Using a Concentrated Heat System to Shock the P53 Protein to Direct Cancer Cells into Apoptosis

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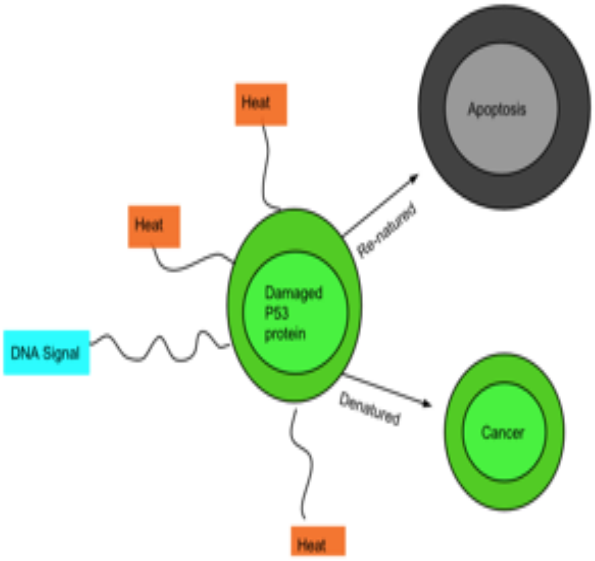
Team 91
Monte del Sol



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Executive Summary

This experiment set out to determine if applying concentrated heat on a cellular level could be used as an alternate way to kill cancer cells. We did this by creating two NetLogo computer models: one that showed how the mutated P53 protein is molecularly altered by heat and the other to show how efficient nanorobots can apply that heat to kill cancer cells. P53 is a tumor suppressor protein within all cells that, when mutated, will not signal the cell to undergo apoptosis when DNA damage occurs (Hainaut). In this model, we used concentrated heat to renature the mutated P53 protein, so it would send out the signal for the cell to die. We tested the effects of raising cell temperatures by four different heat intensities: 13, 23, 100, and 113℃. We chose these increases because 13℃ is the amount needed to break hydrogen bonds, 23℃ to break ionic bonds, 100℃ to break hydrophobic interactions, and 113℃ to break covalent bonds. We found out that 13℃ could possibly kill the cancer cells without seriously altering the environment of the cell by using the specific heat equation ($Q = mc\Delta T$) (BBC). By using two nanorobots in one kilogram of blood, we found that the P53 protein would renature 94% of the time at an increase of 13 degrees Celsius, thus sending out the signal for the cell to undergo apoptosis or programmed cell death in our protein model. Furthermore, at this same temperature, 66% of the time, all of the cancer cells were killed in our cellular model. Twenty-three degrees also showed promise with a cure rate of 62%, but it is likely that it could cause harm to the cell. The most promising temperature is 13℃ because it is hot enough to break hydrogen bonds, which promote refolding and function of the P53 protein.

Introduction

We used NetLogo to model how concentrated heat affects the tertiary structure and function of the P53 protein. Nanorobots were used to detect cancer cells, while not attacking healthy cells; they could go against the flow of blood and be able to obey commands sent from an outside computer (Mali). The nanorobot has a needle in its body that, when it detects a cancer cell, will transfer heat to the cell. The heat will shock the P53 protein, making the protein send a signal out to destroy the cell. We used the specific heat equation in order to determine how certain temperatures could affect the outside environment. The specific heat formula is, $Q = mc\Delta T,$ where the transfer of heat in joules (Q) equals the mass of water in grams (m) * specific heat capacity (c) * change in Temperature (Δ T) (BBC). Using this formula, we figured out how much the temperature of the cell needed to rise to renature the P53 protein but not destroy the cell.

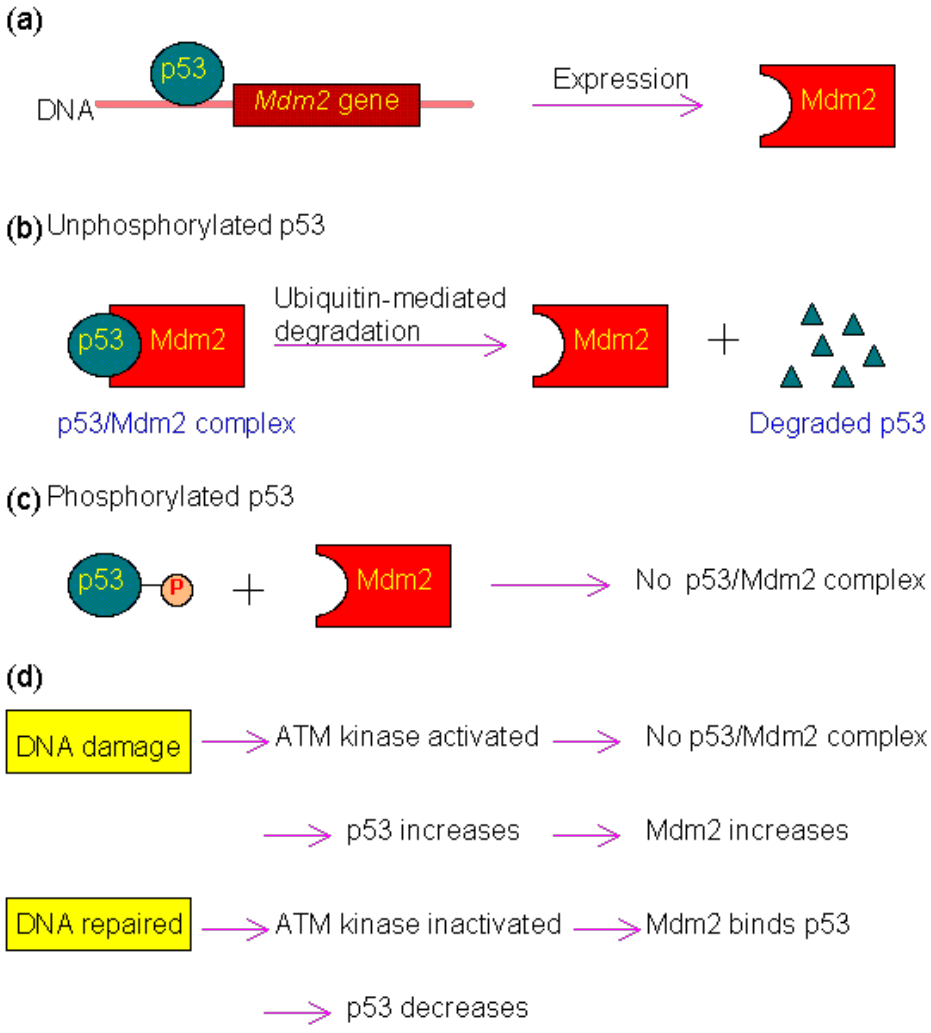
Background

What is the P53 gene?

The p53 gene is one of the tumor suppressing genes, whose main function is to regulate the cell cycle. P53 is the intrinsic pathway to command the cell to go through apoptosis (death or destruction of a cell). The p53 gene activates BAX (another protein), which goes to the mitochondria and releases cytochrome-c. Cytochrome-c then

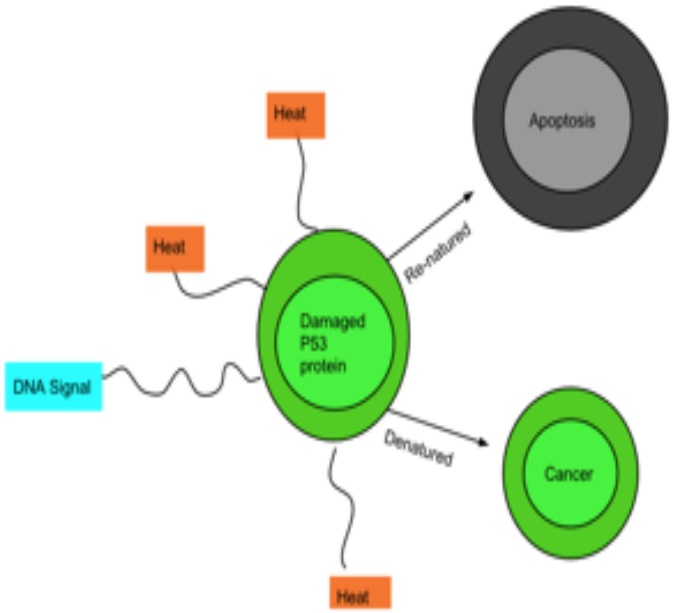
activates caspase 9, which destroys the proteins in the cell and destroys the cell. When the p53 gene is mutated, there is no command sent for the cell to go through apoptosis. The cell can then become cancerous by dividing uncontrollably and creating tumors (Onkoview).

Figure 1: How the P53 Gene Works. http://www.bioinformatics.org/p53/introduction.html



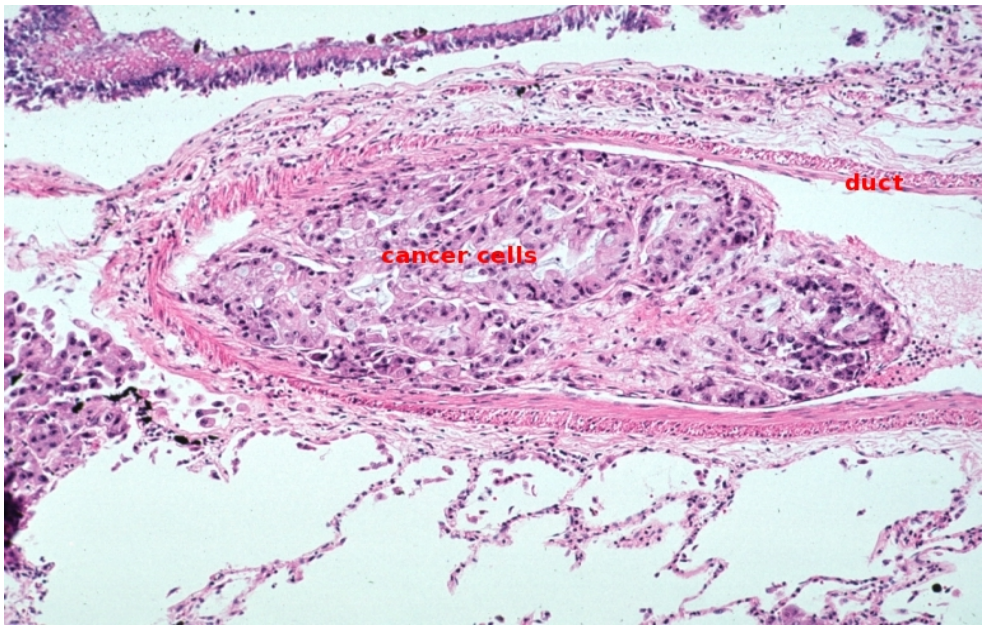
The p53 gene will respond differently to different concentrated heat temperatures.When a mutation occurs in the P53 protein, cancer cells likely develop.

Figure 2: How the P53 Protein Responds to Heat. DNA sends off the ATM signal to the damaged (denatured) protein. Heat then is added and shocks the protein by denaturing it to possibly make it renature itself. Depending on whether or not the protein renatures itself, it sends the cancer cell through apoptosis. If the protein is not renatures the cell continues on as cancerous.



