Corona Simulations - Documentation

1. Preface

This Simulation is based on a model devised by Prof. Yinon Ashkenazy, Dr. Michael Assaf, and Prof. Doron Gazit, and implemented by Prof. Nadav Katz, Yuval Zamir, Samuel Goldstein, Shimon Nowik, Roee Grant and Snir Avraham.

2. General description

The COVID-19 pandemic outbreak has highlighted the need for models of the epidemic that could help manage its progress, and understand its course, given governmental measures undertaken to contain and mitigate it. The code described here simulates evolution of infected, hospitalized, critically ill, dead, and recovered populations.

The simulation implements an age aware SIR model with rate equations as described in Fig. 1. The age awareness is an important ingredient for COVID-19 due to the strong demography dependence of the mortality and hospitalization rates [1]. Thus, all transition probabilities are age dependent, e.g., B_i which is the transition probability from the group of infected people I_i^{NR} to the group of hospitalized people H. The results of the simulation are continuously compared to empiric data from the Israeli public, as infection spreads.

Simulations in general are sensitive to the choice of parameters, this is particularly true for COVID-19, for which basic parameters are still somewhat unknown. Thus, the results of the simulations should not be taken nominally, but as a tool to manage the outbreak and map different strategies.

3. Model Description - rules and resulting limitations

    a)   The population is divided into age groups according to Israel's demographic tables.

b) Each age group can be infected by all other age groups in accordance with the infection rate.

c) We assume the entire population is susceptible to the disease. Otherwise, a new compartment S' has to be defined from which one cannot get infected.

d) We assume that only part of the infected population is identified using PCR tests and that only a fixed part of the infected population is thus measured, but that all infected population transmits the disease at a fixed rate. This is a limitation as the current policy in Israel and many other states is that the person quarantines oneself once symptoms onset, thus, probably resulting in a smaller number of infections. On the other hand, it is reasonable to assume that high viral load in symptomatic patients may lead to higher early infection rate. Thus, at the current state of knowledge we assume that infection rate is not affected by the state of diagnosis of the specific patient. Of course, hospitalized patients are taken out of the infection pool.

e) The infection rate in the simulation is both age and time dependent. We assume that closure measures can gradually or abruptly change the infection rate.

f) One can account for various medications that are tested, especially on critical patients, by changing the vector Γ_i.

g) The model is well-mixed. That is, it does not have spatial dependence in it. In order to take spatial dependence into account, in the simplest way, equations have to be written for the various compartments, S, I, H, C, D, R, for each spatial degree of freedom. That is, assuming the individuals are living on a network, where each individual has a degree k (number of people he/she interacts with), a differential equation for each k has to be written separately. Naturally, high-degree individuals, which have many interactions, have a higher probability of getting infected or infecting others. In Israel, which has different sectors in its population with very different demographic properties, such simplification might induce problems in the validity of the simulation, which should be tested in future work.

h) The model is sensitive to all parameters, especially to the various infection and recovery rates. In the current status of the outbreak, in which many aspects are unknown, both qualitatively and quantitatively, the parameters are merely an estimation from current data. Consequently, the strength of the model is not predicting absolute numbers of infected/critical/dead individuals. Rather, the strength of the model is in predicting how various measures such as lockdown, or gradual release from lockdown can relatively affect these numbers, compared to the absence of such measures.

i) All transition rates (β, γ, δ, δ', ε, ε') are age independent (except for the infection rate α which can also be set to be age dependent), whereas the transition probabilities (A,

B, Γ) are age dependent. e.g., once a patient is determined to be hospitalized, progress in the clinical timeline of the patientis independent of age. However, probability of being hospitalized, i.e., ending up in the H_i^{NR} group (destined for a critical state), is age dependent.

j) Total population size is conserved (deceased are counted as part of the population too).

