EXPERIMENTAL POPULATION GENETICS OF MEIOTIC DRIVE SYSTEMS[1,2] I. PSEUDO-*Y* CHROMOSOMAL DRIVE AS A MEANS OF ELIMINATING CAGE POPULATIONS OF *DROSOPHILA MELANOGASTER*

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ABSTRACT

The experimental population genetics of *Y*-chromosome drive in *Drosophila melanogaster* is approximated by studying the behavior of *T(Y;2),SD* lines. These exhibit "pseudo-*Y*" drive through the effective coupling of the *Y* chromosome to the second chromosome meiotic drive locus, Segregation distorter (*SD*). *T(Y;2),SD* males consequently produce only male offspring. When such lines are allowed to compete against structurally normal *SD+* flies in population cages, *T(Y;2),SD* males increase in frequency according to the dynamics of a simple haploid selection model until the cage population is eliminated as a result of a deficiency in the number of adult females. Cage population extinction generally occurs within about seven generations.—Several conclusions can be drawn from these competition cage studies:

(1) Fitness estimates for the *T(Y;2),SD* lines (relative to *SD+*) are generally in the range of 2–4, and these values are corroborated by independent estimates derived from studies of migration-selection equilibrium.

(2) Fitness estimates are unaffected by cage replication, sample time, or the starting frequency of *T(Y;2),SD* males, indicating that data from diverse cages can be legitimately pooled to give an overall fitness estimate.

(3) Partitioning of the *T(Y;2),SD* fitnesses into components of viability, fertility, and frequency of alternate segregation ($Y + SD$ from $X + SD+$) suggests that most of the *T(Y;2),SD* advantage derives from the latter two components. Improvements in the system might involve increasing both the viability and the alternate segregation to increase the total fitness.

While pseudo-*Y* drive operates quite effectively against laboratory stocks, it is less successful in eliminating wild-type populations which are already segregating for suppressors of *SD* action. This observation suggests that further

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studies into the origin and rate of accumulation of suppressors of meiotic drive are needed before an overall assessment can be made of the potential of *Y*-chromosome drive as a tool for population control.

IN recent years, there has been an increased interest in the use of genetic methods for the control of the size or genetic composition of natural populations. Most of these methods are variations of: (1) the mass release of sterilized males to reduce population size, (2) the mass release of translocation- or compound-autosome-bearing individuals to force fixation of desirable linked traits, and (3) meiotic drive to obtain the results of (2). A detailed description of these techniques and the associated literature can be found in, for example, PAL and WHITTEN (1975). In this report, we focus specifically on control techniques involving meiotic drive.

SANDLER and NOVITSKI (1957) have defined a meiotic drive locus as one which, as a result of the mechanics of the meiotic divisions, leads to a nonrandom recovery (specifically, an excess) of the driven allele in the gametes of heterozygous individuals. Several researchers have demonstrated theoretically that alleles showing meiotic drive will become fixed under a wide variety of conditions (HARTL 1972; HIRAIZUMI, SANDLER and CROW 1960; PROUT, BUNDGAARD and BRYANT 1973). Meiotic drive systems can thus be used either to carry valuable linked traits to fixation (HICKEY and CRAIG 1966; VON BORSTEL and BUZZATI-TRAVERSO 1962), or, in the case of sex-linked drive, to cause extinction of a population owing to a deficiency of one sex (HAMILTON 1976).

Meiotic drive offers advantages in population control over other methods in that it requires only small initial releases of individuals into the target population, the effect of these releases is propagated through many generations, and the drive-altered population is less affected by immigration. On the other hand, there are at least two potential drawbacks to the use of drive systems—their apparent rarity, and their tendency to accumulate drive suppressors (either true suppressors at other loci, or drive-insensitive alleles at the drive locus itself). The first problem may be more apparent than real, because meiotic drive is difficult to detect in nature. This follows from the consideration that in order to be discovered, drive must be at the same time strong enough to eclipse statistical fluctuations from the expected 1:1 segregation, and not so strong as to cause fixation of the driven element. The second drawback is more serious because most known drive systems suffer from it. Thus, if a drive allele is either slow to fix, or reaches a polymorphic equilibrium, there will generally be enough time for natural selection to operate in the direction of inactivating the drive through the accumulation of suppressors (see HARTL 1975, for a particularly lucid discussion of the whole modifier question). It would seem, therefore, that to be effective in population control a drive system must go to fixation rapidly.

Meiotic drive mutants showing *Y*-chromosome drive satisfy this requirement. (For the purposes of this paper, the term *Y* chromosome will be presumed to also include that chromosome carrying the permanently heterozygous gene in single-locus sex determination systems, as in mosquito.) When *Y*-chromosome drive is complete (that is, a male carrying the driven *Y* produces only male offspring),

the fixation of the *Y* chromosome means the extinction of any population carrying it. HAMILTON (1967) has shown that such *Y*-drive loci go to fixation much more rapidy than equivalent loci on the *X* chromosome or autosomes, owing primarily to the fact that a *Y*-chromosome drive locus is subject to selection every generation, while the others are not. Moreover, not only does *Y* drive cause extinction of the target population when fixed, but it also depresses population fecundity throughout the process of replacement (if it is assumed that egg, not sperm, production is the limiting factor in population fecundity).

Unfortunately, the very efficiency of *Y*-chromosome drive makes it practically impossible to observe in nature, and in fact it is only in the mosquito that a clear case of *Y* drive has been isolated (HICKEY and CRAIG 1966). This scarcity also makes it difficult to study the experimental population genetics of *Y*-chromosome drive. One way around this problem is to use a well-characterized autosomal locus showing complete meiotic drive and to link it to the *Y*-chromosome by way of chromosomal rearrangements, thus generating what might be called pseudo-*Y* drive.

In this report, we present an analysis of a case of pseudo-*Y* drive involving the second chromosome meiotic drive locus, Segregation-distorter (*SD*), of *Drosophila melanogaster*. The linkage of *SD* and the *Y* chromosome was accomplished by X-irradiating *SD* males to give a series of *T(Y;2),SD* lines. The males of these lines exhibit complete *Y* drive as a result of: (1) an excess of alternate segregation of the *Y* and *SD* chromosomes from their *X* and SD^+ homologues at the first meiotic division, with the subsequent *SD*-induced dysfunction of the $X;SD^+$ bearing sperm, and (2) aneupoidy of the *X,SD*-bearing gametes from adjacent segregations leading to their elimination as zygotic lethals. A series of such *T(Y;2),SD* lines was tested against structurally normal SD^+ flies in competition cages, and the rate of male genotypic frequency change was used to estimate the fitness of the *T(Y;2),SD* lines. The results of these cage studies demonstrate (a) that pseudo-*Y* drive lines can fix rapidly in target populations to cause their ultimate extinction; (b) that the fixation process follows the simple dynamics predicted by haploid selection theory; and (c) that the effects of immigration on the process are minimal. In additon, a partition of the *T(Y;2),SD* fitness advantage into components of viability, fertility, and frequency of alternate segregation shows that the latter two components contribute most to the success of the pseudo-*Y* drive. Finally, in at least one case, we will demonstrate that the prior existence of drive suppressors segregating in target populations can be enough to allow natural selection to oppose and eventually eliminate the pseudo-*Y* drive.

MATERIALS AND METHODS

A. SD *stocks*

Segregation-distorter (SD): A complex of loci located on chromosome *2* of *D. melanogaster* capable of exhibiting meiotic drive (SANDLER, HIRAIZUMI and SANDLER 1959). The complex seems to consist of at least an *Sd* locus, currently mapped to the basal euchromatin of *2L*, where the action of Segregation-distorter is presumed to originate; a locus herein called Responder (*Rsp*), which is the target for the *Sd* action and is probably located in the centromeric heterochromatin of *2R*; and a series of loci that act as modifiers of *Sd* strength, most of small effect,

spread at least throughout *2R* (SANDLER and CARPENTER 1972; HARTL 1974). The current interpretation of the *SD* phenomenon is that the action of *Sd* is directed to cause dysfunction of any sperm carrying a sensitive *Rsp* allele. Consequently, the *SD* chromosome is thought to carry the *Sd* allele and an insensitive Responder (*Sd Rsp+*) while the *SD+* chromosome carries a sensitive Responder (*Sd+ Rsp*). *SD* operates in *SD/SD+* males to give an excess of *SD* bearing sperm, the excess being due to the dysfunction and loss of *SD+* bearing sperm resulting from the action of *SD*. The extent of this dysfunction in a particular line is measured by the *K*-value, defined in Table 1. A review of the discussions on the nature of *SD* chromosome structure and function can be found in HARTL and HIRAIZUMI (1975). The *SD* line used in the current study was:

SD-72: one of the original *SD* lines isolated by HIRAIZUMI (SANDLER, HIRAIZUMI and SANDLER 1959) from a natural population of *D. melanogaster*. As well as the *SD* complex, this line carries two inversions: (1) a small pericentric inversion with breakpoints at 39–40 and 42A, and (2) an inversion in distal *2R*, *In(2R)NS*, with breakpoints at 52A2-B1 and 56F 9–13 (LEWIS 1962). It is a strong distorter ($K \approx 1.00$). *SD-72* and all other *SD* stocks used in this study were maintained by repeated backcrossing of *SD/cn bw* males to *cn bw* females each generation.

B. *Standard* D. melanogaster *stocks*

cn bw: a stock carrying two second chromosome mutants (cinnabar and brown eye color, respectively). The *cn bw* chromosome is an *SD+* chromosome that is typically extremely sensitive to *SD* action, and it is used as the standard *SD+* in this study.

Canton-S, *Tokyo* +: two standard stocks used as a source of wild-type chromosomes.

c-scan: a multiply marked stock used for linkage detection; carries *sc f*; *al b sp*; *ve st ca*.

Further information on these stocks and a detailed description of the individual mutants can be found in LINDSLEY and GRELL (1968).

C. *Estimation of* k *values*

The *k*-values of individual *SD* males were determined by matings with 2–3 *cn bw* females. The matings were generally brooded after 8 days, the parents being discarded after 8 more days. Progeny from the matings were counted for no more than 19 days, thus avoiding contamination from a second generation. These *k*-values were then used to calculate the mean *K* values for a given *SD* line.

D. *Fitness studies on* T(Y;2),SD *lines*

Induction of translocations: Week-old *SD-72* males were subjected to an X-ray dose of 4000r (dose rate $\approx$ 400r/min) in order to induce *Y;SD* translocations in mature sperm. Sons of these irradiated males were mated individually, and those producing only male offspring were selected as *T(Y;2),SD-72* lines. Since the function of *SD* is sensitive to temperature perturbations, these *SD* lines were always kept at 25°, unless otherwise noted. Each *T(Y;2),SD-72* line was given a designation *T-i*, where *i* is a number denoting the particular independent translocation event from which the line was derived.

Competition between T(Y;2),SD *and standard males*: The total fitness of each *T(Y;2),SD* male line was measured against the fitness of standard *cn bw* males by assaying the relative frequency of the two types, through time, when competing for *cn bw* females in population cages. Each cage was maintained with fourteen shell vials, cycled so that each vial remained in the cage for 17 days. Cages were initiated with 200 males (a given proportion of which are *SD*s) and 500 *cn bw* females, the excess of females used to minimize stochastic fluctuations in the initial matings. The frequency changes through time were assayed by total counts of the adult cage population every 14 days, the first such count being made 17 days after cage initialization. After these counts were made, a transformation of the rate of change of ln (frequency of *SD* males/frequency of *cn bw* males) through time was used as an estimate of the fitness of the particular *T(Y;2),SD-72* line (see Table 1).

