Introduction to Computational Science

Assignment First

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1 Introduction

It is becoming apparent that infectious diseases are a threat that need to be studied more in depth. One way to do this is with the use of mathematical models. By formulating hypotheses, estimating parameters with the help of epidemiological data we can understand, predict and control more efficiently the system's dynamics.
For that, we detail at first the most basic epidemiological model and the assumptions made. We proceed to analyse its dynamics and some of its variations, which predict more accurately the physical world. The present assignment is heavily based on the book *"Modeling Infectious Diseases in Humans and Animals"* by Matt J. Keeling, Pejman Rohani[1].

2 Basic model

In general, the diseases are organized according to overlapping classifications. We focus specifically on infectious diseases caused by micro-parasites, described by a rapid increase in numbers in a host, and being transmitted by direct contact.
The basic blocks of the model in discussion are tree population categories. The susceptible(S), the infected(I) and the recovered(R), hence the model's name SIR. In this definition we ignore population demographics. The chain of events are as follows. First, a host comes with direct contact with an infectious person and becomes infected(S–>I). The host's immune response in these diseases is typically fast to remove them after a period of time and in developing lifelong immunity(I–>R). The first process depends on the number of susceptible, infected and the probability of transmission given contact, assuming homogenous contact interactions and probability of transmitting/contracting across the population. The second process depends on for how long a person is infected, which for simplicity assumed constant.
Combining the above, the differential equation describing the epidemiological model SIR are:

$$ds/dt = -\beta SI$$

$$dI/dt = \beta SI - \gamma I$$

$$dR/dt = \gamma I$$

,where β is the rate of infection and γ is the recovery rate. Note that the terms are proportional to the population N, meaning that in a closed community with no demographics S+I+R=1. For that it is only essential to solve only for the S, I. The system of equations is solved numerically (Figure 1), by implementing the 4th order Runge-Kutta with the initial conditions obeying the S(0)>0, I(0)>0, R(0)=0. Usually, the starting value of I is very small.

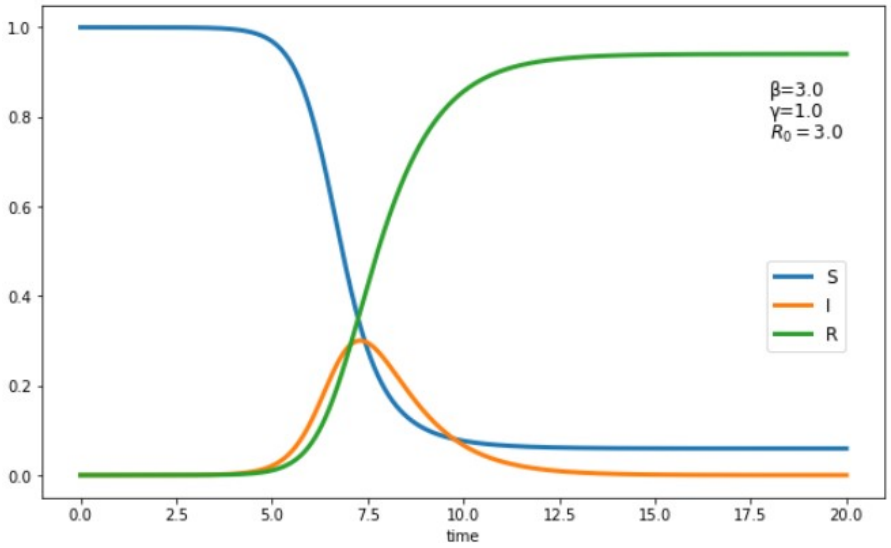

Figure 1: SIR model. Initial values are S(0)=1, I(0)=1e-4, R(0)=0.

3 Epidemic/no epidemic

Examining the equation for the susceptible population, rearranging the terms such as $dI/dt = I(\beta S - \gamma)$, we can see that in order for the rate to be negative, meaning that the disease will eventually die out, $S < \gamma/\beta$. One of the most valued quantity in epidemiology is the basic reproduction number $R_0 = \beta/\gamma$. When this is greater than $R_0 > 1$, which can be interpreted as the recovery being slower than the infection rate, the pathogen will spread to the population. From a different perspective there is a susceptible threshold $S < 1/R_0$, when the disease will not spread further. Also when $S(0) < 1/R_0$ it will not invade.

4 Phase space analysis

After an infection is introduced to the population and in the long term the system moves towards the fixed point $(S^*, I^*, R^*) = (1 - R(\infty), 0, R(\infty))$, when all the infected have recovered. Dividing the differential equations of the S, R we obtain $S(t) = S(0)e^{-R(t)R_0}$. Given that the right-hand terms are always positive, there will be susceptible population who escaped infection. We can see that for $0 \leq R(t) < 1 \Rightarrow S(0)e^{-R_0} \leq S(t) \leq S(0)$.
From the Figure 2 we observe that for values of $S(0) < 1/R_0$ the decease doesn't invade and for the values of $S < 1/R_0$, namely left of the horizontal dashed line, it dies out. All curves move towards their fixed point.

