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Simulating inbreeding depression through the mutation accumulation theory

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Abstract

Using the Penna model for biological aging, which is based on the mutation accumulation theory, we show that the number of homozygous loci corresponding to deleterious mutations is higher in small populations than in large ones. This decrease of heterozygosity may drive small populations to extinction even when no drastic change of the environment occurs.

Keywords: Ageing; Penna model; Monte Carlo simulations

1. Introduction

Inbreeding depression, the decline in fitness arising from increased homozygosity of offspring produced by the mating of close relatives, is a potencially major factor influencing the survival of bottlenecked populations [1–3]. It has been observed that such phenomenon contributes to the decline and extinction of small and isolated populations [4,5] as well as in captivity [6–8]. Although some authors suggest that, in natural populations, the environmental conditions have a much stronger effect than the inbreeding depression on the population survival [9,10], recent results in natural populations of the Glanville fritillary butterfly [11] and also of greater prairie chickens [12] have shown that indeed extinction risk increases significantly with decreasing heterozygosity. In

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this way, inbreeding depression can be considered an important extinction mechanism, although not the single one.

The Penna model for biological aging [13] is a Monte Carlo simulation technique based on the mutation accumulation hypothesis. It has successfully reproduced many different characteristics of living species, such as the catastrophic senescence of pacific salmon [14,15] and the inheritance of longevity [16,17]. It is also in agreement with the Gompertz law of exponential increase of mortality with age [18]. Using this model, we have also obtained that the decrease of heterozygosity in small populations reduces the life expectancy and may lead to extinction such populations. Furthermore, when some of these individuals are periodically replaced by the same amount of individuals randomly chosen from larger populations, heterozygosity increases and the extinction of the small population may be avoided.

This paper is organized as follows: in the next section we review the sexual version of the Penna model; in Section 3 we present our simulations and results and in Section 4, conclusions.

2. The Penna model for sexual populations

Each individual of a population is represented by a "chronological genome" that consists of two bit-strings (diploid) of 32 bits (zeroes and ones). The strings of each individual are read in parallel, which means that each position (locus) is associated to two bits (allele). One time step corresponds to read the next position of each genome. The first position contains the information about the individual's first period of life, the second one about the second period and so on. In this way, each individual can live at most for 32 periods. Here we will arbitrarily call one period as one year. Genetic defects (harmful mutations) are represented by bits 1. Homozygous loci (positions) are those with two equal alleles (bits). On the other side heterozygous loci are those corresponding to different alleles, meaning that the individual inherited opposite informations from each parent. If an individual has two bits 1 (homozygous) at the third position, for instance, it starts to suffer the effects of a genetic defect at its third year of life. If it is an homozygous position with two bits zero, no disease appears at that age. If the individual is heterozygous in some position, it will become sick only if the mutation at this position has dominant effect. Six of the 32 bits positions (loci) are randomly chosen at the beginning of the simulation to have their alleles 1 dominant; in the remaining 26 positions the corresponding allele is recessive. These dominant positions are the same for all individuals and kept dominants during all the process. When the number of accumulated diseases of any individual reaches a threshold value T, the individual dies.

If a female succeeds in surviving until the minimum reproduction age R, it generates b offspring every year until death. The female randomly chooses a male to mate, with age also greater or equal to R. The offspring genome is constructed from the parents' ones; first the strings of the mother are randomly crossed, and a female