Analogous cage studies were carried out using one of the *T(Y;2),SD-72* lines (*T-6*) in competition with + + flies, in order to simulate more closely the expected behavior of *T(Y;2),SD-72*

lines when introduced into natural populations. For several of the *T(Y;2),SD-72* vs. *cn bw* studies, as well as all the *T-6* vs. + + cases, measurements were made on the initial and final *k*-values in order to ascertain whether modifiers of *SD* had accumulated.

Immigration studies: For some *T(Y;2),SD-72* lines, total fitness was independently measured by ascertaining the equilibrium frequency of *SD* males in population cages which were subjected to repeated immigrations of *cn bw* males. Immigrations were carried out at either one or two generation intervals by replacing a fraction of the *SD* males by an equivalent number of *cn bw* flies from control *cn bw* cage populations, with *cn bw* virgin females added simultaneously to maintain cage fecundity. It is presumed that the age distribution for the two classes of male adults (immigrant and non-immigrant) should be roughly equivalent, since both groups are from equivalent population cages. The fraction replaced was dependent on the immigration rate used, which in these studies was either 10, 25, or 30%.

The fitness estimates from these immigration studies were compared to those derived from the competition cage experiments in order to test the reliability of the latter estimates. Finally, the final *k*-values from the immigration cages were also assayed to check for modifier accumulation.

Partitioning of total fitness. The total fitness estimates from the competition cages were broken down into components attributed to male fertility, viability, and segregation (that is, the frequency with which *Y* and *SD* segregate from *X* and *cn bw*). The segregation frequency *c* can be independently measured from studies of egg hatchability as the number of eggs receiving *Y;SD* or *X;cn bw* gametes (*i.e.*, euploid zygotes, which are able to hatch) divided by the total number of fertilized eggs (*i.e.*, euploid and aneuploid zygotes combined). Similarly, the frequency of fertilized eggs which survive to be adult male *SD* flies, divided by the number of adult male *cn bw* flies in control groups, is an estimate of segregation and viability taken together (denoted by *cv*). Using these two estimates it is possible to specify the magnitude of the three components of total fitness, and the exact procedure for extracting these quantities is discussed in subsequent sections.

The eggs for these experiments were collected in the following way. An excess number of the males to be tested were mated with *cn bw* females in highly yeasted food bottles, and allowed to mate for several days, so that the females were all presumed to be mated. The parents were then transferred to empty bottles and the females allowed to lay eggs on specially prepared 2% agar plates with a charcoal background to increase contrast. To facilitate egg laying by the females, the plates were coated with a thin layer of yeast dissolved in equal parts of ethyl alcohol and acetic acid. The plates were changed and eggs counted at 8 hour intervals, and estimates of hatchability were made after two days, when all viable eggs should have hatched. In all cases, corrections were made for unfertilized eggs. Control studies were carried out in the same manner on separate groups of eggs derived from *cn bw* × *cn bw* matings.

THEORY

(See Table 1 for a summary of the quantities discussed in this section.)

Population dynamics of competition cages

A. *Total fitness estimates from rate of cage extinction*: Each competition cage described above is assumed to be a replicate of the same genetic process; that is, the replacement of a normal *Y* chromosome by the translocation *Y* of a specific *T(Y;2),SD*. Figure 1 illustrates the meiotic segregation products for such a *T(Y;2),SD* male. We will first describe a general discrete generation model of the replacement process which allows for the survival of the hyperploid males in Figure 1. This discrete generation model is expected to give a reasonably good approximation to the continuous replacement process actually occurring.

TABLE 1

A summary of the relevant parameters and estimates for pseudo-Y drive systems involving SD

f = fertility of a *T(Y;2),SD* male relative to a standard male (usually *cn bw* in these studies).

v = viability of a *T(Y;2),SD* male relative to a standard male.

c = frequency of alternate segregation ($Y + SD$ from $X +$ *cn bw*) in a *T(Y;2),SD* male. This quantity is defined to be 0.5 in nontranslocated lines.

z = probability of *SD* induced dysfunction of a *SD*+-bearing sperm in a *SD/SD*+ male.

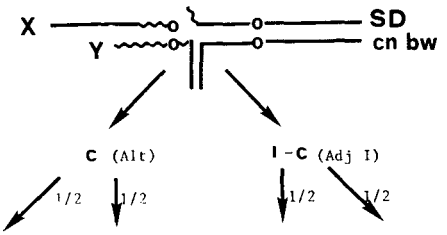
k = the observed proportion of *SD*-bearing sperm among all functional sperm of a *SD/SD*+ male.

K = the mean k value of a stock or line.

$W = \frac{2fcv}{2\text{-}z}$ = total fitness of a *T(Y;2),SD* male relative to a standard male.

$\ln\left(\frac{q_{g+1}}{p_{g+1}}\right) \ln\left(\frac{q_g}{p_g}\right) = \ln(W)$ = one successive difference in a cage where

$\ln\left(\frac{q_g}{p_g}\right) = \ln\left(\frac{\#\ T(Y;2),SD \text{ males at generation } g}{\#\ cn\ bw \text{ males at generation } g}\right)$



Gametic type	X;cn bw	Y;SD	X;SD	Y;cn bw
Frequency	$\frac{c}{2}^{*}$ (1-z)	$\frac{c}{2} \cdot 1$	$\frac{1-c}{2} \cdot 1$	$\frac{1-c}{2} \cdot (1-z)^{**}$
Zygotic type^{+}	cn bw female	T(Y;2)SD male	lethal	hyperploid male--generally lethal or sterile

*c = proportion of meioses in which Y;SD segregates from X;cn bw (proportion of alternate segregation)

**$1-z = \frac{1-k}{k}$ = proportion of surviving SD^{+} gametes (see Table 1)

+when male is mated to a cn bw female

FIGURE 1.—Segregation in *T(Y;2),SD* males. When the hyperploid males are lethal or sterile, the only important products are the two resulting from alternate segregation. Within this class, the parameter z determines the sex ratio in the progeny. It is assumed that only one of the adjacent segregations (Adj I) occurs with significant frequency.

Since a competition cage has only *cn bw* females, a population segregating for *T(Y;2)*, SD and *cn bw* (normal *Y*) males can be completely described by the frequencies of the various male types. Figure 2 depicts the one generation change in these male frequencies, where each generation is measured at the adult stage. Since each new frequency is a complex function of the frequencies in the previous generation it is difficult to work with the male frequencies directly, but this complexity can be removed by using the ratio of the male frequencies instead of the individual values. From Figure 2 it is clear that

$$\frac{q_{g+1}}{p_{g+1}} = \frac{2fcv}{2\text{-}z} \quad \frac{q_g}{p_g} \,. \tag{1}$$

Taking logarithms and rearranging gives

$$\ln\left(\frac{q_{g+1}}{p_{g+1}}\right) - \ln\left(\frac{q_g}{p_g}\right) = \ln\left(\frac{2fcv}{2\text{-}z}\right). \tag{2}$$

If the parameters f, e, v, and z are all constant (and hence independent of p_g and q_g), the difference equation (2) can be used to estimate the fitness advantage of the *T(Y;2),SD* males. For purposes of simplification, let

$$Y_g = \ln\left(\frac{q_{g+1}}{p_{g+1}}\right) - \ln\left(\frac{q_g}{p_g}\right)$$

and

$$W = \frac{2fcv}{2\text{-}z} \,, \tag{3}$$

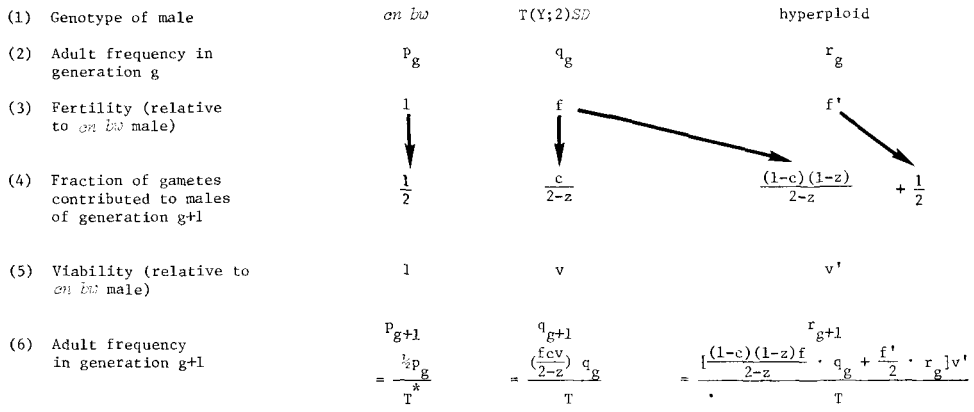
where W measures the fitness of the $Y + SD$ chromosomes in *T(Y;2),SD* males relative to the Y and *cn bw* chromosomes in *cn bw* males. Equation (2) then becomes

$$Y_g = \ln W \tag{4}$$

Each cage yields several such successive differences, and these can be used as random variables in an analysis of variance treatment to give the best available estimate of W, the total fitness. The mechanics of the ANOVA approach will be discussed subsequently.

The fitness estimate derived from the general model is not dependent on the lethality or sterility of the hyperploid males. This follows from the observation that r_g does not enter into the difference equation. The hyperploids, when present, act only as background noise in the cages, although they could conceivably contribute enough female offspring to prevent the ultimate extinction of the population. In any case, for the lines utilized in these experiments the parameter z is essentially equal to one, and no functional hyperploid gametes will ever be produced (see Figure 2); the "hyperploid noise" will therefore be negligible.

B. *Analysis of variance:* Equations (2) and (4) are the deterministic representations of the one generation change in *T(Y;2),SD* frequency in a single cage. Typically, a single cage can be sampled at least several times and thus provides several Y_g values, where $g = 1, 2, \ldots, n$. Each of these values of Y



*T = sum of numerators

FIGURE 2.—One generation change in *T(Y;2),SD* male frequencies in competition cages. Note that the *T(Y;2),SD* males contribute to two males classes in the next generation, while the other male types contribute only to their own class. The values for the gamete fractions from the *T(Y;2),SD* males are determined as the frequency of that class among all gametes in Figure 1, divided by the total frequency of surviving gametes.

provides an estimate of ln W for the particular translocation line being investigated. If we set $\mu' = \ln W$, an equivalent statistical representation of (4) is the linear model

$$Y_g = \mu' + \varepsilon_g \tag{5}$$

where ε_g = random error associated with the gth sample time. However, a given *T(Y;2),SD* line is represented by more than one cage; in fact, there are generally three different starting frequencies, each represented by three replicate cages. Moreover, we may wish to compare several *T(Y;2),SD* lines simultaneously. The changes introduce further linear effects due to *SD* line, sample time, replication, and initial cage condition (starting frequency). Equation (5) can be expanded to give the full linear model

$$Y_{ijkg} = \mu + C_i + S_j + CS_{ij} + K_{ij} + T_g + \varepsilon_{ijkg} \tag{6}$$

where:

C_i = effect of i^{th} *T(Y;2),SD* line
S_j = effect of j^{th} starting frequency (*i.e.*, 10%, 30%, 50%)
CS_{ij} = interaction between i^{th} line and j^{th} starting frequency
K_{ijk} = effect of k^{th} cage replication
T_g = effect of g^{th} sample time
ε_{ijkg} = random error

Equation (6) represents a modified split-plot design, with T_g acting as an additional crossed effect within each cage.

