Infectious Disease Modelling Using Ordinary Differential Equations

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Abstract

A mathematical model based on ordinary differential equations is proposed for a quantitative description of the outbreak of infectious disease like Covid-19. These models form the basis of more detailed models currently used by world health organizations, both to predict the future spread of disease and to develop strategies for containment and eradication. The well-known SIR models have been around for many years. Under some suitable assumptions, the models provide information about when does the epidemic occur and when it doesn't and analyze the outcome mathematically. We will be studying several SIR models and their application, And try to answer some questions about disease progression in a set population.

1 Problem and Motivation

Facing an imminent epidemic, public health authorities will be looking for answers to the following important questions:

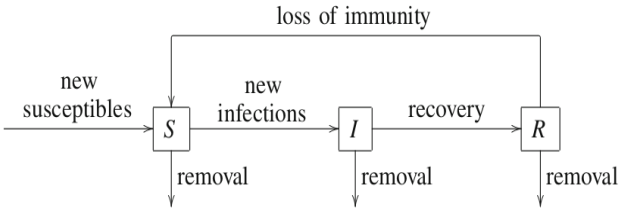
- How severe will the epidemic be?
- How long will it last? When will it peak? What will be its time course?
- How effective will quarantine or vaccination be?
- What are effective measures to contain, control, and eradicate an endemic disease?

Mathematical modeling can provide an understanding of the underlying mechanisms of disease transmission and spread, help to pinpoint key factors in the disease transmission process, suggest effective control and preventive measures and provide an estimate for the severity and potential scale of the epidemic. Put it simply, mathematical modeling should become part of the toolbox of public health research and decision-making.

2 Literature review

2.1 Deterministic Epidemic Models: Compartmental Approach

We first partition the host population into mutually exclusive groups.
S : Susceptible hosts(someone at risk),
I : Infectious hosts (infected ones),
R : Recovered hosts



The goal of modeling is to track the number of hosts in each of the three compartments at any given time t and we denote these numbers by $S(t)$, $I(t)$, and $R(t)$ accordingly.
To set up the compartmental model, we consider a small-time interval $[t, t+\Delta t]$ and the net change in the number of individuals in each compartment.
The net change of the number of hosts in a compartment is the number coming into the compartment minus the number leaving the compartment during the time interval. Applying this principle to each compartment, we arrive at the following equations:
$\Delta S(t)$ = new susceptible + transfer from R – new infections – removal from S
$\Delta I(t)$ = new infections – transfer into R – removal from I
$\Delta R(t)$ = transfer from I –transfer into S – removal from R

If we divide both sides of these equations by Δt and let Δtß0, then the left-hand side will be the derivatives $S'(t)$, $I'(t)$ and $R'(t)$.We thus have the following differential equations:

$$S'(t) = \boxed{\text{influx of new susceptibles}} + \boxed{\text{transfer rate from } R} - \boxed{\text{incidence rate}} - \boxed{\text{removal rate from } S}$$

$$I'(t) = \boxed{\text{incidence rate}} - \boxed{\text{transfer rate into } R} - \boxed{\text{removal rate from } I}$$

$$R'(t) = \boxed{\text{transfer rate from } I} - \boxed{\text{transfer rate into } S} - \boxed{\text{removal rate from } R}.$$

If we express all the terms on the right-hand side as functions of $S(t)$, $I(t)$, and $R(t)$, we will obtain a system of differential equations for $S(t)$, $I(t)$, and $R(t)$, which will form our mathematical model. It is important to note that how these terms are expressed as functions of $S(t)$, $I(t)$, and $R(t)$ is based on our hypotheses regarding the biological processes of disease transmission and population transfer among compartments. Therefore, different hypotheses will give rise to different forms of the model and may lead to different model outcomes. The model I am going to discuss is **Kermack-McKendrick Model**.

2.2 Kermack - McKendrik Model

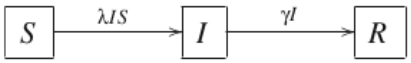
To demonstrate how various rates may depend S(t), I(t) and R(t), we take the following hypothesis for this model:

- Transmission occurs horizontally between host.
- Mixing of individual host is homogeneous thus the Law of Mass Action holds: The number of contacts between hosts from different compartments depends only on the number of hosts in each compartment. In particular, the incidence rate **(number of new infection per unit time)** can be expressed as $\lambda I(t)S(t)$, where λ is called the transmission coefficient.
- Rate of transfer from a compartment is proportional to the population size of the compartment. For instance, the rate of transfer from I to R, the recovery rate, can be written as $\gamma I(t)$, for some rate constant γ.
- Infected individuals become infectious upon infection with no latency period.

