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Monte Carlo simulation of inherited longevity

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Abstract

Within the Penna model of biological ageing, we show that longevity is heritable, for both sexual and asexual reproduction.

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1. Method

It is well known that longevity in humans is partly inherited: If the parents lived very long, then their children have a higher chance to live long. More quantitatively, Perls et al. [1] showed that brothers and sisters of centenarians have a four times higher survival chance at old age than the siblings of people who died at a normal age of 73 years. The present paper aims to check this by Monte Carlo simulations of a suitable model, first for asexual and then for sexual reproduction.

The most widely studied microscopic model of ageing is at present the Penna bit-string model [2]. It has succeeded in explaining for instance, why the salmon dies soon after reproduction, the positive female survival probability after menopause, and is in agreement with the Gompertz law and the Azbel theory of mortality (for a review, see e.g. [3,7,8]). The human genome is here reduced to the 32 bits of one computer

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word, where each bit represents a life-threatening inherited disease. The lifespan is divided into 32 intervals each corresponding to one bit position; for humans therefore one interval consists of 4–7 years, depending on the parameters chosen. A zero bit means health; a bit set to one means that starting from that age interval until death one additional disease is diminishing the health. T such diseases, i.e. T bits set to one in the bitstring from age zero to the current age, kill the individual. People who survive up to the reproductive age R get from then on B children per time interval. Each child differs in M randomly selected bit positions from the parent; if a position is selected which has already its bit set to one, then the bit is set back to zero. Besides these genetic deaths, our simulations also allow for deaths because of the lack of food and space through a Verhulst factor; but such deaths are ignored in all the statistics of the present paper.

The computer program thus does not have to wait until an individual dies. Already at birth the time of death is programmed in the genome. Thus when a baby is born, the histogram element $H(i,k)$ of the correlation matrix H is increased by unity, where i is the genetic age of death for the parent and k that for the newly born child. Complete correlation would mean that the matrix $H(i,k)$ is diagonal while complete statistical independence for the ages of death would mean that the matrix elements have the same shape as a function of k, independent of the line i of the matrix.

The above description refers to asexual reproduction. For sexual reproduction the child gets a random section of genes from the mother and the others from the father (see [3,4,7–9] for a more precise description of the now diploid genome and its recombination). The histogram $H(i,j,k)$ has now three indices, for the death ages i,j,k of father, mother and child. Six of the 32 bit positions are randomly selected (same for the whole population) as indicating dominant diseases affecting the child already when one of the parents has the disease. For the other (recessive) positions the health of the child is diminished only when both parents carry this mutation.

2. Results

For asexual reproduction, the histogram in Fig. 1 shows clearly the correlations between the age of death of parents and children: The numbers $H(i,i)$ in the main diagonal are clearly bigger than away from it. Thus long-lived parents get long-lived children. In observations of human populations, such studies would take much longer than the funding periods of typical grants, and thus Perls et al. [1] instead observed correlations between the age of death of brothers and sisters within the same family. Fig. 2 shows from the same simulations used for Fig. 1 a very clear correlation between the age of death for the first child in the family, and the average age of death for the other children. In both Figs. 1 and 2 the histograms are normalized such that the sum of the elements within one line, i.e. for a fixed age of the parent or first child, equals 100. Fig. 3 shows how the average age of death within one generation of one family depends on the oldest age of death in that group; this figure is nearly the same

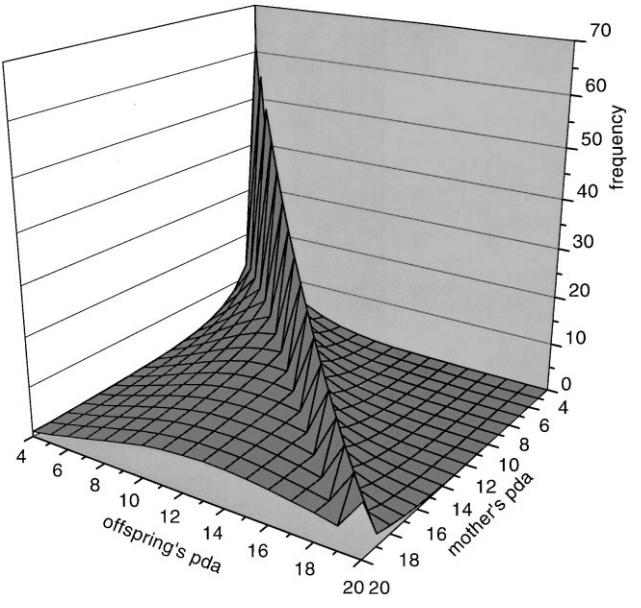

Fig. 1. Histogram (in percent) of child's programmed death age (pda) versus parental death age. For a given genetic death age for the mother we plot the distribution of the ages of genetic death for the offspring. The sharp ridge in the diagonal shows that children die mostly at the same age as their parent, in this asexual model. Note that the horizontal axes do not start at zero. Since we allowed back mutations from one to zero for the bit-string, some children can live longer than their parents.