k) The unknown part of infected patients, i.e., those who are not tested or undetected, is expressed by the factor η, defined as the fraction of identified patients from the total number of patients. η ultimately affects the total number of critical patients and fatalities, but not the general trends (such as the relative decrease in fatalities achieved by lockdown). We typically use $\eta = 0.1$. We note that previous estimates of this number using asymptomatic carriers as derived from "Diamond Princess" [9] are limited due to using PCR rather than post case serological rests and the lack of availability of PCR tests of asymptomatic patients in early stages. Actually, this number represents one of the biggest unknowns for COVID-19, as it folds both the unknown fraction of asymptomatic cases (which currently are estimated to be about 50% of the cases, but numbers in the literature vary substantially daily), and the undetected symptomatic cases, due to limited numbers of tests available, and other limitations of tests in each specific country.

l) All age specific rates and reactions are defined using clinical ratios as described in (see table 1 in the UCL paper) and are consistent with recent observations (see USA reports). All clinical data related to deterioration ratios between hospitalized and icu patients, and there is no reliable information regarding the total infected population including unidentified infected population.
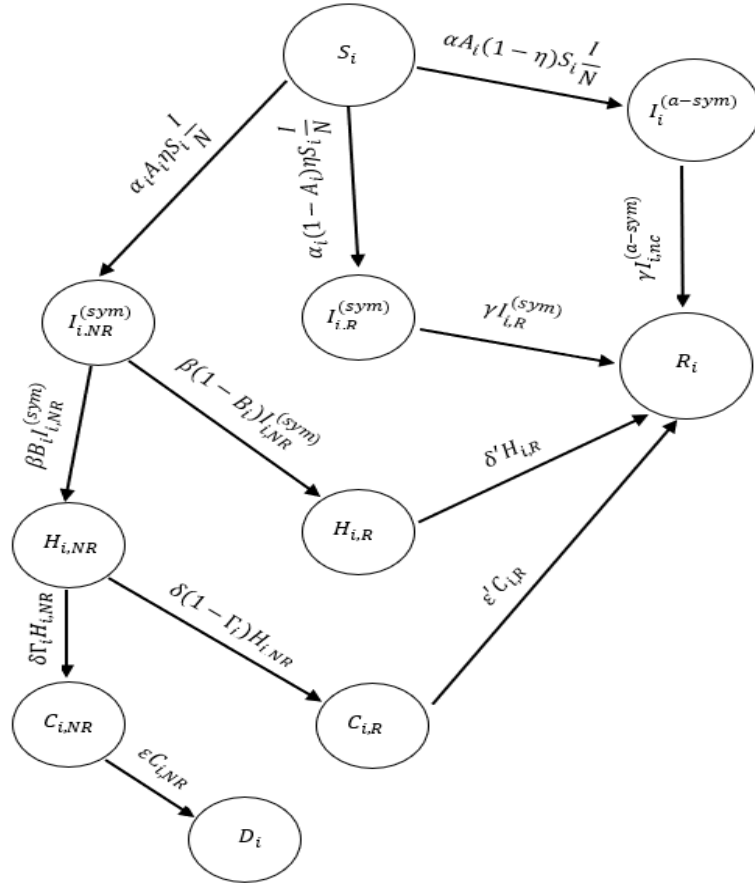
Figure 1 - Model, topology and rates indicated

Notations:

<u>Groups and related parameters</u>

S_i – age-based vector of susceptible individuals

I_i – age-based vector of infected individuals; ($I = \Sigma I_i$)

H_i – age-based vector of hospitalized patients

C_i – age-based vector of critical patients

D_i – age-based vector of dead patients

R_i – age-based vector of recovered patients

N – total population ($N = 9*10^6$)

S_0 – age-based initial condition for the susceptible individuals. This vector is varied per country in accordance with recent local population census. For Israel we used the 2019 census data.

S_0 = N*[0.197, 0.164, 0.14, 0.131, 0.118, 0.091, 0.081, 0.048, 0.03]

η – fraction of identified patients out of total infected population (typically taken at 0.1). This is based on the assumption that light symptoms, do not necessarily lead to test or hospitalization [11]. Named *DetectedI* in code.

