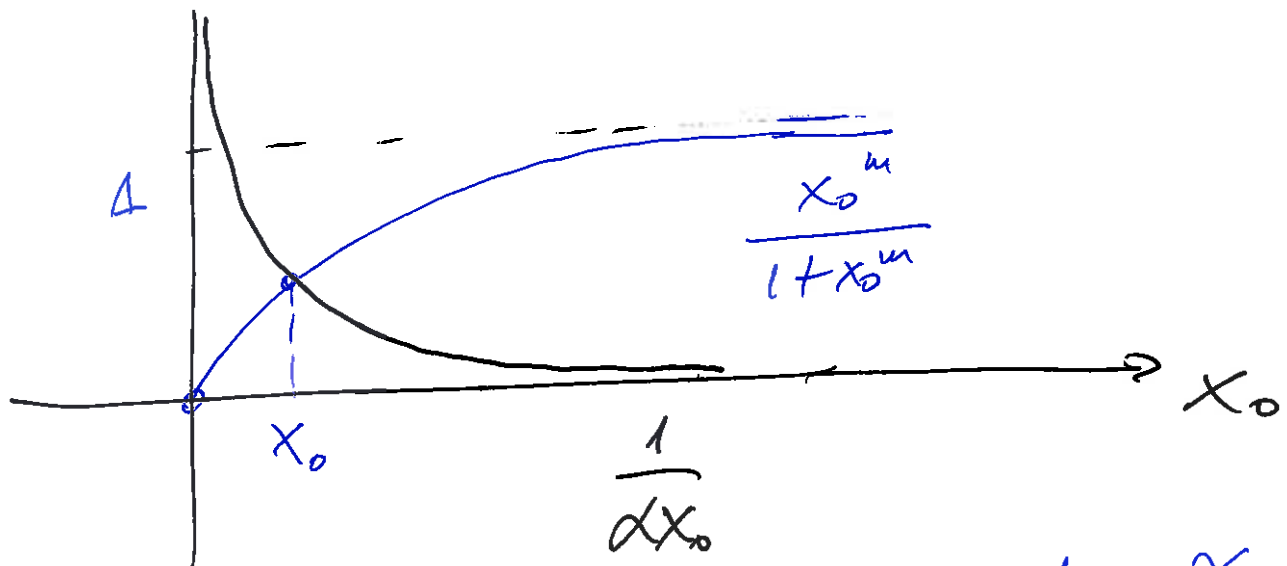
$$\frac{x_0^m}{1+x_0^m}$$

unique positive steady state x_0.

Linear stability analysis

$$x(t) = x_0 + u(t) \qquad |u| \ll 1$$

$$\frac{dx(t)}{dt} = \frac{du(t)}{dt}, \qquad V(x) = V(x_0) + \underbrace{V'(x_0)(x-x_0)}_{u}$$

$$V(x(t)) = V(x_0) + V_0' \cdot u(t) = V_0 + V_0' u(t)$$

$$x'(t) = 1 - \alpha x(t) V(x(t-T))$$

$$u'(t) = 1 - \alpha [x_0 + u(t)] \cdot [V_0 + V_0' u(t-T)]$$

$\uparrow t-T$

$$u'(t) = \underbrace{1 - \alpha x_0 V_0}_{0} - \alpha u(t) V_0 - \alpha x_0 V_0' u(t-T) + \cdots \quad \begin{array}{c} u \cdot u \\ \text{neglect} \end{array}$$

Since $1 - \alpha x_0 \dfrac{x_0^m}{1+x_0^m} = 0$

$$\boxed{u'(t) = -\alpha V_0 u(t) - \alpha x_0 V_0' u(t-T)}$$

$$A = \alpha V_0 = \alpha \frac{x_0^m}{1+x_0^m} > 0$$

$$B = \alpha x_0 V_0' > 0$$

$$V_0' = \frac{d}{dx_0}\left(\frac{x_0^m}{1+x_0^m}\right) = \frac{m x_0^{m-1}(1+x_0^m) - x_0^m \cdot m x_0^{m-1}}{(1+x_0^m)^2}$$

$$= \frac{m x_0^{m-1}}{(1+x_0^m)^2} > 0 \quad , \quad \underline{m > 0}$$

$$\boxed{u'(t) = -Au(t) - B u(t-T)} , \quad \underline{A, B > 0}$$

Looking for solutions $u = k e^{\lambda t}$

$$k\lambda e^{\lambda t} = -A k e^{\lambda t} - B k e^{\lambda(t-T)}$$

$$\boxed{\lambda = -A - Be^{-\lambda T}} \quad \text{Transcendental eqn. for } \lambda$$

$$\lambda = \mu + i\omega$$

$$\mu + i\omega = -A - Be^{-T\mu - iT\omega}$$

$$\mu + i\omega = -A - Be^{-\mu T}\left(\cos\omega T - i\sin\omega T\right)$$

Euler's formula: $e^{-i\omega T} = \cos(-\omega T) + i\sin(-\omega T)$

$$= \cos\omega T - i\sin\omega T$$

$$\mu + i\omega = -A - Be^{-\mu T}\cos\omega T + iBe^{-\mu T}\sin\omega T$$

$$\begin{vmatrix} \mu = -A - Be^{-\mu T}\cos\omega T \\ \omega = Be^{-\mu T}\sin\omega T \end{vmatrix}$$

$$\mu = \mu(T), \qquad \omega = \omega(T)$$

start from $T = 0$, $\mu = -A - B < 0$
the system is stable.
'Bifurcation' occurs when $\mu(T_c) = 0$

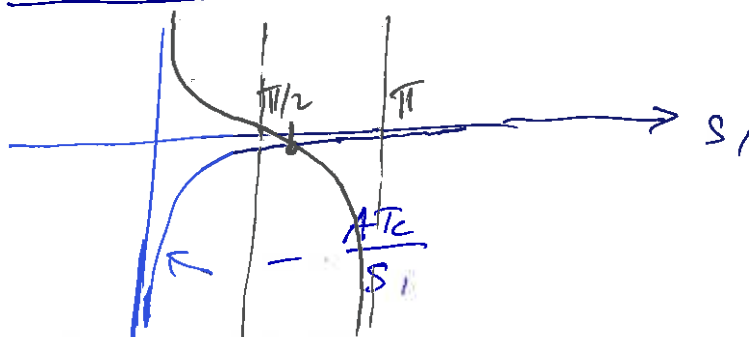$$\begin{vmatrix} 0 = -A - B\cos\omega T_c \\ \omega = B\sin\omega T_c \end{vmatrix}$$

$$\begin{vmatrix} A = -B\cos\omega T_c \\ \omega = B\sin\omega T_c \end{vmatrix} \qquad S_1 = \omega T_c$$

$$\frac{AT_c}{\omega T_c} = -\frac{\cancel{B}\cos\omega T_c}{\cancel{B}\sin\omega T_c} = -\cot(\omega T_c)$$

$$\boxed{\frac{AT_c}{S_1} = -\cot(S_1)} \qquad - \frac{AT_c}{S_1} = \cot S_1$$
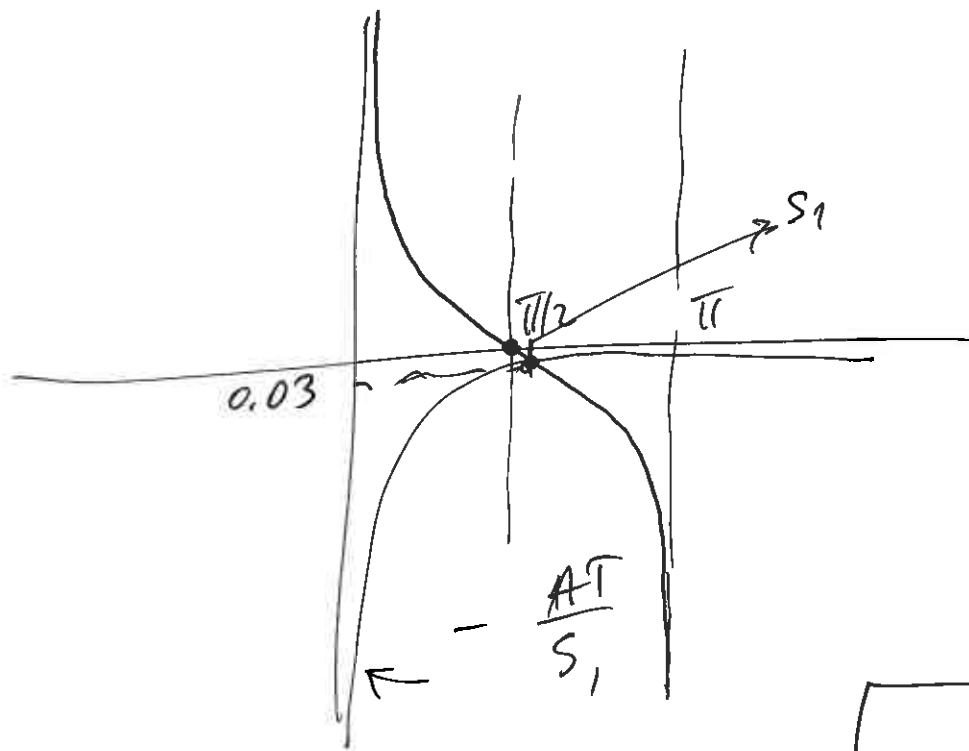
$$\frac{\pi}{2} < S_1 < \pi$$

Can we justify that $\boxed{S_1 \approx \dfrac{\pi}{2}}$

$$AT \ll 1$$

Experimental data : $C_0 = 40 \text{ mm Hg}$
$$p = 6 \text{ mm Hg} / min$$
$$T = 0.25 \text{ min}$$

$AT = \alpha V_0 T$ But $\alpha x_0 V_0 = 1$ $\left(V_0 = \dfrac{1}{\alpha x_0} \right)$

$$AT = \frac{1}{x_0} T = \frac{T}{x_0} = \frac{\frac{p}{a} T_{dimensional}}{x_0} =$$

$$= \frac{p \, T_{dimensional}}{a x_0} = \frac{p \, T_{dim}}{C_0} = 0.0375 \ll 1$$

$$-\frac{AT}{S_1} \approx -\frac{0.0375}{\pi/2} \ll 1 \implies \boxed{S_1 \approx \frac{\pi}{2}}$$

$$S_1 \approx \frac{\pi}{2} = \omega T_c$$

Second equ. $T_c \omega = B T_c \sin \omega T_c$

$$\frac{\pi}{2} = B T_c \boxed{\left(\sin \frac{\pi}{2} \right)}$$

$$\| $$
$$1.$$

$$T_c = \frac{\pi}{2B} = \frac{\pi}{2 \alpha X_o V_o'}$$

$$0 < T < T_c = \frac{\pi}{2 \alpha X_o V_o'} \qquad \underline{\text{stability condition}}$$

$$\boxed{V_o' < \frac{\pi}{2 \alpha X_o T}} \qquad - \text{ stability condition}$$

Gradient of the ventilation at the steady state

$$V_o' \sim 7.44 \text{ litre}/\text{min mm Hg}$$

$$V_o' = \frac{m X_o^{m-1}}{(1 + X_o^m)^2}$$

$$\frac{m X_o^{m-1}}{(1 + X_o^m)^2} < \frac{\pi}{2 \alpha X_o T}$$

$$m T < \frac{\pi}{2 \alpha} \cdot \frac{(1 + X_o^m)^2}{X_o^m}$$

Regulation of Haematopoiesis

$C(t)$ ~ concentration of blood cells

$$[c] = \frac{cells}{mm^3}$$

$T = 6$ days.