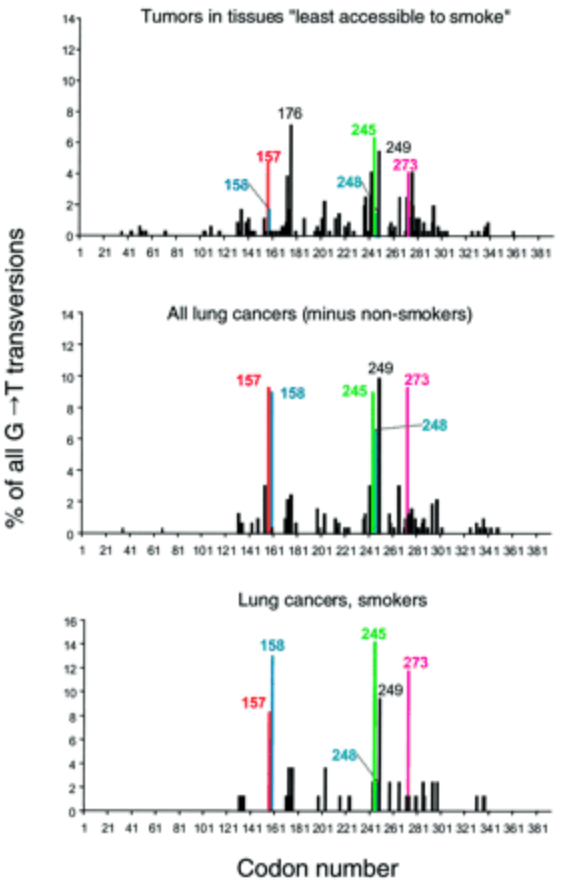
In our model, we are going to simulate adenocarcinoma, which is a type of non-small lung cancer. Adenocarcinoma accounts for 40% of all lung cancers that both smokers and non-smokers get. Non-small cell cancer doesn't respond well to chemotherapy or radiation therapy, so that is why we are going to try concentrated heat (cancer.org).

Figure 3: Adenocarcinoma, http://www.bio.davidson.edu/people/kabernd/berndcv/lab/epithelialinfoweb/Glandular%20Epithelium.html



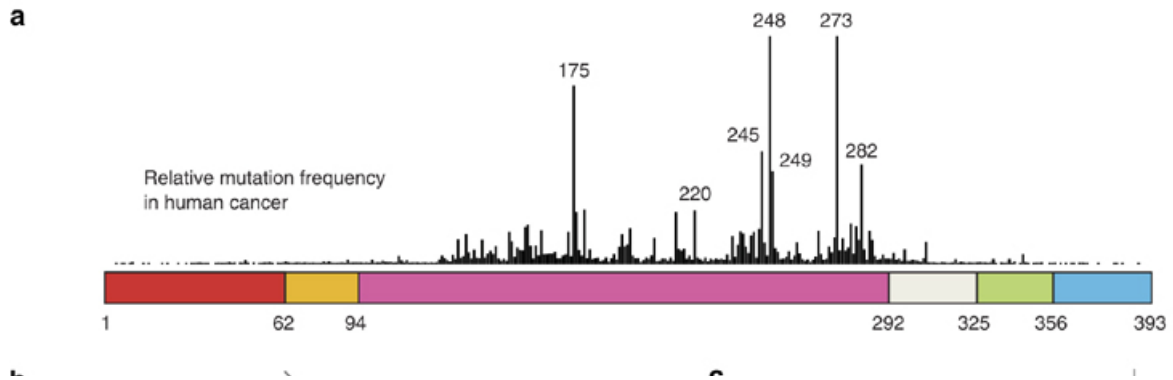
Codon 248 in the DNA-binding core domain is responsible for causing the inactivity of almost all lung cancers. It is a G:C → A:T transversion mutation and is a mutational hotspot as it is the cause of 1544 different mutations as seen in figure 4.

Figure 4: The Frequency of Mutations on Certain Codons.
http://carcin.oxfordjournals.org/content/22/3/367.full#abstract-1



It is also going to be the target of our plan to denature this part of the protein and then allow the protein to renature itself into its natural state, telling the cell it needs to die. If the protein does not renature itself, then it is our hope that the heat will disrupt all of the other proteins and the cell will die (Mogi). In Figure 5, the red region is the N-terminal transactivation domain, the orange is the proline-rich region, the pink is the DNA-binding core domain, the green is the tetramerization domain, and the blue is the negative regulatory domain.

Figure 5: The Domains of the P53 Gene,
http://www.nature.com/onc/journal/v26/n15/fig_tab/1210291f1.html#figure-title



We used nanorobots to detect and destroy cancer cells using concentrated heat. The nanorobots do this by “fixing” the P53 protein so it can send out a signal to destroy the cell.

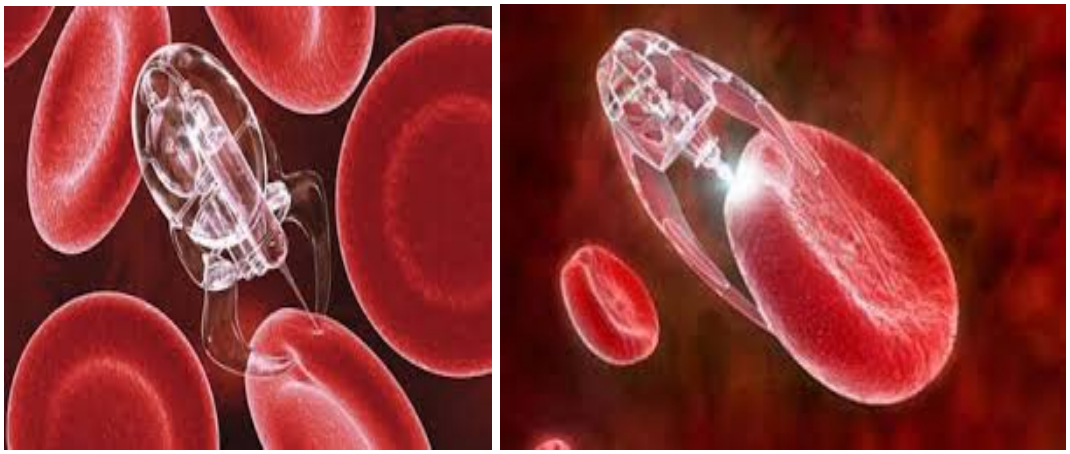
Nanorobots are between 0.05 and 1.00 micrometers; to put this in perspective a red blood cell is 8 micrometers.Nanorobots can travel against the flow of blood while not triggering the immune system (Mali). An outside computer communicates with the nanorobots by a computer chip inside the nanorobots. The nanorobots are told where in the body to go and the amount of heat needed to raise the cancer cells’ temperature to denature the P53 protein. The heat will be added into the cell by a laser inside the nanorobot that will come out once the cell has been grabbed and a needle has punctured the cell. A sensor on the nanorobots can distinguish between cancerous cells and normal blood cells, which allows for a more efficient way of killing the cancer cells.

Figure 6: Nanorobot, One on the Left

http://space.dawsoncollege.qc.ca/explorations/article/the_future_of_medicine_nanorobotics

Figure 7: Nanorobot, One on the Right

http://www.radikal.com.tr/yasam/tipta_nano_robot_devrimi-1079657



Problem Statement

The objective of this project is to determine if using concentrated heat delivered by nanorobots can be used as an alternative way to killing cancer cells without seriously harming surrounding cells and chemotherapy. We thought, based on the research that we had done that if we were given cancer cells with a transversion mutation at codon 248 and nanorobots that increase the temperature two degrees Celsius, then the protein structure will be denatured and then able to renature its structure without affecting the environment because when using the specific heat equation, 2 degrees is the most the temperature can be increased before the environment becomes affected.

System Model

We used the agent based modeling system Netlogo, in which we created a protein model and a cellular model. In the cellular model, we used a random probability to determine if the protein is going to renature or not. Once we got the probability of the bonds renaturing at a certain temperature from the protein model, we programmed that probability into the cellular model to determine the probability of cancer cells dying. For example, at 13℃, the probability is 94% chance of the cell dying. In the cellular model, we included sliders for pH, humidity, and temperature of the body to make it more realistic. If the slider is moved above or below the normal body condition (pH: 7.4, Humidity: 50%, and Temperature: 36℃) all the cells die, the program doesn't run and the person is dead. In our cellular program, we begin with two nanorobots.

The command "Mitosis-for-grandual-epithelial-cells" divides a cell into 2 new cells (or the amount shown on the slider) when the count is less than 50. When the count is over 50, some cells randomly die off. If the malignant-grandular-epithelial-cells take over the interface (population of the cells in the body) the person has died of cancer so the program stops. When the cancer cells reaches the age of 50, 1 cancer cell is 'hatched', at the age of 100: 2 cells are 'hatched' and 3 cells are 'hatched' when the cancer cells are of the age 150.

Method and Solution

P53 protein reacts to heat by denaturing to renature itself. To create the protein model, we used a reference model from http://www.ncbi.nlm.nih.gov/. We were able to create a 3-D P53 protein model to show bonds between different amino acids in the protein

and how they react to different intensities of heat. Through our research, we determined which types of bonds (ionic, covalent, hydrogen bonds and hydrophobic interactions) may form between amino acids and programmed that into our model using “links” of different colors to represent where the bonds would exist. The bonds also have different strengths to determine if they will break.

Figure 8: Code that shows how bonds are made

```
ask serines ;; hydrogen bonds between serines and lysines
[ create-links-with lysines in-radius 10
  create-links-with asparagines in-radius 10
  create-links-with arginines in-radius 10
  create-links-with histidines in-radius 10]
  ask links
  [if color = gray[set color blue]]

  ask lysines ;; creates ionic bonds
  [ create-links-with aspartic-acids in-radius 10
    create-links-with glutamic-acids in-radius 10
    ask links
    [if color = gray[set color green]]]
```

The image above shows a portion of our code that codes for hydrogen and ionic bonds to be created between various amino acids. The next thing we did is program different intensities of heat that would be applied to the protein. We chose four different increases in heat intensity: 13°, 23°, 100°, and 113℃. We chose these temperatures because an increase in 13℃ is enough to break hydrogen bonds, 23℃ for ionic bonds, 100℃ for hydrophobic interactions, and 113℃ for covalent bonds. With this, we then created a probability portion of our model that will determine if the protein will renature based on how many bonds there are in the protein. Limitations with NetLogo led us to

have to have some of the bonds to "die," in order for the probability portion to work. This image shows the probability code for 13℃.

Figure 9: Probability Portion of Code for 13℃

```
if temperature <= 13 ;; minimum temperature for hydrogen bonds to break
[
  let probability random 122 / 486
  let n count links
  ask (n-of(probability * n)links) [die]
  print count links
  if count links <= 364
[
  make-protein-structure
  print "yes"
  ask turtle 154
  [
    setxyz 13 6 -16
  ]
]
 ]
```

Then, based on the data that we obtained from running trials with the protein model, we put them into our second computer model, the cellular model. Our cell model is one that shows whether the cancer cells would die under these parameters. The focus of the second model was the specific heat equation which determined how much of the environment might be affected by the heat.

