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HIGHER MORTALITY OF THE YOUNGEST ORGANISMS PREDICTED BY THE PENNA AGING MODEL

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We have simulated the evolution of population using the Penna model of aging. In populations of diploid organisms, without recombination between haplotypes or with low cross-over rate, a specific distribution of defective genes has been established. As an effect, relatively higher mortality is observed during the earliest stages of life. When two independently evolving populations were mixed and co-evolved in one environment without crossbreeding, one population won after several generations and this winning population showed stronger "early" death effect. We conclude that in the environmentally limited size of a population (in the model limit set by Verhulst factor) it is a better strategy to sacrifice younger individuals — higher fractions of such populations reach the reproduction age.

Keywords: Biological aging; Monte Carlo simulation; recombination; genetic linkage.

1. Introduction

It seems trivial, from the biological point of view, that genes expressed after the organism reaches its reproduction age, are under weaker selection pressure than genes which are indispensable for development, being necessary to reach the reproduction age. This problem has been discussed several times.[1,2] The Penna model has been used several times to show the differences in the strength of selection pressure exerted on genes expressed at different periods during the life span (see Ref. 3 for review). In this model, genes are switched on chronologically, but one can easily observe that the fraction of defective genes switched on before the minimum reproduction age is low and stable, while the fraction of defective genes switched on after the minimum reproduction age is growing with age and eventually reaches 1.

Simulations of population evolution with the Penna model can predict that populations are much more stable and resistant to deleterious mutations if recombination is allowed (cross-over between two haplotypes during gamete production).[4]

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It is necessary to admit that genetic linkage in the model is not natural. The genetic linkage is defined as a measure of probability that two markers (genes) are separated by cross-over during meiosis — genes which are not linked assort independently, even if they stay at the same chromosome. The linked genes in the Penna model are expressed one after another during the development. Thus, there is a full co-linearity between the genetic "map" (or linkage map) and the time order of gene expression. This is not necessarily true for the natural genomes.

In the biological populations, mortality of the youngest is high. It has been found, using the Penna model, that populations which sacrifice the youngest individuals, when forced to adapt to the finite size of the environment win against populations which sacrifice randomly individuals of any age.[6] This strategy of adaptation to the environment capacity ameliorates the genetic pool of populations, too. The higher mortality rate of children has been obtained in simulation by the Penna model with some additional assumptions. Berntsen[5] has assumed the lower threshold T for babies. A. Strotman (cited in Ref. 3) has assumed that during childhood more genes are switched in one time step, which seems to be a very reasonable assumption. Nevertheless, the life span of the human being should be counted from the very conception and it is well documented that the mortality of the human embryos is of the order of 0.6,[7,8] which means that about 60% of zygotes are never born. This huge zygotic death could be predicted if we assume that a large fraction of genes is expressed during the development before the organisms reach the minimum reproduction age.[9] In this paper we will show that the higher mortality rate of the youngest individuals could also evolve as an inherent property of the population if the lower recombination frequency allows generating a specific genetic linkage.

2. Model

For the standard Penna model see its detailed description in Refs. 3, 10 and 11. In our simulations the individual is represented by its diploid genome, consisting of two strings of 64 loci each, switched on chronologically. If a gene in the locus has value 0 — it means that the allele is correct, if the value is 1 — the allele is defective. In this version of the model all defective alleles are recessive, which means that both alleles at a given locus have to be defective to determine a deleterious phenotype. An organism can reproduce if it reaches the minimum reproduction age R. To reproduce, the organisms form haploid gametes. During the gamete production, the two strings of the diploid parental genome exchange homologous fragments at randomly chosen position with probability C. One of the two new strings is randomly chosen and a mutation is introduced into a randomly chosen locus with a probability M. If a defective allele is chosen for mutation — it stays defective, its value stays 1. Each female at the reproduction age produces a gamete, which is joined with a gamete produced by a randomly chosen male organism, also at reproduction age. A newborn organism has no switched-on genes. In the first year (time step) both alleles in the first locus of a newborn are switched on. If at least one

is correct, the determined phenotype is also correct. If both alleles are mutated the defect is expressed. At the second year, the alleles in the second locus are switched on and so on. If the number of expressed defects reaches a declared value T — the organism dies. The organism dies also when it reaches the maximum age (the alleles of the last locus are switched on). It never happens in simulations with our values of parameters — all last genes in the strings are set for one and all organisms die before they reach this maximum allowed age. That is why we have used the last bit of the string to mark the haplotype (a or b) while simulating a competition between two populations a and b evolving in one environment. To avoid unlimited growth of the population, the Verhulst factor V is introduced: $V = 1 - N_t/N_{\max}$ where $N_{\max}$ — the maximum population size — is often called the capacity of the environment, and N_t is the current population size. For each zygote a random number between 0 and 1 is generated and if it is greater than V, the zygote dies. Note that in our simulations the Verhulst factor operates only at conception, which implies that after conception there are no random deaths in the population. This influences the structure of the genetic pool and the age structure of the population when comparing with simulations where the Verhulst factor operates randomly at all ages.[6]

