The Physics of Darwinian Evolution

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1. Abstract
This paper describes the physical (thermodynamic) laws that govern Darwinian Evolution. When one understands how to apply these laws of physics, it becomes clear how clinical, experimental, and empirical examples of Darwinian Evolution behave the way they do. In particular, this paper shows which thermodynamic laws need to be applied to model and describe the evolution of antimicrobial drug resistance and the diversification of cancer cells.

2. Introduction
This paper is written in response to the Fisher Memorial Lecture 2018 by Joe Felsenstein [1], sponsored by Cambridge University. In this lecture, Professor Felsenstein tries to model biological evolution using the laws of thermodynamics. The relationship between energy and entropy in the process of biological evolution is described here in this paper in a qualitative manner to correctly understand this process. It cannot be overstated the importance of understanding this process. Biological evolution causes drug-resistant bacteria and viruses, herbicide-resistant weeds, pesticide-resistant insects, and failed cancer treatments. The impact of biological evolution has a great effect on the fields of medicine and agriculture.

Darwinian Evolution gives the correct qualitative framework to understand important examples of biological evolution. Darwin identified two of the important processes that occur with this biological phenomenon. From his “Origin of Species”[2]:

“For it should be remembered that the competition will generally be most severe between those forms which are most nearly related to each other in habits, constitution, and structure. Hence all the intermediate forms between the earlier and later states, that is between the less and more improved state of a species, as well as the original parent-species itself, will generally tend to become extinct. So it probably will be with many whole collateral lines of descent, which will be conquered by later and improved lines of descent. If, however, the modified offspring of a species get into some distinct country, or become quickly adapted to some quite new station, in which child and parent do not come into competition, both may continue to exist.”

Darwin, in the above paragraph, is describing two biological processes. The first process is “competition”, the struggle for the existence of different lineages in a population in a given environment. The second process is “adaptation”, the modification of some offspring in a given lineage that gives improved reproductive fitness for that new variant to the given selection conditions of the particular environment. These two biological processes are governed by different laws of thermodynamics.

3. Biological Competition
Biological competition is a deterministic, first law of thermodynamics process. This can be understood by the following logical steps and the control volume for available energy usage shown in the Illustration. First, assume that it takes energy to replicate. The carrying capacity of an environment is the total amount of energy available to a population to be used for survival and replication. That available energy is then competed for by the different variants in that population with the most efficient lineage at using that energy may take over the population while the less efficient users of the available energy are driven to extinction. The “relative” fitness of the different lineage determines which variants win this competition.
In a given environment, there can be multiple different lineages competing for a fixed amount of energy (the carrying capacity). Every generation, the more fit variant(s) produce more offspring than less fit variants until at some point in this evolutionary process, the less fit variants have been driven to extinction and the population consists only of descendants of the more fit variant(s). The carrying capacity, the limitation of energy available for reproduction, has reduced the diversity of the population by natural selection. However, unless some modification to one or more of the descendants of the lineage that has won that competition, the “absolute” fitness will not increase in the given environment (Figure 1).

One could think of the shaded area in the Illustration labeled “Energy used for survival and replication” as the total amount of food available to all populations. The total population size cannot exceed the energy available to support that population, therefore, the population size will be limited by the carrying capacity of that environment. This is significant to the evolutionary process in that the carrying capacity of the environment will limit the total number of replications possible and the replication is the random trial with the possible outcomes are, a mutation occurs, or a mutation does not occur. The smaller the carrying capacity of a given environment, the smaller the population (fewer replications) and the lower the probability that an adaptive mutation can occur on some member of the population.

**Figure 1:** Illustration: Limited carrying capacity control volume in which biological competition takes place.

### 4. Biological (Descent with) Modification and Adaptation

Biological modification and adaptation is a DNA evolutionary process. This process is governed by the second law of thermodynamics. This stochastic (random) process is a Markov random walk process. If one ignores the effects of natural selection, random mutations over generations will lead to random genetic sequences. The frequency of change of any base at any given site in the genome for a single replication is given by the mutation rate. If natural selection is not acting (i.e., neutral evolution) where no mutations give a change in reproductive fitness, over time, the genome will become random sequences of bases. A simple example can be used to demonstrate this.

