THE EVOLUTION OF A SEX-LINKED
GENETIC FACTOR

by

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I. INTRODUCTION

The fact that genes are the primary units responsible for the transmission of heritable characters has led geneticists to study gene distribution. It is not unbelievable that the pressures of environmental factors like mutation, selection, migration and many others, would likely change the genotypic make up of a certain population. Any change that occurs consistently in every generation over a long period of time should gradually change the gene frequencies in a population. This is the simplest way of defining evolution, a sequence of changes in the genes.

Having appropriate population models and assumptions, and by application of probability theories, it is always possible, in the changing states in a population, to determine the transition probabilities. But this is not enough to give us a good knowledge of gene distribution. Previous workers and workers of today in this field have the ultimate aim of finding the probability distribution of the genes. This problem has been solved in principle when genetics became an example of stochastic processes, in which Wright's diffusion theory (14) and earlier, the work of Fisher (6,7), Kolmogorov (9) play a central role. There remains, however, the task of building reasonably adequate models to explain population behaviour, for which the solutions are tractable.

The objectives of this study, through the aid of existing theories in genetics and probability and review of previous results are (i) to establish the transition probabilities for the possible states in the population from time t to time t+1 for a particular model, (ii) to obtain expectations of the change of a properly defined variable for the possible states in the population, (iii) to verify the applicability of the diffusion approximation as used by Watterson (13), and lastly (iv) to find the probability distribution of gene using the diffusion equation (or Fokker-Planck equation) studied extensively by Feller (4) and whose various forms of solutions were discussed by Bharucha-Reid (2), Kimura (8), Li (10), Moran (11,12), Watterson (13), and Wright (14).

In this thesis, we consider one particular population model the study of which has not been done before. Here, we are dealing with sex-linked factors rather than autosomal which previous workers have dealt with. The influences of the environment on the population are mutation, selection, random mating, and overlapping generations. For brief descriptions and definitions of these concepts, we use those given by Moran (11).

The genetic factor is of the simplest type. It is controlled by a single locus on a choromosome, at which either of two alleles "a" or "A" can occur. The

individuals are dioecious, that is either male or female. Since we are dealing with sex-linked genes (genes located on sex chromosomes), the genotypes for the males are haploid, that is either "a" or "A" and for the females, they are diploid and either "aa", "Aa" or "AA". A mutation is a rare instantaneous transition from one gene into its allele, say a →A or A → a. We assume that mutation occurs only among 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 genotypes, or indirectly, by varying the life expectations. We shall use the latter approach. By random mating is meant that, in the case of bisexual organisms as in our case, any one individual of one sex is equally likely to mate any one individual of the opposite sex. In other words, the frequency of a certain type of mating is dictated by chance. The term "panmixia" is sometimes used as a synonym of random mating and the population is said to be panmictic. Finally, the generation structure of the population is overlapping with deaths (and births) occurring one at a time, as opposed to non-overlapping generations in which mating occurs between them (populations with seasonal life cycle).

In the solution of the probability distribution of the "a" gene we are actually dealing with a bivariate case for we have "a" and "A" types of genes. But the difficulty, according to Feller (4) is overcome by the assumption of a large but constant population size, for which it is sufficient to deal with a univariate population of a-gene only and consider the proportion of "a" genes as an approximately continuous variable. This assumption greatly facilitates the mathematical theory. If the population size were itself a random variable, the resulting bivariate process would be extremely difficult to handle.

II. DESCRIPTION OF THE MODEL

Various population models have already been considered by previous workers on the theory of the distribution of gene frequencies. Moran (11) used both overlapping and non-overlapping generations for a single locus in a population of diploid individuals, with two sexes, subject to mutation, non-random mating and phenotypic selection. Further, Watterson (13) has covered the cases for monoecious and dioecious populations, haploid and diploid individuals, random and non-random mating, overlapping and non-overlapping generations, etc., subject to influences of mutation, selection, and migration.

For our case, we deal with a large population usually denoted by N, equal to N_1+N_2, where N_1 and N_2 are the numbers of males and females, respectively. The individuals in the population die one by one and are replaced by others of the same sex.

We consider a single locus at which there is one of two alleles and thus the N_1 haploid individuals in the population have one of the genotypes "a" or "A" and N_2 diploid individuals in the population have the genotypes "aa", "Aa" or "AA". We suppose that the number of these genotypes among the male population at time t are k_t, and N_1-k_t, respectively, and similarly r_t, $N_2-r_t-s_t$, and s_t amongst the females. And therefore, the numbers $(k_t; r_t, s_t)$ define the state of the system at time t. The only environmental factors influencing the population are mutation and selection.

III. THE CASE OF OVERLAPPING GENERATIONS

Unlike the case of non-overlapping generations where the entire population dies at the same time and is replaced by a new generation, overlapping generations deals with the case where individuals die one by one. For our case, we suppose that when one individual dies, it is replaced by one of the same sex.

Summarizing the notation, at any given time t, in the population we have the following:

Table I
Genotypes and Numbers of Individuals
for Males and Females

Sex	:	Males	:	Females		
Genotypes	:	a	A	: aa	Aa	AA
No. of individuals:		k_t	N_1-k_t	: r_t	$N_2-r_t-s_t$	s_t

For convenience we introduce random variables $X_t = k_t/N_1$, $Y_t = r_t/N_2$, and $Z_t = s_t/N_2$. Suppose to get to time t+1, one individual dies and is replaced by one of the same sex. Then we can find the probability of an individual dying at time t. We consider two cases: random deaths and with selection.

Case I. <u>Chosen completely at random from N</u>:

$$Pr \text{ a dies} = k_t/N = N_1 X_t/N$$
$$Pr \text{ A dies} = (N_1-k_t)/N = N_1(1-X_t)/N$$
$$Pr \text{ aa dies} = r_t/N = N_2 Y_t/N \qquad (3.1)$$
$$Pr \text{ Aa dies} = (N_2-r_t-s_t)/N = N_2(1-Y_t-Z_t)/N$$
$$Pr \text{ AA dies} = s_t/N = N_2 Z_t/N$$

Case II. **With selection:**

Let α , β , γ and δ be some constants such that

$$\Pr\{\text{a dies}\} = N_1 X_t (1+\alpha) \Lambda^{-1}/N$$

$$\Pr\{\text{A dies}\} = N_1 (1-X_t) \Lambda^{-1}/N$$

$$\Pr\{\text{aa dies}\} = N_2 Y_t (1+\beta)(1+\delta) \Lambda^{-1}/N \qquad (3.2)$$

$$\Pr\{\text{Aa dies}\} = N_2 (1-Y_t-Z_t)(1+\gamma)(1+\delta) \Lambda^{-1}/N$$

$$\Pr\{\text{AA dies}\} = N_2 Z_t (1+\delta) \Lambda^{-1}/N$$

where δ is a selection constant acting against all females, and for the genotypes with in sexes, α is the selection constant against "a" in males, β is the selection constant against "aa" in females, and γ is the selection constant against "Aa" in females, and

$$\Lambda = N_1 X_t (1+\alpha)/N + N_1(1-X_t)/N$$
$$+[N_2(1+\delta)/N]\left[Y_t(1+\beta)+(1-Y_t-Z_t)(1+\gamma)+Z_t\right] \qquad (3.3)$$

is a normalizing fraction to make the death probabilities sum to unity. As a particular case, when the effect of the "a" gene is simply additive, we might take $\alpha = \gamma$, $\beta = 2\gamma$. In general, however, we allow that the "a" gene may have different effects in the male and female individuals, and that the selection against female aa is not necessarily twice that against the Aa genotype. We assume that α , β , γ and δ are of order of magnitude $O(1/N)$, i.e., $\alpha = \alpha_1/N$, $\beta = \beta_1/N$, $\gamma = \gamma_1/N$, and $\delta = \delta_1/N$ where α_1 , β_1 , γ_1 and δ_1 are constants (w.r.t.N). For, if it were not so, and the

α, β, etc. were constant irrespective of N, then these selective pressures would dominate the sampling variance in large populations and the process would be virtually deterministic. On the other hand, if for example $\alpha = 0(1/N^2)$, then its effect would be asymptotically negligible compared with the sampling variance. As with Moran's paper (11) we will consider the asymptotic behaviour of the system as N tends to infinity and we shall always assume that N_1/N_2 lies between fixed non-zero limits so that N, N_1 and N_2 are all of the same order and we can always replace an expression such as $0(1/N_1)$ by $0(1/N)$. With these assumptions, we have

$$\Lambda = 1 + \frac{1}{N}\left[\alpha N_1 X_t + \gamma N_2(1-Y_t-Z_t) + \beta N_2 Y_t \right.$$
$$\left. + \delta N_2 Y_t + \delta N_2(1-Y_t-Z_t) + \delta N_2 Z_t + 0(1/N) \right]$$

$$\approx 1 + 0(1/N) = 1 + V \text{ say,} \qquad (3.4)$$

and also

$$\Lambda^{-1} \approx 1 - V. \qquad (3.5)$$

Now, the union of male and female gametes will give rise to a new individual. Sex is determined by two chromosomes; the homogametic type CC for the females and the heterogametic type CO (or C-) for the males, where C denotes the sex chromosome. When the C-eggs unite with the O-sperms, they form the male offspring. When they unite with the C-sperms, they form the female offspring. Note that a son always has the father's

O-chromosome. For one generation, we illustrate the formation of sex when male mates with the female.
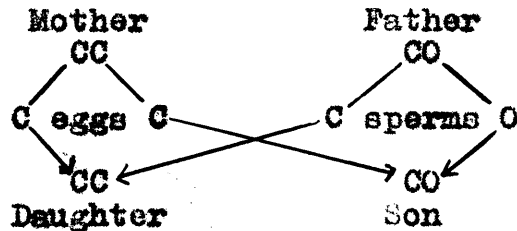
We consider two cases for the development of offspring:

Case I. <u>Choose a male parent at random from N_1 and a female parent at random from N_2</u>:

Under this situation, the following sets of mating probabilities are established at time t:

$$\Pr\{ a \times aa \} = X_t Y_t$$
$$\Pr\{ a \times Aa \} = X_t(1-Y_t-Z_t)$$
$$\Pr\{ a \times AA \} = X_t Z_t \qquad (3.6)$$
$$\Pr\{ A \times aa \} = (1-X_t)Y_t$$
$$\Pr\{ A \times Aa \} = (1-X_t)(1-Y_t-Z_t)$$
$$\Pr\{ A \times AA \} = (1-X_t)Z_t$$

From the preceding results and noting how sex is determined in mating process, we obtained the following table of offspring probabilities, conditional on its sex and on the parents' genotypes:

Table II

Offspring "Conditional" Probabilities

(Without Mutation)

Mating parents:		SEX			
	:	Male		:	Female
a x aa	:	a:1		:	aa:1
a x Aa	:	A:$\frac{1}{2}$	a:$\frac{1}{2}$	:	Aa:$\frac{1}{2}$ aa:$\frac{1}{2}$
a x AA	:	A:1		:	Aa:1
A x aa	:	a:1		:	Aa:1
A x Aa	:	A:$\frac{1}{2}$	a:$\frac{1}{2}$	:	AA:$\frac{1}{2}$ Aa:$\frac{1}{2}$
A x AA	:	A:1		:	AA:1

