THE MEAN TIME FOR ABSORPTION IN A PROCESS OF GENETIC TYPE

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(received 13 October 1962)

1. Introduction

We consider the genetic model introduced by Moran [3] of a haploid population of fixed size M with two genotypes A and a for which the possibility of selection is allowed. In this model an individual is randomly chosen to die and is replaced by a new individual whose probability of being a depends on the selective advantages of the two genotypes and on the number of a individuals before the birth-death event. The probability of eventual elimination of the genotype a, both with and without selection, has been found by Moran [3], while Watterson [4] has found the mean time for absorption and the variance in the case where no selection is allowed. We derive here the mean time and the variance in the case where selection is allowed, thus extending Watterson's result. A diffusion approximation is available for the mean time; it is shown that this gives a very close approximation to the exact value. Comparison is made with the non-overlapping generation model due to Wright [5], and finally some numerical results are exhibited.

2. Derivation of mean time

We suppose that the a and A individuals produce offspring in the relative proportions μ_1 and μ_2. Individuals are randomly chosen to die and are replaced immediately by new individuals which are a or A with probabilities $\mu_1 j\{\mu_1 j+\mu_2(M-j)\}^{-1}$ and $\mu_2(M-j)\{\mu_1 j+\mu_2(M-j)\}^{-1}$ respectively, where j is the number of a individuals before the birth-death event. The number of a individuals is then $j-1$, j, or $j+1$ with probabilities $p_{j,j-1}$, $p_{j,j}$, and $p_{j,j+1}$ respectively, where

$$
\begin{aligned}
p_{j,j-1} &= \mu_2 j(M-j)/[M\{\mu_1 j+\mu_2(M-j)\}] \equiv \pi_j \\
p_{j,j+1} &= \mu_1 j(M-j)/[M\{\mu_1 j+\mu_2(M-j)\}] \equiv \eta_j \\
p_{j,j} &= 1-p_{j,j-1}-p_{j,j+1} \\
p_{j,k} &= 0, \qquad |k-j| \geqq 2.
\end{aligned}
\tag{2.1}
$$

The number of *a* indiviuals is therefore a Markovian variate taking integer values in $[0, M]$ with transition matrix defined by (2.1). We define the state E_j of this chain as "number of *a* individuals $= j$". Moran [3] has shown that the probability P'_0 that the *a* individuals are eventually eliminated is given by

$$P'_0 \equiv 1-P'_M = \frac{\alpha^{M-K}-1}{\alpha^M-1} \tag{2.2}$$

where $\alpha = \mu_1/\mu_2$ and K is the initial number of *a* individuals in the population. We retain these definitions of α and K throughout. (2.2) will be used later in finding the mean time until absorption. Watterson [4] has found the mean time until absorption in the case where there is no selection; the mean time m_K depends on K and is given by

$$m_K = (M-K)\sum_{j=1}^{K}\frac{M}{M-j}+K\sum_{j=1}^{M-K-1}\frac{M}{M-j}. \tag{2.3}$$

In order to find the mean time in the case where selection is allowed we amend the transition probabilities by putting $p_{0K} = p_{MK} = 1$. In this way we replace an absorbing process by a non-absorbing one by starting the process off again whenever one or other genotype is eliminated. All the states E_j of the Markov chain are now persistent, and if we can find the stationary distribution of the amended chain we are able, because of the way in which the original chain was modified, to find the mean time until absorption in the original chain. If we define the amended transition matrix by P, then $I-P$ is given by

$$I-P = \begin{array}{c|cccccccc|} & E_0 & E_1 & E_2 & \cdots & E_K & \cdots & E_M \\ \hline E_0 & 1 & 0 & 0 & \cdots & -1 & \cdots & 0 \\ E_1 & -\pi_1 & \pi_1+\eta_1 & -\eta_1 & \cdots & 0 & \cdots & 0 \\ E_2 & 0 & -\pi_2 & \pi_2+\eta_2 & \cdots & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & & \vdots & & \vdots \\ E_M & 0 & 0 & 0 & \cdots & -1 & \cdots & 1 \end{array}.$$

We denote the stationary distribution of the new process by

$$\boldsymbol{\lambda}' = (\lambda_0\lambda_1\cdots\lambda_M)$$

and put $\lambda_0 = P_0$ (P_0 a constant) for the moment.