- There is no loss of immunity and no possibility of reinfection. This implies that the transfer rate from R back to S is zero.
- There is no input of new susceptible and no removal from any compartments. The influx of new susceptible is zero, and so are the removal rates from all compartments.
- The total host population remains a constant

2.3 SIR MODEL

Based on these assumptions, the transfer diagram for a conceptual model can be translated into



an explicit model as shown in below:
Substituting all terms by our mathematical descriptions, we obtain the following system of differential equations:
$\frac{dS}{dt} = -\lambda IS$ (1)
$\frac{dI}{dt} = \lambda IS - \gamma I$ (2)
$\frac{dR}{dt} = \gamma I$ (3)
with initial conditions
$S(0) = S_0 > 0$, $I(0) = I_0 > 0$ and $R(0) = 0$.
Functions $S(t)$, $I(t)$, and $R(t)$ are variables. Since they denote the number of people, they are expected to take non-negative values. Constants and are model parameters, and they are assumed to be non-negative since they denote rate constant.
If the values of model parameters λ and γ are known, then for each set of initial conditions S_0 and I_0 , model has a unique solution $(S(t), I(t), R(t))$ that produces a prediction for the time course of the epidemic for $t > 0$. Here $t = 0$ marks the beginning of the epidemic.

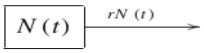
2.4 Some simple observations about the solutions to system

- From equation (1) we obtain
  $\frac{dS}{dt} \leq 0$
  Therefore $S(t)$ is always decreasing. In particular, $S(t) \leq S_0$
- Now for the equation (2)
  $\frac{dI}{dt} = (\lambda S - \gamma)I$, we have the following two cases:
  - If $S_0 < \frac{\gamma}{\lambda}$, then $\frac{dI}{dt} < 0$ at $t = 0$. Since $S(t) \leq S_0 < \frac{\gamma}{\lambda}$, we know $I'(t) < 0$ for all $t \geq 0$, and thus $I(t)$ strictly decreases. As a result no epidemic can occur in this case.
  - If $S_0 > \frac{\gamma}{\lambda}$, then $S(t) > \frac{\gamma}{\lambda}$ for $t \in [0, t)$ for some $t > 0$. This implies $I'(t) > 0$ and thus $I(t)$ strictly increases for $t \in [0, t)$. As a result an epidemic happens.

  This demonstrates the well-known **threshold phenomenon**: There is a threshold value $\frac{\gamma}{\lambda}$, which S_0 must exceed for an epidemic to occur. This threshold value is often called the critical community size for an epidemic.

2.5 Important Concepts in Compartmental Epidemic Models

Consider a general compartment C of total population size $N(t)$, where individuals leave the compartment at a rate $rN(t)$ $(r > 0)$.



Then the equation becomes:
$\frac{dN(t)}{dt} = -rN(t), \qquad r > 0,$
thus $N(t) = N_0 e^{-rt}$, or $\frac{N(t)}{N_0} = e^{-rt}$.
Therefore e^{-rt} gives the fraction of the population that remains in the compartment C. In probability terms e^{-rt} is the probability of an individual entering C at time $t = 0$ and remaining in C at time $t > 0$.
Now consider this equation,

$$F(t) = \begin{cases} 1 - e^{-rt} & t \geq 0 \\ 0 & t < 0 \end{cases}$$

Which gives the fraction of the population that has left C during the time period $[0, t)$, or the probability of an individual who has left C during $[0, t)$. Here we can check that F(t) has the characteristics of a probability distribution.
In fact, if we let X denote the random variable of the residence time of an individual in compartment C, i.e., the time period from entrance to exit, we see that
$F(t) = P[X \leq t]$
In other words, $F(t)$ is the probability distribution function of the individual residence time in C

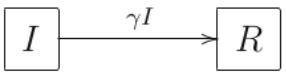
We can also describe the random variable X in terms of the probability density function $f(t) = \frac{dF(t)}{dt}$, namely

$$f(t) = \begin{cases} re^{-rt} & t \geq 0 \\ 0 & t < 0 \end{cases}$$

- The probability density $f(t)$ gives the proportion of individuals with residence time t.
- The expected value, also called the mean value, of X is $E[X] = \int_{\infty}^{-\infty} t f(t)\, dt = \frac{1}{r}$. Therefore the mean residence time is $\frac{1}{r}$.