For convenience, we drop the subscript t throughout the algebraic operations for computations of probabilities. Otherwise, the use of subscript will be retained whenever necessary. Using results obtained in (3.6) and Table II, the probabilities for offspring, conditional on the sex of the dying individual are as follows:

$$p_M(a) = XY + \tfrac{1}{2}X(1-Y-Z) + (1-X)Y + \tfrac{1}{2}(1-X)(1-Y-Z)$$
$$= \tfrac{1}{2}(1+Y-Z)$$

$$p_M(A) = \tfrac{1}{2}X(1-Y-Z) + XZ + \tfrac{1}{2}(1-X)(1-Y-Z) + (1-X)Z$$
$$= \tfrac{1}{2}(1-Y+Z)$$

$$p_F(aa) = XY + \tfrac{1}{2}X(1-Y-Z) = \tfrac{1}{2}X(1+Y-Z) \qquad (3.7)$$

$$p_F(Aa) = \tfrac{1}{2}X(1-Y-Z) + XZ + (1-X)Y + \tfrac{1}{2}(1-X)(1-Y-Z)$$
$$= \tfrac{1}{2}(1+Y-Z+2XZ-2XY)$$

$$p_F(AA) = \tfrac{1}{2}(1-X)(1-Y-Z) + (1-X)Z = \tfrac{1}{2}(1-X)(1-Y+Z)$$

where in the above expressions, for example, the notation $p_M(a)$ denotes the probability that an offspring of type a is produced by the population when a male dies.

The system can move from the state $(k_t; r_t, s_t)$ into one of the eight states below with their corresponding transition probabilities. It can also remain in state $(k_t; r_t, s_t)$, but it is not necessary to calculate explicitly the probability of this happening.

(i) $(k_t+1; r_t, s_t)$ $\frac{1}{N}N_1(1-X)p_M(a)\Lambda^{-1}$

(ii) $(k_t-1; r_t, s_t)$ $\frac{1}{N}N_1(1+\alpha)Xp_M(A)\Lambda^{-1}$

(iii) $(k_t; r_t+1, s_t)$ $\frac{1}{N}N_2(1+\gamma)(1+\delta)(1-Y-Z)p_F(aa)\Lambda^{-1}$

(iv) $(k_t; r_t-1, s_t)$ $\frac{1}{N}N_2(1+\beta)(1+\delta)Yp_F(Aa)\Lambda^{-1}$

(v) $(k_t; r_t+1, s_t-1)$ $\frac{1}{N}N_2(1+\delta)Zp_F(aa)\Lambda^{-1}$

(vi) $(k_t; r_t-1, s_t+1)$ $\frac{1}{N}N_2(1+\beta)(1+\delta)Yp_F(AA)\Lambda^{-1}$

(vii) $(k_t; r_t, s_t+1)$ $\frac{1}{N}N_2(1+\gamma)(1+\delta)(1-Y-Z)p_F(AA)\Lambda^{-1}$

(viii) $(k_t; r_t, s_t-1)$ $\frac{1}{N}N_2(1+\delta)Zp_F(Aa)\Lambda^{-1}$

(3.8)

These probabilities are obtained by multiplying the conditional probabilities (3.7) by the probabilities of deaths in (3.2).

Case II. **With** **mutation**:

We introduce the symbol $\mu = \Pr\{a \to A\}$ as the probability that an "a" gene mutates to "A", and $\zeta = \Pr\{A \to a\}$, and assume $\mu = \mu_1/N$, $\zeta = \mu_2/N$ where

μ_1 and μ_2 are constants (w.r.t.N). As in Case I, we have the random mating probabilities (3.6), but unlike in Case I we must allow for the probability that the gametes from the mating parents may mutate. Then any pair of mating genotypes could give rise to an offspring of any genotype, with the following conditional probabilities:

Table III

Offspring "Conditional" Probabilities
(With Mutation)

Mating parents:	Male		Female		
	a	A	aa	Aa	AA
a x aa	$1-\mu$	μ	$(1-\mu)^2$	$2\mu(1-\mu)$	μ^2
a x Aa	$\frac{1}{2}(1-\mu+\zeta)$	$\frac{1}{2}(1+\mu-\zeta)$	$\frac{1}{2}(1-\mu)(1-\mu+\zeta)$	$\frac{1}{2}[(1-\mu)(1+\mu-\zeta)+\mu(1-\mu+\zeta)]$	$\frac{1}{2}\mu(1+\mu-\zeta)$
a x AA	ζ	$1-\zeta$	$(1-\mu)\zeta$	$(1-\mu)(1-\zeta)+\mu\zeta$	$\mu(1-\zeta)$
A x aa	$1-\mu$	μ	$(1-\mu)\zeta$	$(1-\mu)(1-\zeta)+\mu\zeta$	$\mu(1-\zeta)$
A x Aa	$\frac{1}{2}(1-\mu+\zeta)$	$\frac{1}{2}(1+\mu-\zeta)$	$\frac{1}{2}(1-\mu+\zeta)\zeta$	$\frac{1}{2}[(1-\zeta)(1-\mu+\zeta)+\zeta(1+\mu-\zeta)]$	$\frac{1}{2}(1-\zeta)(1+\mu-\zeta)$
A x AA	ζ	$1-\zeta$	ζ^2	$2\zeta(1-\zeta)$	$(1-\zeta)^2$

Using again (3.6) and Table III, we obtain the offspring probabilities (3.9) where terms of order $O(1/N^2)$ are not explicitly shown. We use a prime to denote offspring probabilities under the pressure of selection and mutation.

$$p'_M(a) = \tfrac{1}{2}\left[1+Y-Z+ \gamma(1-Y+Z)-\mu(1+Y-Z)\right]$$

$$p'_M(A) = \tfrac{1}{2}\left[1-Y+Z- \gamma(1-Y+Z)+\mu(1+Y-Z)\right]$$

$$p'_F(aa) = \tfrac{1}{2}\left[X(1+Y-Z)+ \gamma(1+Y-Z)+2\gamma X(Z-Y)\right.$$
$$\left. -2\mu X(1+Y-Z)+O(1/N^2)\right]$$

$$p'_F(Aa) = \tfrac{1}{2}\left[1+Y-Z+2XZ-2XY- \mu(1+Y-Z)+ \gamma(1-3Y+3Z)\right.$$
$$\left. +2\mu X(1+2Y-2Z)-2\gamma X(1-2Y+2Z)+O(1/N^2)\right]$$

$$p'_F(AA) = \tfrac{1}{2}\left[(1-X)(1-Y+Z)+ \mu(1+Y-Z)+2\mu X(Z-Y)\right.$$
$$\left. -2\gamma(1-Y+Z)+2\gamma X(1-Y+Z)+O(1/N^2)\right]$$

(3.9)

Again, these are conditional on sex only. The eight possible states now will have different transition probabilities as shown below:

(i) $(k_t+1;r_t,s_t)$ $\frac{1}{N}N_1(1-X)p'_M(a)\Lambda^{-1}$

(ii) $(k_t-1;r_t,s_t)$ $\frac{1}{N}N_1(1+\alpha)Xp'_M(A)\Lambda^{-1}$

(iii) $(k_t;r_t+1,s_t)$ $\frac{1}{N}N_2(1+\gamma)(1+\delta)(1-Y-Z)p'_F(aa)\Lambda^{-1}$

(iv) $(k_t;r_t-1,s_t)$ $\frac{1}{N}N_2(1+\beta)(1+\delta)Yp'_F(Aa)\Lambda^{-1}$

(v) $(k_t;r_t+1,s_t-1)$ $\frac{1}{N}N_2(1+\delta)Zp'_F(aa)\Lambda^{-1}$ (3.10)

(vi) $(k_t;r_t-1,s_t+1)$ $\frac{1}{N}N_2(1+\beta)(1+\delta)Yp'_F(AA)\Lambda^{-1}$

(vii) $(k_t;r_t,s_t+1)$ $\frac{1}{N}N_2(1+\gamma)(1+\delta)(1-Y-Z)p'_F(AA)\Lambda^{-1}$

(viii) $(k_t;r_t,s_t-1)$ $\frac{1}{N}N_2(1+\delta)Zp'(Aa)\Lambda^{-1}$

We note that when there are no mutations, results (3.9) and (3.10) are the same as (3.7) and (3.8), respectively.

IV. APPROACH TO GENERAL PROBLEM

We consider now the change in the frequency of "a" genes in the whole population as influenced by the evolutionary factors of mutation and selection. Going from the state at time t to the possible states at time t+1 (equivalent to 1/N generations), the changes in the genotype numbers would also change the gene frequencies in the population. The "a" frequency is

$$\frac{1}{N_1+2N_2}(k_t+2r_t+N_2-r_t-s_t) = \frac{1}{N_1+2N_2}(k_t+N_2+r_t-s_t)$$

$$= \frac{1}{N_1+2N_2}\left[N_1X_t+N_2(1+Y_t-Z_t)\right]$$

$$= \frac{1}{(N_1/N_2)+2}\left[N_1X_t/N_2+(1+Y_t-Z_t)\right] \quad (4.1)$$

However, instead of discussing this variable, we shall define at time t, $U = \frac{1}{3}+\frac{1}{3}(X+Y-Z)$. As $N\to\infty$ and keeping N_1/N_2 constant $= R$ say, we shall subsequently show that, in a certain sense, $X\approx U$, $Y\approx U^2$, $Z\approx(1-U)^2$, and then

$$\frac{1}{(N_1/N_2)+2}\left[N_1X_t/N_2+(1+Y_t-Z_t)\right]\approx \frac{1}{R+2} RU+1+U^2-(1-U)^2$$

$$= \frac{(RU+2U)}{R+2}$$

$$= U \quad (4.2)$$

Thus,

$$U \approx \text{proportion of "a" when } N_1 \neq N_2$$

$$= \text{proportion of "a" when } N_1 = N_2,$$

and, in fact, the determination of the distribution of U is sufficient to completely determine, not only the

behaviour of the true "a" gene frequency, but also that of the individual genotype frequencies. We note the following changes in U from time t to time t+1 corresponding to the possible changes in states of population.