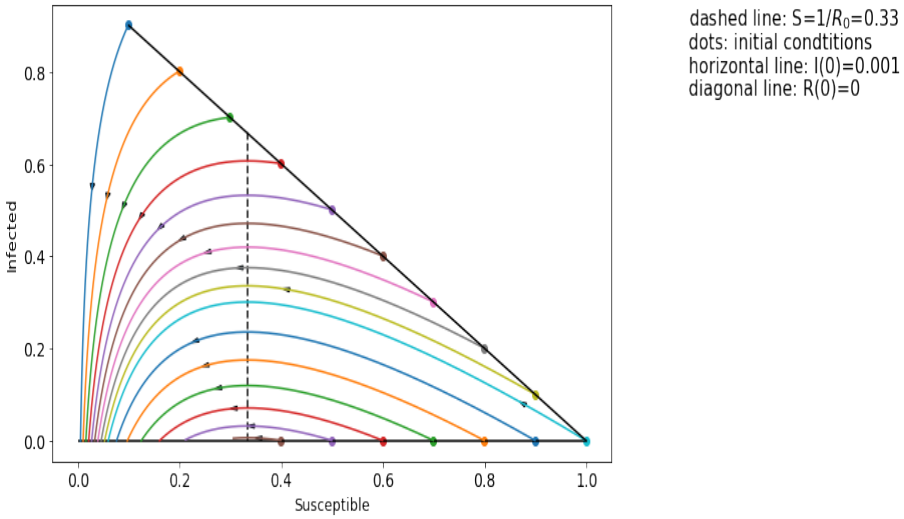

Figure 2: Phase space plot of SIR model in 2D.

5 Fitting Data

This model, despite being very simple, can be very useful and give satisfactory predictions. A working example is that of an influenza outbreak in a British boy's school. One boy started the epidemic in a school population of 763 students. Given the real-world data we can fit the parameters β, γ to the problem (Figure 3), with the outcome in the range of the estimated influenza data in humans. The values calculated are $\beta = 1.67$, $\gamma = 0.45$, $R_0 = 3.72$, which is in the range of the reference value[1] $R_0 = 3 - 4$ (Table 1).

Table 1:
Some Estimated Basic Reproductive Ratios.

Infectious Disease	*Host*	*Estimated R_0*	*Reference*
FIV	Domestic Cats	1.1–1.5	Smith (2001)
Rabies	Dogs (Kenya)	2.44	Kitala et al. (2002)
Phocine Distemper	Seals	2–3	Swinton et al. (1998)
Tuberculosis	Cattle	2.6	Goodchild and Clifton-Hadley (2001)
Influenza	Humans	3–4	Murray (1989)
Foot-and-Mouth Disease	Livestock farms (UK)	3.5–4.5	Ferguson et al. (2001b)
Smallpox	Humans	3.5–6	Gani and Leach (2001)
Rubella	Humans (UK)	6–7	Anderson and May (1991)
Chickenpox	Humans (UK)	10–12	Anderson and May (1991)
Measles	Humans (UK)	16–18	Anderson and May (1982)
Whooping Cough	Humans (UK)	16–18	Anderson and May (1982)

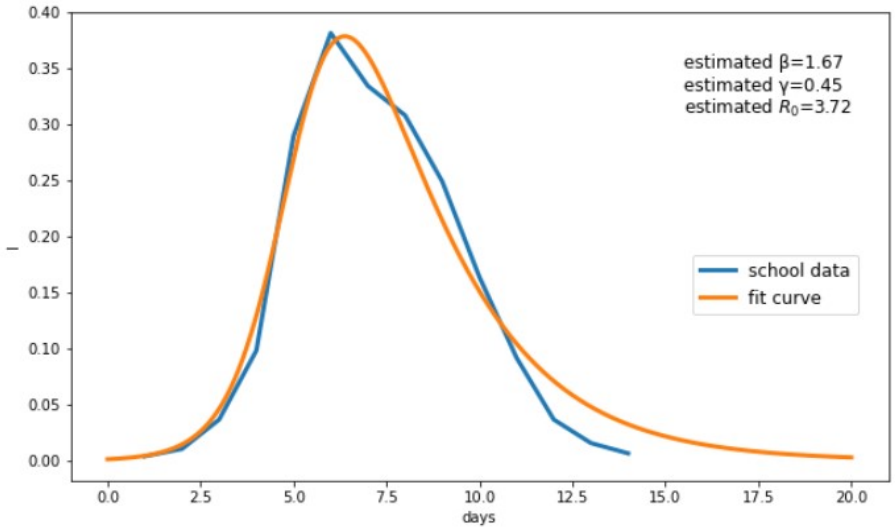

Figure 3: Estimating parameters β, γ by fitting SIR model with real world data.

