Modélisation des processus et systèmes prévisionnels
Lecture 3

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Introduction

Population biology of infectious diseases

- *Microparasitic* diseases are caused by viruses and bacteria and are transmitted directly from human to human. Examples:
  - Viruses: influenza, measles, rubella, chicken pox.
  - Bacteria: tuberculosis, meningitis, gonorrhea.
- *Macroparasitic* diseases are caused by worms or insects and are transmitted from human to agents and then to human. Examples:
  - malaria (mosquitos), black plague (rats), rabies (foxes).
- An *epidemic* is a sudden outbreak of a disease.
- A disease is *endemic* if it is always present in the population.

Introduction

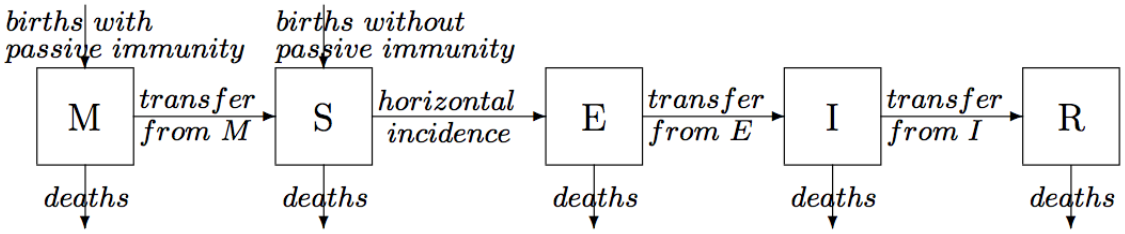
Modelling epidemics

Comportmental models are widely used to model the evolution of a disease. They consider differents population classes:

- The *passively immune* population $M(t)$ composed of infants with passive immunity.
- The *susceptible* population $S(t)$ composed of individuals who are not yet infected.
- The *exposed* population $E(t)$ composed of infected individuals that are not yet infectious.
- The *infective* population $I(t)$ composed of individuals who are infected at time t and are able to spread the disease by contact with susceptibles.
- The *removed* population $R(t)$ composed of individuals who have been infected and then removed from the possibility of being infected again or spreading the disease (either immunized or separated from the rest or dead)

Introduction

Modelling epidemics



Acronyms for epidemiology models are based on the flow patterns between the compartments such as MSEIR, SEIR, SIR, SIRS, SIS, etc. Depending on the model, the class R can be composed of all "removed" individuals or only (temporally) immune individuals.

SIR Epidemics

Model equations

Let us assume that (1) the total population N is constant, (2) the gain in the infective class is at a rate proportional to the number of infectives and susceptibles (rSI, where $r > 0$), (3) the rate of removal of infectives to the removed class is proportional to the number of infectives (aI, where $a > 0$) and (4) the incubation period is short enough to be negligible.
The model equations then read:

$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= -rSI, \\ \frac{\mathrm{d}I}{\mathrm{d}t} &= rSI - aI, \\ \frac{\mathrm{d}R}{\mathrm{d}t} &= aI, \end{aligned}$$

where $r > 0$ is the infection rate and $a > 0$ is the removal rate of infectives ($1/a$ is the average infectious period).

SIR Epidemics

Qualitative analysis

Since $N = S + I + R$ is constant, we can drop the 3rd equation and only consider the equations for S and I:

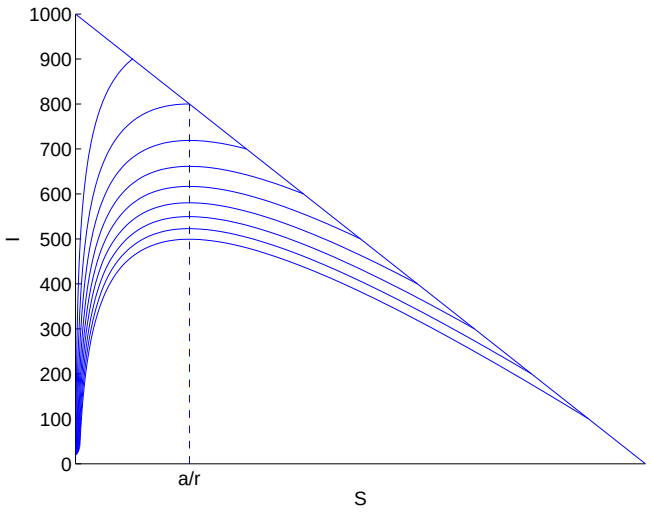
$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= -rSI, \\ \frac{\mathrm{d}I}{\mathrm{d}t} &= rSI - aI. \end{aligned}$$

1. If $S_0 < a/r$, then $I(t)$ is a decreasing function which tends to 0, and $S(t)$ is also decreasing and tends to a constant level greater than 0. Note that in this case: $S(t) \leq S_0 < a/r$.
2. If $S_0 > a/r$, S(t) is also decreasing and tends to a constant level greater than 0, but $I(t)$ will first increase in a time period $[0, T_0]$ and then tend to 0 after T_0.

