Introduction

Higher organisms have “phenotypic plasticity”, meaning that they adapt within a lifetime to demands of the particular environment that they experience. Can these acquired traits be passed to the individual’s offspring?

This is how the question of Lamarckism is classically posed. We now know the answer to this version of the question is “yes”. Still, Lamarckism is dismissed on grounds that become ever narrower. The last remaining domino is the question: In multi-celled organisms, can an individual’s response to the environment influence DNA sequence of its offspring in adaptive way? Few biologists realize that this question has never been tested, and that is what I propose to propose.

History

The nineteenth century history of evolutionary theory is often caricatured by distinguishing Darwinism from Lamarckism. In the caricature, Lamarck said that giraffes stretch their necks to reach higher branches, and this leads to longer necks in their offspring. In the caricature, Darwin says that mutations are the result of accident, purely random and blind to their consequence; so that selection must do all the work of separating a tiny set of adaptive mutations from a much larger set of detrimental mutations.

But in fact, Darwin was a Lamarckian. He believed that genetic variation is partly random, and partly guided by experience in the environment. He summarizes his theory on the last page of *Origin of Species*, listing among the ingredients, “Variability from the indirect and direct action of the conditions of life, and from use and disuse”. Darwin uses the phrase “use and disuse” referring to the idea that those capacities that an individual uses actively become stronger, not just for the individual itself, but in a heritable way. In a letter late in his life, he was most explicit:

> In my opinion, the greatest error which I have committed has been not allowing sufficient weight to the direct action of the environments, i.e. food, climate, etc., independently of natural selection. . . . When I wrote the “Origin,” and for some years afterwards, I could find little good evidence of the direct action of the environment; now there is a large body of evidence. (From a letter to Moritz Wagner, 1876)

Historically, there were three steps in the rejection of Lamarckism by the scientific community:

1. August Weismann conducted a test of his version of Lamarckism by cutting off the tails of 20 generations of rats, to see if the tails of the offspring would be shorter. He found no effect.
2. In the highly politicized science of the Soviet Union in the 1930s, Trofim Lysenko claimed to establish Lamarckian inheritance with a series of experiments that were poorly design and ideologically motivated.

3. Perhaps most important, after the discovery of the structure of DNA and subsequent elucidation of the genetic code, it seemed that there was no biochemical pathway by which present experience of the individual could be fed back into the germ line.

Evidence for Lamarckian inheritance

1. "Epigenetics" is the science of modifications to DNA transcription. At any given time, in any given cell, most of the DNA in the nucleus is inactive, while some of it is being actively transcribed. The choice about which genes to transcribed is influenced by chemical add-ons, methyl and acetyl groups that are attached to the DNA itself or to the histone spool around which the DNA is wound. This "language" of transcription is complex, and is currently the subject of intense study.

   The body actively manages transcription, both from moment to moment and from year to year. At least some of the transcription markers are copied when DNA is replicated during cell division.

   Just in the last decade, it has been firmly established that heritable epigenetic changes can be acquired in a way adaptive to life conditions, and transmitted to offspring for multiple generations. For example, the traumatic experience of Holocaust survivors is detectable in the epigenetic markers of their grandchildren. Mice that have been experienced weeks of low food availability adapt metabolically in a way that is passed to their offspring at least 6 generations in the future. [Ref]

2. Mutation rates vary across the genome in a way that promotes change in those parts of the genome most likely to create adaptive variation. Conversely, genes that code for core metabolic processes, unchanged over hundreds of millions of years, are well protected from mutation, and show mutational change that is orders of magnitude lower than the most variable segments of the genome. [Ref]

3. Stressful environments trigger higher mutation rates generally [Ref].

4. Bacteria actively and adaptively modify their own genomes. This phenomenon has been studied and documented by James Shapiro.

5. Transposons are snippets of DNA that can copy themselves and insert in different locations, even crossing chromosomes. Recently, it has been realized that some of these transposons have effect on transcription of nearby genes. Retrotransposns as Regulators of Gene Expression

6. Most generally and most speculatively, many theorists have noted that the efficiency and historic speed of evolutionary change are difficult to reconcile with the hypothesis that all genetic variation is purely random.

In summary, Lamarckian epigenetic inheritance is well-established. Lamarckian genetic inheritance is observed in bacteria (where there is no soma, and all chromosomes are germ line). Though the mechanisms are unknown, it is well-established that (in multi-celled organisms) life experience of the soma can be fed back to modify the germ line. It remains only to ask whether this happens in a way that modifies DNA sequence "permanently" and not just in ways that modify histones and methylation "temporarily".

Proposed experiment

Experiments can be done with large animals or plants; in this case the generation time is long and the lab population is small, so the challenge is to see an effect that may be small. Alternatively, experiments can be done with large populations of C elegans worms. In this case, the challenge is to clearly distinguish breeding from mutations.

1. There is a Mexican fish [Borowsky, 2023] that has a blind cave-dwelling variety and a sighted stream-dwelling variety. The experiment would be to cross a blind fish with a sighted fish, and hatch half the eggs in darkness and the other half in a fully-lighted tank. Collect offspring of the population raised in darkness and the population raised in light, and compare how many of them have eyes.

   It will then be necessary to analyze the two genomes to demonstrate that the difference is really genetic and not epigenetic.

2. Choose a salt-tolerant annual plant. And grow 100 different plants in graded conditions of salinity, such that plant #1 is watered with no salt at all, and plant #100 gets a lethal salt concentration. Grow a second generation, 1 seed from each of the 100 plants, self-pollinated, and expose them all to a high but sub-lethal salt concentration. Measure the productivity of these 100 plants, and see if their productivity correlates with the salt to which their parent was exposed.

   Use sequencing to check that the difference is genetic and not only epigenetic.

3. There are known single-gene mutations in *C elegans* worms that confer tolerance to, respectively, Zn and Cu. (A million worms can easily be grown in a test tube.)

   Grow generations of *C elegans* worms in high, sub-lethal concentrations of Zn. In parallel, grow generations of worms in higher, sublethal concentrations of Cu.

After each generation, siphon off half the worms from each population and expose half of each half to what would be lethal concentrations of Zn and to lethal concentrations of Cu. This is a way to assay for the mutations that confer resistance to the respective toxicities.

The Lamarckian prediction is that in the populations grown in Zn have a higher probability of mutating to Zn immunity and the worms grown in Cu will have a higher probability of mutating to Cu immunity.