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On the Fixation of Genes of Large Effects Due to Continued Truncation Selection in Small Populations of Polygenic Systems with Linkage[1]

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Summary. The proportion of fixed loci for desirable genes and the time required for fixation is studied in simulated diploid populations, which have initially a HARDY-WEINBERG structure. A symmetric ten-locus system of additive or dominant genes is simulated with linkages between adjacent loci varying as .005, .05, or .5. A constant degree of upper truncation selection within a population is considered over the generations. In different populations the intensity of truncation is varied as N/N, $N/N+2$, $N/N+4$, . . ., where N is the parental population size, specified as 2, 4, 8 or 16. The selection differential in initial generation, $\bar{\imath}$, thereby varies from zero to more than two standard deviations in some cases. The initial mean gene frequency, p, simulated in an initial population is .1 or .5.

It is pointed out that when selective advantage of a gene is large and is changing with gene frequency, diffusion approximations assuming constant selective advantage, gives higher values for proportion of fixed genes in the case of p equal to .1 and lower values for p equal to .5. With parental population size of 16 or less, a relation with $N\bar{\imath}$ alone does not give the proportion of fixed genes. Higher order terms of $N\bar{\imath}$ appear to be involved in the relation. For the same $N\bar{\imath}$, the proportion is much higher for low N.

The depressing effect of low recombinations between loci is of different magnitude for different N and p for a given $N\bar{\imath}$. The increase in the proportion of fixed genes due to increasing N is not as large when p is low. High intensity of selection offsets considerably the effects of population size and linkage when gene effects are large. It appears that with increased inbreeding and selection intensity, almost all the genes of large effects and at intermediate frequencies can be rapidly fixed regardless of linkage.

Linkage has been shown to cause faster fixation of genes in the absence of selection. With selection, linkage tends to delay fixation. But in the case of very low recombinations, there appears to be a level of population size and selection intensity, below which there is more rapid fixation because of linkage. Selection for dominant genes in the case of very close linkage, delays fixation for a number of generations and this delay results in reducing the depressing effect of linkage.

I. Introduction

The present mathematical theory of the chance of fixation of a gene with selective advantage segregating in a finite population, stems essentially from FISHER (1930) and WRIGHT (1931). Using WRIGHT's model and a diffusion approximation of the process, KIMURA (1957) has derived a solution for $u(p)$, the chance of fixation of a gene with initial frequency p, as

$$u(p) = \frac{\int_0^p e^{-2Ns(2h-1)x(1-x)-2Nsx}\,dx}{\int_0^1 e^{-2Ns(2h-1)x(1-x)-2Nsx}\,dx}, \qquad (1)$$

where N denotes parental population size, s is the selective advantage of a dominant homozygote and sh is the selective advantage of a heterozygote. The theory is developed for a single locus with constant N, s and sh, and is essentially haploid except that diploid selective values are used to derive an equivalent haploid selective value. The approximations leading to equation (1) are made on the assumption of a large N and a very small s. EWENS (1963) has shown by powering a transition matrix for a haploid model of a gene acting additively that the error of diffusion approximation in (1) is negligible for N equal to 12 when s is very small and constant, but it increases when s is large. For s equal to 0.1 the error in $u(p)$ is shown to be of the order of about .01 depending upon p.

ROBERTSON (1960) has applied KIMURA's results to non-epistatic polygenic systems ignoring linkages between loci and the effects of gametic disequilibria that may arise due to selection. He has used the relation

$$s = \bar{\imath}\, a/\sigma \qquad (2)$$

to deduce from (1) expressions for quantitative response, where $\bar{\imath}$ is the standard selection differential and a/σ is the proportionate effect of a gene assumed to be very small and constant over generations. LATTER (1965a) shows that the approximations used in obtaining (2) may lead to appreciable error in predicting response if a/σ is large, especially with intense selection. Also, the assumption of constant a/σ is not realistic since the gene frequency is changing with selection.

With selection, extension of a single locus theory to polygenic systems is not simple, as discussed recently by QURESHI and KEMPTHORNE (1968) from the point of view of gametic disequilibria arising in the population. The cumulative build-up of these disequilibria over generations in finite populations results in an excess of repulsion type gametes at fixation (HILL and ROBERTSON, 1966). A direct Monte Carlo study of polygenic systems (QURESHI et al., 1968) has demonstrated certain linkage, selection intensity and population size effects on total response. HILL and ROBERTSON (1966) have examined in detail the case of two linked genes and have pointed out the effect of recombination frequency on the chance of fixation of various gametes and on

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the change in gene frequencies. Their study and that of LATTER (1965b) deal with haploid selection and follow the assumptions of the mathematical model referred to above as they use theoretical frequency functions to generate samples of gametic populations on a computer.

In natural populations, especially of domesticated animals and plants, polygenic situations are commonly encountered where rapid changes in the genetic structure result due to rapid inbreeding and selection of diploid individuals. A question arises whether the simplifying assumptions of the mathematical model hold for such situations. It appears that some answers to the question can be provided by simulation studies. The present study is undertaken to examine the fixation of genes of large effects by directly simulating on a computer the processes of truncation selection and Mendelian segregation with ten linked loci. In the simulation the diploid nature of the process is followed throughout.