6 Vaccination plan

In this section it is attempted a naive implementation of a vaccination plan (Figure 4), using the SIR model and the data from the fitting process. The goal that is being set is decreasing the peak number of infected to around the half of what would be, while also minimizing the people what should be vaccinated. To do that we chose an upper limit of $I_{max} = 0.2$. It is assumed that the vaccine is immediately and 100% effective and the students won't act as carriers. The way that the vaccination plan should be carried is by subtracting an amount of people from the susceptible pool and moving them directly to the recovered at a specific day. While subtracting a fixed amount at a specific day we also check the equation are following the restrictions of $S, I, R > 0$. By implementing the plan, we find that the day of vaccination is the 4th day and 121 people should get the vaccine dose.

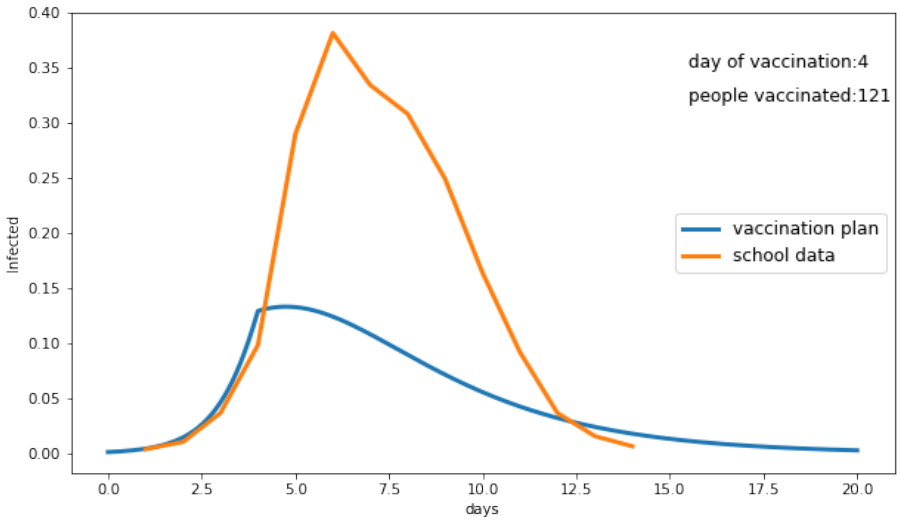

Figure 4: Effect of vaccination plan on development of the school outbreak.

7 Natural death and birth

The basic SIR model represents fast outbreaks in short periods of time. One approach more realistic, is introducing demographic characteristics (deaths, births) to the model. We can do that by incorporating one more parameter, the natural mortality μ. This isn't connected with the mortality induced by the decease. Also, assuming that this parameter represents the birth rate $\nu = \mu$, the population remains constant.

$$dS/dt = \nu - \beta SI - \mu S$$
$$dI/dt = \beta SI - \gamma I - \mu I$$
$$dR/dt = \gamma I - \mu R$$
$$R_0 = \frac{\beta}{\gamma + \mu}$$

8 Endemic/ Oscillation

There are two equilibrium states for the SIR model with demographics. The decease free scenario $(S^*, I^*, R^*) = (1, 0, 0)$ (Figure 5) and the endemic state $(S^*, I^*, R^*) = (1/R_0, \mu/\beta(R_0 - 1), 1 - S^* - I^*)$ (Figure 6). With basic demographics, the endemic equilibrium is stable if $R_0 > 1$, else the decease free equilibrium is stable. In the endemic state the system moves towards the equilibrium by damped oscillation.

