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Modeling the interplay between epidemics and regional socio-economics

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ABSTRACT

In this study we present a dynamical agent-based model to investigate the interplay between the socio-economy of and SEIRS-type epidemic spreading over a geographical area, divided to smaller area districts and further to smallest area cells. The model treats the populations of cells and authorities of districts as agents, such that the former can reduce their economic activity and the latter can recommend economic activity reduction both with the overall goal to slow down the epidemic spreading. The agents make decisions with the aim of attaining as high social positions as possible relative to other agents. They evaluate their social positions based on the local and regional infection rates, compliance to the authorities’ regulations, regional drops in economic activity, and the efforts they make to mitigate the spread of epidemic. We find that the willingness of populations to comply with authorities’ recommendations has the most drastic effect to the spreading of epidemic: periodic waves spread almost unimpeded in non-compliant populations, while in compliant ones the spread is minimal with a chaotic spreading pattern and significantly lower infection rates. Health and economic concerns of agents turned out to have lesser roles, the former increasing their efforts and the latter decreasing them.

Introduction

In today’s world variably populated urban and rural areas and especially people moving around and between them, are the main causes for infectious diseases spreading and wide-spread epidemic. This can cause health and economic concerns among general public as well as governments and local authorities as to what kind of individual and/or societal level measures, such as recommendations and restrictions of various kinds to confine the epidemic spreading and mitigate its effects, to put in place. How effective these non-pharmaceutical interventions (NPIs) turn out to be, depends to large extent on the compliance of individuals. Thus the epidemic spread and the behaviour of people are intertwined, as the individuals’ movements and interactions between individuals serve as the main engines of disease spreading. Apart from the NPIs by the authorities of countries or its districts, there is yet another issue for them to consider, namely how to keep the society, economy, and social functions running in some sort of balance. In order to understand the epidemic spreading and its socio-economic effects, we consider the complex dynamics of the whole societal system, resulting in from an interplay of mutually intertwined epidemic spreading, population as disease carrier and acting on NPIs, and authorities implementing NPIs to take care of social and economic welfare.

In order to understand the complex dynamics of epidemic spreading and issues related to it, modelling has turned out to be the main methodological approach. In terms of modelling the epidemic itself, one identifies four categories (see¹):

(i) **compartmental models** with population divided to compartments reflecting its health status,
(ii) **metapopulation models** based on networks of sub-populations connected by mobility,
(iii) **statistical models** capturing the evolution of epidemic by inferring key parameters and behaviour from data,
(iv) **agent-based models** capturing the spreading patterns at the level of single individuals.

Of these models the compartmental approach has become popular and quite successful in predicting the course of epidemics, because it can be extended to take into account different epidemiological properties of the infection spreading. However, in the present study we need to go further and describe the intertwined process of the epidemic, behaviour of population, authorities NPIs, and society level welfare. For doing this we will construct a hybrid model of compartmental epidemics, linked with population agents and authority agents, the building blocks of which we discuss next.

For the basic building block we choose the compartmental model, which, in its original form, is the SIR (Susceptible, Infected, Recovered) model²–⁴. This model has been modified and adapted to predict the spreading of various infectious diseases, as was demonstrated, e.g., in the case of swine flu (AH1N1) pandemic, by a SEIRS model (E stands for Exposed).
developed by Barrio et al. Recently this model was applied to COVID-19 pandemic and it turned out to describe its course in various countries quite realistically. We adopt this SEIRS model to describe the epidemic spreading over geographical area in our hybrid model. The main characteristics of this model are: 1) it considers that the probability of infection transmission from one compartment to the other is proportional to the probability of having at least one contact that is proportional to the population density and includes time delays that define the progression of the disease in an infected person; 2) it considers a geographical area divided into a two dimensional grid of cells, in each of which a SEIRS model is evolving with time, according to the population density of the cell; 3) the probability of infection is assumed stochastic and dependent on mobility parameters that are used to simulate a network of contacts and reflect the consequences of distancing measures and regional authorities’ interventions to mitigate the disease spreading; 4) network of connections between non-neighbour or distant cells can be defined to simulate transportation (aerial or road) routes that enable e.g. the disease spreading between cities far apart.

As the other building blocks of our hybrid model we introduce two types of agents, namely the population agents in each of the SEIRS model grid cell of the geographical area of a country and the authority agents governing the population agents in the collections of grid cells constituting districts of that country. These two types of agents are introduced to describe the interactions between the popular and authorities’ responses to epidemics and the epidemics itself, from the socio-economic or welfare perspective. The behaviour of both of these agents is based on a single assumption of status maximization as the source of human motivations, called Better Than Hypothesis (BTH), developed in our previous studies. The BTH shares its basic assumption about the human motivation as being rooted in human psychology to the behavioural concepts of superiority and inferiority, with social sciences to the desire for gaining status, and with neurological studies to how human brain processes status-relevant information. Therefore, it makes sense to use an approach like BTH in the context of comprehensive agent-based social simulations, given the ubiquity of social hierarchies in human societies.

In the context of COVID-19 pandemic an agent-based model was employed to study the economic effects of lockdowns propagating through supply chains, but the model did not contain any feedback from the economy to the epidemic itself. Only recently a study has raised questions about the impact of epidemic on economy and whether and how well various NPIs are able to mitigate it. There are also two agent-based model studies addressing the connection between economy and public health. In these studies the observed economic decline is caused by factors such as morbidity instead of the agents making conscious decisions in trying to protect themselves from the disease by, e.g., reducing their risk for getting infected in situations like shopping, public gatherings or other similar activities. Naturally, the questions of the psychological impacts of pandemic on both individual and societal levels are complex, making them challenging to model, but the BTH-approach allows systematic inclusion of different psychological effects to agent-based models.

