Theoretical approach to biological aging

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We present a model for biological aging that considers the number of individuals whose (inherited) genetic charge determines the maximum age for death: each individual may die before that age due to some external factor, but never after that limit. The genetic charge of the offspring is inherited from the parent with some mutations, described by a transition matrix. The model can describe different strategies of reproduction and it is exactly soluble. We applied our method to the bit-string model for aging and the results are in perfect agreement with numerical simulations.

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I. INTRODUCTION

Aging is an extremely complex biological phenomenon of immense importance and interest. Recent progress in studying aging (or senescence) has pointed out the importance of both genetic and environmental components [1–3]. Although no single theory fully explains all aspects of the aging phenomena, the evolutionary and free radical theories, in particular, are supported by significant observational and experimental evidence. Evolutionary explanations of aging fall into two classes. First, according to the optimality theory, organisms might have evolved the optimal life history, in which survival and fertility late in life are sacrificed for the sake of early reproduction. Second, the life history might be depressed below this optimal compromise by the influence of deleterious mutations; since selection against late-acting mutations is weaker, deleterious mutations will accumulate, i.e., impose a greater load late in life.

Besides experiments with flies and data from human populations, computer simulations are a widely used tool to study aging [3–6]. The recently introduced bit-string model [7], based on the mutation accumulation hypothesis [1–3], is able to reproduce the exponential increase of the mortality with age [8] - this behavior is known as the Gompertz's law. Some applications of this model have been reviewed [5,9] for both asexual and sexual versions, with emphasis on computer simulations. However, only a few analytical results on this model are available. Namely the exact results for the survival rates [10,11] and dynamical aspects [12] of the catastrophic senescence of the Pacific salmon and the description of stationary states through Leslie matrices [13]. In this work, we present analytical results for a general asexual model for different strategies of reproduction. Even for the special cases where analytical results for the bit string model are available, our techniques are more easily and efficiently implemented. This paper is organized as follows: in the next section, we present a general formalism to biological aging. In section 3, we review the bit-string model and build the mutation matrix for it. In section 4 we present comparisons with computer simulations. Finally, we present our conclusions.

II. THE MODEL

Consider a population with $N(t)$ individuals living in an environment with finite resources at time t, and with diverse genetic charges which determine different limit ages m, beyond which the individuals cannot survive. Suppose the natural resources allow a maximum population N_{max}, to be considered in a logistic (Verhulst) factor. We note $x(a,m,t)$ as the relative number of individuals with age a and programmed death age m at time t, that is,

$$x(a,m,t) = \frac{N(a,m,t)}{N_{max}} \quad . \tag{1}$$

Also, consider the initial and final reproduction ages as R and R_f. The evolution of the population in a discrete time is described by

$$\begin{aligned} x(a+1,m,t+1) &= [1-x(t)]\,x(a,m,t) \qquad \text{for } 1 \le a < m-1 \\ x(a+1,m,t+1) &= 0 \qquad \text{for } a \ge (m-1) \end{aligned} \tag{2}$$

$$x(1,m,t+1) = b[1-x(t)] \sum_{m'} A_{mm'} \sum_{a=R}^{R_f} x(a,m',t) \quad ,$$

where

$$x(t) = \sum_{m} \sum_{a=1}^{m-1} x(a,m,t) \quad , \tag{3}$$

b is the number of offspring in each reproduction and $A_{mm'}$ is the birth matrix, that gives the probability of an m'-parent having an m-offspring. When no mutation is allowed, $A_{mm'} = \delta_{m\,m'}$. We also considered $a = 1$ to be the first year of life, so that $a \geq 1$. Note that the maximum age a reached by an individual is $m - 1$.

Eqs.(2) describe the evolution of populations whose transmitted genetic charge contains the information about the maximum age of death; the way this genetic charge may change from parent to offspring through mutations as well as how the maximum age of death is distributed among the population depends on further details, typical of each species or theoretical model. The solution to equations (2) strongly depends on the form of the birth matrix A.

Hence, to completely investigate the evolution problem given by equations (2), we must first choose a transition matrix A. For that we consider in the next sections the bit-string model for biological aging, that seems to have grasped some of the interesting features of the age structure of populations.

On the other hand, when this transition matrix satisfies some general features, the present model is exactly soluble, and before applying it to the bit-string model, we present this exact *stationary* solution.

From eqs.(2) one obtains

$$x(a,m) = (1-x)^{a-1}\, x(1,m) \qquad \text{for } 1 < a < m \quad , \tag{4}$$

where we explicitly assume the stationary solution and from now on will not write the time dependence. Our methods thus do not deal with mutational meltdown where the population is doomed to extinction.

