SBIC02BL - compléments de mathématiques pour la bioinformatique

Nom et prénom : Yorgo EL MOUBAYED
Numéro étudiant : e16027493
Email : yorgo.EL-MOUBAYED@etu.univ-amu.fr

This project:

- Describes the SIRC (susceptible-infectious-recovered-carrier) epidemiological model.
- Integrates the model equations in python code.
- Describes the system's parameters and their influences by solving the system of ordinary differential equations for different initial conditions and different parameter values.

1. Introduction

Models of disease dynamics are quite diverse, ranging from caricatures to very detailed simulations. These models are expressed mathematically as difference equations (discrete time) or differential equations (continuous time). In the simplest form, these models do not take into consideration either individual heterogeneity or the local nature of transmission events. Increased realism is achieved by structuring the population according to age, risk behavior, sex, susceptibility, or other category associated with different risk of getting or transmitting the disease. When other species are involved in the transmission process (non-human hosts and vectors), these are also considered as compartments that may be sub-divided as well according to covariates associated with the risk of acquiring or transmitting the disease. In this context, epidemiological models take the form of multi-compartmental models where each compartment is a well-mixed homogeneous population. The model describes the transition of the individuals in this population through a sequence of disease-related stages.

A first fundamental mathematical model for epidemic diseases was formulated by *Kermack & McKendrick* in 1927. This model applies for epidemics that have a relatively short duration and take the form of an outbreak of a disease that infects a portion of the population in a region before it disappears. In this model, the population is classified into three groups:

- The individuals who are uninfected and **susceptible (S)** of catching the disease.
- The individuals who are **infected (I)** by the concerned pathogen.
- The **recovered (R)** individuals who have acquired a permanent immunity to the disease.

2. Infections with a carrier state

2.1. Model description

Although SIR-type paradigms capture mainly the epidemiological characteristics of many infectious diseases (such as chicken-pox or measles), other infections (such as tuberculosis and hepatitis B) may have more elaborate schemes. To incorporate such complexities into the model, *Keeling & Rohani* proposed a SIRC model in 2008, in which a proportion of infected individuals may become chronic carriers but can transmit infections at a low rate for many years. Considering features of these infections, individuals of a given population can be in one of four states: susceptible individuals (S) can be infected both by acutely infectious individuals (I) and by carriers (C). It is assumed that individuals infected by carriers and those infected by acutely infectious individuals are indistinguishable. After a given period, an acutely infectious individual either recovers completely (R) or moves into the carrier state. The compartmental diagram is schematically depicted in **figure 1**.

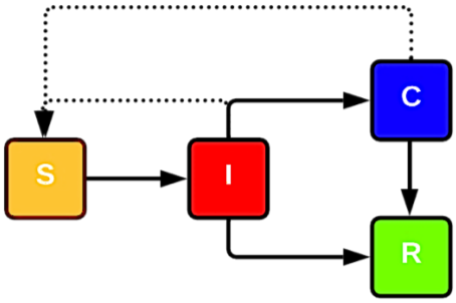

Figure 1 - compartmental diagram of the SIRC model. ***Solid lines*** represent the transfer diagram of the model: **susceptible** individuals can be **infectious**, infectious individuals can be **carriers** or **recover**, carriers can recover. ***Dashed lines*** represent that susceptible individuals can be infected both by acutely infectious individuals and by carriers.

The model is derived under three main assumptions:

- A closed population without demography (no births, no deaths, no migration).
- Spatial homogeneity.
- Disease transmission by contact between susceptible and infected individuals.

2.2. Model equations

Based on the compartmental diagram (**figure 1**) and the above assumptions, the model is represented by the following system of ordinary differential equations that describe the rate at which the proportions of sub-populations change over time:

$$\mathbf{1.}\quad \frac{dS}{dt} = (-\beta I - \varepsilon\beta C)\, S$$

$$\mathbf{2.}\quad \frac{dI}{dt} = (\beta I + \varepsilon\beta C)\, S - \gamma I$$

$$\mathbf{3.}\quad \frac{dR}{dt} = (1 - \rho)\,\gamma I + \tau C$$

$$\mathbf{4.}\quad \frac{dC}{dt} = \rho\gamma I - \tau C$$

In these equations:

