PROBABILITY THEORY APPLIED TO GENETIC POPULATIONS

by

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This work is a thesis submitted for the degree of Doctor of Philosophy in the Australian National University.

1960.

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Preface.

My supervisor, Professor P.A.P. Moran, suggested most of the problems of this thesis, and some of the methods for their solution. He has generously guided and instructed me throughout the work, and it was he who first interested me in population genetics. To Professor Moran I give my sincere thanks. I also wish to thank Mr. J.E. Moyal for some suggestions concerning chapters 1 and 12, and discussion on the writing of the final draft of the thesis.

The material of chapter 1 and chapters 2-5 has been submitted to a journal for publication, (31), (32). That of chapter 7 forms part of a joint paper (with P.A.P. Moran) already published, (27). Chapters 8-10 and chapter 11 have also been published, (29) and (30) respectively.

The results derived in this thesis are original unless otherwise indicated, and except for certain parts of chapter 7 which were investigated jointly with Professor Moran. Moran had studied several special cases of populations by the methods of chapter 7, and the contribution I made was the introduction of the general model giving rise to the generating functions $P_1(z)$ and $P_2(z)$, and the algebra associated with sex-linked genes. The presentation differs from that of the published paper (27) in that the results here are derived from a more compact specification of the population model; to this extent their derivation is new. Material due solely to Moran has been omitted.

The population models (as distinct from the derivation of results) are not all original formulations. In particular, the models B and C discussed in chapters 3 and 4 were first considered by Moran (25), (24) and those of chapters 9 and 10 are generalizations to the case with non-random mating of models used by Wright (36) and Moran (22). The model of chapter 12 was also introduced by Moran (22). Model A of chapter 2 is a generalization to the case with mutation of a model first discussed by Moran and myself jointly (27); the compact specification in probability terms is new. Models D and E of chapters 5, 6, and 11 are original.

In the text, as in this preface, the work of others is indicated by numbered references, these being tabulated after chapter 12. The equations are numbered with chapter prefixes. The distinction between reference and equation numbers is that the latter always have a decimal point, whilst the former do not.

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0. Introduction and summary.

This thesis is concerned with certain aspects of the genetic behaviour of a zoological or botanical population. Broadly speaking, the models used here to describe populations are 'natural', in the sense that they subject the individuals to mainly random influences, as opposed to the controlled environments and breeding programmes found in commercial populations such as poultry and many vegetable crops. The aim is to discover the evolutionary significance of these random influences by the application of probability theory; an analysis is made of the possible states of the population after a considerable number of generations has elapsed from some initial instant.

The most severe assumption made in all the models is that the number of individuals in the population at any time is a constant (usually denoted by N), and is often assumed large. This restriction is imposed so that the population cannot die out, but immediately limits the applicability of the theoretical model in a practical situation; but the deductions drawn from the model should be, at least qualitatively, correct for populations in a fairly stable environment. A start has been made by Feller (7) to remove such a restriction, but is not pursued here. The influences of the environment on the population which are considered are mutation, selection, non-random mating, migration, offspring distributions, and overlapping and non-overlapping generations. A brief des-

cription of these concepts as applied in the models follows.

The genetic factor with which we are concerned is of the simplest type. We assume it to be controlled by a single locus on a chromosome, at which either of two alleles 'a' or 'A' can occur. The genotypes are usually diploid, that is either 'aa', 'Aa', or 'AA', but some instances are treated when they are haploid and either 'a' or 'A'. Again, the individuals are usually dioecious, that is either male or female, but sometimes monoecious models are discussed, for which any individual can behave as both male and female. A mutation is a rare, instantaneous transition from one gene into its allele, say $a \rightarrow A$ or $A \rightarrow a$. The physical reason for such a transition is unimportant for our purposes, and it is convenient to assume that mutations occur only among the gametes produced by an individual, so that its own genotype remains unchanged throughout its life. Selection is the term used to describe variation in the average numbers of offspring produced by the different genotypes. This variation can be caused either directly, by varying the numbers of gametes produced per genotype, or indirectly, by varying the life expectations. By non-random mating is meant the possibility of gametes or zygotes uniting in non-random proportions to form new zygotes. For example, in practice this can be brought about if individuals of like genotype prefer to mate with each other, and this is called positive assortative mating. Migration is not discussed in great detail, but one model is considered in which two sub-populations exist and do not inter-

mingle except for the exchange of a few individuals per generation. Some consideration is given to the problem of how offspring are distributed amongst the parents. The number of offspring per person is a random variate, and a particular case was investigated by Lotka (21), who found that the probability distribution for the number of children born to American parents was a modified geometric. Finally, the generation structure of the population is considered, that is, whether all generations are non-overlapping and no mating occurs between them (for example populations with a seasonal life cycle) or whether they are overlapping with deaths (and births) occurring one at a time.

Before proceeding to a summary of the models, methods, and results in this thesis, it is convenient to give here a brief account of the main objectives in general terms. Finite genetic populations, such as those discussed in this thesis, can have only a finite number of possible genetic states; the numbers of the various genotypes in the population at any time are limited to being non-negative integers, and cannot exceed the total population size. A population model can be described by postulating the probabilities that a given state will change to another state during a birth-death event. These probabilities may either be written down explicitly (as will be done in § 4.1 and § 5.1) or given implicitly by means of generating functions (as in § 2.1 and § 3.1). If the population states are ordered according to some convention, the probabilities can be tabulated as a matrix array called a

'transition matrix', and the successive states form a 'Markov chain' because the transition matrix is assumed to depend on the immediately preceding state only. Given the initial state, one can write down the probabilities that the population is in the various states at any subsequent time. Denote them by the vector $\underline{P}_t$ at time t, and the transition matrix by $\underline{T}$. Then

$$\underline{P}_t = \underline{T}\,\underline{P}_{t-1} = \underline{T}^t\,\underline{P}_0 \qquad (0.1)$$

provided $\underline{T}$ is independent of time, and $\underline{P}_0$ is a vector of zeros apart from a single unity representing the initial state. We are interested in the behaviour of $\underline{P}_t$ as $t \to \infty$.

Following Bartlett (2) p.33, a Markov chain is called 'positively regular' if $\underline{P}_t$ converges to a limit as $t \to \infty$, such that all elements of $\underline{P}_\infty$ are positive and independent of the initial state. A necessary and sufficient condition for this to be true is that the matrix $\underline{T}^t$ has all non-zero elements for some finite t. When the models considered later are subject to mutation this criterion is satisfied; for example the models discussed in § 2, § 3 and § 6 satisfy it with $t = 1$, but for those of § 4 and § 5, t would need to be of the order of the population size N, and a proof would be difficult to give by this method. We shall show directly that $\underline{P}_\infty$ does have non-zero elements even in these cases.

The practical significance of $\underline{P}_\infty$ is that it is a

stable distribution, because

$$\underline{P}_\infty = \underline{T}\,\underline{P}_\infty \,.$$

Thus it describes the behaviour of the population after many generations have elapsed, and provides a measure of the effect on evolution of the environmental influences included in the model. A second quantity of interest is the largest non-unit eigenvalue of the matrix $\underline{T}$, for it is this value which governs the rate that the population approaches its stationary distribution. This is so because of the spectral decomposition of $\underline{T}^t$, from which (0.1) may be written

$$\underline{P}_t = \sum_i \underline{\Sigma}_i(t)\,\lambda_i^t \qquad \text{(c/f.(2) p.32)} \qquad (0.2)$$

where the λ_i are the eigenvalues of $\underline{T}$ and the $\underline{\Sigma}_i(t)$ are vectors whose components are polynomials in t of degree at most $n_i - 1$, where n_i is the multiplicity of λ_i. The largest eigenvalue must be unity since $\underline{T}$ is a stochastic matrix, whilst the effect of the smaller ones is damped away. Asymptotically, only the largest of these latter eigenvalues will contribute to the time-dependence of the process.

It is unfortunately true that, for reasonably general models with environmental influences, no exact determinations of $\underline{P}_\infty$ and the λ_i have been made. Perhaps the simplest finite population model that has been considered is that introduced by Wright (36), (39), and further investigated by Feller (7). The population is composed of monoecious haploid individuals whose genotypes are either a or A. The popu-

[illegible]

and will be denoted by $2N$ for comparisons with a diploid population of size N. Suppose that at the t-th generation there are j individuals of type a and $2N-j$ of type A. Just before the death of the generation, the individuals produce gametes; a proportion α_1 of the a gametes however mutate to A, and α_2 is the mutation rate in the reverse direction. The next generation (which does not overlap with the previous) is formed by random sampling with replacement amongst these gametes. The probability of transition to a state with i a genes is then T_{ij} (say) where

$$T_{ij} = \binom{2N}{i}\left[(1-\alpha_1)\frac{j}{2N} + \alpha_2\left(1-\frac{j}{2N}\right)\right]^i\left[\alpha_1\frac{j}{2N} + (1-\alpha_2)\left(1-\frac{j}{2N}\right)\right]^{2N-i} \qquad (0.3)$$

Since $T_{j,0} > 0$ for all i,j, we know that $\mathbb{P}_\infty$ exists, and is independent of $\mathbb{P}_0$. Weiler shown, (7), that the eigenvalues of the transition matrix $\mathbb{T} = (T_{ij})$ are

$$\lambda_s = (1-\alpha_1-\alpha_2)^s\binom{2N}{s}\frac{s!}{(2N)^s}, \quad s = 0, 1, 2, \ldots, 2N, \qquad (0.4)$$

but the vector $\mathbb{P}_\infty$ has not been found. Of the eigenvalues (0.4), we see that the first is unity, and the next largest are

$$\lambda_1 = 1-\alpha_1-\alpha_2, \quad \lambda_2 = (1-\alpha_1-\alpha_2)^2\left(1-\frac{1}{2N}\right). \qquad (0.5)$$

A second model that has been treated successfully is that introduced by Moran (22). This is again a haploid model, but as the individuals die one at a time, at random, the generations are overlapping. The transition matrix is defined by the elements

$$T_{j-1,j} = \frac{j}{2N}\left[\alpha_1\frac{j}{2N} + (1-\alpha_2)(1-\frac{j}{2N})\right],$$

$$T_{jj} = \frac{j}{2N}\left[(1-\alpha_1)\frac{j}{2N} + \alpha_2(1-\frac{j}{2N})\right] + (1-\frac{j}{2N})\left[\alpha_1\frac{j}{2N} + (1-\alpha_2)(1-\frac{j}{2N})\right], \qquad (0.6)$$

$$T_{j+1,j} = (1-\frac{j}{2N})\left[(1-\alpha_1)\frac{j}{2N} + \alpha_2(1-\frac{j}{2N})\right],$$

$$T_{ij} = 0 \quad \text{if} \quad i > j+1 \quad \text{or} \quad i < j-1,$$

and Moran shows that the probability of the model being in the state i, after the stationary distribution has been attained, is:

$$p_i^{(0)} = p_0^{(0)} \frac{\Gamma(2N+1)}{\Gamma(i+1)\Gamma(2N-i+1)} \frac{\Gamma\left(\frac{2N\alpha_2}{1-\alpha_1-\alpha_2}+i\right)\Gamma\left(\frac{2N(1-\alpha_2)}{1-\alpha_1-\alpha_2}-i\right)}{\Gamma\left(\frac{2N\alpha_2}{1-\alpha_1-\alpha_2}\right)\Gamma\left(\frac{2N(1-\alpha_2)}{1-\alpha_1-\alpha_2}\right)}, \quad i=1,2,\ldots,2N$$

where

$$p_0^{(0)} = \frac{\Gamma\left(\frac{2N\alpha_2}{1-\alpha_1-\alpha_2}\right)\Gamma\left(\frac{2N(1-\alpha_2)}{1-\alpha_1-\alpha_2}\right)}{\Gamma\left(\frac{2N}{1-\alpha_1-\alpha_2}\right)\Gamma\left(\frac{2N\alpha_2}{1-\alpha_1-\alpha_2}\right)}$$ These are clearly independent of α_2.

In an appendix to (2.1), Moran states that the eigenvalues of $\underline{T}$ in the case without mutation ($\alpha_1 = \alpha_2 = 0$) are

$$\lambda_s = 1 - \frac{s(s-1)}{(2N)^2}, \quad s = 0, 1, 2, \ldots, 2N, \qquad (0.7)$$

but the proof appears to be incorrect, since the collinearity transformations he uses do not reduce $\underline{T}$ to triangular form as asserted. Nevertheless, the eigenvalues (0.7) are correct, as we shall prove in chapter 12 (see equation (12.39)). Moran

shows that, with mutation, the two largest non-unit eigenvalues of $\underline{T}$ are

$$\lambda_1 = 1 - \frac{\alpha_1+\alpha_2}{2N} \quad , \quad \lambda_2 = 1 - \frac{(1-\alpha_1-\alpha_2)}{2N^2} - \frac{\alpha_1+\alpha_2}{N} \quad , \qquad (0.8)$$

at least if α_1 and α_2 are small. Note that as α_1 and α_2 become zero, the values of (0.8) equal those of (0.7), but the unit root becomes multiple.

When mutation is absent the above theory deserves closer investigation. In this case, the first two eigenvalues in (0.4) and (0.7) are unity, and the same will be true for more general models. As a result of this, the Markov process is not regular, nor even ergodic (see again (2) p.33), and the limiting value of $\underline{P}_t$ will not be independent of the initial state. That $\underline{P}_\infty$ exists follows from the fact that there are no complex eigenvalues of modulus one. In genetical terms, there exist two absorbing states corresponding to fixation of one or other gene, and there may be others (c/f. § 11). Eventually, one of these states will be reached, and the limiting vector $\underline{P}_\infty$ will consist of zeros for all non-absorbing states; the probability of reaching a particular absorbing state will depend on the initial genotype numbers. In this situation, it is still interesting to find $\underline{P}_\infty$ and the eigenvalues which determine the rate of approach to homozygosity. Further, in the case without mutation, there is some interest in finding the probability distribution of the time taken to reach an absorbing state, or the moments of the time. To the author's

knowledge, this has never been done in the context of genetics, probably because of the complicated matrix theory involved. In chapter 12 we give the solution for Moran's model (0.6) above, and in § 1.4 an approximate solution for a large, fairly general population. The approximate result (1.35), (1.36) for the mean of the absorption time is used in §§ 2 - 6 for the models A - E.

In short, the aim of this thesis is to find P_∞, the largest non-unit eigenvalue, and the behaviour of the absorption time when appropriate, for various population models some of which are more general than those considered by previous writers. The conclusions to be drawn from these results are the evolutionary effects of the environmental factors included in the models.

It has already been pointed out that the calculation of P_∞ seems to be intractable in general; in fact, the example (0.6) is the only one with mutation to yield to analysis so far, and it does not include the effects of assortative mating or selection. The exact results which can be found are usually confined to special cases of more complex models, but for these latter, approximate results can be deduced. For this reason, the approximate results are presented first (§§ 1-6) and exact ones later (§§ 7-12).

Wright (41), Feller (7), Kimura (6), (18), Moran (24), (25), and others have successfully treated certain models by approximate methods, and in particular by differential equations of the diffusion type. Diffusion equations were employed

in probability theory in a basic paper by Kolmogorov (19), and since then various theoretical papers have been written about them (e.g. (14), (8), (9)), but to the author's knowledge no rigorous proof of their applicability has been given in the genetic situation. This is probably because the frequency of a gene in a population is generally not a Markov variate, and because the time scale is essentially discrete, not continuous. Therefore, in chapter 1 the justification is given for the approximation procedures under certain sufficient conditions, and these conditions are wide enough to include genetic problems as special cases.

In chapters 2-6 are discussed five population models to which the approximation theory is applicable. This represents an advance for two reasons; firstly, without a knowledge of some sufficient conditions previous writers have had to assume applicability, or else seek answers to the simpler problems by other methods, and secondly, on the occasions when diffusion equations have been employed, the parameters have not usually been related to specific population models at all, but only described in general terms. Diffusion theory has sometimes been applied uncritically, for example by not allowing for fixation or loss when there is no mutation (c.f. Li (20) p.338 § 6) and by not recognising the limiting processes involved (c.f. Li (20) p.350 exercise 7). Here it is hoped that such pitfalls are avoided by careful descriptions and explicit assumptions for the models concerned.

The five model types are labelled A, B, C, D, and

E, and approximate results are given for them in chapters 2-6 respectively. All models are subject to gene mutation, but differ in other details. The models A, B, C, and D represent populations with dioecious diploid individuals, whilst model E is for monoecious haploids and is the only model having a migration scheme. Models A, B, and E have non-overlapping generations whilst C and D have overlapping. Model A has a general offspring distribution, random mating and there are no selection pressures, whereas the other models have particular offspring distributions, and have non-random mating and selection. When mutation is present, the most useful result obtainable by approximate methods is the stationary probability distribution P_∞ for the frequency of a particular allele. Without mutation, various quantities are of interest, and whenever possible, the approximations to them are compared with exact results to ascertain the discrepancy, if any.

One type of model which is not discussed in this thesis is one in which the population size N is so large as to be effectively infinite. Such a model gives rise to a deterministic process, in which there are no random variates at all. The next simplest models for which exact results can be found are those without selection and mutation, and it is with such models that the chapters 7-12 are concerned.

In general, for a population without mutation, the mating and random segregation of gametes to form offspring zygotes eventually causes one or other allele to be completely

'lost' from the population, and the others to be 'fixed'. This state of fixation is permanent thereafter since there is no source of new alleles. One exceptional case is mentioned in chapter 11, where all individuals are eventually homozygous, that is of types aa or AA, but are not necessarily all of the one type; this is brought about by a very special non-random mating scheme. The two quantities of most interest are the time-rate of approach to homozygosity, and the probability that a given gene (say a) will eventually become fixed. Suppose that time t is measured in units of one generation, and that the number of heterozygotes (Aa) in the population at time t is u_t. Then for large t, it is often found that the quantities $E(u_t)$ and $P_r(u_t \neq 0)$ are approximately proportional to $e^{-\mathcal{R}t}$ or $(1-\frac{\mathcal{R}}{N})^{Nt}$, and $\mathcal{R}$ is called the rate of approach to homozygosity. $\mathcal{R}$ is usually small, so that $E(u_t) \doteq (1-\mathcal{R})E(u_{t-1})$ and the heterozygotes decrease roughly by a proportion $\mathcal{R}$ per generation. Here, $\mathcal{R}$ is related to the largest non-unit eigenvalue of $\underline{T}$; for examples, Wright's and Moran's models give the eigenvalues $\lambda_2 = 1 - \frac{1}{2N}$ from (0.5) and $\lambda_2 = 1 - \frac{1}{2N^2}$ from (0.7) respectively, and on a generation time scale we have the rates of approach

$$\mathcal{R} = 1-\lambda_2 = \frac{1}{2N} \quad \text{and} \quad \mathcal{R} = 1-\lambda_2^{2N} = 1-(1-\tfrac{1}{2N})^{2N} \doteq \frac{1}{N} \qquad (0.9)$$

respectively. Note that 2N birth-death events of Moran's model correspond to one generation of Wright's.

In chapters 7, 9-12, the rate of approach to homo-

zygosity and the probability of gene fixation are found for five different types of models. In chapter 7, the dioecious diploid model A with arbitrary offspring distributions is discussed, but this time without mutation. This is an advance on Wright's work (37), (40) dealing with monoecious populations, especially as Wright used analogy rather than proof to ascertain the rate of approach.

In chapter 8 there is a discussion of non-random mating in general terms, and of the definition of a coefficient to measure the degree of non-randomness in monoecious and dioecious populations. The coefficient is a generalization of one introduced by Wright (35); but it is not a trivial generalization because for some mating systems it is found that assortative mating does not have even the same qualitative effect as it does in other systems (c/f chapters 9-11).

The general positive assortative mating system described in chapter 8 is utilised in chapters 9, 10, and 11 to study the effect of assortative mating on different population models. These models are similar to types B, C, and D used before, but differ by having no mutation, no selection, and a more general mating system than B and C. Further, both monoecious and dioecious models are considered.

Then in § 12, we revert to finding rather special results for the simple model (0.6). We assume that mutation and selection are absent, that the model has haploid individuals, and that mating is at random. Moran (22), (23) has

given a broad account of the model's properties, some of which have been summarized above. The material presented in § 12 is an extension of Moran's work.

The conclusions which can be drawn from the study of the various models are:

i. The genetic behaviour of a population can generally be found by approximate methods for large populations, and by exact methods in the simpler models.

ii. The behaviour of a population is (at least qualitatively) insensitive to changes in the method of introducing mutation and selection. Even if the mutation rates are small, say of the order of magnitude of the reciprocal of the population size, a stable probability distribution will be reached for the genotype frequencies with all genotypes represented. If mutation is absent, all individuals will be homozygous eventually, and usually of the same type. The rate of loss of heterozygotes is increased by a small selective advantage for a recessive gene and decreased for a dominant gene (c/f § § 2-6).

iii. The behaviour may or may not be sensitive to whether generations are overlapping or not (c/f § § 4,5,10, 11).

iv. The behaviour is definitely affected by changing the method of non-random mating, and the offspring distributions. When mutation is absent, the rate of loss of heterozygotes is directly related to the offspring distributions' variances, but can be increased or decreased by posi-

tive assortative mating (c/f §§ 2,3,7,9,10,11).

v. If two large sub-populations have an inter-migration rate proportional to some power of the population size, they behave effectively as a single population (c/f § 6).

These conclusions can be drawn even though not all possible permutations and combinations of factors are considered; a complete account would involve considerable repetition and needless algebra.

1. Discrete and Continuous Diffusion Processes

1.0 Introduction

The relative frequency of a gene in a genetic population of size N is a random variable which may take one of a discrete set of values on the interval $(0,1)$. A change in the variate can be brought about by births, deaths, migrations and gene mutations, all of which occur at discrete times. The gene frequency is generally not a Markov variable because it depends on the frequencies in the male and female sub-populations. Nevertheless, useful mathematical models have been devised in which the population size is assumed sufficiently large to ensure that the behaviour of the gene frequency is approximately that of a continuous Markov diffusion process. The justification for this procedure is at present based on heuristic arguments only, so the aim of this chapter is to give a rigorous demonstration.

Consider a random variate $x(t)$, such that $0 \leqslant x(t) \leqslant 1$, and that as a function of time, $x(t)$ changes only at $t = 1, 2, 3, \ldots$. These jumps are assumed to be of order of magnitude N^{-m} say, where $m = 1$ or 2 in most genetic applications. In order to accumulate a non-degenerate change from the initial state $x(0)$, a time lag $t = N^{m}u$ (say) will be necessary. Suppose the probability distribution of $x(t)$ is the continuous to the right function

$$F_N(x,t) = \Pr\left\{x(t) \leqslant x\right\}.$$

Then it is shown that under certain conditions on the $x(t)$

process, $F_N(x,N^m u)$ converges to a limiting distribution $F(x,u)$ as N increases, and this latter function corresponds to a diffusion process satisfying a Fokker-Planck equation. A summary of some old and some new results for the limiting distribution is given, including the stationary distribution, the probability of gene fixation and the time for this to occur, and the concept of entropy. In chapters 2-6, examples are given of population models of finite size, for which these results hold as approximations.

1.1. Assumptions for discrete process

In genetics, the probability distribution of the gene frequency $x(t+1)$ depends not only on the previous frequency $x(t)$ but also on the individual diploid genotype frequencies within the male and female sub-populations at time t. Roughly, the assumptions to be made here are that the moments of the jump $x(t+1) - x(t)$ are nearly functions of $x(t)$ only, and that the third and higher moments are negligible compared with the first two. Precisely, the assumptions are

(A1) The conditional expectation satisfies[1]

$$\mathcal{E}\left\{e^{\theta[x(t+1)-x(t)]}-1\right\} = N^{-m}\theta\left\{M[x(t)] + \tfrac{1}{2}\theta V[x(t)] + W_N(\theta,t)\right\},$$

where (A2) $m=1$ or 2 or 3 or .... , and is chosen so that

both

$$M(x) = m_0+m_1x+m_2x^2 +\ldots + m_kx^k,$$

and

$$V(x) = v_0 + v_1x + v_2x^2 + \ldots + v_kx^k$$

---

1. Throughout this thesis, the following convention will be used: moments conditional on the occurrence of an event (e.g. a given state of a population in the preceeding generation) will be denoted by $\mathcal{E}$, $\mathcal{V}$ar, $\mathcal{C}$ov, etc. with script capitals and unconditional moments by E, Var, Cov.

are independent of N ; further

$1-x \geqslant N^{-m}M(x) \geqslant -x$ for all $0 \leqslant x \leqslant 1$,

$V(x) > 0$ for all $0 < x < 1$, but $V(0)=V(1)=0$.

In particular, $m_0 > 0$, $\sum_0^k m_i < 0$, $v_0 = \sum_0^k v_i = 0$.

and (A3) For Θ in any bounded interval $(-B,B)$, and for all $u > 0$, there exists a quantity $C_N(B)$ such that the unconditional expectation of $W_N(\Theta, N^n u)$ satisfies, for some n such that $0 \leqslant n < m$, and all $u > 0$,

$$E\left|W_N(\Theta, N^n u)\right| \leqslant C_N(B) \to 0 \quad \text{as} \quad N \to \infty.$$

(A4) The initial probability distribution $F_N(x,0)$ is known and is independent of N. We shall write $F_N(x,0) = F(x,0)$, which will be consistent with the notation used in the introduction to describe the limiting distribution.

These assumptions are sufficient but not necessary for the theory to be developed in the following sections. (A2) and (A4) are certainly more restrictive than they need be, but do cover most genetic applications met in the literature. Thus, $M(x)$ has been at most a cubic polynomial, and $V(x)$ has usually been proportional to $x(1-x)$ or $x^2(1-x)^2$. One exception is found in the paper by Crow and Kimura (6), where $V(x)$ is proportional to $\left(x - \frac{1}{2}\right)^2$; this should be a simpler case to discuss than the one treated here, since it has only one singularity, not two.

On the other hand, (A1) and (A3) must be very nearly nec-

essary, as well as sufficient. They imply that $\mathcal{E}\left[x(t+1) - x(t)\right]$ and $\mathcal{E}\left[x(t+1) - x(t)\right]^2$ are nearly $N^{-m}M\left[x(t)\right]$ and $N^{-m}V\left[x(t)\right]$ respectively, whilst the residual function $W_N(\theta, t)$, which might depend on $x(t)$ and other variates as well, is small for large N, t. A case when $N^{-m}M(x) < -x$, or $N^{-m}M(x) > 1-x$, c/f (A2), could not arise since exit from the region $(0,1)$ is assumed impossible.

The formulation of the problem in terms of moment generating functions, implicit in (A1), is convenient from the point of view of considering specific examples of population models. Theoretically, one could equally well deal in terms of transition probabilities, but their enumeration in a practical case would often be tedious.

1.2. Transition to the limit.

Define the moment generating function of $x(t)$ as

$$\phi_N(\theta,t) = E\left\{e^{\theta x(t)}\right\} = \int_{0-}^{1} e^{\theta x}\, d_x F_N(x,t) \;;$$

this function exists because $x(t)$ and all its moments are bounded on $(0,1)$. For the integral, d_x denotes integration with respect to x, and the range is chosen to include the jumps (if any) in $F_N(x,t)$ at $x = 0$ and 1 because it is continuous to the right. Of course, $F_N(x,t)$ is non-decreasing with respect to x, and is identically zero for $x < 0$, identically unity for $x \geqslant 1$. Further, both $F_N(x,t)$ and $\phi_N(\theta,t)$ are step functions with respect to t.

In one time unit, the moment generating function changes by an amount

$$\phi_N(\theta,t+1) - \phi_N(\theta,t) = E\left[e^{\theta x(t+1)} - e^{\theta x(t)}\right]$$

$$= E\left[e^{\theta x(t)}\left(e^{\theta[x(t+1)-x(t)]} - 1\right)\right],$$

and by (A1) and (A2) this equals

$$N^{-m}\theta\, E\left\{e^{\theta x(t)}\left[M(x(t)) + \tfrac{1}{2}\theta V(x(t))\right]\right\} + N^{-m}\theta\,\varepsilon_N(\theta,t)$$

$$= N^{-m}\theta \sum_{i=0}^{R}\left(m_i + \tfrac{1}{2}\theta v_i\right)\frac{\partial^i \phi_N(\theta,t)}{\partial \theta^i} + N^{-m}\theta\,\varepsilon_N(\theta,t),$$

where $\varepsilon_N(\theta,t) = E\left[e^{\theta x(t)} W_N(\theta,t)\right]$. (A3) implies that

$$|\varepsilon_N(\theta, N^m u)| \leq e^B C_N(B) \to 0 \text{ as } N \to \infty \text{ for } |\theta| \leq B,\ u > 0. \quad (1.1)$$

In the equation

$$N^m\left[\phi_N(\theta,t+1) - \phi_N(\theta,t)\right] = \theta \sum_{i=0}^{k} \left(m_i + \tfrac{1}{2}\theta v_i\right) \frac{\partial^i \phi_N(\theta,t)}{\partial \theta^i} + \theta \varepsilon_N(\theta,t) \quad (1.2)$$

it would be simple to assume that $\phi_N(\theta, N^m u)$ converges to a limit $\phi(\theta,u)$ (say) as N increases, that this limit has suitable differentiability properties, and that it satisfies

$$\frac{\partial \phi(\theta,u)}{\partial u} = \theta \sum_{i=0}^{k} \left(m_i + \tfrac{1}{2}\theta v_i\right) \frac{\partial^i \phi(\theta,u)}{\partial \theta^i} .$$

Then, assuming the solution is a moment generating function of a random variable on $(0,1)$, say $\phi(\theta,u) = \int_{0-}^{1} e^{\theta x} dF(x,u)$, the equation can be reduced to

$$\frac{\partial F(x,u)}{\partial u} = \tfrac{1}{2} \frac{\partial}{\partial x}\left[V(x) \frac{\partial F}{\partial x}\right] - M(x) \frac{\partial F}{\partial x} ,$$

or, writing $f(x,u) = \dfrac{\partial F(x,u)}{\partial x}$,

$$\frac{\partial f(x,u)}{\partial u} = \tfrac{1}{2} \frac{\partial^2}{\partial x^2}\left[V(x) f(x,u)\right] - \frac{\partial}{\partial x}\left[M(x) f(x,u)\right] .$$

This is the diffusion equation used in genetic practice. However, the above argument is not rigorous, and seems very difficult to justify directly. The main stumbling block is the discrete nature of the time scale, and to remove this difficulty, a second generating function will be introduced which

removes discontinuities with respect to t in much the same way that $\phi_N(\theta, t)$ removes the discreteness due to the x variate.

Define the mixture of probability distributions by

$$\alpha_N(x,s) = \left(1-e^{-sN^{-m}}\right)\sum_{t=0}^{\infty} e^{-sN^{-m}t} F_N(x,t), \quad s>0. \tag{1.3}$$

This mixture is itself a probability distribution on $(0,1)$ and is continuous to the right. The moment generating function of the mixture will be written as

$$\mathfrak{F}_N(\theta,s) = \int_{0-}^{1} e^{\theta x}\, d_x \alpha_N(x,s),$$

and by the definition of $\alpha_N(x,s)$ equals

$$\int_{0-}^{1} e^{\theta x} d_x \left\{\left(1-e^{-sN^{-m}}\right)\sum_{t=0}^{\infty} e^{-sN^{-m}t} F_N(x,t)\right\}$$

$$= \left(1-e^{-sN^{-m}}\right)\sum_{t=0}^{\infty} e^{-sN^{-m}t}\int_{0-}^{1} e^{\theta x} d_x F_N(x,t),$$

$$= \left(1-e^{-sN^{-m}}\right)\sum_{t=0}^{\infty} e^{-sN^{-m}t}\, \phi_N(\theta,t), \tag{1.4}$$

the interchange of the order of integration and summation being justified by a limit theorem such as that given by Kendall and Stuart (17) p.104.

From equation (1.2), we can find a similar equation for the function $\mathfrak{F}_N(\theta,s)$. Multiply both sides of (1.2)

by $(1-e^{-sN^{-m}})e^{-sN^{-m}t}$ and add over all t. Consider the terms individually; firstly, we get

$$N^m\left(1-e^{-sN^{-m}}\right)\sum_{t=0}^{\infty} e^{-sN^{-m}t}\phi_N(\theta,t+1)$$

$$= N^m\left(1-e^{-sN^{-m}}\right)e^{sN^{-m}}\sum_{t=0}^{\infty} e^{-sN^{-m}(t+1)}\phi_N(\theta,t+1)$$

$$= N^m e^{sN^{-m}}\left[\Phi_N(\theta,s)-\left(1-e^{-sN^{-m}}\right)\phi_N(\theta,0)\right]$$

by (1.4),

where by (A4) the initial function $\phi_N(\theta,0)=\phi(\theta,0)\,dy=\int_{0-}^{1}e^{\theta x}d_xF(x,0)$ is assumed known. The second term of (1.2) becomes just $-N^m\Phi_N(\theta,s)$. From terms on the right hand side of (1.2) we get, firstly,

$$\theta\left(1-e^{-sN^{-m}}\right)\sum_{i=0}^{k}\left(m_i+\tfrac{1}{2}\theta v_i\right)\sum_{t=0}^{\infty}e^{-sN^{-m}t}\frac{\partial^i\phi_N(\theta,t)}{\partial\theta^i}$$

$$= \theta\sum_{i=0}^{k}\left(m_i+\tfrac{1}{2}\theta v_i\right)\frac{\partial^i\Phi_N(\theta,s)}{\partial\theta^i},$$

the interchange of the order of summation and differentiation being justified by the fact that the series $\sum_{t=0}^{\infty}e^{-sN^{-m}t}\frac{\partial^i\phi_N}{\partial\theta^i}$ is composed of continuous functions and is uniformly convergent with respect to θ - it is dominated by $e^{B}\sum_{t=0}^{\infty}e^{-sN^{-m}t}$ for θ in any bounded region $(-B,B)$. Finally, the last term becomes

$$\theta\left(1-e^{-sN^{-m}}\right)\sum_{t=0}^{\infty}e^{-sN^{-m}t}\varepsilon_N(\theta,t) \;=\; \theta\,\xi_N(\theta,s) \qquad \text{, say.}$$

But

$$\delta_N(\theta,s) = (1-e^{-sN^{-m}})\Big(\sum_{t=0}^{N^n u-1} + \sum_{t=N^n u}^{\infty}\Big) e^{-sN^{-m}t}\,\varepsilon_N(\theta,t)$$

for all $u > 0$ such that $N^n u$ is an integer. According to (1.1),

$$|\delta_N(\theta,s)| \leq \left(1-e^{-sN^{-m+n}u}\right) \operatorname*{Max}_{0\leq t\leq N^n u-1} |\varepsilon_N(\theta,t)| + e^{-sN^{-m+n}u} e^{B} C_N(B)$$

$$\longrightarrow \quad 0 \quad \text{as} \quad N \quad \text{increases, since in (A3),} \qquad (1.5)$$

$0 \leq n < m$. Collecting terms together, we have

$$\theta \sum_{i=0}^{k} \left(m_i + \tfrac{1}{2}\theta v_i\right) \frac{\partial^i \Xi_N(\theta,s)}{\partial \theta^i} - N^m\left(e^{sN^{-m}}-1\right)\Xi_N(\theta,s)$$

$$= -N^m\left(e^{sN^{-m}}-1\right)\phi(\theta,0) - \theta\,\delta_N(\theta,s). \qquad (1.6)$$

For fixed values of s, (1.6) may be regarded as an ordinary differential equation with non-homogeneous terms. Our immediate problem is to show that its solution converges to a unique limit as N increases. Consider the distributions $\{\alpha_N(x,s)\}$. Either this sequence converges as $N \to \infty$, or there exist two or more sub-sequences which converge to different limit functions. By the Montel-Helly theorem, Kendall and Stuart (17) p.103, we can in either case pick a subsequence $\{\alpha_{N'}(x,s)\}$ converging for all x to a monotonic limit $\alpha(x,s)$ say, which will itself be a probability distribution since it must be zero for $x < 0$ and unity for

$x \geqslant 1$. We shall subsequently prove that $\alpha(x,s)$ is uniquely determined by (1.6), and it follows that the entire sequence $\{\alpha_N(x,s)\}$ converges to this limit.

By the first limit theorem (Kendall and Stuart (17) p.104: note that continuity of the limit function is not necessary) we see that the sub-sequence of generating functions also converges, $\Phi_{N^*}(\theta,s) \to \Phi(\theta,s)$ say, where $\Phi(\theta,s)$ is the generating function corresponding to $\alpha(x,s)$, and this convergence is uniform with respect to θ in any bounded region. But for each i ,

$$\frac{\partial^i}{\partial\theta^i}\Phi_N(\theta,s) = \int_{0-}^{1} x^i e^{\theta x} d_x \alpha_N(x,s) \quad , \quad \frac{\partial^i}{\partial\theta^i}\Phi(\theta,s) = \int_{0-}^{1} x^i e^{\theta x} d_x \alpha(x,s)$$

(c/f Widder (33) p.59), so the derivatives of the $\Phi_{N^*}(\theta,s)$ converge to the corresponding derivatives of $\Phi(\theta,s)$. Thus, taking the limit of (1.6) over this particular sub-sequence gives

$$\theta \sum_{i=0}^{k} (m_i + \tfrac{1}{2}\theta v_i) \frac{\partial^i \Phi(\theta,s)}{\partial\theta^i} - s\,\Phi(\theta,s) = -s\,\phi(\theta,0),$$

that is

$$\theta \sum_{i=0}^{k} (m_i + \tfrac{1}{2}\theta v_i) \frac{\partial^i}{\partial\theta^i} \int_{0-}^{1} e^{\theta x} d_x \alpha(x,s) - s \int_{0-}^{1} e^{\theta x} d_x \alpha(x,s)$$

$$= -s \int_{0-}^{1} e^{\theta x} d_x F(x,0) . \qquad (1.7)$$

The limiting operation above changes the discrete process to one characterised by (1.7), which turns out to be a continuous diffusion process. Differentiating under the integral sign in (1.7), and introducing the functional notation of (A2) for $M(x)$ and $V(x)$ we have

$$\theta\int_{0-}^{1} e^{\theta x}\left[M(x)+\tfrac{1}{2}\theta V(x)\right]d_x\prec(x,s) - s\int_{0-}^{1} e^{\theta x} d_x\prec(x,s)$$

$$= -s\int_{0-}^{1} e^{\theta x} d_x F(x,0).$$

Integrating the latter two terms by parts results in

$$\theta\int_{0-}^{1} e^{\theta x}\left[M(x)+\tfrac{1}{2}\theta V(x)\right]d_x\prec(x,s) + s\theta\int_{0-}^{1} e^{\theta x}\left[\prec(x,s) - F(x,0)\right]dx$$

$$= s\left[e^{\theta x}\prec(x,s) - e^{\theta x}F(x,0)\right]_{0-}^{1}$$

$$= 0, \qquad (1.8)$$

and a second integration by parts for those terms involving θ but not θ^2 gives

$$\tfrac{1}{2}\theta^2\int_{0-}^{1} e^{\theta x} V(x) d_x\prec(x,s) = s\theta^2\int_{0-}^{1} e^{\theta x}\left[s^{-1}H(x,s) + K(x,s) - G(x,0)\right]dx$$

$$-s\theta\left[e^{\theta x}\left(s^{-1}H(x,s)+K(x,s)-G(x,0)\right)\right]_{0-}^{1}, \qquad (1.9)$$

where

$$G(x,0) = \int_{0-}^{x} F(x,0)dx,$$

$$H(x,s) = \int_{0-}^{x} M(x)d_x \alpha(x,s),$$

$$K(x,s) = \int_{0-}^{x} \alpha(x,s)dx.$$

If $\theta \neq 0$, (1.8) gives

$$\int_{0-}^{1} e^{\theta x}\left[M(x) + \tfrac{1}{2}\theta V(x)\right] d_x \alpha(x,s) + s\int_{0-}^{1} e^{\theta x}\left[\alpha(x,s) - F(x,0)\right] dx = 0.$$

But this equation holds also for $\theta = 0$ by continuity, and there we get

$$\left[s^{-1} H(x,s) + K(x,s) - G(x,0)\right]_{0-}^{1} = 0.$$

So finally, (1.9) becomes

$$\tfrac{1}{2}\int_{0-}^{1} e^{\theta x} V(x)\, d_x \alpha(x,s) = s\int_{0-}^{1} e^{\theta x}\left[s^{-1}H(x,s) + K(x,s) - G(x,0)\right] dx, \quad (1.10)$$

which holds at $\theta = 0$ by continuity.

By the uniqueness theorem for Laplace-Stieltjes transforms (Widder (33) p.63) the equality (1.10) ensures that

$$\tfrac{1}{2}\int_{0-}^{x} V(x)\, d_x \alpha(x,s) = s\int_{0-}^{x}\left[s^{-1}H(x,s) + K(x,s) - G(x,0)\right] dx \quad (1.11)$$

at least for almost all x. The right hand side is a continuous function of x, however, so that (1.11) in fact holds everywhere; the left hand side is monotonic since $V(x)$ is non-negative over the range of increase of $\alpha(x,s)$. Further,

because the right hand side of (1.11) is differentiable with respect to x, so too is the left hand side, and so too is $\alpha(x,s)$ except possibly where $V(x) = 0$, namely at $x = 0$ or 1. Hence, within the interval $(0,1)$ we have

$$\tfrac{1}{2}V(x)\frac{d\alpha}{dx} = H(x,s) + sK(x,s) - sG(x,0). \qquad (1.12)$$

But within the same interval, the right hand side is differentiable, so

$$\tfrac{1}{2}\frac{d}{dx}\left[V(x)\frac{d\alpha}{dx}\right] = M(x)\frac{d\alpha}{dx} + s\alpha - sF(x,0), \qquad (1.13)$$

that is

$$\tfrac{1}{2}V(x)\frac{d^2\alpha}{dx^2} + \left(\tfrac{1}{2}\frac{dV}{dx} - M\right)\frac{d\alpha}{dx} - s\alpha = sF(x,0). \qquad (1.14)$$

Equation (1.14) is a differential equation of a type studied by Feller (8), and from here on, we essentially reproduce his arguments in reverse order, applying them to our particular case. Firstly, to solve (1.14) uniquely two boundary conditions may be required at $x = 0$ and $x = 1$. To investigate what form these take, suppose there are jumps $\rho(0,s)$ and $\rho(1,s)$ in $\alpha(x,s)$ at $x = 0$ and 1 respectively. Letting $x \to 0+$ in (1.12) gives

$$\tfrac{1}{2}\lim_{x\to 0+} V(x)\frac{d\alpha}{dx} = M(0)\rho(0,s) + \lim_{x\to 0+}\int_{0+}^{x}\left[M(x)\frac{d\alpha}{dx} + s\alpha(x,s) - sF(x,0)\right]dx$$

$$= M(0)\rho(0,s).$$

But by assumption (A2), $V(x)$ has a zero of order unity or more at $x = 0$, and if $M(0)\,\rho(0,s) \neq 0$, then $\frac{d\alpha}{dx}$ has a pole of the same order. But this is impossible since $\frac{d\alpha}{dx}$ is integrable, and therefore $M(0)\,\rho(0,s) = 0$, and by symmetry, $M(1)\,\rho(1,s) = 0$.

