#### Scaling effects in the Penna ageing model

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Abstract: We have analysed the possibility of scaling the sexual Penna ageing model. Assuming that the number of genes expressed before the reproduction age grows linearly with the genome size and that the mutation rate per genome and generation is constant, we have found that the fraction of defective genes expressed before the minimum reproduction age drops with the genome size, while the number of defective genes eliminated by the genetic death grows with genome size. Thus, the evolutionary costs decrease with enlarging the genome. After rescaling the time scale according to the mutational clock, age distributions of populations do not depend on the genome size. Nevertheless, enlarging the genome increases the reproduction potential of populations.

Keywords: Biological Ageing, Monte Carlo Simulation, Penna model, scaling.

## 1 Introduction

The Penna ageing model [1] is the most often used Monte Carlo model for simulating the dynamics of age-structured populations. Properly rescaled and interpreted simulation results mimic very well the age distribution of real populations, including the human one [2]. Changing only one parameter describing the relations between the genotype (phenotype) and the environment, it is possible to simulate the changes of the age distribution of human populations during the last centuries and predict the human life expectancy in the future [3], [4]. One of the most important problems concerning this model is the question how the genome size in the model influences the results of simulations. Thus far, the genome size implemented in the sexual model as two bit-strings, with relatively low number of bits (genes) (from 8 up to around 1000 bits), does not correspond to the real sizes of natural genomes, which in the case of higher eukaryotes are of the order of dozens of thousands of genes. Our question was if it is possible to generate in simulations populations with similar age distributions independently of the genome size. This problem was already addressed by [5] without conclusive results and recently by [6] whose results suggested roughly the scaling properties of the model. In our analyses we have tried to show how the parameters describing the simulated populations change depending on the length of the genomes.

#### 2 Model

In the Penna sexual model each individual is represented by its genome composed of two bitstrings — each L bits long. Bits (genes) are switched on in pairs, consecutively, one pair during each Monte Carlo step. If a bit is set for 0 it means that it is functional, if it is set for 1, it is defective. Defective genes are recessive — both bits (alleles) in the same locus have to be defective to determine the defective phenotype. After a defined number of steps, and switching on the corresponding pairs of bits, the individual reaches the minimum reproduction age R. An individual of reproductive age produces gametes by crossing over its parental bit-strings at a randomly chosen point with a declared probability C. One mutation is added to the recombined strings in one randomly chosen locus. If the bit chosen for mutation is already set to 1 it stays 1, so there are no reversions. A gamete produced by a female is joined by another one produced by a male and offspring is born. Each female produces an offspring with a declared probability during each MC step. The sex of the newborn is randomly chosen with an equal probability for male and female. If, after switching on bits in consecutive loci, the declared number T of defective phenotypes is reached — the individual dies because of its genetic status. 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. Thus, there could be three different causes of death: — genetic death caused by reaching the threshold T of the number of expressed deleterious genes; — random death because of overcrowded environment; — death at maximum age which corresponds to the total number of bits in the bit-string. In practice, organisms do not reach the maximum allowable age determined by the length of the bit-strings. Since random deaths caused by the Verhulst factor could happen only at birth, the only deaths observed in the evolving populations are genetic deaths caused by surpassing the declared threshold T. Summing up, there are only a few parameters crucial for the final state of the population simulated by the Penna model: T - the upper limit of expressed phenotypic defects, at which an individual dies; R - minimum reproduction age; B - birth rate, the number of offspring produced by each female at reproduction age at each time step; M - mutation rate, the number of new mutations introduced into the haploid genome during gamete production; C - the probability of cross-over between parental haplotypes during gamete production or the number of cross-overs.

## 3 Scaling experiments

We have performed three different sets of simulations (parameters shown in Table 1). Note that the cross-over frequency per bit was constant for all simulations and no dominant loci were declared.

a) M per bit and R constant.

In the first series, the minimum reproduction age (8) and M = 1 per bit was constant. Under such parameters, in equilibrium, in the population with the shortest genome (L = 32), all bits beyond the 15th turned out to be set to 1. It means that the rest of the genome is dispensable. Since in the simulations with larger genomes the parameters in the first part (call it the monomer genome) are the same, the results of simulations are also the same. All genes (and further monomers) expressed after the first 15 loci are dispensable and set for 1. In fact only the first "monomer genome" is responsible for the age structure of populations. The results are trivial. This is not a scaling. b) M per bit constant, R proportional to the genome size.

In the second series, where the mutational pressure per bit was constant and the minimum reproduction age was proportional to the genome size, the mutational pressure exerted on the genes expressed before reproduction grew and as a result the populations with longer genomes died out. The conclusion seems to be obvious - species with larger genomes require higher fidelity of replication.

c) M per genome constant, R proportional to genome size.

In the third series of simulations the mutation rate per genome and generation was constant. The constant mutational pressure per genome seems to be biologically legitimate. Besides the conclusions from the second series of simulations, many experiments on living systems [7] as well as theoretical considerations [8] indicate that the mutational pressure is of the order of one mutation per genome replication independently of the size of the genome. Thus, the time of the simulations may be measured in MC steps (each step corresponding to a single bit) or by the "mutational clock" ticking slower for longer genomes. In this series, the minimum reproduction age was proportional to L. The most critical was the birthrate which was set for 1 per MC step. Under such a parameter the reproduction potential was regulated only by Verhulst factor which controls the population size by killing the newborns, and the value of Verhulst factor could be considered a real birthrate regulation [9]. In fact, instead of the birthrate parameter, we have the reproduction potential of the population which is an output of the model rather than its parameter.