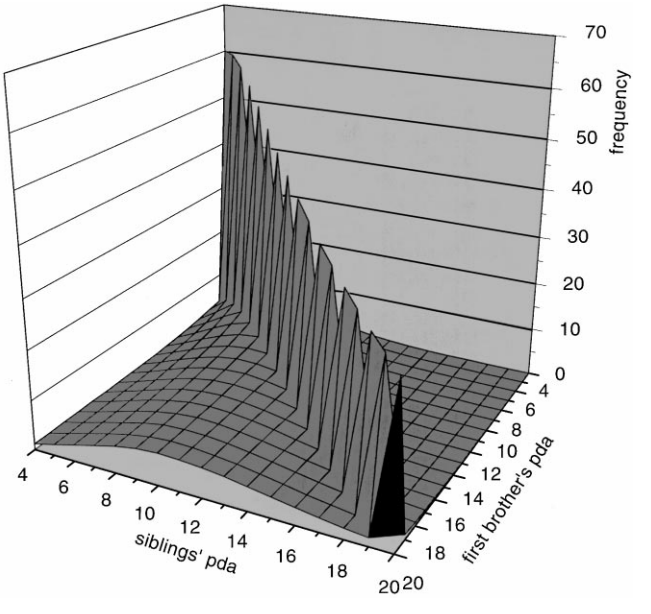

Fig. 2. Histogram (in percent) of child death age versus death age of first-born child. Compared with Fig. 1, we only replaced the mother's age of death by that of the first-born child.

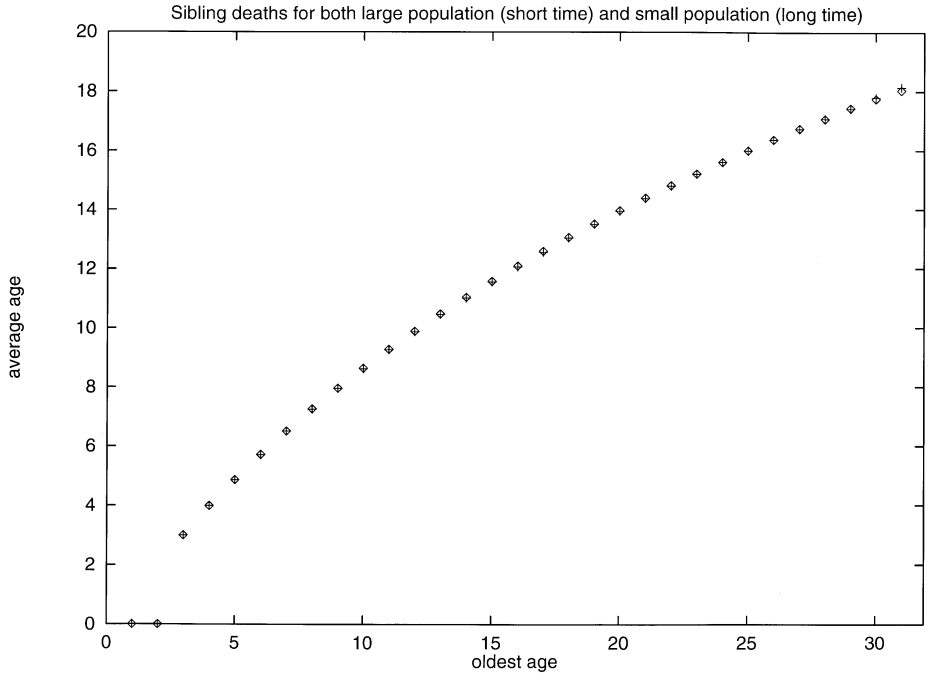

Fig. 3. Average death age of children versus death age of the oldest child in the family. Instead of the full histogram as in Figs. 1 and 2 we show here only the average.

as that in a preliminary publication of the authors [Lancet 352 (1998) 911], where much more iterations and a smaller population were used.

(As parameters for these figures we took $T = R = 3, M = 4, B = 1$. Then at age 13 about 99.8% of the population died, which correponds to an age of about 100 years for the present German population. The mutation rate $M = 4$ was taken unusually [2,3,7,8] large to avoid that nearly all brothers and sisters die at the same age. The minimum reproduction age $R = 3$ was taken unusually low to correspond to human marriage customs.)

