Simulation of Genetic Systems. XI. Inversion Polymorphism

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FRASER *et al.* (1966), working with a six-locus genetic simulation computer program, have examined the effects of introduction of inversions into populations which were in gametic equilibrium for $q_i = 0.5$. They found that stable polymorphism can evolve for such inversions if (a) selection strongly favors a phenotypic intermediate, i.e., is normalizing, (b) the genetic constitution of the inversion is only moderately unbalanced, and (c) the initial frequency of the inversion exceeds a fairly critical value. The frequency dependence is also a feature of analogous multiple allelic systems. Following a suggestion by Alan Robertson (personal communication), we have found that the effect of normalizing selection on such a genetic system can best be understood by first considering a multiple allelic system. Suppose a single locus with three alleles, a_0, a_1, and a_2, which form a series in potency. In the absence of dominance and interaction, the phenotypes of this system can be represented by the following matrix, and double truncation selection for the intermediate phenotype will transform this phenotype matrix into a fitness matrix.

	a_0	a_1	a_2
a_0	0	1	2
a_1	1	2	3
a_2	2	3	4

Phenotype

	a_0	a_1	a_2
a_0	0	0	1
a_1	0	1	0
a_2	1	0	0

Fitness (a)

Although the genetic system is additive on the primary scale of determination of phenotypes, it is marked by complex interactions on the secondary scale of reproductive fitness.

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In this model, there are two stable equilibria. If the frequencies of the three alleles are q_0, q_1, and q_2, then the equilibria are

(1) $q_0 = q_2 = 0$; $q_1 = 1.0$, $\overline{w} = 1.0$ (fixation)
(2) $q_0 = q_2 = 0.5$; $q_1 = 0.0$, $\overline{w} = 0.5$ (stable polymorphism)

There is a third equilibrium when all three alleles are at equal frequencies. This is dependent on the two selected genotypes a_0a_2 and a_1a_1 having different probabilities of producing selected offspring even though they have the same probability of producing offspring. They have different genetic survivals which are markedly frequency dependent.

If the frequencies of a_0a_2 and a_1a_1 are x and y, respectively, then the matrix of mating frequencies is

	a_0a_2	a_1a_1
a_0a_2	x^2	xy
a_1a_1	xy	y^2

(b)

Only two of these matings will produce surviving offspring: $a_0a_2 \times a_0a_2$ and $a_1a_1 \times a_1a_1$. Half of the progeny of the former type of mating will survive as parents compared to all of the progeny of the latter mating.

$$\triangle x = 0 \text{ when } x = 2y$$

This will only hold for

(3) $q_0 = q_1 = q_2 = 0.\dot{3}$, $\overline{w} = 0.\dot{3}$ (unstable polymorphism)

A population which contains all three alleles at equal frequency will be in a state of equilibrium at which any deviation from equality will result in the population shifting to the equilibrium appropriate to the allele with the greatest frequency. If a population is initiated with all three alleles present at different frequencies, selection for a phenotypic intermediate will result in the eventual elimination of the minority allele or alleles. However, if the frequency of a minority allele is increased sufficiently in some way then the progression can be reversed.

A genotype can be said to have a component of its reproductive fitness which is independent of its competitive ability to produce functioning gametes. This component can be termed its combining ability—the proportion of its gametes which combine with the gametic output in general to reproduce the parental genotype. Clearly, the combining ability is frequency dependent, increasing with increase of the frequency of the specific genotype.

The same logic developed for the multiple allele case can be applied to a multigenic system. Suppose a two-locus system with two alleles per locus: a_0,a_1 and b_0,b_1. The phenotype matrix will be

	a_0b_0	a_0b_1	a_1b_0	a_1b_1
a_0b_0	0	1	1	2
a_0b_1	1	2	2	3
a_1b_0	1	2	2	3
a_1b_1	2	3	3	4

(c)

and, if double truncation selection for the phenotypic intermediate occurs, this phenotype matrix is transformed into a fitness matrix.

	a_0b_0	a_0b_1	a_1b_0	a_1b_1
a_0b_0	0	0	0	1
a_0b_1	0	1	1	0
a_1b_0	0	1	1	0
a_1b_1	1	0	0	0

(d)

The suppression of recombination will reduce this system to the equivalent of three alleles at a single locus.

	a_0b_0	a_0b_1, a_1b_0	a_1b_1
a_0b_0	0	0	1
a_0b_1 / a_1b_0	0	1	0
a_1b_1	1	0	0

(e)

If, as in the simulations discussed by Fraser *et al.* (1966), the initial populations involve equal allelic frequencies and gametic equilibrium, then the frequencies of the gametic classes a_0b_0, $a_0b_1 + a_1b_0$, and a_1b_1 are 0.25, 0.50, and 0.25, respectively. Selection will result in the elimination of the a_0b_0 and a_1b_1 classes, with fixation of the (a_0b_1, a_1b_0) class. If, however, the frequency of the a_0b_0 or a_1b_1 class is increased sufficiently, then selection will result in a balanced polymorphism for $a_0b_0//a_1b_1$, with elimination of the (a_0b_1, a_1b_0) class, since the increased frequency of the a_0b_0 or a_1b_1 class results in an in-

creased probability of these combining to produce fit phenotypes. If this increase of the combining ability is such as to exceed that of the (a_0b_1, a_1b_0) class, then selection will result in a stable polymorphism. Recombination between the a and b loci precludes such a stable polymorphism, and the only stable end points will be when fixation has occurred for either a_0b_1 or a_1b_0. The $a_0b_1//a_1b_0$ and $a_0b_0//a_1b_1$ double heterozygotes will have a recombinational disadvantage relative to the homozygotes, $a_0b_1//a_0b_1$ and $a_1b_0//a_1b_0$, resulting in the latter increasing in frequency. If the two balanced homozygotes occur at equal frequencies, there are no differences upon which selection can act. Perturbation of the genetic system resulting in one homozygote occurring at a greater frequency than the other will confer an increased combining ability to this class and the population will, eventually, become fixed for this homozygous combination.

If an inversion is introduced into such a population, then inversion polymorphism is possible if the inversion has a genetic content of a_0b_0 or a_1b_1. The probability that a stable inversion polymorphism will evolve is dependent upon the frequency of the inversion, the conformation of the array of frequencies of normal chromosomes, and the intensity of normalizing selection. There will be two trends of change of the conformation of the array of frequencies of normal chromosomes. In one trend, towards inversion polymorphism, the normalizing selection will tend to increase coupling linkages, changing gene frequencies in the noninverted chromosomes to fixation for a complementary potency to that contained in the inversion. In the other trend, towards fixation of an intermediate, selection will tend to increase repulsion linkages, changing gene frequencies first to equality ($q_i = 0.5$), followed eventually by fixation of opposite acting alleles at the two loci.

Normalizing selection, in the presence of tight linkage, tends to increase the frequencies of repulsion types, decreasing the recombinational load (Lewontin, 1965). The advantage of an inversion will, therefore, decrease with tight linkage. Inbreeding will increase the trend to fixation of an intermediate type, also reducing the fitness of an inversion. Reduction of population size on the other hand, by causing an increased variation of gametic frequencies, will tend to increase the advantage of an inversion.

Fraser *et al.* (1966) have shown that the establishment of inversion polymorphism is possible in a six-locus model if the minimum initial frequency of an inversion exceeds a value of approximately 10%. They conclude that the establishment of a stable polymorphism would only be possible from mutational frequencies in population structures favoring marked genetic drift, or if the inversion had an inherent advantage independent of the six locus system.