We consider the stationary solution and the mutation matrix $A_{mm'}$ to fulfill the following assumptions:

1. $x(1, m \to \infty) = 0$, what is observed in living populations since offspring with unlimited expected life length are not possible (in the bit-string model this condition is equivalent to $x(1, B + T) = 0$, where B is the bit-string length and T the lethal number of accumulated diseases);

2. $A_{mm'}$ is a triangular matrix such that $A_{mm'} = 0$ for $m > m'$, that is, parents cannot give birth to offspring with larger life expectancy (which corresponds to only bad mutation in the bit-string model). This is not biologically unrealistic for well adapted populations - advantageous mutations are expected to be extremely rare due to the large times required for noticeable species evolution;

3. $A_{mm} \neq 0$, that is the probability that the parent gives birth to offspring with the same expected life length is different from zero. This condition is also expected in biological populations and

4. $A_{mm} < A_{m'\,m'}$ if $m > m'$, the probability that a parent gives birth to offspring with the same expected life length m decreases with m. In other words, the larger the parent expected life length is, the larger the probability that a difference in the genetic charge of the offspring effectively reduces their expected life length (the better the genetic code, the larger the number of events that can spoil it).

The solutions to eqs.(2) depend on the reproduction features of the populations. We consider two cases: the first, when the individuals reproduce only once, that is $R_f = R$, and the second case, when $R_f > R$ and the individuals reproduce every year after the reproduction age, until they die.

A. Case R_f=R

For semelparous populations (that reproduce only at age R), the relative number $x(1,m)$ of m-babies can be written as

$$x(1,m) = b(1-x) \sum_{m'} A_{mm'} x(R,m') \quad . \tag{5}$$

We first observe that as $x(a,m) = 0$ for $a \geq m$ the individuals with programmed death age m below $R + 1$ do not reproduce. Nevertheless these individuals keep being born from parents with $m \geq R + 1$, due to mutations.

In a population we assume a maximum life expectancy $m = \nu$ (in the bit-string model discussed in the next section, ν can be taken as $B + T$) and we assume $x(1, m) = 0$ for $m > \nu$. Now we can write eq.(5) for $m = \nu$:

$$x(1,\nu) = b\,(1-x)^R\, A_{\nu\nu} x(1,\nu) \ , \tag{6}$$

since we are assuming a triangular matrix and $x(1, m) = 0$ for $m > \nu$. Hence, either $x(1, \nu) = 0$ or $b\,(1 - x)^R\, A_{\nu\nu} = 1$. Now, the expression for $m = \nu - 1$ reads

$$x(1,\nu-1) = b\,(1-x)^R\,[A_{\nu-1\,\nu-1} x(1,\nu-1) + A_{\nu-1\,\nu} x(1,\nu)] \ . \tag{7}$$

If $x(1, \nu) \neq 0$, then $b(1 - x)^R = A_{\nu\nu}^{-1}$ and the above equation reduces to

$$\left(1 - \frac{A_{\nu-1\,\nu-1}}{A_{\nu\nu}}\right) x(1,\nu-1) = \frac{A_{\nu-1\,\nu}}{A_{\nu\nu}} x(1,\nu) \ , \tag{8}$$

which is not possible because $x(1, m) \geq 0$ for all m and the left hand side is negative as a consequence of $A_{mm} < A_{m-1\,m-1}$ (assumption 4). Hence $x(1, \nu) = 0$ and the solutions to eq.(7) are either $x(1, \nu - 1) = 0$ or $b(1 - x)^R A_{\nu-1\,\nu-1} = 1$. This situation repeats on and on up to $m = R + 1$, such that $x(1, m) = 0$ for $m > R + 1$.

The equation for $m = R + 1$ leaves us with two possibilities: either $x(1, R + 1) = 0$ or

$$b(1-x)^R A_{R+1\ R+1} = 1 \ . \tag{9}$$

The first solution reduces to no population at all, since for $m < R + 1$ individuals cannot reproduce. On the other hand, the expression for $x(1, m)$ when $m < R + 1$ no longer presents the diagonal term and hence does not give place to non-positive solutions, that is,

$$x(1,m) = \frac{A_{m\,R+1}}{A_{R+1\,R+1}} x(1,R+1) \ , \qquad \text{for } m < R+1 \ . \tag{10}$$

Using eqs.(3) and (9), we can obtain $x(1, R + 1)$:

$$x(1,R+1) = \frac{x^2 A_{R+1\,R+1}}{\sum_m^{R+1} A_{m\,R+1}\,[1-(1-x)^{m-1}]} \ . \tag{11}$$

From eq.(9) the total population may be easily obtained:

$$x = 1 - \left(\frac{1}{b A_{R+1\,R+1}}\right)^{1/R} \ , \tag{12}$$

and a critical number of offspring per reproduction b_c may be defined from eq.(12):

$$b_c = \frac{1}{A_{R+1\,R+1}} \ . \tag{13}$$

If $b < b_c$ the only solution is $x = 0$. The population age structure is given by the relative number $x(a)$ of individuals at age a:

$$x(a) = (1-x)^{a-1} \sum_{m=a} x(1,m) \ . \tag{14}$$

The catastrophic senescence effect [10,11] is clearly present, since eq.(14) implies that $x(a) = 0$ for $a > R$ since $x(1, m) = 0$ for $m > R + 1$. Hence the observable quantities x and $x(a)$ of the stationary solution are explicitly calculated by the transition matrix A and the parameters b and R.

The birth matrix $A_{mm'}$ is a central point of the model. As stated before, it describes the probability of an m'-parent to give birth to an m-offspring, and hence it is closely related to the probability of mutations during the birth process. However, assuming that the birth matrix is triangular and fulfills the basic assumptions 2, 3 and 4 for a single mutation, then it is triangular and fulfills the same assumptions also for M multiple mutations, since in this later case the resulting birth matrix is the product of M single mutation birth matrices. In other words, if the above results apply to a model with a single mutation per birth, they also apply to M multiple mutations, provided that the birth matrix is taken as the product of M single mutation matrices.