Figure 10: Specific Heat and Probability Code for 13℃

```
let n count links
let x (3617 * heat)
let probability random 50
   if heat = 13
    [
if any? malignant-grandular-epithelial-cells in-radius 5
[
  ask one-of malignant-grandular-epithelial-cells in-radius 5
  [
      print probability
      if probability < 47
  [
 ask one-of malignant-grandular-epithelial-cells
 [
   set color blue
   set shock true
   if color = blue and probability < 47 ;; probability of renature gotten from 3D protein model
   [
   die]
if x = 47021 and probability < 47
[ask malignant-grandular-epithelial-cells in-radius 10
  [die
  ask grandular-epithelial-cells in-radius 10
  [die]]]]]]]
```

Figure 11: Specific Heat and Probability Code of 23℃

```
      if heat = 23
      [
      if any? malignant-grandular-epithelial-cells in-radius 5
[
  ask one-of malignant-grandular-epithelial-cells in-radius 5
  [
      print probability
      if probability < 18 ;;36% chance that protein will renature (gotten from protein model)
  [
 ask one-of malignant-grandular-epithelial-cells ;; ask cancer cells if renature probability is true to die
 [
   set color blue
   set shock true
   if color = blue and probability < 18
   [
   die]
if x = 83191 and probability < 18 ;; tells cells in the radius of cancer cell being exposed to heat to die.
[ask malignant-grandular-epithelial-cells in-radius 20
  [die
  ask grandular-epithelial-cells in-radius 20
  [die]]]]]]]]
```

Figure 12: Specific Heat and Probability Code for 100℃

```
      if heat = 100
      [ if any? malignant-grandular-epithelial-cells in-radius 5
[
  ask one-of malignant-grandular-epithelial-cells in-radius 5
  [
      print probability
      if probability < 4 ;;8% chance that protein will renature (gotten from protein model)
  [
 ask one-of malignant-grandular-epithelial-cells ;; asks cancer cells if renature probability is true to die
 [
   set color blue
   set shock true
   if color = blue and probability < 4
   [
   die]
if x = 83191 and probability < 4 ;; asks cells within a certain radius of cancer cell being exposed to heat to di
[ask malignant-grandular-epithelial-cells in-radius 30
  [die
  ask grandular-epithelial-cells in-radius 30
  [die]]]]]]]]
```

Figure 13: Specific Heat and Probability Code for 113℃

```
    if heat = 113
    [if any? malignant-grandular-epithelial-cells in-radius 5
[
  ask one-of malignant-grandular-epithelial-cells in-radius 5
  [
      print probability
      if probability < 0 ;; 0% chance that protein will renature (gotten from protein model)
   [
 ask one-of malignant-grandular-epithelial-cells
 [
   set color blue
   set shock true
   if color = blue and probability < 0
   [
   die]
if x = 83191 and probability < 0 ;;asks cells within a certain radius of the cancer cell being exposed to heat to
[ask malignant-grandular-epithelial-cells in-radius 40
  [die
  ask grandular-epithelial-cells in-radius 40
  [die]]]]]]]]]
```

Simulation

We ran fifty trials at each temperature and discovered that an increase in 13℃ is the optimal temperature for the protein renature and signal the cancer cell to die. The second best temperature was 23℃, where the protein sometimes renatured and killed the cancer cells. Our data showed that probability was very low for the protein to renature itself at 100℃ . An increase of 113℃ made the protein so denatured that is did not renature itself so the cancer cells are not told to die.

Results

Table 1: Temperature Data from Our Protein Model at 13℃

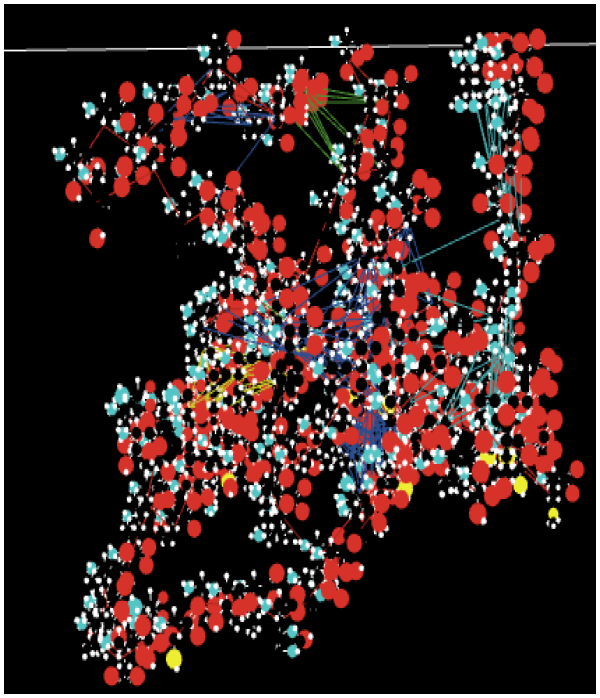
Trial number	Did it renature?	Probability(%) that it would renature *
1	yes	73%
2	yes	71%
3	yes	71%
4	yes	57%
5	yes	66%

6	yes	74%
7	yes	61%
8	yes	63%
9	yes	66%
10	yes	65%
11	yes	65%
12	yes	61%
13	yes	69%
14	yes	71%
15	yes	66%
16	yes	57%
17	no	24%
18	yes	70%
19	yes	71%
20	yes	66%
21	yes	61%
22	yes	64%
23	yes	67%
24	yes	59%
25	yes	65%
26	yes	62%
27	yes	65%
28	yes	65%
29	yes	70%
30	yes	63%

31	yes	61%
32	yes	74%
33	yes	61%
34	yes	66%
35	yes	68%
36	no	24%
37	yes	64%
38	yes	70%
39	yes	59%
40	yes	70%
41	yes	66%
42	yes	68%
43	yes	60%
44	no	22%
45	yes	63%
46	yes	73%
47	yes	57%
48	yes	65%
49	yes	65%
50	yes	63%

*As reported by our computer program

Figure 14: Renatured Protein



The top picture is of the protein after it renatures itself.
The following pictures, from our model, shows how an increase in 13℃ affects the P53 protein

Figure 15: Trial 17 Denature Protein Temperature 13℃

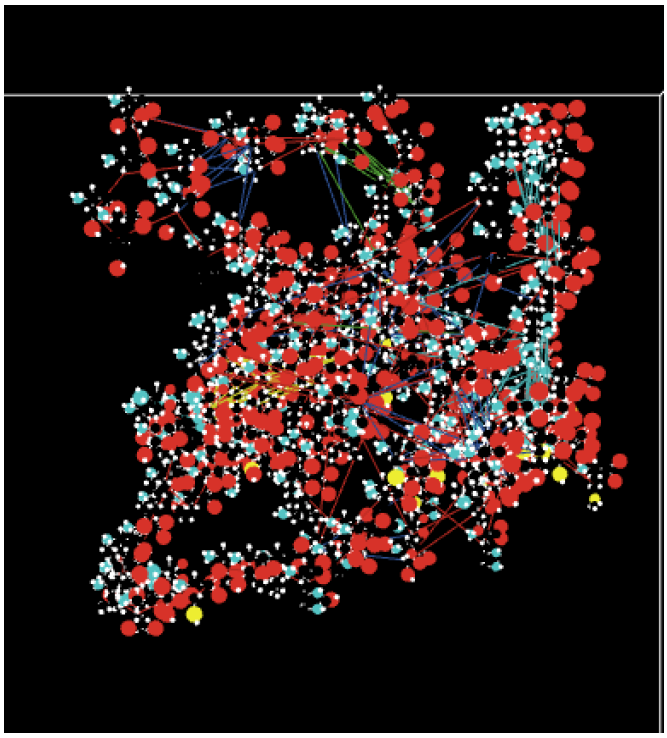


Figure 16: Trial 36, Denatured Protein Temperature 13℃

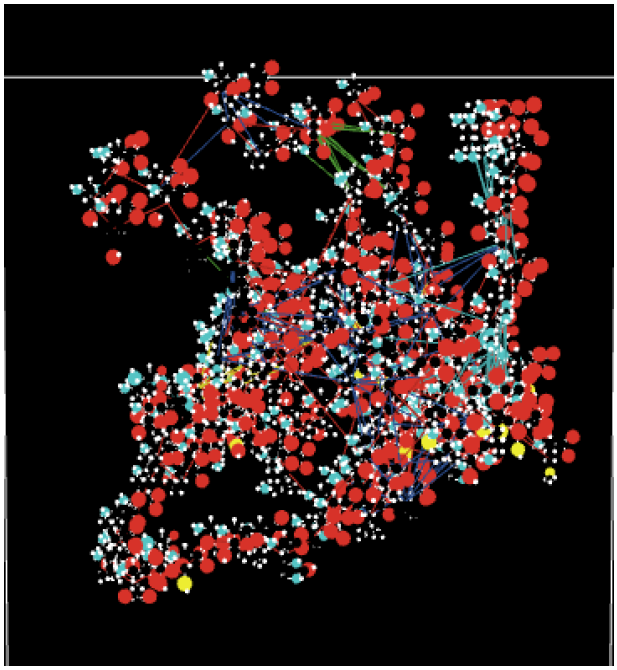


Figure 17: Trial 44 Denatured Protein Temperature 13℃

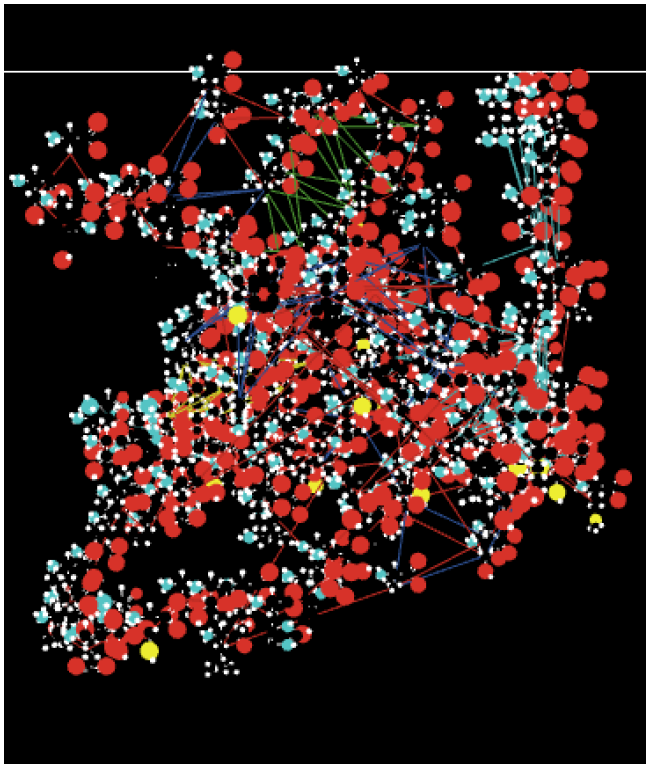


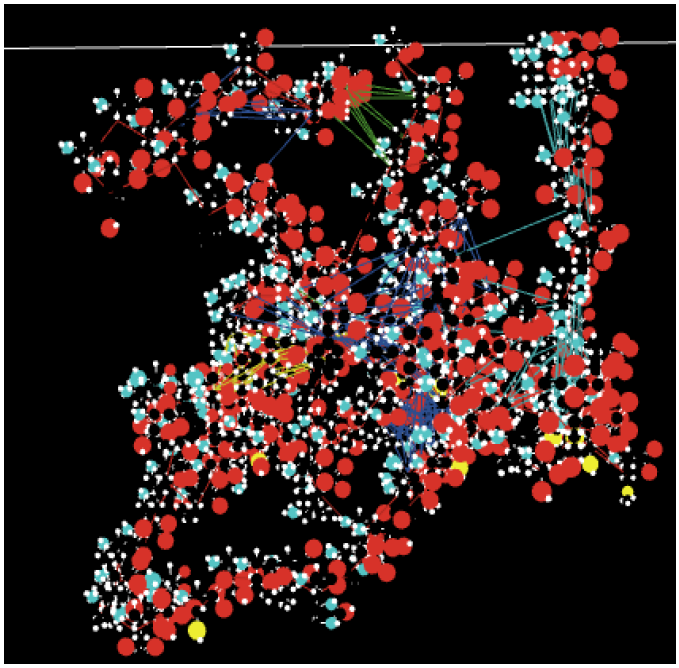
Table 2: Temperature Data from Our Protein Model at 23℃

Trial number	Did the protein re-nature?	Probability(%) that the protein would renature
1	no	25%
2	no	28%
3	no	43%
4	yes	58%
5	yes	57%
6	no	31%
7	yes	54%
8	yes	58%
9	no	47%
10	no	46%
11	yes	51%
12	no	38%
13	yes	51%
14	no	48%
15	yes	61%
16	no	29%
17	yes	57%
18	no	29%
19	no	28%
20	no	38%
21	no	27%
22	no	21%
23	no	48%

24	no	45%
25	no	45%
26	no	36%
27	no	40%
28	no	41%
29	yes	51%
30	no	42%
31	no	34%
32	no	49%
33	yes	50%
34	yes	53%
35	no	33%
36	no	41%
37	yes	59%
38	no	40%
39	no	44%
40	no	28%
41	no	29%
42	no	45%
43	yes	61%
44	no	22%
45	yes	50%
46	no	23%
47	yes	51%
48	yes	58%

49	yes	52%
50	yes	51%

Figure 18: Renatured Protein



The top picture is of the protein after it renatures itself.
The following picture, from our model, shows how 23℃ affects the P53 protein.