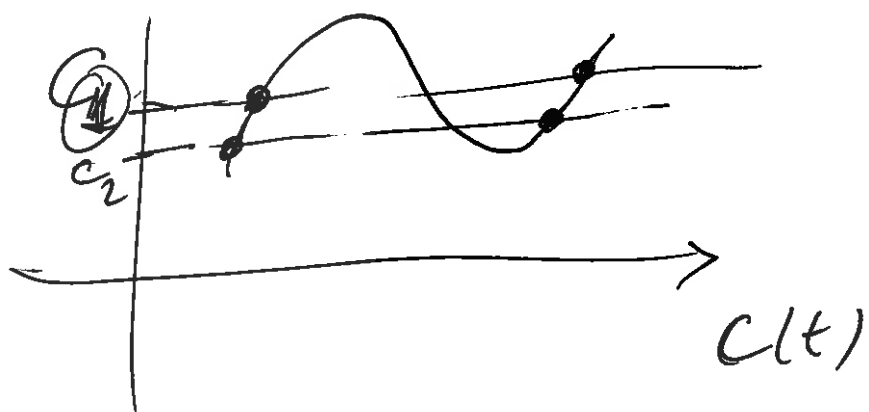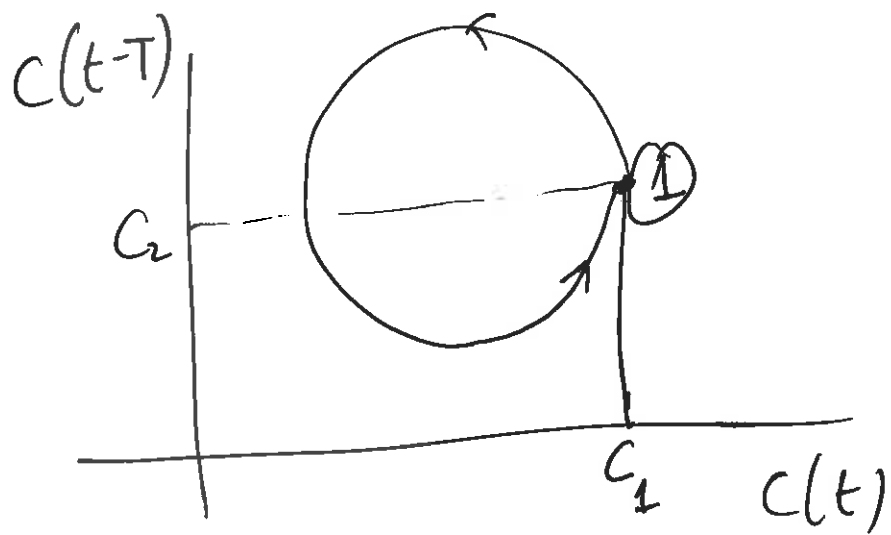$$\frac{dc}{dt} = F\left(c(t-T)\right) - g\, C(t)$$

$$[g] = day^{-1}$$

$$\frac{dc}{dt} = \frac{\lambda a^m\, c(t-T)}{a^m + c^m(t-T)} - g\, c(t)$$

Mackey & Glass (1977)

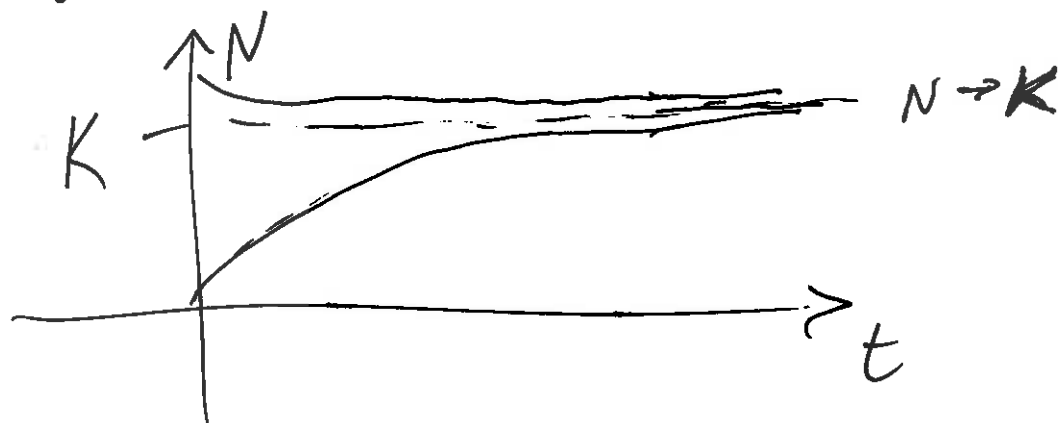λ, a, g, T, m positive constant.

Chaos aperiodic behavior in a deterministic system which depends intimately on the initial conditions

$C(t-T)$

C_2

C_1

$C(t)$

$C(t-T)$

C_2

$C(t)$

Harvesting a single Natural Population

24/10/2011

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right)$$

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right) - EN = f(N)$$

$E = \text{const}$ (effort)

'Constant effort' $Y = \textcircled{E}N$

Steady state $f(N) = 0$

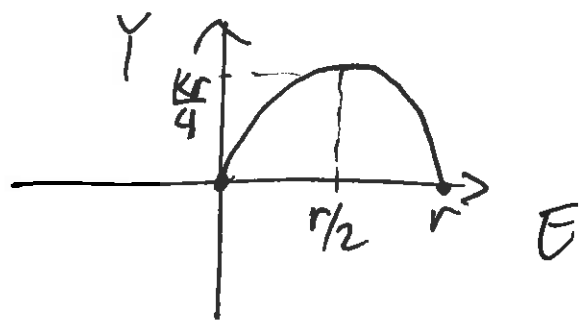$$rN\left(1 - \frac{N}{K}\right) - EN = 0 \quad , \quad \underline{\underline{N = 0}}$$

$$r\left(1 - \frac{N}{K}\right) - E = 0 \implies r - E = r\frac{N}{K}$$

$$N_h = K\left(1 - \frac{E}{r}\right) > 0 \quad \text{if} \quad E < r$$
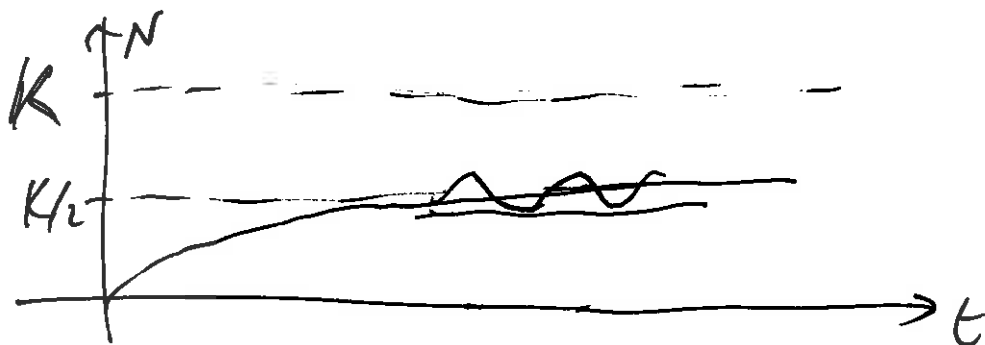
$$0 < E < r$$

'Yield' is $Y = E N_h = E K \left(1 - \frac{E}{r}\right)$

$Y(E) = K E \left(1 - \frac{E}{r}\right)$

$Y_{max} = Y\left(\frac{r}{2}\right) = K \frac{r}{2} \underbrace{\left(1 - \frac{r/2}{r}\right)}_{1/2} = \frac{Kr}{4}$

$N_h\left(\frac{r}{2}\right) = K \left(1 - \frac{r/2}{r}\right) = \frac{K}{2}$

Analysis of the behaviour around N_h

$$N = N_h + n \qquad n - \text{small.}$$

$$\frac{dN}{dt} = 0 + \frac{dn}{dt}$$

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right) - EN = f(N)$$

$$\frac{dn}{dt} = r(N_h + n)\left(1 - \frac{N_h + n}{K}\right) - E(N_h + n)$$

$$\boxed{f(N_h) = 0} \quad \text{steady state.}$$

$$\frac{dn}{dt} = \underset{\substack{\| \\ 0}}{f(N_h)} + \left(\frac{\partial f}{\partial N}\right)_{N=N_h} \underbrace{(N - N_h)}_{n}$$

$$\frac{dn}{dt} = 0 + \left(\frac{\partial f}{\partial N}\right)_{N=N_h} \cdot n$$

$$\frac{\partial f}{\partial N} = r - \frac{2Nr}{K} - \epsilon, \quad \left(\frac{\partial f}{\partial N}\right)_{N_h} = r$$

$$\left(\frac{\partial f}{\partial N}\right)_{N_h} = r - \frac{2r}{K} \cdot \cancel{K}\left(1 - \frac{\epsilon}{r}\right) - \epsilon = r - 2r\left(1 - \frac{\epsilon}{r}\right) - \epsilon =$$

$$= r - 2r + 2\epsilon - \epsilon = \epsilon - r = -(r - \epsilon) < 0$$

$$\text{when} \quad \underline{0 < \epsilon < r}$$

$$\frac{dn}{dt} = -(r - \epsilon) \cdot n \implies n = n_0 \, e^{-(r-\epsilon)t}$$

$$\boxed{N = N_h + n = N_h + n_0 \, e^{-(r-\epsilon)t}}$$

$$\underset{\substack{\downarrow \\ 0 \text{ when } \epsilon < r}}{\underbrace{\phantom{e^{-(r-\epsilon)t}}}}$$

$$N = N_h + n_0 \, e^{-\frac{t}{\tau}}, \quad \tau = \frac{1}{r - \epsilon} > 0$$

