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Penna ageing model and improvement of medical care in 20th century

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Abstract

In Penna's model for biological ageing we reduce after equilibration the influence of acquired diseases and get, similar to reality, the observed increase of the Gompertz slope for the human mortality curves.

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Keywords: Penna model; Biological ageing

In the last 200 years, human life expectancy in rich countries has increased rapidly [1], reaching about 80 years for girls born now, Fig. 1. This change is too rapid to be explained by genetic reasons alone and is due to improved medical care, better food, etc.; war deaths are omitted in Fig. 1. Can we model these effects on a computer?

The Penna ageing model is now the most widespread one for Monte Carlo simulations of many individuals [2–4] (see Refs. [5,6] for alternatives), though biologically there is no consensus on the main reasons for ageing. This Penna model deals with the accumulation of deleterious mutations in the inherited genome; its mortality function [$q = -\mathrm{d}\ \ln(\text{survivors})/\mathrm{d}$ age at age x] agrees roughly with the biologically observed Gompertz law for adults:

$$q(x) \propto \mathrm{e}^{bx} .$$

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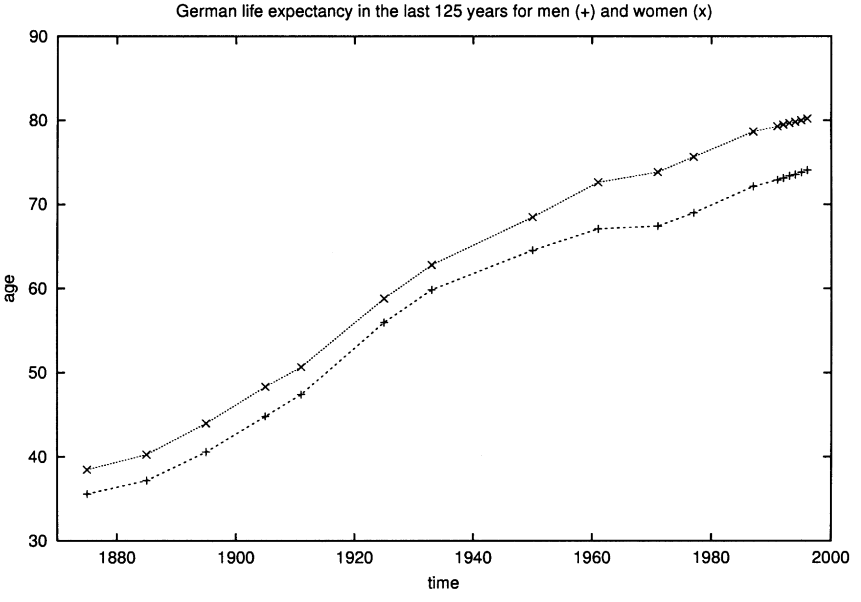

Fig. 1. German life expectancies (male lower than female) during recent history, from various issues of the statistical yearbook of the German government.

Inspection of $q(x)$ for various years, like in Fig. 1.1 of Moss et al. [4], and the quantitative analysis of Azbel [7,8] show that the free parameter in this equation, the Gompertz slope b, increased as a function of time from about 0.07 at the beginning of this century to about 0.09 at its end (in reciprocal years; for German males). A fixed point is seen [7–10] in the sense that the suitably defined mortality function for centenarians barely changed.

Racco et al. [11, Fig. 2.4.5 of Moss et al., Ref. [4]] found good agreement with this Azbel universality but they looked at different populations having different random number seeds and otherwise the same parameters. This situation does not correspond to our attempt to simulate improving health care by changing parameters with time.

The Penna model, as introduced originally, does not explicitly include medical care, only deaths due to bad mutations and due to lack of space and food (Verhulst factor). The latter can be alleviated by increasing the carrying capacity in the Verhulst factor, but this increases only the population, not its equilibrium age distribution. Thus, we include medical care indirectly by changing the genetic death age x_d; in the Penna model, an individual is killed at age x_d when it suffers from T or more mutations (hereditary life-threatening diseases.) In the normal Penna model, this x_d can be calculated for each individual at birth. Actual death occurs at x_d, or earlier through Verhulst deaths.

Now we assume that infections and other acquired (not inherited) diseases, including somatic mutations, reduce this age of death. Thus at each time step and separately for each individual, with probability p the integer x_d is reduced by one unit, to account for

