

# Generalizing Fisher's "reproductive value": Overlapping and nonoverlapping generations with competing genotypes†

(dilute systems/homogeneous functions/Hardy-Weinberg model/biparental genetics)

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**ABSTRACT** How to go beyond Fisher's 1930 linear eigenvector definition of reproductive value has been established for dilute systems whose dynamic relations are first-degree-homogeneous functions so that intensive ratios are scale-free. Here such an extension is applied to standard mendelian models. It is shown that, aside from singular cases like that of the Hardy-Weinberg razor's-edge labile equilibrium, such general systems are irreducibly nonlinear and admit of reproductive-value functions that are calculable only in an infinite number of steps.

Before an age-structured dynamic system in population genetics settles down into its state of balanced exponential growth or stationarity, it may first display quasi-oscillatory transients that depend on its initial conditions. The concept of *reproductive value* was introduced by Fisher (1, Chap. 2) to summarize how the ultimate level of the system's growth mode depends upon the initial values of the separate phase variables. Keyfitz (2) represents one valuable use of essentially this concept in his measurement of the "momentum" of a population that suddenly shifts from high-growth fertility to stationary-growth fertility. How high the population will continue to grow, in the ensuing several decades required to iron out the distortions in the system's initial age distribution inherited from past high fertility, can be estimated by Keyfitz's ingenious variant of the Fisher concept.

A possible purpose of reproductive value is to provide an appropriate surrogate model that is *immediately* in equilibrium and replaces the more complicated true system's initial gyrations and transients. Thus, consider a simple diploid model with AA, aa, and Aa (or aA) numbers, involving *overlapping generations and age-phased differences in mortality and fertility*. Then the simple Hardy-Weinberg property is lost in which the proportions of AA, aa, and Aa genotypes settle down *immediately* to their equilibrium values. Can we perhaps hope to approximate from the beginning such a system's ultimate equilibrium proportions and scale by means of some clever (*finutely*-calculable!) weightings of the initial age-and-genotype classes along the lines of Fisher's reproductive-value concept or from its patent generalizations in Samuelson (3, 4)? Some such hope seems to have been nurtured, but detailed investigation of its practicality has been neglected in the two generations since Fisher's classic 1930 treatise. The present paper explores the application of reproductive value to some standard nonlinear models of simplest mendelian genetics. The limitations of the concept, as well as its successes, are revealed.

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## The Hardy-Weinberg case

First, consider the simplest monoecious model of nonoverlapping generations, involving genotypes AA, aa, and Aa or aA. If all genotypes have the same fertilities and mortalities and mating is independently random rather than assortative, the Hardy-Weinberg law will obtain and the system will settle down in one generation to its ultimate genotype proportions. The common mortalities and fertilities could depend on the size of the total adult population,  $N(t)$ , relative to the carrying capacity of the environment without necessarily affecting this truth about *intensive* proportions or ratios; moreover, the *extensive* dynamic relation relating total  $N(t+1)$  to  $N(t)$  could be such that ultimately the system's malthusian parameter of growth dampens down to zero. Until a sequel, such density-dependent effects will be ignored in order to parallel Fisher's original derivation of reproductive value.

Denote the respective numbers at time  $t$  of adults of types AA, aa, and Aa (aA is included with Aa) by  $[N_{AA}(t), N_{aa}(t), N_{Aa}(t)]$ . The total population,  $N(t)$ , is defined at each time by the relations

$$\begin{aligned} N &= N_{AA} + N_{aa} + N_{Aa} \\ &= (N_{AA} + \frac{1}{2}N_{Aa}) + (N_{aa} + \frac{1}{2}N_{Aa}) \\ &= N_A + N_a = (p + q)N. \end{aligned} \quad [1]$$

The totals of A and a alleles,  $N_A$  and  $N_a$ , are implicitly defined in Eqs. 1, as are the intensive proportions.

Under completely nonassortative mating, with no differential selective effects on fertilities or mortalities, the number of births of type AA and of adults of that type will each be proportional to the product  $N_A^2$ ; those of type aa will be proportional to  $N_a^2$ ; those of type Aa will be proportional to  $2N_A N_a$ . The factor of proportionality appropriate for adults of the next generation, which will itself be the product of fertility and mortality-survivorship factors, can be written as  $\lambda/N$ . (If increases in  $N$  lower  $\lambda$  because of saturation effects of higher densities in a limited environment,  $\lambda$  is short for  $\lambda[N]$ , where  $\lambda'[N] \leq 0$ . In a sequel, the effects on the concept of reproductive value of having  $\lambda[N]$  drop below  $\lambda[0] = \lambda$  will be analyzed in detail.)