The fitness of an inversion is determined to a large degree by the frequency of the complementary normal chromosome. This will, in its turn, be determined by the number of loci in the model and by the tightness of their linkage. It is pertinent to expand the earlier study to models involving greater numbers of loci, over a range of rates of recombination. In this paper, results are detailed and discussed for genetic models of 4, 6, 12, 18, and 30 loci for a range of rates of recombination and degrees of gametic disequilibrium.

GENETIC MODEL

The computer program used in this study is the GSD-2 program run on an IBM 7044 computer. This program allows simulation of multigenic systems of up to 30 loci, in populations of up to 1,024 parents. The number of progeny is unrestricted, being defined by the intensity of selection, e.g., if the intensity of selection is 25%, then the number of progeny produced, in runs with 1,024 parents, is 4,096.

Selection is based on the additive phenotype which has been illustrated above for a two-locus model (c). The additive phenotype is transformed into a probability of selection as a parent (p_s) on the following function

$$p_s = 1 - \left| \frac{n - p_a}{n} \right|^{\beta}$$

where n = number of loci and p_a = additive phenotype.

The term β is a constant which specifies the intensity of the normalizing selection. A series of curves of the relation of p_s to p_a for different values of β are shown in Fraser *et al.* (1966). The notation used below has been described by Fraser *et al.* (1966).

All runs were based on a genetic system of two alleles at n loci, located along a single chromosome with a rate of recombination of r between adjacent loci. The initial population was specified as being in gametic equilibrium for gene frequencies of 0.5, over all loci. The population size was set at 256 parents. Inversion chromosomes were substituted for normal chromosomes with a defined probability. Only one type of inversion was introduced into a particular population. Recombination was completely suppressed in inversion heterozygotes. The program contained a test for establishment of inversion polymorphism. The frequency of the inversion was tested to determine whether it lay within the bounds, 0.45–0.55. If such a test was successful for four successive generations, the run was terminated. Runs were otherwise continued to 50 generations. In some runs, the frequency of the inversion had increased over the initial frequency but had not reached the stable frequency of 0.50 by the 50th generation. A judgment of whether inversion polymorphism would have been established if selection were continued was made. This source of misclassification was of minor importance.

RESULTS AND DISCUSSION

The number of possible types of chromosomes is 2^n where n is the number of loci. The genetic model is based on all loci having equal effects, and it is, therefore, possible to group the types of chromosomes into classes in which the criterion is the number of 0 and 1 alleles, i.e., chromosomes of equal potency are grouped. The formula $1^i\,0^{n-i}$ can signify chromosomes with i loci having 1 allele, and $n - i$ loci having 0 alleles. The number of classes is $n + 1$, ranging from $1^0 0^n$ through $1^{n/2}0^{n/2}$ to $1^n 0^0$ classes. Comparisons of potency for systems involving different number of loci where selection is normalizing can be based on the degree of balance where $1^{n/2}0^{n/2}$ has a balance of unity, and

1^n0^0, 1^00^n have a balance of zero. This is illustrated in Table 1 for genetic systems of 4, 6, 18, and 30 loci.

The initiation of populations with equal allelic frequencies at gametic phase balance results in the classes of chromosomes occurring in binominal proportions. This is illustrated in Table 1 for 4, 6, 18, and 30-locus models. These frequencies apply to the noninverted chromosomes. Introduction of inversion chromosomes results in gametic disequilibrium, but the relative proportions of the classes of noninverted chromosomes will still be in binominal proportions as in Table 1.

Sets of replicate runs were made for inversions differing in their potency, introduced at a range of frequencies, for multigenic systems of 2, 4, 6, 12, 18, and 30 loci. The number of runs in which polymorphism was established is compared in Table 2 with the number of runs in which the inversion was lost. These data are shown as percentages in Fig. 1.

A feature of these runs is the lack of consistent differences between the runs made at recombination rates of 0.25 and 0.50. Figure 2 shows the correlation between analogous runs made at these two recombination rates. This comparison excludes runs in which the probability of polymorphism was 0.0 or 1.0. It is possible that a more extensive comparison would demonstrate an effect of this difference of recombination rate, but it is apparent that any such difference will be small and the data can be grouped to simplify this study.

Grouping the data from runs made with recombination set at 0.25 and 0.50 allows a comparison between analogous runs with (a) effectively free recombination (0.25 + 0.50) and (b) fairly tight linkage (0.025). This is shown in Fig. 3 for the runs involving the least unbalanced types of chromosomes, e.g., $1^{14}0^{16}$, 1^80^{10}, etc. There is an interaction between the number of loci in the model and the effect of the difference of recombination. The effect of the difference of recombination is at a maximum for the 12-locus model, decreasing with increase or decrease of the number of loci.

A set of runs were made for the 6, 12, 18, and 30-locus models and the 1^20^4, 1^50^7, 1^80^{10}, and $1^{14}0^{16}$ inversions, in which the rates of recombination were set to equalize the recombinational lengths of the inversions, i.e., at 0.145 for the six-locus model, 0.0659 for the 12-locus model, 0.0426 for the 18-locus model, and 0.025 for the 30-locus model, each specifying a total recombination length of 0.725. The results of these runs are shown in Fig. 4. There is a progression, from the six to the 30-locus model, of decrease of the minimum frequency at which inversion polymorphism will evolve.

It is apparent from these various sets of runs that the initial frequency of an inversion from which a stable polymorphism will occur with a reasonable probability rapidly decreases with increase of the number of loci, reaching mutational frequencies in the 18 and 30-locus models. (Mutational frequency is specified as $1/2N$, $2/2N$, etc., rather than the frequency at which chromosomes mutate to an inverted form.) This aspect has been investigated in more detail for the $1^{14}0^{16}$ inversion in the 30-locus model. Runs were made in which the inversion was introduced at frequencies of $1/2N$, $2/2N$, and $3/2N$, over a range of rates of recombination.

TABLE 1. THE GAMETIC TYPES, THEIR BALANCE AND THEIR FREQUENCIES (WHERE $q_1 = 0.5$), FOR 30, 18, 6, AND 4 LOCI

$n = 30$

Gametic type	$1^{0}0^{30}$	$1^{1}0^{29}$	$1^{2}0^{28}$	$1^{3}0^{27}$	$1^{4}0^{26}$	$1^{5}0^{25}$	$1^{6}0^{24}$	$1^{7}0^{23}$	$1^{8}0^{22}$	$1^{9}0^{21}$	$1^{10}0^{20}$	$1^{11}0^{19}$	$1^{12}0^{18}$	$1^{13}0^{17}$	$1^{14}0^{16}$	$1^{15}0^{15}$
Balance	0.00	0.07	0.13	0.20	0.27	0.33	0.40	0.47	0.53	0.60	0.66	0.73	0.80	0.87	0.93	1.00
Frequency	—	—	—	—	—	—	0.0005	0.002	0.005	0.012	0.028	0.045	0.084	0.116	0.129	0.145

$n = 18$

Gametic type	$1^{0}0^{18}$	$1^{1}0^{17}$	$1^{2}0^{16}$	$1^{3}0^{15}$	$1^{4}0^{14}$	$1^{5}0^{13}$	$1^{6}0^{12}$	$1^{7}0^{11}$	$1^{8}0^{10}$	$1^{9}0^{9}$
Balance	0.00	0.11	0.22	0.33	0.44	0.55	0.66	0.77	0.88	1.00
Frequency	—	—	—	—	0.01	0.03	0.07	0.12	0.17	0.19