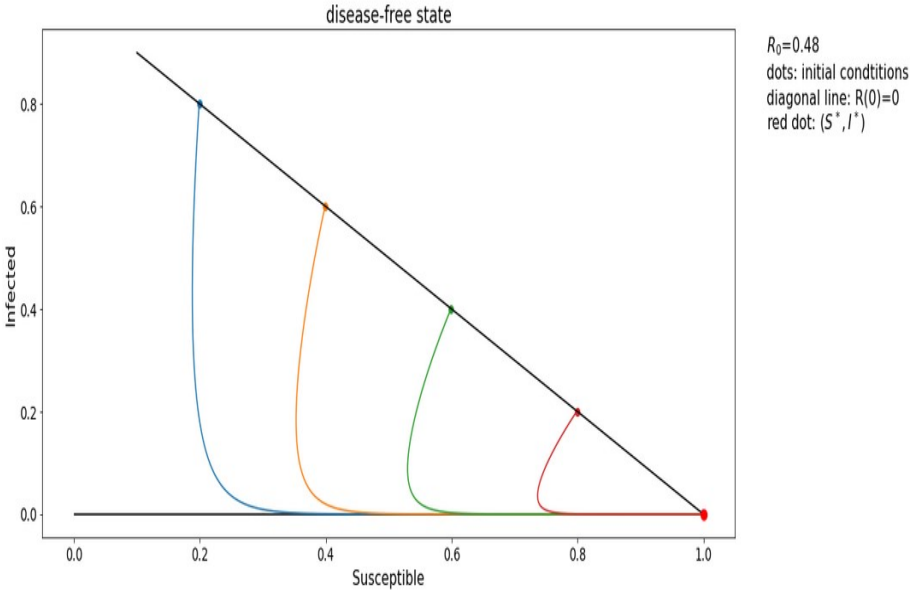

Figure 5: Disease free scenario of SIR model with demographics.

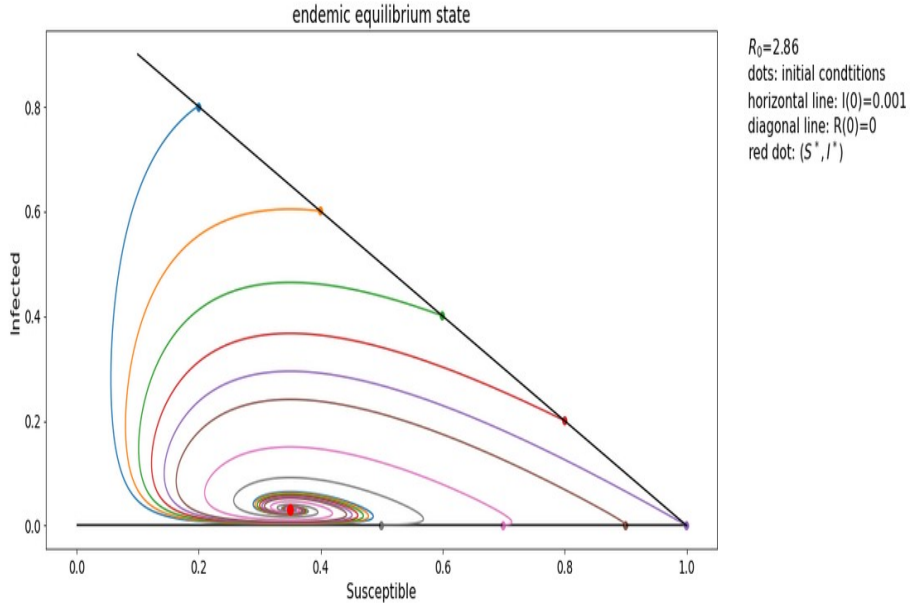

Figure 6: Endemic state of SIR model with demographics.

To investigate the system's dynamics further, we examine what happens when the variables are shifted by a small value form the equilibrium state (e.g., $S = S^* + e$). First, we calculate the Jacobian matrix and then the characteristic polynomial and eigenvalues for the two states.

$$\text{J}=\begin{bmatrix} \text{-}\beta I^* - \mu & \text{-}\beta S^* \\ \beta I^* & \beta S^* - (\gamma + \mu) \end{bmatrix}$$

For the free-state the characteristic polynomial is: $(-\mu-\lambda)(\beta-(\mu+\gamma)-\lambda) = 0$. The two solutions are $\lambda_1 = -\mu, \lambda_2 = \beta - (\mu + \gamma)$. For it to be stable the eigenvalues must be negative, thus $\beta < \mu + \gamma$.
For the endemic: $\lambda^2 + \mu R_0 \lambda + (\mu + \gamma)\mu(R_0 - 1) = 0$ and the solutions are $\lambda_{1,2} = -\mu R_0/2 \pm \sqrt{(\mu^2 R_0^2 - 4/AG)/2}$, $A = 1/\mu(R_0 - 1)$, $G = 1/(\mu + \gamma)$.By assuming that $\mu^2 R_0^2$ is small $\lambda_{1,2} = -(\mu R_0)/2 \pm i/\sqrt{AG}$. The eigenvalues are complex numbers with a negative real part, so the system is characterized by oscillations and the endemic state (i.e., when $R_0 > 1$) is always stable creating an inward spiral. The period of oscillations is $T = 2\pi\sqrt{AG} \approx 60$. (Figure 7).

