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The probability of survival of a mutant gene in an age-structured population and implications for the evolution of life-histories

By BRIAN CHARLESWORTH* and JOHN A. WILLIAMSON†

Department of Genetics, University of Liverpool and Department of Mathematics, University of Colorado, Boulder, Colorado, U.S.A.

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SUMMARY

An expression is derived for determining the probability of survival of a new favourable mutation in a large random-mating population with overlapping generations. For a gene of small effect, in a near-stationary population, an approximate formula similar to the usual one for discrete generations is obtained. The implications of these results for the evolution of life histories are discussed, using the partial derivatives of the chance of survival of a gene, with respect to changes in age-specific fecundities and survival probabilities. The properties of these derivatives are very similar to those of the derivatives of the intrinsic rate of increase, analysed by Hamilton (1966), thus providing a genetical basis for his conclusions concerning the evolution of life histories.

1. INTRODUCTION

The probability of survival of a mutant gene with a specified effect on fitness is one of the classic problems of population genetics (Fisher, 1922; Haldane, 1927; Kimura, 1962). The results derived up to now have ignored age-structuring of the population. As pointed out by Charlesworth (1973), the standard evolutionary arguments concerning the long-term relative effectiveness of selection on genes acting at different ages (e.g. Williams, 1957; Hamilton, 1966) can be translated into statements about the survival probabilities of genes with age-specific effects, since the probability of survival of a mutant gene with a given effect on a character determines what Robertson (1960) has called the limit to selection for that character. It is thus of particular importance to obtain a workable expression for the probability of survival of a mutant gene in an age-structured, diploid, sexually-reproducing population. The aim of this paper is to derive such an expression and to relate its properties to the type of evolutionary argument mentioned above.

* Present address: School of Biological Sciences, University of Sussex.

† This work was done while this author was visiting the Department of Probability and Statistics, University of Sheffield.

2. PROBABILITY OF SURVIVAL OF A MUTANT GENE

Our method is an extension of the standard branching process technique to the case of a mutant gene introduced into a large, age-structured population. We will mostly work with a discrete age-class model of the type introduced by Leslie (1945). Only individuals of reproductive and pre-reproductive age need be considered. Let unity be the index of the birth age-class, b that of the age of first reproduction, and d that of the age of last reproduction. Let p_x be the chance of survival of an individual from age x to $x+1$, and l_x be the chance of survival from conception to age x ($l_x = \prod_{y=1}^{x-1} p_y$; $l_1 = 1$). We shall adopt the convention that $p_d = l_{d+1} = 0$, since we are not interested in individuals past reproductive age. Let m_x be half the expected number of offspring at age x (we are considering either a monoecious species or one where demographic differences between the sexes can be assumed to be absent).

A new mutant gene will first manifest itself in individuals of age-class 1. In a large population mating at random, it is well known that for many generations after its appearance the mutant will be carried overwhelmingly in heterozygous individuals. In such a population the problem therefore reduces to one of finding the probability of survival of the line descended from a single individual of age-class 1, with the life history characteristics of the heterozygote for the mutant gene. We shall write this probability as u. If we count all the progeny produced by a given individual during its life-time as belonging to the same 'generation,' it is easily seen that the probability of extinction, $q = 1-u$, is given as the smallest value of z in the interval $0 \leqslant z \leqslant 1$ which satisfies the standard branching process equation:

$$h(z) = z, \tag{1}$$

where $h(z)$ is the generating function of the distribution of the life-time heterozygous offspring number, of individuals heterozygous for the mutant gene.

It follows from standard theory that $u > 0$ if and only if the mean number of offspring, $M = \Sigma l_x m_x$, is greater than one. This is also the condition for the intrinsic rate of increase, r, to be positive, where r is defined as the real number which satisfies the equation

$$\Sigma e^{-rx} l_x m_x = 1. \tag{2}$$

The functional form of $h(z)$ can be obtained as follows. Let the generating function for the distribution of heterozygous offspring produced by a heterozygote aged x be $h_x(z)$. (If the generating function for all types of offspring is $g_x(z)$, $h_x(z) = g_x(\frac{1}{2} + \frac{1}{2}z)$.) Assuming that, for a parent who has survived to a given age, the offspring distributions for different, earlier ages are independent, the generating function for the distribution of offspring produced after attaining age b by an individual aged x ($x \geqslant b$) is