SIR Epidemics

Qualitative analysis

We can thus define a dimensionless quantity $R_0 = \frac{rS_0}{a}$, which is called the *reproduction rate*. If we introduce a small number of infectives I_0 in a susceptible population, then an epidemic will occur if $R_0 > 1$, *i.e.* if $S_0 > a/r$.



Some estimated values of the reproduction rate R_0

Infectious Disease	**Host**	**R_0**
Tuberculosis	Cattle	2.6
Influenza	Humans	3-4
Foot-and-Mouth Disease	Livestock farms (UK)	3.5-4.5
Smallpox	Humans	3.5-6
Rubella	Humans (UK)	6-7
Chickenpox	Humans (UK)	10-12
Measles	Humans (UK)	16-18
Whooping Cough	Humans (UK)	16-18

from *Keeling M.J. and Rohani P. (2007)*

SIR Epidemics

How to prevent an epidemic?

Reduce the reproduction rate $R_0 = \frac{rS_0}{a}$. This can be achieved through:

- Immunization: reduce S_0, transfer S to R.
- Isolation: isolate the known infectives, reduce r.
- Medical improvement: increase a.

SIR Epidemics

Analytical results

We can rewrite the model equations as follows

$$\frac{\mathrm{d}I/\,\mathrm{d}t}{\mathrm{d}S/\,\mathrm{d}t} = \frac{\mathrm{d}I}{\mathrm{d}S} = \frac{rSI - aI}{-rSI} = -1 + \frac{a}{rS},$$
$$S(0) = S_0, \quad I(0) = I_0, \quad R(0) = 0,$$

which give us:

$$I(t) = cst - S(t) + \frac{a}{r}\log S(t)$$

and since

$$I(0) = cst - S_0 + \frac{a}{r}\log S_0 = N - S_0,$$

we finally have:

$$I(t) = N - S(t) + \frac{a}{r}\log(S(t)/S_0).$$

SIR Epidemics

Analytical results

The severity of the epidemic can be estimated by computing the the maximum of $I(t)$, which occurs at $S = a/r$:

$$I_{max} = N - \frac{a}{r} + \frac{a}{r}\log(\frac{a}{rS_0}).$$

For any initial values I_0 and $S_0 > \frac{a}{r}$, the phase trajectory starts with $S > \frac{a}{r}$ and we see that I increases from I_0 until it reaches I_{max} and hence an epidemic ensues. It may not necessarily be a severe epidemic as is the case if I_0 is close to I_{max}.

SIR Epidemics

Analytical results

Since $\lim_{t\to\infty} I(t) = 0$, we can see that $S_\infty = \lim_{t\to\infty} S(t)$, the population that never caught the disease, is the solution of the following equation:

$$S_\infty - \frac{a}{r}\log(S_\infty/S_0) = N.$$

The total number of susceptibles who catch the disease is thus:

$$I_{total} = I_0 + S_0 - S_\infty.$$

Since $I(t) \to 0$ and $S(t) \to S_\infty$, the disease dies out from a lack of infectives and not from a lack of susceptibles.

SIR Epidemics

Analytical results

In practice, it is not always easy to estimate dI/dt as it represents the number of new infectives per unit time. It is often better to know the number removed per unit time, *i.e.* dR/dt.
We can first express S in terms of R since

$$\frac{\mathrm{d}S}{\mathrm{d}R} = -\frac{r}{a}S \equiv -\frac{S}{\rho},$$

where $\rho = a/r$. Hence $S = S_0 e^{-R/\rho}$.
We then have the following equation for R:

$$\begin{aligned}\frac{\mathrm{d}R}{\mathrm{d}t} &= aI \\ &= a(N - R - S) \\ &= a(N - R - S_0 e^{-R/\rho})\end{aligned}$$

This equation can be solved numerically provided that we know a, r, S_0 and N.

