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Research Project

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Evolution

March 22, 2010

Where is the tipping point where mutation stops being beneficial to the fitness of a species and becomes detrimental to their fitness?

Introduction:

Recent studies have shown that there is an optimal mutation rate, and that any mutations that exceed this rate become deleterious mutations. "The optimal mutation rate must balance the genetic loads caused by deleterious mutations [1]." Many scientific experiments pertaining to mutation and adaptation of bacteria use various strains of *E.coli,* a highly adaptable bacterium due to its high frequency of mutation. One experiment used 12 strands of genetically identical *E.coli* bacteria to show the effects of mutation on genetic variation. "Because the populations were founded from a single ancestral clone, mutation provided their only source of genetic variation [2]." Many bacteria, like *E.coli* develop high mutation rates to produce genetic variation. In this experiment, scientists predicted, "fitness will be higher on average in mutator populations [2]." In another experiment, a highly mutative strain of *E.coli* bacteria due to a defective protein was used to show the effects of mutation in mouse guts. Through the examination of the mice feces, scientists noticed that the mutative bacteria adapted to very well to the digestive tract of one specific mouse. However, when placed in the digestive tract of a mouse infected with a different strand of *E.coli*, the mutations that allowed the first strand to adapt so efficiently became deleterious mutations. Ultimately, the scientists conducting the experiment concluded "a high mutation rate was initially beneficial because it allowed faster mutation, but this benefit disappeared once adaptation was achieved [3]."

Given that a slight mutation is beneficial for the fitness of a bacterial colony, and that anything above that is detrimental to the fitness of a bacterial colony, I aimed to determine when the fitness of a bacteria colony reached its apex due to mutation, and when it began to harm the fitness of a bacteria colony. Is there a tipping point where mutation in a species ceases to be advantageous to a species and becomes detrimental to their survival? If there is a tipping point, how does mutation effect a population once it becomes problematic?

Hypothesis:

Both a 1% mutation rate and a 2% mutation rate (as determined by a previous experiment on Avida-ED) are beneficial to the fitness and population of a bacterial colony. I hypothesized that the optimal mutation of a bacterial colony will occur at roughly a 1.5% mutation rate because 1.5% is the mean of these two percentages, there would be enough of a mutation to cause a significant increase in mean fitness without being too large a mutation to cause harm to the numbers of organisms within the bacterial colony. A 3% mutation rate was the point at which deleterious mutations started to occur, I hypothesized that an approximate 2.5% mutation rate would be the point at which deleterious mutations began to occur, based off of the results from the previous experiment.

Methods:

Using the Avida-ED program, an experiment was designed in order to determine if a point existed after which deleterious mutations occur. 26 different trials were performed and data was collected from each trial. The effects of mutation upon the fitness of a bacterial colony were tested in increments of .1%, beginning with .5% mutation and ending with 3% mutation. Trial 1 had a 0.5% mutation, trial 2 had a 0.6% mutation, trial 3 had a 0.7% mutation and so on and so forth, increasing by increments of .1% until a mutation rate of 3% was reached.

For a control in this experiment, a Petri dish with a 0% per site mutation rate was used. To show moderately deleterious mutations, a Petri dish with a 4% per site mutation rate was used. To show extreme deleterious mutations, a Petri dish with a 10% per site mutation rate was used.

A total of 29 trials were performed. Each trial was performed under the same conditions, and the data was collected each time after 500 time steps. There were 60 cells in each Petri dish, and each offspring was placed near their parent. The repeatability mode was set to "Experimental" to allow for natural variation. These conditions remained constant throughout every trial. After 500 steps in each trial, data was collected for average fitness, maximum fitness, and population size of the bacterial colony.

<u>Results</u>:

After all data was gathered from the 29 trials and organized into a chart (Fig. 1), the relationship between mutation and fitness became apparent. There were noted leaps in average fitness at .8% mutation, 1.3% mutation, 1.7% mutation, 1.8% mutation, and 2.4% mutation (Fig. 2). At these percentages, the average fitness reached 44.9761, 17.9289, 16.2887, 50.2451, and 24.1905 respectively. The highest average fitness was reached at 1.8% mutation, and the highest maximum fitness of 1071.4 was reached at the 2.4% mutation rate.