$n = 6$

Gametic type	$1^{0}0^{6}$	$1^{1}0^{5}$	$1^{2}0^{4}$	$1^{3}0^{3}$
Balance	0.00	0.33	0.66	1.00
Frequency	0.02	0.09	0.23	0.31

$n = 4$

Gametic type	$1^{0}0^{4}$	$1^{1}0^{3}$	$1^{2}0^{2}$
Balance	0.00	0.50	1.00
Frequency	0.06	0.25	0.375

TABLE 2. NUMBER OF RUNS IN WHICH POLYMORPHISM WAS ESTABLISHED (P) AND IN WHICH THE INVERSION WAS LOST (N), FOR DIFFERENT RATES OF RECOMBINATION (r) AND DIFFERENT INITIAL FREQUENCIES OF THE INVERSION (f_I)

(A)

$1^{1}0^{3}$

	r = 0.025		r = 0.25		r = 0.50	
f_I	P	N	P	N	P	N
0.375	—	—	—	—	—	—
0.250	6	4	4	6	5	5
0.188	0	10	1	9	0	10
0.156	—	—	—	—	—	—
0.125	0	10	0	10	0	10
0.094	—	—	—	—	—	—
0.063	—	—	—	—	—	—
0.047	—	—	—	—	—	—
0.031	—	—	—	—	—	—
0.023	—	—	—	—	—	—
0.016	—	—	—	—	—	—
0.008	—	—	—	—	—	—

$1^{1}0^{2}$

	r = 0.025		r = 0.25		r = 0.50	
f_I	P	N	P	N	P	N
0.250	10	0	10	0	10	0
0.200	9	1	10	0	9	1
0.188	4	6	8	2	8	2
0.156	4	6	2	8	5	5
0.125	2	8	2	8	3	7
0.094	1	9	0	10	0	10
0.063	0	10	0	10	0	10
0.047	—	—	—	—	—	—
0.031	0	10	0	10	0	10
0.023	—	—	—	—	—	—
0.016	—	—	—	—	—	—
0.008	—	—	—	—	—	—

$1^{5}0^{7}$

	r = 0.025		r = 0.25		r = 0.50	
f_I	P	N	P	N	P	N
0.375	10	0	—	—	20	0
0.250	10	0	—	—	—	—
0.190	10	0	—	—	—	—
0.156	8	2	10	0	10	0
0.125	7	3	—	—	—	—
0.094	5	5	10	0	10	0
0.063	2	8	9	1	10	0
0.047	4	6	9	1	10	0
0.031	1	9	9	1	6	4
0.023	0	10	9	1	8	2
0.016	0	10	5	5	5	5
0.008	—	—	5	5	2	8

$1^{4}0^{8}$

	r = 0.025		r = 0.25		r = 0.50	
f_I	P	N	P	N	P	N
0.375	—	—	—	—	—	—
0.250	7	3	6	4	5	5
0.190	0	10	2	8	0	10
0.156	0	10	0	10	0	10
0.125	0	10	0	10	0	10
0.094	—	—	—	—	—	—
0.063	—	—	—	—	—	—
0.047	—	—	—	—	—	—
0.031	—	—	—	—	—	—
0.023	—	—	—	—	—	—
0.016	—	—	—	—	—	—
0.008	—	—	—	—	—	—

(B)

	$1^{9}0^{10}$						$1^{7}0^{11}$					
	r						r					
	0.025		0.25		0.50		0.025		0.25		0.50	
f_I	P	N	P	N	P	N	P	N	P	N	P	N
0.250	—	—	10	0	—	—	20	0	10	0	—	—
0.219	—	—	—	—	—	—	—	—	—	—	—	—
0.200	—	—	—	—	—	—	16	4	—	—	18	2
0.188	—	—	—	—	—	—	6	4	8	2	9	1
0.156	—	—	—	—	—	—	4	6	6	4	8	2
0.125	10	0	5	0	—	—	0	10	4	6	3	7
0.094	9	1	—	—	—	—	—	—	0	10	2	8
0.063	8	2	20	0	—	—	—	—	0	10	0	10
0.047	5	5	—	—	—	—	—	—	—	—	—	—
0.031	2	8	20	0	—	—	—	—	0	10	—	—
0.023	1	9	18	2	8	2	—	—	—	—	—	—
0.016	0	10	17	3	7	3	—	—	—	—	—	—
0.008	—	—	—	—	4	6	—	—	—	—	—	—
$3/2N$	0	3	2	4	—	—	—	—	—	—	—	—
$2/2N$	0	20	4	6	5	5	—	—	—	—	—	—
$1/2N$	0	22	9	15	—	—	—	—	—	—	—	—

(C)

	$1^{14}0^{16}$ r						$1^{13}0^{17}$ r						$1^{12}0^{18}$ r						$1^{11}0^{19}$ r						$1^{2}0^{4}$ r		$1^{5}0^{7}$ r		$1^{8}0^{10}$ r		$1^{14}0^{16}$ r	
	0.025		0.25		0.50		0.025		0.25		0.50		0.025		0.25		0.50		0.025		0.25		0.50		0.145		0.0659		0.0426		0.0250	
f_I	P	N	P	N	P	N	P	N	P	N	P	N	P	N	P	N	P	N	P	N	P	N	P	N	P	N	P	N	P	N	P	N
0.250	10	0	4	0	—	—	—	—	4	0	—	—	17	3	19	1	8	2	4	6	7	13	2	8	—	—	—	—	—	—	—	—
0.219	—	—	—	—	—	—	—	—	—	—	—	—	17	3	18	2	9	1	0	10	2	18	1	9	—	—	—	—	—	—	—	—
0.188	—	—	—	—	—	—	10	0	19	0	—	—	8	12	16	4	7	3	1	9	0	20	0	10	16	4	—	—	—	—	—	—
0.156	—	—	—	—	—	—	19	1	20	0	—	—	5	15	6	14	5	5	—	—	—	—	—	—	5	15	—	—	—	—	—	—
0.141	—	—	—	—	—	—	—	—	—	—	—	—	3	17	5	15	1	9	—	—	—	—	—	—	—	—	—	—	—	—	—	—
0.125	—	—	5	0	—	—	16	4	19	1	—	—	6	34	2	58	2	8	—	—	—	—	—	—	3	17	19	1	—	—	—	—
0.109	—	—	—	—	—	—	—	—	—	—	18	2	0	20	0	20	—	10	—	—	—	—	—	—	—	—	—	—	—	—	—	—
0.094	—	—	—	—	—	—	15	5	19	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
0.078	—	—	—	—	—	—	12	8	19	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
0.063	20	0	4	0	—	—	8	32	14	6	17	3	—	—	—	—	—	—	—	—	—	—	—	—	—	—	7	13	19	1	20	0
0.047	20	0	—	—	—	—	—	—	—	—	13	7	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	20	0
0.031	16	4	5	0	—	—	0	20	4	16	5	15	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	19	6	14	6	4
0.023	—	—	—	—	20	0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
0.016	13	7	19	1	17	3	—	—	2	18	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2	18	13	7
$3/2N$	2	3	2	1	—	—	—	—	0	5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2	3
$2/2N$	2	8	4	4	11	36	—	—	0	5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2	8
$1/2N$	1	20	6	18	8	20	—	—	0	20	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	20

