PENNA MODEL OF BIOLOGICAL AGING ON A LATTICE*

Danuta Makowiec

Institute of Theoretical Physics and Astrophysics, Gdańsk University
Wita Stwosza 57, 80-952 Gdańsk, Poland
e-mail: fizdm@univ.gda.pl

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We implement the Penna bit-string model of biological aging on a square lattice to study the evolution of the spatial distributions of the population when some rules for the coexistence for nearest lattice neighbors are introduced. By doing like this, we want to avoid the usage of the, so-called, Verhulst factor, which role has been disscused lately. The basic characteristics: population size, survival rates and mutation distribution, obtained in the lattice asexual Penna model occur different from the corresponding ones which are recorded in the standard Penna model.

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1. Introduction

Recently, many problems have been studied in the interface between statistical physics and biology. Computer simulations have helped us to understand several biological processes and, in particular, population dynamics studies have had significant advances due to the development of this tool. As an important example, theories about the evolution of biological aging have been tested by means of computer simulations.

There exist over 300 theories to explain why the earth creatures, especially human beings, aging when their life time passes and then they die not because of the lack of food or an enviroment disaster but because of senescence. The evolutionary approach to the aging problem predicts that Darwinian selection becomes weaker when the reproduction starts. This implies that the genetic harmful mutations which would lead to genetic diseases but which affect at older ages, will spread in the population, thus causing senescence and eventually death. This is known as *the mutation-accumulation*

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hypothesis, see [1]. The biological motivation for this hypothesis is that the Alzheimer disease activates at old ages only, although the desease is present in the genetic code since birth.

Evolutionary hypotheses are rather difficult to test. There are few reliable experiments done by biologists supporting the hypothesis of mutation-accumulation theory, see [2]. Therefore, solutions derived from mathematical and/or computational models are an interesting way to deal with them.

The Penna aging model is by now the most widespread one for Monte Carlo simulations, see [3,4]. The Penna model deals with the accumulation of deleterious mutations in the inherited genome. The distinguish success of this model arrives from the fact that it is the only Monte Carlo model giving approximately the exponential increase of mortality of adults that agrees with the biological observations.

1.1. Some facts about biological aging

The process of aging can be measured by the so-called mortality, *i.e.*, by the probability that an individual of a given species will die in a next time period. It occurs that the mortality depends on the life period of a individual. The still good proposal for the dependence of the mortality for humans on the age comes from the XIX century proposition, made by Gompertz. This fact is known as the *Gompertz law*. It states that the probability to die within the next time interval grows exponentially:

$$\text{mortality (age)} \propto \mathrm{e}^{b\ \text{age}}, \tag{1}$$

where b is of the order of $0.09(1/\text{year})$. Of course, the Gompertz law becomes wrong for individuals in their old age because the probability to die becomes larger than unity.

The newest investigations, based on the populations of Japan, Sweden and Germany during the past 200 years, done by Azbel, modificate the Gompertz law to the following one, the so-called *Azbel law*, see [5],

$$\frac{\text{mortality (age)}}{b} \propto \mathrm{e}^{b\ (\text{age}-\boldsymbol{X})}. \tag{2}$$

Here the characteristic age $\boldsymbol{X}$ is the same for the whole species and specifies the maximum age reachable by any individual of the considered species. The Azbel observed that in the case of humans the maximum age is $X = 103 \pm 1$ year. However, humans were reliable reported to live until the age 122 years [6]. This contradiction to the Azbel prediction is explained that the Azbel law (2) applicates for the homogeneous population and describes people at their average. Whithin one population there are rare families with small b (or even with $b \to 0$) and for such little b the statistics other than exponential

have to be considerd, see [4,7]. Therefore, there are individuals that can live longer, see [4] for the further disccusion.

It can be frustrating that each of us has to die at its genetically determinded age. The progress in human living conditions can influence the slope b of the Gompertz law but it cannot change $\boldsymbol{X}$, see [5, 8] for quantitative analysis.