2.6 Transfer from I to R

For transfers from compartment I to R, the residence time is the period between time of infection and time of recovery, which is the infectious period.



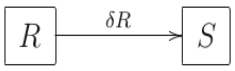
The following transfer diagram is equivalent to assuming that the infectious period of individuals has an exponential distribution

$$F(t)=\begin{cases} 1-e^{-\gamma t} & t \geq 0 \\ 0 & t < 0 \end{cases}$$

where $\frac{1}{\gamma}$ is the mean infectious period.

2.7 Transfer from R to S

For transfers from compartment R to S, the residence time is the immune period **the period recovered individuals are protected from reinfection**.



The proportionate rate δR assumes that the immune period of the individuals have an exponential distribution.

$$F_1(t)=\begin{cases} 1-e^{-\delta t} & t \geq 0 \\ 0 & t < 0 \end{cases}$$

where $\frac{1}{\delta}$ is the mean immune period.

2.8 Modeling Disease Incidence

The incidence term in the Kermack–McKendrick model is given by βIS, which is often called simple mass-action incidence.
The way to derive disease incidence is the following: let $S(t), I(t), R(t)$, and $N(t) = S(t)+I(t)+R(t)$ denote the sizes of the susceptible, infectious, recovered, and total population, respectively. Let be the average per person contact number among individuals per unit time, and p the probability that a contact will produce an infection. Then the incidence(rate at which new infections occur) is given by:
$p\lambda\frac{S(t)}{N(t)}I(t)$
which can be interpreted as

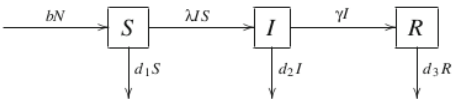
average number of effective contacts produced by each infectious individual	·	probability that a contact is made with a susceptible individual	·	total number of infectious individuals

If we combine the probability p with the contact number λ, so that λ is the per person effective contact number, then the incidence is given by $\frac{\lambda}{N}IS$.
When the total population is constant then the incidence form is same as assumed, with $\beta = \frac{\lambda}{N}$. But when $N(t)$ varies with t, things become complicated. We consider here two cases:

- The effective contact number is independent of the total population size. In this case, the incidence is given by
  $\frac{\lambda I(t)S(t)}{N(t)}$
  This form is called standard incidence.
- The effective contact number is proportional to the total population size, namely $\lambda = \beta N$, then the incidence is again of simple mass-action form $\beta I(t)S(t)$.

2.9 Demography: Birth, Death, and Population Growth

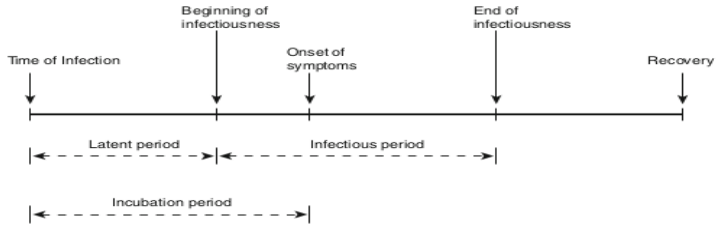
To incorporate demographic factors into the Kermack-McKendrick model, we need to make various assumption on the birth, death and growth of the host population.the simplest of which is the proportional rate assumption that the birth or death rate is proportional to the population size of the respective compartment.



Here b is the natural birth rate constant, and d_1, d_2 and d_3 are death rate constant for the respective compartment.
Now the set of equations become:
$S'(t) = bN(t) - \lambda I(t)S(t) - d_1 S(t)$
$I'(t) = \lambda I(t)S(t) - (\gamma + d_2)I(t)$
$R'(t) = \gamma I(t) - d_3 R(t)$
$N(t) = S(t) + I(t) + R(t)$

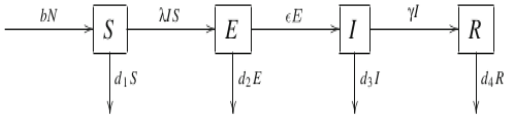
2.10 Disease Latency: Latency and Incubation Period

The period from time of infection to time of onset of symptoms is called the incubation period.
The period from time of infection to time of being contagious or infectious is called the latent period.
The period during which the host is infectious is called the infectious period .
To incorporate the disease latency in a mathematical model, we need to make some basic assumptions about the latency of the disease. The simplest is to divide the infected compartment into two compartments: a latent compartment E and an infectious compartment I, and assume that the transfer from E to I satisfies the proportional rate assumption, namely, given by ϵE with rate constant ϵ



A graphical illustration of incubation, latent and infectious period.