II. Simulation of the Process

The processes of generating initial genotypes, selecting random pairs of individuals for mating, producing a random gamete from each parent with specified frequency of cross-overs, computing genotypic values, and selecting parental population from an ordered array of genotypes are programmed in their logical sequence on an IBM-360 computer system. The generation of random numbers and programming procedure is the same as described by QURESHI et al. (1968). The direct simulation procedure followed here assumes only the Mendelian mechanism of inheritance and mimics selection experiments conducted with biological organisms of known genotypes.

Genetic Models and Structure

We consider an initial population of dioecious individuals with ten segregating loci controlling the expression of a quantitative trait. The population is in HARDY-WEINBERG equilibrium with frequency (p) of plus gene at each locus. With this symmetry of gene frequencies and effects, the genotypic value (g) of an individual is a function of the number of $--$, $+-$, and $++$ phases in the genotype, denoted by n_0, n_1, and n_2 respectively. For the models of gene action studied:

Additive model: $g = n_{1/2} + n_2$

Complete dominance: $g = n_1 + n_2$

The cases of $p = .1$ and $p = .5$ are simulated for each model and no environmental variance is considered. The quality σ in formulae such as $\bar{i}\, a/\sigma$ then refers to the variance associated with all loci but any one locus under consideration. The proportionate effects of genes (a/σ) in the initial population are as follows:

	Additive gene action	Dominance
$p = .1$	1.49	.81
$p = .5$	.89	.73

The size of a/σ, realized in this study of a ten-locus system, is very large and represents a biological situation where the expression of a trait is controlled by a few genes.

For the models specified, using equation (2) and following ROBERTSON's premises, equation (1) becomes:

Additive model:

$$u(p) = \frac{1 - e^{-cp}}{1 - e^{-c}}, \tag{3}$$

Dominance model:

$$u(p) = \frac{\int_0^p e^{c(1-x)^2}\, dx}{\int_0^1 e^{c(1-x)^2}\, dx}, \tag{4}$$

where $c = 2N\bar{i}\, a/\sigma$.

For the purpose of this study we consider a situation where the expected gametic disequilibrium in the initial population is zero. In order to treat the situations where recombination value between loci is less than .5, we assume that all ten loci are situated on a single chromosome and the recombination values between adjacent loci (r) are equal. Three cases of r equal to .005, .05, and .5 are simulated. Only the cases of close linkages are studied since Monte Carlo studies (e.g. LATTER, 1965b) have demonstrated that the recombinations of more than 10 percent do not have considerable effect on long-term response. Although the recombination values specified between adjacent loci are low, high recombination values are realized between distant loci on the same chromosome. Following the argument of QURESHI et al. (1968), the expected recombination value between two loci k recombination sites apart is as follows:

$k =$	2	3	4	5	6	7	8	9
$r = .005$:	.01	.015	.02	.025	.029	.034	.039	.043
$r = .05$:	.095	.136	.172	.205	.234	.261	.285	.306

The expected average recombination value of a random pair of loci is .018 and .151 for r equal to .005 and .05, respectively. A gene cluster on the chromosome is simulated when recombination frequency between adjacent loci is as low as .005.

Selection Procedure

We establish subpopulations of size $N + 2$, $N + 4, \ldots$ (equal number in each sex) by random sampling from the initial population specified and select N parents ($N/2$ in each sex) on the basis of high genotypic value. The selected parents are sampled with replacement for mating and to produce $N + 2$, $N + 4, \ldots$ offspring in various populations. The process of truncation selection and reproduction is continued until all the loci are fixed. The proportion selected in different populations therefore varies as $N/N + 2$, $N/N + 4, \ldots$, and remains constant over generations in a population. The intensity of selection is simulated up to a level where the average number of plus genes fixed is fairly high. The fraction selected each generation in each sex for various N is varied in different populations as follows:

$N = 2$: 1/2, 1/3, 1/4, . . .
$N = 4$: 2/3, 2/4, 2/5, . . .
$N = 8$: 4/5, 4/6, 4/7, . . .
$N = 16$: 8/9, 8/10, 4/11, . . .

Fifty replications were generated for each treatment combination in each of the additive and dominance models. The size of N simulated here varies from the smallest possible to as large as commonly met in isolated natural populations and closed herds of domestic animals. The intensity of selection is increased to a very high level in some cases to study the potential of response, although high intensities of selection are biologically possible only in prolific species.