(a) $\qquad$ $X \longrightarrow X + \frac{1}{N_1}$ $\qquad\qquad$ $U \longrightarrow U + \frac{1}{3N_1}$

$\qquad$ or $X \longrightarrow X - \frac{1}{N_1}$ $\qquad\qquad$ $U \longrightarrow U - \frac{1}{3N_1}$

(b) $\qquad$ $Y \longrightarrow Y + \frac{1}{N_2}$ $\qquad\qquad$ $U \longrightarrow U + \frac{1}{3N_2}$

$\qquad$ or $Y \longrightarrow Y - \frac{1}{N_2}$ $\qquad\qquad$ $U \longrightarrow U - \frac{1}{3N_2}$ $\qquad\qquad$ (4.3)

(c) $\qquad$ $Y \longrightarrow Y + \frac{1}{N_2}$, $Z \longrightarrow Z - \frac{1}{N_2}$ $\quad$ $U \longrightarrow U + \frac{2}{3N_2}$

$\qquad$ or $Y \longrightarrow Y - \frac{1}{N_2}$, $Z \longrightarrow Z + \frac{1}{N_2}$ $\quad$ $U \longrightarrow U - \frac{2}{3N_2}$

(d) $\qquad$ $Z \longrightarrow Z + \frac{1}{N_2}$ $\qquad\qquad$ $U \longrightarrow U - \frac{1}{3N_2}$

$\qquad$ or $Z \longrightarrow Z - \frac{1}{N_2}$ $\qquad\qquad$ $U \longrightarrow U + \frac{1}{3N_2}$

We consider now the contributions to $E(U_{t+1}-U_t)$ and $E(U_{t+1}-U_t)^2$ for each case above. We shall establish these expectations separately for selection pressure alone, and for selection and mutation pressures combined. For the moment, the expectations are taken conditional on a given state in the population at time t.

4.1 Expectations under the influence of selection:

Using results (3.5), (3.7), (3.8), and (4.3), we obtain the following, neglecting terms of order higher than $O(1/N^2)$:

Case (a). When $X \longrightarrow X + \frac{1}{N_1}$ or $X \longrightarrow X - \frac{1}{N_1}$

$$
\begin{aligned}
E(U_{t+1} - U_t) &= \frac{1}{3N_1}\Big[\Pr\{k_t+1; r_t, s_t\} - \Pr\{k_t-1; r_t, s_t\} \Big] \\
&= \frac{1}{3N_1 N}\Big[N_1(1-X)p_M(a) - (1+\alpha)Xp_M(A) \Big]\Lambda^{-1} \\
&= \frac{1}{6N}\Big[(1-X)(1+Y-Z) - X(1-Y+Z) \Big] \\
&\quad + \frac{V}{6N}\Big[X(1-Y+Z) - (1-X)(1+Y-Z) \Big] \\
&\quad - \frac{1}{6N}\alpha\, X(1-Y+Z) \qquad\qquad (4.4)
\end{aligned}
$$

$$
\begin{aligned}
E(U_{t+1} - U_t)^2 &= (1/9N_1^2)\Big[\Pr\{k_t+1; r_t, s_t\} + \Pr\{k_t-1; r_t, s_t\} \Big] \\
&= (N_1/9N_1^2 N)\Big[(1-X)p_M(a) + (1+\alpha)Xp_M(A) \Big]\Lambda^{-1} \\
&= \frac{1}{18N_1 N}\Big[(1-X)(1+Y-Z) + X(1-Y+Z) \Big] \qquad (4.5)
\end{aligned}
$$

Case (b). When $Y \longrightarrow Y + \frac{1}{N_2}$ or $Y \longrightarrow Y - \frac{1}{N_2}$

$$
\begin{aligned}
E(U_{t+1} - U_t) &= \frac{1}{3N_2}\Big[\Pr\{k_t; r_t+1, s_t\} - \Pr\{k_t; r_t-1, s_t\} \Big] \\
&= \frac{1}{3N_2 N}\Big[N_2(1+\gamma)(1+\delta)(1-Y-Z)p_F(aa) \\
&\qquad - (1+\beta)(1+\delta)Yp_F(Aa) \Big]\Lambda^{-1} \\
&= \frac{1}{6N}\Big[X(1-Y-Z)(1+Y-Z) - Y(1+Y-Z+2XZ-2XY) \Big] \\
&\quad - \frac{1}{6N}\beta\, Y(1+Y-Z+2XZ-2XY) \\
&\quad + \frac{1}{6N}\gamma\, X(1-Y-Z)(1+Y-Z) \\
&\quad + \frac{1}{6N}\delta\Big[X(1-Y-Z)(1+Y-Z) - Y(1+Y-Z+2XZ-2XY) \Big] \\
&\quad - \frac{1}{6N}V\Big[X(1-Y-Z)(1+Y-Z) - Y(1+Y-Z+2XZ-2XY) \Big] \quad (4.6)
\end{aligned}
$$

$$E(U_{t+1}-U_t)^2 = (1/9N_2^2)\Big[\Pr\{k_t;r_t+1,s_t\}+\Pr\{k_t;r_t-1,s_t\}\Big]$$

$$= (N_2/9N_2^2N)\Big[(1+\gamma)(1+\delta)(1-Y-Z)p_F(aa)$$

$$+(1+\beta)(1+\delta)Yp_F(Aa)\Big]\Lambda^{-1}$$

$$= \frac{1}{18N_2N}\Big[X(1-Y-Z)(1+Y-Z)+Y(1+Y-Z+2XZ-2XY)\Big] \quad (4.7)$$

Case (c). When $Y \rightarrow Y + \frac{1}{N_2}$ and $Z \rightarrow Z - \frac{1}{N_2}$

or $Y \rightarrow Y - \frac{1}{N_2}$ and $Z \rightarrow Z + \frac{1}{N_2}$

$$E(U_{t+1}-U_t) = \frac{2}{3N_2}\Big[\Pr\{k_t;r_t+1,s_t-1\}-\Pr\{k_t;r_t-1,s_t+1\}\Big]$$

$$= \frac{2}{3N_2N_2}N_2\Big[(1+\delta)Zp_F(aa)-(1+\beta)(1+\delta)Yp_F(AA)\Big]\Lambda^{-1}$$

$$= \frac{1}{3N}\Big[XZ(1+Y-Z)-Y(1-X)(1-Y+Z)\Big]$$

$$-\frac{1}{3N}\beta\, Y(1-X)(1-Y+Z)$$

$$+\frac{1}{3N}\delta\Big[XZ(1+Y-Z)-Y(1-X)(1-Y+Z)\Big]$$

$$-\frac{\gamma}{3N}\Big[XZ(1+Y-Z)-Y(1-X)(1-Y+Z)\Big] \quad (4.8)$$

$$E(U_{t+1}-U_t)^2 = (4/9N_2^2)\Big[\Pr\{k_t;r_t+1,s_t-1\}+\Pr\{k_t;r_t-1,s_t+1\}\Big]$$

$$= (4N_2/9N_2N)\Big[(1+\delta)Zp_F(aa)+(1+\beta)(1+\delta)Yp_F(AA)\Big]\Lambda^{-1}$$

$$= \frac{2}{9N_2N}\Big[XZ(1+Y-Z)+Y(1-X)(1-Y+Z)\Big] \quad (4.9)$$

Case (d). When $Z \longrightarrow Z + \frac{1}{N_2}$ or $Z \longrightarrow Z - \frac{1}{N_2}$

$$E(U_{t+1}-U_t) = \frac{1}{3N_2}\left[\Pr\{k_t; r_t, s_t-1\} - \Pr\{k_t; r_t, s_t+1\}\right]$$

$$= \frac{1}{3N_2 N}N_2\left[(1+\delta)Zp_F(Aa)-(1+\gamma)(1+\delta)(1-Y-Z)p_F(AA)\right]\Lambda^{-1}$$

$$= \frac{1}{6N}\left[Z(1+Y-Z+2XZ-2XY)-(1-X)(1-Y-Z)(1-Y+Z)\right]$$

$$\quad - \frac{1}{6N}\gamma(1-X)(1-Y-Z)(1-Y+Z)$$

$$\quad + \frac{1}{6N}\delta\left[Z(1+Y-Z+2XZ-2XY)-(1-X)(1-Y-Z)(1-Y+Z)\right]$$

$$\quad - \frac{V}{6N}\left[Z(1+Y-Z+2XZ-2XY)-(1-X)(1-Y-Z)(1-Y+Z)\right] \quad (4.10)$$

$$E(U_{t+1}-U_t)^2 = (1/9N_2^2)\left[\Pr\{k_t; r_t, s_t+1\} + \Pr\{k_t; r_t, s_t-1\}\right]$$

$$= (N_2/9N_2^2 N)\left[(1+\gamma)(1+\delta)(1-Y-Z)p_F(AA)\right.$$

$$\quad \left. +(1+\delta)Zp_F(Aa)\right]\Lambda^{-1}$$

$$= \frac{1}{18N_2 N}\left[(1-X)(1-Y-Z)(1-Y+Z)\right.$$

$$\quad \left. +Z(1+Y-Z+2XZ-2XY)\right] \quad (4.11)$$

The four contributions to the expectations can be added to give

$$E(U_{t+1}-U_t) = \frac{1}{6N}\delta(2X-Y+Z-1) - \frac{1}{6N}\alpha X(1-Y+Z)$$

$$\quad - \frac{1}{6N}\beta Y(3-2X-Y+Z) - \frac{1}{6N}\gamma(1-Y-Z)(2X+Y-Z-1) \quad (4.12)$$

and

$$E(U_{t+1}-U_t)^2 = \frac{1}{18N_1 N}(1+Y-Z+2XZ-2XY)$$

$$\quad + \frac{1}{18N_2 N}\left[1+3Y+Z+2(Z-Y)(X+Y-Z)\right] \quad (4.13)$$

In terms of U, and making the substitutions $X \approx U$, $Y \approx U^2$, and $Z \approx (1-U)^2$, the last two equations simplify to

$$E(U_{t+1} - U_t) \approx \frac{U(1-U)}{3N}\left[2(2U-1)\gamma - 2U\beta - \alpha\right], \quad (4.14)$$

and

$$E(U_{t+1} - U_t)^2 \approx \frac{2U(1-U)}{9N}\left[\frac{1}{N_1} + \frac{2}{N_2}\right] \quad (4.15)$$

4.2 Expectations under the influence of selection and mutation:

Results are obtained using (3.5), (3.9), (3.10), and (4.3). Like the previous expectations, results obtained here involve only terms of $O(1/N)$ and $O(1/N^2)$ and all other higher order terms are neglected.