It is possible to analyze the various effects in equation (6) by way of a nested two-way analysis of variance. This will be a mixed model ANOVA, since the

starting frequency effects (S_j) and time effects (T_g) are fixed, while the effects of cage replication (K_{ijk}) and *T(Y,2),SD* line (C_i) are random. The ANOVA approach allows us to partition the total variation of the Y_{ijkg} values into components attributable to each of the effects in equation (6). Appropriate F-tests may then be employed to ascertain the statistical significance of each component. If the effects S_j, CS_{ij}, K_{ijk} and T_g are all statistically nonsignificant, the basic model reduces to

$$Y_{ijkg} = \mu + C_i + \varepsilon_{ijkg}. \tag{7}$$

Each Y_{ijkg} from a given *T(Y;2),SD* line would be a direct estimate of $\mu + C_i = \mu'_i = \ln W_i$; that is, $Y_{i...}$ will be the best unbiased estimate of $\ln(2fcv/2\text{-}z)$ for *T(Y;2),SD* line *i*. Contrarily, statistical significance of any of these effects would mean that the estimate of $\ln(2fcv/2\text{-}z)$ depends on some extraneous variable such as sample time, cage, or starting frequency. Such a variable would have to be corrected for in any final estimate of total fitness.

C. *Total fitness estimates from migration cages:* The observed equilibrium values in the migration cages offer an independent estimate of total fitness of the *T(Y;2),SD* line. These experiments were run using only *T(Y;2),SD* lines which showed complete distortion ($K \cong 1$, $z \cong 1$). Therefore, in the general model of Figure 2, $r_g = 0$ for all g. This implies $p_g + q_g = 1$, and this identity coupled with the equation (1) leads directly to the expression for the change in *T(Y;2)SD* frequency in one generation

$$\Delta q = q_{g+1} - q_g$$

$$= \frac{\frac{2fcv}{2\text{-}z} \cdot q_g}{\frac{2fcv}{2\text{-}z} \cdot q_g + p_g} - q_g = \frac{Wq_g}{Wq_g + p_g} - q_g ,$$

which leads to

$$\Delta q = \frac{(W\text{-}1)\, p_g \cdot q_g}{Wq_g + p_g}, = \frac{s \cdot p_g \cdot q_g}{W} \tag{8}$$

where W-1 is the selection coefficient(s) associated with the *T(Y;2),SD*. Equation (8) is identical to the results for a one generation frequency change for cases of haploid selection (CROW and KIMURA 1970). This is not surprising, since the competition in the cages is effectively between two different Y; autosome haploid complements, with the *cn bw* females acting as the limiting "substrate" for these competing haploids. Equation (8) can be extended to show that after n generations Δq becomes

$$\Delta_n q = \frac{(W^n\text{-}1) \cdot p_g \cdot q_g}{W^n \cdot q_g + p_g} \tag{9}$$

The migration model assumes that at one or two generation intervals a fixed fraction (m) of the adult males in a cage are replaced by immigrant *cn bw*

TABLE 2

Equilibrium in competition cages subjected to migration pressure in the form of cn bw *flies*

W \ m	.05	.10	.15	.20	.25	.30	.35	.40	.45
1.0	L*	L	L	L	L	L	L	L	L
1.1	.450	L	L	L	L	L	L	L	L
1.2	.700	.400	.100	L	L	L	L	L	L
1.3	.783	.567	.350	.130	L	L	L	L	L
1.4	.835	.650	.475	.300	.125	L	L	L	L
1.5	.850	.700	.550	.400	.250	.100	L	L	L
1.6	.867	.733	.600	.467	.333	.200	.067	L	L
1.7	.878	.757	.636	.514	.393	.271	.150	.029	L
1.8	.888	.775	.662	.550	.438	.325	.212	.100	L
1.9	.894	.789	.683	.577	.472	.367	.261	.156	.050
2.0	.900	.800	.700	.600	.500	.400	.300	.200	.100
2.1	.905	.809	.714	.618	.523	.427	.332	.236	.141
2.2	.908	.817	.725	.633	.542	.450	.359	.267	.175

a) Equilibrium frequency of T(Y;2)*SD* males with immigration every generation, where $\hat{q} = 1 - (Wm/W-1)$.

W \ m	.05	.10	.15	.20	.25	.30	.35	.40	.45
1.0									
1.1	.712	.424	.136	L*	L	L	L	L	L
1.2	.836	.673	.509	.345	.182	.028	L	L	L
1.3	.878	.755	.633	.510	.388	.265	.143	.020	L
1.4	.898	.796	.694	.592	.490	.388	.285	.183	.081
1.5	.910	.820	.730	.640	.550	.460	.370	.280	.190
1.6	.918	.836	.754	.672	.590	.508	.426	.344	.262
1.7	.924	.847	.771	.694	.618	.541	.465	.388	.312
1.8	.928	.855	.783	.711	.638	.566	.494	.421	.349
1.9	.931	.862	.793	.723	.654	.585	.516	.447	.378
2.0	.933	.867	.800	.733	.667	.600	.533	.467	.400

b) Equilibrium frequency of T(Y;2)*SD* males with immigration every two generations, where $\hat{q} = 1 - (W^2m/W^2-1)$.

W = fitness of *T(Y;2),SD* males relative to *cn bw* males (see Table 1). m = migration rate in terms of fraction of *T(Y;2)SD* males replaced by *cn bw*. The figures in the body of the table represent the theoretical equilibrium frequencies, $\hat{q}$.

* L = *T(Y;2)SD* is lost from population.

males, and that this immigration acts oppose the intrinsic selective increase in *T(Y;2),SD* frequency. A stable equilibrium is attained whenever the two forces are in balance; that is, whenever

$$\frac{(W\text{-}1).p_g q_g}{W.q_g + p_g} - m.q_{g+1} = \Delta q \quad = 0$$

for migration at one generation intervals. After substituting as before for q_{g+1} and rearranging, the equilibrium value for q can be shown to be

$$\hat{q} = 1 - \frac{W.m}{W\text{-}1} \tag{10}$$

This result can also be extended to include the general case of a population with migration occurring every n generations, the equilibrium being defined as

$$\hat{q} = 1 - \frac{W^n.m}{W^n\text{-}1} \ . \tag{11}$$

For the special cases $n = 1$, $n = 2$, Tables 2a and 2b tabulate the $\hat{p}$ values corresponding to various W and m values.

Once $\hat{q}$ is measured in the equilibrium migration cages, it can be used with m to derive W from equation (11). This value of W can be compared to the corresponding estimate derived from the ANOVA analysis of equation (7) to give information on the reliability of the latter estimate. Note that it is implicitly assumed here that $\hat{q}$ is measured *after* migration. If the frequency was measured *before* migration, both sides of equation (10) would simply be multiplied by $1/(1-m)$. This would not change the estimate of W derived from either (10) or (11) however, so I have arbitrarily chosen to use the post-migration frequency as the quantity of interest.

RESULTS

I. *Generation of* T(Y;2),SD-72 *lines*

A total of 33 *T(Y;2),SD-72* translocations were recovered from 950 tested progeny of irradiated *SD-72* males, and ten of these lines were chosen at random for more detailed analysis. The exact position of the translocation breaks was determined by salivary gland analysis, and the results are listed in Table 3. The striking fact is that 9 of the 10 translocations showed breaks in or around the centromeric heterochromatin of the second chromosome; that is, near the site of the *Sd* locus. This nonrandomness in the position of second chromosome breaks is a bit surprising. Although LINDSLEY *et al.* (1972) have demonstrated that a nonrandom distribution of break-points exists for *Y;2* translocations, with an excess in the heterochromatic regions ($\approx 26\%$ for the centromeric heterochromatin), the 9:1 ratio observed here is too high to be explained on this basis.

The *K*-values for the *T(Y;2),SD-72* lines are listed in Table 3 along with the value for the control *SD-72* stock. As is apparent from the table, none of the *K*-values seem to be affected by the translocation process itself. The other surviving *T(Y;2),SD-72* lines show similar high K values. These results are somewhat surprising in view of a study by NOVITSKI and EHRLICH (1970) which suggested that *SD* action is very sensitive to the presence of chromosomal rearrangements. In fact, the *K*-values for four *T(Y;2),SD* lines examined in that report were not only extremely low, but generally showed self-distortion (see Table 3). These two characteristics of the present *T(Y;2),SD-72* lines, that is, the

TABLE 3

Description of SD *lines examined*

Stock or line	K-value (total progeny or tested males on which estimate is based)	Translocation type	Autosomal breakpoints
(1) T(Y;2)SD-72 lines			
T-1	≈1.00 (3812 progeny)	T(Y;2L)	26B9-10
T-6	≈1.00 (2020 progeny)	T(Y;2L;(4?))	≈41; fourth chromosome often associated with centromere of SD chromosome
T-12	≈1.00 (6057 progeny)	T(Y;2L;3L)	41A-B; 62F5-6
T-22	≈1.00 (2355 progeny)	T(Y;2L)	36B-C
T-23	≈1.00 (2743 progeny)	T(Y;2L)	39B-C
T-24	≈1.00 (2868 progeny)	T(Y;2)	≈41
T-25	≈1.00 (1703 progeny)	T(Y;2R)	very near centromere in middle of SD-72 pericentric inversion
T-31	≈1.00 (3631 progeny)	T(Y;2L)	≈41
T-32	≈1.00 (4223 progeny)	T(Y;2L)	38A
T-41	≈1.00 (3056 progeny)	T(Y;2L) + In(2L)	Y-2 translocation breakpoint at 41B-C; distal inversion breakpoint at ≈25A
(2) Special cases			
SD-72	≈1.00 (8298 progeny)		
T-6/++	≈1.00 (38 males)		
(3) Stocks from Novitski and Ehrlich (1970)			
† T(Y;2)SD, EM106	.555	T(Y;2L)	31D
† T(Y;2)SD, j-4	.336	T(Y;2L)	37B
† T(Y;2)SD, EM135	.132	T(Y;2R)	42A
T(Y;2)SD, CB-1c	.456	T(Y;2R)	44D

† derived from an SD line with $y^{+}YB^{S}$

K-values are listed with the total progeny number on which the estimates were based (or the number of males tested to give the estimate), except for the lines from NOVITSKI and EHRLICH (1970) for which the corresponding progeny numbers are not known. The breakpoints for the translocation were determined from salivary gland squashes.

concentration of break points in the centromeric heterochromatin of chromosome *2* and the uniformly high *K*-values, are thus somewhat surprising in view of previously reported experimental results. The final resolution of the significance of these discrepancies must await the analysis of more translocation lines.

II. *Estimation of* T(Y;2),SD *fitness*

A. T(Y;2),SD-72 *vs.* cn bw *competition cages*: The total fitness for each of the ten induced *T(Y;2),SD-72* lines was estimated from competition cages according to the protocol described previously in the THEORY section. In that section, (equation 3 and Table 1) the total fitness was defined as $W = \frac{2fcv}{2-z}$. However, since all of the ten *T(Y;2),SD-72* lines examined here had *K*-values of ~ 1.00, then $z \approx 1.00$ (see Table 1), and thus for the purposes of our estimation procedures here, $W = 2fcv$ = total fitness. For experimental purposes, the ten lines were broken into two groups.

