

The Everest Hypothesis: mate selection for replicative fidelity

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Abstract

Mutations must occasionally arise in all genes, including the genes that encode the proteins that replicate genetic material – the nucleic acid polymerases and their associated proteins. Some of these mutations must reduce the fidelity of DNA replication (or RNA replication in RNA viruses), without actually being fatal. Lineages that replicate with reduced fidelity must therefore exist in all biological kingdoms, although we do not know how common they are. A fundamental problem at the heart of evolutionary biology is, therefore, to explain how high-fidelity replication originally evolved, and what selective pressures now maintain it. As part of a solution to this problem, I present a simple “Everest hypothesis”. This proposes that natural selection consistently adds unnecessary complexity to the mechanisms that transfer genetic material between individuals. Many sexual organisms choose their mates (I suggest) by monitoring a variety of complex behaviours, physical displays and biochemical mechanisms, often generated by the interaction of many gene products acting together or in sequence so that a defect in a single gene can result in failure to accomplish genetic transfer. Individuals with defective DNA polymerases are likely to have more mutations in these (and all other) genes, and, since most mutations are deleterious, the chance of transferring genes that encode error-prone polymerases is reduced. Many puzzling biological phenomena among sexual organisms can be explained along these lines. The migration and spawning of Atlantic salmon and the complex displays of birds of paradise may, for example, be best understood as “tests” to establish whether potential sexual partners are capable of high-fidelity genetic replication. (Other explanations of these phenomena in the scientific literature may be correct but less important.) Animals that have developed physical handicaps that appear to be harmful, such as peacocks, and animals that undertake remarkable migrations, such as arctic terns, may be special (extreme) cases. I also present suggestions for experiments to test the hypothesis.

Introduction

Imagine a woman who announces publicly that she will have sex with any man, but only on the summit of Mount Everest. Moreover, the potential partners must have solved a difficult sudoku puzzle that they pick up on the way up, and (so that she can choose quickly) they must write – *display* – their solutions in large numerals on a banner that they have to bring along. If it were practical this would be a reasonable mating strategy for both partners: both mother and father are likely to have better-than-average genes. In this paper I present the “Everest hypothesis”, which suggests that many plants and animals use similar strategies: they set up practical “obstacle courses” for potential mates, and may also demand complicated physical displays that can only be generated by the interaction of many genes. These strategies can signal to individuals that potential mates

have good-quality genes, and, in particular, that they are capable of high-fidelity genetic replication, before they agree to mate with them. The hypothesis is built upon four observations and a premise:

(1) mutations must occasionally arise in all genes, including the genes that encode the DNA polymerases that replicate the genetic material of all organisms, and these mutations normally increase the replicative error rate.

(2) When biological entities are subject to strong selection by being “thrust into environments that they are not well-adapted to”, a greater proportion of mutations are beneficial [Duffy, 2018], suggesting that lineages with high mutation rates may gain a short-term selective advantage over their high-fidelity competitors.

(3) However, lineages with high mutation rates are likely to produce offspring that are less fit in the long run, and they are prone to eventual error catastrophe.

(4) Recombination can restore fidelity.

Key premise: the more genes are involved in the mechanism of recombination – including genes that usually do something else – the lower the chance that defective DNA polymerase genes with mutator mutations will be transferred.

By “DNA polymerase genes” I mean all the proteins that make up the DNA polymerase complexes that replicate the genetic material, as well as all other proteins that contribute to replicative fidelity. I will refer to these here as polymerase-associated proteins, or PAPs.

Most advanced organisms, the hypothesis suggests, are therefore sexual, because sex allows mate selection, and, by seeking mates with characters (including displays, behaviours and physiological features) that can only be created by the interaction of many genes, organisms can identify potential mates that are likely to have high-fidelity PAPs.

Natural phenomena that can be explained by the Everest Hypothesis

The hypothesis can explain many natural phenomena that have puzzled evolutionary biologists. Some species use a combination of special displays and behaviour during mating. For example, many finely-tuned gene products must be required to create the colourful feathers of a cock bird of paradise, while other genes generate the complex behaviour to display them effectively. Still other genes allow a female bird of paradise to identify the “correct” feathers and display. Deleterious mutations in any of these genes are likely to prevent mating. Songbirds with a high rate of mutation are likely to be less able to produce diverse and elaborate bird song. Some animals undertake dangerous migrations to overwinter or breed in remote locations. You might expect natural selection to favour lineages that avoid both the risk involved and the expenditure of energy that is required for long journeys. However, migratory species persist. Atlantic salmon are able to migrate from fresh water to the ocean, and then return, with both sexes undertaking dangerous journeys, including adapting to changing salinity, leaping up waterfalls, avoiding predators, and swimming in shallow water, to return to the streams where they hatched in order to mate. Presumably lineages have appeared in the past that bred in less demanding freshwater or saltwater locations, but, I suggest, they didn’t thrive because they lacked this very effective strategy for eliminating individuals with more mutator mutations and slightly higher mutation rates. Arctic terns complete the longest migrations known in the animal kingdom, with birds that nest in Iceland and Greenland completing annual round-trip migrations that are over 70,000 km. With an estimated two million individuals, the species is successful. In many migratory species, “breakaway” populations that either do not migrate or migrate less far exist, but they do not generally outcompete the populations that