1.2. The Penna model

In the asexual Penna bit-string model each individual is characterized by a string of 32 bits, called *genome*. Each bit of a genome represents one subsequent period of life, called *year*. If at age i the ith bit in the genome is set to one, the individual suffers the effect of a deleterious mutation, called *disease*, from this age until death. If the ith bit is set to zero no new disease occurs. When the total number of accumulated diseases reaches a value greater than or equal to a limit T, the individual dies. The individual can also die because of the lack of food and space. This is taken into account through the so-called *Verhulst factor*:

$$V = 1 - \frac{N(t)}{N_{\max}}, \tag{3}$$

where $N(t)$ is the current poplulation size and $N_{\max}$ is the maximum carrying capacity of the environment, defined at the beginning of the simulation. The Verhulst factor determines for each individual, independently of the individual both genome and age, the probability to survive. After reaching the minimum reproduction age R, each year an individual generates b offspring. The baby's genome differs from the parent's one by m bits, randomly selected. Only deleterious mutations are allowed. If a selected bit is equal to one, it remains set to one in the offspring's genome. Otherwise, if the selected bit is equal to zero, the offspring carries an additional deleterious mutation when compared to its parent.

The results of the simulations of this basic Penna model and its sexual version can be found in [4] and in references given there.

1.3. Why Penna model on a lattice?

The assumptions of the Penna model have been critically revised by the brave Polish geneticist, Cebrat, who not only did take a challange to understand the physicists idea of aging , but also actively joined the physicist community to work on this model, see [9]. One of the assumptions of the Penna model, negatively evaluated by Cebrat, is the relation between the developing population and the external environment. This relation is realised by the described above Verhulst factor. After the time when the

self-organization process inside a population performs itself to develope the population that is best fitted to the model parameters, the evolution becomes stationary, see [10]. The Verhust factor overdominates the evolution. The evolution becomes as it is governed by the logistic equation, see [10,11].

By introducing the lattice structure to the Penna model we obtain the other from the logistic equation type condition for modelling the restrictive enviroment capacity. Moreover, in a similar way as in the famous Conway's "Game of Life" we are free to consider any additional rules for life and death; rules conditioned by the nearest neighbors interactions.

2. Model description

The population is the collection of individuals living on a square lattice. Each lattice site is occupied by at least one individual. Each individual is characterized by:
Bit-string: the life history inherited from a parent and additionally mutated at the birth with the ratio m. The genome consists of 32 bits which denote the same as in the standard Penna model described in the previous section.
Age: if an individual survives during one iteration then it will get older by one time unit. Similarly to the standard Penna model we assume that if an individual is mature enough (its age is greater than or equal to R) then it will give b offspring. An individual dies because of suffering from too many diseases. T denotes the threshold of the allowed diseases.

The extra killing factor arrises from the overcrowding of a space and only acts on newborn kids. A parent chooses randomly among its four nearest neighboring sites a place to put a newborn kid. If the chosen site is occupied then the newborn kid dies. If at the same time two parents choose the same place then at the equal to each other probability only one of these parents wins.

Thus individuals older than the newborn ones die only because of too many diseases carried in their genotypes.

By implementing the evolution of the Penna system on a lattice we can consider distinct boundary conditions. In the following we examine two types of boundary conditions:

(a) free boundary: to imitate close systems like lakes or islands,

(b) periodic boundary: to mimic unrestricted life space what can be represent by oceans or large forests.

Our model can be compared to the model described by Sousa *et al.*, see [12]. However, the problem of Verhulst factor influence is not considered there. In [12] it is assumed that each node of the lattice has its own

maximum capacity, *i.e.*, its own Verhulst factor. So that in the evolution there is present a constant killing term coming from these Verhulst factors and therefore the results obtained by the authors do not provide any new effects.

The model considered by us can be seen as imitation of the biological population of plants which can give offspring only in the free nearby area. Our rules for nearest neighbors interactions are similar to the rules considered by Wallinga in the model of annual weeds, see [13]. However our "weeds", thanks to the age progress in Penna dynamics, live longer than a year.

3. Results

The Penna lattice system is considered on a square lattice with the linear size $L = 680$. This size establishes the maximal environment capacity to 462 400 individuals. The initial population consists of 100 individuals with random genomes and with the common age of 1. Individuals are scattered randomly on the lattice. The stationary population is reached in less than 5000 iterations. All statistics is made over 10 000 iterations of a stationary population and over at least three independent experiments.