<u>Probabilities</u>

A_i – age-based vector describing the probability to become hospitalized. As this number was calculated as part of the identified population, we assume that indeed this is per age ratio is taken out of the identified patients in each age group [4]. Named *pIH* (probability to move from I to H) in code.
A_i = [0.001, 0.003, 0.012, 0.032, 0.049, 0.102, 0.166, 0.243, 0.273]

B_i – age-based vector describing the probability to reach critical conditions given that a patient is hospitalized. Named *pHC* in code.
B_i = [0.05, 0.05, 0.05, 0.05, 0.063, 0.122, 0.274, 0.432, 0.709]

Γ_i – age-based vector describing mortality of critical patients ([4]). Name *pCD* in code.
Γ_i = [0.4, 0.4, 0.5, 0.5, 0.486, 0.482, 0.484, 0.486, 0.481]
(The above three tables are taken from [4] which was based on wide survey in China and agrees with the resulting probabilities gathered in the US[3])

Rates

α_i – baseline (without lock-down) age-based infection rate (for the initial growth period α_i = 1/3.4). This was taken as initially uniform and was fitted to universal observed growth rates.
β – rate of hospitalization of symptomatic patients (β = 1/5)
γ – rate of recovery of infected patients (γ = 1/14)
δ – rate of a hospitalized patient becoming critical (δ = 1/10)
δ' – rate of a hospitalized patient recovering (δ' = 1/20)
ε – rate of a critical patient dying (ε = 1/8)
ε' – rate of a critical patient recovering (ε' = 1/14)
NR/R – non-recovering/recovering track
   All rates are expressed in units of [1/days] and were taken using average rates as described in clinical study [2].

Governing differential equations:

$$(1) \quad \dot{S}_i = -\alpha S_i \frac{I}{N}$$

$$(2) \quad \dot{I}_{i,NR}^{(sym)} = \alpha A_i \eta S_i \frac{I}{N} - \beta I_{i,NR}^{(sym)}$$

$$(3) \quad \dot{I}_{i,R}^{(sym)} = \alpha(1 - A_i)\eta S_i \frac{I}{N} - \gamma I_{i,R}^{(sym)}$$

$$(4) \quad \dot{I}_i^{(a-sym)} = \alpha(1 - \eta)S_i \frac{I}{N} - \gamma I_i^{(a-sym)}$$

$$(5) \quad \dot{H}_{i,NR} = \beta B_i I_{i,NR}^{(sym)} - \delta H_{i,NR}$$

$$(6) \quad \dot{H}_{i,R} = \beta(1 - B_i)I_{i,NR}^{(sym)} - \delta'H_{i,R}$$

$$(7) \quad \dot{C}_{i,NR} = \delta \Gamma_i H_{i,NR} - \varepsilon C_{i,NR}{}^1$$
$$(8) \quad \dot{C}_{i,R} = \delta(1 - \Gamma_i) H_{i,NR} - \varepsilon' C_{i,R}$$
$$(9) \quad \dot{D}_i = \varepsilon C_{i,NR}$$
$$10 \quad \dot{R}_i = \beta I_{i,NR}^{(sym)} + \gamma I_i^{(a-sym)} + \delta' H_{i,R} + \varepsilon' C_{i,R}$$