The public health vs. economy discourse concerns, in essence, societal values, thus raising the question which one to prioritize over the other? This question could be phrased as “is it better to safeguard one at the expense of the others?”, from which one can readily see how BTH relates to the topic of this study. However, there is a deeper connection between the BTH and societal values that stems from the simple fact that different people use different criteria to assess their overall social positions. In the context of a epidemic people may, for example, value their personal freedom over the authorities recommendations, and the authorities may value economic growth over mitigating the epidemic. Using the BTH one can model the effects of these attitudes on the behaviour of different human groups and, in the epidemic context, how this behaviour affects the spreading patterns of the disease.

Methods

In order to investigate the interactions between the responses of the population and authorities to the epidemics and epidemics itself as well as their interplay with economics, we devise a human society and geographical area model of compartmental epidemics and socio-economic with populations and authorities as separate agents, as depicted in Fig. 1. The model consists of a large geographical area of a country divided into several smaller jurisdictions or districts with their own authorities and socio-economy. These districts are further subdivided into geographical cells, each with its own population. The epidemic spreading takes place among the population of each cell as well as between the populations of different cells. In addition, the socio-economy of a country is included in the model by introducing the behavioural dynamics of district authorities and geographical cell population agents, as illustrated in Fig. 1.

Here the spreading of epidemic is based on the SEIRS model introduced by Barrio et al., in which the epidemic can spread from one cell to a neighboring cell with probability γ, or to a more distant cell with some other probability to mimic different means of transportation e.g. air, rail, or roads. In the present study, and for the sake of simplicity, such longer distance spreading is not considered. The SEIRS model has the following set of parameters that govern the epidemic spreading in each geographical grid cell: (i) the period of latency before those who contract the disease become infectious ε, (ii) the period of infectiousness σ, (iii) the period of immunity ω, (iv) the transitivity of the disease β, and (v) the mortality rate μ. The time-evolution of the epidemic, i.e. the numbers of susceptible (S), exposed (E), infected (I) and recovered (R), are governed by
Figure 1. A flowchart of the model. The blue oval is describing the BTH-agent model components, while the yellow oval the SEIRS epidemic spreading model components. The red line separates the different scales of the model: above it there are the districts, and below the local populations. The rectangular grid in the upper right-hand corner illustrates the relative scale and division of the geographical area (largest square) to districts (9 smaller squares, numbered) and further to grid cells (smallest squares). The parameters and set values of the SEIRS model are as follows: (i) the period of latency $\varepsilon = 1$; (ii) the period of infectiousness $\sigma = 14$; (iii) the period of immunity $\omega = 140$; (iv) the transmission rate in cells $\beta = 0.91$; (v) the mortality rate $\mu = 3.69 \times 10^{-5}$; (vi) the survival parameter $\lambda = 0.9973$; (vii) the spreading probability $v_c = 0.1$. Note that the used value of the $v_c$ parameter is different from that of the original papers, where values in between 0.08 – 0.33 were adopted.

The populations of the geographical grid cells and district authorities of our socio-economic model are treated as agents, whose behavior is characterized by the choices they make to lower their economic activity in order to lower the chances of the epidemic spreading. This requires a model of the dependence of probability $v_t^i$ of the epidemic spreading from one geographical cell to the next on their economic activity. For the sake of simplicity, this relation is assumed to be linear:

$$v_t^i = v_0 - x_i v_{\text{max}},$$  

where $v_0$ is the maximum possible value of the mobility parameter, $0 \leq x_i \leq 1$ is the proportional reduction of the socio-economic activity of the population agent $i$, and $v_{\text{max}} < v_0$ is the maximum reduction in the infectiousness of the disease that the
socio-economic measures can deliver. We assume that the population agents will not reduce their economic activity below the level necessary for their survival, meaning that $x_i$ as defined above refers specifically to the non-essential part of the economic activity of the agents. This encompasses basically anything not related to acquiring bare necessities such as food, clothing, electricity, paying rents and the like.

The role of the district authorities is to set recommendations for the minimum economic activity reduction $0 \leq X_i \leq 1$ that the population in their districts are encouraged to observe, while the population agents react directly to these recommendations and to the epidemic itself. Again, we assume that the district authorities’ recommendations concern the non-essential economic activities. From now on, the quantities denoted by upper case letters refer to those belonging to the district authority agents, while the lower case letters refer to the quantities associated with the population agents. The district authority regulations basically reflect to those restrictions that affect the spending patterns of the populations, ranging from simple proximity rules to outright business closures. For the sake of simplicity, the businesses of the geographical cells are thought to be incorporated into the concern they have for the relative mean reduction of the economic activity, $X_i$.