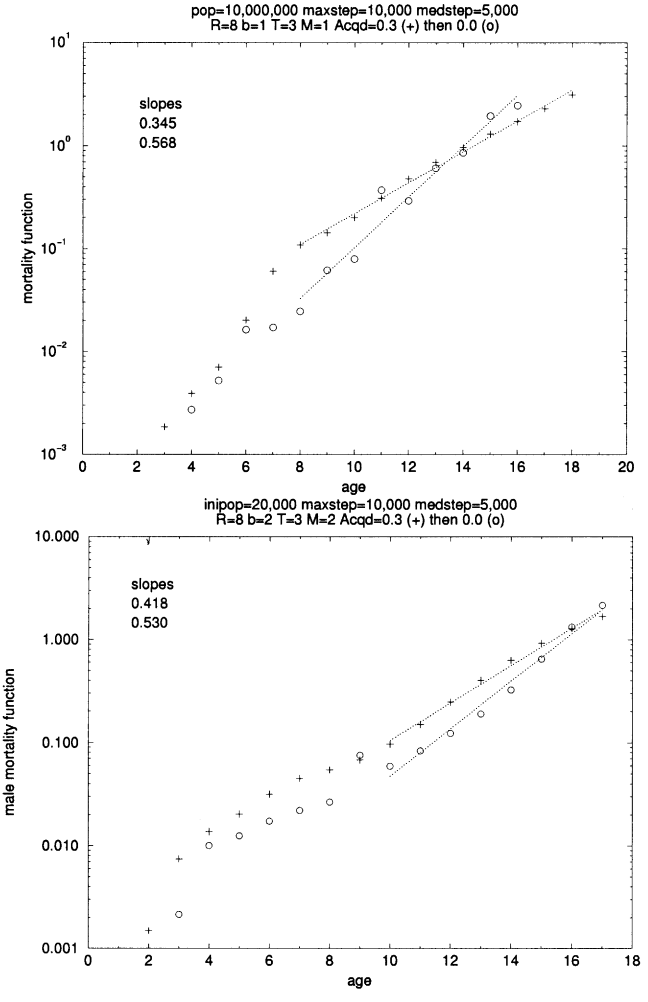

Fig. 2. Mortality function (without Verhulst deaths) for fixed $T = 3$ and with p jumping after equilibration (10^4 iterations) from 0.3 (smaller slope) to zero (larger slope). Part a uses asexual, part b sexual reproduction. The parameter p measures the yearly probability each individual has of acquiring non-heritable diseases.

these deaths related neither to inherited diseases nor to overpopulation. Earlier centuries are treated by assuming $p = 0.3$, and the present situation in rich countries by $p = 0$. Fig. 2a shows that similar to reality the Gompertz slope changes somewhat leading to the desired merging of the two curves at old age (Azbel–Thatcher fixed point). During the less than 100 iterations of the second phase ($p = 0$), the distribution of mutations as a function of the age of the individual cannot change much, just as during the 20th century the human genome did not adjust much to the changing environment. In order to get the same quality for statistical averages, during the second phase we restart the system many times, always from the same initial equilibrium population, and each time

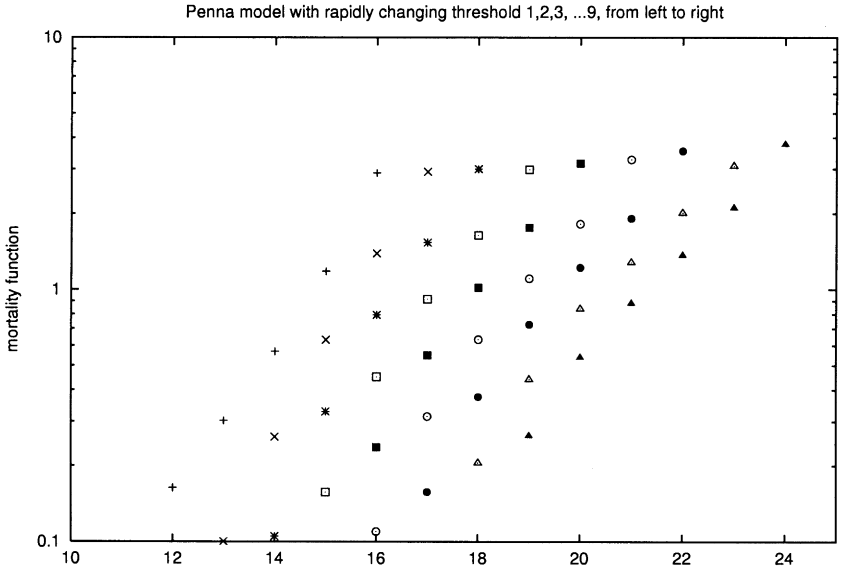

Fig. 3. Mortality function (without Verhulst deaths; $p=0$) with threshold T rapidly increasing from 1 (left) to 9 (right), averaged over 8 populations starting with 4 million individuals each.

with a different set of random numbers. (Although we have a non-equilibrium situation, we got the same mortalities when making the second phase as long as the first one, without restarts.) With sexual instead of asexual reproduction we get the same change of slope, Fig. 2b.

We have simulated also another possibility, by changing the threshold T instead of changing x_d. Thus, we first let the population in the asexual Penna model equilibrate at $T=1$ through 10,000 iterations; each iteration may correspond to several human years. Then, every 10 iterations we increase T by one, until T reaches 9.

Fig. 3 shows that the increase of T shifts the old-age mortality curves to older ages without changing their shape. This agrees with the increase in human life expectation but not with the increase in the Gompertz slope b. When after each change in T we let the genome re-equilibrate, the mortality curves barely change. Thus, this modification is too simple to reproduce all the changes in adult human mortality during this century. Basically, the maximum life span is reached in the Penna model near the age starting from which all bits are set to represent life-threatening diseases. Thus shifting T by one unit shifts all the genetic deaths in this old-age region also by one unit. Perhaps taking 10^3 bits would give better results, shifting the maximum lifespan by a relatively tiny amount if T increases by a few units. At younger ages, where only a minority of bits are set to danger status, shifting T by one unit should shift the death by *more than one* unit, just as we want it. However, our computational statistics was insufficient to show this effect since in the non-equilibrium situations we only looked at the population at one time step, while for equilibrium we averaged over 10^4 iterations.

To improve the situation we switched from asexual to sexual reproduction, omitted dominant diseases, varied the bit-string length from 32 to 16 and to 64 bits, and applied the Verhulst factor to the babies only instead of to the whole population independent of age. Always, the mortality functions at old age were shifted to higher ages, corresponding to the shift in T, without changing their slopes significantly. This finding does not seem to agree with the nearly fixed mortality of human centenarians [7–10]. However, restricting the Verhulst factor to babies not only may be biologically more realistic for many animals, but also made superfluous the distinction between genetic and Verhulst deaths necessary for past simulations of the Penna model.

In summary, the results of the 20th century medicine, dealing mostly with acquired diseases like infections and not with genetic diseases, could be reproduced very well by the simple Penna model. The observed gradual increment in Gompertz slopes could be reproduced by decreasing the rate of acquired diseases, but not by improving the care concerning only genetic diseases.

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