Relationship between the selection pressure and rate of mutation accumulation.

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Abstract

Medawar claimed that the force of natural selection weakens with increasing age which strongly influences the structure of our genomes. A weaker selection pressure enables the accumulation of mutations in the individual's genome in the late expressed genes. Consequences of genetic defects which appear late in the lifetime may be completely unimportant from the evolution point of view since they affect a small number of individuals but they shorten the individuals' lifespan. This phenomenon is known as mutation accumulation theory of ageing.

The Penna model confirms this theory. It assumes chronological activation of genes during individual's life, which leads to accumulation of defective genes expressed late during the lifespan rendering the specific age structure of the population. Genes switched on before reproduction age are under strong selection pressure and fraction of defects in this set of genes is low. Genes switched on after the minimum reproduction age are under weaker selection pressure and increasing fractions of defects are observed in the part of the genome expressed later during the lifespan. We have studied the effect of prolonged release from selection of specific genes expressed earlier or later in life on accumulation of defects in such loci. It mimics the medical care or complementation of some defective metabolic functions, for example treating some metabolic diseases caused by the lack of one active enzyme like phenylketonuria or alkaptonuria. Genes expressed earlier, especially before reproduction age, are essential for individual's life and for its inclusive fitness. That is why the fraction of defective genes expressed during this period stays very low even if the environmental demand for their function is very rare. For the set of genes expressed during reproduction age, we observed that, the later selection pressure is decreased the faster the fraction of defective genes grows.

In nature, the number of individuals in the population depends on limited space and food availability. Due to these restrictions some individuals have to die, more or less randomly. In the Penna model, size of the population is regulated by a parameter which can operate only on newborns or on the whole populations. In the first strategy there are no random deaths during life – the Medawar's weakened selection on individuals due to their older age disappears. Nevertheless, the gradient of accumulated defects and specific age structure of population still persist.

We have also presented a model of evolution of the age structured population based on the Monte Carlo method where the health status of an individual is described by variance of its fluctuations. Each expressed deleterious mutation increases the fluctuations. Additionally, the fluctuations of the environment are superimposed on the fluctuations of individuals in the population. These environmental fluctuations play the role of selection which theoretically should cause an exponential decay of the population with the age. In the model the individual dies if the combination of both stochastic processes trespasses the limit (level of homeostasis) set as the model parameter. The genes are switched on chronologically, like in the Penna model, what leads to accumulation of defective genes expressed during the late periods of life in the genetic pool of the population. That results in the specific age structured population, in accordance with the predictions of Medawar's hypothesis of ageing and the results of the standard Penna model simulations. A decrease of the variation of the environmental noise,

corresponding to the decrease in the selection pressure, increases the average expected lifespan of individuals.