Case (a). When $X \longrightarrow X + \frac{1}{N_1}$ or $X \longrightarrow X - \frac{1}{N_1}$

$$
\begin{aligned}
E(U_{t+1} - U_t) &= \frac{1}{3N_1}\left[Pr\{k_t+1; r_t, s_t\} - Pr\{k_t-1; r_t, s_t\}\right] \\
&= \frac{1}{3N_1}N_1\left[(1-X)p_M'(a) - (1+\alpha)Xp_M'(A)\right]\Lambda^{-1} \\
&= \frac{1}{6N}\left[(1-X)(1+Y-Z) - X(1-Y+Z)\right] \\
&\quad - \frac{1}{6N}\alpha X(1-Y+Z) + \frac{1}{6N}\zeta(1-Y+Z) - \frac{1}{6N}\mu(1+Y-Z) \\
&\quad + \frac{V}{6N}\left[X(1-Y+Z) - (1-X)(1+Y-Z)\right] \quad (4.16)
\end{aligned}
$$

$$
\begin{aligned}
E(U_{t+1} - U_t)^2 &= (1/9N_1^2)\left[Pr\{k_t+1; r_t, s_t\} + Pr\{k_t-1; r_t, s_t\}\right] \\
&= (N_1/9N_1^2 N)\left[(1-X)p_M'(a) + (1+\alpha)Xp_M'(A)\right]\Lambda^{-1} \\
&= \frac{1}{18N_1 N}\left[(1-X)(1+Y-Z) + X(1-Y+Z)\right] \quad (4.17)
\end{aligned}
$$

Case (b). When $Y \rightarrow Y + \frac{1}{N_2}$ or $Y \rightarrow Y - \frac{1}{N_2}$

$$E(U_{t+1}-U_t) = \frac{1}{3N_2}\left[\Pr\{k_t;r_t+1,s_t\} - \Pr\{k_t;r_t-1,s_t\}\right]$$

$$= \frac{1}{3N_2N}N_2\left[(1+\gamma)(1+\delta)(1-Y-Z)p'_F(aa)\right.$$

$$\left. - (1+\beta)(1+\delta)Yp'_F(Aa)\right]\Lambda^{-1}$$

$$= \frac{1}{6N}\left[(1-Y-Z)X(1+Y-Z)-Y(1+Y-Z+2XZ-2XY)\right]$$

$$+ \frac{1}{6N^2}\left[(1-Y-Z)(1+Y-Z+2XZ-2XY)\right.$$

$$\left. -Y\{1-3Y+3Z-2X(1-2Y+2Z)\}\right]$$

$$+ \frac{1}{6N}\mu\left[Y(1+Y-Z)-2XY(1+2Y-2Z)-2X(1+Y-Z)(1-Y-Z)\right]$$

$$- \frac{1}{6N}\beta\, Y(1+Y-Z+2XZ-2XY)$$

$$+ \frac{1}{6N}\gamma\,(1-Y-Z)X(1+Y-Z)$$

$$+ \frac{1}{6N}\delta\left[(1-Y-Z)X(1+Y-Z)-Y(1+Y-Z+2XZ-2XY)\right]$$

$$+ \frac{V}{6N}\left[Y(1+Y-Z+2XZ-2XY)-(1-Y-Z)X(1+Y-Z)\right] \quad (4.18)$$

$$E(U_{t+1}-U_t)^2 = (1/9N_2^2)\left[\Pr\{k_t;r_t+1,s_t\} + \Pr\{k_t;r_t-1,s_t\}\right]$$

$$= (N_2/9N_2^2N)\left[(1+\gamma)(1+\delta)(1-Y-Z)p'_F(aa)\right.$$

$$\left. + (1+\beta)(1+\delta)Yp'_F(Aa)\right]\Lambda^{-1}$$

$$= \frac{1}{18N_2N}\left[(1-Y-Z)X(1+Y-Z)+Y(1+Y-Z+2XZ-2XY)\right] \quad (4.19)$$

Case (c). When $Y \longrightarrow Y + \frac{1}{N_2}$ and $Z \longrightarrow Z - \frac{1}{N_2}$

or $Y \longrightarrow Y - \frac{1}{N_2}$ and $Z \longrightarrow Z + \frac{1}{N_2}$

$$
\begin{aligned}
E(U_{t+1}-U_t) &= \frac{2}{3N_2}\left[\Pr\{k_t; r_t+1, s_t-1\} - \Pr\{k_t; r_t-1, s_t+1\}\right] \\
&= \frac{2}{3N\,N_2}N_2\left[(1+\delta)Zp_F^!(aa)-(1+\beta)(1+\delta)Yp_F^!(AA)\right]\Lambda^{-1} \\
&= \frac{1}{3N}\left[XZ(1+Y-Z)-Y(1-X)(1-Y+Z)\right] \\
&\quad + \frac{1}{3N}\S\left[Z(1+Y-Z+2XZ-2XY)+2Y(1-X)(1-Y+Z)\right] \\
&\quad - \frac{1}{3N}\mu\left[XZ(1+Y-Z)+Y(1+Y-Z+2XZ-2XY)\right] \\
&\quad + \frac{1}{3N}\delta\left[XZ(1+Y-Z)-Y(1-X)(1-Y+Z)\right] \\
&\quad - \frac{1}{3N}\beta\,Y(1-X)(1-Y+Z) \\
&\quad + \frac{V}{3N}\left[Y(1-X)(1-Y+Z)-XZ(1+Y-Z)\right] \qquad (4.20)
\end{aligned}
$$

$$
\begin{aligned}
E(U_{t+1}-U_t)^2 &= (4/9N_2^2)\left[\Pr\{k_t; r_t+1, s_t-1\} + \Pr\{k_t; r_t-1, s_t+1\}\right] \\
&= (4N_2/9N_2^2 N)\left[(1+\delta)Zp_F^!(aa)+(1+\beta)(1+\delta)Yp_F^!(AA)\right]\Lambda^{-1} \\
&= \frac{2}{9N_2 N}\left[XZ(1+Y-Z)+Y(1-X)(1-Y+Z)\right] \qquad (4.21)
\end{aligned}
$$

Case (d). When $Z \longrightarrow Z + \frac{1}{N_2}$ or $Z \longrightarrow Z - \frac{1}{N_2}$

$$E(U_{t+1}-U_t) = \frac{1}{3N_2}\left[\Pr\{k_t;r_t,s_t-1\} - \Pr\{k_t;r_t,s_t+1\}\right]$$

$$= \frac{1}{3N_2N}N_2\left[(1+\delta)Zp_F'(Aa)-(1+\gamma)(1+\delta)(1-Y-Z)p_F'(AA)\right]\Lambda^{-1}$$

$$= \frac{1}{6N}\left[Z(1+Y-Z+2XZ-2XY)-(1-Y-Z)(1-X)(1-Y+Z)\right]$$

$$+ \frac{1}{6N}\beta\left[Z\{1-3Y+3Z-2X(1-2Y+2Z)\}\right.$$
$$\left.+2(1-Y-Z)(1-X)(1-Y+Z)\right]$$

$$\doteq \frac{1}{6N}\mu\left[Z\{(1+Y-Z)-2X(1+2Y-2Z)\}\right.$$
$$\left.+(1-Y-Z)(1+Y-Z+2XZ-2XY\right]$$

$$+ \frac{1}{6N}\delta\left[Z(1+Y-Z+2XZ-2XY)-(1-Y-Z)(1-X)(1-Y+Z)\right]$$

$$- \frac{1}{6N}\gamma(1-Y-Z)(1-X)(1-Y+Z)$$

$$+ \frac{1}{6N}V\left[(1-Y-Z)(1-X)(1-Y+Z)\right.$$
$$\left.-Z(1+Y-Z+2XZ-2XY)\right] \qquad (4.22)$$

$$E(U_{t+1}-U_t)^2 = (1/9N_2^2)\left[\Pr\{k_t;r_t,s_t+1\} + \Pr\{k_t;r_t,s_t-1\}\right]$$

$$= (N_2/9N_2^2N)\left[(1+\gamma)(1+\delta)(1-Y-Z)p_F'(AA)\right.$$
$$\left.+(1+\delta)Zp_F'(Aa)\right]\Lambda^{-1}$$

$$= \frac{1}{18N_2N}\left[(1-X)(1-Y-Z)(1-Y+Z)\right.$$
$$\left.+Z(1+Y-Z+2XZ-2XY)\right] \qquad (4.23)$$

In the same manner as with the effect of selection alone, we obtain the expectations of the change in U as the sum of the contributions from the four cases previously developed. Thus, in terms of X, Y, and Z

$$
\begin{aligned}
E(U_{t+1}-U_t) = & \frac{1}{3N}\zeta(2-X-Y+Z)-\frac{1}{3N}\mu(1+X+Y-Z) \\
& + \frac{1}{6N}\delta(2X-Y+Z-1)-\frac{1}{6N}\beta Y(3-2X-Y+Z) \\
& + \frac{1}{6N}\gamma(1-Y-Z)(2X+Y-Z-1) \\
& - \frac{1}{6N}\alpha X(1-Y+Z)
\end{aligned}
\tag{4.24}
$$

and

$$
\begin{aligned}
E(U_{t+1}-U_t)^2 = & \frac{1}{18N_1 N}(1+Y-Z+2XZ-2XY) \\
& + \frac{1}{18N_2 N}\left[1+3Y+Z+2(Z-Y)(X+Y-Z)\right]
\end{aligned}
\tag{4.25}
$$

In terms of U, (4.24) and (4.25) becomes

$$
\begin{aligned}
E(U_{t+1}-U_t) \approx & \frac{1}{N}\left[\zeta(1-U)-\mu U\right] \\
& + \frac{U(1-U)}{3N}\left[2(2U-1)\gamma-2U\beta-\alpha\right]
\end{aligned}
\tag{4.26}
$$

and

$$
E(U_{t+1}-U_t)^2 \approx \frac{2U(1-U)}{9N}\left[\frac{1}{N_1}+\frac{2}{N_2}\right]
\tag{4.27}
$$

We proceed now to justify the approximations $X \approx U$, $Y \approx U^2$, $Z \approx (1-U)^2$ used above.

V. APPLICABILITY OF DIFFUSION APPROXIMATION

As before, we define $U_t = \frac{1}{3} + \frac{1}{3}(X_t + Y_t - Z_t)$. We will consider now the expectations of $(X_{t+1} - U_{t+1})^2$, $(Y_{t+1} - U_{t+1}^2)^2$, and $\left[Z_{t+1} - (1 - U_{t+1})^2 \right]^2$.

By the aid of (4.3), the possible differences between X_{t+1} and U_{t+1} are as follows:

(a) $X_{t+1} - U_{t+1} = X_t - U_t + \frac{2}{3N_1}$ or $X_t - U_t - \frac{2}{3N_1}$

(b) $X_{t+1} - U_{t+1} = X_t - U_t - \frac{1}{3N_2}$ or $X_t - U_t + \frac{1}{3N_2}$

(c) $X_{t+1} - U_{t+1} = X_t - U_t - \frac{2}{3N_2}$ or $X_t - U_t + \frac{2}{3N_2}$ (5.1)

(d) $X_{t+1} - U_{t+1} = X_t - U_t + \frac{1}{3N_2}$ or $X_t - U_t - \frac{1}{3N_2}$

Then, the conditional expectation[1] of the differences is

$$
\begin{aligned}
E(X_{t+1} - U_{t+1}) = {} & X_t - U_t \\
& + \frac{2}{3N_1}\left[\Pr\{k_t+1; r_t, s_t\} - \Pr\{k_t-1; r_t, s_t\} \right] \\
& - \frac{1}{3N_2}\left[\Pr\{k_t; r_t+1, s_t\} - \Pr\{k_t; r_t-1, s_t\} \right] \\
& - \frac{2}{3N_2}\left[\Pr\{k_t; r_t+1, s_t-1\} - \Pr\{k; r_t-1, s_t+1\} \right] \\
& + \frac{1}{3N_2}\left[\Pr\{k_t; r_t, s_t+1\} - \Pr\{k_t; r_t, s_t-1\} \right]
\end{aligned}
$$

(5.2)

---

1. From now on, we distinguish conditional expectations by the symbol E, from unconditional expectations denoted by $\mathcal{E}$. Up till now, only conditional expectations have been needed.