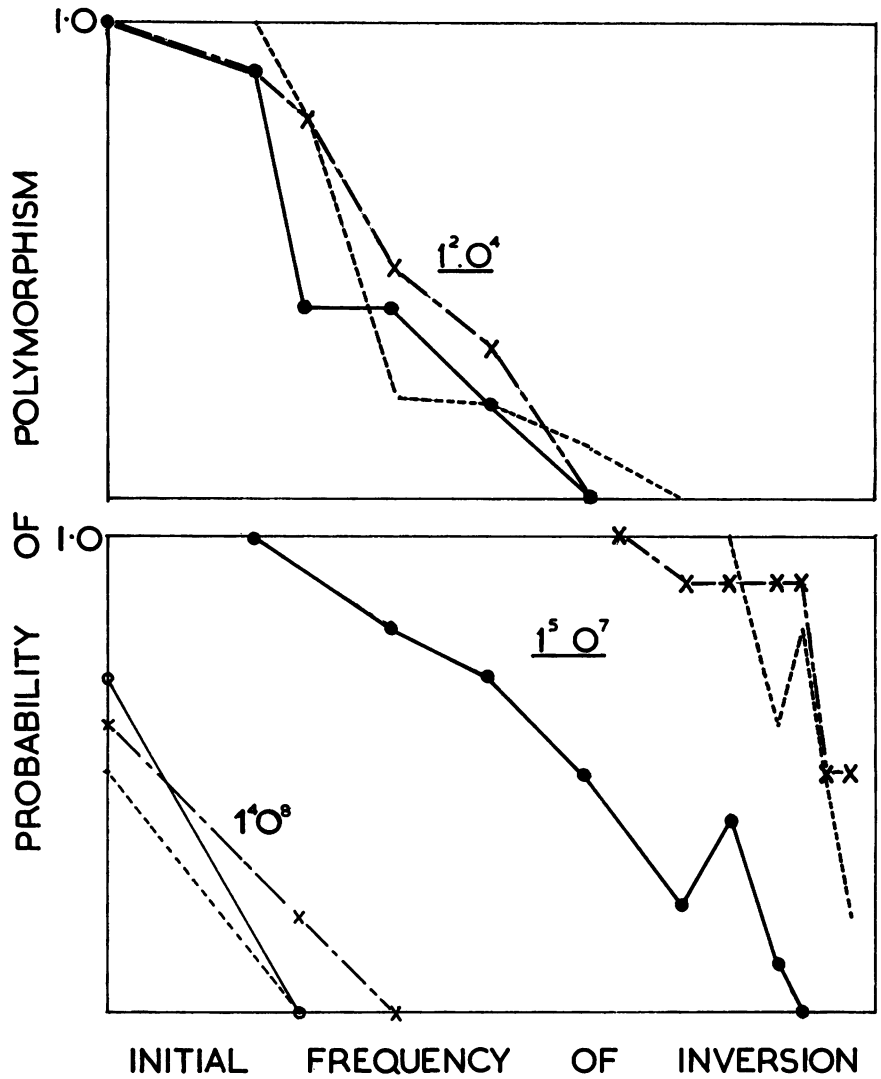

FIG. 1A. The probability of establishment of stable polymorphism is shown against the initial frequency of inversion for a series of inversions. Results are shown for 6, 12, 18, and 30-locus models. Selection was maintained at $\beta = 0.1$, in populations of 256 parents. Runs were made at three rates of recombination in homomorphic individuals: x–x = 0.5, - - - - = 0.25, and O–O = 0.025.

There is a marked decrease of the probability of polymorphism with decrease of the recombination rate below a few per cent (Fig. 5). It would appear that the suppression of recombination in heteromorphic individuals only confers an effective advantage when the rate of recombination between adjacent loci in homomorphic standard chromosomes exceeds a fairly critical value of 1% to 2%. It would appear that the multigenic system becomes essentially a multiple allelic system when the rate of recombination drops below this value.

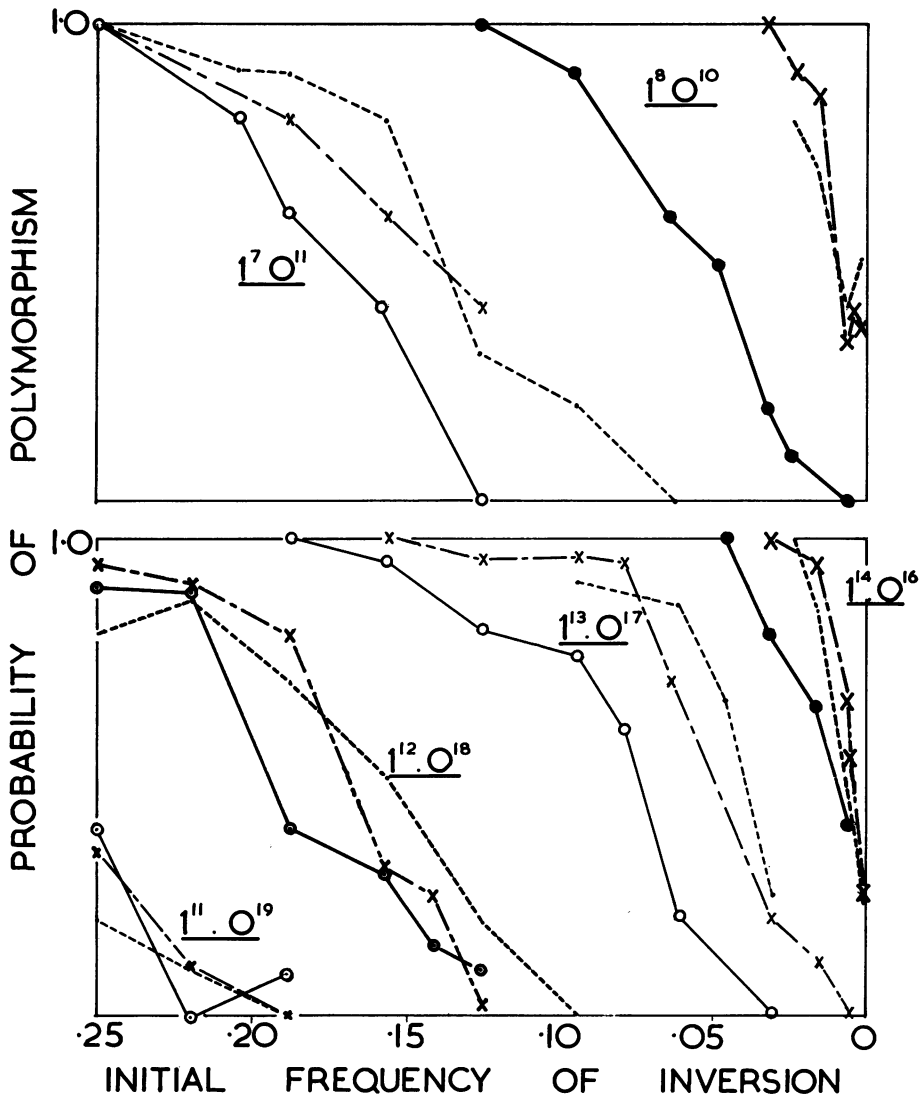

FIG. 1B. (See legend on page 278).

Fraser (1958) found that the interaction of intensity of selection with population size to produce discontinuities in the effectiveness of directional selection is not manifest at rates of recombination of more than a few percent. Lewontin (1964), in a study of the effects of normalizing selection, found that such selection can result in gametic disequilibrium if the rates of recombination between adjacent loci are small.

