Ageing with Sexual and Asexual Reproduction: Monte Carlo Simulations of Mutation Accumulation

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Computer simulations of ageing, based on the Penna bitstring model, are reviewed, generalized to sexual reproduction, and compared with real death rates for humans.

I. Introduction

People, animals and plants all get old, and recent years have seen an upsurge in the computer simulation of this biological process[1–3]. One possible reason for senescence is the accumulation of bad hereditary mutations over the many generation a species has existed: If some damage to our set of genes (the genome) kills us before we reach reproductive age, then we do not give this dangerous mutation on to our offspring. On the other hand, such a genetic desease will be given on, if it affects our health strongly only after typical age of reproduction. Thus bad mutations at young age are much more weeded out by Darwinistic selective pressure compared with such mutations at old age.

This theory of mutation accumulation is not the only one, but it is particularly suitable for computer simulations by observing life and death in large populations studied by Monte Carlo methods. Alternative theories claim that we die if during our life we have consumed more than ten oxygen molecules per body molecule[4], that programmed cell death is responsible[5], that oxygen radicals destroyed parts of our DNA, or that more generally ageing depends on the environment and not the genes of the individual[6]. Biologists recently summarized: "Virtually all of many efforts to find a unifying theory of aging have foundered when rigorous questions were asked"[7]. In this spirit we concentrate here on the accumulation of genetic random mutations since it is suitable for treatment similar to computational statistical physics. We have also included somatic deseases acquired during the individual's life and not transmitted to the offspring. We do not claim that it is the best biological explanation of ageing.

The situation up to the fall of 1994 was already reviewed in this journal, but that review triggered the development of the Penna model[8] on which most of the more recent Monte Carlo simulations of ageing were based. The present paper summarizes this progress, with particular emphasis on sexual reproduction, and compares the results with the male and female death rates in West Germany 1987[9].

Usually these death rates are the ratio of the number of deaths between the ages a and $a+1$, divided by the number $N(a)$ of survivors of age a. This ratio $(N(a)-N(a+1))/N(a)$ cannot be larger than one, though Perls asserted otherwise[10]. However, the separation into discrete time steps is often arbitrary, and with

$$D(a) = \ln(N(a)/N(a+1))$$

we get a death rate which can become arbitrarily large. The Gompertz law of the 19th century states that death rates increase exponentially with age, and with our definition for D this law is not obviously wrong. Fig. 1 shows this rate for the West German population around 1987, and we see a roughly exponential increase over three orders of magnitude, except for very young age.

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The aim of our ageing simulations here is to recover this exponential increase.

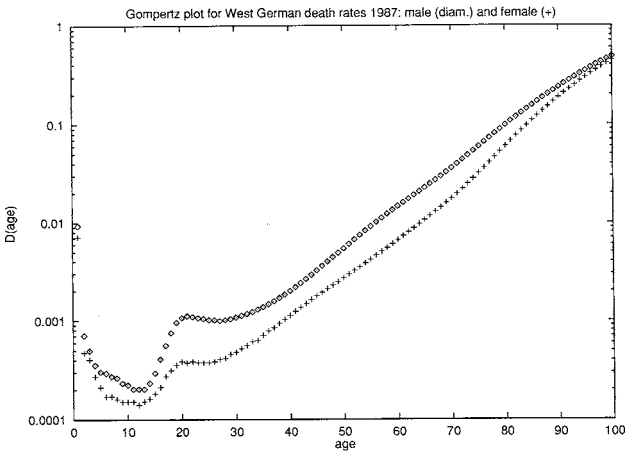

Figure 1. Death rate D as a function of age calculated from the deaths in West Germany around 1987 with our definitions of D. The upper data refer to male, the lower data to female mortality. The age is measured in real years.

Asexual Penna Model

Each year (or other time interval) in the life of an individual is represented by one bit of a 32-bit computer word. This bit is set if starting from that year a serious hereditary disease affects our health, and three or T such diseases kill us. Each year each survivor older than the minimum reproductive age of e.g. eight years give birth to b children (or one child with probability $b < 1$). This child has the same genome (same 32-bit word) as the parent except that at one randomly selected bit position the bit is set to one (serious discase); if the selected bit is already set to one it stays at one. In this way, random deleterious hereditary mutations are simulated; mutations with positive effects are much rarer in nature and neglected here. This is the Penna model[8]. Fig. 2 shows that this model agrees reasonably with the exponential increase of the Gompertz law.

Some medflies become healthier at old age[11], and such deviations from Gompertz's law also may exist for humans[4]. Modifications of the Penna model allow for similar effects[11] but we should remind the reader that only about one percent of the medflies survive to the age where these healthy effects show up. Other applications and modifications described the vanishing of codfish off Newfoundland[12], the survival of Alaskan wolves[13], effects of predators or warfare[14], parental care[15], self-organization of the minimum reproduction age[16] and of the longevity of trees[17]. More than two states per year did not change much[18]. Also exact solutions are possible[19]. Of particular interest for the next section is a simulation[20] showing that no asexual animal can survive in the long run after the maximum age of reproduction, an effect seen most drastically in salmon: These fish die soon after producing offspring.