Meaning of τ : (Recovery time)

$$e^{-\frac{t}{\tau}} \longrightarrow t=\tau \implies e^{-1} \approx \frac{1}{2.71} \approx 0.37$$

$$t=2\tau \implies e^{-2} \approx 0.14$$

$$t=3\tau \implies e^{-3} \approx 0.05$$

$$T_R(E) \approx \tau(E) = \frac{1}{r-E}$$

$$\frac{T_R(E)}{T_R(0)} = \frac{\frac{1}{r-E}}{\frac{1}{r-0}} = \frac{r}{r-E} = \frac{1}{1-\frac{E}{r}} \quad (*)$$
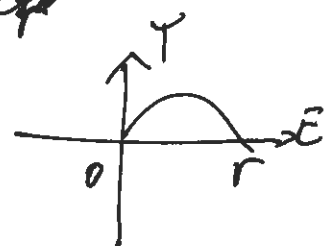
'Max yield' when $E = r/2$

$$\frac{T_R(r/2)}{T_R(0)} = \frac{1}{1-\frac{1}{2}} = 2$$

$$T_R(r/2) = 2 T_R(0)$$

$\frac{T_R(E)}{T_R(0)}$ in terms of Y

$$Y = EK\left(1 - \frac{E}{r}\right)$$

$$-\frac{K}{r}E^2 + KE - Y = 0 \quad | r$$

$$-KE^2 + rKE - rY = 0 \implies E = \frac{-rK \pm \sqrt{r^2K^2 - 4KrY}}{-2K}$$

$$E = \frac{r}{2} \pm \frac{1}{2}\sqrt{r^2 - \frac{4Yr}{K}} = \frac{r}{2}\left(1 \pm \sqrt{1 - \frac{4Y}{rK}}\right)$$
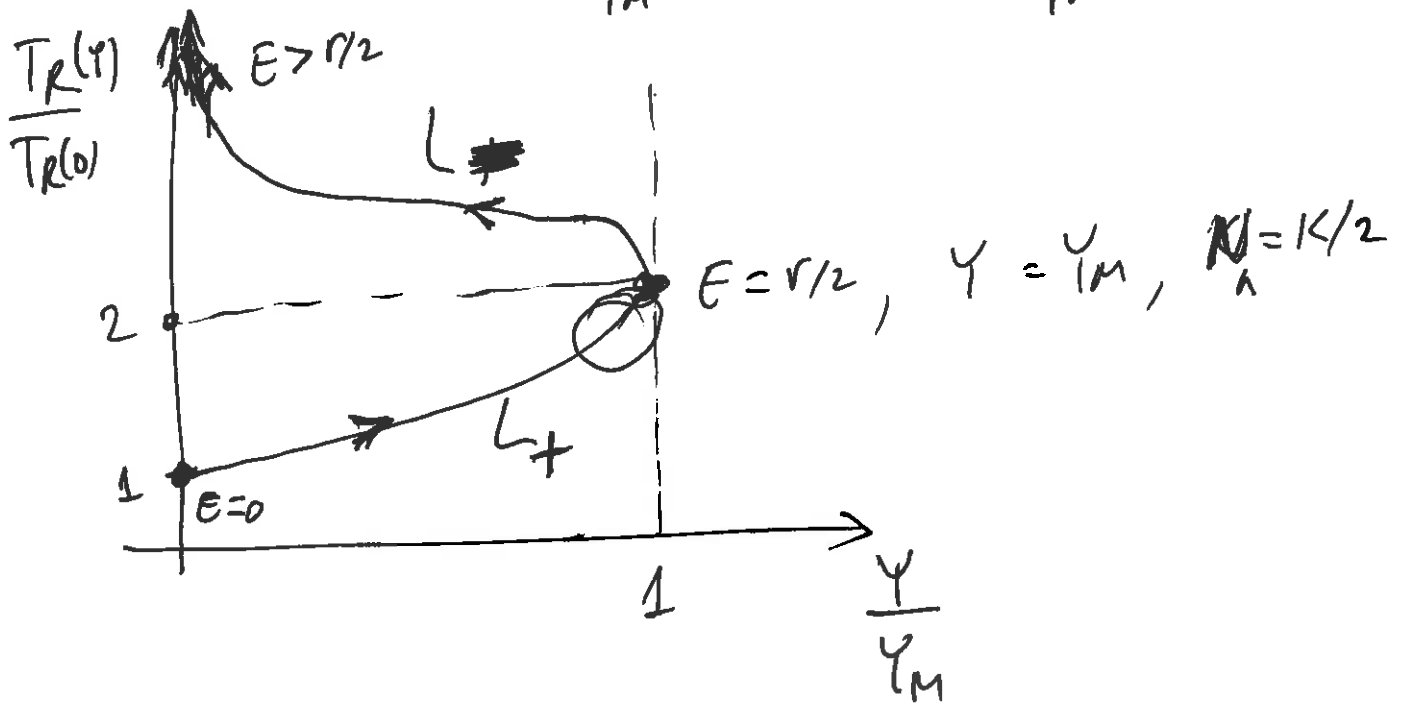
$$E = \frac{r}{2}\left(1 \pm \sqrt{1 - \frac{4Y}{rK}}\right) \qquad Y_M = Y_{max} = \frac{Kr}{4}$$

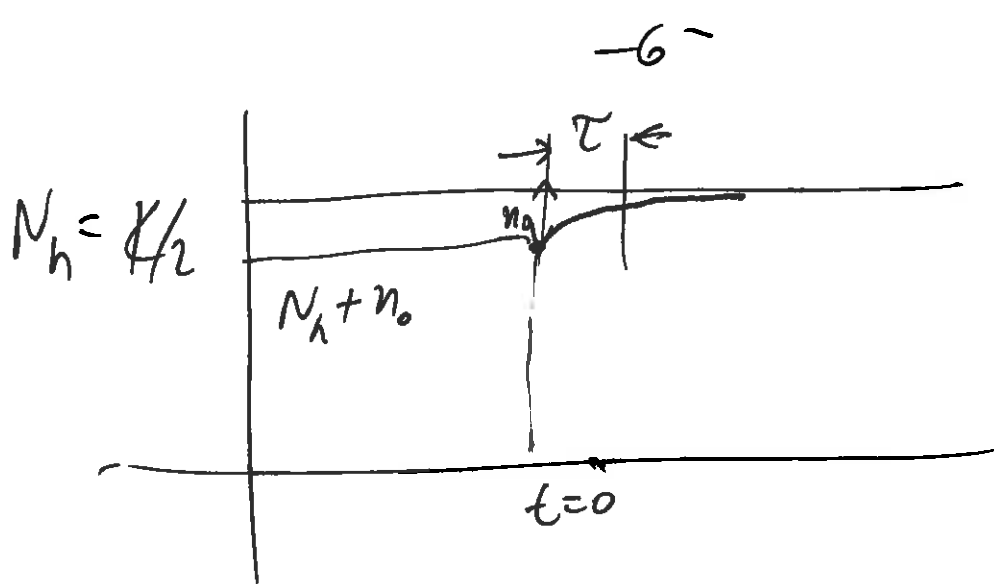$$E = \frac{r}{2}\left(1 \pm \sqrt{1 - \frac{Y}{Y_M}}\right)$$

$$\frac{T_R(Y)}{T_R(0)} = \frac{1}{1 - \frac{E}{r}} = \frac{1}{1 - \frac{1}{r}\cdot\frac{r}{2}\left(1 \pm \sqrt{1 - \frac{Y}{Y_M}}\right)} = \frac{1}{1 - \frac{1}{2} \pm \frac{1}{2}\sqrt{1 - \frac{Y}{Y_M}}}$$

$$\frac{T_R(Y)}{T_R(0)} = \frac{1}{\frac{1}{2} \pm \frac{1}{2}\sqrt{1 - \frac{Y}{Y_M}}} = \frac{2}{1 \pm \sqrt{1 - \frac{Y}{Y_M}}}$$

$E = r/2$, $Y = Y_M$, $N = K/2$

$$Y = 0 \qquad \frac{T_R(Y)}{T_R(0)} \rightarrow \frac{2}{1 \pm 1} = \begin{cases} \frac{2}{2} = 1 & (E = 0) \\ \frac{2}{0} = \infty & E > r/2 \end{cases}$$
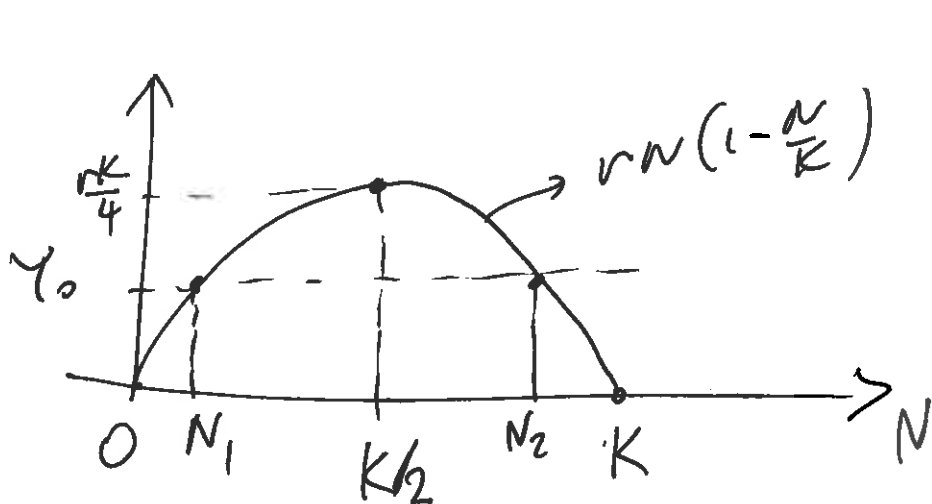
$$Y = Y_\mu \qquad \frac{T_R(Y_\mu)}{T_R(0)} = \frac{2}{1 \pm 0} = 2 \qquad \text{when } E = r/2$$

$$N = N_h + n_0 e^{-\frac{t}{\tau}}$$

Harvesting with constant yield

$$\frac{dN}{dt} = \underbrace{r N\left(1 - \frac{N}{K}\right) - Y_0}_{f(N)}, \qquad Y_0 = \text{const}$$

$$Y_0 = r N\left(1 - \frac{N}{K}\right)$$

$\underset{\text{line}}{Y_0} \quad \underset{\text{parabola}}{rN\left(1-\frac{N}{K}\right)}$

At $N = K/2$ the logistic term is $r\frac{K}{2}\left(1 - \frac{K/2}{K}\right) = \frac{rK}{4}$

$$(Y_0)_{max} = \frac{rK}{4}, \qquad 0 < Y_0 < \frac{rK}{4}$$
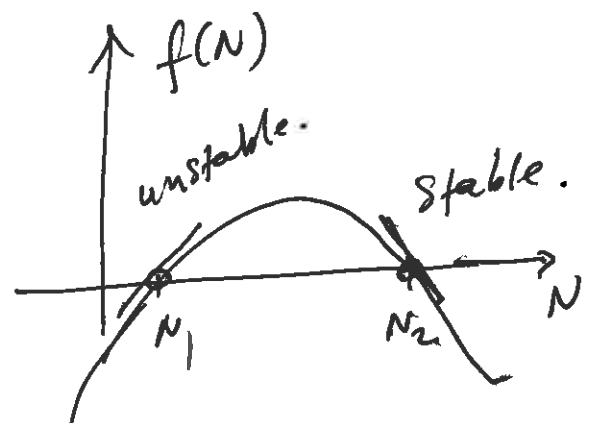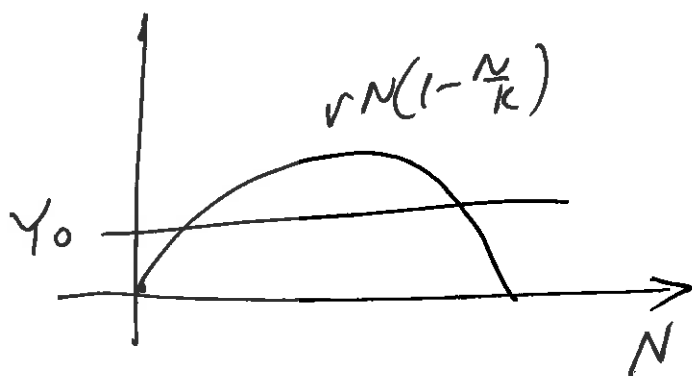
$f(N) = 0 \implies N_1 \ \& \ N_2 \ \text{steady states}$