We varied the population between 32 and 5×10^7, and the number of iterations between 150 and 2000 million, without clear changes seen in the histograms for ages up to 15 intervals. However, the survival probabilities for ages beyond 10 depended strongly on the size of the population as seen in Fig. 4; data with the same population size but different numbers of iterations roughly overlap. These straight lines correspond to the simple Gompertz law of an overall mortality increasing exponentially with age, while the less steep increase of the mortality for the oldest old may correspond to human reality [5,10–14]. For the parameters used in Refs. [2–4] with higher R and lower M, these deviations from the Gompertz lines were much weaker. (The

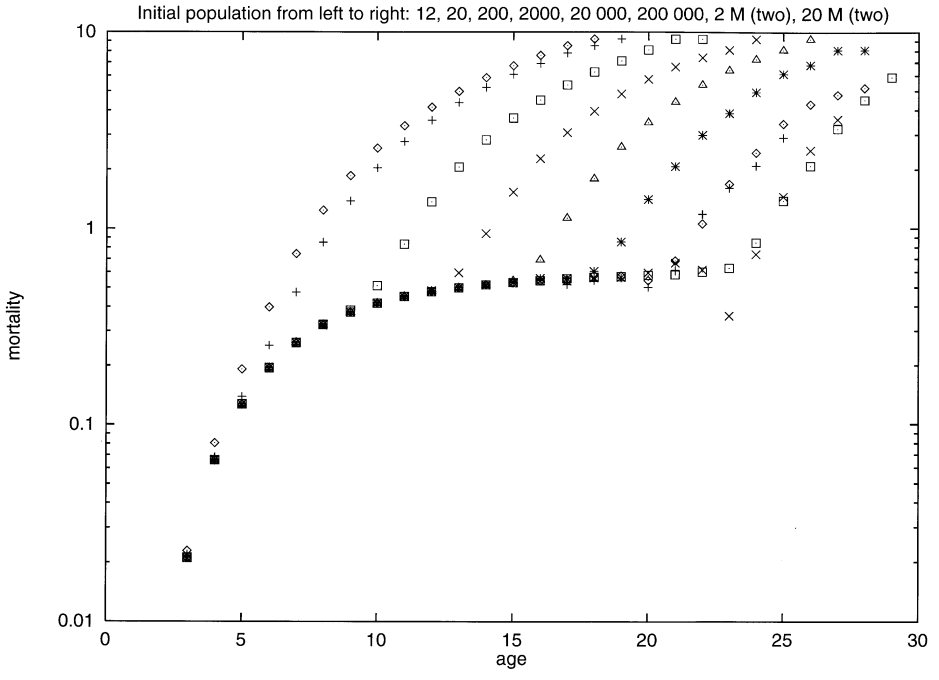

Fig. 4. Mortality versus age, with initial population increasing from 12 (left) to 20 million (right) as given in the top line of the figure. The time varies between 150 (right) and 2000 million (left) iterations. The many curves show that by decreasing the population the end of the plateau is shifted to the left, by an amount logarithmic in the population size. This size effect vanishes and a plateau is reached already for averages over many small populations, if we first average over the populations and then determine the joint survival rates. In this paper, however, we first determine the survival rates and then average over time.

mortality is $q(a) = \ln[S(a)/S(a+1)]$ as a function of age a, where S is the number of survivors.)

For sexual reproduction, we have to correlate the death ages of father (i), mother (j) and child (k). In particular, we want to know if the distribution of the age of death for the children is bimodal (close to the age of death for the father or for the mother) or unimodal (close to the average age of death for the parents). Fig. 5 shows clearly the bimodal character of the distribution: the probability of the children to die is particularly high at the age of the mother's death and at the age of the father's death. We see this from the cross structure in Fig. 5a where the child age was selected to be on one of the recessive positions. In Fig. 5b the child age corresponds to one of the dominant positions in the bit-string, and the cross structure is less pronounced. In short, the danger to die is particularly high at the age of the parental death and at the age where dominant diseases strike. We are not aware of quantitative human studies with which we can compare this result.