Assume there is a simple replicator composed of four DNA bases. Let those bases be all adenine (A) bases in the initial generation. With every replication of that genome, there is a small probability that one of the other three bases (cytosine, guanine, and thymine, C, G, T, respectively) might be substituted. That small probability is the mutation rate. In the first generation, the genetic sequence will be AAAA. However, with each replication, the genetic sequence for the descendant will have a small probability of transitioning to one of the other bases. When the number of replications reaches about 1/(mutation rate), the probability of finding any one of the four different bases, A, C, G, or T will be equally likely, 0.25 at any site in the genome. This is demonstrated by the Jukes-Cantor model.[3] The way this can be interpreted is that it will take about 1/(mutation rate) replications for a particular mutation to occur at a particular site in some descendant in a lineage. This is simply the mean value of a binomial probability distribution problem.

If one considers natural selection, the probability will approach 1 for a certain base occurring at a particular site for a single selection pressure process in about 1/(mutation rate) replications of that site. However, it will take exponentially more replications if one considers 2 or more sites getting particular adaptive mutations at those sites. This is due to the multiplication rule of probabilities. One must consider the joint probabilities of two or more adaptive mutations occurring in a lineage to multiple simultaneous selection pressures. This is the same principle as selecting a single particular card from a card deck versus selecting two particular cards from a card deck. For example, the selection of an ace from a card deck has a probability of 4/52. The probability of drawing a second ace (assuming the first card is replaced) will again be 4/52. The joint probability will be (4/52)*(4/52).

Instead of considering random mutations as a disordering process for a genome, this can be interpreted as becoming less certain of the base at a given site with each replication of the genome. In the first generation, we are certain that the four bases are AAAA. With each generation, we are less certain that the base at a given site is an A until after many generations, the base at a given site will be equally likely A, C, G, or T. The system has reached equilibrium and minimum certainty of the base at any given site. The entropy of the system has been maximized.

### 5. The Interaction of Biological Competition and Biological Modification (Adaptation)

Once it is recognized that biological competition and biological modification are distinct physical processes, how does the inter-
action of these two processes affect biological evolution? There are two good experiments, the Kishony Mega-Plate Experiment (KMPE) [4,6] and the Lenski Long-Term Evolution Experiment (LTEE) [7] that demonstrate this effect.

The KMPE and LTEE both use Escherichia Coli populations. The environments of the two experiments are different. The KMPE is performed in a rectangular acrylic dish (120 x 60 cm) while the LTEE is performed in a test tube with a volume of 10cc. This allows for much larger populations in the KMPE (multiple billions) while the LTEE can only achieve a population size of 500 million before the population must be bottle-necked to 5 million and nutrients replenished. The selection pressure for the KMPE is an antibiotic while for the LTEE, it is starvation. What the Lenski team is doing is putting his population into an intensely competitive environment due to the limited carrying capacity. The effect of this is that it takes many more generations for the most fit variant to achieve the 1/(mutation rate) replications necessary for that lineage to have a variant with the next adaptive mutation.

The LTEE forces its multiple lineages to compete for limited food while the KMPE’s much larger carrying capacity allows for multiple colonies of a billion or more members to be formed by a colony founder in just 30 generations (doublings). Biological competition slows biological adaptation because this competition process limits all lineages in achieving that 1/(mutation rate) replications to give a reasonable probability that lineage will get the next beneficial mutation.

This is a general rule that applies to all biological evolutionary processes. Biological competition will always slow biological adaptation (DNA evolution) because it limits the size of all populations (lineages) involved in this biological evolutionary process. The laws of thermodynamics govern biological evolutionary processes and determine which mathematical rules that need to be used to model this process.

6. Conclusion

Darwinian evolution can be more easily understood if the physical process of each component is understood. This description only includes biological competition and biological descent with modification. Not considered in this description are recombination, lateral transfer of genetic material and other possible mechanisms of genetic change. The reason is that the other mechanisms of genetic, transformation have minimal or no effect on adaptation. Recombination which can cause moths to change from white to black is not creating new alleles. Only those variants with the correct alleles survive predation and those alleles become predominate in the population. It is biological descendant with modification and adaptation that causes the evolution of drug resistance when treating infectious diseases and cancers. Biological competition has minimal effect in this evolution of drug resistance because the carrying capacity of the environment is extremely large in this case. The human body can support a bacterial load in trillions or more. Very small cancer cell volumes can still reach a population size of a billion. These kinds of population sizes will give diverse populations and a high probability that resistant variants will exist in those populations. This must be considered when using targeted selection pressures to try and control or kill these populations. Unless a given targeted selection pressure can kill all variants in a population, that targeted selection pressure will ultimately fail. Multiple selection pressures will need to be used as shown by the use of combination therapy for the treatment of HIV. These same principles are demonstrated with vaccines in that multiple vaccines need to be used in an attempt to control influenza.

A correct understanding of Darwinian evolution gives the framework for understanding the problem of the evolution of drug resistance.

References

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