Individual-based epidemic simulator with vaccination and virus variants for scenario analysis *

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Abstract: The author extended his individual-based epidemic simulator [1] so as to handle a number of different types of vaccination and virus variants. To simulate epidemic dynamics on the infection network among people, this system manages a large number of individuals moving in a two dimensional space for gatherings and long distance jumps. The main objective of the system is to analyze the possible sequences of events that would happen under a variety of assumed scenario. To realize this functionality, the system has a GUI-based user interface that enables the user to specify a number of vaccines with different protocols and efficacies. The features of virus variants, this system employ a reproduction rate of virus within an infected patient, that indicates how fast the virus reproduce themselves in his/her body. The algorithm is improved to manage one million individuals in a single two dimensional space utilizing a type of parallel processing by multicore CPU. By preparing the appropriate settings of parameters and scenario, it is possible to trace the trends of several indexes observed in the real world. Some cases of simulation results of this simulator have been reported in the meetings of governmental committee of the experts to suggest the strategy of countermeasures.

Keywords: multi-agent system, infectious disease, epidemic dynamics, scenario analysis

1 INTRODUCTION

Since the epidemic of SARS-CoV-2 expanded through the world in early 2020, a lot of people have been struggling to cope with the tragic situation not only on health but also almost all of the fields including economy and culture. Multi-agent based simulation, one of the popular software approach in Artificial Life researches, has also been employed to see what was, is, and will be happened; under expectation to provide an appropriate suggestion for planning the countermeasures. Similarly to another project for COVID-19, such as Covasim [2], the author is also involved in the development of an individual-based epidemic simulator [1]. This paper describes new features of the system that enables it to handle a number of different types of vaccination and virus variants. The simulator was designed under assumption that viruses spread among people mainly through contacts between individuals via spray and aerosol. To simulate epidemic dynamics on the infection network, this system manages a large number of individuals moving in a two dimensional space for gatherings and long distance jumps. The main objective of the system is to analyze the possible sequences of events that would happen under a variety of assumed scenario about the countermeasures, invasion of a new variant, and other conditions. To realize this functionality of flexible scenario settings, the system has a GUI-based user interface that enables the user to edit a number of vaccines with different protocols and efficacies, accompanying a text description in JSON format for batch jobs.

The following sections describes a short summary of the overall model, a detail of the models of virus variants and vaccines, the design of user interface, the algorithm for acceleration, some examples of simulation results, and then concluding remarks.

2 SHORT SUMMARY OF THE MODEL

Differently from the mathematical model widely used for epidemic simulation, such as SIR model based on differential equations [3], multi-agent based model is useful to introduce concrete characteristics of people's behavior and countermeasures, even though those features make hard to apply analytic mathematical methods for the implication. It also provides a source of visualization that helps our intuitive understanding of the complex phenomena. The model and algorithm are inherited from the authors previous work [4] on evolutionary simulation for sexual dimorphism and speciation. The models of individual behavior, pathogenesis, and measures are implemented. The individuals move in a two-dimensional Euclidean space basically following a simple Newtonian mechanics with mass and friction, affected by repulsion forces for collision avoid-

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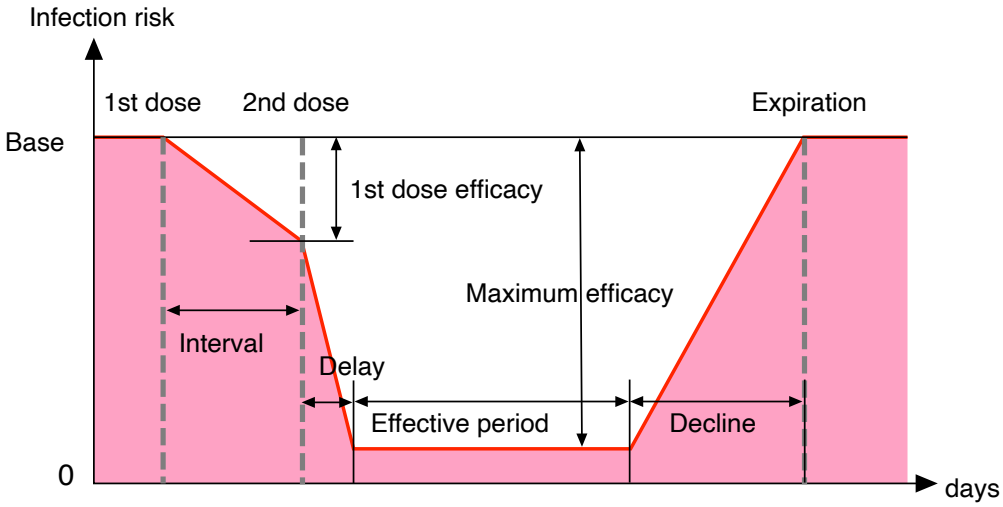