- **S**, **I**, **R** and **C** denote respectively the number of susceptibles, acutely infectious, recovered individuals with permanent immunity to the disease and carriers at time **t**. The total population N = S + I + R + C is constant by assumption since we have:
$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} + \frac{dC}{dt} = 0$$
- **β** denotes the rate at which susceptible individuals become infectious by contact.
- **γ** denotes the recovery rate.
- **ε** denotes the reduced transmission rate from chronic carriers compared with acutely infectious individuals.
- **τ** denotes the rate at which individuals leave the carrier state and enter the recovered state.
- **ρ** denotes the proportion of acute infections that become carriers while the remaining **(1 - ρ)** denotes the rate at which infectious individuals recovers.

2.3. Basic reproductive ratio R_0

It is important to understand when an epidemic can occur and hence to calculate the basic reproductive ratio, R_0. It describes the ratio between the frequency of contacts to the frequency of recovery. For infections with a carrier state, R_0 has two components: one comes from acutely infectious individuals, the other comes from infections caused while in the carrier state and must take into account the fraction of infected becoming carriers:

$$R_0 = \frac{\beta}{\gamma} + \frac{\rho\gamma}{\gamma}\frac{\varepsilon\beta}{\tau},$$

Where $\frac{\rho\gamma}{\gamma}$ accounts for the infectious individuals that go on to become carriers. Therefore, the fact that infected individuals can enter an infectious carrier state rather than simply recovering decreases the value of R_0. The most important uses of R_0 are determining if an emerging infectious disease can spread in a population and determining what proportion of the population should be immunized through vaccination to eradicate a disease. When $R_0 > 1$ the infection will be able to start spreading in a population, but not if $R_0 < 1$. $R_0 = 1$ is a threshold between epidemic/no epidemic. Generally, the larger the value of R_0, the harder it is to control the epidemic. Furthermore, an epidemic will occur if the proportion of infectious individuals increases with time: $\frac{dI}{dt} > 0$.

2.4. Python code model integration

The model ODEs were integrated in Python code using the 'odeint' library from 'scipy'. The parameter space dimension is five. A GitLab repository (https://gitlab.com/Yorgomoubayed/sirc-model) contains:

- The source code of the SIRC model Python implementation.
- Detailed information setting up and running custom simulations are available on GitLab. The parameters must be indicated when creating a new instance of the model.

2.4.1. Changing model parameters

Variables and parameters and represented according to the source code.

Dynamics parameters

- β = contact rate * transmission probability
- γ = 1 / infectious period
- ε = reduced transmission rate
- τ = 1 / length of time in carrier state
- ρ = acute infections proportion

These are impacted by,

- 'contact rate' (number of contacts per day).
- 'transmission probability' (transmission probability).
- 'infectious period' (infectious period).

- ‘reduced transmission rate’ (chronic carriers compared to acute infections).
- ‘acute infections proportion’ (acute infections that become carriers).
- ‘length of time in carrier state’ (length of time in carrier state).

Initial values of sub-populations

- ‘S’ (susceptible hosts).
- ‘I’ (infectious hosts).
- ‘R’ (recovered hosts).
- ‘C’ (carrier hosts).

- ‘N’ = S + I + R + C (total population).

Initial state values for the differential equations: $S_0 = \frac{S}{N}$, $I_0 = \frac{I}{N}$, $R_0 = \frac{R}{N}$, $C_0 = \frac{C}{N}$.

2.4.2. Model simulations

A. Let us consider an epidemic outbreak in a population where, at the initial time, only a few individuals are infected (20). The initial conditions are as in **figure 2**.

In **figure 2**, the number of susceptible (**blue**) continually decreases as more people are exposed, but the susceptible population never recovers because once a person has recovered, they can no longer be susceptible in this model. Meanwhile the infectious (**red**) reach a peak when the at the time point where the susceptibles drop to the lowest. The number of recovered individuals (**green**) spikes very soon after the number of infectious hosts spikes. The carriers (**black**) have a chronic form of the disease. They are less infectious than those with the acute form. They heal more slowly, so they stay in the carrier state for a long time.