Parameters Observed

For a given initial gene frequency, p, and a model of gene action, all the populations simulated have initially the same expected genotypic mean and variance regardless of the parental population size (N), recombinations between adjacent loci (r), and the degree of truncation selection specified. For the fraction of progeny selected to be parents in each sex, one can calculate the selection differential in standard units from FISHER and YATES (1953), Table XX, on the assumption of approximately normal distribution of genotypic values in the initial generation. We shall denote these selection differentials as $\bar{i}$ and use these values in the results to indicate the intensity of truncation selection. We also denote m_t ($t = 0, 1, \ldots, T$) as the genotypic mean in generation t, where T denotes the generation number when all the loci are fixed. The quantitative response in generation t is denoted by R_t, where $R_t = m_t - m_0$.

Since the genotypic value of a ++ phase at a locus is specified as one for both the models, m_T is equal to the number of plus genes fixed in the populations. The proportion of loci at which plus genes are fixed is therefore $m_T/10$, which we denote as P. P may also be considered as a measure of probability of fixation of a plus gene under the specified set of conditions. In order to describe the process at fixation for various conditions of N, r, and $\bar{i}$ in the case of a given p and mode of gene action, the following parameters are observed in each case.

1. Proportion of loci fixed for plus gene: $P = m_{T/10}$ and its variance, $V(P)$.
2. Number of generations to fixation at all loci, T, and its variance, $V(T)$.
3. The ratio of total response to initial response, R_T/R_1, where $R_1 = m_1 - m_0$ and $R_T = m_T - m_0$, averaged over all replications.

The means of P and T and the variances $V(P)$ and $V(T)$ are the sample statistics based on data in 50 replications in each case.

III. Results and Discussion

Before examining the limits at fixation of all loci, one must keep in view the process of change in frequency of genes leading to their fixation. For the process simulated, the probability of fixation of a gene and the mean time for fixation are complex functions of N, r, $\bar{i}$ and a/σ. $\bar{i}$ and a/σ are specified for initial generation and change over the generations according to changes in the distribution of genotypic values and in the gene frequency. Changes in a/σ correspond to changes in genotypic variance (σ^2) with inbreeding, gametic disequilibria, and changes in gene frequency with selection, as discussed in QURESHI and KEMPTHORNE (1968). Also, the change in gene frequency due to selection depends on a/σ in that generation.

For the purpose of presentation of results, $\bar{i}$, although not constant over generations, is used to study P and T under various conditions of N and r. P is plotted for different N and r in Figures 1 to 4 against $N\bar{i}$, since P has the same origin at $\bar{i}$ equal to zero for all values of N and r and a given p. The values of T are different for different N at $\bar{i}$ equal to zero. T is therefore plotted against $\bar{i}$ in Figures 5 and 6. Similarly, linkage effects are more clearly illustrated by plotting R_T/R_1 against $\bar{i}$ as presented in Figures 7 and 8.

Mean Proportion of Genes Fixed

Calculated values of $u(p)$ from equations (3) and (4) are also presented in Figures 1 to 4, along with the observed values of P from populations with free recombinations among loci. The purpose of this comparison is to assess the nature and magnitude of the differences in the results because of discrepancy in the premises of the diffusion model and of the experimental model of this study. It is, however, not reasonable to compare diffusion approximations with simulation results from populations with linkage.

Comparison of P in the case of free recombination between loci with $u(p)$ shows larger values of P when initial gene frequency is .5 and smaller values when the frequency is .1. For lower values of p, the difference is larger in the case of additive genes as compared with that for dominant genes. The difference between P and $u(p)$ is due to continuization

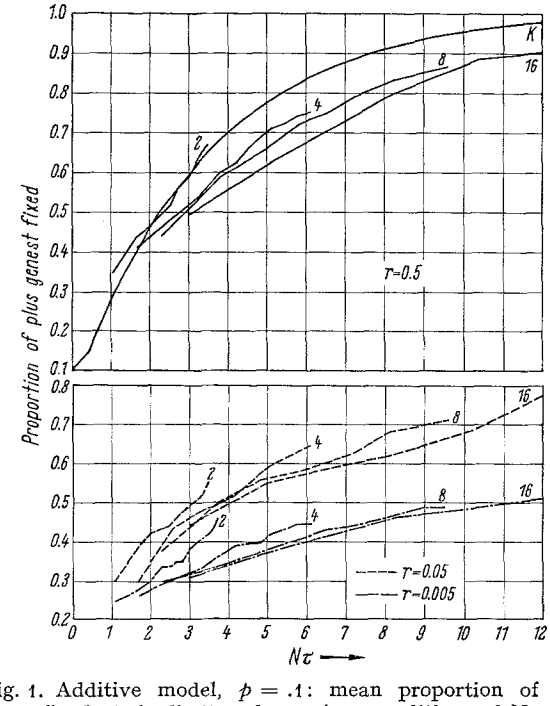

Fig. 1. Additive model, $p = .1$: mean proportion of plus genes fixed at the limit under various conditions of N and r. Curve K is calculated from equation (3)