1. *Lines used to analyze components of variation: Modified split-plot design.* One group of three lines (*T-1*, *T-6* and *T-12*) was examined at three starting frequencies for the *T(Y;2),SD-72* males (10, 30, and 50%), each with three

replicates, with the exception that *T-1* was not examined at the 50% starting frequency. This is the modified split-plot design described in part B of the THEORY section. Figures 3, 4, and 5 represent $\ln(q/p)$ graphed against time for each competition cage of *T-6*, *T-12* and *T-1*, respectively. The results from the figures are clear. In most cages the *T(Y;2),SD-72* line rapidly increased in frequency until it was fixed in the population, fixation being defined as having occurred when less than 7 *cn bw* females remained in the cage. This criterion is generally satisfied when $\ln(q_g/p_g) > 3$, *i.e.*, when the frequency of *T(Y;2),SD-72* males was > 0.95. The reason for choosing this seemingly arbitrary cut-off point was the fact that cages with fewer than 7 females seem to be unable to produce new offspring and are in fact apt to collect mold and mite infestations, and it was deemed best to discontinue them at this point. Fixation was rapid, the rate being dependent, of course, on the particular line used and its starting frequency. For the most part, the fixation time was on the order of 100 days ($\approx$ 7 generations). As an example of the gross fixation process, Table 3A gives observed population

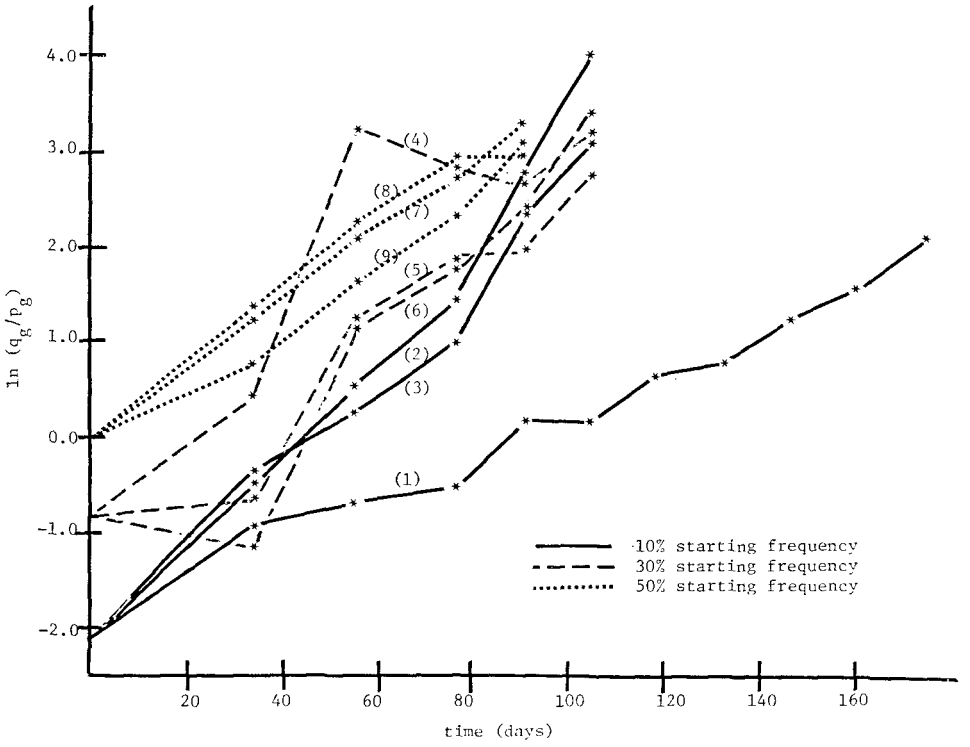


FIGURE 3.—Results of *T-12* competition cages. The quantity $\ln(q_g/p_g)$ is used as the ordinate to describe the process of fixation (see Table 1) in this figure and also Figures 4 and 5, since the change in $\ln(q_g/p_g)$ is expected to be roughly linear under the haplo selection model (see text). Numbers refer to the particular cage to which the labeled curve corresponds. Calculations are based on the magnitude of the change in $\ln(q_g/p_g)$ from one sample time to another, with the exception of the initial jump (from time = 0 to time = 36) which is not used in analysis.

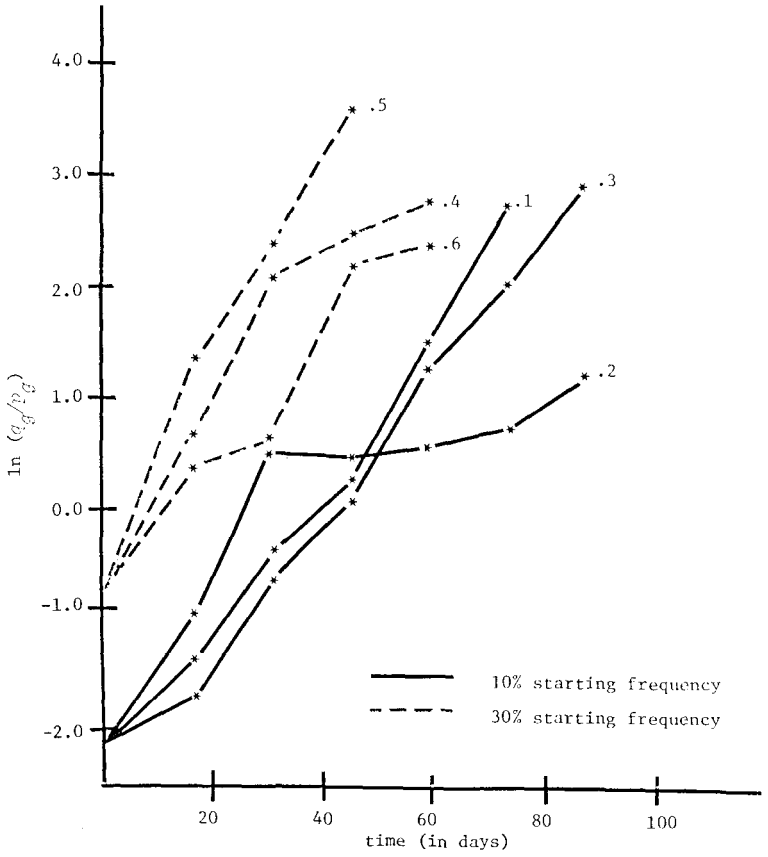


FIGURE 4.—Results of *T-1* competition cages. (See Figure 3 caption for explanation.)

values for the T-6 cages charted in Figure 5. Two important conclusions emerge from the table. First, the populations remain roughly constant in size through the early sample times. Total fecundity is apparently not reduced significantly until the number of females in the cage is on the order of 80 or less, suggesting that density compensation is occurring throughout the initial stages of the competition, but fails when females are required to produce more than 15–20 offspring each to attain the carrying capacity of the cage. Secondly, the number of males remains high until the final population crash, suggesting that these populations would be buffered with respect to immigration throughout the fixation process. Data from the other nine lines give similar results, though not presented here.

For a more detailed examination of the fixation process, the successive differences between sample points were then used as the basic observations in the ANOVA scheme described in the THEORY section. Before using the analysis, one further transformation was carried out on the successive differences. That is, cage generation length in all these studies is taken to be 12 days at 25° (J.

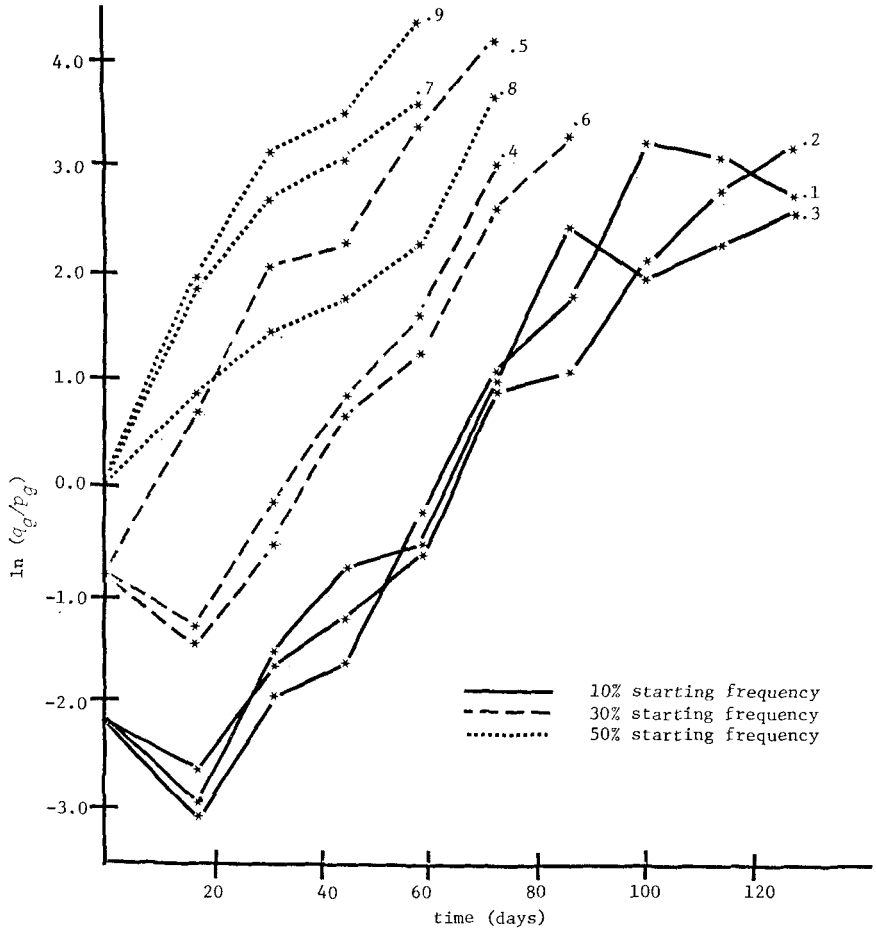


FIGURE 5.—Results of *T-6* competition cages. (See Figure 3 caption for explanations.)

MITCHELL, personal communication), but the original data was collected at 14-day intervals. Therefore, each Y_g should presumably estimate $\frac{14}{12}\ln W$ (or $\frac{14}{b}\ln W$ if the real generation length $b \neq 12$ days), and each datum was so transformed before the ANOVA was carried out. The results of this analysis are reproduced in Table 4. It was not clear at first that the transformed quantity used as the basic unit of data in the ANOVA, $\ln(q_{g+1}/p_{g+1})$, could still be assumed to have a normal distribution, which is a usual assumption in the use of F-tests. To check for normality, the residuals for lines *T-1*, *T-6* and *T-12* were grouped together and their distribution analyzed. The distribution did not show any significant deviations from normality; and indeed, plots on normal probability paper with concomitant checks of skewness and kurtosis from moment statistics reveal no non-normal tendencies in the data. Therefore, we assume that the F-tests are in fact valid.

TABLE 3A

Total population counts for line T-6

T-6 CAGE NUMBER / SAMPLE TIME	10% T-6			30% T-6			50% T-6		
	1	2	3	4	5	6	7	8	9
INITIAL	200/500=700	200/500=700	200/500=700	200/500=700	200/500=700	200/500=700	200/500=700	200/500=700	200/500=700
1	707/646=1353	768/586=1354	704/460=1164	705/518=1223	1137/360=1497	723/529=1252	1421/231=1652	1044/380=1424	1428/200=1628
2	644/280=924	704/236=940	640/223=863	810/106=916	1267/56=1323	857/160=1017	759/22=781	887/74=961	697/13=710
3	724/309=1033	691/216=907	637/189=826	726/143=869	587/27=614	498/133=631	431/8=439	523/12=535	402/7=409
4	701/252=953	551/231=782	641/223=864	714/53=767	586/12=598	1006/147=1153	183/0=183	172/6=188	155/0=155
5	1230/120=1350	1047/116=1163	935/97=1032	641/3=644	657/1=658	1051/13=1064		115/0=115	
6	621/39=660	674/55=729	482/16=498			513/5=518			
7	817/16=833	642/39=681	336/10=346						
8	370/6=376	550/7=557	315/7=322						
9	95/0=95	74/0=74	143/0=143						

Each entry in the body of the table represents (#males/#females = total) for a given sample time (which, with the exception of sample 1, were taken at approximately 2-week intervals). Each group of three cages represents replicates at one initial *T-6* male frequency, as is demonstrated by Figure 5.

