Exercise 2 - Systems Biology

Eyal Haluts, ID: 318456290
Tomer Rozenstine, ID: 315718908

Comment: We didn't attach our plots, as they are too big as HTML files, and very hard to capture the essence of them in a png / static image. They will be generated by running both python scripts.

Question 1

a. HIV equations:

Verbal Equations:
Change in Uninfected = Production of Uninfected - (Uninfected percentage * Viruses density * Infection coefficient (K_1)) - (Uninfected percentage * Uninfected death coefficient (K_2))

Change in Infected = (Uninfected percentage * Viruses density * Infection coefficient (K_1)) - (Infected percentage * Infected death coefficient (K_3)) - (Infected percentage * Lithic explosion coefficient(K_4))

Change in Virus density = Infected percentage * Lithic explosion coefficient(K_4) * Viruses per lithic explosion - Viruses degradation coefficient(K_5) * Viruses density

Mathematical Equations:

$$\frac{dU}{dt} = P - U \cdot V \cdot K_1 - U \cdot K_2$$
$$\frac{dI}{dt} = U \cdot V \cdot K_1 - K_3 \cdot I - K_4 \cdot I$$
$$\frac{dV}{dt} = I \cdot K_4 \cdot \alpha - K_5 \cdot V$$

b. Updated Equations, with Latent cells population:

$$\frac{dU}{dt} = P - U \cdot V \cdot K_1 - U \cdot K_2$$
$$\frac{dI}{dt} = 0.8 \cdot U \cdot V \cdot K_1 + K_6 \cdot L - K_3 \cdot I - K_4 \cdot I$$
$$\frac{dL}{dt} = 0.2 \cdot U \cdot V \cdot K_1 - K_6 \cdot L - K_7 \cdot L$$
$$\frac{dV}{dt} = I \cdot K_4 \cdot \alpha - K_5 \cdot V$$

Where K_6 Is the Latent to Infected coefficient, and K_7 Is the Latent death coefficient.

c. See generated plots, in HTML files, named:

a. HIV Model Latent from Beginning.html - Where the latent cells transforms to infected cells in a steady rate from the beginning
b. HIV Model Latent after Equilibrium.html - Where the latent cells transform to infected cells only after reaching equilibrium

Question 2

We ran the model twice, once with treatment that doubled the virions death rate, and once with the same treatment, but also made the latent cells transform to infected cells at 10 times higher rate. The results are generated as plots with the following names:

1. HIV Model Treatment.html
2. HIV Model Treatment and Latent.html

As observed in our model, the treatment without the higher transformation to infected rates, showed better results - the peak virus number was smaller, we had fewer outbreaks, and both ended with approximately the same number of virions, and uninfected cells.
The only improvement by the higher transformation rate was that it slightly shortened the first and most aggressive outbreak duration.
We tested several changes in our model:

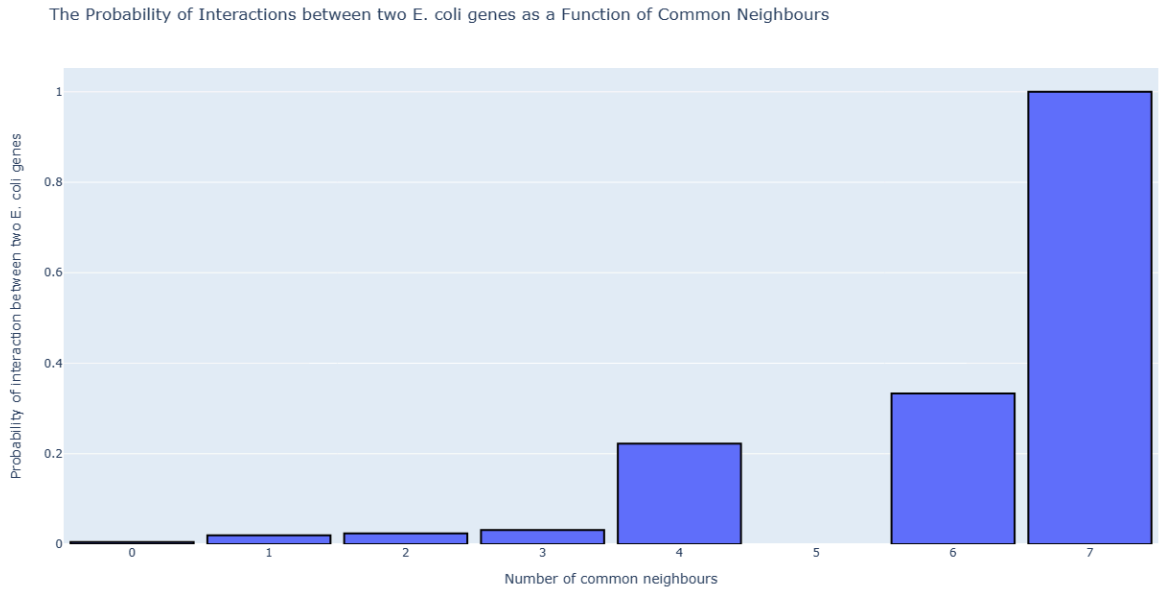
1. Latent to infected cells occur at steady rate, or only after a certain period (in various lengths)
2. Latent to infected cells occurs only during outbreaks, that repeat every specific time period, and for a specific time period (both vary in length)
3. Various treatment virus kill rate

All of these eventually resulted in the same conclusion. Therefore, we believe that the expanded treatment, also increasing latent to infected cells rate, does not improve the results of the treatment.