Our assumptions lead to the following dynamic recursion relations for successive generations of  $[N_{AA}(t), N_{aa}(t), N_{Aa}(t)]$ , where the operator symbol  $E$  is used to shorten the written difference equations by being given the meaning  $EN_{AA} = N_{AA}(t+1)$ ,

$$EN_{AA} = N^{-1}[N_{AA} + \frac{1}{2}N_{Aa}]^2\lambda \quad [2.1]$$

$$EN_{aa} = N^{-1}[N_{aa} + \frac{1}{2}N_{Aa}]^2\lambda \quad [2.2]$$

$$EN_{Aa} = 2N^{-1}[N_{AA} + \frac{1}{2}N_{Aa}][N_{aa} + \frac{1}{2}N_{Aa}]\lambda. \quad [2.3]$$

Under our assumptions of common fertilities and mortalities, the total population satisfies a simple relation that is indepen-

† This is paper no. 3 in a series. Paper no. 2 is ref. 3.

dent of its relative genotype composition: adding the above three relations yields

$$EN(t) = N(t)\lambda. \quad [2.4]$$

The behavior of the subaggregates is determinable from adjoining to Eq. 2.4 the following relation deducible from Eqs. 2.1-2.3:

$$Ep(t) = p(t), \quad t \geq 0$$

$$EN_{AA}(t) = N(t)p(t)^2, \quad EN_{aa}(t) = N(t)[1 - p(t)]^2. \quad [2.5]$$

Eqs. 2.5 are the embodiment of what is called the Hardy-Weinberg law, in which the system settles down in one generation to its stable ( $p^2, q^2, 2pq$ ) proportions (see for example ref. 5). From them and Eq. 2.4 we can write down at once the system's explicit solution, which grows from the beginning proportionally to the geometric progression  $(1 + r^*)^t$ :

$$N(t) = (1 + r^*)^t N^0, \quad t \geq 0; \quad 1 + r^* = \lambda \quad [3.1]$$

$$N_{AA}(t) = p(0)^2 (1 + r^*)^t N^0$$

$$N_{aa}(t) = q(0)^2 (1 + r^*)^t N^0$$

$$N_{Aa}(t) = 2p(0)q(0)(1 + r^*)^t N^0 \quad [3.2]$$

$$N_A(t) = p(0)(1 + r^*)^t N^0, \quad p(0) + q(0) = 1$$

$$N_a(t) = q(0)(1 + r^*)^t N^0. \quad [3.3]$$

This simple Hardy-Weinberg case has no need for a surrogate system based upon some prior calculated reproductive value. It is its own surrogate. The question is whether systems that are not so degenerately simple as the Hardy-Weinberg case can be artificially given its simplicity by means of artful calculation of fisherine reproductive values.

### Nonuniform fertilities and mortalities

The general case will involve different fertilities and mortalities for the different genotypes, ( $\lambda_{AA}, \lambda_{aa}, \lambda_{Aa}$ ) rather than the common  $\lambda$  of the Hardy-Weinberg example. For almost all values of these three  $\lambda$ s, the system's asymptotic growth mode will have its [ $n_{AA}^*, n_{aa}^*, n_{Aa}^*; p^*, 1 - p^*$ ] proportions generally independent of the positive initial conditions [ $N_{AA}^0, N_{aa}^0, N_{Aa}^0$ ]. Hence, essentially one reproductive-value function  $v[N_{AA}^0, N_{aa}^0, N_{Aa}^0]$ , will be definable. Now the general dynamic relations become

$$EN_{AA} = N^{-1}N_{AA}^2\lambda_{AA} = N^{-1}[N_{AA} + \frac{1}{2}N_{Aa}]^2\lambda_{AA}$$

$$EN_{aa} = N^{-1}N_{aa}^2\lambda_{aa} = N^{-1}[N_{aa} + \frac{1}{2}N_{Aa}]^2\lambda_{aa}$$

$$EN_{Aa} = 2N^{-1}N_{Aa}N_a\lambda_{Aa}$$

$$= 2N^{-1}[N_{AA} + \frac{1}{2}N_{Aa}][N_{aa} + \frac{1}{2}N_{Aa}]\lambda_{Aa}. \quad [4]$$

Relations 4 are like those met in standard mendelian genetics, as in ref. 5, but with this generalization: the total number,  $N$ , is not assumed to necessarily stay the same from generation to generation; how the total  $N(t)$  changes will ultimately depend upon how large  $N(t)$  is in comparison with the environment's carrying capacity; but so long as  $N(t)$  is small enough so that the system can be regarded as dilute, how fast  $N(t)$  grows depends only upon the proportions of the different genotypes (or, under random mating, on the proportions of the gene totals).