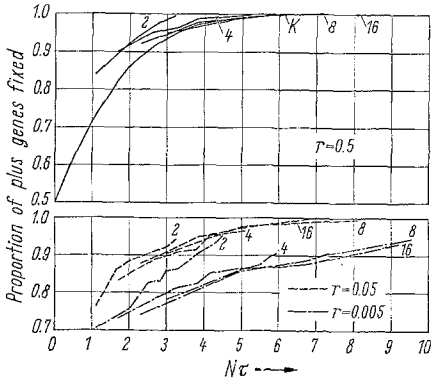

Fig. 2. Additive model, $p = .5$: mean proportion of plus genes fixed at the limit under various conditions of N and r. Curve K is calculated from equation (3)

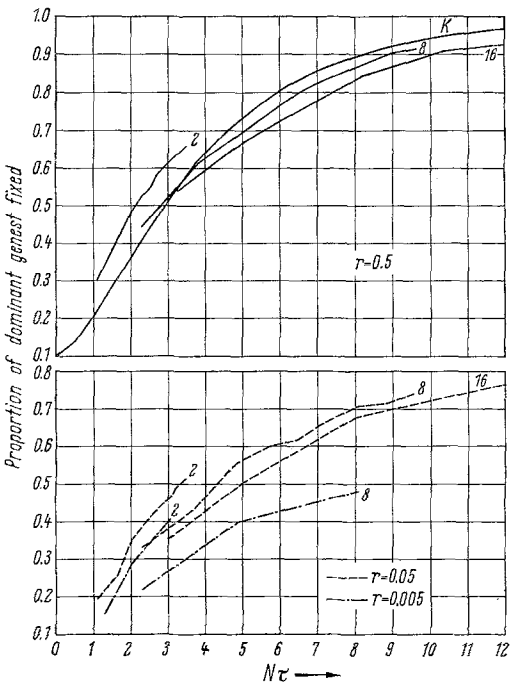

Fig. 3 (right). Dominance model, $p = .1$: mean proportion of plus genes fixed at the limit under various conditions of N and r. Curve K is calculated from equation (4)

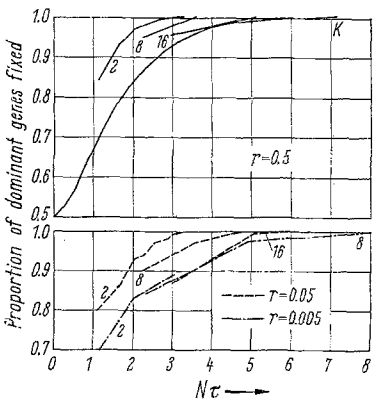

Fig. 4. Dominance model, $p = .5$: mean proportion of plus genes fixed at the limit under various conditions of N and r. Curve K is calculated from equation (4)

of the time parameter and approximations used in the derivation of Equations (3) and (4) besides the effect on P of changes in the selective value ($\bar{\imath}\, a/\sigma$). EWENS (1963) has shown that if the changes in selective value are ignored, $u(p)$ calculated from diffusion approximation is larger for all values of p between zero and one. The effect of changes in the selective value for the cases of p equal to .1 and .5 are demonstrated by the observed values of P compared with $u(p)$ in Figures 1 to 4.

For the same values of $N\bar{\imath}$, P is greater for smaller N. In small populations, increase in the intensity of selection results in the fixation of larger proportion of plus genes than that described by a relationship with $N\bar{\imath}$. For populations smaller than 8 this effect is quite considerable. At $N\bar{\imath}$ equal to 3, P with full sibbing is greater by about .1 than with N equal to 16 in the case of initial gene frequency of .1. When p is .5, this difference is of the order of about .05. It is apparent that at least for parental populations of 16 or less and the modes of gene action studied, P is not a function of $N\bar{\imath}$ alone for a given p, but also involves high order functions of $N\bar{\imath}$.

For the close linkages simulated, the decrease in P is considerably large and this serves to demonstrate clearly linkage effects under various conditions of N and $\bar{\imath}$. It has been shown earlier (QURESHI and KEMPTHORNE, 1968) that with additive genes and low recombinations between loci, the change in gene frequency over generations is consistent with the decrease in the genotypic variance and there is rapid approach to fixation. For dominant genes an 'operational plateau' with respect to change in mean gene frequency is noticed over a number of generations after an initial phase of consistent increase. The dominance component of the genotypic variance is increased at the plateau because of the gametic disequilibria in the population. With decrease in heterozygosity due to increased inbreeding in later generations, the dominance variance is reduced and a second phase of increase in gene frequency is seen. It is interesting to note here that this pattern of change in the mean frequency of dominant genes results in the fixation of a higher proportion of genes. It may be seen from Figures 1—4 that the reduction in P due to low recombination is not as large for dominant genes as it is for additive genes.

