

ASO: Mathematical Modelling in Biology

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We will follow **Ruth Baker's** Lecture Notes, but please read the course synopsis carefully:

Chapter 2, **Section 3.5** and **Section 5.2** in those Lecture Notes are no longer in the course.

Enzyme-Substrate kinetics and the **Hodgkin-Huxley model and excitable kinetics** have been added to the course.

AIMS

Introduce you to the art of mathematical modelling in biology, chemistry, ecology, epidemiology and medicine.

Use techniques you have already learnt in applied mathematics (ordinary differential equations, discrete equations) to analyse these models.

Introduce you to new analysis techniques.

Lay the foundation for future courses, such as Part B Further Mathematical Biology, and Part C Mathematical Physiology.

Continuous-time models for a single species

(Ruth Baker notes Chapter 3.)

1.1 Introduction

We start with the **conservation law**:

$$\begin{aligned} \text{rate of increase of population} &= \text{birth rate} - \text{death rate} \\ &+ \text{rate of immigration} - \text{rate of emigration.} \end{aligned} \tag{1.1}$$

We make the following assumptions:

A.1. The system is closed - no immigration, no emigration.

A.2. There is no spatial dependence (Part B: Further Mathematical Biology)

A.3. Time is continuous - overlapping generations.

We can therefore represent the population by $N(t)$, where $t \in [0, \infty)$ is time, and $N(t) \in [0, \infty)$ is population density (or biomass).

Equation (1.1) can be written:

$$\frac{dN}{dt} = f(N) = Ng(N), \tag{1.2}$$

where $g(N)$ is defined to be the *intrinsic growth rate (per capita growth rate)*.

Examples

Eg 1. Malthus Model (1798)

$$g(N) = b - d \tag{1.3}$$

where b is the constant (non-negative) per capita birth rate, and d is the constant (non-negative) per capita death rate. Therefore, Equation (1.2) becomes

$$\frac{dN}{dt} = rN \tag{1.4}$$

where $r = b - d$. Assume initial condition $N(0) = N_0$. Hence the solution is $N(t) = N_0 e^{rt}$.

This model then predicts that populations either grow to ∞ , decay to zero or, in the very special case $r = 0$, remain constant.

Not very realistic.

Eg 2. Verhulst (logistic growth) Model (1836)

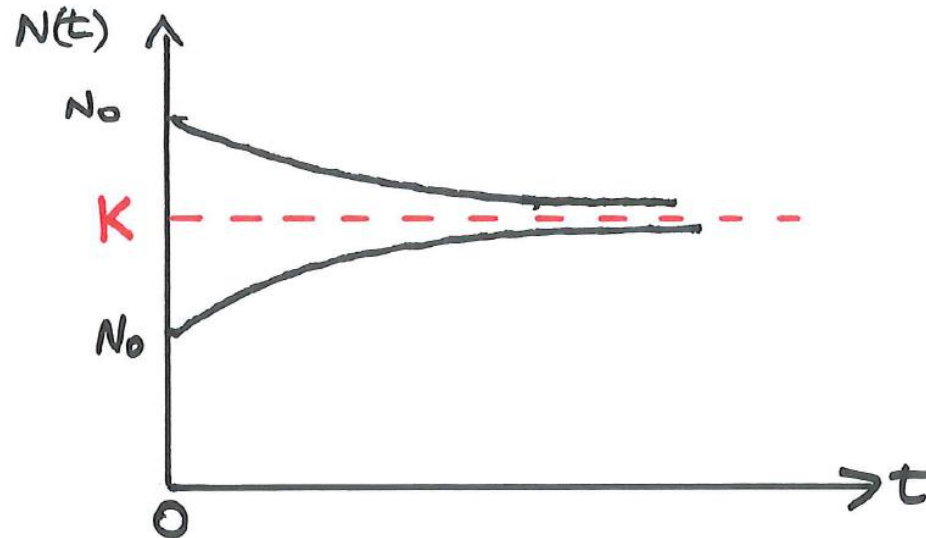
Assume that as N increases, the intrinsic growth rate decreases due to overcrowding, lack of food, competition, *etc.* The simplest such growth rate is:

$$g(N) = r\left(1 - \frac{N}{K}\right), \quad (1.5)$$

where r (positive constant) is linear growth rate, and K (positive constant) is the *carrying capacity*. Substituting this into Equation (1.2) leads to the logistic growth model:

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right). \quad (1.6)$$

Exercise: Show that the solution to the logistic growth model is $N(t) = \frac{N_0 K e^{rt}}{K + N_0(e^{rt} - 1)}$.



Logistic growth is a very good fit for bacterial growth, rats, yeast ...

1.2 Steady States and Linear Stability

Definition: The *steady states* of $\frac{dN}{dt} = f(N)$ are the constants N_s such that $f(N_s) = 0$.

So, for example, in the logistic growth model, there are 2 steady states: $N_s = 0, N_s = K$.

Definition: *Stability.* Roughly speaking “if every initial state sufficiently close to the steady state N_s continues to be permanently close to it, then N_s is stable”. There are lots of different types of stability.

1.2.1 Linear (or Local) Stability

$$\frac{dN}{dt} = f(N). \quad (1.7)$$

Steady states of Equation (1.7): $f(N) = 0 \implies N = N_s$.

Set $N(t) = N_s + n(t)$, where $|n(t)| \ll |N_s|$.

Now Taylor expand $f(N)$:

$$f(N) = f(N_s + n) = f(N_s) + f'(N_s)n + h.o.t \quad (1.8)$$

where dash is derivative with respect to N . Substituting this expansion into Equation (1.7) and noting the definition of steady state, we have (neglecting higher order terms) the linear system:

$$\frac{dn}{dt} = f'(N_s)n \implies n(t) = n_0 e^{f'(N_s)t}, \quad (1.9)$$

where n_0 is the size of the initial perturbation from the steady state.

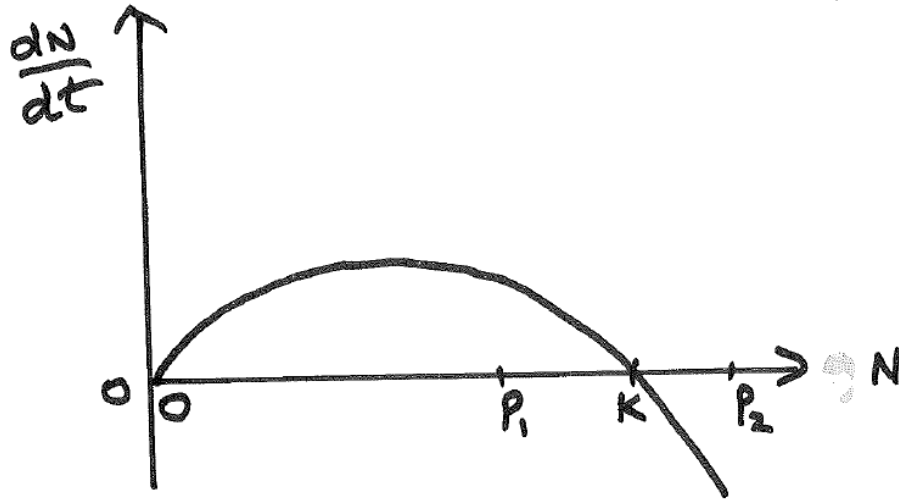
Therefore, if $f'(N_s) > 0$, then $n(t)$ grows so the system moves away from the steady state. We say that the steady state is linearly unstable.

On the other hand, if $f'(N_s) < 0$, then $n(t)$ goes to zero, so the system moves towards the steady state. We say that the steady state is linearly stable, and $\frac{1}{|f'(N_s)|}$ is called the *recovery time* - the time taken for a perturbation to decrease by a factor of e , as predicted by linear analysis. Hence, it is a measure of the time taken for the population to recover from a perturbation.