In terms of total genes as phase variables, [ $N_A(t), N_a(t)$ ], the dynamic laws of motion of the system 4 can be written under random mating as

$$EN_A = [N_A + N_a]^{-1}N_A[N_A\lambda_{AA} + N_a\lambda_{Aa}]$$

$$EN_a = [N_A + N_a]^{-1}N_a[N_a\lambda_{aa} + N_A\lambda_{Aa}]. \quad [5]$$

Replacing [ $N_A, N_a$ ] by phase variables

$$N = N_A + N_a, \quad Z = N_A - N_a; \quad z = Z/N$$

$$N_A = \frac{1}{2}[N + Z], \quad N_a = \frac{1}{2}[N - Z] \quad [6]$$

we have as an equivalent to Eqs. 5

$$Ez = \frac{[1 + z]^2\lambda_{AA} - [1 - z]^2\lambda_{aa}}{[1 + z]^2\lambda_{AA} + [1 - z]^2\lambda_{aa} + 2[1 + z][1 - z]\lambda_{Aa}} = \psi(z) \quad [6.1]$$

$$EN = \frac{1}{4}N\{[1 + z]^2\lambda_{AA} + [1 - z]^2\lambda_{aa} + 2[1 - z^2]\lambda_{Aa}\}. \quad [6.2]$$

Eq. 6.1 is an autonomous difference equation for  $z(t)$  alone. To solve for a stationary solution,  $z(\infty)$ , we equate  $Ez$  and  $z$  in Eq. 6.1. The resulting cubic equation in  $z$  has three real roots:  $(1, -1, z^*)$ . The first two correspond to axis solutions where but one of the homozygous genotypes obtains:

$$N_{aa}(t) \equiv 0 \equiv N_{Aa}(t), \quad [z(t), p(t), q(t)] \equiv [1, 1, 0] \quad [7.1]$$

$$N_{AA}(t) \equiv 0 \equiv N_{Aa}(t), \quad [z(t), p(t), q(t)] \equiv [-1, 0, 1]. \quad [7.2]$$

Provided the third root, call it  $z^*$ , falls on the interval  $-1 < z < +1$ , we have genotypes coexisting in equilibrium. The equilibrium will be stable:

$$\lim_{t \rightarrow \infty} z(t) = z^* = \psi(z^*) \text{ if } -1 < \psi'(z^*) < 1. \quad [8.1]$$

The ultimate geometric rate of growth of  $N(t)$ , proportional to  $(1 + r^*)^t$ , is at a rate given by

$$1 + r^* = \frac{1}{4}\{[1 + z^*]^2\lambda_{AA} + [1 - z^*]^2\lambda_{aa} + 2[1 + z^*][1 - z^*]\lambda_{Aa}\} \quad [8.2]$$

$$\lim_{t \rightarrow \infty} \frac{N(t)}{(1 + r^*)^t} = v[N_{AA}^0, N_{aa}^0, N_{Aa}^0], \text{ by definition} \quad [8.3]$$

$$\lim_{t \rightarrow \infty} [N_A(t), N_a(t)](1 + r^*)^{-t} = [p^*, q^*]v[N_{AA}^0, N_{aa}^0, N_{Aa}^0] = [\frac{1}{2} + z^*, \frac{1}{2} - z^*]v[N_{AA}^0, N_{aa}^0, N_{Aa}^0] \quad [8.4]$$

$$\lim_{t \rightarrow \infty} [N_{AA}(t), N_{aa}(t), N_{Aa}(t)](1 + r^*)^{-t} = [n_{AA}^*, n_{aa}^*, n_{Aa}^*]v[N_{AA}^0, N_{aa}^0, N_{Aa}^0] = [(1 + z^*)^2\lambda_{AA}, (1 - z^*)^2\lambda_{aa}, 2(1 + z^*)(1 - z^*)\lambda_{Aa}] \times \frac{v[N_{AA}^0, N_{aa}^0, N_{Aa}^0]}{4(1 + r^*)}. \quad [8.5]$$

### Case of heterozygous fitness

An interesting example of the previous section's analysis is the case where the heterozygous state,  $Aa$ , is superior in fitness to either of the homozygous states,  $AA$  or  $aa$ . We then expect that there will be a stable ultimate equilibrium with both  $A$  and  $a$  coexisting. It will simplify the arithmetic to set  $\lambda_{AA}$  and  $\lambda_{aa}$  equal, a transparent symmetric case. Thus, suppose

$$\lambda_{AA} = \lambda_{aa} = \lambda < \lambda_{Aa} = \lambda\gamma, \quad \gamma > 1. \quad [9]$$

From the symmetry of  $AA$  and  $aa$ ,

$$[z^*, p^*, q^*] = [0, \frac{1}{2}, \frac{1}{2}]$$

$$[n_{AA}^*, n_{aa}^*, n_{Aa}^*] = [\frac{1}{2}, \frac{1}{2}, \gamma](1 + \gamma)^{-1} \quad [10.1]$$

$$1 + r^* = \frac{1}{2}(1 + \gamma)\lambda > \lambda \quad [10.2]$$

$$v[N_{AA}^0, N_{aa}^0, N_{Aa}^0] \equiv v[N_{aa}^0, N_{AA}^0, N_{Aa}^0]. \quad [10.3]$$

If the heterozygous state had lacked fitness,  $\gamma < 1$  and  $p^* = q^* > \frac{1}{2}$ , the interior equilibrium would have represented an

*unstable* equilibrium: any slightest perturbation of  $N_{AA}/N_{aa}$  away from unity would have been followed by further movement in the same direction—until only one homozygous genotype remained.