The results of this third series of simulations should be discussed separately for the part of the genome expressed before the minimum reproduction age (lets call them the housekeeping genes), and the part expressed after the minimum reproduction age, i.e. during the ageing period (death genes) [10]. One of the measures of the genetic status of genomes or populations is the genetic load, the fraction or frequency of defective genes in the genome. From the point of view of the evolutionary costs, the winning strategy is the strategy which eliminates more defects by one genetic death. Simulations show that under the constant mutational pressure per genome, the proportional increase of the number of housekeeping genes (Figs. 1a and 1b), while the number of defective genes eliminated by a single genetic death grows with the genome length (Table 2). We would like to stress that the results of simulations with haploid genomes or with diploid genomes but with declared dominance of defective genes would be different. In such simulations, the number of defective genes among the housekeeping genes is rather constant and set by the threshold T parameter.

One of the important features of populations with larger genomes is their higher reproduction potential. As a result, the populations' size grows and the limitations set by the Verhulst factor are stronger. One can expect further amelioration of the genetic pool of populations with larger genomes if the random death introduced by Verhulst factor is replaced by selection mechanisms. The results of simulations, shown as a fraction of populations at a given age are shown in Fig. 2. The age axis co-ordinates correspond to the length of the genomes and the consecutive genes switched on. Since the numbers of genes in the genomes and the minimum reproduction age increases, the life span of organisms is increasing on this bit scale, too. The plots in Fig. 3 show the age distribution of the populations shown in Fig. 2 after normalization of the y-axis scale. Note, that the time scale in the plots is still in MC steps. Fig. 4 shows the results of normalization when the mutational clock is the base of the time scale, which means that the x-axis is reduced to the scale corresponding to the frequency of mutations. In this figure, the plots representing the age structure of all simulations give similar results. One can conclude that the Penna model has scaling properties when simulations are performed under specifically related simulation parameters. These results are in better agreement with scaling than those obtained by [6]. Nevertheless, it is important to note that populations with different sizes of the genomes and very similar age distributions are characterised by very different other parameters describing their genetic status as well as reproduction potential. The values of the parameters describing the populations are shown in Table 2.

# 4 Conclusions

It is possible to generate similar age distributions of populations with different sizes of genomes of their individuals. Thus the properties of the model have become independent of the choice of the Monte Carlo time step. The main feature of populations with larger genomes is the higher fidelity of their genome replication: it has to be constant per genome rather than per length unit. Populations with larger genomes are characterised by higher reproduction potential which results in better filling the available environment. The fractions of defective genes among the genes indispensable for reaching the reproduction age in larger genomes are lower but the number of genes eliminated from the genetic pool by one genetic death is higher. The last property is true only for diploid organisms and the fraction of loci where the defects are recessive. Haploid, asexually reproducing organisms have to keep the same number of defects in this part of the genome.

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L	R	M	B	C	T
32	8	1	1	0.015	3
64	8	2	1	0.03	3
128	8	4	1	0.06	3
256	8	8	1	0.12	3
512	8	16	1	0.24	3
32	8	1	1	0.015	3
64	16	2	1	0.03	3
128	32	4	1	0.06	3
256	64	8	1	0.12	3
512	128	16	1	0.24	3
32	8	1	1	0.015	3
64	16	1	1	0.03	3
128	32	1	1	0.06	3
256	64	1	1	0.12	3
512	128	1	1	0.24	3

Table 1: Parameters for three series of simulations, where M = mutation rate per genome.

L	R	maxgen	defects	V	Pop	Eliminated
32	8	15	0.387	0.443	5568	6.2
64	16	25	0.283	0.304	6963	9.0
128	32	48	0.198	0.188	8124	12.7
256	64	94	0.139	0.095	9050	17.8
512	128	202	0.093	0.040	9603	23.9

Table 2: Characteristics of the populations for third series. L and R - parameters of simulations; maxgen - the first locus, where all bits in the genetic pool are set for 1; defects - average fraction of defective genes in the section of housekeeping genes; V - fraction of surviving newborns (since the birthrate in all simulations was set to B = 1 per MC step, in fact, Verhulst factor controlled the reproduction rate); Pop - size of populations in equilibrium,  $N_{max} = 10000$ ; Eliminated average number of defects in the housekeeping genes of one genome.



Figure 1: Part a: Distribution of defective genes in the genomes of different length. Simulation parameters as shown in Table 1 for third series. X-axis co-ordinates correspond to the number of bits in the bitstring. Part b: Fraction of defective genes in the sections of housekeeping genes in genomes of different length (right scale, empty circles); average number of defective house keeping genes in diploid genomes, genes eliminated by one "genetic death" (left axis, filled squares).



Figure 2: Age distribution of populations with different length of genomes; y-axis shows fractions of populations at a given age.



Figure 3: Normalized age distribution of populations. Age scale still in MC steps or numbers of bits in the bitstrings.



Figure 4: The same as in Fig. 3 but the age axis is rescaled according to the mutational pressure (see text for detailed explanation).