What if $f'(N_s) = 0$?

Exercise: Show that the steady state $N_s = 0$ for the logistic model is linearly unstable, and that the steady state $N_s = K$ is linearly stable.

N.B. $N_s = K$ is, in fact, stable in $(0, \infty)$.



$f'(0) > 0 : f'(K) < 0$
 If we start at P_1 : $f \text{ (ie } \frac{dN}{dt}) > 0 \therefore N \uparrow$
 " " " " P_2 $< 0 \therefore N \downarrow$

Summary

- Deriving a model
- Steady states
- Linear stability analysis

End of Lecture 1-1

Summary of Previous Lecture

- Deriving a model
- Steady states
- Linear stability analysis

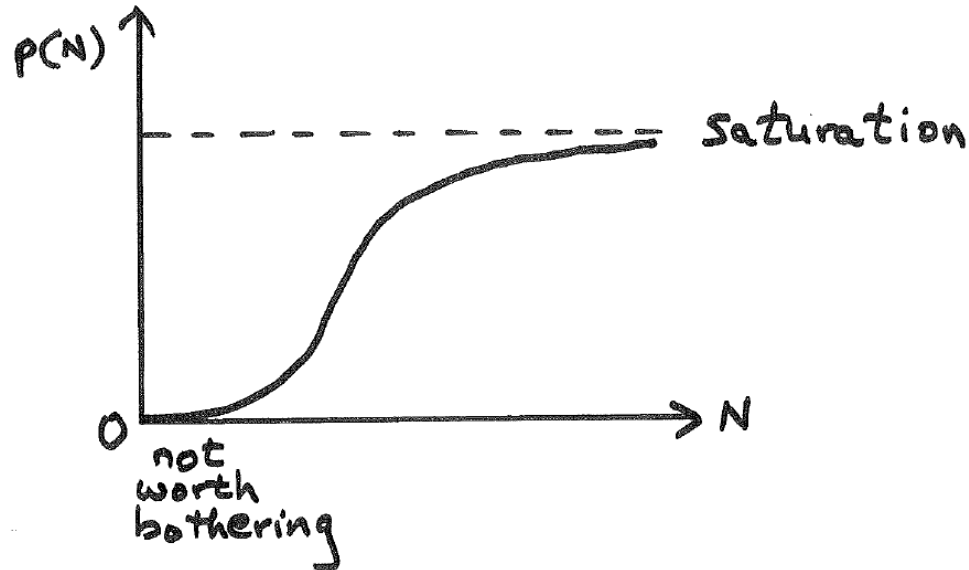
1.3 Non-dimensionalisation and Hysteresis

1.3.1 The Spruce Budworm Model

Introduced by Don Ludwig in 1978, this model proposes that the dynamics of the budworm can be modelled via logistic growth and predation. The model takes the form:

$$\frac{dN}{dt} = r_B N \left(1 - \frac{N}{K_B}\right) - p(N), \quad p(N) := \frac{BN^2}{A^2 + N^2}. \quad (1.10)$$

Here, $N(t)$ is the budworm density (or biomass) at time t , the parameters r_B and K_B are, respectively the linear growth rate and carrying capacity, and $p(N)$ is predation due to birds. A and B are also positive parameters.



Non-dimensionalisation

Equation (1.10) has four parameters: r_B (dimensions, 1/time), K_B (dimensions, biomass), B (dimensions, biomass x 1/time), and A (dimensions, biomass).