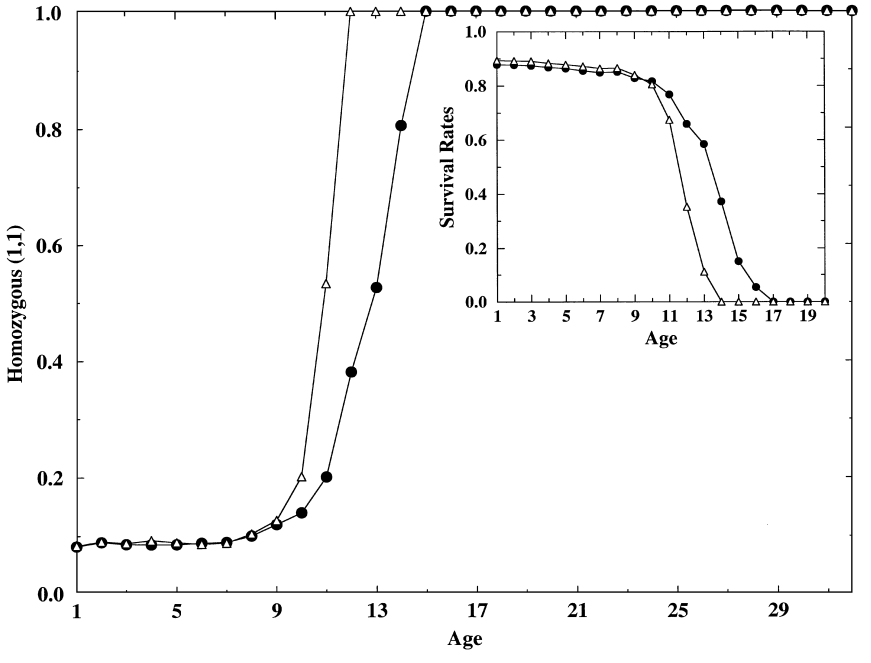

Fig. 1. Percentage of fixed homozygous loci (1,1) as a function of age for small (triangles – 300 initial individuals) and large (circles – 10 000 initial individuals) populations. Since locus (1,1) contains one deletrious mutation in each allele, it is necessarily related to a disease active in that age. The inset shows the corresponding survival rates for small (triangles) and large (circles) populations. We can observe that small populations live three years lesser than large ones, in agreement with the earlier fixation of deleterious alleles.

gamete is produced. M_m deleterious mutations are then randomly introduced. The same process occurs with the father's genome (with M_f mutations), and the union of the two remaining gametes form the new genome. The sex of the baby is randomly chosen, each one with probability 50%. This procedure is repeated for each of the b offspring.

Deleterious mutation means that if the randomly chosen bit of the parent's genome is equal to 1, it remains 1 in the offspring genome, but if it is equal to zero in the parent's genome, it is set to 1 in the baby genome. The most important characteristic of this dynamics is that the bits 1 accumulate, after many generations, at the end part of the genomes, that is, after the minimum reproduction age R. For this reason aging appears: the survival probabilities decrease with age.

Although only harmful mutations are considered, a population that increases exponentially in time is obtained. In order to avoid this exponential increase, at every timestep each individual has a probability to die. This probability is given by the Verhulst factor

$$V = N(t)/N_{\max} ,$$

where $N(t)$ is the number of individuals at time t and $N_{\max}$ is the maximum carrying capacity which is defined at the beginning. At every time step, for each individual, a

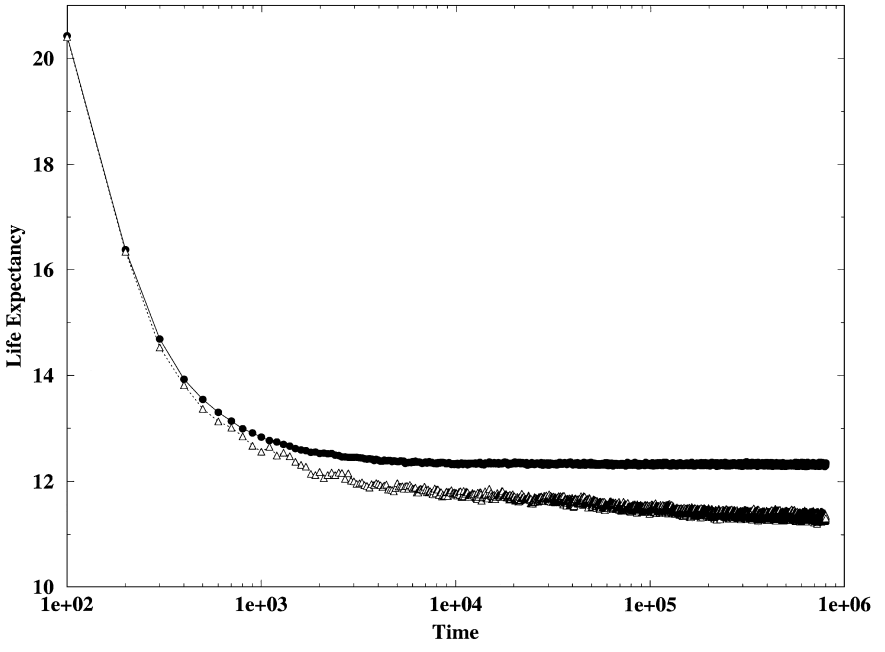

Fig. 2. The life expectancy for small (lower curve) and large (upper curve) populations. We can see that the average life expectancy for small populations tends to stabilize in a much lower value than for large ones. The initial population sizes are the same of Fig. 1.

