CSE 440

02 July 2017

Assignment 4

Monte Carlo Reinforced Virus Population Growth Modeling and Simulation

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Abstract

In this assignment, we modeled the effects of using drugs for treating viral infections. Using randomness, we ran simulations on how some viruses might gain resistances to administered drugs and how that would affect the chances of patients getting cured. We tried to figure out how delay in treatments affects curing of patients. We also considered the effects of using single and multiple drugs.

To gain reasonable insights, we ran 500 trials for all our simulations. All our code could be found in the **`ps8.py`** file.

Problem 1: Implementing a Simulation with Drugs

This problem required us to implement the **`ResistantVirus`** and **`Patient`** classes according to the provided specifications. The implementations of these classes could be found in the **`ps8.py`** file.

Problem 2: Running and Analyzing a Simulation with a Drug

In this problem, we considered the effects of both administering drugs to the patient and the ability of virus particle offspring to inherit or mutate genetic traits that confer drug resistance. Drugs were given to a patient using the **`addPrescription()`** method of the **`Patient`** class. The drugs we consider do not directly kill virus particles lacking resistance to the drug, but prevent those virus particles from reproducing. Virus particles with resistance to the drugs continue to reproduce normally. All viruses start off with no resistance to the drugs, but as time goes by virus offspring randomly gain resistance to the administered drugs.

The common trend observed in Figures 1, 2, and 3 by adding a single drug at different time steps shows that after drug is induced, the average total virus population decreases dramatically at that very step in all cases. This happens because the drug prevents the viruses, who did not mutate to gain drug resistance, from reproducing. Hence the average total virus populations in all cases drop.

In addition, the average guttagonol resistant virus populations demonstrate an upward trend. After the introduction of the drug, viruses that got favorable drug resistance mutations get higher chances of reproduction owing to the reduced population density. In fact, after some time steps only the drug resistant viruses survive and represent the total virus population.