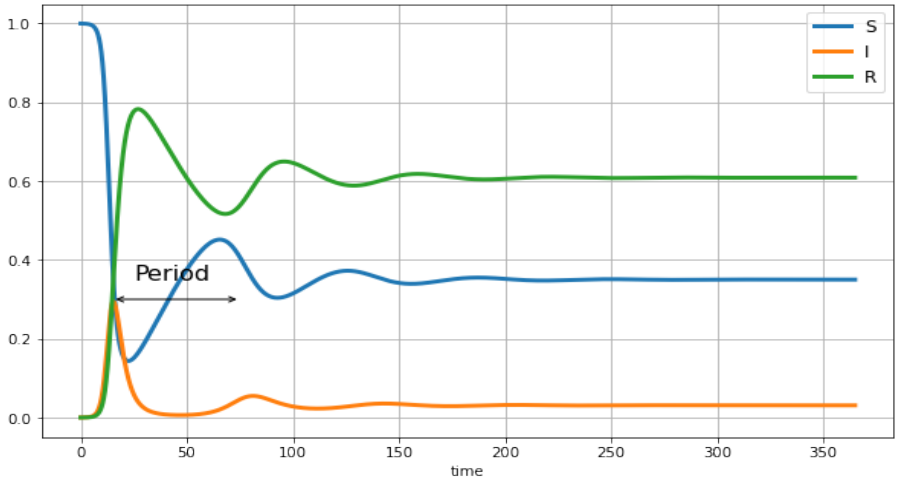

Figure 7: Oscillatory dynamics of the SIR model with demographics. Initial conditions are $S(0) = 1$, $I(0) = 1e - 4$, $R(0) = 0$. The model parameters are $\beta = 1$, $\gamma = 1/3$, $\mu = 1/60$.

9 Infection induced mortality

One of the possible outcomes of contracting a disease is the death of the host. For that we subtract a fraction of the population of the infected, which can be formulated by introducing the per capita probability of dying from the infection ρ. It takes values from zero to one, meaning that there is an increasing effect on the death rate by the disease. The population can no longer be assumed constant and the ODEs must be re-evaluated. We can no longer deal with fraction of the population categories; thus, we replace the fractions S,I,R with the number of people occupying each category X,Y,Z respectively. We assume as before that approximately $\nu = \mu$.

$$dX/dt = \nu - \beta Y/N - \mu X$$

$$dY/dt = \beta XY/N - (\gamma + \mu)Y/(1 - \rho)$$

$$dZ/dt = \gamma Y - \mu Z$$

$$R_0 = \frac{\beta(1-\rho)}{\mu+\gamma}$$

The equilibrium states are again the disease-free and the endemic state. The first is mathematically formulated by the simple $(X^*, Y^*, Z^*) = (\nu/\mu, 0, 0)$. The later is calculated by setting the rates equal to zero and this produces the values:

$$X^* = N/R_0 \Rightarrow S^* = 1/R_0$$

$$Y^* = \frac{\nu\beta(1-\rho)^2 - \nu(\mu+\gamma)(1-\rho)}{(\mu+\gamma)(\beta(1-\rho) - \mu\rho - \gamma\rho)} \Rightarrow I^* = \frac{\mu}{\beta(1-\rho)}(R_0 - 1) \rightarrow \text{if } R_0 > 1 \text{ the disease invades}$$