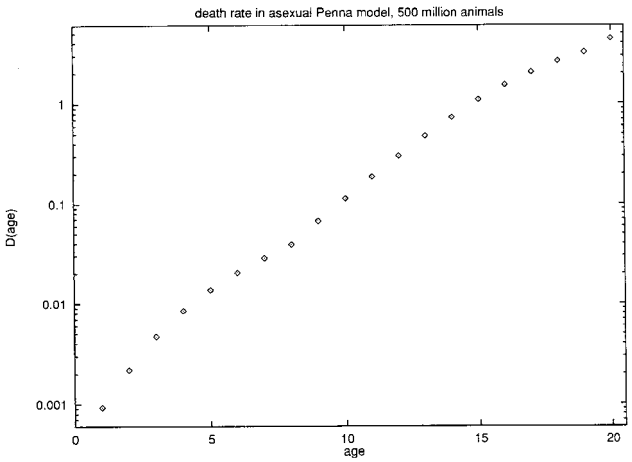

Figure 2. Example of death rate in assexual Penna model, based on hundreds of millions of simulated individuals. The age is measured in bits (i.e. in iterations). Due to nonequilibrium effects (insufficient computer time), for high age the plotted death rate is slightly lower than its equilibrium value. The Gompertz law corresponds to a straight line in this plot. (As in the sexual case below, the numerical survival rate were normalized to unity at young age in order to exclude deaths from the Verhulst factor in the plotted death rate.

Sexual aging model

Most "higher" species, i.e. the more complicated animals, prefer sexual to asexual reproduction. We do not discuss here the intermediate forms where one animal or plant recombines its own genes[21]. Thus sex mixes for the offspring the genes of father and mother in a more or less random way. The details are complicated and at least partially not relevant as far as our numerical results are concerned[22]. Each parent has a genome of two 32-bit words, and sexual reproduction selects one of these two words randomly from each parent. The resulting two 32-bit strings cross over by combining the first k bits from one word with the last 32 - k bits from the other word. In this way the child has again two 32-bit words as a genome which are a mixture of the parental genomes.

It seems controversial[23] among biologists why nature prefers this complicated way of reproduction over

the simpler asexual way. We claim[22] that sex avoids the detrimental effects of most bad mutations: If a bit from the father's genome is mutated and that of the mother's genome is not, or the other way around, then the child not necessarily suffers from the father's genetic disease. Most inherited diseases are recessive and affect us only if both father and mother had them, not if only one of that had this mutation. Only the dominant mutations make us sick already if only one of the parents had it. Most genetic diseases are recessive and not dominant, and thus the genetic sexual recombination pushes back the bad effects of most mutations. Our computer simulations[22] confirm the earlier work of Bernardes[21,24] that a species survives better when it uses recombination.

According to Redfield[23], males produce more mutations than females. Nevertheless, the numbers of surviving females is just as large as the male number if the child's sex is selected randomly. Moreover, even if all females stop reproduction at some age below the maximal age of 32 ("menopause") and men continue up to their death, both males and females survive equally beyond the end of female reproduction; compare Fig. 3. Only if both males and females stop reproducing after a certain age do we recover the salmon result[20,19] of catastrophic senescence.

This model gives already for old age about the same exponential increase of the death rates with age as the asexual Penna model. However, there is no quantitative agreement with the German population data. One reason is that the computer simulations usually assume a finite supply of food (animals) or space (trees), realized by an additional Verhulst death rate proportional to $N(t)$, as in the logistic map. In a rich and peaceful society, deaths from hunger are rare. One can take into account this effect by simply normalizing the simulated survival rates by the survival rate at very young age where mutations are unimportant, or better, by counting as deaths only those due to mutations, not those due to the Verhulst factor. Then the roughly exponential increase of the death rate with age is found over a much wider range (Fig.3).

However, it is well known that women live longer than men, and Fig.1 shows that this difference in the death rates of the two sexes appears already for babies. Increasing the genetic mutation rate for males but not for females does not produce a difference in the two death rates. However, we may introduce in addition to the hereditary mutations discussed so far also somatic mutations which do not affect our germ cells and thus are not given on to the offspring. An example is skin cancer from too much sunshine on the beach. These somatic mutations can happen anywhere in the body, and thus occur with a much higher frequency, though less effect from each single mutation. Thus we may neglect fluctuations in the number of somatic mutations and assume e.g. that each year the survival probability is reduced by a tenth of a percent due to the somatic mutations. Then we get the other curves in Fig.3, and they show a clear difference between the male and female death rates due to (hereditary + somatic) mutations. Only at old age, where the deaths due to inherited mutations dominate over those from somatic effects, do the death rates of males and females approach each other, just as in the real world of Fig.1.