The above runs were all based on the noninverted chromosomes occurring in gametic equilibrium which specifies that the frequency distribution of potency classes has binominal proportions. (See Table 1.) The degree of potency of a chromosome is, therefore, confounded with its frequency, and it is not

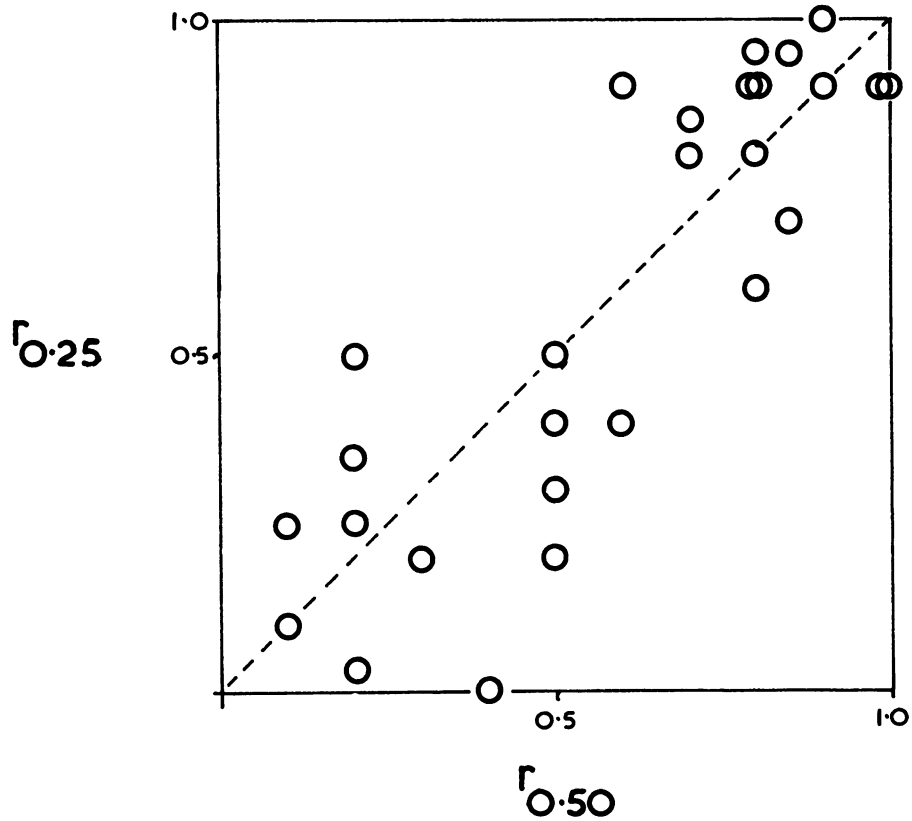

FIG. 2. Comparison between the $r = 0.5$ and $r = 0.25$ rates of recombination of the probability of establishment of stable polymorphism. The comparison excludes runs in which the probability of polymorphism was 0 or 1.

possible to determine whether differences of fitness between inversions are due to their differing in potency or to their complementary normal chromosomes differing in frequency. Runs were made, therefore, for populations in which the array of normal chromosomes did not occur in gametic equilibrium.

Gametic disequilibrium can be introduced by initiating each population in full coupling and interpolating a generation without selection at some specific rate of recombination. With the rate of recombination for this interpolated generation set at 0.50, gametic equilibrium will result, whereas if it is set at 0.00 then the original coupling disequilibrium will be maintained, and if it is set at 1.00 then a repulsion disequilibrium will be generated. A series of distributions of gametic classes produced in this way are shown in Fig. 6 for the 30-locus model.

Runs were made at various degrees of disequilibrium from full coupling to full repulsion for the $1^{13}0^{17}$ inversion. The results are given in Fig. 7.

The fitness of an inversion appears, as would be expected, to be minimal when the gametic phase is in strong repulsion disequilibrium; it increases to a maximum when the gametic phase is in intermediate coupling dis-

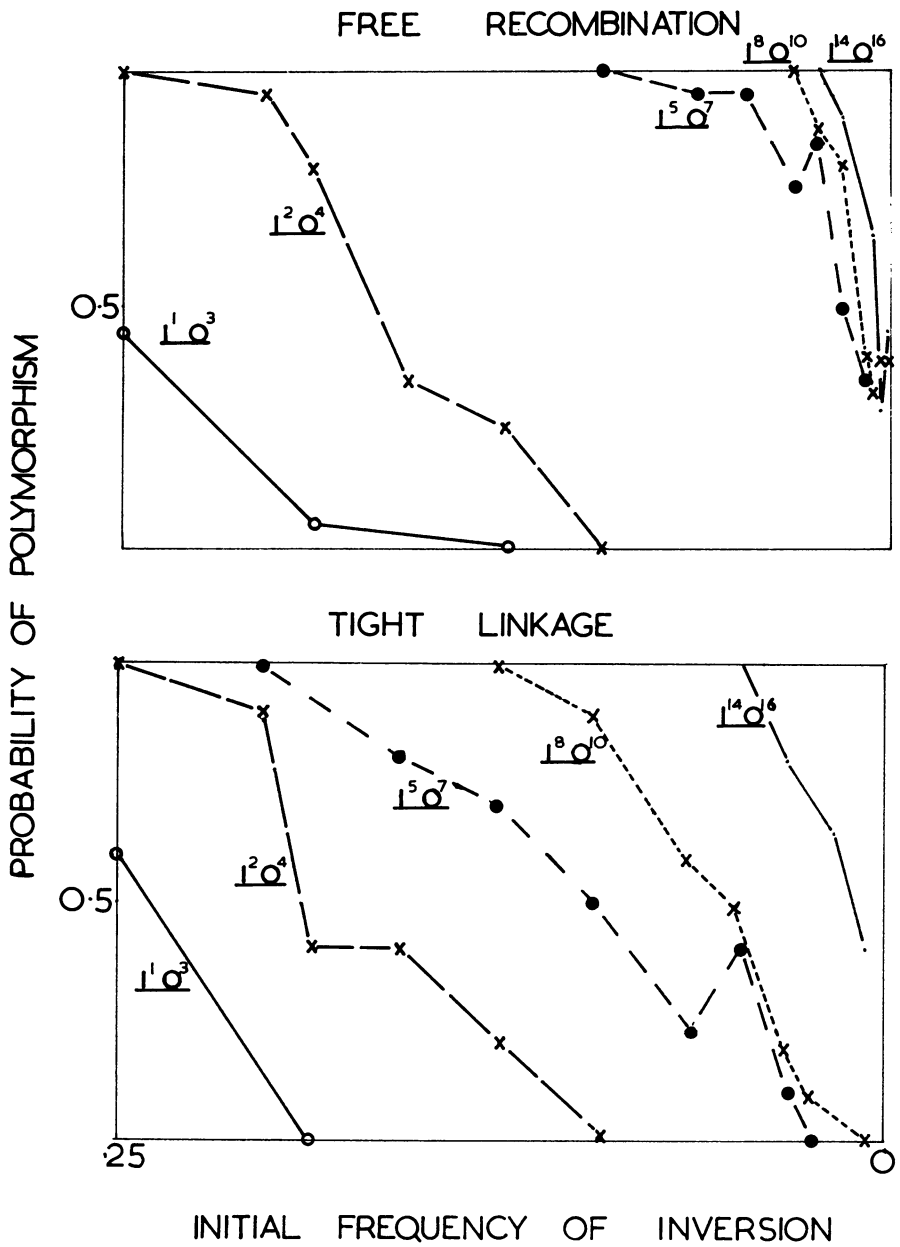

FIG. 3. The probability of establishment of polymorphism is shown against the initial frequency of the inversion for free recombination (0.25 and 0.5) and tight linkage (0.025) in homomorphic individuals.