In the BTH for the population agents, we take into account the values that they associate with their economic contribution to fighting the epidemic. In the BTH, their utility takes the form

$$u_i = w_i^x (x_i - X_i^0) + w_i^y (y_i - X_i^0) + w_i^c (c_i - X_i^0),$$

where $x_i$ is any measure by which agent $i$ can be compared to others, $e_i$ is the set of agents which agent $i$ compares itself with, and $w_i^x$, $w_i^y$, and $w_i^c$ are the weights that determine how important it is for the agent $i$ to rank high on the comparison scale $a$, i.e., how much value agent $i$ places on $a$. Analogously to the population agents, the district authority agents, too, value making efforts to keep the epidemic at bay, which in their case amounts making recommendations or restrictions for the population agents to follow, while aiming at low infection rates. These values are defined by the weights $W_i^X$ and $W_i^Y$, respectively, for the district authority agent $i$. As the setters of restrictions or rules, they do not have the compliance characteristic of the population agents. Instead, we have chosen to include the concern they have for the relative mean reduction of the economic activity, $Z_i'$, in their districts, defined as follows

$$Z_i' = \frac{1}{|P_i|} \sum_{x_k \in P_i} Z_i' = 1 - Z_i'. $$

where $P_i$ is the set of all population agents residing in the geographical area the district authority agent $i$ governs. The gross domestic product (gdp) $Z_i$ of the district $i$ is related to $Z_i'$ in the following manner:

$$Z_i = 1 - Z_i'. $$
The weight that describes the value the district authority agent attaches to \( Z_i' \) is denoted with \( W_i^Z \). With these choices for the district authority concerns, their utility function takes the form,

\[
U_i = W_i^X (X_i + \sum_{j \in E_i} (X_i - X_j)) + W_i^Y (Y_i + \sum_{j \in E_i} (Y_i - Y_j)) + W_i^Z (Z_i' + \sum_{j \in E_i} (Z_i' - Z_j)),
\]

(10)

where \( Y_i \) is the average infection rate of district \( i \). Just like in the case of the population agents, it is assumed that the district authority agents want to keep the restrictions to the minimum, meaning that they choose their recommendations or restrictions \( X_i \) so that \( U_i = 0 \). Again, this implies \( W_i^X < 0 \) for all authority agents. Hence from Eq. (10) we obtain:

\[
X_i = \frac{1}{|E_i| + 1} (\sum_{j \in E_i} X_j - \frac{W_i^Y}{W_i^X} (Y_i + \sum_{j \in E_i} (Y_i - Y_j)) - \frac{W_i^Z}{W_i^X} (Z_i' + \sum_{j \in E_i} (Z_i' - Z_j))).
\]

(11)

In Eqs. 7 and 11 we assume that if \( x_i \) and \( X_i \) are outside their range, they are set to 0 or 1, appropriately, depending on whether the result is below the former, or larger than the latter. One of the basic properties of these value variables is that their sign determines, whether agents seek to minimize or maximize the quantity that the parameter refers to, while the absolute value of the parameter determines the strength of this tendency. Thus, for example, a district authority agent with negative \( W_i^Y \) would seek to minimize the infection rates in its own district, whereas an authority agent with positive \( W_i^Y \) would take the herd immunity approach and seeks to encourage the spread of the epidemic. However, it should be noted that in deriving Eqs. 7 and 11 we have assumed that the agents will do the minimum allowed by their utilities, so studying the effects of a true herd immunity approach is beyond the scope of this study. Hence, we generally also assume that \( W_i^Y < 0 \) for all the district authority agents, and \( w_i^Y < 0 \) for all the population agents.

Here it is assumed that the district authority agents compare themselves to all other district authority agents in the model, while the population agents only compare themselves to their eight neighboring agents, if they have that many: in this study we use wall boundary conditions, so the population agents in the corners of the whole model area only have three comparison targets, while other agents on the boundary have five. There are no such phenomena as reflection of the spread of the epidemic from a rigid boundary. In other words, \( E_i \) contains all regional authority agents except the agent \( i \), and \( e_i \) contains the population agents that share a side or a corner with population agent \( i \), which means that \( |E_i| = N_x - 1 \), when the number of all the district authority agents is \( N_x \), and \( |e_i| = 8, 5 \) or 3 depending on the geographical location of the population agent \( i \).

Our hybrid model with SEIRS-epidemics and BTH agents for populations of grid cells and authorities of districts are set on a large square-shaped geographical area of a country. As depicted in Fig. 1 this area is divided to a grid of \( N=51 \times 51 \) cells, each of which has a BTH population agent and in each of which the epidemic follows the SEIRS-dynamics. This grid is grouped to larger 3x3 grid or \( N_e = 9 \) jurisdiction or governance districts (each with 17x17 population cells) for BTH-authority agents. The numbers of cells and districts were chosen odd to set the epidemic starting from the center of the geographical area of the country and its district in the middle.

**Results**

In this section we present the results for our hybrid model based on SEIRS epidemic spreading and BTH agents of district authorities and local geographical grid cell populations, which we from now on call the hybrid BTH-SEIRS model. We start by conducting control runs of the pure SEIRS model with the parameters that were found to describe the current COVID-19 pandemic well\(^6,7\), the values of which are listed in the caption of Fig. 1. These results are then compared with those of the BTH-SEIRS model using the same SEIRS parameters, while adopting variable BTH value parameters for all the agents (next section). Then we proceed by running the BTH-SEIRS model with different BTH value parameters to illustrate their effects and isolate the most important of them for the system dynamics (the rest of the results section). To keep the dynamical system as simple as possible, we set the parameter values the same for all the authority agents and the population agents, and study the effects of changing them in various ways.