At a .8% mutation rate, the average fitness of the colony remained low but then increased to 44.9761 towards the very end of the allotted 500 steps. This indicates that the mutation did not immediately help the fitness of the population. There was an initial peak in the growth of the number of organisms, but these organisms had a low fitness level. A slight plateau in growth followed this peak. At this plateau, the bacteria with a low fitness level died off and bacteria with a high fitness level due to mutation were growing. This plateau immediately preceding the peak in average fitness indicates that the bacteria first growing on the Petri dish were harmed by the mutation. The unfit bacteria died off, and the remaining organisms had a high average fitness level due to mutation. This is evidence of selection. Here, the mutation rids the population of the weak, leaving a strong population with a high average fitness level. This remaining population was better adapted to their surroundings than the initial population.

The most consistent growth in population and the most consistent average fitness are seen at the 1.3% mutation rate. At this rate, the average fitness was 17.9289, the maximum fitness was 134.43, and the number of organisms was 3583. If you look at Fig. 4, fitness rose immediately and then remained for most of the 500 steps. During this period of uniform fitness, there was a large, consistent growth in the number of the organisms, indicating the health of the population.

Although the average fitness of the population is highest at a 1.8% mutation rate, the population is lowest out of all the mutation rates between 0% and 4%. In Fig. 6, there is a slow initial growth of bacteria, followed by a plateau in growth. This indicates that while many new bacteria were growing, the ones unfit for survival due to mutation died off. The population growth of the organisms at the 1.8% mutation rate was not as consistent as in the other experiments, but the average fitness of the bacteria increased much earlier. The line indicating average fitness fluctuated, indicating rapid increases and decreases in fitness from the middle to the end of the 500 steps. The slow population growth, combined with the rapid increases and decreases in average fitness indicates that the mutation hindered the growth and fitness of many organisms, but still provided for a high average fitness after the 500 steps. What was left after these 500 steps was a smaller colony of bacteria with a higher average fitness level overall, however the mutation did not allow the population to flourish as greatly as it did in the other trials. The mortality rate due to mutation is much higher at a 1.8% rate.

At 2.4% mutation, the maximum fitness of the organisms peaks at 1071.4, significantly higher than the maximum fitness at any other rate of mutation, and yet the average fitness of the colony is 34.1905. When looking at the Fig. 7, there was consistent growth in the number of organisms, which slowed as time progressed, indicating that there was a regulated population. There was a noticeable initial spike in average fitness, after which the average fitness of the population remained consistent and then increased at the very end of the experiment. This explains the average fitness of 34.1905 and the maximum fitness of 1071.4. The mutation caused this level of average fitness almost immediately in the population, and then caused a select few to mutate with a maximum fitness level of 1071.4, significantly higher than the rest of the population. In this instance, the mutation caused a high average fitness, and a select few “super bacteria”.

Instead of the predicted consistent increase in average fitness as mutation rates approached 2.5%, the average fitness overall is fairly uniform, with spikes (Fig. 13) in average fitness at the .8%, 1.3%, 1.7%, 1.8%, and 2.4% mutation rates. However, this is not evidence against my conclusion, because the maximum fitness of bacterial colonies between the .05% mutation rate and the 2.5% mutation rate are consistently high. As soon as the mutation rate reaches 2.6%, the maximum fitness drops. Although there is another spike at 2.9%, this is not indicative of the overall health of the population.

Although a maximum fitness of 62.177 is shown at the 2.9% mutation rate (Fig. 2), the average fitness is only 2.96165. Also, the population level decreases from 3529 at the 2.4% mutation rate to 3178 at the 2.9% mutation rate. These are indications that deleterious mutations are occurring. Here the mutation produced a few organisms with a maximum fitness of 62.177, but for the vast majority of the organisms, the average fitness was 2.96165. Here the mutation did not produce a more fit population overall. For a few, their mutations allowed them to reach a fitness level of 62.177. However, the vast majority of the colony were experiencing deleterious mutations.