3.1. Free versus periodic boundary conditions

We perform simulations for both free and periodic boundary condistions to consider dependence of the results on the boundary type. In Figs 1,2,3 we

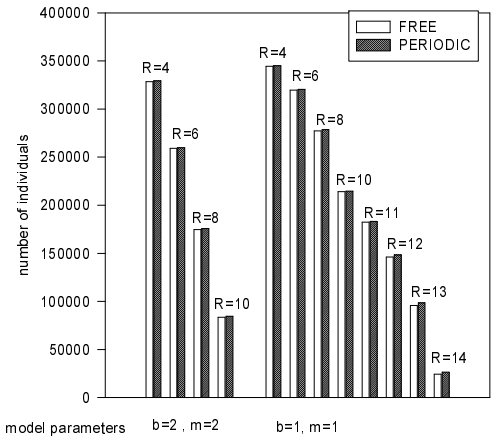
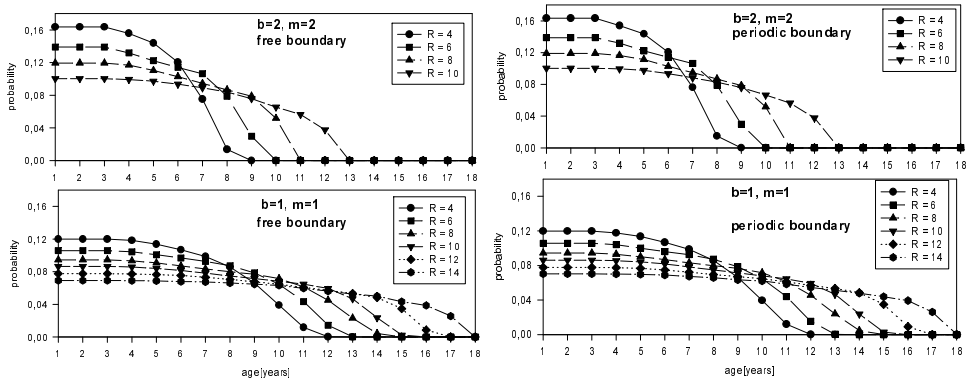
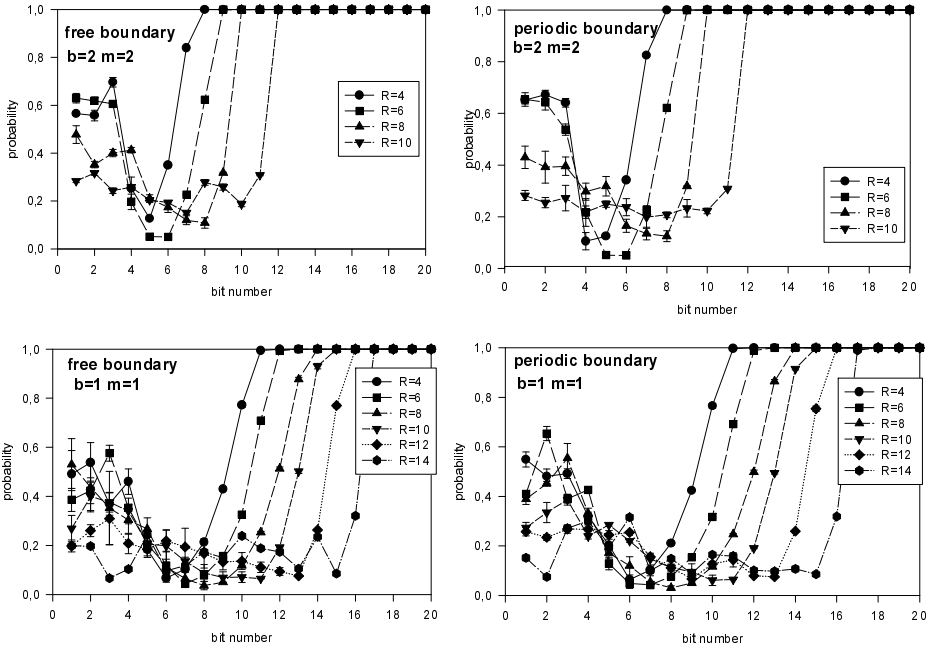


Fig. 1. Size of the stationary population developed under different Penna model parameters and different boundary conditions: free boundary conditions and periodic boundary conditions.



(a) (b)

Fig. 2. Age distribution in the stationary population developed under different Penna model parameters and different boundary conditions: (a) — free boundary conditions (b) — periodic boundary conditions.



(a) (b)

Fig. 3. Mutations distribution in the stationary population developed under different Penna model parameters and different boundary conditions:(a) free boundary conditions, (b) periodic boundary conditions.

present the basic characteristics of the models: Fig. 1 is to compare the sizes of the stationary populations developed under different model parameters and lattice boundary conditions. Fig. 2 is to show the age distribution, *i.e.*, the probability to meet an individual at a given age in stationary populations. Fig. 3 presents the distrubution of bad mutations, *i.e.*, the probability that an individual has a given bit of its genome set to 1.