Figure 19: Denatured Protein 1 Temperature 23℃

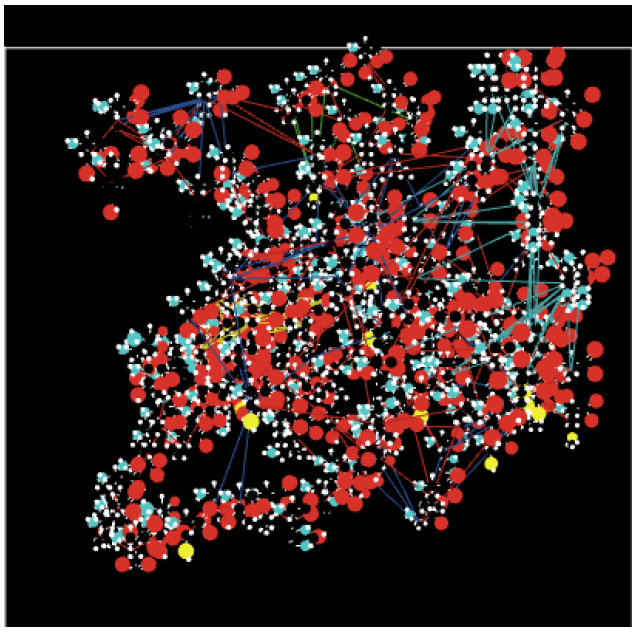


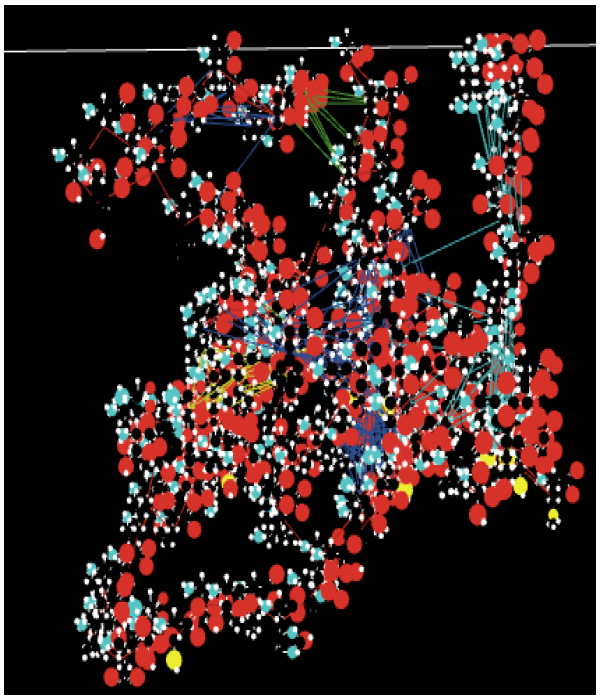
Table 3: Temperature Data from Our Protein Model at 100℃

Trial number	Did the protein re-nature?	Probability(%) that the protein will renatue
1	no	49%
2	no	43%
3	no	54%
4	no	38%
5	no	73%
6	no	59%
7	no	70%
8	no	43%
9	no	63%
10	no	72%
11	no	74%
12	no	66%
13	no	51%
14	no	75%
15	no	44%
16	yes	80%
17	no	46%
18	no	44%
19	no	66%
20	no	24%
21	no	57%
22	yes	75%

23	no	49%
24	no	34%
25	no	74%
26	no	70%
27	no	60%
28	no	51%
29	no	30%
30	yes	79%
31	no	36%
32	no	62%
33	no	65%
34	no	51%
35	no	40%
36	no	38%
37	no	50%
38	no	68%
39	no	68%
40	no	71%
41	yes	77%
42	no	44%
43	no	43%
44	no	24%
45	no	47%
46	no	66%
47	no	36%

48	no	66%
49	no	61%
50	no	50%

Figure 20: Renatured Protein



The top picture shows the protein after it renatures itself.
The following picture, from our model, shows how an increase of 100℃ affects the P53 protein.

Figure 21: Denatured Protein 1 Temperature 100℃

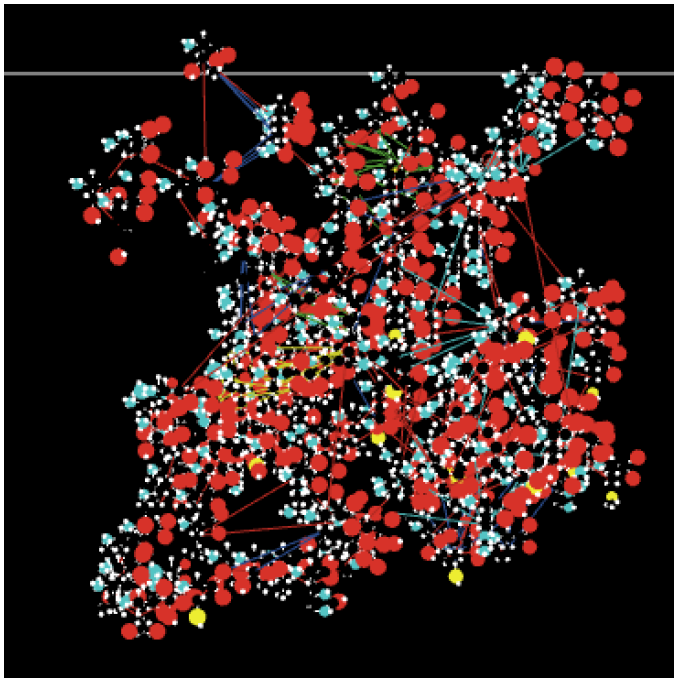


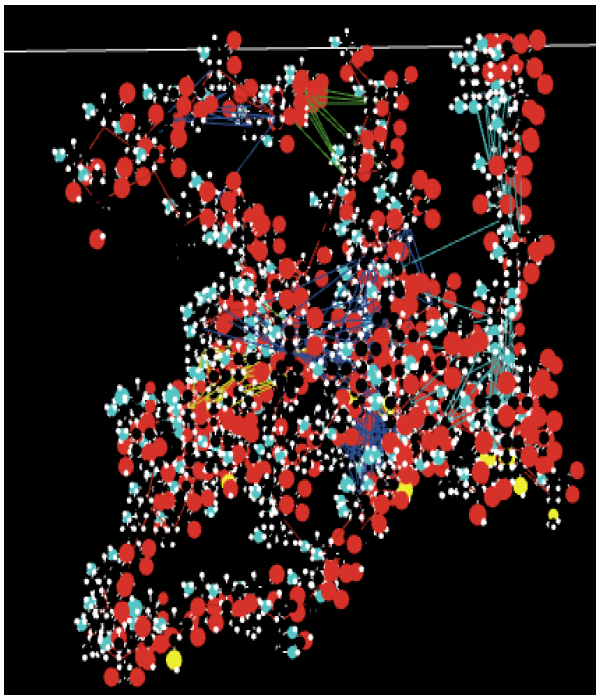
Table 4: Temperature Data from Our Protein Model at 113℃

Trial number	Did the protein re-nature?	Probability(%) that the protein would renature
1	no	38%
2	no	36%
3	no	4%
4	no	70%
5	no	62%
6	no	29%
7	no	73%
8	no	53%
9	no	69%
10	no	25%
11	no	12%

12	no	26%
13	no	5%
14	no	15%
15	no	53%
16	no	7%
17	no	37%
18	no	63%
19	no	18%
20	no	28%
21	no	12%
22	no	52%
23	no	53%
24	no	41%
25	no	29%
26	no	25%
27	no	8%
28	no	71%
29	no	5%
30	no	40%
31	no	62%
32	no	46%
33	no	66%
34	no	43%
35	no	17%
36	no	38%

37	no	57%
38	no	20%
39	no	35%
40	no	56%
41	no	4%
42	no	10%
43	no	26%
44	no	71%
45	no	27%
46	no	19%
47	no	49%
48	no	51%
49	no	67%
50	no	67%

Figure 22: Renatured Protein



The top picture is of the protein once it is renatures itself.
The following picture, from our model, shows how 113℃ affects the P53 protein.
Figure 23: Denatured Protein 1 Temperature 113℃

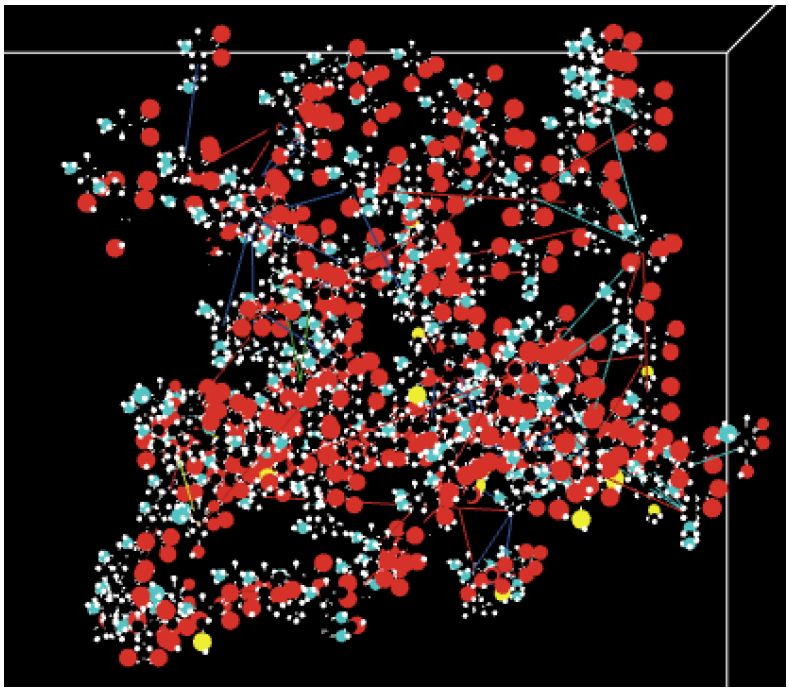


Table 5: Time taken for Cell Death to Occur in Cellular Model at 13℃

Trial number	Were all of the cancer cells killed?	Time (Minutes)
1	yes	232
2	yes	155
3	yes	52
4	yes	36
5	yes	386
6	yes	13
7	no	786
8	yes	330
9	no	288

10	yes	619
11	no	632
12	yes	24
13	yes	540
14	yes	11
15	yes	158
16	yes	343
17	yes	934
18	yes	107
19	yes	150
20	no	664
21	yes	62
22	yes	844
23	no	451
24	yes	198
25	yes	19
26	no	415
27	yes	40
28	yes	198
29	yes	12
30	yes	147
31	no	263
32	no	1198
33	no	249
34	yes	1176

35	no	332
36	no	342
37	no	239
38	yes	42
39	no	491
40	yes	265
41	yes	28
42	yes	607
43	yes	49
44	no	329
45	no	252
46	no	463
47	yes	494
48	no	574
49	yes	26
50	yes	20

Table 6: Time taken for Cell Death to Occur in Cellular Model at 23℃

Trial number	Were all of the cancer cells killed?	Time (Minutes)
1	yes	91
2	yes	24
3	yes	391
4	yes	369
5	yes	48
6	yes	51

