Model of a Human Bloodstream

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By Eli Echt-Wilson and Corey Miner

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Executive Summary

Our supercomputing project is a model and simulation of a human blood stream. Our main goal was to create a testbed that allows experimentation of different problems within the blood stream. The model simulates the flow and function of the major components in human blood. Each cell in the blood stream is programmed to follow a certain set of rules that corresponds to the behavior of a normal, healthy blood cell. We can manipulate this model to explore, investigate, and help solve different problems that a human blood stream encounters. So far, we have modeled a few different problems such as cuts and simple viruses.

Our blood model represents a human blood stream because it incorporates all of the major components such as platelets, red-blood cells, white-blood cells, and antibodies. We represent these major components as breeds of agents. The agents are all programmed to circulate appropriately in the environment and have accurate life spans and production rates. In addition, each individual breed has a specific purpose in the model. Red-blood cells transport oxygen, white-blood cells produce antibodies to fight disease, antibodies destroy viruses, and platelets clot cuts. We critically researched the correct ratios between all of the major blood components and replicated these ratios in our model. Because we accurately assign behaviors to the correct agents in the correct ratios, our model behaves in a very similar way to a healthy human blood stream.

Using this blood system model, we can investigate different problems within a human blood stream. We extensively tested a simple virus to determine when the virus cell production rate overcomes the white-bloods cells ability to destroy it. We also tested the amount of blood lost for different sized cuts before the platelets could scab the cut. These are just examples of our overall goal to produce a blood model that can test various situations in a blood stream. There are many other ways for our model to be extended.

Overall, we successfully created a blood model that correctly resembles a blood stream in the human body. We did not create this model to solve one particular problem, but instead, to serve as a testbed for investigating multiple blood system problems.

Project Background

In coming up with an idea for our project, our team wanted to pick a project that was relevant to our lives today. Creating a blood model was a perfect fit, because two of our team's very close family members are suffering from blood diseases. One of our parents very recently had a pulmonary embolism, which is a blood clot in the lungs. Because of this clot, he is on blood thinning chemicals so that his blood has a much lower risk of clotting. Another family member currently has myelofibrosis which is a disease where the bone marrow in your body stops producing red blood cells. Because of this, she has been on many different types of medication over the past year and a half. Our goal for this project was to create a realistic blood model that could be used to explore these types of blood system problems and others. Eventually, our blood model could be used to explore blood clots and myelofibrosis. We did not have one specific problem in the human blood that we were trying to solve; however, our model allowed us to test two problems that occur in human blood streams. The two problems that we tested were the point at which a virus gets out of control, and how much blood is lost from a cut. These problems are only two out of many that can potentially be tested using our model.

Programming Environment

Our team decided to use the NetLogo programming interface and environment to create our model. NetLogo does have limitations: the size of our model is limited to about 4,500 agents (due to the amount of memory java allows), and java only allows the use of one core. In spite of these limitations, NetLogo is the right choice for us because, it is a simple, agent-based environment that has a very good interface for creating models and testing them. In addition, our team members each knew different languages, and NetLogo seemed to be the easiest for everyone to learn quickly. While we still believe NetLogo was the correct choice, it has definitely created challenges on our project that are hard to overcome. Our blood model only represents about a microliter of blood, because of the limitation on the number of agents. To put this into perspective, our model has 3-4 white-blood cells where in the human body there are actually 25,200,000,000 white-blood cells. In order to model a larger blood volume, we would need to choose a different programming language that allowed more agents and the use of more cores.

Our team had ready access to several intel-based desktop computing systems. On our highest performing computer, each run took about six seconds. On our slowest performing computer, each run took about 30 seconds. Due to the limitations of these computers, one of our experiments took two and a half days to run. If we want to experiment with larger volumes of blood, we need a much higher performing computer. This might be a great model to run on a supercomputer, but it requires migrating from NetLogo to a different language such as RePast.

Baseline Model

We used a step-by-step process in producing this model. First, we created the three major components of a blood stream using the correct ratios corresponding to human blood. In a human blood stream the ratio for white-blood cells, red-blood cells, and platelets is 1:700:32. We modeled this ratio exactly. The next step was to make these components circulate around the NetLogo world to emulate a flowing blood stream. Figure 1 shows an image of the agents circulating around the NetLogo world. This will be explained further below.

