

Genetics and The Likelihood Of Disease

New Mexico Adventures in
Supercomputing Challenge

Final Report

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Team 069

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TABLE OF CONTENTS

Executive Summary.....	3
Introduction.....	4
Table 1.....	5
Problem Definition.....	6
Problem Solution.....	6
Results.....	7
Table 2.....	8
Figure 1.....	9
Conclusions.....	9
Recommendations.....	10
Acknowledgments.....	10
References.....	11
Appendix A.....	12

Executive Summary

When we started this project we wanted to make a computational model using a simple mathematical problem. We also wanted to use a subject that affected many people and was widely known. Using this information it seemed like the subject of breast cancer was all around us.

Once we chose the subject of breast cancer we began to think about what angle we wanted to take. We found that identifying the spread of breast cancer could help identify how the disease works. As we took this idea we also wanted to make it realistic, taking in factors such as age and genetics. We started off making a random population using the StarLogo agent-based modeling program. Then we went on to give them breeds of male and female. Obviously they would have to meet the opposite sex, become a couple, and reproduce. Although they can move randomly on their own they can only reproduce with their partner.

The major factors affecting this model were breast cancer statistics and population genetics. We programmed in the real statistics from our research on how many people inherit the mutated gene for breast cancer as well as what percentage will die from breast cancer. This model also took into account the factors affecting population equilibrium, such as genetic drift or mutation. The population in this model maintained equilibrium except for manipulation of the breast cancer gene.

The program that we wrote effectively displayed the breast cancer gene and how it is spread through genetics. We feel that this is a realistic and useful model. We ultimately were successful and feel that this could be effectively used to better grasp the spread of this disease.

Introduction

Description

This project involves heredity and the likelihood of disease appearing in later generations. We took a random population and modeled how a breast cancer gene propagates through the population. We used the Star Logo agent-based modeling program to examine each generation and the likelihood of the disease showing up, noting any changes. We also modeled its distribution in populations, among different ages and males and females.

Ultimately we wanted to predict if future generations would have the same disease. The reason that we chose breast cancer as the disease to monitor is because it is widely known. Almost everyone knows someone with breast cancer or has been affected by it. We hope that this may aid or increase the amount of study about breast cancer. We also hope that in some small way this could maybe be a step to one day find a cure to breast cancer.

We expected to be able to explain how breast cancer propagates throughout a population. We also expected to see a slow increase in cases of breast cancer genotype as time goes on because as population increases we expect the number of cases of breast cancer will likewise increase. All in all, the model helped to explain how quickly the breast cancer gene was passed on given different population size and distribution.

Background

Breast Cancer is caused by a mutation of two genes, BRCA-1 and BRCA-2. One out of every 400 people carry this mutated gene. Men and women can develop breast cancer once they have this gene. For every 400 men with breast cancer there are 40,000 women with breast cancer. Men only have a .26 percent chance of developing breast cancer. There are about

212,600 new cases of breast cancer each year and about 40,200 expected deaths. The following table shows the percent increase in the risk of women getting breast cancer with age.

Table 1: Percent Chance of Breast Cancer Development in Women

Age	Percent in Women
30	.15%
40	.48%
50	.92%
60	1.28%
70	1.5%
80	1.54%

If a population stays the same with out change it is said to be in equilibrium. When we established our beginning population, we factored in the basic genetic equation, or Hardy-Weinberg Equation, $p^2+2pq+q^2=1$. This states that in the absence of other factors, genetic makeup of population does not change. We took into account these factors, which are:

*Large populations

*No gene migration

*No mutation

*Random mating

After establishing these parameters of equilibrium in the model, we then manipulated the factors of mutation and genetic inheritance to show the spread of breast cancer.

Genes are the traits passed down from parents to their offspring. They are either dominant or recessive. The parents each pass on one gene type or allele to their offspring. Each parent passes on one allele, giving the offspring a possible combination of pure dominant, heterozygous, or pure recessive. This combination is called the genotype. This model used pure recessive genotype as the type that gives rise to breast cancer.

Problem Definition

Our model examined population genetics and the likelihood of disease. Breast cancer is the specific disease that we monitored throughout the population. We want to look at the chances of it reoccurring with each generation. The goal of this project was to develop a computational model to show the chances people have of getting breast cancer.

Problem Solution

We used the Star Logo program of agent based modeling to solve our problem. We took the basic assumptions of population equilibrium set forth by the Hardy-Weinberg rule and created a large population with a random genetic makeup. The turtles randomly reproduced and had no outside physical or environmental effects of change on them. After creating the population in equilibrium, we were able to input and manipulate the breast cancer mutation.