In fact, the Penna model has only a few parameters important for the final genetic state of population (parameters' values in our simulations are given in parentheses):

- M — mutation rate, the number of new mutations introduced into the haploid genome during the gamete production — ($M = 1$ per haploid genome per generation);
- B — birth rate, the number of offspring produced by each female at reproduction age at each time step — ($B = 1$);
- R — minimum reproduction age — ($R = 20$);
- T — the upper limit of expressed defects, at which an individual dies — ($T = 3$);
- C — the probability of cross-over between parental haplotypes during gamete production or the number of cross-over if $C \geq 1$. We have performed simulations with $C \leq 1$.

3. Results

In the first experiments we performed simulations with diploid populations without cross-overs during gamete production, which means that offspring was produced by joining two complete, not recombined haplotypes (bitstrings) derived from female and male organisms, each in reproduction age. Each haploid genome (haplotype) was represented by 63 bits (genes). The last one (64th) bit in the string was used to mark the haplotype — a or b. We have produced 100 populations, each of them evolved independently during 100 000 time steps in the environment of $N_{\max} = 10\,000$. Then we have used pairs of such independently obtained populations for simulations of co-evolution. Two populations after 100 000 MCS of inde-

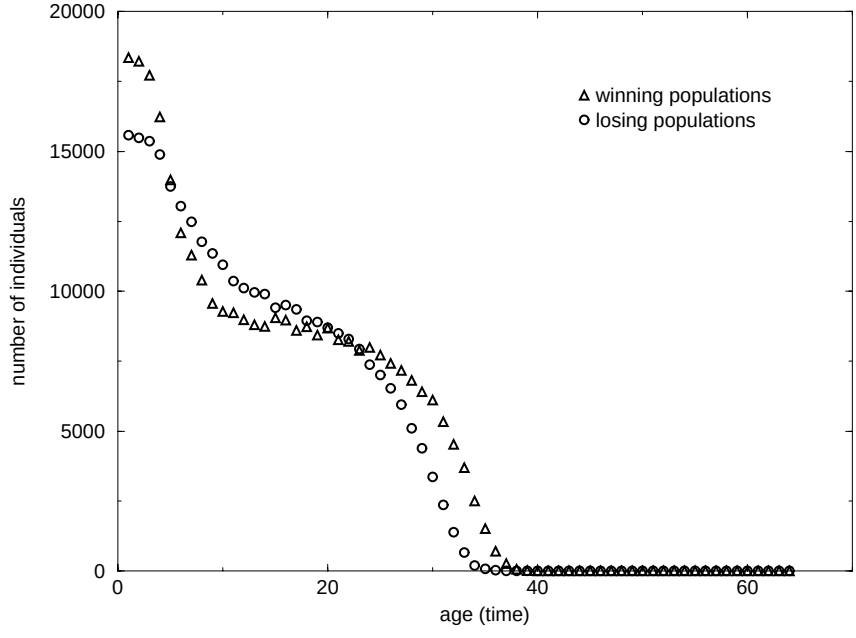

Fig. 1. Age distributions of two groups of populations. One hundred populations were simulated for 100 000 MCS without cross-over with $N_{\max} = 10\,000$. Then pairs of such populations evolved without cross-breeding in one environment with $N_{\max} = 20\,000$ unit one population was extinct. Plots represents the data averaged separately for pools of 50 winning and 50 losing populations.

