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# Modelling the effect of SARS-CoV-2 variants on morbidity of COVID-19

## Introduction

COVID-19 is an infectious respiratory disease caused by the SARS-CoV-2 novel coronavirus that was first identified in late 2019[1]. It belongs to the Coronaviridae family, which are single stranded enveloped RNA viruses with viral spike proteins that commonly infect birds and mammals[3]. These viruses can cause the common cold, Severe Acute Respiratory Syndrome (SARS), and Middle East Respiratory Syndrome (MERS) in humans. COVID-19 was declared a global pandemic by the World Health Organization in March 2020[2]. The virus spreads primarily through respiratory droplets and aerosols when someone coughs, sneezes, or talks, and infects individuals when it is inhaled or comes in contact with the mucous membranes of the nose, mouth, or eyes[4].

New viral genetic variants are constantly being reproduced through genetic changes caused by recombination. These genetic changes result in differences in the offspring's virulence and ability to spread from host to host. However, mutations caused by recombination result in changes to the variant's function only when they alter the shape of a protein. Recombination takes place during replication when two parent strains infect the same host cell, resulting in a new viral progeny that has the DNA of both parent strains and acts as a new variant[5].

According to Emma Hodcroft, a molecular epidemiologist at the University of Basel, SARS-CoV-2 acquires a two letter mutation in its genome each month. This rate of mutation is much slower in comparison to most RNA viruses due to the presence of proofreading enzymes that correct these mutations[6].

Some variants in Scotland and the UK have been found to have mutations in the receptor binding domain of the spike protein, which allows it to enter host cells more easily by increasing protein expression. Since this specific mutation is not always detected by antibodies, it is now present in the majority of the viral strains in Europe[6].

Mutations in the SARS-CoV-2 virus are inevitable, but it is unknown exactly how they could affect the behaviour of the virus. This research study uses COBWEB simulation software (Complexity & Organized Behaviour within Environmental Bounds) to evaluate the effect of random SARS-CoV-2 variants on the morbidity of COVID-19.

This research study investigates the relationship between the time it takes for a susceptible population to become extinct and the number of viral agents. It is hypothesized that if there is an increase in viral agents as a result of a random mutation, then a higher percentage of the susceptible population will become infected and the number of ticks it takes for the population to become extinct will be smaller, thus increasing the morbidity of SARS-CoV-2. Two scenarios will be compared: an experimental scenario with random SARS-CoV-2 variants and a control scenario without.

**Methods**

Twenty trials were conducted for each scenario. There were two types of agents, agent 1 representing a sample population of humans and agent 2 representing the SARS-CoV-2 virus. The purpose of having an agent represent the virus was so the agent could be mutated using the genetics tab in COBWEB. The disease feature was used to represent the spread of the virus.

In the experimental scenario, 100 human agents and 20 virus agents were positioned randomly within a 40 by 40 COBWEB grid. In each trial, 2% of the human agents were initially infected. The environment had sufficient resources for both human and virus agents so they were not endangered by starvation. The transmission rate of the disease was set to 1, which is the highest under COBWEB's limitations. Step energy, which is how much energy is needed for an agent to take a step, was set to 1. Infected human agents had a step energy factor of 5, so therefore they would need five times the energy to move one grid square compared to an uninfected human agent to simulate the fatal effects of COVID-19.

The breed energy of virus agents, which is how much energy is necessary for reproduction, was set to 60. Breed energy was mutated at a rate of 0.05 in order to simulate the changing severity of COVID-19 from random mutations. Depending on the mutation generated, virus agents would require either more or less energy to reproduce, leading to an increase or decrease in population of virus agents, therefore changing how likely it is for human agents to get infected and the morbidity of COVID-19. Virus agents could only transmit disease to human agents but virus agents could not transmit to other virus agents. This was so that human agents would always be affected by the changing number of virus agents. A different randomly generated AI seed was used for virus agents every trial to randomize mutations. The AI seed was kept constant and the mutation rate was 0 for human agents.

In the control scenario, parameters were exactly the same, however the mutation rate for virus agents was set to 0 so there were no SARS-CoV-2 variants. Each trial used a corresponding AI seed from the experimental scenario.

For each scenario, the total number of ticks that it takes for human agents to become extinct as a result of being infected was recorded. This was done to compare the morbidity of

COVID-19 with SARS-CoV-2 variants and without. Morbidity is the rate of disease in a population.

**Results**

As shown in Table 1, 10 out of the 20 trials indicated that the experimental scenario required less ticks for the human agent population to go extinct compared to the control scenario. Therefore, the mutated SARS-CoV-2 variant was more virulent than the control for half of the trials. The other 10 trials indicated that the experimental scenario required more ticks for the human agent population to go extinct compared to the control scenario. Therefore, the mutated SARS-CoV-2 variant was less virulent for the other half of the trials.