In genetics, if there exists migration between populations, or gene mutation, neither $M(0)$ nor $M(1)$ are zero. Then $\rho(0,s) = \rho(1,s) = 0$, and the boundary conditions to be applied to (1.14) are

$$\alpha(0+,s) = \alpha(0,s) = 0, \quad \alpha(1-,s) = \alpha(1,s) = 1. \qquad (1.15)$$

These are sufficient to ensure a unique solution (see later).

Suppose now that $M(0) = M(1) = 0$, corresponding to no migration nor mutation. Then the above argument does not show that $\alpha(x,s)$ is continuous at 0 and 1. If jumps exist, they can be found from (1.13) to have the values

$$\rho(0,s) = \alpha(0+,s) = \lim_{x\to 0+}\left\{\tfrac{1}{2}s^{-1}\frac{d}{dx}\left(V\frac{d\alpha}{dx}\right) + F(x,0)\right\},$$
$$\rho(1,s) = 1-\alpha(1-,s) = -\lim_{x\to 1-}\left\{\tfrac{1}{2}s^{-1}\frac{d}{dx}\left(V\frac{d\alpha}{dx}\right) + F(x,0) - 1\right\}, \qquad (1.16)$$

because $M(x)\frac{d\alpha}{dx} \to 0$ as $x \to 0$ or 1. It is impossible to impose specific boundary conditions, and the question arises as to how to determine an appropriate solution. Feller's (8) studies of diffusion equations show that (1.14) has only one solution which is a probability distribution.

The assertions in the previous two paragraphs can be amplified somewhat. Make a transformation to a new variable defined by

$$\varphi(x) = \sqrt{2} \int_{\frac{1}{2}}^{x} V^{-\frac{1}{2}}(y)\, dy .$$

Because $V(y) > 0$ in the interior of $(0,1)$, this transform is monotonic; suppose it turns the points 0, 1 into r_1, r_2 respectively, where $-\infty \leq r_1 < 0 < r_2 \leq \infty$. Using the same function symbols after transformation, equation (1.14) becomes

$$\frac{d^2\alpha}{d\varphi^2} + \left(\tfrac{1}{2} V^{-1} \frac{dV}{d\varphi} - \sqrt{2}\, M V^{-\frac{1}{2}}\right) \frac{d\alpha}{d\varphi} - s\alpha = s\, F(\varphi, 0), \qquad (1.17)$$

for which we require a solution that is a probability distribution on (r_1, r_2) . Consider the homogeneous equation

$$\frac{d^2\alpha}{d\varphi^2} + \left(\tfrac{1}{2} V^{-1} \frac{dV}{d\varphi} - \sqrt{2}\, M V^{-\frac{1}{2}}\right) \frac{d\alpha}{d\varphi} - s\alpha = 0 . \qquad (1.18)$$

Hille (16) has shown, and the result is also quoted by Feller (8) p.483, (9)p.13, that there exist two non-negative solutions of (1.18), one of which is non-increasing, the other non-decreasing. Neither are identically zero, nor constants. Call these solutions α_1 and α_2 respectively; then if α_0 is a particular integral of (1.17), the general solution can be written as

$$\alpha = A\alpha_1 + B\alpha_2 + \alpha_0$$

where A and B are constants. In the problem where $M(r_1)$ and $M(r_2)$ are not zero, A and B are chosen so that α satisfies the boundary conditions equivalent to (1.15). Uniqueness depends on the fact that the determinant

$$\begin{vmatrix} \alpha_1(r_1) & \alpha_2(r_1) \\ \alpha_1(r_2) & \alpha_2(r_2) \end{vmatrix}$$

does not vanish, since $\alpha_1(r_1) > \alpha_1(r_2)$, $\alpha_2(r_2) > \alpha_2(r_1)$.

However, the case where $M(r_1)$ and $N(r_2)$ vanish is more interesting because there are no specific boundary conditions. If the particular integral α_0 is chosen to be a probability distribution on (r_0, r_1) , then it must be shown that the general solution is only a distribution when $A=B=0$, otherwise uniqueness would not be present. Consider the function

$$B(\xi) = \int_0^{\xi} \left[\tfrac{1}{2}V^{-1}\frac{dV}{d\xi} - \sqrt{2}\,MV^{-\frac{1}{2}}\right] d\xi = \int_{\frac{1}{2}}^{x} \left[\tfrac{1}{2}V^{-1}\frac{dV}{dx} - 2MV^{-1}\right] dx.$$

If $M(r_1) = M(r_2) = 0$, it may be shown (see appendix to this chapter) that

$$e^{B(\xi)} \quad , \quad e^{-B(\xi)}$$

are not both integrable, nor is

$$e^{-B(\xi)} \int_0^{\xi} e^{B(s)}\, ds$$

integrable, at either terminal r_1 or r_2 . Thus the boundaries r_1 and r_2 are, in Feller's notation (8) p.487,

either ENTRANCE or NATURAL boundaries.[1] But for such boundaries, Feller (8) p.488 shows that α_1 and α_2 can be chosen as being bounded at r_2 and r_1 respectively, but are then unbounded at r_1 and r_2 respectively. Consequently no linear combination can be a probability distribution, and the solution α_0 is unique.

It is unnecessary to consider separately the cases where $M(x)$ vanishes at one boundary but not the other, since the results follow immediately from the above considerations. Nor will we employ Green's functions or other techniques to find the actual solution of (1.14), but in the next section the nature of the solution will be discussed in terms of diffusion equations.

1: To avoid confusion with later terminology, it should be explained that these classifications refer to equation (1.18) considered as a mathematical entity, and not to the actual physical diffusion process. Feller (8) p.486 points out that if $B(\xi)$ is replaced by $-B(\xi)$, what was previously called an entrance boundary would be renamed EXIT The latter is the correct physical interpretation in our case, because for a population without mutation the boundaries act as absorbing barriers.

1.3. Nature of the solution.

The solution of (1.14), subject to the boundary conditions (1.15) when applicable, is

$$\alpha(x,s) = s\int_0^\infty e^{-su}F(x,u)\,du \quad , \tag{1.19}$$

where

(a) For $0 < x < 1$, $0 < u < \infty$,

$$\frac{\partial F}{\partial u} = \frac{1}{2}\frac{\partial}{\partial x}\left[V(x)\frac{\partial F}{\partial x}\right] - M(x)\frac{\partial F}{\partial x} \ . \tag{1.20}$$

(b) The notation $F(x,u)$ is consistent with the given initial function $F(x,0)$ when $u = 0$.

(c) If $M(0) = M(1) = 0$, no lateral conditions can be imposed at the boundaries $x = 0, x = 1$. At these points $F(x,u)$ has jumps

$$\begin{aligned} F(0+,u) &= F(0+,0) + \lim_{x\to 0+}\frac{1}{2}\int_0^u \frac{\partial}{\partial x}\left[V(x)\frac{\partial F(x,v)}{\partial x}\right]dv, \\ 1-F(1-,u) &= 1-F(1-,0) - \lim_{x\to 1-}\frac{1}{2}\int_0^u \frac{\partial}{\partial x}\left[V(x)\frac{\partial F(x,v)}{\partial x}\right]dv. \end{aligned} \tag{1.21}$$

If neither $M(0)$ nor $M(1)$ are zero, then there are no jumps in $F(x,u)$ and we impose the lateral conditions

$$\begin{aligned} F(0+,u) &= F(0,u) = 0, \\ F(1-,u) &= F(1,u) = 1. \end{aligned} \tag{1.22}$$

This solution is easily verified to satisfy (1.14); the jumps (1.21) are obtained from (1.16), and the boundary conditions (1.22) from (1.15). That (1.20), coupled with the conditions imposed, determines a unique function follows from Feller's paper (8). We shall refer to this point again later. Firstly,

however, we can give a precise meaning to the above result. We have shown that $\alpha(x,s)$ is uniquely determined, and therefore the whole sequence $\{\alpha_N(x,s)\}$ converges to this limit. From (1.3) and (1.19) we have that

$$(1-e^{-sN^{-m}})\sum_{t=0}^{\infty} e^{-sN^{-m}t} F_N(x,t) \to s\int_0^{\infty} e^{-su} F(x,u)\,du \quad \text{as } N\to\infty.$$

The left hand side can be written as an integral expression

$$(1-e^{-sN^{-m}})N^m \int_0^{\infty} e^{-s[N^m u]N^{-m}} F_N(x, N^m u)\,du,$$

where $[N^m u]$ denotes the integral part of $N^m u$. Now as N increases

$$(1-e^{-sN^{-m}})N^m e^{-s[N^m u]N^{-m}} \to se^{-su},$$

so we may write, for all $s>0$,

$$\lim_{N\to\infty} \int_0^{\infty} e^{-su} F_N(x,N^m u)\,du = \int_0^{\infty} e^{-su} F(x,u)\,du.$$

By the uniqueness theorem for Laplace transforms, this implies that

$$F_N(x,N^m u) \to F(x,u)$$

at least for all values of u for which the right hand side is continuous; the differentiability implicit in (1.20) ensures the convergence holds for all u. With respect to x, the limit can be made to hold for all x by arbitrarily de-

fining $F(x,u)$ as being continuous to the right at $x = 0$, $x = 1$, whenever jumps occur.

Thus for large N, and a suitably chosen time scale, $F(x,u)$ is an approximation to the probability distribution of the variate $x(N^m u)$. Many genetic problems have already been solved by the application of partial differential equations, for example Fisher (11), (12), Wright (41), Feller (7), and Crow and Kimura (6), but the rigorous study of the passage from a discrete to a continuous process seems not to have been given except for one special case, when Moran (24) found the approximate stationary distribution $F(x, \infty)$, or at least its derivative. Some of Moran's methods have been used above.

In practice, it has been usual to discuss the derivative, $\frac{\partial F(x,u)}{\partial x} = f(x,u)$ say, rather than the cumulated distribution itself. Differentiating (1.20) with respect to x gives the familiar Fokker-Planck diffusion equation

$$\frac{\partial f(x,u)}{\partial u} = \frac{1}{2}\frac{\partial^2}{\partial x^2}\left[V(x) f(x,u)\right] - \frac{\partial}{\partial x}\left[M(x) f(x,u)\right], \qquad (1.23)$$

which holds for all $0 < x < 1$. The boundary conditions to be applied are

(a) $f(x,u) \to \frac{d F(x,0)}{dx}$ as $u \to 0$, for all x for which the latter exists. In practice, when the initial gene frequency $x(0)$ is often a given constant, $f(x,u)$ converges to an improper 'delta function', a requirement to be interpreted in the sense of convergence of the integrals.

(b) If $M(0) = M(1) = 0$, no lateral conditions can be imposed on (1.23), and the time rates of accumulation of probability at the boundaries are, from (1.21),

$$\frac{dF(0+,u)}{du} = \lim_{x \to 0+} \tfrac{1}{2} \frac{\partial}{\partial x}\left[V(x) f(x,u)\right], \qquad (1.24)$$

$$\frac{d[1-F(1-,u)]}{du} = -\lim_{x \to 1-} \tfrac{1}{2} \frac{\partial}{\partial x}\left[V(x) f(x,u)\right].$$

If neither $M(0)$ nor $M(1)$ are zero, no accumulations of probability occur, and the solution $f(x,u)$ must represent a probability density. The lateral conditions to be imposed are

$$\tfrac{1}{2} \frac{\partial}{\partial x}\left[V(x) f(x,u)\right] - M(x) f(x,u) \to 0 \quad \text{as } x \to 0, 1. \qquad (1.25)$$

These conditions follow from (1.20) and (1.22).

That the conditions (a) and (b) are sufficient to determine a unique solution of (1.23) follows from Feller (8). For, consider the function

$$W(x) = \exp\left\{-2 \int_{1/2}^{x} M(y) V^{-1}(y)\, dy\right\}.$$

Feller introduces the terminology that a boundary, say $x = 1$, is called

REGULAR if $W(x)$ and $V^{-1}(x)W^{-1}(x)$ are integrable at $x = 1$, EXIT if $V^{-1}W^{-1}$ is not integrable, but $W \int^{x} V^{-1}(y)W^{-1}(y)dy$ is, ENTRANCE if not regular, and $V^{-1}W^{-1}$ and $V^{-1}W^{-1} \int^{x} W(y)dy$ are integrable, NATURAL if not of the other three types.

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This terminology is applicable to the diffusion process defined in (1.23), but not for the ordinary differential equation (1.14). In our case, when $M(x)$ and $V(x)$ are polynomials, it can be shown (see appendix) that the boundaries $x = 0$ and $x = 1$ are either exit or natural if $M(0) = M(1) = 0$, whilst they are either regular or entrance depending on the magnitude of the non-zero quantities $M(0)$ and $M(1)$. Feller (8) § 23 shows that exit and natural boundaries do not require lateral conditions for the solution of (1.23) but only the specification of the initial function $F(x,0)$, and the solution corresponds to a probability 'density' with end point accumulations. Further, for regular and entrance boundaries, the lateral conditions of zero flux, (1.25), make the solution a probability density without accumulations.

1.4. Applications to general genetical problems

In chapters 2-6 are given specific examples of population models having a finite number of individuals, and verifying for them that the above theory is applicable. For the present, it is assumed that such a model is available, and its genetic behaviour can be approximately described by the diffusion equation (1.23).

For definiteness, consider a model having

$$V(x) = \tfrac{1}{2}ax(1-x),\ M(x) = b-(b+c)x + sx(1-x)\left[\tfrac{1}{2}(d+1)-dx\right] \qquad (1.26)$$

Diffusion processes of this type have been considered in particular by Feller (7), Kimura (18), Crow and Kimura (6). The interpretations to be attached to the parameters are

a depends on the effective population size (which may not equal N),

b and c are non-negative mutation rates from one allele to the other, or migration rates from outside populations, d and s are selection coefficients measuring the selective advantage of one gene over the other. For no dominance $d = 0$, whilst for complete dominance $d = 1$ or -1 depending on which gene is the dominant. For no selection, $s = 0$.

Non-random mating may also influence all parameters. The diffusion equation can be used for two main purposes. For the case with mutations, $b > 0$, $c > 0$, it gives rise to a

probability density for the gene frequency, and of most interest is the 'stationary distribution'. This is the limiting value of $f(x,u)$ as $u \to \infty$, and is obtained from (1.23) by equating $\frac{\partial f}{\partial u}$ to zero. Dropping the dependence on u, the first integral of (1.23) becomes

$$\tfrac{1}{2}\frac{d}{dx}[V(x)\ f(x)] - M(x)\ f(x) = 0,$$

the constant of integration being zero in view of the boundary conditions (1.25). A second integration gives

$$f(x) = CV^{-1}(x)\ \exp\left\{2\int^{x} M(y)V^{-1}(y)dy\right\},$$

where the constant C is chosen to make $\int_0^1 f(x)\,dx = 1$. This solution was first used by Wright (38). For our example, we get

$$f(x) = C\,2a^{-1}\exp\left\{2a^{-1}[(d+1)x - dx^2]\right\}\ x^{4ba^{-1}-1}(1-x)^{4ca^{-1}-1}, \qquad (1.27)$$

which is similar in form to results found by Moran (24), (25) for specific overlapping and non-overlapping generation models. As for the classification of the boundaries, it is easily checked (see appendix to this chapter) that the boundary $x = 0$ is either regular or entrance depending on whether $0 < 4ba^{-1} < 1$, or $4ba^{-1} \geq 1$. Similarly, the boundary $x = 1$ is regular or entrance depending on whether $0 < 4ca^{-1} < 1$ or $4ca^{-1} \geq 1$.

For the case without mutation, one is most interested in the rate of approach to homozygosity, that is, the rate at which fixation or loss of the gene takes place in the popula-

tion. With $b = c = 0$, the boundaries are classified as exits, and the final distribution has

$$F(0+, \infty) + 1 - F(1-, \infty) = 1$$

$$f(x, \infty) = 0 \quad \text{for} \quad 0 < x < 1$$

According to Feller (9) p.11, an exit boundary is 'accessible', that is, there is a positive probability that it will be reached from the interior of $(0,1)$ in a finite time (here measured in u-units). He gives several theorems concerning first passage times, which are given here in our notation.

Firstly, let $p = x(0)$ be the initial value of the gene frequency, and $G(p,u) = 1 - F(1-,u)$ the probability that absorption at the boundary $x = 1$ has taken place before time u. Then, if the Laplace transform of G is

$$z(p, \lambda) = \int_0^\infty e^{-\lambda u} G(p,u)\, du ,$$

this satisfies the equation

$$\tfrac{1}{2} V(p) \frac{\partial^2 z}{\partial p^2} + M(p) \frac{\partial z}{\partial p} - \lambda z = 0 ,$$

with boundary conditions $z(0+,\lambda) = 0, z(1-,\lambda) = \lambda^{-1}$. More directly, Kimura (18) p.896 uses the equivalent result that

$$\tfrac{1}{2} V(p) \frac{\partial^2 G}{\partial p^2} + M(p) \frac{\partial G}{\partial p} = \frac{\partial G}{\partial u} , \qquad (1.28)$$

with boundaryconditions $G(0+,u) = 0, G(1-,u) = 1$. Note that these methods are alternatives to the application of (1.21),

which involves knowledge of the solution of the diffusion equation (1.23). Equation (1.23) is the formal adjoint of (1.28).

Secondly, the probability of ultimate absorption at $x = 1$, $G(p, \infty)$, is given by the solution of

$$\frac{1}{2} V(p) \frac{d^2 G(p,\infty)}{dp^2} + M(p) \frac{dG(p,\infty)}{dp} = 0, \qquad (1.29)$$

with boundary conditions $G(0+, \infty) = 0, G(1-, \infty) = 1$.

Thirdly, writing $U(p)$ as the expected time (in u-units) to reach one or other boundary $x = 0$, $x = 1$ then U is the solution of

$$\frac{1}{2} V(p) \frac{d^2 U}{dp^2} + M(p) \frac{dU}{dp} = -1, \qquad (1.30)$$

with boundary conditions $U(0+) = U(1-) = 0$.

For our particular example (1.26), no solution of (1.28) has yet been obtained, but Kimura (18) p.896 has obtained its smallest eigenvalue λ_0 as a power series expansion in the selection coefficients d and s. Thus[1]

$$2a^{-1}\lambda_0 = 1 + K_1 sa^{-1} + K_2(sa^{-1})^2 + K_3(sa^{-1})^3 + K_4(sa^{-1})^4 + \ldots \qquad (1.31)$$

---

1. The notation λ_0 used here is conventional for d.e.'s, but differs from the eigenvalues of the transition matrix $\underline{T}$ introduced in (0.1). It is, of course, related to the largest non-unit eigenvalue of $\underline{T}$.

where

$$K_1 = -\tfrac{1}{5}d, \quad K_2 = \frac{1}{2.5} + \frac{2^2.3}{5^3.7}d^2, \quad K_3 = \frac{1}{2.5^3.7}d - \frac{2^2}{5^5.7}d^3,$$

$$K_4 = -\frac{1}{2^3.5^3.7} - \frac{7^3}{2.3^3.5^5}d^2 - \frac{2^2.3^5}{5^6.7^3.11}d^4.$$

However, Kimura gives solutions, or at least methods for solution, for the particular cases $d = 0$, $d = 1$, and $d = -1$, and also the case with no selection at all, $s = 0$, $M(x) \equiv 0$. This latter case has the probability of absorption

$$G(p,u) = p + \sum_{i=1}^{\infty}(2i+1)p(1-p)(-1)^i F(1-i, i+2, 2, p)\, e^{-\frac{1}{4}i(i+1)au}, \qquad (1.32)$$

a result which may also be obtained indirectly from (1.21), using the diffusion equation solution

$$f(x,u) = \frac{\partial F(x,u)}{\partial x} = \sum_{i=1}^{\infty}\frac{2i+1}{i(i+1)}4p(1-p)T_{i-1}'(1-2p)T_{i-1}'(1-2x)\, e^{-\frac{1}{4}i(i+1)au},$$

(c/f Kimura (18) p.890).

The solution of (1.29) can however be found in the general case, and the result is (Kimura (18) p.896)

$$G(p,\infty) = \int_0^p e^{-2sa^{-1}[(d+1)x - dx^2]}dx \Big/ \int_0^1 e^{-2sa^{-1}[(d+1)x - dx^2]}dx. \qquad (1.33)$$

In particular, with no selection, $s = 0$, this reduces to

$$G(p,\infty) = p. \qquad (1.34)$$

(1.33) has been used to find the probability of survival of a single mutant in a population, by taking $p = \frac{1}{2}N^{-1}$; it seems intuitively reasonable, but does not follow from our previous

theory, that this procedure results in a good approximation for a finite population. Previously we had assumed that the initial variate $x(0)$ had a distribution independent of N. Nevertheless, verification can be made with some specific population models, and in particular, (1.34) is often exactly correct even for finite populations.

Finally, the evaluation of the expected time to reach homozygosity seems not to have been made before. For our example (1.25), without mutation, the solution of (1.30) is easily shown to be

$$U(p) = 4a^{-1}\Big[\int_0^p e^{-4sa^{-1}[\frac{1}{2}(d+1)-dx]}\Big[\int_{\frac{1}{2}}^x e^{4sa^{-1}[\frac{1}{2}(d+1)-dy]}\, y^{-1}(1-y)^{-1}dy\Big]dx$$

$$-\int_0^p e^{-4sa^{-1}[\frac{1}{2}(d+1)-dx]}\Big[\int_{\frac{1}{2}}^x e^{4sa^{-1}[\frac{1}{2}(d+1)-dy]}\, y^{-1}(1-y)^{-1}dy\Big]dx\Big]. \qquad (1.35)$$

In the case of no selection, $s = 0$, this simplifies to

$$U(p) = 4a^{-1}\log\left[p^{-p}(1-p)^{-(1-p)}\right], \qquad (1.36)$$

and can be verified as being the mean of the distribution obtained by summing (1.32) and the equivalent probability for the $x = 0$ boundary, namely $G(1-p,u)$. As would be expected, (1.36) represents a bell-shaped curve with maximum at $p = \frac{1}{2}$, when the initial gene frequency is furthest from a boundary. Clearly it is connected with the 'entropy' of the population at time $u = 0$. Suppose we define the entropy of a population in state x to be $S(x) = U(x)$, where $U(x)$ is defined in (1.35) for the general case. Then we have the immed-

iate result that the expected time for the population to reach homozygosity (a state of zero entropy) is equal to the initial entropy. The expected value of the entropy at time u, $H(u)$ say, is

$$H(u) = \int_{0-}^{1} S(x)\, d_x F(x,u) = \int_{0+}^{1-} S(x) f(x,u)\, dx \quad \text{since} \quad S(0) = S(1) = 0,$$

and the time required for this expected entropy to become zero is greater than $U(p)$. Differentiating with respect to u gives

$$\begin{aligned}
\frac{dH}{du} &= \int_{0+}^{1-} S(x) \frac{\partial f}{\partial u}\, dx, \\
&= \int_{0+}^{1-} S(x) \left[\tfrac{1}{2} \frac{\partial^2 V f}{\partial x^2} - \frac{\partial M f}{\partial x} \right] dx \quad \text{by (1.23)}, \\
&= -\int_{0+}^{1-} \frac{dS}{dx} \left[\tfrac{1}{2} \frac{\partial V f}{\partial x} - M f \right] dx, \quad \text{integrating by parts}, \\
&= \int_{0+}^{1-} \left[\tfrac{1}{2} V \frac{d^2 S}{dx^2} + M \frac{dS}{dx} \right] f\, dx, \quad \text{by parts, with } \left[\tfrac{1}{2} V f \frac{dS}{dx} \right]_0^1 = 0, \\
&= -\int_{0+}^{1-} f(x,u)\, dx \quad \text{by (1.30)}, \\
&= -[1 - F(0+,u) - G(p,u)], \\
&\leqslant 0.
\end{aligned}$$

Hence

$$H(u) - H(0) = -u + \int_0^u [F(0+,v) + G(p,v)]\, dv,$$

and when $H(u) = 0$, we have

$$u = H(0) + \int_0^u [F(0+,v) + G(p,v)]\, dv \geqslant H(0) = U(p). \qquad (1.37)$$

At least in the case when $s = 0$, an approximate solution of (1.37) could be obtained by substituting for $F(0+,v) = G(1-p,v)$ from (1.32)

In the results of § 1.4, we have used throughout the time scale of u, not t. In subsequent chapters, it will be shown that one u-unit corresponds to N generations in the finite population, or to N^2 individual-birth-death events. Thus, scaling the eigenvalue (1.31), the population approaches homozygosity at the rate $N^{-1}\lambda_0 = \mathcal{R}$ (say) measured in generations, and the expected time for this state to be reached is $NU(p)$ generations.

Concerning the accuracy of using diffusion theory for a finite population, some remarks can be made. Firstly, for the stationary density function (1.27), if selection is absent the formula reduces to a beta-distribution. Now in § 0 an exact distribution is given for Moran's model (0.6), and Moran (22) showed that the limit of this distribution as N increases can be obtained by using Stirling's formula for the gamma functions involved. He found a beta-distribution as the result, which suggests that (1.27) is as good an approximation for a finite population as Stirling's formula is for a gamma function.

Secondly, in most chapters of this thesis, we mention the fact that (1.34) is exactly correct for the model under discussion, provided selection is not present.

Thirdly, in (12.18) we show for Moran's model (0.6) that the expected time to reach an absorbing state can be expressed as a finite sum of terms, and that if this summation is replaced by integration, (1.36) is obtained as an approximation. Hence the accuracy of (1.36) can be ascertained in this case.

Finally, the rate of approach to homozygosity, $\mathscr{R} = N^{-1}\lambda_0$ where λ_0 is given by (1.31), will be shown to agree with the exact determinations except for terms of order N^{-2}, at least for models without selection.

1.5. Appendix

This appendix is concerned with verifying the nature of the boundaries $x = 0$, $x = 1$ for various functions $M(x)$ and $V(x)$. Only the boundary $x = 0$ need be investigated since the other follows by symmetry.

Firstly, we are concerned with the differential equation (1.14), or its transformed version (1.17). In the text, it was stated that when the function M vanishes at the boundaries, $e^{B(\xi)}$ and $e^{-B(\xi)}$ are not both integrable, nor is $e^{-B(\xi)}\int_0^{\xi} e^{B(s)}\,ds$ integrable, in particular at $\xi = r_1$. The proof is as follows. Transforming back into the original x variable, we require to prove that

$$c(x) = e^{-2\int_{1/2}^{x} M(y)V^{-1}(y)\,dy} \quad \text{and} \quad d(x) = V^{-1}(x)\, e^{2\int_{1/2}^{x} M(y)V^{-1}(y)\,dy}$$

are not both integrable, nor is

$$e(x) = V^{-1}(x)\, e^{2\int_{1/2}^{x} M(y)V^{-1}(y)\,dy}\left[\int_{1/2}^{x} e^{-2\int_{1/2}^{y} M(z)V^{-1}(z)\,dz}\,dy\right],$$

at $x = 0$. It is only necessary to consider cases where $d(x)$ is integrable, for otherwise $e(x)$ is not integrable either. Feller (8) lemma 9.2 states this result, without proof; it follows from the equality

$$\int_0^{1/2} e(x)\,dx = -\int_0^{1/2} c(x)\left[\int_0^{x} d(y)\,dy\right] dx.$$

Now consider the various possibilities. Suppose that for small x, $M(x) \doteqdot bx^p, V(x) \doteqdot \frac{1}{2}ax^q$, where the symbol $\doteqdot$ here implies that second order terms are neglected. Since, for the present purpose $M(0)=V(0)=0$, we have $p \geqslant 1$, $q \geqslant 1$. Then $M(x)V^{-1}(x) \doteqdot 2ba^{-1}x^{p-q}$, and $2\int_{\frac{1}{2}}^{x} MV^{-1}dx \doteqdot 4ba^{-1}(p-q+1)^{-1}x^{p-q+1}$ + constant if $p \neq q-1$, or $2\int_{\frac{1}{2}}^{x} MV^{-1}dx \doteqdot 4ba^{-1}\log x$ + constant if $p = q-1$. Thus

$$e^{2\int_{\frac{1}{2}}^{x} MV^{-1}dx} \doteqdot \text{constant}.\ e^{4ba^{-1}(p-q+1)^{-1}x^{p-q+1}} \quad \text{if } p \neq q-1,$$

$$\doteqdot \text{constant}.\ x^{4ba^{-1}} \quad \text{if } p = q-1.$$

Although apparently excluded above, the case when $M(x) \equiv 0$ is a special case of the second result with $b = 0$, for now $e^{2\int_{\frac{1}{2}}^{x} MV^{-1}dx} \equiv 1$. Otherwise we assume that $ba^{-1} \neq 0$.

Now

$$d(x) \doteqdot \text{constant}\ x^{-q}\ e^{4ba^{-1}(p-q+1)^{-1}x^{p-q+1}} \quad \text{if } p \neq q-1,$$

$$\doteqdot \text{constant}\ x^{4ba^{-1}-q} \quad \text{if } p = q-1,$$

and we are only concerned with cases when these are integrable. The first is integrable only when $p-q+1 < 0$ and $4ba^{-1} > 0$, for otherwise it exceeds a non-integrable function, constant $\times x^{-q}$, for sufficiently small x. The second is integrable only when $4ba^{-1}-q > -1$, that is, when $4ba^{-1} > p \geqslant 1$. In these circumstances, we need to show that $c(x)$ and $e(x)$ are not integrable. Now

$$e(x) \doteqdot \text{constant.}\ e^{4ba^{-1}(q-p-1)^{-1}x^{-(q-p-1)}} \quad \text{if } p \neq q-1,$$

$$\doteqdot \text{constant.}\ x^{-4ba^{-1}} \quad \text{if } p = q-1,$$

and obviously neither are integrable under the restrictions.

Again

$$e(x) = d(x)\int_{1/2}^{x} c(y)\,dy$$

$$\doteqdot \text{constant.}\ x^{-q} e^{-4ba^{-1}(q-p-1)^{-1}x^{-(q-p-1)}} \int_{1/2}^{x} e^{4ba^{-1}(q-p-1)^{-1}y^{-(q-p-1)}}\,dy$$

$$\doteqdot \text{constant.}\ x^{-p} \quad \text{if } q-1 \neq p \geq 1$$

or

$$\doteqdot \text{constant.}\ x^{4ba^{-1}-q}\int_{1/2}^{x} y^{-4ba^{-1}}\,dy \quad \text{if } p = q-1 \geq 1$$

$$\doteqdot \begin{cases} \text{constant.}\ x^{-p} & \text{if } 4ba^{-1} \neq 1 \\ \text{constant.}\ x^{-p}\log x & \text{if } 4ba^{-1} = 1. \end{cases}$$

In all of the above alternatives, it is clear that $e(x)$ is not integrable. This justifies the assertion in the text.

Turning now to the diffusion equation (1.23), it is necessary to show that the case when $M(0) = M(1) = 0$ corresponds to exit or natural boundaries. This follows immediately from the above argument, because for the diffusion equation the integrability of $e(x)$ and $d(x)$ implies a regular boundary, and of $e(x)$ implies an entrance boundary; both such possibilities have been disproved above. Again, in reference to (1.23) it was stated that when $M(0) \neq 0, M(1) \neq 0$, the boundaries are regular or entrance. To prove this, we now need to prove integrability of $e(x)$ and $d(x)$, or of $e(x)$ In the above notation, $p = 0, q \geq 1$, and in view of

(A2), $b = M(0) > 0$, $a > 0$. Thus when $q > 1$,

$$d(x) \doteqdot \text{constant.}\ x^{-q} e^{-4ba^{-1}(q-1)^{-1}x^{-(q-1)}},$$

$$e(x) \doteqdot \text{constant.}\ e^{4ba^{-1}(q-1)^{-1}x^{-(q-1)}},$$

$$c(x) \doteqdot \text{constant},$$

and both $d(x)$ and $e(x)$ are integrable whilst $c(x)$ is not. Hence the boundary is always an entrance. Alternatively, if $q = 1$, then

$$d(x) \doteqdot \text{constant.}\ x^{4ba^{-1}-1},$$

$$e(x) \doteqdot \text{constant.}\ x^{-4ba^{-1}},$$

$$e(x) \doteqdot \text{constant if } 4ba^{-1} \neq 1,$$

$$\doteqdot \text{constant.}\ \log x \text{ if } 4ba^{-1} = 1.$$

Clearly, $d(x)$ is always integrable, and $c(x)$ is integrable if $0 < 4ba^{-1} < 1$. In this case we have a regular boundary. If $4ba^{-1} \geqslant 1$, then $c(x)$ is not integrable but $e(x)$ is, so that the boundary is again an entrance. These conclusions are stated in § 1.4 for the particular case (1.26).

2. Model A: Offspring distributions.

2.0. Introduction

The previous chapter outlined a method for obtaining the stochastic behaviour of a genetic population under certain sufficient conditions. In §§ 2-6 we give examples of particular models for which the theory is applicable.

The first population model to be considered is a generalization of a model studied by Moran and Watterson (27) (see § 7 below) to the case when mutation is present. The population is of constant size, has non-overlapping generations, is not subject to selective pressures, and practices a restricted form of random mating. The distinctive feature of the model is that the probability distributions for the number of offspring, per parent, are to a considerable degree arbitrary. The only previous work of this kind concerned monoecious diploid populations without mutation, reference to which will be made in § 7.0. Here, we discuss dioecious diploid populations with mutation.

2.1 Description of model.

Suppose the population has N_1 males and N_2 females, making up a total of $N = N_1+N_2$ diploid individuals. The next generation consists of individuals, each formed by the mating of one male and one female. Write q_{1n} for the probability that a particular male has n offspring, with the generating function $Q_1(z) = \sum_{n=0}^{\infty} q_{1n}z^n$, and similarly let $Q_2(z)$ be the generating function for a particular female

As we assume selection is absent, then $Q_1(z)$ and $Q_2(z)$ apply to all males and females of the parent generation, respectively. The expected number of offspring is

$$N_1 Q_1'(1) = N_2 Q_2'(1),$$

which is a restriction on the otherwise arbitrary $Q_1(z)$, $Q_2(z)$.

The joint probability generating function for the numbers of offspring from male parents is

$$Q_1(z_1)\, Q_2(z_2) \ldots Q_1(z_{N_1})$$

assuming independence. However, as we do not wish the population to die out, we make the strong restriction that N_1 and N_2 are constants through all generations, and the above approach must be modified. A suitable joint generating function to ensure this is, for males,

$$\frac{\text{coefficient of } w^N \text{ in } Q_1(wz_1)Q_1(wz_2)\ldots Q_1(wz_{N_1})}{\text{coefficient of } w^N \text{ in } \left[Q_1(w)\right]^{N_1}},$$

and for females

$$\frac{\text{coefficient of } w^N \text{ in } Q_2(wz_1)Q_2(wz_2)\ldots Q_2(wz_{N_2})}{\text{coefficient of } w^N \text{ in } \left[Q_2(w)\right]^{N_2}}.$$

This means that the generating function for a particular parent

must also be modified, and becomes for males

$$P_1(z) = \frac{\text{coefficient of } w^N \text{ in } Q_1(wz)\left[Q_1(w)\right]^{N_1-1}}{\text{coefficient of } w^N \text{ in } \left[Q_1(w)\right]^{N_1}},$$

and for females (2.1)

$$P_2(z) = \frac{\text{coefficient of } w^N \text{ in } Q_2(wz)\left[Q_2(w)\right]^{N_2-1}}{\text{coefficient of } w^N \text{ in } Q_2(w)^{N_2}}.$$

One can easily show that the means of these distributions are

$$P_1'(1) = N N_1^{-1}, \quad P_2'(1) = N N_2^{-1}, \qquad (2.2)$$

and provided also that $N = N_1 Q_1'(1) = N_2 Q_2'(1)$, then as N_1 and N_2 increase we have $P_1(z) \to Q_1(z)$ and $P_2(z) \to Q_2(z)$. This convergence was proved by Moran (27).

The joint generating function for two male parents is

$$R_1(z_1,z_2) = \frac{\text{coefficient of } w^N \text{ in } Q_1(wz_1)Q_1(wz_2)\left[Q_1(w)\right]^{N_1-2}}{\text{coefficient of } w^N \text{ in } \left[Q_1(w)\right]^{N_1}},$$

and for females (2.3)

$$R_2(z_1,z_2) = \frac{\text{coefficient of } w^N \text{ in } Q_2(wz_1)Q_2(wz_2)\left[Q_2(w)\right]^{N_2-2}}{\text{coefficient of } w^N \text{ in } \left[Q_2(w)\right]^{N_2}}.$$

Because the total offspring from the N_1 males is exactly N, its variance must be zero, so we have

$$N_1\left[P_1''(1) + P_1'(1) - \left(P_1'(1)\right)^2\right] + N_1(N_1-1)\left[\frac{\partial^2 R_1}{\partial z_1 \partial z_2}\Big|_{z_1=z_2=1} - \left(P_1'(1)\right)^2\right] = 0,$$

or

$$\left[N_1^{-1}N(N-1) - P_1''(1)\right](N_1-1)^{-1} = \left.\frac{\partial^2 R_1}{\partial z_1 \partial z_2}\right|_{z_1=z_2=1}.$$

Similarly. (2.4)

$$\left[N_2^{-1}N(N-1) - P_2''(1)\right](N_2-1)^{-1} = \left.\frac{\partial^2 R_2}{\partial z_1 \partial z_2}\right|_{z_1=z_2=1}.$$

Further relations exist between joint moments of higher order.

Suppose the population consists of individuals of one or other of the genotypes aa, Aa, and AA , and let the number of males of each type be k_t , u_t , l_t at the t-th generation, and the number of females be r_t , v_t , s_t respectively.[1] The state of the population is determined by the four variates (k_t , l_t , r_t , s_t) since $u_t=N_1-k_t-l_t$ and $v_t=N_2-r_t-s_t$. Define p_1 , p_2 , p_3 as the probabilities that a parent of genotype aa, Aa, AA passes on a gamete of type a to his offspring, and write $q_i = 1 - p_i$ as the probability that a gene of type A is passed on. If the mutation rates are α_1 and α_2 for $a \to A$ and $A \to a$ respectively, then we have

i	1	2	3
p_i	$1-\alpha_1$	$\frac{1}{2}(1-\alpha_1+\alpha_2)$	α_2
q_i	α_1	$\frac{1}{2}(1+\alpha_1-\alpha_2)$	$1-\alpha_2$

(2.5)

1. The notation $k_t, u_t, l_t, r_t, v_t, s_t$ will be used often throughout this thesis to represent genotype numbers.

Our problem is to find the behaviour of the population during a transition from one generation to the next. This is solved in (2.13) where the probability generating function for $(k_{t+1},u_{t+1},l_{t+1},r_{t+1},v_{t+1},s_{t+1})$ conditional on a fixed state $(k_t,u_t,l_t,r_t,v_t,s_t)$ of the population at time t is given.

Denote the numbers of offspring coming from matings of type $i \times j$ by x_{ij}, and write $x_{i.}$ and $x_{.j}$ for the marginal totals. That is, the offspring numbers form a contingency table

Male parents.

Female parents		aa	Aa	AA	
	aa	x_{11}	x_{12}	x_{13}	$x_{1.}$
	Aa	x_{21}	x_{22}	x_{23}	$x_{2.}$
	AA	x_{31}	x_{32}	x_{33}	$x_{3.}$
		$x_{.1}$	$x_{.2}$	$x_{.3}$	N

(2.6)

As $x_{.1}$ represents the number of offspring from k_t males, and $x_{.2}$ and $x_{.3}$ come from u_t and l_t males, the generating function associated with these variates is (conditional on fixed k_t,u_t,l_t)

$$\left.\begin{aligned}\mathcal{E}\left(z_1^{x_{.1}}z_2^{x_{.2}}z_3^{x_{.3}}\right) &= \frac{\text{coefficient of } w^N \text{ in } [Q_1(z_1,w)]^{k_t}[Q_1(z_2,w)]^{u_t}[Q_1(z_3,w)]^{l_t}}{\text{coefficient of } w^N \text{ in } [Q_1(w)]^N},\\ \text{and similarly,}\\ \mathcal{E}\left(z_1^{x_{1.}}z_2^{x_{2.}}z_3^{x_{3.}}\right) &= \frac{\text{coefficient of } w^N \text{ in } [Q_2(z_1,w)]^{r_t}[Q_2(z_2,w)]^{v_t}[Q_2(z_3,w)]^{s_t}}{\text{coefficient of } w^N \text{ in } [Q_2(w)]^N}\end{aligned}\right\} \quad (2.7)$$

Now conditional on fixed values of the $x_{i.}$ and $x_{.j}$ we assume mating is at random, that is, that the row and column classifications in (2.6) are independent. This is, of

course, a restricted type of random mating in the sense that the parent population has fixed (but fairly arbitrary) offspring distributions according to (2.1).

Of the x_{ij} offspring, we denote the number of males by m_{ij} and the number of females by f_{ij}. Assuming that sex is determined at random subject to the restriction that N_1 males and N_2 females must be born, then the rows and columns of the 2 x 9 contingency table

$$\begin{array}{cccc|c} m_{11} & m_{12} & \cdots & m_{33} & N_1 \\ f_{11} & f_{12} & \cdots & f_{33} & N_2 \\ \hline x_{11} & x_{12} & \cdots & x_{33} & N \end{array} \qquad (2.8)$$

are independent.