7	no	205
8	no	571
9	yes	482
10	no	648
11	yes	592
12	yes	257
13	yes	311
14	yes	42
15	yes	63
16	no	702
17	yes	262
18	no	361
19	yes	300
20	yes	266
21	no	490
22	yes	26
23	yes	46
24	no	476
25	no	505
26	yes	1754
27	yes	18
28	yes	510
29	no	419
30	no	368
31	yes	577

32	no	306
33	no	268
34	yes	58
35	no	941
36	yes	24
37	yes	32
38	no	396
39	no	334
40	no	213
41	no	974
42	yes	26
43	yes	290
44	yes	105
45	no	351
46	yes	355
47	yes	137
48	yes	152
49	no	370
50	yes	40

Table 7: Time taken for Cell Death to Occur in Cellular Model at 100°C

Trial number	Were all of the cancer cells killed	Time (minutes)
1	no	166
2	no	192
3	no	175

4	no	242
5	no	198
6	no	162
7	no	290
8	no	247
9	no	219
10	no	268
11	no	205
12	no	198
13	no	211
14	no	188
15	no	222
16	no	173
17	no	166
18	no	180
19	no	182
20	no	230
21	no	390
22	no	204
23	no	203
24	no	270
25	no	205
26	no	210
27	no	207
28	no	329

29	no	267
30	no	243
31	no	229
32	no	162
33	no	190
34	no	201
35	no	173
36	no	221
37	no	284
38	no	239
39	no	167
40	no	222
41	no	166
42	no	184
43	no	210
44	no	211
45	no	208
46	no	221
47	no	191
48	no	187
49	no	141
50	no	270

Table 8: Time taken for Cell Death to Occur in Cellular Model at 113℃

Trial number	Were all of the cancer cells killed?	Time (Minutes)
1	no	166
2	no	140
3	no	218
4	no	151
5	no	211
6	no	161
7	no	149
8	no	153
9	no	197
10	no	175
11	no	193
12	no	189
13	no	178
14	no	236
15	no	158
16	no	177
17	no	152
18	no	157
19	no	184
20	no	169
21	no	163
22	no	191
23	no	222

24	no	167
25	no	160
26	no	215
27	no	197
28	no	183
29	no	147
30	no	165
31	no	280
32	no	198
33	no	165
34	no	170
35	no	148
36	no	148
37	no	186
38	no	179
39	no	166
40	no	150
41	no	168
42	no	211
43	no	153
44	no	178
45	no	153
46	no	239
47	no	169
48	no	188

49	no	168
50	no	151

Statistical Analysis

Table 9: Averages

Temperature(℃)	13	23	100	113
Protein Model percentage of renatured proteins	62.94	42.52	55.52	37.80
Cellular Model ps punt of time to renature	325.70	331.94	214.38	177.84

The following graphs of averages show that the percentage of renatured proteins decreases as temperature increases in the protein model (see figure 24). In the cellular model, the time to renature drastically decreases as temperature increases (see figure 25).

Figure 24: Protein Average

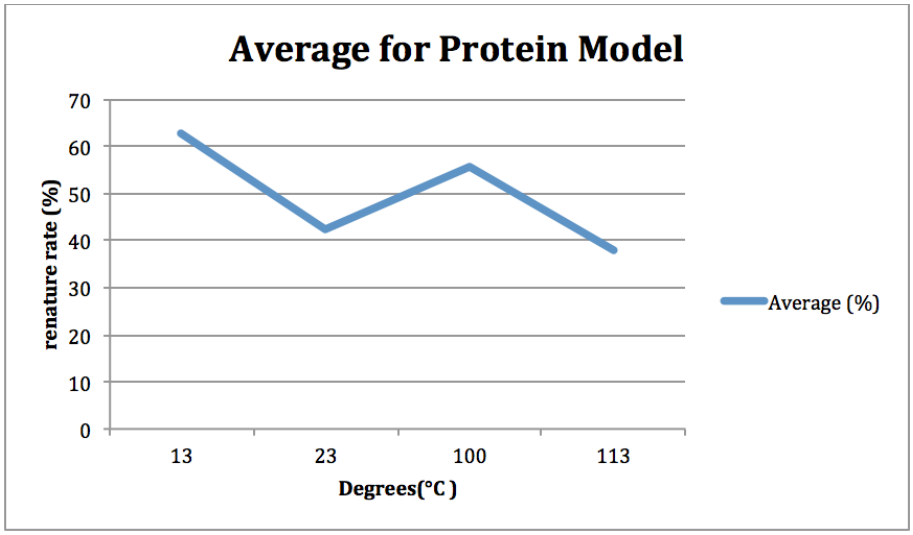


Figure 25: Cell Time Average

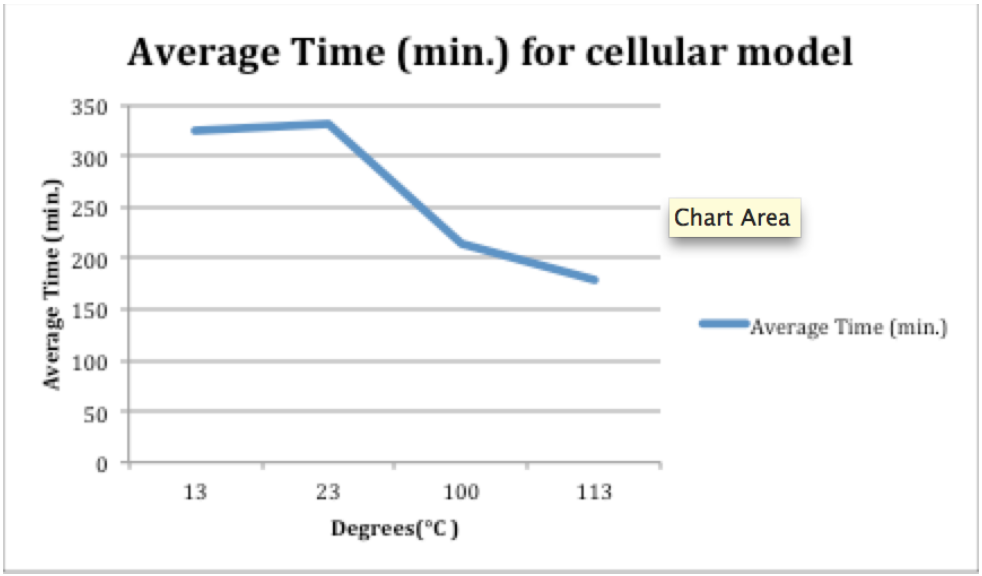


Table 10: Standard Deviation

Temperature (℃)	13	23	100	113
Protein	0.110	0.118	0.152	0.217
Cellular Model	298.784	310.840	45.837	28.261

Standard deviation($s = \frac{\sqrt{\Sigma(x_i - x)^2}}{n-1}$) is the amount that the data will vary from the mean. For example, for 13℃ the mean is 62.94 for the protein, and the standard deviation is 0.110. The data collectively will vary by 0.110 from the mean, 62.94. For the protein model, as the temperature goes up, the standard deviation goes up. For the cellular model, as the temperature goes up the standard deviation falls drastically.

Table 11: T-Test

Temperature(℃)	13 and 23	13 and 100	13 to 113
Protein	0.000	0.006	0.000
Cellular	0.919	0.012	0.001

Table 12: T-Test

Temperature(℃)	23 to 13	23 to 100	23 to 113
Protein	0.000	0.000	0.181
Cellular	0.919	0.000	0.181

Table 13: T-Test

Temperature(℃)	100 to 13	100 to 23	100 to 113
Protein	0.006	0.000	0.000
Cellular	0.012	0.000	0.000

Table 14: T-Test

Temperature(℃)	113 to 13	113 to 23	113 to 100
Protein	0.000	0.181	0.000
Cellular	0.001	0.181	0.000

The T-test shows how much two data sets vary from each other and is used to see if there is a statistically noticeable difference. We used a type 3, two-tailed T-test. Type 3 is used for data sets that are unrelated to each other. The two-tailed part of the T-test is to see if there is variance in the unpaired data. The T-test measures if there is a difference among the temperatures, not the change over time. The variance from 13 and 23 ℃ is 0.000 for the protein, but for 13 and 23 ℃; in the cellular model, is 0.919. The variance for the protein level is not significant, meaning there is no real basis to say they are different. For the cellular model, the variance is enough to say that there is a difference between 13 and 23 ℃ . The null hypothesis (stating that there is no significant difference from one temperature to another) is accepted if the value is lower than the critical value. The null hypothesis is rejected if the T-test value is higher than

the critical value of 2.01, meaning there is a significant difference between the two data sets. Since all of our T-test values fall below 2.01, this means that there is not a statistical difference between all of the data sets compared.

Figure 26: Excel Spreadsheet Formula for the T-test

Figure 27: Excel Spreadsheet Formula for Standard Deviation

Analysis

Based on the data generated in our model, when using two nanorobots in one kilogram of blood and raising the temperature of the body by 13℃, 94% of the trials produced a renatured protein, signaling the cell that it needs to die. When input into our cellular model, 66% of the trials resulted in the cancerous cells dieing. As for the temperatures of 23°, 100°, and 113℃, the cancer cells had a lower probability dying because the P53 protein was less likely to renature because too many bonds had been broken.

There were some limitations and potential errors that could have taken place in this experiment. The big thing for this experiment is that the only way to get any randomness in the protein model for the links is to make a portion of them die. Another problem was that the exact probability that the protein would renature is unknown, so the probability of the P53 protein renaturing in the protein model was an estimate based on the knowledge we had previously known about how the types of bonds work and

how often in nature proteins themselves renature.There were also some limitations with the specific heat portion of our project; we had to calculate the values outside of the program and then estimate how those numbers would affect the program to determine how the specific heat directly affects the environment of the cells. Once the cancer cells reached an age of 200, we had to make them die to keep the program from freezing up. Finally, the structure of the P53 protein we have in our protein model is an estimated model. We based our model off of a model protein structure by NCBI, but because we had to program it in ourselves instead of being able to upload the structure, it is probably not an exact model. This is given that the model protein that we used was a estimate of what the real thing looks like, which is unknown.

Conclusion

The purpose of this experiment was to determine if using concentrated heat could be an alternate way to kill cancer cells. We did this by creating two computer models: first, a model of the mutant P53 protein in the cancer cells that shows how the bonds of the structure are affected and if the protein is able to renature, and, second, a model of how the cancer cells respond to heat delivered by nanorobots. Our results showed us that the most promising results occurred when the nanorobots raised the temperature of the cancer cells by 13℃. This resulted in a 94% chance that the protein will renature and about a 66% chance of killing all of the cancer cells. This shows that our hypothesis was wrong because we had thought that 2℃ was enough to break bonds in the protein structure. As a result, 13℃ would be the ideal temperature to further explore effects of renaturation rate and apoptosis in our molecular and cellular models. Our code worked

in that we found out that the nanorobots only needed to raise the cells temperature 13℃.

