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IMMUNITY IN THE NOISY PENNA MODEL

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We have modified the Penna standard sexual model in such a way, that the state of each individual has been determined by the individual fluctuation and the fluctuation of the environment. If the sum of both fluctuations is higher than the assumed limit, the organism dies. Additionally, the individuals can learn the trends of the environment's fluctuations, diminishing their deleterious effects. This mechanism leads to the higher mortality of the youngest individuals and the lowest mortality of individuals just before reaching the minimum reproduction age. These phenomena are observed in any mortality curve describing the age structures of human populations.

Keywords: Penna model; immunity.

1. Introduction

In the standard Penna ageing model with sexual reproduction,[1–3] individuals are represented by two bitstrings (haplotypes). Bits at the same position in the bitstrings represent alleles and are switched on simultaneously and chronologically which means that the age of individual corresponds to the number of switched on loci. The genetic death in the model is determined by the threshold number T of switched on defective genes (bits set for 1 in both loci at the same position). That is why the standard version of the model cannot predict the higher mortality rate of the youngest individuals. However, the phenomenon of the higher mortality of newborns is well known in the natural populations. The genetic defects are responsible for a fraction of cases of the newborns' deaths, but the other fraction probably is caused by the stress connected with the adaptation of new organisms to the quite new environment. The results of higher mortality of the youngest organisms can be obtained in the Penna model by introducing some additional assumption into it. Berntsen[4] has assumed lower threshold T of defective genes for the "babies". Strotman, as cited in Ref. 2, has assumed that the number of genes switched on in one time unit during the childhood is higher than during the later periods of life. Keeping the same assumption as Strotman and additionally introducing genes which are switched on in the period between the conception and the birth, Niewczas *et al.*,[5]

have got the effect of spontaneous abortion at the level corresponding to the mortality of the human embryos[6,7] and the increased mortality of the youngest individuals. Higher mortality of the youngest organisms (still above the age corresponding to the threshold T) could be also predicted by the Penna model simulations when the recombination rate between haplotypes during the gamete production is reduced.[8] Nevertheless, the genetic death in the model cannot occur before the threshold T is reached. In the modified, so called "noisy" Penna model[9] the newborns can die during the first time unit even if T is higher than 1. It is possible because the "health status" of individual fluctuates (we prefer to use the term of homeodynamics[12] for description of such a dynamic state of living systems instead of homeostasis.) If fluctuations pass beyond the limits set for homeodynamics, the organism dies. However, this mortality is still lower for the youngest individuals when comparing with older fractions.

In the model presented below we have assumed that individuals after the birth can "learn" the new environmental conditions. The learning process corresponds to the immunization of young organisms.

2. Model

Consider a population of N individuals. In the noisy Penna model[9] the state of ith individual in time t is an extrapolation of two factors, the inner state of the individual is denoted as $P_i(t)$ and the state of the environment is denoted as $E(t)$, thus

$$I_i(t) = E(t) + P_i(t)\,. \tag{1}$$

The individual dies if its state crosses the level of homeodynamics $I_i(t) \leq F$. Both $E(t)$ and $P_i(t)$ are Gaussian stochastic processes with means $\mu_E(t)$ and $\mu_{P_i}(t)$ equal to zero. The variation of $E(t)$ is constant and equal to σ_e^2 since the variation of $P_i(t)$ is equal to $\sigma_i^2(t)$ and increases with increasing number of expressed defective loci. This model behaves in similar way as the well known standard Penna model with sexual reproduction.[1,9] Thus, during the evolution of population, the defective alleles are accumulated in the loci expressed later during the lifespan — after reaching the minimum reproduction age. The mortality curve shows the lowest mortality for the youngest individuals and increased to 1 for the oldest ones.

In this paper we have introduced the learning mechanism into the noisy Penna model. The mechanism is designed to mimic the immune system. We have put a signal into the environment and have equipped the individuals with a possibility to learn this signal.

The signal in the environment is introduced as a nonzero periodic function $\mu_E(t + D) = \mu_E(t)$ with period D. Thus, the average value of the environment state changes periodically.