random number between 0 and 1 is generated and compared to V: if this number is smaller than V the individual dies independently of its age and genome. This death probability also simulates the dispute for space and food and, in this way, environmental conditions are included.

3. Results

In this paper we compare the results obtained for small populations with those for large ones. It has been pointed out that inbreeding seems to produce fixation of recessive deleterious alleles affecting longevity [19]. We have just observed this effect in our simulations, as showed in Figs. 1 and 2.

In Fig. 1, we have measured the percentage of homozygous locus with both alleles equal to one as a function of age, in small (triangles) and large (circles) populations. As can be seen, in small populations deleterious mutations get fixed at younger ages. This earlier fixation is due to the inbreeding which produces a loss of genetic diversity. The inset shows the corresponding survival rates $S(a)=N(a)/N(a-1)$, where $N(a)$ is the number of individuals with age a. Due to the fact that the small populations begin to fix deleterious mutations three years earlier than the large ones, their survival rates also drop to zero three years earlier.

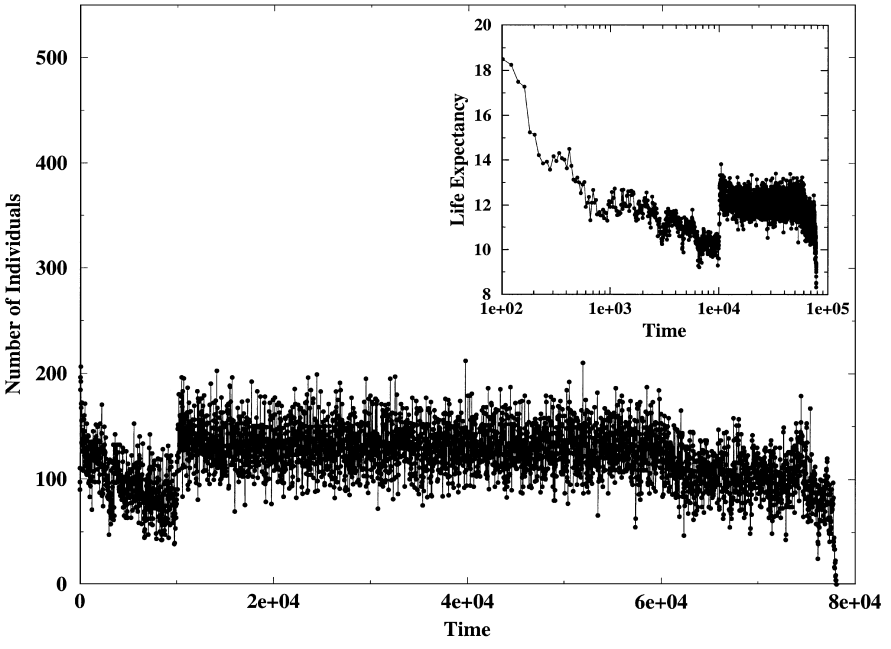

Fig. 3. Number of individuals as a function of time for a small population in which 20% of its individuals are periodically replaced by new ones originated from large populations. The inset shows the corresponding life expectancy. It can be noticed that when the replacements stop at step 60 000, the population extincts after a few time steps. The initial populationn contains 110 individuals and the replacements start at step 10 000.

In Fig. 2, we show the average life expectancy for small (lower curve) and large (upper curve) populations. The reason for the initial decay of both curves is that we start the simulations with all the genomes free of mutations (only bits zero). It can be noticed that while the upper curve stabilizes, the lower one tends to zero. To measure the life expectancy we have computed, for each baby genome, the age of programmed death (according to the limit T). In this way the environmental effects, as we explained before, are disregarded in what concerns life expectancy, since even if the baby dies in the next step due to predation, for instance, its age of programmed death has already been computed.