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Appendix A: Molecular Model Code

```
links-own [strength]
breed [serines serine]
breed [valines valine]
breed [prolines proline]
breed [glutamines glutamine]
breed [lysines lysine]
breed [threonines threonine]
breed [tyrosines tyrosine]
breed [glycines glycine]
breed [phenylalanines phenylalanine]
breed [arginines arginine]
breed [leucines leucine]
breed [histidines histidine]
breed [cysteines cysteine]
breed [asparagines asparagine]
breed [methionines methionine]
breed [tryptophans tryptophan]
breed [aspartic-acids aspartic-acid]
breed [alanines alanine]
breed [isoleucines isoleucine]
breed [glutamic-acids glutamic-acid]
to setup
clear-all
create-aspartic-acids 8
create-glutamic-acids 11
create-serines 18
create-valines 15
create-prolines 14
create-glutamines 7
create-lysines 7
create-threonines 14
create-tyrosines 8
create-glycines 14
create-phenylalanines 5
create-arginines 17
create-leucines 15
create-histidines 7
```

```
create-cysteines 10
create-asparagines 9
create-methionines 6
create-tryptophans 1
create-alanines 7
create-isoleucines 6
 ask turtles
 [
   set size 4
]
make-protein-structure
  ask links
  [ if color = yellow
    [
      set strength random 6 + 15 ;; between 15 - 20 covalent
    ]
    if color = green
    [
      set strength random 6 + 5 ;; between 5 - 10 ionic
    ]
    if color = blue
    [
      set strength random 5 ;;between 0 - 5 hydrogen
    ]
    if color = cyan
    [
      set strength random 6 + 10 ;; between 10 - 15 hydrophobic interactions
    ]
    if color = red
    [
       set strength 50
    ]
  ]
end
  to make-protein-structure
  ask turtle 0 [ set shape "serine" setxyz 0 24 -24 create-link-with turtle 1 ]
  ask turtle 1 [set shape "serine" setxyz 0 24 -22 create-link-with turtle 2]
  ask turtle 2 [set shape "serine" setxyz 0 24 -20 create-link-with turtle 3]
  ask turtle 3 [set shape "valine" setxyz -2 22 -18 create-link-with turtle 4]
```

```
ask turtle 4 [set shape "proline" setxyz -4 20 -16 create-link-with turtle 5]
ask turtle 5 [set shape "serine" setxyz -6 22 -15 create-link-with turtle 6]
ask turtle 6 [set shape "glutamine" setxyz -2 20 -14 create-link-with turtle 7]
ask turtle 7 [set shape "lysine" setxyz -7 23 -13 create-link-with turtle 8]
ask turtle 8 [set shape "threonine" setxyz -9 20 -12 create-link-with turtle 9]
ask turtle 9 [set shape "tyrosine" setxyz -11 19 -11 create-link-with turtle 10]
ask turtle 10 [set shape "glutamine" setxyz -13 17 -10 create-link-with turtle 11]
ask turtle 11 [set shape "glycine"setxyz -15 18 -9 create-link-with turtle 12]
ask turtle 12 [set shape "serine" setxyz -17 15 -8 create-link-with turtle 13]
ask turtle 13 [set shape "tyrosine" setxyz -15 13 -7 create-link-with turtle 14]
ask turtle 14 [set shape "glycine" setxyz -11 15 -8 create-link-with turtle 15]
ask turtle 15 [set shape "phenylalanine" setxyz -9 12 -9 create-link-with turtle 16]
ask turtle 16 [set shape "arginine" setxyz -7 13 -9 create-link-with turtle 17]
ask turtle 17 [set shape "leucine" setxyz -5 10 -8 create-link-with turtle 18]
ask turtle 18 [set shape "glycine" setxyz -3 7 -7 create-link-with turtle 19]
ask turtle 19 [set shape "phenylalanine" setxyz -1 4 -6 create-link-with turtle 20]
ask turtle 20 [set shape "leucine" setxyz 2 2 -5 create-link-with turtle 21]
ask turtle 21 [set shape "histidine" setxyz 4 3 -4 create-link-with turtle 22]
ask turtle 22 [set shape "serine" setxyz 6 0 -4 create-link-with turtle 23]
ask turtle 23 [set shape "glycine" setxyz 8 2 -1 create-link-with turtle 24]
ask turtle 24 [set shape "threonine" setxyz 10 4 -2 create-link-with turtle 25]
ask turtle 25 [set shape "alanine" setxyz 12 0 -3 create-link-with turtle 26]
ask turtle 26 [set shape "lysine" setxyz 14 -2 -4 create-link-with turtle 27]
ask turtle 27 [set shape "serine" setxyz 12 -4 -4 create-link-with turtle 28]
ask turtle 28 [set shape "valine" setxyz 10 -3 -2 create-link-with turtle 29]
ask turtle 29 [set shape "threonine" setxyz 8 -1 -6 create-link-with turtle 30]
ask turtle 30 [set shape "cysteine" setxyz 6 2 -7 create-link-with turtle 31]
ask turtle 31 [set shape "threonine" setxyz 7 4 -7 create-link-with turtle 32]
ask turtle 32 [set shape "tyrosine" setxyz 6 6 -7 create-link-with turtle 33]
ask turtle 33 [set shape "serine" setxyz 7 8 -8 create-link-with turtle 34]
ask turtle 34 [set shape "proline" setxyz 5 10 -8 create-link-with turtle 35]
ask turtle 35 [set shape "alanine" setxyz 8 12 -9 create-link-with turtle 36]
ask turtle 36 [set shape "leucine" setxyz 7 13 -10 create-link-with turtle 37]
ask turtle 37 [set shape "asparagine" setxyz 4 11 -11 create-link-with turtle 38]
ask turtle 38 [set shape "lysine" setxyz 6 9 -11 create-link-with turtle 39]
ask turtle 39 [set shape "methionine" setxyz 4 7 -11 create-link-with turtle 40]
ask turtle 40 [set shape "phenylalanine" setxyz 6 5 -11 create-link-with turtle 41]
ask turtle 41 [set shape "cysteine" setxyz 4 3 -12 create-link-with turtle 42]
ask turtle 42 [set shape "glutamine" setxyz 3 1 -13 create-link-with turtle 43]
```

```
ask turtle 43 [set shape "leucine" setxyz 1 -1 -14 create-link-with turtle 44]
ask turtle 44 [set shape "alanine" setxyz -1 -3 -15 create-link-with turtle 45]
ask turtle 45 [set shape "lysine" setxyz -3 -5 -12 create-link-with turtle 46]
ask turtle 46 [set shape "threonine" setxyz -5 -3 -12 create-link-with turtle 47]
ask turtle 47 [set shape "cysteine" setxyz -6 -2.5 -13 create-link-with turtle 48]
ask turtle 48 [set shape "proline" setxyz -7 -2 -12 create-link-with turtle 49]
ask turtle 49 [set shape "valine" setxyz -8 -1.5 -13 create-link-with turtle 50]
ask turtle 50 [set shape "glutamine" setxyz -9 -1 -12 create-link-with turtle 51]
ask turtle 51 [set shape "leucine" setxyz -10 -0.5 -13 create-link-with turtle 52]
ask turtle 52 [set shape "tryptophan" setxyz -11 0 -12 create-link-with turtle 53]
ask turtle 53 [set shape "valine" setxyz -12 0.5 -12.5 create-link-with turtle 54]
ask turtle 54 [set shape "aspartic acid" setxyz -13 1 -11.5 create-link-with turtle 55]
ask turtle 55 [set shape "serine" setxyz -14 0 -11.5 create-link-with turtle 56]
ask turtle 56 [set shape "threonine" setxyz -13 -1.5 -11 create-link-with turtle 57]
ask turtle 57 [set shape "proline" setxyz -12 -2 -14 create-link-with turtle 58]
ask turtle 58 [set shape "proline" setxyz -13 -5 -15 create-link-with turtle 59]
ask turtle 59 [set shape "proline" setxyz -11 -7 -16 create-link-with turtle 60]
ask turtle 60 [set shape "glycine" setxyz -10 -5 -17 create-link-with turtle 61]
ask turtle 61 [set shape "threonine" setxyz -9 -3 -18 create-link-with turtle 62]
ask turtle 62 [set shape "arginine" setxyz -8 -4 -18 create-link-with turtle 63]
ask turtle 63 [set shape "valine" setxyz -7 -2 -18 create-link-with turtle 64]
ask turtle 64 [set shape "arginine" setxyz -6 0 -19 create-link-with turtle 65]
ask turtle 65 [set shape "alanine" setxyz -5 2 -18 create-link-with turtle 66]
ask turtle 66 [set shape "methionine" setxyz -4 4 -19 create-link-with turtle 67]
ask turtle 67 [set shape "alanine" setxyz -2 6 -18 create-link-with turtle 68]
ask turtle 68 [set shape "isoleucine" setxyz 0 10 -19 create-link-with turtle 69]
ask turtle 69 [set shape "tyrosine" setxyz 2 14 -19 create-link-with turtle 70]
ask turtle 70 [set shape "lysine" setxyz 4 18 -18 create-link-with turtle 71]
ask turtle 71 [set shape "glutamine" setxyz 6 22 -19 create-link-with turtle 72]
ask turtle 72 [set shape "serine" setxyz 4 26 -20 create-link-with turtle 73]
ask turtle 73 [set shape "glutamine" setxyz 8 23 -21 create-link-with turtle 74]
ask turtle 74 [set shape "histidine" setxyz 7 18 -20 create-link-with turtle 75]
ask turtle 75 [set shape "methionine" setxyz 4 18 -22 create-link-with turtle 76]
ask turtle 76 [set shape "threonine" setxyz 5 14 -23 create-link-with turtle 77]
ask turtle 77 [set shape "glutamic acid" setxyz 6 12 -24 create-link-with turtle 78]
ask turtle 78 [set shape "valine" setxyz 5 10 -23 create-link-with turtle 79]
ask turtle 79 [set shape "valine" setxyz 6 8 -22 create-link-with turtle 80]
ask turtle 80 [set shape "arginine" setxyz 7 6 -23 create-link-with turtle 81]
ask turtle 81 [set shape "arginine" setxyz 8 4 -22 create-link-with turtle 82]
```

```
ask turtle 82 [set shape "cysteine" setxyz 9 5 -23 create-link-with turtle 83]
ask turtle 83 [set shape "proline" setxyz 10 3 -25 create-link-with turtle 84]
ask turtle 84 [set shape "histidine" setxyz 11 1 -23 create-link-with turtle 85]
ask turtle 85 [set shape "histidine" setxyz 10 -1 -22 create-link-with turtle 86]
ask turtle 86 [set shape "glutamic acid" setxyz 9 0 -23 create-link-with turtle 87]
ask turtle 87 [set shape "arginine" setxyz 10 -2 -25 create-link-with turtle 88]
ask turtle 88 [set shape "cysteine" setxyz 9 -3 -23 create-link-with turtle 89]
ask turtle 89 [set shape "serine" setxyz 8 -4 -22 create-link-with turtle 90]
ask turtle 90 [set shape "aspartic acid" setxyz 7 -3 -21 create-link-with turtle 91]
ask turtle 91 [set shape "serine" setxyz 6 -4 -22 create-link-with turtle 92]
ask turtle 92 [set shape "aspartic acid" setxyz 5 -5 -22 create-link-with turtle 93]
ask turtle 93 [set shape "glycine" setxyz 4 -3 -23 create-link-with turtle 94]
ask turtle 94 [set shape "leucine" setxyz 3 -1 -22 create-link-with turtle 95]
ask turtle 95 [set shape "alanine" setxyz 4 0 -21 create-link-with turtle 96]
ask turtle 96 [set shape "proline" setxyz 5 1 -22 create-link-with turtle 97]
ask turtle 97 [set shape "proline" setxyz 6 2 -22 create-link-with turtle 98]
ask turtle 98 [set shape "glutamine" setxyz 7 3 -20 create-link-with turtle 99]
ask turtle 99 [set shape "histidine" setxyz 6 4 -19 create-link-with turtle 100]
ask turtle 100 [set shape "leucine" setxyz 7 4 -18 create-link-with turtle 101]
ask turtle 101 [set shape "isoleucine" setxyz 4 7 -17.5 create-link-with turtle 102]
ask turtle 102 [set shape "arginine" setxyz 9 1 -17 create-link-with turtle 103]
ask turtle 103 [set shape "valine" setxyz 10 -1 -16.5 create-link-with turtle 104]
ask turtle 104 [set shape "glutamic acid" setxyz 7 -3 -16 create-link-with turtle 105]
ask turtle 105 [set shape "glycine" setxyz 4 -6 -15.5 create-link-with turtle 106]
ask turtle 106 [set shape "asparagine" setxyz 1 -9 -16 create-link-with turtle 107]
ask turtle 107 [set shape "leucine" setxyz -2 -6 -16.5 create-link-with turtle 108]
ask turtle 108 [set shape "arginine" setxyz -3 -4 -17 create-link-with turtle 109]
ask turtle 109 [set shape "valine" setxyz -2 -2 -18 create-link-with turtle 110]
ask turtle 110 [set shape "glutamine" setxyz -3 0 -19 create-link-with turtle 111]
ask turtle 111 [set shape "tyrosine" setxyz -2 2 -20 create-link-with turtle 112]
ask turtle 112 [set shape "leucine" setxyz -3 4 -21 create-link-with turtle 113]
ask turtle 113 [set shape "aspartic acid" setxyz -1 7 -22 create-link-with turtle 114]
ask turtle 114 [set shape "aspartic acid" setxyz -4 10 -23 create-link-with turtle 115]
ask turtle 115 [set shape "arginine" setxyz -6 13 -24 create-link-with turtle 116]
ask turtle 116 [set shape "asparagine" setxyz -8 16 -26 create-link-with turtle 117]
ask turtle 117 [set shape "threonine" setxyz -6 16 -25 create-link-with turtle 118]
ask turtle 118 [set shape "phenylalanine" setxyz -4 13 -24 create-link-with turtle 119]
ask turtle 119 [set shape "arginine" setxyz -2 10 -23 create-link-with turtle 120]
ask turtle 120 [set shape "histidine" setxyz -4 7 -22 create-link-with turtle 121]
```

```
  ask turtle 121 [set shape "serine" setxyz -6 4 -21 create-link-with turtle 122]
  ask turtle 122 [set shape "valine" setxyz -8 1 -20 create-link-with turtle 123]
  ask turtle 123 [set shape "valine" setxyz -10 -1 -19 create-link-with turtle 124]
  ask turtle 124 [set shape "valine" setxyz -12 -4 -18 create-link-with turtle 125]
  ask turtle 125 [set shape "proline" setxyz -14 -7 -17 create-link-with turtle 126]
  ask turtle 126 [set shape "tyrosine" setxyz -15 -10 -16 create-link-with turtle 127]
  ask turtle 127 [set shape "glutamic acid" setxyz -16 -12 -14 create-link-with turtle 128]
  ask turtle 128 [set shape "proline" setxyz -16 -10 -13 create-link-with turtle 129]
  ask turtle 129 [set shape "proline" setxyz -16 -12 -12 create-link-with turtle 130]
