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A computer simulation for biological ageing

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Abstract. — Here we present the computer simulation of a model for ageing, which incorporates hereditary mutations and favours in some way deleterious mutations to advantageous mutations. We simulated the behaviour for infinite population and have studied through finite size scaling how the behaviour of a finite system approaches that of an infinite system.

By now it has been demonstrated that computer simulation does provide a way to attack the problem of ageing (Stauffer and Jan [1], Ray [2], Vollmar and Dasgupta [3], and for a different approach, Kowald and Kirkwood [4]), at least as long as sex is ignored. This paper presents a computer simulation, the basic idea of which is to associate every living being (of some species) with a point in a 'fitness surface' and to represent the mutation as a random walk to the nearest neighbouring site in that plane. This approach has been applied with success to the study of evolution (Kauffman [5]) but has not yet been tested on the ageing problem (to our knowledge). Recently, we published [3] a simulation study of the ageing problem with a somewhat different model (called model 1 or M1 below) and our present model (called model 2 or M2) has some similarities and some differences with M1, which will be discussed below. We consider only hereditary mutations and show (with M2) that under such mutations a system attains a stationary state for reasonable values of the parameters and investigate how this stationary state depends on the size of the system. The size dependence is studied for M1 also.

Our model is basically as follows: following the two-age model of Partridge and Barton [6] we consider a population consisting of 'babies', 'juveniles', and 'adults', having ages 0, 1, 2 respectively. (Hotzel [7] has shown for M1 that a generalization to more than two age steps is reduced after many generations to this two-age model.) At each time step ('generation') the babies (juveniles) suffer hereditary mutations ( - somatic mutations are neglected all through) and after that mature to juveniles (adults) with survival probability $J(A)$ and give birth to $B$ babies. The adults die out after giving birth. Thus, (i) a baby is born having the same $J$, $A$ values as those of its parent (adult or juvenile), (ii) suffers mutation which changes $J$, $A$ to $J'$, $A'$, (iii) matures with probability $J'$ to a juvenile (iv) gives birth to $B$ babies each having

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probabilities $J'$, $A'$ (v) in the next generation suffers mutation again, thus getting probabilities altered from $J''$, $A''$ to $J'''$, $A'''$, (vi) matures with probability $A''$ to an adult (vii) gives birth to $B$ babies each having probabilities $J''$, $A''$ and finally (viii) dies. Up to this point the models $M1$ and $M2$ are the same (for $M1$ $B$ was set equal to 1). The crucial point in $M2$ is that we consider here a two-dimensional ‘fitness plane’ where $J$ and $A$ values are plotted along $X$ and $Y$ axes. The actual values of $J$ and $A$ can be anything between 0 and 1 but here we divide this range into $L$ parts and assume that the possible values are $0, 1/L, 2/L, ..., (L - 1)/L, 1$. Thus on this plane we now have an $L \times L$ square lattice. The whole system is then described by the populations at every point $(J, A)$ of that lattice, that is, by the number of babies, juveniles and adults having survival probabilities $J$ and $A$. As regards mutation, we assume that for an individuum at some lattice point 7 possibilities are equally probable: (i) it may stay unmoved, or it may move one step (ii) upwards or (iii) downwards or (iv) to the left or (v) to the right, or it may move two steps (vi) to the left or (vii) downwards. (Thus the survival probabilities may be decreased by $1/L$ or $2/L$ but can be increased only by $1/L$. This asymmetry between good and bad mutations is essential for the model, as will be discussed below.) For an infinite population, an $1/7$-th fraction will have each possibility but for a finite number of individuals there will be departures (‘fluctuations’) from an exact $1/7$-th value. To have the effect of such fluctuations we have simulated the process by Monte Carlo algorithm determining through a random number call which of these 7 possibilities is taken. One starts with $n$ babies all at $J = A = 1$ and observes the variation of the population (of babies, juveniles and adults) with generation. The crucial aspects of the model are that there are only two parameters $B$ and $L$ and that one can simulate an infinite population simply by measuring population in units of some large number $N$.

There are two basic differences of the present model ($M2$) with the previous one ($M1$), where for each individuum a random number determined the change in $J$ and $A$. One is that now we can simulate a large population since the size of computer memory required for $M2$ is proportional to $L^2$ whereas the same for $M1$ is proportional to the population. The other difference refers to the food restriction and reduction by a factor of 10. In the previous simulations [1, 3] one had to take special measures to ensure that the population does not exceed the size which the available computer memory can tackle. Thus, one had to multiply the survival probability by the ‘food restriction’ factor (also called Verhulst factor) $(1 - n_t/n_l)$ where $n_t$ is the total population and $n_l$ is some limiting population. This factor implies that when the population increases too much, there is some extraneous factor (unrelated to mutation) which restricts the population. Another alternative to this is to reduce artificially the population (when it exceeds some chosen limit) by a factor of 10. But in the model $M2$ even without such restrictions or reductions one can deal with a change of population by 60 orders of magnitude.