The results exhibited in Figs. 1 and 2 correspond to already stable small (initial population of 300 individuals) and large (initial population of 10 000 individuals) populations. A stable population means that the number of individuals of any given age a is already constant in time. To obtain each of them, we have simulated 50 different populations (50 different initial seeds) during 800 000 Monte Carlo steps and averaged the final results. In fact, the small populations were also evolved for 3 million time steps, confirming the results obtained with 800 000. The general parameters used in all simulations here are:

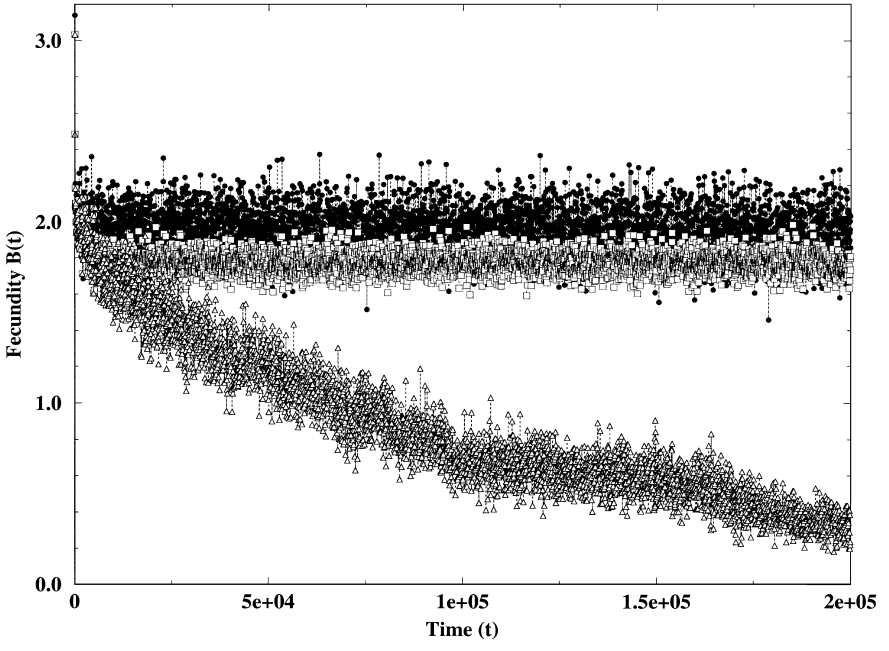

Fig. 4. Average fecundity $B(t)$ as a function of time. Upper curve: initial population = 300 individuals; lower curve: initial population = 100 individuals; middle curve: initial population = 100 individuals with periodic replacements. In all cases $B_{\max} = 5$ offspring per female. The replacements are enough to increase and stabilize the average fitness of populations that would disappear.

- maximum population size $N_{\max} = 10$ times initial population;
- limit number of allowed diseases $T = 3$;
- minimum reproduction age $R = 8$;
- number of offspring per year per female $b = 2$;
- number of mutations at birth $M_m = M_f = 1$.

In order to confirm that the decrease of life expectancy in small populations is really due to inbreeding depression and not to the finite size of the habitat [20], we adopted the following strategy: We began with a small population (110 individuals) that we previously knew would vanish at around 45 000 Monte Carlo steps. After 10 000 steps, we started to replace twenty percent of its individuals by new ones randomly chosen from a large stable population. The replacements were performed periodically at every 50 time steps, during a total of 60 000 steps. Observe that since we are simply replacing the individuals, the population size does not change and so we can maintain the same carrying capacity. In Fig. 3 we show the evolution of the population in time. It can be noticed that when the replacements start (at step 10 000) the population increases and stabilizes in a higher value. However, when we stop to replace the individuals (after 60 000 steps) the population decreases and tends to extinction. The inset shows the corresponding life expectancy. This same procedure was repeated for 10 000 different

initial populations (seeds), and the same result was obtained for 93% of them: 7% was not able to survive even with the replacements.