4. Code Description

The code is divided into three main parts – system initialization and parameters, dynamics and plots. In the first part the simulation parameters (length, time step, case constants – see below) and constants (e.g. probabilities and rates) are set, and the data structures are initialized (most importantly – the infection rate matrix). In the second part the model described in the previous part is implemented via a loop over time steps. This simplistic method was chosen over advanced methods of ODE solution (such as RK45) in order for the user and developer to have greater control over the system's dynamics. The last part produces four figures – three of them depict the number of infected, hospitalized, critical patients and deceased at each point in time. The first of these three one shows the data per age group (see Figure 2 in this document), while the other two show the total amount in population (first in regular, and the other in log scale - Figure 3 and Figure 4). The last figure depicts both the conservation of population along the simulation, and the infection rate for each age group along the simulative time (see Figure 5).
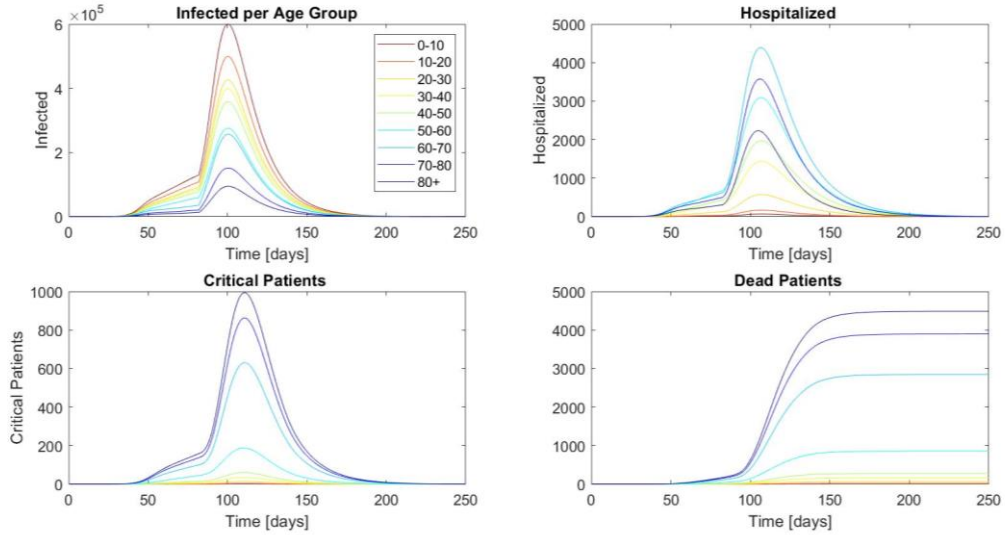

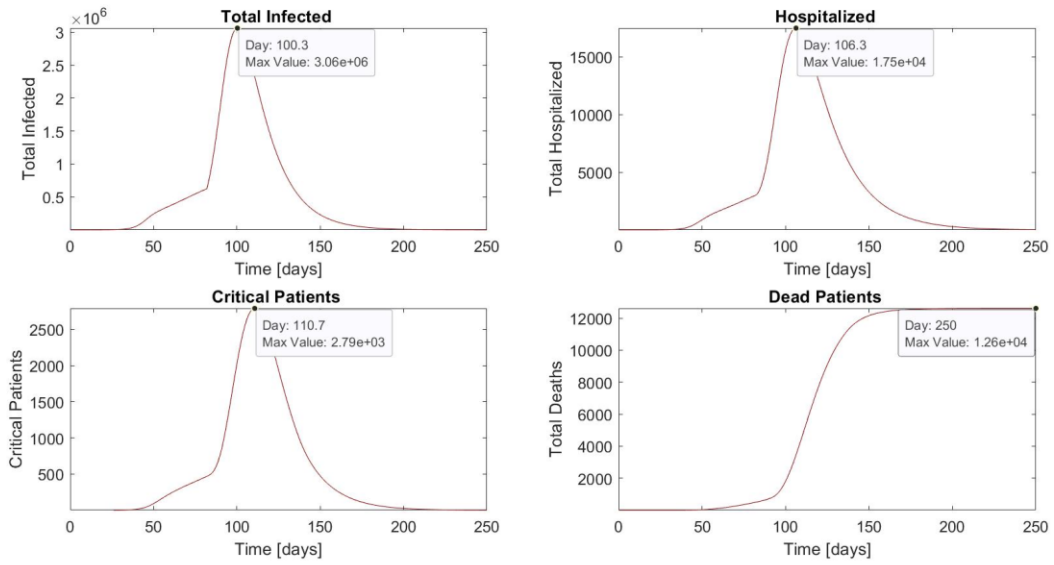*Figure 2 - Simulation results per age group - "Exit" case*