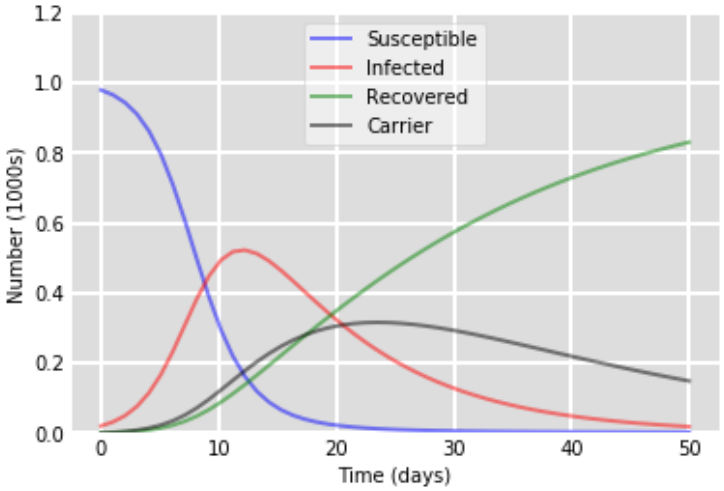

Figure 2 - disease dynamics characterized by parameters β=7*0.08, γ=10, ε=0.09, τ=1/20, ρ=0.67 in a population of N=1000 on a course of 50 days. The model is started with 980 susceptibles, 20 infectious, 0 carriers and 0 recovered on day 0.

B. Let us consider an epidemic outbreak in a population where, at the initial time, only a few individuals are infected and the contact rate β increases. The initial conditions are as in **figure 3**. When β increases, we expect a decrease in the proportion of susceptibles and an increase in the proportion of infectious individuals over time. This is supported by the model's ODEs:

In equation (1), an increase in β induces a decrease in $(-\beta I - \varepsilon\beta C)\, S$ then in $\frac{dS}{dt}$.

In equation (2), an increase in β induces an increase in $(\beta I + \varepsilon\beta C)\, S$ then in $\frac{dI}{dt}$.

As expected, in **figure 3**, the number of susceptible (**blue**) rapidly decreases as more people are exposed. There are the infectious (**red**), which rapidly peak at the time point where the susceptibles drop to the lowest. The number of recovered individuals (**green**) spikes very soon after the number of infectious hosts spikes.

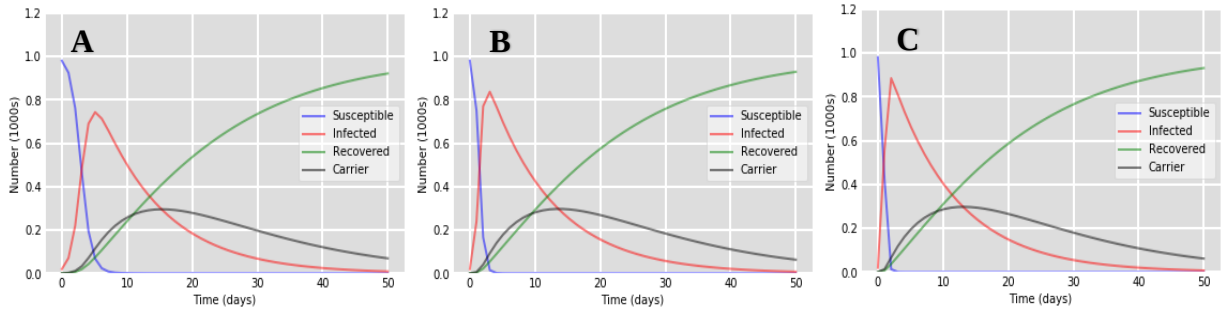

Figure 3 - disease dynamics characterized by parameters:
(A) β=7*0.2, γ=10, ε=0.09, τ=1/20, ρ=0.67
(B) β=7*0.4, γ=10, ε=0.09, τ=1/20, ρ=0.67
(C) β=7*0.6, γ=10, ε=0.09, τ=1/20, ρ=0.67
In a population of N=1000 on a course of 50 days. The model is started with 980 susceptibles, 20 infectious, 0 carriers and 0 recovered on day 0.

C. Let us consider an epidemic outbreak in a population where, at the initial time, only a few individuals are infected and the infectious period increases, with the recovery rate γ = 1/infectious period. The initial conditions are as in **figure 4**. When the infectious period increases, it is expected that the proportion of infectious individuals would dominate over time. It would take more time for the population to recover from the disease or may not recover at all. This is supported by:

In equation (2), a decrease in γ induces a decrease in γI, then a slight decrease in $\frac{dI}{dt}$.