Then since $\boldsymbol{\lambda}'(I-P) = \mathbf{0}$ we have

$$\lambda_0-\lambda_1\pi_1 = 0$$

$$\lambda_1(\pi_1+\eta_1)-\lambda_2\pi_2 = 0$$

giving

$$\lambda_1 = P_0/\pi_1 \tag{2.3}$$
$$\lambda_2 = P_0(1+\alpha)/\pi_2$$

where α has been defined previously.

Also $\lambda_i (1 \leqq i \leqq K-3)$ obeys the recurrence relation

$$-\eta_i\lambda_i + (\eta_{i+1}+\pi_{i+1})\lambda_{i+1} - \pi_{i+2}\lambda_{i+2} = 0. \tag{2.4}$$

Put

$$\pi_i\lambda_i = \xi_i.$$

Then $\eta_i\lambda_i = \alpha\xi_i$ and (2.4) becomes

$$-\alpha\xi_i + (\alpha+1)\xi_{i+1} - \xi_{i+2} = 0. \tag{2.5}$$

The solution of this difference equation is

$$\xi_i = A + B\alpha^i \qquad (A, B, \text{ arbitrary constants}).$$

The boundary conditions (2.3) are more conveniently written

$$\xi_1 = P_0 \tag{2.6}$$
$$\xi_2 = P_0(1+\alpha).$$

These conditions fix A and B as

$$A = -P_0/(\alpha-1), \qquad B = P_0/(\alpha-1)$$

so that

$$\xi_i = P_0(\alpha^i - 1)/(\alpha-1)$$

and hence

$$\lambda_i = \frac{P_0(\alpha^i-1)}{\pi_i(\alpha-1)} \qquad (i = 1, 2, \cdots, K-1). \tag{2.7}$$

We now find the elements $\lambda_{K+1} \cdots \lambda_M$. If we put for the moment $\lambda_M = P_M$ (P_M a constant) we have

$$-\eta_{M-1}\lambda_{M-1} + P_M = 0$$

$$-\eta_{M-2}\lambda_{M-2} + (\pi_{M-1}+\eta_{M-1})\lambda_{M-1} = 0.$$

Hence

$$\lambda_{M-1} = P_M/\eta_{M-1} \tag{2.8}$$
$$\lambda_{M-2} = P_M(1+\alpha^{-1})/\eta_{M-2}.$$

Suppose we now define $\xi_i = \eta_i\lambda_i$.

Then from the recurrence relation (2.4) we obtain

$$-\xi_i + (1+\alpha^{-1})\xi_{i+1} - \alpha^{-1}\xi_{i+2} = 0$$

or

$$-\alpha\xi_i + (\alpha+1)\xi_{i+1} - \xi_{i+2} = 0$$

which is the same as (2.5). Thus the general solution is

$$\xi_i = C + D\alpha^i \qquad (C, D, \text{ arbitrary constants})$$

subject to the boundary conditions (2.8), which are more conveniently written

$$\xi_{M-1} = P_M$$
$$\xi_{M-2} = P_M(1+\alpha^{-1}).$$

These conditions fix C and D as

$$C = P_M \alpha^M/(\alpha^M - \alpha^{M-1}), \qquad D = -P_M/(\alpha^M - \alpha^{M-1}).$$

Therefore

$$\xi_i = P_M(\alpha^M - \alpha^i)/(\alpha^M - \alpha^{M-1})$$

and

$$\lambda_i = \frac{P_M(\alpha^M - \alpha^i)}{\eta_i(\alpha^M - \alpha^{M-1})} \qquad (i = K+1, \cdots, M-1). \tag{2.9}$$

It remains to evaluate λ_K. We have

$$-\lambda_0 - \eta_{K-1}\lambda_{K-1} + (\eta_K + \pi_K)\lambda_K - \pi_{K+1}\lambda_{K+1} - \lambda_M = 0$$

or

$$\lambda_K = \left\{P_0 + P_M + P_0\left(\frac{\alpha^K - \alpha}{\alpha - 1}\right) + P_M\left(\frac{\alpha^{M-1} - \alpha^K}{\alpha^M - \alpha^{M-1}}\right)\right\} \div \{\pi_K + \eta_K\} \tag{2.10}$$