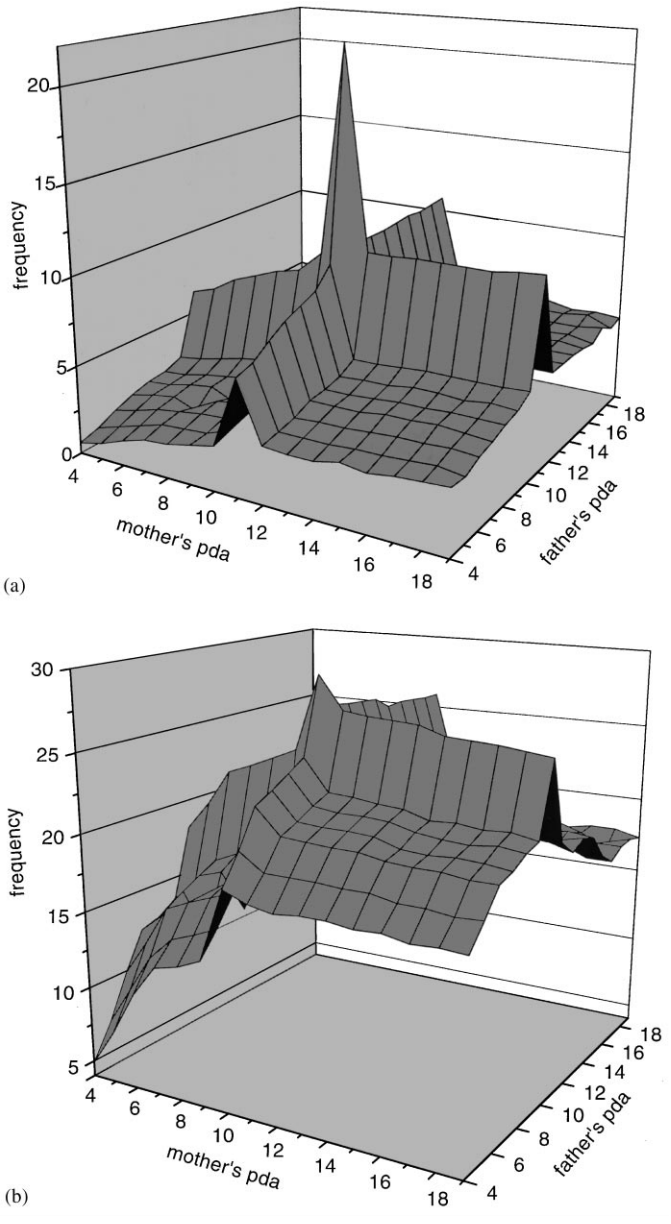

Fig. 5. Histogram of the probability (in percent) to die at age 11 (part a) and 10 (part b), versus the death ages of father and mother. The ages with dominant mutations are 5, 6, 10, 14, 21, and 30. The two ridges show that children die mostly at the same age as one of their parents, in this sexual model.

3. Summary

In conclusion, the Penna model of mutation accumulation agrees nicely with the observed heredity of longevity [1], because it is based on population genetics. This success does not exclude, however, alternative theories of ageing [6] like oxygen radicals; for example the sensitivity to these radicals damaging the DNA could also be inherited.

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References

[1] T.T. Perls, E. Bubrick, C.G. Wager, J. Vijg, L. Kruglyak, Lancet 351 (1998) 1560.
[2] T.J.P.P. Penna, J. Stat. Phys. 78 (1995) 1629.
[3] S. Moss de Oliveira, Physica A 257 (1998) 465.
[4] D. Stauffer, P.M.C. de Oliveira, S. Moss de Oliveira, R.M. Zorzenon dos Santos, Physica A 231 (1996) 504.
[5] J.W. Vaupel et al., Science 280 (1998) 855.
[6] K.W. Wachter, C.E. Finch, Between Zeus and the Salmon, The Biodemography of Longevity, National Academy Press, Washington, DC, 1997.
[7] A.T. Bernardes, in: D. Stauffer (Ed.), Annual Reviews of Computational Physics, p. 359, vol. IV, World Scientific, Singapore, 1996.
[8] S. Moss de Oliveira, P.M.C. de Oliveira, D. Stauffer, Nontraditional Applications of Computational Statistical Physics, to be published.
[9] S. Moss de Oliveira, P.M.C. de Oliveira, D. Stauffer, Braz. J. Phys. 26 (1996) 626.
[10] M.Ya. Azbel, Proc. Roy. Soc. London B 263 (1996) 1449.
[11] M.Ya. Azbel, Phys. Rep. 288 (1997) 545.
[12] M.Ya. Azbel, Physica A 249 (1998) 472.
[13] L.D. Mueller, M.R. Rose, Proc. Natl. Acad. Sci. USA 93 (1996) 15 249 S.D. Pletcher, J.W. Curtsinger, Evolution 52 (1998) 454.
[14] S. Moss de Oliveira, P.M.C. de Oliveira, D. Stauffer, Physica A 215 (1995) 298.