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Comment on "A Bit-String Model for Biological Aging"[1]

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The bit-string model of biological aging introduced by Penna is investigated. This is a well-established model, making use of mutation accumulation theory. However, it turns out that a correct use of the *Verhulst* factor is not made and therefore in a certain limiting case the model does not produce proper results. Furthermore, care has to be taken when chosing the time steps in the model to avoid unrealistic effects.

KEY WORDS: Aging, Penna bit-string model; Monte Carlo simulations.

1. INTRODUCTION

Aging is a process characterized by the loss of functional abilities predominantly after maturation. In a mathematical language, aging, or senesence, is defined as the decrease of the survival probability of an organism from one period of time to another. Several factors are blamed for the cause of senesence: the environment, metabolism, and so forth. Evolution theorists(2, 7) have pointed out that genetic factors may play a major role, especially antagonistic pleiotropy and mutation accumulation.

During the last years various models have been simulated by means of Monte Carlo.(3, 8, 9) According to Stauffer,(8) the most successful approach is the bit-string model introduced by Penna (Penna-Bit-String Model, PM),(1, 4–6) which makes use of mutation accumulation theory. The main focus of this comment is the investigation of this model with respect to the asymptotic dynamics of a simulated population since it is usually used for

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the gain of demographic parameters.(2) In particular the way to keep the population within the computer memory limits is investigated, and the effects of this limitation are pointed out. In section two the model is shortly summarized, followed by its investigation in section three, and the conclusion in section four.

II. THE MODEL

In the PM,(4) an initial population of $N(t = 0)$ individuals is generated. Each individual is characterized by a word of B bits related to its genetic code. The age is considered as a discrete variable running for an individual from 1 to B. The units of time are arbitrary, but mostly chosen as years. If at age i the ith bit equals one, the individual is supposed to suffer the effects of a deleterious mutation for the rest of his "life". It dies when the number of such mutations exceeds a certain threshold T. The parameters of the model are usually chosen to prevent an individual reaching the age B.

When an individual arrives at a reproduction age R it produces b offsprings. Since mutations are hereditary, an offspring gets the parental bit-string, except M bits, which are randomly chosen. By this procedure, deleterious and helpful mutations are possible. To keep the population within the computer memory limits, "(the) effect of food and space restriction is taken into account by an age-independent Verhulst factor, which gives to each individuum a probability $[1 - N(t)/N_{\max}]$ of staying alive; $N_{\max}$ is typically ten times greater than the initial population $N(0)$, and represents the maximum possible size of the population."(6)

III. INVESTIGATION OF THE MODEL

A. Asymptotic Population Dynamics

A population simulated by the PM can be subdivided into groups of individuals all having the same genetic code. Since the genetic codes are related to finite bit-strings the number of such groups is also finite. The course of a simulation is cyclic and one cycle can be divided into two steps:

1. birth, heredity and death due to mutation accumulation
2. application of the Verhulst factor.

In the following the population dynamics is at first investigated without taking into account the Verhulst factor. It is then *density-independent* (cf. ref. 2) since the growth-rate does not depend on the total population size. The process of birth, heredity and death due to mutation accumulation now introduces a random (logarithmic) growth rate $r_k(t)$ for the size $n_k(t)$ of each group k

$$\begin{aligned} n_k(t+1) &= \exp(r_k(t))\, n_k(t) \\ &= \exp\left(\sum_{s=0}^{t} r_k(s)\right) n_k(0) \end{aligned}$$

which is time dependent, e.g., due to fluctuations caused by the Monte Carlo simulation. All groups k which die out at a finite time t (mutational meltdown, cf. e.g. ref. 1) can be neglected since they do not play any role for the long-term evolution of the population ($t \to \infty$). For the other groups the introduction of averaged growth rates

$$\bar{r}_k = \lim_{t \to \infty} \frac{1}{t} \sum_{s=0}^{t-1} r_k(s)$$

is convenient. For the existence of these limits the expressions

$$\frac{1}{t} \sum_{s=0}^{t-1} (r_k(s) - \bar{r}_k)$$

must be bounded for all t, which implies reasonable fluctuations. This requirement shows that not all cases can be treated by this framework, but a lot of relevant ones are covered. The largest value $r = \max\{\bar{r}_k\} \geqslant 0$ is called *intrinsic rate of increase*$^{(2)}$ since it dominates the asymptotic population dynamics of a density-independent population, and the total population size $n(t)$ then approximately grows as[3]

$$n(t+1) = e^r n(t), \qquad t \gg 1 \tag{1}$$

$$n(t+1) - n(g) = (e^r - 1)\, n(t), \qquad (\Delta t = 1) \tag{2}$$

Now the second step of a cycle in a simulation is considered: the application of the Verhulst factor. For the further investigation the two steps of the simulation are exchanged. This is an alternative but equivalent point of view possibly implying an incomplete first cycle. In each cycle the population is then first reduced by a factor $1 - n(t)/N_{\max}$ and afterwards (asymptotically) increased by a factor e^r. Equation (1) now reads

$$n(t+1) = n(t)\, e^r \left(1 - \frac{n(t)}{N_{\max}}\right) \tag{3}$$

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[3] For a continuous-time model the equation $dn(t)/dt = rn(t)$ corresponds to Eq. (2).