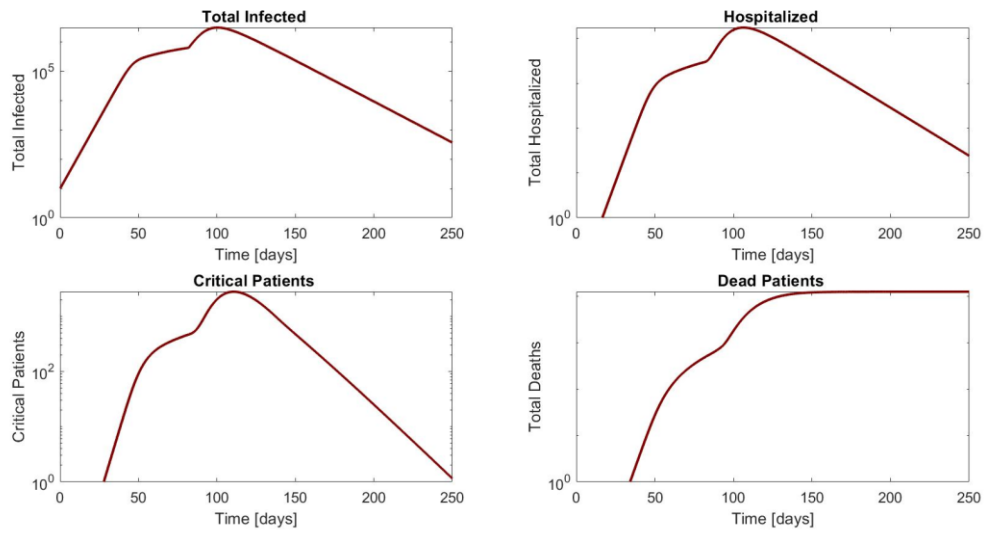*Figure 3 - Simulation results for entire population - "Exit" case*

Figure 4 - Simulation results for entire population, log scale - "Exit" case
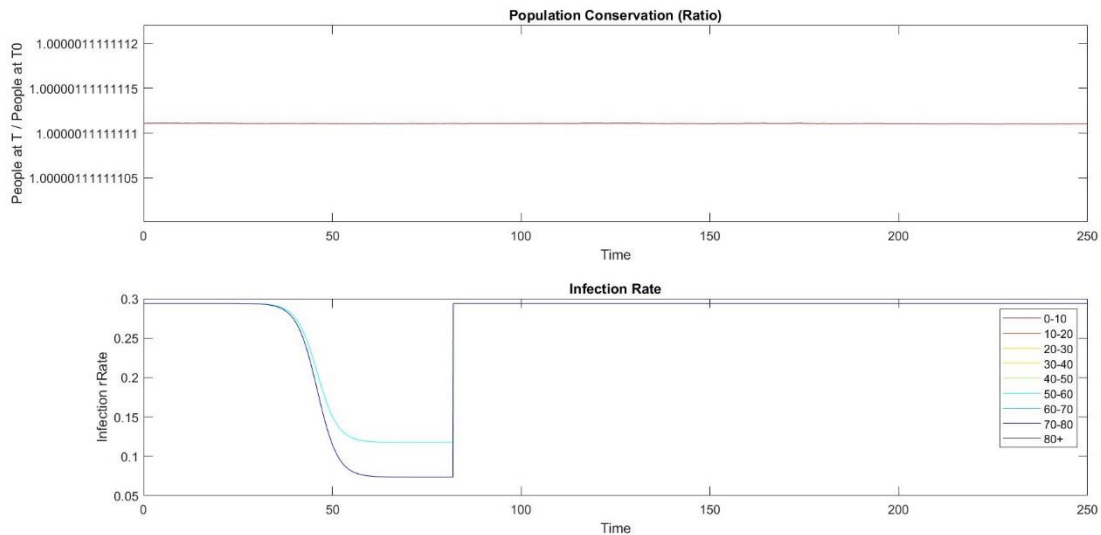
Figure 5 - Population conservation and infection rate vs. time - "Exit" case