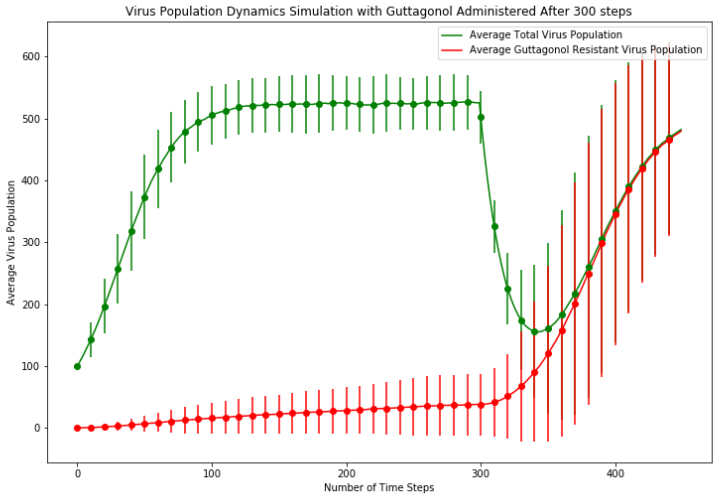

Figure 1

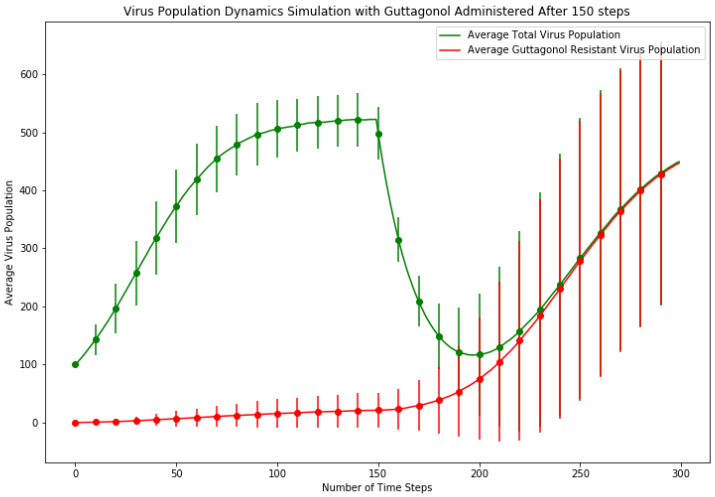

Figure 2

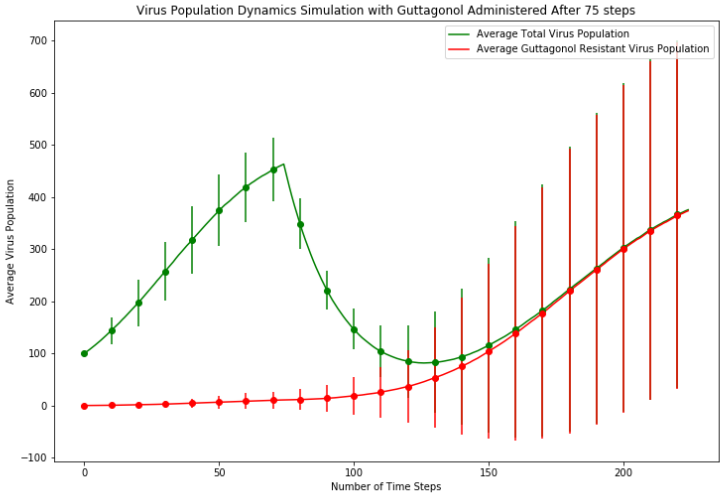

Figure 3

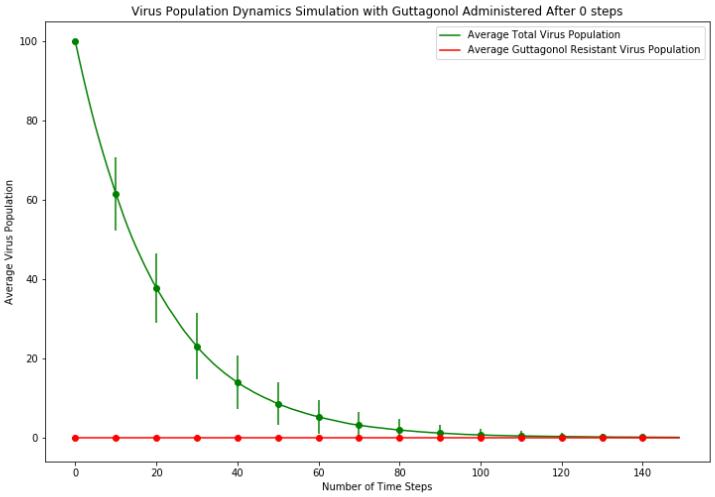

Figure 4

A different trend is observed in Figure 4. When the drug is introduced right after the loop is initiated at 0^{th} step, average total virus population steeps down while average resistant virus population shows no increase in population. This happens because no virus is out there which is outside the effect of the drug and could continue to produce more viruses. If 100 viruses are present at the start, all of them get influenced by the drug, and the number of resistant viruses stays almost at 0. Since mutations are very unlikely to occur (1 in 200), very few resistant viruses are born.

These trends are consistent with our intuition.

Problem 3: The Effect of Delaying Treatment on Patient Outcome

The histograms in Figures 5, 6, 7, and 8 demonstrate how administering a drug in 300, 150, 75, and 0 time steps delay affect patient outcome. We ran our each of our simulations 500 times and the reasonability of our chosen number of trials is justified by the intuitive histograms.