$$H_x(z) = \prod_{y=b}^{x} h_y(z). \tag{3}$$

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By partitioning the life-history into disjoint events, it is easy to see that

$$h(z) = (1-l_b)+\Sigma(l_x-l_{x+1})H_x(z). \tag{4}$$

In the important case when the offspring distribution for each age-class is Poisson, the survival probability, u, is thus given as the appropriate root of equation (5)

$$(u-l_b)+\Sigma(l_x-l_{x+1})e^{-M_x u}=0, \tag{5}$$

where

$$M_x = \sum_{y=b}^{x} m_y.$$

From Jensen's inequality (Feller, 1966, p. 151) applied to the convex function $e^{-(1-z)M_x}$ we find from equations (1), (4) and (5) that $h(z)$ is strictly greater than $e^{-(1-z)M}$ in all age-structured models with a Poisson distribution in each age-class. Hence the survival probability in this case is always strictly less than the survival probability for the non-overlapping generation model with a Poisson offspring distribution and the same mean. This effect can be fairly substantial, as is shown by numerical calculations. For example, with demographic data on an 1830 cohort of French women (Jacquard, 1974, Chap. 7) M is 1·02, with a u of 0·013, assuming a Poisson distribution for each age-class. This is about sixty per cent of the value for a discrete generation model with the same mean.

For u close to 0 and M close to 1, equation (1) can be approximated (e.g. Ewens, 1969, p. 80) to give

$$u \approx 2(M-1)/V, \tag{6}$$

where V is the variance of the overall offspring distribution. (In the case of a Poisson distribution for each age-class, $V \approx \Sigma(l_x-l_{x+1})\,M_x^2$ when $M \approx 1$.)

Equation (6) enables u to be related to the intrinsic rate of increase of the mutant heterozygotes as follows. When $M \approx 1$, r is given by the approximate expression

$$r \approx (M-1)/T, \tag{7}$$

where $T = \Sigma_x l_x m_x$, and is a rough measure of the generation time of the mutant. u and r are thus related by the equation

$$u \approx 2rT/V. \tag{8}$$

It will be seen from equations (6) and (8) that small changes in M and r alone have much bigger effects on u than changes in V or T alone (for small u, and $M \approx 1$). This implies that the probability of survival of a mutant gene of small effect in a near-stationary population is largely determined by its effect on M or, equivalently, r. Since most populations in nature are probably regulated by density-dependent factors, it is not unreasonable to assume stationary population size in general.

3. LIFE-HISTORY IMPLICATIONS

The results of the last section justify (as an approximation) the procedure of using r in arguments concerning the evolution of life-history phenomena (e.g. Lewontin, 1965; Hamilton, 1966; Gadgil & Bossert, 1970), as far as stationary populations are concerned. Similarly, the work of Williams (1957), which is based on M, is given a genetic basis. Charlesworth (1973) pointed out that such arguments ought strictly to be based on survival probabilities of mutant genes, advanced a crude demonstration that these are determined by the effects of the genes on r. This depended on the idea that the deterministic rate of increase in gene frequency away from zero should determine the probability of survival of a gene, and this rate of increase could in turn be shown to depend on r. As far as they go, the above results agree with this conclusion.

Some authors have, however, considered the problem of the evolution of life-histories in a colonizing environment, where the population is increasing rapidly. In such cases, it is no longer reasonable to assume $u \approx 0$, and it is extremely difficult to obtain an explicit expression such as equation (6). Some insight into the relative evolutionary advantages of genes affecting different parts of the life-cycle, on the lines of the discussions of Hamilton (1966) and Charlesworth (1973), can be obtained as follows. Consider an initial population with $r > 0$. If a new mutant with no effect on the life-history is introduced into this population, it will have a non-zero chance of survival u given by equations (1) and (4), using the l_x and m_x values for the initial population. A gene which increases survival or fecundity will have chance of survival $u^* > u$. The difference, $u^* - u$, measures the contribution of natural selection to the probability of establishment of this gene in the population. For genes of small effect, $u^* - u$ can be approximated adequately by the total differential $\mathrm{d}u$, given the effects of the gene on fecundity ($\mathrm{d}m_x$) and on survival ($\mathrm{d}p_x$). It is therefore of interest to evaluate the partial derivatives of u with respect to the variables p_x and m_x, and to compare their values for different x's, on lines similar to the analyses of Hamilton (1966) and Goodman (1971) of the partials of r.