2.11 SEIR Model

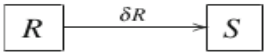


Transfer diagram for an SEIR model.

$S'(t) = bN(t) - \lambda I(t)S(t) - d_1 S(t)$
$E'(t) = \lambda I(t)S(t) - (\epsilon + d_2)E(t)$
$I'(t) = \epsilon E(t) - (\gamma + d_3)I(t)$
$R'(t) = \gamma I(t) - d_4 R(t)$
$N(t) = S(t) + E(t) + I(t) + R(t)$

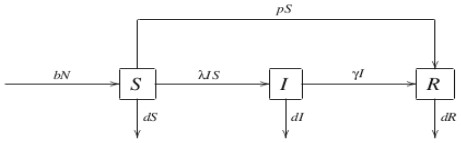
2.12 Acquired Immunity: SEIRS Model

In terms of compartmental models, loss of immunity results in a transfer of recovered individuals back to the susceptible compartment. We assume that the transfer rate is proportional to the size of the compartment.

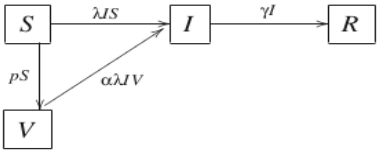


2.13 Disease Control and Prevention Measures: Immunization and Quarantine

Apart from medical treatment, two of the most effective and widely used prevention and control measures for infectious diseases are immunization and quarantine.By immunizing a large portion of the susceptible host population before or at the early phase of a disease outbreak, we can reduce the initial number S_0 of susceptible to a level that is below the threshold $\frac{\gamma}{\lambda}$, and by our threshold result.
From a compartmental modeling viewpoint, vaccination moves susceptible hosts directly to the recovered compartment without going through the I compartment. If we assume that a fraction p of all susceptible is vaccinated per unit time, then the new compartmental model will be,



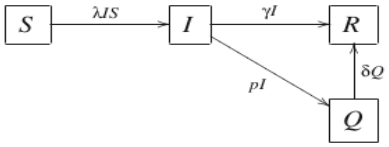
Issues with vaccination is that some vaccination can be leaky or imperfect; namely immunized host can still get infected, with smaller probability than unvaccinated host. Now to model this situation, we add a new compartment V of vaccinated host and an additional incidence term $\alpha\lambda VS$ due to the infection of vaccinated individuals. We obtain the transfer diagram,



Here $0 < \alpha \leq 1$ denotes the reduced probability of transmission due to immune protection from the vaccine.

Quarantine is a measure that isolates infectious individuals and hence prevents them from infecting others. We introduce a new compartment Q for the quarantined individuals and assume that quarantine is carried out in such a way that a fraction $0 < p \leq 1$ of infectious individuals will be

isolated.The transfer diagram is depicted where δ is the rate constant for the recovery of quarantined individuals.



2.14 The basic Reproduction Number R_0

The basic reproduction number R_0 ,is the single most important parameter in epidemic modeling. It measures the average number of secondary infections caused by a single infectious individual in an entirely susceptible population during the mean infectious period.In the context of the Kermack–McKendrick model, R_0 can be expressed as: $\lambda S_0 \frac{1}{\gamma}$. Which can be interpreted as,

average number of effective contacts of a single infectious host	·	initial susceptible population	·	mean infectious period

Using R_0 , the threshold phenomenon described earlier can be expressed as follows:
If $R_0 < 1$, then an epidemic will not occur;
If $R_0 > 1$, an epidemic will occur.
When models get more complex, R_0 may be harder to derive directly from the transfer diagram. Other methods for deriving R_0 exist. Most of them are based on the stability analysis of the disease-free equilibrium.

2.15 Analysis of Kermack McKendrick Model

$\frac{dS}{dt} = -\lambda IS$ (1)
$\frac{dI}{dt} = \lambda IS - \gamma I$ (2)
$\frac{dR}{dt} = \gamma I$ (3)
with initial conditions
$S(0) = S_0 > 0$, $I(0) = I_0 > 0$ and $R(0) = 0$.