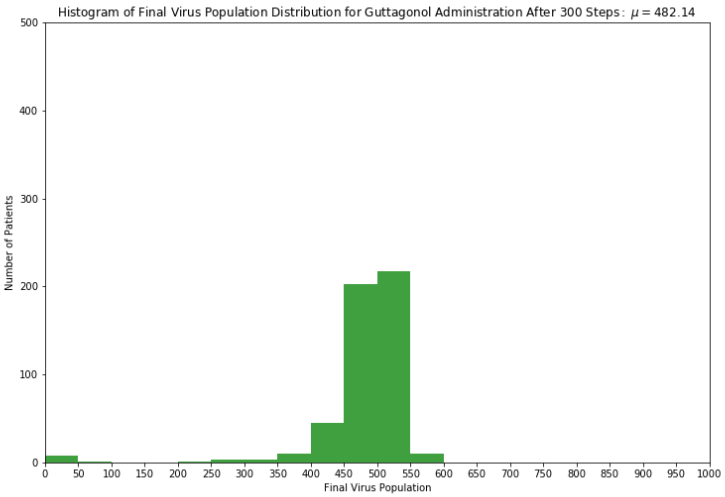

Figure 5

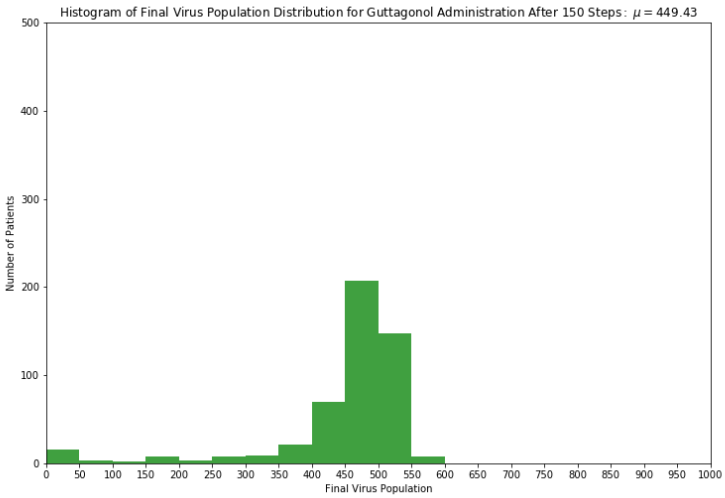

Figure 6

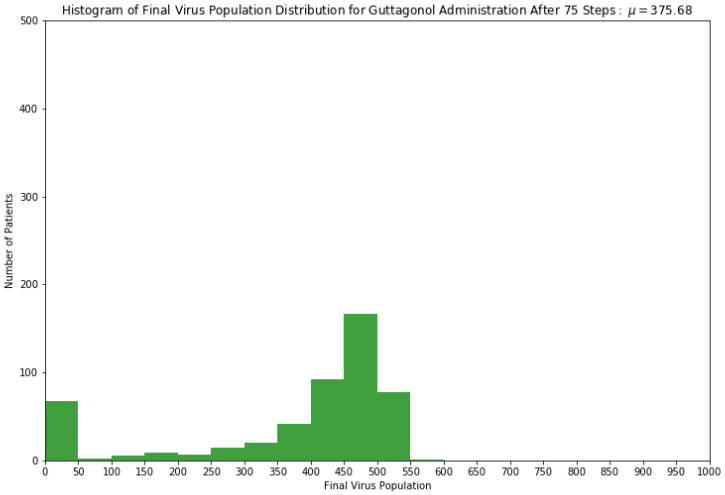

Figure 7

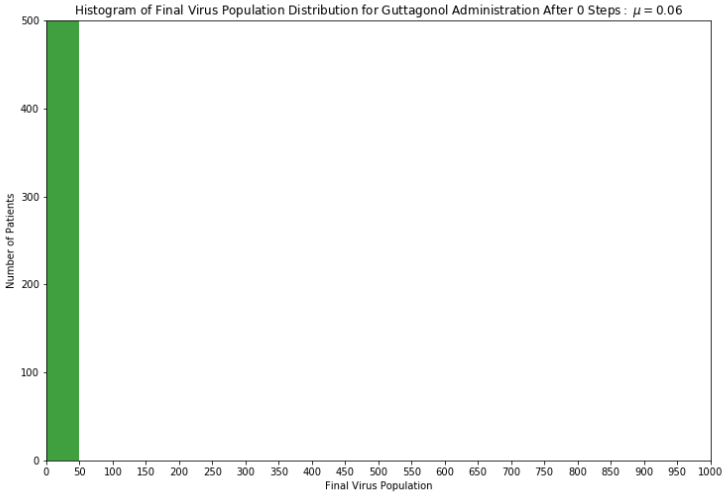

Figure 8

Considering a patient's final count being between 0 and 50 as the patient being cured or in remission, we find that there is an inversely proportional relationship between the time delay of drug administration and the number of patients being cured. This means that the more delay there is in drug administration, the smaller number of patients are cured and vice versa.