<u>Discussion</u>:

At the mutation rates between 1.8% mutation and 2.4% mutation, the average fitness was low, yet the maximum fitness was high. The most stable and consistent population arose at the 1.3% mutation rate. Because the healthiest overall population was noticed at a 1.3% mutation rate, and because the peak in average fitness of the bacterial colony occurred at a 1.8% mutation rate, it can be concluded that my hypothesis was correct. I predicted that the health of a bacterial colony would peak at approximately a 1.5% mutation rate. The data collected in my experiment was significant. In the scope of mean fitness, a 1.8% mutation rate was the most effective. However, when the number of organisms was taken into consideration, the population at 1.8% was low. The higher mortality rate of the colony meant that deleterious mutations were occurring, but not at such a substantial frequency that the fitness of the population was affected. The bacteria at the 1.3% mutation rate were consistently healthy with a much lower mortality, meaning less deleterious mutations. Although the average fitness was low compared to the 1.8% mutation rate, there was a higher population and less fluctuation in the average fitness.

I also predicted that the highest deleterious mutations would occur around a 2.5% mutation rate. The average fitness was low after reaching the 2.4% mutation rate and decreased even more in the trials that followed. Also, there was an overall decline in number of organisms after the 2.4% mutation rate. Both of these findings support my initial hypothesis.

This in vitro study shows that although mutation rates are beneficial to the survival and adaptation of bacteria. However, the greater their mutability, the more deleterious these mutations are to their health. This experiment may inspire studies on drug resistance due to adaptation in pathogens. Many bacteria have a very high mutative rate, which makes them highly adaptive. If these bacteria are pathogens in human diseases, their highly adaptive nature can make them resistant to medication or treatment, making them infinitely more dangerous to people afflicted by them. The fitness of a bacterium is directly proportional to its survival rate. In highly adaptive bacteria, their adaptations become their demise.

Works Cited:

1. Adaptive Evolution of Highly Mutable Loci in Pathogenic Bacteria, http://www.fas.harvard.edu/~ped/people/faculty/publications_nowak/CurBio94.pdf, Accessed March 21, 2010

2. Evolution of High Mutuation Rates in Experimental Populations of *E.coli*, http://myxo.css.msu.edu/lenski/pdf/1997,%20Nature,%20Sniegowski%20et%20al.pdf, Accessed March 21, 2010

3. Costs and Benefits of High Mutation Rates: Adaptive Evolution of Bacteria in the Mouse Gut, http://isites.harvard.edu/fs/docs/icb.topic459133.files/Papers/Giraud-et-al-2001.pdf, Accessed March 22, 2010

Appendix A

Fig. 1) All experimental data:

A Closer examination of Fitness and Population

% mutation	avg. fitness	max fitness	population
0%	0.25268	0.2526	3600
0.50%	1.06892	4.2247	3597
0.60%	1.75446	17.655	3597
0.70%	1.07289	16.259	3594
0.80%	44.9761	266.12	3155
0.90%	5.88654	24.188	3580
1%	9.97997	33.265	3418
1.10%	1.8126	4.8205	3595
1.20%	4.80099	16.804	3314
1.30%	17.9289	134.43	3583
1.40%	0.715322	3.832	3589
1.50%	2.62357	16.898	3586
1.60%	2.66491	35.929	3588
1.70%	16.2887	109.21	3590
1.80%	50.2451	164.84	2552
1.90%	4.20366	24.188	3392
2.00%	3.35733	17.355	3564
2.10%	0.998945	9.8461	3579
2.20%	0.420119	1.071	3589
2.30%	0.983173	16.265	3480
2.40%	34.1905	1071.4	3529
2.50%	0.741603	8.533	3320
2.60%	0.312891	0.7272	3541
2.70%	0.827424	7.8659	3554
2.80%	0.414077	4.1513	3578
2.90%	2.96165	62.177	3178
3.00%	0.421819	2.0324	3513
4.00%	0.264757	1.4222	3515
10.00%	0.172771	0.3076	351