From its intrinsic definition in Eq. 8.3,  $v[N_{AA}(t), N_{aa}(t), N_{Aa}(t)] = V(t)$  is a scalar that grows from the beginning at the percentage rate  $(1 + r^*)$ :

$$V(t + 1) = (1 + r^*)V(t). \quad [11.1]$$

Similarly, the following surrogate vector grows like  $(1 + r^*)^t$ :

$$\begin{aligned} [n_{AA}^*, n_{aa}^*, n_{Aa}^*]V(t) &= V(t) \\ V(t + 1) &= (1 + r^*)V(t). \end{aligned} \quad [11.2]$$

One interprets this as a surrogate system, which replaces the true  $[N_{AA}^0, N_{aa}^0, N_{Aa}^0] = N^0$  and implied true  $N(t)$  by new fisherine initial conditions that are in equilibrium proportions,  $V(0)$ ; after the period of transient delay, this surrogate system ultimately closely approximates the original system—in the vectoral sense that

$$\lim_{t \rightarrow \infty} \frac{N(t) - V(t)}{(1 + r^*)^t} = 0 \quad [12]$$

However, we were not able to use this concept of reproductive value  $V(0)(1 + r^*)^t$  to *learn* what the equilibrium will be: rather, it was the case that *after* we had *already* learned what the equilibrium was we were then able to arrive at Eq. 8.3's definition of reproductive value. It remains true that the recipe for cooking the pie of reproductive value must begin with the instruction: First, you must catch your bird.

### Biparental genetic models

Now we can come to grips with reproductive value in a two-sex model where males,  $M(t)$ , are of respective genotypes  $AA$ ,  $aa$ , or  $Aa$ ; and where females,  $F(t)$ , are likewise. Using letters with obvious mnemonic properties to denote sex, we write down the many convenient notational identities:

$$\begin{aligned} N &= M + F = (m + f)N, f = 1 - m \\ &= [M_{AA} + M_{aa} + M_{Aa}] + [F_{AA} + F_{aa} + F_{Aa}] \\ &= [m_{AA} + m_{aa} + m_{Aa}]N + [f_{AA} + f_{aa} + f_{Aa}]N \\ &= [F_{AA} + \frac{1}{2}F_{Aa}] + [F_{aa} + \frac{1}{2}F_{Aa}] \\ &\quad + [M_{AA} + \frac{1}{2}M_{Aa}] + [M_{aa} + \frac{1}{2}M_{Aa}] \\ &= [M_A + M_a] + [F_A + f_a] = [m_A + m_a + f_A + f_a]N \\ &= N_A + N_a = [n_A + n_a]N \\ &= N_{AA} + N_{aa} + N_{Aa} = [n_{AA} + n_{aa} + n_{Aa}]N. \end{aligned} \quad [13]$$

To avoid the complexities involved with natural selection for the male-female sex ratio at birth,  $g/(1 - g)$ , I shall usually assume that  $g$  is the same parameter for all genotypes of the parental matings and offsprings. I begin by assuming no overlapping of generations and that all mating is strictly independent-random.

The dynamic relations for the six phase variables  $[M_{AA}(t), \dots, F_{Aa}(t)]$  now are assumed to be

$$\begin{aligned} EN_{AA} &= g^{-1}EM_{AA} = (1 - g)^{-1}EF_{AA} = N^{-1}M_A F_A \lambda_{AA} \\ EN_{aa} &= g^{-1}EM_{aa} = (1 - g)^{-1}EF_{aa} = N^{-1}M_a F_a \lambda_{aa} \\ EN_{Aa} &= g^{-1}EM_{Aa} = (1 - g)^{-1}EF_{Aa} \\ &= N^{-1}[M_A F_a + M_a F_A] \lambda_{Aa}. \end{aligned} \quad [14]$$

Deducible from Eqs. 14 are

$$\begin{aligned} EN &= N[m_A f_A \lambda_{AA} + m_a f_a \lambda_{aa} + (m_A f_a + m_a f_A) \lambda_{Aa}] \\ &= N\theta(m_A, m_a, f_A; \lambda_{AA}, \lambda_{aa}, \lambda_{Aa}) \text{ for short, } t \geq 0 \\ &= Ng(1 - g)[n_A^2 \lambda_{AA} + (1 - n_A)^2 \lambda_{aa} \\ &\quad + 2n_A(1 - n_A) \lambda_{Aa}], t \geq 1 \end{aligned} \quad [15.1]$$

$$\begin{aligned} En_A &= \frac{m_A f_A \lambda_{AA} + \frac{1}{2}(m_A f_a + m_a f_A) \lambda_{Aa}}{\theta(m_A, m_a, f_A; \lambda_{AA}, \lambda_{aa}, \lambda_{Aa})}, t \geq 0 \\ &= \frac{n_A^2 \lambda_{AA} + n_A(1 - n_A) \lambda_{Aa}}{n_A^2 \lambda_{AA} + (1 - n_A)^2 \lambda_{aa} + 2n_A(1 - n_A) \lambda_{Aa}}, t \geq 1 \\ &= \phi[n_A] \text{ for short; } |\phi'[n_A]| < 1. \end{aligned} \quad [15.2]$$