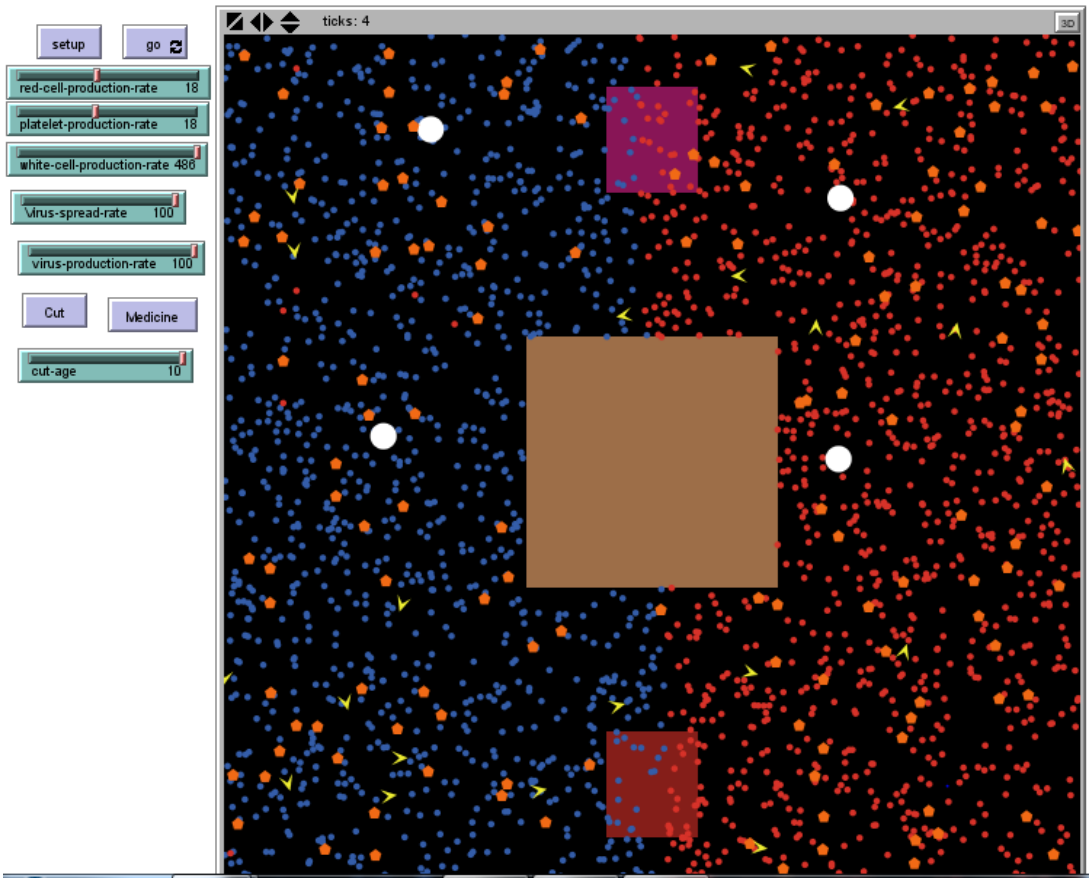

FIGURE 1: Blood Agents in NetLogo World

The next step was to program the functions of the red-blood cells, white-blood cells, antibodies, and platelets. Using the interface in NetLogo, the world that we created is a relatively small square. In order to optimally use the entire square, the blood component agents in the program circulate counterclockwise around the square. This created a graphical representation of blood circulation. Red-blood cells (or erythrocytes), transport oxygen from the lungs to other parts of the body. Red-blood cells are a deep blue color when they do not carry oxygen (as seen on the left side of the world in figure 1), but turn red when they do carry oxygen (as seen on the right side of the world). The purple colored small square at the top of the screen represents a part of the body where the blood drops off oxygen. The blood continues to circulate around the world, and picks up oxygen from the lungs which is represented by the red square at the bottom. Red-blood cells have an average lifespan of 120 days, which we duplicated in our model. In addition, our model contains white-blood cells (or leukocytes) which are represented by the larger white circles in figure 1. White-blood cells are the control factors of the body's immune system. The white-blood cells control the amount of antibodies that are sent out to fight a virus in our blood stream. White-blood cells come in many different varieties, and each variety has a different average lifespan. However, the main white blood cells for fighting common viruses are the lymphocytes. Lymphocytes, on average, live for around 4 years, or 1460 days. When a virus is present, white-blood cells release antibodies to fight the disease. Antibodies are represented by yellow arrows in our model. Antibodies latch on to a virus, and kill the virus. During this process, the antibody itself is killed. Antibodies in our model are released when a white-blood cell is near a virus. The antibodies then naturally search out the virus and kill it. Antibodies have an average lifespan of 25 days. Platelets, as well as the white-blood cells, can have multiple purposes in the human body. Platelets are represented by orange hexagons in our model. We used platelets to scab over a cut, and stop bleeding. When a cut is produced, blood flows into the cut and is lost from the body. In our model, the red-blood cells disappear. The platelets' purpose in our model is to rush to the cut and stop the bleeding as quickly as possible. Platelets have an average life span of 4-6 days. In our model, one of our main focuses was to represent the ratios and lifespans of all the major blood components as accurately as possible.