Basic Usage

The main two parameters which should concern the basic user are – the length of the simulation, and the case being tested. Simulation length is set using simLength variable and it's units are days. The "Case" variable is a bit more complicated. Each case simulates the pandemic dynamics given some policiy, which effect the infection rate differently:

a. **Business as usual** – no protective measures are taken onceover. This means that the infection rate is fixed to it's basic value for all age group throughout the simulation. This, naturally, leads to very poor result. To use this case place 'BAU' as the value for the Case variable.
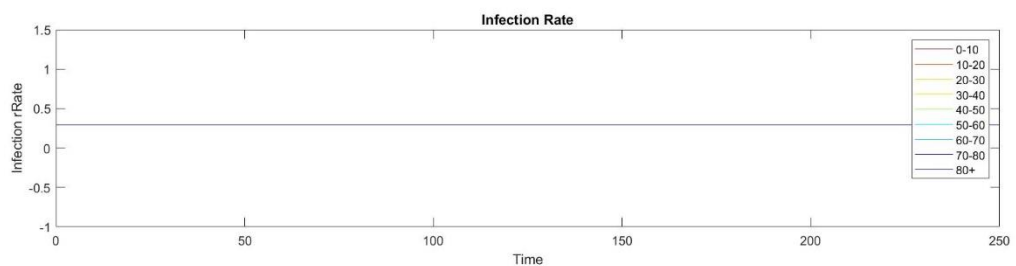

Figure 6 - Infection rate vs. time - "Business As Usual" case

b. **Lockdown** – Protective measures are taken to a severe state (25% of the base infection rate for the elderly, 40% for young people – see values for variables youngFactor and oldFactor), but no "exit strategy" is implemented. This case yields the best results but is obviously not realistic. It is worth noting that the restriction do not take in effect at once, but are gradually imposed along several days (the length of this period is determined by the restLength variable which

is set to 12 days). The process of gradually imposing the restrictions is simulated using a hyperbolic tangent function. The case label is LockDown.
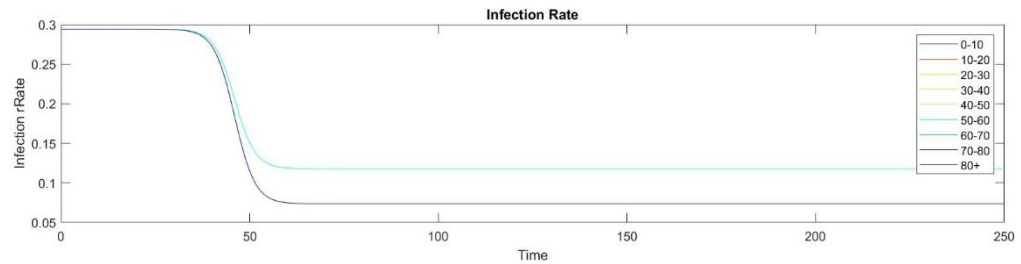

Figure 7 - Infection rate vs. time - "Lockdown" case

c. **Exit** - Same as the Lockdown case, yet at some point young and elderly population is returned back to normal (meaning – the infection rate goes back up to it's original value). The timing of the removal of the restriction for the young and elderly can differ – it is controlled via OpendDay1 and OpenDay2 variables (set by default to 6 and 11 weeks after the beginning of the restrictions). As opposed to the gradual imposing of the restrictions, their removal is almost instantaneous (as we believe will happen in reality). Use "Exit" label for this case.
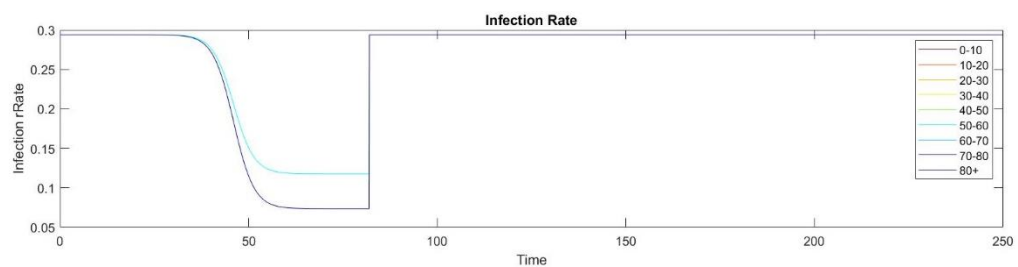