Appendix B

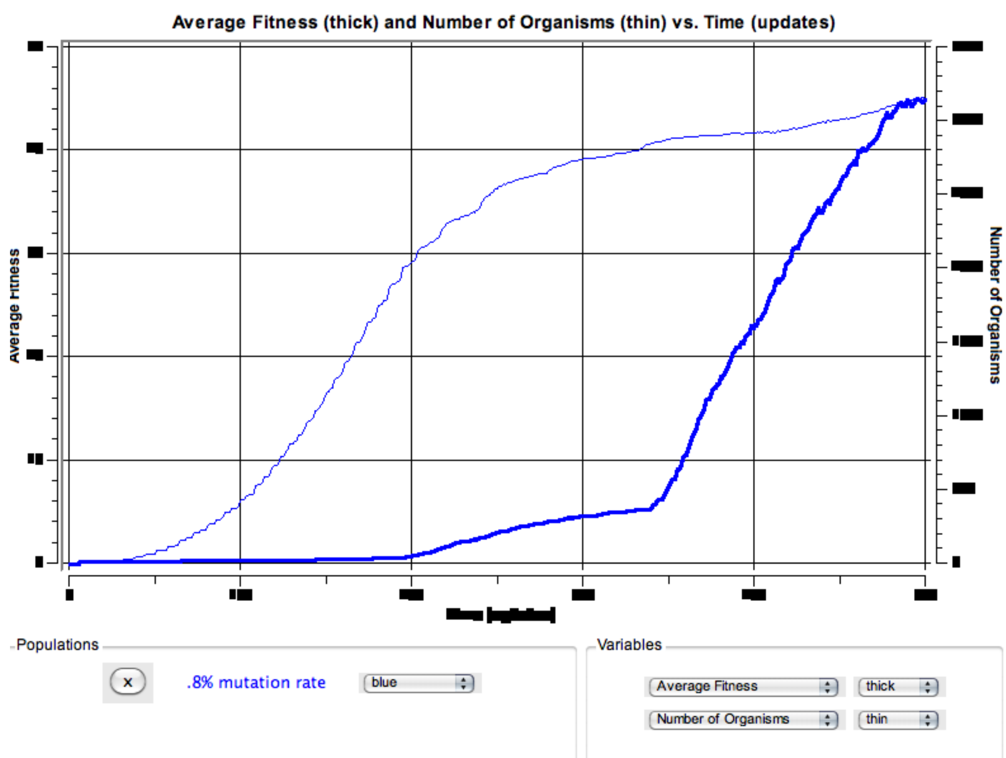
Fig. 2) Key points where average fitness or maximum fitness are highest:

A Closer examination of Fitness and Population

% mutation	avg. fitness	max fitness	population
0%	0.25268	0.2526	3600
0.50%	1.06892	4.2247	3597
0.60%	1.75446	17.655	3597
0.70%	1.07289	16.259	3594
0.80%	44.9761	266.12	3155
0.90%	5.88654	24.188	3580
1%	9.97997	33.265	3418
1.10%	1.8126	4.8205	3595
1.20%	4.80099	16.804	3314
1.30%	17.9289	134.43	3583
1.40%	0.715322	3.832	3589
1.50%	2.62357	16.898	3586
1.60%	2.66491	35.929	3588
1.70%	16.2887	109.21	3590
1.80%	50.2451	164.84	2552
1.90%	4.20366	24.188	3392
2.00%	3.35733	17.355	3564
2.10%	0.998945	9.8461	3579
2.20%	0.420119	1.071	3589
2.30%	0.983173	16.265	3480
2.40%	34.1905	1071.4	3529
2.50%	0.741603	8.533	3320
2.60%	0.312891	0.7272	3541
2.70%	0.827424	7.8659	3554
2.80%	0.414077	4.1513	3578
2.90%	2.96165	62.177	3178
3.00%	0.421819	2.0324	3513
4.00%	0.264757	1.4222	3515
10.00%	0.172771	0.3076	351