This resulted in the baseline model. Using this model, many different aspects of a blood system can be explored. We decided to run two experiments: testing outcomes from a simple virus and testing how much blood was lost from different sized cuts Yet, there are many different

experiments and problems that could be run based around our blood model. The next sections detail the experiments and results.

Experiment 1: Fighting a Simple Virus

Problem:

The first experiment was designed to explore the behavior of a simple virus. The problem we examined was to find the point at which the virus overwhelmed the white-blood cells as the virus spread and production rate changed.

Hypothesis:

If the model is functioning correctly, we should see an increase of viruses and antibodies as the virus production and spread rate increase. At some point we expect the number of viruses to overwhelm the body and our model should stop.

Procedure:

The experiment tested the model at various combinations of two variables: virus spread rate and virus production rate. The virus produces randomly according to an input parameter controlled by the slider "virus production rate" in the NetLogo interface. We also control how fast the virus spreads, with another slider "virus spread rate". Both of these sliders are inversely proportional to the rate, meaning as the slider value gets lower, the production rate gets higher and vise versa. We ran the experiment, testing each variable from 1 to 30 in increments of 1. We ran the experiment 3 times and averaged the results.

Results:

The purpose of this experiment was to find the point at which a virus can no longer be controlled. After running our code 2700 times, we discovered a few things. The results are shown in figure 2. We learned that when the inverse virus spread rate is in the range between 1-4 (ie virus spread rate is at its maximum this can be seen on the far left side of figure 2), the virus almost always gets out of control and is not stoppable by the antibodies and white-blood cells. As we increased the inverse virus spread rate past 12, there was a distinct drop off in virus growth (as seen on the right side of figure 2). By the end of the test, the inverse virus spread rate is as large as possible (the virus spread rate is as small as possible) and the antibodies and white-

blood cells fight off the virus before it can spread at all.