If we can evaluate P_0 and P_M, and then normalize $\boldsymbol{\lambda}'$ so that $P_0 + P_M = 1$, we shall have, because of the way in which we have amended the absorbing Markov chain, the mean time until absorption in the absorbing case as the sum of the elements in $\boldsymbol{\lambda}'$, less $P_0 + P_M$. This follows directly from relations connecting absorbing and associated persistent Markov chains. Now clearly

$$\frac{P_0}{P_M} = \frac{\text{Prob \{absorption at } 0 \text{ in absorbing case\}}}{\text{Prob \{absorption at } M \text{ in absorbing case\}}}$$
$$= \frac{\alpha^{M-K} - 1}{\alpha^M - 1} \div \frac{\alpha^M - \alpha^{M-K}}{\alpha^M - 1} \quad \text{from (2.2).}$$

Since we now put $P_0 + P_M = 1$, we have

$$\begin{aligned} P_0 &= \frac{\alpha^{M-K} - 1}{\alpha^M - 1} = P_0' \\ P_M &= \frac{\alpha^M - \alpha^{M-K}}{\alpha^M - 1} = P_M'. \end{aligned} \tag{2.11}$$

With P_0 and P_M given by (2.11), all elements in $\boldsymbol{\lambda}'$ are now given explicitly by (2.7), (2.9) and (2.10).

Furthermore, it is easily shown, using (2.11), that (2.10) reduces to

$$\lambda_K = \frac{(\alpha^K-1)(\alpha^{M-K}-1)}{(\alpha-1)(\alpha^M-1)\pi_K}.$$

Thus the mean time m_K is given by

$$m_K = \frac{\alpha^{M-K}-1}{\alpha^M-1}\sum_{i=1}^{K}\frac{\alpha^i-1}{\pi_i(\alpha-1)} + \frac{\alpha^M-\alpha^{M-K}}{\alpha^M-1}\sum_{i=K+1}^{M-1}\frac{\alpha^M-\alpha^i}{\eta_i(\alpha^M-\alpha^{M-1})}. \tag{2.12}$$

As a check, it is a simple but lengthy matter to show that m_K, as defined by (2.12), satisfies the difference equation

$$m_K = \pi_K m_{K-1} + (1-\pi_K-\eta_K)m_K + \eta_K m_{K+1} + 1$$

which is the difference equation for m_K obtained by comparing the mean time until absorption at two consecutive birth-death events.

Further, if we let $\mu_1 \to \mu_2$, so that $\alpha \to 1$, then equation (2.12) becomes

$$\begin{aligned} m_K &= (M-K)\sum_{i=1}^{K}\frac{M}{M-i} + K\sum_{i=K+1}^{M-1}\frac{M}{i} \\ &= (M-K)\sum_{i=1}^{K}\frac{M}{M-i} + K\sum_{i=1}^{M-K-1}\frac{M}{M-i} \end{aligned}$$

which is the result obtained by Watterson [4].

3. The diffusion approximation

In the case where $\mu_1/\mu_2 = 1+0(M^{-1})$ a diffusion theory approximation is available for the mean time until absorption. In the case where there is no selection, Watterson [4] has shown that the diffusion theory result gives a very close approximation to the true value. We now show that this continues to hold for the case where selection is allowed.

We firstly find an approximation to (2.12). If we put $\alpha = \mu_1/\mu_2 = 1+h^*M^{-1}$, then

$$\alpha^M \approx e^{h^*} \tag{3.1}$$

and if $y = iM^{-1}$, $\alpha^i \approx e^{h^*y}$.