With reference to the genotypes of these offspring, the probability that the mating of two parents of types i x j produces an offspring of type aa is $p_i p_j = p_{ij}$ (say), where the p_i are defined in (2.5). Similarly, the probability of a genotype AA is $q_i q_j = q_{ij}$ (say), and of Aa is $1-p_{ij}-q_{ij}$. Consider now the m_{ij} male offspring from matings of type i x j ; of these, let k_{ij} be of aa genotype, u_{ij} be Aa , and l_{ij} be AA . Then the probability of such a distribution is

$$\Pr\{k_{ij}, u_{ij}, \ell_{ij}\} = \frac{m_{ij}!}{k_{ij}!\, u_{ij}!\, \ell_{ij}!}\, p_{ij}^{k_{ij}} (1-p_{ij}-q_{ij})^{u_{ij}} q_{ij}^{\ell_{ij}}.$$

Similarly, define r_{ij} , v_{ij} , s_{ij} as the numbers of females of types aa, Aa , and AA out of the f_{ij} female offspring from i x j matings. We have (2.9)

$$\Pr\{r_{ij}, v_{ij}, s_{ij}\} = \frac{f_{ij}!}{r_{ij}!\, v_{ij}!\, s_{ij}!}\, p_{ij}^{r_{ij}} (1-p_{ij}-q_{ij})^{v_{ij}} q_{ij}^{s_{ij}}.$$

The specification of the population model will be completed if we can obtain the probability generating function for the t+1 th generation genotype numbers, namely of

$$k_{t+1} = \sum_{ij} k_{ij}\ ,\ u_{t+1} = \sum_{ij} u_{ij}\ ,\ \ell_{t+1} = \sum_{ij} \ell_{ij}\ ,\ r_{t+1} = \sum_{ij} r_{ij}\ ,\ v_{t+1} = \sum_{ij} v_{ij}\ ,\ s_{t+1} = \sum_{ij} s_{ij}.$$

Write this function as

$$W_{t+1}(\kappa, \chi, \lambda, \rho, \psi, \sigma) = E\left(\kappa^{k_{t+1}} \chi^{u_{t+1}} \lambda^{\ell_{t+1}} \rho^{r_{t+1}} \psi^{v_{t+1}} \sigma^{s_{t+1}}\right),$$

and denote a conditional expectation by $\mathcal{E}$, and a conditional value of W_{t+1} by $\mathcal{W}_{t+1}$. Now, conditional on fixed values of n_{ij} and f_{ij} , the variates k_{ij} etc. are multinomial variates with distributions given by (2.9). Thus the conditional function is

$$\mathcal{W}_{t+1} = \prod_{ij} \mathcal{E}\left(\kappa^{k_{ij}} \chi^{u_{ij}} \lambda^{\ell_{ij}}\right) \mathcal{E}\left(\rho^{r_{ij}} \psi^{v_{ij}} \sigma^{s_{ij}}\right),$$

$$= \prod_{i,j} \left[p_{ij}\kappa + (1-p_{ij}-q_{ij})\chi + q_{ij}\lambda \right]^{m_{ij}} \left[p_{ij}\rho + (1-p_{ij}-q_{ij})\psi + q_{ij}\sigma \right]^{f_{ij}},$$

$$= \prod_{i,j} g_{ij}^{m_{ij}} h_{ij}^{f_{ij}} \quad \text{say},$$

where

$$\begin{aligned} g_{ij} &= p_{ij}\kappa + (1-p_{ij}-q_{ij})\chi + q_{ij}\lambda \,, \\ h_{ij} &= p_{ij}\rho + (1-p_{ij}-q_{ij})\psi + q_{ij}\sigma \,. \end{aligned} \tag{2.10}$$

If the m_{ij} and f_{ij} are allowed to vary subject to fixed values of the marginal totals x_{ij}, N_1, N_2, then $\mathcal{W}_{t+1}$ is the probability generating function for variates from the contingency table (2.8), with independent classifications. The general result for contingency tables is that if $y_{ij} (i = 1, 2, \ldots n, j = 1, 2, \ldots, m)$ are variates of a contingency table with independent classifications, the probability generating function can be written as

$$\mathcal{E}\left(\theta_{11}^{y_{11}} \theta_{12}^{y_{12}} \ldots \theta_{nm}^{y_{nm}}\right) = \frac{\prod y_{ij}!}{y_{..}!} \text{ coefficient of } \varphi_1^{y_{.1}} \varphi_2^{y_{.2}} \ldots \varphi_m^{y_{.m}} \text{ in} \tag{2.11}$$

$$\left(\varphi_1\theta_{11} + \varphi_2\theta_{12} + \cdots + \varphi_m\theta_{1m}\right)^{y_{1.}} \left(\varphi_1\theta_{21} + \cdots + \varphi_m\theta_{2m}\right)^{y_{2.}} \cdots \left(\varphi_1\theta_{n1} + \cdots + \varphi_m\theta_{nm}\right)^{y_{n.}},$$

conditional on fixed values of the marginal totals $y_{i.}$, $y_{.j}$ (see Wilks (34) p.215).

Applying this result gives

$$W_{t+1} = \mathcal{E}\left[\prod_{ij} g_{ij}^{m_{ij}} h_{ij}^{f_{ij}}\right]$$

$$= \frac{N_1! N_2!}{N!} \text{ coefficient of } \gamma_1^{N_1}\gamma_2^{N_2} \text{ in } \prod_{ij}\left(\gamma_1 g_{ij} + \gamma_2 h_{ij}\right)^{x_{ij}}.$$

The variates x_{ij} are themselves restricted to a contingency table (2.6) with independent classifications; hence applying (2.11) conditional on fixed values of the $x_{i.}$ and $x_{.j}$ gives

$$W_{t+1} = \frac{N_1! N_2!}{N!} \text{ coefficient of } \gamma_1^{N_1}\gamma_2^{N_2} \text{ in}$$

$$\frac{x_{1.}! x_{2.}! x_{3.}!}{N!} \text{ coefficient of } \mu_1^{x_{1.}}\mu_2^{x_{2.}}\mu_3^{x_{3.}} \text{ in}$$

$$\prod_j\left[\gamma_1 \sum_i \mu_i g_{ij} + \gamma_2 \sum_i \mu_i h_{ij}\right]^{x_{.j}},$$

which may be rewritten

$$W_{t+1} = \frac{N_1! N_2!}{N!} \frac{x_{1.}! x_{2.}! x_{3.}!}{N!} \frac{x_{.1}! x_{.2}! x_{.3}!}{N!} \text{ coefficient of } \gamma_1^{N_1}\gamma_2^{N_2}\mu_1^{x_{1.}}\mu_2^{x_{2.}}\mu_3^{x_{3.}}\nu_1^{x_{.1}}\nu_2^{x_{.2}}\nu_3^{x_{.3}}$$

$$\text{in } \left[\gamma_1 \sum_{ij}\mu_i\nu_j g_{ij} + \gamma_2 \sum_{ij}\mu_i\nu_j h_{ij}\right]^N,$$

$$= \frac{\prod x_{i.}! \prod x_{.j}!}{(N!)^2} \text{ coefficient of } \mu_1^{x_{1.}}\mu_2^{x_{2.}}\mu_3^{x_{3.}}\nu_1^{x_{.1}}\nu_2^{x_{.2}}\nu_3^{x_{.3}}$$

$$\text{in } \left[\sum_{ij}\mu_i\nu_j g_{ij}\right]^{N_1}\left[\sum_{ij}\mu_i\nu_j h_{ij}\right]^{N_2}. \qquad (2.12)$$

The actual values of g_{ij} and h_{ij} were given in (2.10), and remembering that $p_{ij} = p_i p_j$ and $q_{ij} = q_i q_j$, we get

$$\sum_{ij} \mu_i \nu_j g_{ij} = (\kappa - \chi)(\Sigma p_i \mu_i)(\Sigma p_i \nu_i) + \chi(\Sigma \mu_i)(\Sigma \nu_i) + (\lambda - \chi)(\Sigma q_i \mu_i)(\Sigma q_i \nu_i),$$

$$\sum_{ij} \mu_i \nu_j h_{ij} = (\rho - \psi)(\Sigma p_i \mu_i)(\Sigma p_i \nu_i) + \psi(\Sigma \mu_i)(\Sigma \nu_i) + (\sigma - \psi)(\Sigma q_i \mu_i)(\Sigma q_i \nu_i)$$

Therefore, after some algebra,

$$\left(\sum_{ij} \mu_i \nu_j g_{ij}\right)^{N_1} \left(\sum_{ij} \mu_i \nu_j h_{ij}\right)^{N_2} = \sum_{\gamma_1 \gamma_2 \gamma_3} \left(\frac{\gamma_1! \gamma_2! \gamma_3!}{N!}\right)^2 \text{coefficient of } (\beta_1 \delta_1 \varepsilon_1)^{\gamma_1} (\beta_2 \delta_2 \varepsilon_2)^{\gamma_2} (\beta_3 \delta_3 \varepsilon_3)^{\gamma_3}$$

$$\text{in } \left\{\beta_1(\kappa - \chi) + \beta_2 \chi + \beta_3(\lambda - \chi)\right\}^{N_1} \left\{\beta_1(\rho - \psi) + \beta_2 \psi + \beta_3(\sigma - \psi)\right\}^{N_2}$$

$$\times \left[\delta_1 \Sigma p_i \mu_i + \delta_2 \Sigma \mu_i + \delta_3 \Sigma q_i \mu_i\right]^{N} \left[\varepsilon_1 \Sigma p_i \nu_i + \varepsilon_2 \Sigma \nu_i + \varepsilon_3 \Sigma q_i \nu_i\right]^{N},$$

where the summation is over non-negative integers $\gamma_1, \gamma_2, \gamma_3$ whose total is N. The expressions in square brackets are linear functions of the μ_i and ν_i, and so re-grouping terms and substituting back into (2.12) gives

$$W_{\theta_1} = \sum_{\gamma_1 \gamma_2 \gamma_3} \left(\frac{\gamma_1! \gamma_2! \gamma_3!}{N!}\right)^2 \text{coefficient of } (\beta_1 \delta_1 \varepsilon_1)^{\gamma_1} (\beta_2 \delta_2 \varepsilon_2)^{\gamma_2} (\beta_3 \delta_3 \varepsilon_3)^{\gamma_3} \text{ in}$$

$$\left[\beta_1(\kappa - \chi) + \beta_2 \chi + \beta_3(\lambda - \chi)\right]^{N_1} \left[\beta_1(\rho - \psi) + \beta_2 \psi + \beta_3(\sigma - \psi)\right]^{N_2}$$

$$\times \left(\delta_1 p_1 + \delta_2 + \delta_3 q_1\right)^{\alpha_{11}} \left(\delta_1 p_2 + \delta_2 + \delta_3 q_2\right)^{\alpha_{12}} \left(\delta_1 p_3 + \delta_2 + \delta_3 q_3\right)^{\alpha_{13}}$$

$$\times \left(\varepsilon_1 p_1 + \varepsilon_2 + \varepsilon_3 q_1\right)^{\alpha_{21}} \left(\varepsilon_1 p_2 + \varepsilon_2 + \varepsilon_3 q_2\right)^{\alpha_{22}} \left(\varepsilon_1 p_3 + \varepsilon_2 + \varepsilon_3 q_3\right)^{\alpha_{23}}.$$

Taking expectations with respect to the $x_{i\circ}$ and $x_{\circ j}$ in accordance with (2.7) gives

$$\mathcal{W}_{t+1} = \mathcal{E}\left(\pi^{k_{t+1}} \chi^{u_{t+1}} \lambda^{l_{t+1}} \rho^{r_{t+1}} \psi^{v_{t+1}} \sigma^{s_{t+1}}\right)$$

$$= \sum_{\gamma_1,\gamma_2,\gamma_3} \left(\frac{\gamma_1!\,\gamma_2!\,\gamma_3!}{N!}\right)^2 \text{coefficient of } (\beta_1\delta_1\varepsilon_1)^{\gamma_1}(\beta_2\delta_2\varepsilon_2)^{\gamma_2}(\beta_3\delta_3\varepsilon_3)^{\gamma_3} \text{ in}$$

$$\left[\beta_1(\pi-\chi)+\beta_2\chi+\beta_3(\lambda-\chi)\right]^{N_1}\left[\beta_1(\rho-\psi)+\beta_2\psi+\beta_3(\sigma-\psi)\right]^{N_2}$$

$$\times\left[Q_1(\varepsilon_1\beta_1+\varepsilon_2+\varepsilon_2\eta_1)\right]^{k_t}\left[Q_1(\varepsilon_1\beta_2+\varepsilon_2+\varepsilon_3\eta_2)\right]^{u_t}\left[Q_1(\varepsilon_1\beta_3+\varepsilon_2+\varepsilon_3\eta_3)\right]^{l_t}$$

$$\times\left[Q_2(\delta_1\beta_1+\delta_2+\delta_3\eta_1)\right]^{r_t}\left[Q_2(\delta_1\beta_2+\delta_2+\delta_3\eta_2)\right]^{v_t}\left[Q_2(\delta_1\beta_3+\delta_2+\delta_3\eta_3)\right]^{s_t}$$

$$\times\left\{\text{coefficient of } \omega_1^N\omega_2^N \text{ in } \left[Q_1(\omega_1)\right]^{N_1}\left[Q_2(\omega_2)\right]^{N_2}\right\}^{-1}, \qquad (2.13)$$

the summation being over non-negative integers $\gamma_1, \gamma_2, \gamma_3$ whose total is N .

Equation (2.13) is the major equation for future discussion, since it completely defines the stochastic behaviour of the population at generation $t+1$ conditional on a given state of the population at time t . However, an even more general result can be obtained by once again taking expectations over the variates k_t etc., without any conditional constraints. We get a type of difference equation for the unconditional probability generating function $W_t = E(\mathcal{W}_t)$.

namely,

$$W_{t+1}(\kappa,\chi,\lambda,\rho,\psi,\sigma) = \sum_{\gamma_1,\gamma_2,\gamma_3} \left(\frac{\gamma_1!\,\gamma_2!\,\gamma_3!}{N!}\right)^2 \text{coefficient of } (\beta_1\xi_1\varepsilon_1)^{\gamma_1}(\beta_2\xi_2\varepsilon_2)^{\gamma_2}(\beta_3\xi_3\varepsilon_3)^{\gamma_3}$$

$$\text{in } [\beta_1(\kappa-\chi)+\beta_2\chi+\beta_3(\lambda-\chi)]^{N_1}[\beta_1(\rho-\psi)+\beta_2\psi+\beta_3(\sigma-\psi)]^{N_2}$$

$$\times W_t[Q_1(\varepsilon_1\beta_1+\varepsilon_2+\varepsilon_3\eta_1),\ Q_1(\varepsilon_1\beta_2+\varepsilon_2+\varepsilon_3\eta_2),\ Q_1(\varepsilon_1\beta_3+\varepsilon_2+\varepsilon_3\eta_3),$$

$$Q_2(\xi_1\beta_1+\xi_2+\xi_3\eta_1),\ Q_2(\xi_1\beta_2+\xi_2+\xi_3\eta_2),\ Q_2(\xi_1\beta_3+\xi_2+\xi_3\eta_3)]$$

$$\times \left\{\text{coefficient of } \omega_1^{N_1}\omega_2^{N_2} \text{ in } [Q_1(\omega_1)]^{N_1}[Q_2(\omega_2)]^{N_2}\right\}^{-1}.$$

This equation, together with the (assumed) known starting value N_0, completely determines the whole stochastic behaviour of the model. But to make any worthwhile deductions from it about the a gene frequency $y_t = \frac{1}{2} + \frac{1}{2}N^{-1}(k_t - l_t + r_t - s_t)$, for large values of t, seems hopeless except in the simplest of cases. Some results are found in § 7 when no mutation is allowed, that is, when $p_1=1$, $p_2=\frac{1}{2}$, $p_3 = 0$; it is the aim at present to find approximate results in the general case when N_1 and N_2 may be assumed large.

2.2. Applicability of diffusion approximation.

In § 1, it was shown that under certain conditions a discrete stochastic process of the above type may be approximated by a diffusion process, for which many results are already known. We proceed to verify that this model does satisfy such conditions, and hence deduce its approximate behaviour.

As mentioned above, the relative frequency of the a gene in the population at time t is $y_t=\frac{1}{2}+\frac{1}{2}N^{-1}(k_t-l_t+r_t-s_t)$. It turns out that this function is not suitable for direct study; instead we consider the variate $x_t=\frac{1}{2}+\frac{1}{2}N_1^{-1}(k_t-l_t)+\frac{1}{2}N_2^{-1}(r_t-s_t)$ and shall show that x_t-y_t converges in probability to zero as N_1 and N_2 increase. This implies (see Cramer (4) p.254) that y_t and x_t have the same asymptotic distribution and approximations valid for one will hold for the other also.

The moment generating function of x_{t+1} conditional on a given state of the population at the t-th generation is

$$\mathcal{E}\left(e^{\theta x_{t+1}}\right) = e^{\frac{1}{2}\theta}\,\mathcal{E}\left\{\exp\tfrac{1}{4}\theta\left[N_1^{-1}(k_{t+1}-l_{t+1})+N_2^{-1}(r_{t+1}-s_{t+1})\right]\right\},$$

and substituting

$$\kappa = e^{\frac{1}{4}N_1^{-1}\theta},\quad \chi=1,\quad \lambda=e^{-\frac{1}{4}N_1^{-1}\theta},\quad \rho=e^{\frac{1}{4}N_2^{-1}\theta},\quad \psi=1,\quad \sigma=e^{-\frac{1}{4}N_2^{-1}\theta}$$

into (2.13) results in

$$\mathcal{E}(e^{\theta x_{t+1}}) = e^{\frac{1}{2}\theta} \sum_{\gamma_1,\gamma_2,\gamma_3} \left(\frac{\gamma_1!\,\gamma_2!\,\gamma_3!}{N!}\right)^2 \text{coefficient of } (\beta_1\delta_1\varepsilon_1)^{\gamma_1}(\beta_2\delta_2\varepsilon_2)^{\gamma_2}(\beta_3\delta_3\varepsilon_3)^{\gamma_3}$$

$$\text{in } \left[\beta_1(e^{\frac{1}{2}N_1^{-1}\theta}-1)+\beta_2+\beta_3(e^{-\frac{1}{2}N_1^{-1}\theta}-1)\right]^{N_1}\left[\beta_1(e^{\frac{1}{2}N_2^{-1}\theta}-1)+\beta_2+\beta_3(e^{-\frac{1}{2}N_2^{-1}\theta}-1)\right]^{N_2}$$

$$\times\left[Q_1(\varepsilon_1\beta_1+\varepsilon_2+\varepsilon_3\gamma_1)\right]^{k_t}\left[Q_1(\varepsilon_1\beta_2+\varepsilon_2+\varepsilon_3\gamma_2)\right]^{u_t}\left[Q_1(\varepsilon_1\beta_3+\varepsilon_2+\varepsilon_3\gamma_3)\right]^{\ell_t}$$

$$\times\left[Q_2(\delta_1\beta_1+\delta_2+\delta_3\gamma_1)\right]^{r_t}\left[Q_2(\delta_1\beta_2+\delta_2+\delta_3\gamma_2)\right]^{v_t}\left[Q_2(\delta_1\beta_3+\delta_2+\delta_3\gamma_3)\right]^{s_t} \qquad (2.14)$$

$$\times\left\{\text{coefficient of } w_1^{N}w_2^{N} \text{ in } \left[Q_1(w_1)\right]^{N_1}\left[Q_2(w_2)\right]^{N_2}\right\}^{-1}.$$

To verify the applicability of the theory of § 1, we need to investigate the conditional expectation $\mathcal{E}\left[e^{\theta(x_{t+1}-x_t)}-1\right]$. Expanding by Taylor's theorem gives

$$\mathcal{E}\left[e^{\theta(x_{t+1}-x_t)}-1\right] = \theta\,\mathcal{E}(x_{t+1}-x_t) + \tfrac{1}{2}\theta^2\mathcal{E}(x_{t+1}-x_t)^2$$

$$+\tfrac{1}{6}\theta^3\mathcal{E}(x_{t+1}-x_t)^3+\tfrac{1}{24}\theta^4\mathcal{E}\left[(x_{t+1}-x_t)^4 e^{\theta\varphi(x_{t+1}-x_t)}\right],$$

where φ is a random variable with $0<\varphi<1$. Because $|\varphi(x_{t+1}-x_t)|<1$, the absolute value of the last term is

$$\tfrac{1}{24}\theta^4\left|\mathcal{E}\left[(x_{t+1}-x_t)^4 e^{\theta\varphi(x_{t+1}-x_t)}\right]\right| < \tfrac{1}{24}e^{\theta}\theta^4\,\mathcal{E}(x_{t+1}-x_t)^4.$$

We need to find two functions $N^{-m}M(x_t)$ and $N^{-m}V(x_t)$ which are approximately equal to $\mathcal{E}(x_{t+1}-x_t)$ and $\mathcal{E}(x_{t+1}-x_t)^2$ respectively, and to show that the remainder of the series is small for sufficiently large N and t. Firstly, we con-

sider

$$\mathcal{E}(x_{t+1}-x_t) = \frac{d}{d\theta}\left(\mathcal{E}e^{\theta x_{t+1}}\right)\Big|_{\theta=0} - x_t .$$

Differentiating (2.14) once with respect to θ, and evaluating the result at $\theta=0$, gives

$$\frac{d}{d\theta}\left(\mathcal{E}e^{\theta x_{t+1}}\right)\Big|_{\theta=0} = \frac{1}{2} + \sum_{\gamma_1,\gamma_2,\gamma_3}\left(\frac{\gamma_1!\,\gamma_2!\,\gamma_3!}{N!}\right)^2 \text{coefficient of } (\beta_1\delta_1\varepsilon_1)^{\gamma_1}(\beta_2\delta_2\varepsilon_2)^{\gamma_2}(\beta_3\delta_3\varepsilon_3)^{\gamma_3}$$

$$\text{in } \tfrac{1}{2}\beta_2^{N-1}(\beta_1-\beta_3)\left[Q_1(\varepsilon_1\beta_1+\varepsilon_2+\varepsilon_3\eta_1)\right]^{R_t}\left[Q_1(\varepsilon_1\beta_2+\varepsilon_2+\varepsilon_3\eta_2)\right]^{U_t}\left[Q_1(\varepsilon_1\beta_3+\varepsilon_2+\varepsilon_3\eta_3)\right]^{L_t}$$

$$\times\left[Q_2(\delta_1\beta_1+\delta_2+\delta_3\eta_1)\right]^{r_t}\left[Q_2(\delta_1\beta_2+\delta_2+\delta_3\eta_2)\right]^{u_t}\left[Q_2(\delta_1\beta_3+\delta_2+\delta_3\eta_3)\right]^{s_t} \qquad (2.15)$$

$$\times\left\{\text{coefficient of } w_1^N w_2^N \text{ in } \left[Q_1(w_1)\right]^{N_1}\left[Q_2(w_2)\right]^{N_2}\right\}^{-1}.$$

As usual, the summation on the right hand side is over non-negative integers $\gamma_1, \gamma_2, \gamma_3$ whose total is N, and terms with $\gamma_1=1, \gamma_2=N-1, \gamma_3=0$ or $\gamma_1=0, \gamma_2=N-1, \gamma_3=1$ are non-zero.
For example, consider the evaluation of

$$\text{coefficient of } \varepsilon_1\varepsilon_2^{N-1} \text{ in } \left[Q_1(\varepsilon_1\beta_1+\varepsilon_2+\varepsilon_3\eta_1)\right]^{R_t}\left[Q_1(\varepsilon_1\beta_2+\varepsilon_2+\varepsilon_3\eta_2)\right]^{U_t}\left[Q_1(\varepsilon_1\beta_3+\varepsilon_2+\varepsilon_3\eta_3)\right]^{L_t}$$

$$\times\left\{\text{coefficient of } w_1^N \text{ in } \left[Q_1(w_1)\right]^{N_1}\right\}^{-1}.$$

By differentiating with respect to ε_1 , this equals

$$\text{coefficient of } \varepsilon_2^{N-1} \text{ in } (k_t p_1 + u_t p_2 + l_t p_3)\, Q_1'(\varepsilon_2)\, Q_1^{N-1}(\varepsilon_2) \times \{\text{coefficient of } \omega_1^N \text{ in } [Q_1(\omega_1)]^{N_1}\}^{-1},$$

which by (2.1) and (2.2) is just

$$(k_t p_1 + u_t p_2 + l_t p_3) P_1'(1) = (k_t p_1 + u_t p_2 + l_t p_3) N N_1^{-1} .$$

Substituting for this and similar terms into (2.15) gives

$$\frac{d}{d\theta}\left(\mathcal{E} e^{\theta x_{t+1}}\right)\Big|_{\theta=0} = \tfrac{1}{2} + \tfrac{1}{2} N_1^{-1} N_2^{-1}\left[(k_t p_1 + u_t p_2 + l_t p_3)(r_t p_1 + v_t p_2 + s_t p_3) - (k_t q_1 + u_t q_2 + l_t q_3)(r_t q_1 + v_t q_2 + s_t q_3)\right],$$

and introducing the values of p_i , q_i from (2.5) we get

$$\frac{d}{d\theta}\left(\mathcal{E} e^{\theta x_{t+1}}\right)\Big|_{\theta=0} = \tfrac{1}{2}(1-\alpha_1+\alpha_2) + \tfrac{1}{4}(1-\alpha_1-\alpha_2)\left[N_1^{-1}(k_t - l_t) + N_2^{-1}(r_t - s_t)\right]$$

$$= \tfrac{1}{2}(1-\alpha_1+\alpha_2) + \tfrac{1}{2}(1-\alpha_1-\alpha_2)(2x_t - 1) .$$

Thus

$$\mathcal{E}(x_{t+1} - x_t) = \frac{d}{d\theta}\left(\mathcal{E} e^{\theta x_{t+1}}\right)\Big|_{\theta=0} - x_t = \alpha_2 - (\alpha_1 + \alpha_2) x_t .$$

Similarly, with the aid of (2.3), (2.4), and (2.5) it may be shown that

$$\mathcal{E}(x_{t+1}-x_t)^2 = \frac{d^2}{d\theta^2}\left(\mathcal{E}e^{\theta x_{t+1}}\right)\Big|_{\theta=0} - 2x_t\frac{d}{d\theta}\left(\mathcal{E}e^{\theta x_{t+1}}\right)\Big|_{\theta=0} + x_t^2$$

$$= \tfrac{1}{4}\left[N_1^{-1}(\beta_t+\ell_t)-N_1^{-2}(\beta_t-\ell_t)^2\right]\left[N^{-2}N_1P_1''(1)-N_1^{-1}\right]$$

$$+\tfrac{1}{4}\left[N_2^{-1}(\gamma_t+\delta_t)-N_2^{-2}(\gamma_t-\delta_t)^2\right]\left[N^{-2}N_2P_2''(1)-N_2^{-1}\right]$$

$$+\tfrac{1}{2}(N_1^{-1}+N_2^{-1})\left[1+N_1^{-1}N_2^{-1}(\beta_t-\ell_t)(\gamma_t-\delta_t)-2(2\alpha_t-1)^2\right]$$

$$+ O(N^{-2}) .$$

Finally, one can show that $\mathcal{E}(x_{t+1}-x_t)^3$ and $\mathcal{E}(x_{t+1}-x_t)^4$ are both bounded by a constant of order of magnitude N^{-2}, but the algebra for proving the last three results is tedious and is omitted.

In view of these results, we can write for the Taylor expansion

$$\mathcal{E}\left[e^{\theta(x_{t+1}-x_t)}-1\right] = \theta\left[\alpha_t-(\alpha_1+\alpha_2)x_t\right]$$

$$+\tfrac{1}{32}\theta^2\Big\{\left[N_1^{-1}(\beta_t+\ell_t)-N_1^{-2}(\beta_t-\ell_t)^2\right]\left[N^{-2}N_1P_1''(1)-N_1^{-1}\right]$$

$$+\left[N_2^{-1}(\gamma_t+\delta_t)-N_2^{-2}(\gamma_t-\delta_t)^2\right]\left[N^{-2}N_2P_2''(1)-N_2^{-1}\right]$$

$$+\tfrac{1}{2}(N_1^{-1}+N_2^{-1})\left[1+N_1^{-1}N_2^{-1}(\beta_t-\ell_t)(\gamma_t-\delta_t)-2(2\alpha_t-1)^2\right]$$

$$+ O(N^{-2})\Big\} ,$$

where $O(N^{-2})$ represents a random variable bounded by a constant of order of magnitude N^{-2}, provided Θ is restricted to a finite region. For the theory of § 1 to be applicable, this function must be expressible in the form $\Theta N^{-m}\left[M(x_t)+\frac{1}{2}\Theta V(x_t)+W_N(\Theta,t)\right]$ where M and V are functions independent of N, and W is small for large N and t. The choice of these three functions is of course not arbitrary, nor is it obvious how they are defined. As a start, one might guess that the Hardy-Weinberg law holds for large N, so that k_t, l_t, r_t and s_t might approximate $N_1x_t^2$, $N_1(1-x_t)^2$, $N_2x_t^2$ and $N_2(1-x_t)^2$ respectively. Further, for large N we know that $P_1(z) \doteqdot Q_1(z)$, and $P_2(z) \doteqdot Q_2(z)$, at least provided N_1 and N_2 increase in such a way that the ratios NN_1^{-1} and NN_2^{-1} are constant and equal $Q_1'(1)$ and $Q_2'(1)$ respectively. Making these substitutions, the coefficient of $\frac{1}{2}\Theta^2$ is approximately

$$\tfrac{1}{8}N^{-2}\left[N_1Q_1''(1)+N_2Q_2''(1)\right]x_t(1-x_t)$$

and therefore for m we choose $m=1$, and for $V(x)$,

$$V(x)=\tfrac{1}{8}N^{-1}\left[N_1Q_1''(1)+N_2Q_2''(1)\right]x(1-x).$$

This function satisfies the assumptions made about it in § 1.1, provided, of course, that N_1 and N_2 are increased in a fixed proportion so that $V(x)$ is independent of the value of N. With $m=1$, the function $M(x)$ is now determined by the coefficient of ΘN^{-1}, namely

$$M(x)=N\left[\alpha_2-(\alpha_1+\alpha_2)x\right].$$

This satisfies the assumptions of § 1.1 provided $N\alpha_1$ and $N\alpha_2$ are independent of N, that is, provided α_1 and α_2 are inversely proportional to the population size. This requirement has practical fulfilment when the mutation rates are small; if α_1 and α_2 are constants independent of N, then the diffusion theory breaks down and the limiting case (as N increases) is a deterministic process outside the scope of the thesis.

Finally, the third function is now

$$W_N(\theta,t) = \frac{1}{32}\theta\Big\{\big[N_1^{-1}(A_t+\ell_t)-N_1^{-2}(A_t-\ell_t)^2-2x_t(1-x_t)\big]\big[N^{-1}N_1P_1''(0)-NN_1^{-1}\big]$$
$$+\big[N_2^{-1}(r_t+s_t)-N_2^{-2}(r_t-s_t)^2-2x_t(1-x_t)\big]\big[N^{-1}N_2P_2''(0)-NN_2^{-1}\big]$$
$$-\tfrac{1}{8}N(N_1^{-1}+N_2^{-1})\big[N_1^{-1}(A_t-\ell_t)-N_2^{-1}(r_t-s_t)\big]^2$$
$$+2x_t(1-x_t)N^{-1}\big[N_1P_1''(0)+N_2P_2''(0)-N_1Q_1''(0)-N_2Q_2''(0)\big]$$
$$+O(N^{-1})\Big\}.$$

We need to show that there exists some number $n\,(0\leqslant n<m=1)$ such that the unconditional expectation of $\left|W_N(\theta,N^n u)\right|$, for all $u>0$, converges to zero as $N\to\infty$. It will be sufficient if we can show

$E\left|W_N(\theta,t)\right|\to 0$ as $N\to\infty$, the convergence being uniform for all $t>1$, and all θ in $(-B,B)$.

This does not quite fulfil the assumption with $n=0$ since $t=1$ is excluded from the convergence. However for any $n>0$ the validity will follow in view of the uniformity con-

dition (on t) here imposed.

Now

$$|W_N(\theta,t)| \leqslant \tfrac{1}{32}|\theta| \Big\{ \big|N_1^{-1}(k_t+l_t) - N_1^{-2}(k_t-l_t)^2 - 2x_t(1-x_t)\big| \cdot \big|N^{-1}N_1 P_1''(1) - NN_1^{-1}\big|$$

$$+ \big|N_2^{-1}(r_t+s_t) - N_2^{-2}(r_t-s_t)^2 - 2x_t(1-x_t)\big| \cdot \big|N^{-1}N_2 P_2''(1) - NN_2^{-1}\big|$$

$$+ \tfrac{1}{8} N(N_1^{-1}+N_2^{-1}) \big[N_1^{-1}(k_t-l_t) - N_2^{-1}(r_t-s_t)\big]^2$$

$$+ 2x_t(1-x_t)N^{-1} \big|N_1 P_1''(1) + N_2 P_2''(1) - N_1 Q_1''(1) - N_2 Q_2''(1)\big|$$

$$+ O(N^{-1}) \Big\} ,$$

so it will be sufficient to prove that

$$\begin{aligned}
&E\big[N_1^{-1}(k_t-l_t) - N_2^{-1}(r_t-s_t)\big]^2 \to 0 , \\
&E\big[N_1^{-1}(k_t+l_t) - N_1^{-2}(k_t-l_t)^2 - 2x_t(1-x_t)\big]^2 \to 0 , \\
&E\big[N_2^{-1}(r_t+s_t) - N_2^{-2}(r_t-s_t)^2 - 2x_t(1-x_t)\big]^2 \to 0 , \\
&N^{-1}\big|N_1(P_1''(1) - Q_1''(1)) + N_2(P_2''(1) - Q_2''(1))\big| \to 0 ,
\end{aligned} \tag{2.16}$$

as $N \to \infty$, uniformly for all $t > 1$.

To prove the first result, the moment generating function for $N_1^{-1}(k_t-l_t) - N_2^{-1}(r_t-s_t)$ can be obtained from (2.13) by putting $\kappa = e^{\theta N_1^{-1}}$, $\gamma = 1$, $\lambda = e^{-\theta N_1^{-1}}$, $\rho = e^{-\theta N_2^{-1}}$, $\psi = 1$, $\sigma = e^{\theta N_2^{-1}}$, and replacing t by $t-1$. This will be a function conditional on fixed values of the k_{t-1} , etc. From it, one sees that

$$E\big[N_1^{-1}(k_t-l_t) - N_2^{-1}(r_t-s_t)\big]^2 = O(N^{-1}).$$

In fact, the following identity is true (c/f equation (7.9))

$$\mathcal{E}\left[N_1^{-1}(k_t - l_t) - N_2^{-1}(r_t - s_t)\right]^2 \equiv N_1^{-2}\,\mathcal{E}(k_t + l_t) + N_2^{-2}\,\mathcal{E}(r_t + s_t) - (N_1^{-1} + N_2^{-1})N_1^{-1}N_2^{-1}\,\mathcal{E}(k_t - l_t)(r_t - s_t),$$

and the right hand side is clearly $O(N^{-1})$ uniformly for t. As N increases, the unconditional expectation also converges to zero. In passing, note that because $N_1^{-1}(k_t - l_t)$ and $N_2^{-1}(r_t - s_t)$ converge in probability, so too will x_t and y_t, and this justifies our fixing attention on x_t rather than to the actual gene frequency, y_t.

The two middle results of (2.16) follow similarly. For example, from (2.13) one can show by suitable differentiations that

$$\mathcal{E}\left[N_1^{-1}(k_t + l_t) - N_1^{-2}(k_t - l_t)^2 - 2x_t(1 - x_t)\right]^2 = \frac{1}{64}\left[N_1^{-1}(k_{t-1} - l_{t-1}) - N_2^{-1}(r_{t-1} - s_{t-1})\right]^2 + O(N^{-1}),$$

and the unconditional expectation of the right hand side is $O(N^{-1})$ by the previous result. At least, this holds uniformly for $t > 1$, for otherwise fixed initial values k_0, l_0, r_0, and s_0 would be encountered. The last result of (2.16) follows from the fact that $P_i(z) \to Q_i(z)$ as $N \to \infty$ if the ratio $N_1 N_2^{-1}$ is kept constant.

This completes the verification of the assumptions of § 1.1.

2.3. Asymptotic behaviour of model.

In equation (1.26) an example was given of which the present model is a particular case, with the notational substitutions

$$a = \tfrac{1}{4}N^{-1}\left[N_1 Q_1''(1) + N_2 Q_2''(1)\right] , \quad b = N\alpha_2 , \quad c = N\alpha_1 ,$$

$$s = d = 0.$$

From (1.27), the stationary density for x (and hence for the gene frequency y) is approximately equal to the beta-density

$$\left[B(4N_V\alpha_2 , 4N_V\alpha_1)\right]^{-1} x^{4N_V\alpha_2 - 1}(1-x)^{4N_V\alpha_1 - 1} , \qquad (2.17)$$

where we have written

$$N_V = \frac{x(1-x)}{2V(x)}N = 4N^2\left[N_1 Q_1''(1) + N_2 Q_2''(1)\right]^{-1} \qquad (2.18)$$

as the 'variance effective population size' (c/f Crow (5) p.551).[1]

Suppose that there is no mutation, that is $\alpha_1 = \alpha_2 = 0$, and that the initial value of x is $p = \frac{1}{2} + \frac{1}{4}N_1^{-1}(k_0 - l_0) + \frac{1}{4}N_2^{-1}(r_0 - s_0)$. Of course, p is

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1. This definition of N_V is not particularly suitable for haploid populations, especially for those with overlapping generations.

not exactly the initial value of the a gene frequency in general, but is so if $N_1 = N_2$. Then the rate of approach to homozygosity is approximately

$$\mathscr{R} \doteq N^{-1}\lambda_0 = \tfrac{1}{2}aN^{-1} = \tfrac{1}{8}N^{-2}\left[N_1Q_1''(1) + N_2Q_2''(1)\right] = \tfrac{1}{2}N_V^{-1},$$

per generation, by (1.31). The probability of ultimate fixation of the a gene is $G(p,\infty) \doteq p$, (1.34), and the expected value of the time for the a gene to be either fixed or lost from the population is $NU(p) \doteq 4N_V \log p^{-p}(1-p)^{-(1-p)}$ generations, (1.36). All the approximations are valid for large N_1 and N_2 , and some are exact or good approximations for small populations. Thus, in (7.13) it is shown that $G(p,\infty) = p$ exactly, and also in (7.11) that for the finite population the rate of approach to homozygosity is

$$\mathscr{R} \doteq N^{-1}\lambda_0 \doteq \tfrac{1}{8}N^{-2}\left[N_1P_1''(1) + N_2P_2''(1)\right]$$

ignoring terms of order N^{-2} . The approximate result above will be of the same accuracy whenever $P_i''(1) - Q_i''(1) = O(N^{-1})$; for example, when all individuals of the same sex produce exactly the same number of offspring, we have $P_i(z) \equiv Q_i(z) = z^{NN_i^{-1}}$, and

$$\mathscr{R} \doteq N^{-1}\lambda_0 = \tfrac{1}{8}N^{-1}(N^2N_1^{-1}N_2^{-1} - 2).$$

This particular case is the one for which N_V is maximum and $\mathscr{R}$ minimum; when the offspring distributions have variances, the corresponding N_V is reduced. This example proves that $N_V \leqslant 2N$, with equality holding only when $N_1 = N_2$ and Q_1 and Q_2 have zero variances.

The most important special case of the above model is that considered by Wright (36), in which offspring are produced by completely random mating (with replacement) amongst the parent generation. For this population the offspring probability distribution, per parent, is binomial, and the generating functions are

$$P_1(z)=(1-N_1^{-1}+N_1^{-1}z)^N \quad , \quad P_2(z)=(1-N_2^{-1}+N_2^{-1}z)^N .$$

The corresponding limiting distributions are Poisson, with

$$Q_1(z)=e^{+(z-1)NN_1^{-1}} \quad , \quad Q_2(z)=e^{+(z-1)NN_2^{-1}} \quad ,$$

and the variance effective population size is

$$N_v = 4N_1N_2N^{-1} .$$

Thus the stationary distribution for a large population has the approximate density

$$f(x) = \left[B(16N_1N_2N^{-1}\alpha_2 \, , \, 16N_1N_2N^{-1}\alpha_1)\right]^{-1} x^{16N_1N_2N^{-1}\alpha_2-1}(1-x)^{16N_1N_2N^{-1}q-1} \qquad (2.19)$$

with mutation, and the rate of approach to homozygosity, per generation, is $\frac{1}{8}NN_1^{-1}N_2^{-1}$ without mutation. Both these results are well known (c/f (25) p.116, (20) p.212).

Other special cases will be considered in connection with models B , C , and D below, where their discussion is more appropriate than here. But we will now give one final example concerning human populations.

Lotka (21) found from American population statistics for 1920 that the probability of a given male having n offspring could be written $\gamma_{1,n} = \gamma_{1,1}\,\gamma^{n-1}$ for $n \gg 1$, and

for $n = 0$, $q_{1,0} = 1 - q_{1,1}\sum_{n=1}^{\infty}\gamma^{n-1} = 1 - \frac{q_{1,1}}{1-\gamma}$. The parameter values were $q_{1,1} = 0.1707$, $\gamma = 0.7358$, $q_{1,0} = 0.3540$. Actually, Lotka had incorrectly calculated $q_{1,0}$ as being 0.3686; this is inconsistent with the other two parameter values which were obtained by least squares fitting to observed data. The generating function for the male population is then

$$Q_1(z) = \sum_{n=0}^{\infty} q_{1,n} z^n = 1 - \frac{q_{1,1}}{1-\gamma} + \frac{q_{1,1} z}{1-\gamma z} ,$$

and the expected value of the number of offspring is

$$Q_1'(1) = \frac{q_{1,1}}{(1-\gamma)^2} .$$

Now consider a population model having non-overlapping generations, such that the sex numbers are equal and constant (or at least their expectations) through all generations, and that the offspring probabilities are the same for both sexes. We suppose that $N_1 = N_2 = \frac{1}{2}N$, and

$$Q_1(z) = Q_2(z) = 1 - \frac{q_{1,1}}{1-\gamma} + \frac{q_{1,1} z}{1-\gamma z} .$$

These assumptions are not, of course, valid for the American population. With $Q_1'(1) = Q_2'(1) = 2$ we find

$$q_{1,1} = 2(1-\gamma)^2 , \quad q_{1,0} = 2\gamma - 1 ,$$

and if $\gamma = 0.7358$ as above, we get $q_{1,1} = 0.1396$, $q_{1,0} = 0.4716$, which are not too dissimilar from the actual parameters. The

effective population size is then

$$N_V = \frac{4N^2}{\frac{1}{2}N\left[Q_1''(1) + Q_2''(1)\right]} = N\frac{1-\gamma}{\gamma}$$

$$= 0.3591\,N,$$

or roughly one third of the total size.

3. Model B: Selection and non-random mating

3.0. Introduction.

We turn now to a model which incorporates a degree of selection and non-random mating, and so is more general (in this sense) than model A. However, to get an amenable model we sacrifice the previous model's main attribute, namely the arbitrary nature of the generating functions $P_1(z)$ and $P_2(z)$. The model we discuss was that introduced by Moran (25); he obtained the asymptotic stationary distribution by a somewhat different method to that used here, but did not deal with the problems arising when no mutation is present. Nevertheless, we are able to use some of the results he proves for our own purposes. The model concerns dioecious diploid individuals with non-overlapping generations.