A cursory examination of Figures 3, 4, and 5 shows that the cages all seem to be acting as satisfactory replicates of the same process. Only 2 of the 24 analyzed cages show any anomalous behavior, these being cage #1 in Figure 3 and cage #2 in Figure 4. Both of these cages showed much lower rates of *T(Y;2),SD-72* increase compared to the other replicates of their respective lines. One possible explanation for this behavior was that the *K*-value had somehow been reduced in these anomalous cages, perhaps due to the presence of some background *SD* suppressors in the initial cage populations. However, tests on *T(Y;2),SD-72* males from these cages showed that their *K*-value was indistinguishable from the stock *K*-values (*i.e.*, ≈ 1.00). Regardless of the cause for the behavior of these cages, it should be emphasized that the vast majority (22 out of 24) of the competition cages behaved in a quite orthodox and satisfactory way.

The subjective evaluation of cage homogeneity obtained from the figures is verified by the more reliable *F*-tests of Table 4. That is, no significant contribution to the total variation was made by *T(Y;2),SD-72* line, starting frequency, or cage. In fact, the only significant component of variation is that attributable to sample time, most of the significance being derived from the last one or two sample times in each cage. These often showed rates of increase in *T(Y;2),SD-72* male frequency which were lower than equivalent measurements derived from earlier sample times. These low values have a reasonable biological explanation. The fitness estimates derived from these competition cages are determined by

the rate of increase in *T(Y;2),SD-72* frequency, which is reflected in the successive differences. The successive differences are in turn determined mainly by differences in birth rate for *T(Y;2),SD-72* and *cn bw* males. However, by the time the last one or two samples are taken the process of cage extinction has been carried to the point where only 30 or fewer females are left in a given cage, and at this point new births become relatively rare. This means that the last few successive differences are in reality mainly measuring the differential survivability of adult *T(Y;2),SD-72* and *cn bw* males. That is, the persistence of adult males from previous generations exerts a relatively large effect on the total fitness estimate when compared to the contribution from new birth. If this effect of sample time is real, the bias it introduces is not unimportant, but the next section will show that the effect is transitory and in fact disappears when other sets of experimental cages are examined. Therefore, we will include these points in the estimates of total fitness for the purposes of this analysis, with the added note that the inclusion makes the total fitness estimates somewhat conservative in nature, since these last samples will generally fail to take into account any fertility advantage of the *T(Y;2),SD* males.

2. *Lines analyzed only for fitness effects.* Since the starting frequency had no significant effect on the fitness estimates, the remaining seven lines were examined at only one initial frequency (30%), with four replicates. This meant that

TABLE 4

ANOVA table for competition cages involving lines T-1, T-6 *and* T-12

Source	d.f.	M.S.	E.M.S.	F-test
C_i	2	.09789	$\sigma^2_\varepsilon + .294\ \phi_T + 4.765\ \sigma^2_K + 2.637\ \sigma^2_{CS} + .804\ \phi_S + 33.840\ \sigma^2_C$	.70†
S_j	2	.10785	$\sigma^2_\varepsilon + 1.125\ \phi_T + 4.342\ \sigma^2_K + 12.732\ \sigma^2_{CS} + 31.602\ \phi_S$	1.93†
CS_{ij}	3	.05581	$\sigma^2_\varepsilon + .242\ \phi_T + 4.308\ \sigma^2_K + 12.580\ \sigma^2_{CS}$	.40†
K_{ijk}	16	.14011	$\sigma^2_\varepsilon + .078\ \phi_T + 4.359\ \sigma^2_K$	.64†
T_g	7	.75466	$\sigma^2_\varepsilon + 11.714\ \phi_T$	3.45††
error (residual)	75	.21860	σ^2_ε	
Total (adjusted for mean)	105			

For this table and Table 5, the M.S. values were calculated with the appropriate term reordered last in the partition of the sums of squares. Since C_i and CS_{ij} are both random effects, their F-tests are calculated using K_{ijk} (or K_{ik} in Table 5) as the standard, while the fixed effect S_j is treated against the interaction component CS_{ij}. K_{ijk}, K_{ik}, and T_g are all tested against the residual error for their respective F-tests. Higher order interaction terms are ignored in these analyses.

† Nonsignificant at the $\alpha = 0.10$ level.
†† Significant at the $\alpha = 0.01$ level.

each line in these groups was represented in only four cages, rather than the nine total cages which were generally allocated to the lines in group (1). This reduction in information per line was compensated for by an increase in the total number of lines examined. The ANOVA results for these seven lines are reduction in information per line was compensated for by an increase in the are nonsignificant, as was the case for the lines in group (1). However, the effect of sample time is now nonsignificant as well. This result is at variance with the significant sample time effect found for the group (1) lines. Unfortunately, the data for all 10 lines cannot be legitimately pooled to test the overall significance of sample time, since the two groups were tested at different times during the course of the experiments. Nevertheless, the fact that there is not a stable, consistent effect of sample time on the change in T(Y;2),*SD-72* male frequency (and thus on the T(Y;2),*SD-72* fitness estimate as well) would seem to indicate that it is acceptable to pool fitness estimates from different sample times to give an overall estimate of fitness for a particular line.

The last three columns of Table 6 summarize the fitness estimates for the 10 lines examined in this selction. The important column is the one headed by $\widehat{2fcv}$, the estimate of total fitness for a given translocation line. With the exception of *T-12*, which will be discussed subsequently, the fitnesses are generally ≥ 2. This is a very large selective advantage and explains the rapidity with which the translocation lines were able to fix in populations to cause their ultimate extinction. Of course, these fitnesses are measured relative to a standard laboratory strain (*cn bw*) which is certainly much lower in fitness than a corresponding wild-type strain would be expected to be. Therefore, it is not really the absolute

TABLE 5

ANOVA table for competition cages involving the remaining T(Y;2),SD-72 *lines*

Source	d.f.	M.S.	E.M.S.	F-test
C_i	6	.12384	$\sigma_\varepsilon^2 + .313\ \phi_T + 2.444\ \sigma_K^2 + 9.493\ \sigma_C^2$	1.23†
K_{ik}	21	.10031	$\sigma_\varepsilon^2 + .095\ \phi_T + 2.369\ \sigma_K^2$	.39†
T_g	3	.15321	$\sigma_\varepsilon^2 + 13.000\ \phi_T$	.60†
error (residual)	36	.25647	σ_ε^2	
Total (adjusted for mean)	66			

These seven lines were examined at only one starting frequency (30%) and therefore the S_j and CS_{ij} terms disappear from the analysis.

† Nonsignificant at the $\alpha = 0.10$ level.

value of the total finess that is important, but rather it is whether such a fitness excess was enough to insure population extinction (it was) and whether the extinction process proceeded in a uniform way (it did). The value of having the estimate of total fitness itself lies in our ability to partition that fitness into components due to fertility, viability, and meiotic segregation in the *T(Y;2),SD-72* males. Such a partitioning should, we hope, make it possible to ascertain which of these components of fitness can be most easily altered to produce the largest increase in total fitness, and hence increase the efficiency of pseudo-*Y* drive.

B. *Migration cage studies.* As a test of the validity of the fitness estimates derived from the competition cages, fitness estimates were also derived from the equilibrium frequencies observed in cages where the selective advantage of *T(Y;2),SD-72* males was offset by the immigration of *cn bw* males. The approach to equilibrium under immigration pressure was investigated using two replicate cages each of lines *T-12* (30% *cn bw* immigration every two generations), *T-1* and *T-6* (both with 25% *cn bw* immigration every generation). The results from these cage experiments are found in Figure 6. Additional *T-12* replication cages

TABLE 6

Fitness components of T(Y;2),SD-72 *lines*

SD line	$\hat{c}$ estimates												
	A*	B**	$\hat{c}$	$s_{\hat{c}}^2(s_{\hat{c}})$	$\hat{cv}$	$\hat{cv}'$	$\hat{v}$	$s_{\hat{v}}^2(s_{\hat{v}})$	$\hat{f}$	$s_{\hat{f}}^2(s_{\hat{f}})$	$\widehat{ln2fcv}$	$\widehat{2fcv}$	$s^2_{\widehat{2fcv}}(s_{\widehat{2fcv}})$
T-1	587	888	.661	.0003 (.0161)	.483	.456	.696	.0013 (.0361)	2.118	.0178 (.1335)	.6586	1.932	.0097 (.0987)
T-6	408	556	.734	.0004 (.0190)	.251	.381	.520	.0007 (.0239)	2.554	.0816 (.2856)	.6658	1.946	.0013 (.0365)
T-12	561	803	.699	.0003 (.0161)	.477	.502	.718	.0017 (.0412)	1.664 ($\hat{f}^*$=2.636)	.0142 (.1191)	.5134	1.671	.0042 (.0647)
T-22	406	656	.619	.0004 (.0190)	.329	.424	.685	.0012 (.0339)	2.935	.1805 (.4248)	.9119	2.489	.0587 (.2422)
T-23	519	837	.620	.0003 (.0167)	.559	.564	.910	.0026 (.0506)	3.018	.0874 (.2956)	1.2250	3.404	.0810 (.2846)
T-24	566	828	.684	.0003 (.0161)	.549	.560	.819	.0014 (.0381)	1.785	.0063 (.0796)	.6926	1.999	.0009 (.0297)
T-25	561	833	.673	.0003 (.0161)	.508	.515	.766	.0019 (.0431)	3.017	.1114 (.3338)	1.1340	3.108	.0892 (.2986)
T-31	463	719	.644	.0003 (.0179)	.452	.531	.825	.0014 (.0370)	1.957	.0184 (.1355)	.7314	2.078	.0063 (.0797)
T-32	366	743	.493	.0003 (.0184)	.326	.371	.752	.0016 (.0400)	3.093	.0436 (.2088)	.8307	2.295	.0066 (.0815)
T-41	563	845	.666	.0003 (.0161)	.500	.500	.751	.0019 (.0431)	3.019	.0432 (.2078)	1.1049	3.019	.0184 (.1357)
cn bw	825	845	na†	na	na	na	defined to be 1	na	defined to be 1	na	na	na	na
SD-72	892	935	na	na	na	na	.977	.0024 (.0488)	na	na	na	na	na

Empirical variances are calculated according to the procedures outlined in the text.
* Hatched eggs.
** Fertile eggs.
† Not applicable.

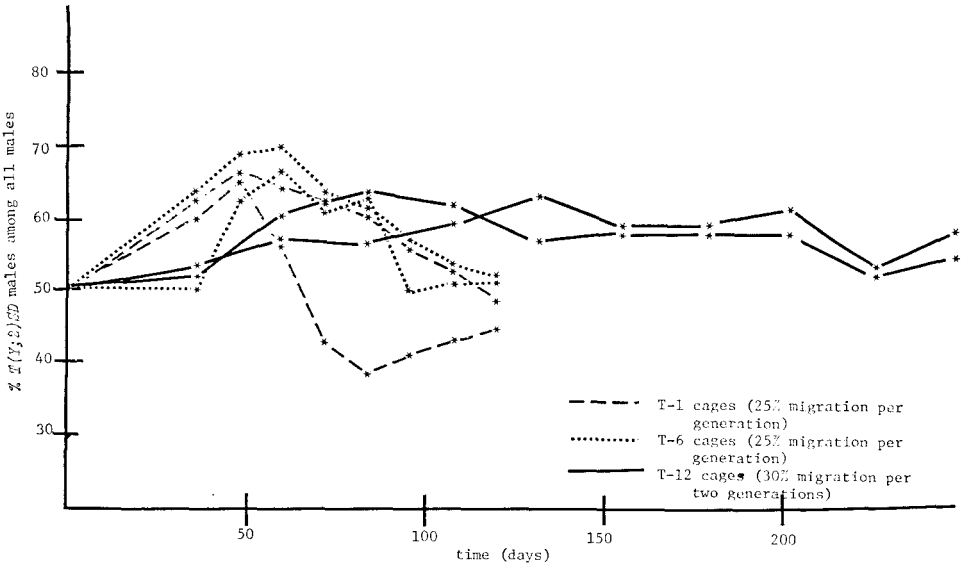


FIGURE 6.—Migration cage results. Fraction of *T(Y;2),SD* males among all males was measured at each sample time after immigration has taken place. Each of the replicate cages was started with 50% *T(Y;2),SD* males and an excess of *cn bw* females.

with 10% immigration every two generations were begun, but it proved impossible to keep these cages from becoming fixed for the *T(Y;2),SD-72*. Generation length was taken to be 12 days in cages at 25°.