Using (3.8), (5.2) becomes

$$E(X_{t+1} - U_{t+1})$$

$$= X_t - U_t + \Lambda^{-1} \frac{2}{3N}\left[(1-X)p_M(a) - (1+\alpha)Xp_M(A)\right]$$

$$- \Lambda^{-1}\frac{1}{3N}\left[(1+\gamma)(1+\delta)(1-Y-Z)p_F(aa) - (1+\beta)(1+\delta)Y_F(Aa)\right]$$

$$- \Lambda^{-1}\frac{2}{3N}\left[(1+\delta)Zp_F(aa) - (1+\beta)(1+\delta)Yp_F(AA)\right]$$

$$+ \Lambda^{-1}\frac{1}{3N}\left[(1+\gamma)(1+\delta)(1-Y-Z)p_F(AA) - (1+\delta)Zp_F(Aa)\right]$$

Ignoring terms of order $O(1/N^2)$, we get

$$E(X_{t+1} - U_{t+1})$$

$$= X_t - U_t + \frac{1}{3N}\left[(1-X)(1+Y-Z) - X(1-Y+Z)\right]$$

$$- \frac{1}{6N}\left[X(1-Y-Z)(1+Y-Z) - Y(1+Y-Z+2XZ-2XY)\right]$$

$$- \frac{1}{3N}\left[XZ(1+Y-Z) - Y(1-X)(1-Y+Z)\right]$$

$$+ \frac{1}{6N}\left[(1-Y-Z)(1-X)(1-Y+Z) - Z(1+Y-Z+2XZ-2XY)\right]$$

$$+ O(1/N^2) \tag{5.3}$$

Therefore, since

$$E\left[X_{t+1} - U_{t+1} - (X_t - U_t)\right]^2 = E(X_{t+1} - U_{t+1})^2$$

$$-2(X_t - U_t)E(X_{t+1} - U_{t+1}) + (X_t - U_t)^2$$

$$= O(1/N^2) \quad \text{because from (5.1), we}$$

see that $X_{t+1} - U_{t+1} - (X_t - U_t)$ is of order $O(1/N)$ and

squaring it will give the magnitude of order $O(1/N^2)$.

Then

$$E(X_{t+1} - U_{t+1})^2$$

$$= (X_t - U_t)^2 + \frac{2}{3N}(X_t - U_t)\left[(1-X)(1+Y-Z) - X(1-Y+Z)\right]$$

$$- \frac{1}{3N}(X_t - U_t)\left[X(1-Y-Z)(1+Y-Z) - Y(1+Y-Z+2XZ-2XY)\right]$$

$$- \frac{2}{3N}(X_t - U_t)\left[XZ(1+Y-Z) - Y(1-X)(1-Y+Z)\right]$$

$$+ \frac{1}{3N}(X_t - U_t)\left[(1-Y-Z)(1-X)(1-Y+Z) - Z(1+Y-Z+2XZ-2XY)\right]$$

$$+ O(1/N^2)$$

$$= (X_t - U_t)^2 + \frac{1}{3N}(X_t - U_t)(3+3Y-3Z-6X) + O(1/N^2) \qquad (5.4)$$

Expressing (5.4) in terms of X and U, it becomes

$$E(X_{t+1} - U_{t+1})^2 = (X_t - U_t)^2 + \frac{1}{3N}(X_t - U_t)(9U_t - 9X_t) + O(1/N^2)$$

$$= (1 - \frac{3}{N})(X_t - U_t)^2 + O(1/N^2) \qquad (5.5)$$

Let us consider now the differences between Y_{t+1} and U_{t+1}^2. Using (4.3) and the definition for U_t, we obtain the following possible changes from $Y_t - U_t^2$:

(a) $Y_{t+1} - U_{t+1}^2 = Y_t - U_t^2 - \frac{2}{3N_1}U_t - \frac{1}{9N_1^2}$ or $Y_t - U_t^2 + \frac{2}{3N_1}U_t - \frac{1}{9N_1^2}$

(b) $Y_{t+1} - U_{t+1}^2 = Y_t - U_t^2 + \frac{1}{3N_2}(3-2U_t) - \frac{1}{9N_2^2}$

$$\text{or } Y_t - U_t^2 - \frac{1}{3N_2}(3-2U_t) - \frac{1}{9N_2^2} \qquad (5.6)$$

(c) $Y_{t+1} - U_{t+1}^2 = Y_t - U_t^2 + \frac{1}{3N_2}(3-4U_t) - \frac{4}{9N_2^2}$

$$\text{or } Y_t - U_t^2 - \frac{1}{3N_2}(3-4U_t) - \frac{4}{9N_2^2}$$

(d) $Y_{t+1} - U_{t+1}^2 = Y_t - U_t^2 + \frac{2}{3N_2}U_t - \frac{1}{9N_2^2}$ or $Y_t - U_t^2 - \frac{2}{3N_2}U_t - \frac{1}{9N_2^2}$

Again, ignoring terms of order $O(1/N^2)$,

$$E(Y_{t+1}-U_{t+1}^2) = Y_t-U_t^2 - \frac{1}{3N}U_t\left[(1-X)(1+Y-Z)-X(1-Y+Z)\right]$$

$$- \frac{1}{3N}U_t\left[X(1-Y-Z)(1+Y-Z)-Y(1+Y-Z+2XZ-2XY)\right]$$

$$- \frac{2}{3N}U_t\left[XZ(1+Y-Z)-Y(1-X)(1-Y+Z)\right]$$

$$+ \frac{1}{3N}U_t\left[(1-Y-Z)(1-X)(1-Y+Z)-Z(1+Y-Z+2XZ-2XY)\right]$$

$$+ \frac{1}{2N}\left[X(1-Y-Z)(1+Y-Z)-Y(1-X)(1-Y+Z)\right]$$

$$+ \frac{1}{2N}\left[XZ(1+Y-Z)-Y(1-X)(1-Y+Z)\right]$$

$$+ O(1/N^2) \tag{5.7}$$

Therefore

$$E(Y_{t+1}-U_{t+1}^2)^2$$

$$= (Y_t-U_t^2)^2 - \frac{2}{3N}U_t(Y_t-U_t^2)\left[(1-X)(1+Y-Z)-X(1-Y+Z)\right]$$

$$- \frac{2}{3N}U_t(Y_t-U_t^2)\left[X(1-Y-Z)(1+Y-Z)-Y(1+Y-Z+2XZ-2XY)\right]$$

$$- \frac{4}{3N}U_t(Y_t-U_t^2)\left[XZ(1+Y-Z)-Y(1-X)(1-Y+Z)\right]$$

$$+ \frac{2}{3N}U_t(Y_t-U_t^2)\left[(1-Y-Z)(1-X)(1-Y+Z)-Z(1+Y-Z+2XZ-2XY)\right]$$

$$+ \frac{1}{N}(Y_t-U_t^2)\left[XZ(1+Y-Z)-Y(1-X)(1-Y+Z)\right]$$

$$+ \frac{1}{N}(Y_t-U_t^2)\left[(1-Y-Z)(1+Y-Z)X-Y(1+Y-Z+2XZ-2XY)\right]$$

$$+ O(1/N^2)$$

$$= (Y_t-U_t^2)^2 + \frac{1}{N}(Y_t-U_t^2)(X-2Y-XZ+XY) \tag{5.8}$$

Expressing (5.8) in terms of Y and U^2, X and U, the equation simplifies as

$$E(Y_{t+1} - U_{t+1}^2)^2$$

$$= (Y_t - U_t^2)^2 + \frac{1}{N}(Y_t - U_t^2) - 2(Y_t - U_t^2) + (2U_t - X_t)(U_t - X_t) + O(1/N^2)$$

$$= (1 - \frac{2}{N})(Y_t - U_t^2)^2 + \frac{1}{N}(Y_t - U_t^2)(2U_t - X_t)(U_t - X_t) + O(1/N^2)$$

$$(5.9)$$

Taking unconditional expectations of both sides of (5.5) and (5.9), we have the difference equations

$$\mathcal{E}(X_{t+1} - U_{t+1})^2 = (1 - \frac{3}{N})\mathcal{E}(X_t - U_t)^2 + O(1/N^2) \qquad (5.10)$$

and

$$(Y_{t+1} - U_{t+1}^2)^2 = (1 - \frac{2}{N})\mathcal{E}(Y_t - U_t^2)^2$$

$$+ \frac{1}{N}\mathcal{E}(Y_t - U_t^2)(2U_t - X_t)(U_t - X_t) + O(1/N^2)$$

$$(5.11)$$

Let $\mathcal{E}(X_t - U_t)^2 = A_t$. For some n, $2 > n > 1$ and also for n = 2, and for any given δ, $\varepsilon > 0$, there exists an $N_{\delta, \varepsilon}$ such that

$$A_N n_s \leq \delta \quad \text{for all } N > N_{\delta, \varepsilon} \text{ and all } s > \varepsilon \qquad (5.12)$$

that is,

$$A_N n_s \rightarrow 0 \text{ as } N \rightarrow \infty \text{ uniformly for s in } (\varepsilon, \infty) \text{ for}$$

any $\varepsilon > 0$. $\qquad (5.13)$

To show (5.13) is true, we proceed by considering (5.10) which can be written as

$$A_N{}^n{}_s = \left(1 - \frac{3}{N}\right)^{N^{3/2}\varepsilon} \cdot A_N{}^n{}_{s-N^{1/2}\varepsilon} + O(1/N^{1/2}) \quad \text{for any } n \geqslant \frac{3}{2} \tag{5.14}$$

Now

$$\left(1 - \frac{3}{N}\right)^{N^{3/2}\varepsilon} \leq \left| e^{-3N^{1/2}\varepsilon} \right| \to 0 \text{ as } N \to \infty \text{ for all } \varepsilon > 0,$$

$$\left| A_N{}^n{}_{s-N^{1/2}\varepsilon} \right| \leq \left(\frac{2}{3}\right)^2 \text{ for all } s \text{ because}$$

$$X - U = \frac{2}{3}X + \frac{1}{3}Z - \frac{1}{3}Y - \frac{1}{3} \text{ with } \max(X-U) = \frac{2}{3} \text{ (when } X=Z=1, Y=0)$$

$$\min(X-U) = -\frac{2}{3} \text{ (when } X=Z=0, Y=1)$$

and

$$O(1/N^{1/2}) \to 0 \text{ as } N \to \infty \text{ uniformly with } s \geqslant \varepsilon > 0.$$

For, the term $O(1/N^2)$ in (5.10) is a random variable dependent on time. At any time, this random variable is bounded by a certain constant of order $(1/N^2)$ and hence $O(1/N^{1/2})$ above also represents a bound uniform in time. Hence we have proved $A_N{}^n{}_s$ converges to zero as $N \to \infty$ uniformly for s in (ε, ∞) for any $\varepsilon > 0$.