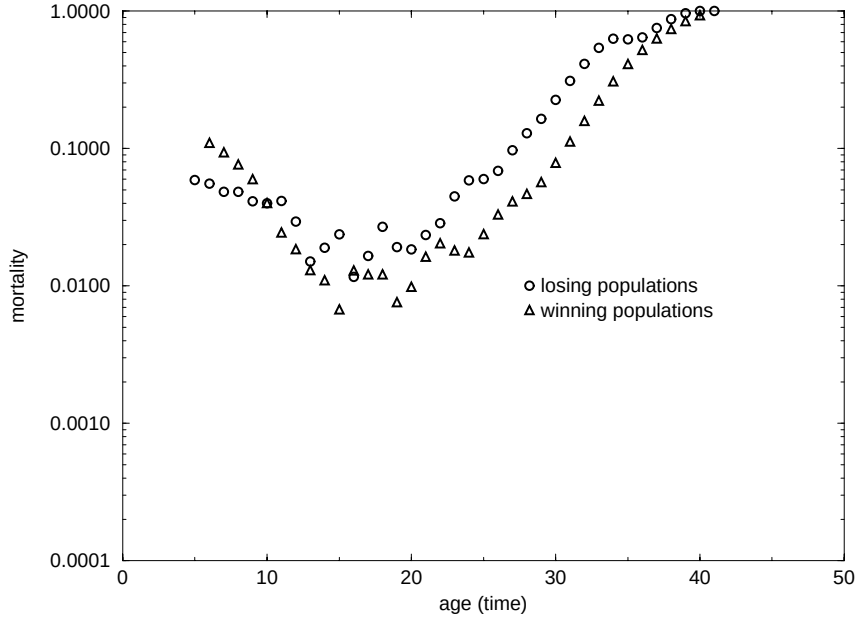

Fig. 2. Averaged mortality in sets of populations described in Fig. 1.

pendent evolution were put into one environment of doubled size ($N_{\max} = 20\,000$) and allowed to co-evolve until one of them was extinct. Then we look at 50 winning populations and 50 losing populations. In Fig. 1 we have shown the average age distributions of both groups of populations and in Fig. 2 the mortalities for these populations. A characteristic of the winning populations was relatively higher mortality during the first stages of life, in agreement with reality and in disagreement with the traditional $C = 1$ Penna model results. On average, the total sizes of the winning populations were higher than sizes of losing populations. Furthermore, the fractions of individuals in the fertility period was higher for the winning population.

One can argue that the effect is not natural, because there was no recombination between haplotypes. That is why we performed the further simulations with parameter $C = 0.001$. In Fig. 3 we have shown the age distribution of the populations simulated under these conditions. The effect of higher mortality of the younger individuals was still observed for this frequency of recombination and again populations with stronger effect of "early death" won when they co-evolved and competed in one environment. This effect disappeared when each haploid genome of a gamete was a product of one cross-over between two parental haplotypes ($C = 1$). In Fig. 4 we compared the mortality in populations simulated with $C = 1$ and averaged mortality of 50 winning populations with $C = 0.001$. Populations with low cross-over frequencies show the minimum mortality at the age just before reaching the reproduction age, which is also observed in the natural human populations.

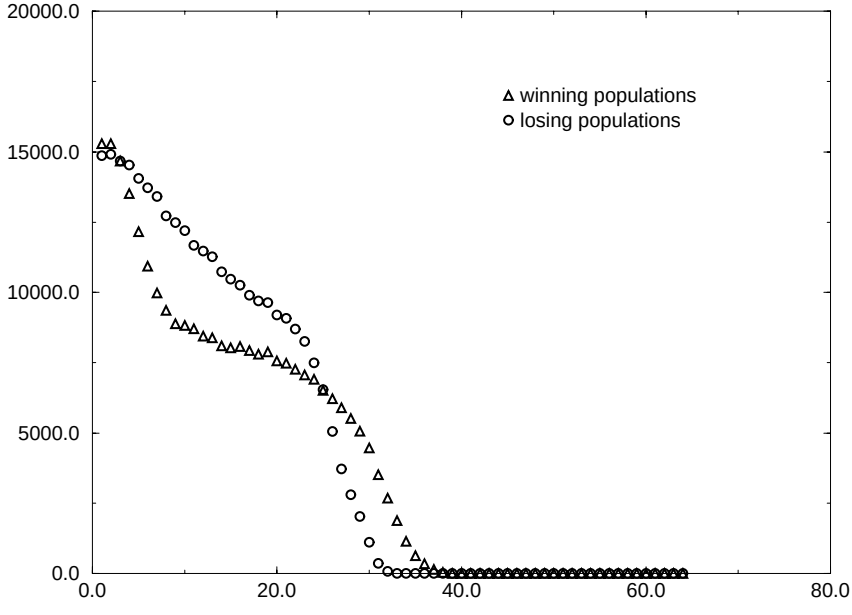

Fig. 3. Age distributions for two groups of populations obtained as described in Fig. 1, but with cross-over frequency $C = 0.001$ per gamete formation.

