

# Mathematical Epidemiology – Lecture 1

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*Epidemiology* is the subject that studies the spread of diseases in populations, and primarily the human populations.

- XIX century – William Farr's statistics
- XIX century – Pasteur's germ theory of infection
- 1880 – notice of measles' periodic behaviour by Arthur Ransome
- 1906 – discrete time epidemic model for transmission of measles by William Hamer
- 1927 – simplest mathematical model by Kermack and McKendrick.

## Mathematical epidemiology

Mathematical epidemiology is concerned with quantitative aspects of the subjects and usually consists of:

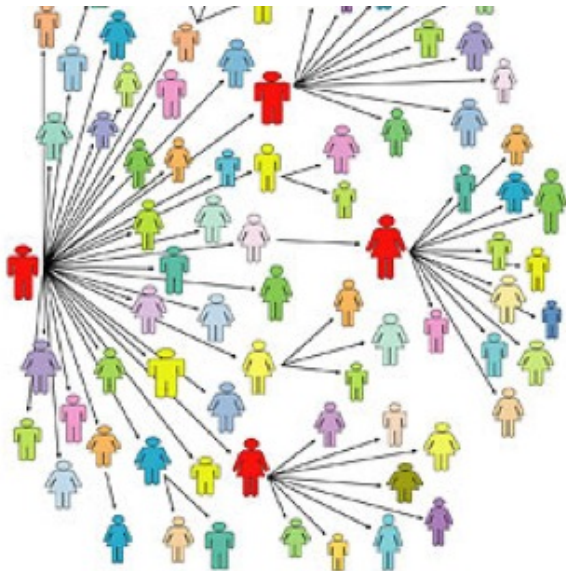
- model building,
- estimation of parameters,
- investigation of the sensitivity of the model to changes in the parameters,
- simulations.

## Mathematical modelling

The diseases which are modeled most often are the so called *infectious diseases*, that is, diseases that are contagious and can be transferred from one individual to another through *contact*.

Examples are: measles, rubella, chicken pox, mumps, HIV, hepatitis, tuberculosis, as well as the very well known influenza.

For various diseases different types of contact are needed in order for the disease to be transmitted.

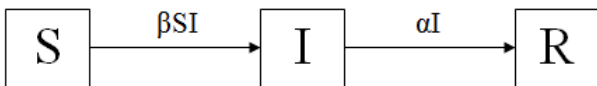


## Disease classes

When a disease spreads, the population is divided into nonintersecting classes:

- Susceptible individuals (susceptibles)
- Infective individuals (infectives)
- Removed/Recovered individuals.

An optional class is also Latent or Exposed.



Kermack and McKendrick, 1927

$$\frac{dS}{dt} = -\beta SI \quad (1)$$

$$\frac{dI}{dt} = \beta SI - \alpha I \quad (2)$$

$$\frac{dR}{dt} = \alpha I \quad (3)$$

## Parameter estimation

Estimation of the parameters in ODE models relies on one observation of how various class exit rates relate to reality.

To see how that relates to  $\alpha$ , the recovery/removal rate, let us assume that there is no inflow in the infectious class.

Then the differential equation that gives the dynamics of this class is

$$I'(t) = -\alpha I, \quad I(0) = I_0$$



## Solution

The Kermack-McKendrick model is a relatively simple epidemiological model. Quite a bit of analysis is possible to be done "manually", for instance, we can obtain an implicit solution, which is rarely possible for epidemic models.

$$I + S - \frac{\alpha}{\beta} \ln S = C \quad (4)$$

$$R = N - I - S \quad (5)$$

The Kermack-McKendrick model is equipped with initial conditions:  $S(0) = S_0$  and  $I(0) = I_0$ . Those are assumed given.

We assume also that  $\lim_{t \rightarrow \infty} I(t) = 0$  while  $S_\infty = \lim_{t \rightarrow \infty} S(t)$  gives the final number of susceptible individuals after the epidemic is over.

The implicit solution holds both for  $(S_0, I_0)$  and for  $(S_\infty, 0)$ . Thus

$$\frac{\beta}{\alpha} = \frac{\ln \frac{S_0}{S_\infty}}{S_0 + I_0 - S_\infty}$$

## The Great Plague of Eyam

The village of Eyam near Sheffield, England, suffered an outbreak of bubonic plague in 1665-1666. The source of that plague was believed to be the Great Plague of London. The community has persuaded quarantine itself. Detailed records were preserved.

The initial population of Eyam was 350. In mid-May 1666 there were 254 susceptibles and 7 infectives.

## Plague data

Date 1666	Susceptibles	Infectives
Mid-May	254	7
July 3/4	235	14.5
July 19	201	22
August 3/4	153.5	29
August 19	121	21
September 3/4	108	8
September 19	97	8
October 3/4	Unknown	Unknown
October 19	83	0

These data give the following values:  $S_0 = 254$ ,  $I_0 = 7$ ,  $S_\infty = 83$ .

From these we obtain  $\frac{\beta}{\alpha} = 0.00628$

The infective period of bubonic plague is about 11 days. Since the data is given in months, we convert days to months

$$11 \text{ days} = 0.3548387 \text{ months}, \quad \alpha = \frac{1}{0.3548387} = 2.82$$

$$\beta = 0.00628\alpha = 0.0177$$

## Maximum number of infectives

When  $I = 0$  we can find the maximal number of infected individuals

$$I_{\max} = -\frac{\alpha}{\beta} + \frac{\alpha}{\beta} \ln \frac{\alpha}{\beta} + S_0 + I_0 - \frac{\alpha}{\beta} \ln S_0$$

Then for the Eyam plague we get  $I_{\max} = 27.5$ , with the real data pointing at 29.

Models which do not include explicitly births and deaths in the population are called **epidemic models without explicit demography**.