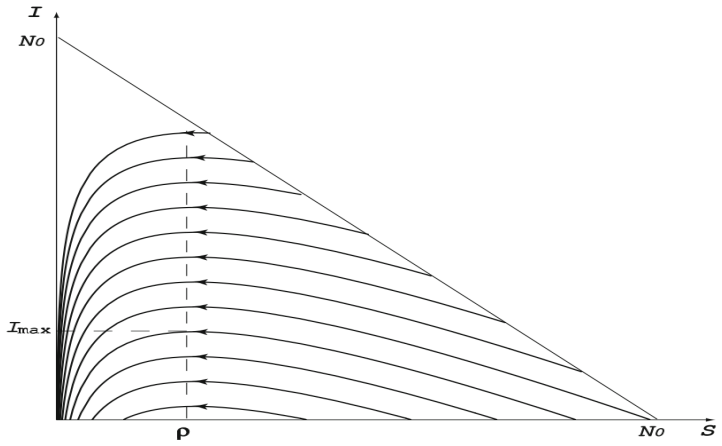
Simple Properties of Solutions
Property 1. Model is well posed.
We mean that non-negative initial conditions lead to non-negative solutions, namely, $S_0 \geq 0$, $I_0 \geq 0$, and $R_0 \geq 0$ imply $S(t) \geq 0$, $I(t) \geq 0$, and $R(t) \geq 0$ for $t \geq 0$.Another way to describe this is that the non-negative cone of $\mathbb{R}^3$, $\mathbb{R}^3_+ = \{(S, I, R) \in \mathbb{R}^3 | S \geq 0, I \geq 0, R \geq 0\}$, is positively invariant.
Property 2. Total population is constant.
Let $N(t) = S(t) + I(t) + R(t), N_0 = S_0 + I_0 + R_0$.
We obtain $N'(t) = 0$ for all $t \geq 0$, which implies $N(t) = N_0$ for all $t \geq 0$.
Property 3. Limit $\lim_{t\to\infty}(S(t), I(t), R(t)) = (S(\infty), I(\infty), R(\infty))$
we know $S'(t) = -\lambda I(t)S(t) \leq 0$.
Therefore, $S(t)$ is decreasing and bounded below by 0, and thus $S(\infty)$ exists.
Similarly, $R'(t) = \gamma I(t) \geq 0$ and $R(t)$ increasing and bounded above by N_0. Therefore, $R(\infty) \geq 0$

exists.
From $I(t) = N_0 - S(t) - R(t)$ we know that $I(\infty) = N_0 - S(\infty) - R(\infty) \geq 0$ exists.

2.16 Phase Portrait in the SI-Plane: Epidemic Curves

For a better understanding of the behaviors of solutions, we try to view their orbits in the SI-plane. Consider only the S, I equations:
$\frac{dS}{dt} = -\lambda IS$ (1)
$\frac{dI}{dt} = \lambda IS - \gamma I$ (2)
Dividing the two equations we obtain,
$\frac{dI}{dS} = -1 + \frac{\gamma}{\lambda S} = -1 + \frac{\rho}{S}$,where $\rho = \frac{\gamma}{\lambda}$ is the threshold number for S_0.
Integrating we obtain, $\phi(S, I) = I + S - \rho \log S = C$, where C is integration constant and can be determined from S_0 and I_0. Therefore function $\phi(S, I)$ remains constant along all the solutions. This implies that trajectories of system are given by the family of level curves $\phi(S, I) = c$.

2.17 Family of epidemic curves



- The maximum value I_{max} of I is achieved when $S = \rho$, the threshold value. This fact is also clear from the equation of I, since I' = 0 if and only if $S = \rho$, and $S = \rho$ is a critical point for I.
- If $S_0 < \rho$, then $I(t)$ decreases monotonically as t increases and the epidemic declines and no new outbreaks occur.
- If $S_0 > \rho$, then $I(t)$ initially increases monotonically while $S(t)$ decreases, $I(t)$ peaks when $S = \rho$, and then as $S(t)$ decreases below ρ, $I(t)$ decreases to 0. This gives the rise–peak–decline cycle of an epidemic.