3.1. Description of model.

Moran introduced selection by assuming that the genotypes aa , Aa , and AA produce gametes in the proportions $1-\vartheta_1 : 1 : 1+\vartheta_2$ and he defined mutation rates α_1 and α_2 as above in model A. All the coefficients ϑ_1 , ϑ_2 , α_1 and α_2 are assumed to be proportional to N^{-1} , and are thus small. If selection occurs before mutation, the proportions of the two genes in the gametic output of the sexes are (c/f (25)p.114)

$$p_M(a) = \tfrac{1}{2}(N_1 - \nu_1 k_t + \nu_2 \ell_t)^{-1}\left[N_1(1-\alpha_1+\alpha_2) + (1-\alpha_1-\alpha_2)(k_t-\ell_t) - 2k_t\nu_1(1-\alpha_1) + 2\ell_t\nu_2\alpha_2\right],$$

$$p_M(A) = \tfrac{1}{2}(N_1 - \nu_1 k_t + \nu_2 \ell_t)^{-1}\left[N_1(1+\alpha_1-\alpha_2) - (1-\alpha_1-\alpha_2)(k_t-\ell_t) - 2k_t\nu_1\alpha_1 + 2\ell_t\nu_2(1-\alpha_2)\right],$$

(3.1)

$$p_F(a) = \tfrac{1}{2}(N_2 - \nu_1 r_t + \nu_2 s_t)^{-1}\left[N_2(1-\alpha_1+\alpha_2) + (1-\alpha_1-\alpha_2)(r_t-s_t) - 2r_t\nu_1(1-\alpha_1) + 2s_t\nu_2\alpha_2\right],$$

$$p_F(A) = \tfrac{1}{2}(N_2 - \nu_1 r_t + \nu_2 s_t)^{-1}\left[N_2(1+\alpha_1-\alpha_2) - (1-\alpha_1-\alpha_2)(r_t-s_t) - 2r_t\nu_1\alpha_1 + 2s_t\nu_2(1-\alpha_2)\right].$$

When these gametes unite to form zygotes, Moran postulated that there is a degree f of non-randomness in the pairing so that zygotes are formed in the proportions[1]

$$\begin{aligned} p(aa) &= (1-f)p_M(a)p_F(a) + \tfrac{1}{2}f\left[p_M(a)+p_F(a)\right], \\ p(Aa) &= (1-f)\left[p_M(a)p_F(A) + p_M(A)p_F(a)\right] \\ p(AA) &= (1-f)p_M(A)p_F(A) + \tfrac{1}{2}f\left[p_M(A)+p_F(A)\right]. \end{aligned} \qquad (3.2)$$

Finally, from these gametes the new generation is formed by random sampling, to give the probability generating function conditional on a given population at time t ,

$$\mathcal{E}\left(\kappa^{k_{t+1}}\chi^{u_{t+1}}\lambda^{\ell_{t+1}}\rho^{r_{t+1}}\psi^{v_{t+1}}\sigma^{s_{t+1}}\right) = \left[p(aa)\kappa + p(Aa)\chi + p(AA)\lambda\right]^{N_1}\left[p(aa)\rho + p(Aa)\psi + p(AA)\sigma\right]^{N_2}.$$

---

1. An extensive discussion of non-random mating is given in § 8, for which this is a special case.

3.2. Applicability of diffusion approximation

As for model A , we consider the variates $x_t = \frac{1}{2} + \frac{1}{2}N_1^{-1}(k_t - l_t) + \frac{1}{2}N_2^{-1}(r_t - s_t)$ rather than the actual gene frequency $y_t = \frac{1}{2} + \frac{1}{2}N^{-1}(k_t - l_t + r_t - s_t)$. Moran (25) shows that these converge in probability, so they have asymptotically the same distribution. The conditional moment generating function of x_{t+1} is

$$\mathcal{E}(e^{\theta x_{t+1}}) = e^{\frac{1}{2}\theta}\left[p(aa)e^{\frac{1}{4}N_1^{-1}\theta} + p(Aa) + p(AA)e^{-\frac{1}{4}N_1^{-1}\theta}\right]^{N_1}\left[p(aa)e^{\frac{1}{4}N_2^{-1}\theta} + p(Aa) + p(AA)e^{-\frac{1}{4}N_2^{-1}\theta}\right]^{N_2}$$

and substituting for the p(aa) etc. from (3.2), we have

$$\begin{aligned}\mathcal{E}\left[e^{\theta(x_{t+1}-x_t)}-1\right] &= e^{-\theta x_t}\,\mathcal{E}(e^{\theta x_{t+1}}) - 1\\ &= \theta\Big[\alpha_2 - (\alpha_1+\alpha_2)x_t - \tfrac{1}{4}(\nu_1 N_1^{-1}k_t + \nu_1 N_2^{-1}r_t + \nu_2 N_1^{-1}l_t + \nu_2 N_2^{-1}s_t)\\ &\qquad + \tfrac{1}{4}(\nu_1 k_t - \nu_2 l_t)(k_t - l_t)N_1^{-2} + \tfrac{1}{4}(\nu_1 r_t - \nu_2 s_t)(r_t - s_t)N_2^{-1}\Big]\\ &\quad + \tfrac{1}{16}\theta^2(N_1^{-1}+N_2^{-1})\left[1+f+(1-f)(k_t-l_t)(r_t-s_t)N_1^{-1}N_2^{-1} - 2(2x_t-1)^2\right]\\ &\quad + \theta\,O(N^{-2}).\end{aligned}$$

This can be written in the form

$$\theta\, N^{-m}\left[M(x_t) + \tfrac{1}{2}\,\theta\, V(x_t) + W_N(\theta, t)\right]$$

by taking $m = 1$,

$$M(x) = N\alpha_2 - N(\alpha_1+\alpha_2)x - \tfrac{1}{2}(1+f)N(\nu_1+\nu_2)x(1-x) - \tfrac{1}{2}(1-f)N(\nu_1-\nu_2)(2x-1)x(1-x),$$

$$V(x) = \tfrac{1}{8}N(N_1^{-1}+N_2^{-1})(1+f)x(1-x),$$

$$W_N(\theta,t) = N\theta^{-1}\mathcal{E}\left[e^{\theta(x_{t+1}-x_t)}-1\right] - M(x_t) - \tfrac{1}{2}\theta V(x_t),$$

and these three functions satisfy the assumptions of § 1.1, because, in particular, M and V ~~is~~ are independent of N if $N\alpha_1, N\alpha_2, N\nu_1, N\nu_2$ are assumed constants, and because Moran has, in effect, shown that $E|W_N(\theta, t)| \to 0$ as N_1 and N_2 increase with their ratio kept constant.

3.3. Asymptotic behaviour of model.

This model is therefore a special case of the one treated in (1.26), with

$$a = \tfrac{1}{4}N(N_1^{-1} + N_2^{-1})(1+f),\ b = N\alpha_2,\ c = N\alpha_1,$$

$$s = -N(1+f)(\nu_1+\nu_2),\quad d = -(1-f)(\nu_1-\nu_2)\left[(1+f)(\nu_1+\nu_2)\right]^{-1}.$$

As in (2.18), one can define the variance effective population size, and here it becomes

$$N_v = 4N_1N_2N^{-1}(1+f)^{-1}. \tag{3.3}$$

The interpretation of the constants a, b, and c is now clear, for they represent the ratio NN_v^{-1}, the mutation rate from A to a (scaled) and the reverse rate from a to A, respectively. The interpretation of s and d is not so simple since they are a compounding of selection and non-random mating coefficients; for no selection $(\nu_1=\nu_2=0)$, $s=0$, for no dominance $(\nu_1=\nu_2)$, $d=0$, and for random mating $(f=0)$ d is simply a measure of dominance, since for a dominant $(\nu_1=0)$, $d=1$, and for a recessive $(\nu_2=0)$, $d=-1$.

With mutation operating, the asymptotic stationary distribution of x (and y) is, from (1.27),

$$f(x) = 2N^{-1}N_V C \exp\left\{-4N_V(\nu_2+\nu_1 f)x - 2N_V(1-f)(\nu_1-\nu_2)x^2\right\} . x^{4N_V\alpha_2-1}(1-x)^{4N_V\alpha_1-1}, \quad (3.4)$$

and agrees with that deduced by Moran (25) by different methods. In the special case without selection and with random mating, $\nu_1 = \nu_2 = f = 0$, the model becomes a special case of model A, and (3.4) reduces to (2.19).

When $\alpha_1 = \alpha_2 = 0$, the population eventually reaches a stage where one or other gene is fixed. The rate at which this occurs depends on the eigenvalue

$$\lambda_0 = \tfrac{1}{2}a\left[1 + K_1 sa^{-1} + K_2(sa^{-1})^2 + K_3(sa^{-1})^3 + K_4(sa^{-1})^4 + \ldots\right], \quad \text{(see (1.31))}$$

when time is measured in units $u = N^m t = Nt$, so that, per generation, we have the rate of approach to homozygosity

$$\mathcal{R} \doteq N^{-1}\lambda_0 = \tfrac{1}{2}N_V^{-1}\left[1 + K_1(sN_VN^{-1}) + K_2(sN_VN^{-1})^2 + K_3(sN_VN^{-1})^3 + K_4(sN_VN^{-1})^4 + \ldots\right]. \quad (3.5)$$

Here

$$K_1 = -\frac{1}{5}d, \quad K_2 = \frac{1}{2.5} + \frac{2^2.3}{5^3.7}d^2, \quad K_3 = \frac{1}{2.5^3.7}d - \frac{2^2}{5^5.7}d^3,$$

$$K_4 = -\frac{1}{2^3.5^3.7} - \frac{7^3}{2.3^3.5^5}d^2 - \frac{2^2.3^5}{5^6.7^3.11}d^4.$$

Provided s is sufficiently small to make the second and higher powered terms of (3.5) negligible, then $\mathcal{R}$ is less than $\frac{1}{2}N_V^{-1}$ if selection is in favour of a dominant gene ($s > 0, d > 0$ or $s < 0, d < 0$) and $\mathcal{R}$ is greater then $\frac{1}{2}N_V^{-1}$ if selection is in favour of a recessive gene ($s > 0$, $d < 0$ or

$s \leqslant 0, d > 0$) . This was pointed out by Kimura (18) p.896, but he did not deal with a specific model. The probability of ultimate fixation of the a gene is, according to (1.33),

$$G(p,\omega) \doteqdot \frac{\int_0^p e^{-\phi}\left\{2N_V[(1+f)(v_1+v_2)-(1-f)(v_1-v_2)]x+2N_V(1-f)(v_1-v_2)x^2\right\}dx}{\int_0^1 e^{-\phi}\left\{2N_V[(1+f)(v_1+v_2)-(1-f)(v_1-v_2)]x+2N_V(1-f)(v_1-v_2)x^2\right\}dx}, \quad (3.6)$$

and the expected time for the a gene to be either fixed or lost is

$$\begin{aligned} N\,U(p) \doteqdot\ & 4N_V p\int_0^1 e^{-4sa^{-1}\left[\frac{1}{2}(d+1)-dx\right]}\left[\int_{1/2}^{x} e^{4sa^{-1}\left[\frac{1}{2}(d+1)-dy\right]}y^{-1}(1-y)^{-1}dy\right]dx \\ & -4N_V\int_0^p e^{-4sa^{-1}\left[\frac{1}{2}(d+1)-dx\right]}\left[\int_{1/2}^{x} e^{4sa^{-1}\left[\frac{1}{2}(d+1)-dy\right]}y^{-1}(1-y)^{-1}dy\right]dx, \end{aligned} \quad (3.7)$$

measured in generations. As in model A , p is not necessarily the initial a gene frequency, but rather, $p = \frac{1}{2} + \frac{1}{4}N_1^{-1}(k_0 - l_0) + \frac{1}{4}N_2^{-1}(r_0 - s_0)$.

When no selection operates in the model, it is shown in equation (9.14) that (3.6) gives exactly correct results, whilst (3.5) is correct except for terms of order N^{-2}, even though finite populations be considered, see (9.13). Unfortunately, no exact determinations have yet been made for models with selection.

4. Model C: Overlapping generations.

4.0. Introduction

Models A and B just considered are both of a type where the generations of the populations do not overlap, but rather, the entire population dies and is replaced simultaneously. Models D, and C which we now describe, are of quite a different type in that individuals die one at a time, and each is immediately replaced by a new individual. As before, the model is of dioecious diploid type.

Model C was introduced by Moran (24), who found the asymptotic stationary distribution; we shall change his notation slightly but use essentially the same model. By application of the diffusion approximation, we extend Moran's work to the case when mutation is absent, and the stationary distribution degenerate.

4.1. Description of model.

In model B, the selection effect was assumed to take place at the production of gametes for the gene pool, so that genotypes aa, Aa , and AA produced gametes in the proportions $1-\gamma_1 : 1 : 1+\gamma_2$. Following the production, mutation took place at the rates α_1 and α_2 , and then the gametes combined to form zygotes with the (non-random) probabilities given in (3.2). In the present model, selection is not introduced in this way. Here, the offspring zygotes are assumed to occur in the proportions given formally by (3.2), but with

$\nu_1 = \nu_2 = 0$ in the gamete proportions (3.1).

Selection is introduced by varying the average lifetimes of the three genotypes. Suppose that at a death, the probability that a dying individual is of a particular type is given by (c/f. (24) p.104)

male	aa	$(1+\nu_1)k\Lambda^{-1}$
male	Aa	$(N_1-k-\ell)\Lambda^{-1}$
male	AA	$(1-\nu_2)\ell\Lambda^{-1}$
female	aa	$(1+\nu_1)r\Lambda^{-1}$
female	Aa	$(N_2-r-s)\Lambda^{-1}$
female	AA	$(1-\nu_2)s\Lambda^{-1}$,

(4.1)

where (k,l,r,s) is the state of the population immediately preceding the death, $\Lambda = (1+\nu_1)(k+r)+(N-k-\ell-r-s)+(1-\nu_2)(\ell+s)$, and ν_1 and ν_2 are selection coefficients measuring the deviation from completely random deaths. Note that if ν_1 is small and positive, $1+\nu_1$ represents a relatively shorter life for aa individuals, thus reducing the average number of offspring to being proportional to $(1+\nu_1)^{-1} \doteq 1-\nu_1$. This is just the quantity used in the model B for selection against aa. Similarly, $(1-\nu_2)^{-1} \doteq 1+\nu_2$. Therefore the quantities ν_1, ν_2 in this model have, at least qualitatively, the same interpretation as those used previously, although they arise from quite a different population model.

At the death of an individual, the population is kept at constant size by choosing a new individual of the same sex at random from the zygote pool. Thus the state may remain

(k,l,r,s) or may change to another with the following probabilities:

$(k-1,l,r,s)$	$(1+\nu_1)\, k\Lambda^{-1}\, p(Aa)$
$(k-1,l+1,r,s)$	$(1+\nu_1)\, k\Lambda^{-1}\, p(AA)$
$(k+1,l,r,s)$	$(N_1-k-l)\Lambda^{-1}\, p(aa)$
$(k,l+1,r,s)$	$(N_1-k-l)\Lambda^{-1}\, p(AA)$
$(k+1,l-1,r,s)$	$(1-\nu_2)\, l\Lambda^{-1}\, p(aa)$
$(k,l-1,r,s)$	$(1-\nu_2)\, l\Lambda^{-1}\, p(Aa)$
$(k,l,r-1,s)$	$(1+\nu_1)\, r\Lambda^{-1}\, p(Aa)$
$(k,l,r-1,s+1)$	$(1+\nu_1)\, r\Lambda^{-1}\, p(AA)$
$(k,l,r+1,s)$	$(N_2-r-s)\Lambda^{-1}\, p(aa)$
$(k,l,r,s+1)$	$(N_2-r-s)\Lambda^{-1}\, p(AA)$
$(k,l,r+1,s-1)$	$(1-\nu_2)\, s\Lambda^{-1}\, p(aa)$
$(k,l,r,s-1)$	$(1-\nu_2)\, s\Lambda^{-1}\, p(Aa)$.

4.2. Applicability of diffusion approximation

As before, we define $x_t=\frac{1}{2}+\frac{1}{2}N_1^{-1}(k_t-l_t)+\frac{1}{2}N_2^{-1}(r_t-s_t)$. From the transition probabilities, it is easily verified that the t-th birth-death event is such that

$$\mathcal{E}\left[e^{\theta(x_{t+1}-x_t)}-1\right] = \theta N^{-1}\left[\alpha_1-(\alpha_1+\alpha_2)x_t-\tfrac{1}{2}\nu_1(N_1^{-1}k_t+N_2^{-1}r_t)(1-x_t)-\tfrac{1}{2}\nu_2(N_1^{-1}l_t+N_2^{-1}s_t)x_t\right]$$

$$+\tfrac{1}{32}\theta^2N^{-1}\left\{N_1^{-2}(k_t+l_t)+N_2^{-2}(r_t+s_t)-2(2x_t-1)\left[N_1^{-2}(k_t-l_t)+N_2^{-2}(r_t-s_t)\right]\right.$$

$$\left.+\tfrac{1}{2}(N_1^{-1}+N_2^{-1})\left[1+\xi+(1-\xi)N_1^{-1}N_2^{-1}(k_t-l_t)(r_t-s_t)\right]\right\}$$

$$+\ \theta\, O(N^{-2}).$$

The right hand side can be written as $\theta N^{-m}\left[M(x_t) + \tfrac{1}{2}\theta V(x_t) + W_N(\theta,t)\right]$ if we take

$$
\begin{aligned}
&m = 2\,,\\
&M(x) = N\left[\alpha_2 - (\alpha_1+\alpha_2)x - x(1-x)\left(\nu_1 f + \nu_2 + x(\nu_1-\nu_2)(1-f)\right)\right],\\
&V(x) = \tfrac{1}{4}N\left(N_1^{-1}+N_2^{-1}\right)(1+f)\,x(1-x)\,,\\
&W_N(\theta,t) = N\left[\nu_1(1-x_t)+\nu_2 x_t\right]\left[x_t f + x_t^2(1-f) - \tfrac{1}{2}N_1^{-1}k_t - \tfrac{1}{2}N_2^{-1}r_t\right]\\
&\qquad -\tfrac{1}{32}\theta N\Big\{\left(2x_t-1\right)\left(N_1^{-1}-N_2^{-1}\right)\left[N_1^{-1}(k_t-l_t)-N_2^{-1}(r_t-s_t)\right]-\tfrac{1}{4}\left(N_1^{-1}+N_2^{-1}\right)(1-f)\left[N_1^{-1}(k_t-l_t)-N_2^{-1}(r_t-s_t)\right]^2\\
&\qquad\qquad +N_1^{-1}\left[1-2(1-f)x_t(1-x_t)-N_1^{-1}(k_t+l_t)\right]+N_2^{-1}\left[1-2(1-f)x_t(1-x_t)-N_2^{-1}(r_t+s_t)\right]\Big\}\\
&\qquad + O(N^{-1})\,.
\end{aligned}
\tag{4.2}
$$

Obviously, if we assume $N\alpha_1, N\alpha_2, N\nu_1, N\nu_2$ are kept constant as N increases, the functions M and V satisfy the assumptions of § 1.1. It remains to show, that for θ bounded, there exists some number n such that $0 \leqslant n < m = 2$ and $E\left|W_N(\theta, N^n u)\right| \to 0$ for $N \to \infty$ and all $u > 0$. Moran showed, (24), that (in effect) $E\left|W_N(\theta, t)\right| \to 0$ provided t was sufficiently large for a steady state to exist, but this is not sufficiently precise for our purpose. In fact, in general $E\left|W_N(\theta, t)\right|$ does not converge to zero for fixed t.

The absolute value of $W_N(\theta, t)$ is bounded by the sum of the absolute values of the terms on the right hand side of (4.2). One such term is $\frac{1}{32}\theta N\left(N_1^{-1}+N_2^{-1}\right)(1-f)\left[N_1^{-1}(k_t-l_t)-N_2^{-1}(r_t-s_t)\right]^2$. Let us write $Z_t = N_1^{-1}(k_t - l_t) - N_2^{-1}(r_t - s_t)$. Then from the transition probabilities, the conditional expectation is

$$\mathcal{E}(Z_t^2) = Z_{t-1}^2 + 2Z_{t-1}\Lambda^{-1}\Big\{-(1+\nu_1)(N_1^{-1}\ell_{t-1} - N_2^{-1}r_{t-1})\big(p(Aa)+2p(AA)\big)$$
$$-\big[N_1^{-1}(\ell_{t-1}+\ell_{t-1}) - N_2^{-1}(r_{t-1}+s_{t-1})\big]\big[p(aa)-p(AA)\big]$$
$$+(1-\nu_2)(N_1^{-1}\ell_{t-1} - N_2^{-1}s_{t-1})\big(2p(aa)+p(Aa)\big)\Big\}$$
$$+\Lambda^{-1}N_1^{-1}\Big\{(1+\nu_1)N_1^{-1}\ell_{t-1}\big(p(Aa)+4p(AA)\big) + N_1^{-1}(N_1-\ell_{t-1}-\ell_{t-1})\big(p(aa)+p(AA)\big)$$
$$+(1-\nu_2)N_1^{-1}\ell_{t-1}\big(4p(aa)+p(Aa)\big)\Big\}$$
$$+\Lambda^{-1}N_2^{-1}\Big\{(1+\nu_1)N_2^{-1}r_{t-1}\big(p(Aa)+4p(AA)\big) + N_2^{-1}(N_2-r_{t-1}-s_{t-1})\big(p(aa)+p(AA)\big)$$
$$+(1-\nu_2)N_2^{-1}s_{t-1}\big(4p(aa)+p(Aa)\big)\Big\}$$
$$= Z_{t-1}^2(1-2N^{-1}) + O(N^{-2}).$$

Taking unconditional expectations of both sides we have the difference equation

$$E(Z_t^2) = (1-2N^{-1})E(Z_{t-1}^2) + O(N^{-2}). \qquad (4.3)$$

Therefore, for any number $n, 1 < n < m = 2$, we have

$$E(Z_{N^{n_u}}^2) = (1-2N^{-1})^{N^{n_u}} E(Z_0^2) + O(N^{-(2-n)})$$
$$\longrightarrow 0 \quad \text{as} \quad N \to \infty,$$

since $E(Z_0^2) = Z_0^2$ is bounded. Similarly, one could show

$$E\big[1-2(1-f)x_{N^{n_u}}(1-x_{N^{n_u}}) - N_1^{-1}(\ell_{N^{n_u}}+\ell_{N^{n_u}})\big]^2 \to 0,$$

$$E\big[1-2(1-f)x_{N^{n_u}}(1-x_{N^{n_u}}) - N_2^{-1}(r_{N^{n_u}}+s_{N^{n_u}})\big]^2 \to 0,$$

$$E\big[x_{N^{n_u}}f + x_{N^{n_u}}^2(1-f) - \tfrac{1}{2}N_1^{-1}\ell_{N^{n_u}} - \tfrac{1}{2}N_2^{-1}r_{N^{n_u}}\big]^2 \to 0 \quad \text{as} \quad N \to \infty.$$

Thus $E\big|W_N(\theta, N^{n_u})\big| \to 0$ as required. Hence the theory of § 1 applies to the present population model variate x; to show that it applies to the actual gene frequency y, it is

sufficient to prove that $x_N 2_u$ and $y_N 2_u$ converge in probability, and for this to be true it is sufficient to prove that $E(Z^2_N 2_u) \to 0$. By slightly modifying the above argument, we have from (4.3) that

$$E(Z^2_{N^2u}) = (1-2N^{-1})^{N^{3/2}u} E(Z^2_{N^2u(1-N^{-1/2})}) + O(N^{-1/2}),$$

and the right hand side converges to zero as required, since all Z_t^2 and their expectations are bounded.

4.3. Asymptotic behaviour of model

This population model is again a special case of one given in (1.26) with the parametric values

$$N_v = 2N_1N_2N^{-1}(1+f)^{-1}, \qquad (4.4)$$

$$a = NN_v^{-1}, \quad b = N\alpha_2, \quad c = N\alpha_1,$$

$$s = -N(1+f)(\nu_1+\nu_2), \quad d = -(1-f)(\nu_1-\nu_2)\left[(1+f)(\nu_1+\nu_2)\right]^{-1}.$$

Comparing these with the similar quantities for model B, one sees that this model is identical in asymptotic behaviour to that of B except for a halving of the variance effective number N_V (c/f (3.3)). In particular, the stationary distribution with mutation is formally identical with (3.4), a result found by Moran (24). Without mutation, the asymptotic properties are described by equations (3.5) - (3.7), with of course the appropriate modification of N_V. The time scale here represents birth-death events, and transforming to the

units of $u = N^{-m}t = N^{-2}t$, each unit corresponds to N^2 birth-death events or to N generations each of N deaths.

There are several interesting conclusions which may be drawn from the similarity of models B and C. It appears that the order in which mutation and selection are introduced is not important, and the actual method of selection, whether it be on the proportions of gametes produced or on the life-time distributions, seems to have had no effect.

The only difference between the asymptotic behaviours is in the effective sizes of the populations; however, it is incorrect to ascribe this difference as being due to the fact that one model has overlapping generations, the other not. Rather, it is due to changes in the manner in which offspring are distributed amongst the parents.

Consider the special case without selection and with random mating $(\nu_1 = \nu_2 = f = 0)$. For model C, the generating functions for offspring, per person, can be found as follows. The probability of any given individual dying at a birth-death event is N^{-1} , and of having a lifetime of exactly t units is $N^{-1}(1-N^{-1})^{t-1}$, $t = 1,2,3, \ldots$. This may be expressed by saying that $t-1$ has a geometric distribution; the expected lifetime is N and is the number of time units corresponding to one generation in a non-overlapping model. At each instant at which a death occurs, including its own, the individual has a probability N_1^{-1} of becoming a parent if male, and N_2^{-1} if female. So the probability generating

function of the number of offspring per male is

$$P_1(z) = \sum_{t=1}^{\infty} N^{-1}(1-N^{-1})^{t-1}\left(1-N_1^{-1}+N_1^{-1}z\right)^t$$

$$= (N_1-1+z)\left[N+N_1-1-(N-1)z\right]^{-1},$$

and similarly for the females

$$P_2(z) = (N_2-1+z)\left[N+N_2-1-(N-1)z\right]^{-1},$$

(4.5)

and the limiting values of these as N_1 and N_2 increase in such a way as to keep their ratio constant are

$$Q_1(z) = N_1\left[N_1+N(1-z)\right]^{-1},\quad Q_2(z) = N_2\left[N_2+N(1-z)\right]^{-1},$$

corresponding to geometrically distributed variates. Note that $P_i(z)$ and $Q_i(z)$ are <u>not</u> connected by (2.1), since for model C, a parent can have more than N offspring. Now a population model of type A with non-overlapping generations can be set up having these functions Q_i as a basis, and according to (2.18) the effective size would be

$$N_v = 4N^2\left[N_1Q_1''(1)+N_2Q_2''(1)\right]^{-1},$$

$$= 2N_1N_2N^{-1},$$

which is identical with (4.4) when $f = 0$. That is, in some circumstances overlapping and non-overlapping populations can have the same asymptotic behaviour. However, model D (later) furnishes an example of the opposite.

In the simplest example of this population, that is when $\alpha_1 = \alpha_2 = \gamma_1 = \gamma_2 = f = 0$, the rate of approach to homozygosity is $R \doteq N^{-1}\lambda_0 = \frac{1}{2}N_v^{-1} = \frac{1}{4}NN_1^{-1}N_2^{-1}$ which is twice that for the simplest

case of model B; this result was pointed out by Moran (22) when he first considered a simpler overlapping model. More generally, even when the mating is non-random, but $\nu_1 = \nu_2 = \alpha_1 = \alpha_2 = 0$, the probability of ultimate fixation of the a gene is exactly $p = \frac{1}{2} + \frac{1}{4}N_1^{-1}(k_0 - l_0) + \frac{1}{4}N_2^{-1}(r_0 - s_0)$ and the rate of approach to homozygosity is $\frac{1}{2}N_v^{-1}$ ignoring terms of order N^{-2}; see (10.11), (10.10). Thus application of equations (1.34) and (1.31) to this case gives rather better results than might be expected from the approximation procedure involved.

5. Model D: Overlapping generations, an exceptional case

5.0. Introduction

The purpose of including model D as an example of diffusion theory is to illustrate that the preceding three models are not representative of all possible populations. In particular, it will be shown that non-random mating can be introduced in a different fashion to B and C, with a dramatic change in asymptotic behaviour, and further, that overlapping generations can sometimes invalidate the application of the theory for model A, in contrast to the equivalence found between special cases of A and C in § 4.3. Here again, the individuals are dioecious diploids; the model is original.

5.1. Description of the model.

The model to be considered is like model C, in that it has birth-death events occurring separately at discrete time intervals. We assume, as before, that the deaths occur according to the probabilities (4.1), but we postulate a different mating system and consequently a different offspring distribution. At each birth-death event, the dying individual acts as one parent of the new individual, whilst the other parent is chosen from the opposite sex at random (with probability $1-f$) or to have the same genotype as the dying individual (with probability f). Thus f is a measure of positive assortative mating within the population, and acts at the zygote level rather than between gametes as in models B and C. We ignore the difficulty that positive assortative

mating is not always possible in a two sex population when a particular genotype might be absent from one sex but present in the other; in any case, this same difficulty occurs with respect to models B and C as well.

Under the above assumptions, we can write down the probabilities that the dying individual will mate with the other parent of specified genotype

		Other parent		
		aa	Aa	AA
Male	aa	$(1-f)N_2^{-1}r+f$	$(1-f)N_2^{-1}(N_2-r-s)$	$(1-f)N_2^{-1}s$
	Aa	$(1-f)N_2^{-1}r$	$(1-f)N_2^{-1}(N_2-r-s)+f$	$(1-f)N_2^{-1}s$
	AA	$(1-f)N_2^{-1}r$	$(1-f)N_2^{-1}(N_2-r-s)$	$(1-f)N_2^{-1}s+f$

Dying individual (5.1)

	aa	$(1-f)N_1^{-1}k+f$	$(1-f)N_1^{-1}(N_1-k-l)$	$(1-f)N_1^{-1}l$
Female	Aa	$(1-f)N_1^{-1}k$	$(1-f)N_1^{-1}(N_1-k-l)+f$	$(1-f)N_1^{-1}l$
	AA	$(1-f)N_1^{-1}k$	$(1-f)N_1^{-1}(N_1-k-l)$	$(1-f)N_1^{-1}l+f$,

where (k,l,r,s) is the state of the population before the death.

As in model A, we suppose that the three genotypes aa Aa , and AA pass on gametes of type a or A with probabilities p_i or q_i according to (2.5). Therefore, in this model we assume that the mutations occur after selection and mating, but from the results we will find that by comparison with previous models this ordering does not appear critical. Write $P(aa|aa,M)$ as the probability that a dying male of genotype aa produces an offspring of type aa , and similar expressions for the other possibilities. From (5.1) and (2.5)

we get

$$
\begin{aligned}
P(aa|aa,M) &= \tfrac{1}{2}(1+f)(1-2\alpha_1) + \tfrac{1}{2}(1-f)\alpha_2 + \tfrac{1}{2}(1-f)N_1^{-1}(r-s)(1-2\alpha_1-\alpha_2) + O(N^{-2}),\\
P(Aa|aa,M) &= \tfrac{1}{2}(1-f)(1-\alpha_2) + \tfrac{1}{2}(1+3f)\alpha_1 - \tfrac{1}{2}(1-f)N_2^{-1}(r-s)(1-3\alpha_1-\alpha_2) + O(N^{-2}),\\
P(AA|aa,M) &= \tfrac{1}{2}(1-f)\alpha_1 - \tfrac{1}{2}(1-f)N_2^{-1}(r-s) + O(N^{-2}),\\
P(aa|Aa,M) &= \tfrac{1}{4}(1-2\alpha_1+2\alpha_2) + \tfrac{1}{4}(1-f)N_2^{-1}(r-s)(1-2\alpha_1) + O(N^{-2}),\\
P(Aa|Aa,M) &= \tfrac{1}{2} + \tfrac{1}{2}(1-f)N_2^{-1}(r-s)(\alpha_1-\alpha_2) + O(N^{-2}),\\
P(AA|Aa,M) &= \tfrac{1}{4}(1-2\alpha_2+2\alpha_1) - \tfrac{1}{4}(1-f)N_2^{-1}(r-s)(1-2\alpha_2) + O(N^{-2}),\\
P(aa|AA,M) &= \tfrac{1}{2}(1-f)\alpha_2 + \tfrac{1}{2}(1-f)N_2^{-1}(r-s)\alpha_2 + O(N^{-2}),\\
P(Aa|AA,M) &= \tfrac{1}{2}(1-f)(1-\alpha_1) + \tfrac{1}{2}(1+3f)\alpha_2 + \tfrac{1}{2}(1-f)N_2^{-1}(r-s)(1-\alpha_1-2\alpha_2) + O(N^{-2}),\\
P(AA|AA,M) &= \tfrac{1}{2}(1+f)(1-2\alpha_2) + \tfrac{1}{2}(1-f)\alpha_1 - \tfrac{1}{2}(1-f)N_2^{-1}(r-s)(1-\alpha_1-2\alpha_2) + O(N^{-2}),
\end{aligned}
\qquad (5.2)
$$

and similar equations hold for the females' offspring except that $N_2^{-1}r$ is replaced by $N_1^{-1}k$, and $N_2^{-1}s$ by $N_1^{-1}\ell$.

Our model assumes that each unit of time corresponds to one birth-death event, and if the state was (k,l,r,s) just before an event, then after the death the state might remain unchanged, or might become one of the following with quoted probabilities:

$$
\begin{aligned}
&(k-1,l,r,s) && (1+v_1)\,k\,\Lambda^{-1}\,P(Aa|aa,M),\\
&(k-1,l+1,r,s) && (1+v_1)\,k\,\Lambda^{-1}\,P(AA|aa,M),\\
&(k+1,l,r,s) && (N_1-k-\ell)\,\Lambda^{-1}\,P(aa|Aa,M),\\
&(k,l+1,r,s) && (N_1-k-\ell)\,\Lambda^{-1}\,P(AA|Aa,M),\\
&(k+1,l-1,r,s) && (1-v_2)\,\ell\,\Lambda^{-1}\,P(aa|AA,M),\\
&(k,l-1,r,s) && (1-v_2)\,\ell\,\Lambda^{-1}\,P(Aa|AA,M),\\
&(k,l,r-1,s) && (1+v_1)\,r\,\Lambda^{-1}\,P(Aa|aa,F),\\
&(k,l,r-1,s+1) && (1+v_1)\,r\,\Lambda^{-1}\,P(AA|aa,F),\\
&(k,l,r+1,s) && (N_2-r-s)\,\Lambda^{-1}\,P(aa|Aa,F),\\
&(k,l,r,s+1) && (N_2-r-s)\,\Lambda^{-1}\,P(AA|Aa,F),\\
&(k,l,r+1,s-1) && (1-v_2)\,s\,\Lambda^{-1}\,P(aa|AA,F),\\
&(k,l,r,s-1) && (1-v_2)\,s\,\Lambda^{-1}\,P(Aa|AA,F).
\end{aligned}
\qquad (5.3)
$$

5.2. Applicability of diffusion approximation

With $x_t = \frac{1}{2} + \frac{1}{4}N_1^{-1}(k_t - l_t) + \frac{1}{4}N_2^{-1}(r_t - s_t)$, we have

$$\mathcal{E}\left[e^{\theta(x_{t+1}-x_t)}-1\right] = \theta N^{-1}\Big\{\alpha_2 - (\alpha_1+\alpha_2)x_t - \tfrac{1}{8}(1-f)\big(\nu_1 N_1^{-1}k_t + \nu_2 N_1^{-1}l_t + \nu_1 N_2^{-1}r_t + \nu_2 N_2^{-1}s_t\big)$$
$$+ \tfrac{1}{8}(1-f)\big[N_1^{-1}(k_t-l_t)N_2^{-1}(\nu_1 r_t - \nu_2 s_t) + N_2^{-1}(r_t-s_t)N_1^{-1}(\nu_1 k_t - \nu_2 l_t)\big]\Big\}$$
$$+ \tfrac{1}{64}\theta^2 N^{-1}\Big\{(N_1^{-1}+N_2^{-1})\big[1-(1-f)N_1^{-1}N_2^{-1}(k_t-l_t)(r_t-s_t)\big] - f\big[N_1^{-2}(k_t+l_t)+N_2^{-2}(r_t+s_t)\big]\Big\}$$
$$+ \theta\, O(N^{-3}).$$

The right hand side can be written as $\theta N^{-m}\big[M(x_t) + \tfrac{1}{2}\theta V(x_t) + W_N(\theta,t)\big]$ if we take

$m = 2$

$$M(x) = N\Big\{\alpha_2 - (\alpha_1+\alpha_2)x - \tfrac{1}{2}\tfrac{1-f}{2-f}x(1-x)\big[\nu_1(f+2(1-f)x) + \nu_2(f+2(1-f)(1-x))\big]\Big\},$$

$$V(x) = \tfrac{1}{4}N(N_1^{-1}+N_2^{-1})\tfrac{1-f}{2-f}x(1-x),$$

$$W_N(\theta,t) = -\tfrac{1}{8}N\nu_1(1-f)\big[N_1^{-1}N_2^{-1}k_t(N_2-r_t+s_t) + N_1^{-1}N_2^{-1}r_t(N_1-k_t+l_t) - \tfrac{f}{2-f}x_t(1-x_t)(f+2(1-f)x_t)\big]$$
$$- \tfrac{1}{8}N\nu_2(1-f)\big[N_1^{-1}N_2^{-1}l_t(N_2+r_t-s_t) + N_1^{-1}N_2^{-1}s_t(N_1+k_t-l_t) - \tfrac{f}{2-f}x_t(1-x_t)(f+2(1-f)(1-x_t))\big]$$
$$+ \tfrac{1}{64}\theta N\Big\{\tfrac{1}{4}(1-f)(N_1^{-1}+N_2^{-1})\big[N_1^{-1}(k_t-l_t) - N_2^{-1}(r_t-s_t)\big]^2$$
$$+ f\big[(N_1^{-1}+N_2^{-1})\big(1-\tfrac{4(1-f)}{2-f}x_t(1-x_t)\big) - N_1^{-2}(k_t+l_t) - N_2^{-2}(r_t+s_t)\big]\Big\}$$
$$+ O(N^{-1}),$$

and provided $N\alpha_1$, $N\alpha_2$, $N\nu_1$, $N\nu_2$ are independent of N , and that N_1 and N_2 are increased in a fixed ratio, the functions M and V satisfy the assumptions for applicability of the diffusion approximation, § 1.1. We have to prove further that there exists some $n\,(0 \leq n < m = 2)$ for which $E\left|W_N(\theta, N^n u)\right| \to 0$ as $N \to \infty$. To do this, it will be sufficient to show

$$E\left[N_1^{-1}(k_{N^n u} - l_{N^n u}) - N_2^{-1}(r_{N^n u} - s_{N^n u})\right]^2 \longrightarrow 0,$$

$$E\left[N_1^{-1}N_2^{-1}k_{N^n u}(N_2 - r_{N^n u} + s_{N^n u}) + N_1^{-1}N_2^{-1}r_{N^n u}(N_1 - k_{N^n u} + l_{N^n u}) - \tfrac{f}{2-f}x_{N^n u}(1-x_{N^n u})(f+2(1-f)x_{N^n u})\right]^2 \to 0,$$

$$E\left[N_1^{-1}N_2^{-1}l_{N^n u}(N_2 + r_{N^n u} - s_{N^n u}) + N_1^{-1}N_2^{-1}s_{N^n u}(N_1 + k_{N^n u} - l_{N^n u}) - \tfrac{f}{2-f}x_{N^n u}(1-x_{N^n u})(f+2(1-f)(1-x_{N^n u}))\right]^2 \to 0,$$

$$N E\left[(N_1^{-1}+N_2^{-1})\big(1-\tfrac{4(1-f)}{2-f}x_{N^n u}(1-x_{N^n u})\big) - N_1^{-2}(k_{N^n u}+l_{N^n u}) - N_2^{-2}(r_{N^n u}+s_{N^n u})\right]^2 \longrightarrow 0, \text{ as } N \to \infty.$$

To prove the first of these results, write $Z_t = N_1^{-1}(h_t - l_t) - N_2^{-1}(r_t - s_t)$; then the transition probabilities give, for the conditional expectation of z_t^2

$$\mathcal{E}(Z_t^2) = \left[1 - 2(1-f)N^{-1}\right] Z_{t-1}^2 + O(N^{-2}),$$

and the unconditional expectations satisfy

$$E(Z_t^2) = \left[1 - 2(1-f)N^{-1}\right] E(Z_{t-1}^2) + O(N^{-2}).$$

This equation is almost identical with (4.3) found for model C, and by the same arguments used there, $E(Z_{N^n u}^2) \to 0$ as $N \to \infty$ for all $u > 0$ and all $n > 1$, provided $f \neq 1$. This is sufficient to show that the actual gene frequency $y_{N^2 u}$ converges in probability to $x_{N^2 u}$. The other convergence relations can be shown similarly. The exceptional case when $f = 1$ is degenerate in the sense that the gene frequency does not behave, even asymptotically, as a diffusing variate. Some consideration is given to this case in § 11, but when there is neither mutation nor selection.

5.3. Asymptotic behaviour of model.

The parameters introduced in (1.26) are, for this model,

$$\begin{aligned} a &= N N_V^{-1}, \quad b = N\lambda_2, \quad c = N\lambda_1, \\ s &= -N\frac{1-f}{2-f}(\nu_1+\nu_2), \quad d = -(1-f)\frac{\nu_1-\nu_2}{\nu_1+\nu_2}, \end{aligned}$$

where

$$N_V = 2N_1N_2N^{-1}(2-f)(1-f)^{-1}, \tag{5.4}$$

and comparing these with the similar quantities for models B and C there are some interesting differences. Firstly, the non-random mating parameter f appears in quite a different way, and this is due to the facts that here, assortative mating acts at the zygote level, not the gametic as before, and also it is the dying individual irrespective of sex who selects the mating partner, whereas in (3.2) the sexes are weighted with equal importance although they are not necessarily equal in numbers. The outcome is that the variance effective size is increased by assortative mating, instead of decreased as in previous models.

Secondly, for random mating, the selection coefficients ν_1 and ν_2 enter with only half the effect they had in models B and C, although qualitatively they are similar. This is because in this model a high selection against a genotype does not stop that genotype from producing offspring, as it did in the previous models. Here, the death of an individual automatically implies that it have one offspring, at least.

Thirdly, with random mating ($f = 0$) the variance effective size (5.4) is equal to that for model B, (3.3), and half that for model C, (4.4). The importance of this result is that it is not what one would expect. Consider the case with random mating and no selection, $f = \nu_1 = \nu_2 = 0$. The probability of a given individual living for exactly t time units is $N^{-1}(1-N^{-1})^{t-1}$ with $t = 1,2,3, \ldots$ as in model C. But the probability of its being a parent at any stage is altered since it must always be a parent at its own death. Con-

sider a birth-death event not of the given individual but of one of the remaining $N-1$ individuals. If the original individual was male, then for it to be a parent at a death other than its own, the dying individual must be female (with probability $N_2(N-1)^{-1}$) and the original individual must be chosen as second parent from N_1 males. The probability of its being a parent at an event other than its own death is therefore $N_2(N-1)^{-1}N_1^{-1}$, and the probability generating function for the total number of offspring, per male, is

$$P_1(z) = \sum_{t=1}^{\infty} N^{-1}(1-N^{-1})^{t-1}\left[1-N_2(N-1)^{-1}N_1^{-1}+N_2(N-1)^{-1}N_1^{-1}z\right]^{t-1} z = zN_1(N-N_2z)^{-1}.$$

Similarly for females

$$P_2(z) = zN_2(N-N_1z)^{-1},$$

and letting N_1 and N_2 increase with a fixed ratio, the limiting functions are also given by the same formulae,

$$Q_1(z) = zN_1(N-N_2z)^{-1}, \qquad Q_2(z) = zN_2(N-N_1z)^{-1}.$$

The $P_i(z)$ and $Q_i(z)$ are not connected by (2.1) because the model has overlapping generations. A model of type A with these Q's for basic generating functions, would have an effective size given by (2.18), namely

$$N_v = 4N^2\left[N_1Q_1''(1) + N_2Q_2''(1)\right]^{-1} = \frac{2NN_1N_2}{N_1^2+N_2^2}.$$

This differs from the result actually found for model D, (5.4), unless $N_1=N_2$. In other words, (2.18) happens to be correct for one overlapping model (C), but not correct for another (D).