Next we put $\mathcal{E}(Y_t - U_t^2)^2 = B_t$ and $\mathcal{E}(Y_t - U_t^2)(2U_t - X_t)(U_t - X_t) = C_t$ in (5.11). Then we get

$$B_{t+1} = \left(1 - \frac{2}{N}\right)B_t + \frac{1}{N}C_t + O(1/N^2) \tag{5.15}$$

For $n \geqslant \frac{3}{2}$ and v chosen such that $N^{3/2}v$ is an integer, $N^{3/2}v < N^n s$, we have

$$B_N{}^n{}_s = \left(1 - \frac{2}{N}\right)^{N^{3/2}v} B_N{}^n{}_{s-N^{3/2}v}$$

$$+ \frac{1}{N}\left[\sum_{w=0}^{N^{3/2}v-1} C_N{}^n{}_{s-N^{3/2}v+w}\left(1 - \frac{2}{N}\right)^{N^{3/2}v-w-1}\right] + O(1/N^{1/2}) \tag{5.16}$$

Now $|B|$ is bounded by 1, hence

$$(1-\frac{2}{N})^{N^{3/2}v}B \to 0 \text{ as } N \to \infty \text{ and } 0(1/N^{\frac{1}{3}}) \to 0 \text{ as } N \to \infty$$

Further

$$\left| \frac{1}{N}\sum_{w=0}^{N^{3/2}v-1} C(1-\frac{2}{N})^{N^{3/2}v-w-1} \right| \le \frac{1}{N}\left[\text{Max} |C| \right] \sum_{w}(1-\frac{2}{N})^{N^{3/2}v-w-1}$$

$$\le \left[\text{Max} |C| \right] \frac{1-(1-2/N)^{N^{3/2}v}}{N[1-(1-2/N)]}$$

$$< \left[\text{Max} |C| \right] \cdot \frac{1}{2} \text{ for } N > 2$$

Now $\displaystyle \text{Max}_{0 \le w \le N^{3/2}v-1} \left| C_N n_{s-N^{3/2}v+w} \right| = 0(1/N^{\frac{1}{4}}) \to \theta \text{ as } N \to \infty$

Proof:

$$\left| (Y_t-U_t^2)(2U_t-X_t)(U_t-X_t) \right| \le \left| Y_t-U_t^2 \right| \left| 2U_t-X_t \right| \left| U_t-X_t \right|$$

$$\left| C_t \right| \le \xi \left| Y_t-U_t^2 \right| \left| 2U_t-X_t \right| \left| U_t-X_t \right|$$

$$\le \xi \left[1 \cdot 2 \left| U_t-X_t \right| \right]$$

$$\le 2\sqrt{\xi (U_t-X_t)^2}$$

$$\therefore C_t^2 \le 4\xi(U_t-X_t)^2 = 4A_t$$

where $A_t = (1-\frac{3}{N})A_{t-1} + 0(1/N^2)$. Thus

$$A_N n_{s-N^{3/2}v+w} = (1-\frac{3}{N})^{N^{3/2}v} A_N n_{s-2N^{3/2}v+w} + 0(1/N^{\frac{1}{2}})$$

$$= 0(1/N^{\frac{1}{2}}) \text{ for all } w \text{ in } (0,N^{3/2}v-1)$$

Hence $\left| C_t \right| \le 2A_t^{\frac{1}{2}} = 0(1/N^{\frac{1}{4}})$.

Therefore we have shown that $B_N n_s$ converges to zero as $N \to \infty$ uniformly for $s > v > 0$ for $2 > n > 1$ and also for $n = 2$.

Similarly,

$$\left[Z_N n_s - (1 - U_N n_s)^2 \right]^2 \to 0 \text{ as } N \to \infty \text{ by symmetry.}$$

In particular, this means that X_{N2_s} converges in
mean square (m.s.) to U_{N2_s}, therefore it converges in
probability, and therefore the distribution of X_{N2_s}
converges to distribution of U_{N2_s}. Also, Y_{N2_s} converges
in m.s. to $U^2_{N2_s}$, therefore it converges in probability
and therefore the distribution of Y_{N2_s} converges to
distribution of $U^2_{N2_s}$. This concept of convergence is
given by Bartlett (1). We can deduce because of symmetry,
that the distribution of Z_{N2_s} converges to distribution
of $(1-U_{N2_s})^2$ by the same argument. And further, "true
gene frequency" and U have asymptotically the same
distribution.

VI. JUSTIFICATION OF THE DIFFUSION EQUATION

Consider the conditional expectation of

$\left[e^{\theta(U_{t+1}-U_t)}-1\right]$. Using the previous results we have

$$E\left[e^{\theta(U_{t+1}-U_t)}-1\right] = \frac{\theta}{1!}E(U_{t+1}-U_t) + \frac{\theta^2}{2!}E(U_{t+1}-U_t)^2$$

$$+ \frac{\theta^3}{3!}E(U_{t+1}-U_t)^3 + \frac{\theta^4}{4!}E(U_{t+1}-U_t)^4 + \cdots$$

$$= \frac{\theta}{N^2}\Big\{ \zeta'(1-U_t) - \mu'U_t$$

$$+ \frac{1}{3}U_t(1-U_t)\left[2(2U_t-1)\gamma' - 2U_t\beta' - \alpha'\right]\Big\}$$

$$+ \frac{\theta^2}{2}\frac{1}{N^2}\frac{2}{9}U_t(1-U_t)\left[\frac{N}{N_1} + \frac{2N}{N_2}\right]$$

$$+ \frac{\theta}{1!}\Big[E(U_{t+1}-U_t) - \frac{1}{N^2}\Big\{\zeta'(1-U_t) - \mu'U_t$$

$$+ \frac{1}{3}U_t(1-U_t)\left[2(2U_t-1)\gamma' - 2U_t\beta' - \alpha'\right]\Big\}\Big]$$

$$+ \frac{\theta^2}{2!}\Big[E(U_{t+1}-U_t)^2 - \frac{1}{N^2}\frac{2}{9}U_t(1-U_t)\left(\frac{N}{N_1} + \frac{2N}{N_2}\right)\Big]$$

$$+ \frac{\theta^3}{3!}\, 0(1/N^3) \tag{6.1}$$

because $|U_{t+1}-U_t| \leq \max\left(\frac{1}{3N_1}, \frac{2}{3N_2}\right)$ and so

$E(U_{t+1}-U_t)^3 = 0(1/N^3)$, etc. We write (6.1) as

$$E\left[e^{\theta(U_{t+1}-U_t)}-1\right] = \frac{1}{N^2}\Big[\theta b(U_t) + \frac{\theta^2}{2}\, a(U_t) + \theta W_N(\theta, t)\Big] \tag{6.2}$$

where

$$b(U_t) = \zeta'(1-U_t) - \mu'U_t$$

$$+ \frac{1}{3}U_t(1-U_t)\left[2(2U_t-1)\gamma' - 2U_t\beta' - \alpha'\right]$$

$$a(U_t) = \frac{2}{9}U_t(1-U_t)\left[\frac{N}{N_1} + \frac{2N}{N_2}\right]$$

$$W_N(\theta,t) = E(U_{t+1}-U_t) - \left\{\zeta'(1-U_t) - \mu'U_t \right.$$
$$\left. + \frac{1}{3}U_t(1-U_t)\left[2(2U_t-1)\gamma' - 2U_t\beta' - \alpha'\right]\right\}$$
$$+ \theta\left[E(U_{t+1}-U_t)^2 - \frac{2}{9}U_t(1-U_t)\left(\frac{N}{N_1} + \frac{2N}{N_2}\right)\right]$$
$$+ \frac{\theta^2}{6} O(1/N)$$

Let $t = N^2s$, (6.2) becomes

$$E\left[e^{\theta(U_{N^2s+1} - U_{N^2s})} - 1\right] = \frac{1}{N^2}\left[\theta b(U_{N^2s}) + \frac{\theta^2}{2} a(U_{N^2s}) \right.$$
$$\left. + \theta W_N(\theta,N^2s)\right] \quad (6.3)$$

Now, let $\varphi_N(\theta,t) = E[e^{\theta U_t}] = $ m.g.f. of U_t. Then

$$\varphi_N(,N^2s) = E\left[e^{\theta U_{N^2s}}\right], \quad \varphi_N(\theta,N^2s+1) = E\left[e^{\theta U_{N^2s+1}}\right], \text{ and}$$

$$\varphi_N(\theta,N^2s+1) - \varphi_N(\theta,N^2s)$$
$$= E\left[e^{\theta U_{N^2s+1}}\right] - E\left[e^{\theta U_{N^2s}}\right]$$
$$= E\left[e^{\theta(U_{N^2s+1} - U_{N^2s})} \cdot e^{\theta U_{N^2s}}\right] - E\left[e^{\theta U_{N^2s}}\right]$$
$$= E\left[e^{\theta U_{N^2s}}E\left\{e^{\theta(U_{N^2s+1} - U_{N^2s})}\right\}\right] - E\left[e^{\theta U_{N^2s}}\right]$$
$$= E\left[e^{\theta U_{N^2s}}\left\{E\left[e^{\theta(U_{N^2s+1} - U_{N^2s})} - 1\right]\right\}\right]$$
$$= \frac{1}{N^2}E\left\{e^{\theta U_{N^2s}}\left[\theta b(U_{N^2s}) + \frac{\theta^2}{2}a(U_{N^2s}) + \theta W_N(\theta,N^2s)\right]\right\}$$

$$(6.4)$$

Dividing both sides of (6.4) by $(1/N^2)$, we get

$$\frac{\varphi_N(\theta,N^2s+1) - \varphi_N(\theta,N^2s)}{(1/N^2)} = \xi\left\{e^{\theta U_{N^2s}}\left[\theta b(U_{N^2s}) + \frac{\theta^2}{2}a(U_{N^2s}) + \theta W_N(\theta,N^2s)\right]\right\}$$

(6.5)

Now

$$\xi\left[e^{\theta U_{N^2s}}\theta b(U_{N2s})\right] = \xi\left[e^{\theta U_{N^2s}}\theta\left\{\zeta'(1-U) - \mu'U + \frac{1}{3}U(1-U)\left[2(2U-1)\gamma' - 2U\beta' - \alpha'\right]\right\}\right]$$

$$= \theta\left\{\zeta'\xi\left[e^{\theta U}\right] - \left(\zeta' + \mu' + \frac{2}{3}\gamma' + \frac{1}{3}\alpha'\right)\xi\left[U e^{\theta U}\right]\right.$$

$$+ \left(2\gamma' - \frac{2}{3}\beta' - \frac{1}{3}\alpha'\right)\xi\left[U^2 e^{\theta U}\right]$$

$$\left. + \left(\frac{2}{3}\beta' - \frac{4}{3}\gamma'\right)\xi\left[U^3 e^{\theta U}\right]\right.$$

$$= \theta\left\{\zeta'\varphi_N(\theta,N^2s) - \left(\zeta' + \mu' + \frac{2}{3}\gamma' + \frac{1}{3}\alpha'\right)\frac{\partial\varphi_N(\theta,N^2s)}{\partial\theta}\right.$$

$$+ \left(2\gamma' - \frac{2}{3}\beta' - \frac{1}{3}\alpha'\right)\frac{\partial^2\varphi_N(\theta,N^2s)}{\partial\theta^2}$$

$$\left. + \left(\frac{2}{3}\beta' - \frac{4}{3}\gamma'\right)\frac{\partial^3\varphi_N(\theta,N^2s)}{\partial\theta^3}\right.$$