Let

$$N = N^*u, \quad t = t^*\tau, \quad (1.11)$$

where N^* has units of biomass, and t^* has units of time, with N^* and t^* constant. Then u and τ are non-dimensional (dimensionless) and satisfy the equation (using the fact that $\frac{d}{dt} = \frac{d}{d\tau} \frac{1}{t^*}$)

$$\frac{N^*}{t^*} \frac{du}{d\tau} = r_B N^* u \left(1 - \frac{N^* u}{K_B} \right) - \frac{B(N^*)^2 u^2}{A^2 + (N^*)^2 u^2}, \quad (1.12)$$

$$\implies \frac{du}{d\tau} = r_B t^* u \left(1 - \frac{N^* u}{K_B} \right) - \frac{B t^* N^* u^2}{A^2 + (N^*)^2 u^2}. \quad (1.13)$$

Now, if we set:

$$N^* = A, \quad t^* = \frac{A}{B}, \quad r = r_B t^* = \frac{r_B A}{B}, \quad q = \frac{K_B}{N^*} = \frac{K_B}{A}, \quad (1.14)$$

we have

$$\frac{du}{d\tau} = ru \left(1 - \frac{u}{q} \right) - \frac{u^2}{1 + u^2} := f(u; r, q). \quad (1.15)$$

Now we only have 2 parameters!

Exercise: Check that r and q are dimensionless, and that N^* and t^* have the correct dimensions.

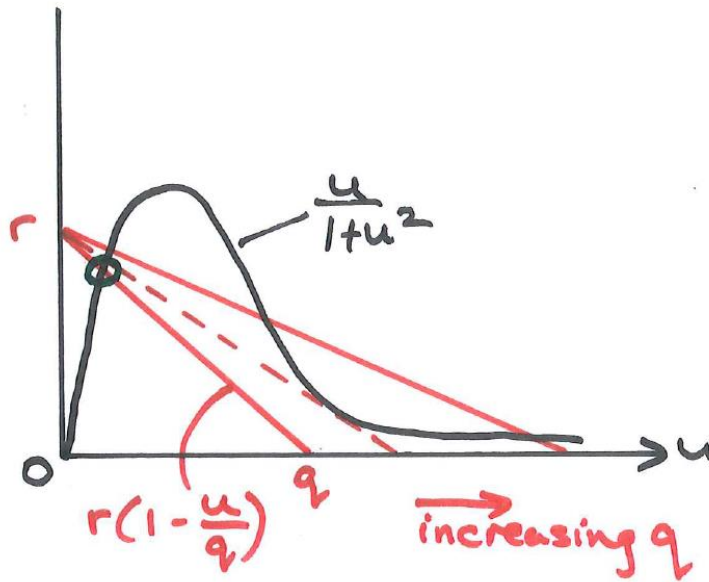
Steady states

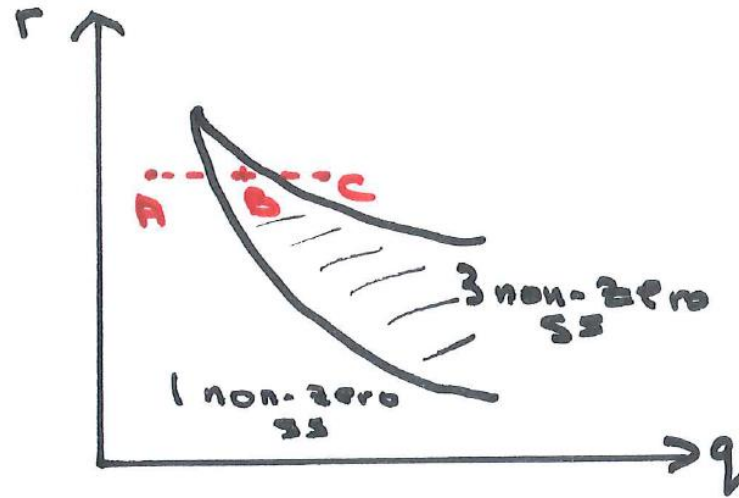
The steady states are given by the solutions of

$$ru \left(1 - \frac{u}{q} \right) - \frac{u^2}{1+u^2} = 0. \quad (1.16)$$

Clearly $u_s = 0$ is a steady state. We proceed graphically to consider the other steady states which are given by the intersection of the graphs

$$f_1(u) = r \left(1 - \frac{u}{q} \right) \quad \text{and} \quad f_2(u) = \frac{u}{1+u^2}. \quad (1.17)$$