Fig. 1: Model of vaccination efficacy.

ance and attraction forces for gatherings. They could also jump to another position as a model of long distance travel. The measures include social distancing, mobility restriction, gathering restriction, tests, quarantine, and contact tracing. Vaccination was newly introduced and the detail is explained the following section. All of these features are adjustable by specification of the parameter settings on the probabilities of occurrence and the frequency distribution of continuous values.

Relating to the main theme of this paper, the probability $P_{a\to b}$ of infection of virus from a patient a to a susceptible person b is represented in the model as the following equation.

$$P_{a\to b} = F \cdot R_v \cdot C_a \cdot D_{ab} \cdot (1 - I_b) \tag{1}$$

where C_a is contagious factor of a, D_{ab} is the factor of physical distance between a and b, and I_b is on the immunity of b. R_v is the reproductivity of the virus v that described in later section. F is the effect of environmental factors such as ventilation, sanitization, face mask, and so on. The details of C_a and D_{ab} are available in the project Web site [5].

3 MODEL OF VIRUS VARIANTS AND VACCINES

The vaccination is a powerful countermeasure to prevent the explosive spread of infectious diseases by assisting the immune system of individual body. Immunity against a specific pathogen is naturally acquired after the patient is infected by the pathogen. It is not only to produce antigen but also to make some types of immune cells to memorize the key to trigger the efficient immune response. The antigen is effective to suppress the activity of pathogen. The immune memory is effective for quick response to produce appropriate antigen for infection in the next occasion. Such effect usually becomes stronger after the exposure within a number of days, then gradually declines through some months or years. The duration of efficacy depends on the type of pathogen and the individual characteristics. The vaccination triggers the same response of immune system without real infection.

3.1 Vaccination

Each type of vaccine has its own recommended protocol that specifies how it should be treated. It is sometimes required to conduct the second dose some days or weeks after the first dose to achieve the enough level of efficacy. Figure 1 illustrates the model of time transition of efficacy on an individual in case the second dose is necessary. It is difficult to measure the efficacy directly, in terms of reduction of infection and severe symptom risk, but it is possible to estimate it from the results of clinical trials. The parameter values of both efficacy and duration are given from the reports of a clinical trial such as [6]. Because the efficacy of vaccination depends on the types of target virus variants, the parameter set is in a form of a table of rows and columns as shown in the later section of GUI design. The efficacy of acquired immunity by infection is also in a same form. It is also possible to add an application schedule for each vaccine to the scenario.

3.2 Virus variants

Virus has an ability to evolve by erroneous copy of genetic information that happens when it replicates itself. As coronavirus uses RNA to convey the information, the mutation rate is relatively higher than other DNA-based organisms. This means new variants are frequently produced in the patient body. The mutation usually bring a decay of reproductivity as the replica-

tion mechanism is complicated somehow, but in a probability it provides a more sophisticated mechanism of efficient reproduction. The features of virus variants are usually described in basic reproduction rate R_0 in terms of the average number of infection cases from single spreader to other persons under assumption without any special countermeasures. Because this index depends on a lot of environmental condition, this system employ a reproduction rate within an infected patient instead, that indicates how fast the virus reproduce themselves in his/her body. In the case new coronavirus, the variants vary in the efficiency of invasion into host cells depending on the type of spike protein. When this index is high, the incubation period becomes shorter and the immune response tends to be late to prevent a severe symptom.