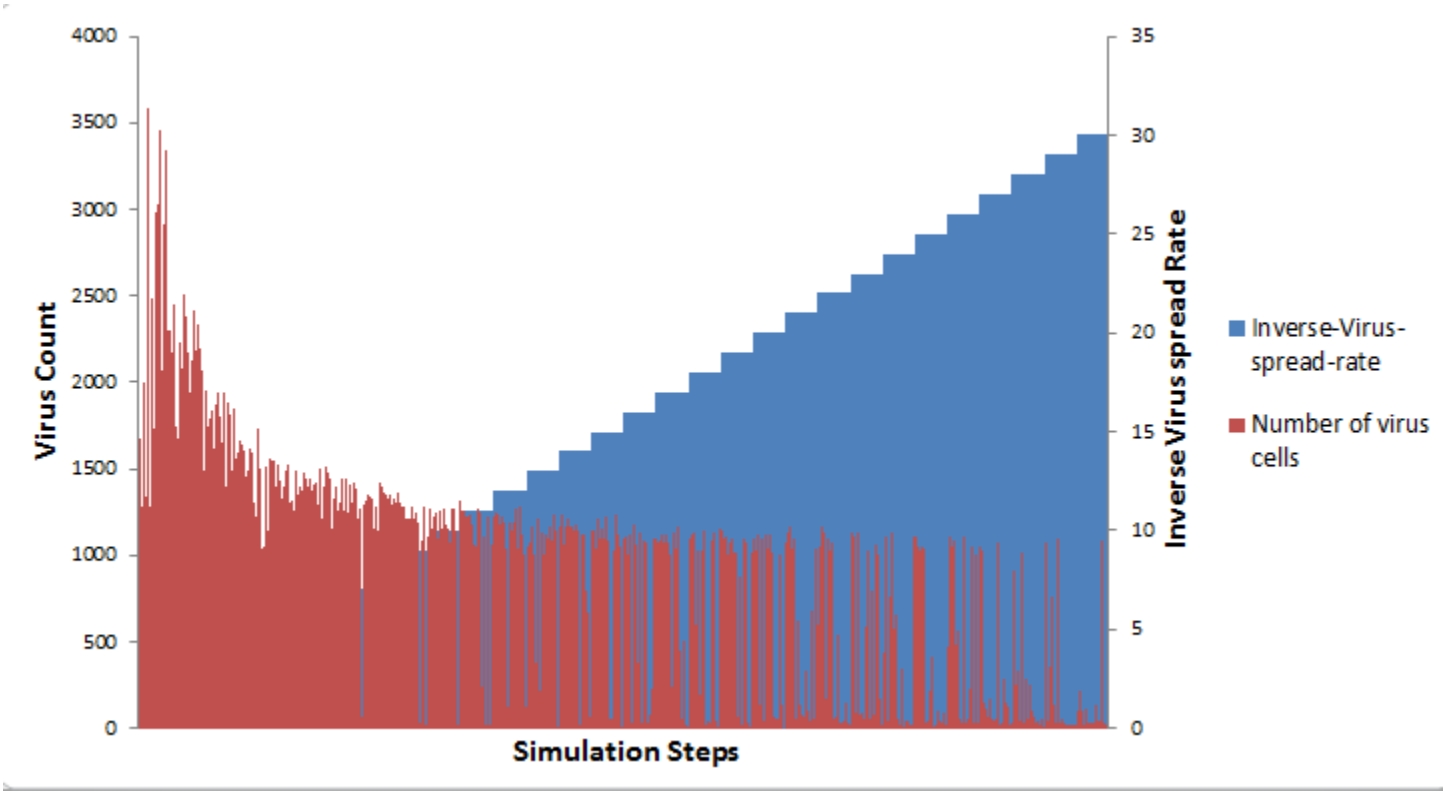

Figure 2: Simple Virus Results

Discussion:

From these results we determined that the model is functioning correctly as we hypothesised. We learned that it would be helpful to have a more powerful computer to test our model, as it took 2 and a half days of constantly running the test to collect all the data. Lastly, we were not able to take our conclusions and apply them to human life. We know that the point at which viruses get out of control is when the inverse virus production rate is 4 or below. But, what does that mean? While our model can be used to understand and test these viruses, we cannot necessarily apply those numbers to a human body because our model represents such a small portion of a blood stream.

Experiment 2: Blood Loss Through Cuts

Problem:

The second experiment was designed to test the amount of blood lost and the time it took to heal different sized cuts.

Hypothesis:

Based on the rules we set for this experiment, we believe the results should show that as the cut gets larger, the body should lose more blood. Yet we should not see the body loose so much blood that is cannot function anymore.

Procedure:

The second experiment changed one variable: the size of a cut. We decided to create a cut which is produced by a button on the NetLogo interface. The cut's size changed according to an input parameter controlled by the slider "cut-age". We ran the experiment, testing the size of the cut from 1 to 10 in increments of 1. For each cut size, we collected how long the cut took to heal, and how much blood was lost in the process. The only way the cut could heal was by platelets passing through and clotting the cut. This experiment had much more variability than the last experiment, so we ran the experiment 5 times instead of 3. In reality we should run the experiment many more times than this but we were limited by our computer resources.We took these 5 experiment runs and averaged the results.

Results:

Our second experiment's purpose was to see how much blood would be lost and how much time it took to heal the cut based on the size of a cut. After running our code 1700 times, our data really surprised us. The results are shown in figure 3. The first half of our results agreed with our hypothesis. As the cut grew in size, the amount of blood lost increased. But halfway through the simulation, the data points showed that the blood loss did not follow any particular pattern. The time it took to heal the cut in general increased as the cut size grew as we predicted. However again, there was a substantial amount of variability in the resulting data.

Discussion:

In this experiment we did find that the platelets did stop the bleeding by clotting the cut. We were also able to see that the larger the cut, the longer it took for it to heal. This demonstrated how our base model was performing according to expectations in general. Yet upon closer examination of these results, we found that the data we collected varied unexpectedly and dramatically. This variability can be seen in figure 3. We determined that this variability was most likely caused by a flaw in the rules controlling the experiment. We also believe that we did not run the test enough times to eliminate a suitable amount of error. Based on these findings, this experiment requires additional refinement and modifications.

