

# II Southern-Summer School on Mathematical Biology

Roberto André Kraenkel, *IFT*

<http://www.ift.unesp.br/users/kraenkel>

Lecture IV

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- 1 Historical background...
  - The Plague of Athens
  - Plague
  - The 1918 Influenza pandemic

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- 2 Models
  - The SIR model

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# Epidemics: some history



For the disorder first settled in the head, ran its course from thence through the whole of the body, and even where it did not prove mortal, it still left its mark on the extremities; for it settled in the privy parts, the fingers and the toes, and many escaped with the loss of these, some too with that of their eyes. Others again were seized with an entire loss of memory on their first recovery, and did not know either themselves or their friends."

## The Plague of Athens.

- The Plague of Athens was an epidemic that raged in Athens in year 430(AC), during the Peloponnesian war .
- It was described by Thucydides: heats in the head, hard cough. discharges of bile of every kind, violent spasms, ...
- 1/3 of the population died, including *Pericles*.
- We don't know for sure what disease was responsible for the epidemic. . Epidemic typhus is currently considered the most probable cause. The etiological agent is a bacterium ( *Rickettsia prowazekii*) transmitted by lice.
- Epidemic came from Africa.

*Cito, longe, tarde.*



## Plague

- Plague is an infectious disease caused by the bacterium *Yersinia pestis*. It comes in three forms;
  - **pneumonic**, affecting the lungs and being transmissible between humans.
  - **bubonic**, infection of the lymph glands transmitted by infected flea (*Xenopsylla cheopis* (the rat flea).) The fleas get infected when they bite infected rats and mouse.
  - **septicemic**, passing through the blood, and potentially infecting many organs.
- If not treated they lead to death in a high proportion. Antibiotics are efficient .
  - If treated in a few hours!

# Stories of the Plague.

*The "Red Death" had long devastated the country. No pestilence had ever been so fatal, or so hideous. Blood was its Avator and its seal — the redness and the horror of blood. There were sharp pains, and sudden dizziness, and then profuse bleeding at the pores, with dissolution. The scarlet stains upon the body and especially upon the face of the victim, were the pest ban which shut him out from the aid and from the sympathy of his fellow-men. And the whole seizure, progress and termination of the disease, were the incidents of half an hour. (E.A. Poe, in The Masque of the Red Death).*

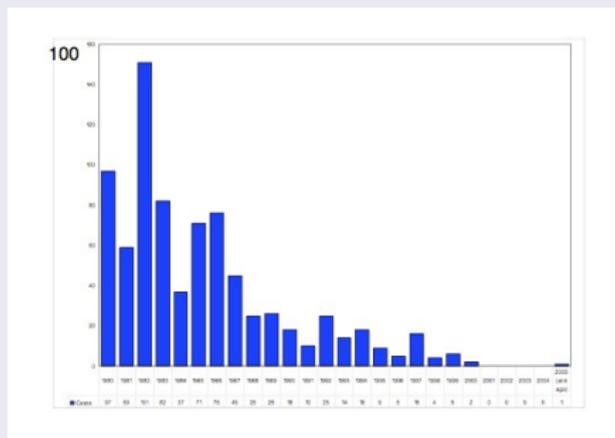
## The Plague.

- Three pandemics ;
  - *The Plague of Justinian*, (541 A.D.), Spreading from Constantinople and killing 25 % of the Mediterranean population. It did not propagate much inland, except by the borders of big rivers.
  - *The Black Death*, (1347), entering Europe at Sicily , it killed 1/3 of the European population.
  - The *third* pandemic, begun in China in 1855 and killed 12 millions in China in India.
  - Paul Louis Simond; "Ce jour-la, le 2 juin 1898, j' éprouvais une émotion inexprimable à la pensée que je venais de violer un secret qui angoissait l'humanité depuis l'apparition de la peste au monde".
- There still exist plague in our times. Mainly in arid regions of US. It usually does not lead to death due to the use of antibiotics.



# Stories of the Plague

## Plague in Brazil



**Figura :** Plague in Brazil from 1980 to 2005. Most cases occurred in rural areas of Minas Gerais and Northeastern states. Over this period, there were six death cases.

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## The 1918 Influenza Pandemic - Spanish Flu



- The *1918 influenza pandemic* was a particularly severe (*influenza A*) pandemic.
- It lasted from 1918 to 1919.
- It attained almost all regions of the world.
- Approximately 50 millions of humans beings died of it. 500 millions (1/3 of the world population) were infected.
- It is a human-to-human transmission route.
- In São Paulo, the first death occurred October 21, 1918. By the end of november it was almost extinct.

## Simple model: building blocks

- Let us begin with some simplifications
  - The populations is well-mixed.
  - It is spatially homogeneous.
- This defines implicitly time and space scales,
- We will classify individuals in three compartments:
  - $S$  susceptibles;
  - $I$  infectious ( we will use "infected" interchangeably);
  - $R$  recovered (including immune and dead)
- From population biology point of view, we have a structured population.