To solve our problem we had to give each turtle its own properties. One such property is genotype. The genes were identified as alleles 0 or 1, with 1 being the dominant and 0 being the recessive gene. When the recessive genotype (0,0) appears the agent would develop breast cancer. We used the statistics from our research, to input the probability of breast cancer occurrence. One in 400 people would randomly mutate to the breast cancer gene. Those offspring who inherited the recessive genotype (0,0) would also develop breast cancer. We also input the probability of breast cancer death, based on the statistics in Table 1. We made this

model realistic in that if the turtle carries this gene they have a certain percentage risk of dieing from breast cancer.

Results

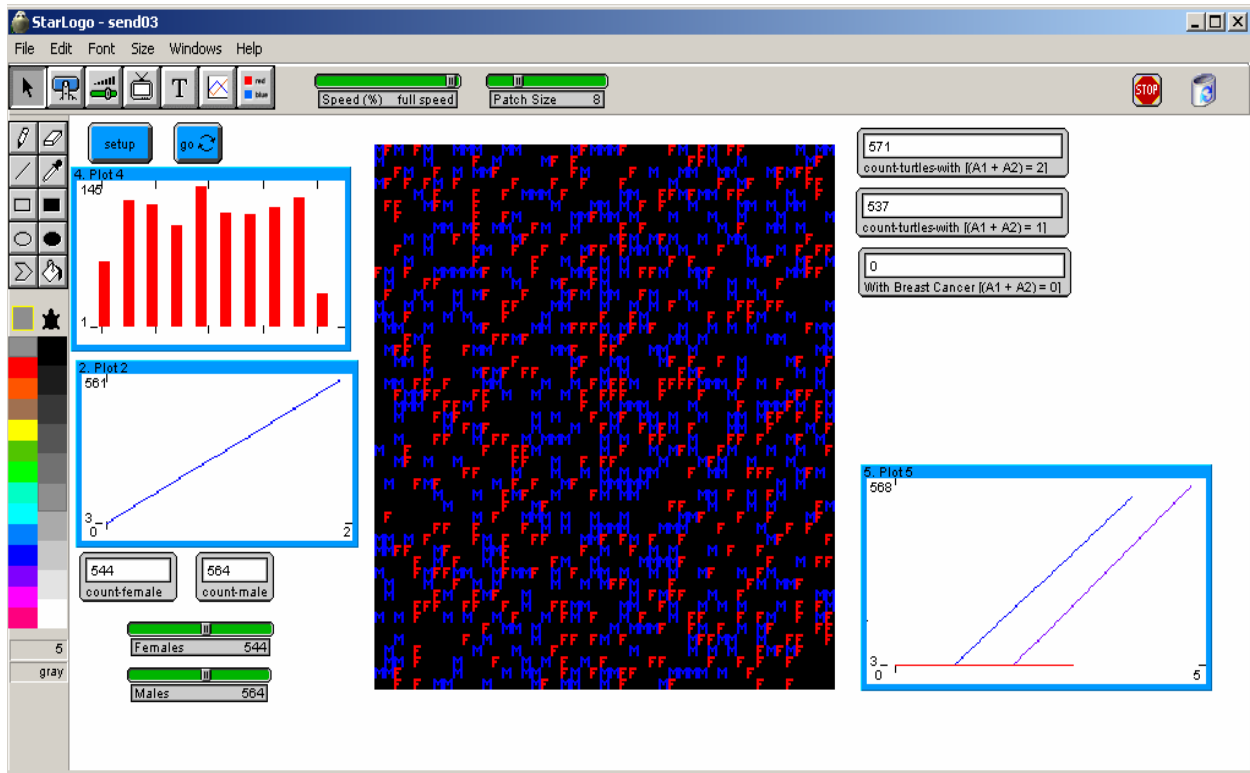
After running this model many times we found that while population does not decline or decrease, the amount of breast cancer in the population does increase because of reproduction. We also found that in smaller populations there is a rapid increase in the amount of breast cancer found most likely due to the fact that they have a smaller number of people reproducing and a limited age to reproduce. We found that in larger populations there were less people getting breast cancer. All in all we found that the total increase in breast cancer was between 3 and 6 percent. Specific results can be found in the following table.

Table 2: Findings From Model Test Runs

Trial	Male/Female	A1+A2=0	A1+A2=1	A1+A2=2	Time	Results
1	Begin 400/400 End 856/840	Begin 0 End 51	Begin 401 End 792	Begin 399 End 853	136	The end result was 51 cases of breast cancer. This is a 3% increase.
2	Begin 200/200 End 655/706	Begin 0 End 81	Begin 200 End 537	Begin 200 End 743	348	We ended with 81 cases of breast cancer. Showing about a 6% increase
3	Begin 150/150 End 547/473	Begin 0 End 33	Begin 143 End 390	Begin 157 End 597	251	The end result was 33 cases of breast cancer. This is about a 3 % increase.
4	Begin 400/400 End 971/939	Begin 0 End 62	Begin 399 End 795	Begin 401 End 1053	202	The end result was 62 cases of breast cancer. This is also a 3% increase.
5	Begin 200/200 End 788/819	Begin 0 End 77	Begin 213 End 665	Begin 187 End 865	503	We ended with 77 cases of breast cancer. Showing about a 5% increase
6	Begin 150/150 End 507/495	Begin 0 End 29	Begin 142 End 401	Begin 158 End 572	360	The end result was 29 cases of breast cancer. This is almost a 3 % increase.