**Comparison between pure SEIRS and hybrid BTH-SEIRS models**

In this subsection we investigate what the agent-based features add to the descriptive power of the original SEIRS-model. Obviously some effect could be expected, as the addition of the BTH-agents introduces a connection between the epidemic and its social and economic effects. The fact that the probability of the epidemic spreading to new areas is linked to the responses of the local population and district authority agents, brings in new geographical variability to the time evolution of the epidemic. In this section we demonstrate the basic properties of the epidemic spreading patterns in both the original SEIRS model and the agent-based BTH socio-economic epidemic model.
Figure 2. (A) Snapshot of the epidemic spreading over a single region without agent activity. The spreading probability, \( \nu \), is 0.1 everywhere. (B) Same as (A) but with agents’ activities enabled, in which case \( \nu \) changes according to Eq. (3). We vary the value parameters for population and authority agents in nine different districts.

**SEIRS model**

Since in the case of the pure SEIRS model the epidemic spreading probability is the same everywhere, it is straightforward to demonstrate the different cases of spreading dynamics. A simple consideration of either very small or very large spreading probabilities over a geographical area of two-dimensional grid of cells reveals two extreme spreading patterns: one in which the epidemic spreads almost unimpeded as wave fronts, like ripples in water, and another in which the spread is very slow and lacks any discernible geometric shape. The spreading probability 1 will cause the infection in a cell to spread at every time step to all the available geographical cells in the cardinal directions (up, down, left, right) of our model, and thus result in a perfectly regular diamond shaped wave pattern of the epidemic. When the spreading probability is decreased, the spreading patterns gradually lose their regularity, until all cohesion is lost and the pattern appears random. This happens when the spreading probability is set to a value below approximately 0.02. In Fig. 2(A) we show the epidemic spreading when the spreading probability \( \nu \) is set to a constant 0.1 everywhere. In this case the epidemic spreads as wave fronts that resemble highly distorted diamond patterns, which attests the resilience of the diamond pattern found in the case of large spreading probabilities.

**BTH-SEIRS model**

For the BTH-SEIRS model we first define the parameter values to characterize the authority agents of districts and population agents of geographical cells, along with the maximum spreading probability and its maximal reduction achievable by agent action. Here we choose the maximum epidemic spreading probability \( \nu_0 = 0.5 \), while for the maximal reduction to this probability \( \nu_{max} = 0.49 \), which means that the minimum possible spreading probability is \( \nu_0 = 0.01 \). In the case of pure SEIRS model these extreme spreading probability values are found to produce almost completely random or nearly regular diamond-shaped spreading patterns, the former for the minimum value and the latter for the maximum value. As for the parameter values for the district authority and population agents we choose them random with uniform distribution of width one and centered around representative mean values as follows 

\[
-1.5 \leq W_x^i \leq -0.5, \quad -10.5 \leq W_y^i \leq -9.5, \quad -0.5 \leq W_z^i \leq 0.5, \\
-1.5 \leq w_x^i \leq -0.5, \quad -100.5 \leq w_y^i \leq -99.5 \quad \text{and} \quad -0.5 \leq w_c^i \leq 0.5.
\]

The simulated spreading pattern resulting for these parameter value choices is shown in Fig. 2(B). Here the epidemic spreads in waves that are roughly diamond shaped in the vicinity of the center of the epidemic outbreak but quickly become irregular, as the spreading speed is highly dependent on the actions of the local population agents, which vary from time to time and place to place. For example, the diamond shaped spreading pattern in the center suggests that the agents did not take significant action to curtail the epidemic right at the start, but as it spread, the countermeasures by the agents increased. There are also significant local variations in the spread of the epidemic both between and within the districts that are not present in the pure SEIRS model.
BTH-SEIRS model results for different parameter values

In this subsection we have run numerous BTH-SEIRS model simulations, isolated the most important parameter values, and discuss their effects. It turns out that the easiest way to make the simulated epidemic to exhibit either the random or diamond shaped spreading behaviours is to change the sign of the compliance \( w_c \) of the population agents. In the simulations we observe the epidemic wave front being diamond shaped for non-compliant populations \((w_c < 0)\), while simulation for the compliant populations \((w_c > 0)\) exhibit random pattern. On the other hand increasing the concern for health in the population agents (i.e. \( w_y \)) causes the spreading patterns to fall in between these two extremes.

Compliance

As stated above, the extreme spreading patterns of our model come to fore in situations where there is no significant variance in the parameter values of the population agents and, crucially, the signs of all the parameters are the same for all the agents. We found this out when we were investigating the effect of the compliance parameter \( w_c \) of the population agents by setting the values of the district authority agents as follows: \( W^X_i = W^Z_i = -1, W^Y_i = -10 \). Here the infection parameter value \( W^Y_i \) was set to be much lower than the other two parameters so that the authority agents would insist on relatively tough measures against the epidemic, which in turn will make the compliance more relevant. We have made two sets of runs one with \( w_x = w_y = -1 \) and \( w_c = -2 \), and the other with \( w_x = w_y = -1 \) and \( w_c = 2 \), and name them the cases of Non-compliance and Compliance, respectively. Note that the absolute value of 2 for \( w_c \) was chosen to avoid division by zero in Eq. 7.