This equation serves as a starting point for the further discussion. It is appropriate for the study of the asymptotic population dynamics in the PM since for bounded $n(t)$ only those groups will survive in the long run which intrinsically grow at the largest averaged rate r.

B. Population Limitation

In the following the means used to limit the total population size of the PM are investigated. Since there is some confusion, first the concept of the Verhulst factor is reviewed. According to Charlesworth,(2)

> "the classical approach to modelling a density-dependent population is to write down a differential equation which describes the rate of increase in the number of individuals, n, in a local population
>
> $$\frac{dn}{dt} = ng(n) \qquad (4)$$
>
> where $g(n)$ is a continuous, decreasing function of n. ...The simplest and most widely used form for $g(n)$ is that of the *logistic growth* or *Pearl–Verhulst* equation
>
> $$g(n) = \alpha - \beta n\text{"}$$

For a discrete-time model like the PM ($\Delta t = 1$) Eq. (4) reads

$$n(t+1) - n(t) = n(t)\; g(n(t))$$

$$n(t+1) = n(t)(g(n(t)) + 1)$$

First of all, the use of a Pearl–Verhulst factor is rather unrealistic, since one assumes that both death-rates and fecundities, which regulate the growth of a population, are independent of age but depend on the total population size (cf. ref. 2). Furthermore, comparing this concept with the situation in the PM, it becomes clear that the growth of a population and **not** its total size if affected by the Verhulst factor. Thus the PM does not make proper use of it. Considering Eqs. (1) and (2) a possible choice is

$$g(n(t)) = (e^r - 1)\left(1 - \frac{n(t)}{N_{\max}}\right)$$

yielding

$$n(t+1)-n(t)=n(t)(e^r-1)\left(1-\frac{n(t)}{N_{\max}}\right) \tag{5}$$

$$n(t+1)=n(t)\left((e^r-1)\left(1-\frac{n(t)}{N_{\max}}\right)+1\right) \tag{6}$$

but rather than Eq. (6), the asymptotic population dynamics is actually described in the PM by Eq. (3).

C. Effects of the Limitation

Equation (3) is a well-known logistic equation.[10] For moderate r ($e^r < 3$) a stable equilibrium population size n_s is reached, but for large r the dynamics becomes chaotic which may lead to bad results. This can be avoided if smaller time steps are chosen in the model such that r has an appropriate value.

The following discussion is now restricted to the case of moderate r. Inserting $n(t+1)=n(t)=n_s$ in Eq. (3) yields

$$1=e^r\left(1-\frac{n_s}{N_{\max}}\right)$$

$$n_s=(1-e^{-r})\,N_{\max}$$

and the latter equation is now discussed:

1. For $r=0$, n_s equals zero and the population dies out as in the case of a mutational meltdown. This is an effect of the population limitation concept changing the original population dynamics, i.e., the population, which is stationary without limitation, vanishes independently of its current size. Since for rather small populations restriction of food and space normally do not exist, this is an undesired result.

2. For $r>0$ the desired stationary, finite population is obtained. However, if r is rather small the stationary population size n_s is also rather small. This might impede the determination of reliable demographic parameters for which the population has to be sufficiently large. To avoid this effect, larger time steps can be chosen such that r has an appropriate value.

IV. CONCLUSIONS

As pointed out in Section III the PM[4] does not make a correct use of the Verhulst factor. Due to its limitation scheme the PM does not produce proper results in situations when the intrinsic rate of increase r is rather small or large. In the former case, reliable demographic parameters can hardly be determined since the equilibrium population is rather small; in the latter case, the asymptotic dynamics becomes chaotic and bad results may occur. Both cases can be avoided by the appropriate choice of the time steps in the model such that r has a moderate value.

However, in the limiting situation when r equals zero one obtains the same result as for a mutational meltdown independently of the time steps. This should not occur since the corresponding unrestricted population is stationary. For moderate r the model works well and produces reasonable results.

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NOTE ADDED IN PROOF

After completion of this comment the author received a publication of Bernardes *et al.* [Eur. Phys. J. B 1, 393 (1998)] on "Simulation of chaotic behaviour in population dynamics" confirming the results in section IIIC.

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