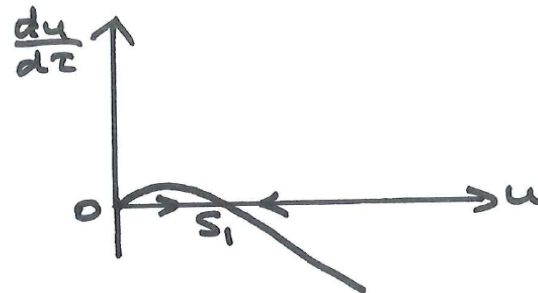


ss - steady
state

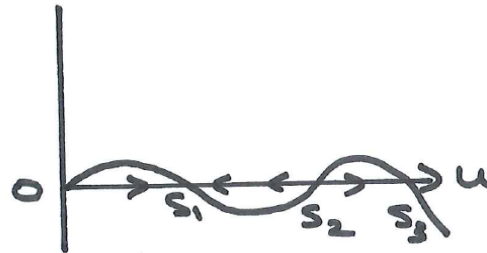
Parameter Space

A:
(q small)
Small non-zero
ss

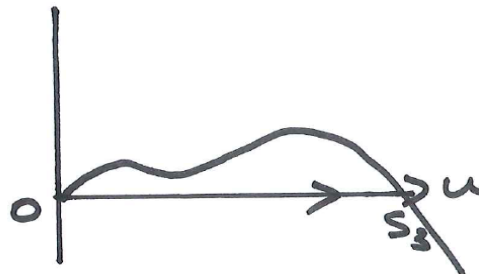
$$\frac{du}{d\tau} = ru(1 - \frac{u}{q}) - \frac{u^2}{1+u^2}$$