The asymptotic behaviour of the gene frequency can be inferred from § 1 provided $0 \leq f < 1$; in the extreme case $f = 1$, the approximation theory has not been justified. When there exists mutation, the stationary asymptotic density is given by (1.27) as

$$f(x) = 2N^{-1}N_V C \exp\left\{-2N_V \frac{1-f}{2-f}\left[2v_2 + f(v_1-v_2)\right]x - 2N_V \frac{(1-f)^2}{2-f}(v_1-v_2)x^2\right\} x^{4N_V v_2 - 1}(1-x)^{4N_V v_1 - 1}.$$

Without mutation, the rate of approach to homozygosity is formally that in (3.5), with however the appropriate parameters for this model. In particular, when there is no selection, the rate is

$$R \doteq N^{-1}\lambda_0 = \tfrac{1}{2}N_V^{-1} = \tfrac{1}{4}N_1^{-1}N_2^{-1}N(1-f)(2-f)^{-1} \qquad (5.5)$$

per generation, and this differs from the exact quantity found in (11.15) by terms at most of order of magnitude N^{-2} . We note that the rate decreases with increasing f , which is contrary to the behaviour found for models B and C.

According to (1.33), the probability of ultimate fixation of the a gene is approximately

$$G(p,w) = \frac{\int_0^p e^{\frac{1}{2}N_1N_2N^{-1}\left[\left(2v_2 - f(v_1-v_2)\right)x + \left(1-f\right)(v_1-v_2)x^2\right]}\,dx}{\int_0^1 e^{\frac{1}{2}N_1N_2N^{-1}\left[\left(2v_2 - f(v_1-v_2)\right)x + \left(1-f\right)(v_1-v_2)x^2\right]}\,dx},$$

and in the special case without mutation, this becomes

$$G(p,\infty) = p \equiv \tfrac{1}{2} + \tfrac{1}{4}N_1^{-1}(k_0 - l_0) + \tfrac{1}{4}N_2^{-1}(r_0 - s_0), \qquad (5.6)$$

which is exactly correct (see (11.21)). Finally, the expected time for the a gene to be either fixed or lost from the population is as in (3.7), with appropriate values for the parameters. No exact determination of this quantity has yet been made.

6. Model E: Migration

6.0. Introduction

Unlike the previous four models, we now consider a population of monoecious haploid individuals, whose genotypes are either a or A. To be comparable with a diploid model, it is assumed that the population size is constant at $2N$ individuals. Further, the total is divided into two sub-populations each of size N. Clearly the model could be generalized in many ways, but even for this simple model the notation and algebra are quite difficult enough without the introduction of two sexes and three genotypes. The essential difference between this and previous models is that migration is introduced by assuming M individuals (chosen at random) cross over from each sub-population to the other, just after the birth of a new generation. The model, of course, has non-overlapping generations.

Migration has been considered by other authors, but not in the same way as discussed here. For example, Crow and Kimura (6) considered two sub-populations, one of finite size, the other infinite. Thus in their model, the proportion of migrants of genotype a coming from the infinite sub-population was fixed through all generations. Here, this is not so because random fluctuations occur in the gene frequencies of both finite sub-populations. Again, Moran (26) has considered a population sub-divided many times but without mutation and selection; here these factors will be introduced.

6.1. Description of model

Because of the sub-division, a notation differing from that of previous chapters will be used. Write α_1 and β_1 for the mutation rates of $a \to A$ in the first and second sub-population, respectively, and α_2 and β_2 for the reverse rates of $A \to a$. Similarly, let μ and γ be the selective advantage of the a-gene in the two sub-populations. These definitions allow the environments of the two groups to differ. Denote by k_t and l_t the numbers of a individuals in the respective sub-populations just before the $t+1$ th mating season.

As a result of mutation and selection, the proportion of gametes produced in the first sub-population during the $t+1$ th mating season is a:A as $p_1 : q_1$, where

$$p_1 = \frac{k_t(1-\alpha_1-\alpha_2)+\alpha_2 N}{N+\mu[k_t(1-\alpha_1-\alpha_2)+\alpha_2 N]}(1+\mu), \quad q_1 = 1-p_1 = \frac{-k_t(1-\alpha_1-\alpha_2)+(1-\alpha_2)N}{N+\mu[k_t(1-\alpha_1-\alpha_2)+\alpha_2 N]}, \quad (6.1)$$

(c/f. (3.1) for diploids). From these gametes, the new generation is formed by random sampling with replacement, that is, by random mating. Write k_t' and k_t'' as the numbers of new a individuals which stay in the first sub-population or migrate to the second, respectively. Then the conditional probabilities attached to these numbers are

$$Pr\{k_t' | k_t\} = \binom{N-M}{k_t'} p_1^{k_t'} q_1^{N-M-k_t'}, \quad Pr\{k_t'' | k_t\} = \binom{M}{k_t''} p_1^{k_t''} q_1^{M-k_t''}.$$

Similarly, define l_t' and l_t'' as the numbers of a individuals born in the second sub-population which stay there or mi-

grate to the first sub-population respectively. We have

$$\Pr\{l'_t \mid k_t\} = \binom{N-M}{l'_t} p_2^{l'_t} q_2^{N-M-l'_t}, \quad \Pr\{l''_t \mid l_t\} = \binom{M}{l''_t} p_2^{l''_t} q_2^{M-l''_t},$$

where p_2 and q_2 are defined similarly to (6.1) with the α's replaced by β's, μ by γ, and k_t by l_t. The next generation takes the final state (k_{t+1}, l_{t+1}) with $k_{t+1} = k'_t + l''_t$, $l_{t+1} = l'_t + k''_t$.

6.2. Applicability of diffusion approximation

Conditional on fixed values of k_t and l_t, the moment generating function of k_{t+1} and l_{t+1} is

$$\mathcal{E}\left(e^{\theta k_{t+1} + \phi l_{t+1}}\right) = \left[p_1 e^{\theta} + q_1\right]^{N-M} \left[p_2 e^{\theta} + q_2\right]^{M} \left[p_1 e^{\phi} + q_1\right]^{M} \left[p_2 e^{\phi} + q_2\right]^{N-M}. \tag{6.2}$$

The a gene relative frequency in the total population of $2N$ individuals is now $x_{t+1} = \frac{1}{2}N^{-1}(k_{t+1} + l_{t+1})$ with moment generating function

$$\begin{aligned}\mathcal{E}\left(e^{\theta x_{t+1}}\right) &= \left[p_1 e^{\frac{1}{2}N^{-1}\theta} + q_1\right]^{N} \left[p_2 e^{\frac{1}{2}N^{-1}\theta} + q_2\right]^{N} \\ &= \left[p_1 p_2 e^{N^{-1}\theta} + (p_1 q_2 + p_2 q_1) e^{\frac{1}{2}N^{-1}\theta} + q_1 q_2\right]^{N}.\end{aligned} \tag{6.3}$$

Using this result, one easily obtains

$$\mathcal{E}\left[e^{\theta(x_{t+1} - x_t)} - 1\right] = \tfrac{1}{2}N^{-1}\theta\left[k_t(\mu - \alpha_1 - \alpha_2 - k_t N^{-1}\mu) + l_t(\gamma - \beta_1 - \beta_2 - l_t N^{-1}\gamma) + N(\alpha_2 + \beta_2)\right]$$

$$+ \tfrac{1}{2}N^{-1}\theta^2\left[\tfrac{1}{2}x_t + \tfrac{1}{2}k_t l_t N^{-2} - x_t^2\right] + \theta\, O(N^{-2}).$$

In order to apply the theory developed in chapter 1, this function must be written in the form

$$\theta\, N^{-m}\left[M(x_t) + \tfrac{1}{2}\,\theta\, V(x_t) + W_N(\theta, t)\right]$$

where m is an integer, $M(x)$ and $V(x)$ are polynomials independent of N, $V(0) = V(1) = 0$, and $E\left|W_N(\theta, N^n u)\right| \to 0$ for all bounded θ and some n such that $0 \leq n < m$. It is not obvious how this may be accomplished, but suppose we start by assuming that $k_t N^{-1}$, $l_t N^{-1}$ and x_t converge in probability as N increases. Then we would take

$$m = 1$$

$$M(x) = \tfrac{1}{2} N\left\{ x\left[\mu+\eta-\alpha_1-\alpha_2-\beta_1-\beta_2-x(\mu+\eta)\right] + \alpha_2+\beta_2 \right\},$$

$$V(x) = \tfrac{1}{2} x(1-x),$$

$$W_N(\theta,t) = -\tfrac{1}{2} N\left\{ (x_t-k_t N^{-1})\left[\mu-\alpha_1-\alpha_2-(x_t+k_t N^{-1})\mu\right] + (x_t-l_t N^{-1})\left[\eta-\beta_1-\beta_2-(x_t+l_t N^{-1})\eta\right] \right\}$$
$$- \tfrac{1}{16}\,\theta\,(k_t N^{-1} - l_t N^{-1})^2 + O(N^{-1}).$$

To satisfy assumption (A2), our model must be such that all the α's, β's, μ and η must be proportional to N^{-1}. To prove (A3) applies, we need to show that $E(k_t N^{-1} - l_t N^{-1})^2$, $E\left|x_t - k_t N^{-1}\right|$, and $E\left|x_t - l_t N^{-1}\right|$ converge to zero for $t = N^n u$ and $N \to \infty$. In fact, it will be sufficient to prove $E(k_{N^n u} N^{-1} - l_{N^n u} N^{-1})^2 \to 0$ where $0 < n < 1$; therefore consider the function $U_t = N^{-1}(k_t - l_t)$. From (6.2) we get

$$\mathcal{E}(e^{\theta U_t}) = \left[p_1 p_2 + q_1 q_2 + p_1 q_2 e^{\theta N^{-1}} + p_2 q_1 e^{-\theta N^{-1}}\right]^{N-M}\left[p_1 p_2 + q_1 q_2 + p_2 q_1 e^{\theta N^{-1}} + p_1 q_2 e^{-\theta N^{-1}}\right]^{M},$$

so that

$$\mathcal{E}(U_t^2) = \left(1-\tfrac{2M}{N}\right)^2 (p_1-p_2)^2 + N^{-1}(p_1q_1+p_2q_2)$$

$$= \left(1-\tfrac{2M}{N}\right)^2 U_{t-1}^2 + O(N^{-1}).$$

Taking unconditional expectations of both sides gives

$$E(U_t^2) = \left(1-\tfrac{2M}{N}\right)^2 E(U_{t-1}^2) + O(N^{-1}).$$

For any pair of numbers n,i with $0 < i < n < 1$ we have

$$E(U^2_{N^n u}) = \left(1-\tfrac{2M}{N}\right)^{2N^{n-i}u} E\left(U^2_{N^n u(1-N^{-i})}\right) + O(N^{-1-i+n}).$$

As N increases, the last term on the R.H.S. approaches zero. The U's, and hence the U^2's, are bounded, so it remains to show that

$$\left(1-\tfrac{2M}{N}\right)^{2N^{n-i}u} \longrightarrow 0 \quad \text{as} \quad N \to \infty .$$

A sufficient condition for this to be true is that M is not a constant, but has the form $M = LN^j$, where $0 < L < 1$, and $0 < 1+i-n < j \leq 1$. (Note: $j > 1$ is unrealistic since not more than N individuals can migrate). But because n and i are otherwise arbitrary, they can be chosen so that the latter inequalities are true for any given j; thus the assumption (A3) has been verified. The above argument breaks down, in particular, when M is a constant, and this case will be mentioned again later.

6.3. Asymptotic behaviour of model

Summarizing the above, we can say that the diffusion theory approximation of chapter 1 is applicable to this population model provided that N is large, the mutation and selection coefficients are inversely proportional to N, and the migration rate is directly proportional to some positive power of N with constant of proportionality L bounded in the open interval $(0,1)$. In fact, the model is a special case of (1.26) discussed previously. We have here

$$a = 1, \quad b = \tfrac{1}{2}N(\alpha_2+\beta_2), \quad c = \tfrac{1}{2}N(\alpha_1+\beta_1), \qquad d = 0, \quad s = N(\mu+\gamma). \tag{6.4}$$

From (1.27), the stationary distribution for the a gene relative frequency is approximately

$$f(x) = C\{\exp\{2N(\mu+\gamma)x\}\cdot x^{2N(\alpha_2+\beta_2)-1}(1-x)^{2N(\alpha_1+\beta_1)-1}, \tag{6.5}$$

where C is a normalizing constant. Without mutation, we see from (1.31) that the rate of approach to homozygosity is approximately

$$R \doteq N^{-1}\lambda_0 = \tfrac{1}{2}N^{-1}\left[1 + \frac{N^2(\mu+\gamma)^2}{10} - \frac{N^4(\mu+\gamma)^4}{7,000} - \frac{N^6(\mu+\gamma)^6}{1,050,000} - \cdots\right], \tag{6.6}$$

when time is measured in units of one generation (for the last given term of this expansion see (6) (7.21)).

By considering (6.4), (6.5), and (6.6) it is clear that the population behaviour is asymptotically independent of the migration rate M, provided M increases with N.

It is therefore equivalent to a united population of size $2N$ subject to mutations at the average rates $\frac{1}{2}(\alpha_1+\beta_1)$ and $\frac{1}{2}(\alpha_2+\beta_2)$, and to the average selection $\frac{1}{2}(\mu+\gamma)$. If there were no selection nor mutation, then the rate of approach to homozygosity would be just $\frac{1}{2}N^{-1}+O(N^{-2})$, which is a special case of a result given by Moran (26) for a population subdivided many times. Moran used exact methods to obtain his results. As well as this, Moran shows that if the migration rate M is a constant independent of N (the case not covered by the above theory) then the rate of approach is smaller than $\frac{1}{2}N^{-1}$. Write it as $\mathcal{R} = \frac{1}{2}\nu N^{-1}$; then ν has the values

M	1	2	4	8	16	100
ν	0.8769	0.9378	0.9688	0.9844	0.9922	0.9988

and $\nu \to 1$ as $M \sim N \to \infty$. As mentioned above, in the case where M is constant the approximate procedure does not work; whether Moran's results could be generalized to the case with selection by consideration of a bivariate diffusion approximation is not known.

Again, in the case without mutation, (1.33) gives the approximate probability of ultimate fixation of the a gene given an initial starting frequency $p=x_0=\frac{1}{2}N^{-1}(k_0+1_0)$, and (1.35) gives the expected time for either allele to become fixed in units of $u = N^{-1}t$. In the case with no selection, these expressions simplify to (1.34) and (1.36). One can show that (1.34) is exactly correct in this case, for consider the equality $Pr(x_\infty = 1) = E(x_\infty)$. From (6.3), we obtain

$$\mathcal{E}(x_{t+1}) = x_t \quad , \text{ for all } t,$$

by a single differentiation with respect to θ , and so

$$P_r\{x_\infty = 1\} = E(x_\infty) = x_0 = p = \tfrac{1}{2}N^{-1}(k_0 + l_0) .$$

7. Model A: Approach to homozygosity, without mutation.

7.0. Introduction

The previous chapters have been concerned with finding approximate descriptions for the asymptotic behaviour of fairly general population models. In this, and subsequent chapters, we turn our attention to obtaining exact results, but in doing so, lose a certain generality by assuming that no mutation or selective pressures exist in the models.

As was pointed out in § 0, a population with no mutation will eventually become homozygous, and usually all genes will be of the one type. According to (0.2), the time rate for this to occur depends on the largest non-unit root (say λ_2 if $\lambda_0=\lambda_1=1$) of the transition matrix $\underline{T}$. In (0.9) we have defined the 'rate of approach to homozygosity' as being $\mathcal{R}=1-\lambda_2$ for non-overlapping generation models, and $\mathcal{R}=1-\lambda_2^{2N}$ or $\mathcal{R}=1-\lambda_2^{N}$ for overlapping models with $2N$ haploid or N diploid individuals, respectively. The quantity $\mathcal{R}$, or rather λ_2 , could sometimes be found directly from the transition matrix, as was in fact done for the two models leading to (0.9). But for the more complex models this procedure seems unwieldy, and Moran (22) used another method for obtaining (0.8). This method we now briefly describe, since it will be used repeatedly.

For at least one of the absorbing states of the system, the corresponding element of $\underline{P}_t$ in (0.2) must contain a non-zero component in λ_2^t , unless the population is initi-

ally in an absorbing state. Ignoring the latter trivial case, suppose a quadratic function of the genotype numbers at time t is constructed, which is always non-negative, and is strictly positive in the aforementioned state. Then the expectation of this function will contain a term proportional to λ_2^t, and possibly other terms in the smaller eigenvalues as well.[1] It is thus sufficient to consider, not the transition matrix itself, but the behaviour of certain quadratic moments of the genotype numbers, in order to find λ_2. A specific example of the use of Moran's method will follow in § 7.1.

In this chapter we deal with model A discussed in § 2, but with the limitation that there is no mutation in the population. Remembering that the model is for dioecious diploid individuals, and that the genotype numbers were written $(k_t,u_t,l_t;r_t,v_t,s_t)$ at generation t, the conditional probability generating function for the next generation is given by (2.13) with the substitutions $p_1=1$, $p_2=\frac{1}{2}$, $p_3=0$,

1. The requirement of non-negativity of the function removes any possibility of the terms in λ_2^t cancelling; Wright has frequently used the number of heterozygotes (a linear function) for this purpose, but obtains a difference equation involving several generations whereas a quadratic function leads to a system of simultaneous difference equations of first order.

[illegible] (c/f. (2.5)). Thus

$$[illegible] \qquad (7.1)$$

$$[illegible]$$

The [illegible] to the author's knowledge, the first [illegible] to derive a discrete model having [illegible] for the number of offspring, [illegible] of constant size through all generations.

The history of the topic seems to start with Bartlett's paper (1), in which he considers only the heterozygotes in a monoecious population, when self mating is precluded. The possible number of heterozygotes is not limited by consideration of total population size. Bartlett discusses two cases, one for which each individual produces a fixed number of offspring, and the second, when the offspring numbers are independently Poisson distributed. He finds the mean and variance for the number of heterozygotes at any (non-overlapping) generation as functions of the mean number of offspring per individual (which is the only parameter in either of his offspring distributions).

A result which is more pertinent to our development

in that due to Wright for a monoecious population practising restricted random mating. Wright allows the offspring distribution to be arbitrary, and independent between parents, so that here also the population size is a random variable. By comparing the proportion of pairs of gametes derived from the same parent among all possible pairs of gametes, with the similar proportion in a completely random mating population, Wright obtains (see Li (20) p.321) the 'effective population size' as

$$\hat{N} = \frac{4N - 2}{\sigma^2 + 2} \qquad (7.2)$$

where we have written m and σ^2 as the mean and variance of the actual number of gametes produced per individual, and N as the population size. However, the concept of 'effective population size' as used here is not particularly useful, because it involves (in statistical language) sample estimates m and σ^2 rather than the population parameters μ and σ^2 of the gamete-number distribution. Even if the population is sufficiently large to write

$$\hat{N} = \frac{4N - 2}{\sigma^2 + 2} \qquad (7.3)$$

there is still some difficulty in interpretation. There are at least three distinct definitions of 'effective population size', but they are often treated as being equivalent in the literature (e.g. Li (20) pp.320-325). That they are not necessarily equivalent was recognised by Crow (5). The origi-

tions are:

The effective population size, $\tilde{N}$, is

1) $\tilde{N} = \frac{1}{2}\mathcal{R}^{-1}$, where $\mathcal{R}$ is the rate of approach to homozygosity,

or 2) [illegible] , see (2.18),

or 3) $\frac{\text{number of possible remote pairs}}{\text{number of remote pairs derived from the same parent}}$.

We have used the second definition, and the terminology 'variance effective population size' . Wright is here using the third definition.

Now definition 1) assumes the population does approach homozygosity, which is not correct if mutation is present, whilst in 2) it is implicitly assumed that the diffusion approximation is applicable, and 3) is limited to nonoverlapping generations. Apart from these general differences, even when all the assumptions are defined they are not necessarily equal, although they may be so. For example, in (3.3) we see that 1) and 2) can certainly differ, and 3) implies that [illegible] is constant but in 1) and 2) this is not necessarily so (see (3.5) and (3.7) where the non-random mating parameter f can be functional). Now it is not a conclusive argument to calculate $\tilde{N}$ for definition 3) and infer that $\mathcal{R} = \frac{1}{2}\tilde{N}^{-1}$, and Wright's conclusions (3.2) and (3.3) are open to this objection. Another additional one is that (3.2) is defined for a given k , but in general could vary from one generation to the next, and even cyclically, in which latter case it is [illegible]

valid if we take $m = \mu = 2$, and keep N constant. Then instead of (7.2) one has

$$\tilde{N} = \frac{4N-2}{S^2+2} \doteqdot \frac{4N-2}{\sigma^2+2} \qquad \text{(see (37),(40))}, \qquad (7.4)$$

a formula obtained also by Haldane (15) and Fisher (13).

For dioecious populations of diploid individuals only particular examples have been studied by exact methods. Wright (36) found that the rate of approach to homozygosity for a population of N_1 males and N_2 females practising random mating is

$$R \doteqdot \frac{1}{8N_1N_2} \qquad (7.5)$$

for autosomal genes, and for sex-linked genes

$$R \doteqdot \frac{N_2+2N_1}{9N_1N_2} . \qquad (7.6)$$

In Wright's model, the generations are non-overlapping, and constitute special cases of models A and B (c/f. § 2.3, § 3.3). This particular model will be generalised to non-random mating in § 9. An alternative model with overlapping generations was considered by Moran (22), and will be generalized to non-random mating in § 10. Finally, Moran considered several special models with non-overlapping generations, and the present author collaborated with him to extend these to the case with general offspring distributions considered here; the results were published jointly, (27). However, the compact specification of the model (7.1), and the derivation of results from it, is new.

7.1. Approach to homozygosity

It is clear from the verbal description of model A given in § 2.1, that when mutation is absent there are only two absorbing states in the Markov chain. These correspond to fixation of either the a or A genes, and thus either $k=N_1$, $r=N_2$, $u=v=l=s=0$, or $l=N_1$, $s=N_2$, $u=v=k=r=0$. However, it is less obvious that the above statements are correct if one considers only the mathematical formulation (7.1), and we proceed to verify that the two states mentioned are in fact absorbing. It is sufficient to discuss one state only, for the other follows by symmetry. We have to verify that if $k_t=N_1, r_t=N_2, u_t=v_t=l_t=s_t=0$, then $k_{t+1}=N_1$, $r_{t+1}=N_2$, $u_{t+1}=v_{t+1}=l_{t+1}=s_{t+1}=0$. That is, from (7.1),

$$\mathcal{E}\left(\kappa^{k_{t+1}}\chi^{u_{t+1}}\lambda^{l_{t+1}}\rho^{r_{t+1}}\psi^{v_{t+1}}\sigma^{s_{t+1}}\right) = \kappa^{N_1}\rho^{N_2} \qquad (7.7)$$

$$= \sum_{\gamma_1,\gamma_2}\left(\frac{\gamma_1!\,\gamma_2!}{N!}\right)^2 \text{coefficient of } (\beta_1\delta_1\varepsilon_1)^{\gamma_1}(\beta_2\delta_2\varepsilon_2)^{\gamma_2} \text{ in}$$

$$\left[\beta_1(\kappa-\chi)+\beta_2\chi\right]^{N_1}\left[\beta_1(\rho-\psi)+\beta_2\psi\right]^{N_2}$$

$$\times\left[Q_1(\varepsilon_1+\varepsilon_2)\right]^{N_1}\left[Q_2(\delta_1+\delta_2)\right]^{N_2}$$

$$\times\left\{\text{coefficient of } \omega_1^{N}\omega_2^{N} \text{ in } \left[Q_1(\omega_1)\right]^{N_1}\left[Q_2(\omega_2)\right]^{N_2}\right\}^{-1},$$

where the terms in $\beta_3, \delta_3, \varepsilon_3$ are missing, and the summation extends over γ_1, γ_2 with $\gamma_1+\gamma_2 = N$. Now the only terms in the expansion of $\left[Q_1(\varepsilon_1+\varepsilon_2)\right]^{N_1}$ which are of order N with respect to $\varepsilon_1, \varepsilon_2$ are contained in

$$\text{coefficient of } \omega_1^{N} \text{ in } \left[Q_1(\omega_1)\right]^{N_1}(\varepsilon_1+\varepsilon_2)^{N} = \text{coefficient of } \omega_1^{N} \text{ in } \left[Q_1(\omega_1)\right]^{N_1}\sum_{\gamma_1,\gamma_2}\frac{N!}{\gamma_1!\,\gamma_2!}\varepsilon_1^{\gamma_1}\varepsilon_2^{\gamma_2},$$

and similarly for the terms in ξ_1, ξ_2 . Hence the right hand side of (7.7) becomes

$$\sum_{\gamma_1,\gamma_2} \text{coefficient of } \beta_1^{\gamma_1}\beta_2^{\gamma_2} \text{ in } [\beta_1(\kappa-\chi)+\beta_2\chi]^{N_1}[\beta_1(\rho-\psi)+\beta_2\psi]^{N_2}.$$

But in the expansion of the square brackets, all terms are of order N with respect to β_1, β_2 , so the sum of the coefficients can be obtained by putting $\beta_1=\beta_2=1$ in the function; hence the right hand side of (7.7) reduces to $\kappa^{N_1}\rho^{N_2}$ as required. To verify that there are <u>only</u> two absorbing states seems to be very difficult algebraically, if one starts from (7.1); it is obvious, if one follows through the derivation of (7.1) in § 2.1.

The function $(k_t-l_t)^2$ is non-negative, and is strictly positive for each of the two absorbing states. Hence its expectation must contain a term proportional to λ_2^t . It is convenient to introduce four additional quantities, and the following notation will be used:

$$\underline{M}_{t+1} = \begin{bmatrix} M^1_{t+1} \\ M^2_{t+1} \\ M^3_{t+1} \\ M^4_{t+1} \\ M^5_{t+1} \end{bmatrix} = \begin{bmatrix} N_1^{-1}E(k_{t+1}+l_{t+1}) \\ N_2^{-1}E(r_{t+1}+s_{t+1}) \\ N_1^{-1}N_2^{-1}E(k_{t+1}-l_{t+1})(r_{t+1}-s_{t+1}) \\ N_1^{-2}E(k_{t+1}-l_{t+1})^2 \\ N_2^{-2}E(r_{t+1}-s_{t+1})^2 \end{bmatrix}$$

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By an argument similar to that used to evaluate (3.15) we get

$$N_1^{-1}\mathcal{E}(k_{t+1}+l_{t+1}) = N_1^{-1}N_2^{-1}\left[(k_t+\tfrac{1}{2}a_t)(r_t+\tfrac{1}{2}u_t)+(\tfrac{1}{2}k_t+a_t)(\tfrac{1}{2}r_t+s_t)\right]$$

$$= \tfrac{1}{2} + \tfrac{1}{2}N_1^{-1}N_2^{-1}(k_t-l_t)(r_t-s_t)\,,$$

since $a_t = N_1-k_t-l_t$, $u_t = N_2-r_t-s_t$.

Taking unconditional expectations of both sides gives

$$N_1^{-1}E(k_t+l_t) = \tfrac{1}{2}+\tfrac{1}{2}N_1^{-1}N_2^{-1}E(k_t-l_t)(r_t-s_t).$$

that is

$$H^1_{t+1} = \tfrac{1}{2}+\tfrac{1}{2}H^3_t \quad .$$

Similarly,

$$H^2_{t+1} = H^1_{t+1} = \tfrac{1}{2}+\tfrac{1}{2}H^3_t \, .$$

A somewhat more complicated algebraic argument involving second order derivatives of (7.1) gives

$$H^3_{t+1} = \tfrac{1}{2}N^{-1}(N-1)^{-1}\Big\{\left[N(N-1)-N_1P_1''(0)\right]N_1(N_1-1)^{-1}H^5_t + \left[N(N-1)-N_2P_2''(0)\right]N_2(N_2-1)^{-1}H^5_t$$
$$- \left[N(N-1)-N_1^2P_1''(0)\right](N_1-1)^{-1}H^1_t - \left[N(N-1)-N_2^2P_2''(0)\right](N_2-1)^{-1}H^2_t$$
$$+ 2N(N-1)H^3_t \Big\} \quad ,$$

$$H^4_{t+1} \equiv (1-N_1^{-1})H^3_{t+1} + N_1^{-1}H^1_{t+1} \quad , \qquad (7.8)$$

$$H^5_{t+1} \equiv (1-N_2^{-1})H^3_{t+1} + N_2^{-1}H^2_{t+1} \quad ,$$

which were derived in (27) by a more pedestrian method. In the derivation of the latter two members of (7.8) it is incidently seen that

$$\mathcal{E}\left[N_1^{-1}(k_{t+1}-l_{t+1})-N_2^{-1}(r_{t+1}-s_{t+1})\right]^2 \equiv N_1^{-2}\mathcal{E}(k_{t+1}+l_{t+1})+N_2^{-2}\mathcal{E}(r_{t+1}+s_{t+1}) \qquad (7.9)$$
$$-(N_1^{-1}+N_2^{-1})N_1^{-1}N_2^{-1}\mathcal{E}(k_{t+1}-l_{t+1})(r_{t+1}-s_{t+1}),$$

an identity which holds also when saturation is present (c/f. p. 72).

Substituting for M^2_t, M^4_t, M^5_t into the right hand side of M^3_{t+1} in (7.8), we finally have the two first order difference equations

$$M^1_{t+1} = \tfrac{1}{2} + \tfrac{1}{2} M^2_t ,$$

$$M^3_{t+1} = \tfrac{1}{2} n'(\zeta-\nu') \left\{ [n_1 P_1'(0) + n_2 P_2'(0)] M^1_t + [n(n-1) - n_1 P_1''(0) - n_2 P_2''(0)] M^3_t \right\} .$$

These may be written

$$\begin{bmatrix} M^1_{t+1} \\ M^3_{t+1} \end{bmatrix} = \underline{Q} \begin{bmatrix} M^1_t \\ M^3_t \end{bmatrix} + \begin{bmatrix} \frac{1}{2} \\ 0 \end{bmatrix} ,$$

where

$$\underline{Q} = \begin{bmatrix} 0 & \frac{1}{2} \\ \dfrac{n_1 P_1'(0) + n_2 P_2'(0)}{2n'(\zeta-\nu')} & 1 - \dfrac{n_1 P_1''(0) + n_2 P_2''(0)}{2n'(\zeta-\nu')} \end{bmatrix} ,$$

and the solution has the form

$$M^1_t = 1 - \alpha_2 \lambda_2^t - \alpha_3 \lambda_3^t ,$$

$$M^3_t = 1 - \beta_2 \lambda_2^t - \beta_3 \lambda_3^t .$$

Here, the λ's are the eigenvalues of $\underline{Q}$ and the α's and β's are constants chosen to satisfy the initial conditions. If λ_2 is the larger eigenvalue, then from the middle member of (7.8), M^4_t, contains a term proportional to λ_2^t as well, and λ_2 is therefore the largest non-unit eigenvalue of the transition matrix defined implicitly by (7.1).

Consider the general 2×2 matrix

$$Q = \begin{bmatrix} a & b \\ c & d \end{bmatrix}.$$

Its characteristic equation is

$$|Q - \lambda I| = \lambda^2 - (a+d)\lambda + ad - bc = 0,$$

and provided $|bc| \ll |a-d|^2$, the eigenvalues are approximately

$$a + \frac{bc}{a-d}, \qquad d - \frac{bc}{a-d}. \tag{7.10}$$

Applying this to the matrix under consideration, the larger eigenvalue is approximately

$$\lambda_2 \doteq 1 - \frac{N_1 P_1''(0) + N_2 P_2''(0)}{4N(N-1)} - \frac{N_1 P_1''(0) + N_2 P_2''(0)}{8N(N-1)} \left[\frac{N_1 P_1''(0) + N_2 P_2''(0)}{4N(N-1)} - 1 \right]^{-1}$$

$$\doteq 1 - \frac{N_1 P_1''(0) + N_2 P_2''(0)}{8N^2},$$

or exactly, the larger solution of

$$\lambda^2 - \left[1 - \frac{N_1 P_1''(0) + N_2 P_2''(0)}{4N(N-1)} \right] \lambda - \frac{N_1 P_1''(0) + N_2 P_2''(0)}{8N(N-1)} = 0.$$

Therefore, ignoring terms of order N^{-2}, the rate of approach to homozygosity is

$$\mathcal{R} = 1 - \lambda_2 \doteq \frac{1}{8} N^{-1} \left[N_1 P_1''(0) + N_2 P_2''(0) \right] \tag{7.11}$$

measured in time units of τ, that is, in generations. This result is very similar to that obtained in § 2.3 by approximate methods, namely

$$\mathcal{R} \doteq \frac{1}{8} N^{-1} \left[N_1 Q_1''(0) + N_2 Q_2''(0) \right].$$

By considering the expectations of $(k_{t+1}, l_{t+1}, r_{t+1}, s_{t+1})$ in terms of those at generation t, we can easily find the probabilities of ultimate absorption in one or other of the absorbing states $(N_1, 0, N_2, 0)$, $(0, N_1, 0, N_2)$. Thus, the probability of absorption in the former is the ultimate value of $N_1^{-1}E(k_{t+1})$ which may be denoted by $N_1^{-1}E(k_\infty)$. We know already that

$$N_1^{-1}E(k_\infty) = N_2^{-1}E(r_\infty), \quad N_1^{-1}E(l_\infty) = N_2^{-1}E(s_\infty), \tag{7.12}$$

$$N_1^{-1}E(k_\infty + l_\infty) = 1 = N_2^{-1}E(r_\infty + s_\infty).$$

Further, in § 6.2 it was shown that

$$\mathcal{E}(s_{t+1} - s_t) = \alpha_2 - (\alpha_1 + \alpha_2)s_t,$$

and in our present notation with no mutation this is equivalent to

$$\mathcal{E}\left[N_1^{-1}(k_{t+1} - l_{t+1}) + N_2^{-1}(r_{t+1} - s_{t+1})\right] = N_1^{-1}(k_t - l_t) + N_2^{-1}(r_t - s_t).$$

Thus

$$E\left[N_1^{-1}(k_\infty - l_\infty) + N_2^{-1}(r_\infty - s_\infty)\right] = N_1^{-1}(k_0 - l_0) + N_2^{-1}(r_0 - s_0).$$

Substituting from (7.12) for the unwanted quantities on the left hand side, we get the probability of fixation of the a gene as

$$P\{k_\infty = N_1\} = N_1^{-1}E(k_\infty) = \tfrac{1}{2} + \tfrac{1}{2}N_1^{-1}(k_0 - l_0) + \tfrac{1}{2}N_2^{-1}(r_0 - s_0) = p(x_0), \tag{7.13}$$

which is the sum of the relative frequencies of the a gene in the males and females of the initial population. We notice in particular that it is only equal to the overall initial frequency of a when $N_1 = N_2$. Note also that (7.13) was obtained exactly in § 2.3 by approximate methods.

The whole of the above calculations have been repeated by the author for the case when the males are haploid and the females diploid, which is effectively so for sex-linked genes. Nothing in the new analysis warrants its inclusion here, since it follows step by step that given above. Denote the genotype numbers by k, N_1-k for the male a and A, and r, r_1, s $(r+r_1+s=N_2)$ for the female aa, Aa, and AA. Then the state of the population is determined by the three variates (k,r,s) and the two possible absorbing states are $(N_1,N_2,0)$ and $(0,0,N_2)$. It can be shown that the rate of approach to one or other of these states is

$$\mathcal{R} \doteq \tfrac{1}{4}\pi^2\left(N_1 P_1''(0) + 2N_2 P_2''(0)\right), \tag{7.14}$$

where the symbols have the same meanings as before. The probability of ultimate fixation of the a genes is now

$$\tfrac{1}{2} + \tfrac{1}{6}(2k_0 - N_1)N_1^{-1} + \tfrac{1}{3}(r_0 + s_0)N_2^{-1}.$$

For the present general model, it seems exceedingly difficult to find the exact expected time to reach homozygosity, but in § 2.3 an approximation is given for this quantity in the autosomal gene case.

Because of the close agreement between approximate and exact results, it is unnecessary to repeat examples of

special models for which the above theory is applicable; these have been given already in §§ 2.3, 4.3, 5.3. We note in particular, that Wright's model given in § 2.3 is an example for which (7.11) and (7.14) reduce to (7.5) and (7.6), as they should.

8. Systems of non-random mating

8.0. Introduction

In this chapter, various systems of non-random mating are considered for both monoecious and dioecious populations. As before, the individuals are diploids, with possible genotypes aa, Aa, or AA. The total population size, N, is assumed constant through all generations, and so too are the sex numbers N_1 and N_2 in the dioecious case.

Genetically speaking, the birth of an individual in a population is caused by the union of two gametes to form a new zygote. If we disregard the fact that these gametes come from diploid patents and treat them as independent entities, then we refer to the mating system as being on a 'gametic basis'; but on the other hand, if we consider offspring as coming specifically from the mating of two diploid parents, then the mating will be on a 'zygotic basis'. Non-random mating is a result of one gamete (or zygote) type being more likely to unite with a certain gamete (zygote) type than the assumption of random encounters suggests. Thus positive assortative mating results when a gamete or zygote prefers to mate with another of the same type, whilst negative assortative mating occurs when union with a different type is preferable. The extreme cases when all unions are of the same, or different, types are called complete positive, and complete negative, assortative mating, respectively. We propose to approximate to actual population behaviour by assuming it to

be a mixture of random, complete positive, and complete negative assortative mating systems, but we shall also indicate another method of representation.

So far, only one measure of non-randomness of mating has achieved wide usage, the so called 'coefficient of inbreeding' (denoted by F or f) introduced by Wright (35). This coefficient measures the correlation between uniting gametes in a monoecious population, or a dioecious population with both sexes having the same genotypic proportions. To calculate the correlation, the alleles a and A are scored 0 and 1 on a numerical scale. Moran (24) has recently extended this theory to two-sex populations with unequal genotype proportions by analogy with Wright's system, and has devised a somewhat different formulation for negative assortative mating. However, each of these systems is on a gametic basis only.

In the following sections, we discuss the problem from first principles, and obtain some non-random mating systems which are sufficiently general to cover both gametic and zygotic cases, and which include Wright's and Moran's systems as special cases. For examples of positive assortative mating, one can refer back to models B, C, and E (chapters 3, 4, and 6) on a gametic basis, and to model D (chapter 5) on a zygotic basis.

8.1. Monoecious population, gametic basis.

Suppose we have a population of size N, consisting of $k, N-k-l$, and l individuals of genotypes aa, Aa, and AA respectively. The number of a genes in this population is $2k+(N-k-l)$, and of A genes is $(N-k-l)+2l$, so that the gametic proportions are

$$p(a) = \tfrac{1}{2}(N+k-l)N^{-1}, \quad p(A) = \tfrac{1}{2}(N-k+l)N^{-1}$$

If random mating occurs, the proportions of the various possible gametic unions are

	a	A
a	$p(a)^2$	$p(a)p(A)$
A	$p(a)p(A)$	$p(A)^2$

When completely positive assortative mating occurs, the offspring are always homozygous, with proportions

	a	A
a	$p(a)$	0
A	0	$p(A)$

For completely negative assortative mating, it is not always possible for a union of opposite allele types to occur, because the entire population may be of one type. In this exceptional circumstance, we allow homozygotic offspring, but in gen-

eral offspring will be heterozygotic. The proportions are

		First gamete chosen: a	First gamete chosen: A
Second gamete chosen	a	$p(a)(1-\beta)$	$p(A)\alpha$
	A	$p(a)\beta$	$p(A)(1-\alpha)$

where $\alpha = 1, 0$ if $p(a) > 0, = 0$, and $\beta = 1, 0$ if $p(A) > 0, = 0$. α and β are functions included to account for the exceptional case, and should not be confused with mutation rates as used in previous chapters. Here, neither mutation nor selection are considered.

To combine these systems into a general population model, suppose that a new zygote is formed by the union of two gametes, the first being chosen at random from all the population output, the second chosen according to either random mating, complete positive, or complete negative assortative mating with probabilities f_1, f_2, f_3 respectively. We must have

$$f_1 + f_2 + f_3 = 1 .$$

The offspring now has the following probabilities of being of a certain genotype:

$$\begin{aligned} P_{aa} &= f_1 p(a)^2 + f_2 p(a) + f_3 p(a)(1-\beta), \\ P_{Aa} &= 2 f_1 p(a) p(A) + f_3 [p(a)\beta + p(A)\alpha], \\ P_{AA} &= f_1 p(A)^2 + f_2 p(A) + f_3 p(A)(1-\alpha) . \end{aligned} \tag{8.1}$$

A more general (and more plausible) system of non-random mating is possible for the population, and is one which satisfies a law of 'Mass Action'. Suppose that the gametic unions have the probabilities

	a	A
a	$p(a)^2(1+b)\Delta^{-1}$	$p(a)p(A)(1+c)\Delta^{-1}$
A	$p(a)p(A)(1+c)\Delta^{-1}$	$p(A)^2(1+d)\ \Delta^{-1}$

where $\Delta = p(a)^2(1+b) + 2p(a)p(A)(1+c) + p(A)^2(1+d)$,
and $-1 \leqslant b, c, d \leqslant 1$. Then since all probabilities are non-negative, the system is a true probability distribution, and the constants b, c, and d measure the deviation from randomness. A similar system may be used for zygotically based systems, or for dioecious populations; however, we shall not pursue its study further because the probabilities are rational functions of the gene frequencies (instead of being polynomials), for which it appears to be too difficult to solve population problems by exact methods.

8.2. Monoecious populations, zygotic basis

Let us denote the genotype proportions in the population by $X = kN^{-1}$, $Y = lN^{-1}$ for types aa and AA respectively, and the proportion of heterozygotes is then $1 - X - Y$.

The mating system practised by a population on a zygotic basis will be defined by the following rule. A new zygote is formed by union of two gametes, one of which is chosen at random from a diploid parent, itself chosen at random from the population. The second gamete is chosen at random from a diploid parent, such that the two parents are either random mates, completely positive, or completely negative assortative mates, with probabilities f_1, f_2, f_3 respectively. Note that this does not exclude self-mating by a parent, that is, two zygotes from the same parent may unite.