SIR Epidemics

Analytical results

In practice, we do not often know all these parameters and a best fit procedure must then be carried on. If we can assume that the epidemic is not large, *i.e.* if R/ρ is small, we can approximate the exponential by its Taylor series expansion and obtain:

$$\begin{aligned}\frac{\mathrm{d}R}{\mathrm{d}t} &\approx a[N - R - S_0(1 - R/\rho - R^2/2\rho^2)] \\ &= a\left[N - S_0 + \left(\frac{S_0}{\rho} - 1\right)R - \frac{S_0 R^2}{2\rho^2}\right]\end{aligned}$$

That equation can then be solved analytically and the solution reads:

$$R(t) = \frac{\rho^2}{S_0}\left[\left(\frac{S_0}{\rho} - 1\right) + \alpha \tanh\left(\frac{\alpha a t}{2} - \phi\right)\right]$$

$$\alpha = \left[\left(\frac{S_0}{\rho} - 1\right)^2 + \frac{2S_0(N - S_0)}{\rho^2}\right]^{1/2}, \quad \phi = \tanh^{-1}\frac{1}{\alpha}\left(\frac{S_0}{\rho} - 1\right)$$

SIR Epidemics

Analytical results

The removal rate is then given by

$$\frac{\mathrm{d}R}{\mathrm{d}t} = \frac{a\alpha^2\rho^2}{2S_0}\mathrm{sech}^2\left(\frac{\alpha a t}{2} - \phi\right),$$

which involves only 3 parameters, namely, $a\alpha^2\rho^2/(2S_0)$; αa and ϕ that can be estimated by fitting the above function to the public health records.

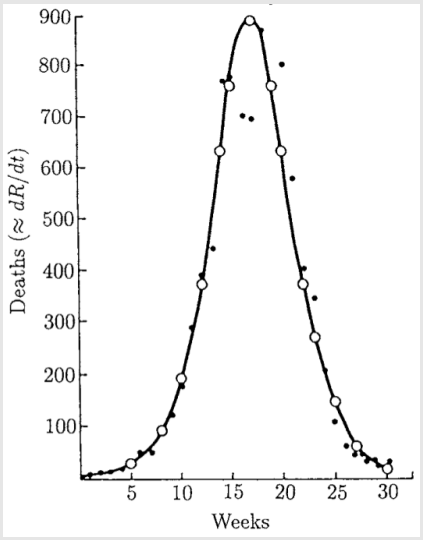
Model application

Example 1: Bombay Plague Epidemic 1905-1906

This epidemic lasted for almost a year. Since most of the victims who got the disease died, the number of removed per week, dR/dt, was approximately equal to the number of deaths per week.

Since that epidemic was not severe (relative to the population size), it was possible to fit the "sech" solution to the actual data and obtain:

$$\frac{\mathrm{d}R}{\mathrm{d}t} = 890\ \mathrm{sech}^2(0.2t - 3.4).$$

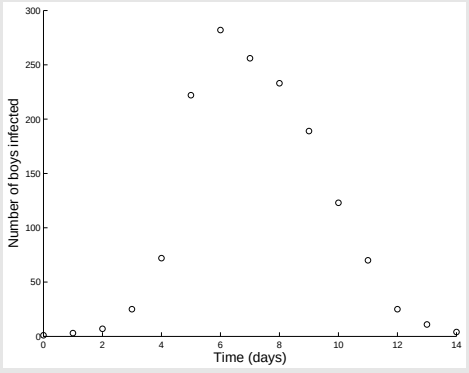


Model application

Example 2: Influenza Epidemic in an English Boarding School 1978

A flu occured in a boys boarding school with a total of 763 boys. Of these, 512 were confined to bed during the epidemic, which lasted from 22nd January to 4th February 1978. It seems that one infected initiated the epidemic.

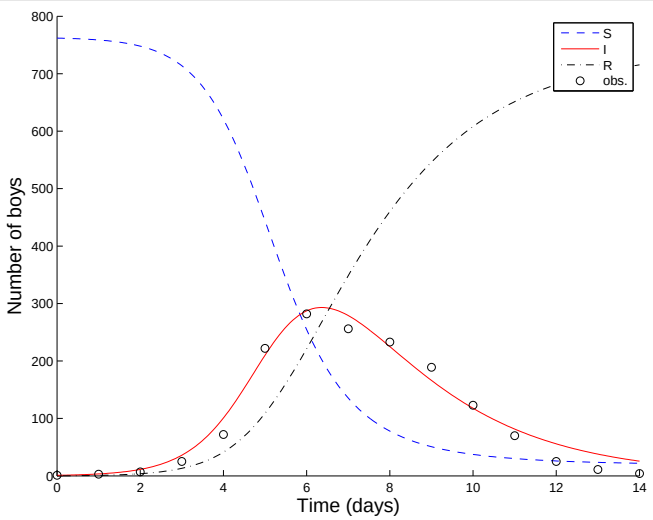
For this example, the disease is of short duration, thus birth and death do not need to be considered, and the population is confined to one location, so no spatial effects. However, the epidemic was severe (relative to the population size) and the full system has to be used. When a boy was infected, he was put to bed and so we have $I(t)$ from the data.