equilibrium and decreases for strong coupling disequilibrium. It is pertinent to consider the change from gametic phase balance which would occur under normalizing selection in the absence of an inversion. This is illustrated in Fig. 8 for two runs of the $1^{12}0^{17}$ inversion in populations with an initial disequilibrium

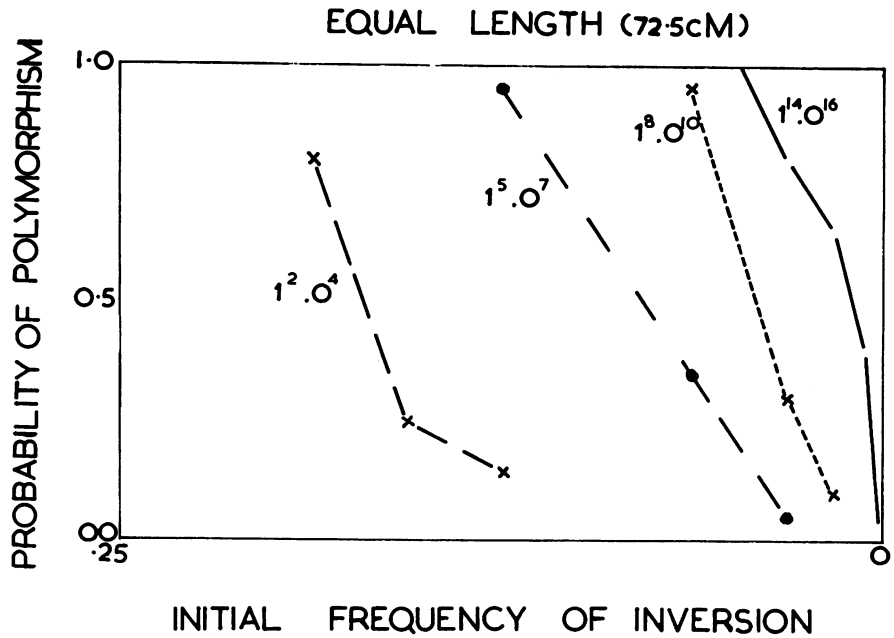

FIG. 4. As in Fig. 3 for inversions of the same recombinational length (72.5 centimorgans).

of 0.4375, i.e., in coupling disequilibrium. In one of these runs, the population became established in inversion polymorphism; in the other, the inversion decreased in frequency and the gametic phase changed to a repulsion disequilibrium. Lewontin (1965), Gill (1965), and Fraser *et al.* (1966) have shown that normalizing selection results in repulsion imbalance for multigenic systems involving tight linkage, and, consequently, any consideration of the probability of establishment of inversion polymorphism for a multigenic system under normalizing selection needs to be based on estimates of the degree of repulsion imbalance which would be expected to occur.

SUMMARY

The simulations of inversion polymorphism with a six-locus model by Fraser *et al.* (1966) showed that the model of additivity on the phenotypic scale with interaction imposed by a normalizing mode of selection can only account for the establishment of inversion polymorphism in a fairly restricted set of circumstances. The present extension of this model to a larger number of loci has shown that the restrictions decrease with increase of the number of loci. In models of 18 and 30 loci, the establishment of inversion polymorphism would appear to be adequately explicable without reference to inversions having specific advantages outside the framework of the basic model. A major deficiency of this work is that it is based on the existence of a multigenic

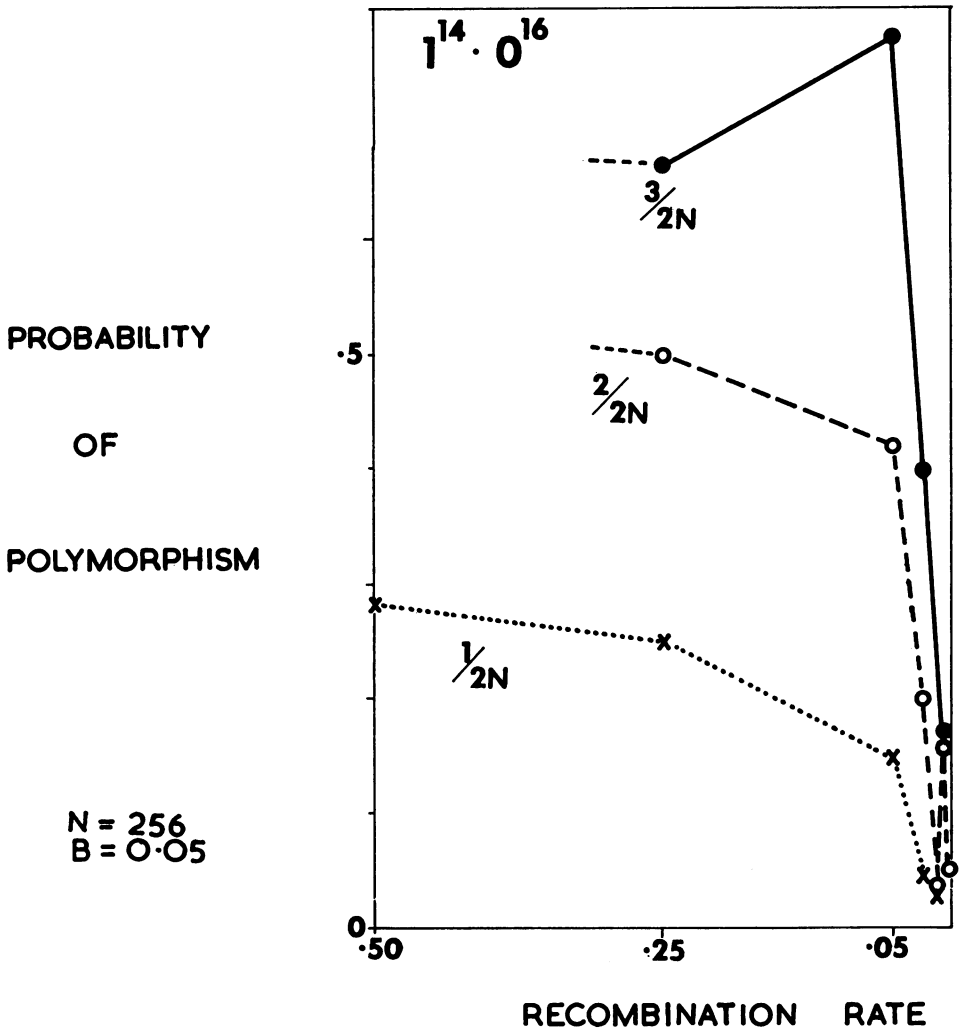

FIG. 5. The probability of establishing stable polymorphism of the $1^{14}0^{16}$ inversion from initial frequencies of $1/2N$, $2/2N$, and $3/2N$ is shown for different rates of recombination in homomorphic individuals.

polymorphism at intermediate allelic frequencies. So far, there has not been any adequate demonstration that such a multigenic polymorphism can be maintained in the absence of generalized overdominance, i.e., an advantage of heterozygosity *per se* in Lerner's (1954) terms. It is, therefore, pertinent to examine our model in terms of the existence of such overdominance to determine, firstly, the minimal degree of such overdominance necessary to maintain intermediate gene frequencies and, secondly, to determine the effects of introducing inversions into such populations. This will be the next step in our investigation of this model.