According to the above presented results there is no noticable difference between boundary conditions introduced. Therefore, in our further investigations we restrict our considerations to the model with periodic boundary conditions.

3.2. Lattice versus standard Penna model

Just by the eye inspection one can notice that the mutation distribution in the population developed on a lattice is different from the corresponding characteristics found for the standard Penna model, see [10]. If the reproduction age is low, *e.g.* $R \leq 10$, then we observe the additional mutation accumulation area which is concentrated at the youth of individuals.

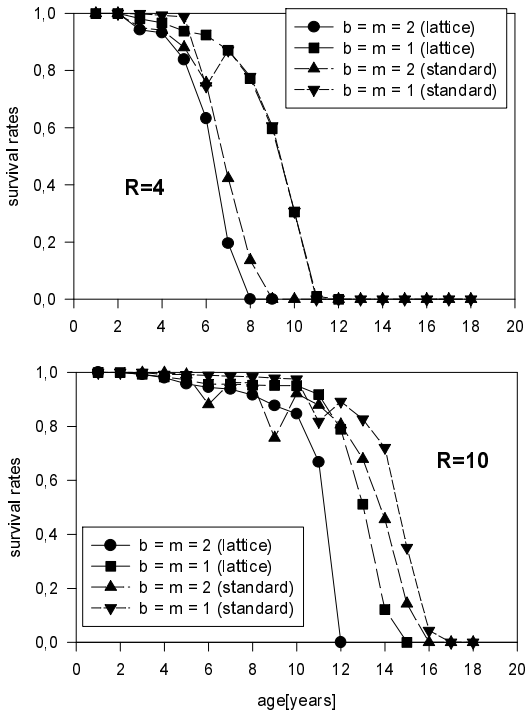


Fig. 4. Survival rates for Penna standard model and Penna model on the lattice

In Fig. 4 we present the survival rates, *i.e.*,

$$\text{survival\_rate(age)} = \frac{\text{number\_of\_individuals(age + 1)}}{\text{number\_of\_individuals(age)}} \tag{4}$$

for the populations obtained in the lattice and standard Penna models under different model parameters to compare the distribution of age. In the case of the standard Penna model the survival rates are normalized, *i.e.*, divided by the survival_rate(1). It occurs that the lattice structure has little influence on the survival rates if the reproduction age starts at the young age. However, the noticable difference appears if the reproduction in the population starts later on, see, *e.g.*, the curves corresponding to $R = 10$ in Fig. 4. The population of the standard Penna model occurs to be not as sensitive to the changes in the mutation ratio as the lattice system.

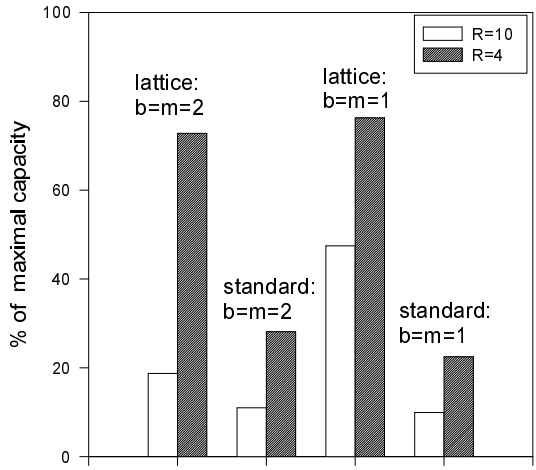


Fig. 5. The percentage of the maximal environment capacity occupied by a population.

The most evident discrepancy between the two systems discussed appears when the population sizes are compared. In Fig. 5 we present the percentage of the maximal environment capacity occupied by stationary populations. It occurs that random deaths affecting all individuals of the whole population at the same rate, namely, at the rate given by the Verhulst factor, sqeezes artificially the population size.

3.3. Spatial evolution

In the present subsection we consider the space distribution of the Penna lattice system. In Fig. 6 we show the snapshots of the populations obtained after first iterations to observe the spatial self-organization. In Fig. 7 one can see the zoomed parts of these snapshots to analize the age distribution in the space.