2.18 Final Size Formula and the Severity of an Epidemic

3 Application

3.1 SIR Model Simulation

The Model

Here follow the 3 equations that govern the model dynamics:

$\frac{dS}{dt} = -\lambda SI + \delta R$

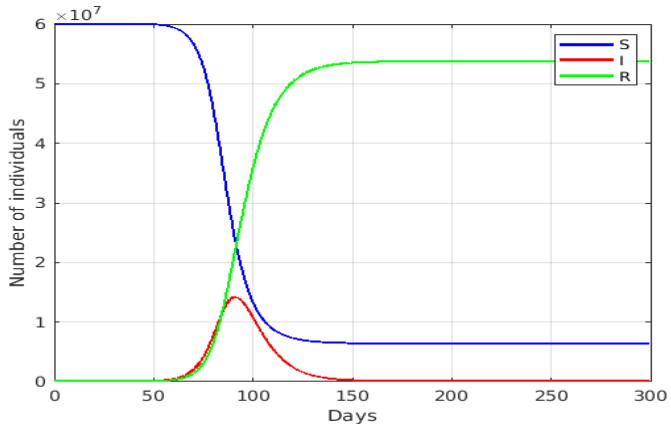
$\frac{dI}{dt} = \lambda SI - \gamma I$

$\frac{dR}{dt} = \gamma I - \delta R$

3.2 Model simulation code

```
% Model parameters
lambda = 5*10^-9; % rate of infection
gamma = 0.12; % rate of recovery
delta = 0.0; % rate of immunity loss
N = 6*10^7; % Total population N = S + I + R
I0 = 10; % initial number of infected
T = 300; % period of 300 days
dt = 1/4; % time interval of 6 hours (1/4 of a day)
fprintf('Value of parameter R0 is %.2f',N*lambda/gamma)
% Calculate the model
[S,I,R] = sir_model(lambda,gamma,delta,N,I0,T,dt);
% Plots that display the epidemic outbreak
tt = 0:dt:T-dt;
% Curve
plot(tt,S,'b',tt,I,'r',tt,R,'g','LineWidth',2); grid on;
xlabel('Days'); ylabel('Number of individuals');
legend('S','I','R');
% Map
plot(I(1:(T/dt)-1),I(2:T/dt),"LineWidth",1,"Color",'r');
hold on; grid on;
plot(I(2),I(1),'ob','MarkerSize',4);
xlabel('Infected at time t'); ylabel('Infected at time t+1');
hold off;
```

3.3 Graph



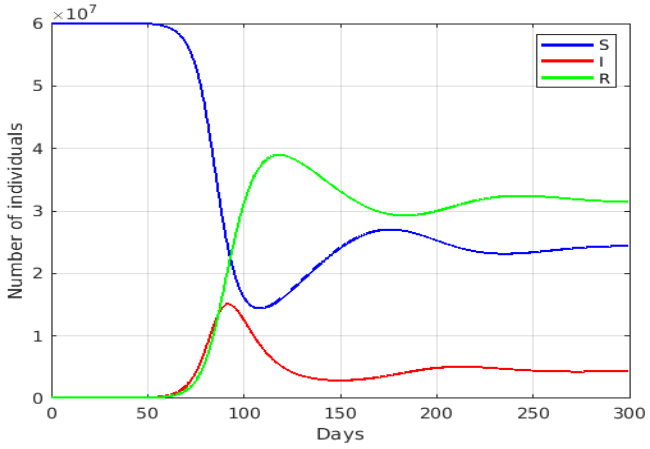
3.4 What if we consider immunity loss?

In a more general model, recovered individuals could lose their immunity after some time. Let's assume that immunity is lost, on average, after 60 days from recovery (delta = 1/60), and display the new simulation.

```
delta = 1/60; % rate of immunity loss
% Calculate the model
[S,I,R] = sir_model(lambda,gamma,delta,N,I0,T,dt);
% Curve
plot(tt,S,'b',tt,I,'r',tt,R,'g','LineWidth',2); grid on;
xlabel('Days');ylabel('Number of individuals');
legend('S','I','R');
```

```
function [S,I,R] = sir_model(lambda,gamma,delta,N,I0,T,dt)
    % if delta = 0 we assume a model without immunity loss
    S = zeros(1,T/dt);
    S(1) = N;
    I = zeros(1,T/dt);
    I(1) = I0;
    R = zeros(1,T/dt);
    for tt = 1:(T/dt)-1
        % Equations of the model
        dS = (-lambda*I(tt)*S(tt) + delta*R(tt)) * dt;
        dI = (lambda*I(tt)*S(tt) - gamma*I(tt)) * dt;
        dR = (gamma*I(tt) - delta*R(tt)) * dt;
        S(tt+1) = S(tt) + dS;
        I(tt+1) = I(tt) + dI;
        R(tt+1) = R(tt) + dR;
    end
end
```

3.5 Graph after immunity loss



4 Refrences

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