$$r N \left(1 - \frac{N}{K}\right) - Y_0 = 0$$

$$r N - \frac{r}{K} N^2 - Y_0 = 0$$

$$- \frac{r}{K} N^2 + r N - Y_0 = 0 \qquad (- K)$$

$$+ r N^2 - r K N + Y_0 K = 0$$

$$N_{1,2} = \frac{r K \pm \sqrt{r^2 K^2 - 4 r Y_0 K}}{2 r} = \frac{K}{2} \left(1 \pm \sqrt{1 - \frac{4 Y_0}{r K}}\right)$$

$$N_2 = \frac{K}{2} \left(1 + \sqrt{1 - \frac{4 Y_0}{r K}}\right) - stable.$$

$$Y_M = \frac{r K}{4} \ ; \qquad N_2 = \frac{K}{2} \left(1 + \sqrt{1 - \frac{Y_0}{Y_M}}\right)$$

$$N = N_2 + n, \quad n \ll 1$$

$$\frac{dN}{dt} = \frac{dn}{dt} = \underbrace{f(N_2)}_{0} + \left(\frac{\partial f}{\partial N}\right)_{N_2} \underbrace{(N - N_2)}_{n} + \cdots$$

$$\frac{dn}{dt} = \left(r - \frac{2 N r}{K}\right)_{N=N_2} \cdot n$$

$$\frac{dn}{dt} = r \left[1 - \frac{2}{K} \cdot \frac{K}{2} \left(1 + \sqrt{1 - \frac{Y_0}{Y_M}}\right)\right] n = - \sqrt{1 - \frac{Y_0}{Y_M}} \ n$$

$$\frac{dn}{dt} = -r\sqrt{1-\frac{Y_0}{Y_M}}\, n \implies n = n_0 e^{-r\sqrt{1-\frac{Y_0}{Y_M}}\, t}$$

$$T_R(Y_0) = \frac{1}{r\sqrt{1-\frac{Y_0}{Y_M}}} \quad , \qquad T_R(0) = \frac{1}{r}$$

$$\boxed{\frac{T_R(Y_0)}{T_R(0)} = \frac{1}{\sqrt{1-\frac{Y_0}{Y_M}}}} \quad , \qquad Y_M = \frac{rK}{4}$$

$$Y_0 \to Y_M \qquad T_R(Y_M) \to \infty$$

$N \to 0$ <u>behaviour</u>:

$$\frac{dN}{dt} = r\cancel{N} - \frac{K\cancel{N^2}}{\cancel{K}} - Y_0$$

$\underset{\text{small}}{}$

$$\frac{dN}{dt} = -Y_0 \implies N(t) \cong \underset{\text{small}}{\underline{N(0) - Y_0 t}}$$

Fisher – Kolmogoroff Equation

Diffusion process
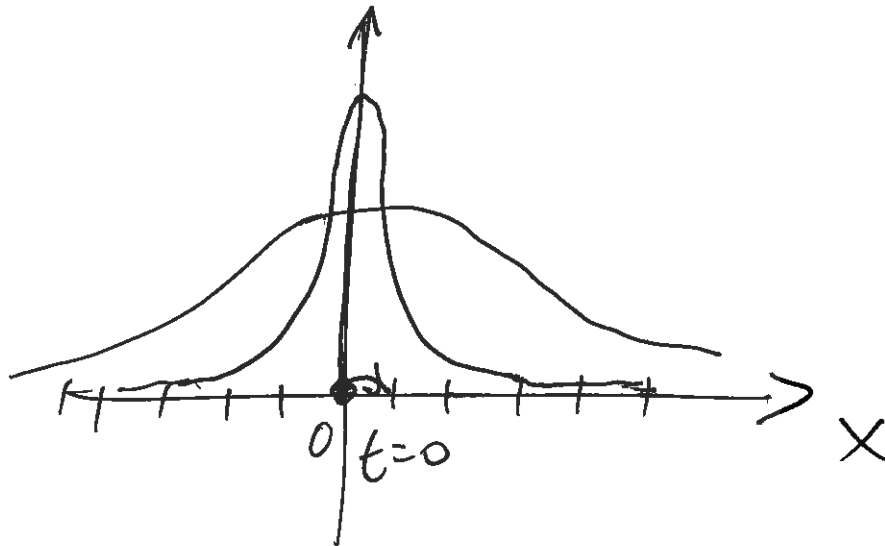
$$t = n \Delta t$$
$$x = n \Delta x$$

$$p(x, t) = \frac{1}{2} p(x - \Delta x, t - \Delta t) + \frac{1}{2} p(x + \Delta x, t - \Delta t)$$

$$= \frac{1}{2} \left[p(x, t) + \frac{\partial p}{\partial x}(-\Delta x) + \frac{\partial p}{\partial t}(-\Delta t) + \frac{1}{2} \frac{\partial^2 p}{\partial x^2}(\Delta x)^2 \right.$$
$$\left. + \frac{1}{2} \frac{\partial^2 p}{\partial t^2}(\Delta t)^2 + \frac{\partial^2 p}{\partial x \partial t}(-\Delta x)(-\Delta t) \right]$$

$$+ \frac{1}{2} \left[p(x, t) + \frac{\partial p}{\partial x}(\Delta x) + \frac{\partial p}{\partial t}(-\Delta t) + \frac{1}{2} \frac{\partial^2 p}{\partial x^2}(\Delta x)^2 + \frac{1}{2} \frac{\partial^2 p}{\partial t^2}(\Delta t)^2 + \frac{\partial^2 p}{\partial x \partial t}(\Delta x)(-\Delta t) \right]$$

$$p(x, t) = p(x, t) + \frac{\partial p}{\partial t}(\Delta t) + \frac{1}{2} \frac{\partial^2 p}{\partial x^2}(\Delta x)^2 + \frac{1}{2} \frac{\partial^2 p}{\partial t^2}(\Delta t)^2$$

$$\frac{\partial p}{\partial t} \Delta t = \frac{1}{2} \frac{\partial^2 p}{\partial x^2}(\Delta x)^2 + \frac{1}{2} \frac{\partial^2 p}{\partial t^2}(\Delta t)^2$$

$$\frac{\partial p}{\partial t} = \frac{\partial^2 p}{\partial x^2} \frac{(\Delta x)^2}{2 \Delta t} + \frac{1}{2} \frac{\partial^2 p}{\partial t^2} \Delta t \qquad \Delta t \to 0$$

$$\lim_{\substack{\Delta x \to 0 \\ \Delta t \to 0}} \frac{(\Delta x)^2}{2\Delta t} = D = \text{const} \quad (\text{diffusion coefficient})$$

(I) $$\boxed{\frac{\partial p}{\partial t} = D \frac{\partial^2 p}{\partial x^2}}$$ Diffusion equation
   Heat equation

$$\frac{\partial N}{\partial t} = D \frac{\partial^2 N}{\partial x^2}$$

$$\frac{\partial N}{\partial t} = D \left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2} \right) N = D \Delta N$$

$$\underbrace{\phantom{\left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2} \right)}}_{\Delta}$$

(?) $$p(x, t) = \frac{C}{2\sqrt{\pi D t}} e^{-\frac{x^2}{4Dt}} \qquad t > 0$$

Initial conditions $p(x, 0) = ?$

$$p(x, 0) = \lim_{t \to 0} \frac{C}{2\sqrt{\pi D t}} e^{-\frac{x^2}{4Dt}} = C \delta(x)$$

$$\boxed{\frac{\partial N}{\partial t} = rN\left(1 - \frac{N}{K}\right) + D \Delta N} \qquad \text{Fisher (1937)}$$

$$N = N(t, x, y, z)$$

Fisher-Kolmogoroff equation.

$$\frac{\partial N}{\partial t} = rN\left(1 - \frac{N}{K}\right) + D\frac{\partial^2 N}{\partial x^2}$$

$$u = \frac{N}{K}$$

$$\frac{\partial(N/K)}{\partial t} = r\frac{N}{K}\left(1 - \frac{N}{K}\right) + D\frac{\partial^2(N/K)}{\partial x^2}$$

$$\frac{\partial u}{\partial t} = ru(1-u) + D\frac{\partial^2 u}{\partial x^2} \qquad \left| \cdot \frac{1}{r} \right.$$

$$\frac{\partial u}{\partial(rt)} = u(1-u) + \frac{D}{r}\frac{\partial^2 u}{\partial x^2}$$

$$\tau = rt \qquad , \quad \cancel{X} = x\sqrt{\frac{r}{D}} \quad , \quad x = X\sqrt{\frac{D}{r}}$$

$$\frac{\partial u}{\partial \cancel{\tau}} = u(1-u) + u_{\cancel{xx}}$$

$$\frac{\partial u}{\partial \tau} = u(1-u) + \frac{\partial^2 u}{\partial X^2}$$

$$u_t = u(1-u) + u_{xx}$$

$$u(x,t) = U(x - ct)$$

travelling wave solutions

$$u = U(x - ct) \quad, \quad z = x - ct$$

$$u_t = \frac{dU}{dz} \cdot \frac{dz}{dt} = U'(-c) = -c\, U'(z)$$

$$u_x = U'(z) \quad, \quad u_{xx} = U''(z) \qquad \left(\frac{\partial z}{\partial x} = 1 \right)$$

$$u_t = u(1-u) + u_{xx}$$

$$\boxed{-c\, U' = U(1-U) + U'' \qquad\qquad ODE}$$

c is the wavespeed.

Biological Waves: Single Species Models
7/11/2011

Fisher-Kolmogoroff equation

$$\frac{\partial u}{\partial t} = r u (1-u) + D \Delta u$$

$r, D = $ const. $u = N/K$

$$\Delta = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}$$

in one-dimension

$$u_t = r u (1-u) + D u_{xx}$$
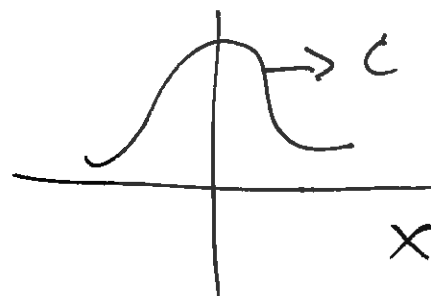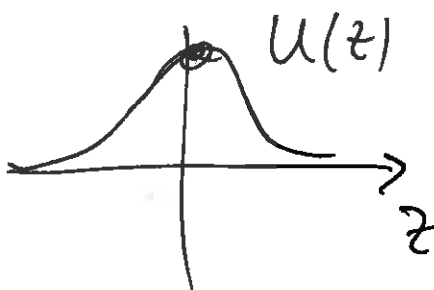
$t \to r t$ $x \to x \sqrt{\frac{r}{D}}$

$$\boxed{u_t = u(1-u) + u_{xx}}$$

Nonlinear PDE

Travelling wave solution

$$u(x,t) = U(x-ct), \qquad c = \text{const.}$$

$z = x - ct$ $u(x,t) = U(z)$

$z = x - ct$ $-z-$

Fix $\otimes$, $c > 0 \Rightarrow$ $t = -\infty$ $z = \infty$ 'past'