Hence if we put $KM^{-1} = x$, we find that m_K may be approximated by

$$\frac{M^2}{h^*}\left[\frac{e^{h^*(1-x)}-1}{e^{h^*}-1}\int_0^x (e^{h^*y}-1)k_1(y)dy + \frac{e^{h^*}-e^{h^*(1-x)}}{e^{h^*}-1}\int_x^1 \frac{e^{h^*}-e^{h^*y}}{e^{h^*}}k_2(y)dy\right] \tag{3.2}$$

where $k_1(y)$, $k_2(y)$ are the "continuity" analogues of $1/\pi_i$ and $1/\eta_i$ and are

$$\frac{\mu_1 y+\mu_2(1-y)}{\mu_2 y(1-y)} \quad \text{and} \quad \frac{\mu_1 y+\mu_2(1-y)}{\mu_1 y(1-y)} \quad \text{respectively.}$$

For the diffusion equation we must measure time in units of M^2 birth-death events. If we define $m(x)$ as the mean time until absorption for initial proportion x, then the diffusion differential equation satisfied by $m(x)$ is (Feller [1])

$$M(x)m'(x)+\tfrac{1}{2}V(x)m''(x) = -M^{-2} \tag{3.3}$$

where $M(x)$ is the expected value of the increase of the proportion of a individuals after one birth-death event when the proportion of a individuals is x, and is given by

$$M(x) = \frac{(\mu_1-\mu_2)x(1-x)}{M\{\mu_1 x+\mu_2(1-x)\}}\,.$$

Similarly $V(x)$ is the expected value of the square of the increase of the proportion of a individuals, and is given by

$$V(x) = \frac{(\mu_1+\mu_2)x(1-x)}{M^2\{\mu_1 x+\mu_2(1-x)\}}\,.$$

Inserting these values in (3.3) and simplifying, we obtain

$$m''(x)+hm'(x) = -k(x) \tag{3.4}$$

where $h = \dfrac{2\mu_2 h^*}{\mu_1+\mu_2}$ and

$$k(x) = \frac{2\{\mu_1 x+\mu_2(1-x)\}}{(\mu_1+\mu_2)x(1-x)}\,.$$

The general solution of (3.4) is easily obtained, and the solution satisfying the boundary conditions $m(0) = m(1) = 0$ is found to be

$$m(x) = C\{1-e^{-hx}\}-\int_0^x e^{-hz}\int_0^z e^{hy}k(y)\,dy\,dz \tag{3.5}$$

where

$$C = \left[\int_0^1 e^{-hz}\int_0^z e^{hy}k(y)\,dy\,dz\right]\Big/\,[1-e^{-h}].$$

Equation (3.5) is simplified by an integration by parts, which gives eventually

$$\begin{aligned} m(x) = \frac{M^2}{h}\Bigg[&\frac{e^{h(1-x)}-1}{e^h-1}\int_0^x (e^{hy}-1)k(y)\,dy \\ &+\frac{e^h-e^{h(1-x)}}{e^h-1}\int_x^1 \frac{e^h-e^{hy}}{e^h}\,k(y)\,dy\Bigg] \end{aligned} \tag{3.6}$$

where we have now rescaled $m(x)$ so that the mean time is now in terms of birth-death events. Since $\mu_1-\mu_2$ is $0(M^{-1})$ we find that $h-h^*$ is $0(M^{-1})$, and similarly both $k_1(x)$ and $k_2(x)$ differ from $k(x)$ by a term of this order. Thus comparing (3.2) and (3.6) it is clear that the diffusion equation gives a very close approximation to the true mean time.

4. The variance

We denote by Q the submatrix of P corresponding to transition probabilities from a state in $(E_1, \cdots, E_{M-1})$ to another state in this set. Then it is easily shown that the elements in the Kth row of $(I-Q)^{-1}$ are the various elements constituting the sums in (2.12). Specifically, if we put

$$\theta_{ij} = \frac{\alpha^{M-i}-1}{\alpha^M-1} \cdot \frac{\alpha^j-1}{\pi_j(\alpha-1)}$$

$$\psi_{ij} = \frac{\alpha^M-\alpha^{M-i}}{\alpha^M-1} \cdot \frac{\alpha^M-\alpha^j}{\eta_j(\alpha^M-\alpha^{M-1})}$$

then

$$(I-Q)^{-1} = \begin{vmatrix} \theta_{11} & \psi_{12} & \psi_{13} & \psi_{14} & \cdots & \psi_{1,M-1} \\ \theta_{21} & \theta_{22} & \psi_{23} & \psi_{24} & \cdots & \psi_{2,M-1} \\ \theta_{31} & \theta_{32} & \theta_{33} & \psi_{34} & \cdots & \psi_{3,M-1} \\ \vdots & \vdots & \vdots & \vdots & & \vdots \\ \theta_{M-1,1} & \theta_{M-1,2} & \theta_{M-1,3} & \theta_{M-1,4} & \cdots & \theta_{M-1,M-1} \end{vmatrix} .$$