Figure 6 indicates that the equilibrium values for *T-12*, *T-1*, and *T-6* in these cages are approximately 0.58, 0.465, and 0.51, respectively. The theoretical values for $\hat{q}$ under migration pressure were presented in Table 2. Using the observed equilibrium values for $\hat{q}$ and the experimentally imposed immigration rates of m, it is possible to read the fitnesses for *T-1*, *T-6*, and *T-12* directly from the table, and these values turn out to be approximately 1.9, 2.05, and 1.9, respectively. Examination of Table 6 shows that these values are reasonably close approximations to the fitness estimates derived from the competition cages. If any directional bias exists, it is that the migration cages seem to overestimate the fitness, since even while immigrants are being added new flies are eclosing to augment the cage populations. These flies are predominantly *T(Y:2),SD-72* males, and their addition makes the effective immigration rate lower than the actual fraction of flies exchanged for *cn bw* males. This would lead to an overestimate of fitness. On the other hand, it was pointed out in an earlier section that the competition cage estimates of total fitness may themselves be conservative. The fact that these conservative estimates correspond rather closely to the presumably liberal migration cage estimates suggests that the methods of estimation used produce results which are quite reliable.

None of the results from these equilibrium populations are in conflict with earlier findings. Since the fitness estimates of *T-1*, *T-6* and *T-12* obtained from the migration studies are clearly compatible with those derived from the com-

petition cages (Table 6), we can be fairly confident that the latter estimates are valid measures of total *T(Y;2),SD-72* fitness, and these estimates will be used in subsequent analyses.

C. *Modifier accumulation in long-term* T(Y;2),SD-72 *lines.* Several of the *T(Y;2)SD-72* competition and migration cages remained segregating for periods of time which were presumably long enough for *SD* suppressors to accumulate. With this in mind, the following *T(Y;2),SD-72* cage lines were assayed for changes in K-value at the time of cage termination (where 10% refers to the initial frequency of *SD* males):

(1) *T-12* 10% competition cages; one examined at day 174;
(2) *T-6* 10% competition cages; three examined at day 130;
(3) *T-1* 10% competition cages; one examined at day 90;
(4) *T-12* migration cages, two examined at day 250;
(5) *T-1, T-6* migration cages, two from each line examined at day 120.

None of these cases showed any significant reduction in K-value below the control values of $K \approx 1.00$. Of course, the life span of even these long term cages is not so long that we would expect accumulation of much new mutation, so it is likely that only preexisting suppressors could have been accumulated rapidly enough to oppose the spread of the *T(Y;2),SD* complex. This result suggests that pseudo-*Y* drive can at least be expected to be successful in populations which are not already segregating for significant numbers of background suppressors of drive strength.

III. *Partitioning of total fitness.*

Each of the total fitness estimates derived from the competition cages was partitioned into segregation, viability and fertility estimates, according to the protocol described in MATERIALS AND METHODS. These estimates, along with their standard errors, are presented in the body of Table 6.

The results of the egg hatch studies are tabulated in the first three columns of the table. The estimate $\hat{c}$ in the third column is the ratio of the number of hatched eggs (column #1) divided by the total number of fertilized eggs (column #2). For the numbers in column #2, it was necessary to count the unfertilized eggs directly rather than to simply use the unfertilized fraction in the *SD-72* cross as a control. Such a simple control correction was impossible in view of the rather large line-to-line variability in the proportion of fertilized eggs which is evident in column #2. The fraction of fertilized eggs is especially low for the *T-6* and *T-22* crosses, and these values might be particularly hard to explain when it is recalled that the *T(Y;2),SD-72* × *cn bw* matings were made with an excess of males in highly yeasted food bottles, in order to maximize fertile egg production. On the other hand, large line-to-line variances in the fraction of fertilized eggs seems to be a common problem in egg hatch studies (C. P. LIU, personal communication). Most of the other *T(Y;2),SD-72* crosses, as well as the *cn bw* and *SD-72* controls, showed fertilized egg fractions which were at least commensurate with those reported in the experimental literature (BROWN 1940).

The distribution of values for $\hat{c}$ is about what would be expected for *T(Y;2)* lines having break points in the centromeric regions of the second chromosome, if similar experimental studies can be taken as a guide. R. GETHMANN (personal communication) has found that centromeric *Y-2* translocations give corrected alternate segregation rates in the range of 0.252–0.749, with the mean approximately 0.575. Since nine of the ten induced translocations in this study involved centromeric breaks, the observed values for $\hat{c}$ should be roughly comparable to GETHMANN's results. The range here was from 0.493–0.734, with a mean of 0.649. These values are perhaps a little higher than those indicated by GETHMANN, but they are certainly in the same area. Values of c greater than 0.5 are of course quite desirable in these pseudo-*Y* drive lines, since such a value would imply that the *T(Y;2),SD-72* male has a higher proportion of *Y*-bearing sperm than a normal Drosophila male would be expected to have. This in turn implies that the *T(Y;2),SD-72* male actually has a comparatively greater number of sons than does a normal male. Of course, this whole argument rests on the assumption that *SD* activity does not reduce the total fecundity of carrier males, and it is well known that *SD* males are in actuality less fertile than their normal counterparts (PEACOCK and ERICKSON 1965; HARTL, HIRAIZUMI and CROW 1967). However, if we look at the detailed results of HARTL, HIRAIZUMI and CROW quite closely, we find that for a period of approximately two weeks *SD* males are able to ejaculate as many functional sperm as control males. After this time the *SD* males are sterile, while the control males go on producing functional sperm for an average of two more weeks. In other words, during their fertile life span *SD* and control males are about equally fecund; but *SD* males only stay fertile about half as long as their non-*SD* counterparts. It is seldom the case in population cages that a male fly would be able to participate in a mating as late as two weeks after eclosing. The excess of males and the relatively short life span ($\approx$ 7 days, personal communication from J. MITCHELL) effectively excludes this from happening. We can therefore be fairly sure that the number of functional sperm will hardly ever be the limiting factor on the fecundity of cage matings.

The values for $\widehat{cv}$ are calculated as numbers of adult males hatching from *T(Y;2),SD* $\times$ *cn bw* matings divided by the numbers of adult *cn bw* males from separate *cn bw* $\times$ *cn bw* matings, each measured per 1000 eggs, and corrected for unfertilized eggs. Values for $\widehat{cv}$ are listed in column #4 of Table 6.

The ratio of $\widehat{cv}$ to $\hat{c}$ is taken as an estimate of the relative viability ($\hat{v}$) of each *T(Y;2),SD-72* line and these estimates are listed in Table 6. These viability estimates are generally less than one. Part of this reduction may be attributable to the *SD-72* stock from which the *T(Y;2),SD-72* lines were derived, since in these studies *SD-72* appears to have a slightly reduced viability relative to *cn bw* (see Table 6), but most of the viability effect can probably be attributed to the presence of the translocation itself, or the associated lesions incurred in the irradiation processes which generated the translocation lines. It is important to note that the egg to adult studies on which the $\widehat{cv}$ values were based (and therefore the $\hat{v}$ values as well) were done under uncrowded conditions, with 100 eggs allocated to

each food vial. The viability estimates for the *T(Y;2),SD-72* lines might be higher under the crowded conditions prevailing in population cages.

Fertility estimates ($\hat{f}$) are obtained from ratios of $2f\hat{c}\hat{v}$ and $2\hat{c}\hat{v}$, and these also appear with their standard deviations in Table 6. The values of $\hat{f}$ for the various lines show a rather interesting pattern. Five values (for *T-22*, *T-23*, *T-25*, *T-32*, *T-41*) are clustered closely around 3.000, and it is tempting to speculate that the fertility of *SD-72* would also be around 3.000. Unfortunately, no independent estimate of *SD-72* fertility is available to check the plausibility of the speculation. The other five lines shown relatively reduced fertility, although all values of $\hat{f}$ are large relative to the standard *cn bw* value. Again, the specific translocation induced is presumably responsible for these fertility changes. One of the lines (*T-12*) with a low $\hat{f}$ value offers a complex problem. Table 3 indicates that *T-12* is a T(Y;2;3)*SD-72*. Males hyperploid for the tip of the third survive, but are sterile. Normal and hyperploid males are indistinguishable under cage conditions, and they were necessarily treated as one class for counting purposes. This means that the overall estimate of fertility is a weighted average of the real fertility exhibited by normal males (f^*) and a sterility ($f = 0$) of the hyperploid males. The weighting is determined by the relative segregation of the two classes of males from the matings of normal *T-12* males and *cn bw* females. This segregation parameter has been measured independently from crosses of the type:

$$T\text{-}12/c\text{-}scan\ \delta \times c\text{-}scan\ \varphi$$

The relative proportion of $ve^+\ st^+\ ca^+$ males to $ve^+\ st\ ca$ males can be used as an estimate of the euploid:hyperploid segregation parameter, which turns out to be 0.631. It is then possible to estimate the actual fertility of the *T-12* line as

$$\hat{f}^* = \frac{1.664}{0.631} = 2.636.$$

This value is listed in Table 6 along with the uncorrected $\hat{f}$ estimate for *T-12*. The correction brings the *T-12* fertility estimate up into the general vicinity of the $\hat{f}$ values observed for the other *T(Y;2),SD-72* lines.

It must be remembered that the transformation of the data to 12 day generation length means that $\hat{f}$, which measures the residual fitness component of W after $\hat{c}$ and v are removed, should really be estimating $\hat{f}(12/b)$. If the real generation length $\neq$ 12 days, this will introduce a corresponding error in the f value obtained. However, the values presented in Table 6 are so large that even a 15% error (obtained for an $\hat{f}$ of 3.0 if $b = 10$ or 14) would not change the qualitative results much, so we will simply note this possible extra source of error in $\hat{f}$ without attempting to correct for it in detail.

Some general inferences about *T(Y;2),SD-72* fitness can be drawn from the estimates of Table 6. Clearly, both segregation and fertility are generally high for these lines, while viability is generally less than in the *cn bw* control. This suggests that viability is the component of *T(Y;2),SD-72* fitness that would be most amenable to improvement in future experiments. This might be done through the recombinational incorporation of beneficial alleles into the *Y-SD*

complex; or alternatively, by incorporating the *SD* complex into a *Y-2* translocation which is already known to have high viability. The segregation values, while high, are still low enough to allow for the possibility of marked enhancement of *T(Y;2),SD* fitness through increases in the frequency of alternate segregation, perhaps by further structural alterations in the *SD* and *Y* chromosomes. Table 6 also suggests that viability, segregation, and fertility differences contribute approximately equally to the variation in total fitness, although fertility may show slightly less variability as a result of the clustering of values around $\hat{f} = 3.000$.

This dissection of total fitness into its components is quite informative, but it should be reiterated that any strong conclusions await the analysis of more *T(Y;2),SD* lines, especially those with breaks in different areas of the second chromosome. It should also be reemphasized that it is the *relative* importance of the various fitness components that is most significant, since the *absolute* values of the components are probably artificially inflated when measured against the *cn bw* laboratory stock.