The differences in P due to parental population size for a given $N\bar{\imath}$ appear to be of similar nature with linkage as in the case of free

Table 1. *Additive model: observed variance of P, V(P), compared with the binomial variance, σ_p^2*

		$\bar{\imath} \doteq .5$			$\bar{\imath} \doteq 1.0$		
		P	$V(P)$	σ_p^2	P	$V(P)$	σ_p^2
$p = .1$							
	$N = 2$, $r = .005$	.246	.008	.019	.298	.007	.021
	$r = .05$	.300	.011	.021	.422	.011	.024
	$r = .5$	.347	.015	.023	.462	.010	.025
	$N = 8$, $r = .005$	.332	.004	.022	.454	.009	.025
	$r = .05$	.498	.013	.025	.688	.015	.021
	$r = .5$	.594	.023	.024	.810	.012	.015
	$N = 16$, $r = .005$	.454	.014	.025	—	—	—
	$r = .05$	.664	.015	.022	—	—	—
	$r = .5$	.790	.011	.017	—	—	—
$p = .5$							
	$N = 2$, $r = .005$	.727	.011	.020	.780	.006	.017
	$r = .05$	.810	.008	.015	.896	.009	.009
	$r = .5$	.834	.015	.014	.938	.004	.006
	$N = 8$, $r = .005$	.806	.010	.016	.920	.007	.007
	$r = .05$	.944	.005	.005	.990	.002	.001
	$r = .5$	.976	.003	.002	1.0	.0	—
	$N = 16$, $r = .005$	.896	.005	.009	—	—	—
	$r = .05$	.988	.001	.001	—	—	—
	$r = .5$	.998	.000	.0	—	—	—

recombination. But the decrease in P due to linkage is different for different N and p. In the case of p equal to .1 the decrease in P with linkage, at a given $N\bar{\imath}$, is larger for large N and is smaller with increasing N when p is .5. It appears that for populations with low initial gene frequency, increase in parental size up to 16 results in smaller increase in P with similar selection intensity. With high initial gene frequency and close linkage, the increase in P is larger with increasing N. Increased selection intensity, even with r as low as .005, appears to counteract the effects of linkage and results in an increase in P more than that explained by a relation with $N\bar{\imath}$.

It is of interest to find the distribution of P, especially when linkage is present between loci. Under conditions of free recombination and no selection, the distribution is apparently binomial with index n, the number of loci under consideration. In order to get some ideas about the departure of the observed distribution from the binomial, we have compared the observed variance of P, a parameter of interest denoted by $V(P)$, with the binomial variance, σ_p^2, which is equal to $P(1-P)/10$. These are presented in Tables 1 and 2 in the case of selection intensities for which $\bar{\imath}$ is approximately equal to .5 and 1.0. Chi-Squares calculated from data in 50 replications were not consistent but were significant mostly in cases of low recombinations.

Table 2. *Dominance model: observed variance of P, V(P), compared with the binomial variance, σ_p^2*

		$\bar{\imath} = .5$			$\bar{\imath} = 1.0$		
		P	$V(P)$	σ_p^2	P	$V(P)$	σ_p^2
$p = .1$							
	$N = 2$, $r = .005$	.216	.007	.017	.385	.011	.024
	$r = .05$	.298	.011	.021	.452	.009	.025
	$r = .5$	.300	.013	.021	.490	.008	.025
	$N = 8$, $r = .005$	.496	.008	.025	.578	.010	.024
	$r = .05$	.538	.013	.025	.804	.012	.016
	$r = .5$	.614	.013	.024	.862	.011	.012
$p = .5$							
	$N = 2$, $r = .005$	.695	.015	.021	.846	.011	.013
	$r = .05$	.800	.017	.016	.934	.007	.006
	$r = .5$	.842	.011	.013	.972	.002	.002
	$N = 8$, $r = .005$	.924	.005	.007	.969	.002	.002
	$r = .05$	.972	.002	.003	1.0	.0	.0
	$r = .5$	.994	.001	.001	1.0	.0	.0

Table 3. *Additive model: mean number of generations to fixation (T) and its variance, V(T), in certain cases*

		$N = 2$		$N = 8$		$N = 16$	
		T	$V(T)$	T	$V(T)$	T	$V(T)$
$p = .1$							
	$\bar{\imath} = 0$, $r = .005$	6.18	13.3	29.9	247.1	57.0	1072.3
	$r = .05$	8.1	30.2	32.5	444.1	65.9	781.2
	$r = .5$	7.9	30.9	37.0	295.3	72.8	1405.5
	$\bar{\imath} = .5$, $r = .005$	7.0	22.5	16.9	75.5	25.8	259.0
	$r = .05$	8.3	12.1	20.0	33.2	27.1	35.4
	$r = .5$	9.3	7.5	19.4	18.5	23.5	14.3
	$\bar{\imath} = 1.0$, $r = .005$	5.5	7.4	11.5	77.9	—	—
	$r = .05$	6.8	6.0	12.9	7.3	—	—
	$r = .5$	6.8	2.3	11.5	1.7	—	—
$p = .5$							
	$\bar{\imath} = 0$, $r = .005$	8.9	29.4	37.7	421.5	75.9	841.0
	$r = .05$	10.7	23.5	51.3	452.8	90.2	976.2
	$r = .5$	13.5	28.3	51.7	390.0	97.9	1218.8
	$\bar{\imath} = .5$, $r = .005$	5.2	6.5	17.2	103.0	19.9	102.0
	$r = .05$	9.8	19.2	19.0	36.0	22.8	30.1
	$r = .5$	9.6	5.5	16.6	10.1	15.3	5.5
	$\bar{\imath} = 1.0$, $r = .005$	5.6	10.3	9.4	16.2	—	—
	$r = .05$	6.2	3.7	8.4	3.8	—	—
	$r = .5$	6.9	2.3	7.4	0.7	—	—