Relation 15.2 is an autonomous first-order difference equation for  $n_A(t)$  alone, just as Eq. 6.1 was for  $z(t)$ ; indeed, relations exactly like 15.1 and 15.2 could have been written in place of 6.2 and 6.1 for the monoecious case. For, as is noted by Crow and Kimura (5, P. 45), so long as the relevant sex ratios are uniform, the dioecious case can be reduced *after one extra generation* to the monoecious case. Therefore, we need not duplicate the details of our earlier analysis. Thus, greater fitness of the heterozygous state will lead to a unique equilibrium of coexisting genotypes, approached asymptotically over infinite time from any initial conditions that involve positive  $(M_A, F_A)$  or  $(M_a, F_a)$ . The results of Eqs. 8 apply once we follow obvious steps in calculating  $[N_{AA}(1), N_{aa}(1), N_{Aa}(1)]$  from  $[M_{AA}(0), M_{aa}(0), M_{Aa}(0), F_{AA}(0), F_{aa}(0), F_{Aa}(0)]$ .

Also, in the Hardy-Weinberg case when all  $\lambda$ s are equal, results just like Eqs. 2 and 3 apply—but now only after two generations rather than one. This means that the ultimate  $(p^*, q^*)$  mendelian probabilities are equal to the  $[p(1), 1 - p(1)]$  numbers; and although these are not the same as the crude  $[p(0), 1 - p(0)]$  numbers derived from pooling the originally present genotypes without respect to their partition between initial males and females, they are easily calculated in a small finite number of steps from the initial  $[m_A^0, m_a^0, f_A^0, f_a^0]$  data by use of Eqs. 15 as applied to  $t = 0$ . Hence, there could in this case be analytical profit from the concept of reproductive value.

### Linearizable cases of overlapping generations

There are some special cases where a diploid genetic model could yield to Fisher-Lotka linear eigenvector algorithms. One such is where (i) male and female mortalities are identical, (ii) the male/female sex ratio at birth is always the same  $g/(1 - g)$ , or (iii) only parents of the same age mate together and at rates independent of the numbers of persons of other ages (see ref. 6). Another is that where all who mate do so at random without regard to their respective ages and where their fertilities and sex ratio of offspring are the same at all ages of the parents. When  $B_t$  is thus linearly determined by  $(B_{t-1}, \dots, B_{t-K})$ , the 1930 Fisher concept applies. When its true nonlinear relation is perturbed only slightly away from such a singular linear case, the latter's eigenvector gives *approximate* reproductive-value weights that *approximately* wipe out initial age oscillations.

### Age-phased reproductive value

Now I face up to the fact that adults reproduce at more than one age, so that generations cannot be nonoverlapping. If there is only one parent and the system is dilute, the standard linear demographic models of Sharpe and Lotka (7) and Leslie (8) could give Fisher his simple 1930 reproductive value formulas. But when biparental reproduction is involved, none of this remains generally valid.

I now apply the methods and definitions of refs. 3 and 4 to show how reproductive value is to be properly computed for such nonlinear systems in their dilute, homogeneous stages. Begin with a dioecious, diploid model where at first only one genotype is involved. Denote the number of males at time  $t$  by  $M(x, t)$  and the number of females of age  $x'$  at  $t$  by  $F(x', t)$ . Suppose time and age are observed at discrete equally spaced intervals,  $(t = \dots, -1, 0, 1, 2, \dots)$  and  $(x, x' = 0, 1, 2, \dots, K)$ , where  $K$  is the oldest relevant age and age 0 represents new births.

As in standard demography, begin by assuming invariant age-specific mortalities for each sex (initially independent of genotype). The fraction of males newborn at age 0 who survive to age  $x$  is written as  $l_M(x)$ ; the similar fraction of surviving females is written as  $l_F(x')$ :

$$1 = l_M(0) \geq l_M(1) \geq \dots \geq l_M(K) > 0$$

$$1 = l_F(0) \geq l_F(1) \geq \dots \geq l_F(K) > 0. \quad [16]$$

Then, much as in refs. 9 and 10,

$$M(x,t) = \frac{l_M(x)}{l_M(x-\theta)} M(x-\theta, t-\theta), \quad x \geq \theta, \quad t \geq \theta$$

$$= l_M(x)M(0, t-x) = l_M(x)B_M(t-x), \quad t \geq x \quad [17.1]$$

$$F(x',t) = \frac{l_F(x')}{l_F(x'-\theta)} F(x'-\theta, t-\theta), \quad x' \geq \theta, \quad t \geq \theta$$

$$= l_F(x')F(0, t-x') = l_F(x')B_F(t-x'), \quad t \geq x'.$$

Our assumptions about fertilities cannot be so conventional, having to go beyond those of the standard one-sex demographic model. Total births of each sex at  $t$  equals the sum of the births of that sex born at  $t$  to parents of all ages  $x$  and  $x'$ :

$$B(t) = M(0,t) + F(0,t) = B_M(t) + B_F(t) \quad [17.2]$$

$$= \sum_{x=0}^K \sum_{x'=0}^K [g(x,x') + \{1 - g(x,x')\}]B(x,x',t) \quad [17.3]$$

Here  $g(x,x')$  is the fraction of births that are male born to a father of age  $x$  and mother of age  $x'$ . (Initially, genotype is considered irrelevant.) For  $x$  or  $x'$  outside the fertile ages,  $B(x,x',t) = 0$  and we have no need to define  $g(x,x')$ .