$t = +\infty$ $z = -\infty$ future'

$$u_t = \frac{\partial u}{\partial t} = \frac{dU}{dz}\frac{\partial z}{\partial t} = -c\, U'(z)$$

$$u_x = \frac{\partial u}{\partial x} = \frac{dU}{dt}\frac{\partial z}{\partial x}^{(-c)} = U'(z)$$

$$u_t = u(1-u) + u_{xx}$$

$$-c\, U' = U(1-u) + U''$$ $\underline{ODE}$

$$\boxed{U'' + cU' + U(1-u) = 0}$$

Two constant solutions $U = 0$, $U = 1$

Linearize near $U = 0$ and $U = 1$

$$U = 0 + n, \quad n - \text{'small'}, \quad n^2 \to 0$$

$$n'' + cn' + n(1-n) = 0$$

$$n'' + cn' + n - \cancel{n^2} = 0 \qquad n = n_0 e^{\lambda z}$$

$$n_0 \lambda^2 e^{\lambda t} + c n_0 \lambda e^{\lambda z} + n_0 e^{\lambda z} = 0$$

$$\lambda^2 + c\lambda + 1 = 0 \quad \text{characteristic equ.}$$

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

$$\lambda = \frac{-c \pm \sqrt{c^2 - 4}}{2}$$

$\underline{I}$ $\quad c^2 - 4 \geq 0$

$U = n = n_0 e^{-\frac{c}{2}}$

Two negative <u>roots</u> $\lambda_1, \lambda_2 < 0$

$$U = n_{0_1} e^{\lambda_1 z} + n_{0_2} e^{\lambda_2 z} \rightarrow 0$$

$U = 0$ is a stable equilibrium

$\underline{II}$ $\quad c^2 - 4 < 0$ complex roots

$$U = n_0 \left(e^{-\frac{cz}{2}} \right) \cos\left(\sqrt{4 - c^2} \, z + \varphi_0 \right)$$

$\downarrow$

0

$U(z)$, z
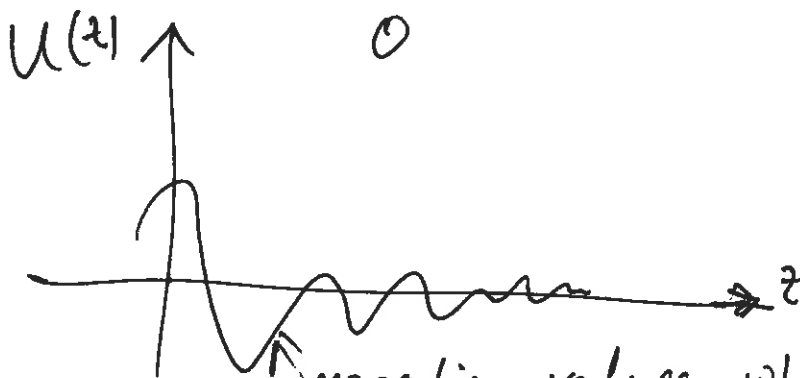
negative values, which are not possible.

Case $\underline{II}$ not possible.

Case $\underline{I}$: $\quad c^2 - 4 \geq 0 \implies \boxed{c \geq 2}$

$\boxed{c_{min} = 2}$

$$u = 1 \implies u = 1 + n, \qquad |n| \ll 1$$

$$u'' + cu' + u(1-u) = 0$$

$$n'' + cn' + (1+n)(\cancel{1} - \cancel{1} - n) = 0$$

$$n'' + cn' - n - \cancel{n^2} = 0$$

$$n'' + cn' - n = 0 \quad , \qquad n = n_0 e^{\lambda z}$$

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

$$\lambda_\pm = \tfrac{1}{2}\left(-c \pm \sqrt{c^2 + 4}\right)$$

$$n = n_{0_1} e^{\lambda_- z} + n_{0_2} e^{\lambda_+ z} \qquad \underline{\text{unstable}}$$

$$\downarrow \qquad\qquad \downarrow$$
$$0 \qquad\qquad \infty$$

$$n = n_{0_1} \underset{\substack{\downarrow \\ 0}}{e^{\lambda_- z}} + n_{0_2} \underset{\substack{\downarrow \\ \infty}}{e^{\lambda_+ z}} \;\to\; \infty$$

$$u(z) = 1 \quad \text{is} \quad \text{unstable equilibrium}$$

$$u(-\infty) = -1 \qquad\qquad u(\infty) = 0$$
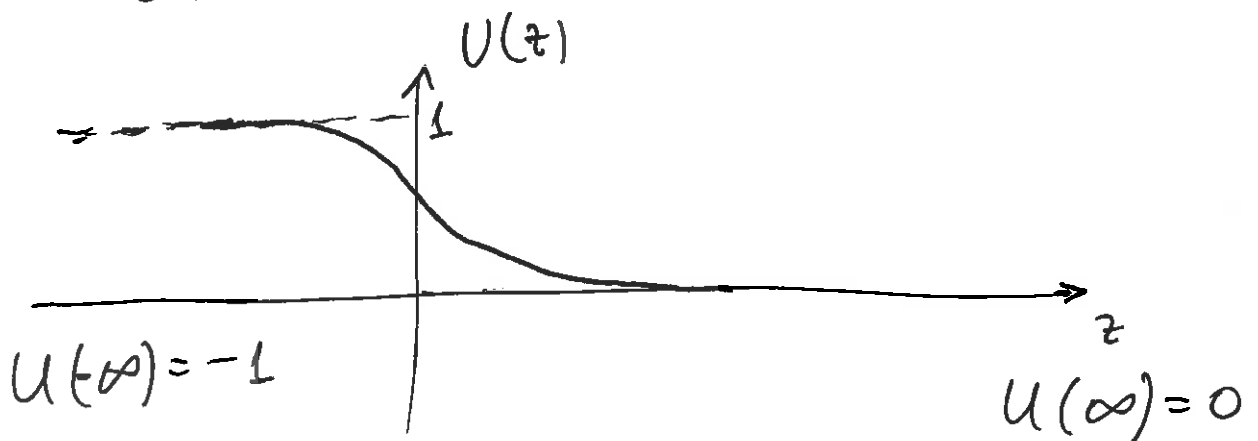
$$\boxed{z = x - ct}$$
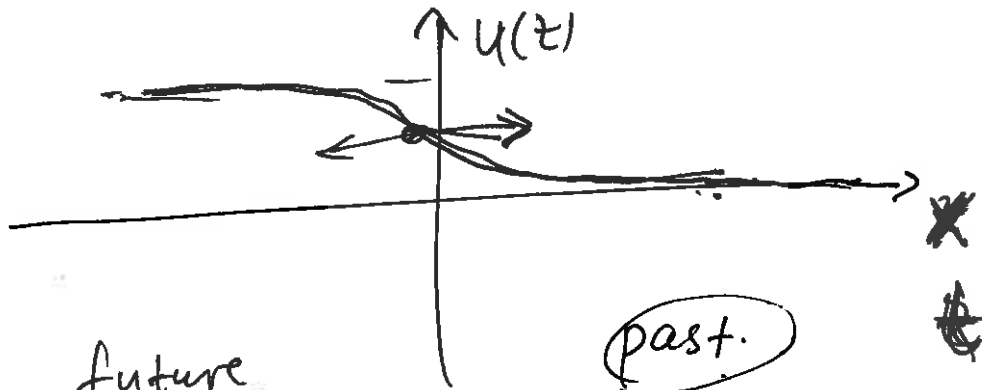
future
$$u(-\infty) = 1.$$

past.

$$u(\infty) = 0 \quad (\text{stable})$$

$$\boxed{c \geq 2} \quad C_{min} = \underline{\underline{2}}$$

$$\textcircled{X} \to x\sqrt{\frac{r}{D}} \qquad t \to rt$$

$$1 = \left\lfloor \frac{x}{t} \right\rfloor \to \frac{\sqrt{\frac{r}{D}}}{r} = \frac{1}{\sqrt{rD}} \quad \text{C dim.}$$

$$\boxed{C_{min} = 2\sqrt{rD}}$$

Kolmogoroff:
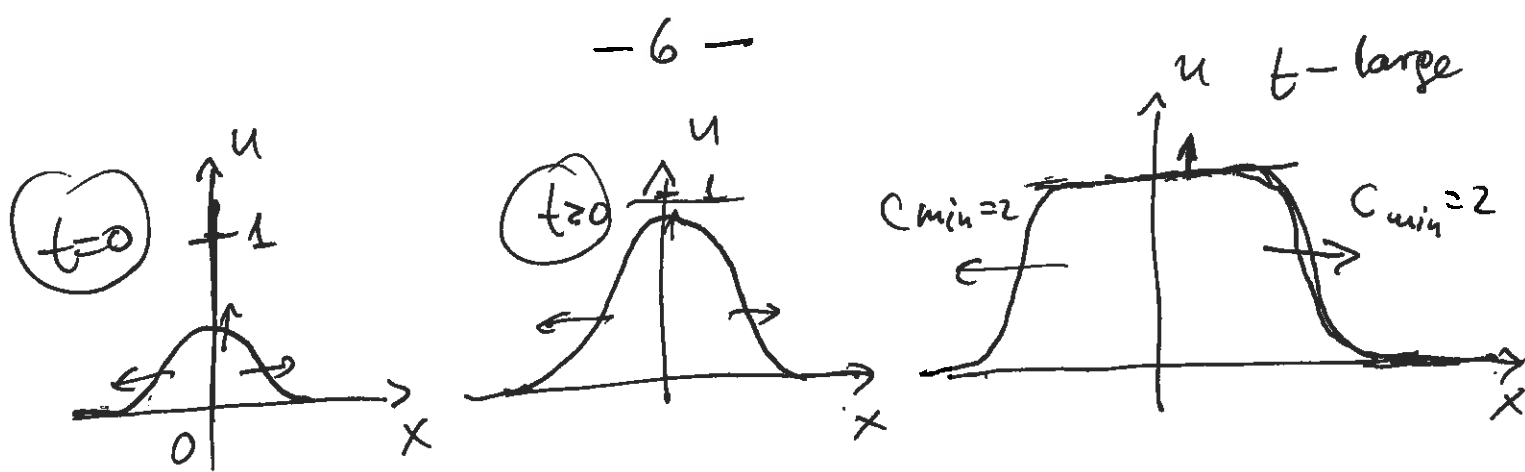
$$u(x, 0) = \begin{cases} 1, & x < x_1 \\ 0 & x > x_2 \end{cases}$$

Then $u(x, t)$ is a travelling wave
with $c = 2 = C_{min}$

C depends on $u(x, 0)$ at $\pm\infty$

$$u_t = u(1-u) + u_{xx}, \qquad x \to \boxed{-x}$$

$U(x \mp ct)$ is solution so is $U(x \mp ct)$

$$-x - ct = -\boxed{(x + ct)}, \qquad \boxed{\pm c}$$

$$\lim_{x \to \infty} u(x,t) = \lim_{z \to -\infty} U(z) = 1 \qquad z = \boxed{x} - ct.$$