(6.6)

Similarly

$$\frac{\theta^2}{2}\xi\left[e^{\theta U_{N^2s}}a(U_{N2s})\right] = \frac{\theta^2}{2}\left[\frac{2}{9}\left(\frac{N}{N_1} + \frac{2N}{N_2}\right)\left[\frac{\partial\varphi(\theta,N^2s)}{\partial\theta} - \frac{\partial^2\varphi_N(\theta,N^2s)}{\partial\theta^2}\right]\right]$$

(6.7)

Finally

$$\left| \theta \, \mathcal{E}\left[e^{\theta U_{N^2 s}} W_N(\theta, N^2 s) \right] \right| \le |\theta| \, \mathcal{E} \left| e^{\theta U_{N^2 s}} W_N(\theta, N^2 s) \right|$$

$$\le |\theta| e^{|\theta|} \, \mathcal{E} |W_N(\ , N^2 s)| \quad \text{since} \ |U_{N^2 s}| < 1$$

$$\longrightarrow 0 \ \text{as} \ N \longrightarrow \infty \qquad (6.8)$$

because $\mathcal{E}|W_N(\theta, N^2 s)| \le \sqrt{\mathcal{E}[W_N(\theta, N^2 s)^2]}$

$$\longrightarrow 0 \ \text{as} \ N \longrightarrow \infty$$

as we have shown that all terms in $W_N(\theta, N^2 s)$ converge to zero in m.s. sense. This point will be taken up again following (6.11).

Suppose now $\varphi_N(\theta, N^2 s) \rightarrow \varphi(\theta, s)$ as $N \rightarrow \infty$ and

$$\frac{\varphi_N(\theta, N^2 s + 1) - \varphi_N(\theta, N^2 s)}{(1/N^2)} \rightarrow \frac{\partial \varphi(\theta, s)}{\partial s}$$

Then

$$\frac{\partial \varphi(\theta, s)}{\partial s} = \theta \Big[\gamma' \varphi(\theta, s) - (\gamma' + \beta' + \frac{2}{3}\gamma' + \frac{1}{3}\alpha') \frac{\partial \varphi(\theta, s)}{\partial \theta}$$

$$+ (2\gamma' - \frac{2}{3}\beta' - \frac{1}{3}\alpha') \frac{\partial^2 \varphi(\theta, s)}{\partial \theta^2}$$

$$+ (\frac{2}{3}\beta' - \frac{4}{3}\gamma') \frac{\partial^3 \varphi(\theta, s)}{\partial \theta^3}$$

$$+ \frac{\theta^2}{2} \Big[\frac{2}{9} (\frac{N}{N_1} + \frac{2N}{N_2}) \Big] \Big[\frac{\partial \varphi(\theta, s)}{\partial \theta} - \frac{\partial^2 \varphi(\theta, s)}{\partial \theta^2} \Big]$$

$$(6.9)$$

Suppose $\varphi(\theta,s)$ is a m.g.f. of U_{N^2s} as $N \to \infty$ with distribution $F(u,s)$, i.e. $\varphi(\theta,s) = \int_0^1 e^{u\theta} dF(u,s)$. Substituting into (6.9) and integrating by parts [see e.g. (13)] we find that

$$\frac{\partial F(u,s)}{\partial s} = \frac{1}{2} \frac{\partial}{\partial u}\left[a(u)\frac{\partial F(u,s)}{\partial u}\right] - b(u)\frac{\partial F(u,s)}{\partial u} \qquad (6.10)$$

and if $f(u,s) = \dfrac{\partial F(u,s)}{\partial u}$, then

$$\frac{\partial f}{\partial s} = \frac{1}{2}\frac{\partial^2 [a(u)f(u,s)]}{\partial u^2} - \frac{\partial [b(u)f(u,s)]}{\partial u} \qquad 0 < u < 1 \qquad (6.11)$$

Now, we need to show that $\mathcal{E}[W_N(\theta,N^2s)]^2 \to 0$ as $N \to \infty$. More strictly, Watterson (13) has shown that all the above assumptions are justified in this case if $\exists \; n \ni 1 < n < 2 \ni \mathcal{E}[W_N(\theta,N^2s)]^2 \to 0$ as $N \to \infty$ uniformly for $s > \xi$ for all $\xi > 0$. In (6.2), $W_N(\theta,t)$ is expressed as a difference between exact and approximate (i.e. X replaced by U, etc.) moments of $U_{t+1}-U_t$. For $t = N^n s$ $(n \geq \frac{3}{2})$ we have shown in section 5 that $X_{N^n s}$, $Y_{N^n s}$, $Z_{N^n s}$ converge in m.s. to $U_{N^n s}$, $U_{N^n s}^2$, $(1-U_{N^n s})^2$, respectively, and hence functions of the former will converge in m.s. to functions of the latter; in particular therefore $\mathcal{E}[W_N(\theta,N^2s)]^2 \to 0$ as $N \to \infty$.

VII. DIFFERENTIAL EQUATION AND ITS SOLUTION

Let $U_N 2_s$ have a distribution $F_N(u,s)$. Under the assumptions we have already verified,

$$F_N(u,s) \longrightarrow F(u,s) \text{ as } N \longrightarrow \infty$$

and if $f(u,s) = \dfrac{\partial F(u,s)}{\partial u}$, then

$$\frac{\partial f}{\partial s} = \frac{1}{2}\frac{\partial^2 [a(u)f]}{\partial u^2} - \frac{\partial [b(u)f]}{\partial u} \qquad 0 < u < 1 \qquad (7.1)$$

We have justified this type of equation in the previous section; for our case, $a(u)$ and $b(u)$ are defined in (6.2). This equation, known also as "Fokker-Planck equation" is mostly used in diffusion processes. It has been studied extensively by Feller (4) and various forms of solutions were discussed by Bharucha-Reid (2), Kimura (8), Li (10), Moran (11,12), Watterson (13), and Wright (14).

To solve (7.1) for $f(u,s)$, we assume first that s is so large that a stationary distribution has been attained; i.e. we find $\lim\limits_{s \to \infty} f(u,s) = f(u)$ say. We can write (6.10) as

$$\frac{\partial F(u,s)}{\partial s} = \frac{1}{2}\frac{\partial [a(u)f(u,s)]}{\partial u} - b(u)f(u,s) \qquad (7.2)$$

As $u \longrightarrow 1-0$,

$$\frac{\partial F(u,s)}{\partial s} = \frac{\partial}{\partial s}\Pr\{U_s \le u\} = \frac{\partial}{\partial s}\Pr\{U_s < u\} \text{ for } u < 1$$
$$\longrightarrow \frac{\partial}{\partial s}\Pr\{U < 1\} = \frac{\partial(1)}{\partial s} = 0 \text{ if there is}$$

mutation.

$$\therefore \lim_{u \to 1-0}\left[\frac{1}{2}\frac{\partial [a(u)f(u,s)]}{\partial u} - b(u)f(u,s)\right] = 0 \text{ for all s. } (7.3)$$

In particular, when "$s = \infty$". This is a boundary condition on Fokker-Planck equation. If there is no mutation, no boundary condition is needed [Feller (4)], apart from the requirement that the solution must be consistent at s = 0 with an assumed given initial distribution.

Similarly, as $u \to 0 + 0$

$$b(u)f(u, \infty) = \frac{1}{2} \frac{\partial [a(u)f(u, \infty)]}{\partial u} + 0 \qquad (7.4)$$

With mutation, there is no probability that $U_s = 0$ nor $U_s = 1$. Then $f(u,s)$ really is a density function, thus $\int_0^1 f(u,s)du = 1$.

Equating $\frac{\partial f}{\partial s}$ to zero, the first integral of (7.1) becomes

$$\frac{1}{2} \frac{\partial [a(u)f]}{\partial u} - b(u)f = 0, \qquad (7.5)$$

the constant of integration being zero in view of the boundary conditions (7.3). According to Li (10), $b(u)f$ represents the portion of the distribution that tends to be carried past a given value of u by the systematic pressure $b(u)$ in each generation. Li further added that since the distribution is stationary,

$$\frac{1}{2} \frac{\partial [a(u)f]}{\partial u} = \frac{1}{9} \left[\frac{N}{N_1} + \frac{2N}{N_2} \right] \frac{d}{du} u(1-u)f$$

must be the portion of the distribution which tends to be scattered away in opposite direction by the random deviations in each generation.

To facilitate the second integration, we rewrite (7.5) as follows:

$$\frac{b(u)}{a(u)}[a(u)f] = \frac{1}{2}\frac{d}{du}[a(u)f]$$

$$\text{or}\quad \frac{2b(u)}{a(u)} = \frac{\frac{d}{du}[a(u)f]}{a(u)f} \tag{7.6}$$

Integrating (7.6) gives

$$f(u) = Ca^{-1}(u)\exp\left\{2\int^{u}b(x)a^{-1}(x)dx\right\}, \quad 0 < u < 1 \tag{7.7}$$

where the constant C is chosen to make $\int_{o}^{1}f(u)du = 1$.
This solution was first used by Wright (14). For our case, we get

$$f(u) = Cu^{C_1-1}(1-u)^{C_1-1}\exp\left\{\frac{1}{3}C_1\left[(2\gamma'-\beta')u^2-(2\gamma'+\alpha')u\right]\right\} \tag{7.8}$$

where $C_1 = \dfrac{9R}{(R+1)(R+2)}$. This solution is similar in form to results found by Kimura (8), Moran (11,12), and Watterson (13).

We observe that δ', a measure of the selection acting against females as a whole, has asymptotically no effect. Presumably as this acts for all female genotypes, the individual gene frequencies are unaffected. If the condition that female number N_2 be constant had been dropped from our initial model, of course selection against females would have an effect.

The effects of mutation and selection can be discussed separately since $f(u)$ is so factorized in (7.8). Before doing so, we note that the effect of sex-ratio, R, is to multiply the effects of mutation and selection. As $C_1 = \dfrac{9R}{(R+1)(R+2)}$, with $0 < R < \infty$ has a maximum at $R = \sqrt{2}$, this sex-ratio ($N_1 : N_2$ as $\sqrt{2} : 1$) produces the greatest magnification of environmental effects.

Special Cases:

1. Assume $\gamma' > 0, \mu' > 0$, mutation is present.

    1(a). If there is no selection, $\alpha' = \beta' = \gamma' = 0$.

        Then

$$f(u) = Cu^{C_1\gamma'-1}(1-u)^{C_1\mu'-1} \qquad 0 < u < 1 \qquad (7.9)$$

represents a beta density with $C = \dfrac{1}{B(C_1\gamma', C_1\mu')}$.

