Did you know? How Simulations May Help Us to Understand the Dynamics of COVID-19 Spread. – Visualizing Non-Intuitive Behaviours of a Pandemic (pansim.uni-jena.de)

The new coronavirus SARS-COV-2 is currently impacting life around the globe.[1] The rapid spread of this viral disease might be highly challenging for health care systems. This was seen in Northern Italy and in New York City for example.[2] Governments reacted with different measures such as shutdown of all schools, universities and up to a general curfew. All of those measures have a huge impact on the economy. The United Nations secretary general has stated recently: "The COVID-19 pandemic is one of the most dangerous challenges this world has faced in our lifetime. It is above all a human crisis with severe health and socio-economic consequences".[3] According to the European mortality observing network[4]: "Pooled mortality estimates from the EuroMOMO network continue to show a markedly increased level of excess all-cause mortality overall for the participating European countries, coinciding with the current COVID-19 pandemic" (see Figure 1).

There are many aspects that need to be considered when considering measures such as lockdowns. One of the main problems is that aspects of the dynamical behaviour are hard to grasp with our thinking in the context of our experiences. Our understanding of cause and relationship is mostly related to "linear thinking". This means that there is a linear relationship between a potential influence and a result. An example would be "If you buy twice as many apples you have to pay twice the amount of money." This concept however does not work for exponential growth rates. Those are governed by rules that are highly sensitive to the conditions of the underlying process. In the context of a viral disease we can consider the concept of growth rate describing the factor that describes the number of affected individuals divided by the number the previous day. For example, if you change the growth rate in an ideal exponential scenario from 1.1 by 10% to 1.21 you will get after only 10 days more than twice and after 20 days more than six times the amount (see Figure 2). In the case of COVID-19 it has been estimated that the reproductive number can be as large as 3.9[5] in this particular study. The exponential growth however could only be found in a situation where there are an infinite number of individuals that can get viral disease. This is obviously not the case. Exponential-like growth can be observed only in the beginning of the spread, where the number of people who do not have the disease is a lot bigger in comparison to the infectious individuals. In order to understand the spread and aspects of the dynamics of the disease we can use a modelling approach.[6]

Here we explore an agent-based model where dots as surrogates for individuals move around in a given space. The simulation can be found at https://pansim.uni-jena.de. Each of the dots has one of the following states: susceptible, infectious without symptoms, infectious with symptoms, recovered and immune. Once infected, the dots go through the disease cycle described by the states. The dots move around in the space with a given "mobility". Once the dots get aware of the disease they change their mobility.

The ultimate goal would be to eradicate the SARS-2 virus worldwide. This is unlikely to achieve on a short-term scale because of its pandemic characteristic. When the pandemic runs through the population a key figure is the maximum number of active cases. Since a certain percentage of the active cases will require intensive care the maximum number of active cases determines whether or not the healthcare system runs at its limit or not.

In order to model different theoretical scenarios, we have implemented predefined parameter settings. The different scenarios described in the following relate a "default" parameter setting that is used to compare the modifications.

1 | SCENARIO I: LESS INITIALLY INFECTED

This scenario describes a situation where the initial number of people who are infected in the model population is reduced in comparison to the default situation. It is interesting that the number is important since the initial phase of an epidemic might be therefore an important point of attack for containment measures.
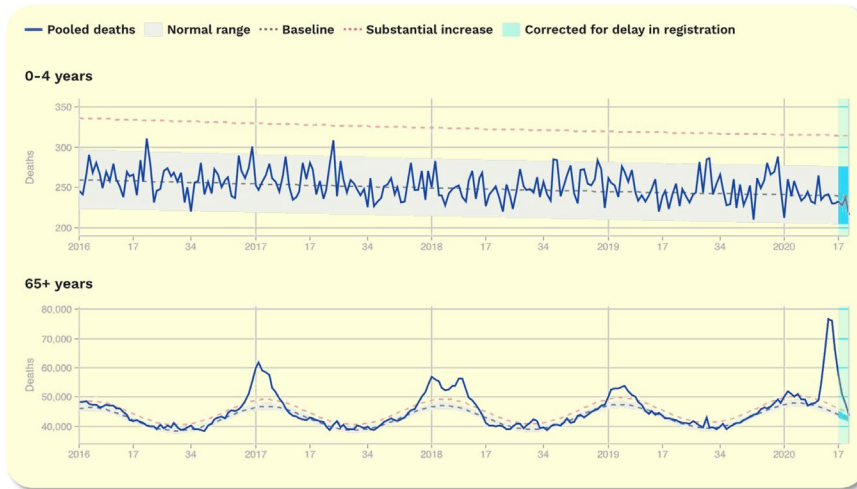
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FIGURE 1 Mortality in Europe over time according to age groups. The y-axis refers to the number of deaths per week. A clear excess of overall mortality is seen in the beginning of week 15 of the year 2020 as compared to the previous years. Modified from: https://www.euromomo.eu/graphs-andmaps/ [28 May 2020]
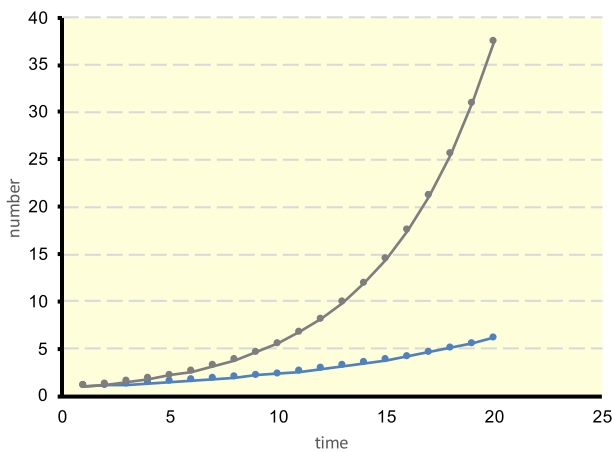