Asymptotic Solution

$$C \geq 2, \qquad \varepsilon = \frac{1}{c^2} < \frac{1}{C^2_{min}} = \frac{1}{4} = 0.25$$

$$U'' + c\,U' + U(1-U) = 0$$

$$U(z) = g(\xi), \qquad \xi = \frac{z}{c} = \sqrt{\varepsilon}\, z$$

$$g(\xi) = g_0(\xi) + \varepsilon g_1(\xi) + \varepsilon^2 g_2(\xi) + \cdots$$

$$g(-\infty) = 1, \qquad g(\infty) = 0, \qquad g(0) = \frac{1}{2}$$

$$U(z) = g(\xi) \quad , \quad \xi = \frac{z}{c}$$

$$\frac{dU}{dz} = \frac{dg}{d\xi} \cdot \frac{d\xi}{dz} = \frac{1}{c} g' = \sqrt{\varepsilon} \frac{dg}{d\xi}$$

$$\frac{dU}{dz} = \sqrt{\varepsilon} \frac{dg}{d\xi}$$

$$U'' + cU' + U(1-U) = 0$$

$$\varepsilon \frac{d^2g}{d\xi^2} + c \cdot \frac{1}{c} \frac{dg}{d\xi} + g(1-g) = 0$$

$$\varepsilon \frac{d^2g}{d\xi^2} + \frac{dg}{d\xi} + g(1-g) = 0$$

$$g = g_0 + \varepsilon g_1 + \varepsilon^2 g_2 + \text{- - -}$$

$$\varepsilon \left(g_0'' + \varepsilon g_1'' + \text{- -} \right) + \left(g_0' + \varepsilon g_1' + \text{- -} \right) +$$

$$+ \left(g_0 + \varepsilon g_1 + \text{-} \right) \left(1 + g_0 - \varepsilon g_1 \text{- -} \right) = 0$$

$$0 = \varepsilon g_0'' + \varepsilon^2 g_1''' + g_0' + \varepsilon g_1' + g_0 + \varepsilon g_1 - g_0^2 - \varepsilon g_1 g_0 - \varepsilon g_0 g_1 + \text{-}$$

$\boxed{\varepsilon^0}$ $\qquad g_0' + g_0(1-g_0) = 0 \qquad \longrightarrow$ solve for g_0

$\boxed{\varepsilon^1}$ $\qquad g_0'' + g_1' + g_1 - 2g_0 g_1 = 0 \longrightarrow$ solve for g_1

$$g_0(\xi) = \frac{1}{1+e^\xi}$$

$$u(z) = \frac{1}{1+e^{z/c}} + O(\varepsilon)$$

⊛ $\quad g_1' + (1-2g_0)g_1 = -g_0''$

$$\boxed{y' + P(\xi)\,y = Q(\xi) \quad - \text{ linear } 1^{st} \text{ order}}$$

$$1 - 2g_0$$

$\boxed{Eq. \text{ for } g_0}: \quad g_0' + g_0(1-g_0) = 0$

$$g_0' + g_0 - g_0^2 = 0 \quad \Rightarrow \quad g_0'' + g_0' - 2g_0 g_0' = 0$$

$$g_0'' + (1-2g_0)g_0' = 0$$

'Trick'
$$\boxed{1 - 2g_0 = -\frac{g_0''}{g_0'}}$$

$$g_1' \cancel{=} \frac{g_0''}{g_0'} g_1 = -g_0'' \qquad \Big| \cdot \frac{1}{g_0'}$$

$$\frac{g_1' g_0' - g_0'' g_1}{(g_0')^2} = -\frac{g_0'' A}{g_0' A} \qquad \left[\frac{g_1}{g_0'}\right]' = \big(- \ln|A\,g_0'|\big)'$$

$$\frac{g_1(\xi)}{g_0'} = -\ln|A\,g_0'| \quad \Rightarrow \quad \boxed{g_1(\xi) = -g_0' \ln|A\,g_0'|}$$

$$g_0 = \frac{1}{1+e^\xi} \quad , \quad g_0' = -\frac{e^\xi}{(1+e^\xi)^2}$$

$$g_1 = -g_0' \ln |A g_0'|$$

$$g_1(\xi) = \frac{e^\xi}{(1+e^\xi)^2} \ln \frac{A e^\xi}{(1+e^\xi)^2} \qquad \underline{g_1(0) = 0}$$

$$g_1(0) = \frac{1}{2^2} \ln \left(\frac{A}{2^2}\right) \implies A = 2^2 = \underline{\underline{4}}$$

$$\boxed{g_1(\xi) = \frac{e^\xi}{(1+e^\xi)^2} \ln \frac{4 e^\xi}{(1+e^\xi)^2}} \qquad \cancel{z} \, \boxed{\xi = \frac{z}{c}}$$

$$U(z) = g_0 + \varepsilon g_1 + O(\varepsilon^2) \qquad \boxed{\varepsilon = \frac{1}{c^2}}$$

$$U(z) = \frac{1}{1+e^{z/c}} + \frac{1}{c^2} \cdot \frac{e^{z/c}}{(1+e^{z/c})^2} \ln \left[\frac{4 e^{z/c}}{(1+e^{z/c})^2}\right] + O\left(\frac{1}{c^4}\right)$$

$$\boxed{c \geq 2}$$

Density - Dependent Diffusion Models

$$\frac{\partial u}{\partial t} = f(u) + \frac{\partial}{\partial x}\left[D(u) \frac{\partial u}{\partial x} \right]$$

Typically $f(u)$ has zeroes at $u=0$ & $u=1$

$$f(u) = u^p(1-u^q) \quad , \quad P, q > 0$$

$$D(u) = D_o u^m \quad , \quad D_o, m > 0$$

$$\frac{\partial u}{\partial t} = r u^p(1-u^q) + D_o \frac{\partial}{\partial x}\left(u^m \frac{\partial u}{\partial x} \right)$$

$$\frac{\partial u}{\partial t} = u^p(1-u^q) + \frac{\partial}{\partial x}\left(u^m \frac{\partial u}{\partial x} \right)$$

An example of an exact solution

take $\underline{p=1, \quad m=0}$

$$\left| \begin{array}{l} \frac{\partial u}{\partial t} = u(1-u^q) + \frac{\partial^2 u}{\partial x^2} \quad , \quad q>0 \\[4mm] u = U(z) \quad, \quad z = x - ct \quad, \quad U(-\infty) = 1, \quad U(\infty) = 0 \end{array} \right.$$

$$L(U) = U'' + c U' + U(1-U^q) = 0$$

$$U(z) = \frac{1}{(1+ae^{bz})^s} \qquad \underline{a, b, s > 0}$$

$$U = \frac{1}{(1+ae^{bz})^S} = (1+ae^{bz})^{-S}$$

$$U' = \frac{-Sabe^{bz}}{(1+ae^{bz})^{S+1}} = -Sab \frac{e^{bz}}{(1+ae^{bz})^{S+1}}$$

$$U'' = -Sab \frac{be^{bz}(1+ae^{bz})^{S+1} - e^{bz}(S+1)(1+ae^{bz})^{S}abe^{bz}}{(1+ae^{bz})^{2S+2}}$$

$$U'' = -Sab^2(1+ae^{bz})^{-S-2}e^{bz}\left[1+ae^{bz} - (S+1)ae^{bz}\right]$$

$$U'' = -Sab^2e^{bz}(1+ae^{bz})^{-S-2}(1-Sae^{bz})$$

$$U' = -Sabe^{bz}(1+ae^{bz})^{-S-1}$$

$$U = (1+ae^{bz})^{-S}$$

$$U'' + cU' + U(1-U^q) = 0$$

$$-Sab^2e^{bz}(1+ae^{bz})^{-S-2}(1-Sae^{bz})$$
$$\ \ c\,Sabe^{bz}(1+ae^{bz})^{-S-1} \quad + (1+ae^{bz})^{-S} - (1+ae^{bz})^{-S(q+1)}$$

$$(1+ae^{bz})^{-S-2}\left[-Sab^2e^{bz}(1-Sae^{bz}) - cSabe^{bz}(1+ae^{bz})\right.$$
$$\left. + (1+ae^{bz})^2 - (1+ae^{bz})^{2-Sq}\right] = 0$$

$$e^0\, e^{bz},\quad e^{2bz}$$

$$\boxed{2-Sq = 0, 1, 2}$$

$z = sq$, $s = \frac{2}{q}, \frac{1}{q}$, $\cancel{sq \neq 0}$. $\quad \underline{\dfrac{s > 0}{q > 0}}$

Consider $\quad s = \frac{1}{q} \qquad sq = 1$

$$-sab^2 e^{bz} + s^2 a^2 b^2 e^{2bz} - csabe^{bz} - csa^2 b e^{2bz}$$

$$+ \cancel{1} + 2ae^{bz} + a^2 e^{2bz} - \cancel{1} - ae^{bz}$$

$\left. e^{bz} \right|$ $\quad -sab^2 - csab + 2a - a = 0$

$\qquad\quad -sb\alpha (b+c) + \alpha = 0 \qquad\qquad a > 0$

$$\boxed{1 = sb(b+c)}$$

$\left. e^{2bz} \right|$ $\quad s^2 a^2 b^2 - csa^2 b + a^2 = 0$

$\qquad\qquad s^2 b^2 - csb + 1 = 0$

$\qquad\qquad \underline{sb(sb - c) = \boxed{-1} = -sb(b+c)}$

$$\underline{sb}(sb - c) + \underline{\underline{sb}}(b+c) = 0$$

$$sb(sb - \cancel{c} + b + \cancel{c}) = 0$$

$$sb^2(s + 1) = 0 \qquad\qquad \text{Not possible !}$$

$$s = \frac{1}{q} \text{ not possible .}$$

$$\frac{Sq = 2}{}$$

$$- Sab^2 e^{bz} + s^2 a^2 b^2 e^{2bz} - csabe^{bz} - csa^2 b\, e^{2bz}$$

$$+ \cancel{1} + 2ae^{bz} + a^2 e^{2bz} - \cancel{1} = 0$$

$$e^{bz} \bigg/ \quad - sab^2 - csab + 2a = 0$$

$$- s\alpha b\,(b+c) + 2\cancel{a} = 0$$

$$\boxed{2 = sb\,(b+c)}$$

$$e^{2bz} \bigg/ \quad s^2 \textcircled{a^2} b^2 - cs\textcircled{a^2} b + \textcircled{a^2} = 0$$

$$sb\,(sb - c) + 1 = 0$$

$$2sb\,(sb-c) + 2 = 0$$

$$2\textcircled{sb}\,(sb-c) + \textcircled{sb}\,(b+c) = 0$$

$$\textcircled{sb}\,(2sb - 2c \pm b + c) = 0$$

$$(2s + 1)b - c = 0$$

$$(2s+1)b = c \quad \Rightarrow \quad \boxed{b = \frac{c}{1+2s}}$$

$$s = \frac{2}{9}, \quad b = \frac{9}{[2(9+2)]^{1/2}}, \quad c = \frac{9+4}{[2(9+4)]^{1/2}}$$

$\boxed{q=1}$ Fisher — Kolmogoroff.