## Simple model: time scales

- We are however not so much interested in the dynamics of the population itself.
- What we want is to study the characteristics of the epidemic, the conditions for its occurrence, its prevalence, and if it will come to an end or not.
- Separating both dynamics of the populations and the of the epidemics is possible **if the typical time scale associated with the disease is much shorter than the time scale for changes in the population.**
- If this is the case,, we can take the population as a constant.,  $N$ .
- We will consider this case. It is valid for a large range of diseases: influenza, rubella, measles, ....

# The Kermack & McKendrick (1927) model

The *per capita* rate of change of susceptibles is proportional to the number of infected:

$$\frac{dS}{dt} = -rSI$$

where  $r$  is the infection rate.

An important point about  $r$  is that it must depend on the size of the population  $r \sim 1/N$ , or

$$r = \frac{\beta}{N} ,$$

where  $\beta$  does not depend on  $N$ . This means that the equation above ( and the ones that will follow) depends only on the proportion of infected, susceptibles and recovered in the population. This means, in particular that the dynamics of the epidemic is independent of the size of the population of, say, a city. Only absolute numbers will differ. This is valid for epidemics affecting humans, as the number of infectious contacts of each individual depends more on the social structure than on the size of the population. For plant and animal diseases, this might not be true.

# The Kermack & McKendrick (1927) model

The *per capita* rate of change of the infected is proportional to the number of susceptibles minus a factor accounting for the removal of this class.

$$\frac{dS}{dt} = -rSI$$

$$\frac{dI}{dt} = rSI - aI$$

# The Kermack & McKendrick (1927) model

The rate of change of the recovered is proportional to the number of infected .

$$\frac{dS}{dt} = rSI$$

$$\frac{dI}{dt} = rSI - aI$$

$$\frac{dR}{dt} = aI$$

# The Kermack & McKendrick (1927) model

Three equations, three variables. Perfect!:

$$\frac{dS}{dt} = -rSI$$

$$\frac{dI}{dt} = rSI - aI$$

$$\frac{dR}{dt} = aI$$

Let us study these equations

$$\frac{dS}{dt} = -rSI \quad \frac{dI}{dt} = rSI - aI \quad \frac{dR}{dt} = aI$$

- Notice that, if we add all the equations, we get just:

$$\frac{d(S + I + R)}{dt} = 0 \Rightarrow S + I + R = N$$

where  $N$  is the total population, a constant, as it should.

- But now let us be more precise about the question we want to answer:
  - Say at  $t = 0$ , we have :  $S(0) = S_0$ ,  $I(0) = I_0$  and  $R(0) = 0$ .
  - That is, we have a certain number of infected ( $I_0$ ) and of susceptibles ( $S_0$ ).
  - Given  $r$ ,  $a$ ,  $S_0$  e  $I_0$ , we want to know if **there will be an epidemic or not**. Which we characterize by  $I(t) > I_0$  for some time  $t$ .

$$\frac{dS}{dt} = -rSI \quad \frac{dI}{dt} = rSI - aI \quad \frac{dR}{dt} = aI$$

- We notice that at  $t = 0$ :

$$\left[ \frac{dI}{dt} \right]_0 = rS_0 I_0 - aI_0 = I_0(rS_0 - a)$$

- If  $S_0 < a/r$  then  $\left[ \frac{dI}{dt} \right]_0 < 0$ .
- If  $S_0 > a/r$  then  $\left[ \frac{dI}{dt} \right]_0 > 0$  (Epidemic!)
- On the other hand,  $S < S_0$  for all  $t$ , as  $dS/dt < 0$ .
- So, if  $S_0 < a/r$  then  $S(t) < a/r$  for all  $t$

$$\frac{dI}{dt} = rSI - aI = I(rS - a) < 0$$

and thus  $I(t) < I_0$  and there is no epidemic.

- If  $S_0 > a/r$  there will be an epidemic ( as  $\left[ \frac{dI}{dt} \right]_0 > 0$ ). But pay attention to the fact that  $I(t)$  does not grow forever

## In summary...

- If  $S_0 > a/r$  we have an epidemic, and if  $S_0 < a/r$ , there is none.
- Or:

$$R_0 \equiv \frac{S_0 r}{a} > 1$$

is the condition for the existence of an epidemic

- $R_0$  is called **basic reproductive ratio**.
- Even in more complex models, we usually define an analogous quantity .

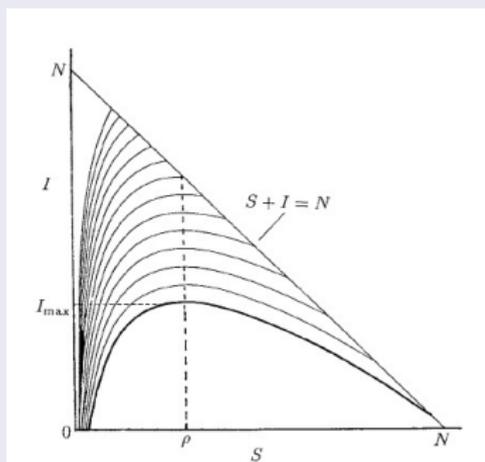
$$\frac{dS}{dt} = -rSI \quad \frac{dI}{dt} = rSI - aI \quad \frac{dR}{dt} = aI$$

Making sense of  $R_0 > 1$ .