![Figure 3. The results for the Non-compliance case, i.e., simulating non-compliant populations. The four panels on the left show, from bottom to top, the average infection rate, gross domestic product, average degree of compliance of the populations, and district authorities’ regulations, while the panel on the right shows the spreading pattern of the epidemic. Districts are numbered as in Fig. 1.](image-url)

The results for the Non-compliance case, in which the population agents’ values are strongly against the district authorities’ regulations, are shown in Fig. 3. In the left panels (from bottom to top) we show the average infection rate, the gdp \( Z_i \), the average degree of compliance of geographical cell populations, and the regulations of district authorities as functions of time. The right panel shows the characteristic spreading pattern after the first wave of the epidemic has reached all the districts. Here the spreading pattern appears to be of diamond-shaped with somewhat rounded edges, which is consistent with fast epidemic propagation speed, discussed above. Due to the rapid propagation and the relatively small size of the simulation domain, the later waves of the epidemic have not yet materialized. However, as the simulation progresses, new waves emerge periodically from the origin following the very same pattern as the first wave. The time period between the epidemic wave fronts is determined for the most part by the length of immunity parameter \( \omega \).

The seasonal nature of the epidemic is clearly visible in the periodicity of the infection rates. Quite understandably, the behaviour of the different districts is strongly dependent on their distance from the origin of the epidemic, but the fact that equidistant areas show almost identical trends in every tracked quantity is remarkable. Especially the infection rates are almost the same for the areas in the cardinal directions (2, 4, 6 and 8, hereafter called adjacent areas) from the origin area (5), and the diagonally neighbouring areas (1, 3, 7 and 9, hereafter diagonal areas) likewise show similar infection rates all the times.

An interesting detail that can be extracted from the infection rate curves is that their overall shapes can be deduced from the underlying epidemic spreading pattern. The central district (number 5) experiences a very steep rise and fall in its infection rate,
because the epidemic spreads there in the full diamond-like pattern, while other districts only get to experience the traveling wave fronts of the epidemic. Thus the peak infection rate of approximately 0.35 in the central district is roughly twice that of the other districts showing similar peak rates.

We note that the direction from which the wave front arrives plays a crucial role in determining the shape of the infection rate outside the central district: As the epidemic enters the adjacent districts from the side, the evolution of the epidemic in these districts resembles a wedge travelling through them along the cardinal directions. The result is that the infection rates reach their peak quite fast, but then linger there until the wedge of the epidemic front exits the district, which is seen in Fig. 3 as a kind of flat top of the infection curve. In contrast, in the diagonal districts the epidemic enters from their corners and spreads as a front perpendicular to the diagonal direction. This causes the infection rates to climb and decline slower than in the other districts, since the peak occurs when the epidemic front runs diagonally from one corner of the district to the other.

The general behaviour of district authorities, as depicted in Fig. 3, is characterised by periods of high economic restrictions reaching even the maximum level of 1 and intervening periods with all the restrictions lifted up. Like for the infection rates, the patterns repeat themselves cyclically, although they do not fully settle until the second wave. There is also a similar correspondence between the actions of district authorities controlling geographically similarly positioned districts, i.e. authorities of adjacent districts follow the same trend as other adjacent districts. The same holds for the diagonally located districts. However, while the policies of the authorities of adjacent districts are almost identical at all times, the authorities of diagonal districts have more variation among their policies when lifting restrictions.

An interesting observation can be made by comparing the district authorities’ restrictions and infection dynamics. The district authority agents tend to impose restrictions before the epidemic arrives, but drop them as it takes hold, as if they were giving up after failing to contain the outbreak. Even more interestingly, the district 5, where the epidemic starts, does not put up any restrictions initially, and is introducing them for the first time only after the adjacent areas have dropped theirs.

The reason for this behaviour can be found in Eq. 11. If there are significantly more infections in the district governed by its authority agent $i$ than there are in the other districts the second term of this equation has an overall negative sign for the district authority agent $i$. Since $W^I$ is much larger than $W^X$ and $W^Z$, the other terms cannot compensate for it, and so the regulations are set to remain at the minimum possible value of 0 until the epidemic intensifies in the other districts. At this point the second term acquires positive sign and causes restrictions to be imposed. Besides this attempted prevention and giving up dynamics, the actions of the district authorities also clearly influence each other, as dictated by the first term of Eq. 11, since the introduction of restrictions by the central district coincides with the tightening of restrictions in the diagonal districts and the reintroduction of restrictions in the adjacent districts similarly seems to encourage tighter restrictions in the central district.

The actions of the population agents, as seen in the gdp and compliance degree curves, are also very heavily determined by the district of the population. Again, the population agents of the adjacent and diagonal districts behave very similarly within themselves, while the population in the central area follows its own behavioural pattern. The degree of compliance of people is low, about 0.25 at best. As one would expect from the choice of the compliance value parameter, it is often negative, attaining values as low as the minimum of $-1$. There is a clear correspondence between the tightening of the restrictions by the district authorities and the lowering of the degree of compliance. This is apparently driven primarily by extremely fast impositions of
restrictions by the district authority agents, rather than by active resistance to these restrictions by the population agents. This is because we observe the GDP curves also falling at the same time as the degree of compliance curve. However, the actions of population agents rarely meet the regulatory demands, and as a result the GDP in any of the districts never falls to less than 40% of the pre-epidemic levels at most. From the GDP curve one can also see that the population agents tend to act to prevent the epidemic, and give up when they fail. This is evident from the fact that the deepest fall in the GDP occurs immediately before the epidemic again picks up in a district. As the epidemic worsens, the population agents increase their spending, in accordance with how the district authority agents lessen the restrictions during the worsening phase of the epidemic.