The reproductivity affects the pathogenic mechanism as follows. It is assumed that the incubation period and the time to death are shortened in proportion to the this rate. The larger reproductivity increases the viral load excreted by infected individuals. The resulting changes in infectivity and toxicity are also in line with the reproductivity, therefore it affects the coefficient R_v in the equation (1) of infection probability. In addition, under the assumption that the larger value of R_v results the faster the symptom progress, the values are divided by $\sqrt[3]{R_v}$ for all of the pathogenic mechanism including incubation period, recovery start period, contagious delay, and period to contagious peak.

The number of false negative cases in the tests to check the individual infection is also affected by reproductivity because the specimen includes more the viral load. This means that the larger reproductivity causes the higher sensitivity of the tests. Here the sensitivity S_e is revised using the following equation.

$$S_e = 1 - (1 - S_1)^{R_v} \tag{2}$$

where S_1 is the standard sensitivity when $R_v = 1$.

The effect of acquired immunity is represented in a same form of the case of vaccination, that is, a table form whose cells contain the scalar values that indicate how much effective the immunities are against each known type of virus variants.

4 USER INTERFACES

Figure 2 shows a sample of screenshot of the GUI panel to specify the parameter values on virus variants and vaccines. The lower part of the panel has six sliders and digits fields to specify the standard efficacy. The upper part has two tables that specify the efficacy rate for each combination between the acquired immunity by infection in the upper table, and vaccination in the lower table. For example, the top row of the upper table indicates the reproductivity of the original variant is 1.0 in the second column, and the effectiveness of the acquired immunity by infection of original variant is 1.0, 0.9, 0.8 and 0.7 against the exposure to the original, alpha, delta, and omicron

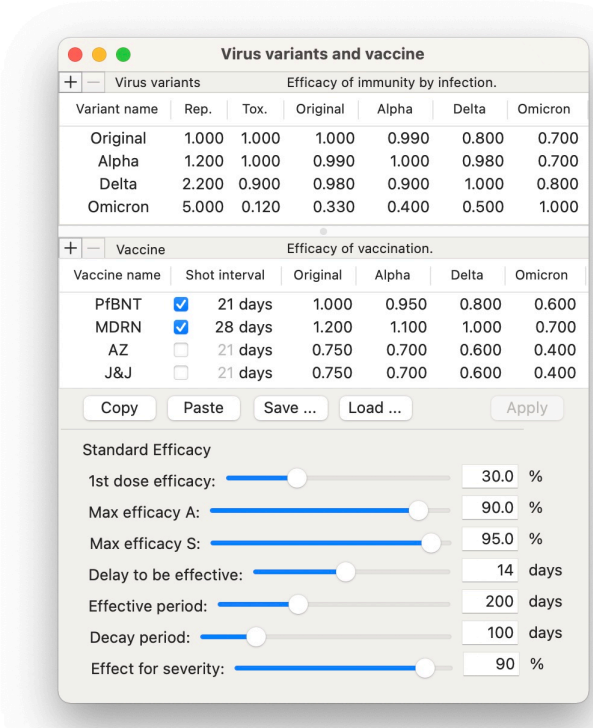

Fig. 2: GUI for setting virus variants and vaccines.

variants respectively. The table on vaccines includes the interval between the first and the second doses if required. A user is allowed to copy, paste, save, and load the settings in convenience for his/her editing tasks to examine a variety of different settings. All of these operations use JSON format to read and write the information so that it makes easy to use this panel as an editor to organize a task specification for batch jobs.

Figure 3 is a sample code that specifies the virus variants in three lines from the second line, the vaccine in three lines from the fifth line, the scenario, and the statistical indexes to be recorded. The tenth line in the scenario indicates that the performing speed of vaccination is gradually changed toward 0.6% of the population per day spending two weeks. The eleventh line specifies the invasion of alpha variant with ten infected patients at random locations. As described in [1], the web server version of this simulator accepts a specification of batch job in the payload part of "POST" method in HTTP/1.1 protocol.