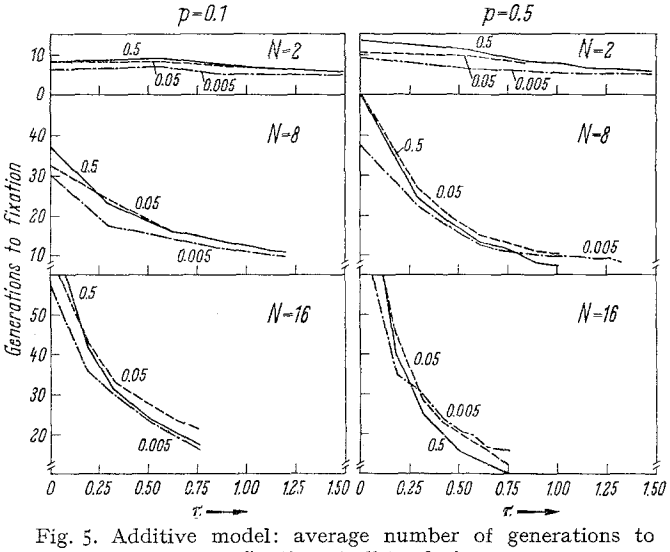

Fig. 5. Additive model: average number of generations to fixation at all ten loci

It appears that $V(P)$, given in Tables 1 and 2, is reduced with increasing intensity of selection and this reduction is more with free recombination. $V(P)$ appears to be reduced with low recombinations in very small populations but appears to increase when N is as large as 16. When N is equal to 8, there is an increase in $V(P)$ with low recombination at high initial gene frequency. A comparison of $V(P)$ and σ_p^2 gives a more clear picture. $V(P)$ gets smaller than σ_p^2 with decreasing N and $\bar{\imath}$ and with increasing $\bar{\imath}$. The difference due to selection intensity is small and in the case of free recombination it is negligible.

Mean Number of Generations to Fixation

Theoretical solutions for mean time for fixation, $m(t)$, can be derived from diffusion models (e.g. EWENS, 1963) for a single segregating gene. For a set of genes with identical selective advantage located at freely segregating loci, $m(t)$ corresponds to the time required for fixation of any one of the loci. It is of interest to find the number of generations

required for fixation of all the loci under consideration, especially in the case of linkage. This parameter, denoted by T in this study, is expected to be greater than $m(t)$ but smaller than $n[m(t)]$, where n is the number of loci.

With no selection, close linkage causes rapid fixation of genes as shown in Table 3. This suggests that when a multi-locus situation is considered, the rate of inbreeding in finite populations is higher with restricted recombination among loci. Looking at the observed values of T as a multiple of N, say $X\,N$, the following values of X are obtained:

	$N=2$	$N=8$	$N=16$
$p=.1$, $r=.005$	3.1	3.7	3.6
.05	4.1	4.1	4.1
.5	4.0	4.6	4.6
$p=.5$, $r=.005$	4.5	4.7	4.8
.05	5.4	6.4	5.6
.5	6.8	6.5	6.1

It appears that there is a tendency for the coefficient to increase with increasing N. The inconsistencies to this trend are accounted for by the large variance of T in the particular cases as shown in Table 3. In general, $V(T)$ in relation to its mean appears to be similar in all cases of N and s simulated.

Selection for additive genes causes rapid fixation of genes as seen in Figure 5. The decrease in T with increasing selection intensity appears to follow a complex exponential relation in terms of N and $\bar{i}$. For the same $N\,\bar{i}$, T is much smaller for smaller N. With full-sibbing, there is rapid fixation with selection when r is .05 or lower. In parental populations of 8 or more, fixation is delayed when r is equal to .05 and this delay is increased with increasing N. With increased intensity and larger populations T is increased even when r is as low as .005. This type of relationship between N and r suggests that for a given level of linkage there is a level of N and $\bar{i}\,a/\sigma$ above which fixation is delayed in comparison with free recombination. With decrease in population size or selection pressure below this level, linkage will cause more rapid fixation of genes. Tables 3 and 4 show that the variance of T in relation to its mean generally increases with N and r but decreases with increasing selection intensity.

