Mutational Meltdown: Dawn of an extinction

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Abstract

Many a times when extinction of species is mentioned, it can be attributed to several different factors such as destruction of habitat, indiscriminate hunting, inability to cope with changing environmental conditions or even a highly skewed sex ratio. There is always a chance if none of these factors are pre dominantly responsible for loss of a species, a mutational meltdown has occurred leading to its untimely demise. A mutational meltdown can be described as an eco-evolutionary process in which, due to the accumulation of deleterious mutations in an isolated population results in reduced fitness of an organism eventually leading to the loss of a species. A sub class of the extinction blackhole, it occurs as a consequence of environmental and genetic components working alongside each other, indirectly working against the fitness of the organism. Mutational meltdowns have been reported to occur in both sexual and asexually reproducing populations. The present article aims to describe mutational meltdown and its consequences in detail.

Introduction

Over the past few millennia several species have either gone extinct or were on the brink of extinction. While many of these species recovered either in full or partially, they were unable to go back to their original population size without facing adversities. In addition to environmental factors like habitat loss, alternations in climatic conditions and human interference, there is also a loss of genetic diversity due to a higher level of inbreeding amongst the surviving population. It has been reported that in smaller populations, genetics plays a pivotal role in ensuring the fertility and viability of progeny for future generations to survive. By studying data over time and geographical locations we can understand the role of genetic factors in the process of extinction. However, majority of these studies focus only on the data surrounding few generations once the population has started to recover and not data from the original base population. This has led to difficulty differentiating between the initial genetic consequences of the rapid decline in population and long-term inbreeding depression as well as the possible accumulation of deleterious mutations.

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Woolly mammoth populations were plentiful 45,000 years ago, but went into genomic freefall as their numbers dwindled around 4,000 years ago.

Why does it happen?

Over time, due to repeated inbreeding within a population, recessive mutations started showing up with a higher frequency compared to, if the population was a large random mating population. The accumulation of these deleterious mutations is known as Muller's ratchet termed so, after Hermann Joseph Muller (Muller, 1964). The effects of deleterious mutations can be either mild or high and can result in behavioral and developmental defects. The cumulative buildup of such mutations resulted in reduced fitness in an organism and as a consequence, a decrease in the population size. The synergistic interaction between the reduced population size and the accumulation of deleterious mutations resulted in an extinction process termed 'mutational meltdown'. It can occur in populations that reproduce asexually as well as those that reproduce sexually.

In asexual populations mutational meltdowns can happen due to the absence of recombination, resulting in increased mutation rates. Such populations can suffer if the mutation rate is high or the population size is small or a combination of both. If back mutations are rare, then due to the absence of

recombination the progeny of an individual will have more deleterious mutations than the carrier parent itself. The possibility always exists that, by chance, the class of individuals with lowest fitness will not produce offspring in some generation. After this class of individuals has been lost, the second-best class is expected to ultimately suffer the same fate, and so on.

In sexual populations mitochondrial DNA inherited via the maternal parent has a high mutation rate and accounts for majority of the known inherited diseases. Although the frequency of these diseases is high, the mutations causing them are very less in comparison (Wallace et al., 2007). Recombination slows down mutational meltdown since it helps in the production of progeny with the best possible outcome for survival. Another contributing factor is the larger population size which reduces chances of inbreeding.

Examples of mutational meltdown

The best example of mutational meltdown studied in detail is the Woolly mammoth (Mammuthus primigenius). These mammals were distributed across Siberia, Beringia, and North America, during the Pleistocene and early Holocene period. When scientists sequenced the genomes of two specimens, they found that while one was from the mainland from 45,000 years ago, the second one was identified to be from an isolated population on Wrangel Island in the Artic Sea, 4500 years ago. Another isolated population was found to be present on St. Paul Island in the Bering Sea over 5000 years ago. While the animals on the mainland passed away due to hunting and habitat loss, rising sea levels and scarcity of water resulted in the loss of mammoths on St. Paul's Island. However, neither was the case for the mammoths from Wrangel island. It was reported that the mammoths from Wrangel island had more deleterious mutations in their genome when compared to their counterparts from the mainland. These mutations ranging in size from 10kb to 269kb were found to modify the coding regions which resulted in a modification in physiological functions. Rogers and Slatkin in 2017 reported that genes related to smell and urinary proteins, which in modern elephants are important for eliciting mating behaviours or signalling social status were shut down by deleterious mutations. They also reported the presence of a mutation in a gene, FOXQ1 which conferred the mammoths with a satin coat phenotype. In 2020, Fry *et al*., reported how the mutations identified by them in the woolly mammoth population were responsible for the loss of male fertility and the cause of neurological defects.

The treatment of RNA virus infections can incorporate the application of mutational meltdown. Compared to other viruses, RNA viruses have a higher mutation rate which makes them susceptible to mutational meltdowns. Mutagenic drugs like favipiravir have been designed to increase the mutation rate in viral infections, resulting in a mutational meltdown. However, it was reported that this same drug when used against influenza strains in the laboratory, due to a high mutation rate the strain developed a genetic resistance to it (Goldhill et al. 2018). It was also proposed that the same concept can be applied to the treatment of the COVID19 virus.

Conclusion

Several factors affect mutational meltdown in a species, the most important being the size and location of the deleterious mutation and the effective population size. Climatic and topographical factors play an additional role in contributing to extinction of a species. Studying of these mutations along with the cumulative effect of non-genetic factors can provide us with a better understanding of the evolutionary process as a whole.

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