In equation (3), a decrease in γ induces a decrease in $(1 - \rho)\, \gamma I$, then a decrease in $\frac{dR}{dt}$.

In equation (4), a decrease in γ induces a decrease in $\rho\gamma I$, then a decrease in $\frac{dC}{dt}$.

As expected, in **figure 4**, when γ decreases, the number of carriers (**black**) decreases over time, less individuals enter the recovery state (**green**), and the number of infectious (**red**) individuals spikes at the beginning but decreases slowly over time.

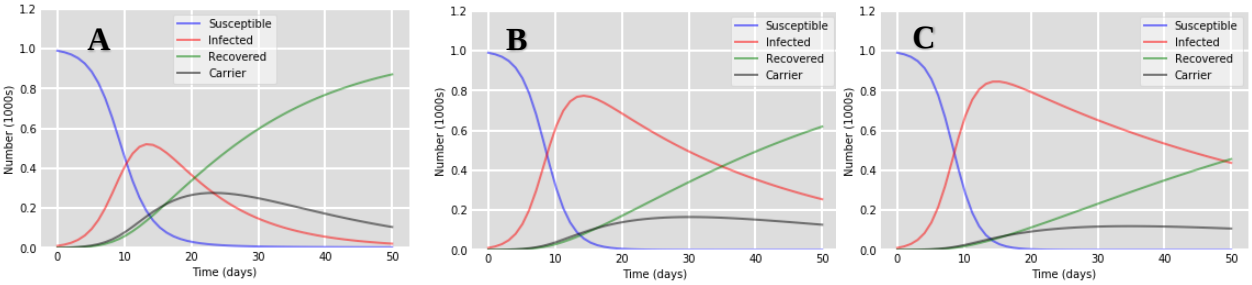

Figure 4 - disease dynamics characterized by parameters:
(A) β=7*****0.2, **γ=1/10**, ε=0.09, τ=1/20, ρ=0.67
(B) β=7*****0.4, **γ=1/30**, ε=0.09, τ=1/20, ρ=0.67
(C) β=7*****0.6, **γ=1/50**, ε=0.09, τ=1/20, ρ=0.67
In a population of N=1000 on a course of 50 days. The model is started with 980 susceptibles, 20 infectious, 0 carriers and 0 recovered on day 0.

D. Let us consider an epidemic outbreak in a population where, at the initial time, only a few individuals are infected and the proportion of acute infections that become carriers ρ increases. The initial conditions are as in **figure 5**. When ρ increases, it is expected that the proportion of carrier individuals would dominate over time. This would impact the number of recoveries. The carriers have a chronic form of the disease. They heal more slowly, so they stay in the carrier state for a long time. This is supported by:

In equation (3), an increase in ρ induces a decrease in *(1 - ρ)* then $\frac{dR}{dt}$.

In equation (4), an increase in ρ induces an increase in $\rho\gamma I$ then in $\frac{dC}{dt}$.

As expected, in **figure 5**, when ρ increases, the number of carriers (**black**) increases over time and the population takes more time to enter the recovery state (**green**).