SIR Epidemics

Example 2: Model results

Starting with 1 infective individual and 762 susceptibles (*i.e.* $S_0 = 762$, $I_0 = 1$ and $R_0 = 0$) and taking $r = 2.18 \times 10^{-3}/(\text{day}\times\text{ind})$ and $a = 0.44$ /day, we obtain:



SIR Epidemics

Example 2: Inverse modeling with `fminsearch`

To find the model parameters corresponding to experimental data or observations, we need to minimize the difference between model results and observations for a range of parameter values. That can be done with the Matlab function `fminsearch`, which finds the minimum of a scalar function of several variables, starting at an initial estimate.

The syntax is

```
[x,fval] = fminsearch(fun,x0)
```

where `x` is the local minimizer of the function described by `fun`, `x0` is the starting value for `x` and `fval` is the function value at `x`.

SIR Endemics

Under what conditions is a disease endemic?

For an endemic disease, we are interested in long-term behaviour and can no longer neglect birth and disease-unrelated death. It is also no longer sensible to lump together immune and dead people into the same (removed) class. R should now be considered as the immune class. In order to keep the total population constant, we will assume that the birth rate b is equal to the death rate d. Also, it is assumed that all births enter the susceptible population. The model equations then read:

$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= -rSI + bN - dS, \\ \frac{\mathrm{d}I}{\mathrm{d}t} &= rSI - aI - dI, \\ \frac{\mathrm{d}R}{\mathrm{d}t} &= aI - dR, \end{aligned}$$

where we will assume that $d = b$ so that $N = S + I + R$ is constant.

SIR Endemics

Reproduction rate and steady states

We see that initially, I will increase if $rS_0 > a + b$. If we assume that the entire population is susceptible to the disease, we can define the reproduction rate R_0 as

$$R_0 = \frac{rN}{a+b}.$$

Different behaviors are expected for R_0 larger or smaller than 1.

The model equations also have 2 steady states (S^*, I^*, R^*):

- disease-free: $(S^*, I^*, R^*) = (N, 0, 0)$
- endemic disease: $(S^*, I^*, R^*) = (\frac{a+b}{r} = \frac{N}{R_0}, \frac{b(R_0-1)}{r}, N - \frac{N}{R_0} - \frac{b(R_0-1)}{r})$

SIR Endemics

Stability analysis

Around a steady state (S^*, I^*, R^*), we can approximate the model equations as

$$\frac{\mathrm{d}}{\mathrm{d}t}\begin{pmatrix} S \\ I \\ R \end{pmatrix} = \begin{pmatrix} f_S(S,I,R) \\ f_I(S,I,R) \\ f_R(S,I,R) \end{pmatrix} \approx \begin{pmatrix} f_S(S^*,I^*,R^*) \\ f_I(S^*,I^*,R^*) \\ f_R(S^*,I^*,R^*) \end{pmatrix} + J(S^*,I^*,R^*)\begin{pmatrix} f_S - f_S^* \\ f_I - f_I^* \\ f_R - f_R^* \end{pmatrix}$$

where

$$J(S,I,R) = \begin{pmatrix} \frac{\partial f_S}{\partial S} & \frac{\partial f_S}{\partial I} & \frac{\partial f_S}{\partial R} \\ \frac{\partial f_I}{\partial S} & \frac{\partial f_I}{\partial I} & \frac{\partial f_I}{\partial R} \\ \frac{\partial f_R}{\partial S} & \frac{\partial f_R}{\partial I} & \frac{\partial f_R}{\partial R} \end{pmatrix} = \begin{pmatrix} -rI - b & -rS & 0 \\ rI & rS - (a+b) & 0 \\ 0 & a & b \end{pmatrix}$$

is the Jacobian of the system right-hand side. A steady state is stable if all the eigenvalues of the Jacobian, computed at the steady state, have a negative real part. These eigenvalues are denoted λ and can be obtained by computing

$$\begin{aligned} \det(J^* - \lambda\mathbb{I}) &= (-b-\lambda)\Big[(-rI - b - \lambda)(rS - (a+b) - \lambda) + r^2 SI\Big] \\ &= 0, \end{aligned}$$

where $J^* = J(S^*, I^*, R^*)$.