5 ALGORITHM FOR ACCELERATION

In addition to these extension concerning the model, the algorithm is improved to manage one million individuals in a single two dimensional space utilizing a type of parallel processing by

```
{"stopAt":200,"n":8,
"variants":[
  {"name":"Original","reproductivity":1.0,"Alpha":0.8},
  {"name":"Alpha","reproductivity":1.2,"Original":0.8}],
"vaccines":[
  {"name":"PfBNT","interval":21,
    "Original":1.0,"Delta":0.9}],
"scenario":[
  "days >= 50",["gatheringFrequency",0.75,11],
  "days >= 83",["vaccinePerformRate",6,14],
  "days >= 85",[10,0,"Alpha"],
  ],
"out":["asymptomatic","symptomatic","recovered",
  "died","vaccinated",
  "dailyTestPositive","dailyTestNegative",
  "severityStats","variantsStats"]}
```

Fig. 3: A sample code in JSON format for a batch job.

multicore CPU. The most heaviest part of computation in the simulation is for aggregation of mutual effects between all of the combination of individuals. It would waste the computing time proportional to the square of the population size by a naive algorithm to sequentially enumerate all of possible pairs. In a similar manner with an algorithm for simulation of flocking behavior in Euclidean space, such as BOIDS [7], it is possible to improve the performance by restring the relations only into the relatively adjacent individuals, because the interaction between the individuals in distance is usually very small. There are a number of possible methods to achieve such improvement, we employed a method to divide the space into a uniform partition in the square lattice. It is enough to calculate the interaction between individuals in the same or neighboring partition. This method has an advantage to allow the separated partitions in parallel utilizing the multithreading. The process is sequentially conducted with nine subprocesses for interaction between individuals (1) within a same partition, (2) vertically neighboring partitions of even number rows, (3) vertically neighboring partitions of odd number rows, (4) horizontally neighboring partitions of even number columns, (5) horizontally neighboring partitions of odd number columns, (6) orthogonally neighboring partitions by upper left of even number rows and lower right, (7) orthogonally neighboring partitions by upper left of odd number rows and lower right, (8) orthogonally neighboring partitions by upper right of even number rows and lower left, and (9) orthogonally neighboring partitions by upper right of odd number rows and lower left. By tuning the number of threads and reorganization of memory structure for a population, it achieved the throughput time as approximately 70 steps per minute for one million individuals on Mac mini M1. By giving an array of parameters to the code unit of submodule instead of the each single value, it makes easy for the compiler to find the part of code to be compiled into a short code sequence utilizing the vector processor in CPU.

6 RESULT EXAMPLE

By preparing the appropriate settings of parameters and scenario, it is possible to trace the trends of several indexes observed in the real world.

Figure 4 is a sample screen image in Mac Application version, where the scenario including both vaccination and virus variants. The main part of the screen is occupied by the animation of individuals' movements attached with two special area indicating quarantine and death at the right edge of the screen. Each dot is corresponding to each individual in the field. The population includes 16,000 individuals in this cases. The yellow circles shown in the field indicate the gatherings. The frequency of gatherings is reduced under the governmental declaration of emergency. The left edge is a stack of the control panel and six trend graphs showing statistical indexes, including population distribution of individual states of health, the numbers of newly detected infected patients, proportion of severity levels, the number of patients by the type of infecting virus variants, and frequency histograms of incubation period, and so on. Figure 5 is the screen capture of the scenario panel used for this simulation. This GUI panel allows the user to add a new item in the scenario by clicking one of the buttons in the top row of the panel. The upper two items specify that the parameter value of "gathering frequency" is set to 10 immediately when the statistic index named "symptomatic" becomes larger than 1,000. The text "Lockdown" is drawn in the trend graph when this condition is satisfied.

