LINMA2370 - Project (Part 1)
The Dynamics of Infectious Diseases

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Version 1.6

Introduction

Infectious diseases are caused by the transmission of pathogenic microorganisms (e.g. bacteria, parasites, viruses) from one person to another. Examples of major epidemics in history include the plague[1] and the smallpox[2], as well as the very recent Covid-19 worldwide crisis. Despite advances in modern medicine, infectious diseases are still an important cause of mortality. Therefore, predicting the evolution of an outbreak in the population and adopting strategies in order to control the epidemic are major challenges in public health.

In this project, we will explore how mathematical modelling can help us to understand the spread of infectious diseases in a large population. The models covered here are not intended to provide an exact and realistic view on specific diseases, but rather to illustrate some concepts mathematically. Never forget the famous quote[3] :

"All models are wrong, but some are useful."

1 A Simple Model

Let us consider a population of constant size N divided into three non-overlapping groups:

- The individuals who can become infected (susceptible)
- The individuals who contracted the disease (infected)
- The individuals who acquired permanent immunity following their infection and recovery (recovered)

Let $S(t)$, $I(t)$ and $R(t)$ respectively denote the numbers of susceptible, infected and recovered individuals in the population at time t. Because we consider a large population, we will further assume that S, I and R are real continuous variables. For this first model, we consider the following modelling assumptions:

- The birth rate (constant) is denoted by μ and is valid for the whole population, no matter if they are susceptible, infected or recovered. Each individual entering the population is susceptible.
- The death rate (constant) is equal to the birth rate, so that the population size N remains constant. All individuals die at the same rate, no matter if they are susceptible, infected or recovered.
- The contact rate between susceptible and infected individuals is proportional to the *density* of infected individuals in the population. We further assume that the population mixes homogeneously.
- When a contact between a susceptible individual and an infected one occurs, the disease is transmitted at a constant rate β.
- Infected individuals either recover from the disease and acquire a permanent immunity at a constant rate γ, or die.

[1] https://en.wikipedia.org/wiki/Plague_(disease)
[2] https://en.wikipedia.org/wiki/Smallpox
[3] Which is attributed to George E.P. Box, see https://en.wikipedia.org/wiki/All_models_are_wrong

1. Derive a state-space model for S, I and R and explain your reasoning.

2. Why is it sufficient to consider a planar system although there are three state variables? Which state variable is the easiest to remove from the model? Justify and provide the reduced state-space model.

3. Implement a function that will numerically simulate the full system (cfr. question 1) as it evolves from the initial condition `x0`, over a time period going from 0 to `Tend`. The pseudo-signature of the function is

   ```
   [T,Y] = epidemic(N,mu,beta,gamma,Tend,x0)
   ```

   `T` is a vector containing the time steps of the simulation and `Y` is an array whose columns contain the temporal evolution of each state variable . Try with the following sets of parameters at least (you are free to explore the parameter space by yourself of course):

N	μ [years^{-1}]	β [years^{-1}]	γ [years^{-1}]	`Tend` [years]	`x0`
10^7	1/80	60	7	300	$[N-10, 10, 0]$
10^7	1/80	21	23	300	$[N-10, 10, 0]$

   Provide at least a plot of the temporal evolution of the state variables[4] and a plot of the phase plane of the planar system derived in question 2.

Considering the planar system that you derived, there exist two equilibria: the disease-free equilibrium and the endemic equilibrium. Interestingly, the physical existence of the later depends on a dimensionless threshold quantity denoted by R_0. For the system that we consider, we have for example that $R_0 = \frac{\beta}{\gamma+\mu}$.

4. Derive the two equilibria of the planar system and express them as a function of R_0 (if possible). Comment on the physical existence of the endemic equilibrium.

5. Provide an intuitive interpretation of the quantity R_0 in terms of its parameters and comment on your numerical simulations.

2 Stratified Age Groups

It is commonly observed that the spread of a disease in the population impacts individuals differently depending on their age. For instance, older people can be considered *at risk* while young children could transmit the disease at a higher rate to adults than to other children. An approach to take the age into account is to explicitly add it as a continuous variable along with the time variable in the previous model. However, for the sake of simplicity[5], we will instead consider *stratified age groups*.