SIR Endemics

Stability of the disease-free steady state $(S^*, I^*, R^*) = (N, 0, 0)$

We easily see that one eigenvalue is always $\lambda_1 = -b$, which is always negative. The remaining 2 eigenvalues are the solutions of

$$(-b-\lambda)(rN - (a+b) - \lambda) = 0$$

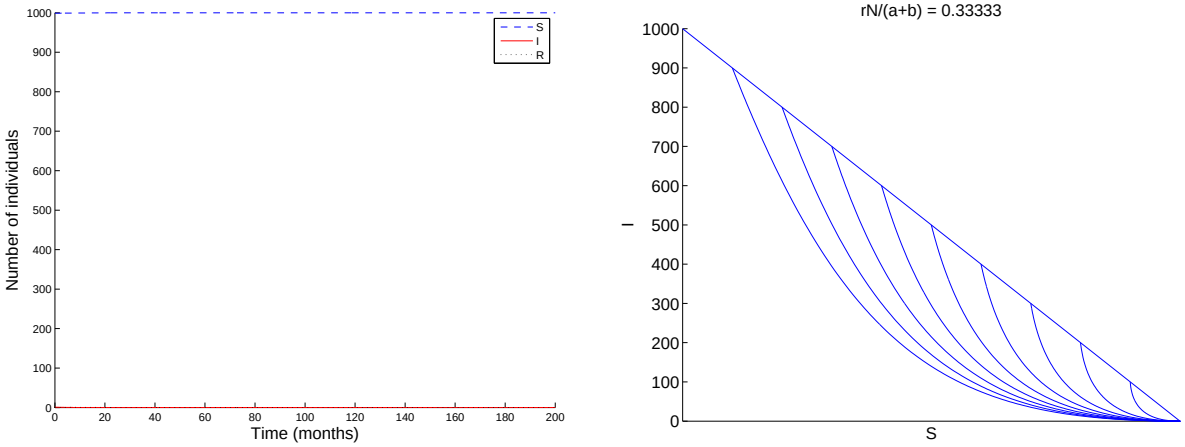
and hence

$$\begin{aligned} \lambda_2 &= -b < 0, \\ \lambda_3 &= rN - (a+b) = (a+b)(R_0 - 1). \end{aligned}$$

The eignevalue λ_3 is thus negative only if $R_0 < 1$, which confirms that the system will be converge towards a disease-free equilibrium when $R_0 < 1$.

SIR Endemics

Example of convergence towards a disease-free equilibrium



When $R_0 < 1$, all solution paths approach the disease-free equilibrium given by $S = N$.

SIR Endemics

Stability of the endemic steady state $(S^*, I^*, R^*) = (\frac{N}{R_0}, \frac{b(R_0-1)}{r}, N - \frac{N}{R_0} - \frac{b(R_0-1)}{r})$

We still have the eigenvalue $\lambda_1 = -b$, which is always negative. The remaining 2 eigenvalues are the solutions of

$$\lambda^2 + bR_0\lambda + rbN\frac{R_0 - 1}{R_0} = 0$$

and hence

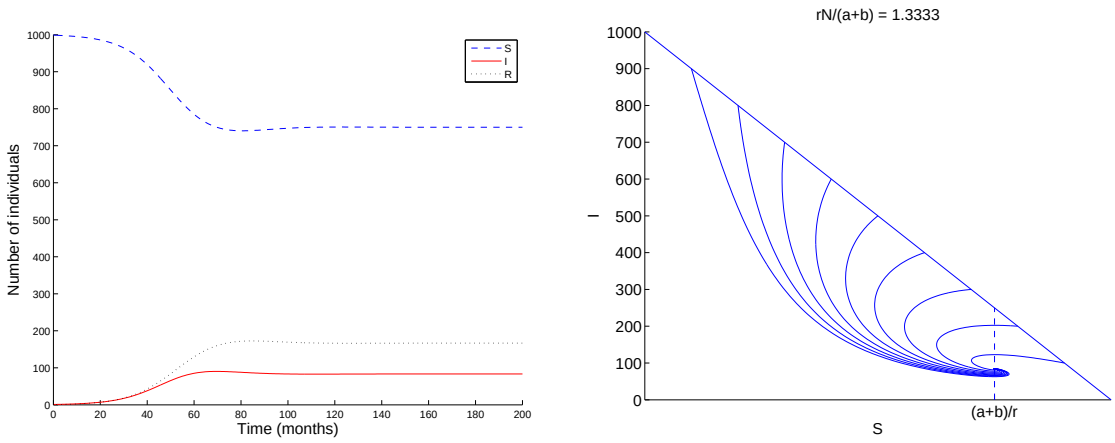
$$\lambda_{2,3} = \frac{-bR_0}{2} \pm \frac{1}{2}\sqrt{(bR_0)^2 - 4rbN\frac{R_0 - 1}{R_0}}$$
$$\approx \frac{-bR_0}{2} \pm i\sqrt{rbN\frac{R_0 - 1}{R_0}},$$

since $(bR_0)^2$ is usually negligible in front of the other term. The eigenvalues $\lambda_{2,3}$ have thus a negative real part if $R_0 \geq 1$, which confirms that the system will be converge towards an endemic-disease equilibrium when $R_0 \geq 1$.