$S = 2$, $b = \frac{1}{\sqrt{6}}$ $c = \frac{5}{\sqrt{6}} = 2.04 > \underline{\underline{2}}$

$U(0) = \frac{1}{2}$ $\Rightarrow \underline{a = \sqrt{2} - 1}$

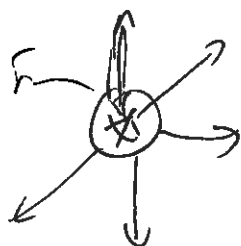$$U(z) = \frac{1}{\left(1 + (\sqrt{2}-1)\, e^{z/\sqrt{6}}\right)^2}$$

$c = \frac{5}{\sqrt{6}}$ — waves for specific $\underline{speed}$!

$$\frac{14/11/2011}{}$$

$$\frac{\partial u}{\partial t} = u(1-u) + \boxed{\frac{\partial^2 u}{\partial x^2}} \quad (1)$$

$u = 0$ steady state   stable

$u = 1$ unstable

$$z = x - ct$$

$$u'' + cu' + u(1-u) = 0 \qquad U = U(z)$$

$$c \geq 2$$

$$\varepsilon = \frac{1}{c^2} < \frac{1}{4} = 0.25 \quad \text{is small parameter}$$

$$U(z) = \frac{1}{1+e^{z/c}} + \frac{1}{c^2} \cdot \frac{e^{z/c}}{(1+e^{z/c})^2} \ln\left[\frac{4e^{z/c}}{(1+e^{z/c})^2}\right] + O\left(\frac{1}{c^4}\right)$$

$$u(\infty) = 0 \quad , \quad u(-\infty) = 1 \quad , \quad U(0) = \frac{1}{2}$$

-2-

$$\frac{\partial u}{\partial t} = u\left(1 - u^q\right) + \frac{\partial^2 u}{\partial x^2}$$

$$\underline{q > 0}$$

$$u(x,t) = U(z) \qquad z = x - ct$$
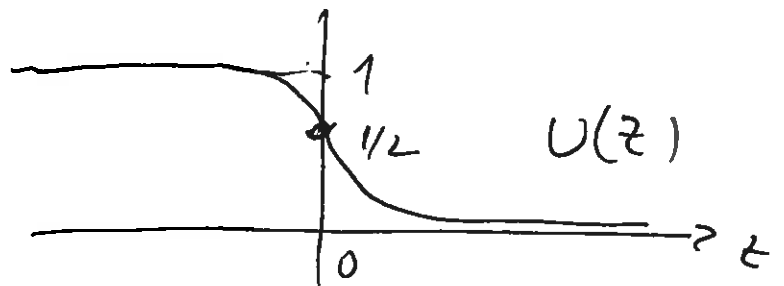
$$U(-\infty) = 1, \qquad U(\infty) = 0$$

Exact solution $\quad U(z) = \dfrac{1}{\left(1 + ae^{bz}\right)^s}$

$$s = \frac{2}{q}, \quad b = \frac{1}{\sqrt{2\,(q+2)}}, \quad c = \frac{q+4}{\sqrt{2(q+4)}}$$

when $q = 1$ Fisher - Kolmogoroff

$$s = 2 \qquad b = \frac{1}{\sqrt{6}} \qquad c = \frac{5}{\sqrt{6}} = 2.04 \geqslant 2$$

$$U(0) = \frac{1}{2}$$

$U(z)$

$$U(0) = \frac{1}{2} = \frac{1}{(1 + a\cdot 1)^2} \quad \Rightarrow \quad \sqrt{2} = 1 + a$$

$$\boxed{a = \sqrt{2} - 1}$$

$$U(z) = \frac{1}{\left(1 + (\sqrt{2}-1)e^{z/\sqrt{6}}\right)^2}, \qquad \boxed{z = x - \frac{5}{\sqrt{6}}t}$$

$$\frac{\partial u}{\partial t} = ru(1-u) + \frac{\partial}{\partial x}\left(D(u)\frac{\partial u}{\partial x}\right)$$

$$D = D_0 u^m, \quad D_0 > 0 \text{ is a constant}$$

$$\frac{\partial u}{\partial t} = ru(1-u) + D_0 \frac{\partial}{\partial x}\left(u^m \frac{\partial u}{\partial x}\right)$$

$$t \to rt \qquad x \to x\sqrt{\frac{r}{D_0}}$$

$$\frac{\partial u}{\partial t} = u(1-u) + \frac{\partial}{\partial x}\left(u^m \frac{\partial u}{\partial x}\right)$$

$$m > 0 \quad \text{is a constant}$$

Example: $m = 1$

$$\frac{\partial u}{\partial t} = u(1-u) + \frac{\partial}{\partial x}\left(u\frac{\partial u}{\partial x}\right)$$

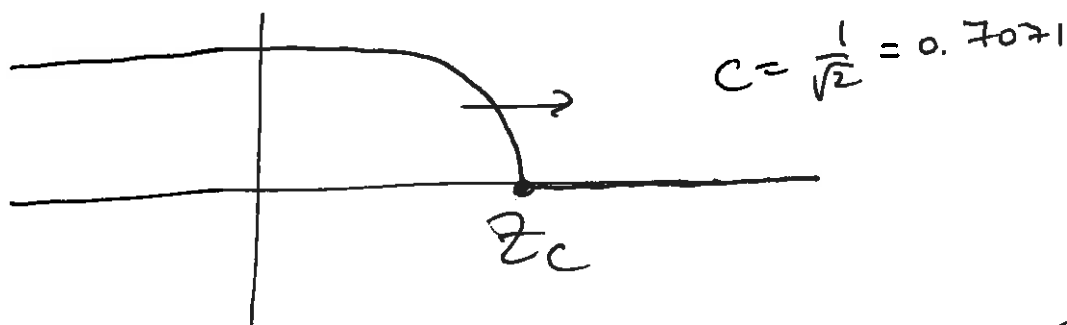two nonlinear terms.

Travelling wave solution $U = U(z) = u(x,t)$

$$\frac{\partial u}{\partial t} = -cU' \qquad \frac{\partial u}{\partial x} = U', \quad z = x - ct$$

$$\boxed{(UU')' + cU' + U(1-U) = 0}$$

Exact travelling wave solution $^{-4-}$

$$U(z) = \left[1 - e^{\frac{z-z_c}{\sqrt{2}}}\right]\theta(z_c - z)$$

$c = \frac{1}{\sqrt{2}} = 0.7071$

$\cancel{tt=}$ $u(x,t) = U(\cancel{x \pm ct}) + \boxed{U_2(x-ct)}$

$$U' = -\frac{1}{\sqrt{2}} e^{\frac{z-z_c}{\sqrt{2}}}\theta(z_c - z) + \left(1 - e^{\frac{z-z_c}{\sqrt{2}}}\right)\delta(z_c-z)(-1)$$

$\underbrace{(1-1)}_{0} \longleftarrow z = z_c$

$$\boxed{U' = -\frac{1}{\sqrt{2}} e^{\frac{z-z_c}{\sqrt{2}}}\theta(z_c - z)}$$

$$UU' = \left(1 - e^{\frac{z-z_c}{\sqrt{2}}}\right)\theta(z_c-z)\left(-\frac{1}{\sqrt{2}}\right)e^{\frac{z-z_c}{\sqrt{2}}}\underline{\theta(z_c-c)}$$

$$= \left(-\frac{1}{\sqrt{2}} e^{\frac{z-z_c}{\sqrt{2}}} + \frac{1}{\sqrt{2}} e^{2\frac{z-z_c}{\sqrt{2}}}\right)\theta(z_c - z)$$

$$(UU')' = \left(-\frac{1}{\sqrt{2}}\cdot\frac{1}{\sqrt{2}} e^{\frac{z-z_c}{\sqrt{2}}} + \frac{1}{\sqrt{2}}\cdot\frac{2}{\sqrt{2}} e^{2\cdot\frac{z-z_c}{\sqrt{2}}}\right)\theta(z_c-z) +$$

$$\underbrace{\left(-\frac{1}{\sqrt{2}} e^{\frac{z-z_c}{\sqrt{2}}} + \frac{1}{\sqrt{2}} e^{2\left(\frac{z-z_c}{\sqrt{2}}\right)}\right)}_{0}\delta(z_c-z)(-1)$$

$z = z_c$

$$(uu')' = \left(-\frac{1}{2}e^{\frac{z-z_c}{\sqrt{2}}} + e^{2\frac{z-z_c}{\sqrt{2}}}\right)\theta(z_c - z)$$
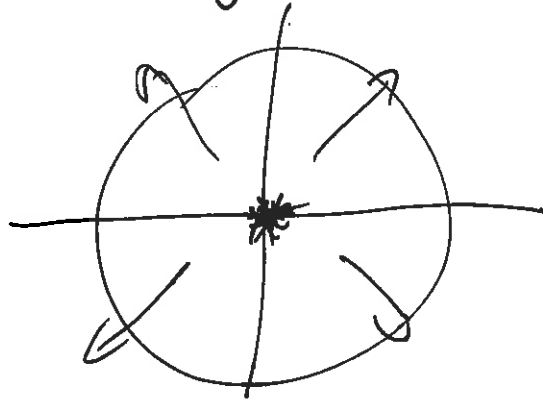
$$cu' = -\frac{c}{\sqrt{2}}\, e^{\frac{z-z_c}{\sqrt{2}}}\,\theta(z_c - z)$$

$$u(1-u) = \left(1 - e^{\frac{z-z_c}{\sqrt{2}}}\right)e^{\frac{z-z_c}{\sqrt{2}}}\,\theta(z_c - z)$$

$$(uu')' + cu' + u(1-u) =$$

$$\theta(z_c-z)\left\{-\frac{1}{2}e^{\frac{z-z_c}{\sqrt{2}}} + e^{2\frac{z-z_c}{\sqrt{2}}} - \frac{c}{\sqrt{2}}e^{\frac{z-z_c}{\sqrt{2}}} + e^{\frac{z-z_c}{\sqrt{2}}} - e^{2\frac{z-z_c}{\sqrt{2}}}\right\}$$

$$= \theta(z_c-z)\left(\frac{1}{2} - \frac{c}{\sqrt{2}}\right)e^{\frac{z-z_c}{\sqrt{2}}} = 0 \quad \text{when } c = \frac{1}{\sqrt{2}}$$

Radial symmetry

$$\frac{\partial u}{\partial t} = \underline{\underline{\varepsilon u}} + D\Delta u$$

Linear!