Although ages of human fathers and mothers often tend to bunch close together, it is only realistic to recognize that births to parents of ages  $x$  and  $x'$  might depend on more than their own respective numbers,  $M(x,t)$  and  $F(x',t)$ . Thus, the number of females 1 year younger than a given female will reduce her chance to mate with a male of any age. The number of infants, although each is in an infertile age, may well influence the probability of their relatives bearing offspring. Even if no one mated with a person more than one period different in age, it could still be the case that the fertility of 20 year olds could be influenced by the relative numbers of middle-aged persons. Therefore, our general fertility function must become

$$B(x,x',t+1) = f[x,x';M(0,t), \dots, M(K,t)F(0,t), \dots, F(K,t)]$$

$$= f[x,x';M(t),F(t)] \text{ for short.} \quad [17.4]$$

So long as the system remains sparse or "dilute" relative to the environment's limited resources,  $f[\ ]$  can be expected to be a first-degree-homogeneous function of all of its arguments, albeit not linear in them, i.e.,

$$f[x,x';qM(0,t), \dots, qF(K,t)] \equiv qf[x,x';M(0,t), \dots, F(K,t)], \quad q > 0. \quad [17.5]$$

The generality of  $f[\ ]$  in Eqs. 17, like that of  $f^i[\ ]$  in Eqs. 20 is more than enough to permit the usual geneticist's quasi-random-mating specialization (as in Eqs. 18). However, the generality of Eqs. 17 is not excessive: to handle the fact that humans mate with people near their own age but are affected in doing so by the number of people present of varying ages, one must go beyond the conventional mendelian formulas.

Combining Eqs. 16-17.5, we derive valid recursive relations for  $[B_M(t), B_F(t)]$ , holding after  $K$  periods have passed and all the initial living individuals have been replaced by individuals whose numbers have been obeying our postulated mortality and fertility laws:

$$B_M(t) = \Phi_M[B_M(t-1), B_M(t-2), \dots, B_M(t-K), B_F(t-1), \dots, B_F(t-K)]$$

$$= \Phi[B_M(t), B_F(t)] \text{ for short}$$

$$B_F(t) = \Phi_F[B_M(t), B_F(t)]$$

$$\Phi_M[qB_M(t), qB_F(t)] \equiv q\Phi_M[B_M(t), B_F(t)]$$

$$\Phi_F[qB_M(t), qB_F(t)] \equiv q\Phi_F[B_M(t), B_F(t)]. \quad [17.6]$$

Although an exponential-growth solution to Eqs. 17.6 is no longer guaranteed now that  $\Phi_M$  and  $\Phi_F$  are nonlinear functions and possibly no longer monotone-increasing in all of their arguments, under specifiable conditions of some plausibility there will be a stable exponential solution of the form:

$$[B_M(t), B_F(t)] = c[l, \beta^*](1 + r^*)^t. \quad [17.7]$$

Here  $[1 + r^*, \beta^*]$  are the positive roots for  $[R, \beta = B_F/B_M]$  in

$$1 = \Phi_M[R^{-1}, \dots, R^{-K}, \beta R^{-1}, \dots, \beta R^{-K}]$$

$$\beta = \Phi_F[R^{-1}, \dots, R^{-K}, \beta R^{-1}, \dots, \beta R^{-K}] \quad [17.8]$$

and  $c$  is a scalar proportional to generalized fisherine reproductive value and dependent on the system's initial conditions.

From any initial state of positive  $[M(0,0), M(1,0), \dots, F(0,0), \dots, F(K,0)]$ ,

$$\lim_{t \rightarrow \infty} \frac{B_M(t+1)}{B_M(t)} = \lim_{t \rightarrow \infty} \frac{B_F(t+1)}{B_F(t)} = 1 + r^* \quad [17.9]$$

$$\lim_{t \rightarrow \infty} \frac{N(t)}{(1 + r^*)^t} = v[M(0,0), M(1,0), \dots, M(K,0), F(0,0), \dots, F(K,0)]$$

$$= v[M(0), F(0)] \text{ for short} \quad [17.10]$$

$$\lim_{t \rightarrow \infty} \frac{M(x,t)}{M(0,t)} = l_M(x)(1 + r^*)^{-x}$$

$$\lim_{t \rightarrow \infty} \frac{F(x',t)}{F(0,t)} = l_F(x')(1 + r^*)^{-x'}. \quad [17.11]$$

In Eq. 17.10,  $N(t)$  is the sum of all individuals of all ages and sex,  $\sum_x [M(x,t) + F(x,t)]$ , and  $v[M(0), F(0)]$  is the well-defined reproduction-value function of the system, generalized to nonlinear homogeneous systems, with  $v[\ ]$  itself being first-degree-homogeneous in its arguments. Any other extensive variable of the system beside  $N$ , as for example  $M(3,t)$ , has defined for it a reproductive value function that is its appropriate equilibrium proportion times  $v[\ ]$  of Eq. 17.10.