The fact that $\lambda_{2,3}$ are complex conjugates means that the endemic equilibrium is approached via a damped oscillatory dynamics. The period of these oscillations is $T = 2\pi(rbN\frac{R_0-1}{R_0})^{-1/2}$.

SIR Endemics

Example of convergence towards an equilibrium where the disease is endemic

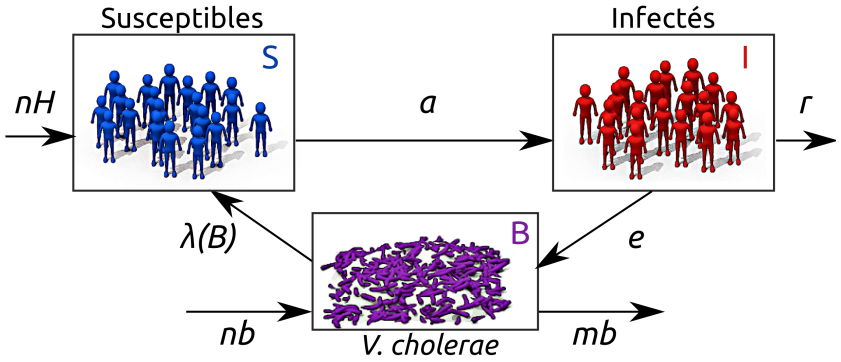


Here $R_0 = \frac{rN}{a+b} > 1$ and all solution paths converge towards the endemic steady state given by $S_e = \frac{a+b}{r}$ and $I_e = \frac{b(R_0-1)}{r}$.

A simple model of the cholera disease transmission

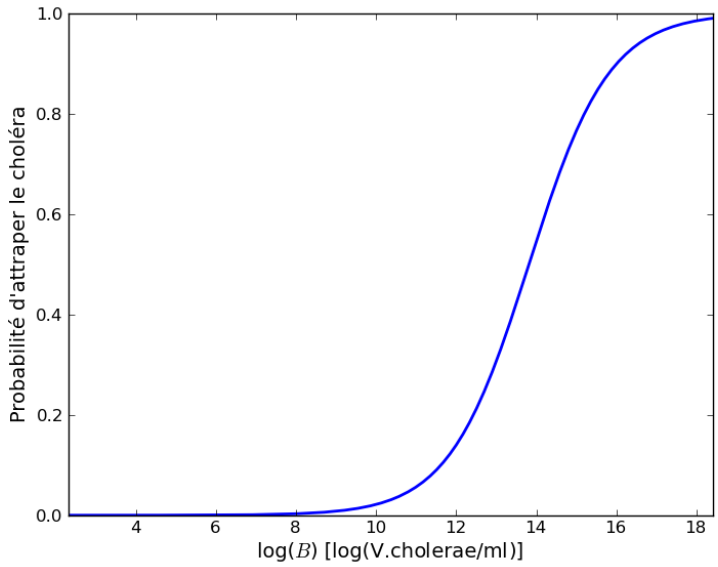
$$\frac{dS}{dt} = n(H - S) - a\lambda(B)S,$$
$$\frac{dI}{dt} = a\lambda(B)S - rI,$$
$$\frac{dB}{dt} = B(n_b - m_b) + eI,$$

where H is the total human population and B represents the population of bacteries. We have assumed that the birth rate is equal to the death rate, and that infected individuals only die from the disease at a rate r.



The probability of catching the disease depends on the concentration of *V. cholerae* in the water

$$\lambda(B) = \frac{B}{K + B}$$



Endemic and epidemic dynamics of cholera

It can be shown that the reproduction number has the following expression:

$$R_0 = \frac{aeS_0}{rK(m_b - n_b)},$$

which indicates that the arrival of infectives into a community with S_0 larger then a critical value S_c will trigger an outbreak. The critical value reads:

$$S_c = \frac{rK(m_b - n_b)}{ae}.$$

The outbreak will stabilize into an endemic equilibrium if the birth rate n and the initial number of infectives are large enough.