complete the longer migrations. For example, some populations of monarch butterflies do not migrate, while many North American populations east of the Rocky Mountains complete a dangerous multi-generational migration between overwintering sites (the largest being in Michoacán in Mexico, where around 150 million monarchs overwinter) and their northern breeding grounds, mainly near the Great Lakes. Note that this cycle requires four generations to complete, so many of the genetically-encoded behaviours and physiological changes involved cannot be conserved by selection en route. In other species, biochemical mechanisms are available to prevent the transfer of low-fidelity PAP genes. For example, the fertilization of flowering plants is highly complex, involving multi-layered signalling pathways, with many gene products that are expressed in both pollen and the female tissues (figure 1). The Everest hypothesis suggests that this complexity reduces the chance that low-fidelity strains will successfully reproduce.

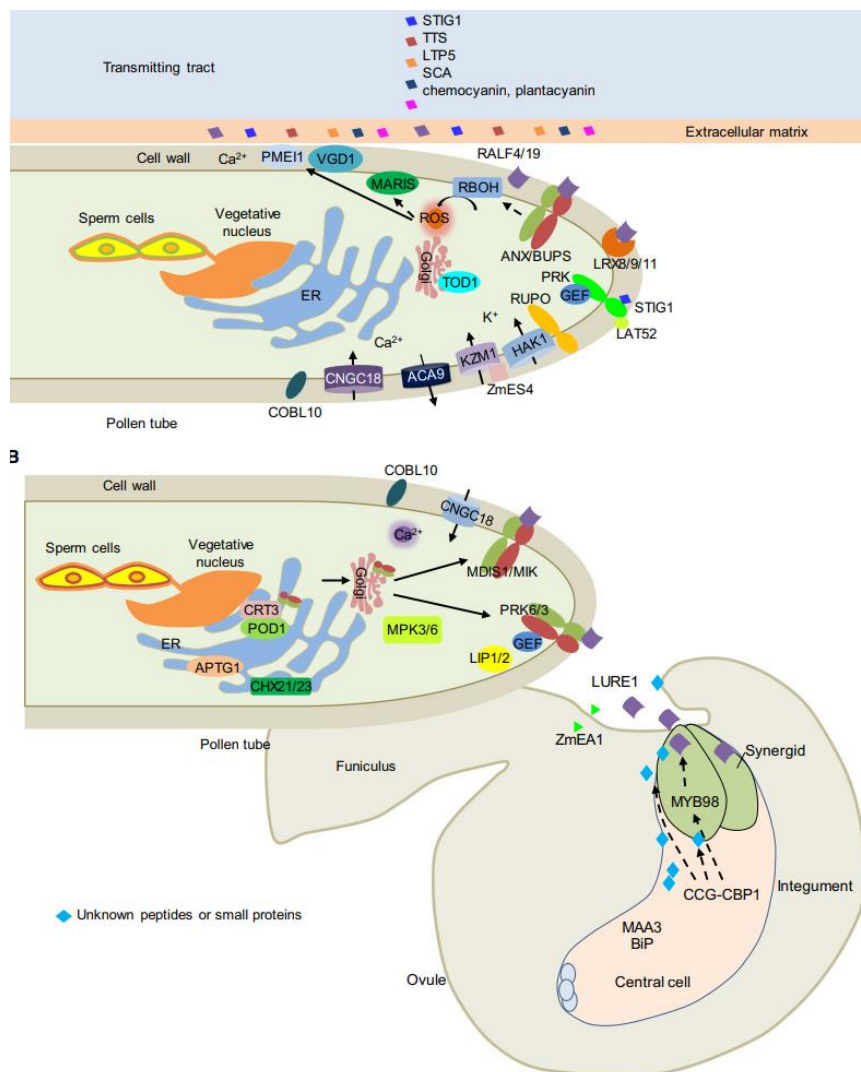


Figure 1. Fertilization in flowering plants. Pollen tube elongation in the maternal tissue and navigation to the ovule require intimate successive cell–cell interactions between the tube and female tissues [Li et al, 2018]. This procedure can create complex tests for pollen grains (which should be thought of as haploid organisms that are capable of producing sperm) using multi-layered signalling pathways that involve many gene products, which can weed out many error-prone lineages.