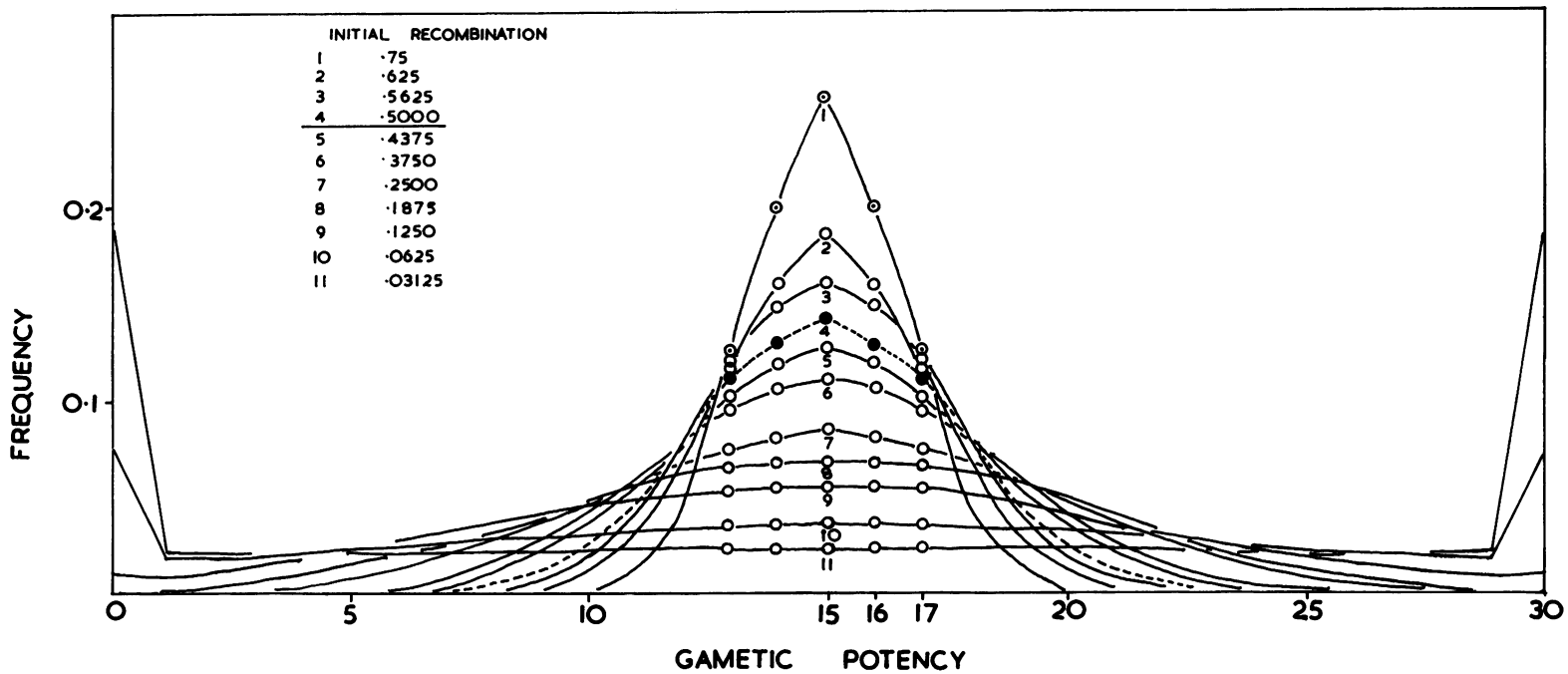

FIG. 6. The frequency distributions of potency classes for different degrees of gametic disequilibrium. The disequilibrium was produced as described in the text.

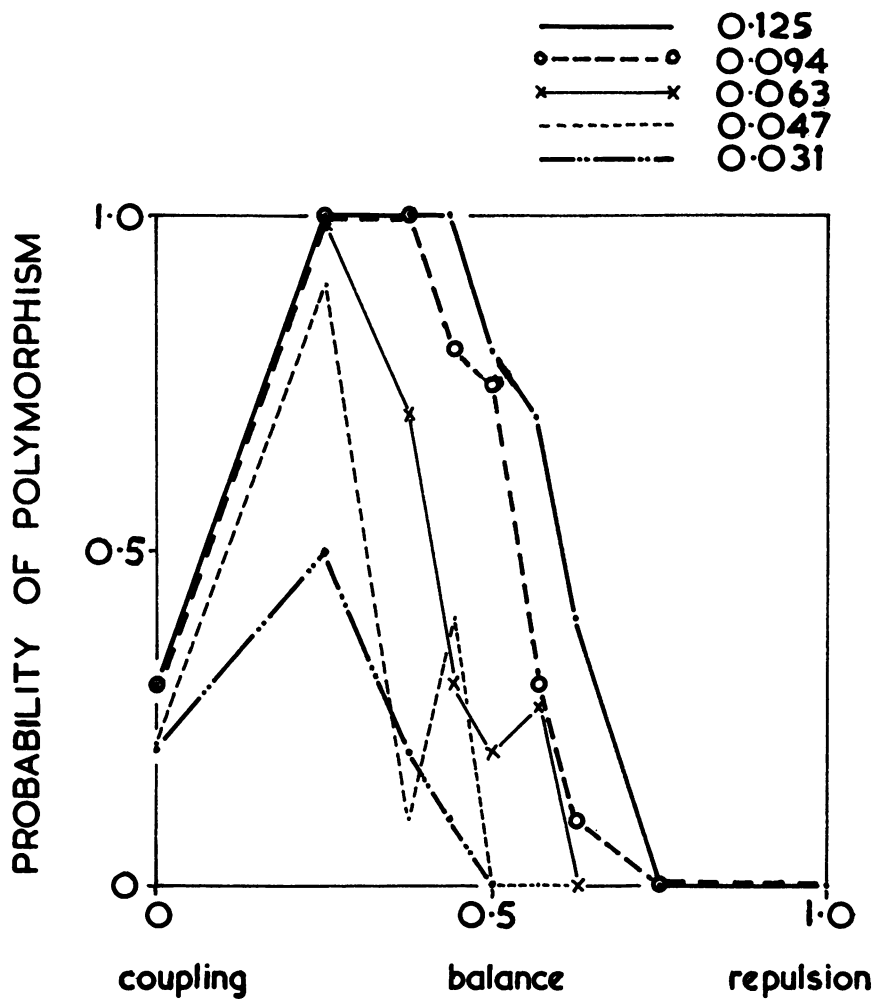

FIG. 7. The probability of establishing stable polymorphism for the $1^{13}0^{17}$ inversion introduced at a series of frequencies into populations with various degrees of gametic disequilibrium of the noninverted chromosomes.