In the random mating system, the zygotic mating probabilities are

	aa	Aa	AA
aa	X^2	$X(1-X-Y)$	XY
Aa	$X(1-X-Y)$	$(1-X-Y)^2$	$Y(1-X-Y)$
AA	XY	$Y(1-X-Y)$	Y^2

For the completely positive assortative mating with no dominance, the probabilities are

	aa	Aa	AA
aa	X	0	0
Aa	0	1-X-Y	0
AA	0	0	Y

Various interpretations of completely negative assortative mating are possible, but we shall consider only one at this stage. We suppose that an aa parent mates only with an AA parent, and vice versa; and that an Aa parent mates with aa and AA with equal probabilities $\frac{1}{2}, \frac{1}{2}$. Of course, adjustments must be made when one or more of these matings is impossible because of genotypes being missing from the population. For simplicity, we might assume that if the required genotype is not present, the parent self-mates. Under such a system, the mating proportions are

Second zygote chosen \ First zygote chosen	aa	Aa	AA
aa	$X(1-\beta)$	$\frac{1}{2}\alpha(1-X-Y)$	αY
Aa	0	$\frac{1}{2}(1-X-Y)(2-\alpha-\beta)$	0
AA	βX	$\frac{1}{2}\beta(1-X-Y)$	$Y(1-\alpha)$

where $\alpha = 1, 0$ if $X > 0$, $= 0$; $\beta = 1, 0$ if $Y > 0$, $= 0$.

α and β are introduced to allow for the exceptional cases.

The offspring probabilities are

$$P_{aa} = f_1 \tfrac{1}{4}(1+X-Y)^2 + f_2 \tfrac{1}{4}(1+3X-Y) + f_3 \tfrac{1}{8}(2+\alpha-\beta+6X-\alpha X-7\beta X-2Y-\alpha Y+\beta Y),$$

$$P_{Aa} = f_1 \tfrac{1}{2}(1+X-Y)(1-X+Y) + f_2 \tfrac{1}{2}(1-X-Y) + f_3 \tfrac{1}{2}(2\beta X+1-X-Y+2\alpha Y), \qquad (8.2)$$

$$P_{AA} = f_1 \tfrac{1}{4}(1-X+Y)^2 + f_2 \tfrac{1}{4}(1+3Y-X) + f_3 \tfrac{1}{8}(2-\alpha+\beta+6Y-\beta Y-7\alpha Y-2X-\beta X+\alpha X).$$

Another type of zygotic mating occurs when one gene is dominant over the other. Suppose that A is dominant over a , so that Aa and AA genotypes are indistinguishable phenotypically. Then, complete positive assortative mating would allow mates between two such genotypes. The proportions of such mates would be

First zygote chosen

Second zygote chosen	aa	Aa	AA
aa	X	0	0
Aa	0	$(1-X-Y)^2(1-X)^{-1}$	$Y(1-X-Y)(1-X)^{-1}$
AA	0	$Y(1-X-Y)(1-X)^{-1}$	$Y^2(1-X)^{-1}$

For the general population with dominance, the offspring probabilities would be rational functions of X and Y, and involve the factor $1-X$ in the denominator. Our problems seem too difficult to solve under such a system, and therefore in what follows, we assume no dominance is present in the genotypes.

8.3. Dioecious populations, gametic basis

The mating systems to be treated here are generalizations of the monoecious systems above. Suppose that there are k, N_1-k-l and l male genotypes of the forms aa, Aa, and AA respectively, with corresponding numbers of female genotypes r, N_2-r-s and s. The gametic proportions are now

$$p_M(a)=\tfrac{1}{2}(N_1+k-l)N_1^{-1}\ , \quad p_F(a)=\tfrac{1}{2}(N_2+r-s)N_2^{-1}\ ,$$

$$p_M(A)=\tfrac{1}{2}(N_1-k+l)N_1^{-1}\ , \quad p_F(A)=\tfrac{1}{2}(N_2-r+s)N_2^{-1}\ .$$

A new zygote is formed by the union of two gametes, one of which must come from the male sub-population output, the other from the female. This restriction removes the possibility of self-mating which was allowed for the monoecious population, and hence completely positive, as well as completely negative assortative mating, may not always be possible when a gene is absent from one or other sex. Several systems of mating are possible, and we consider three in detail.

I. General system

Under the general mating system, a new zygote is produced by the union of two gametes, one of which is chosen completely at random from the population gametic output, the other is chosen from the opposite sex according to random mating, complete positive or complete negative assortative mating, with probabilities f_1, f_2, f_3 respectively.

For this system, the probability that the first gamete chosen is male is N_1N^{-1} , that it is both male and of type a is $N_1N^{-1}p_M(a)$. Obvious relations hold for the other possibilities. With random mating, the mating proportions are

		Male: a	Male: A
Female	a	$p_M(a)p_F(a)$	$p_M(A)p_F(a)$
	A	$p_M(a)p_F(A)$	$p_M(A)p_F(A)$.

For completely positive assortative mating, offspring will be homozygotic, whenever possible. The mating proportions are

		Male: a	Male: A
Female	a	$N_1N^{-1}p_M(a)\gamma + N_2N^{-1}p_F(a)\alpha$	$N_1N^{-1}p_M(A)(1-\delta) + N_2N^{-1}p_F(a)(1-\alpha)$
	A	$N_1N^{-1}p_M(a)(1-\gamma) + N_2N^{-1}p_F(A)(1-\beta)$	$N_1N^{-1}p_M(A)\delta + N_2N^{-1}p_F(A)\beta$

where $\alpha = 1, 0$ if $p_M(a) > 0, = 0$, $\beta = 1, 0$ if $p_M(A) > 0, = 0$,

$\gamma = 1, 0$ if $p_F(a) > 0, = 0$, $\delta = 1, 0$ if $p_F(A) > 0, = 0$.

α, β, γ and δ are introduced to allow for the exceptional cases. Similarly, for completely negative assortative mating,

the probabilities of union of various gamete types are

Female \ Male	a	A
a	$N_1N^{-1}p_M(a)(1-\delta)+N_2N^{-1}p_F(a)(1-\beta)$	$N_1N^{-1}p_M(A)\gamma+N_2N^{-1}p_F(a)\beta$
A	$N_1N^{-1}p_M(a)\delta+N_2N^{-1}p_F(A)\alpha$	$N_1N^{-1}p_M(A)(1-\gamma)+N_2N^{-1}p_F(A)(1-\alpha)$

Combining these probabilities, we get the offspring frequencies:

$$P_{aa} = f_1 p_M(a)p_F(a) + f_2\left[N_1N^{-1}p_M(a)\gamma+N_2N^{-1}p_F(a)\alpha\right] + f_3\left[N_1N^{-1}p_M(a)(1-\delta)+N_2N^{-1}p_F(a)(1-\beta)\right],$$

$$P_{Aa} = f_1\left[p_M(a)p_F(A)+p_M(A)p_F(a)\right] + f_2\left[1-N_1N^{-1}p_M(a)\gamma-N_2N^{-1}p_F(a)\alpha-N_1N^{-1}p_M(A)\delta-N_2N^{-1}p_F(A)\beta\right] \quad (8.3)$$
$$+ f_3\left[N_1N^{-1}p_M(a)\delta+N_2N^{-1}p_F(a)\beta+N_1N^{-1}p_M(A)\gamma+N_2N^{-1}p_F(A)\alpha\right],$$

$$P_{AA} = f_1 p_M(A)p_F(A) + f_2\left[N_1N^{-1}p_M(A)\delta+N_2N^{-1}p_F(A)\beta\right]+f_3\left[N_1N^{-1}p_M(A)(1-\gamma)+N_2N^{-1}p_F(A)(1-\alpha)\right].$$

II. Symmetric system

A second mating system, which treats the two sexes equally, is the following:

A new zygote is produced by first choosing a sex with equal probabilities, then randomly choosing the first gamete from this sex. The second gamete is chosen from the opposite sex according to either a random mating system, complete positive, or complete negative assortative mating with probabilities f_1, f_2, and f_3 respectively.

The only change that this system makes over the general system I above, is that the weights N_1N^{-1} and N_2N^{-1} of

equations (8.3) are replaced by $\frac{1}{4}$, $\frac{1}{2}$.

III. Asymmetric system

For a population in which one sex takes the initiative in finding a mate, the above systems are not applicable. Instead, we may postulate a mating system as follows:

A new zygote is produced by the union of two gametes, the first of which is chosen from the male sex, at random, and the second is chosen from the female gametes according to random mating, complete positive, or complete negative assortative mating, with probabilities f_1, f_2, f_3 respectively.

Such a system gives the initiative to the male sex, but of course, the other case may be deduced by symmetry. We shall not dwell on the derivation of the probabilities of the various offspring genotypes, but these are easily seen to be

$$
\begin{aligned}
P_{aa} &= f_1 p_M(a) p_F(a) + f_2 p_M(a)\gamma + f_3 p_M(a)(1-\delta), \\
P_{Aa} &= f_1 \left[p_M(a) p_F(A) + p_M(A) p_F(a) \right] + f_2 \left[p_M(a)(1-\gamma) + p_M(A)(1-\delta) \right] \\
&\quad + f_3 \left[p_M(a)\delta + p_M(A)\gamma \right], \\
P_{AA} &= f_1 p_M(A) p_F(A) + f_2 p_M(A)\delta + f_3 p_M(A)(1-\gamma).
\end{aligned}
\tag{8.4}
$$

8.4. Dioecious population, zygotic basis.

In the monoecious population case of zygotic mating, § 8.2, we saw that many alternative systems were possible, and likewise for the dioecious, gametic mating populations in § 8.3. We shall not attempt to unite all these possibilities into the case under discussion, but consider one simplified case only. Suppose that there is at least one of each genotype in each sex; that is, that X, $1-X-Y$, Y, W, $1-W-Z$, Z are all non-zero, where $X = kN_1^{-1}$, $Y = lN_1^{-1}$, $Z = sN_2^{-1}$, $W = rN_2^{-1}$. Then, complete positive assortative mating is always possible, being the mating of two similar parents; further, it is always possible for an aa parent to mate with an AA parent and vice versa, and for an Aa parent to find a mate with an aa or an AA with probabilities $\frac{1}{2}, \frac{1}{2}$, hence complete negative assortative mating is also possible. Suppose now, that a new offspring is formed by the union of two gametes, the first being chosen at random from the two possible gametes of one parent, itself being chosen at random from the population. The second gamete is chosen at random from another parent, which is of opposite sex to the first, and chosen so that the two parents mate according to either random mating, complete positive, or complete negative assortative mating systems, with probabilities f_1, f_2, f_3 respectively.

The offspring probabilities will then be:

$$
\begin{aligned}
P_{aa} &= f_1 \tfrac{1}{4}(1+X-Y)(1+W-Z) + f_2 \tfrac{1}{4}[1+N_1N^{-1}(3X-Y)+N_2N^{-1}(3W-Z)] \\
&\quad + f_3 \tfrac{1}{4}[1-N_1N^{-1}(X+Y)-N_2N^{-1}(W+Z)], \\
P_{Aa} &= f_1 \tfrac{1}{4}[(1+X-Y)(1-W+Z)+(1-X+Y)(1+W-Z)] \\
&\quad + f_2 \tfrac{1}{2}[1-N_1N^{-1}(X+Y)-N_2N^{-1}(W+Z)] + f_3 \tfrac{1}{4}[1+N_1N^{-1}(X+Y)+N_2N^{-1}(W+Z)], \\
P_{AA} &= f_1 \tfrac{1}{4}(1-X+Y)(1-W+Z) + f_2 \tfrac{1}{4}[1+N_1N^{-1}(3Y-X)+N_2N^{-1}(3Z-W)] \\
&\quad + f_3 \tfrac{1}{4}[1-N_1N^{-1}(X+Y)-N_2N^{-1}(W+Z)].
\end{aligned}
\tag{8.5}
$$

To account for the exceptional cases when complete positive or negative assortative mating is impossible, equations (8.5) would have to be modified by non-analytic factors equivalent to α, β etc. introduced in previous systems. However, in § 8.5 below, we simplify all systems by disregarding α, β etc., so that the more correct version of (8.5) will not be required.

8.5. Simplifications.

A trivial special case of the above mating schemes is obtained with $f_2 = f_3 = 0$, when the equations (8.1) to (8.5) reduce to the well-known panmictic proportions. With $f_3 = 0$, equations (8.1) become the usual inbred offspring probabilities, and in this case f_2 is identical to Wright's coefficient of inbreeding.

For many practical purposes, neither gene will be absent from the population, nor will any genotype be missing from either sex, and consequently $\alpha = \beta = \gamma = \delta = 1$. With

this substitution, the equations (8.1) to (8.4) are seen to have a much simplified form. Moran (24) has used a system of non-random mating equivalent to the symmetrical system of § 8.3 above for the special cases $f_2 = 0$ or $f_3 = 0$; for a homogeneous population it seems unlikely that both positive and negative assortative mating could be practised simultaneously, and hence Moran's special cases are probably of most importance.

For studies with mutation, it may well be sufficient to use (8.1) to (8.5) ignoring the exceptional cases which necessitated the introduction of the quantities $\alpha, \beta, \gamma, \delta$. Such a procedure cannot be recommended in general, however, because when no mutations are allowed in a population, it will eventually become homozygous after a sufficiently long time, and indeed, fixation of one gene will occur. To this extent, the simplification cannot be used unless $f_3 = 0$, because no fixation would be allowed by the model. For this reason, we shall limit ourselves to the case of positive assortative mating only, the equations to account for negative mating being too difficult to deal with because of the non-linear quantities $\alpha, \beta, \gamma, \delta$.

The simplification of omitting the quantities $\alpha, \beta, \gamma, \delta$ introduces another, less major, difficulty. In the monoecious population, $p_M(a)$ equals $p_F(a)$, since sexes are ignored. Hence, positive assortative mating is always possible. However, for the dioecious population, these two quantities need not be equal, although for large popula-

tions they will be approximately so. The simplified versions of (8.3), (8.4), and (8.5), with $f_3 = 0$, allow a non-zero probability of getting aa offspring when in fact there are no a gametes in the female population. However, for large populations, this discrepancy should not affect the essential behaviour of the population model.

We shall now unify the simplified mating systems described above. We propose to use a general form for offspring probabilities, which will include many cases of interest. For a monoecious population, practising positive assortative mating, the offspring probabilities may be written

$$P_{aa} = \tfrac{1}{4}(1-f)(1+X-Y)^2 + f\,L_1(X,Y) ,$$

$$P_{AA} = \tfrac{1}{4}(1-f)(1-X+Y)^2 + f\,L_2(X,Y) , \qquad (8.6)$$

$$P_{Aa} = 1 - P_{aa} - P_{AA} .$$

where we have put $f_2 = f$, $f_1 = 1 - f$, and L_1 and L_2 denote linear functions of their arguments. Similarly, many cases of dioecious population mating systems are included in the equations

$$P_{aa} = \tfrac{1}{4}(1-f)(1+X-Y)(1+W-Z) + f\,L_3(X,Y,W,Z) ,$$

$$P_{AA} = \tfrac{1}{4}(1-f)(1-X+Y)(1-W+Z) + f\,L_4(X,Y,W,Z) , \qquad (8.7)$$

$$P_{Aa} = 1 - P_{aa} - P_{AA} ,$$

where L_3 and L_4 are again linear functions. The systems (8.6) and (8.7) assume that offspring probabilities are quadratic functions of the genotype frequencies, and that non-randomness is introduced by the linear functions L_1, L_2, L_3 and L_4. We may immediately impose some restrictions on these linear functions, because a practical population must, at least, satisfy the following requirements:

(1) When the total population is of type aa, then all offspring must also be of that type.

(2) When the total population is of type AA, then all offspring must also be of that type.

(3) The gene types a and A are symmetrical, in that if the numbers of aa and AA individuals are equal in each sex, then the corresponding offspring probabilities must also be equal.

Symbolically, these conditions are:

(1) $P_{aa} = 1$, $P_{AA} = 0$ when $X=W=1$, $Y=Z=0$,

(2) $P_{aa} = 0$, $P_{AA} = 1$ when $X=W=0$, $Y=Z=1$,

(3) $P_{aa} = P_{AA}$ when $X=Y$, $W=Z$.

It is a simple matter to show that these conditions require that the offspring probabilities are given implicitly by

$$\begin{aligned} P_{aa}+P_{AA} &= \tfrac{1}{2}\left[1-f(1-2\varepsilon)\right] + \tfrac{1}{2}(1-f)(X-Y)^2 + f(1-\varepsilon)(X+Y), \\ P_{aa}-P_{AA} &= X-Y, \\ P_{Aa} &= 1-P_{aa}-P_{AA}, \end{aligned} \tag{8.8}$$

for the monoecious case, and in the dioecious case by

$$
\begin{aligned}
P_{aa} + P_{AA} &= \tfrac{1}{2}\left[1 - f(1-2\varepsilon)\right] + \tfrac{1}{2}(1-f)(X-Y)(W-Z) + \tfrac{1}{2}f(1-\varepsilon)(X+Y+W+Z) \\
&\quad + \tfrac{1}{4}f\left[\xi(X-W) + \eta(Y-Z)\right], \\
P_{aa} - P_{AA} &= \tfrac{1}{2}(1+f\rho)(X-Y) + \tfrac{1}{2}(1-f\rho)(W-Z), \\
P_{Aa} &= 1 - P_{aa} - P_{AA},
\end{aligned}
\tag{8.9}
$$

where $\varepsilon, \xi, \eta, \rho$ are arbitrary constants, but restricted to make all probabilities non-negative and not greater than unity. By inspection, we may verify that $\varepsilon = 1$ corresponds to gametic mating (equations (8.1), (8.3), and (8.4), and $\varepsilon = \frac{1}{2}$ corresponds to zygotic mating (equations (8.2) and (8.5)). For a dioecious population, $\xi = \eta = 0$ for gametic mating, and either the general system, the symmetric system, or the asymmetric system is given when $\rho = (N_1 - N_2)N^{-1}$, 0, 1 respectively. For the one zygotic mating system considered, equations (8.5) give $\xi = \eta = \rho = (N_1 - N_2)N^{-1}$, which correspond to the general system; the other systems would be given by $\rho = 0$, and $\rho = 1$.

Of the two systems of gametic and zygotic mating, the former involves the concept of a gene pool with like genes having a higher probability of uniting than unlike genes. Clearly, this system will have few (if any) counterparts in actual populations, and the zygotic system will be predominant. Further, although the symmetric system produces rather simple results, most actual populations probably approximate to either the general or the asymmetrical system.

In the following two chapters, the effect these general systems of non-random mating have on the behaviour of non-overlapping and overlapping generation populations will be investigated. Finally, in chapter 11 another special case will be considered.

9. Model B: Approach to homozygosity

9.0. Introduction

We now consider a population model similar to that of chapter 3, in that it has non-overlapping generations, and the genotype numbers are random variables determined from the previous generation by trinomial distributions. However, here a more general mating system is prescribed along the lines of § 8, and mutation and selection are assumed absent. We shall discuss both the monoecious and dioecious cases of diploid individuals.

9.1. Monoecious population

Wright's birth-death model for a population asserts that one generation is replaced by another with genotype numbers drawn from a genotype pool by random sampling with replacement. If the probabilities of one offspring being of genotypes aa, Aa, AA are P_{aa}, P_{Aa}, P_{AA} respectively, then the state of the new generation has genotype numbers k,u,l $(k+u+l = N)$ with probability

$$P\{k,u,l\} = \frac{N!}{k!\,u!\,l!}\, P_{aa}^{k}\, P_{Aa}^{u}\, P_{AA}^{l} . \qquad (9.1)$$

In a panmictic population, Wright (36) has shown that the expected number of heterozygotes, $E(N - k - l)$ decreases asymptotically by an amount $\frac{1}{2}N^{-1}$ per generation c/f (0.9); finally, the population will be homozygous with either $k = N$, $u = l = 0$ or $k = u = 0$, $l = N$, correspond-

ing to fixation of one or other gene. We extend this result to the case where the offspring probabilities are given by (8.8).

At the t-th generation, the genotype proportions are denoted by $X_t = kN^{-1}$, $Y_t = lN^{-1}$ and $1 - X_t - Y_t$ taken in the order aa, AA, Aa. The state of the population at any time is specified by the two quantities X_t, Y_t, but it would be difficult to find the rate of approach to homozygosity via the eigenvalues of the transition matrix of this Markov chain. Instead we use the method of moments described in § 7.0 and exemplified in § 7.1 for model A.

From the well-known theory of multinomial distributions, the conditional moments of the t+1 th generation variates are

$$\begin{aligned} &\mathcal{E}(X_{t+1}) = P_{aa}, \qquad \mathcal{E}(Y_{t+1}) = P_{AA}, \\ &\mathcal{V}ar(X_{t+1}) = P_{aa}(1-P_{aa})N^{-1}, \quad \mathcal{V}ar(Y_{t+1}) = P_{AA}(1-P_{AA})N^{-1}, \\ &\mathcal{C}ov(X_{t+1}, Y_{t+1}) = -P_{aa}P_{AA}N^{-1}. \end{aligned} \tag{9.2}$$

Writing

$$\underline{M}_t = \begin{bmatrix} M_t^1 \\ M_t^2 \end{bmatrix} = \begin{bmatrix} E(X_t + Y_t) \\ E(X_t - Y_t)^2 \end{bmatrix},$$

we have from (9.2) and (8.8)

$$M'_{t+1} = E(P_{aa}+P_{AA}) = f(1-\varepsilon)M'_t + \tfrac{1}{2}(1-f)M^2_t + \tfrac{1}{2}[1-f(1-2\varepsilon)] ,$$

$$M^2_{t+1} = E(P_{aa}-P_{AA})^2(1-N^{-1}) + E(P_{aa}+P_{AA})N^{-1}$$

$$= M^2_t(1-N^{-1}) + \tfrac{1}{2}N^{-1}[2f(1-\varepsilon)M'_t + (1-f)M^2_t + 1 - f(1-2\varepsilon)]$$

$$= f(1-\varepsilon)N^{-1}M'_t + [1-\tfrac{1}{2}(1+f)N^{-1}]M^2_t + \tfrac{1}{2}N^{-1}[1-f(1-2\varepsilon)] ,$$

which may be re-written

$$\underline{M}_{t+1} = \underline{Q}\,\underline{M}_t + \tfrac{1}{2}[1-f(1-2\varepsilon)]\begin{bmatrix} 1 \\ N^{-1} \end{bmatrix} , \qquad (9.3)$$

where

$$\underline{Q} = \begin{bmatrix} f(1-\varepsilon) & \tfrac{1}{2}(1-f) \\ f(1-\varepsilon)N^{-1} & 1-\tfrac{1}{2}(1+f)N^{-1} \end{bmatrix} .$$

Now the solution of (9.3) has the form

$$M'_t = 1 + \alpha_2\lambda_2^t + \alpha_3\lambda_3^t ,$$

$$M^2_t = 1 + \beta_2\lambda_2^t + \beta_3\lambda_3^t ,$$

where the λ's are the eigenvalues of the matrix $\underline{Q}$, and the α's, β's are constants depending on the initial state of the population. If λ_2 is the larger of the two roots of $\underline{Q}$, then it is also the largest non-unit root of the transition matrix, $\underline{T}$, implicitly defined by (9.1); the first two roots of $\underline{T}$ will of course be unity.

According to (7.10), the larger root of $\underline{Q}$ is given

approximately by

$$\lambda_2 \doteqdot 1 - \tfrac{1}{2}(1+f)N^{-1} + \tfrac{1}{2}(1-f)f(1-\varepsilon)N^{-1}\left[1 - f(1-\varepsilon) - \tfrac{1}{2}(1+f)N^{-1}\right]^{-1} \qquad (9.4)$$

$$\doteqdot 1 - \tfrac{1}{2}\left[1 - f(1-2\varepsilon)\right]N^{-1}\left[1 - f(1-\varepsilon)\right]^{-1},$$

and its exact value (a solution of a quadratic equation) differs from this by terms of at most $O(N^{-2})$. The rate of approach to homozygosity is therefore

$$\mathcal{R} = 1 - \lambda_2 \doteqdot \frac{1 - f(1-2\varepsilon)}{2N\left[1 - f(1-\varepsilon)\right]} . \qquad (9.5)$$

The special cases of gametic and zygotic mating systems ($\varepsilon = 1, \tfrac{1}{2}$) have the rates $\tfrac{1}{2}(1+f)N^{-1}$ and $\tfrac{1}{2}(1-\tfrac{1}{2}f)^{-1}N^{-1}$ respectively, and we note that both these are equivalent to that found by Wright for random mating populations, $\tfrac{1}{2}N^{-1}$, when we substitute $f = 0$. Thus positive assortative mating increases the asymptotic rate of approach to homozygosity by a factor between 1 and 2, but in general the zygotic system has a slower rate than the less likely gametic system.

To ascertain the probabilities associated with the two types of ultimate fixation, we have

$$E(X_\infty) = \Pr(X_\infty = 1).$$

Now the moment formulae (9.2), (8.8) give

$$E(X_{t+1} - Y_{t+1}) = E(P_{aa} - P_{AA}) = E(X_t - Y_t),$$

so that if the initial values of X and Y are X_0 and Y_0, then

$$E(X_t - Y_t) = X_0 - Y_0$$

for all t. But because the limit is fixation,

$$E(X_\infty + Y_\infty) = 1,$$

and the two equations taken together give

$$\begin{aligned} \Pr\{X_\infty = 1\} &= E(X_\infty) = \tfrac{1}{2}(1 + X_0 - Y_0) = \tfrac{1}{2} + \tfrac{1}{2}N^{-1}k_0 - \tfrac{1}{2}N^{-1}l_0 \\ \Pr\{Y_\infty = 1\} &= E(Y_\infty) = \tfrac{1}{2}(1 - X_0 + Y_0) = \tfrac{1}{2} - \tfrac{1}{2}N^{-1}k_0 + \tfrac{1}{2}N^{-1}l_0, \end{aligned} \qquad (9.6)$$

which is of interest because of the independence from f.

9.2. Dioecious population

We come now to the more realistic case of a population consisting of two sexes of fixed numbers, and assume that positive assortative mating is practised according to equations (8.9). At any instant in time, the state of the population will be completely determined by the four variates k, l, r, s, being the numbers of aa and AA genotypes for males and females. For Wright's simultaneous birth-death model, the probability that the population will be in this state is given by the product of two trinomial distributions:

$$\Pr\{k, l, r, s\} = \frac{N_1!}{k!(N_1-k-l)!\,l!} P_{aa}^{k} P_{Aa}^{(N_1-k-l)} P_{AA}^{l} \times \frac{N_2!}{r!(N_2-r-s)!\,s!} P_{aa}^{r} P_{Aa}^{(N_2-r-s)} P_{AA}^{s},$$

where P_{aa}, P_{Aa} and P_{AA} refer to the previous generation.

For a random mating population, Wright (36) has shown that the expected number of heterozygotes decreases at the asymptotic rate

$$R = \tfrac{1}{2}\left(1+\frac{N}{4N_1N_2}\right)-\tfrac{1}{2}\left[1+\left(\frac{N}{4N_1N_2}\right)^2\right]^{\frac{1}{2}} \doteq \frac{N}{8N_1N_2} \qquad \text{(c/f.(7.5))}$$

where $N = N_1 + N_2$, per generation. For positive assortative mating, we expect by analogy with the previous case that this rate would increase somewhat. In fact, however, this is not necessarily true. Consider moments of the variates

$$X = kN_1^{-1},\ Y = lN_1^{-1},\ W = rN_2^{-1},\ Z = sN_2^{-1}.$$

At the $t+1$ th generation, conditional on the t-th generation values, we have

$$\begin{aligned}
&\mathcal{E}(X_{t+1}) = \mathcal{E}(W_{t+1}) = P_{aa}, && \mathcal{E}(Y_{t+1}) = \mathcal{E}(Z_{t+1}) = P_{AA},\\
&\mathcal{V}ar(X_{t+1}) = P_{aa}(1-P_{aa})N_1^{-1}, && \mathcal{V}ar(Y_{t+1}) = P_{AA}(1-P_{AA})N_1^{-1},\\
&\mathcal{V}ar(W_{t+1}) = P_{aa}(1-P_{aa})N_2^{-1}, && \mathcal{V}ar(Z_{t+1}) = P_{AA}(1-P_{AA})N_2^{-1},\\
&\mathcal{C}ov(X_{t+1}, Y_{t+1}) = -P_{aa}P_{AA}N_1^{-1}, && \mathcal{C}ov(W_{t+1}, Z_{t+1}) = -P_{aa}P_{AA}N_2^{-1}.
\end{aligned} \qquad (9.7)$$

Write $M_t^{\,1} = E(X_t + Y_t)$,

$M_t^{\,2} = E(X_t - Y_t)(W_t - Z_t)$,

$M_t^{\,3} = E(X_t - Y_t)^2$,

$M_t^{\,4} = E(W_t - Z_t)^2$.

Then using (9.7), (8.9), we get

$$M_{t+1}^{\,1} = E(X_{t+1}+Y_{t+1}) = E(W_{t+1}+Z_{t+1}) = E(P_{aa}+P_{AA}) = f(1-\varepsilon)M_t^{\,1} + \tfrac{1}{2}(1-f)M_t^{\,2} + \tfrac{1}{2}[1-f(1-2\varepsilon)]. \qquad (9.8)$$

Similarly, because of the independence of male and female distributions

$$M^2_{t+1} = E\left[\mathcal{E}(X_{t+1}-Y_{t+1})\mathcal{E}(W_{t+1}-Z_{t+1})\right] = E(P_{Aa}-P_{AA})^2$$

$$= \tfrac{1}{4}\left[2(1-f^2\rho^2)M^2_t + (1+f\rho)^2 M^3_t + (1-f\rho)^2 M^4_t\right]. \qquad (9.9)$$

But,

$$M^3_{t+1} = (1-N_1^{-1})E(P_{aa}-P_{AA})^2 + N_1^{-1}E(P_{aa}+P_{AA}),$$

so that at the t-th generation we have

$$M^3_t = (1-N_1^{-1})M^2_t + N_1^{-1}M^1_t,$$

and similarly

$$M^4_t = (1-N_2^{-1})M^2_t + N_2^{-1}M^1_t.$$

Substituting the last two equations into (9.9) gives

$$M^2_{t+1} = \tfrac{1}{4}\left[(1+f\rho)^2N_1^{-1} + (1-f\rho)^2N_2^{-1}\right]M^1_t + \tfrac{1}{4}\left[4-(1+f\rho)^2N_1^{-1}-(1-f\rho)^2N_2^{-1}\right]M^2_t. \qquad (9.10)$$

The equations (9.8), (9.10) can be written

$$\begin{bmatrix} M^1_{t+1} \\ M^2_{t+1} \end{bmatrix} = \underline{Q}\begin{bmatrix} M^1_t \\ M^2_t \end{bmatrix} + \begin{bmatrix} \tfrac{1}{2}\left[1-f(1-2\epsilon)\right] \\ 0 \end{bmatrix},$$

where

$$\underline{Q} = \begin{bmatrix} f(1-\epsilon) & \tfrac{1}{2}(1-f) \\ \tfrac{1}{4}(1+f\rho)^2N_1^{-1} + \tfrac{1}{4}(1-f\rho)^2N_2^{-1} & 1-\tfrac{1}{4}(1+f\rho)^2N_1^{-1} - \tfrac{1}{4}(1-f\rho)^2N_2^{-1} \end{bmatrix}.$$

According to the approximation (7.10), the larger characteristic root of this matrix is approximately

$$\lambda_2 \doteq 1 - \tfrac{1}{4}(1+f\rho)^2 N_1^{-1} - \tfrac{1}{4}(1-f\rho)^2 N_2^{-1} + \tfrac{1}{8}(1-f)\left[(1+f\rho)^2 N_1^{-1} + (1-f\rho)^2 N_2^{-1}\right]\left[1 - f(1-\varepsilon) - \tfrac{1}{4}(1+f\rho)^2 N_1^{-1} - \tfrac{1}{4}(1-f\rho)^2 N_2^{-1}\right]^{-1}$$

$$\doteq 1 - \tfrac{1}{8}\left[(1+f\rho)^2 N_1^{-1} + (1-f\rho)^2 N_2^{-1}\right]\left[1 - f(1-2\varepsilon)\right]\left[1 - f(1-\varepsilon)\right]^{-1},$$

when both N_1 and N_2 are large. Therefore, the expected number of heterozygotes decreases asymptotically by a proportion

$$\mathcal{R} = 1 - \lambda_2 \doteq \tfrac{1}{8}\left[(1+f\rho)^2 N_1^{-1} + (1-f\rho)^2 N_2^{-1}\right]\left[1 - f(1-2\varepsilon)\right]\left[1 - f(1-\varepsilon)\right]^{-1} \qquad (9.11)$$

per generation, a result equivalent to Wright's random mating rate when $f = 0$. The results for other particular cases are

	$\varepsilon = 1$	$\varepsilon = \frac{1}{2}$
$\rho = 0$	$\frac{N}{4N_1N_2}(1-f)$	$\frac{N}{8N_1N_2}(1-\frac{1}{2}f)^{-1}$
$\rho = (N_1-N_2)N^{-1}$	$\frac{N}{8N_1N_2}\left[1-f(2-f)(N_1-N_2)^2N^{-2}\right](1+f)$	$\frac{N}{8N_1N_2}\left[1-f(2-f)(N_1-N_2)^2N^{-2}\right](1-\frac{1}{2}f)^{-1}$
$\rho = 1$	$\frac{N}{8N_1N_2}\left[1+f^2-2f(N_1-N_2)N^{-1}\right](1+f)$	$\frac{N}{8N_1N_2}\left[1+f^2-2f(N_1-N_2)N^{-1}\right](1-\frac{1}{2}f)^{-1}$

(9.12)

For symmetric mating ($\rho = 0$), the rate increases with the degree of non-randomness f, but for the more practical cases of general or asymmetric mating this need not hold if the sex numbers N_1 and N_2 are substantially unequal. Positive assortative mating does increase the rate if $|N_1-N_2|N^{-1} < 0.5$; otherwise, each case needs to be examined

separately. As for the monoecious population § 9.1, zygotic ($\varepsilon = \frac{1}{2}$) has a slower rate of approach than gametic mating ($\varepsilon = 1$), except of course when $f = 0$. It is interesting to note that the rates are independent of the values of γ and η of equation (8.9).

In § 3, a population model was discussed in which selection, non-random mating, and mutation operated. In the special case without selection and mutation, the model is a special case of that considered here, with symmetry of sexes ($\rho = 0$) and gametic mating ($\varepsilon = 1$). Apart from terms of order N^{-2}, the exact result found here is

$$\mathcal{R} = \frac{N}{8N_1N_2}(1+f), \tag{9.13}$$

which agrees with the rate found by approximate methods in (3.5).

From (9.7), (8.9), we have

$$E(X_{t+1}-Y_{t+1}) = E(P_{AA}-P_{Aa}) = \tfrac{1}{2}(1+f\rho)E(X_t-Y_t) + \tfrac{1}{2}(1-f\rho)E(W_t-Z_t)$$

$$= E(X_t-Y_t) \quad \text{for } t \geq 1,$$

so that in the limit

$$E(X_\infty-Y_\infty) = \tfrac{1}{2}(1+f\rho)(X_0-Y_0) + \tfrac{1}{2}(1-f\rho)(W_0-Z_0).$$

But also

$$E(X_\infty+Y_\infty) = 1,$$

so the probabilities of fixation are

$$\Pr\{X_\infty=1\} = \Pr\{W_\infty=1\} = \tfrac{1}{2} + \tfrac{1}{4}(1+f\rho)(X_0-Y_0) + \tfrac{1}{4}(1-f\rho)(W_0-Z_0) = E(X_\infty), \tag{9.14}$$

$$\Pr\{Y_\infty=1\} = \Pr\{Z_\infty=1\} = \tfrac{1}{2} - \tfrac{1}{4}(1+f\rho)(X_0-Y_0) - \tfrac{1}{4}(1-f\rho)(W_0-Z_0) = E(Y_\infty).$$

These probabilities are independent of f when $\rho = 0$, and are always independent of whether mating was gametic or zygotic. Again, the case when $\rho = 0$, $\varepsilon = 1$ is a special case of the model in § 3, and the approximate methods leading to (3.6) in fact give exactly correct results. In terms of the notation of § 3, the probability of fixation of the a gene was

$$G(p,\infty) \doteq p = \tfrac{1}{2} + \tfrac{1}{4}N_1^{-1}(k_0 - \ell_0) + \tfrac{1}{4}N_2^{-1}(r_0 - s_0)$$

in the case without selection, which agrees with the exact result (9.14) with $\rho = 0$.

10. Model C: Approach to homozygosity

10.0. Introduction

The model here considered has overlapping generations, because at each time unit only one birth-death event occurs. As usual for finding exact results, we assume there is no selection, and that the dying individual is chosen at random from the population. Non-random mating is introduced via the general equations (8.8) or (8.9) for offspring, depending on whether monoecious or dioecious models are considered. Moran (22) has shown that with random mating, the expected number of heterozygotes decreases asymptotically (and approximately) by a proportion N^{-2} per death, or N^{-1} per generation, in the monoecious case (see (0.9)), and by $\frac{1}{4}NN_1^{-1}N_2^{-1}$ per generation in the dioecious.

10.1. Monoecious population

If the genotype numbers just before a birth-death event are $k, N-k-1, 1$ in the order aa, Aa, AA , then the probability that a dying individual is of a particular genotype are the random proportions

$$\Pr(\text{death of aa}) = kN^{-1} = X ,$$

$$\Pr(\text{death of Aa}) = (N-k-1)N^{-1} = 1 - X - Y ,$$

$$\Pr(\text{death of AA}) = 1N^{-1} = Y .$$

The state of the system at any time is specified by the two quantities k and l, or X and Y. Given that a death occurs, the state changes from (k,l) to another state with probabilities

$$\begin{aligned}
&(k+1,l): \quad (1-X-Y)P_{aa}, && (k-1,l): \quad XP_{Aa},\\
&(k+1,l-1): \quad YP_{aa}, && (k-1,l+1): \quad XP_{AA}, \qquad (10.1)\\
&(k,l-1): \quad YP_{Aa}, && (k,l+1): \quad (1-X-Y)P_{AA},\\
&(k,l): \quad P_{Aa}+X(P_{aa}-P_{Aa})+Y(P_{AA}-P_{Aa}),
\end{aligned}$$

where the offspring probabilities P_{aa} etc. are given by (8.8). By enumerating the possibilities, we have the conditional moment at time $t+1$ given the state at time t,

$$\mathcal{E}(X_{t+1}+Y_{t+1}-X_t-Y_t) = N^{-1}(P_{aa}+P_{AA}-X_t-Y_t).$$

Define $M_t^1 = E(X_t+Y_t)$ as an unconditional moment; then

$$M_{t+1}^1 = \left[1-(1-f(1-\varepsilon))N^{-1}\right]M_t^1 + \tfrac{1}{2}(1-f)N^{-1}M_t^2 + \tfrac{1}{2}\left[1-f(1-2\varepsilon)\right]N^{-1},$$

where $M_t^2 = E(X_t-Y_t)^2$. Similarly,

$$M_{t+1}^2 = \left[1+f(1-\varepsilon)\right]N^{-2}M_t^1 + \left[1-\tfrac{1}{2}(3+f)N^{-2}\right]M_t^2 + \tfrac{1}{2}\left[1-f(1-2\varepsilon)\right]N^{-2}.$$

As in § 7, the solution of these difference equations depends on the eigenvalues of the matrix

$$\underset{\sim}{Q} = \begin{bmatrix} 1-\left[1-f(1-\varepsilon)\right]N^{-1} & \tfrac{1}{2}(1-f)N^{-1} \\ \left[1+f(1-\varepsilon)\right]N^{-2} & 1-\tfrac{1}{2}(3+f)N^{-2} \end{bmatrix}.$$

The approximation (7.10) applies when N is large, so that the larger eigenvalue is

$$\lambda_2 \doteq 1 - \tfrac{1}{2}(3+f)N^{-2} + \tfrac{1}{2}(1-f)[1+f(1-\varepsilon)]N^{-2}\left[1 - f(1-\varepsilon) - \tfrac{1}{2}(3+f)N^{-1}\right]^{-1},$$

$$\doteq 1 - [1-f(1-2\varepsilon)]N^{-2}\left[1-f(1-\varepsilon)\right]^{-1}.$$

The rate of approach to homozygosity is therefore

$$\mathcal{R} = 1 - \lambda_2^N \doteq \frac{1-f(1-2\varepsilon)}{N[1-f(1-\varepsilon)]}, \qquad (10.2)$$

where time is measured in generations, that is in N birth-death events. This is twice the rate found for Wright's non-overlapping model (9.5), and agrees with Moran's result when $f = 0$. As other special cases, gametic mating reduces to the rate $(1+f)N^{-1}$ with $\varepsilon = 1$, whilst for zygotic mating $(\varepsilon = \frac{1}{2})$, the rate is $N^{-1}(1-\frac{1}{2}f)^{-1}$.

To determine the probabilities of fixation, we know

$$E(X_\infty + Y_\infty) = 1.$$

Also using (10.1) and (8.8),

$$E(X_{t+1} - Y_{t+1}) = (1-N^{-1})E(X_t - Y_t) + N^{-1}E(P_{aa} - P_{AA})$$
$$= E(X_t - Y_t)$$

so that

$$E(X_t - Y_t) = X_0 - Y_0 \qquad \text{for all } t,$$

and finally

$$\Pr\{k_\infty = N\} = E(X_\infty) = \tfrac{1}{2}(1 + X_0 - Y_0) = \tfrac{1}{2} + \tfrac{1}{2}N^{-1}(k_0 - \ell_0),$$
$$\Pr\{\ell_\infty = N\} = E(Y_\infty) = \tfrac{1}{2}(1 - X_0 + Y_0) = \tfrac{1}{2} - \tfrac{1}{2}N^{-1}(k_0 - \ell_0). \qquad (10.3)$$

These probabilities are exactly those found for Wright's model also, (9.6), and are independent of f and ε .