Summary

The Penna model and its sexual variants[21,22,24] were shown here to reproduce the well-known Gompertz law of an exponential increase of the death rate with age, and of higher death rates for men due to their higher mutation rates[23]. More precisely, our data suggest that men age more rapidly than women because of somatic effects. Hereditary mutations influence men and women equally and dominate at old age, where both in reality and in our simulations the male and female death rates approach each other. This does not exclude that other causes of ageing[5] exist but should be a challenge to find out if the models corresponding to these alternatives give similar or even better agreement with nature.

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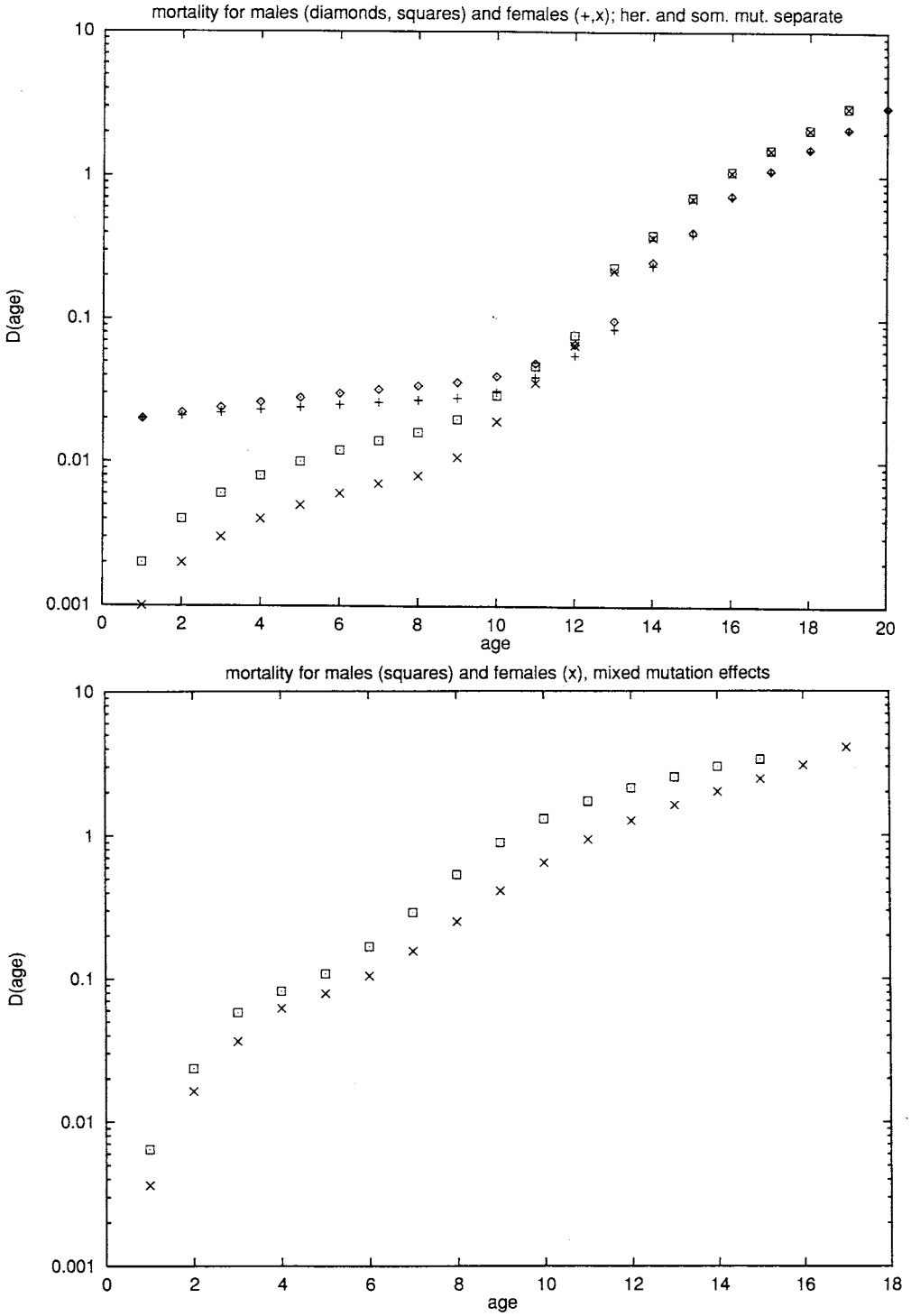

Figure 3. Example of death rated for males (upper data) and females (lower data); female reproduction between 10 and 15, male between 10 and 32; mutation rate 2 for males and 1 for females (per word and per generation); dominance 6 of 32 bits. Part a assumes somatic mutations to decrease survival probabilities by 0.2 (males, diamonds and squares) and 0.1 (females, + and x) percent for each year in life; $T = 10$. Deaths due to the Verhulst factor are ignored (squared and x) or counted (diamonds, +). In part b the symbols mean the same and refer to the mixed model where a somatic mutation reduces lifespan by the same amount as an inherited mutation but only with a probability of 0.65 (males) and 0.45 (females); minimum reproduction age = 6 and $T = 3$.