The results for the Compliance case are shown in Fig. 4. In this simulation, the populations act decisively to halt the spread of the epidemic, which is clearly seen in the GDP and degree of compliance curves, as they tend to their minimum and maximum values, respectively. This results in the epidemic spreading pattern being random and taking a long time to reach other areas outside the starting central district 5. The authorities of the district 5 are not found to issue any restrictions at all, so the degree of compliance curve for that district is a mirror image of the GDP curve. While all the district authorities other than that of the central district 5 put in place some restrictions, they again tend to drop them some time before the epidemic enters their areas. As one would expect, the rule of thumb is that the adjacent areas drop theirs first, and the diagonal areas last, but due to the chaotic spreading of the epidemic this pattern is somewhat blurred.

It should be noted that both the infection rates and the restrictions by the district authorities are much lower in this case than in the case of Non-compliance. Furthermore, it could be said that in this case the district authorities to some extent cede their responsibility for mitigating the spread of epidemic within the population of the district.

The results for the Prohealth case are depicted in Fig. 5. As can be seen from the spreading pattern, there is much more geographical variability in the propagation of the epidemic, since there is more space between consequent wave fronts in the cardinal directions than in the diagonal directions. The population agents are also much more willing and consistent in limiting the spread of epidemic, as can be seen in the GDP and degree of compliance curves. While the latter approaches values near the maximum value of 1 for all districts, with the exception of dips caused by the seasonal tightening of restrictions by the district authorities, in the former we observe relaxation to values much lower than those found in the Non-compliance simulation. In the end state the GDP-curves are all periodic, with the central area experiencing larger amplitudes than the adjacent districts, which in turn have larger amplitudes than the diagonal districts.

Figure 5. The results of the Prohealth case, i.e, simulating health-conscious population agents. Panels as in Fig. 3.

Populations’ health concerns
It is clear from the results of the previous subsection that the compliance characteristic of the population agents has a significant effect on their behaviour and the spreading of the epidemic, but what can be said of the effects of other parameters? Could it be, for example, that if the population agents were more averse to the disease spreading to them, would they attempt to moderate the rapid spread seen in the case of Non-compliance? To study this question we made a simulation called Prohealth, where we used otherwise the same parameters as in the case of Non-compliance, but changed \( w_i \), describing the value that the population agents give for staying healthy, i.e. to the value \(-50\) for all the population agents. We chose to modify the parameters of the Non-compliance simulation because of its regular behaviour, which makes it relatively easy to compare its results with the new simulations.

The results for the Prohealth case are depicted in Fig. 5. As can be seen from the spreading pattern, there is much more geographical variability in the propagation of the epidemic, since there is more space between consequent wave fronts in the cardinal directions than in the diagonal directions. The population agents are also much more willing and consistent in limiting the spread of epidemic, as can be seen in the GDP and degree of compliance curves. While the latter approaches values near the maximum value of 1 for all districts, with the exception of dips caused by the seasonal tightening of restrictions by the district authorities, in the former we observe relaxation to values much lower than those found in the Non-compliance simulation. In the end state the GDP-curves are all periodic, with the central area experiencing larger amplitudes than the adjacent districts, which in turn have larger amplitudes than the diagonal districts.
In the infection rate curves we see that apart from the central district, which experiences a seasonal re-emergence of the epidemic, the disease becomes almost endemic in the other districts, with the infection rates varying between the maximal value of about 0.2 and a minimum value of about 0 in the adjacent districts and fluctuating around approximately 0.07 in the diagonal districts. However, in all districts the maximal infection rates are slightly below those of the Non-compliance case.

The restrictions imposed by the district authority agents are at the beginning of epidemic rather similar to those in Non-compliance case, but they become somewhat subdued in the end state of the simulation. Most of the areas drop their restrictions entirely, only to reintroduce them seasonally in the latter part of the time series. These seasonal adjustments seem to follow similar pattern as the runs of Non-compliance case, i.e. restrictions are raised when infection rates are low.

**Authorities’ economic concerns**

Next we investigate how does the district authorities’ concerns for the economy influence the behavior of the population agents and the spread of the epidemic. We again use the Non-compliance case model as our basis, but we set $W_i^Z$ of all district authority agents to $-10$, and call it the Proeconomy simulation. The results of this simulation are depicted in Fig. 6.

Figure 6. The results of the Proeconomy case, i.e., simulating district authority agents being conscious of economy. Panels as in Fig. 3.

Here the spreading pattern and time-evolution of the infection rates are essentially the same as in the case of Non-compliance simulation, but there are substantial differences in the behaviour of the district authority and population agents. Most obvious of these is that the district authorities are much less stringent when enacting restrictions: while in the initial epidemic wave their restrictions may reach values as high as the maximum level of 1.0, once the later waves start rolling in, they raise them to a little over 0.5 at most. This is naturally reflected in the degree of compliance curve, which indicates that in this case the population agents are often compliant with the lax restrictions by the district authorities.