T-6 vs. ++ *competition cages*. Since the *cn bw* laboratory stock used as a standard in the previous experiments undoubtedly has a lower absolute fitness than a comparable wild-type chromosome, the competitive advantage of a *T(Y;2),SD-72* lines is increased above its expected value in natural populations. With this in mind, the change in frequency of males in competition with ++ males was used to more closely simulate the behavior of *T(Y;2),SD* lines in natural populations. The ++ stock used was a mixture of *Canton-S*, *Tokyo*-+ and inbred lines derived from two natural populations, which was maintained in population cages for one year (≈ 30 generations) in order to enhance genetic variability. The *T-6* vs. ++ cages were initiated with equal numbers of *T-6* and ++ males. Three replicates were maintained, and a ++ cage was kept as a control. Since the *T-6* males were phenotypically indistinguishable from their ++ counterparts (except by progeny tests), the sex ratio in the competition cages was used as a measure of *T-6* success. That is, if the sex ratio (frequency of males) increases, we presume that this is due to the proliferation of *T-6* males with their concomitant unisexual progeny. The ++ cage is necessary to control for environmentally induced sex ratio shifts. Figure 7 depicts the change in sex ratio through time for the experimental and control cages. It is clear that the natural variation in the sex ration from time to time is great enough to obscure any but the most qualitative conclusions concerning the change in frequency of the *T-6* males in the experimental populations. One interesting fact which should be noted from Figure 7 is that the control sex ratio is usually > 0.50. This is not an unexpected result in these population cages, where the females spend most of their time in the food vials (and hence often die from being stuck in the food), while the males usually stay in the upper portion of the cage.

Despite the large variance, it is clear from Figure 7 that the sex ratio in the experimental cages is generally higher than that of the control cage. This presumably at least indicates the persistence of *T-6* when in competition with ++ males. To check this, fifty males from each experimental population were prog-

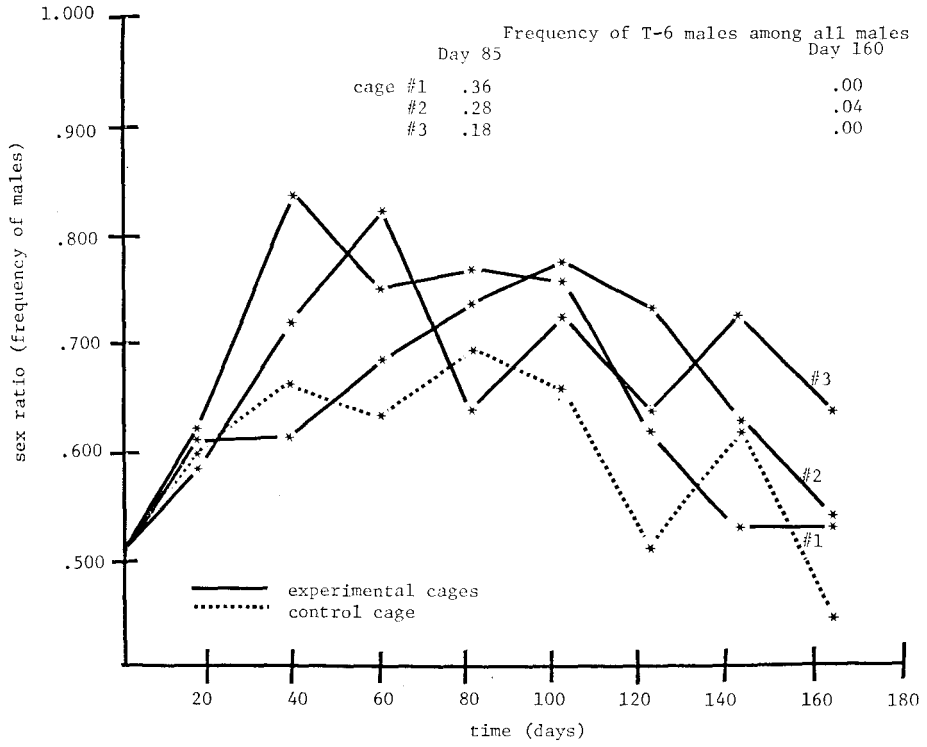


FIGURE 7.—Sex ratio *vs.* time in *T-6* versus ++ competition cages. The control cage consisted solely of the ++ mixture. All cages were started with equal numbers of males and females. An excess of males (compared to the control cage) presumably indicates the presence of *T-6* males giving unisexual progeny. The frequency of *T-6* males among all males was determined by individual progeny tests of 50 males randomly sampled from each experimental cage at each of the two sample times.

eny tested at day 85 and at cage termination (day 160). These sample frequencies of *T-6* males for each cage are also listed in the figure. Obviously *T-6* is not able to cause extinction of these wild populations, although it remains segregating for long periods of time. There are at least three reasonable explanations for this failure. First of all, the choice of *T-6* as the testor line was an unfortunate one. These competition cages were originated before the fitness of the various *T(Y;2),SD-72* lines were determined, and *T-6* was simply chosen at random from the ten available *T(Y;2),SD-72* lines. Unfortunately, Table 6 indicates that *T-6* is one of the least fit of the analyzed lines, and in fact has the lowest viability. It was therefore probably the worst line that could have been selected to compete against the wild populations. Secondly, it is quite likely that the great fertility advantage enjoyed by *T-6* over *cn bw* males disappears when in competition with ++ flies. This results in an even further lowering of the already low relative fitness of *T-6*. A similar drawback has been encountered in at least one study involving the use of compound autosome lines for genetic control of natural populations. CANTELO and CHILDRESS (1974) found that such

lines worked effectively in eliminating laboratory populations of *D. melanogaster*, but proved to be ineffective against wild-type strains encountered in field studies. The third explanation has to do with the segregation of drive modifiers. When *T-6*/++ males were tested as controls for the effect of the ++ chromosomes on *K*-value, it was found that the overall *K*-value did not change significantly (Table 3). However, 1 of the 38 ++ chromosome complements showed a *k*-value of 0.61 when tested over *T-6*, presumably indicating that a dominant *SD* suppressor was present in that ++ complement. The magnitude of the suppressor effect (*k* is lowered from 1.00 to 0.61) suggests that it is probably an insensitive *Rsp* allele that is segregating, rather than a simple quantitative suppressor. This would not be surprising, since insensitive SD^+ chromosomes have repeatedly been found segregating in natural populations (HARTL 1970b, HIRAIZUMI, SANDLER and CROW 1960). The prior presence of such SD^+ elements might allow ++ populations challenged by pseudo-*Y* drive rapidly to increase the SD^+ frequency in order to inactivate the distorting ability of the *T(Y;2), SD-72* line. Reexamination of equation (3) suggests that the effect of such a loss

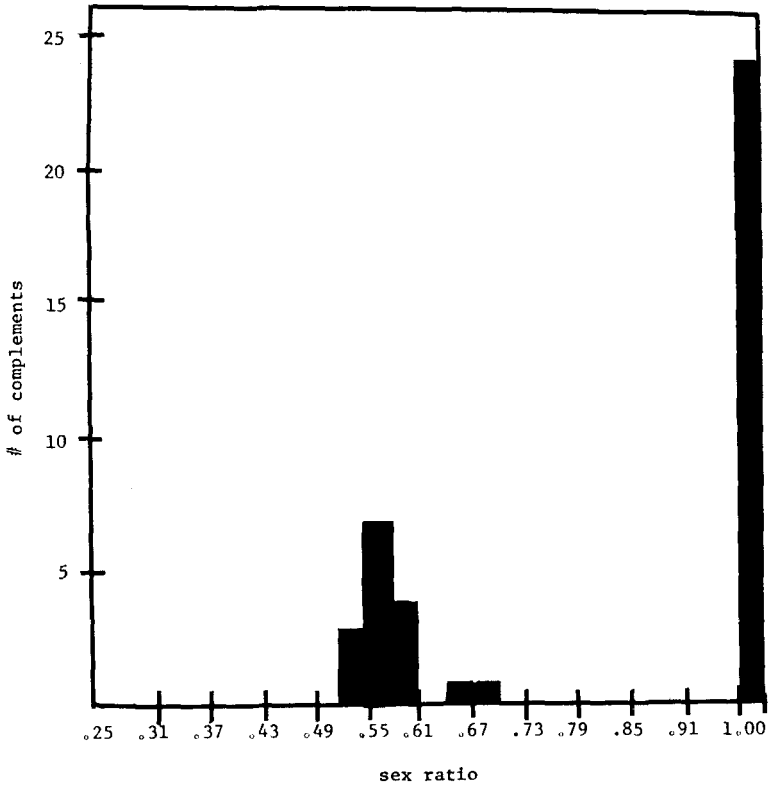


FIGURE 8.—Distribution of *k*-values of *T-6*/++*. The ++* complements were derived from cage #1 in Figure 7 at day 160, and the *T-6* chromosome is from a standard stock. The bimodality of the distribution suggests that a strong *SD* suppressor (presumably an insensitive responder) is segregating among the ++* chromosomes.

of drive would be approximately to halve the total relative fitness of the *T(Y;2), SD-72*. That is, loss of distortion is reflected by a change in z from one to zero, doubling the denominator of $W = 2fcv/2\text{-}z$. Since *T-6* already has reduced viability, the value of W might therefore drop below one, resulting in the disappearance of *T-6* from the population, as was observed. In fact, a small sample of ++ chromosome complements taken from cage #1 at day 160 and tested over *T-6* showed 16 out of 40 complements giving greatly decreased distortion ($k \leq 0.70$, see Figure 8). This indicated that insensitive alleles were in fact accumulating to suppress the action of *SD*.

The ultimate loss of the *T-6* lines can therefore be attributed to one or more of the three reasons discussed above. This poor showing of *T-6* makes it clear that improvements must be made in the *T(Y;2),SD* system before it will be fully competitive with natural populations.

DISCUSSION

The main purpose of this investigation was to ask whether experimental populations challenged by pseudo-*Y* drive evolved in a manner compatible with the theoretical dynamics of regular *Y* chromosome drive. That is, does fixation of the drive element (and concomitant population extinction) occur, and if so, does the replacement process follow the kinetics of haploid competition, as predicted by the simple discrete generation model considered above? The analysis of the competition cage studies demonstrates that the answer to both these questions is the affirmative: under a wide range of starting frequencies and migration pressures, *T(Y;2),SD* lines are capable of causing the extinction of populations harboring them. This statement as it stands is probably only applicable when the target population is a laboratory mutant stock such as *cn bw*; in the one case of *T(Y;2),SD-72* vs. ++ competition examined, the *T(Y;2),SD-72* was eventually lost from the population. Rather than relying on such a qualified conclusion, it might be better to restate the general conditions under which population extinction will occur, and then to ascertain which of the experimental cages satisfy those general conditions. From equation (2) we can clearly see that the frequency of the *T(Y;2),SD-72* will increase and the competition populations will become extinct whenever the fitness $W = (2fcv)/(2\text{-}z) > 1$. These conditions clearly hold in the *T(Y;2),SD-72* vs. *cn bw* cages, but not in the case of *T-6* vs. ++ competition, where z and f are almost certainly reduced in magnitude. Clearly, the success of a *T(Y;2),SD* line is quite dependent on the target population in question. Nevertheless, the fact that some of the *T(Y;2),SD-72* vs. *cn bw* migration cages could withstand 25% migration every generation without losing the *SD* is an impressive example of the potential staying power of these pseudo-*Y* drive lines under laboratory conditions.