B:
(3 ss)
non-zero

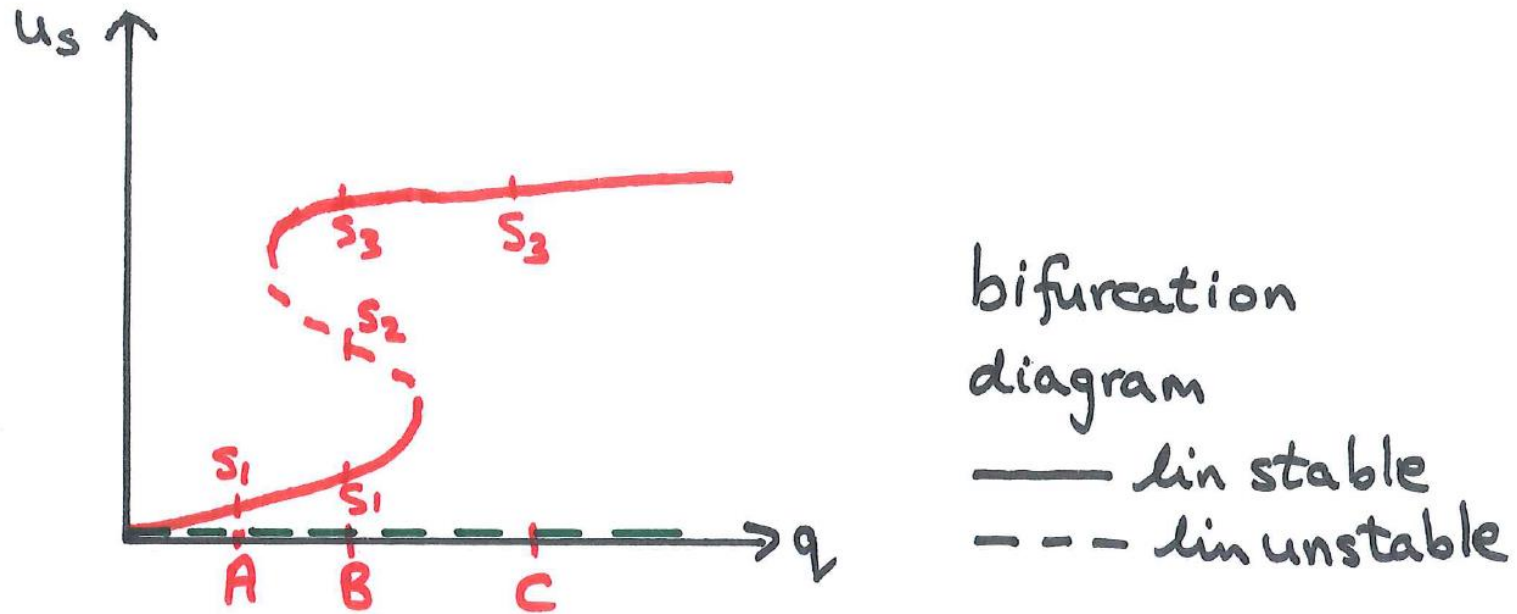


C:
non-zero
(one ss: large)
q large



parameter
behaviour

$\xleftarrow{\text{green}} \quad \xrightarrow{\text{red}}$
 A $\xrightarrow{\text{red}}$ B $\xrightarrow{\text{red}}$ C
 $S_1 \xrightarrow{\text{red}} S_1 \xrightarrow{\text{red}} S_3$
 $S_1 \xleftarrow{\text{green}} S_3 \xleftarrow{\text{green}} S_3$



Bifurcation: Point at which the stability of a solution changes.

Crucially we see what is called a **hysteresis loop**: As we change a parameter, we go through a sequence of steady states of the system. When we reverse the change in parameter, *we come back to the state at which we started, but in a different sequence.*

Biological Insights

The biological insight from this analysis is that we cannot eliminate the budworm (zero steady state is unstable) but if we reduce either r or q then we force the budworm into a small steady state.

Recall:

$r = \frac{r_B A}{B}$ there we could reduce r_B (sterile insect release).

$q = \frac{K_B}{A}$ so we could reduce K_B by spraying the trees.

1.4 Harvesting

We want *Maximum Sustainable Yield* (MSY).

Suppose the population grows logistically. That is:

$$\frac{dN}{dt} = rN \left(1 - \frac{N}{K}\right). \quad (1.18)$$

Non-zero steady state is $N = K$. Suppose we perturb it, so that $N = K + n$, where $|n|$ is small. Then, ignoring higher order terms:

$$\frac{dn}{dt} = -rn \quad \Rightarrow \quad n = n(0)e^{-rt}. \quad (1.19)$$

Hence, the logistic growth model predicts a recovery time of $1/r$ for the non-zero steady state.

1.4.1 Constant Effort

In this case,

$$\frac{dN}{dt} = rN \left(1 - \frac{N}{K}\right) - EN := f(N; E), \quad (1.20)$$

where E is a positive constant (the effort we put in to harvest).

The yield, $Y(E)$ is EN and we want to maximise Y but make sure that the steady state still recovers (MSY). The steady states, N_s , are such that $f(N_s; E) = 0$. Therefore, the non-zero steady state is

$$N_s(E) = \frac{(r - E)K}{r} = \left(1 - \frac{E}{r}\right) K, \quad (1.21)$$

and hence

$$Y_s(E) = EN_s(E) = \left(1 - \frac{E}{r}\right) KE. \quad (1.22)$$

Note: Must take $E < r$,

Note that this means that one yield can be obtained from two different efforts.

To maximise the yield, we take $E = \frac{r}{2}$.

Hence the maximum yield, Y_S^{max} , is $\frac{rK}{4}$ and is achieved for the steady state value $N_s = \frac{K}{2}$.