$$N^* = \frac{\nu}{\mu}\frac{R_0(1-\rho)}{R_0-\rho}$$

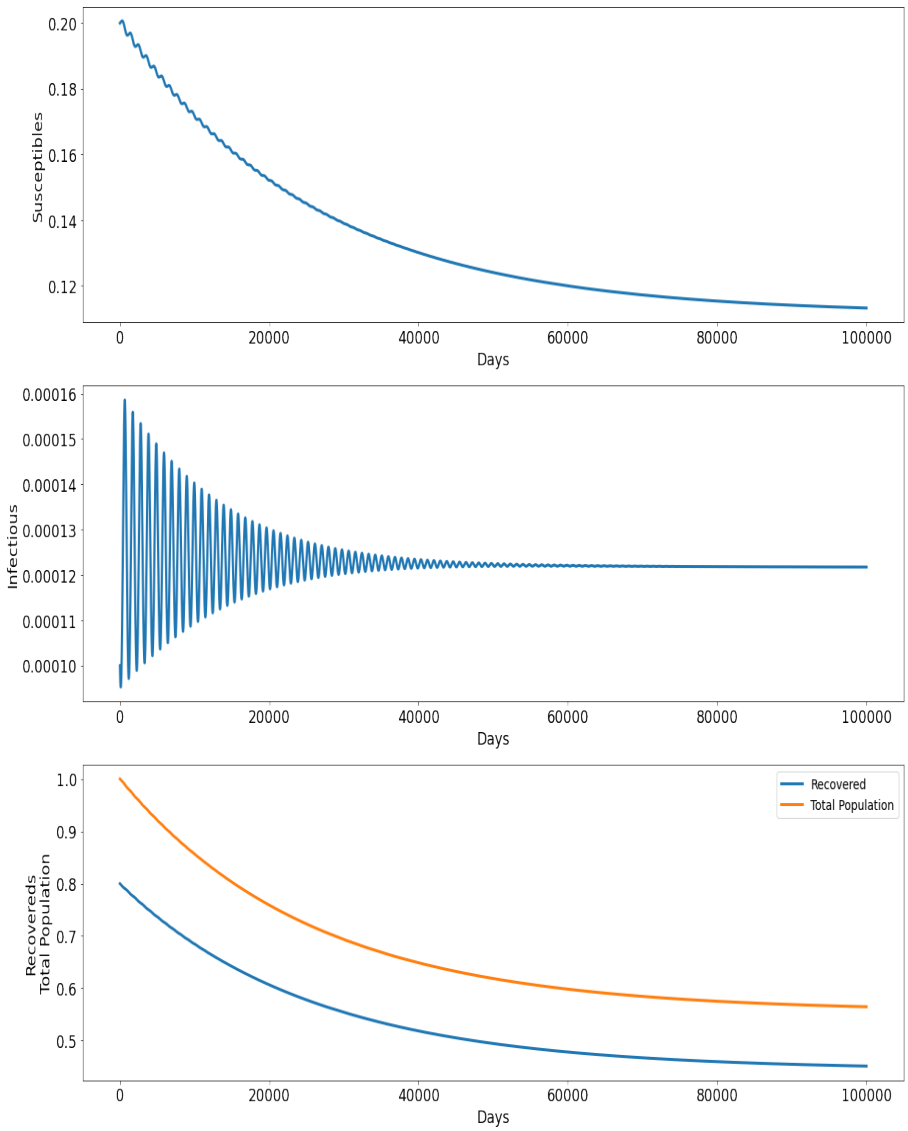

Figure 8: SIR model with introduced mortality. System dynamics with parameters $\beta = 520$ per year, $\gamma = 1/7$ days, $\mu = 1/70$ years and initial values $N(0) = 1, X(0) = 0.2, Y(0) = 1e-4, Z(0) = 1 - X(0) - Y(0)$.

For the parameter ρ we can say that plays a very important role and behaves just like we want to. For increasing values, the total population equilibrium decreases (Figure 9), being that the disease is more deadly. In the process of making the plot we run into some stability problems with overflowing, due to possibly a very small time step value in the equations and may be the reason for the step-like plot line.

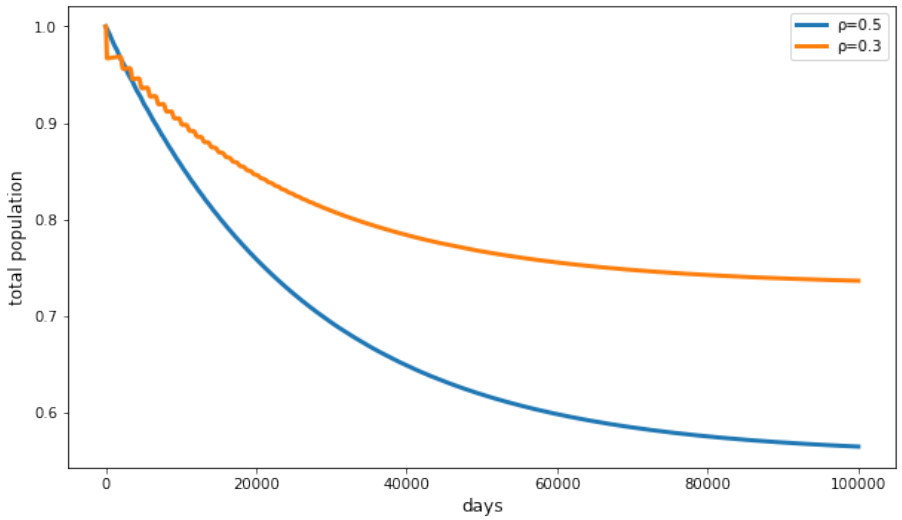

Figure 9: Effect of value ρ in the total population.

10 The SIS model variation

Tackling one other assumption that we made, that of the lifelong immunity, the SIS model is described below. People can be infected multiple times in their lifetime and develop no immune response to the pathogen. So, they move directly from the infected category back to the susceptible pool. For simplicity we ignore the demography of the population and despite not accounting for deaths and births(i.e. $S + I = 1$), the disease can have a long-lasting imprint of the population if invades. Finally, everyone is at equal risk.

$$dS/dt = \gamma I - \beta SI$$

$$dI/dt = \beta SI - \gamma I$$

$$R_0 = \beta/\gamma$$

For the equilibrium point and because the population remain the same, we substitute $S = I - 1$ to the infected equation and solve for zero. That gives $(S^*, I^*) = (1/R_0, 1 - 1/R_0)$. Interpreting the results, this state is stable for

$R_0 > 1$ and the disease will persist, as long it invades and no immunity is developed (Figure 10), because the susceptible pool keeps replenishing.