  ask turtle 130 [set shape "glutamic acid" setxyz -14 -14 -11 create-link-with turtle 131]
  ask turtle 131 [set shape "valine" setxyz -16 -13 -10 create-link-with turtle 132]
  ask turtle 132 [set shape "glycine" setxyz -14 -14 -9 create-link-with turtle 133]
  ask turtle 133 [set shape "serine" setxyz -12 -13 -10 create-link-with turtle 134]
  ask turtle 134 [set shape "aspartic acid" setxyz -12 -12 -11 create-link-with turtle 135]
  ask turtle 135 [set shape "cysteine" setxyz -10 -13 -10 create-link-with turtle 136]
  ask turtle 136 [set shape "threonine" setxyz -8 -11 -11 create-link-with turtle 137]
  ask turtle 137 [set shape "threonine" setxyz -6 -11 -10 create-link-with turtle 138]
  ask turtle 138 [set shape "isoleucine" setxyz -4 -11 -11 create-link-with turtle 139]
  ask turtle 139 [set shape "histidine" setxyz -2 -12 -10 create-link-with turtle 140]
  ask turtle 140 [set shape "tyrosine" setxyz 0 -11 -10.5 create-link-with turtle 141]
  ask turtle 141 [set shape "asparagine" setxyz 2 -9 -11 create-link-with turtle 142]
  ask turtle 142 [set shape "tyrosine" setxyz 4 -7 -11.5 create-link-with turtle 143]
  ask turtle 143 [set shape "methionine" setxyz 6 -5 -12 create-link-with turtle 144]
  ask turtle 144 [set shape "cysteine" setxyz 8 -3 -12.5 create-link-with turtle 145]
  ask turtle 145 [set shape "asparagine" setxyz 10 -1 -12 create-link-with turtle 146]
  ask turtle 146 [set shape "serine" setxyz 12 1 -13 create-link-with turtle 147]
  ask turtle 147 [set shape "serine" setxyz 15 -1 -14 create-link-with turtle 148]
  ask turtle 148 [set shape "cysteine" setxyz 18 -3 -16 create-link-with turtle 149]
  ask turtle 149 [set shape "methionine" setxyz 21 -5 -17 create-link-with turtle 150]
  ask turtle 150 [set shape "glycine" setxyz 19 -3 -18 create-link-with turtle 151]
  ask turtle 151 [set shape "glycine" setxyz 17 -1  -17 create-link-with turtle 152]
  ask turtle 152 [set shape "methionine" setxyz 19 2 -16 create-link-with turtle 153]
  ask turtle 153 [set shape "asparagine" setxyz 15 4 -16 create-link-with turtle 154]
  ask turtle 154 [set shape "leucine" setxyz 13 6 -18 create-link-with turtle 155] ;;
hydrogen bond that was there before deosnt exist
  ask turtle 155 [set shape "arginine" setxyz  11 8 -17 create-link-with turtle 156]
  ask turtle 156 [set shape "proline" setxyz 9 7 -16 create-link-with turtle 157]
  ask turtle 157 [set shape "isoleucine" setxyz 7 6 -15 create-link-with turtle 158]
  ask turtle 158 [set shape "leucine" setxyz 5 6 -15 create-link-with turtle 159]
```

```
ask turtle 159 [set shape "threonine" setxyz 3 4 -14 create-link-with turtle 160]
ask turtle 160 [set shape "isoleucine" setxyz 1 5 -13 create-link-with turtle 161]
ask turtle 161 [set shape "isoleucine" setxyz -1 3 -12 create-link-with turtle 162]
ask turtle 162 [set shape "threonine" setxyz -3 4 -11 create-link-with turtle 163]
ask turtle 163 [set shape "leucine" setxyz -5 3 -10 create-link-with turtle 164]
ask turtle 164 [set shape "glutamic acid" setxyz -7 2 -11 create-link-with turtle 165]
ask turtle 165 [set shape "aspartic acid" setxyz -9 1 -11 create-link-with turtle 166]
ask turtle 166 [set shape "serine" setxyz -9 0 -12 create-link-with turtle 167]
ask turtle 167 [set shape "serine" setxyz -9 1 -13 create-link-with turtle 168]
ask turtle 168 [set shape "glycine" setxyz -7 3 -13 create-link-with turtle 169]
ask turtle 169 [set shape "asparagine" setxyz -8 5  -13 create-link-with turtle 170]
ask turtle 170 [set shape "leucine" setxyz -7 7 -12 create-link-with turtle 171]
ask turtle 171 [set shape "leucine" setxyz -8 6 -11 create-link-with turtle 172]
ask turtle 172 [set shape "glycine" setxyz -6 7 -10 create-link-with turtle 173]
ask turtle 173 [set shape "arginine" setxyz -4 7 -10 create-link-with turtle 174]
ask turtle 174 [set shape "asparagine" setxyz -2 6 -9 create-link-with turtle 175]
ask turtle 175 [set shape "serine" setxyz 0 5 -10 create-link-with turtle 176]
ask turtle 176 [set shape "phenylalanine" setxyz 2 4 -9 create-link-with turtle 177]
ask turtle 177 [set shape "glutamic acid" setxyz 4 3 -11 create-link-with turtle 178]
ask turtle 178 [set shape "valine" setxyz 6 2 -13 create-link-with turtle 179]
ask turtle 179 [set shape "arginine" setxyz 8 1 -13 create-link-with turtle 180]
ask turtle 180 [set shape "valine" setxyz 11 0 -11 create-link-with turtle 181]
ask turtle 181 [set shape "cysteine" setxyz 14 -1 -10 create-link-with turtle 182]
ask turtle 182 [set shape "alanine" setxyz 17 -2 -9 create-link-with turtle 183]
ask turtle 183 [set shape "cysteine" setxyz 15 -1 -8 create-link-with turtle 184]
ask turtle 184 [set shape "proline" setxyz 14 -1 -7 create-link-with turtle 185]
ask turtle 185 [set shape "glycine" setxyz 15 0 -6 create-link-with turtle 186]
ask turtle 186 [set shape "arginine" setxyz 16 2 -7 create-link-with turtle 187]
ask turtle 187 [set shape "aspartic acid" setxyz 15 4 -8 create-link-with turtle 188]
ask turtle 188 [set shape "arginine" setxyz 14 6 -7 create-link-with turtle 189]
ask turtle 189 [set shape "arginine" setxyz 15 8 -6 create-link-with turtle 190]
ask turtle 190 [set shape "threonine" setxyz 16 10 -7 create-link-with turtle 191]
ask turtle 191 [set shape "glutamic acid" setxyz 15 12 -8 create-link-with turtle 192]
ask turtle 192 [set shape "glutamic acid" setxyz 14 14 -7 create-link-with turtle 193]
ask turtle 193 [set shape "glutamic acid" setxyz 15 16 -6 create-link-with turtle 194]
ask turtle 194 [set shape "asparagine" setxyz 16 18 -7 create-link-with turtle 195]
ask turtle 195 [set shape "leucine" setxyz 15 20 -6 create-link-with turtle 196]
ask turtle 196 [set shape "arginine" setxyz 14 20 -6 create-link-with turtle 197]
ask turtle 197 [set shape "lysine" setxyz 13 20 -6 create-link-with turtle 198]
```

```
  ask turtle 198 [set shape "lysine" setxyz 12 20 -6]
  ask links
[set color red]

ask cysteines
[ create-links-with other cysteines in-radius 10 ;; represent disulfide bonds between two
cysteines
 ask links
 [if color = gray[set color yellow]]]

ask threonines ;; hydrogen bonds between serine, threonine, and tyrosine,
[ create-links-with serines in-radius 10
  create-links-with tyrosines in-radius 10
ask links
[if color = gray[set color blue]]]

ask aspartic-acids ;; hydrogen bonds
[ create-links-with tyrosines in-radius 10
  create-links-with glutamic-acids in-radius 10]
    ask links
    [if color = gray[set color blue]]

ask serines ;; hydrogen bonds between serines and lysines
[ create-links-with lysines in-radius 10
  create-links-with asparagines in-radius 10
  create-links-with arginines in-radius 10
  create-links-with histidines in-radius 10]
  ask links
  [if color = gray[set color blue]]

  ask lysines ;; creates ionic bonds
  [ create-links-with aspartic-acids in-radius 10
    create-links-with glutamic-acids in-radius 10
    ask links
    [if color = gray[set color green]]]

  ask aspartic-acids ;; ionic bonds
  [ create-links-with arginines in-radius 10
    create-links-with lysines in-radius 10
```

```
    create-links-with histidines in-radius 10
    ask links
    [if color = gray[set color green]]]

  ask glutamic-acids ;; ionic bonds
  [ create-links-with arginines in-radius 10
    create-links-with lysines in-radius 10
    create-links-with histidines in-radius 10
    ask links
    [if color = gray[set color green]]]

    ask arginines ;; ionic bonds
  [ create-links-with aspartic-acids in-radius 10
    create-links-with glutamic-acids in-radius 10
    ask links
    [if color = gray [set color green]]]

    ask histidines ;; ionic bonds
  [ create-links-with aspartic-acids in-radius 10
    create-links-with glutamic-acids in-radius 10
    ask links
    [if color = gray[set color green]]]

   ask alanines ;; hydrophobic interactions
   [ create-links-with valines in-radius 10
     create-links-with leucines in-radius 10
     create-links-with isoleucines in-radius 10
     create-links-with methionines in-radius 10
     create-links-with phenylalanines in-radius 10
     create-links-with tryptophans in-radius 10
     ask links
     [if color = gray[set color cyan]]]
 end
to heat
 ask links
 [if temperature >= 13
     [if strength <= 7
       [ask both-ends
         [ask other-end
```

```
          [forward random 3]]
          die]]
   if temperature >= 23
    [if strength <= 11
      [ask both-ends
        [ask other-end
          [forward random 3]]
        die]]
    if temperature >= 100
    [if strength <= 15
      [ask both-ends
        [ask other-end
          [forward random 3]]
        die]]
    if temperature >= 113
    [if strength <= 20
      [ask both-ends
        [ask other-end
          [forward random 3]]
        die]]
   ]
 ask cysteines
[ create-links-with other cysteines in-radius 10 ;; represent disulfide bonds between two
cysteines
 ask links
 [if color = gray[set color yellow]]]

ask threonines ;; hydrogen bonds between serine, threonine, and tyrosine,
[ create-links-with serines in-radius 10
  create-links-with tyrosines in-radius 10
ask links
[if color = gray[set color blue]]]

ask aspartic-acids ;; hydrogen bonds
[ create-links-with tyrosines in-radius 10
  create-links-with glutamic-acids in-radius 10]
    ask links
    [if color = gray[set color blue]]
```

```
ask serines ;; hydrogen bonds between serines and lysines
[ create-links-with lysines in-radius 10
  create-links-with asparagines in-radius 10
  create-links-with arginines in-radius 10
  create-links-with histidines in-radius 10]
  ask links
  [if color = gray[set color blue]]

  ask lysines ;; creates ionic bonds
  [ create-links-with aspartic-acids in-radius 10
    create-links-with glutamic-acids in-radius 10
    ask links
    [if color = gray[set color green]]]

  ask aspartic-acids ;; ionic bonds
  [ create-links-with arginines in-radius 10
    create-links-with lysines in-radius 10
    create-links-with histidines in-radius 10
    ask links
    [if color = gray[set color green]]]

  ask glutamic-acids ;; ionic bonds
  [ create-links-with arginines in-radius 10
    create-links-with lysines in-radius 10
    create-links-with histidines in-radius 10
    ask links
    [if color = gray[set color green]]]

    ask arginines ;; ionic bonds
  [ create-links-with aspartic-acids in-radius 10
    create-links-with glutamic-acids in-radius 10
    ask links
    [if color = gray[set color green]]]

      ask histidines ;; ionic bonds
  [ create-links-with aspartic-acids in-radius 10
    create-links-with glutamic-acids in-radius 10
    ask links
     [if color = gray[set color green]]]
```

```
ask alanines ;; hydrophobic interactions
[ create-links-with valines in-radius 10
  create-links-with leucines in-radius 10
  create-links-with isoleucines in-radius 10
  create-links-with methionines in-radius 10
  create-links-with phenylalanines in-radius 10
  create-links-with tryptophans in-radius 10
  ask links
  [if color = gray[set color cyan]]]

  if temperature <= 13 ;; minimum temperature for hydrogen bonds to break
  [
    let probability random 122 / 486
    let n count links
    ask (n-of(probability * n)links) [die]
    print count links / 486
    if count links <= 364
  [
    make-protein-structure
    ask turtle 154
    [
      setxyz 13 6 -16
    ]
  ]
   ]
  if temperature = 23
       [
    let probability random 243 / 486
    let n count links / 486
    ask (n-of(probability * n)links) [die]
    print count links
    if count links <= 243
  [
    make-protein-structure
    ask turtle 154
    [
      setxyz 13 6 -16
    ]
```

```
    ]
    ]
    if temperature = 100
        [
      let probability random 365 / 486
      let n count links / 486
      ask (n-of(probability * n)links) [die]
      print count links
      if n <= 121
    [
      ask turtles[
      make-protein-structure
      ask turtle 154
      [
        setxyz 13 6 -16
      ]
    ]
         ]]
   if temperature >= 113
        [
      let probability random 481 / 486
      let n count links / 486
      ask (n-of(probability * n)links) [die]
      print count links
      if n <= 5
    [
      make-protein-structure
      ask turtle 154
      [
        setxyz 13 6 -16
      ]
    ]
    ]
end
```