In the experimental scenario, human agents became extinct at an average of 10731.5 ticks while in the control scenario, human agents became extinct at an average of 11044.35 ticks. A t-test was conducted to determine if there was a statistically significant difference between the experimental and control trials. As seen in Table 2, the calculated P(T<=t) two-tail value was 0.615, greater than the chosen level of significance of 0.05. In addition, the t-Stat value of -0.507 did not have a greater absolute value than the t Critical two-tail value of 2.02. As such, the results of the experimental scenario did not have a statistically significant difference from the results of the control scenario.

**Discussion**

The results of this model show that there is no statistically significant difference between the number of ticks required for the human population to become extinct in the experimental scenario compared to the control scenario. Therefore, there is no relationship between the presence of mutations in the viral agent and morbidity in the human population. Random SARS-CoV-2 variants have the potential to be equally either more or less virulent.

A source of error in the model was that all agents were in one contained area with no barriers between them. This is not realistic since agents are closer together which can lead to a faster transmission of COVID-19. Another source of error was that breed energy had to be mutated to simulate the changing virulence of COVID-19 instead of disease transmission rate, which affected the accuracy of the results. Assumptions made to reflect COVID-19 were that 2% of the human population was initially infected and the mutation rate of the virus agent's breed energy was 0.05.

Error was reduced by providing enough resources for all agents so human agents could only die from being infected and not from other causes such as starvation. Human agents could not transmit disease to other human agents. Instead, only virus agents could infect human agents,

so the likelihood of a human agent being infected was always affected by the amount of virus agents that varied depending on the mutation.

This preliminary model of mutations in the SARS-CoV-2 virus could lead to more detailed models of the effect of SARS-CoV-2 variants as well as other viruses. A possible extension to this model includes using a larger COBWEB grid where agents are more spread out or using barriers to give a more realistic simulation of spread. Also, other parameters besides breed energy, such as step energy or breed chance, could be mutated to see if COVID-19 would spread differently.

**Conclusion**

This model demonstrates that random SARS-CoV-2 variants may either increase or decrease the morbidity of COVID-19. When comparing two scenarios where the likelihood of infection of COVID-19 is randomly mutated versus when there are no mutations, there were an equal number of trials where the variant caused an increase in morbidity and a decrease in morbidity. The results support the hypothesis because some random mutations caused the breed energy of virus agents to decrease, and as a result, the number of virus agents increased because less energy was required to reproduce. This increased virulence of COVID-19 caused the human agents to die out faster.

**References**

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## Appendix

**Table 1.** Raw data - number of ticks for human population to become extinct for each trial of the experimental and control scenario. The number of ticks determines if the experimental scenario is more or less virulent than the control scenario.

| Trial | Ticks for human population to become extinct - experimental scenario | Ticks for human population to become extinct - control scenario | Experimental scenario more or less virulent than control? |
|---|---|---|---|
| 1 | 10019 | 9810 | less |
| 2 | 7473 | 11430 | more |
| 3 | 8808 | 8316 | less |
| 4 | 11630 | 10150 | less |
| 5 | 10650 | 9767 | less |
| 6 | 9748 | 16248 | more |
| 7 | 11654 | 14950 | more |
| 8 | 8522 | 10458 | more |
| 9 | 10780 | 9111 | less |
| 10 | 10366 | 11930 | more |
| 11 | 12602 | 11616 | less |
| 12 | 13729 | 11015 | less |
| 13 | 9265 | 9303 | more |
| 14 | 14542 | 10340 | less |
| 15 | 9898 | 7510 | less |
| 16 | 13288 | 11696 | less |
| 17 | 8957 | 12104 | more |
| 18 | 9493 | 10655 | more |
| 19 | 11865 | 12370 | more |
| 20 | 11341 | 12108 | more |

**Table 2.** t-test results including the average and variance of the number of ticks for the human population to become extinct in the experimental and control scenario.

| | Experimental scenario | Control scenario |
|---|---|---|
| Mean | 10731.5 | 11044.35 |
| Variance | 3431534.474 | 4193752.976 |
| Observations | 20 | 20 |
| Hypothesized mean difference | 0 | |
| df | 38 | |
| t-Stat | -0.5066675 | |
| P(T<=t) one-tail | 0.307657799 | |
| t Critical one-tail | 1.68595446 | |
| P(T<=t) two-tail | 0.615315598 | |
| t Critical two-tail | 2.024394164 | |