It is well known (cf. Kemeny and Snell [2], p. 51), that the variance of the absorption time is the Kth element in the column vector

$$\{2(I-Q)^{-1}-I\}(I-Q)^{-1}\xi-\boldsymbol{m}^2$$

where ξ is a column vector all of whose elements are unity and $\boldsymbol{m}^2$ is a column vector of the m_K^2's. It follows that

$$\text{(4.1)} \qquad \begin{aligned} \sigma_K^2 &= 2\sum_{i=1}^{K} \theta_{Ki}\left\{\sum_{j=1}^{i} \theta_{ij} + \sum_{j=i+1}^{M-1} \psi_{ij}\right\} \\ &\quad + 2\sum_{i=K+1}^{M-1} \psi_{Ki}\left\{\sum_{j=1}^{i} \theta_{ij} + \sum_{j=i+1}^{M-1} \psi_{ij}\right\} - m_K - m_K^2 . \end{aligned}$$

If we let $\alpha \to 1$ we have

$$\theta_{ij} = M(M-i)/(M-j), \qquad \psi_{ij} = Mi/j$$

and it is easily checked that (4.1) agrees with the formula found by Watterson [4].

Equation (4.1) may also be approximated by an equation involving integrations, but owing to the complexity of these integrations and the fact that they cannot be evaluated explicitly, there seems to be no point in making this approximation.

5. Comparion with Wright's model

In a second model due to S. Wright [5], all M individuals in the population die simultaneoulsy and are replaced immediately by a new generation of M individuals, the number of a individuals in the new generation being determined by the number in the previous generation as well as by the selective advantages. For this model, no exact expression is available for either the probability of elimination of either genotype or for the mean time until elimination. However, a diffusion approximation is available for the mean time, and is approximately given by (3.3) if we replace $V(x)$ by $\frac{1}{2}V(x)$. In the case where $M(x) = 0$, so that there is no selection, this has the effect of doubling the mean time until elimination. When $M(x)$ is not zero the effect is more complicated but the mean time is still approximately doubled.

In order to test the adequacy of the diffusion approximation and to compare the mean absorption times in each case, the following numerical results were obtained. They refer to a population of twelve individuals, which is about the largest number for which calculations are readily made. The results for the Moran model (Model I) were derived from (2.12). Those for Wright's model (Model II) were obtained numerically by a matrix inversion (c.f. Theorem 3.2.4 in Kemeny and Snell [2]), and subsequently multiplied by 12, since they were originally given in terms of generations rather than birth-death events.

TABLE 1

Mean number of birth-death events until absorption

Initial number of a individuals $= K$
Selective advantage of a individuals $= S$

$S = 0$

K	1	2	3	4	5	6	7	8	9	10	11
Model I	36.24	59.39	75.33	85.95	92.06	94.06	92.06	85.95	75.33	59.39	36.24
Model II	73.77	117.19	147.68	168.05	179.81	183.66	179.81	168.05	147.68	117.19	73.77

$S = .1$

K	1	2	3	4	5	6	7	8	9	10	11
Model I	37.22	59.26	72.85	80.49	83.47	82.65	78.45	71.11	60.62	46.60	27.85
Model II	88.27	133.83	159.46	171.36	173.31	167.71	156.08	139.27	117.54	90.42	49.14

In the case $S = 0$, the values in the first row are almost exactly half those in the seond, the result suggested by the diffusion equation. For $S = .1$ this is still approximately true, as we again expect. We infer that even for such a small population the comparisons between the mean times suggested by the diffusion equation are still remarkably accurate.

References

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