A special case happens when no mutation at all is considered. In this case $A_{mm'} = \delta_{mm'}$ does not fulfill the basic assumptions but the problem is still exactly soluble. In this case,

$$x_{M=0} = 1 - \left(\frac{1}{b}\right)^{1/R} \tag{15}$$

and the age structure of the population is determined by the values assumed for $x(1, m)$, that must only satisfy

$$x = \sum_{m}^{R+1} \frac{1-(1-x)^{m-1}}{x} x(1,m) \quad . \tag{16}$$

B. Case $R_f > R$

It is interesting to investigate what happens when the individuals may reproduce more than once, that is, for $a \geq R$. We will first consider that an individual reproduces from age R until its death (iteroparous population). In this case, birth is described by the equation

$$x(1,m) = b(1-x) \sum_{m'} A_{mm'} \sum_{a=R}^{m'-1} (1-x)^{a-1} x(1,m') \quad . \tag{17}$$

Summing over a we have

$$x(1,m) = b(1-x)^R \sum_{m'=R+1} A^*_{mm'} x(1,m') \tag{18}$$

where

$$A^*_{mm'} = A_{mm'} \frac{1-(1-x)^{m'-R}}{x} \quad . \tag{19}$$

It is straightforward to verify that since $x < 1$ the renormalized birth matrix A^* does not necessarily conserve the required properties for a catastrophic senescence solution, that is, A^*_{mm} could increase with m. However in order to have $x \neq 0$ there must exist some m_ℓ such that $x(1, m_\ell) \neq 0$ and $x(a, m) = 0$ for $m > m_\ell$. If $m_\ell > R+1$, that is, the senescence is not catastrophic, then the following must hold:

$$\frac{A_{m_\ell - 1\, m_\ell - 1}}{A_{m_\ell\, m_\ell}} \frac{[1-(1-x)^{m_\ell - 1 - R}]}{[1-(1-x)^{m_\ell - R}]} < 1 \quad , \tag{20}$$

so that the equation for $x(1, m_\ell - 1)$ has a non null solution, in analogy to eq.(8). The ratio between the matrix terms is larger than one, and so the second ratio in the left hand side of the above equation must be small enough to compensate. Given an $m_\ell > R+1$ that satisfies eq.(20), the total population is obtained from the solution of

$$\frac{(1-x)^R - (1-x)^{m_\ell}}{x} = \frac{1}{b A_{m_\ell\, m_\ell}} \quad . \tag{21}$$

Observe that when $m_\ell = R+1$, the above equation reduces to the result obtained in the previous section with $R_f = R$, as it should.

It is possible to obtain the maximum m_ℓ for a given birth matrix A, that is, the maximum death age of an iteroparous population. It is useful then to define a maximum death age limit μ:

$$\mu = \max\{m_\ell\} \quad . \tag{22}$$

where all m_ℓ satisfy eqs.(20) and (21). When starting from an initial population containing death ages larger than μ, the solution converges to $m_\ell = \mu$. However, depending on the structure of the birth matrix, it can happen that eq.(20) never holds for $m_\ell > R+1$. In this case, the system organizes itself as a semelparous population and all results of the previous section apply. Also, when the population initially contains only individuals with death age $m < \mu$, then $m_\ell < \mu$, because the birth matrix A is triangular.

An intermediary case, when $R+1 < R_f < \mu$, may also be considered. In this case the solution is $m_\ell = R_f + 1$ for initial conditions where $m > R_f + 1$ are present.

The solution to the problem is complete with the values of $x(1,m)$ for $R+1 \leq m \leq m_\ell$, that are obtained by finding the solution to the eigenvalue equation

$$x(1,m) = \frac{1}{A_{m_\ell\, m_\ell}[1-(1-x)^{m_\ell - R}]} \sum_{m'=R+1}^{m_\ell} A_{m\, m'}[1-(1-x)^{m'-R}]x(1,m') \quad , \tag{23}$$

for $R+1 \leq m \leq m_\ell$, that satisfies the normalization condition given by

$$x = \sum_m \sum_{a=1}^{m-1} x(a,m) \tag{24}$$

where $x(a,m) = (1-x)^{a-1}x(1,m)$.

Here we can also discuss the case where mutations are absent. As before, $A_{mm'} = \delta_{mm'}$. The eigenvalue equation reduces to

$$x(1,m) = b\frac{(1-x)^R - (1-x)^m}{x} x(1,m) \quad \text{for } m > R. \tag{25}$$

That means that for every $m^* > R$ there is a different solution, where the population consists only of m^*-individuals and the total population x satisfies the above equation for $m = m^*$. The final state depends on the initial conditions and the system always converges to a solution with m_ℓ given by the largest m present in the initial population.

In the next sections we apply our approach to the bit-string model.