- What does the condition  $R_0 \equiv \frac{S_0 r}{a} > 1$  tell us ?
- Step by step:
  - $1/a$  is the characteristic time of the infectious period.
    - The smaller  $a$ , the longer the infection, and an epidemic is more likely to occur. *Makes sense.*
    - We can lower this time by public health measures.
  - The larger  $S_0$  large  $R_0$ . Or, if we have more susceptibles there are more chances to occur an epidemic, as there is a larger recruitment pool. *It makes also sense.*
  - $r$  measures the transfer tax of susceptibles to infected. The higher, more infective is the disease. It will be more likely to have an epidemic. *Once more, it makes sense!*

## Graphics!

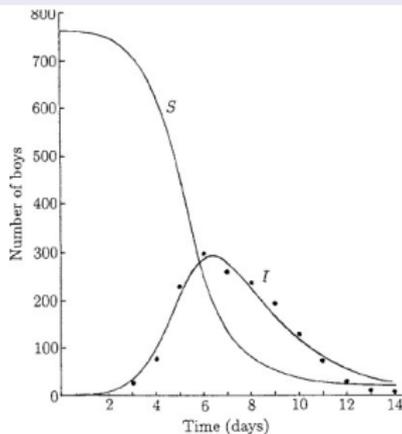
- Let us look at the dynamics in the **phase space**.
- We have **three** variables, but as  $S + I + R = N$ , we can eliminate one of them. Say,  $R$ . So we now have a two-dimensional phase space  $S$  e  $I$ .



Note that on this plot all trajectories end in  $I = 0$  when  $t \rightarrow \infty$ . The epidemic burns out.

Further, notice that  $S(t \rightarrow \infty) \neq 0$ . Not everybody gets infected.

# In praise of the SIR model



- It is simple.
- For a certain number of diseases it is good model. Mainly, for diseases with a human-to-human route.
- Take a look at the plot comparing SIR theory and data from a flu epidemic in a boarding school in UK..
- The curves were obtained by numerics.

- We can use the model as a starting point
- We can consider, for example, *new compartments*.
- And also *demographic growth*.
- We can also consider a spatial version of it.
- Let us see some examples.

## Take vital dynamics into account

- You may couple vital dynamics. You will have birth and deaths terms. Here is a SIR model with vital dynamics **but still with a constant population**:

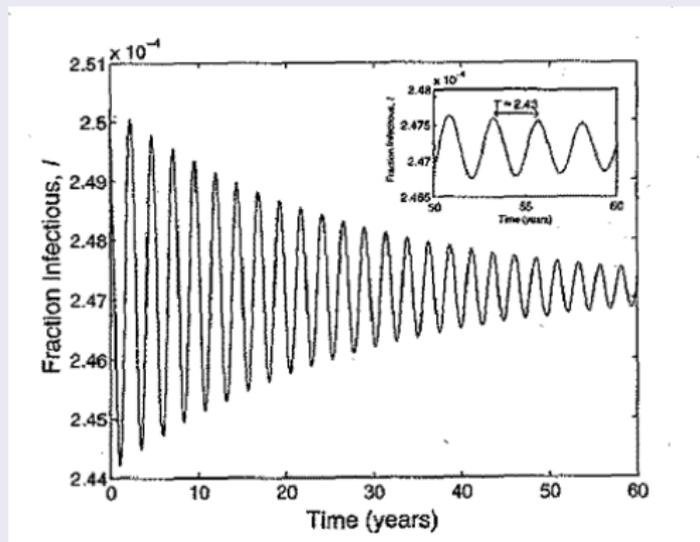
$$\frac{dS}{dt} = \mu N - rSI - \mu S$$

$$\frac{dI}{dt} = rSI - aI - \mu I$$

$$\frac{dR}{dt} = aI - \mu R$$

- This model has a new stable equilibrium point: the endemic state.
- $R_0 = \frac{\beta}{\gamma + \mu}$ .
- If  $R_0 < 1$  then the disease-free equilibrium is stable. If not, the endemic equilibrium is stable.

## SIR model with vital dynamics



**Figura :** The Sfr model's damped oscillations. The main figure shows how the fraction of infectives oscillates with decreasing amplitude as it settles toward the equilibrium. Taken from Keeling and Rohani:

## More models

- More compartments
- Disease induced mortality
- Loss of immunity
- Non-human reservoirs
- Age and social structure
- Vectorial transmission
- Control measures
- Temporal variability
- Spatial models
- Structure of contacts

# Bibliography

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