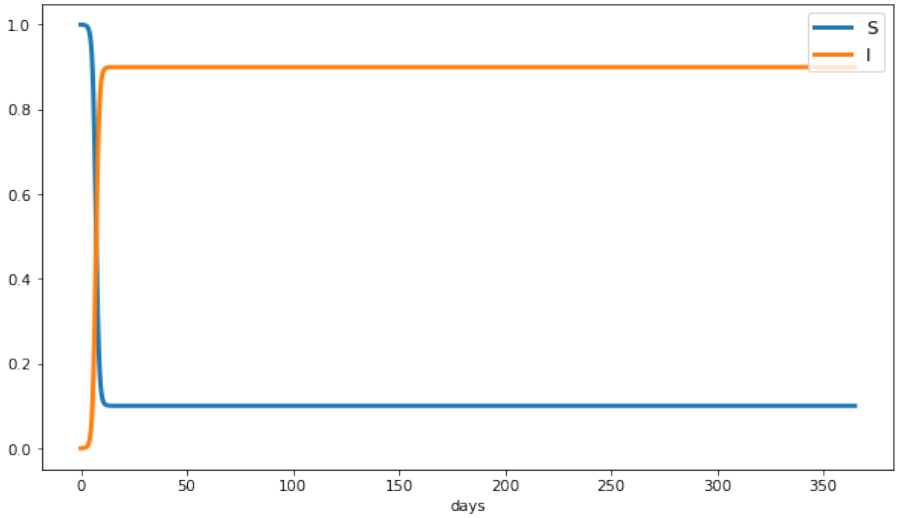

Figure 10: SIS model. System parameters and initial values respectively are: $\beta = 520$ per year, $\gamma = 1/7$ days, $S(0) = 1 - 1e - 4, I(0) = 1e - 4$

11 Seasonality

Not all data can be explained by the SIR model described previously. The parameters of a disease outbreak are complicated. In some cases, there is recurrent outbreaks of infectious diseases that can not be explain by the SIR model as formulated above. The disease doesn't oscillate toward an equilibrium but it is seasonal. For that we construct a forced model to understand the mechanisms and dynamics of such diseases. It is found that a factor that can lead to such a behaviour is by incorporating an agitation effect in the transmission rate, which in a way translates to varying conditions of close human contacts interactions.

$$\beta(t) = \beta_0(1 + \beta_1 cos(\omega t))$$

The term β_0 is the mean transmission rate, ω the period of forcing, $\beta_1 \leq 1$ the amplitude of sinusoidal forcing. Finally:

$$dS/dt = \nu - \beta(t)SI - \mu S$$

$$dI/dt = \beta(t)SI - \gamma I - \mu I$$

$$dR/dt = \gamma I - \mu R$$

$$R_0 = \beta_0/\gamma$$

The modified term introduced produces seasonal oscillations(Figure 11,12). Depending on the natural period and the seasonal forcing we get different result patterns.

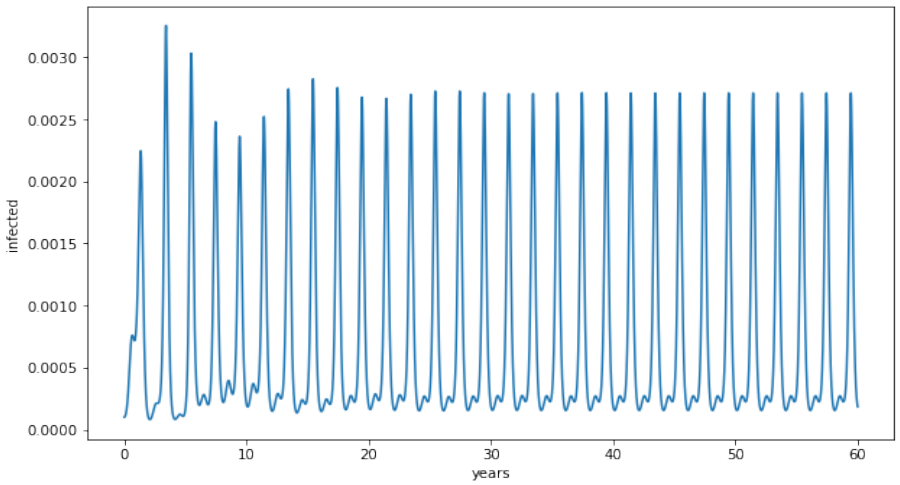

Figure 11: Periodic behaviour of system with enforced seasonality. Initial values and parameters $S(0) = 0.0588, I(0) = 1e-4, R(0) = 1 - S(0) - I(0)$, $\beta_0 = 1.308$ days, $\gamma = 0.077$ days,$\mu = 1/50$ years