Figure 8 - Infection rate vs. time - "Exit" case

d. **Gradual Exit –** Very similar to the last case, yet the restrictions are removed gradually. The relieve is divided to four steps – first step is still complete lockdown (25% infection rate for the elderly, 40% for the young), major restrictions in the second stage step (90% restrictions up to 50 years old, 40% for 50-60, and still 25% for older), minor restrictions in the third stage (115% for people up to 50, 90% for 50-60, and yet still 25% for the elderly), and finally back to normal in the last stage (115% for all). This case attempts to emulate the leading strategy chosen by the Israeli ministry of health at the middle of April 2020. Notice that the removal of the restrictions is gradual in the sense that it is implemented steps (and not at once), but the change in the infection rate is not smooth as the imposing of the restriction (described in the Lockdown case) but is still discrete. For this case use "GradualExit" label.
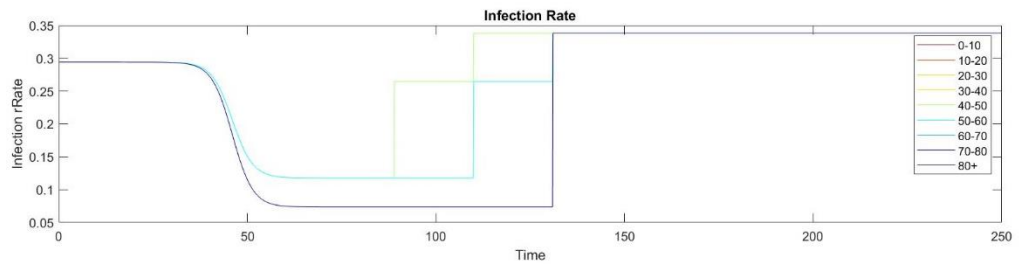
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Figure 9 - Infection rate vs. time - "Gradual Exit" case

Notice that any of the values mentioned in this section could be changed, yet they (as other undiscussed parameters) were chosen to best fit empirical results. Therefore, it is encouraged not to change values which control past behavior (such as restLength or youngFactor), but to focus on variables which control future results (such as the stages' infections rates).

Advanced Usage

Once mastered the basic usage of the simulation, the code offers more flexibility in the manner of its execution. Firstly, one can **create their own case** by simply changing some values of the infection rate over time. Note that rI is indeed a matrix with rows as the numbers of the time steps, and columns as the numbers of the age groups (9). By changing future values or rI, one can create their own exit strategy. It is recommended to keep the restrictions imposing part as is (for it describes well the past policy and it's results in Israel), and to change only future events. Note that the first day of the simulation correlates with the 12th of February (when there were about ten patients in Israel).

Some other key parameters of the simulation, which a more advanced user should know of are **maxCriticalPatients** (which describes the health system's capacity for critical patients), **DetectedI** (corresponding with η at chapter 3, describing the percentage of detected patients out of infected, set by default to 1/10) and **restDay0** (matches the first day of the restrictions, around the 21st of March).

The simulation can easily be modified to match other countries by changing the ages distribution (pAge) and population size (N), assuming other parameters hardly change between countries (have to do mostly with the disease features, not with the country). Yet some calibration will be required before properly executing the code (dates of restriction imposing for instance, and the intensity of the lockdown). This procedure has already been done, and one can read about it's results in an article being written these days. If one wants to examine the code please contact Yuval Zamir (yuval.zamir@mail.huji.ac.il).

5. Contacts

For bug reports and code related questions please contact Yuval Zamir (yuval.zamir@mail.huji.ac.il). For detailed data about the model please contact Dr. Michael Assaf (michael.assaf@mail.huji.ac.il).

6. Releases

Version 1.0.0 – released 13th of April.

7. References

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