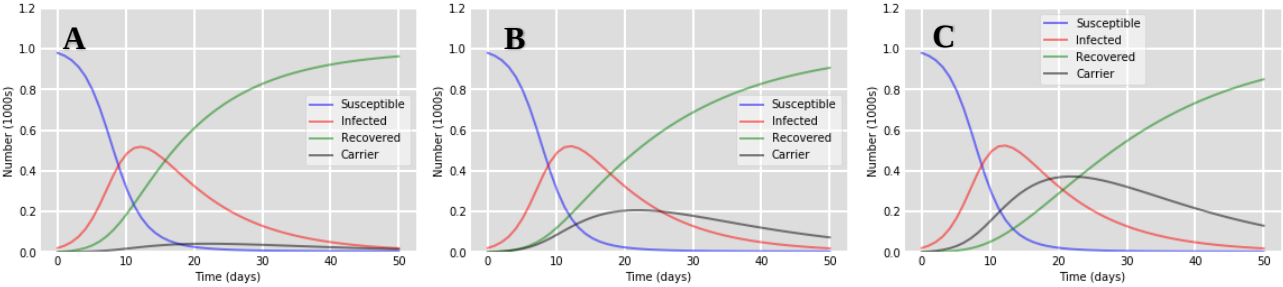

Figure 5 - disease dynamics characterized by parameters:
(A) β=7*0.08, γ=1/10, ε=0.09, τ=1/20, **ρ=0.1**
(B) β=7*0.08, γ=1/10, ε=0.09, τ=1/20, **ρ=0.5**
(C) β=7*0.08, γ=1/10, ε=0.09, τ=1/20, **ρ=0.9**
In a population of N=1000 on a course of 50 days. The model is started with 980 susceptibles, 20 infectious, 0 carriers and 0 recovered on day 0.

D. Let us consider an epidemic outbreak in a population where, at the initial time, only a few individuals are infected and the rate at which individuals leave the carrier state and enter the recovered state τ increases or decreases. The initial conditions are as in **figure 6**. When τ increases, it is expected that the proportion of recovered individuals increases and the proportion of carriers decreases over time. Inversely, when τ decreases, it is expected that the proportion of recovered individuals decreases and the proportion of carriers increases over time. This is supported by:

In equation (3), an **increase**/decrease in τ induces an **increase**/decrease in τC then in $\frac{dR}{dt}$

In equation (4), an **increase**/decrease in τ induces a **decrease**/decrease in τC then in $\frac{dC}{dt}$

As expected, in **figure 6**, when τ increases, the number of carriers (**black**) decreases and the number of recovered individuals (**green**) increases over time. While, when τ decreases, the number of carriers (**black**) increases and the number of recovered individuals (**green**) decreases over time.

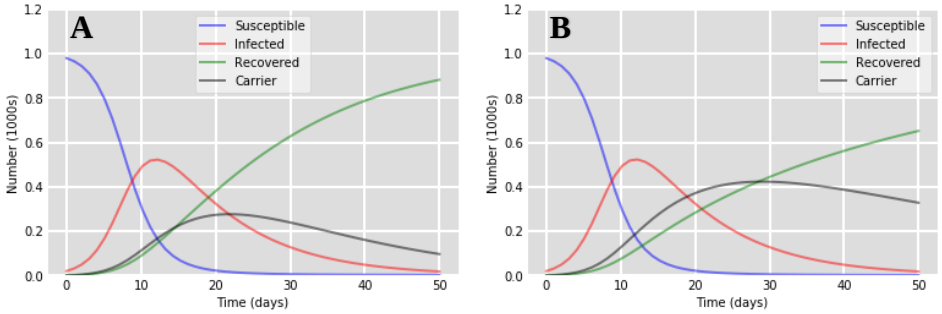

Figure 6 - disease dynamics characterized by parameters:
(A) β=7*0.08, γ=1/10, ε=0.09, **τ=1/15**, ρ=0.67
(B) β=7*0.08, γ=1/10, ε=0.09, **τ=1/45**, ρ=0.67
In a population of N=1000 on a course of 50 days. The model is started with 980 susceptibles, 20 infectious, 0 carriers and 0 recovered on day 0.

3. Conclusions and perspectives

Epidemics can be represented by compartmental ODE models. Even the simplest epidemiological models require computer algorithms to estimate prevalence profiles. But criteria for invasion and for equilibrium conditions can be derived analytically. The basic reproductive ratio R_0 is a key epidemiological measure affecting criteria for invasion extinction and size of the epidemic.

In the absence of demography, strongly immunizing infections will always go extinct eventually and not all individuals will have become infected. Thus, it would be interesting to add demography to the model. This creates the possibility of an endemic equilibrium, where the disease remains present in the population because of the birth of new susceptible individuals. In the SIR model, it can be shown that this equilibrium is always globally stable. In the SIRC model, given the results of the study from *Wang et al*[1] on overall stability, it seems to be the same.

References

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2.**Lectures on Mathematical Modelling of Biological Systems**, G. Bastin, 2018. https://perso.uclouvain.be/georges.bastin/lectures-bio.pdf

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4.**The SIR epidemic model**. https://scipython.com/book/chapter-8-scipy/additional-examples/the-sir-epidemic-model/

5.**Modeling Infectious Diseases in Humans and Animals** by Matt J. Keeling and Pejman Rohani.