A newborn individual does not know the signal, but during its life it learns the expected value of the signal. There are many different ways to introduce the

learning mechanism. We have assumed that realistic learning mechanisms fulfill the following conditions:

- the learning process starts at the time of birth of the individual and the knowledge about the signal is not inherited,
- the accuracy of learning is an increasing function of age (on average, the older individuals better predict the value of the signal),
- after some time of the learning process, if the state of environment is unnoised, the individual approaches the perfect knowledge of the signal value i.e., $\mu_E(t)$,
- the last remembered period has higher impact on the learning effect than earlier periods.

We chose the weighted averaging as the mechanism that fulfills all above-mentioned conditions. The individual predicts a state of the environment as the weighted average from the survived periods

$$\mu_{P_i}(t) = \sum_{j=1}^{\infty} L(i, t - j * D) w_j E(t - j * D)$$

where $L(i,t) = 1$ if individual i has been living at time t and 0 otherwise, weights w_j are decreasing

$$w_j = e^{-(j-1)/\lambda} - e^{-j/\lambda},$$

since $E(t - j * D)$ is the state of environment in time $t - j * D$ (that is j periods before t).

The λ coefficient corresponds to the speed of learning. If this coefficient is low then individuals learn intensively but mainly from the latest periods, otherwise, if this coefficient is high, the individuals learn slower, from larger number of periods with more balanced weights.

In comparison to the noisy Penna model only the means μ_E and μ_{P_i} are modified. During the simulations in each step and for each individual the state $P_i(t)$ is computed with experienced states of $E(t)$) taken into the consideration. Then the state of $E(t)$ is computed and individuals for which extrapolation of these states crossed the homeodynamic level are killed. Survivors which are in the reproduction age (their age is larger than R) mate and produce B children per pair. Reproduction follows exactly the Penna algorithm — random mutations, recombinations and random choosing the partner. A Verhulst factor is introduced to control the birthrate: $V = 1 - N_t/N_{\max}$, where V describes the survival probability of the newborn, N_t corresponds to the actual size of the population and $N_{\max}$ is called the maximum capacity of the environment.

The learning of the environmental signal reduces the deleterious effects of the environment changes and decreases the mortality rate. But very young individuals who have not managed to learn the signal die more often than a little bit older individuals with "more experience".

3. Results

All simulations have been performed for diploid genome with haplotypes $L = 64$ bits long. The reproduction age was set to $R = 10$, the number of offspring per pair was $B = 1$.

The signal in the environment has been modeled as sinusoidal rhythm $\mu_E(t) = A * \sin(t * 2\pi/D)$. The amplitude of signal was $A = 2$ and period $D = 12$ if not otherwise noted.

The most adequate plot to compare results of different simulations is the Gompertz plot,[10] showing the logarithm of mortality rate of individuals at given age as a function of their age.

In Fig. 1 we plot results for different λ's. The environmental noise is relatively small, $\sigma_e = 0.3$, in comparison to the signal. (Here and later, the horizontal axis gives the age and the vertical one the mortality.)

If the amplitude of signal is high and the environmental noise is low (the lower plot in Fig. 1) we see that differences in mortality occur only in early stages of life while for individuals older than 10 years, the mortality does not depend on λ.