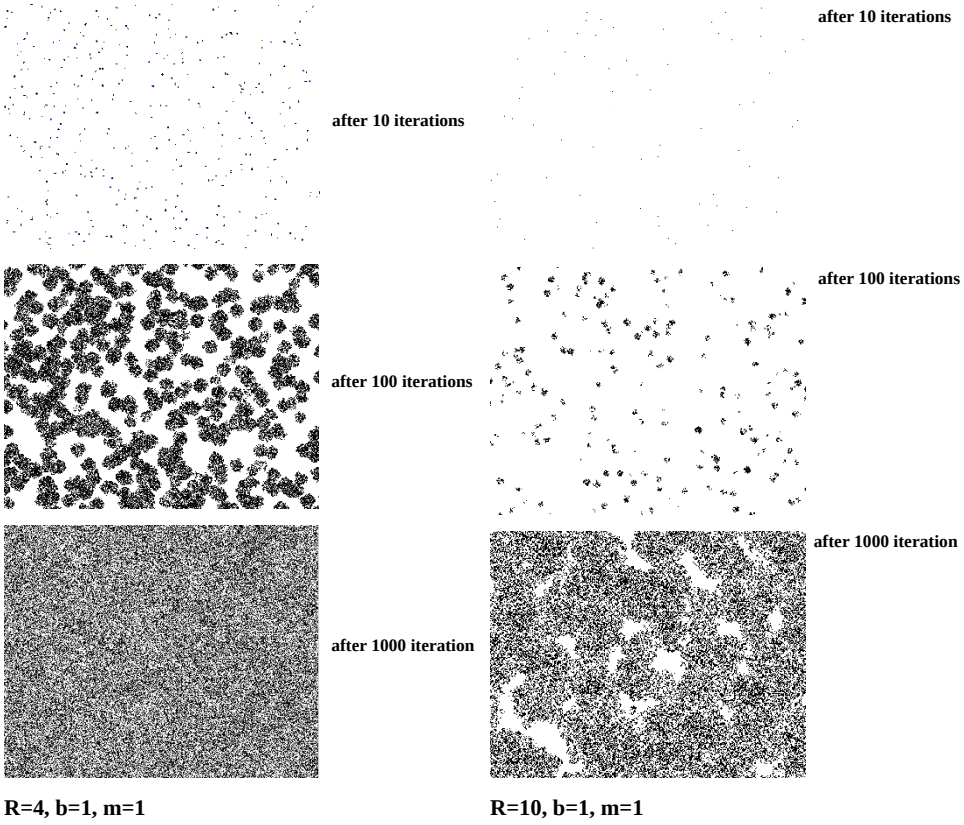


Fig. 6. Snapshots of the lattice sites for the Penna model when the reproduction start at (a) $R = 4$ (b) $R = 10$ after fixed number of iterations. Black dots denote occupied sites, white dots denote free space.