Time Steps Before Drug Administration	Percentage of Patients Cured (or in Remission)
300	1.40
150	3.00
75	13.40
0	100

Table 1: Effects of Administering One Drug at Varying Time Steps

Essentially, the more delay there is in inducing a drug, the more drug resistant viruses are likely to be born within the host. These resistant viruses continue to produce of offspring even after the drug is administered and thus offset the effects of the drug. On the other hand, smaller delay in administering the drug means there will be less drug resistant viruses and the drug would be able to affect more viruses. Smaller delay in drug administration thus leads to more patients getting cured.

This can be verified by the produced histograms. In Figure 5, where the drug is induced after 300 steps, the mean final virus population is almost 482. In fact, most patients have 450 – 550 viruses within them, where very few patients are cured. This supports the "the more delay in treatment, the less successful the medication" policy.

In Figure 6, the drug is administered after 150 time steps. The mean final virus population here is almost 449 which is less than the mean population after 300 steps. Again, more number of patients are in the cure range than before. Also, the number of patients carrying higher virus population (400-600) has also decreased. And more number of patients are found over the range of (0-400) showing more number of patients are on the way to be cured faster.

In Figure 7, the mean final population for drug administration after 75 time steps is almost 376 which is quite smaller than the previous figures. Number of patients on the cure range is almost 70, greater than previous plots. Also, number of patients carrying higher population of virus has declined and highest virus population is nearly limited to 550 now. More number of patients are distributed between (0-400) indicating that more people are carrying less virus population.

In contrast, the mean final virus population in Figure 8, where the drug is administered after 0 steps, is almost 0. The is far lesser than the previous histograms. In this plot, all 500 patients are in the cure range, which indicates a 100% successful drug application. This verifies the idea that "the smaller delay in treatment, the more successful the medication."

Problem 4: Designing a Treatment Plan with Two Drugs

In this problem, we consider the effects of using two drugs for treatment. To model make the model more realistic, we opted to introduce the drug after 150 time steps and varied the number of time steps for the introduction of the second drug. In general, we found an inversely proportional relationship between the number of patients cured (or in remission) and the time between administering the two drugs. Larger delay in between the drug administrations meant fewer patients getting cured, and smaller delay in between the drug administrations meant more patients getting cured. This happens because the viruses continue to produce offspring and genetic mutation give those offspring drug resistance. More time allotted to the virus before introducing the second drug only makes them more resistant against the drug effect.

Steps Before Administering the First Drug	Steps Before Administering the Second Drug	Percentage of Patients Cured (or in Remission)
150	300	5.00
150	150	10.00
150	75	45.40
150	0	84.80

Table 2: Effect of Administering Two Drugs at Varying Time Steps

Nevertheless, dual drug treatment has an average better outcome of cured patients than the single drug treatment provided that the first drug induced already reduces some of the virus population. Although the final trial produces 84.8 % of cured patients whereas single drug treatment produced 100% cure rate, this happens due to gap maintained at the beginning before introducing the first drug. In this case, some of the virus remain unaffected by both the drugs and continue to reproduce.