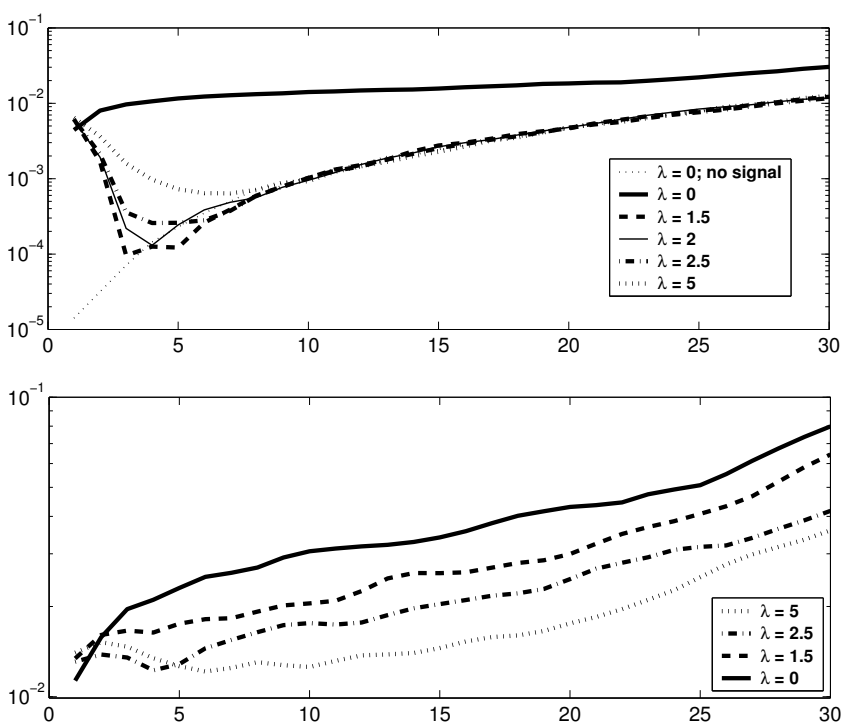

Fig. 1. Mortality curves for different λ's. The mortality is defined as the fraction of individuals that die in given age. On the upper plot the amplitude of signal and noise are $A = 1$, $\sigma_e = 0.5$ respectively. Results presented on the lower plot are for $A = 2$ and $\sigma_e = 0.3$, respectively, except the bold solid line which corresponds to $A = 0$ i.e., lack of signal. Lines marked as $\lambda = 0$ correspond to the lack of learning (i.e., all $w_j = 0$).

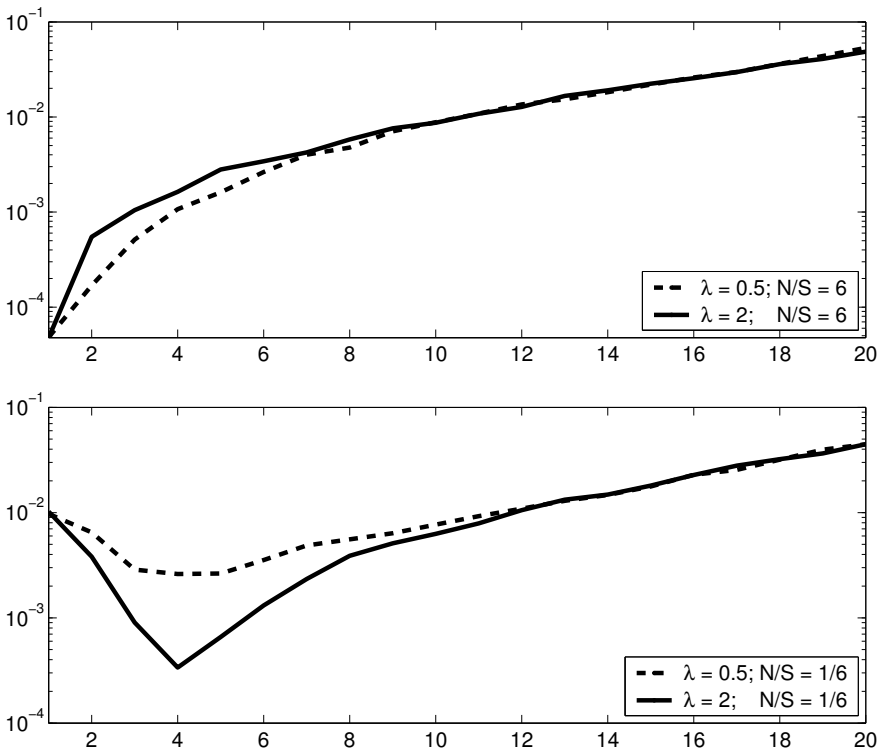

Fig. 2. Mortality curves for speed ($\lambda = 2$) and slow ($\lambda = 0.5$) learning for different noise/signal ratios.

After this time in all scenarios individuals learn the signal and if the σ_e is small, individuals predict the environment nearly perfectly. The mortality in early stages of life depends on λ. For higher λ (slow learning) there is higher mortality of newborn babies than for small λ. This conclusion is true for the low noise/signal ratio and it cannot be transferred to the case when noise/signal ratio is high. In the upper part of Fig. 2 we see that high noise in connection to fast learning results in higher mortality.