(i) *Partials of u with respect to m_x*

Using the rule for the differentiation of an implicit function, equations (1) and (4) yield the result

$$\frac{\partial u}{\partial m_x} = -\frac{1}{K}\frac{\partial h}{\partial m_x}$$

$$= -\frac{1}{Kh_x}\frac{\partial h_x}{\partial m_x}\sum_{y=x}^{d}(l_y - l_{y+1})H_y, \qquad (9)$$

where

$$K = 1 - \frac{\partial h}{\partial z}.$$

From the shape of the graph of $h(z)$ against z, we have $K > 0$. It is evident from equation (9) that the relation of $\partial u/\partial m_x$ to x will in general depend on the behaviour

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of $\partial h_x/\partial m_x$. In the case of a Poisson distribution for each age-class, equation (9) simplifies to

$$\frac{\partial u}{\partial m_x} = \frac{u}{K}\sum_{y=x}^{d}(l_y - l_{y+1})e^{-uM_y} \quad (u>0). \tag{10}$$

When the demographic parameters of the population are such that u approaches zero, equation (10) breaks down since both top and bottom of the right hand side become 0. If we expand equation (1) in a Taylor's series about the point $z = 1$ ($u = 0$) and combine terms, we have

$$K = 1 - h'(z) = \tfrac{1}{2}uh''(1) + o(u).$$

Letting u approach 0 in the Poisson case then gives the limiting value

$$\frac{\partial u}{\partial m_x} = \frac{2l_x}{\Sigma(l_y - l_{y+1})M_y^2}. \tag{11}$$

$\partial u/\partial m_x$ thus has the same shape as l_x when u is very close to 0, provided the offspring distributions are Poisson. (The same can be shown to be true for geometric offspring distributions.)

These properties of $\partial u/\partial m_x$, for the case of Poisson offspring distributions, are similar to those derived by Hamilton (1966) for the partial derivatives of r; they imply that genes increasing fecundity have a greater chance of incorporation into the population if they act early rather than late in the life-cycle, other things being equal. Equation (10) implies that, at least for a Poisson distribution for each age-class, $\partial u/\partial m_x$ falls off faster with increasing x, the higher u. Similarly, high mortality means a high rate of decline of $\partial u/\partial m_x$.

(ii) *Partials of u with respect to log p_x*

Hamilton (1966) argued that it was biologically more meaningful to deal with partial derivatives with respect to log p_x rather than p_x itself, since independent effects are more likely to be additive on a log scale. We shall therefore consider $\partial u/\partial \log p_x$ here.

(a) *Pre-reproductive ages* ($x < b$)

For $u > 0$, we have:

$$\frac{\partial u}{\partial \log p_x} = \frac{1}{K}\left((l_b - \sum_{y=b}^{d}(l_y - l_{y+1})H_y)\right). \tag{12}$$

When $u \approx 0$,

$$\frac{\partial u}{\partial \log p_x} \approx \frac{M}{K^*}, \tag{13}$$

where

$$K^* = \tfrac{1}{2}h''(1).$$

These expressions imply that, as with the corresponding partials of r (Hamilton, 1966), it is indifferent at what pre-reproductive age genes affecting survivorship act.

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(*b*) *Reproductive ages* ($b \leqslant x \leqslant d$)

For $u > 0$ we have

$$\frac{\partial u}{\partial \log p_x} = \frac{1}{K}\left(l_{x+1} H_x - \sum_{y=x+1}^{d} (l_y - l_{y+1}) H_y,\right), \tag{14}$$

and for $u \approx 0$:

$$\frac{\partial u}{\partial \log p_x} \approx \frac{1}{K^*} \sum_{y=x+1}^{d} l_y m_y. \tag{15}$$

Equation (15) shows that, in a stationary population, $\partial u/\partial \log p_x$ is a decreasing function of x for all reproductive ages. The same is true for populations with $u > 0$; the difference, Δ_x, between the partials for x and $x+1$ is given by

$$\Delta_x = \frac{l_{x+1} H_x}{K}(1 - h_{x+1}), \tag{16}$$

which is always positive or zero.