A more surprising observation is that the gdp is also significantly affected by the change in the $W_i^Z$ parameter, as the formerly very regular curves start oscillating irregularly around some mean values, which seem to be remarkably higher than those of the Non-Compliance case. The root cause for the weaker efforts of the population agents to contain the epidemic can be found in the third term of Eq. 7. With the values of $w_i^c$ and $w_i^x$ we have chosen for Proeconomy simulation we have

$$\frac{w_i^c}{w_i^c + w_i^x} = \frac{2}{3},$$

(12)

from which it follows

$$\frac{w_i^c}{w_i^c + w_i^x} |e_i|X_i^r \geq 0,$$

(13)

where the equality only holds, if there are no regulations imposed by the district authorities, i.e. $X_i^r = 0$. This, in turn, means that if the district authorities issue lighter restrictions, the population agents will likewise lower their contributions to ward off the epidemic, which is seen in the difference between the gdp-curves of Figs. 6 and 3.
Discussion

In this study we devised a human society and geographical area based hybrid model of compartmental SEIRS-type epidemic spreading and dynamics of socio-economic with the local populations and district authorities considered as separate Better-Than-Hypothesis behaving agents, to investigate their mutual interplay. In this hybrid SEIRS-BTH model the epidemic spreading takes place over the entire geographical area, divided to a grid of cells each with a population agent and collections of these cells forming a larger area district governed by its authorities agent. These district agents give recommendations to lower economic activity to stem the tide of the epidemic, and the local population agents can choose to limit their economic activity to lower the transmission rate between adjacent geographical cells. One of the novelties of our model is that the agents, having some information of the epidemic itself, can react to it to mitigate its spreading. Furthermore, our model operates at multiple length scales, i.e. covering local, district, and large geographical areas. For showcasing the basic properties of our model, we used a relatively rapid base spreading rate of the epidemic, and also made the mitigating efforts of epidemic by the population agents relatively effective. As a result the model exhibits rapid and regular or slow, chaotic spreading patterns as extreme cases.

The model in its current form suggests that the willingness by the populations to follow the restrictions implemented by the district authorities turns out to be the most significant factor in reducing the speed at which an epidemic spreads through the whole geographical area. Indeed, the easiest way to change the geographical transmission speed of the epidemic from extremely slow to extremely fast is to give all the population agents the same value parameters with sufficiently large compliance value $w_i$ and switching its sign from positive to negative, respectively. The chaotic nature of the slow spreading pattern resulting from having compliant population agents, $(w_i > 0)$, is generally reflected in the decreased infection rates and the district authorities’ restrictions, but not so much in the gdp, which tends to go to zero almost monotonically. On the other hand the fast epidemic spreading caused by non-compliant population agents, $(w_i < 0)$, results in periodic outbreaks of the disease and periodic responses by both the district authority and population agents.

If one interprets $w_i$ as measuring the adherence to social norms in general, this result is broadly in agreement with the results of\(^\text{1}\) in which it was observed that culturally loose (low adherence) countries have tended to suffer more in the current COVID19-pandemic than culturally tight (high adherence) ones. Other intuitively sensible behavioural patterns arising from our model are the effects of the health and economic concerns on spreading rates, such that higher health concerns drive up efforts to stem the epidemic, while economic concerns drive these efforts down.

While capturing these intuitive features with the model is encouraging, our simulations also exhibit some counter-intuitive ones. One of those is that in our simulations the district authority agents only impose restrictions when the epidemic is at low ebb and scrap them when the epidemic picks up the pace. Remembering the discussion about how this pattern emerges from the second term of Eq. 11, this feature can be understood to be a result of the competitive nature of the agents in our model and their non-existent ability to constrain the epidemic once it has broken loose. If the epidemic is particularly serious in a district relative to others, and the effects of the local restrictions are not significant anyway, why would the authorities of the said district bother putting up any restrictions at all? This situation could change radically if the effects of vaccinations were taken into account, since then the district authorities would have a realistic chance of eliminating the disease altogether.

Some of the imminent future improvements of our model would include taking into account specific NPIs, such as mandatory mask wearing, social distancing, business closures and the like, their economic effects, and improving the decision-making algorithm to handle these more realistic NPIs, e.g., by implementing Monte Carlo methods. The model can also be adapted to study the effects of vaccinations, which requires adding a term describing vaccine hesitancy into the populations’ utility function. Adding economic infrastructure and businesses as economic agents to the simulation are other possible future prospects.

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Author contributions statement

R.A.B. is the main developer of the original SEIRS model. J.E.S. modified the model to include agent-based BTH-aspects. All the authors took part in the planning of the simulation runs to be performed. J.E.S. was responsible for practical design of these
simulations, running them, and analysing their results. J.E.S. was the lead author of the manuscript, while all the co-authors contributed by writing and revising the paper.

Data availability
All data generated, and customised computer programs used to generate them, are available from the corresponding author on reasonable request.

Competing interests
The authors declare no competing interests.

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A. Synthesis of SARS-CoV2-derived RNA and Luciferase RNA fusion gene. Secondary structure prediction by RNA fold based of SARS-CoV-2 5’UTR and Luciferase RNA fusion gene. Design of guide RNA (gRNA) complimenting Luciferase gene.

B. gRNA-dCas13 mediated pull down. gRNA targeting luciferase fragment of 5’UTR RNA-Luciferase fusion. mRNA for dCas13 mediated pull down of 5’UTR RNA bound host RNAs in HEK293T and A549 cells.

C. Trans immunoprecipitation (TRIP) and Purification of host RNAs. Precipitation and purification of 5’UTR bound host RNAs.