It is easier to notice the differences in results if differences in signal/noise ratio are larger. Compare plots in Fig. 2. In the lower one the noise is small in comparison to the signal; in this case we have got lower mortality if the learning is fast. On the upper figure the noise is high and signal very low. Then, in fact, the speed learning may be even harmful to the individual. The slower learning corresponds to the lower mortality.

The goal of introduction of the learning mechanism is to obtain the results of simulations which better fit to the real data. In Fig. 3 we present the rescaled results of simulations and demographic data for German population.

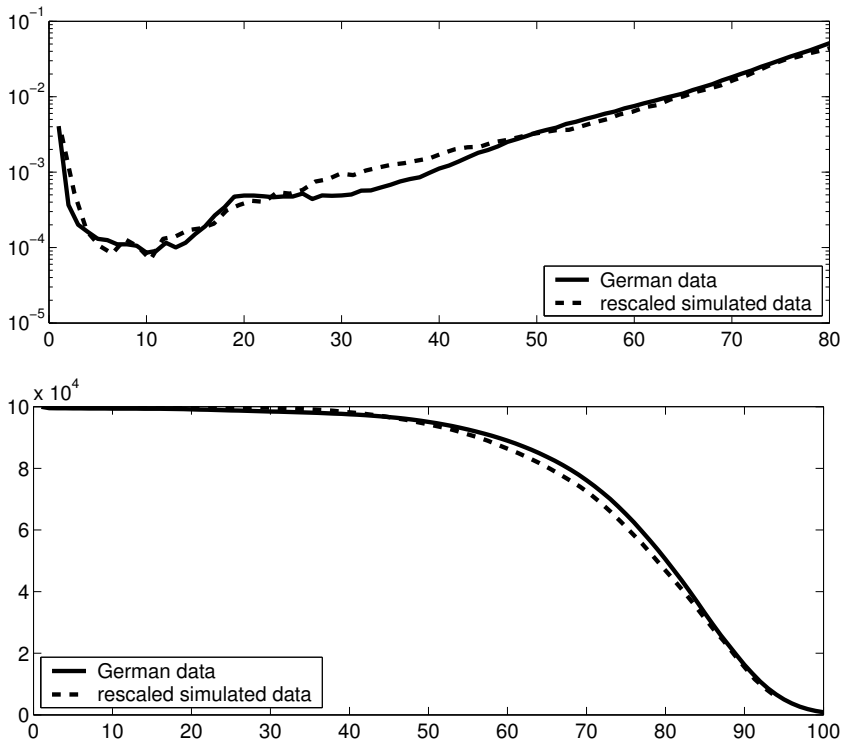

Fig. 3. Mortality curve and age structure for recent demographic German data and the simulated data.

4. Discussion

In this paper we have simulated only one mechanism which could be connected with the phenomenon of higher mortality of the youngest people. In fact, this mechanism rescues organisms from the deleterious influence of the unfriendly environment. In the model, organisms can learn the periodic signal of the environment which could corresponds to the immunization and their higher mortality is observed in the period before they successfully recognize an environmental signal. This mortality could be considered as random death rather than the genetic death. It should be remembered, that if random death is assumed in the population evolution, it is the best if the youngest individuals preferentially die because of it.[11] In Nature, there are other causes of early death — genetic defects. In the standard Penna model genes in the genomes of individuals are checked chronologically, that is why a newborn, before checking the first locus for defects, has a perfect genetic status. The same problem in our model still exists. In the real world, for example in the human populations, newborns have a large fraction of genes already expressed and the most of defective phenotypes are eliminated before birth (estimated 95%). It is also estimated that in the European population about 1% of babies is born with monogenic defects (diseases caused by a defect in only one gene or both genes in one pair of alleles)

and about 0.5% is born with chromosomal aberrations (lost or translocated larger fragment of the chromosome).[7] These babies are much more often hospitalized than babies without any genetic defects and we expect that these babies should be much more susceptible for the influence of the hostile environment. In the previous paper,[5] where about 75% of genes were expressed before birth, the newborns were not genetically perfect any more. It would be interesting to check, how the learning mechanism switched on after birth influences the accumulation rate and frequency of deleterious genes expressed before and after the birth in the evolving populations. Such simulations would be more demanding for computing power.

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