If we relate the average fitness of the population to its average fecundity, we can observe how the fitness of small populations evolves in time. With this purpose, instead of considering a constant birth rate or fecundity b for all females, we adopted the following fecundity equation that depends on the number of deleterious mutations:

$$B(t) = B_{\max} * [1 - (\mathrm{negmut}(t)/T)] ,$$

where $B_{\max}$ is the maximum possible number of offspring that can be generated per female, *negmut* is the average number of current active mutations of the parents at time t and T is the limit number of allowed diseases. In Fig. 4 we show the average fecundity as a function of time for two different initial sizes: upper curve, initial population = 300; lower curve, initial population = 100 and middle curve, initial population = 100 but with the periodical replacements mentioned before. We can see that for small stable populations the fitness stabilizes on a finite constant value, whereas for populations that tends to extinction the fitness goes to zero. Again, the replacements are able to sustain these last populations. Each curve here corresponds to the average obtained for 50 different initial seeds.

4. Conclusions

Using the Penna model for biological aging we obtain that the fixation of deleterious mutations occurs in small populations at younger ages than it occurs in large populations. We show that this loss of genetic variation decreases the life expectancy and may lead to population extinction. Such effect has already been observed in real small and isolated populations [4,5], as well as in natural ones [11,12]. Previous results with the Penna model show [20] that the survival chance of a small population in an environmental of limited carrying capacity grows exponentially with the size of the habitat. In order to isolate inbreeding depression from finite size effects we periodically replace a given percentage of the individuals of a small population by the same amount of individuals from a large population, keeping constant the carrying capacity. We obtain that populations that would extinct are now able to survive as long as the replacements persist.

In summary, we show that the genetic effects due to inbreeding in small populations are well reproduced by the Penna model for biological ageing, and that periodic *replacements* of the individuals by new ones originated from large populations are enough to maintain small populations alive without changing the original carrying capacity.

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References

[1] L.F. Keller, P. Arcese, J.N.M. Smith, W.M. Hochachka, S.C. Stearns, Nature 372 (1994) 356.
[2] R. Frankham, K. Ralls, Nature 392 (1998) 441.
[3] M.E. Soulé, L.S. Mills, Science 282 (1998) 1658.
[4] R. Frankham, Annu. Rev. Genetics 29 (1995) 305.
[5] R. Frankham, Conserv. Biol. 9 (1995) 792.
[6] K. Ralls, J.D. Ballou, A. Templeton, Conserv. Biol. 2 (1988) 185.
[7] D. Charlesworth, B. Charlesworth, Annu. Rev. Ecol. Systems 18 (1987) 237.
[8] I.J. Saccheri, P.M. Brakefield, R.A. Nichols, Evolution 50 (1996) 2000.
[9] T.M. Caro, M.K. Laurenson, Science 263 (1994) 485.
[10] G. Caughley, Animal Ecol. 63 (1994) 215.
[11] L. Saccheri, M. Kuussaari, M. Kankare, P. Vikman, W. Fortelius, I. Hanski, Nature 392 (1998) 491.
[12] R.L. Westemeier, J.D. Brawn, S.A. Simpson, T.L. Esker, R.W. Jansen, J.W. Walk, E.L. Kershner, J.L. Bouzat, K.N. Paige, Science 282 (1998) 1695.
[13] T.J.P. Penna, J. Stat. Phys. 78 (1995) 1629.
[14] T.J.P. Penna, S. Moss de Oliveira, D. Stauffer, Phys. Rev. E 52 (1995) 3309.
[15] T.J.P. Penna, S. Moss de Oliveira, J. Phys. I 5 (1995) 1697.
[16] P.M.C. de Oliveira, S. Moss de Oliveira, A.T. Bernardes, D. Stauffer, Lancet 352 (1998) 911.
[17] P.M.C. de Oliveira, S. Moss de Oliveira, A.T. Bernardes, D. Stauffer, J. Physica A 262 (1999) 242.
[18] S. Moss de Oliveira, P.M.C. de Oliveira, D. Stauffer, Evolution, Money, War and Computers, Teubner, Stuttgart-Leipzig, 1999.
[19] M.R. Rose, Evolutionary Biology of Aging, Oxford University Press, Oxford, 1991.
[20] K.F. Pal, Int. J. Mod. Phys. C 7 (6) (1996) 899.