10.2. Dioecious population

For a two sex population, we again assume that at each birth-death event the dying individual is chosen at random. Hence, the probabilities of it being of a particular type are

	aa	Aa	AA
Male	kN^{-1}	$(N_1-k-l)N^{-1}$	lN^{-1}
Female	rN^{-1}	$(N_2-r-s)N^{-1}$	sN^{-1}

where there are k, N_1-k-l, l and r, N_2-r-s, s individuals of types aa, Aa, and AA in the two sexes. To keep N_1 and N_2 constant, the new individual must be of the same sex as that of the dying one. At such a birth-death event, the state of the system changes from (k,l,r,s) to another state with the following probabilities

$$
\begin{aligned}
&(k+1,l,r,s): && (N_1-k-l)N^{-1}P_{aa}, && (k,l,r+1,s): && (N_2-r-s)N^{-1}P_{aa},\\
&(k+1,l-1,r,s): && lN^{-1}P_{aa}, && (k,l,r+1,s-1): && sN^{-1}P_{aa},\\
&(k,l-1,r,s): && lN^{-1}P_{Aa}, && (k,l,r,s-1): && sN^{-1}P_{Aa},\\
&(k-1,l,r,s): && kN^{-1}P_{Aa}, && (k,l,r-1,s): && rN^{-1}P_{Aa},\\
&(k-1,l+1,r,s): && kN^{-1}P_{AA}, && (k,l,r-1,s+1): && rN^{-1}P_{AA},\\
&(k,l+1,r,s): && (N_1-k-l)N^{-1}P_{AA}, && (k,l,r,s-1): && (N_2-r-s)N^{-1}P_{AA}.
\end{aligned}
\qquad (10.4)
$$

We have omitted the identical transformation $(k,l,r,s) \rightarrow (k,l,r,s)$, which completes all possibilities. In the above, the quantities P_{aa}, etc. are given by (8.9) for positive assortative mating.

Now define the variates $X=kN_1^{-1}$, $Y=lN_1^{-1}$, $W=rN_2^{-1}$, $Z=sN_2^{-1}$, and the vector of unconditional moments by

$$\underline{M}_t = \begin{bmatrix} E[\tfrac{1}{2}(X_t-W_t) + \tfrac{1}{2}(Y_t-Z_t)] \\ E(X_t+Y_t) \\ E(W_t+Z_t) \\ E(X_t-Y_t)(W_t-Z_t) \\ E(X_t-Y_t)^2 \\ E(W_t-Z_t)^2 \end{bmatrix} .$$

From the transition probabilities (10.4) and (8.9), we can show after some algebra that the difference equation for $\underline{M}_t$ is

$$\underline{M}_{t+1} = \underline{Q}\,\underline{M}_t + \underline{K} \quad ,$$

where $\underline{Q}$ is the 6 x 6 matrix

$$\underline{Q} = N^{-1} \begin{bmatrix} N-1 & 0 & 0 & 0 & 0 & 0 \\ \tfrac{1}{4}f & N-1+\tfrac{1}{2}f(1-\varepsilon) & \tfrac{1}{2}f(1-\varepsilon) & \tfrac{1}{2}(1-f) & 0 & 0 \\ \tfrac{1}{4}f & \tfrac{1}{2}f(1-\varepsilon) & N-1+\tfrac{1}{2}f(1-\varepsilon) & \tfrac{1}{2}(1-f) & 0 & 0 \\ 0 & 0 & 0 & N-1 & \tfrac{1}{2}(1+f\rho) & \tfrac{1}{2}(1-f\rho) \\ \tfrac{1}{4}fN_1^{-1} & [1+\tfrac{1}{2}f(1-\varepsilon)]N_1^{-1} & \tfrac{1}{2}f(1-\varepsilon)N_1^{-1} & (1-f\rho)(1-N_1^{-1})+\tfrac{1}{2}(1-f)N_1^{-1} & N-(1-f\rho)-(1+f\rho)N_1^{-1} & 0 \\ \tfrac{1}{4}fN_2^{-1} & \tfrac{1}{2}f(1-\varepsilon)N_2^{-1} & [1+\tfrac{1}{2}f(1-\varepsilon)]N_2^{-1} & (1+f\rho)(1-N_2^{-1})+\tfrac{1}{2}(1-f)N_2^{-1} & 0 & N-(1+f\rho)-(1-f\rho)N_2^{-1} \end{bmatrix} ,$$

and $\underline{K}' = \tfrac{1}{2}\left[1-f(1-2\varepsilon)\right] N^{-1}(0,1,1,0,N_1^{-1},N_2^{-1})$.

The characteristic equation for the matrix may be written most conveniently as

$$|\lambda \underline{I} - \underline{Q}| = N^{-6}(\mu-1)^2(\mu-2)(\mu^3 - A\mu^2 + B\mu - C) = 0 , \qquad (10.5)$$

where

$$\mu = (1-\lambda)N ,$$

$$A = 2 - f(1-\varepsilon) + (1+f\rho)N_1^{-1} + (1-f\rho)N_2^{-1} ,$$

$$B = 1 - f(1-\varepsilon) + \tfrac{1}{4}(1+f\rho)N_1^{-1}[5 - f(3-4\varepsilon) + 2f\rho] + \tfrac{1}{4}(1-f\rho)N_2^{-1}[5 - f(3-4\varepsilon) - 2f\rho]$$
$$+ (1-f^2\rho^2)N_1^{-1}N_2^{-1} ,$$

$$C = \tfrac{1}{4}\left[(1+f\rho)^2N_1^{-1} + (1-f\rho)^2N_2^{-1} + 2(1-f^2\rho^2)N_1^{-1}N_2^{-1}\right]\left[1 - f(1-2\varepsilon)\right] .$$

Now when N_1 and N_2 are both large, the smallest root for μ from the above equation is approximately

$$\mu_2 \doteq \frac{C}{B} \doteq \tfrac{1}{4}\left[(1+f\rho)^2N_1^{-1} + (1-f\rho)^2N_2^{-1}\right]\left[1 - f(1-2\varepsilon)\right]\left[1 - f(1-\varepsilon)\right]^{-1} .$$

This corresponds to the largest non-unit root of the transition matrix $\underline{T}$ defined by (10.4), say λ_2 . Hence the rate of approach to homozygosity, measured in generations of N birth-death events, is

$$R = 1 - \lambda_2^N = 1 - \left(1 - \frac{\mu_2}{N}\right)^N \doteq \mu_2 \doteq \frac{\left[(1+f\rho)^2N_1^{-1} + (1-f\rho)^2N_2^{-1}\right]\left[1 - f(1-2\varepsilon)\right]}{1 - f(1-\varepsilon)} . \qquad (10.6)$$

When mating is at random, (10.6) reduces to

$$\mathcal{R} = \tfrac{1}{4}\frac{N}{N_1 N_2} ,$$

which is the rate found by Moran (22). In general, comparing (10.6) with (9.11), the rate is twice that obtained for model B previously, and values for particular cases are therefore double those of (9.12). As in model B, positive assortative mating may either increase or decrease the rate of approach to homozygosity, depending on the mating system and the divergence of the sex numbers N_1 and N_2 from equality.

To find the probabilities of fixation of the a or A gene, we note that

$$Pr\{X_\infty = 1, W_\infty = 1\} = E(X_\infty) = E(W_\infty),$$
$$Pr\{Y_\infty = 1, Z_\infty = 1\} = E(Y_\infty) = E(Z_\infty).$$

Also, from (10.4) and (8.9) it can be shown that

$$E(X_{t+1} - Y_{t+1}) = (1-N^{-1})E(X_t - Y_t) + \tfrac{1}{2}N^{-1}E\left[(1+f\rho)(X_t - Y_t) + (1-f\rho)(W_t - Z_t)\right], \quad (10.7)$$

$$E(W_{t+1} - Z_{t+1}) = (1-N^{-1})E(W_t - Z_t) + \tfrac{1}{2}N^{-1}E\left[(1+f\rho)(X_t - Y_t) + (1-f\rho)(W_t - Z_t)\right]. \quad (10.8)$$

Write

$$\alpha_t = E(X_t - Y_t + W_t - Z_t) ,$$
$$\beta_t = E(X_t - Y_t - W_t + Z_t) .$$

Then adding and subtracting (10.7), (10.8) gives respectively

$$\alpha_{t+1} = \alpha_t + f\rho N^{-1}\beta_t ,$$

$$\beta_{t+1} = (1-N^{-1})\beta_t ,$$

and the solution of these difference equations is

$$\alpha_t = \alpha_0 + f\rho\beta_0 - f\rho(1-N^{-1})^t\beta_0 ,$$

$$\beta_t = (1-N^{-1})^t\beta_0 ,$$

where α_0, β_0 are initial values. In the limit we get

$$\alpha_\infty = \alpha_0 + f\rho\beta_0 ,$$

$$\beta_\infty = 0 ,$$

that is

$$E(X_\infty - Y_\infty + W_\infty - Z_\infty) = 2E(X_\infty - Y_\infty) = (1+f\rho)(X_0 - Y_0) + (1-f\rho)(W_0 - Z_0).$$

But

$$E(X_\infty + Y_\infty) = 1 ,$$

and the probabilities of ultimate fixation are therefore

$$P_r\{X_\infty = 1, W_\infty = 1\} = E(X_\infty) = \tfrac{1}{2} + \tfrac{1}{4}(1+f\rho)(X_0 - Y_0) + \tfrac{1}{4}(1-f\rho)(W_0 - Z_0),$$

$$P_r\{Y_\infty = 1, Z_\infty = 1\} = E(Y_\infty) = \tfrac{1}{2} - \tfrac{1}{4}(1+f\rho)(X_0 - Y_0) - \tfrac{1}{4}(1-f\rho)(W_0 - Z_0). \qquad (10.9)$$

These probabilities are identical with those found for model B in (9.14).

As a special case of the above results, it is particularly interesting to consider the case of symmetric mating on a gametic basis ($\rho = 0$, $\varepsilon = 1$) since this model was discussed by approximate methods in § 4, with the added complications of mutation and selection. The rate of approach to homozygosity is, from (10.6),

$$\mathcal{R} \doteq \frac{N}{4N_1N_2}(1+f) , \qquad (10.10)$$

and the probability of fixation of the a gene is

$$P\{X_\infty = W_\infty = 1\} = \tfrac{1}{2} + \tfrac{1}{4}(X_0 - Y_0) + \tfrac{1}{4}(W_0 - Z_0) = \tfrac{1}{2} + \tfrac{1}{4}N_1^{-1}(k_0 - l_0) + \tfrac{1}{4}N_2^{-1}(r_0 - s_0), \quad (10.11)$$

from (10.9). The latter result was exactly predicted by the diffusion approximation (c/f (1.34) with $p = x_0 = \frac{1}{2} + \frac{1}{2}N_1^{-1}(k_0 - l_0) + \frac{1}{4}N_2^{-1}(r_0 - s_0)$ from § 4.2). The former was predicted correctly except for terms of order N^{-2} by (1.31) with the appropriate parameters of (4.4).

As was pointed out in § 4.3, the difference in behaviour of models B and C, and in particular the doubling of the rate of approach to homozygosity, is due to differing offspring distributions and not to the overlapping generations of model C.

11. Model D: Approach to homozygosity

11.0. Introduction

In this chapter we deviate from the pattern of the last two chapters in that, here, assortative mating is not introduced in the full generality of § 8. Rather, assortative mating is restricted to the general zygotic system of § 8 because of the particular model D property that each dying individual must be one parent of the replacing individual. In effect, in the dioecious case we treat the special case of model D, § 5, without mutation or selection. However, for completeness, the monoecious model is described and investigated first.

In § 5 it was found that model D was unusual for two reasons; firstly, the diffusion approximation held only if the mating parameter f was less than unity, that is, if complete positive assortative mating did not occur; and secondly, the variance effective population size was not correctly predicted by the application of the non-overlapping generation theory of model A. We shall gain further insight into these characteristics by the exact determination of asymptotic properties.

11.1. Monoecious population

Suppose the population is a mixture of the genotypes aa, Aa, AA in the proportions $X = kN^{-1}$, $1-X-Y = (N-k-1)N^{-1}$, $Y = lN^{-1}$. As in model C, at a time instant when a death occurs, the dying individual is chosen at random with the probabilities

$$\Pr(\text{death of aa}) = X ,$$

$$\Pr(\text{death of Aa}) = 1 - X - Y ,$$

$$\Pr(\text{death of AA}) = Y .$$

Our model further assumes that the dying individual is a parent of its successor, but there are in general three possible genotypes for the second parent, and the probabilities associated with each depends on whether random or positive assortative mating takes place. Suppose there is a probability f that the individual self-mates or mates with another of the same genotype, and a probability $1-f$ that random mating occurs. Such a system was classified in § 8 as being 'positive assortative mating on a zygotic basis'. The mating probabilities are then

Dying parent \ Second parent	aa	Aa	AA
aa	$(1-f)X + f$	$(1-f)(1-X-Y)$	$(1-f)Y$
Aa	$(1-f)X$	$(1-f)(1-X-Y) + f$	$(1-f)Y$
AA	$(1-f)X$	$(1-f)(1-X-Y)$	$(1-f)Y + f$

This system gives rise to offspring in the proportions

Dying parent \ Offspring	aa	Aa	AA
aa	$\frac{1}{2}(1-f)(1+X-Y)+f$	$\frac{1}{2}(1-f)(1-X+Y)$	0
Aa	$\frac{1}{4}(1-f)(1+X-Y)+\frac{1}{2}f$	$\frac{1}{2}$	$\frac{1}{4}(1-f)(1-X+Y)+\frac{1}{2}f$
AA	0	$\frac{1}{2}(1-f)(1+X-Y)$	$\frac{1}{2}(1-f)(1-X+Y)+f$

(11.1)

During a birth-death event, the state of the population may remain the same, or may change from (k,l) to another state with probabilities determined from (11.1):

$$\begin{aligned}
(k+1,l) &: \quad \tfrac{1}{2}(1-X-Y)\left[1+(1-f)(X-Y)\right] , \\
(k,l-1) &: \quad \tfrac{1}{2}(1-f)Y(1+X-Y) , \\
(k-1,l) &: \quad \tfrac{1}{2}(1-f)X(1-X+Y) , \\
(k,l+1) &: \quad \tfrac{1}{2}(1-X-Y)\left[1-(1-f)(X-Y)\right] .
\end{aligned} \tag{11.2}$$

It is instructive to consider the relationship between this model and the models B and C. Each defines a random walk in the two dimensional space (k,l), and because of discreteness, the values of k and l are restricted to non-negative integers with total $k+l \leqslant N$. That is, the state is confined to a triangular lattice of points in the plane. In model B, N birth-death events occur simultaneously, and the state can change to any other state in the next generation, with the two exceptions that once having reached either $(N,0)$ or $(0,N)$ it remains there forever. Model C limits the change of state during one birth-death event to six out of the eight neighbouring points, namely, from (k,l) to either $(k-1,l)$,

$(k-1,l+1)$, $(k,l-1)$, $(k,l+1)$, $(k+1,l-1)$ or $(k+1,l)$, see (10.1). There are obvious exceptions at the boundary of the region, or at either of the two absorbing points $(0,N)$, $(N,0)$ corresponding to gene fixation.

The present model, specified in (11.2), further limits the possible changes of state to four neighbouring ones. When $f = 1$, these are reduced to two states only, $(k,l+1)$ or $(k+1,l)$, because the probabilities for the other states become zero. Supposing that the initial state is (k_0,l_0), this latter model restricts the subsequent states to the triangle $k \geqslant k_0$, $l \geqslant l_0$, $k+l \leqslant N$, and any point reached on the boundary $k+l = N$ will be an absorbing point. There are thus $N-k_0-l_0+1$ absorbing states, and in each the population consists of homozygous individuals only, but gene fixation does not necessarily occur.

These models are illustrated diagrammatically in Fig. 1, p.167, where absorbing points are circled.

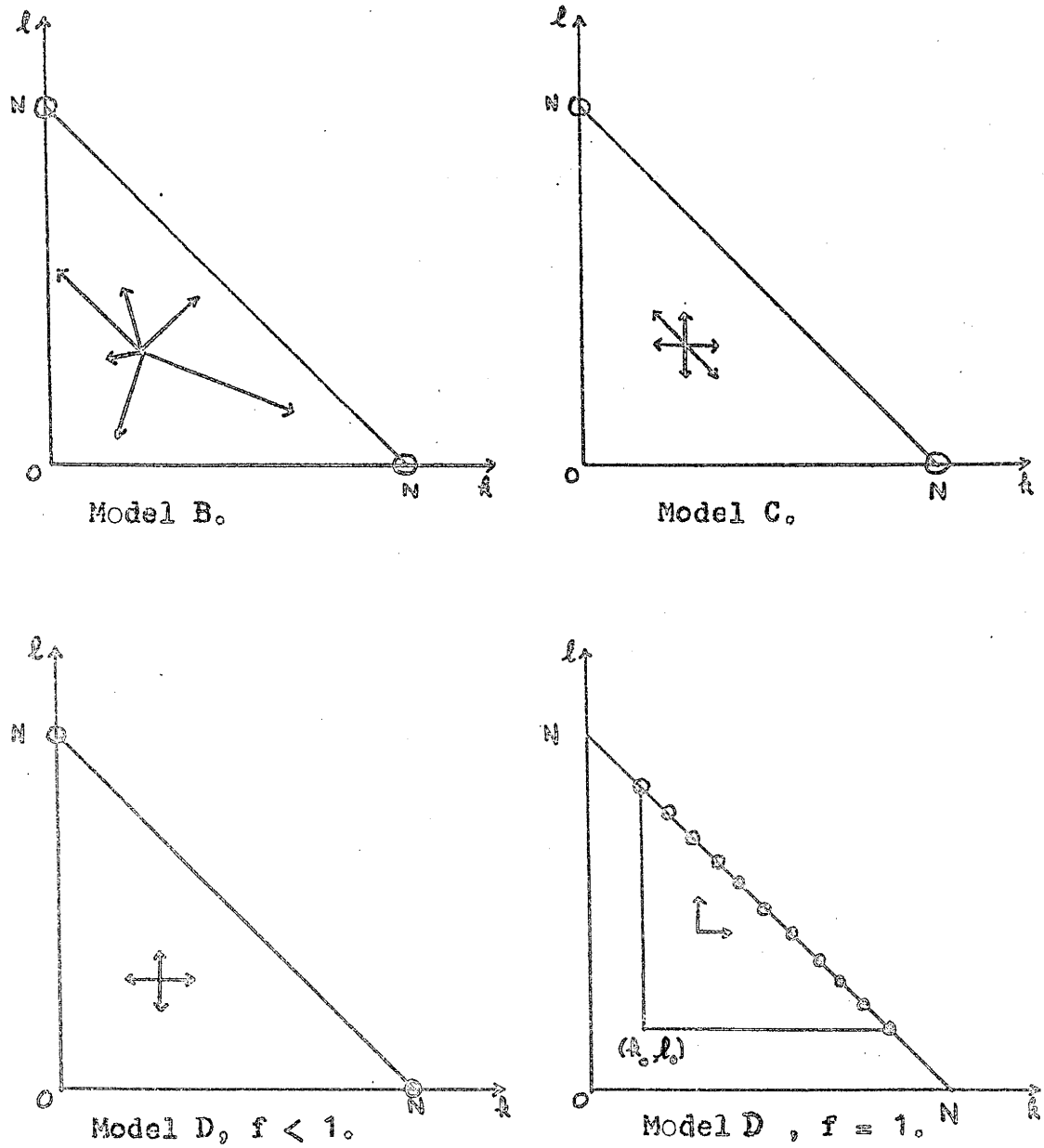

Fig.1. Possible movements for the random walk models, showing absorbing states circled.

As before, the eigenvalues of the transition matrix (11.2) can be found by considering moments of the genotype proportions. Define

$$M_t^1 = E(X_t+Y_t) \ , \quad M_t^2 = E(X_t-Y_t)^2 \ ,$$

taken after the t-th birth-death event. Conditional on a given state at time t, we have from (11.2)

$$\mathcal{E}(X_{t+1}+Y_{t+1}-X_t-Y_t) = \tfrac{1}{2}N^{-1}\left[1-(2-f)(X_t+Y_t)+(1-f)(X_t-Y_t)^2\right],$$

so that

$$M_{t+1}^1 = \left[1-\tfrac{1}{2}(2-f)N^{-1}\right]M_t^1 + \tfrac{1}{2}(1-f)N^{-1}M_t^2 + \tfrac{1}{2}N^{-1} \ .$$

Similarly, it may be shown that

$$M_{t+1}^2 = -\tfrac{1}{2}fN^{-2}M_t^1 + \left[1-\tfrac{1}{2}(1-f)N^{-2}\right]M_t^2 + \tfrac{1}{2}N^{-2} \ .$$

The difference equations have a solution of the form

$$\begin{aligned} M_t^1 &= 1 - \alpha_2\lambda_2^t - \alpha_3\lambda_3^t \ , \\ M_t^2 &= 1 - \beta_2\lambda_2^t - \beta_3\lambda_3^t \ , \end{aligned} \qquad (11.3)$$

where the α's, β's are constants chosen to satisfy the initial conditions, and the λ's are the eigenvalues of the matrix of coefficients

$$\underline{Q} = \begin{bmatrix} 1-\tfrac{1}{2}(2-f)N^{-1} & \tfrac{1}{2}(1-f)N^{-1} \\ -\tfrac{1}{2}fN^{-2} & 1-\tfrac{1}{2}(1-f)N^{-2} \end{bmatrix} .$$

For large N, (7.10) gives the eigenvalues as

$$\lambda_2 \doteqdot 1-(1-f)(2-f)^{-1}N^{-2} ,$$

$$\lambda_3 \doteqdot 1-\tfrac{1}{2}(2-f)N^{-1} .$$

As well as these, the transition matrix will have two unit roots, and other smaller roots. The largest non-unit root is λ_2 for $f < 1$, and its effect will dominate the time-dependence of the solution (11.3) for large values of t. Thus, the rate of approach to homozygosity is

$$\mathcal{R} = 1-\lambda_2^N \doteqdot \frac{1-f}{N(2-f)} , \qquad (11.4)$$

in a generation of N birth-death events, and the limit is ultimate fixation of one or other gene since $M^1_\infty = M^2_\infty = 1$.

When $f = 1$, however, the root λ_2 is itself unity, so the time dependence depends on λ_3. In this special case, (11.3) becomes

$$M^1_t = 1-(1-M^1_0)(1-\tfrac{1}{2}N^{-1})^t \longrightarrow 1 \quad \text{as} \quad t \to \infty ,$$

$$M^2_t = M^2_0+(1-M^1_0)N^{-1}\left[1-(1-\tfrac{1}{2}N^{-1})^t\right] \longrightarrow M^2_0+(1-M^1_0)N^{-1} \quad \text{as} \quad t \to \infty ,$$

so that in the limit, an absorbing state is reached in which all individuals are homozygous, but gene fixation does not necessarily occur unless it was present in the initial state, when $M^1_0 = M^2_0 = 1$ and $M^1_\infty = M^2_\infty = 1$. The rate of approach now becomes

$$\mathcal{R} = 1-\lambda_3^N \doteqdot 1-e^{-\frac{1}{2}} = 0.3935 \quad \text{per} \quad N \quad \text{deaths}, \qquad (11.5)$$

a much faster rate than in the general case, no doubt due to the increased number of absorbing states, and the limitations on the direction of movement in the random walk.

To evaluate the expectations of the genotypes at the absorbing states, we know

$$M'_{\infty} = E(X_{\infty} + Y_{\infty}) = 1. \tag{11.6}$$

From (11.2) it may be shown

$$E(X_{t+1} - Y_{t+1}) = E(X_t - Y_t) \quad \text{for all } t,$$

hence on introducing the initial values X_0, Y_0,

$$E(X_{\infty} - Y_{\infty}) = X_0 - Y_0. \tag{11.7}$$

Taking (11.6) and (11.7) together gives

$$E(X_{\infty}) = \tfrac{1}{2}(1 + X_0 - Y_0), \quad E(Y_{\infty}) = \tfrac{1}{2}(1 - X_0 + Y_0). \tag{11.8}$$

When $f < 1$, there are only two absorbing states, and the frequencies (X_{∞}, Y_{∞}) can only be $(1,0)$ or $(0,1)$. Therefore, the probabilities of fixation are

$$Pr\{X_{\infty} = 1\} = E(X_{\infty}) = \tfrac{1}{2}(1 + X_0 - Y_0); \quad Pr\{Y_{\infty} = 1\} = E(Y_{\infty}) = \tfrac{1}{2}(1 - X_0 + Y_0). \tag{11.9}$$

However, when $f = 1$, there are $N - k_0 - l_0 + 1$ absorbing states, and the probability of reaching one of these must be evaluated by different methods. Let $P(k,l)$ be the probability that the population will sometime pass through the point (k,l). From (11.2) we know that this state can be reached only through $(k-1,l)$ or $(k,l-1)$, so that

$$P(k,l) = \tfrac{1}{2}P(k-1,l) + \tfrac{1}{2}P(k,l-1) \tag{11.10}$$

with the boundary conditions

$$P(k_0,l_0) = 1,\ P(k,l) = 0 \quad \text{if either} \quad k < k_0 \text{ or } l < l_0 .$$

The solution of (11.10) is

$$P(k,l) = 2^{-(k+l-k_0-l_0)} \binom{k+l-k_0-l_0}{k-k_0} ,$$

and the probability of reaching the absorbing state $(k,N-k)$ is

$$P(k,N-k) = 2^{-(N-k_0-l_0)} \binom{N-k_0-l_0}{k-k_0} ; \qquad (11.11)$$

Note that this distribution is consistent with the expectations (11.8).

The expected time to first reach homozygosity has not been found for the general case, but can be when $f=1$ because of the simple nature of the random walk then. Let $u = N-k-l$ be the number of heterozygotes in the population, and t_u be the time (measured in birth-death events) taken by the population to leave this state. According to (11.2), when $f = 1$ the state will either remain unchanged, or change from u to $u-1$ heterozygotes with probability $\frac{1}{2}uN^{-1}$ per birth-death event. The variable t_u-1 has a geometric distribution with parameter $\frac{1}{2}uN^{-1}$, and the mean and variance of t_u are

$$E(t_u) = 2Nu^{-1} , \quad Var(t_u) = 4N^2u^{-2} - 2Nu^{-1} .$$

If T is the total time (measured in birth-death events) to reach homozygosity, the distribution of $T - u_0$ is the convolution of u_0 geometric distributions, and we have

$$T = t_{u_0} + t_{u_0-1} + \dots + t_2 + t_1 \ ,$$

$$E(T) = 2N\sum_1^{u_0} \frac{1}{u} \doteq 2N(0.5772 + \log u_0), \qquad (11.12)$$

$$Var(T) = 4N^2 \sum_1^{u_0} \frac{1}{u^2} - 2N\sum_1^{u_0} \frac{1}{u} \doteq 4N^2 \frac{\pi^2}{6} - 2N(0.5772 + \log u_0) \ ,$$

the approximations holding for large u_0 . To conform with the notation of § 1.4, write $E(T) = N^2U$. Then (11.12) shows that U is not of the form (1.36) suggested by the diffusion theory, because here the gene frequency is not a diffusion variate (c/f. § 5).

11.2. Dioecious population

The dioecious equivalent to the above model has already been described in § 5. Thus the mating probabilities were given in (5.1) and the offspring probabilities in (5.2). Here we assume that there is no mutation and no selection $(\alpha_1 = \alpha_2 = \nu_1 = \nu_2 = 0)$, and the transition probabilities

(5.3) become

$$
\begin{aligned}
(k-1,l,r,s) &: \tfrac{1}{2}N_1N^{-1}(1-f)X(1-W+Z)\ ,\\
(k-1,l+1,r,s) &: 0\ ,\\
(k+1,l,r,s) &: \tfrac{1}{2}N_1N^{-1}(1-X-Y)\left[1+(1-f)(W-Z)\right]\ ,\\
(k,l+1,r,s) &: \tfrac{1}{2}N_1N^{-1}(1-X-Y)\left[1-(1-f)(W-Z)\right]\ ,\\
(k+1,l-1,r,s) &: 0\ ,\\
(k,l-1,r,s) &: \tfrac{1}{2}N_1N^{-1}(1-f)Y(1+W-Z)\ ,\\
(k,l,r-1,s) &: \tfrac{1}{2}N_2N^{-1}(1-f)W(1-X+Y)\ ,\\
(k,l,r-1,s+1) &: 0\ ,\\
(k,l,r+1,s) &: \tfrac{1}{2}N_2N^{-1}(1-W-Z)\left[1+(1-f)(X-Y)\right]\ ,\\
(k,l,r,s+1) &: \tfrac{1}{2}N_2N^{-1}(1-W-Z)\left[1-(1-f)(X-Y)\right]\ ,\\
(k,l,r+1,s-1) &: 0\ ,\\
(k,l,r,s-1) &: \tfrac{1}{2}N_2N^{-1}(1-f)Z(1+X-Y)\ ,
\end{aligned}
\qquad (11.13)
$$

where $X = kN_1^{-1}$, $Y = lN_1^{-1}$, $W = rN_2^{-1}$, $Z = sN_2^{-1}$ are the genotype frequencies.

The theory proceeds analogously to the monoecious case treated in § 11.1, but with somewhat more complication. If we define the vector of moments $\underline{M}_t$ as

$$
\underline{M}_t = \begin{bmatrix} E(X_t + Y_t) \\ E(W_t + Z_t) \\ E(X_t - Y_t)(W_t - Z_t) \\ E(X_t - Y_t)^2 \\ E(W_t - Z_t)^2 \end{bmatrix}\ ,
$$

then the difference equations linking the moments of succeeding states are

$$\underline{M}_{t+1} = \underline{Q}\,\underline{M}_t + \underline{K} \quad , \qquad (11.14)$$

where

$$\underline{K}' = \tfrac{1}{2}N^{-1}(1,1,0,N_1^{-1},N_2^{-1}) \quad ,$$

and

$$\underline{Q} = \begin{bmatrix} 1-\frac{1}{2}(2-f)N^{-1} & 0 & \frac{1}{2}(1-f)N^{-1} & 0 & 0 \\ 0 & 1-\frac{1}{2}(2-f)N^{-1} & \frac{1}{2}(1-f)N^{-1} & 0 & 0 \\ 0 & 0 & 1-(1-f)N^{-1} & \frac{1}{2}(1-f)N^{-1} & \frac{1}{2}(1-f)N^{-1} \\ -\frac{1}{2}f(NN_1)^{-1} & 0 & (1-f)N^{-1}(1-\frac{1}{2}N_1^{-1}) & 1-(1-f)N^{-1} & 0 \\ 0 & -\frac{1}{2}f(NN_2)^{-1} & (1-f)N^{-1}(1-\frac{1}{2}N_2^{-1}) & 0 & 1-(1-f)N^{-1} \end{bmatrix}.$$

Write $\lambda = 1-\mu N^{-1}$.

Then the characteristic equation for $\underline{Q}$ becomes

$$|\underline{Q}-\lambda\underline{I}| = N^{-5}(\mu-1+\tfrac{1}{2}f)(\mu-1+f)(\mu^3-A\mu^2+B\mu-C) = 0,$$

where

$$A = 3-\tfrac{5}{2}f,$$
$$B = 2(1-\tfrac{1}{2}f)(1-f)+\tfrac{1}{4}(1-f)^2(N_1^{-1}+N_2^{-1}) \quad ,$$
$$C = \tfrac{1}{4}(1-f)^2(N_1^{-1}+N_2^{-1}) \quad .$$

The smallest root for μ will correspond to the largest non-unit eigenvalue of the transition matrix, say λ_2. For both

N_1 and N_2 large, this root μ_2 is approximately

$$\mu_2 \doteq \frac{c}{\delta} \doteq \tfrac{1}{4}(1-f)(2-f)^{-1}(N_1^{-1}+N_2^{-1}),$$

and so

$$\lambda_2 \doteq 1-\tfrac{1}{4}N^{-1}(1-f)(2-f)^{-1}(N_1^{-1}+N_2^{-1}).$$

When $f = 1$, the characteristic equation reduces to

$$N^{-5}\mu^3(\mu-\tfrac{1}{2})^2 = 0,$$

so that the largest non-unit eigenvalue is then

$$\lambda_3 = 1-\tfrac{1}{2}N^{-1}.$$

When $f < 1$, the rate of approach to homozygosity is now

$$\mathcal{R} = 1-\lambda_2^N \doteq \frac{N}{4N_1N_2}\cdot\frac{1-f}{2-f}, \qquad (11.15)$$

per generation of N deaths. But when $f = 1$, the rate takes the substantially larger value

$$\mathcal{R} = 1-\lambda_3^N \doteq 1-e^{-\frac{1}{2}} = 0.3935. \qquad (11.16)$$

The change in magnitude of the rate is explained in the same way as for the monoecious population. When $f < 1$, the random walk model has only two absorbing states, with either $k = N_1, l = 0, r = N_2, s = 0$, or $k = 0, l = N_1, r = 0, s = N_2$, whilst when $f = 1$ there are $(N_1-k_0-l_0+1)(N_2-r_0-s_0+1)$ absorbing states typified by

$$(k, N_1-k, r, N_2-r) \quad \text{for} \quad \left\{\begin{matrix} k = k_0, k_0+1, \ldots, N_1-l_0, \\ r = r_0, r_0+1, \ldots, N_2-s_0. \end{matrix}\right\}.$$

Also, when $f = 1$, the number of heterozygotes cannot increase, but it can in the general case.

To investigate the moments of the genotype frequencies in an absorbing state, we know

$$E(X_\infty + Y_\infty) = 1,$$
$$E(W_\infty + Z_\infty) = 1. \tag{11.17}$$

From (11.13), it can be shown that

$$E(X_{t+1} - Y_{t+1} + W_{t+1} - Z_{t+1}) = E(X_t - Y_t + W_t - Z_t),$$
$$E(X_{t+1} - Y_{t+1} - W_{t+1} + Z_{t+1}) = \left[1-(1-f)N^{-1}\right]E(X_t - Y_t - W_t + Z_t)$$

so in the limit, we have

$$E(X_\infty - Y_\infty + W_\infty - Z_\infty) = X_0 - Y_0 + W_0 - Z_0,$$
$$E(X_\infty - Y_\infty - W_\infty + Z_\infty) = \begin{cases} 0 & \text{if } f < 1, \\ X_0 - Y_0 - W_0 + Z_0 & \text{if } f = 1. \end{cases} \tag{11.18}$$

Taking equations (11.17), (11.18) together gives the expectations

$$E(X_\infty) = E(W_\infty) = \tfrac{1}{2} + \tfrac{1}{4}(X_0 - Y_0 + W_0 - Z_0),$$
$$E(Y_\infty) = E(Z_\infty) = \tfrac{1}{2} - \tfrac{1}{4}(X_0 - Y_0 + W_0 - Z_0), \tag{11.19}$$

when $f < 1$, and when $f = 1$,

$$E(X_\infty) = \tfrac{1}{2}(1 + X_0 - Y_0), \quad E(W_\infty) = \tfrac{1}{2}(1 + W_0 - Z_0),$$
$$E(Y_\infty) = \tfrac{1}{2}(1 - X_0 + Y_0), \quad E(Z_\infty) = \tfrac{1}{2}(1 - W_0 + Z_0). \tag{11.20}$$

In the general case, there are only two absorbing states, and therefore the probabilities of gene fixation are, from (11.19),

$$Pr\{X_\infty = W_\infty = 1\} = \tfrac{1}{2} + \tfrac{1}{4}(X_0 - Y_0 + W_0 - Z_0),$$
$$Pr\{Y_\infty = Z_\infty = 1\} = \tfrac{1}{2} - \tfrac{1}{4}(X_0 - Y_0 + W_0 - Z_0). \tag{11.21}$$

But for the particular case $f = 1$, other methods are needed to evaluate the probabilities associated with each absorbing state. Define $P(k,l,r,s)$ as the probability that the population will sometime pass through the point (k,l,r,s). According to (11.13), this state can only be reached through one of the four neighbouring states $(k-1,l,r,s)$, $(k,l-1,r,s)$, $(k,l,r-1,s)$ or $(k,l,r,s-1)$. If the state is actually $(k-1,l,r,s)$ at some instant, then according to (11.13), the probability of reaching (k,l,r,s) in one birth-death event is $\frac{1}{2}N_1N^{-1}(1-X-Y+N_1^{-1})$, and the probability of ever reaching this state is

$$p_1(\text{say}) = \tfrac{1}{2}N_1N^{-1}(1-X-Y+N_1^{-1})\left[1-N_1N^{-1}(X+Y)-N_2N^{-1}(W+Z)+N^{-1}\right]^{-1},$$

$$= \tfrac{1}{2}(N_1-k-l+1)(N-k-l-r-s+1)^{-1}.$$

Similarly, the probability of ever reaching (k,l,r,s) from $(k,l-1,r,s)$ is also p_1, whilst from $(k,l,r-1,s)$ and $(k,l,r,s-1)$ it is

$$p_2(\text{say}) = \tfrac{1}{2}(N_2-r-s+1)(N-k-l-r-s+1)^{-1}.$$

Hence, we get the difference equation

$$P(k,l,r,s) = p_1\left[P(k-1,l,r,s)+P(k,l-1,r,s)\right] + p_2\left[P(k,l,r-1,s)+P(k,l,r,s-1)\right],$$

with the boundary conditions

$$P(k_0,l_0,r_0,s_0) = 1, \quad P(k,l,r,s) = 0$$

if any of $k < k_0$, $l < l_0$, $r < r_0$ or $s < s_0$ hold. It is easily verified that the solution of this set of equations

is

$$P(k,l,r,s) = 2^{-(k+l+r+s-k_0-l_0-r_0-s_0)} \frac{\binom{k+l-k_0-l_0}{k-k_0}\binom{r+s-r_0-s_0}{r-r_0}\binom{k+l+r+s-k_0-l_0-r_0-s_0}{k+l-k_0-l_0}\binom{N-k-l-r-s}{N_1-k-l}}{\binom{N-k_0-l_0-r_0-s_0}{N_1-k_0-l_0}},$$

and therefore the probability of ultimately reaching the absorbing state (k, N_1-k, r, N_2-r) is

$$P(k, N_1-k, r, N_2-r) = 2^{-N+k_0+l_0+r_0+s_0}\binom{N_1-k_0-l_0}{k-k_0}\binom{N_2-r_0-s_0}{r-r_0}. \qquad (11.22)$$

Note that this distribution is consistent with the expectations of equations (11.20) above.

Again, in the special case of $f = 1$, the distribution of T (the total number of birth-death events taken to first reach an absorbing state) is identical with that obtained in the monoecious case (11.12), but with u_0 replaced by $u_0+v_0 = N-k_0-l_0-r_0-s_0$, the number of heterozygotes initially in the population.

Comparing the above results with those obtained for the same model by diffusion approximations in § 5, the reason for the exceptional behaviour when $f = 1$ is easily accounted for; the diffusion theory breaks down since the number of heterozygotes cannot increase. When $f < 1$, the diffusion theory gave the same rate of approach (5.5) as the exact theory (11.15), except for terms of order N^{-2}. The diffusion theory exactly predicted, (5.6), the probability of a gene fixation given

above in (11.21). In the diffusion theory, we were able to find an approximation to the expected time to reach an absorbing state if $f < 1$, but this has not been found in the exact theory. However, when $f = 1$ the exact theory gave the distribution as well as the moments for this time.

11.3. Comparison of models B, C, and D

We here collect together the more important exact results found for the three models B, C, and D in which assortative mating played an important part. Because in model D mating was on the general system with a zygotic basis, the same will be assumed for models B and C, that is we take $\varepsilon = \frac{1}{2}$, and for the dioecious populations, $\xi = \eta = \rho = (N_1 - N_2)N^{-1}$.

Monoecious populations

The rates of approach to homozygosity, per generation, were given in (9.5), (10.2), and (11.4) for the three models as

Mating parameter	Model B	Model C	Model D
$f=0$	$\frac{1}{2}N^{-1}$	N^{-1}	$\frac{1}{2}N^{-1}$
$0 < f < 1$	$\frac{1}{2}N^{-1}(1-\frac{1}{2}f)^{-1}$	$N^{-1}(1-\frac{1}{2}f)^{-1}$	$\frac{1}{2}N^{-1}(1-\frac{1}{2}f)^{-1}(1-\frac{1}{2}f)$
$f=1$	N^{-1}	$2N^{-1}$	$1-e^{-\frac{1}{2}}$

ignoring terms of order N^{-2}. The probabilities of reaching a particular absorbing state are in each case independent of the mating parameter f, and the same for all models, with the one exception of complete assortative mating in model D.

Normally, the probabilities are

$$Pr\{k_\infty = N, l_\infty = 0\} = \tfrac{1}{2}(1 + X_0 - Y_0) = \tfrac{1}{2} + \tfrac{1}{2}N^{-1}(k_0 - l_0),$$

$$Pr\{k_\infty = 0, l_\infty = N\} = \tfrac{1}{2}(1 - X_0 + Y_0) = \tfrac{1}{2} - \tfrac{1}{2}N^{-1}(k_0 - l_0),$$

(c/f. (9.6), (10.3), (11.9)), but in the exceptional case we have

$$Pr\{k_\infty = k, l_\infty = N-k\} = 2^{-N+k_0+l_0}\binom{N-k_0-l_0}{k-k_0}$$

with $k_0 \leq k \leq N-l_0$, from (11.11).

For random mating, model D and model B are identical in both rate and fixation probabilities, but the presence of assortative mating decreases the rate of D in contrast to B and C whose rates increase with f. Hence model D has the slowest rate in general, but the fastest rate if $f=1$. The diverse behaviour of D is understandable in terms of the random walk diagrams, Fig 1, for in general, the state of the population will approach a boundary of the region at quite a fast rate but not reach either of the two absorbing points until much later. As f increases, the tendency is for a drift to the boundary with no heterozygotes, and once near this boundary the probability of the state changing at all is small. When $f=1$, this latter probability is zero along the entire homozygous boundary, and the fast initial rate becomes all-important. The same is not true for the other two models because, for them, the number of heterozygotes may increase with non-zero probability for all values of f, provided fixation has not occurred.

Dioecious populations

The asymptotic rates of approach to homozygosity for the three models are given, to first order in N^{-1}, by (9.11), (10.6) and (11.15), (11.16) as

Mating parameter	Model B	Model C	Model D
$f = 0$	$\frac{N}{8N_1N_2}$	$\frac{N}{4N_1N_2}$	$\frac{N}{8N_1N_2}$
$0 < f < 1$	$\frac{N}{8N_1N_2}\left[1-f(2-f)\left(\frac{N_1-N_2}{N}\right)^2\right](1-\frac{1}{2}f)^{-1}$	$\frac{N}{4N_1N_2}\left[1-f(2-f)\left(\frac{N_1-N_2}{N}\right)^2\right](1-\frac{1}{2}f)^{-1}$	$\frac{N}{8N_1N_2}(1-f)(1-\frac{1}{2}f)^{-1}$
$f = 1$	$\frac{N}{4N_1N_2}\left[1-\left(\frac{N_1-N_2}{N}\right)^2\right]$	$\frac{N}{2N_1N_2}\left[1-\left(\frac{N_1-N_2}{N}\right)^2\right]$	$1-e^{-t}$

All models have the same probability of ultimate fixation,

$$\Pr\{k_\infty = N_1, r_\infty = N_2\} = \tfrac{1}{2} + \tfrac{1}{4}(X_0 - Y_0 + W_0 - Z_0) = \tfrac{1}{2} + \tfrac{1}{4}N_1^{-1}(k_0 - l_0) + \tfrac{1}{4}N_2^{-1}(r_0 - s_0),$$

$$\Pr\{l_\infty = N_1, s_\infty = N_2\} = \tfrac{1}{2} - \tfrac{1}{4}(X_0 - Y_0 + W_0 - Z_0) = \tfrac{1}{2} - \tfrac{1}{4}N_1^{-1}(k_0 - l_0) - \tfrac{1}{4}N_2^{-1}(r_0 - s_0),$$

(see (9.14), (10.9), (11.21)) with the exception of model D subject to complete assortative mating, when we get

$$\Pr\{k_\infty = k, l_\infty = N_1 - k, r_\infty = r, s_\infty = N_2 - r\} = 2^{-N+k_0+l_0+r_0+s_0}\binom{N_1-k_0-l_0}{k-k_0}\binom{N_2-r_0-s_0}{r-r_0}$$

with $k_0 \leq k \leq N_1 - l_0$, $r_0 \leq r \leq N_2 - s_0$.