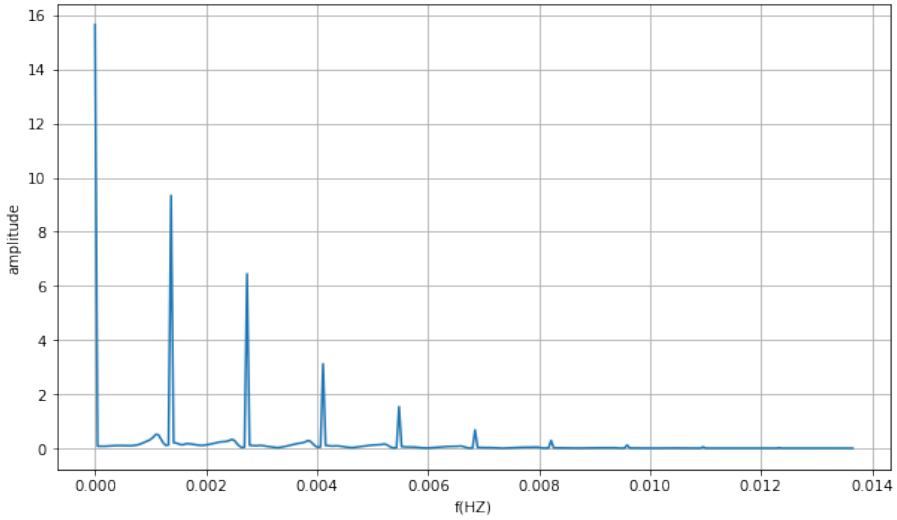

Figure 12: Fourier analysis of seasonality

For a more detailed approach, we visualize the effect on the dynamics by constructing a bifurcation diagram. The control parameter that is changed is β_1. For any of its value four subsequent years are plotted (Figure 13). The initial conditions are the same and the simulation is run until the system is settled to its long-term state.

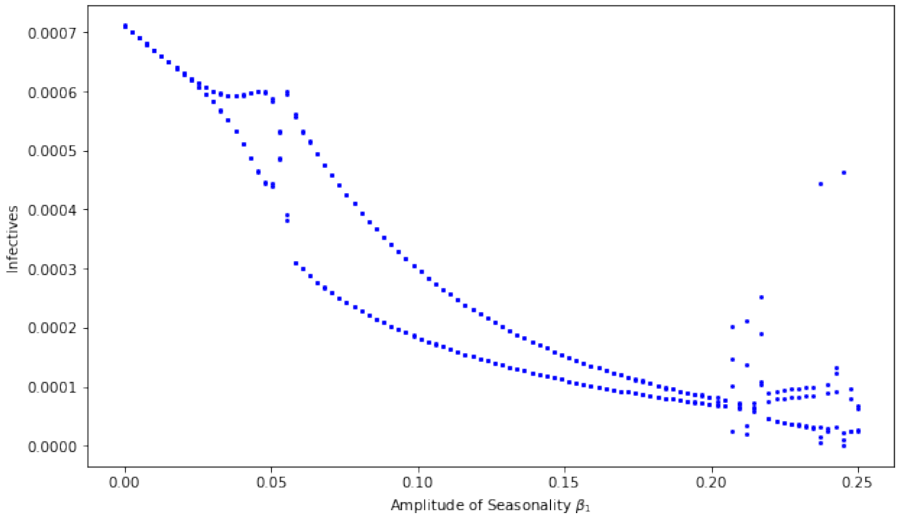

Figure 13: Bifurcation diagram with as β_1 the control parameter. Initial values and parameters $S(0) = 0.5, I(0) = 1e-4, R(0) = 1 - S(0) - I(0)$, $\beta_0 = 1.308$ days, $\gamma = 0.077$ days, $\mu = 1/50$ years.

Examining Figure 13, we count the number of points on a specific β_1 value. For example, at $\beta_1 \approx 0.35$ we number two dots, meaning that the dynamics are biennial. The bifurcation diagram shows that the complexity of the system is increasing with the seasonality, leading eventually to chaos. Many other parameters can could be used and a single diagram can't capture all the possible combinations.

12 Conclusion

It is apparent that the mechanisms governing diseases are very complex. Many factors must be taken into account. The type, the means of transmission, the seasonality, specific groups of population affected, the immune response are a few of them. Although these models in the process of understanding and predicting are sometimes adequate, there is always an aspect that we don't truly understand yet. For that we must evaluate and change the parameters in close collaboration with real world data and study further the many different ways a disease can spread.

13 References

[1] Keeling, M. J., & Rohani, P. (2007). Modeling Infectious Diseases in Humans and Animals. Princeton University Press, pp. 1-52, 155-167.