They are useful for epidemic modeling on a short time scale.

In reality many disease models are not that simple. And therefore, finding their solutions analytically is not possible.

However, parameter estimation is still possible as long as real data is available.

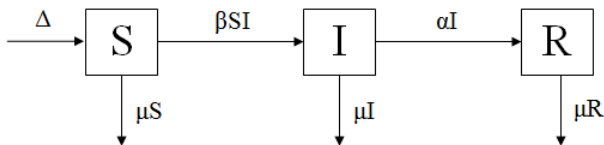
Then the estimation can be done through **least squares** method, that is optimizing parameter values in such a way that the sum of squares of differences between the model and real data

$$SS = \sum_{i=1}^n (f(x_i, \theta) - y_i)^2$$

is **minimized**.



Suppose the total population changes in time according to the simplest demographic model which describes logistic growth.



### Model with explicit demography

$$S'(t) = \Lambda - \beta IS - \mu S \quad (6)$$

$$I'(t) = \beta IS - \alpha I - \mu I \quad (7)$$

$$R'(t) = \alpha I - \mu R \quad (8)$$

We would like to know what will happen to the disease in a long run: will it die out or will it establish itself in the population and become an **endemic**?

To answer this question we have to investigate the long-term behavior of the solution. This behavior depends largely on the **equilibrium points**, that is time-independent solutions of the system, i.e. for  $S'(t) = 0$ ,  $I'(t) = 0$  and  $R'(t) = 0$ .

We get the system

$$0 = \Lambda - \beta IS - \mu S \quad (9)$$

$$0 = \beta IS - \alpha I - \mu I \quad (10)$$

$$0 = \alpha I - \mu R \quad (11)$$

From the last equation

$$R = \frac{\alpha}{\mu} I$$

From the second equation we have either  $I = 0$  or

$$S = \frac{\alpha + \mu}{\beta}$$

## Case $I = 0$

Then  $R = 0$ . From the first equation we have  $S = \frac{\Lambda}{\mu}$ . Thus we have the equilibrium solution

$$\left( \frac{\Lambda}{\mu}, 0, 0 \right)$$

This equilibrium exists for any parameter values. Notice that the number of infectives in it is zero, which means that if a solution of the ODE system approaches this equilibrium, the number of infectives  $I(t)$  will be approaching zero, that is the disease will disappear from the population. That is why it is called the **disease-free equilibrium**.

## Case $I \neq 0$

Then from the first and second equation we have

$$\Lambda = \beta IS + \mu S, \quad \text{and} \quad S = \frac{\alpha + \mu}{\beta}$$

Substituting  $S$  and solving for  $I$  we have

$$I = \frac{\beta\Lambda - \mu(\alpha + \mu)}{\beta(\alpha + \mu)}$$

Clearly,  $I > 0$  if and only if

$$\beta\Lambda > \mu(\alpha + \mu)$$

Thus only then we have the equilibrium

$$\left( \frac{\alpha + \mu}{\beta}, \frac{\beta\Lambda - \mu(\alpha + \mu)}{\beta(\alpha + \mu)}, \frac{\alpha}{\mu} \frac{\beta\Lambda - \mu(\alpha + \mu)}{\beta(\alpha + \mu)} \right)$$

In this equilibrium solution the number of infected is strictly positive. So if some of the solutions of the ODE system  $I(t)$  approaches time goes to infinity this equilibrium the number of infectives will remain strictly positive for a long time and approximately equal to  $I$ . Thus the disease remains in the population and the solution becomes an **endemic equilibrium**.

The condition for existence of an endemic equilibrium can be rewritten in the form

$$\frac{\beta\Lambda}{\mu(\alpha + \mu)} > 1$$

The expression on the left hand side is denoted by  $R_0$

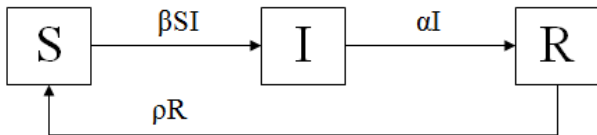
$$R_0 = \frac{\beta\Lambda}{\mu(\alpha + \mu)}$$

The parameter  $R_0$  is called the **reproduction number** of the disease.

Epidemiologically, the reproductive number of the disease tells us how many secondary cases will one infected individual produce in an entirely susceptible population.

- If  $R_0 < 1$  then there exists only the disease-free equilibrium. The equilibrium is attractive so that every solution of the ODE system approaches this equilibrium and the disease disappears from the population.
- If  $R_0 > 1$  then there are two equilibria: the disease-free equilibrium and the endemic equilibrium. Here the disease-free equilibrium is not attractive in the sense that solutions of the ODE system that start very close to it tend to go away. The endemic equilibrium is attractive so that solutions of the ODE system approach it as time goes to infinity. Thus, in this case the disease remains endemic in the population.



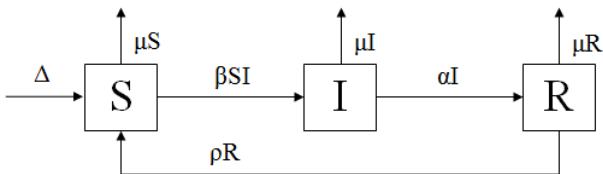


## SIRS

$$\frac{dS}{dt} = -\beta SI + \rho R \quad (12)$$

$$\frac{dI}{dt} = \beta SI - \alpha I \quad (13)$$

$$\frac{dR}{dt} = \alpha I - \rho R \quad (14)$$



## SIRS with demography

$$S'(t) = \Lambda - \beta IS + \rho R - \mu S \quad (15)$$

$$I'(t) = \beta IS - \alpha I - \mu I \quad (16)$$

$$R'(t) = \alpha I - \rho R - \mu R \quad (17)$$