The expected value for the proportion of "a" genes in the population is then

$$\frac{C_1\gamma'}{C_1\mu' + C_1\gamma'} = \frac{\gamma'}{\mu' + \gamma'}$$

which is independent of the sex-ratio R. However, the magnitudes of R and γ', μ' do affect the shape of the distribution. For example when $C_1\gamma' < 1$, $C_1\mu' < 1$ the density function is bimodal(Fig.1).

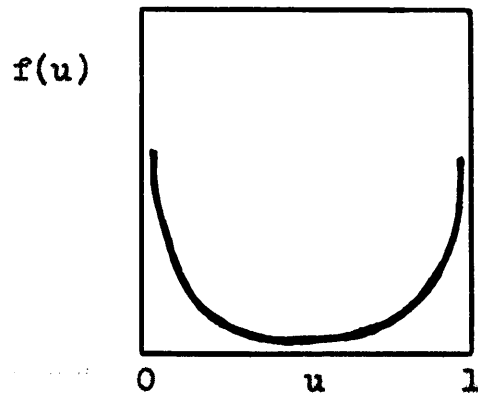Fig. 1. — Distribution (7.9), with $C_1 \gamma' < 1$, $C_1 \mu' < 1$
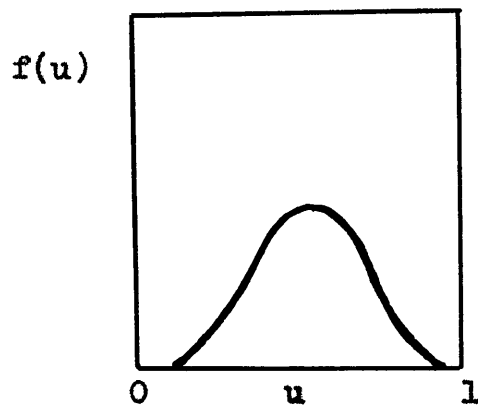

Fig. 2. — Distribution (7.9), with $C_1 \gamma' > 1$, $C_1 \mu' > 1$

This implies that when mutation is small, one or other gene will tend to dominate the population. Another way of looking at this, is as follows: $C_1 < \frac{1}{z'}$ will hold when

$$\frac{9R}{(R+1)(R+2)} < \frac{1}{z'}, \text{ i.e. } R^2 + (3 - 9z')R + 2 > 0.$$

The latter will be true when

$$1 - \frac{\sqrt{8}}{3} < 3z' < 1 + \frac{\sqrt{8}}{3}$$

irrespective of R or, if z' is not within this interval, when

$$R > \frac{9z' - 3 + \sqrt{9(1-3z')^2 - 8}}{2} \text{ or } R < \frac{9z' - 3 - \sqrt{9(1-3z')^2 - 8}}{2}.$$

In these cases $f(u)$ will have an infinite mode at $u = 0$.

Similar conclusions concerning $f(u)$ at $u = 1$ with respect to the relationship of R and μ' can be made.

On the other hand, when $C_1 z' > 1$, $C_1 \mu' > 1$, we see that $f(u)$ has a single mode with $(0,1)$, (Fig. 2). The higher z' is compared to μ', the more will the density become concentrated near $u = 1$. In other words, high mutation rates from A to a will tend to produce asymptotic preponderance of a in the population.

1(b). If there is selection against a but with no
dominance (i.e. Aa is midway between aa, AA in
selective advantage), then $\beta' = 2\gamma'$ and $\beta' > 0$, $\alpha' > 0$.
From (7.8)

$$f(u) = Cu^{C_1\beta'-1}(1-u)^{C_1\gamma'-1}\exp\left\{-\tfrac{1}{3}C_1(2\gamma'+\alpha')u\right\}$$

$$(7.10)$$

and the same general conclusions as in 1(a) can
be made except that the exponential factor has
an increasingly negative exponent as $u \rightarrow 1$ and
shifts the concentration of the density towards
$u = 0$. Of interest in this case, is the fact
that the selection in males (α') is only half
as important as in females (γ') for a single
"a" gene. However, if selection in males acts
in the opposite direction to that in females, the
consequences of selection are not so marked. In
particular when $\alpha' = -2\gamma'$, $f(u)$ reduces to the
beta density in 1(a) obtained with no selection.

1(c). The effect of dominance, $\beta' \neq 2\gamma'$, can be likewise
investigated. For example, if the selection acts
on the phenotypes, and phenotypically Aa, aa are
indistinguishable, then $\beta' = \gamma'$ and the exponent
in (7.8) becomes

$$\tfrac{1}{3}C_1\left[\beta'u^2 - (2\beta'+\alpha')u\right]$$

If α', β' are positive then we see this exponent to be negative since $u > u^2$. This implies that as in 1(b), the exponential factor has an increasingly negative exponent as $u \to 1$ and the concentration of the density would be towards $u = 0$. On the other hand, if α', β' are negative, then the exponent in (7.8) is positive and the same conclusion would be made as in the case of positive exponent in 1(a).

2. When mutation is absent, the above theory does not hold. In particular, because of random fluctuations the boundaries $u = 0$ or $u = 1$ will sometimes be reached and the population will remain unchanged thereafter. This is called "fixation". The limiting $f(u)$ is now of no interest since $\frac{dF(u)}{du} = 0$ for $0 < u < 1$. What is of interest, however, is the probability of ultimate fixation at $U = 1$ say, and also the time rate for fixation to be achieved. Let

$G(p, s) = \Pr\{U_{N^2s} = 1\}$, where $p = U_0 = \frac{1}{3} + \frac{1}{3}(X_0 + Y_0 - Z_0)$,

be the distribution function for the absorption time s at state $U = 1$. Then Kimura (8) has shown that

$$\frac{\partial G(p, s)}{\partial s} = \frac{1}{2}a(p) \frac{\partial^2 G}{\partial p^2} + b(p) \frac{\partial G}{\partial p} \qquad (7.11)$$

with boundary conditions $G(0, s) = 0$, $G(1, s) = 1$. The limiting cas $G(p, \infty)$ is the probability of ever

being absorbed in state U = 1, which satisfies

$$\frac{1}{2}a(p) \frac{d^2G}{dp^2} + b(p) \frac{dG}{dp} = 0 \tag{7.12}$$

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

$$a(p) = \frac{2}{3}p(1-p)\left[\frac{N}{N_1} + \frac{2N}{N_2}\right]$$

$$b(p) = \frac{1}{3}p(1-p)\left[2(2p-1)\gamma' - 2p\beta' - \alpha'\right]$$

$$G(p, \infty) = \frac{\int_0^p e^{-3\left[\frac{N}{N_1} + \frac{2N}{N_2}\right]^{-1}\left[(2\gamma' - \beta')p^2 - (2\gamma' + \alpha')p\right]}\,dp}{\int_0^1 e^{-3\left[\frac{N}{N_1} + \frac{2N}{N_2}\right]^{-1}\left[(2\gamma' - \beta')p^2 - (2\gamma' + \alpha')p\right]}\,dp} \tag{7.13}$$

In particular, when there is no selection,
$(\alpha' = \beta' = \gamma' = 0)$, the solution reduces to

Pr{Ultimate absorption in state U = 1}

$$= G(p, \infty) = p = \frac{1}{3} + \frac{1}{3}\left[\frac{k_0}{N_1} + \frac{r_0}{N_2} - \frac{s_0}{N_2}\right] \tag{7.14}$$

Kimura (8) has found the smallest eigenvalue of the
diffusion equation, which in our case becomes

$$\lambda_0 = \frac{2}{\sigma_1}\Bigg\{ 1 + K_1\left[\frac{-(\alpha' + \beta')C_1}{6}\right] + K_2\left[\frac{-(\alpha' + \beta')C_1}{6}\right]^2$$

$$+ K_3\left[\frac{-(\alpha' + \beta')C_1}{6}\right]^3 + K_4\left[\frac{-(\alpha' + \beta')C_1}{6}\right]^4 + \cdots \tag{7.15}$$

where
$$K_1 = -\frac{1}{5}d, \quad K_2 = \frac{1}{2\cdot 5} + \frac{2^2\cdot 3}{5^3\cdot 7}d^2,$$

$$K_3 = \frac{1}{2\cdot 5^3\cdot 7}d - \frac{2^2}{5^5\cdot 7}d^3,$$

$$K_4 = \frac{1}{2^3\cdot 5^3\cdot 7} - \frac{7^3}{2\cdot 3^3\cdot 5^5}d^2 - \frac{2^2\cdot 3^5}{5^6\cdot 7^3\cdot 11}d^4,$$

and
$$d = \frac{2\gamma'-\beta'}{\alpha'+\beta'}$$

This means, that the leading term in the eigen function expansion of $f(u,s)$ is of the form

$$(\text{function of } u)e^{-\lambda_o s}$$

with other terms being of a similar form but having higher values of λ. However, since λ_o is the smallest value, it determines the asymptotic rate of change in the population distribution. If there is no selection, then $\lambda_o = \frac{2}{C_1}$ which is smallest when $R = \sqrt{2}$, giving the slowest rate of evolution towards fixation.

VIII. SUMMARY

The density function $f(u)$ for the "a" gene frequency is found by applying Wright's diffusion theory (14). It is similar in form to results found by Kimura (8), Moran (11,12), and Watterson (13).

Results show that δ', a measure of the selection acting against females as a whole, has asymptotically no effect. Presumably the gene frequencies are unaffected when δ' acts for all female genotypes. On the other hand, the sex-ratio $R = \sqrt{2}$ is found to multiply the effects of mutation and selection.

When selection is absent, $f(u)$ becomes a beta density function. The diffusion theory does not hold when mutation is absent. However, in this case, the probability of ultimate fixation and also the time rate for fixation to be achieved are found following results given by Kimura (8).

IX. ACKNOWLEDGEMENTS

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ABSTRACT

The genetical theory of evolution is best
understood by a knowledge of the distribution of
gene frequencies. The sequence of changes in genes,
primarily due to effects of mutation, selection,
migration, and many other environmental influences,
would also gradually change gene frequencies after
a long period of time. The distribution of gene
frequencies is determined by application of theories
of probability and mathematics. In particular,
Wright's diffusion theory (14) and early works of
Fisher (6,7) and Kolmogorov (9) play a central role.

The aim of this thesis is to discover the
evolutionary significance of mutation, selection,
and random mating in the case of sex-linked factors
when the generation structure of the population is
overlapping. To facilitate the application of
mathematical theory, we assume the population size
at any time is large and constant denoted by N.

Instead of discussing the individual genotype
frequencies, we introduce a properly defined random
variable U, approximately the proportion of "a" genes
in the population. The first and second moments of

the change in U during the birth-death event are
obtained. For the diffusion process to work out,
we let the time be a function of N, and by moment
generating functions the diffusion equation (or
Fokker-Planck equation) is justified when N tends
to infinity. Following methods of solution given
by Barucha-Reid (2), Kimura (8), Li (10), Moran (11,12),
Watterson (13), and Wright (14), the density function
for the "a" gene frequency is obtained.