Question 3

a. To count the numbers of transcription factors, we counted all the rows in which there is at least one non-zero value. We found out that there are **377** transcription factors in the network.
b. To count how many inhibition interactions there are in the network, we counted the number of -1 values in the network, and similarly to find the number of activation interactions we counted the number of 1 values in the network. We found that there are 214 inhibition interactions and 364 activation interactions, which means **there are more activation interactions.**
c. To find how many unregulated genes there are in the network, we counted how many columns contain only 0 values. We found that there are **307 unregulated genes in the network.**

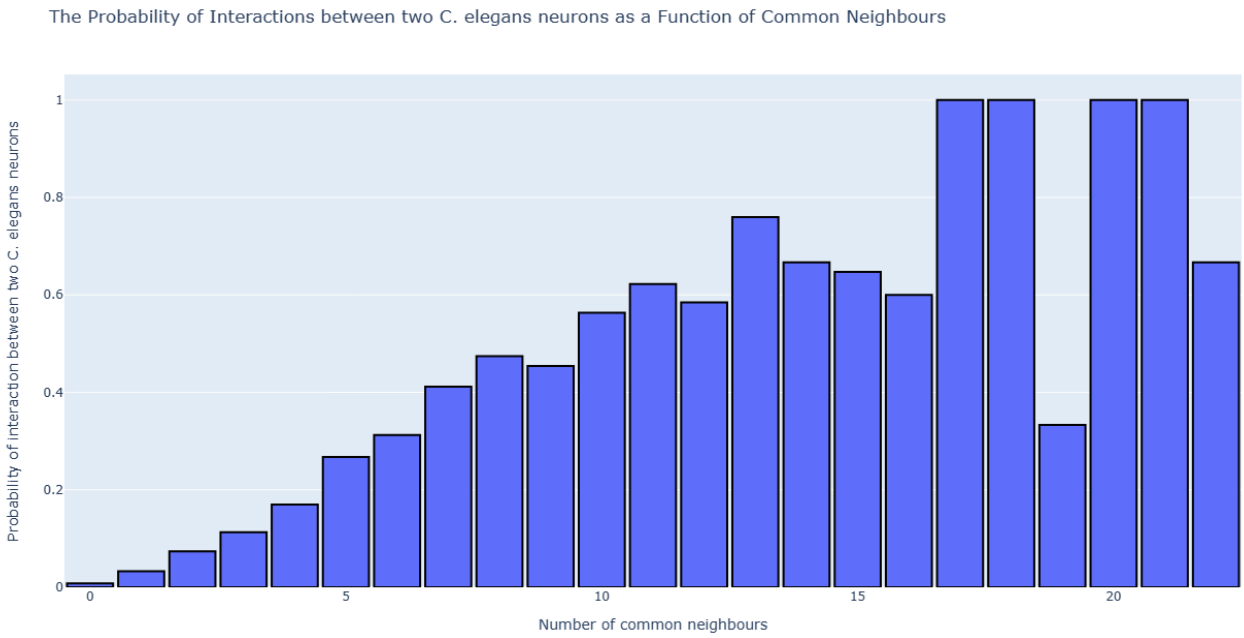
d. To check if the common neighbor rule applies to the network, we calculated the number of common neighbors for each pair of genes. For each number of common neighbors (n) we got, we checked the fraction of pairs with n common neighbors that have at least one interaction between them. The results are shown in the histogram below:



it is clear that the number of common neighbors increases the chance of in-pair interaction.

e. To check if the given structure is a motif in the transcription network, we first checked if there is any pair of genes in the network that regulate each other (for the genes annotated as W and Y). We found that no such pair exists, and therefore it must be that the given structure does not appear in the network at all. Trivially, it is not a motif.

f. To check if the Common Neighbor Rule applies for the C.elegance neuron network, we applied the same logic as in d. We found that the rule does apply, as seen in the histogram below:



g. To check if the given structure is a motif in the C.elegance neuron network, we applied the same logic as in e. In this case, there were many pairs of neurons that regulated each other. For each of these pairs (W,Y), we checked which neurons are regulated by Y and regulate W (X). For each of the triplets (W,X,Y) we found, we checked which neurons are regulated by Y. In each step we also made sure no other interactions that are not part of the structure occur between the neurons.
After applying this procedure, we ended up with 1,201 quadruplets (W,X,Y,Z) which followed the given structure. To see if this is indeed a motif, we shuffled the network 1,000 times, and counted how many times the structure appears in each shuffle (permutation of the original network). We calculated the Z score and found that it was extremely high (>20) across several runs. The p-value that corresponds to this Z score is close to 0. Therefore, we can confidently conclude that this structure is a motif in the C.elegance neuron network.