The relations 17 provide a complete and general solution for the nonlinear, biparental case of overlapping generations. It shows that the infinite number of computations implied by Eq. 17.10 is the irreducible number. Only in special, singular razor's-edge cases that lack structural stability (and hence almost never occur in nature however frequently they appear in textbooks and treatises), like the cases given in the previous section, can the 1930 interest-rate-discount eigenvector formulas of Fisher be applicable.

An interesting nonlinear case is that special one in which (a) effective relative fertilities of each sex show a systematic invariant relationship with adult age, but where (b) the adult mating patterns are random with respect to age. Let  $[\omega_M(x), \omega_F(x)]$  be the weights of relative fertilities by age: thus  $\omega_F(40)/\omega_F(20) = 1/3$  means that one 20-year-old female is like three 40-year-old females in effective fertilities.

From these relative-fertility weightings, we derive the effective number of procreating males and females at time  $t$ ,  $W_M(t)$  and  $W_F(t)$ :

$$W_M(t) = \sum_{x=0}^K \omega_M(x)M(x,t)$$

$$W_F(t) = \sum_{x'=0}^K \omega_F(x')F(x',t). \quad [18.1]$$

Each member of the  $W_M(t)$  category is as likely to mate with any given member of the  $W_F(t)$  category as with any other, the number of births at  $t + 1$  being proportional to the product  $W_M(t)W_F(t)$ . Now we can replace Eqs. 17.3–17.4 by the special relationship

$$B(t + 1) = g^{-1}M(0,t + 1) = (1 - g)^{-1}F(0,t + 1) = \beta \frac{W_M(t)W_f(t)}{W_M(t) + W_F(t)}. \quad [18.2]$$

Adjoining to Eqs. 18.1–18.2 the unchanged mortality relations 17.2, our general recursion relations of 17.6 reduce down to

$$B(t) = \Phi[B(t - 1), \dots, B(t - K)], \quad t \geq K = q^{-1}\Phi[qB(t - 1), \dots, qB(t - K)] \quad [18.3]$$

$$= \frac{\left[ \sum_0^K W_M(x)\phi_M(x)gB(t - x) \right] \times \left[ \sum_0^K W_F(x')\phi_F(x')(1 - g)B(t - x') \right]}{\beta^{-1} \sum_0^K [W_M(x)\phi_M(x)g + W_F(x)\phi_F(x)(1 - g)]B(t - x)} \quad [18.4]$$

Then

$$\lim_{t \rightarrow \infty} \frac{B(t + 1)}{B(t)} = 1 + r^*, \quad [18.5]$$

where  $1 + r^*$  is the positive  $R$  root in

$$1 = \Phi[R^{-1}, \dots, R^{-K}] = \psi(R), \quad \psi'(R) < 0 \quad [18.6]$$

$$\lim_{t \rightarrow \infty} \frac{N(t)}{(1 + r^*)^t} = v[M(0,0), M(1,0), \dots, F(0,0), \dots, F(K,0)] \quad [18.7]$$

$$\lim_{t \rightarrow \infty} \left[ \frac{M(x,t)}{M(0,t)}, \frac{F(x,t)}{F(0,t)} \right] = [l_M(x), l_F(x)](1 + r^*)^{-x}. \quad [18.8]$$

Independently, Crow<sup>‡</sup> has proposed certain genetic variants of the scenario of Eqs. 18.

**Age-structured genotype demographics**

Now we may assume males and females of age  $x$  at time  $t$  are also characterized by their genotype:  $AA, aa, Aa, \dots$ ; or, to simplify notation, by  $A^1A^1, A^2A^2, A^1A^2, A^2A^1, A^3A^3, \dots, A^sA^s$  where  $A^iA^j$  represents the presence of alleles  $A^i$  and  $A^j$ . Now we have

$$N = \sum_{x=0}^K \left\{ \sum_{i=1}^s \sum_{j=1}^s M^{ij}(x,t) \right\} + \sum_{x'=0}^K \left\{ \sum_{i=1}^s \sum_{j=1}^s F^{ij}(x',t) \right\} = \sum_{x=0}^K \left\{ \sum_{i=1}^s M^i(x,t) \right\} + \sum_{x'=0}^K \left\{ \sum_{i=1}^s F^i(x',t) \right\}. \quad [19]$$