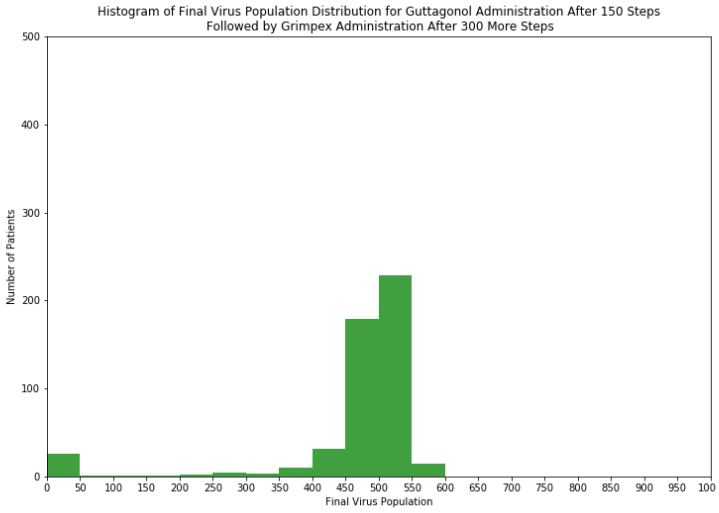

Figure 9

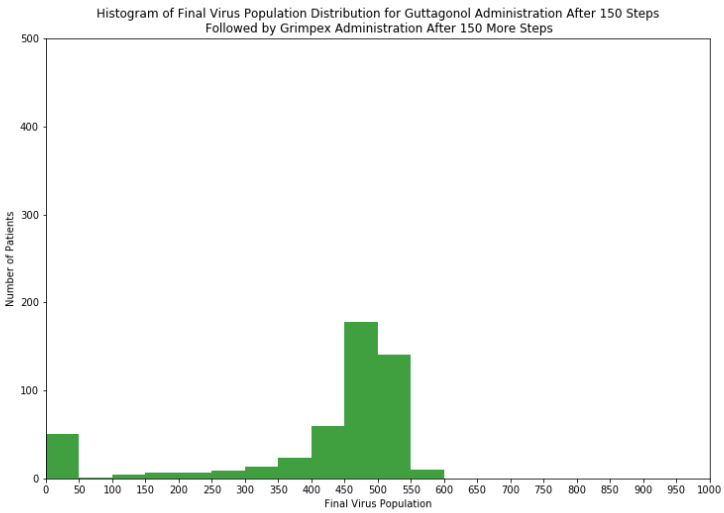

Figure 10

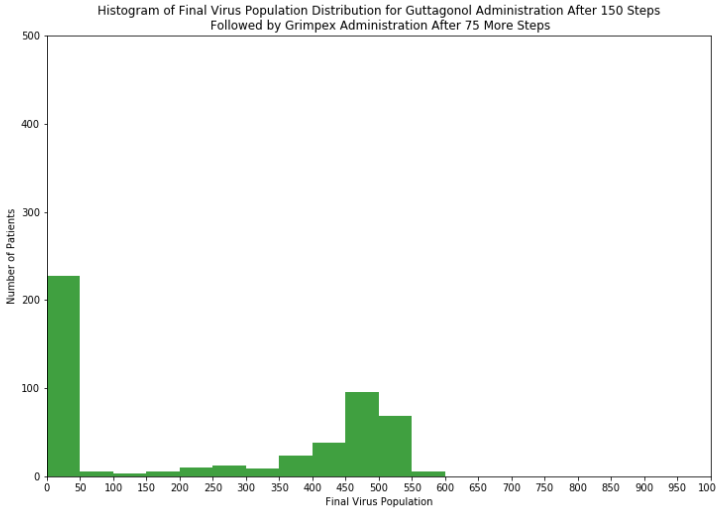

Figure 11

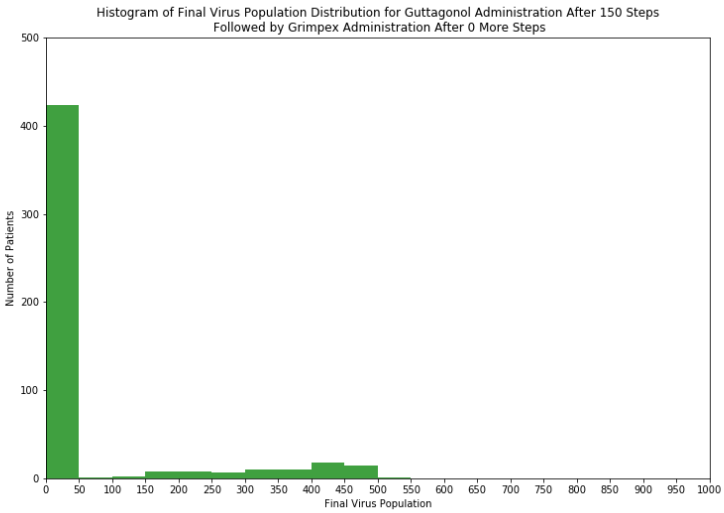

Figure 12

In Figure 9, the second drug, grimpex, is administered 300 steps after the first drug, guttagonol. Here, 5% of the patients are in the cure (or remission) range and most other patients remain in the higher ranges of virus population. Highest virus population reaches 600 and majority of the patients carry 450-550 viruses. Delay in addition of the second drug diminishes the effects of the drugs on the viruses and the remedy turns quite ineffective.