Once it has been determined that the dynamics of the replacement process are behaving in a manner compatible with the basic theory, it is possible to derive a fitness estimate for a particular *T(Y,2),SD-72* line from the rate of increase of the frequency of that line in the competition cages. In this study, an encouraging result from the point of view of experimental methodology is the com-

parability of fitness estimates from sample time to sample time and even from cage to cage, as is demonstrated by the F tests in Tables 4 and 5. Although there may be a slight tendency for a sample time dependence in some of the data (*e.g.*, Table 4) which should be examined in more experimental detail, successive time samples from a given competition cage can be pooled to give a single estimate of *T(Y;2),SD-72* fitness. We can also legitimately pool estimates from replicate cages, even those with widely different starting frequencies, and thus greatly increase the available information on the total *T(Y;2),SD-72* fitness. This allows for the extraction of fitness estimates which are much more reliable than those which are based on only a single cage study.

It is clear from the tables that the *T(Y;2),SD-72* lines used do not contribute any significant component to the variation in fitness estimates. Loosely paraphrased, this means that the irradiation process which converts the *SD-72* chromosome into the several *T(Y;2),SD-72* lines does not induce any appreciable fitness differences among those lines. This is not to say that no differences exist, just that they are not large enough to be picked up against the background noise of random cage-to-cage variation.

It is important to emphasize one statistical point here. Fitness estimates derived from gene (or genotype) frequency changes in cages have often been calculated by fitting a regression line to the data and taking the slope of that line as a source for a fitness estimate. However, since the individual sample points in a cage population assayed through time are serially correlated, the basic assumption of independence of sample points (a necessary condition for valid significance tests and confidence interval estimation on the derived regression estimates) is almost certainly violated. The ANOVA approach used here eliminates that problem by using the *change* in genotype frequency (suitably transformed) as the basic variable. Since the jumps in genotype frequency from one sample time to the next are expected to be independent (that is, no frequency dependence is assumed to exist) this ANOVA approach can produce valid fitness estimates despite the serial correlation in sample frequency which exists in the population cages; that is, ANOVA gives more reliable estimates of variance components than regression might provide. This in turn also allows us to employ the variance components in F-tests (as in Tables 4 and 5) to test for the presence of factors (starting frequency, cage replication, etc.) which might be acting to alter or obscure the desired estimates of real fitness differences. Regression estimates will not necessarily give biased estimates of fitness, but the autocorrelation problem will make the estimates of variance components and confidence intervals more suspect, which in turn may invalidate any F-tests used.

The migration cage studies serve two distinct purposes: (1) they allow a qualitative measurement of the sensitivity of the *T(Y;2),SD-72* lines to pressures opposing fixation (*i.e.*, immigration pressure); and, (2) they allow an independent test of the accuracy of the fitness estimates derived from the replacement process in the competition cages. As described above, the equilibrium in the migration cages are quite commensurate with the predicted values; and this internal consistency allows us to put more faith in the overall estimates of fitness.

It has long been an accepted tenet of population genetics that any autosomal gene causing a deviation from 1:1 in the progeny sex ratio is selectively disadvantageous (FISHER 1930; CROW and KIMURA 1970). Nevertheless, in this report the *T(Y;2),SD-72* flies, which produce only male progeny, have been considered to have a selective advantage. The resolution of this apparent contradiction lies in the fact that the translocation has effectively made this a case of sex-linked sex-ratio distortion. This makes it essential to specify whether the definition of "selective advantage" is at the organismal or chromosomal level. That is, any unlinked suppressor of male drive will have a fitness advantage in the *T(Y;2), SD-72* male. This follows from the fact that, by causing the sex ratio to move closer to 1:1, the presence of drive modifier leads to an increase in the contribution by the carrier male to the genetic material of future generations. On the other hand, the presence of the suppressor leads to a decrease in the fitness of the $Y + SD$ chromosome complex through the reduction it causes in the number of $(Y + SD)$-bearing sperm. This creates a conflict which can be likened to a race. In any population challenged by high-*K T(Y;2),SD-72* males, there is an immediate selective pressure in favor of *SD* suppressors. If the $Y + SD$ complex can replace the normal competing *Y* chromosome before *SD* suppressors can arise and accumulate, then the population will become extinct. Contrarily, if the suppressor accumulates quickly enough, or if the male drive is incomplete and therefore incapable of extinguishing the population completely, the population will eventually return to a 1:1 sex ratio. Such a result was noted by HICKEY and CRAIG (1966) in cage experiments designed to measure the progress of the *Y*-drive element m^D in mosquito populations. They demonstrated that the driven *Y* element was able to spread through the population, but drive suppressors accumulated to prevent population extinction. Moreover, when major modifiers of drive are already segregating in the background of a population, the progress of drive inactivation can be much more rapid, as the results from the *T-6* vs. ++ cages indicate (Figures 7 and 8). In the cases of *T(Y;2),SD-72* vs. *cn bw* competition, however, there apparently were no preexisting modifiers, and population extinction occurred before suppressors could arise *de novo* from mutation.

What is the source of the strong selective advantage for pseudo-*Y* drive? As has been pointed out in the section on the partitioning of fitness, most of the advantage for the *T(Y;2),SD-72* lines is derived from their high relative fertility compared to *cn bw* males (see Table 6), and these values are almost certainly inflated because of the low intrinsic fertility of the latter (due mostly to mating disadvantage rather than reduced sperm production). Nevertheless, the extreme size of the overall fertility advantage for *T(Y;2),SD* males (≈ 3.00 in most cases), which includes any mating advantage as well as sperm transfer disadvantages incurred from *SD* activity, suggests to this author that the latter effect on overall fertility must be small. That is, the high $\hat{f}$ values and the relatively short mean life span for cage flies imply that sperm production is seldom, if ever, the limiting factor in the fecundity of *D. melanogaster* cage matings involving *SD* flies. This is an important conclusion for meiotic drive systems in general, since most such systems rely on gametic dysfunction as the mechanism for drive (HARTL 1968), and this

loss of gametes might be expected to lead to a proportional loss of fecundity (HARTL 1972). For *SD*, at least, this does not seem to be the case. As discussed earlier, the studies of HARTL (1969) and HARTL, HIRAIZUMI and CROW (1967) suggest that *SD* males can produce as many functional sperm per ejaculation as normal males, but reach senescent sterility earlier. *SD* matings in cages will therefore almost always involve the passage of numbers of functional sperm which are nearly equivalent to non-*SD* matings. POLICANSKY (1974) has demonstrated that this is not the case for *sex ratio* (*sr*) in *D. pseudoobscura*, where *sr* × ++ mattings in natural populations are generally less fertile than the corresponding ++ × ++ crosses. Since LEWONTIN and HUBBY (1966) have suggested that natural breeding populations of *D. pseudoobscura* have breeding populations of approximately 500 flies, which is a value analogous to those obtained for the experimental cage populations described here, it might be expected that the fecundities for the drive males would be similar in the two cases. The fact that they demonstrate opposite conclusions should make us cautious in extrapolating the fertility results for one drive system to cases of gametic distortion in other species. We might feel confident in suggesting that the *t* allele system in mouse would more than likely show similarities to the *SD* case, however, since drive derived reduction in sperm production will probably not be the limiting factor in this mammalian system where only a small proportion of sperm are used for actual fertilization of eggs. In any case, high fecundity of drive carriers is almost certainly a prerequisite for the success of a distorting element in natural or experimental populations.

The question of how the mechanism of *SD* action (via sperm dysfunction) affects male fertility is an appropriate lead-in to another important consideration: why it is that *T(Y;2),SD* male lines can become fixed in populations while a structurally normal *SD* chromosome generally reaches a polymorphic equilibrium at best (HIRAIZUMI, SANDLER and CROW 1960; MANGE 1961; HARTL (1970a)? The *T(Y;2),SD* is a more successful drive system for several disparate reasons: (1) Fixation of a *T(Y;2),SD* leads to a population extinction before drive suppressors can accumulate, while fixation of a standard *SD* allows population survival and eventual selection for resistance to drive. (2) Since the mechanism of *SD* action is sperm dysfunction, *SD/SD* homozygotes are often reduced in fertility or even sterile. *T(Y;2),SD* lines can never become homozygous for *SD*, and therefore never suffer this fertility loss. (3) Since the *T(Y;2),SD* lines are permanently heterozygous for the second chromosome, they are able to take advantage of any heterosis available for that chromosome, while structurally normal *SD*'s have no such permanent heterosis available. (4) Normal *SD* chromosomes spend half their time in females where their drive is inoperative, while a translocation *SD* is always in a male where it can take advantage of its selective differential. (5) PROUT, BUNDGARD and BRYANT (1973) and HARTL (1975) have demonstrated that drive enhancers will selectively accumulate whenever they are closely linked to the drive locus. Since in *T(Y;2),SD* lines all of the second chromosome is permanently linked to the *Sd* locus, these translocations will tend to increase drive efficiency by accumulating enhancers of *SD* activity on chromo-

some II which are generally unavailable to structurally normal *SD* chromosomes subject to regular amounts of recombination.

Certainly pseudo-*Y* can offer a potent means for extinction of target populations, but even from the limited studies reported here it is clear that improvements are necessary before such systems could be expected to compete efficiently against natural populations. As was discussed above, the viabilities for the *T(Y;2),SD-72* lines are uniformly low, and methods for increasing these viabilities were considered. A glance at Table 7 will show that the segregation parameters (*c*) also seem to offer room for improvement. We are currently working on an experimental procedure designed specifically to generate a compound *Y* and *SD* chromosome, such that all the fertility factors of the *Y* chromosome are linked to the *SD*. Such a "stitching" translocation might be expected to show a high rate of disjunction of the *X* and SD^+ chromosomes from the "stitched" *Y-SD*; that is, it would exhibit a high value for *c*, with a concomitant reduction in the wastage due to lethal hypoploid progeny.

Finally, as a whole new alternative to the pseudo-*Y* drive system presented here, it might be possible to select for a direct *Y* drive system in Drosophila males. This might be done my moving the *SD* locus directly to the *Y* chromosome, the opposite of the "stitched" *T(Y;2),SD* discussed above. However, the evidence that it is the presence of the SD^+, not the absence of the *SD*, which leads to sperm dysfunction (SANDLER and CARPENTER 1972) makes it probable that this system would simply lead to *Y* chromosome suicide. As an alternate to moving the *SD*, it might be possible to specifically select for *Y* chromosome drive in mutagenized *Y* chromosomes. However it was generated, either *de novo* or by coupling the *SD* directly to the *Y*, such *Y*-drive offers an alternative to the pseudo-*Y* drive of the *T(Y;2),SD-72* lines which avoids many of the segregation problems limiting the effectiveness of the latter systems.

None of the suggested improvements of the *T(Y;2),SD* system can circumvent the biggest barrier of all to effective drive-mediated population control: the prior existence of strong *SD* suppressors in the target populations. One way around this may be to use several different drive systems in succession, so that modifiers accumulating for one will have no effect on the succeeding drive system. Unfortunately, cases of multiple meiotic drive are rare in nature, and are not likely to be induced soon in the laboratory. Alternately, we might circumvent the effects of preexisting suppressors by simply overflooding the target population with *T(Y;2),SD* males, thus employing the strong-arm tactics of the sterile-male technique with the self-perpetuating ability of meiotic drive (HARTL 1975).

Despite the associated problems, some of which are immediately solvable and others which are not, the *T(Y;2),SD* pseudo-*Y* drive system presented here is a first step towards providing some detailed experimental information on the population dynamics of sex chromosome meiotic drive systems, as well as the process of modifier accumulation with which natural selection resists the spread of such driven elements. Further investigations, both theoretical and experimental, will be required before a comprehensive picture can be generated of the evolutionary fate of such systems and their potential as a means of population control.

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