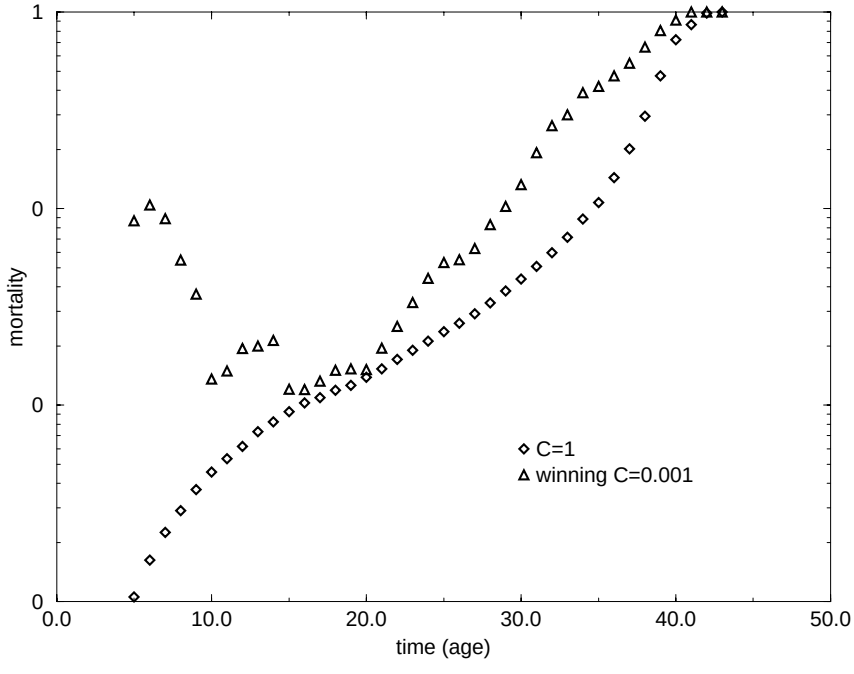

Fig. 4. Mortality for the group of winning populations, with cross-over rate $C = 0.001$ and for populations with $C = 1$.

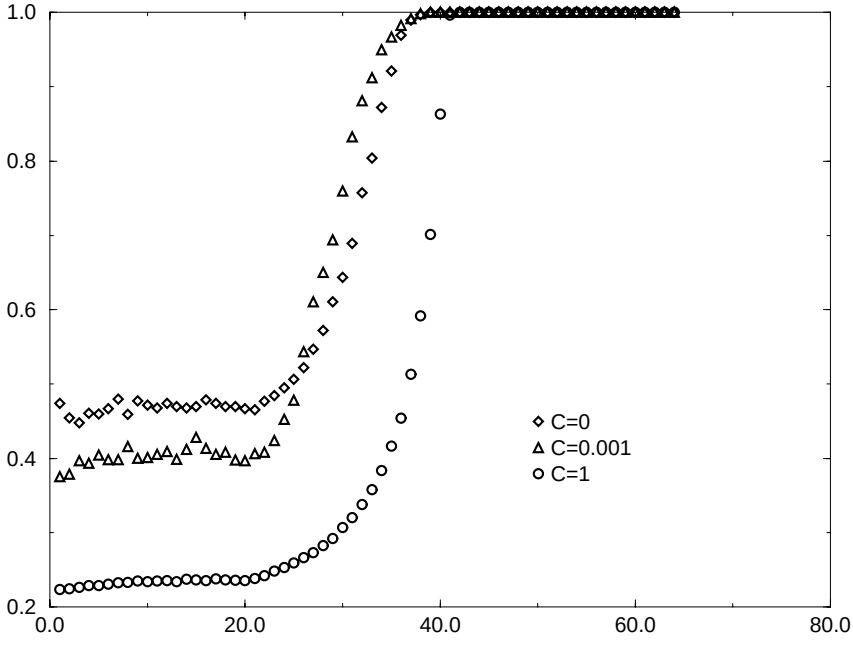

Fig. 5. Distribution of the defective genes in the genomes of three groups of populations evolving at different values of C parameter.

The effect of higher mortality of the youngest individuals is the result of defective genes distribution in genomes. In Fig. 5 the defective gene distribution of three different types of populations (evolving at different values of the C parameter) are shown. On average, the frequency of defective genes expressed before the reproduction age is higher for populations with lower cross-over frequencies. For each population evolving with high cross-over rate, the defective genes are distributed evenly between all loci switched on before the reproduction period, even if the number of these loci is much higher than 20 (i.e. 500 as simulated by Niewczas.[9]) In contrast, the distribution of defective genes in individual genomes and in the whole genetic pool of populations evolving with low recombination rate is very uneven.

4. Conclusions

Genetic linkage between genes expressed chronologically could be an important feature of evolving genomes. Linkages between genes could be responsible for reproduction strategies of populations helping them to fit to the finite size of the environment. Thus, it is not only the risk of recombination associated mutations which could restrict the recombination rate between haplotypes.

Acknowledgments

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