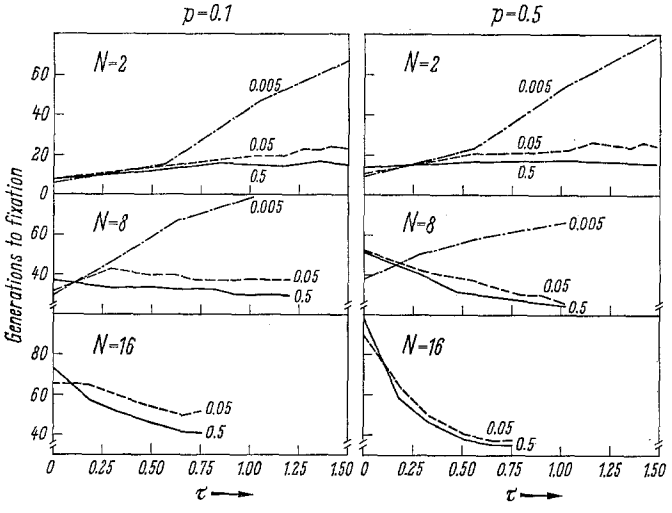

Fig. 6. Dominance model: average number of generations to fixation at all ten loci

Table 4 *Dominance model: mean number of generations to fixation (T) and its variance, $V(T)$, in certain cases*

		$N=2$		$N=8$	
		T	$V(T)$	T	$V(T)$
$p=.1$:					
$\bar{i}=.5$,	$r=.005$	14	92	65	284
	$r=.05$	14	72	39	161
	$r=.5$	13	46	34	120
$\bar{i}=1.0$,	$r=.005$	47	657	64	322
	$r=.05$	20	83	39	93
	$r=.5$	15	50	29	72
$p=.5$:					
$\bar{i}=.5$,	$r=.005$	22	279	57	411
	$r=.05$	20	74	38	154
	$r=.5$	16	36	31	132
$\bar{i}=1.0$,	$r=.005$	53	704	54	418
	$r=.05$	22	168	24	82
	$r=.5$	16	30	24	70

In the case of selection for dominant genes (Figure 6) fixation is always delayed with linkage. With full-sibbing T is slightly increased with increasing $\bar{i}$ even when there is free recombination between loci. The increase in T with linkage may be explained in terms of gametic disequilibria in the population that influence the change in gene frequencies over the generations. The incidence of 'operational plateaus' discussed earlier cause large increase in T when r is as low as .005. For reasons of large number of generations involved, this case of linkage could not be studied for N equal to 16.

Quantitative Response

In our model, all the populations have similar structure in the initial generation. Response in one cycle of selection (R_1) therefore depends on $\bar{i}$ alone and is independent of the effects of N or r. The total response (R_T) depends on the conditions of N, r and $\bar{i}$ simulated in various populations. From the definition of R_T it is obvious that the results given for P also hold for R_T. In a discussion of limits of quantitative response the questions of practical importance pertain to the level of N and $\bar{i}$, for a given r and a/σ, needed to attain total response close to the maximum. The importance of N in this respect has been emphasized in various theoretical and Monte Carlo studies. With genes of large effects, increasing the intensity of selection, if the prolificacy of the species allows, offsets considerably the depressing effects of population size and linkage. Results of this study show that for genes with not very low initial gene frequency, increased selection intensity can result in response close to the maximum even with full-sibbing and close linkages between loci. For example, the following levels of truncation selection in each sex were required in order to attain P of .95, starting with a mean frequency of .5 of additive genes.

	$r=.005$	$r=.05$	$r=.5$
$N=2$	1/51 (2.25)	1/13 (1.67)	1/5 (1.16)
$N=4$	2/28 (1.80)	2/7 (1.06)	2/5 (.83)
$N=8$	4/22 (1.39)	4/7 (.62)	4/6 (.48)
$N=16$	8/15 (.71)	8/10 (.32)	8/9 (.19)

The values in parentheses are of $\bar{i}$ calculated for initial generations. The level of truncation required in the case of dominant genes is much lower than given above.

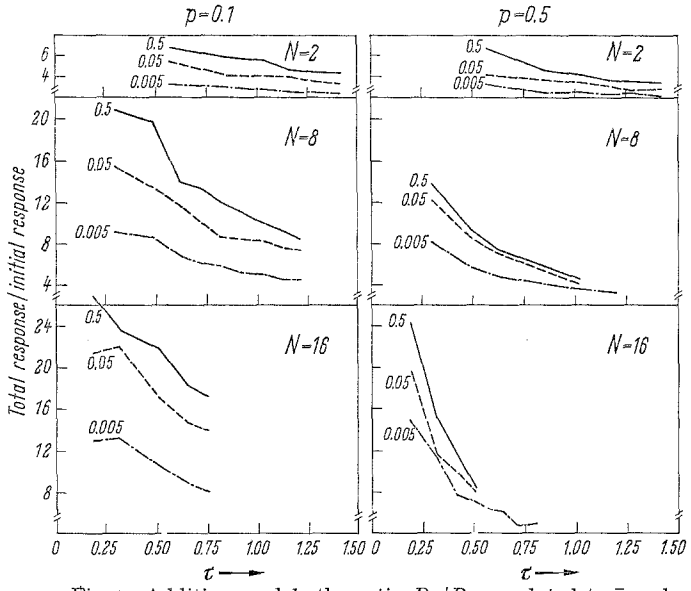

Fig. 7. Additive model: the ratio R_T/R_1 as related to $\bar{\imath}$ under various conditions of N and r.