In Figure 10, grimpex is administer after 150 steps of guttagonol. Here, 10 % of the patients are in the cure (or remission) range which is double of the previous histogram. Most other patients remain in the higher ranges of virus population. Highest virus population reaches 600 and majority of the patients carry 400-550 viruses. Some of the patients discretely carry varied number of virus in the range (100-350) indicating that more number of viruses are affected when the delay time is reduced. Lesser delay in addition of the second drug increases the drugs' effect on virus a bit and the remedy turns somewhat more effective than before.

In Figure 11, where grimpex is administer after 75 more time steps of guttagonol, 45.40 % of the patients are in the cure (or remission) range which is significantly larger than the previous histograms. Moreover, fewer patients carry high number of viruses. It clearly indicates that the lessened delay in addition of second drug accelerated the cure process and more number of patients stay in the cure range of virus population.

In Figure 12, grimpex and guttagonol are administered simultaneously after 150 time steps. Here, 84.80 % of the patients are in the cure (or remission) range which is the highest cure rate among all the histograms. We can also see that few patients have high virus populations. This clearly establishes how small or no delays in drug administration dramatically increase curing chances of patients.

Problem 5: Analysis of Virus Population Dynamics with Two Drugs

In this problem, we examine the effects of using two drugs more closely. Specifically, how the delaying the administration of the second drug when the first drug is administered after 150 steps affects patients.

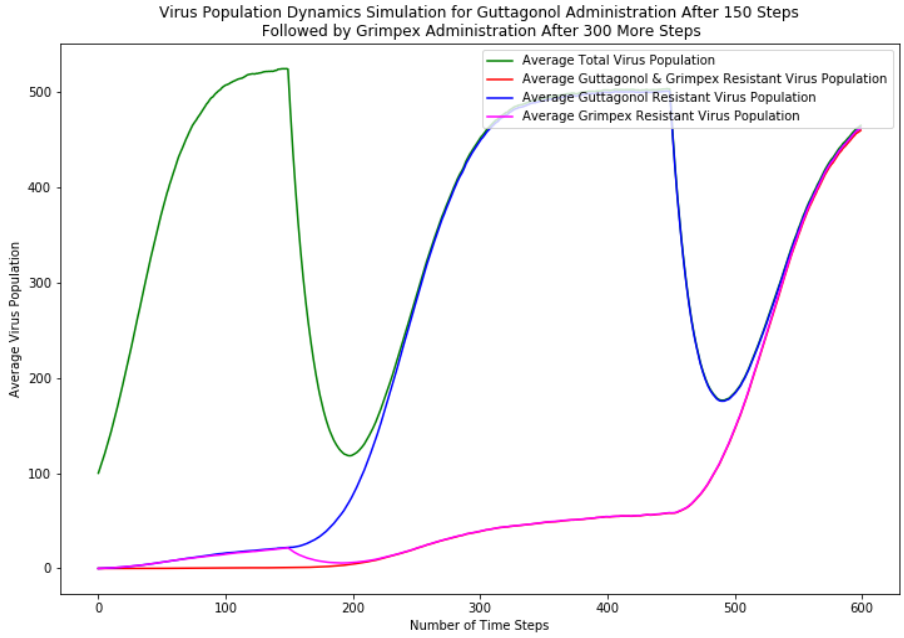

Figure 13

In Figure 13, we model how administering the second drug, grimpex, 300 steps after administering the first drug, guttagonol affect patient outcome. The average total population of viruses rises till step 150. The population of grimpex resistant and guttagonol resistant viruses also increases slowly. However, the population of viruses that are resistant to both grimpex and guttagonol shows the slowest increase, almost none.