We first discuss the results for the case of infinite population (Fig. 1) where we measure the number of individua in units of some large number $N$ (and allow the populations to be any real number, not necessarily an integer). Thus we start with one baby and study the growth of the population for a given value of $L$. It is found that one can control the rate of this growth by adjusting the fertility $B$ (Fig. 1a) and that there is a value $B = B_0$ (which is of course a function of $L$) for which this growth vanishes. With $L = 50, B_0 = 0.697$ and the population increases only two orders of magnitude in 1000 generations but with $L = 200, B_0 = 0.638$ and the population increases to 5 orders of magnitude in 1000 generations. We have chosen the former set for the sake of convenience. This choice implies that the product of fractional change in viability (due to mutation) and the mutation rate (per person per generation) is $(6/7)(1/L) \sim 0.02$ which is of the same order of magnitude as the Lynch and Gabriel [8] estimate of 0.0075. In figures 1b and 1c we plot the total (over all $J$ and $A$) values of populations
Fig. 1. — Results for an infinite population with $L = 50$ when one starts with 1 baby at $J = A = p_0$ (say). The population is measured in units of some very large number $N$. (a) For $p_0 = 1$ and various $B$ value as indicated in the figure. (b) For $p_0 = 1$ and $B = 0.697$. (c) For $B = 0.697$ and $p_0 = 1, 0.9, 0.8$, shown by continuous dashed and chain lines respectively. (d) For $B = 1$ and $p_0 = 0.2, 0.3, . . . 1.0$ for the lowest, next higher, . . . topmost curves respectively.
Fig. 1. — (continued)
of babies, juveniles and adults and the average survival probabilities against generation. The probabilities become constant after a few hundred iterations. The population curves show a downward slope which could be made more horizontal by an adjustment of $B$ in the 4-th place of decimal. We see that in the constant region $A < J$, that is, the old individuals die more often than the younger ones, as desired from ageing theories.

We have also performed the Monte Carlo simulation starting from a finite number ($n$) of population with the same set of parameters. The constant region in the survival probability $v$s. generation curve does not change but the population curve depends strongly on $n$. It is found that as $n$ increases the curve approaches the one for infinite population (Fig. 2). Over the last few decades physicists have gained expertise in what is called ‘finite size scaling’ in such situations (the behaviour of a finite system approaching the infinite size limit with the increase of size). The basic idea of such scaling is to identify a combination of variables on which the system depends, rather than on the individual variables. We have attempted a scaling analysis in the present case also. For this purpose we have started with 50 systems each with $n$ individuals at $J_0 = A_0 = 1$ but having different random number sequence. Different systems then die at different iterations and figure 3a shows that logarithm of the lifespan of a particular system (that is, the generation at which a system dies) is approximately proportional to the logarithm of the starting system size $n$. This shows that the average lifespan of a species increases as a power of the population, thus conforming to the basic idea of Muller’s ratchet [9]. The rectilinear plot of figure 3a also motivated us to plot in figure 3b the number of systems alive (out of 50) after $t$ generations $v$s. the variable $x = \log(n)/\log(t)$ for different values of $t$ and system size ($n$). Instead of getting different curves for different $n$ one now gets a single curve
Fig. 3. Scaling plot for model M2 with $L = 50, B = 0.697$. We start with 50 copies of a system (with $n$ babies at $J = A = 1$) each with a different random number sequence. (a) Plot for lifespan (the generation at which a system dies). The continuous line joins the median for the lifespans at a given $n$. (b) Plot for the number of systems alive after $t$ generations. The data points shown are for $n = 400$ to 20000. In each case iterations were performed till all the 50 systems die.
Fig. 4. — Plot for scaling relationship for the model M1. As in figure 3 we observe 50 replicas starting with \( n \) babies at \( J = A = 1 \), having different random number sequences. Parameter values: \( u = 1, \epsilon_l = 2\epsilon_u \). (a) \( \epsilon_u = 0.02 \). The line joins the median points. (b) \( \epsilon_u = 0.02 \) (crosses) \( \epsilon_u = 0.01, 0.03, 0.04, 0.05 \) (diamonds). Points for \( n = 40 \) to 24000 and \( t \leq 20000 \) were included. \( m \) is \( n\epsilon_u \).
(unless one includes points from too small systems) indicating that the choice of the crucial (scaling) variable $x$ is correct.

Now we make some alterations in the model for infinite population. If one starts with $n$ babies at $J_0 = A_0 < 1$ then the rate of growth (at high generation) of the total number of babies remains the same but there appears a dip at low generations for low values of $J_0 (= A_0)$ (Fig. 1d). The constant values of average $J$ and $A$ remains however the same (Fig. 1c). These constant values are in fact poorly sensitive to $L$ also and remains the same if one uses population reduction [1]. However if one uses food restriction [1, 3] instead of population reduction, these values get changed strongly. We also tried to have five possibilities for mutation: No change of $J$, $A$, increase or decrease $J$ or $A$ by $1/L$. This variant gives equilibrium values of $J$ and $A$ that are too close to each other and hence cannot explain ageing.

We have also performed the finite size scaling analysis for the model M1 using reasonable values of the parameters ($\epsilon_1 = 0.04, \epsilon_u = 0.02, u = 1$) and food restriction factor for both juvenile and adult survival probabilities. (For more details and explanation of the symbols, see [3].) Here also we take 50 systems with different random number sequences and plot (Fig. 4a) the life span of different systems against the number of babies one starts with ($n$). The curve is not a good straight line (there is a bend in the region of high $n$) and as a result the plot (Fig. 4b) of number of systems alive after $t$ generations vs the scaling variable $x = \log(n\epsilon_u)/\log(t/4)$ is rather scattered, but still the scaling is qualitatively obeyed. We could not find any choice of scaling variable which gives a better plot.

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Note added in Proof:

Recently, Hoetzel [7] has also generalised the model M2 to 5 age steps and found that this model is not reduced to 3 age model. Heumann (private communication) has introduced in the model M1 another state with low food consumption and this has resulted in an increased survival probability.

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