The model itself allows the controller to manipulate the initial settings. One can also monitor the frequency, age, and distribution of the breast cancer gene through the graphs displayed on the following screen.

Figure 1: Breast Cancer Model



Conclusion

We feel that we have been successful in that this model works. We feel that it is a good start to more complex and more beneficial models. We feel this was a good way to display how breast cancer is spread throughout a population. This takes into account the factors reflecting population genetics in that we examine mutation and the inheritance of gene. All in all, this

model effectively shows that the larger a population the slower the inheritance of the breast cancer gene. Breast cancers spread is affected by mutation and genetic drift.

Our greatest accomplishment was completing a successful Star Logo computational model. Within the model the greatest accomplishment was developing and writing the code. We feel that this part of the code was the hardest part to write...

```
to reproduce :mom :dad ; parameters passed in the reproduce call
if (age > 19 and age < 40)
[ifelse (random 2) = 0 [let [:gA1 A1-of :mom]] [let [:gA1 A2-of :mom]]]
ifelse (random 2) = 0 [let [:gA2 A1-of :dad]] [let [:gA2 A2-of :dad]]
hatch
[set age 0 set A1 :gA1 set A2 :gA2
ifelse (random 2) = 0
[set breed male setshape 12 setc 107]
[set breed female setshape 13 setc 17]
if (random 400) = 0
[mutation]
]
]
end
```

We feel that this was hard because we had to understand and use parameters and locals. Which neither of us had ever seen before.

Recommendations

If we were to continue with this model we feel that we could make it more realistic by adding more factors such as different races and realistic environmental factors. In real life situations people move in and out changing the population. If we added this it would add more practicality. Time was a major constraint in the development of our population model.

Acknowledgement

We would like to thank all the great people who helped us develop this model. They took out time from their busy lives and schedules to help us make this model the best it can be with the time allotted. They are: James Taylor, Hal Scheintaub, and Rhonda Ward.

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Appendix A

The Code

```

Java StarLogo
2.0
english
`turtle`
breeds [female male]
turtles-own [A1 A2 age coupleID]

to go
  wiggle
  die-of-old-age
end

to wiggle
  fd 1
  rt random 25
  lt random 25
  set age (age + 0.01)
  match2
end

to match2
  if breed = female
  [grab one-of-male-here
  [set coupleID partner
  set coupleID-of partner (who)
  if (age > 18 and age < 100) and
  ((age-of partner) > 18 and (age-of partner) < 100)
  [reproduce who partner]
  ]
  ]
end

to reproduce :mom :dad ; parameters passed in the reproduce call
  if (age > 19 and age < 40)
  [ifelse (random 2) = 0 [let [:gA1 A1-of :mom]] [let [:gA1 A2-of :mom]]
  ifelse (random 2) = 0 [let [:gA2 A1-of :dad]] [let [:gA2 A2-of :dad]]
  hatch
  [set age 0 set A1 :gA1 set A2 :gA2
  ifelse (random 2) = 0
  [set breed male setshape 12 setc 107]
  [set breed female setshape 13 setc 17]
  if (random 400) = 0
  [mutation]
  ]
  ]
end

to mutation

```

```

    if (age > 30 and age < 39) and (random 1000) <= 15
      [die]
    if (age > 40 and age < 49) and (random 1000) <= 48
      [die]
    if (age > 50 and age < 59) and (random 1000) <= 92
      [die]
    if (age > 60 and age < 69) and (random 1000) <= 128
      [die]
    if (age > 70 and age < 79) and (random 1000) <= 150
      [die]
    if (age > 80 and age < 100) and (random 1000) <= 154
      [die]

  end
  to die-of-old-age
    if age > 100 [die]
  end

```

observer

```

to setup
  ca
  create-female-and-do number
  [setc red setshape 13
  set age random 80]
  create-male-and-do number2
  [setc blue setshape 12
  set age random 80]
  ask-turtles
  [setx random 50 sety random 50]
  ask-turtles
  [ifelse (random 400) < 1 [set A1 0 set A2 0]
          [set A2 1 set A1 0]
  ifelse (random 2) = 1
  [set A2 1 set A1 0]
  [set A1 1 set A2 1]
]
end

```