III. THE BIT-STRING MODEL

The bit-string model for biological aging [7] consists in a population of $N(t)$ individuals at time t, each one represented by a bit-string of B bits and subject to aging, reproduction and death. The bit S_i $(i = 1, \ldots, B)$ of the string contains the genetic information of the programmed health status of the associated individuals at age i: when $S_i = 1$ a *genetically programmed* disease is acting for all $a \geq i$. Each individual in the population may survive up to T of these diseases, that is, it cannot survive longer than age m, at which the sum of bits from zero to m is T. Individuals cannot reproduce before age R, when it gives birth to b offspring either once (semelparous) or each year (iteroparous) until death. An offspring has the same string as the parent except for M bits that are randomly changed, to simulate genetic inheritance and mutation. The environment limitations are taken into account through a Verhulst factor, that reduces the number of individuals by $(1 - N/N_{max})$, where N_{max} is the maximum allowed population size. From now on we shall discuss in terms of the relative population quantities $x = N/N_{max}$, $x(a) = N(a)/N_{max}$ and $x(a,m) = N(a,m)/N_{max}$.

Exact results have been available only for semelparous populations with $T = 1$ and deleterious mutations [10]. The analytical approach to aging that we present in eqs.(2) may be adapted to reproduce the simulation model. To account for the finite length of computer bit-strings, we also take $x(a,m,t) = 0$ for $a > B$ whereas $m \geq T$, since in the bit-string model no individual may have its programmed death age below T. Moreover, $m \leq (B+T)$ where $m = B + k$ is associated to individuals with only $k < T$ bits equal to 1.

To describe the bit-string model for biological aging, we note that the probability of finding an individual with programmed death age m is equivalent to the probability of finding the T^{th} genetically programmed disease acting on age m, or to find the T^{th} bit equal to unity in the m^{th} position of the bit-string associated to the individual. Also, the birth matrix A should reflect the change in the death age implied by the flipping of randomly chosen bits when building an offspring bit-string. In a recent work, Ito [18] obtained an analytical approach to the bit-string model by considering the relative number $n(\vec{S}, a, t)$ of different bit-strings $\vec{S} = (S_1, S_2, \ldots, S_B)$ present in the population. The present model reproduces the evolution equations of Ito [18] by summing over all bit-strings with the same death age m, that is $x(a,m,t) = \sum_{\{\vec{S}\}} n(a,\vec{S},t)\delta(\ell - m)$ where ℓ is the position (locus) of the T^{th} inherited disease in the bit-string $\vec{S}$. Due to the form of the birth matrices of the bit-string model, the general calculations performed in the previous sections still apply and exact results may be produced.

A. The mutation matrix

To write the birth matrix $A_{m\,m'}$ for the bit-string model, we first consider the one-mutation matrix F, when at most one bad mutation happens at birth in the bit-string model: a random site is chosen and set to one, regardless its previous state. The mutation matrix is triangular and reads

$$
\begin{aligned}
&\text{for } m' \leq B: \\
&\qquad F_{mm'} = \frac{T}{B}\frac{(m'-T)!\,(m-1)!}{(m-T)!\,(m'-1)!} \qquad \text{for } m \leq m'-1 \\
&\qquad F_{mm'} = \frac{B-m'}{B} + \frac{T}{B} \qquad \text{for } m = m' \\
&\qquad F_{mm'} = 0 \qquad \text{for } m'+1 \leq m \leq B+T \\
&\text{for } m' = B+1: \\
&\qquad F_{mm'} = \frac{T}{B}\frac{(m-1)!\,(B-T+1)!}{(m-T)!\,B!} \qquad \text{for } T \leq m \leq B \\
&\qquad F_{mm'} = \frac{T-1}{B} \qquad \text{for } m = B+1 \\
&\qquad F_{mm'} = 0 \qquad \text{for } m > B+1 \\
&\text{for } B+2 \leq m' \leq B+T \\
&\qquad F_{mm'} = 0 \qquad \text{for } m < m'-2 \\
&\qquad F_{mm'} = \frac{m'-T}{B} \qquad \text{for } m = m'-1 \\
&\qquad F_{mm'} = \frac{B+T-m'}{B} \qquad \text{for } m = m' \\
&\qquad F_{mm'} = 0 \qquad \text{for } m'+1 \leq m \leq B+T
\end{aligned}
$$

The matrix elements are obtained considering that the probabilities of finding a bit one in different ages before age m are not correlated. Now, the string length B and the maximum number of diseases T of the bit-string model have been already taken into account (actually B is necessary only due to the finite limits of computers.

In the case that more than one mutation may happen at birth, say M mutations, the mutation matrix is taken to the power M, that is $A = F^M$. The birth matrix is triangular and considering $R_f = R$ populations, it fulfills the required conditions for a catastrophic senescence for any $M > 0$.

IV. RESULTS

Considering the bit-string model, there are three different ways of obtaining results: analytically as presented in the previous sections, numerically iterated solutions to eqs.(2) and numerical simulations. In what follows we will discuss these three forms, for each case we have considered.