Now, for effort $E < r$, there are two steady states $N_s(E)$ and, linearising by setting $N = N_s(E) + n$ (n small), we find:

$$\frac{dn}{dt} = f'(N_s; E)n = (E - r)n. \quad (1.23)$$

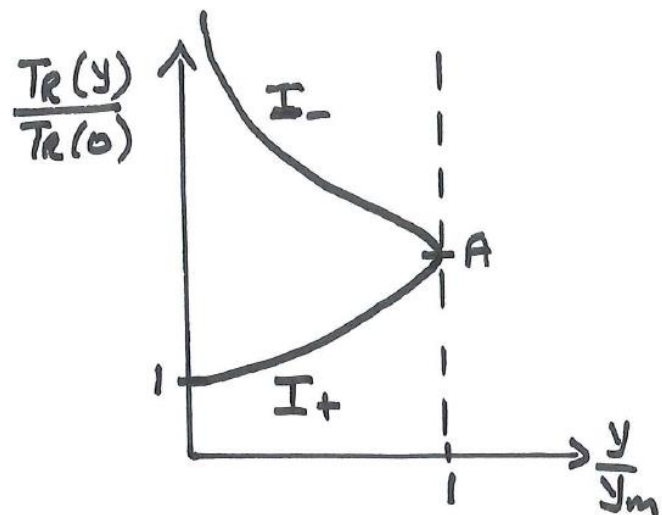
Hence, the recovery time for effort E , $T_R(E) = \frac{1}{r-E}$. Therefore, comparing this to the “natural” recovery time, that is, when there is no harvesting, we have:

$$\frac{T_R(E)}{T_R(0)} = \frac{1}{1 - \frac{E}{r}}. \quad (1.24)$$

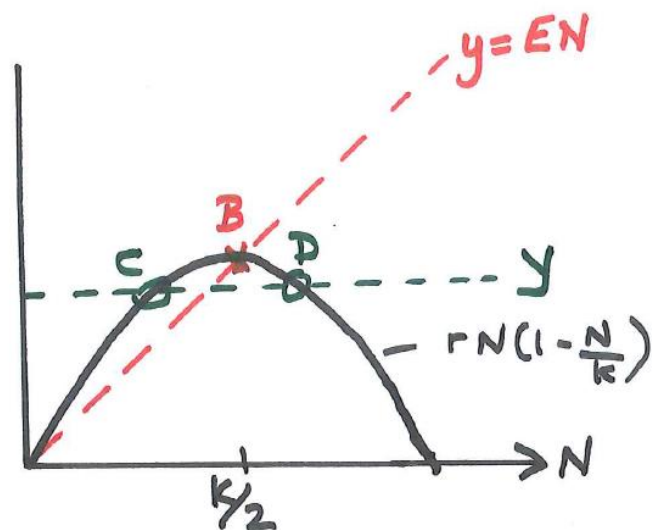
Note that, at MSY, this ratio is 2.

As we typically measure Y , we rewrite everything in terms of Y . Hence, Equation (1.24) becomes:

$$\frac{T_R(Y)}{T_R(0)} = \frac{2}{1 \pm \sqrt{1 - Y/Y_s^{max}}}. \quad (1.25)$$



$y_c = y_0$, but
 $E_c > E_D$
 $\therefore Tr \text{ at } C (= \frac{1}{r-E_c}) >$
 $Tr \text{ at } D$
 $\therefore$ Dis on I_+ branch
 C " " I_- "



B is $\max(N_S^{\max})$ & $E = \frac{r}{2}$
 For yield Y , ($Y < Y_m$),
 we can have two N_S (& therefore two E) - these
 are the pts C & D .

We see that the MSY corresponds to the point A. If we get things slightly wrong, we may end up at the point C. This corresponds to the branch I_- and therefore it will take the population longer to recover. Hence N will be lower than we think so we increase E so that the yield Y is constant. Hence we progress on the I_- branch.

1.4.2 Constant Yield

Exercise.

Summary

- Non-dimensionalisation
- Parameter spaces and bifurcation diagrams
- Hysteresis
- Harvesting

End of Lecture 1-2