Figure 6 shows an example of statistic summary over 128 times of trials with different random number sequences in a single scenario, concerning the number of patients infected by four types of virus variants. The parameter values were tuned to fit with the real observation in the case happened in Tokyo from late of December 2020 to the end of November 2021. The part of December 2021 is the extension using predicted parameter values and some facts revealed on omicron variant. The reason why the replacement of dominating variants is progressing more slowly than expected is that the percentage of infected patients is fewer than 1/1,000 in the population. This means the distribution of contagious individuals is too sparse to fit to a model of differential equations using the variables representing the ratio of each health state in the population.

7 CONCLUDING REMARKS

Some cases of simulation results of this simulator have been reported in the meetings of governmental committee of the experts to suggest the strategy of countermeasures. The reports are accessible from the web site of AI simulation project [8] together with the other sub projects.

One of the general issue in the design of simulation is the choice of parameters from enormous number of features in the real system. Typically in the target area of such epidemic of

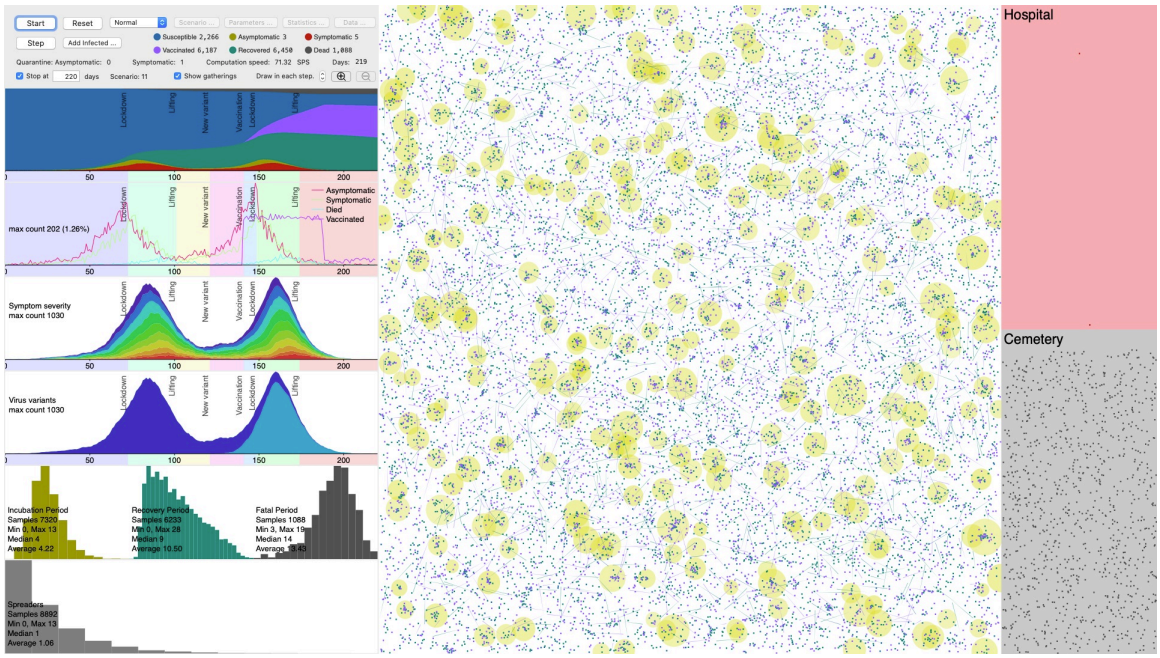

Fig. 4: A sample screen shot of macOS application version.