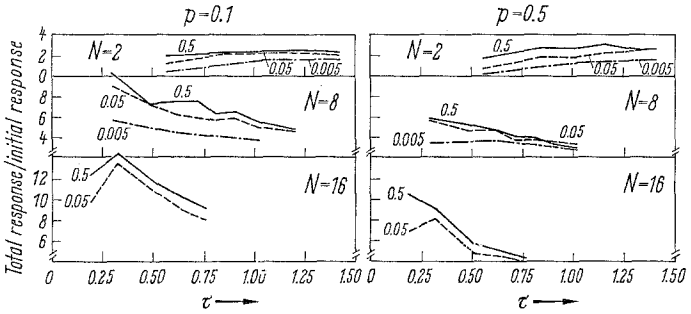

Fig. 8. Dominance model: the ratio R_T/R_1 as related to $\bar{\imath}$ under various conditions of N and r.

It is of interest to describe total response in terms of initial response as attempted by ROBERTSON (1960). The ratio R_T/R_1 is shown in Figures 5 and 6 for additive and dominance models. It appears that attempts to represent total response as $R_T/R_1 = C\,N$ are futile, since C is dependent upon p, N and $\bar{\imath}$ besides r. As expected R_T/R_1 is higher for p equal to .1 and for higher recombinations. The graphs for different linkage groups in Figures 7 and 8 converge with increasing $\bar{\imath}$. This illustrates the effect of increased selection intensity in reducing the depression in total response due to linkage. The ratio R_T/R_1 is lower for dominant genes than for additive genes, which is due to higher values of R_1 realised.

Zusammenfassung

Der Anteil fixierter Loci für erwünschte Gene und die für die Fixierung erforderliche Zeit werden in einer simulierten diploiden Population untersucht, wobei eine ursprüngliche HARDY-WEINBERG-Struktur angenommen wird. Es wird ein symmetrisches 10-Locus-System von additiven oder dominanten Genen mit Koppelung zwischen benachbarten Loci, die von 0,005 über 0,05 bis zu 0,5 variiert wird, simuliert. Hierbei wird ein konstantes Ausmaß von trunkierender (stutzender) Selektion für die Obergrenze der Verteilung in der Population betrachtet. In verschiedenen Populationen wird die Intensität der Verteilungsstutzung variiert in der folgenden Form $N/N, N/N+2, N/N+4, \ldots$, wobei N die elterliche Populationsgröße ist, die mit 2, 4, 8 oder 16 spezifiziert wird. Das Selektionsdifferential der Ursprungsgeneration, i, variiert hierbei in einigen Fällen von 0 bis auf mehr als 2 Standardabweichungen. Die ursprüngliche mittlere Genfrequenz, p, die in einer Ausgangspopulation simuliert wird, ist 0,1 oder 0,5.

Es wird gezeigt, daß, im Vergleich zu großem selektivem Vorteil eines Gens und frequenzabhängiger Änderung des Selektionskoeffizienten, Diffusionsnäherungen, die konstante selektive Vorteile voraussetzen, höhere Werte für den Anteil fixierter Gene im Fall $p = 0{,}1$ und niedrigere Werte für $p = 0{,}5$ ergeben. Mit einer elterlichen Population der Größe 16 oder kleiner ergibt die Beziehung Ni allein nicht den Anteil fixierter Gene, da Termini höherer Ordnung von Ni in die Beziehung einbezogen sind. Bei gleichem Ni ist der Anteil bei kleinem N viel höher. Der reduzierende Effekt einer niederen Rekombinationsrate zwischen den Loci ist von unterschiedlicher Größenordnung bei verschiedenem N und p bei einem gegebenen Ni. Der Zuwachs im Anteil fixierter Gene infolge eines wachsenden N ist nicht so groß, wenn p niedrig ist. Eine hohe Intensität der Selektion gleicht die Wirkungen der Populationsgröße und Koppelung erheblich aus, wenn die Genwirkungen groß sind. Es zeigt sich, daß praktisch alle Gene mit großer Wirkung und intermediärer Frequenz unabhängig von der Koppelung schnell fixiert werden können, wenn eine zunehmende Inzucht und Selektionsintensität vorliegt.

Koppelung hat sich als eine Ursache für eine schnellere Fixierung von Genen in der Abwesenheit von Selektion erwiesen. Mit Selektion tendiert Koppelung dazu, die Fixierung zu verzögern. Es zeigt sich jedoch im Falle einer sehr niederen Rekombinationsrate, daß es für die Populationsgröße und Selektionsintensität einen Schwellenwert zu geben scheint, unterhalb dessen eine schnellere Fixierung als Folge der Koppelung auftritt. Eine Selektion auf dominante Gene verzögert im Fall der sehr engen Koppelung die Fixierung für eine Anzahl von Generationen und diese Verzögerung führt dazu, daß der verlangsamende Effekt der Koppelung reduziert wird.

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