Example

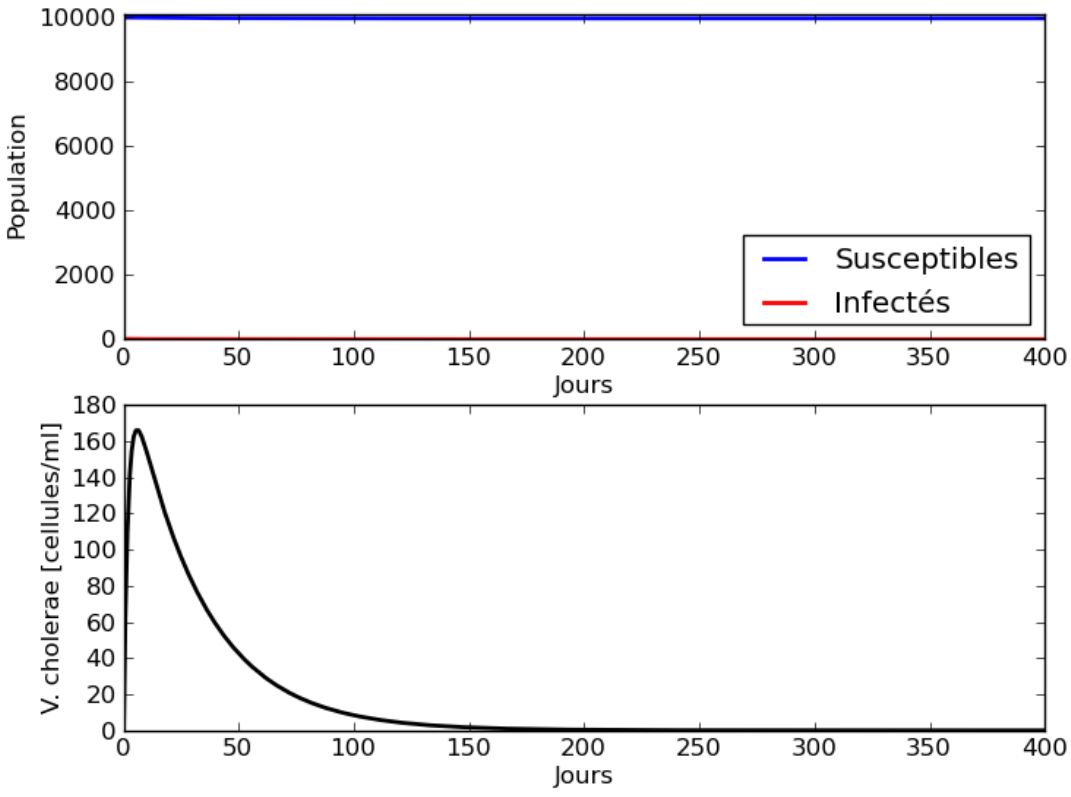
Let us consider 3 different communities with the following parameters values:

	Community 1	Community 2	Community 3
H	10000	10000	10000
n	0.0001	0.0001	0.003
a	0.5	1	1
K	10^6	10^6	10^6
r	0.2	0.2	0.2
$n_b - m_b$	-0.33	-0.33	-0.33
e	10	10	10
R_0	0.76	1.52	1.52
S_c	13200	6600	6600

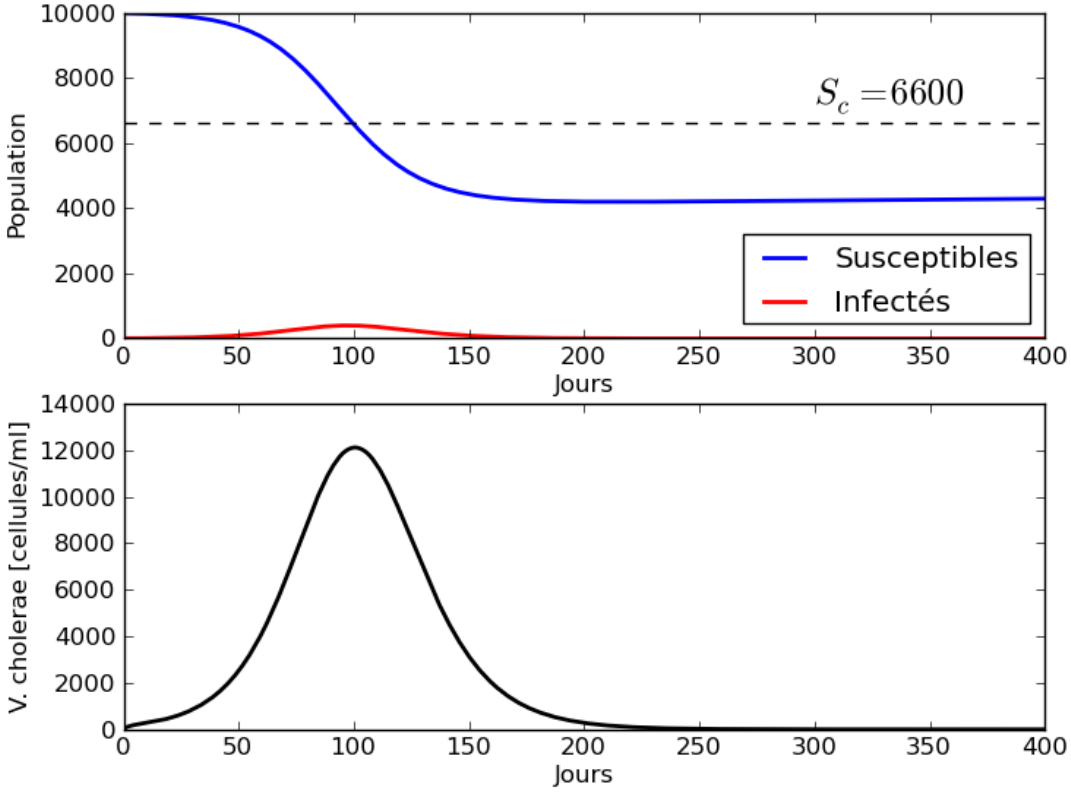
and the same initial conditions:

$$S(0) = H, \quad I(0) = 1, \quad B(0) = 0.$$

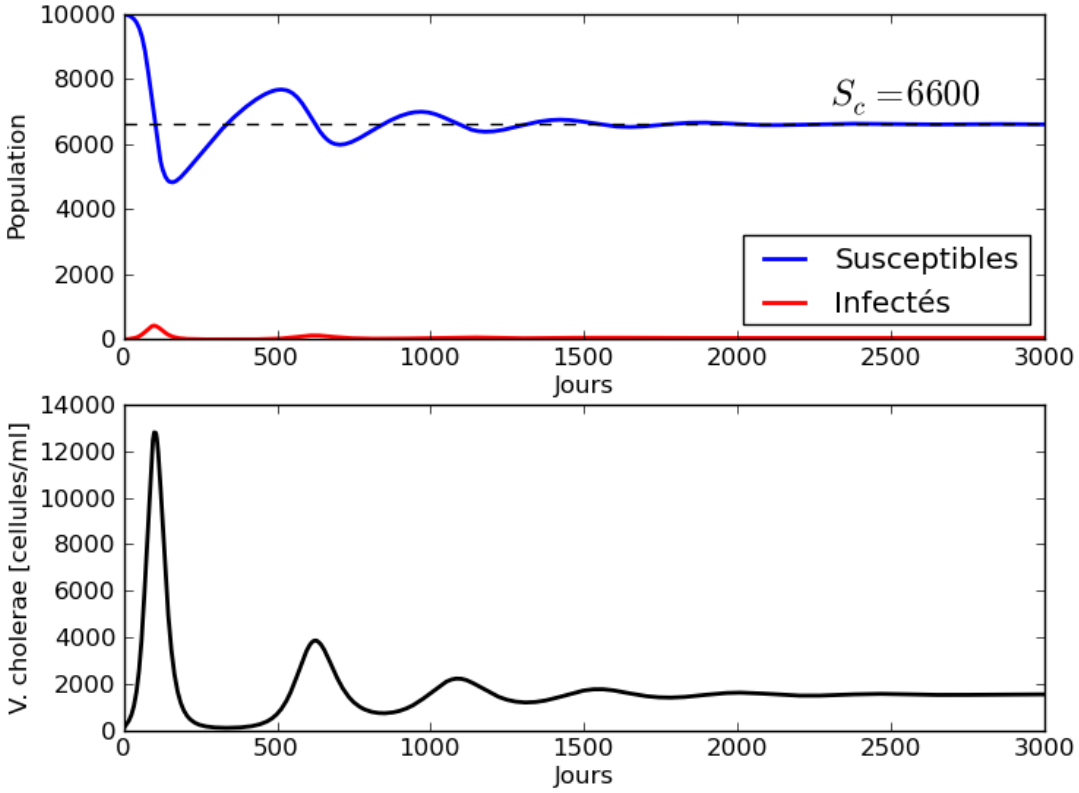
Community 1: cholera-free population



Community 2: Epidemic cholera



Community 3: Endemic cholera



References

For those interested to learn more

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- Wolter, J. (2011) "Modélisation épidémiologique spatio-temporelle sur réseaux: Application au choléra à Haïti". *Mémoire de fin d'études*, UCL/AGRO (copy available on icampus).

Practicals

to do this week...

- Implement the models we have used today and try to produce similar results.
- Do the "Ecosystem collapse" homework.