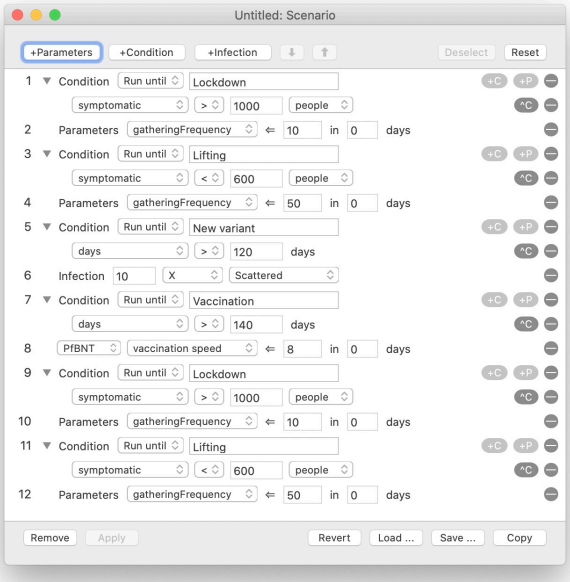

Fig. 5: Scenario setting in the GUI panel used for the simulation process shown in Figure 4.

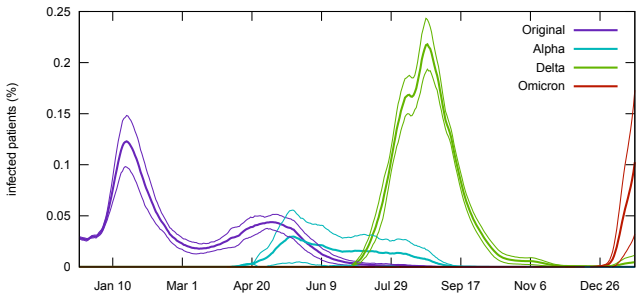

Fig. 6: A sample of simulation result on spread transition of virus variants. The scenario was adjusted so as to fit to the real observation in Tokyo. Thick lines indicate the average values over 128 trials. Thin lines are on the average $\pm$ standard deviation.

infectious diseases, it is necessary to focus on a variety of features in very wide scale from microscopic physiological reaction to macroscopic social phenomena including the natural environment. For the characteristics of new virus variant, omicron, the pathogenesis should be designed more sophisticated so as to represent more precise difference between toxicity and infectiousness, as it is reported a possibility that the toxicity is less than the others though the infectiousness is very strong [9].

We would like to continue our effort to develop the model and simulator to be more helpful for strategic decision and education.

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REFERENCES

[1] T. Unemi *et al.*, "An individual-based epidemic simulator," in *Proceedings of the 26th International Symposium on Artificial Life and Robotics*, Online, January 2021, pp. 12–17.

[2] C. C. Kerr *et al.*, "Covasim: An agent-based model of COVID-19 dynamics and interventions," *PLOS Computational Biology*, vol. 17, no. 7, pp. 1–32, 07 2021. https://doi.org/10.1371/journal.pcbi.1009149

[3] K. W. Ogilvy and A. G. McKendrick, "A contribution to the mathematical theory of epidemics," *Proceedings of the Royal Society A*, vol. 115, no. 772, pp. 700–721, 1927.

[4] T. Unemi and H. Matsumoto, "Loversflow v2 : an individual-based evo-eco simulator on sexual dimorphism – a challenge toward evolutionary aesthetics," in *Proceedings of the 23rd International Symposium on Artificial Life and Robotics*, Beppu, Japan, January 2018, pp. 295–300.

[5] T. Unemi. Simepidemic1: An individual-based epidemic simulator. http://www.intlab.soka.ac.jp/~unemi/SimEpidemic1/info/

[6] CDC, "Information about the Pfizer-BioNTech COVID-19 vaccine," Centers for Disease Control and Prevention, USA, https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/Pfizer-BioNTech.html, Tech. Rep., January 2021.

[7] C. W. Reynolds, "Flocks, herds, and schools: A distributed behavioral model," in *ACM SIGGRAPH '87 Conference Proceedings*, Anaheim, California, July 1987, pp. 25–34.

[8] Cabinet Secretariat of Japan Government. (2021) COVID-19 AI and simulation project. https://www.covid19-ai.jp/en-us/

[9] S. A. The National Institute for Communicable Diseases. (2021, December). https://www.nicd.ac.za/early-assessment-of-the-clinical-severity-of-the-sars-cov-2-omicron