FIGURE 2 Exponential growth is highly sensitive to its parameters. In this example the growth rate of 1.1 (blue) has been increased only by 10% (red)

2 | SCENARIO II: HALF THE INFECTION PROBABILITY

This shows that the infection probability is a central parameter for the spread of the disease and the maximum number of active cases. Any measure that reduces the infection probability will help to reduce the value of the maximum number of active cases. In this context it is worthwhile to think about physical distancing and arguments for or against wearing nose and mouth masks.

3 | SCENARIO III AND IV: FRACTION OF POPULATION IS IMMUNE

This shows the effect of a potential vaccination or if the population has been in contact with the virus previously. In scenario III, a third is immune to the disease, whereas in

scenario IV two thirds is. As expected the maximum number of active cases is drastically reduced.

4 | SCENARIO V: SICK PEOPLE REMAIN MOBILE

If sick people remain mobile, the maximum number of active cases will increase. This suggests that it is beneficial, that the number of contacts of an infectious person is low to slow down the spread.

5 | SCENARIO VI: INFECTION DETECTED EARLIER

This would reflect a situation where testing of the disease is available on a large scale to identify infectious individuals. In the model, infected agents reduce their mobility earlier and therefore the transmission rate is reduced.

6 | SCENARIO VII: SUPER MOBILE EXIST

Here we simulate the case that a given number of individuals have a much higher mobility than the rest of the simulated population. This high mobility is kept at all times in the simulation. The simulation shows much higher values for the maximum number of active cases.

7 | SCENARIO VIII AND IX: LOCKDOWN WITH A THRESHOLD

These scenarios describe a population-wide lockdown based on a threshold of active cases at a given time. The lockdown

measure reduces the maximum number of active cases in the model. If the lockdown is imposed at a lower threshold the effect is stronger. A second value allows setting, to which fraction of the lockdown threshold the number of active cases needs to drop in order to lift the lockdown.

As pointed out earlier, the behaviour of the spread is highly sensitive to the initial parameters. That is why it is difficult to predict the spread and hard to estimate when to impose drastic measures such as lockdowns. There are however features in the model that are important to note and give consistent results over a broad range of parameter sets. For example that if one reduces the infection probability; the speed of the spread is slowed down. That means that any measure that leads to the reduction of that probability would reduce the maximum number of active cases and hence would help to reduce the risk of pushing the health care system to its limit. A complicating issue with COVID-19 is that a substantial number of people show only mild or even no symptoms,[7] hence remaining undetected while spreading the virus.

One other problem of controlling the disease is that there are delays in the underlying biology. It is known systems that have time delays in the feedback loop might exhibit oscillatory behaviour.[8] This is what we see in the model (Figure 3) for the active cases.

Understanding the dynamical aspects of the disease is crucial for proper control. It is therefore important to educate the public about the unintuitive behaviour of the spreading of a disease like COVID-19. The agent-based model might be a good tool to communicate the epidemiological characteristics. The model makes it possible to explore the effects of the different parameters on the behaviour of the spread and key outcomes such as peak number of active cases or total number of affected individuals. The input parameters can be changed interactively on the website.

According to the model one effective way to slow down the disease would be to reduce the contacts of infectious individuals. In this regard it is discussed whether it might be helpful to trace contacts and to test for the disease in a targeted manner.[9]

The World Health Organization (WHO) has defined priorities for research related to COVID-19. Among those top priorities is "the natural history of the virus, its transmission and diagnosis".[10] From an epidemiological point of view the way of transmission has a prominent role. For example, it would have a tremendous impact on the prevention strategy if the virus would be transmitted over food or drinking water such as *Escherichia coli* bacteria or sapoviruses.[11] The model also shows that super mobile individuals that have contact with many others contribute to a faster spread if they are infectious.

It appears to be certain that the topic of COVID-19 with currently 41 36 056 confirmed cases and 283 478 total deaths worldwide (as of 11 May 2020)[12] will engage our interest for the upcoming months. However one should not forget that other health topics are also on the table. According to the latest numbers: "Tobacco kills more than 8 million people globally every year. More than 7 million of these deaths are from direct tobacco use and around 1.2 million are because of non-smokers being exposed to secondhand smoke",[13] this is all because of a behaviour that could been stopped immediately, at least in theory.