Provided there is a non-zero probability of producing offspring in each age-class between b and d, it follows that $\partial u/\partial \log p_x$ is a strictly decreasing function of x. The qualitative properties of $\partial u/\partial \log p_x$ are thus identical with those of $\partial r/\partial \log p_x$, derived by Hamilton (1966), and his conclusions concerning the evolution of senescence can thus be justified genetically in terms of u rather than r.

It may be noted that equations (11), (13) and (15) confirm the conclusion from equations (6) and (8) that, for populations with $M \approx 1$, the effect of a gene on u is determined largely by its effect on M (or r), provided that its effect is small. Apart from a constant of proportionality which is the same for each x, the values of the derivatives of u are the same as those of M.

4. DISCUSSION

The utility of the partial derivatives of u as predictors of the direction of evolutionary change in a life-history may be viewed in the following way. Suppose that we imagine a supply of mutants at independent loci which enter the population from time to time and which affect, say, fecundity. Provided that a significant fraction of these mutants have effects on fecundity which are restricted to only some of the possible age-classes, that there are no physiological constraints on changes in the m_x (e.g. an increase in m_x causing a decrease in m_{x+1}), and that the mutants occur randomly with respect to age-specific effects on fecundity, then the expected increases in m_1, m_2 ..., m_d (after enough evolutionary time had elapsed for some small changes in the life-history to have taken place) will be as $\partial u/\partial m_1$: $\partial u/\partial m_2$ .... : $\partial u/\partial m_d$. In other words, for small enough changes for a differential approximation to be adequate, fecundity is expected to change in the direction of the gradient vector of u with respect to the m_x's. (Mathematically, this corresponds to the direction of the gradient vector being the direction of the maximum directional derivative of a function at a point.) A similar result will obviously hold for the log p_x.

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In actual fact, as discussed by such authors as Hamilton (1966) and Gadgil & Bossert (1970), physiological restrictions of the type referred to above must play a very important role in determining the direction of evolution of a life-history. It is necessary to postulate such effects in order to explain why, for example, organisms do not have their maximum fecundity at birth, as predicted by the above considerations applied to equation (9). Such constraints can be allowed in this approach by taking functional relationships between, for example, m_x and m_{x+1} or p_{x+1} into account in evaluating partial derivatives of u. In certain circumstances, the constraints may lead to the existence of one or more life histories which are 'evolutionarily stable strategies' in the sense of Maynard Smith (1971) (cf. Gadgil & Bossert, 1970). Such a life-history is characterized by having grad $u = 0$, and higher derivatives which satisfy the standard partial derivative test for a relative maximum.

In a density-regulated population where M is held constant at 1 at equilibrium, a given life-history will be evolutionarily stable if and only if M is at a maximum with respect to variations in the non-density-dependent life-history parameters, taking the physiological constraints into account. This follows from the standard condition that $u > 0$ if and only if $M > 1$. In determining whether a given life-history in a density-regulated population is evolutionarily stable, we therefore examine the appropriate partial derivatives of M. They should be computed with the density-dependent parameters treated as constants and with the physiological constraints having been introduced. They should be evaluated using the values of the density-dependent parameters which make $M = 1$ for the life-history under investigation.

The results derived above demonstrate that the qualitative behaviour of the partials of u as x increases is similar to that of the partials of r. For u and r zero, their partials behave identically, but when u is non-zero, the formulae for the partials of u are not identical with those of r (depending partly on the class of offspring distribution assumed for each age-class), and it is therefore possible that the response of u to a mutation affecting the life history in a complex manner might be different from that of r.

It is thus of some interest to examine the partial derivatives of u and r in concrete cases. Fig. 1 shows their values for two human populations, one rapidly growing and with high mortality (the Taiwan population), and the other almost stationary and with low mortality (the U.S. population). It will be seen that the graphs for u and r are very similar for the U.S. population, but not quite as similar in the Taiwan population. In either case there would be no serious error in using r (as has been the practice in the past) for calculations of the effect of natural selection on the life-history. However, there is no more difficulty in doing numerical work with u rather than r. Since u has a more direct relation with the effectiveness of natural selection, we would suggest using it rather than r in future theoretical studies of the evolution of life-histories in colonizing environments, analogous to those of Lewontin (1965).

All our conclusions have been expressed in terms of a discrete age-class model.