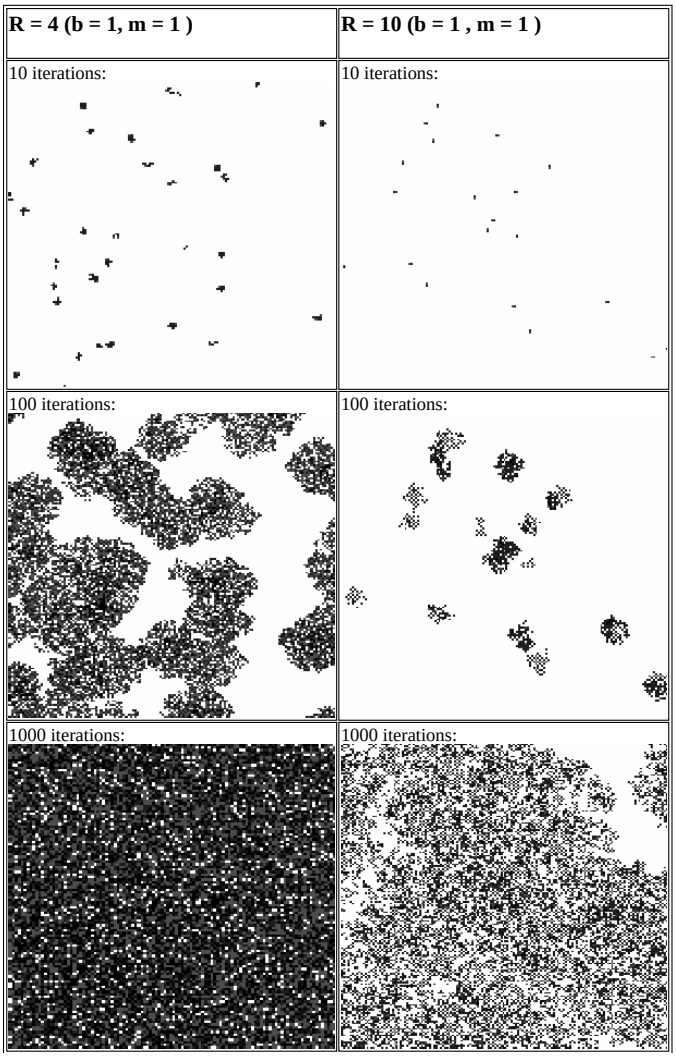


Fig. 7. Parts of the zoomed snapshots of the lattice sites for the Penna model when the reproduction start at (a) $R = 4$ (b) $R = 10$ after fixed number of iterations. Different colors represent individuals of different age: gray dots denote individuals younger than R, balch dots denote individuals at the age of $> R$.

3.4. Mortality

The Penna model on the lattice keeps the property of the exponential increase of mortality for adults, *i.e.*, for individuals of the age $> R$. Fig. 8 presents the mortality obtained for different Penna model parameters.

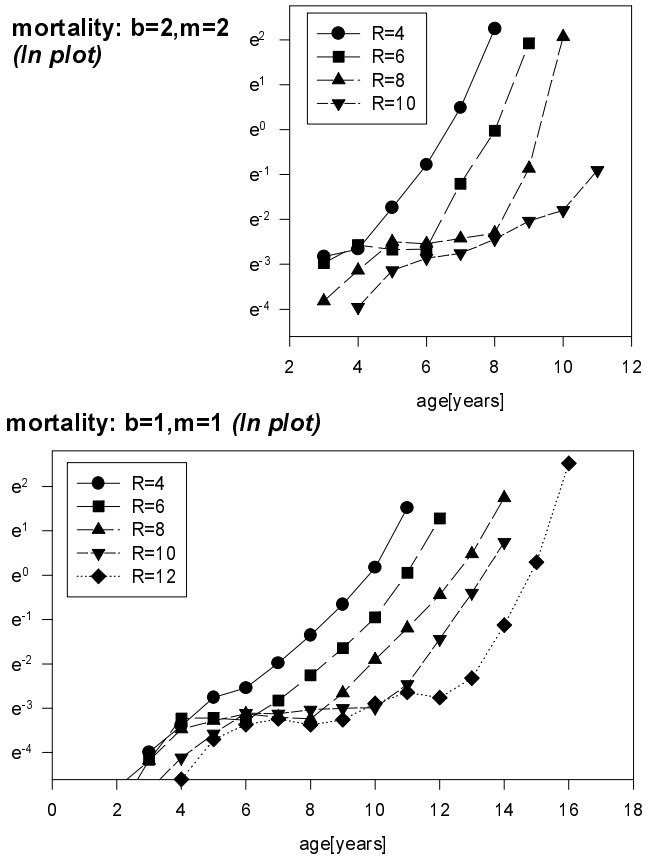


Fig. 8. Mortality of the Penna model on a lattice (log plot)

4. Conclusions

Since the overdominating role of the Verhulst factor in the standard Penna model has been questioned by many authors, see, *e.g.*, [8–10, 14], distinct modifications are formulated to change the model, to improve the result, namely, make the model more close to the real one. Considering the Penna population on a lattice we gain the independence of the random deaths. The adult individuals die only because of passing through too many diseases. Such a situation could be seen as somehow extremal. To improve it one can think of introducing some additional killing factor which provides the extra probability to die for each individual. Unlike the Verhulst factor this killing factor does not need to be connected with restricted environment capacity. Such a factor would represent, for example, the possible weather disasters.

The three important differences are observed when the basic characteristics of the standard Penna model are compared to the Penna model implemented on the lattice. First, the distribution of mutations in the population exhibit the additional acumulation period which affects individuals at their youth. Second, the survival rates depend strongly on the mutational ratio. Third, the sizes reached by the populations developed in the lattice Penna system are noticable greater than the sizes observed in the standard Penna model.

No significant differences are noticed when the two distinct lattice boundary conditions: the free boundary and the periodic boundary, are considered.

Presented results are the preliminary ones and the model designed needs further invesigations. Specially, we plan to consider the properties of the mortality within the Penna lattice model. The reported in the following paper properties of the model allow us to expect to obtain laws for mortality which provide better fits to the life table data actually observed than the original Penna model.

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