Once again, for random mating the present model is very similar to model B, but for the general case the rates of approach differ in behaviour. Incomplete assorative mating in model D slows down the fixation rate, and this may or may

not occur for the other models, depending on whether $(N_1-N_2)^2N^{-2}$ is greater or less than $\frac{1}{2}$. When $f=1$, the models differ fundamentally in that model D approaches an absorbing state with no heterozygotes quite quickly, whereas the other models have a slow drift to gene fixation.

It should be noted that main attention has been focused on the asymptotic rate of approach to homozygosity. However, in many cases smaller eigenvalues of the transition matrix are known, and these correspond to the fast rates at which the population changes initially. Moran (22) has suggested that a root $1-N^{-1}$ (c/f (10.5)) gives the rate at which his overlapping generation population approaches a state where the Hardy-Weinberg law holds. This is certainly of the correct order of magnitude, for in units of one generation we have $(1-N^{-1})^N \doteq e^{-1}$, and in an infinite non-overlapping population the Hardy-Weinberg law holds after one generation for monoecious populations, and after two generations in the dioecious case. Other roots perhaps correspond to the rate of approach to a boundary of the random walk region, suggested of course by the root $1-\frac{1}{2}N^{-1}$ encountered in model D with $f=1$.

12. Model C (haploid, random mating case): Approach to gene fixation.

12.0. Introduction

If a finite Markov chain, in discrete time, has a number of absorbing states, one of these will eventually be reached. In § 12.1 we give theoretical formulae for the probability distribution and the moments of the time taken to first reach an absorbing state. Then in § 12.2 the theory is applied to a genetic population model introduced by Moran (22), but the transition matrix (given above in (0.6)) is simplified by assuming mutation is absent. In genetical terms, we are discussing the time taken for the a gene to become either fixed in, or lost from, the population.

During the derivation, we shall prove that the eigenvalues (0.7) are correct, and shall find the corresponding pre- and post-eigenvectors. An incidental by-product is the proof of certain identities for the Tchebichef polynomials.

Apart from model D subject to complete assortative mating (see (11.12)), the present model is the only one so far to yield to this type of analysis. The model has overlapping generations and some of the other features of the models discussed in § 4 and § 10, and so we have labelled it model C in the chapter heading. However it concerns haploid individuals with random mating, no mutation, and no selection.

12.1. Markov chains with absorbing states

Consider a Markov chain in discrete time and with a finite number of possible states. The states will be labelled $0,1,2, \ldots, N$ and the times $t = 0,1,2,3, \ldots$. Let p_{ij} be the probability that a given state i changes to the state j in one time unit, and write $\underline{P}$ for the $(N+1)$-square transition matrix (p_{ij}). Note that this notation uses a different convention to that in § 0, where the elements of the transition matrix $\underline{T}$, say T_{ij}, represented the probability of transition from state j to state i. Thus the present matrix $\underline{P}$ is the transpose of $\underline{T}$: the change in convention simplifies the writing of certain matrix equations.

We assume that the states 0 and N are absorbing, that is $p_{00} = p_{NN} = 1$, and that the states $1,2,3, \ldots, N-1$ are transient. The following theory could be easily adapted to a chain with more (or less) absorbing states, but the application to genetics makes the specific case important. It is well known that no matter what the state at time $t=0$ may be, eventually one of the absorbing states will be reached; we write T_i for the time taken to first reach an absorbing state, given the initial state was i $(i=0,1,2, \ldots, N)$. Our aim is to find the probability distribution and the moments of T_i. There are two possible approaches to the problem, one allowing i to be any of the possible states, and the second limiting i to being a transient state only. One would think that the difference between these two approaches could be trivial, but in practice this is not so.

(a) Arbitrary initial state

Denote by $S_i^{(t)}$ the probability that $T_i = t$. Clearly, if i is absorbing $T_i \equiv 0$, and therefore

$$S_0^{(0)} = S_M^{(0)} = 1, \quad S_0^{(t)} = S_M^{(t)} = 0 \quad \text{for} \quad t=1,2,3, \ldots \qquad (12.1)$$

If however, i is not an absorbing state, then $T_i \geq 1$, and we have

$$S_i^{(0)} = 0, \quad S_i^{(1)} = p_{i0} + p_{iM} \quad \text{for} \quad i=1,2,3, \ldots, M-1. \qquad (12.2)$$

In this case, an expression for the general $S_i^{(t+1)}$ can be obtained by considering the possible changes from the initial state to another transient state, and the probability of absorption from there in time t. Thus

$$S_i^{(t+1)} = \sum_{j=1}^{M-1} p_{ij} S_j^{(t)} \quad \text{for} \quad t=1,2,3, \ldots. \qquad (12.3)$$

But for $t \geq 1$, $S_0^{(t)}$ and $S_M^{(t)}$ are zero by (12.1), so that (12.3) may be written

$$S_i^{(t+1)} = \sum_{j=0}^{M} p_{ij} S_j^{(t)} \quad \text{for} \quad t=1,2,3, \ldots$$

This actually holds whether i is transient or absorbing, because $p_{0j} = p_{Mj} = 0$ for $j=1,2,3, \ldots, M-1$. Writing

$$S^{(t)} = \begin{bmatrix} S_0^{(t)} \\ S_1^{(t)} \\ \vdots \\ S_M^{(t)} \end{bmatrix},$$

we therefore have

$$\underline{S}^{(t+1)} = \underline{P}\,\underline{S}^{(t)} \qquad \text{for} \quad t=1,2,3, \ldots . \tag{12.4}$$

It follows immediately that

$$\underline{S}^{(t+1)} = \underline{P}^{t}\,\underline{S}^{(1)} \qquad \text{for} \quad t=0,1,2,3, \ldots , \tag{12.5}$$

the case when $t=0$ being obvious. From (12.2) the vector $\underline{S}^{(1)}$ is given as

$$\underline{S}^{(1)} = \begin{bmatrix} 0 \\ p_{1,0}+p_{1,M} \\ p_{2,0}+p_{2,M} \\ \vdots \\ p_{M-1,0}+p_{M-1,M} \\ 0 \end{bmatrix} .$$

The application of (12.5) directly is not usually a simple task, but if the eigenvalues and eigenvectors of $\underline{P}$ are known, (12.5) can be replaced by a more useful expression. Suppose $\underline{K}$ is a $(M+1)$-square matrix whose columns are the post-eigenvectors of $\underline{P}$, and write $\underline{\Delta} = (\delta_{ij}\lambda_j)$ as the matrix whose diagonal elements λ_j are the eigenvalues of $\underline{P}$. By definition,

$$\underline{P}\,\underline{K} = \underline{K}\,\underline{\Delta} . \tag{12.6}$$

The pre-eigenvectors are the rows of $\underline{K}^{-1}$, for (12.6) can be transformed into

$$\underline{K}^{-1}\,\underline{P} = \underline{\Delta}\,\underline{K}^{-1}. \tag{12.7}$$

With these definitions, $\underline{P}^t$ can be written $\underline{K}\,\underline{\Delta}^t\,\underline{K}^{-1}$, and so (12.5) becomes

$$\underline{S}^{(t+1)} = \underline{K}\,\underline{\Delta}^t\,\underline{K}^{-1}\,\underline{S}^{(1)}, \quad t = 0, 1, 2, \cdots \tag{12.8}$$

At least in theory, (12.8) or (12.5) give the complete probability distributions we seek. For practical purposes, it may be preferable to ascertain the moments rather than the distributions, and this may be done by introducing the probability generating functions. We define these as

$$G_i(Z) = E(Z^{T_i}) = \sum_{t=0}^{\infty} S_i^{(t)} Z^t, \tag{12.9}$$

and write

$$\underline{G}(z) = \begin{bmatrix} G_0(z) \\ G_1(z) \\ \vdots \\ G_M(z) \end{bmatrix} = \sum_{t=0}^{\infty} \underline{S}^{(t)} z^t .$$

Substituting from (12.1), (12.8) we have

$$\underline{G}(z) = \begin{bmatrix} 1 \\ 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix} + z \sum_{t=0}^{\infty} \underline{K}\, z^t \underline{\Delta}^t \underline{K}^{-1} \underline{S}^{(1)}$$

$$= \begin{bmatrix} 1 \\ 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix} + z\,\underline{K}\,\underline{D}\,\underline{K}^{-1}\,\underline{S}^{(1)} \text{ say}, \tag{12.10}$$

where $\underline{D}$ is the $(M+1)$-square matrix $\sum_{t=0}^{\infty} z^t \underline{\Lambda}^t = \left(\delta_{ij} \frac{1}{1-z\lambda_j}\right)$, since each diagonal term of $\underline{D}$ is the sum of a geometric series.

(b) Transient initial state.

An alternative approach to the problem can be made by assuming that the initial state i belongs to the set $1,2,3, \ldots, M-1$, thus excluding the absorbing states. The notation employed here is that $(M-1)$-order matrices and vectors are (usually) denoted by script capitals. Write $\mathscr{P}$ for the matrix obtained by eliminating the first and last rows and columns of $\underline{P}$; $\mathscr{P}$ is not stochastic because the states $1,2,3, \ldots, M-1$ are assumed transient and are not a closed set.

Write

$$\underline{\mathscr{S}}^{(t)} = \begin{bmatrix} S_1^{(t)} \\ S_2^{(t)} \\ \vdots \\ S_{M-1}^{(t)} \end{bmatrix} ;$$

then from (12.1), (12.2),

$$\underline{\mathscr{S}}^{(0)} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix}, \quad \underline{\mathscr{A}}^{(1)} = \begin{bmatrix} p_{1,0} + p_{1,M} \\ p_{2,0} + p_{2,M} \\ \vdots \\ p_{M-1,0} + p_{M-1,M} \end{bmatrix} = (\underline{I} - \underline{\mathscr{P}})\underline{1} \qquad (12.11)$$

where $\underline{I}$ is the unit matrix, and $\underline{1} = (1,1,1, \ldots, 1)'$, both of order $M-1$. Equation (12.3) can then be written

$$\underline{\mathcal{S}}^{(t+1)} = \underline{P}\,\underline{\mathcal{S}}^{(t)}, \quad \text{for } t = 1,2,3,\ldots \qquad (12.12)$$

and (12.5) is replaced by

$$\underline{\mathcal{S}}^{(t+1)} = \underline{P}^t \underline{\mathcal{S}}^{(1)} = (\underline{P}^t - \underline{P}^{t+1})\underline{1} \text{ using (12.11)}. \qquad (12.13)$$

For the probability generating function, we have

$$\underline{\mathcal{G}}(z) = \sum_{t=0}^{\infty} z^t \underline{\mathcal{S}}^{(t)},$$

which by (12.11) equals

$$\underline{\mathcal{G}}(z) = z(\underline{I}-\underline{P})\underline{1} + \sum_{t=1}^{\infty} z^{t+1} \underline{\mathcal{S}}^{(t+1)}.$$

Substituting from (12.12),

$$\underline{\mathcal{G}}(z) = z(\underline{I}-\underline{P})\underline{1} + z\sum_{t=1}^{\infty} z^t \underline{P}\,\underline{\mathcal{S}}^{(t)} = z(\underline{I}-\underline{P})\underline{1} + z\underline{P}\,\underline{\mathcal{G}}(z),$$

so that

$$\underline{\mathcal{G}}(z) = (\tfrac{1}{z}\underline{I} - \underline{P})^{-1}(\underline{I}-\underline{P})\underline{1}. \qquad (12.14)$$

Of course, (12.13) and (12.14) must produce results consistent with the corresponding elements of (12.8) and (12.9) respectively, but already we see that this is not immediately obvious.

12.2. Application to a population model

In (0.6) a transition matrix was given for a model introduced by Moran (22). The population size was there written as $2N$, and a different notation was used for the transition probabilities. The fact that $2N$ is even has little significance for the present problem, although it was chosen previously to make the model directly comparable with a diploid population of size N. Here, we shall adhere to the notation of § 12.1. In the model, the state of the population was taken as the number of a individuals. The transition probabilities are

$$\begin{aligned} p_{i,j} &= 0 \quad \text{if} \quad |i-j| > 1 \\ p_{i,i-1} &= \tfrac{i}{M}\left(1-\tfrac{i}{M}\right), \\ p_{i,i} &= 1 - 2\tfrac{i}{M}\left(1-\tfrac{i}{M}\right), \\ p_{i,i+1} &= \tfrac{i}{M}\left(1-\tfrac{i}{M}\right), \end{aligned} \qquad (12.15)$$

where we have assumed there is no mutation. Clearly the states 0 and M are absorbing, and this corresponds to the obvious fact that once all individuals are either A or a, no change in state can occur without mutation.

It is convenient to use approach (b) of § 12.1 first, and so we assume that the initial state i is not absorbing. Consider first the expected value of the absorption time T_i. To conform with the notation of § 1.4, we write this expectation as

$$E(T_i) = M^2 . U(p)$$

where $p = iM^{-1}$ is the initial relative frequency of the a gene. Differentiating (12.14) with respect to z, and evaluating the result at $z=1$ gives

$$\frac{d}{dz}\underline{g}(z)\Big|_{z=1} = \left[\tfrac{1}{z^2}\left(\tfrac{1}{z}\underline{I}-\underline{P}\right)^{-2}\right]_{z=1}(\underline{I}-\underline{P})\underline{1} = (\underline{I}-\underline{P})^{-1}\underline{1}. \qquad (12.16)$$

This equation was given by Feller (10) p.378 ex.17 with a somewhat different notation. To the author's knowledge, it has not been used before for a genetic population model. In the particular model under discussion, we have from (12.15)

$$\underline{I}-\underline{P} = \begin{bmatrix} 2\frac{1}{M}(1-\frac{1}{M}) & -\frac{1}{M}(1-\frac{1}{M}) & 0 & 0 & \cdots & 0 \\ -\frac{2}{M}(1-\frac{2}{M}) & 2\frac{2}{M}(1-\frac{2}{M}) & -\frac{2}{M}(1-\frac{2}{M}) & 0 & & 0 \\ 0 & -\frac{3}{M}(1-\frac{3}{M}) & 2\frac{3}{M}(1-\frac{3}{M}) & -\frac{3}{M}(1-\frac{3}{M}) & & 0 \\ 0 & & & & & \vdots \\ \vdots & & & & & \vdots \\ 0 & & & -\frac{2}{M}(1-\frac{2}{M}) & 2\frac{2}{M}(1-\frac{2}{M}) & -\frac{2}{M}(1-\frac{2}{M}) \\ 0 & 0 & 0 & \cdots\ 0 & -\frac{1}{M}(1-\frac{1}{M}) & 2\frac{1}{M}(1-\frac{1}{M}) \end{bmatrix}$$

and this may be written as a matrix product

$$\begin{bmatrix} \frac{1}{M}(1-\frac{1}{M}) & 0 & 0 & \cdots & 0 \\ 0 & \frac{2}{M}(1-\frac{2}{M}) & 0 & & \vdots \\ 0 & 0 & \frac{3}{M}(1-\frac{3}{M}) & & \vdots \\ \vdots & & & \ddots & 0 \\ 0 & 0 & 0 & \cdots & \frac{1}{M}(1-\frac{1}{M}) \end{bmatrix} \begin{bmatrix} 2 & -1 & 0 & 0 & \cdots & 0 \\ -1 & 2 & -1 & 0 & & \vdots \\ 0 & -1 & 2 & -1 & & \vdots \\ \vdots & & & & & 0 \\ & & & & -1 & 2 & -1 \\ 0 & & & & 0 & -1 & 2 \end{bmatrix}$$

From this the inverse may be found to be

$$(\mathbf{I}-\mathbf{Q})^{-1} = M \begin{bmatrix} M-1 & M-2 & M-3 & \cdots & 3 & 2 & 1 \\ M-2 & 2M-4 & 3M-6 & \cdots & 6 & 4 & 2 \\ \vdots & & & & & & \\ M-i & 2(M-i) & 3(M-i) & \cdots & i(M-i) & \cdots & 2i \quad i \\ \vdots & & & & & & \\ 1 & 2 & 3 & \cdots & M-3 & M-2 & M-1 \end{bmatrix} \begin{bmatrix} \frac{1}{1(M-1)} & 0 & \cdots & \cdots & 0 \\ 0 & \frac{1}{2(M-2)} & & & \vdots \\ \vdots & & \ddots & & \\ & & & & 0 \\ 0 & \cdots & \cdots & 0 & \frac{1}{(M-1)} \end{bmatrix} \tag{12.17}$$

which when substituted back into (12.16) gives for the i-th element

$$E(T_i) = M^2 U(p) = (M-i)\sum_{j=1}^{i} \frac{1}{1-jM^{-1}} + i\sum_{j=1}^{M-i-1} \frac{1}{1-jM^{-1}}, \tag{12.18}$$

and this happens to hold for $i = 0,1,2,\ldots, M-1, M$ because for $i = 0$ or M we have $T_0 \equiv T_M \equiv 0$.

Equation (12.18) is simple to compute if M is reasonably small, but for many natural populations M is large and an approximation to (12.18) is worthwhile. If M is increased but $p = iM^{-1}$ is kept constant, the summations in (12.18) tend to Riemann integrals and therefore

$$U(p) \doteq \log\left[p^{-p}(1-p)^{-(1-p)}\right]. \tag{12.19}$$

This formula could be derived from the applicability of diffusion theory to the model, and (1.36) would give the same approximation for the function $U(p)$. This agreement follows as the parameter a in (1.36) takes the value 4 if the diffu-

sion theory is applied to the model$_\lambda^{\text{with}}$ N of § 1 replaced by M; a different value for a $(a=1)$ arises if N is replaced by $\frac{1}{2}M$ in § 1 because a different time scale is involved. However, we shall not give the justification for the diffusion theory, but remark that (12.18) and (12.19) provide a measure of the accuracy of that theory. If time is measured in generations of M birth-death events the expected time in (12.18) should be divided by M, to give $MU(p)$.

Higher moments of T_i can be obtained by a similar argument. For example, for the second(factorial) moment we have

$$\frac{d^2}{dz^2}\underline{\mathcal{G}}(z)\Big|_{z=1} = \left[-\frac{2}{z^3}\left(\tfrac{1}{2}I-\underline{Q}\right)^{-2}+\frac{2}{z^2}\left(\tfrac{1}{2}I-\underline{Q}\right)^{-3}\right]_{z=1}\left(\tfrac{1}{2}I-\underline{Q}\right)\underline{1}$$

$$= -2\left(\tfrac{1}{2}I-\underline{Q}\right)^{-1}\underline{1}+2\left(\tfrac{1}{2}I-\underline{Q}\right)^{-2}\underline{1}$$

$$= 2\left[\left(\tfrac{1}{2}I-\underline{Q}\right)^{-1}-I\right]\cdot\frac{d}{dz}\underline{\mathcal{G}}(z)\Big|_{z=1}.$$

Using (12.17), (12.18), the i-th element is seen to be

$$2N(N-1)\sum_{k=1}^{i}\left[\sum_{j=1}^{k}\frac{1}{1-jN^{-1}}+\frac{k}{N-k}\sum_{j=1}^{N-k-1}\frac{1}{1-jN^{-1}}\right]+2Ni\sum_{k=1}^{N-i}\left[\sum_{j=1}^{k}\frac{1}{1-jN^{-1}}+\frac{k}{N-k}\sum_{j=1}^{N-k-1}\frac{1}{1-jN^{-1}}\right]$$

$$= 2E(T_i).$$

Hence the variance of T_i is

$$\begin{aligned} Var(T_i) = {} & 2M(M-1)\sum_{k=1}^{i}\left[\sum_{j=1}^{k}\frac{1}{1-jM^{-1}} + \frac{k}{M-k}\sum_{j=1}^{M-k-1}\frac{1}{1-jM^{-1}}\right] \\ & + 2Mi\sum_{k=1}^{M-i-1}\left[\sum_{j=1}^{k}\frac{1}{1-jM^{-1}} + \frac{k}{M-k}\sum_{j=1}^{M-k-1}\frac{1}{1-jM^{-1}}\right] \qquad (12.20) \\ & - E(T_i) - [E(T_i)]^2, \end{aligned}$$

which holds incidently for all i whether absorbing or not. As before, an approximation can be made if M is large, and replacing the summations by integrations gives

$$\begin{aligned} Var(T_{Mp}) \doteq M^4\Big\{ & 4p(1-p) + \tfrac{4}{3}p^2 - 2\log\left[p^{-p^2}(1-p)^{-(1-p)^2}\right] - \left[\log\left(p^{-p}(1-p)^{-(1-p)}\right)\right]^2 \\ & - 2\sum_{r=1}^{\infty}\frac{p^{r+1}+(1-p)^{r+1}}{r^2}\Big\}, \qquad (12.21) \end{aligned}$$

ignoring terms of order less than M^4.

From (12.18) and (12.20) we can infer that the exact expressions for the higher moments will be complicated summations of simple functions, whereas from (12.19) and (12.21) it seems that approximate results will involve non-elementary functions.

An alternative method of derivation of these results was outlined in § 12.1 (a), and this will now be considered. We shall see that an explicit formulation can be given to all moments in terms of comparatively simple series of Tchebichef's orthogonal polynomials. Therefore we start by defining these polynomials.

Write

$$\phi_i(x) = i!\,\epsilon_i\,\Delta^i\binom{x}{i}\binom{x-M}{i}, \quad i = 0, 1, 2, \ldots, M-1, \qquad (12.22)$$

where

$$\Delta f(x) = f(x+1) - f(x) \ , \quad \Delta^i f(x) = \sum_{k=0}^{i} (-1)^k \binom{i}{k} f(x+i-k),$$

and

$$c_i = \left\{ \frac{2i+1}{M(M^2-1^2)(M^2-2^2)\cdots(M^2-i^2)} \right\}^{\frac{1}{2}} .$$

Then $\xi_i(x)$ is a polynomial of degree i in x, and the set is orthonormal in the sense that

$$\sum_{x=0}^{M-1} \xi_i(x)\, \xi_j(x) = \delta_{ij} \ , \quad i,j = 0,1,2,\ldots,M-1, \tag{12.23}$$

see (3) p.223. In particular,

$$\xi_0(x) = \frac{1}{\sqrt{M}} \quad \text{for } x = 0,1,2,\ldots,M-1, \tag{12.24}$$

and

$$\xi_1(x) = \left[\frac{3}{M(M^2-1)}\right]^{\frac{1}{2}} \left[\binom{x+1}{1}\binom{x+1-M}{1} - \binom{x}{1}\binom{x-M}{1} \right]$$

$$= \left[\frac{3}{M(M^2-1)}\right]^{\frac{1}{2}} (2x - M + 1), \quad \text{for } x = 0,1,2,\ldots,M-1. \tag{12.25}$$

In what follows it will be convenient to use the conventions

$$\xi_i(-1) = 0 \quad \text{for } i = 0,1,2,\ldots,M-1, \tag{12.26}$$

and to introduce the new function

$$\xi_{-1}(x) = \begin{cases} 0 & \text{if } x = 0,1,2,\ldots,M-1, \\ 1 & \text{if } x = -1. \end{cases} \tag{12.27}$$

It is clear from (12.23) and the conventions that the augmented set $\{ \varphi_i(x) \}$, $i = -1,0,1,2,\ldots, M-1$, is orthonormal over $x = -1,0,1,2, \ldots , M-1$. The non-trivial values of $\varphi_i(x)$ have been tabulated in (28) for $M = 3(1)52$, $i = 1(1)6$, and references are given there to more extensive tabulations; in each case, the values are multiplied by the smallest constant to make the entries integers.

The functions $\varphi_i(x)$ satisfy the difference equation

$$(x+2)(x-M+2)\Delta^2 \varphi_i(x) + [2x-M+3-i(i+1)]\Delta\varphi_i(x) - i(i+1)\varphi_i(x) = 0,$$

see (3) p.223, and although this is usually proved for $i=0,1, \ldots , M-1$, $x=0,1, \ldots , M-3$, it also holds over the extended range $i = -1,0,1, \ldots , M-1$, $x = -1,0,1, \ldots , M-3$ in view of the conventions (12.26), (12.27). The difference equation can be written in an equivalent form

$$i(i+1)\varphi_i(x+1) = \Delta\left[(x+1)(x-M+1)\Delta\varphi_i(x)\right],$$

and summing over x gives

$$i(i+1)\sum_{x=-1}^{j-2} \varphi_i(x+1) = j(j-M)\Delta\varphi_i(j-1) = j(j-M)\left[\varphi_i(j) - \varphi_i(j-1)\right].$$

The summation on the left hand side can be extended to $x=-2$ because the additional term $\varphi_i(-1)$ is zero for non-negative i from (12.26), and for $i= -1$ the left hand side is identically zero whether $\varphi_{-1}(-1)$ is included or not. Hence

$$i(i+1)\sum_{x=-2}^{j-2} \varphi_i(x+1) = j(j-M)\left[\varphi_i(j) - \varphi_i(j-1)\right], \quad i = -1,0,1,\ldots,M-1.$$

Although the range of j is nominally $j = 1,2, \ldots, N-1$, in fact the equation holds for $j = 0,1,2, \ldots, N$ because the case $j = 0$ is trivial and the case $j = N$ holds by the well known fact that the summation on the left hand side is zero for $i = 1,2, \ldots, N-1$ and the multiplying term is zero if $i = -1$ or 0. A more convenient formulation is got by replacing i by $j-1$, j by i, and x by $k-2$, whence

$$(j-1)j \sum_{k=0}^{i} \xi_{j-1}(k-1) = c(i-N)\left[\xi_{i-1}(i) - \xi_{i-1}(i-1)\right], \quad i,j = 0,1,2,\ldots,N. \tag{12.28}$$

We are now in a position to prove the following theorem.

Theorem For the matrix $\underline{P}$ defined in (12.15),

(a) The eigenvalues are

$$\lambda_j = 1 - \frac{j(j-1)}{N^2}, \quad j = 0,1,2,\ldots,N. \tag{12.29}$$

(b) The post-eigenvectors are the columns $\underline{k}_j$ of the matrix

$$\underline{K} = (\underline{k}_0, \underline{k}_1, \ldots, \underline{k}_N) = \underline{C}\,\underline{\Xi} \tag{12.30}$$

where

$$\underline{C} = \begin{bmatrix} 1 & 0 & 0 & 0 & \cdots & 0 \\ 1 & 1 & 0 & 0 & & \vdots \\ 1 & 1 & 1 & 0 & & \vdots \\ 1 & 1 & 1 & 1 & & \vdots \\ \vdots & & & & \ddots & \vdots \\ 1 & 1 & 1 & 1 & \cdots & 1 \end{bmatrix}, \quad \underline{\Xi} = \begin{bmatrix} \xi_{-1}(-1) & \xi_0(-1) & \cdots & \xi_{N-1}(-1) \\ \xi_{-1}(0) & \xi_0(0) & & \xi_{N-1}(0) \\ \xi_{-1}(1) & \xi_0(1) & & \xi_{N-1}(1) \\ \vdots & \vdots & & \vdots \\ \xi_{-1}(N-2) & \xi_0(N-2) & \cdots & \xi_{N-1}(N-2) \end{bmatrix}$$

and (c) The pre-vectors are the rows of the matrix

$$\underline{K}^{-1} = \underline{\Xi}' \underline{C}^{-1} \qquad (12.31)$$

where $\underline{\Xi}'$ is the transpose of $\underline{\Xi}$, and $\underline{C}^{-1}$ is

$$\underline{C}^{-1} = \begin{bmatrix} 1 & 0 & 0 & 0 & \cdots & 0 \\ -1 & 1 & 0 & 0 & & \vdots \\ 0 & -1 & 1 & 0 & & \vdots \\ 0 & 0 & -1 & 1 & & \vdots \\ \vdots & & & \ddots & \ddots & \vdots \\ \vdots & & & & \ddots & \vdots \\ \vdots & & & & \ddots & \vdots \\ \vdots & & & & -1 & 1 \\ 0 & \cdots & \cdots & \cdots & 0 & -1 \end{bmatrix}$$

Proof: Parts (b) and (c) of the theorem are either true or false together, because $\underline{\Xi}$ is an orthogonal matrix, $\underline{C}^{-1}$ has the stated form, and the inverse of the post-eigenvector matrix gives the pre-vectors, c/f (12.6), (12.7). It will therefore be sufficient to prove that (a) and (b) are correct, and this is done by proving that (12.6) holds for the particular definitions used here. Write $g_{i,j}$ for the typical element of $\underline{P}\,\underline{K}$, and $h_{i,j}$ for the corresponding element of $\underline{K}\,\underline{\Lambda}$; here, $i,j = 0,1,2, \ldots, M$. We have to prove $g_{i,j} = h_{i,j}$ for all relevant i and j.

Multiplying out $\underline{P}\,\underline{K} = \underline{P}\,\underline{C}\,\underline{\Xi}$ we find

$$g_{i,j} = \sum_{k=0}^{M} \left[\varphi_{j-1}(k-1) \sum_{\ell=k}^{M} p_{i,\ell} \right] ,$$

and with the substitutions of (12.15) for the elements of $\underline{P}$ we get

$$g_{ij} = \sum_{k=0}^{i-1} \varphi_{j-1}(k-1) + \left[1 - \frac{i}{M}\left(1-\frac{i}{M}\right)\right] \varphi_{j-1}(i-1) + \frac{i}{M}\left(1-\frac{i}{M}\right) \varphi_{j-1}(i) .$$

Again, multiplying out $\underline{K}\,\underline{\Delta} = \underline{C}\,\underline{\Xi}\,\underline{\Delta}$, we have

$$h_{ij} = \lambda_j \sum_{k=0}^{i} \varphi_{j-1}(k-1) ,$$

which from (12.29) becomes

$$h_{ij} = \left[1 - \frac{j(j-1)}{M^2}\right] \sum_{k=0}^{i} \varphi_{j-1}(k-1) .$$

The equality of $g_{i,j}$ and $h_{i,j}$ follows from (12.28), and this holds for $i,j = 0,1,2, \ldots, M$ as required. This completes the proof of the theorem.

The theorem is not completely new; we mentioned in the introduction, see (0.7), that the eigenvalues (12.29) were already known, but the proof given by Hannan in an appendix to (22) is incorrect[1]. Again, the eigenvectors corresponding to the roots $\lambda_0 = \lambda_1 = 1$, $\lambda_2 = 1-2M^{-2}$, $\lambda_3 = 1-6M^{-2}$, $\lambda_4 = 1-12M^{-2}$ were given explicitly by Moran (23), but although he stated that the pre- vectors can be generated by Heun's differential equation, and

1. Hannan has shown (personal communication) that his published proof of (12.29) can be corrected by some modifications; this was not known until after the above theorem had been proved. The methods of proof are quite dissimilar, the present method giving the eigenvectors explicitly.

the post-vectors obtained from them, he did not find the general vectors. The vectors (12.30), (12.31) agree with the particular ones found by Moran, except possibly for multiplicative constants.

The relationship Moran (23) recognized between the pre- and post-eigenvectors can be proved from the above theorem. We have for the i-th element of the j-th post-eigenvector $\underline{k}_j$,

$$k_{i,j} = \sum_{k=0}^{i} \xi_{j-1}(k-1),$$

and by (12.28) this can be written

$$k_{i,j} = \frac{i(M-i)}{(j-1)\,j}\left[\xi_{j-1}(i-1) - \xi_{j-1}(i)\right].$$

This is perhaps a simpler formulation than that of (12.30). The corresponding element of the pre-vector is from (12.31)

$$\xi_{j-1}(i-1) - \xi_{j-1}(i),$$

and so the two are related by a proportionality factor $\frac{i(M-i)}{(j-1)j}$.

Although not particularly relevant to the subsequent development, it is interesting to note that the last post-eigenvector can be written in terms of binomial coefficients. For, the i-th element of $\underline{k}_M$ in (12.30) is

$$k_{i,M} = \sum_{k=0}^{i} \xi_{M-1}(k-1),$$

and since

$$\xi_{M-1}(k-1) = (-1)^{M+k}\binom{M-1}{k-1}\left[\binom{2M-2}{M-1}\right]^{-\frac{1}{2}}, \quad \sum_{k=0}^{i}(-1)^{M+k}\binom{M-1}{k-1} = (-1)^{M+i}\binom{M-2}{i-1},$$

we have

$$\beta_{i,M} = (-1)^{M+i}\binom{M-2}{i-1}\left[\binom{2M-2}{M-1}\right]^{-\frac{1}{2}}.$$

With these preliminaries, we shall now make use of the theorem to discuss the population model from the standpoint of § 12.1 (a). Equations (12.8), (12.30) and (12.31) imply that the vector of probabilities of absorption at time $t+1$ is

$$\underline{S}^{(t+1)} = C\,\Xi\,\Delta^{t}\,\Xi'C^{-1}\underline{S}^{(1)},$$

where

$$\underline{S}^{(1)} = \begin{bmatrix} 0 \\ \frac{1}{M}(1-\frac{1}{M}) \\ 0 \\ \vdots \\ 0 \\ \frac{1}{M}(1-\frac{1}{M}) \\ 0 \end{bmatrix}.$$

Multiplying out the matrices involved gives for the i-th element

$$S_i^{(t+1)} = \frac{1}{M}(1-\frac{1}{M})\sum_{j=0}^{M}\left\{\left[1-j(j-1)M^{-2}\right]^{t}\left[\xi_{j-1}(0)-\xi_{j-1}(1)+\xi_{j-1}(M-2)-\xi_{j-1}(M-1)\right]\sum_{k=0}^{i}\xi_{j-1}(k-1)\right\}$$

and substituting from (12.23) this becomes

$$S_i^{(t+1)} = \frac{1}{M}(1-\frac{1}{M})\frac{1}{M}(1-\frac{1}{M})\sum_{j=0}^{M}\left\{\left[1-j(j-1)M^{-2}\right]^{t}\left[\xi_{j-1}(0)-\xi_{j-1}(1)+\xi_{j-1}(M-2)-\xi_{j-1}(M-1)\right]\frac{n^{2}}{j(j-1)}\left[\xi_{j-1}(i-1)-\xi_{j-1}(i)\right]\right\}.$$

Various simplifications can be made; firstly, the term corresponding to $j=0$ in the summation is zero because of (12.27). Further,

$$\gamma_{j-1}(0) = \pm \xi_{j-1}(M-1) \quad , \quad \gamma_{j-1}(1) = \pm \xi_{j-1}(M-2) \, ,$$

depending on whether j is odd or even, so only even terms need be considered. Hence

$$\xi_i^{(t+1)} = 2\tfrac{1}{M}(1-\tfrac{1}{M})\tfrac{1}{M}(1-\tfrac{1}{M})\sum_{j=1}^{[\frac{1}{2}M]} \left\{ \left[1-2j(2j-1)M^{-2}\right]^t \left[\gamma_{2j-1}(0)-\xi_{2j-1}(1)\right]\frac{M^2}{2j(2j-1)}\left[\xi_{2j-1}(i-1)-\xi_{2j-1}(i)\right]\right\} \qquad (12.32)$$

where $[\frac{1}{2}M]$ denotes the integral part of $\frac{1}{2}M$. Note that if $M=2N$ as in (0.6), $[\frac{1}{2}M] = \frac{1}{2}M = N$. Putting $i=0$ in (12.28) gives

$$\frac{j(j-1)}{M^2}\,\xi_{j-1}(0) = \tfrac{1}{M}(1-\tfrac{1}{M})\left[\xi_{j-1}(0)-\xi_{j-1}(1)\right] \, ,$$

and substituting in (12.32) we have

$$\xi_i^{(t+1)} = 2\tfrac{1}{M}(1-\tfrac{1}{M})\sum_{j=1}^{[\frac{1}{2}M]} \left\{ \left[1-2j(2j-1)M^{-2}\right]^t \xi_{2j-1}(0)\left[\xi_{2j-1}(i-1)-\xi_{2j-1}(i)\right]\right\} \, . \qquad (12.33)$$

Equation (12.33) is perhaps the simplest explicit form for the probability distribution for general t and i. It is clear that it holds for all i ($i = 0,1,2, \ldots , M$) and all $t \geqslant 0$. However for t reasonably small, equation (12.5) could be used to give another form of solution. For example, with $t = 0$ we know that

$$\xi_i^{(1)} = \left(\xi_{i,1} + \xi_{i,M-1}\right)\tfrac{1}{M}(1-\tfrac{1}{M}) \, ,$$

and comparing this with (12.33) we find the identity

$$(\delta_{i,1}+\delta_{i,M-1})\tfrac{1}{M}(1-\tfrac{1}{M}) \equiv 2\tfrac{1}{M}(1-\tfrac{1}{M})\sum_{j=1}^{[\frac{1}{2}M]} \varphi_{2j-1}(0)\left[\varphi_{2j-1}(i-1)-\varphi_{2j-1}(i)\right], \quad i=0,1,\ldots,M.$$

This, and other identities for the orthogonal polynomials, can be obtained directly from the definition (12.22), or more easily from

$$\underline{K}\,\underline{\Delta}^{t}\underline{K}^{-1} \equiv \underline{P}^{t} \quad \text{for } t=0,1,2,\ldots .$$

We note that (12.33) agrees with (12.1) in so much as the right-hand side is zero when $i=0$ or $i=M$ for all $t \geqslant 0$. Whether (12.33) can be simply approximated for large N but $p = iM^{-1}$ kept fixed is not known, although there is some hope for this to be true since Legendre polynomials are limiting cases of the Tchebichef polynomials used here, see (3) p.223.

The probability generating function corresponding to (12.33) is

$$G_i(z) = \sum_{t=0}^{\infty} S_i^{(t)} z^t ,$$

$$= \delta_{i,0} + \delta_{i,M} + z\sum_{t=0}^{\infty} S_i^{(t+1)} z^t ,$$

$$= \delta_{i,0} + \delta_{i,M} + 2z\tfrac{1}{M}(1-\tfrac{1}{M})\sum_{j=1}^{[\frac{1}{2}M]}\left[\left[1-z\,a_j(a_j-b)^{-1}\right]^{-1}\varphi_{2j-1}(0)\left[\varphi_{2j-1}(i-1)-\varphi_{2j-1}(i)\right]\right]. \quad (12.34)$$

This result could be derived directly from (12.10), and is an alternative form to (12.14) if i is limited to the transient states.

Because $G_i(z)$ is a probability generating function, we must have $G_i(1) = 1$ for all i, and so (12.34) gives another identity for orthogonal polynomials

$$2\tfrac{i}{M}(1-\tfrac{i}{M})\sum_{j=1}^{[\frac{1}{2}M]}\left[1-2j(2j-1)M^{-2}\right]^{-1}\xi_{2j-1}(0)\left[\xi_{2j-1}(i-1)-\xi_{2j-1}(i)\right] \equiv 1-\delta_{i,0}-\delta_{i,M}\ , \quad i=0,1,\ldots,M.$$

(12.34) provides a method for determining the mean and higher moments of the absorption time T_i. We have

$$E(T_i) = \frac{d}{dz}G_i(z)\Big|_{z=1}$$

$$= 2M^2 i(M-i)\sum_{j=1}^{[\frac{1}{2}M]}\left[2j(2j-1)\right]^{-2}\xi_{2j-1}(0)\left[\xi_{2j-1}(i-1)-\xi_{2j-1}(i)\right]\ . \qquad (12.35)$$

But (12.18) is an alternative version of this quantity, and we get the further identity

$$2M^2 i(M-i)\sum_{j=1}^{[\frac{1}{2}M]}\left[2j(2j-1)\right]^{-2}\xi_{2j-1}(0)\left[\xi_{2j-1}(i-1)-\xi_{2j-1}(i)\right]$$

$$\equiv (M-i)\sum_{j=1}^{i}\left[1-jM^{-1}\right]^{-1} + i\sum_{j=1}^{M-i}\left[1-jM^{-1}\right]^{-1}\ , \quad i=0,1,\ldots,M.$$

Consider the second (factorial) moment of T_i. From (12.34) we have

$$\frac{d^2}{dz^2}G_i(z)\Big|_{z=1} = 4M^4 i(M-i)\sum_{j=1}^{[\frac{1}{2}M]}\left[2j(2j-1)\right]^{-2}\left[1-2j(2j-1)M^{-2}\right]\xi_{2j-1}(0)\left[\xi_{2j-1}(i-1)-\xi_{2j-1}(0)\right]\ ,$$

and by (12.35) this equals

$$4M^4 i(M-i)\sum_{j=1}^{[\frac{1}{2}M]}\left[2j(2j-1)\right]^{-3}\varphi_{2j-1}(0)\left[\varphi_{2j-1}(i-1)-\varphi_{2j-1}(i)\right]-2E(T_i).$$

The variance of T_i is therefore

$$\mathrm{Var}(T_i)=\frac{d^2}{dz^2}G_{T_i}(z)\Big|_{z=1}+E(T_i)-\left[E(T_i)\right]^2$$

$$=4M^4 i(M-i)\sum_{j=1}^{[\frac{1}{2}M]}\left[2j(2j-1)\right]^{-3}\varphi_{2j-1}(0)\left[\varphi_{2j-1}(i-1)-\varphi_{2j-1}(i)\right]-E(T_i)-\left[E(T_i)\right]^2,$$

and comparing this with (12.20) we find the identity

$$2M^3 i(M-i)\sum_{j=1}^{[\frac{1}{2}M]}\left[2j(2j-1)\right]^{-3}\varphi_{2j-1}(0)\left[\varphi_{2j-1}(i-1)-\varphi_{2j-1}(i)\right]$$

$$\equiv(M-i)\sum_{k=1}^{i}\left[\sum_{j=1}^{k}\left[1-jM^{-1}\right]^{-1}+\frac{k}{M-k}\sum_{j=1}^{N-k-1}\left[1-jM^{-1}\right]^{-1}\right]+i\sum_{k=1}^{M-i-1}\left[\sum_{j=1}^{k}\left[1-jM^{-1}\right]^{-1}+\frac{k}{M-k}\sum_{j=1}^{M-k-1}\left[1-jM^{-1}\right]^{-1}\right],$$

$$i=0,1,\ldots,M.$$

Higher moments can be obtained by suitable differentiations of (12.34), and will also involve summations of the above type.

Other aspects of the model's behaviour have been given in (22), (23), and need not be included here.

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