We first present the results for $R_f = R = 11$ (age at reproduction of the Pacific salmon, in years). The birth matrix A is obtained from the one mutation matrix F, that is

$$A = F^M \quad \text{for } M > 0 \ , \tag{26}$$

and $A_{mm'} = \delta_{mm'}$ for $M = 0$. In fig. 1 we present a snapshot of the time evolution of x for $M = 1$ and $T = 1$, considering different initial conditions: a) fixed point solution as given by eq.(12) and b) all individuals with age 1 and $m = 32$, i.e, free of mutations. The iteration of eq.(2), starting from the solution of eq.(12) confirms the existence of a fixed point of the dynamics where the system remains for all times. However, for any values of M and T, if $b > b_c$ and $R_f = R$ we also found oscillatory states with period 11 ($= R$). These oscillations may vary in amplitude and phase, depending on the initial condition. They have been previously observed [12,14] and are due to the non-overlap of generations in semelparous populations [12]. The effect of increasing T, the limit number of diseases that kill the individual, is to increase the population. On the other hand, increasing M decreases the total population, because offspring with low m are more frequently generated in each birth process. Simulations show that the fixed point solution is very unstable: any perturbation drives the system slightly away from the fixed point, after a few steps the population is driven to an oscillatory regime. Another point worth noting is the extremely slow convergence of the

age distribution. When the population size reaches the equilibrium (after less than 2000 steps) the population with age one year after the age at reproduction has not vanished. An exponential fitting ($x(a) = A\exp(\alpha t)$) to this age gives a small valued exponent $\alpha = -0.004$ which guarantees that the population older than age at reproduction will eventually vanish.

In fig. 2 we present the survival rates, defined as

$$S(a) = \left(\frac{x(a+1)}{x(a)}\right) \ , \ \ a \geq 1 \quad . \tag{27}$$

The catastrophic senescence effect is clearly present in this figure. The excellent agreement between computer simulations and the analytical results can be also seen.

We consider now $R < R_f$, for the bit-string model. Considering $B = 64$ and reproduction every year until death, our results do not show any oscillatory behavior: regardless the initial conditions the system converges to a fixed point solution. In fig. 3 we present a semi-log plot of the mortality rate at age a defined as [15]

$$q_a = -\ln\left(1 - \frac{S(a)}{S(1)}\right), \tag{28}$$

for $M = 1$,$T = 1$,$b = 0.1$. This normalization has been proved to eliminate the Verhulst factor influence [11]. Using this normalized mortality curve we can see the Gompertz's region (from ages 10 to 25). A clear change in the behavior at the minimum age of reproduction R - where we expect that mutation accumulation effects are not relevant - can be seen in this figure. Another deviation occurs also at older ages. The existence of several Gompertz's regions was proposed by Gompertz [15] and it was already studied in the bit-string framework [16]. To obtain the analytical results for the asymptotic solution we must first obtain the maximum death age of the population. For these parameters, the maximum death age is $\mu = 33$. Starting from an initial condition where $m > 33$ are present, the population stabilizes with $m_\ell = \mu = 33$ (maximum age=$m_\ell - 1$). Solving eq.(21) for the adequate birth matrices A, we can find the asymptotic total population. Again we present computer simulations for comparison. After an enough number of time steps, individuals with advanced ages ($a > 33$) tend to disappear from the population. Our results were obtained from longer series ($3 \times 10^6 timesteps$) than than the ones from intensively parallel simulations by Meisgen [17] (800,000 time steps).

It can be argued about the sizes of the simulated systems. This point is one of the important advantages of the present treatment. We adopted, in computer simulations, population sizes around 300000 individuals (considering $B = 32$ for comparisons, which is the most used value in computer simulations). In a Pentium 150MHz (32Mb RAM) running Linux and using a very optimized code, 1025 sec are needed to simulate 20000 time steps. However, solving the equations for this same time interval, using the present approach only just 20 sec are needed, that is, in our strategy is three orders of magnitude faster than a simulation (for 300000 individuals)! Also, it is worth remarking that no population finite size effects are present in this treatment. (The finite size effects related to the bit string length are exactly taken into account). Moreover the storage needed to simulate it is basically $2 * B \times B \times 8$ bytes (considering double precision float point numbers) whereas a $N = 300000/8$ bytes were required to the computer simulations (using bitwise operations). However, we have to emphasize that in the current approach the computer time increases as B^2 whereas in computer simulations the CPU time increases linearly with B.

In summary, the analytical calculations agree perfectly well with both the stationary solutions found by numerically iterating eqs.(2) and with simulations. For $R = R_f$, oscillatory stable solutions may also be found when solving iteratively the evolution equations. Finally, we observe that the computer time required for numerically iterated solutions for the analytical evolution equations is very short due to the size of the transition matrices ($B \times B$), in comparison to previous models where the birth matrices are $2^B \times 2^B$ [18]. This CPU time required in the present model is still orders of magnitude smaller than that required by computer simulations of systems comparable to real sizes, with the traditional $B = 32$ age intervals.