Always, by our convention,  $M^{ij}(x,t) = M^{ji}(x,t)$  and  $F^{ij}(x',t) = F^{ji}(x',t)$ . Now we have mortality functions by genotype:  $[l_M^i(x), l_F^i(x')]$ , with

$$M^{ij}(x,t) = l_M^i(x)M^{ij}(0,t - x) = l_M^i(x)B_M^i(t - x) F^{ij}(x',t) = l_F^i(x')F^{ij}(0,t - x') = l_F^i(x')B_F^i(t - x'). \quad [20.1]$$

Now our 17.6 fertility relations give  $B_M^i(x,x',t)$  and  $B_F^i(x,x',t)$  in terms of the vector  $[M^{11}(0,t), \dots, M^{11}(K,t), M^{12}(0,t), \dots,$

$M^{12}(K,t), M^{22}(0,t), \dots, M^{ss}(L,t), F^{11}(0,t), \dots, F^{ss}(K,t)] = [M(t), F(t)]$  for short. With prescribed mortality relations of Eqs. 20.1, we can express this last pair of vectors in terms of the past values  $[B_M^i(t - 1), \dots, B_M^i(t - K), B_F^i(t - 1), \dots, B_F^i(t - K)] = [B_M(t - x), B_F(t - x)]$  for short. Thus, for  $(i, j = 1, 2, \dots, s)$ ,

$$B_M^i(t) = \Phi_M^i [B_M(t - x), B_F(t - x)] = q^{-1}\Phi_M^i [qB_M(t - x), qB_F(t - x)] B_F^i(t) = \Phi_F^i [B_M(t - x), B_F(t - x)] = q^{-1}\Phi_F^i [qB_M(t - x), qB_F(t - x)]. \quad [20.3]$$

Under plausible regularity conditions on the  $\Phi^{ij}[\ ]$  functions, we define a stable exponential mode of asymptotic growth

$$\lim_{t \rightarrow \infty} \frac{N(t + 1)}{N(t)} = 1 + r^*, \quad \text{the positive } R \text{ root of} \quad [20.4]$$

$$B_M^i(t) = \Phi_M^i [R^{-1}B_M^1, R^{-2}B_M^1, \dots, R^{-1}B_M^s, \dots, R^{-K}B_F^s], B_F^i(t) = \Phi_F^i [R^{-1}B_M^1, R^{-2}B_M^1, \dots, R^{-1}B_M^s, \dots, R^{-K}B_F^s], \quad (i, j = 1, \dots, s) \quad [20.5]$$

$$\lim_{t \rightarrow \infty} [B_M^i(t), B_F^i(t)]N(t)^{-1} = [B_M^i, B_F^i], \quad [20.6]$$

$$\lim_{t \rightarrow \infty} \frac{N(t)}{(1 + r^*)^t} = v[M(0), F(0)], \quad [20.7]$$

etc.

The present analysis will disappoint readers of Fisher who hoped that the simplicity of his asserted “fundamental theorem of natural selection” could be restored to validity by appeal to reproductive-value weightings (as where in the 1958 edition of ref. 1, p. 38, Fisher says “. . . the ease of its [the ‘fundamental theorem’s’] interpretation may be increased by appropriate conventions of measurement. For example, the frequencies should strictly be evaluated at any instant by the enumeration, not necessarily of the census population, but of all individuals having reproductive value, weighted according to the reproductive value of each.”

The reader of the present series of papers on reproductive value will realize that, trivially special cases aside, there exist no such individual’s weighting to save the theorem. Left for another occasion is exploration of various generalizations of the reproductive-value concept in the direction of defining the approximate effect of initial conditions on penultimate behavior of the system or on its early behavior under dilute conditions, and use of approximate 1930 eigenvector reproductive value to smooth out oscillations in age deviations of systems perturbed only slightly from singular linear cases.

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1. Fisher, R. A. (1930 and 1958) *Genetical Theory of Natural Selection* (Clarendon Press, Oxford), 1st Ed. and 2nd Ed.
2. Keyfitz, N. (1971) *Demography* 8, 71–80.
3. Samuelson, P. A. (1977) *Proc. Natl. Acad. of Sci. USA* 74, 5772–5775.
4. Samuelson, P. A. (1977) *Proc. Natl. Acad. Sci. USA* 74, 5189–5192.
5. Crow, J. F. & Kimura, M. (1970) *An Introduction to Population Genetics Theory* (Harper and Row, New York).
6. Euler, L. (1761) in *Die göttliche Ordnung*, ed. Süßmilch, J. P. Vol. 1, pp. 291–299.
7. Sharpe, F. R. & Lotka, A. J. (1911) *Philos. Mag.* 21, 435–438.
8. Leslie, P. H. (1945) *Biometrika* 33, 183–212.
9. Samuelson, P. A. (1976) *Theor. Popul. Biol.* 9, 82–122.
10. Yellin, J. & Samuelson, P. A. (1976) *Theor. Popul. Biol.* 11, 105–126.

<sup>‡</sup> Crow, J. F. (1977) *Gene frequency and fitness change in an age-structure population*, Working paper from Department of Genetics, University of Wisconsin, Madison, draft of May 1, 1978.