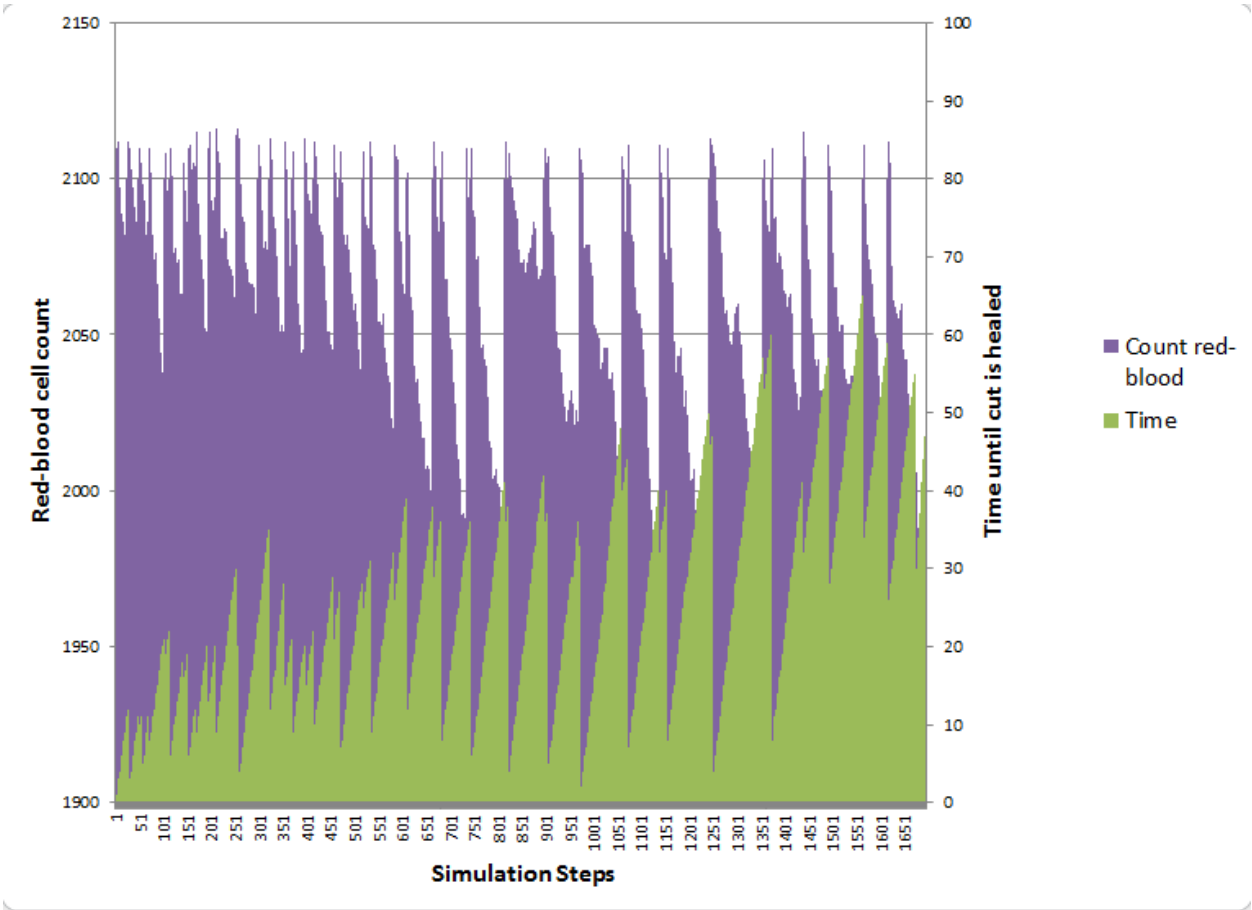

Figure 3: Cut Results

Conclusion

In conclusion, we successfully created a blood system testbed for many different experiments. The two experiments that we were able to test were a simple virus and a cut. We collected extensive data and found clear results for a model of our size. A more powerful computer would allow us to run these simple experiments on a larger volume of blood, more closely emulating a human blood system. Our thoughts for extending our project include doing more research on different diseases and problems. We would also like to conduct more complex experiments such as testing diseases like myelofibrosis and pulmonary embolisms. Conducting these more complex experiments also requires us to extend the model. Our most significant original achievement on this project was: creating a human blood system testbed, based on researched ratios and proportions that can be used to examine different human blood system problems.

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