V. CONCLUSIONS

We have presented a theoretical model to describe how inherited genotypes may determine the age structure of a population. This model takes into account the inherited maximum lifespan, which is passed from parent to offspring according to a birth matrix that may contemplate the possibility of mutations. When this birth matrix is triangular, the stationary solution is obtained analytically for semel- and iteroparous population. Considering that reproduction occurs for $R \leq a \leq R_f$, the expected catastrophic senescence is obtained for $R_f = R$, but it can also occur for $R_f \to \infty$, depending on the structure of the birth matrix. In general cases, successive iterations (not simulations) always reach

asymptotic solutions to the evolution equations that does not require large computational resources. Applying this technique to the bit-string model, we found that iteroparous population always stabilize at the theoretically predicted stationary solution, but semelparous ones may also present stable oscillatory behavior with period R which amplitudes depend on the initial conditions. The agreement with simulation results are noticeable. This approach is at least three orders of magnitude faster than computer simulations and still more memory saving. It is worth to remember that computer simulations have been used up to now, as the most important tool to aging studies. Therefore, we believe that our results can be useful for further studies on biological aging. A natural extension is to consider a continuous time limit, where the time scale is given by R, the biological relevant quantity. This extension is now in progress and will be presented in due time.

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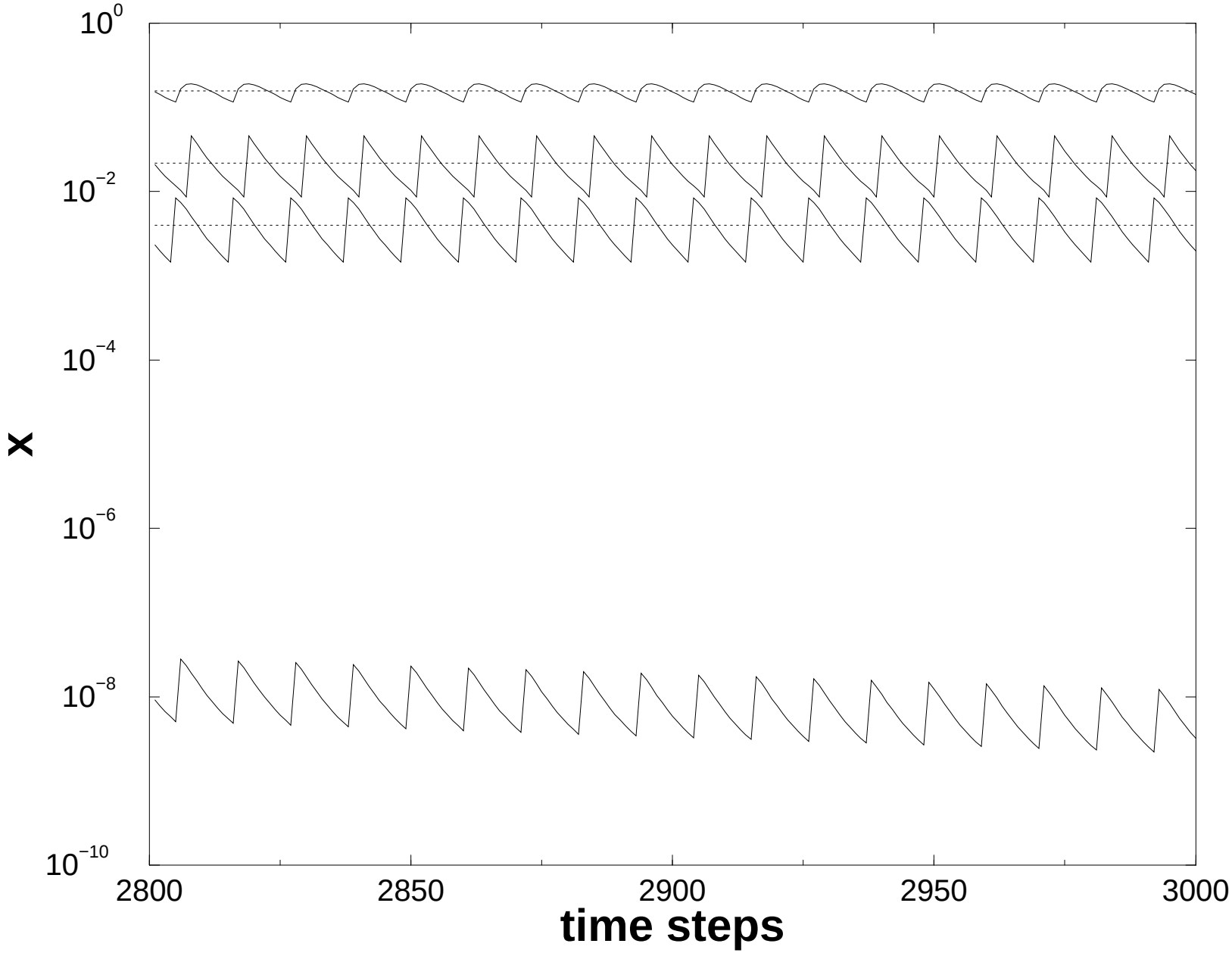
VII. FIGURE CAPTIONS

Figure 1. A snapshot of the time evolution of the population for two different initial conditions: dotted line refer to the fixed point solution of eq.(12) and solid lines to all individuals initially free of mutations. The parameters used in both conditions were: $R_f = R = 11$, $b = 10$, $M = T = 1$. From the top to bottom the solid lines mean the total population, population at ages 1,5 and 12 years. We can note a displacement of the peaks at each age curve. Since the total population is the sum of all ages, these peaks present a smoother aspect. Population vanishes for ages above $R = 11$. However, the decay of these curves for the oscillatory solutions is extremely slow.