Zahavi's handicap principle

Other hypotheses have been put forward to explain some of these phenomena. In 1975 Amotz Zahavi suggested that characteristics, behaviours and structures in animals that confer handicaps may evolve by sexual selection because they “test the quality” of the animals that possess them [Zahavi, 1975]. Like the Everest hypothesis, Zahavi's handicap principle suggests that sought-after characters can advertise the quality of genes whose effects would otherwise be hidden. The hypotheses are, however, distinct. The Everest hypothesis proposes that these sought-after characters must be the product of many genes (which can show up mutations effectively), but they can be either beneficial (such as strong muscles and intelligent brains) or harmful (such as the massive tail of a peacock); by contrast, Zahavi suggests that characters selected in this way must “lower the fitness of the selected sex in relation to the main ecological problems of the species” and must squander a scarce resource [Zahavi, 1975]. According to the Everest hypothesis, peahens might select males by evaluating, in particular, the extraordinary symmetry of peacocks' tails (Figure 2). The handicap principle suggests that peahens would be attracted to peacocks with large tails regardless of symmetry, because large tails lower the fitness of males. The complex eyes on a peacock's tail are, therefore, not well-explained by the principle. Moreover, the handicap principle focuses on biological fitness, which is difficult for scientists to define or quantify. The Everest hypothesis focuses on mutation rates, which are well-defined and can be measured directly by scientists [Nachman *et al.*, 2000]. According to the handicap principle, species and populations with greater handicaps (such as peafowl) are expected to be at a selective disadvantage compared to comparable groups with more modest handicaps. According to the Everest hypothesis, species and populations with more extreme handicaps may be at a long-term selective advantage compared to other comparable groups, and may thrive, if the handicaps successfully reduce the transmission of error-prone PAP genes.



Figure 2. The extraordinary symmetry of a peacock's tail, with the positions and lengths of feathers being carefully controlled to produce regular spacing of the “eyes”. In 1975, Amotz Zahavi proposed the “handicap principle” to explain the evolution of features such as these tails [Zahavi, 1975]. The principle suggests that by squandering scarce resources by growing and maintaining such features, peacocks and other animals show potential mates that they are of “good quality” and are selected. However, the handicap would be almost identical without the elaborate markings and exact symmetry, suggesting that they have some other benefit. Moreover, the barbs outside the eye areas of the feathers are sparse, suggesting that selection favours reduced, rather than enhanced, weight - although enhanced weight

would increase the handicap. The Everest hypothesis notes that a well-formed tail shows that the peacock has an intact set of genes for constructing this feature, suggesting a low mutation rate. Similarly, a female that recognises a well-formed tail has an intact set of genes for tail-recognition.

Other mutations

Note that the mate-selection strategies discussed above can also expose other genetic defects that would otherwise be hidden. For example, complex behaviours, displays and biochemical mechanisms can show up mutations in “house-keeping” genes that are active in all cell-types such as ribosomal and cell-cycle proteins, histones, mitochondrial proteins, as well as factors for transcription, RNA splicing, translation and protein processing.

Suggestions for experimental and observational testing of the Everest hypothesis

Several scientific approaches could be used to test the Everest Hypothesis. Similar studies could be performed with any convenient sexual organisms, including yeasts, protists, insects, flowering plants, fish, mice, birds or mammals (possibly in captivity, for example in zoos.) I suggest experiments along the following lines: (1) sequence PAPs from wild organisms in large populations, which can be assumed to be high-fidelity. (2) Identify or create inbred populations and sequence their PAPs. Identify inbred lineages with mutant PAPs, which will often show increased mutation rates. (3) Set up new colonies, starting each colony with single pairs of organisms. Sequence PAPs and a selection of other genes to identify high-fidelity and low-fidelity colonies. (4) Quantify and compare the health of high and low-fidelity colonies. This can shed light on the expected prevalence and evolution of low-fidelity lineages in nature. (5) Now introduce high-fidelity individuals to low-fidelity colonies, and low-fidelity individuals to high-fidelity colonies; use sequencing to compare the rates at which the two classes of PAP genes invade their respective colonies. The Everest hypothesis predicts that high-fidelity PAP genes will replicate and spread faster. A second experimental approach would test whether the application of strong selective pressures encourages the emergence of low-fidelity lineages. For example, colonies could be sustained on unsuitable foods, or exposed to toxic compounds. Novel behaviours could also be selected, for example by eliminating drosophila and other insects that are attracted to electrical insect killers with UV lamps. Evolutionary theory suggests that low-fidelity lineages will be more prevalent after strong selection and rapid adaptation. A third approach is observational. Since the Everest Hypothesis suggests that long migrations are an effective way to eliminate mutator mutations, it predicts that migratory lineages will infiltrate non-migratory populations more often than the reverse. This prediction could be investigated in monarch butterflies by constructing phylogenetic trees based on monarch sequences.

Zahavi pointed out that the evolution of the sought-after characters can be explained by more than one hypothesis [Zahavi, 1975]. So, I am not saying here that the handicap principle (or any other theory of evolution) is wrong: in the example given in the Introduction, above, if a man arrived on the summit of Mount Everest with a bunch of flowers, he would be applying the handicap principle. It might work. I suggest, however, that the Everest hypothesis provides a simpler and more universal explanation of many surprising features that are apparent in the mate-selection and reproductive strategies of plants and animals, and, presumably, protists and fungi too.

References

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