$$\Delta f = \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial f}{\partial r}\right) + \frac{1}{r^2}\cancel{\frac{\partial^2 f}{\partial \theta^2}}$$

$$u(r,t) = \frac{N_0}{4\pi D t}\, e^{\,\varepsilon t - \frac{r^2}{4Dt}}$$

$$\lim_{t\to 0} u(r,t) = N_0\,\delta(r) = \underline{u(r,0)}$$

$$\frac{\partial u}{\partial t} = -\frac{N_0}{4\pi D t^2}\, e^{\,\varepsilon t - \frac{r^2}{4Dt}} + \frac{N_0\left(\varepsilon + \frac{r^2}{4Dt^2}\right)}{4\pi D t}\, e^{\,\varepsilon t - \frac{r^2}{4Dt}}$$

$$\frac{\partial u}{\partial t} = \left(-\frac{1}{t} + \varepsilon + \frac{r^2}{4Dt^2}\right) u(x,t)$$

$$D\Delta u = D\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u}{\partial r}\right) = \frac{D}{r}\frac{\partial}{\partial r}\left[r\,\boxed{\frac{N}{4\pi D t}}\, e^{\,\varepsilon t - \frac{r^2}{4Dt}}\cdot\left(-\frac{2r}{4Dt}\right)\right]$$

$$= \frac{N_0}{4\pi D t}\cdot\frac{D}{r}\frac{\partial}{\partial r}\left(-\frac{2r^2}{4Dt}\, e^{\,\varepsilon t - \frac{r^2}{4Dt}}\right) =$$

$$= \left(\boxed{\frac{N_0}{4\pi Dt}}\right) \cdot \frac{D}{r} \left[-\frac{4r}{4Dt} - \frac{2r^2}{4Dt}\left(\frac{-2r}{4Dt}\right) \right] \boxed{e^{\left(\varepsilon t - \frac{r^2}{4Dt}\right)}}$$

$$= \left(-\frac{1}{t} + \frac{D}{x} \cdot \frac{4r^2}{4^2 D^2 t^2} \right) u(x,t) =$$

$$= \left(-\frac{1}{t} + \frac{r^2}{4Dt^2} \right) u(x,t) = D \Delta u$$

$$\frac{\partial u}{\partial t} \overset{?}{=} \varepsilon u + D\Delta u \qquad - \text{equation}$$

$$\left(-\frac{1}{t} + \varepsilon + \frac{r^2}{4Dt^2} \right) u \overset{?}{=} \varepsilon u + \left(\frac{1}{t} + \frac{r^2}{4Dt^2} \right) \checkmark$$

u is detectable if $\boxed{u > u^*}$

$$u(r,t) = u^* \implies r(t)$$

$$u^* = \frac{N_0}{4\pi Dt} \exp\left(\varepsilon t - \frac{r^2}{4Dt} \right)$$

$$\ln \frac{4\pi Dt \, u^*}{N_0} = \varepsilon t - \frac{r^2}{4Dt}$$

$$r^2 = \varepsilon t \cdot 4Dt - 4Dt \ln \frac{4\pi Dt u^*}{N_0}$$

$$r^2 = 4D\varepsilon\, t^2 - 4Dt\ln\frac{4\pi Du^* t}{N_0}$$

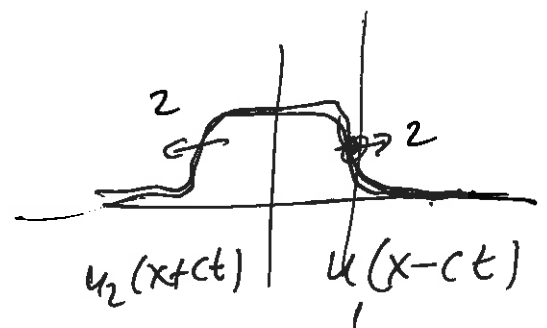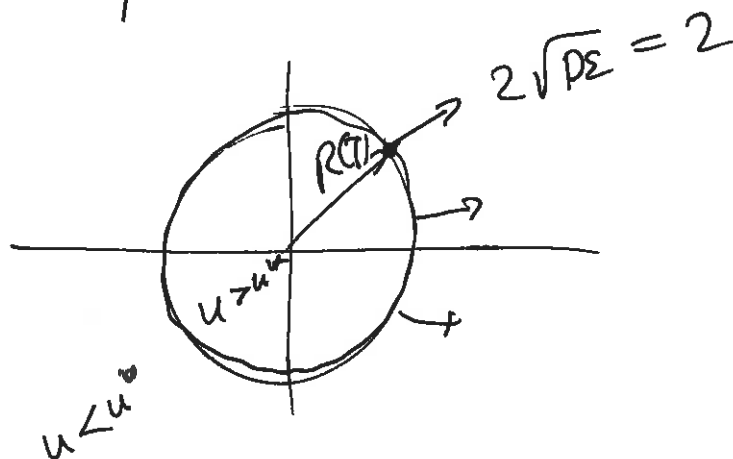$$r(t) = 2t\left(D\varepsilon - \frac{D}{t}\ln\frac{4\pi Du^* t}{N_0}\right)^{1/2}$$

$$R(T) = 2T\left(D\varepsilon + \frac{D}{T}\ln\frac{N_0}{4\pi Du^* T}\right)^{1/2}$$

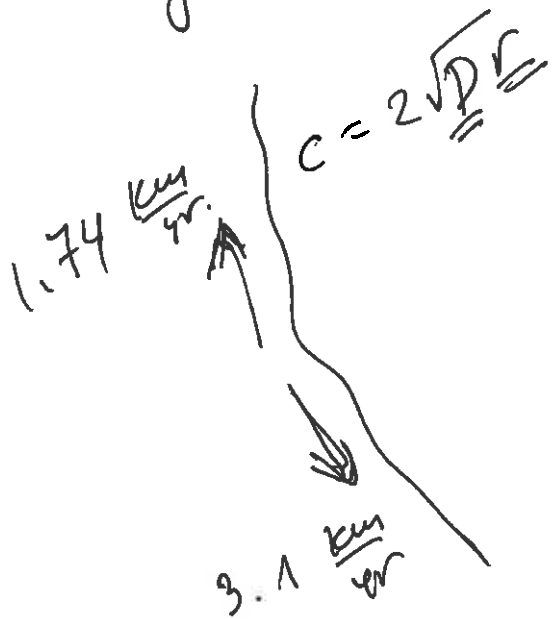$$T \to \infty \qquad \frac{1}{T}\ln\frac{\gamma}{T} \to 0$$

$$\lim_{T\to\infty}\frac{\ln\frac{\gamma}{T}}{T} = \lim_{T\to\infty}\frac{\left[\ln\left(\frac{\gamma}{T}\right)\right]'}{(T)'} = \frac{\frac{T}{\gamma}\left(-\frac{\gamma}{T^2}\right)}{1} = -\frac{1}{T} = 0$$

$$R(T) = 2T\sqrt{D\varepsilon}$$

$$C = \frac{R(T)}{T} \approx 2\sqrt{D\varepsilon} \quad \text{wavespeed.}$$

$$2\sqrt{D\varepsilon} = 2$$

$u > u^*$

$u < u^*$

$R(T)$

$u_2(x+ct)$ $u(x-ct)$

Otter population   central coast of California

'Big Sur'

$$D = 13.5 \; km^2/yr$$

$$c = 2\sqrt{D \cdot r}$$

1.74 $\frac{km}{yr.}$

3.1 $\frac{km}{yr}$

$$D = 54.7 \; km^2/yr, \quad r = 0.056 \; yr^{-1}$$

1938 – 1972

Discrete Population Models
for a Single Species
(Chapter 2 , vol. $\perp$)

$$\frac{dN}{dt} = r N \left(\not{1} - \frac{N}{K} \right)$$

$$\underline{\underline{N(t)}} \longrightarrow N(1), N(2), N(3), \text{--}$$

$$N_1, N_2, N_3, \text{--}$$

$$\frac{N(t+\Delta t) - N(t)}{\Delta t} \approx \frac{N_{t+1} - N_t}{1} \simeq N_{t+1} - N_t$$

$$N_{t+1} = f(N_t) = N_t F(N_t)$$

$$N_{t+1} - N_t = r N_t (1 - N_t)$$

$$N_{t+1} = N_t (1 + r - r N_t)$$

$$N_{t+1} = (1+r) N_t \left(1 - \underbrace{\left(\frac{r}{r+1} N_t \right)}_{X_t} \right)$$

$$X_t = \frac{r}{r+1} N_t , \quad r' = 1+r$$

$$\boxed{X_{t+1} = r' X_t (1 - X_t)}$$

$$N_{t+1} = r N_t \qquad \text{Simplest difference eq.}$$

$$N_t = r^t N_0$$

$$N_{t+1} = r N_t = r(r N_{t-1}) = r^2 N_{t-1} = r^3 N_{t-2}$$

$|r| > 1 \quad$ growth
$|r| < 1 \quad$ decay

Fibonacci Sequence

$$\circledast \qquad N_{t+1} = N_t + N_{t-1} \qquad\qquad \underline{\underline{N_0 = N_1 = 1}}$$

$$1, 1, 2, 3, 5, 8, 13, \cdots$$

linear difference equation

$$N_t = N_0 \lambda^t$$

$$N_0 \lambda^{t+1} = N_0 \lambda^t + N_0 \lambda^{t-1} \qquad \left(\frac{1}{\lambda^{t-1}} \right)$$

$$\boxed{\lambda^2 = \lambda + 1} \quad \text{characteristic equation}$$

$$\lambda_{1,2} = \tfrac{1}{2}\left(1 \pm \sqrt{5}\right)$$

$$\boxed{N_t = C_1 \lambda_1^t + C_2 \lambda_2^t} \qquad \lambda_{1,2} = \frac{1 \pm \sqrt{5}}{2}$$

$$N_0 = 1, \qquad N_1 = 1$$

$$\underline{t=0} \qquad 1 = C_1 \lambda_1^0 + C_2 \lambda_2^0 \Rightarrow \qquad \begin{array}{l} C_1 + C_2 = 1 \\[2mm] C_1 \frac{1+\sqrt{5}}{2} + C_2 \frac{1-\sqrt{5}}{2} = 1 \end{array}$$

$$t=1 \qquad 1 = C_1 \lambda_1 + C_2 \lambda_2$$

$$\underbrace{\boxed{C_1 + C_2}}_{2} \cdot t + \frac{\sqrt{5}(C_1 - C_2)}{2} = 1$$

$$\frac{1}{2} + \frac{\sqrt{5}}{2}(C_1 - C_2) = 1 \Rightarrow \qquad C_1 - C_2 = \frac{1}{2} \cdot \frac{2}{\sqrt{5}} = \frac{1}{\sqrt{5}}$$

$$\left. \begin{array}{l} C_1 + C_2 = 1 \\ C_1 - C_2 = \frac{1}{\sqrt{5}} \end{array} \right| \qquad 2C_1 = 1 + \frac{1}{\sqrt{5}}$$

$$C_1 = \frac{1}{2}\left(1 + \frac{1}{\sqrt{5}}\right), \qquad \underline{C_2 = \frac{1}{2}\left(1 - \frac{1}{\sqrt{5}}\right)}$$

$$N_t = \frac{1}{2}\left(1 + \frac{1}{\sqrt{5}}\right)\lambda_1^t + \frac{1}{2}\left(1 - \frac{1}{\sqrt{5}}\right)\lambda_2^t, \qquad \lambda_{1,2} = \frac{1 \pm \sqrt{5}}{2}$$

$$\lambda_1 = \frac{1+\sqrt{5}}{2} > 1 \qquad \left|\lambda_2\right| = \left|\frac{1-\sqrt{5}}{2}\right| < 1, \qquad \lambda_2^t \to 0.$$

$$\text{For large } t, \qquad \boxed{N_t \approx \frac{1}{2}\left(1 + \frac{1}{\sqrt{5}}\right)\lambda_1^t}$$

$$\lim \frac{N_{t+1}}{N_t} = \frac{\frac{1}{2}\left(1+\frac{1}{\sqrt{5}}\right)\lambda_1^{t+1}}{\frac{1}{2}\left(1+\frac{1}{\sqrt{5}}\right)\lambda_1^{t}} = \lambda_1 = \frac{1+\sqrt{5}}{2}$$

$$\frac{N_t}{N_{t+1}} \longrightarrow \frac{1}{\lambda_1} = \frac{2}{1+\sqrt{5}} \cdot \frac{(\sqrt{5}-1)}{(\sqrt{5}-1)} = \frac{2(\sqrt{5}-1)}{5-1} =$$

$$\lim_{t \to \infty} \frac{N_t}{N_{t+1}} \Longrightarrow \frac{\sqrt{5}-1}{2} \qquad \text{'golden mean'}$$