There is no difficulty in deriving analogues to equations (1) and (3) with a continuous time model. Let l_x be the probability of living to age x, as before, and $\mu_x dx$ and $m_x dx$ be the probabilities of dying and producing an offspring respectively,

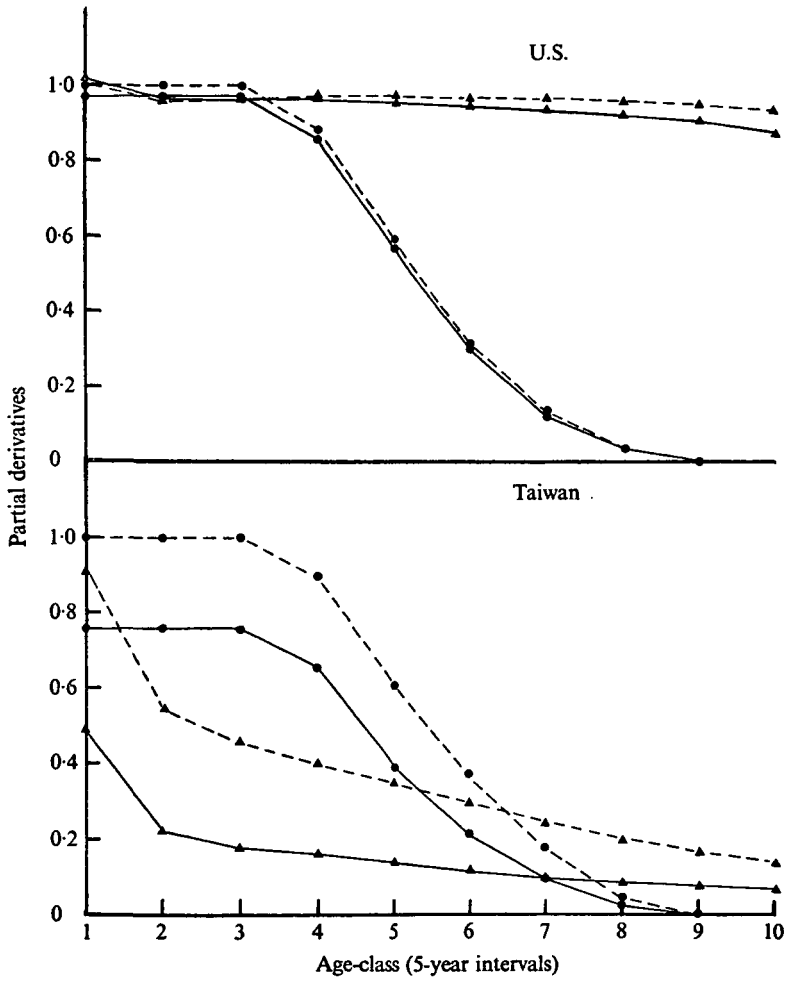

Fig. 1. Partial derivatives of u (dashed lines) and r (full lines) with respect to m_x (triangles) and $\log p_x$ (circles), using census data for the U.S. population of 1939–41 (Grenville, 1946) and the Taiwan population of 1906 (Hamilton, 1966). A Poisson distribution of offspring is assumed for each age-class.

in the age interval x to $x+dx$. On the assumption of independent offspring distributions at different ages, the offspring distribution of individuals who live to age x and die in the interval x to $x+dx$ is a Poisson distribution with parameter

$$M_x = \int_b^x m_x \, dy.$$

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It follows that the overall probability generating function for the life-time offspring distribution is

$$h(z) = (1-l_b) + \int_b^d l_x \mu_x \, e^{-(1-z)M_x} dx. \tag{17}$$

This can be substituted in equation (1) to find u.

Calculations of the sensitivity of u to small changes in μ_x and m_x can be carried out on the lines of Hamilton's (1966) treatment of r, and yield formulae analogous to those derived above for the discrete age-class model, with integration replacing summation.

CORRECTION

Genetical Research **23**, pp. 259–280 (1974).

Inversion polymorphism in a two-locus genetic system

By Brian Charlesworth

Page 263: the vector $\mathbf{c}'$ should be multiplied by $\hat{y}$.

Row 1 of the matrix **A** should be multiplied by $\hat{z}$, row 2 by $\hat{x}_2$, etc.

The determinants $\det_1$, $\det_2$, etc. should be multiplied by $\hat{y}/\hat{z}$.

Page 264: the right hand side of equation (7) should be $-\hat{y}\hat{x}_4 \, w_{14}/\hat{z}\hat{w}$.

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