Specifically, let us consider three groups defined as follows :

- Group A : individuals between 0 and 12 years old
- Group B : individuals between 13 and 60 years old
- Group C : individuals being 61 years old or more

Starting from the modelling assumptions of the first model, we specify the following points :

- All individuals, no matter the group they belong to, die at the same constant death rate μ so that the population size N remains constant[6].
- Individuals from one group can have contacts with individuals from any other group. The transmission rates are constant but depend on the groups in contact, and are not necessarily reciprocal: β_{ij} is the transmission rate from age group i to age group j, and $\beta_{ij} \neq \beta_{ji}$ for all $i \neq j$.

[4] For the infected individuals, you may plot the prevalence (i.e. the percentage of infected individuals in the population) as a function of time.

[5] Although we know that you *love* partial differential equations... ;-)

[6] We are aware that this is a rather unrealistic assumption, but let's keep it simple. However, feel free to relax this assumption and observe the changes in the results if you want !

6. How many state variables do you need to model this situation ? Provide a diagram containing a box for each state variable, and draw the relationships (or *flows*) between them.

7. Derive the corresponding augmented state-space model.

   Hint. Can you check whether the population remains constant ?

8. Simulate the system numerically with the parameters of your choice (an easy choice is to start from the values of question 3). The pseudo-signature of the function is similar to that of question 3, up to some parameters that you may want to add. Try different scenarios by varying the transmission rates inside/between age groups and provide some plots to illustrate your conclusions. For instance, how does the percentage of infected individuals evolve in each group ?

3 Epidemics on networks

Until now, we have considered the spread of an infectious disease in a large, homogeneous population (e.g. a country). At a more local level (e.g. a city, a school), taking into account the contact patterns between individuals can be insightful in order to predict the evolution of an epidemic. Contact patterns can be conveniently represented as a graph (or a network), with nodes being individuals and edges being contacts (see Figure 1 in the Appendix). Each node can either be susceptible, infected or recovered. The numbers of susceptible, infected and recovered individuals are therefore integer variables. We do not take age groups into account for this part.

In order to study the spread of a disease on such a network, we will use *stochastic simulations* (see Appendix) rather than deterministic differential equations. This will allow us to generate (hopefully) more realistic results based on a probabilistic approach. Since the network structure is fixed, i.e. individuals cannot enter or leave the population, the simulated system is slightly different from that of question 1 : births and deaths are neglected, and the time scale is different (e.g. days instead of years).

9. Run the code that comes with this statement[7] on the four networks provided ($N = 1000$ nodes). Describe what you observe in the simulations with respect to the contact patterns. Feel free to tune some parameters (e.g. the initial percentage of infected individuals) and observe their impact.

10. Be creative ! Model *one* sanitary measure of your choice that could help slowing down the spread of the epidemic in the population. Explain it in a few words. Update the network topology, the simulation parameters and/or the code adequately in order to illustrate the effect of this measure. Here are some examples of scenarios that you can investigate, but you are welcome (and encouraged!) to suggest your own ideas :

    - Wearing a mask and washing your hands regularly
    - Applying social distancing after a given threshold of infected individuals is reached
    - Adopting the "5-people-bubble" policy (or 10, 15 ...)
    - Isolating infected individuals from the rest of the population

Practical information

You are asked to work by groups of two students and to write a report (in French or in English) gathering your answers to the above questions. You should submit on Moodle a single zip file containing your report in `pdf` and your codes for questions 3, 8 and 10 (Do not include your codes in your report!). The deadline for the submission is **October 30th 2020 at 11:55 pm**. Feel free to ask your questions on the dedicated forum on Moodle and to ask for an appointment with the teaching assistant in charge of the project (Benjamin Chiêm).

[7] Read the appendix first, and be sure to have the NetworkX and EoN toolboxes correctly installed. For any installation problem, contact Benjamin Chiêm (benjamin.chiem@uclouvain.be) as soon as possible.