8 | METHODS

Agent-based model: The agent-based model (ABM) presented here is based on the idea of the classical SIR model and expanded by additional states. The SIR model describes the spread of an infectious disease in a population using three population state quantities: susceptible (S), infectious (I) and recovered (R).[5] The dynamics of the SIR model is governed by different transition rates between the states, that can be

FIGURE 3 Behaviour of the model with a lockdown criterion based on a threshold (screenshot from https://pansim. uni-jena.de). In this setting a second lockdown was required. Notice that after imposing the lockdown the number is still increasing, in this case by a factor of two to three. This overshoot is much smaller in the second lockdown phase. This is because of the fact that a considerable fraction got infected and turned to the recovered/immune stage. If however this fraction is small, steep increase would be possible again
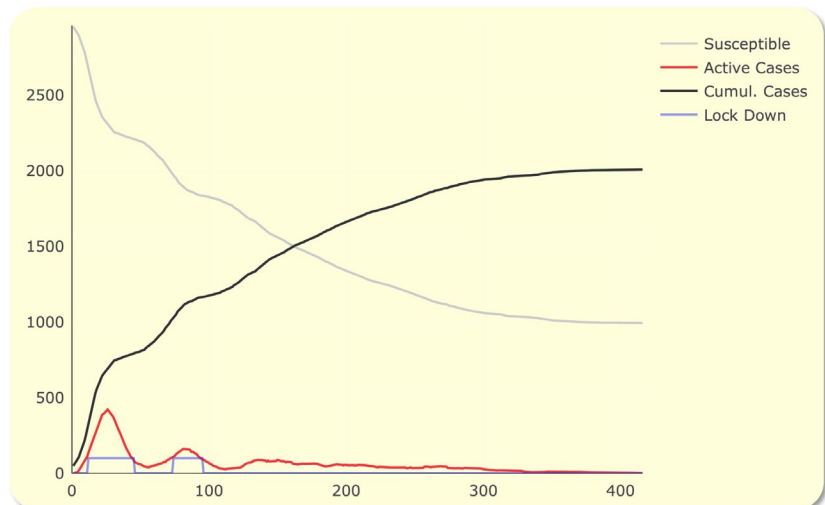
explicitly modelled by a system of differential equations. pansim, on the other hand, simulated a population of entities (agents) that behave individually according to simple rules in a simulation space. In contrast to a mathematically formulated model, such rules can be easily understood and yet can produce similar outcomes despite the stochastic nature of ABMs.[14] A simple ABM can approximate the SIR model by using three instructions that each agent obeys: (a) move through the simulated space, (b) if a susceptible agent is near an infected agent, change state from susceptible to infected, (c) if an agent is infected and a certain time has passed, change the state to recovered (See Figure 1). Behaviour rules can be programmed to reflect individual behaviour of agents even more realistically. This makes it possible to produce complex interactions between agents, which may lead to unexpected, emergent behaviour from those simple rules.[15,16]

Technical implementation: pansim was written in JavaScript using the p5.js[17] and plotly.js[18] libraries. p5.js is a graphical library that allows for simple creation of visual elements in JavaScript. Built-in functions of p5.js were used to create graphical representations of the agents for the pansim simulation. p5.js is built around the 'draw()' main loop function, which is periodically called and is used to update the simulation in time. plotly.js has been used for generating live-updating plots of the data produced during the model run.

The pansim model uses object-oriented programming to produce individual agents with the "Person" object. "Person" describes the states agents can assume (susceptible, infected, recovered, immune), how they behave and how agents are graphically represented. The 'Town' object takes user input and builds a corresponding population of agents and passes down user-defined behaviour parameters to the agents. Thus, users of pansim can change simulation parameters as desired. After the model parameters are set, the simulation starts and updates the agents' position using a random walk by iteratively calling p5.js's 'draw()' function. After each update interval, the agents check if they are in contact with an infected agent, ie if the distance between any agent is less than their radius, and change their status accordingly. The probability of infection upon contact can be specified, so that not every contact leads to an infection. If an agent is infected, an internal timer is incremented after each update interval. An infected agent progresses from an infectious but asymptomatic time interval (time infectious without symptoms, TIWOS) to an infectious time interval with symptoms (TIWS).[19] Agents can change their mobility during the symptomatic time interval. The user can set for how many simulation updates the TIWOS and TIWS phase should last. In addition to the three classic states from the SIR model, a population of super mobile agents can be included. Those agents have three times the mobility of susceptible agents throughout the model run despite their infection state. The user has the option to introduce a population-wise lockdown by specifying a threshold of symptomatic agents. In that case, all agents reduce their mobility except super mobile agents.

The number of susceptible (grey), symptomatic (red) and total number of infected agents (black) is counted after each update interval and displayed in a live-updating plotly.js graph. The fraction of the population that got infected and the maximum fraction of active cases is displayed in the control panel of pansim to allow users to compare different simulation outcomes.

CONFLICT OF INTEREST
None.

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