When guttagonol is administered at step 150, the viruses non-resistant to guttagonol start to die off. From this point forward to step 450, the guttagonol resistant viruses can produce more because of the reduced population density. In this period, the guttagonol resistant represent the majority of the viruses. The only grimpex resistant and both grimpex and guttagonol virus population converge, because only the guttagonol resistant viruses survive, and continue to increase slowly.

When grimpex is administered at step 450, the guttagonol resistant but grimpex non-resistant viruses start to die off. As a result, after some time steps, only the viruses resistant to both the drugs survive and constitute the total virus population.

After 150 steps of grimpex administration, it is seen that only 5% of the patients are cured.

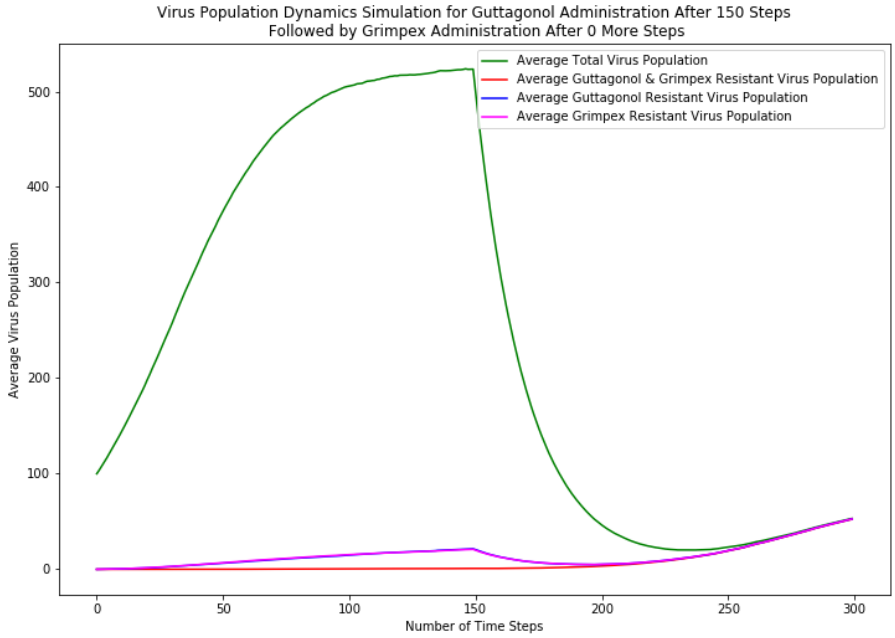

Figure 14

Figure 14, on the other hand, shows what happens when guttagonol and grimpex are administered simultaneously. Before the drugs are administered the virus populations increase as they have previously. When the drugs are administered at time step 150, viruses they are not resistant to both drugs start dying. At the end of 150 additional steps only the viruses resistant to both the drugs survive.

Almost 84.80% of patients are cured here. All patients are not cured because before the administration of the drugs at step 150, genetic mutation conferred resistance to both the drugs to some viruses.

Problem 6: Patient Non-compliance

We can model the randomness in patient compliance by introducing a new property called **`complianceProbabiltiy`** in the **`Patient`** class and changing the **`update()`** method in such way drugs would be added randomly during each call to update.

We can assume 80% of patients have **`complianceProbabiltiy`** over 90%. This means 80% of the patients would take drugs in the right manner 90% of the time. We can further assume 10% of the patients have **`complianceProbabiltiy`** between 75% and 90%, 5% of the patients of **`complianceProbabiltiy`** between 50% and 75%, and 5% have **`complianceProbabiltiy`** below 50%.

We can create the **`Patient`** instances for our trials keeping the **`compliancePrbabiltiy`** distribution in mind. Now in the **`update()`** method, we can check through randomness whether a patient will take the drugs administered to him/her at each time step and update the virus populations accordingly at that time step.

This would give us a reasonable model.

Conclusion

This assignment established that it is best to seek treatment for viral infections as soon as possible as it highly increases the chances of curing.