Figure 2. Survival rates $S(a)$, in units of $S(1)$, for $R_f = R = 11$, $b = 10$, $M = T = 1$. Catastrophic senescence is clearly seen in this plot. Solid lines are the analytical results and the full circles are the results from computer simulations.

Figure 3. Normalized mortality rate $q(a)$ for $R = 8$, $R_f = 64$, $M = T = 1$, and $b = 0.1$. The full line refers to the theoretical predictions after 3 million time steps (this is the longest time series obtained for the model). Computer simulation results after 10^4 steps are represented by circles. The population beyond age 33 will eventually disappear (after one million years, according to the theoretical predictions).

[1] M. Rose, *Evolutionary Biology of Aging*, Oxford University Press, New York (1991).
[2] B. Charlesworth, *Evolution in Age-Structured Populations*, 2nd. edition, Cambridge University Press, Cambridge (1994)
[3] L.Partridge and N.H.Barton, Nature **362**, 305 (1993)
[4] D. Stauffer, Braz.J.Phys. **24**, 900 (1994).
[5] A.T. Bernardes, in *Annual Reviews of Computational Physics*, D. Stauffer (ed.), World Scientific, Singapore (1996).
[6] S. Moss de Oliveira, P.M.C. de Oliveira and D. Stauffer, *Sex, Money, War and Computers: Non-Traditional Applications of Computational Statistical Physics*, Springer-Verlag, to appear (1997).
[7] T.J.P. Penna, J. Stat. Phys **78**, 1629 (1995).
[8] T.J.P.Penna and D. Stauffer, Zeits. Phys. B **101**, 46 (1996).
[9] S. Moss de Oliveira, P.M.C. de Oliveira and D. Stauffer, Braz.J.Phys. **26** 626 (1996).
[10] T.J.P. Penna and S. Moss de Oliveira, J. de Physique I **5**, 1697 (1995).
[11] T.J.P. Penna, S. Moss de Oliveira and D. Stauffer, Phys. Rev **E52**, 3309 (1995)
[12] H. Puhl, D. Stauffer and S. Roux, Physica **A221**, 445 (1995)
[13] A. F. R. Toledo Piza, Physica **A242**, 195 (1997).
[14] J. Thoms, P. Donahue and N. Jan, J.Phys I **5**, 935 (1995).
[15] M.Ya.Azbel, Proc. Royal Soc. of London **B263**, 1449 (1996)
M. Ya Azbel, Phys.Rept. **288**, in press.
[16] A. Racco, M. Argollo de Menezes and T.J.P. Penna, preprint (1997).
[17] F. Meisgen, Int.J.Mod.Phys. **C8**, 575 (1997).
[18] N. Ito, Physica **A232**, 134 (1996).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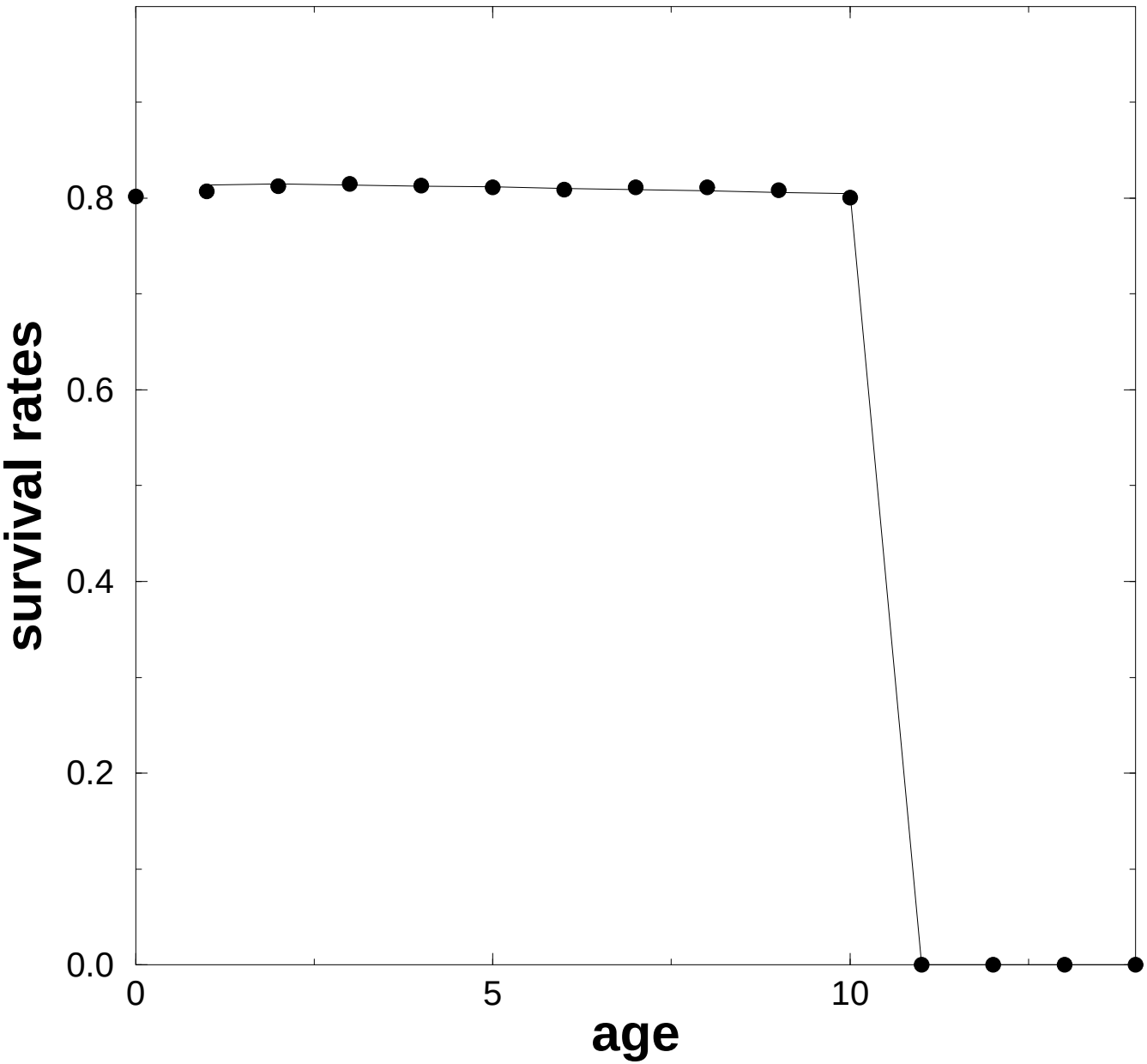
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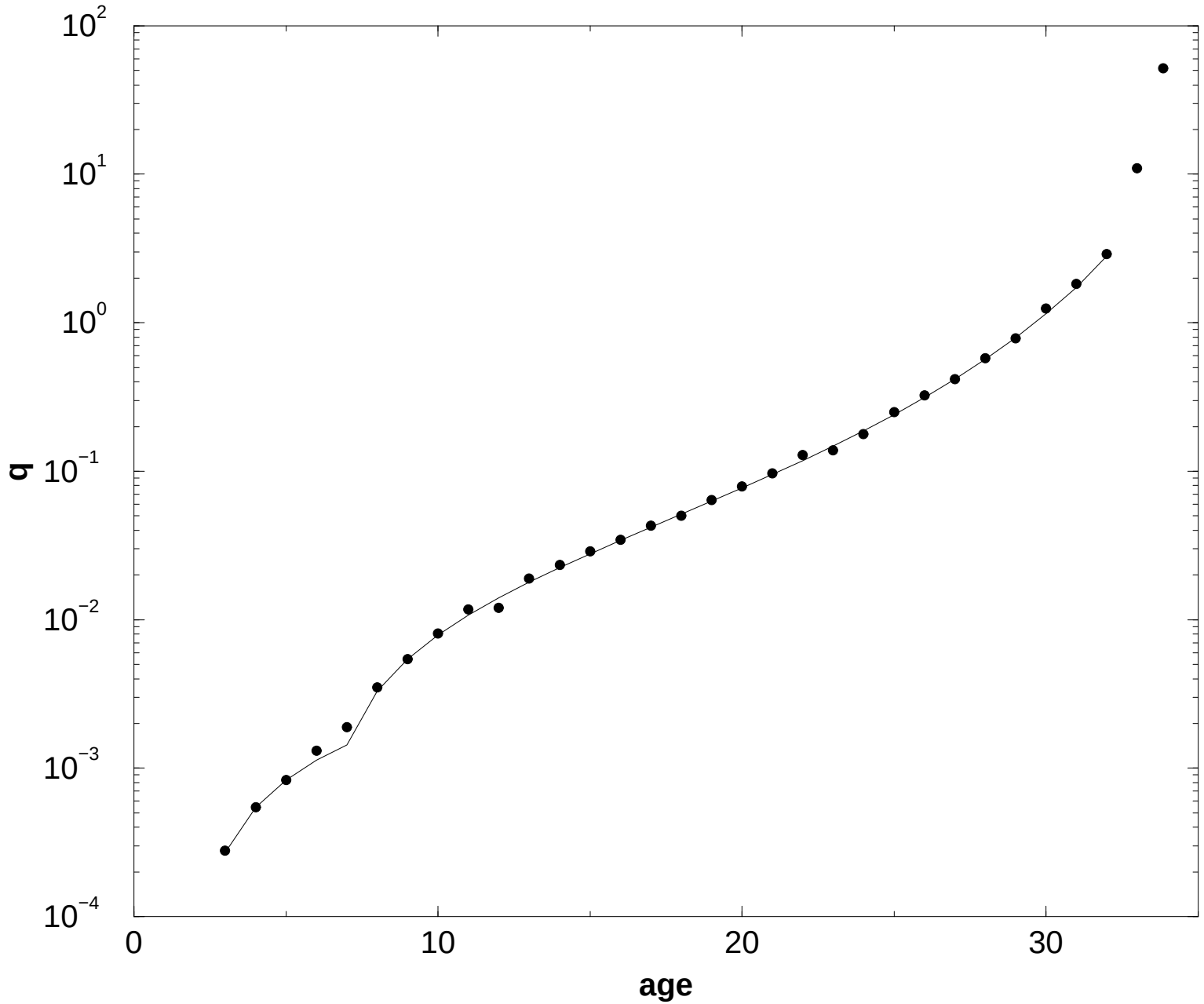
0
5
10
age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