D. RNA-seq and GO enrichment. RNA-seq of precipitated host RNAs and Gene Ontology analysis of enrichment RNAs.

E. Impact of SARS-CoV2-derived 5’UTR in human cells. Verification of gene expression changes in SARS-CoV2-derived 5’UTR RNA overexpressing cells. Identification of translation-suppressing drug candidates via 5’UTR derived from SARS-CoV2.

Figure 1

Workflow of the study.
pGL3-5'UTR construct and Luciferase reporter assay. (a) Vector construction with SARS-CoV-2 5'UTR insert in pGL3 luciferase vector. The genomic architecture of SARS-CoV-2 starts with 5' UTR followed by ORF1 and structural genes. To elucidate the translational mechanism in host cells, 5' UTR segment of the SARS-CoV-2 was inserted in the pGL3 vector between SV40 promoter and luciferase gene. Luciferase gene is a reporter for the transfection efficiency and expression of 5' UTR. Further, luciferase RNA forms the target for crRNA-dCAS13 facilitating Trans immunoprecipitation (TRIP) for 5'UTR bound host translational RNAs. (b) Luciferase transcription induced by the SV40 promoter measured as a function of luminescence in HEK293T cells (left) and A549 cells (right). According to the amount of cell introduction, both pGL3-promoter and pGL3-5'UTR vector increased or decreased the activity of luciferase protein.
Upon introduction of pGL3-5'UTR vector, relative luciferase activity increased more than 10 times to the equivalent amount of pGL3-promoter. Note that the SARS-CoV-2 derived 5'UTR synergistically activated translation in an intracellular factor-dependent manner. Relative luciferase activity was calculated against the activity of endogenous pRL-RSV serving as control (100%). The Mann-Whitney U test was used for statistical significance (p < 0.05).

Figure 3
RNA-immunoprecipitation. (a) Prediction of luciferase mRNA- 5'UTR fusion. Two optimal 28 nt regions gRNAs targeting the luciferase RNA were designed - gRNA1 and gRNA2. (b) gRNA-dCas13 mediated RNA immunoprecipitation of host RNA bound to 5'UTR sequences. RT-qPCR was performed to determine the accumulation of immunoprecipitated 5'UTR sequence (Top) and luciferase RNA (bottom) via gRNA-dCas13 mediated targeting of luciferase RNA. The host RNA bound to 5'UTR was immunoprecipitated and the enrichment factor was calculated as 2 (-ΔΔCt [RIP / background]). The mean and standard error of the three independent experiments is shown. Statistical analysis was performed using a two-sided paired t-test. * Indicates a significant difference from the control sample at a value of p <0.05.
Differential expression by RNA seq analysis. (a) Set of four samples was analyzed for RNA-seq analysis. Each lane is Luciferase RNA-immunoprecipitation sample 38 from no 5'UTR sequence (293L2GL3 and A549L2GL3) and controls, or Luciferase-RNA fused with 5'UTR (293L2CV, A549L2CV, and A549L1Cv) as test samples. (L1 or L2 are guide RNAs targeting Luciferase RNA). Heatmap analysis of differentially enriched genes show enrichment in 293L2CV, A549L2CV, and A549L1Cv immunoprecipitated samples.
(b) Venn diagram showing genes common to the unique genes in the test sample (293L2CV, A549L2CV, and A549L1Cv) that were significantly enriched (p < 0.05) compared to the control (293L2GL3 or A549L2GL3). 293T-XIST is an RNA-immunoprecipitation sample serving as a negative control using HEK293T cells expressing lncRNA XIST-targeting guide RNA and dCas13. The genes enriched by Control-293 vs 293T-L2-CoV2, Control-A549 vs A549-L1-CoV2, and Control-A549-L2-CoV2 are human intracellular factors that interact with 5'UTR derived from SARS-CoV-2. (c) Genes enriched by Control-293 vs 293T-L2-CoV2 dataset were ranked according to their differential enrichment and the resulting enriched GO terms are visualized using a DAG graphical representation with color-coding reflecting their enrichment degree.

**Figure 5**

Motif analysis and host binding factors to 5'UTR. The motif in the 5'UTR in HEK293T cells (top) and A549 cells (bottom) is crucial for binding the host translational factors.
Overexpression of 5'UTR in SARS-CoV-2 alters genes expression involved in the mevalonate pathway in HEK293T and A549 cells. (a) 1 ug of pGL3-promoter and pGL3-5'UTR vectors were introduced into cells cultured in 6 well plates (0.3 x 10^6). Expression of lipid metabolism factors from total RNA was measured. Overexpression of 5'UTR affected the expression of ACAA and HMGCS. Results are shown as mean ± SD, and Student's t-test was used as a test of significance. (b) Outline of metabolic pathway of Acetyl-CoA by overexpression of 5'UTR of SARS-CoV-2 and inhibitory mechanism of HMG-CoA reductase inhibitors like statins. (c) 1 ug of pGL3-promoter and pGL3-5'UTR vectors was introduced in cells cultured in 24 well plates. HMGCoA reductase inhibitors were added to the culture solution at a concentration range of 1nM, 10nM, 100nM and 1,000 nM. Following incubation for 48 hours, the luciferase activity was measured. To assess the effect on the 5'UTR, the pGL3-promoter and luciferase activity from each adjacent well into which the pGL3-5'UTR vector was introduced were subtracted. The internal control used was the sum of each value. The results were shown as mean ± SD and were tested for significance by Student's t-test. The internal control used was the sum of the respective values. Results were shown as mean ± SD, and Student's t-test examined significance.
Supplementary Files

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