Appendix B: Cellular Model Code

```
turtles-own [cancerous? age]
patches-own [temperature]
breed [malignant-grandular-epithelial-cells malignant-grandular-epithelial-cell] ;;
cancer cells
malignant-grandular-epithelial-cells-own [shock]

breed [grandular-epithelial-cells grandular-epithelial-cell] ;; non-cancer cells.
Normal,healthy cells.
breed [nanorobots nanorobot]
to setup
  clear-all
  reset-ticks
  create-turtles 1
  ask turtle 0
  [ setxy 16 16
    set color 136
    set heading 180
    pen-down
    forward 35
    pen-up
    setxy 15.5 16
    pen-down
    forward 35
    pen-up
    setxy 15.4 16
    pen-down
    set color blue
    forward 35
    pen-up
    setxy 14.5 16
    pen-down
    forward 35
    pen-up
    setxy 14.4 16
    set color 136
    pen-down
    forward 35
```

```
  pen-up
  setxy 14 16
  pen-down
  forward 35
  die
]
create-grandular-epithelial-cells 50;; creates 100 healthy cells
create-malignant-grandular-epithelial-cells 20
ask malignant-grandular-epithelial-cells
[ set breed malignant-grandular-epithelial-cells
  set shape "eyeball"
  set color black
  set cancerous? true
  set size 1.5
  set age 50
]
create-nanorobots number-of-nanorobots
ask nanorobots
[
  set shape "rocket"
  set size 1.5
  set color green
]
ask grandular-epithelial-cells
[
  set shape "epithelial cell"
  set size 1.5
  set color green
  set cancerous? false
  set age 50
]
  ask one-of grandular-epithelial-cells
[
  set breed malignant-grandular-epithelial-cells
  set shape "eyeball"
  set color black
  set cancerous? true
]
create-grandular-epithelial-cells 1
```

```
  ask patches
  [
    set temperature heat
  ifelse pxcor >= 14
  [
    set pcolor black ;; represents the color of the blood in the body
  ]
  [
    set pcolor 15
  ]
  ]
  ask turtles
  [
  setxy random-xcor random-ycor
  if pcolor = black
  [
    set xcor random 12.9
  ]
  ]
end

to movement-of-cells
   if count grandular-epithelial-cells = 0 ;; stops the model if "person" is dead
becuase of cancer cells killing all of normal cells
  [
    stop
  ]
  if count malignant-grandular-epithelial-cells = 0
  [stop]
    ask links
    [let n count links
      if n > 1
      [
        ask other links
        [
          die
        ]]]
       ask nanorobots
          [
```

```
 forward 1
right random 180
let n count links
let x (3617 * heat)
let probability random 50
   if heat = 13
    [
if any? malignant-grandular-epithelial-cells in-radius 5
[
  ask one-of malignant-grandular-epithelial-cells in-radius 5
  [
     print probability
     if probability < 47
  [
 ask one-of malignant-grandular-epithelial-cells ;in-radius 5
 [
   set color blue
   set shock true
   if color = blue and probability < 47
   [
   die]
if x = 47021 and probability < 47
[ask malignant-grandular-epithelial-cells in-radius 10
  [die
  ask grandular-epithelial-cells in-radius 10
  [die]]]]]]];ask malignant-grandular-epithelial-cells
    if heat = 23
    [
    if any? malignant-grandular-epithelial-cells in-radius 5
[
  ask one-of malignant-grandular-epithelial-cells in-radius 5
  [
     print probability
     if probability < 32
  [
 ask one-of malignant-grandular-epithelial-cells ;in-radius 5
 [
   set color blue
   set shock true
```

```
  if color = blue and probability < 32
  [
  die]
if x = 83191 and probability < 32
[ask malignant-grandular-epithelial-cells in-radius 20
 [die
 ask grandular-epithelial-cells in-radius 20
 [die]]]]]]]]
  if heat = 100
  [       if any? malignant-grandular-epithelial-cells in-radius 5
[
 ask one-of malignant-grandular-epithelial-cells in-radius 5
 [
    print probability
    if probability < 4
 [
ask one-of malignant-grandular-epithelial-cells ;in-radius 5
[
  set color blue
  set shock true
  if color = blue and probability < 4
  [
  die]
if x = 83191 and probability < 4
[ask malignant-grandular-epithelial-cells in-radius 30
 [die
 ask grandular-epithelial-cells in-radius 30
 [die]]]]]]]]
  if heat = 113
  [if any? malignant-grandular-epithelial-cells in-radius 5
[
 ask one-of malignant-grandular-epithelial-cells in-radius 5
 [
    print probability
    if probability < 0
 [
ask one-of malignant-grandular-epithelial-cells ;in-radius 5
[
  set color blue
```

```
      set shock true
      if color = blue and probability < 0
      [
      die]
    if x = 83191 and probability < 0
    [ask malignant-grandular-epithelial-cells in-radius 20
      [die
      ask grandular-epithelial-cells in-radius 20
      [die]]]]]]]]]

ask malignant-grandular-epithelial-cells
[
  right random 180 ;; has cancer cells do a random wiggle walk
  forward 1
    if pcolor = black
  [
    set xcor 12.9
  ]
  set age age + 1 ;; sets the age for the cancer cells
  if any? grandular-epithelial-cells-here
  [
    ask grandular-epithelial-cells-here ;; healthy cells die when in contact with
cancer cells
    [
      die
    ]
    if any? grandular-epithelial-cells
    [
    if count grandular-epithelial-cells < 50
    [
      ask one-of grandular-epithelial-cells
      [
        hatch mitosis-for-grandual-epithelial-cells
        set age 50
        right random 180
        forward 1
      ]
     ]
    ]
```

```
if age = 50
[
  hatch mitosis-for-malignant-grandual-epithelial-cells + 1 ;; stage one
  set cancerous? true
  set age 1
  right random 180
  forward 1
]
if age >= 100
[
  hatch mitosis-for-malignant-grandual-epithelial-cells + 2 ;; stage two
  set cancerous? true
  set age 1
  right random 180
  forward 1
]
if age >= 150
[
  hatch mitosis-for-malignant-grandual-epithelial-cells + 3 ;; stage three
  set cancerous? true
  set age 1
  right random 180
  forward 1
  ask grandular-epithelial-cells
  [
    if count grandular-epithelial-cells < 50
    [
      ask grandular-epithelial-cells with [age = 1]
      [
      die
      ]
        if any? grandular-epithelial-cells-here
        [
          ask grandular-epithelial-cells-here
          [
            die
          ]
        ]
]
```

```
    ]
  if age >= 200 ;; asks the cancer cells to die if at the age of 150 or greater.
  [
    die
  ]
]
]
ask grandular-epithelial-cells
[
  right random 180
  forward 1
  if pcolor = black
  [
    set xcor 12.9
  ]
  set age random 50
  set age age + 1
]
ask turtles
[
    if temperature-of-body > 37
  [
    die
  ]
  if temperature-of-body < 35
  [
    die
  ]
  if pH > 7.42
  [
    die
  ]
  if pH < 7.38
  [
    die
  ]
  if Humidity > 70
  [
```

```
  ]
  if Humidity < 30
  [

  ]
]
tick
end
```