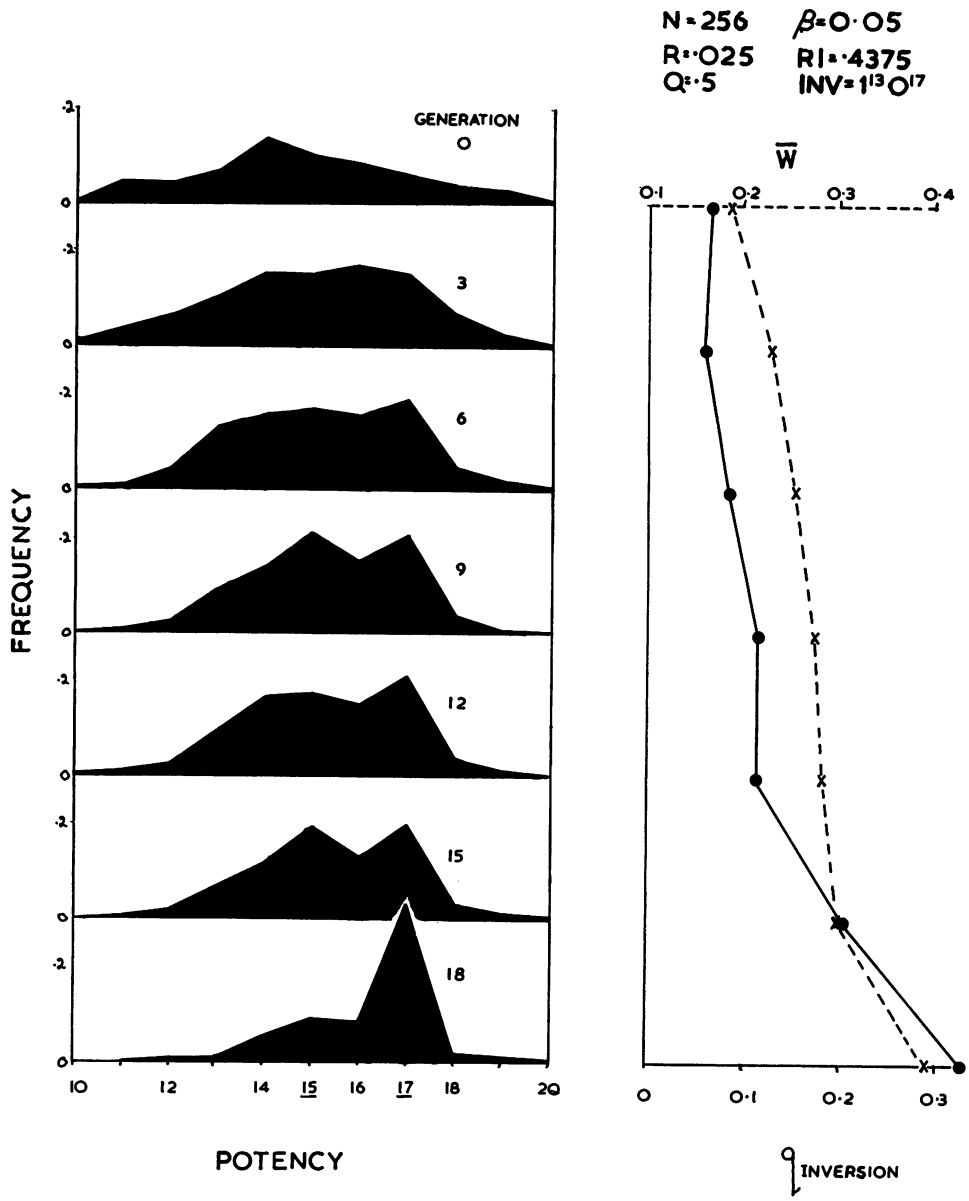

FIG. 8A. The frequency distributions of potency classes for the noninverted chromosomes are shown for two runs in which the $1^{13}0^{17}$ inversion was introduced at an initial frequency of 0.0625. The population of noninverted chromosomes had an initial gametic disequilibrium of 0.4375. The frequency of the inversion and the fitness of the population are also shown.

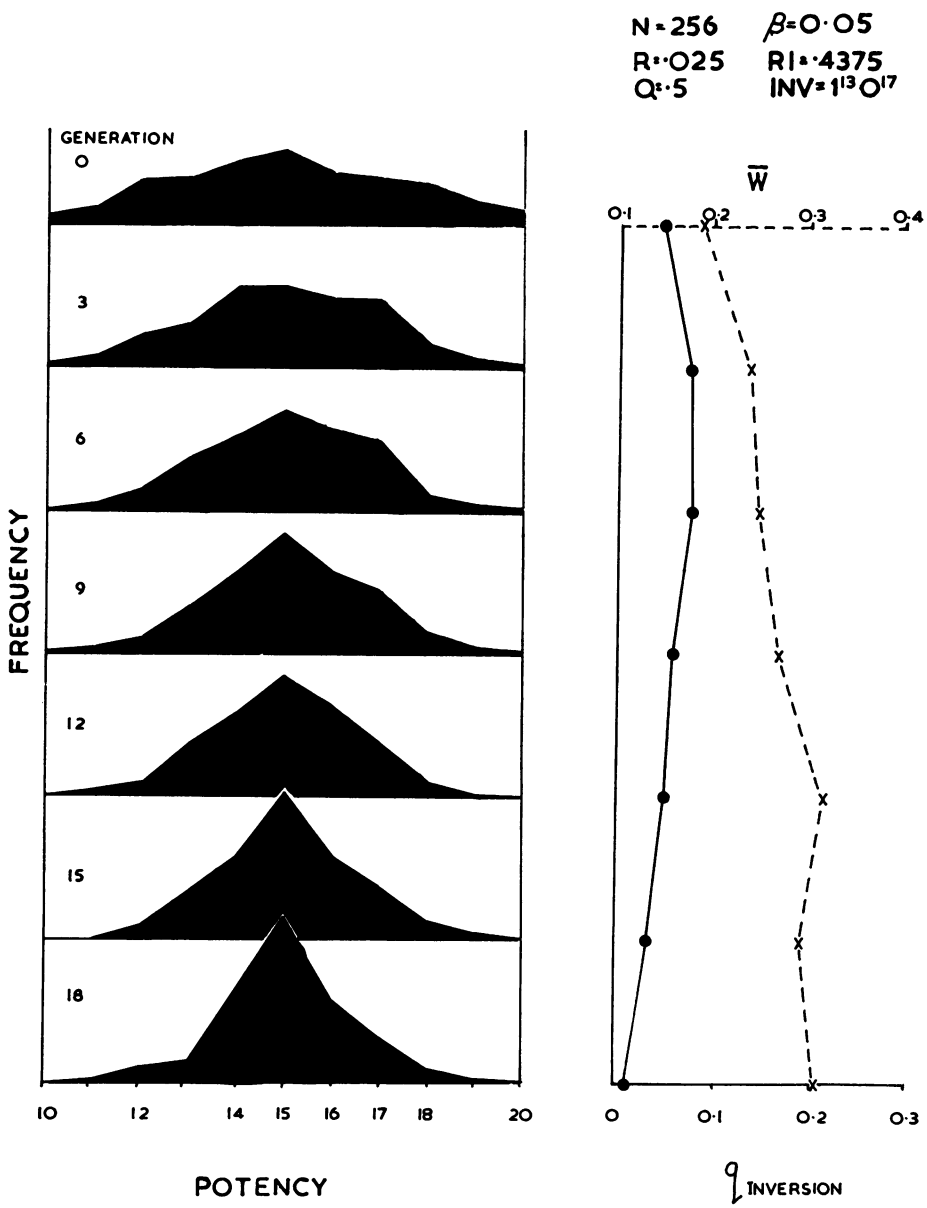

FIG. 8B. (See legend on page 286).

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