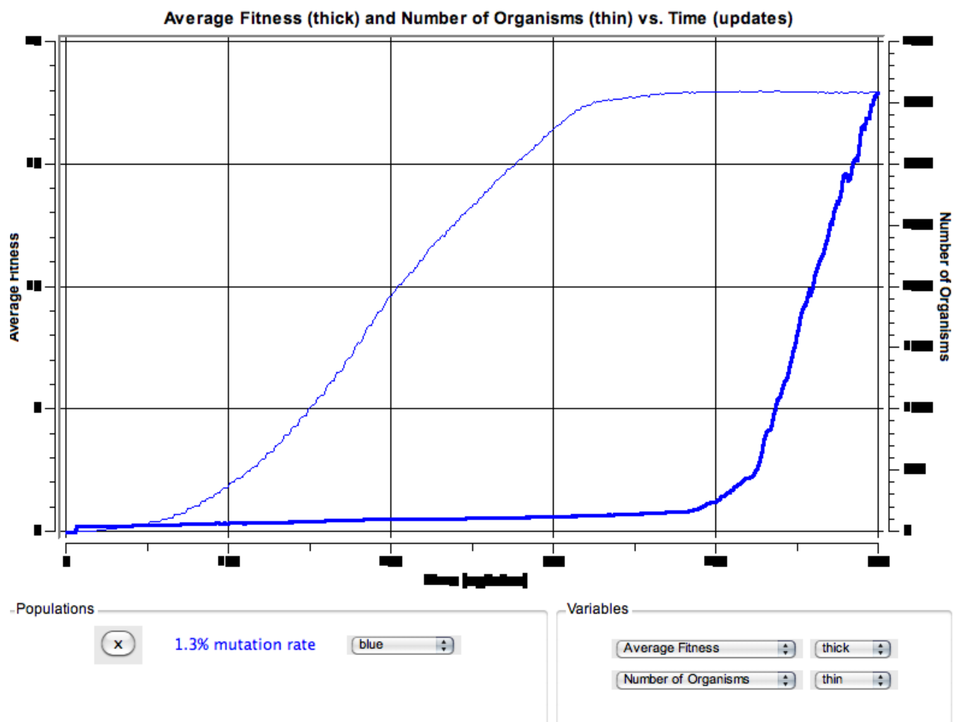
Appendix C

Fig. 3) Graph of average fitness and number of organisms at a .8% mutation rate:



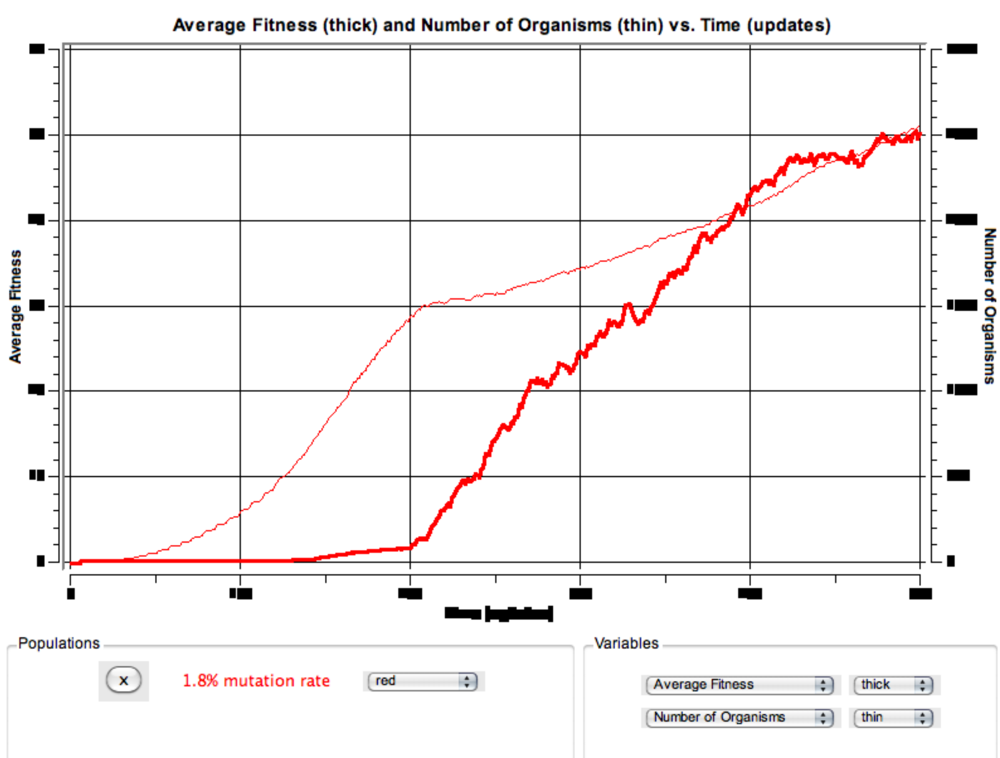
Appendix D

Fig. 4) Graph of average fitness and number of organisms at a 1.3% mutation rate:



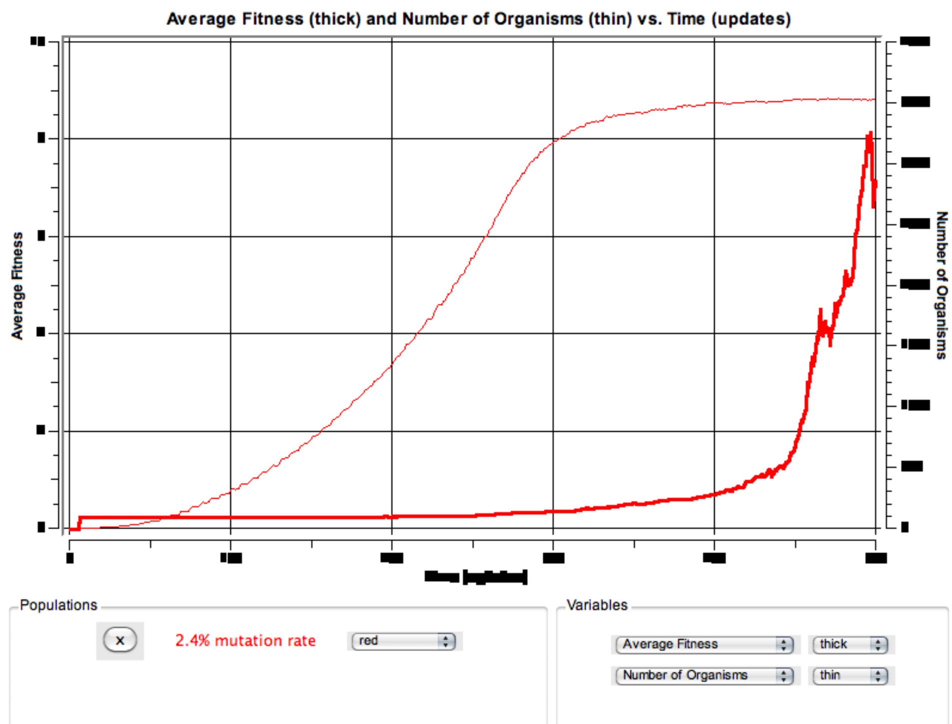
Appendix E

Fig. 6) Graph of average fitness and number of organisms at a 1.8% mutation rate:



Appendix F

Fig. 7) Graph of average fitness and number of organisms at a 2.4% mutation rate:



<u>Appendix G</u>

Fig. 13) Relationship between increasing % mutation and fitness: