THE LOCATION AND PROPERTIES OF SOME OF THE MAJOR LOCI AFFECTING THE SEGREGATION DISTORTION PHENOMENON IN *DROSOPHILA MELANOGASTER*

by

CECIL BERT SHARP
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required standard

THE UNIVERSITY OF BRITISH COLUMBIA
October, 1977

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Department of Zoology

The University of British Columbia
2075 Wesbrook Place
Vancouver, Canada
V6T 1W5

Date Oct. 4, 1977

ABSTRACT

There has recently been renewed interest concerning the location of the major loci responsible for the Segregation Distortion phenomenon in Drosophila melanogaster. Hartl (1974) has shown that two major sites are involved: Sd and Rsp. Rsp confers insensitivity to SD chromosomes, while Sd is considered to be the major locus that initiates distortion. Sd is located to the left of Rsp and both are located between Tft and cn. Ganetzky (1977) has extended these findings by showing that just distal to pr there is a locus that, if deleted on a SD chromosome, eliminates distortion and he argues that this is the Sd site. Ganetzky (1977) also uncovered another important locus, in or near the heterochromatin of 2L, that, if deleted from a SD chromosome, greatly reduces the ability of that chromosome to distort and he argued that this site is an enhancer of SD, E(SD). Ganetzky (1977), also suggests that Rsp might be located very close to the centromere in the proximal heterochromatin of 2R. The results presented here demonstrate the presence of an important component of SD located within the proximal heterochromatin of 2L. These results also show that there is another important site located just distal to pr. However, when this site is removed by recombination from a SD chromosome, a certain level of residual distortion remains. It is argued that the site that Ganetzky (1977) called E(SD) is likely responsible for this residual distortion in the absence of the site just distal to pr. Thus the site near pr is called Sd_1 and the site near lt is called Sd_2. Loss of either site results in a large reduction, but not complete elimination, of the distorting ability of a SD chromosome. Other data are presented that, on the whole, agree with Ganetzky's (1977) proposal that Rsp is located in the centromeric heterochromatin of 2R, very close to the centromere.

Miklos and Smith-White (1971) have suggested that k (the segregation

ratio observed from a given mating) is a deceptive measure of the degree of distortion and they have proposed another method of measuring distortion based on their model of sperm dysfunction. Some of the weak assumptions of this model are discussed and a simpler alternative is presented. The alternative model assumes that the potential segregation ratios of a population of SD males follow a truncated normal distribution. Data are presented that are not necessarily inconsistent with this assumption. The same data show that it is likely that certain SD chromosomes differ in their susceptibility to modifiers of SD. It is concluded that at present k provides the clearest measure of distortion.

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GENERAL INTRODUCTION

Segregation distorter (SD) was first reported by Sandler, Hiraizumi, and Sandler in 1959. They noted that some second chromosomes taken from a natural population near Madison, Wisconsin, showed abnormal segregation ratios. In particular, these chromosomes were recovered far in excess of the 1:1 ratio expected from the cross of SD/cn bw males mated to cn bw/cn bw females. (cn, cinnabar eyes, and bw, brown eyes, together produce a white-eyed phenotype). The recovery ratio, defined as the number of SD progeny divided by the total number of progeny and given the symbol k, was often in excess of 0.9. However, the value of k for the reciprocal cross, SD/cn bw females mated to cn bw/cn bw males, was 0.5.

These results suggested that the mechanism of SD resided in some abnormality of either male spermatogenesis or spermiogenesis. Sandler, Hiraizumi, and Sandler (1959) proposed that SD induced a break in its homologue during prophase I and that this break fused to form a dicentric bridge and acentric fragments during anaphase II. Preliminary cytological evidence indicated that dicentric bridges and acentric fragments could be observed during male meiosis (Sandler, Hiraizumi, and Sandler 1959); however, these observations could not be verified (Peacock and Erickson 1965).

Although this hypothesis does not have direct cytological support, it does have indirect genetic evidence in its favour. Hiraizumi (1961) observed that rare cn bw chromosomes recovered from SD/cn bw males had lower homozygous viabilities than did cn bw chromosomes recovered from SD^+/cn bw males. In addition, Crow, Thomas, and Sandler (1962) found that the response of male recombination to radiation was much greater in SD heterozyous males than in SD^+ heterozyous males. Both of these experiments were consistent with the hypothesis that SD induces chromosome breaks in its homologue.

Peacock and Erickson (1965) were unable to detect any cytological abnorm-

alities in the meiotic divisions of SD males. Because of this and the indirect nature of the evidence in support of the breakage hypothesis, they modified the functional pole hypothesis of Novitski and Sandler (1957) to explain SD. The functional pole hypothesis holds that in male meiosis there are two poles and that the products of one pole function in fertilization, while the products of the other pole are regularly nonfunctional, although motile and transferred to the female. Peacock and Erickson (1965) proposed that SD operates by preferentially orienting the SD chromosome toward the functional pole. In support of this model, Peacock and Erickson (1965) showed that with both SD/cn bw and wild type males the number of progeny a female yielded was equal to approximately one-half the number of sperm transferred to the female. However, Zimmering and Fowler (1968) have shown that the efficiency of sperm utilization varies between females, depending upon their genotype. The y (yellow body colour) females used by Peacock and Erickson normally utilize only about one-half of their stored sperm, whereas Oregon-R (wild type) females use up to eighty per cent of the sperm transferred by Oregon-R males. Thus it would appear that because of the type of female used to obtain progeny to sperm ratios, Peacock and Erickson's (1965) results were atypical. The functional pole hypothesis does not appear to apply generally to Drosophila males and consequently it is a poor starting point from which to develop an hypothesis for explaining mechanisms for the action of SD.

A much more reasonable starting point is provided by the results of Hartl, Hiraizumi, and Crow (1967). They demonstrated that if both SD/cn bw and cn bw/cn bw males were provided with an excess of virgin females until the males became sterile, and if the females were re-brooded until they ceased to lay fertilized eggs, then the cn bw/cn bw males produced twice as many progeny as did the SD/cn bw males. This finding suggested that, compared to cn bw/cn bw males, a SD/cn bw male can produce only one-half the number of functional

sperm. This in turn suggested that in SD/cn bw males the sperm which carry cn bw chromosomes are somehow rendered dysfunctional.

Some of the steps involved in this dysfunction process have recently been elucidated. Tokuyasu, Peacock, and Hardy (1977) have reported a detailed study of spermiogenesis in SD/cn bw males and they have compared those results with earlier observations they made on spermiogenesis in normal males (Peacock, Tokuyasu, and Hardy 1972; Tokuyasu 1974). The earliest differences between normal males and SD/cn bw males are observed during the transformation of the early spherical spermatid nucleus into the highly condensed and compact nucleus of the mature spermatid. In a SD/cn bw male the chromatin of cn bw bearing spermatids fails to condense to the same degree as either the chromatin of SD bearing spermatids or the chromatin of all the spermatids in a normal male. Later in spermiogenesis these spermatids with improperly condensed heads will frequently fail to become individualized by the individualization membrane that delimits the other spermatids from the syncytium in which they were formerly located. In normal males, after individualization the sperm undergo a coiling process prior to release into the testicular lumen. In SD/cn bw males, those sperm which are improperly individualized are frequently not coiled with the rest of the bundle and subsequently degenerate. However, even in SD/cn bw males that have k values near 1.0, one frequently observes among the coiled sperm of a single cyst a few sperm that have improperly condensed chromatin. Thus, although the majority of the cn bw-bearing sperm are lost during spermiogenesis, a few are likely transferred to females, but their ability to function in fertilization is severely limited, probably owing to their abnormally condensed nuclei.

Improper condensation of chromatin suggests that the transition from lysine-rich to arginine-rich histones observed during spermiogenesis in normal

Drosophila males (Das, Kaufmann, and Gay 1964) is somehow impaired in the cn bw-bearing spermatids of SD/cn bw males. In fact, this is likely the case, since Kettanah and Hartl (1976) have found that the lysine-rich to arginine-rich transition cannot be detected cytochemically in SD homozygotes.

Although the first cytochemical and morphological manifestations of segregation distortion occur during the nuclear condensation phase of spermiogenesis, Mange (1968) has shown that the segregation ratios of SD/cn bw males are sensitive to temperature shocks applied during the early stages of meiosis. However, this observation is not necessarily inconsistent with the hypothesis that the mechanism of segregation distortion involves modification of the transition from lysine-rich to arginine-rich sperm histones, since Gould-Somero and Holland (1974) have demonstrated by means of autoradiography that RNA synthesis ceases pre-meiotically in Drosophila males. Because RNA synthesis ceases pre-meiotically it is not unreasonable to assume that the factors which mediate the improper condensation of chromatin in SD^+ bearing spermatids are also present pre-meiotically. Furthermore, it is not unreasonable to assume that temperature shocks can affect these factors in such a way that they will alter the frequency of SD^+ sperm with improperly condensed chromatin.

In spite of the recent advances elucidating the general mechanism by which segregation distortion operates, there is still a lack of solid information concerning the loci involved in the process. Numerous studies have been undertaken to solve this problem; however, the results of these studies have been amazingly ambivalent. The purpose of the present study was to approach this mapping problem by using methods that differed somewhat from those used by previous workers, in the hope that a firmer conclusion could be made concerning the loci involved. This in turn should certainly help to complement biochemical studies determine a more detailed understanding of the mechanisms

involved in segregation distortion.

Previous studies have examined the properties of SD recombinants recovered between pr (purple eyes) and cn (cinnabar eyes) (Sandler and Hiraizumi 1960b, Hiraizumi and Nakazima 1967), Cy (curly wings) and cn (Crow, Thomas and Sandler 1962), and Tft (tufted wings) and cn (Hartl 1974). These pairs of markers provide one locus in the euchromatin of 2L and the other in the euchromatin of 2R. Since the centromeric heterochromatin had not been marked in the earlier studies, one could not position the SD loci relative to this block of heterochromatin. In the present study the marker chromosome used to obtain SD recombinants was b pr lt pk cn. This chromosome carried lt (light eyes), a locus located in the centromeric heterochromatin of 2L (Hilliker and Holm 1975). In addition to recombination, I also employed deletion mapping. However, before examining the results of these mapping experiments, I will present some considerations pertaining to the measurement of distorted segregation ratios.

CHAPTER I

ON MEASURING DISTORTED SEGREGATION RATIOS

INTRODUCTION

One of the most important factors which must be taken into consideration when estimating a genetic segregation ratio is the relative viability of the different genotypes involved. For example, although the chromosomes on which two different alleles of a single gene are located may be segregating randomly, the frequencies of the two alleles in the recovered progeny may not be equal because progeny bearing one of the alleles may be less viable than progeny bearing the other.

In the case of Segregation Distorter in Drosophila melanogaster, one is interested in determining the viability of progeny bearing the SD chromosome relative to the viability of progeny bearing the SD^+ chromosome. One method of doing this makes use of the property that SD operates in males, but not in females. If segregation is random in, for example, SD/cn bw females, then the relative recovery of SD and cn bw-bearing progeny should approximately reflect the relative viability of progeny bearing these chromosomes.

One problem with this method is that recombination does not occur in males, but does occur in females. Thus SD and cn bw progeny recovered from male SD/cn bw parents will not be genotypically identical to progeny of the same visible phenotypes recovered from female SD/cn bw parents. However, this problem is alleviated to a certain extent because most SD chromosomes have one or more inversions, in the right arm of chromosome 2, which greatly reduce the frequency of recombination between cn and bw.

Another problem with this method is that it is possible that the relative viability of SD and cn bw bearing progeny may differ depending upon whether the male or female parent was SD/cn bw. That is, it is conceivable that relative viability may be associated with a maternal effect.

However, I do not feel that the possible effects of either of the above problems would be sufficiently large to nullify the advantages of attempting to measure the relative viability of SD and SD^+ bearing progeny by performing the reciprocal cross, i.e. with SD/SD^+ as the female parent. If one assumes that the method is approximately valid, then one can use the segregation ratio determined from a cross where the female parent is SD/SD^+, given the symbol k_f, to correct the segregation ratio determined from a cross where the male parent is SD/SD^+, given the symbol k_m. This corrected segregation ratio, given the symbol k_c, is obtained as follows:

$$k_c = \frac{k_m}{k_m + (1-k_m)\left(\frac{k_f}{1-k_f}\right)}$$

This formula, however, does not take into account variation in k_m and k_f. One can use the means of k_m and k_f in order to obtain an estimate of k_c, but this estimate will not be the mean of k_c, it will be the mode of k_c. It is generally preferable to use the mean of k_c. Mood, Graybill, and Boes (1974) give the following method for approximating the mean of a derived variable such as k_c:

$$E(k_c) \doteq k_c + \tfrac{1}{2}\,\mathrm{Var}(k_m)\,\frac{\partial^2 k_c}{\partial k_m^2} + \tfrac{1}{2}\,\mathrm{Var}(k_f)\,\frac{\partial^2 k_c}{\partial k_f^2}$$

It is also of interest to know the variance of k_c, in order that confidence limits can be estimated for $E(k_c)$. Mood, Graybill, and Boes (1974) give the following as an estimate of the variance of k_c:

$$\mathrm{Var}(k_c) \doteq \left(\frac{\partial k_c}{\partial k_m}\right)^2 \mathrm{Var}(k_m) + \left(\frac{\partial k_c}{\partial k_f}\right)^2 \mathrm{Var}(k_f)$$

This method of estimating the mean and variance of a derived variable, f(x), depends upon expanding f(x) in a Taylor series about E(x). The accuracy of the approximation depends upon the magnitude of the remainder term in the Taylor series (Johnson and Kotz 1969). As can be seen from Figure 1, the curves of k_m versus k_c could be easily estimated by a Taylor series at values of k_f between 0.3 and 0.7, since the curves are close to being linear. Figure 2 shows that the same holds for curves of k_f versus k_c at values of k_m between 0.3 and 0.7. Thus, I would conclude that it would be quite reasonable to use these approximations if $\bar{k}_m$ and $\bar{k}_f$ are both between 0.3 and 0.7.

The required partial derivatives are given below:

$$\frac{\partial k_c}{\partial k_m} = \left(\frac{k_f}{1-k_f}\right)\left[1 + \left(\frac{k_f}{1-k_f}\right) k_m^{-1} - \left(\frac{k_f}{1-k_f}\right)\right]^{-2} k_m^{-2}$$

$$\frac{\partial k_c}{\partial k_f} = \frac{-\left[\left(\frac{1}{k_m}\right) - 1\right]\left[k_f\left(1-k_f\right)^{-2} + \left(1-k_f\right)^{-1}\right]}{\left[1 + \left(\frac{1}{k_m} - 1\right)\left(\frac{k_f}{1-k_f}\right)\right]^2}$$

$$\frac{\partial^2 k_c}{\partial k_m^2} = -\left(\frac{k_f}{1-k_f}\right)\left\{\frac{2 - 2\left(\frac{k_f}{1-k_f}\right)}{\left[1 + \left(\frac{k_f}{1-k_f}\right) k_m^{-1} - \left(\frac{k_f}{1-k_f}\right)\right]^3} k_m^3\right\}$$

FIGURE 1

The relationships between k_c and k_m at various values of k_f.

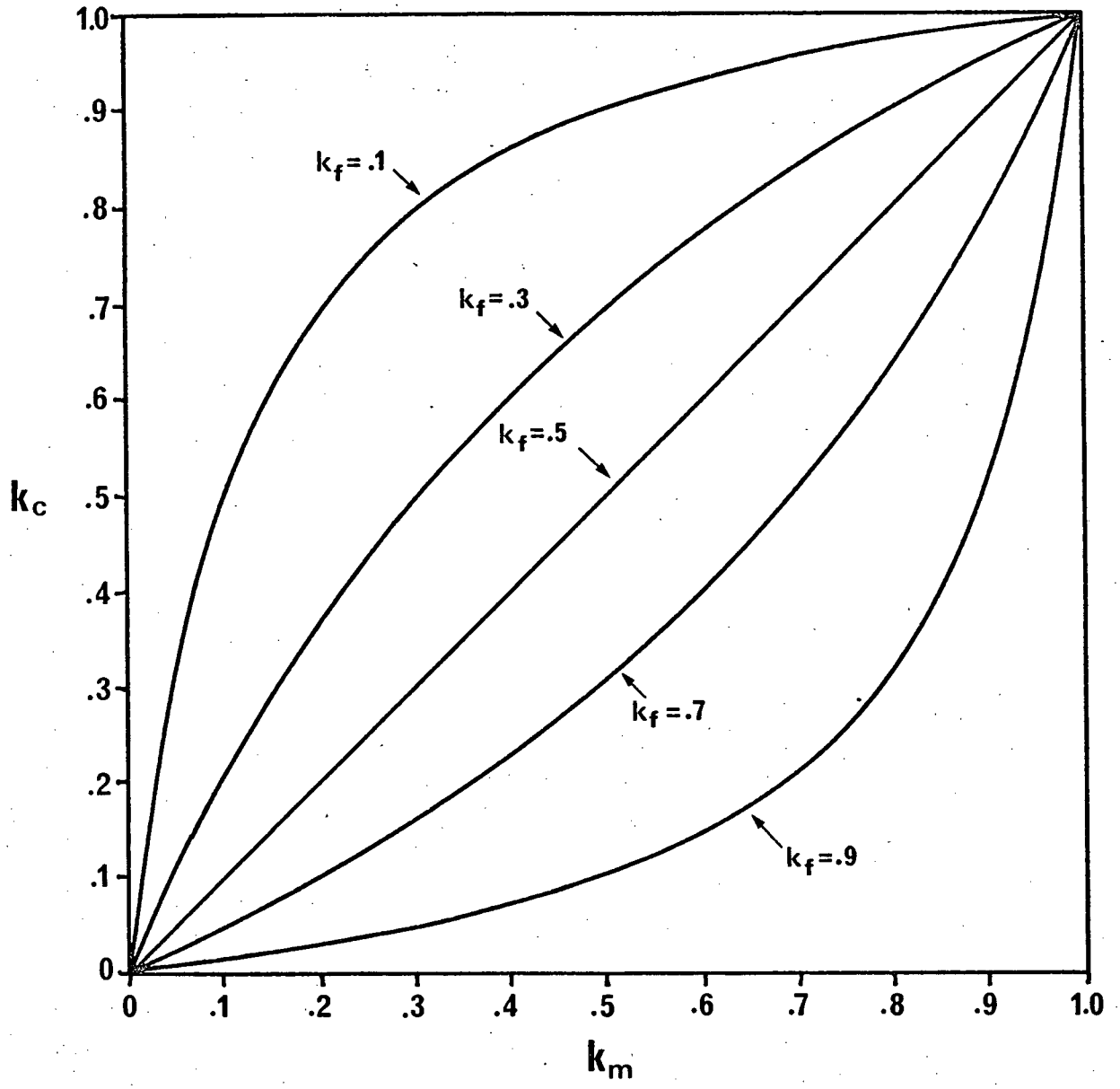
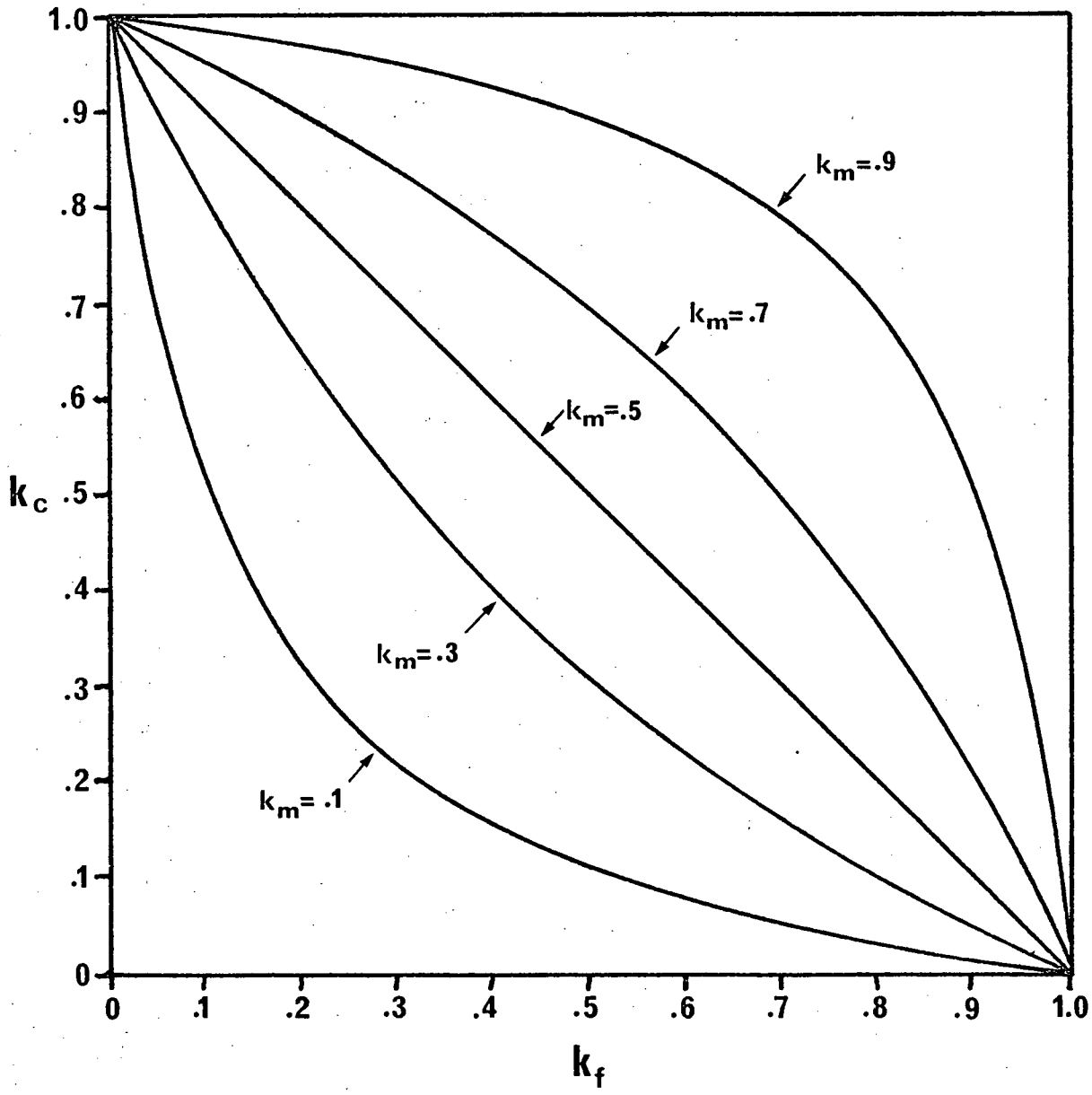

1.0
.9
.8
.7
.6
.5
.4
.3
.2
.1
0
k_c
k_f=.1
k_f=.3
k_f=.5
k_f=.7
k_f=.9
0
.1
.2
.3
.4
.5
.6
.7
.8
.9
1.0
k_m

FIGURE 2

The relationships between k_c and k_f at various values of k_m .


1.0
.9
.8
.7
.6
.5
.4
.3
.2
.1
0
k_c
0
.1
.2
.3
.4
.5
.6
.7
.8
.9
1.0
k_f
k_m=.9
k_m=.7
k_m=.5
k_m=.3
k_m= .1

$$\frac{\partial^2 k_c}{\partial k_f^2} = \frac{-\left(\frac{1}{k_m} - 1\right)}{(1-k_f)^2} \left\{ \frac{\left[1 + \left(\frac{1}{k_m} - 1\right)\left(\frac{k_f}{1-k_f}\right)\right]\left[\left(\frac{1+k_f}{1-k_f}\right) + 1\right] - \left[\left(\frac{k_f}{1-k_f} + 1\right)^2 \frac{\left(\frac{1}{k_m} - 1\right)}{1-k_f}\right]}{\left[1 + \left(\frac{1}{k_m} - 1\right)\left(\frac{k_f}{1-k_f}\right)\right]^3} \right\}$$

The difference between k_c and $E(k_c)$ is usually quite small (in the third decimal place) and consequently for most purposes it would be satisfactory to use k_c in place of $E(k_c)$.

The SD phenomenon called instability by Sandler and Hiraizumi (1960a) has suggested to some (Miklos and Smith-White 1971) that possibly other problems are associated with using k as a measure of the degree of distortion.

Sandler and Hiraizumi (1960a) noted that unrecombined SD chromosomes, such as SD-5 and SD-72, invariably had very high mean k values (approximately 0.99) as well as very small variances of k. Because these unrecombined chromosomes had small variances, they were called stable. However, whenever bw-bearing SD recombinants, derived from SD/cn bw females, were tested, they were found to have lowered mean k values, the lowest of these being about 0.82. In addition, these recombinants always had increased variances of k, and accordingly were called either semistable or unstable, depending upon how great the variance of k was. Unstable lines always had lower mean k values than semistable lines.

Sandler and Hiraizumi (1960a) also observed that if the cn-bearing recombinants, derived from SD/cn bw females, were made heterozygous with bw-bearing semistable recombinants, then the semistable recombinant became stable. Unstable bw-bearing recombinants could be made more stable in this manner, but could not be made completely stable. These observations suggested to these

authors that a stabilizer of SD was located in 2R.

One rather perplexing observation was that by selecting males with low k values a semistable line could be made unstable and the mean k could be reduced, but by selecting males with high k values an unstable line could not be made semistable. However, selection for only one generation was effective in either slightly increasing or slightly decreasing the mean k values of an unstable line, depending upon the direction of selection.

Sandler and Hiraizumi (1960a) reasoned that, since male variation in k showed some evidence of heritability for one generation, selection for high k values should have made an unstable line semistable. Because selection could not produce this effect, they suggested that the high k "states" of unstable lines have a high mutation rate back to low k "states". That is, although a number of genetic modifiers may combine in a male to produce a high level of distortion in that male, the modifiers could not maintain their effect when selected, because they mutated, at a high frequency, to an allelic state that did not contribute to a high level of distortion. I assume that their model implies that selection was effective in the opposite direction because there were certain allelic states of the modifiers present in the cn bw and SD populations that mutated at a very low frequency and did not enhance the degree of distortion.

Sandler and Hiraizumi (1960a) made it quite clear that they could conceive of two possible roles of the stabilizer that were consistent with their data. One role would be simply to increase the degree of distortion associated with any given SD state. This would cause stabilization because almost all states would then have k values of 1.0 and consequently there would be no opportunity for male to male variation. The other possible role they suggest is to decrease the mutation rate to the lower k states. This would result in

an accumulation of males with high k states. However, as I stated in the previous paragraph, I feel that in order to explain the selection of an unstable line from a semistable line there must exist certain allelic forms of the modifiers that do not mutate and do not enhance k. If this were the case and the stabilizer operated by preventing mutation to low k states, then stable lines should have bimodal k distributions. Since they do not, this last possible role for the stabilizer is not consistent with the data available.

Miklos and Smith-White (1971) have criticized the hypothesis of Hiraizumi and Sandler (1960a) on the grounds that it "involves the introduction of new concepts; of SD states, SD-state mutation, and a stabilizer which controls this mutation". As an alternative to these new concepts, Miklos and Smith-White (1971) propose a model that predicts increasing variances of k with decreasing mean values of k, in the range of k's observed by Sandler and Hiraizumi (1960a). Acceptance of this model also requires that one accept that mean k is a deceptive measure of the degree of distortion of a given line. This is why this model is being examined in this chapter.

Before proceeding to describe the model, I should point out that the model does not in any way attempt to explain the pertinent observations of Sandler and Hiraizumi (1960a) that led them to hypothesize SD state mutations. The concept of SD state mutations is the only really novel concept that Miklos and Smith-White should have criticized. The concept of SD states itself should not be construed as being novel. The term SD state, as used by Sandler and Hiraizumi (1960a), is surely meant to imply the potential distorting ability of a given male, depending upon that males genotype with respect to the modifiers of SD. Also, one cannot criticize Sandler and Hiraizumi's entire model on the basis of the proposed role of the stabilizer in reducing the frequency of mutation to lower k states, since an alternative role for the

stabilizer was clearly proposed, that is, increasing the k value of all SD states. This leaves only the concept of SD state mutation to be criticized. SD state mutation was proposed in order to explain the observation that a semistable line could be made unstable by selection, but an unstable line could not be made semistable by selection. Miklos and Smith-White (1971) do not discuss this issue at all, instead they concentrate solely on describing the relationship between mean k and the variance of k.

Miklos and Smith-White (1971) use the concept of "make" in developing their model. This concept is outlined in Rendel's (1967) analysis of the development of scutellar bristles. Rendel defined make (m) as the resultant of all factors leading to the development of a scutellar bristle. The utility of such a concept is that it forces one's attention upon the resultant, and in so doing does not require unnecessary speculation about the magnitude of variables that one cannot measure. Miklos and Smith-White (1971) define make as the "total level of all systems leading to the extinction of SD^+ in heterozygous males". The proportion of SD^+ sperm that fail to function, called e, is related to k as follows: $e = 2 - (\frac{1}{k})$. They further reason that "Extinction or non-extinction of SD^+ involves alternative responses, and therefore there must be some level of m which acts as a threshold or switch point. This threshold is denoted P, and the extinction coefficient measures the proportion of gametes in which m exceeds P". However, it would appear that they have not used the term make as Rendel (1967) proposed that it should be used, because they have resolved two factors contributing to sperm dysfunction, make and threshold of make.

They next assume that the make values of the sperm within a given male are normally distributed and that the thresholds of make of all sperm within a male do not vary. (The latter assumption I find rather difficult to accept.

This point will be returned to later.) Given these assumptions the extinction coefficient is defined by:

$$e = \int_{P}^{\infty} \frac{e^{-\frac{1}{2}\left(\frac{m-\bar{m}}{\sigma_m}\right)^2}}{\sigma_m \sqrt{2\pi}} \, dm .$$

If one measures P in standard deviation units from the mean, then one can deal with a normal distribution with a mean of zero and a standard deviation of one.

i.e. $$e = \int_{\frac{P-\bar{m}}{\sigma_m}}^{\infty} \frac{e^{-\frac{1}{2}m^2}}{\sqrt{2\pi}} \, dm .$$ See Figure 3 for a diagram showing the relationship between e and $\frac{P-\bar{m}}{\sigma_m}$. One can see that if e varies between males, then the best variable for measuring this variation will be $\frac{P-\bar{m}}{\sigma_m}$ i.e., the number of standard deviations of P from the mean of the make distribution. The value $\frac{P-\bar{m}}{\sigma_m}$ can be called m', the make level of an individual male.

If m' values between males are assumed to have a normal distribution, then one can examine the distribution of k values between males at different mean k values, while maintaining the variance of m' constant. It will be easier, however, to just examine the variance of k. The variance of k and the variance of m' are approximately related as follows:

$$\text{Var } k = (dk/dm')^2 \text{Var } m'$$

where $dk/dm' = k^2 \frac{e^{-\frac{1}{2}(m')^2}}{\sqrt{2\pi}}$. The relationship between dk/dm' and mean k is shown in Figure 4. It is apparent that the variance of k will increase as k is reduced to 0.77, then the variance of k will begin to decrease again. One should note here that these variances do not take into account binomial sampling variance.

FIGURE 3

The relationships between the distribution of make values within a male (m), the threshold of dysfunction (P), the proportion of $\underline{SD^+}$ sperm that dysfunction (e), and the make level of a male (m'). Make (m) is measured in standard deviations from the mean of the distribution.

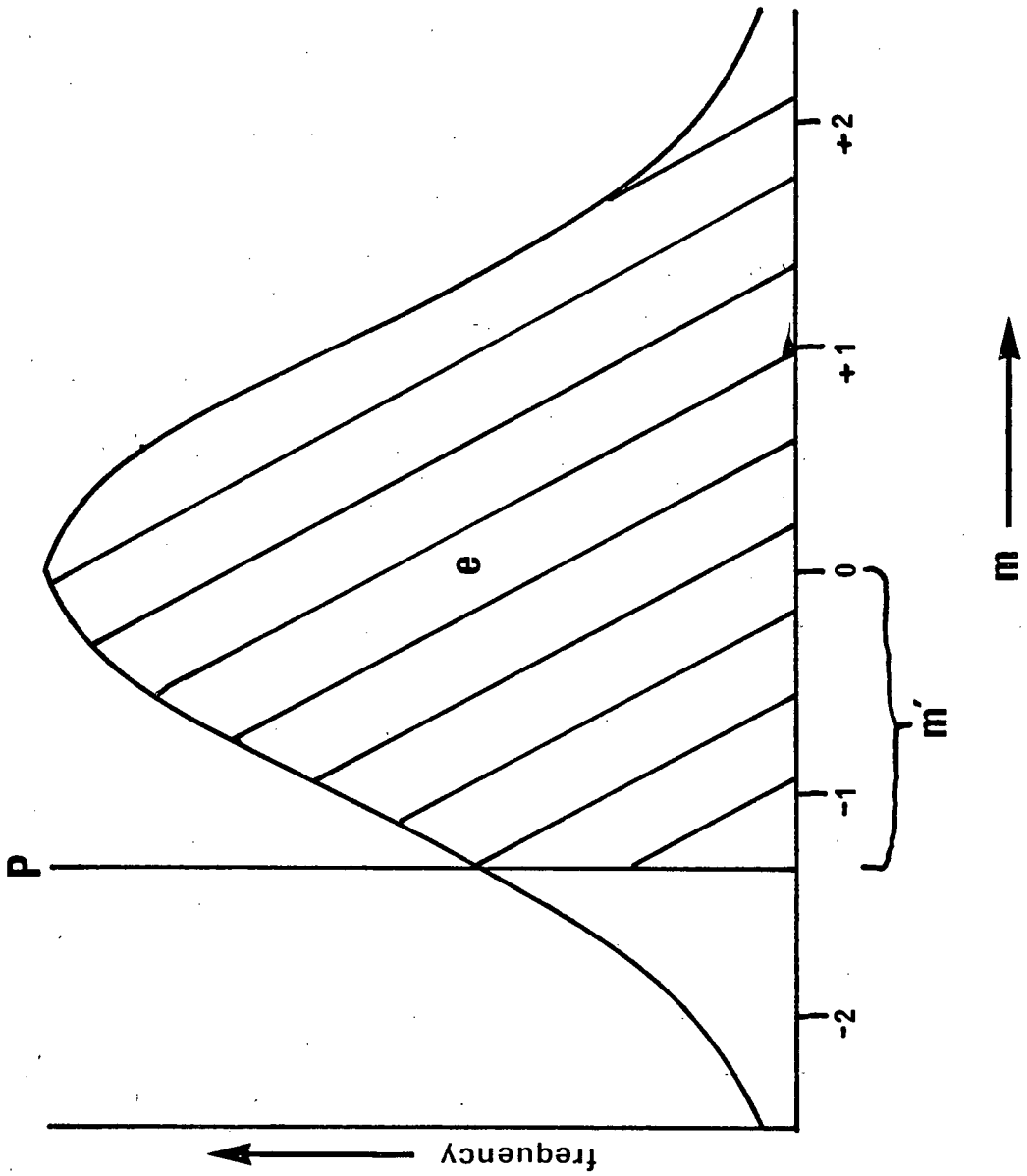
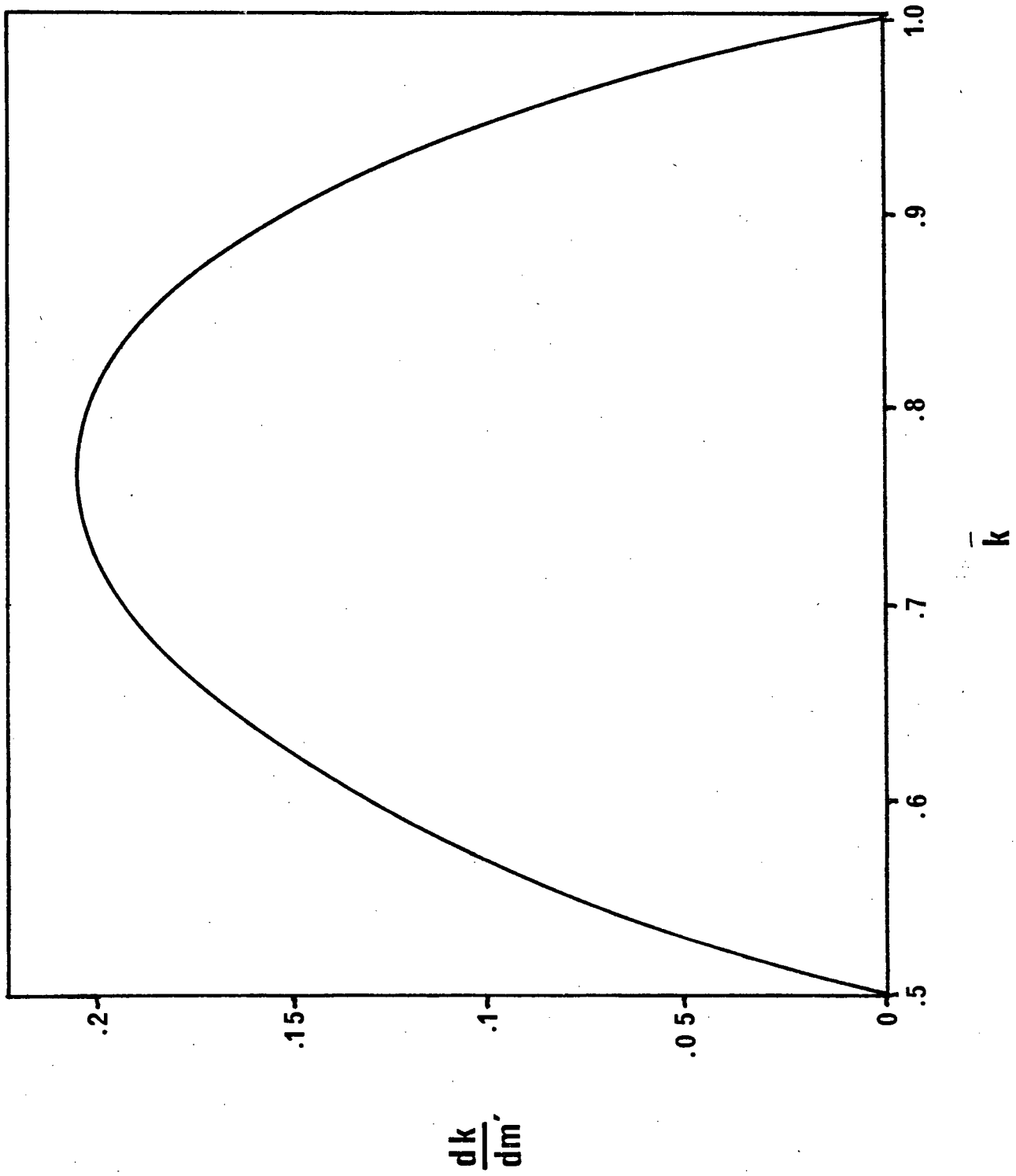

+2
+1
0
-1
-2
m
m'
e
P
frequency

FIGURE 4

The relationship between dk/dm' and mean k.


.2
.15
.1
.05
0
.5
.6
.7
.8
.9
1.0
$\frac{dk}{dm'}$
$\bar{k}$

Miklos and Smith-White (1971) proposed this model in order to describe the increased variability of bw-bearing SD recombinants, as compared to unrecombined SD lines, without the necessity of hypothesizing mutable SD states. However, Sandler and Hiraizumi (1960a) did not hypothesize mutable SD states in order to describe the increased variability of bw-bearing SD recombinants, rather they were hypothesized in order to explain the observation that unstable lines could not be made semistable by selection. Sandler and Hiraizumi (1960a) had already proposed a perfectly reasonable hypothesis to explain the increased variability of bw-bearing SD recombinants. This hypothesis was that the stabilizer of SD operated by simply increasing the k values of all SD states. When the stabilizer was absent the k values of all SD states would be lowered so that variability between the states could then be observed.

It is clearly of importance to choose between these two hypotheses, since acceptance of Miklos and Smith-White's hypothesis requires that one should measure k as m'. In order to make a choice one must first examine the weak points of these hypotheses. In this respect, I feel that Miklos and Smith-White's assumption that the thresholds of m within a male are constant, while m may vary normally, is definitely suspect. I cannot think of any a priori reason why the thresholds of m should be any less variable than m. Since there is no way of measuring either P or m, at present, in order to evaluate the generality of the model one should ask: what are the effects of P varying within males? If the variance of P equaled the variance of m, as in Figure 5, then one can see intuitively that the variance of k will be smallest at k equal to 0.5, but will be greatest close to a k of 1.0. However, at some point close to 1.0 a certain proportion of males will have k equal to exactly 1.0, i.e. all m are greater than P. This truncation effect will begin to reduce the variance of k again as mean k approaches 1.0. Nevertheless, the way in which variance of k changes with mean k will be considerably different if

FIGURE 5

A model similar to Miklos and Smith-White's, except P is allowed to vary and σ_p equals σ_m. The units on the abscissa are standard deviations of m from the mean of each distribution.

frequency
m
-2
-1
0
-2
+1
-1
+2
0
+1
+2
m
e
m'
p

one relaxes the assumption that P is constant. In addition, if P varies, then the relationship between k amd m', as defined by Miklos and Smith-White (1971), will be altered.

In the remainder of this chapter I will present some results from large scale experiments that demonstrate how the variance of k is related to mean k and then I will compare these results with predictions made by the model of Miklos and Smith-White (1971) as well as with predictions made by a model I shall develop, based on my interpretation of Sandler and Hiraizumi's (1960a) discussion of instability.

MATERIALS AND METHODS

The distribution of segregation ratios of six different types of SD second chromosomes were determined when the chromosomes were heterozygous with a cn bw chromosome. All six chromosomes were originally maintained as balanced stocks over In(2LR)SM1,Cy, an effective balancer for chromosome 2 (see Lindsley and Grell 1968). In order to approximate isogenic backgrounds between the different stocks, all of the balanced lines were backcrossed as males to cn bw/cn bw females for four generations. After the fourth backcross generation males that were from two to four days old were collected and mated to females that were homozygous for the genetic markers, cn bw; Ki p^p bx sr e^s. Since these females were homozygous for Ki p^p bx sr e^s, one could easily distinguish a white-eyed SD^+ fly, which would be heterozygous for Ki p^p bx sr e^s, from a white-eyed fly that arose from a non-virgin female.

Single "SD"/cn bw males were placed with two homozygous cn bw; Ki p^p bx sr e^s virgin females in shell vials containing standard Drosophila medium. The parents were left in the vials for four days and then discarded. The progeny were scored 12 to 13 days later. The temperature was maintained at 24±1 ^oC during the experiment.

The modified SD chromosomes used were derived from SD mapping experiments that will be described in the next chapter. The following SD chromosomes were examined:

1. SD-5, an unrecombined SD chromosome.
2. R(SD-5) pk cn, a recombinant of SD-5 with almost all of 2R replaced by the right arm of a b pr lt pk cn chromosome. This recombinant should have lost the stabilizer of Sandler and Hiraizumi (1960a).
3. Df(2L)(SD-5)-8, a 2L heterochromatic deficiency on SD-5 for Group

VIII (lt) and the Group VII site including EMS 56-4 (see Hilliker 1976).

4. RR(SD-5)lt, a double recombinant of SD-5 in which the centromeric heterochromatin of SD-5 was replaced by that of the b pr lt pk cn chromosome.

5. R(SD-5) b pr-5, a recombinant derived from SD-5 and b pr lt pk cn.

6. RR(SD-5) pr lt, a double recombinant of SD-5 and b pr lt pk cn.

RESULTS AND DISCUSSION

The observed frequency distributions of k for the six different "SD" chromosomes are shown in Figure 6. It is apparent that as mean k decreases the variance of k increases for the four chromosomes with mean k above 0.5 and then the variance of k again decreases for the two low k chromosomes.

Sandler and Hiraizumi (1960a) suggested that one way the stabilizer might operate is by simply increasing the k of all SD states such that most states would then have k's of 1.0 and thus variability would not be observed. In order to examine this proposal more carefully, I shall develop it quantitatively.

One can start by assuming that a number of modifiers of distortion, both genetic and environmental, act in such a way that the potential k's of a given population of males will be normally distributed. Furthermore, assume that this distribution of potential k's is unaffected by changes in mean k. This will undoubtedly not be true as mean k approaches 0.5, because when mean k equals 0.5, SD is not operating and one would not expect modifiers of SD to have any effect upon the potential segregation ratio. However, at high mean k's another factor comes into play, and it is this factor which I believe Sandler and Hiraizumi (1960a) alluded to. Since the variance of potential segregation ratios is unaffected by mean k, at high mean k's a certain percentage of the males will have potential segregation ratios greater than or equal to 1.0. Clearly all potential segregation ratios greater than or equal to 1.0 should be placed together into one group with a potential segregation ratio of 1.0 i.e. no chance of recovering an SD^+ sperm. This truncates the normal distribution of potential k values. As the mean of the untruncated distribution increases, a greater percentage of the population falls into the

FIGURE 6

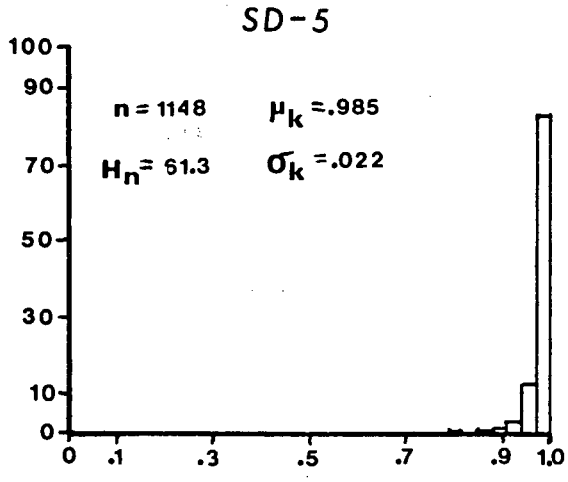
The observed k distributions of the 6 "SD" chromosomes tested. The unit of measurement on the ordinate is the percentage of males having k's within a given interval. The unit of the abscissa is k. The k interval is 0.03.

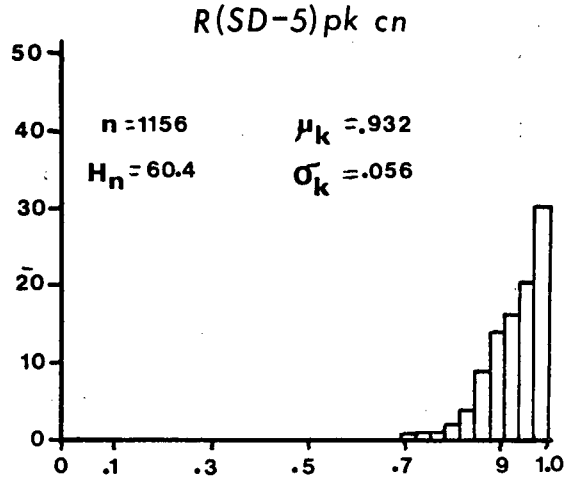
n = the number of males tested

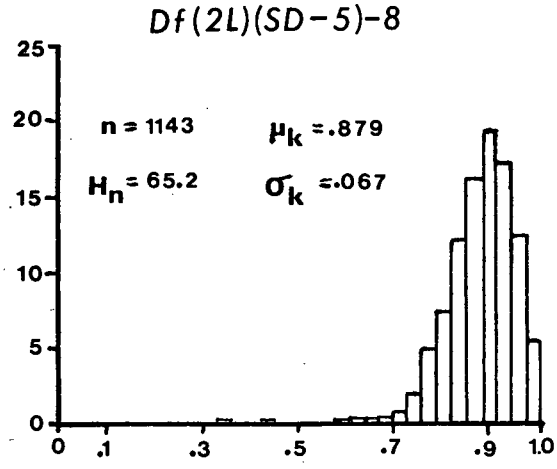
H_n = the harmonic mean number of males

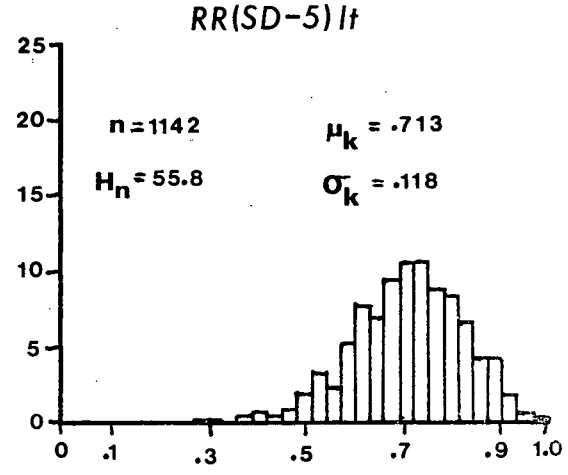
μ_k = the unweighted mean of k's of all the males

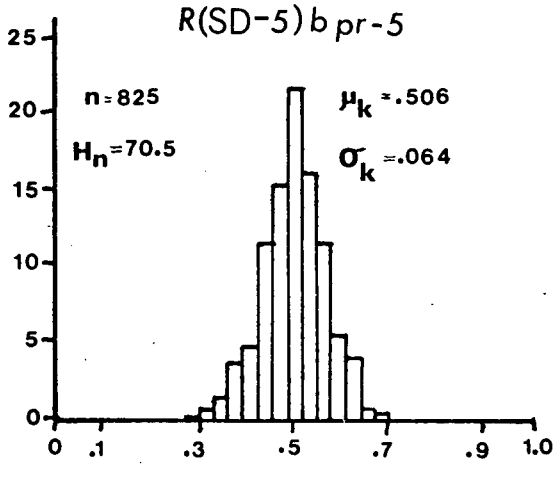
σ_k = the standard deviation of the k's

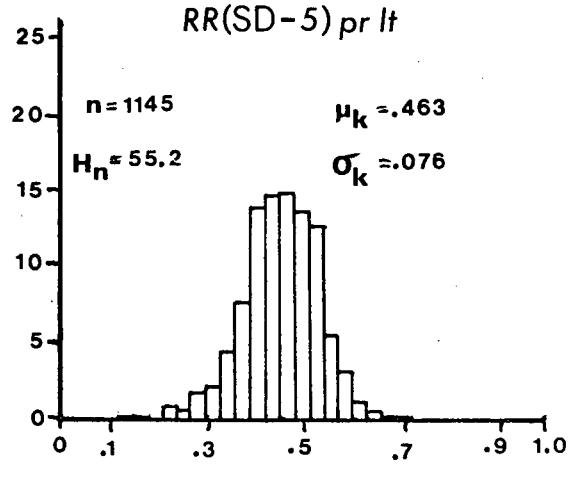

SD-5
n = 1148
μ_k =.985
H_n = 61.3
σ_k =.022
100
90
70
50
30
10
0
0 .1 .3 .5 .7 .9 1.0


R(SD-5)pk cn
n =1156
μ_k =.932
H_n = 60.4
σ_k =.056
50
40
30
20
10
0
0 .1 .3 .5 .7 9 1.0


Df(2L)(SD-5)-8
n = 1143
μ_k =.879
H_n = 65.2
σ_k =.067
25
20
15
10
5
0
0 .1 .3 .5 .7 .9 1.0


RR(SD-5)lt
n =1142
μ_k = .713
H_n = 55.8
σ_k = .118
25
20
15
10
5
0
0 .1 .3 .5 .7 .9 1.0


R(SD-5)b pr-5
n = 825
μ_k =.506
H_n =70.5
σ_k =.064
25
20
15
10
5
0
0 .1 .3 .5 .7 .9 1.0


RR(SD-5)pr lt
n = 1145
μ_k =.463
H_n = 55.2
σ_k =.076
25
20
15
10
5
0
0 .1 .3 .5 .7 .9 1.0

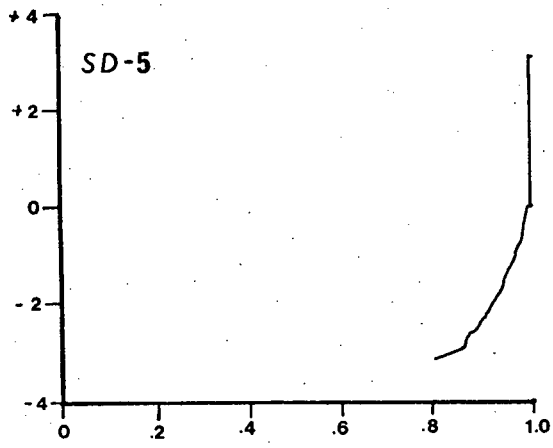
truncated portion and this in turn reduces the variance of the truncated distribution. Thus, on this model the stabilizer is only a strong positive modifier of SD that shifts up the distribution of potential k values such that the majority are truncated at 1.0.

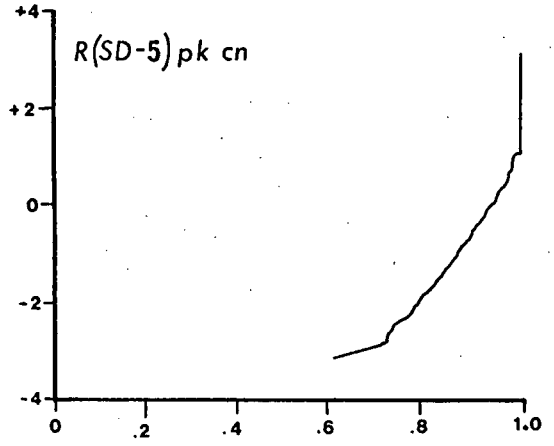
This model predicts that potential segregation ratios will be distributed as truncated normal distributions. However, observed segregation ratios have a binomial sampling component to their distributions and this must be taken into account when observing actual distributions of segregation ratios.

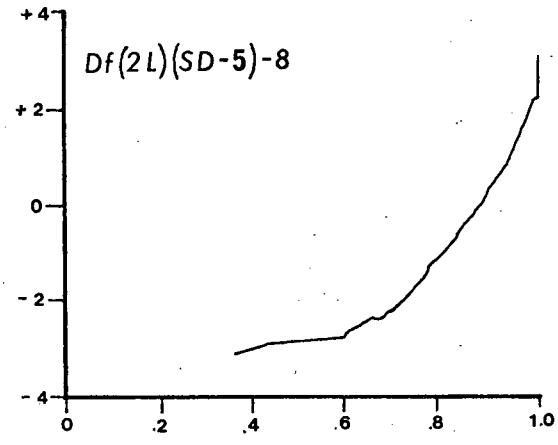
In order to check if the potential segregation ratios follow truncated normal distributions one can use a semigraphical method outlined by Sokal and Rohlf (1969). This involves plotting the cumulative frequencies of successive intervals of a distribution versus the mean value of the interval. Such a plot will be s-shaped if the distribution is normal. If, instead of cumulative frequencies of successive intervals, one uses the probit transformation of that frequency, then the plot will follow a straight line if the distribution is normally distributed. For the present purposes, this technique has been modified somewhat. The individual k values were ranked from the lowest to the highest, and then the quotient of the rank divided by the total number of observations was subjected to the inverse normal integral transformation and then these values were individually plotted versus their respective k's. The points were then joined by straight lines. All of this was performed on a PDP 11 computer. The graphs are shown in Figure 7. Fig. 8 shows graghs constructed in the same manner, except that k was measured as $\arcsin \sqrt{k}$ in order to attempt to remove the effects of binomial sampling. The angular transformation is effective in normalizing a binomial distribution. However, these k distributions are a mixture of a binomial component, and a biological component. I have hypothesized that the biological component follows a truncated

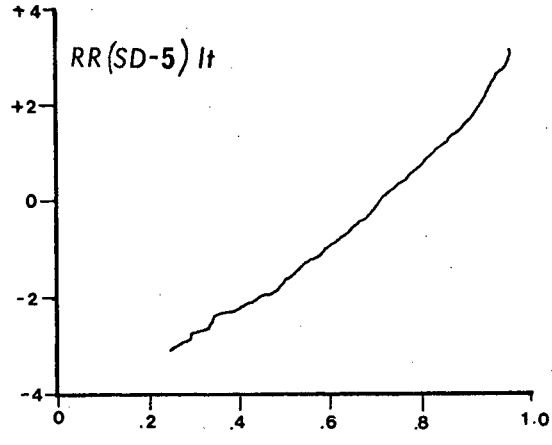
FIGURE 7

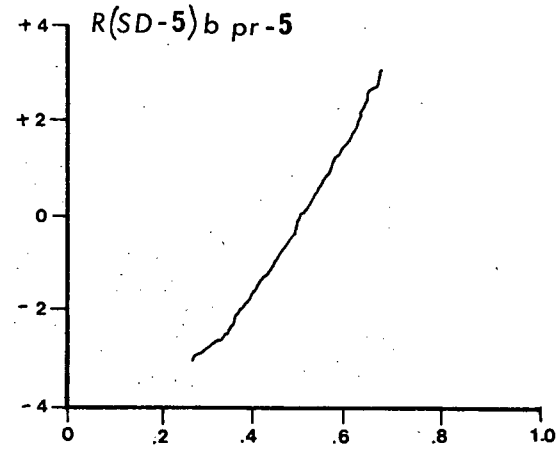
A diagrammatic test for normality of the k distributions of the 6 "SD" chromosomes tested. The unit on the ordinate is standard deviations and the unit on the abscissa is k.


SD-5
+4
+2
0
-2
-4
0
.2
.4
.6
.8
1.0


R(SD-5) pk cn
+4
+2
0
-2
-4
0
.2
.4
.6
.8
1.0


Df(2L)(SD-5)-8
+4
+2
0
-2
-4
0
.2
.4
.6
.8
1.0


RR(SD-5) lt
+4
+2
0
-2
-4
0
.2
.4
.6
.8
1.0


R(SD-5) b pr-5
+4
+2
0
-2
-4
0
.2
.4
.6
.8
1.0

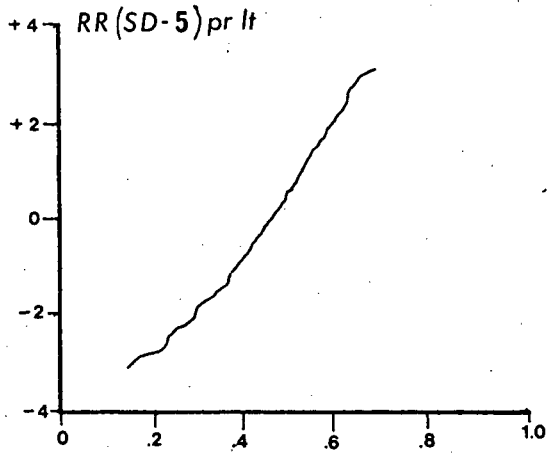
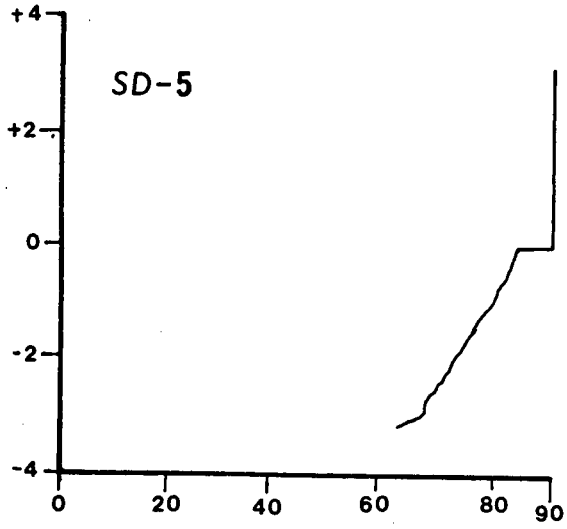
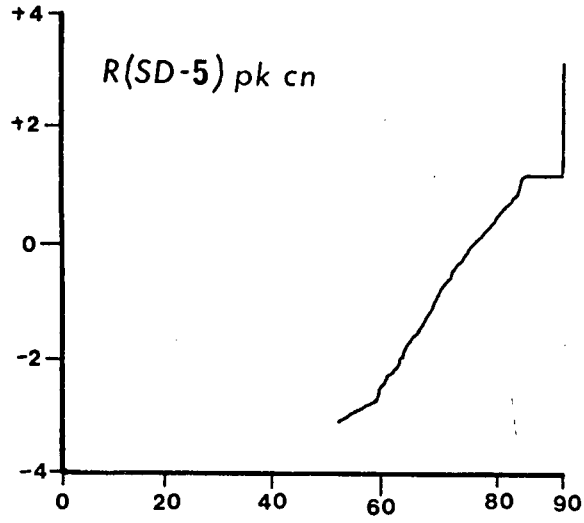
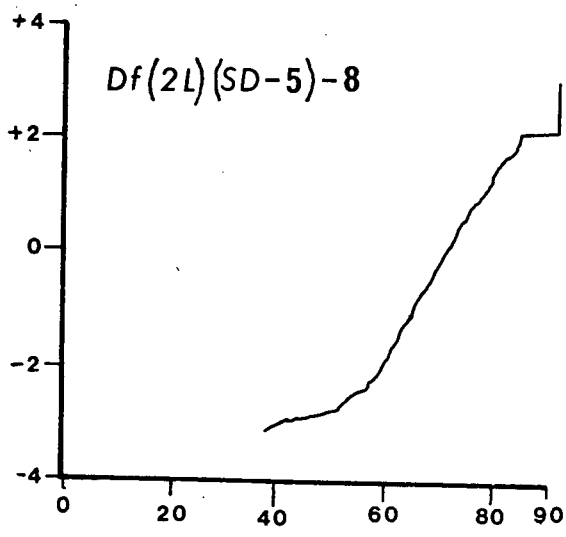

RR(SD-5) pr lt
+4
+2
0
-2
-4
0
.2
.4
.6
.8
1.0

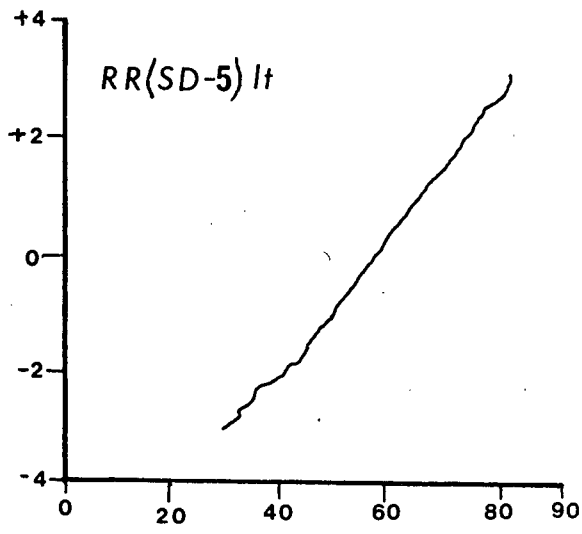
FIGURE 8

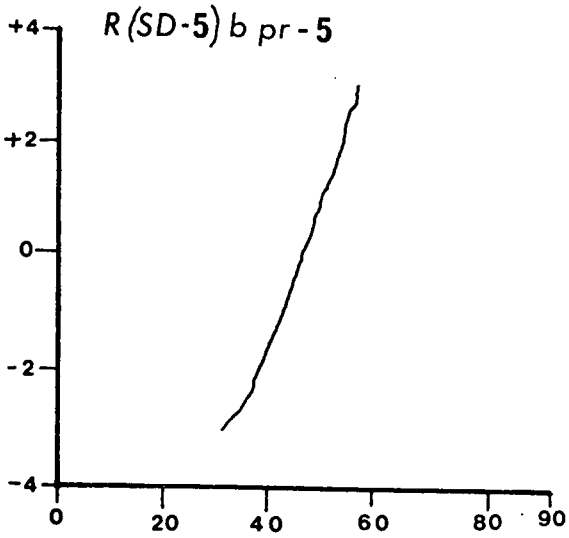
A diagrammatic test for normality of the distributions of arc sin $\sqrt{k}$ of the 6 "SD" chromosomes tested. The unit on the ordinate is standard deviations and the unit on the abscissa is arc sin $\sqrt{k}$.

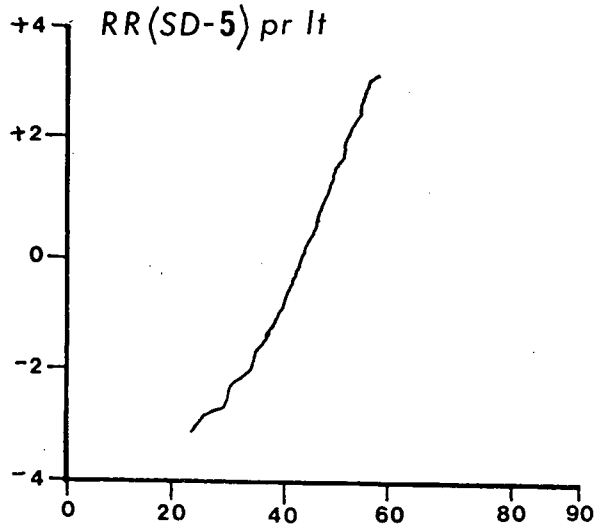

SD-5
+4
+2
0
-2
-4
0
20
40
60
80
90


R(SD-5) pk cn
+4
+2
0
-2
-4
0
20
40
60
80
90


Df(2L)(SD-5)-8
+4
+2
0
-2
-4
0
20
40
60
80
90


RR(SD-5) lt
+4
+2
0
-2
-4
0
20
40
60
80
90


R(SD-5) b pr-5
+4
+2
0
-2
-4
0
20
40
60
80
90


RR(SD-5) pr lt
+4
+2
0
-2
-4
0
20
40
60
80
90

normal distribution. Because the angular transformation is applied to the hybrid distribution, it will only be approximately effective in removing the effects of binomial sampling. The distributions of arcsin $\sqrt{k}$ shown in Figure 8 are truncated normal distributions. These observations support the hypothesis that the biological component of variation follows a truncated normal distribution, but the support should not be considered to be too strong, because of the previously mentioned reservations concerning the effectiveness of the angular transformation in this case. From Figure 8 it is also apparent that the slopes of the resolved portions of the distributions of the four "SD" stocks with mean k's above 0.5 are approximately equal. Although one might be tempted to suggest that this indicates that the variances of the untruncated potential k distributions of the four "SD" stocks with k's above 0.5 are equal, I would hesitate to do so, again because of reservations concerning the efficacy of the angular transformation in removing the effects of binomial sampling from an observed k distribution.

From the distributions shown in Figure 8, it is not at all unreasonable to assume that the potential segregation ratios approximately follow truncated normal distributions. If this assumption is made, then one can determine whether or not truncation alone can account for changes in the observed variance of k between the "SD" stocks with mean k greater than 0.5. Let j be the potential segregation ratio of a male. Binomial sampling from j gives the observed segregation ratio k. The variable j has a normal distribution:

$$f(j) = \frac{e^{-\frac{1}{2}\left(\frac{j-\mu_j}{\sigma_j}\right)^2}}{\sigma_j \sqrt{2\pi}} .$$

Since j is an abstraction, it can possess what seem to be rather peculiar properties. One of these peculiar properties is that it can have values less

than 0 or greater than 1, as well as the usual range from 0 to 1. The more j exceeds 1, the "more impossible" it becomes to recover a fly with the $\underline{SD^+}$ chromosome. Practically, however, one cannot distinguish between different degrees of impossibility. Thus, although in abstract terms j follows a normal distribution, in practical terms j follows a truncated normal distribution, with the distribution being truncated at 0 and 1. What one wishes to determine is how the mean and variance of the truncated distribution vary, when the mean of the untruncated distribution is altered but the variance of the untruncated distribution is maintained at a constant value.

In order to simplify the mathematics of the problem, I shall transform j into z, where $z = \frac{j - \mu_j}{\sigma_j}$. Now the variable z will follow a normal distribution with a mean of 0 and a standard deviation of 1; $f(z) = \frac{e^{-\frac{z^2}{2}}}{\sqrt{2\pi}}$. Instead of being truncated at 1, this distribution will be truncated at $\frac{1 - \mu_j}{\sigma_j}$, which will be designated as z^t. The mean of the truncated z distribution, μ_z^t, can be determined by dividing the distribution into two parts, one part less than z^t and the other part greater than z^t. The part greater than z^t will, because of truncation, have a value of z^t. The proportion of the total distribution contained in this component is given by:

$$\int_{z^t}^{\infty} \frac{e^{-\frac{z^2}{2}}}{\sqrt{2\pi}} \, dz \; .$$

Thus, this component will contribute $z^t \int_{z^t}^{\infty} \frac{e^{-\frac{z^2}{2}}}{\sqrt{2\pi}} \, dz$ towards the mean of the truncated z distribution. The part of the distribution with values of z less z^t will constitute:

$$\int_{-\infty}^{z^t} \frac{e^{-\frac{z^2}{2}}}{\sqrt{2\pi}} \, dz = \int_{-\infty}^{z^t} Z \, dz$$

of the total distribution. In order to calculate the mean of this part of the distribution one must define this part in such a way that the area under this part of the distribution is equal to 1. This can be done by multiplying f(z) by $\left(\int_{-\infty}^{z^t} Z \, dz \right)^{-1}$. The mean of a distribution can be given by $\int_a^b (x) \cdot f(x) \, dx$, if $\int_a^b f(x) \, dx = 1$. Thus the mean of the part of the z distribution less than z^t is given by:

$$\left(\int_{-\infty}^{z^t} Z \, dz \right)^{-1} \left(\int_{-\infty}^{z^t} z \cdot Z \, dz \right).$$

Since this constitutes $\int_{-\infty}^{z^t} Z \, dz$ of the total distribution, this part of the distribution contributes $\int_{-\infty}^{z^t} z \cdot Z \, dz$ towards the mean of the truncated z distribution. Thus the mean of the truncated z distribution is given by:

$$\left(z^t \int_{z^t}^{\infty} Z \, dz \right) + \left(\int_{-\infty}^{z^t} z \cdot Z \, dz \right).$$

The solution of the integral on the right is $\frac{-e^{-\frac{z^{t2}}{2}}}{\sqrt{2\pi}}$, therefore

$$\mu_z^t = \left(z^t \int_{z^t}^{\infty} Z \, dz \right) - \frac{e^{-\frac{z^{t2}}{2}}}{\sqrt{2\pi}}.$$

The variance of the truncated z distribution can be determined in much the same manner, i.e. by dividing the distribution into two parts, one part less than z^t and the other part greater than z^t. In this case one uses the relationship $\sigma_x^2 = \int_a^b f(x)(x-\mu_x)^2 \, dx$, where $\int_a^b f(x) \, dx = 1$. Using this procedure:

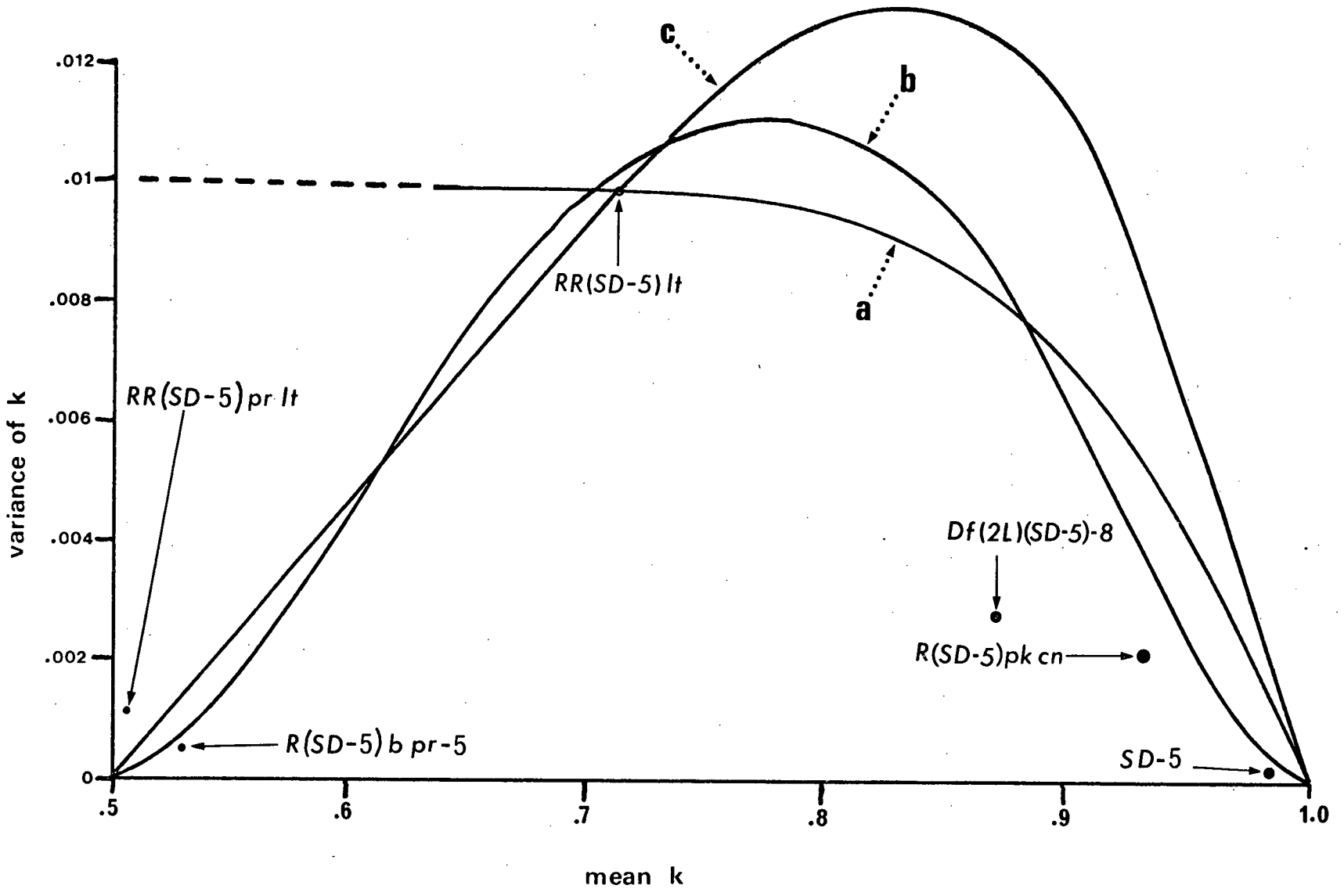
$$\sigma^{t2} = \left(\int_{-\infty}^{z^t} (z - \mu_z^t)^2 \, Z \, dz \right) + \left(\int_{z^t}^{\infty} Z \, dz \right) \left(\mu_z^t - z^t \right)^2.$$

One now knows how to calculate μ_z^t and σ_z^{t2}. In terms of j these parameters are $\mu_j^t = \mu_z^t \sigma_j + \mu_j$ and $\sigma_j^{t2} = \sigma_z^{t2} \sigma_j^2$. In order to compare parameters predicted in terms of j with parameters measured in terms of k one must attempt to remove the effects of binomial sampling from μ_k and σ_k^2. This was done by estimating the variance of a binomial distribution with θ equal to μ_k, and the number of progeny per vial the same as in the observed experiment, and then subtracting this variance from the observed value of σ_k^2. This should give an estimate of σ_j^{t2}. The component of variation contributed by binomial sampling was calculated as $\frac{\mu_k (1-\mu_k)}{H_n}$, where H_n represents the harmonic mean number of progeny per vial. There should be no correction necessary for μ_k, since μ_k should equal μ_j^t.

One can now compare corrected values of μ_k and σ_k^2 with the predicted relationship between μ_j^t and σ_j^{t2}, given some constant value of σ_j^2. One must now choose what the value of σ_j^2 should be. Figures 7 and 8 show that RR(SD-5) 1t/cn bw males had no values of k equal to 1.0. Since the k distribution of these males is not truncated σ_j^2 should equal σ_j^{t2}. Accordingly, this corrected value of σ_k^2 was used as an estimate of σ_j^2. This value of σ_j^2 was used to predict the relationship between μ_j^t and σ_j^{t2} according to the model I have proposed. This relationship is shown in Figure 9 by the curve labelled a. Also shown in Figure 9 are the observed values of μ_k and the corrected values of σ_k^2. Because of the results shown in Figure 8, where the slopes of the resolved portions of the distribution of arc sin $\sqrt{k}$ were similar for RR(SD-5) 1t/cn bw males, Df(2L)(SD-5)-8/cn bw males, R(SD-5) pk cn/cn bw males and SD-5/cn bw males, I expected that curve a in Figure 9 would follow the observed data points for the above males. Clearly it does not. This demonstrates that one must be cautious when interpreting Figure 8. Curve b of Figure 9 shows the prediction made by Miklos and Smith-White's

FIGURE 9

The observed and predicted relationships between the variance of k (without the binomial component) and mean k. Curve a is my prediction with σ_j^2 constant at 0.01. Curve b is the prediction made by Miklos and Smith-White's model (1971) with $\sigma_{m'}^2 = 0.27$. Curve c is my prediction with $\sigma_j^2 = 0.047\ (\mu_j - 0.5)$.


c
b
a
.012
.01
.008
.006
.004
.002
0
variance of k
RR(SD-5) lt
RR(SD-5) pr lt
Df(2L)(SD-5)-8
R(SD-5)pk cn
R(SD-5) b pr-5
SD-5
.5
.6
.7
.8
.9
1.0
mean k

(1971) model. The agreement between this prediction and the observed data points is not much better. In particular, the variance of Df(2L)(SD-5)-8/cn bw males is far below the prediction of either model. Since the variance and mean of RR(SD-5) 1t/cn bw males was used as the reference point through which the curves of both models passed, it is just as likely that, as compared to males with mean k's above the mean k of RR(SD-5) 1t/cn bw males, the SD system in RR(SD-5) 1t/cn bw males was abnormally sensitive to modifiers of SD.

Curve a in Figure 9 was constructed on the assumption that σ_j^2 was constant for all values of μ_j. However, as I previously mentioned, when μ_j is near 0.5 the SD system is either not operating, or only operating at a very low level. Under such circumstances modifiers of segregation distortion should have no effect, i.e. σ_j^2 should be zero. The observations shown in Figure 9 support this contention. Thus it would appear that σ_j^2 must increase as μ_j increases above 0.5. Curve a in Figure 9 is based on the assumption that σ_j^2 does not change after it reaches a value of 0.01 at some point less than μ_j equal to 0.7. Since curve a in Figure 9 does not fit the data, the assumption used to construct it must be incorrect. Perhaps the model would be improved if σ_j^2 was in some manner dependent upon μ_j. The simplest assumption is that σ_j^2 is directly proportional to $(\mu_j - 0.5)$, i.e. $\sigma_j^2 = c(\mu_j - 0.5)$. Again, the variance and mean of RR(SD-5) 1t/cn bw males can be used to estimate c as equal to 0.047. Curve c in Figure 9 shows the prediction when this assumption is applied to the model used to construct curve a. Although this modification renders the model more realistic at low values of μ_k, it does not fit the observations any better at high values of μ_k.

Since none of the predictions shown in Figure 9 fit the observations, it is likely that the SD chromosomes examined in this study differ in their sensitivities to modifiers of segregation distortion. If this is the case, it

must be a consequence of the particular mutations on each of these chromosomes. In this regard, it is interesting to note that RR(SD-5)lt and Df(2L)(SD-5)-8 differ in that the former chromosome was constructed by recombination, while the latter chromosome bears a deficiency of the heterochromatin close to, and including, the lt locus.

CONCLUSION

Although the data obtained in this study do not enable one to choose between the models I have proposed and that of Miklos and Smith-White (1971), I favour my models because their common basic assumption is open to direct refutation. This common basic assumption is that the potential segregation ratios (j) in a population of SD males follow a truncated normal distribution. I attempted to test this assumption, as shown in Figure 8. Figure 8 shows that in all cases arc sin $\sqrt{k}$ is distributed as a truncated normal distribution, but, as previously indicated, I have reservations concerning the efficacy of the angular transformation in this situation, and, accordingly, I consider Figure 8 to be rather weak evidence in support of the assumption that j follows a truncated normal distribution. However, the important point is that, given enough time, it is conceivable that one could compute the exact frequency distribution of k expected for a truncated normal distribution of j and a given distribution of numbers of progeny per vial. Thus this assumption, although not rigourously tested here, is at least potentially verifiable.

On the other hand, Miklos and Smith-White's (1971) model is predicated upon three basic assumptions. The first assumption is that the values of m within a male follow a normal distribution. The second assumption is that within a given male all values of P are invariant. The third assumption is that the values of m' between males of a given population follow a normal distribution. The first two assumptions cannot be tested directly at present, and likely they never will be able to be tested directly. Furthermore, one cannot ascertain the distribution of a variable like m' until one first affirms the validity of the variable, and I have just pointed out that this cannot be done. The only way to test the validity of this triad of assumptions is to test the predictions of the entire model.

In support of their model Miklos and Smith-White (1971) compared calculated frequency distributions of k, which they generated using their model, with observed frequency distributions of k. The comparison they made was incorrect, however, because their predicted distributions of k did not take into account binomial sampling, while the observed k distributions necessarily had a binomial component. If one disregards this gross oversight, it is apparent from their published diagrams that the observed and "predicted" distributions agreed reasonably well. As further support for their model, Miklos and Smith-White (1971) compared the predicted relationship between the standard deviation of k and the mean of k with the observed relationship. Their prediction imposed another assumption on their model, the assumption that σ^2_m, remained constant for all values of μ_k. From the data they presented, the observed relationship agreed reasonably well with the predicted relationship. However, their model, with all four assumptions, did not agree with my observations, as shown in Figure 9. Thus the assumption that σ^2_m, remains constant in flies with similar genetic backgrounds is not generally valid. Proof for the validity of their model must rest on predictions made by the original triad of assumptions. This boils down to comparing observed distributions of k with predicted distributions of k and as I have already pointed out, they failed to do this adequately.

Because my model has only one basic assumption, while Miklos and Smith-White's (1971) model has three basic assumptions, my model is inherently simpler. For this reason, further experiments should concentrate upon attempting to refute my hypothesis, in preference to Miklos and Smith-White's. If it could be adequately verified that j follows a truncated normal distribution, then one could confidently examine changes of σ^2_j between different SD stocks and this might enable one to use μ_j as a measure of distortion, in lieu of k. However, at present, not enough is known about distributions of k in order to

justify any measure of distortion other than k. Accordingly, in what follows I will use either k or k_c as the measure of distortion.

CHAPTER II

ON THE LOCATION AND PROPERTIES OF SOME OF THE LOCI AFFECTING SEGREGATION DISTORTION

INTRODUCTION

To introduce the reader to my results on the location of some of the components of the SD system, I shall first discuss the results of Hartl (1974), since his experiments have avoided some of the complications that had confounded earlier studies on this topic (Hartl and Hiraizumi 1976). Hartl (1974) examined the properties of recombinants recovered from R(SD-36)-1/Tft cn females. The Tft cn chromosome was specifically chosen as it carries no suppressors of SD. The k value of R(SD-36)-1/Tft cn males was 0.95. The recombinants bearing Tft fell into three classes based on their ability to distort cn bw and their sensitivity to another SD chromosome. These three classes were: 1) insensitive distorters (unrecombined SD chromosomes are insensitive distorters), 2) insensitive nondistorters, and 3) sensitive nondistorters. The cn recombinants also fell into three classes. The first class was composed of insensitive distorters. The second and third classes were sensitive nondistorters. These sensitive nondistorters could be further subdivided depending upon their response to the insensitive nondistorter Tft recombinants. One class of the sensitive nondistorter cn recombinants contained chromosomes that were themselves distorted by insensitive nondistorter Tft recombinants. The chromosomes of the other class of sensitive nondistorter cn recombinants were not distorted by the insensitive nondistorter Tft recombinants.

These results suggest that two SD loci are located between Tft and cn. One of these is called Sd and is located to the left of the second locus called Rsp (Responder). A Rsp^+ allele responds to a Sd allele, resulting in the dysfunction of sperm bearing Rsp^+. If a male bears a Rsp^+ allele, but does not have a Sd allele, then there is nothing to cause the Rsp^+ allele to respond, and again segregation will appear normal. If segregation is to appear

abnormal, there must be at least one Sd allele and one each of Rsp and Rsp^+. Thus the recombinants can be classified genotypically as follows: Tft insensitive distorters are Sd Rsp, Tft insensitive nondistorters are Sd^+ Rsp, Tft sensitive nondistorters are Sd^+ Rsp^+, cn insensitive distorters are Sd Rsp, and cn sensitive nondistorters can be divided into two classes since Sd Rsp^+ is distorted by Tft Sd^+ Rsp while Sd^+ Rsp^+ is not distorted by Tft Sd^+ Rsp. A sensitive chromosome such as cn bw, therefore, is Sd^+ Rsp^+.

Ganetzky (1977) has extended Hartl's (1974) analysis by using radiation induced deletions rather than recombinants to map the components of SD. Ganetzky (1977) irradiated SD-5 males with 5000 rads from a cobalt 60 source and then tested the treated chromosomes for their ability to distort cn bw. From 4,000 tested chromosomes, eight were recovered that evidently failed to distort cn bw. However, when tests for distortion of cn bw were repeated using female controls (as I have discussed in Chapter I) it was found that three of these had corrected k values of approximately 0.7, while the other five had corrected k's near 0.5.

Those SD semi-revertants that had Kc's (corrected k values) near 0.7 were also all mutant for lt. Furthermore, when they were complemented with a series of proximal deletions in 2L (Hilliker and Holm 1975), these SD chromosomes behaved as if they all had deletions extending from the position of Group IX lethals to Group VII lethals (Hilliker 1976). These results suggested that an enhancer of SD is located in the centromeric heterochromatin of 2L. Ganetzky (1977) designated this locus as E(SD).

The five complete SD revertants were tested for their ability to induce self distortion of a Sd Rsp^+ chromosome. It was found that four of them did cause Sd Rsp^+ to dysfunction, but one did not. Supposedly the one that did not induce self distortion of Sd Rsp^+ was a powerful suppressor of SD. How-

ever, the other four were candidates for mutations at the SD locus. These four chromosomes were complemented with a series of deletions covering the base of 2L from polytene chromosome band 36F to 40A. They were also examined cytologically. Three of the four chromosomes were fully viable with the deletions and failed to show any new cytological abberations. The fourth chromosome, however, was lethal with some of the deletions and in addition a deletion was observed on this chromosome that extended from 38A6-B2 on the right to 37D2-7 on the left. This deletion is located between the sites of Tft and pr and it suggests that the Sd site of Hartl (1974) is located there also.

Ganetzky (1977) also tested the sensitivity, in males, of 5,160 cn bw chromosomes that were irradiated with 5000 rads of gamma rays. Five chromosomes were recovered that were insensitive to distortion by SD-72. Three of these chromosomes had acquired a new recessive lethal and complementation tests revealed the three lethals to be allelic. By recombination the newly induced insensitivity site was placed between pr and cn.

This is approximately the region where Hartl (1974) placed Rsp. If the newly induced insensitivity alleles are newly induced Rsp alleles, then these insensitive chromosomes should cause distortion of Sd Rsp^{+}. Ganetzky found this indeed to be the case.

Since three of the insensitive cn bw chromosomes had the same recessive lethal in common, it was decided that mapping this lethal should provide information on the location of Rsp. Accordingly, these three chromosomes were complemented with a series of deletions and point mutations of the centromeric heterochromatin of 2R (Hilliker and Holm 1975; Hilliker 1976). It was found that the common recessive lethal was a mutation at the rl locus. One of these chromosomes was mutant only at rl, while the other two appeared to be deletions, one extending into Group I lethals and the other extending both into

Group I and into Group III lethals (Hilliker 1976).

These data alone suggest that Rsp is located near rl. However, Hilliker (personal communication) has tested his proximal 2L and 2R deficiencies and has found that at least one deficiency from each Group is sensitive to distortion. Furthermore, $Df(2R)M\text{-}S2^{10}$, which appears to be both cytologically and genetically deficient for all of the 2R centromeric heterochromatin (Hilliker and Holm 1975), is sensitive to distortion (Ganetzky 1977). In view of these results, it is most unreasonable to maintain that Rsp is located near rl. In order to explain his results in view of Hilliker's findings, Ganetzky (1977) proposes that the Rsp site may be located proximal to Group I. If this were the case, then the insensitive cn bw chromosome that was lethal only for Group II would have to be the result of a double "hit" of some type, one hit causing lethality at Group II and the other hit mutating the Rsp site which is proximal to Group I. Ganetzky also points out that, conceivably, Rsp might occupy different sites on different chromosomes.

In the remainder of this chapter I shall present the results of my findings on the location and properties of Sd, E(SD), and Rsp.

MATERIALS AND METHODS

The SD chromosomes used in this study were SD-5 and SD-72. These chromosomes were obtained by David Holm from the Pasadena stock centre about ten years ago. SD-5 has been maintained as a balanced stock over In(2LR)SM1, Cy and SD-72 over In(2LR)SM5, Cy since that time. SD-5 has two inversions, In(2R)45C-F; 49A and In(2R)NS, while SD-72 has In(2R)NS and a pericentric inversion, In(2LR)39-40; 42A (Lewis 1962).

All experimental crosses were performed in shell vials containing standard Drosophila medium. Segregation ratios from males were always determined from the mean of a number of individual males each mated to two females. Segregation ratios from females were always determined from the mean of a number of individual females each mated to two males. Usually parental flies were allowed to mate and lay eggs for three to four days and then they were discarded.

A cobalt-60 source was used for radiation treatment. Mature males were treated with 2000 rads and then mated with females immediately, in order that mature, irradiated sperm were sampled.

All k values are calculated as the proportion of the total progeny bearing the chromosome that is written first or on top. For example, for the cross $\frac{a}{b}$ mated to $\frac{b}{b}$ (a/b mated to b/b) k refers to the number of progeny bearing a divided by the total number of progeny.

For a description of any visible genetic markers used in this study, see Lindsley and Grell (1968).

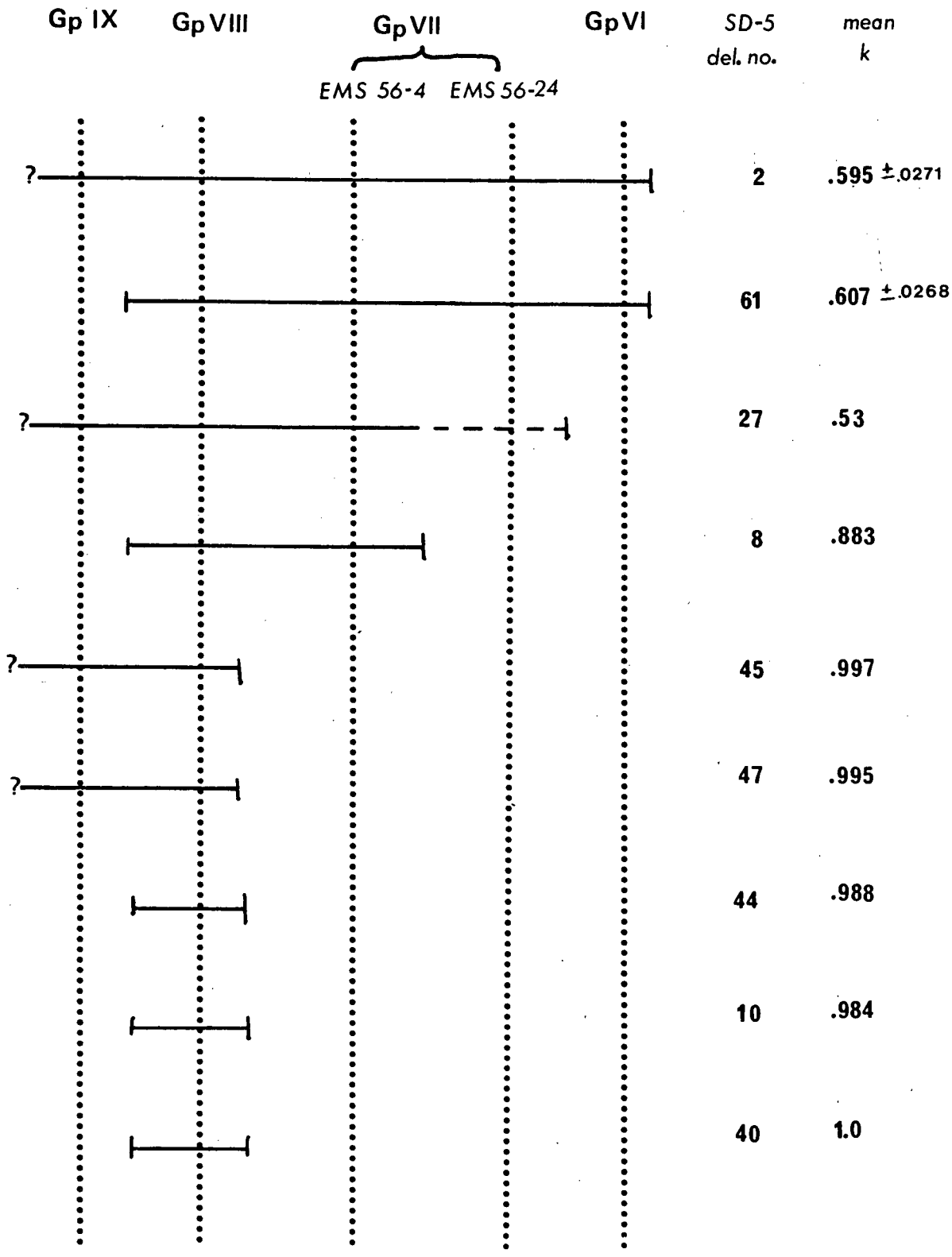
RESULTS AND DISCUSSION

In order to test if there were any components of SD in the centromeric heterochromatin of 2L, I wanted to induce a number of deletions in that region of a SD chromosome. Since lt (light eyes) has an easily detectable phenotype and is located in the centromeric heterochromatin of 2L (Hilliker and Holm 1975) I decided to use γ-rays to induce mutations of lt on SD-5. This was done by irradiating SD-5/SM1 males, mating them to homozygous b pr lt pk cn females and then scoring the non-curly winged progeny for lt eyes (the SM1 chromosome carries the dominant gene Cy, curly wings). The SD-5 chromosomes with newly induced lt mutations were then balanced over SM1. Immediately after being balanced the "lt" SD-5 chromosomes were checked for lethality with Df(2L)PR31, a deficiency of proximal 2L that includes the locus for lt. Since it is known that deficiencies of lt are recessive lethals (Hilliker and Holm 1975), those "lt" SD-5 chromosomes that were lethal with Df(2L)PR31 were retained for further examination, since it was likely that some of them would have heterochromatic deficiencies.

Nine lt SD-5 chromosomes were recovered that were lethal with Df(2L)PR31. All nine chromosomes were tested for their ability to distort cn bw. In addition, they were complemented with a series of deletions of the heterochromatin of 2L (Hilliker and Holm 1975) as well as with some recessive lethal point mutations that comprise Group VII (Hilliker 1976). The results of the complementation and distortion tests are shown in Figure 10. Four of the chromosomes have reduced k values, while the remaining five have k values that are unaffected by the mutations around lt. From the complementation patterns it is apparent that a component of SD is located between EMS 56-4 and the Group VI lethals of Hilliker (1976). The loss of this component results in reducing k from close to 1.0 to approximately 0.6. Likely the reason that

FIGURE 10

The complementation relationships between the putative SD-5 deficiencies and Hilliker's (1976) groups of lethal mutations in the proximal heterochromatin of 2L. The centromere is to the right of Group VI, as drawn in the diagram. Df(2L)(SD-5)-27 was unfortunately lost before its ability to survive with EMS 56-24 was confirmed and a female control to determine k_f was made. The only other chromosomes for which female controls were made were Df(2L)(SD-5)-2 and DF(2L)(SD-5)-61. The mean k shown for these is $E(k_c)$ and the error term is the 95 per cent confidence limits of $E(k_c)$.


Gp IX
Gp VIII
Gp VII
Gp VI
EMS 56-4
EMS 56-24
SD-5 del. no.
mean k
?
2
.595 ±.0271
61
.607 ±.0268
?
27
.53
8
.883
?
45
.997
?
47
.995
44
.988
10
.984
40
1.0

Df(2L)(SD-5)-8 has an intermediate k of 0.88 is that the ability of this SD component to function has only been slightly affected by the proximity of the deletion to it, but the deletion has not removed the SD site. However, it is also possible that more than one SD site resides between Group VIII and Group VI and that Df(2L)(SD-5)-8 has deleted fewer of these than the other three SD-5 deficiencies with reduced k's.

It is also interesting to note that Df(2L)(SD-5)-8 has permitted me to order the two Group VII loci of Hilliker (1976). It is apparent that the locus specified by EMS 56-4 must be distal to the locus specified by EMS 56-24.

Ganetzky (1977) also reported disclosing an important component of SD located in proximal 2L. He did not, however, prove that the component, which he designated as E(SD), was located in heterochromatin. The data presented here confirm the existence of E(SD) and also shows that it is located in the proximal heterochromatin of 2L.

As I did not know of Ganetzky's (1977) work when I had uncovered the component of SD near lt, I wanted to confirm my results in some other manner. Accordingly, I undertook a recombinational analysis of SD-5. The marker chromosome used was b pr lt pk cn. This chromosome was chosen both because of the suitable location of its markers and also because it is very sensitive to SD-5 (from a cross of SD-5/b pr lt pk cn males mated to homozygous b pr lt pk cn females, out of 16,008 total progeny, only six were b pr lt pk cn). From 156 single SD-5/b pr lt pk cn females each mated with two homozygous b pr lt pk cn males the following progeny were recovered: 7,058 wild type, 6,711 b pr lt pk cn, 554 b, 467 lt pk cn or pr lt pk cn (these could not be distinguished without further tests), 4 pk cn, 46 b pr, 2 cn, 2 b pr lt pk, 5 b pr lt, 18 pr, 2 b pk cn, 1 pr lt. It is interesting to note the high frequency of apparent pr double crossovers. These will be discussed later.

Fifteen of the b-bearing recombinants were tested for their ability to distort both cn bw and b pr lt pk cn. The results are shown in Table 1. Eleven of the 15 had high k's over both cn bw and b pr lt pk cn. However, four had reduced k's. When heterozygous with cn bw these four had k's of about 0.55 and when heterozygous with b pr lt pk cn they had k's of about 0.8. This suggests that some component of SD is located between b and pr.

Table II gives the results of tests to determine the abilities of the b pr-bearing recombinants to distort cn bw and b pr lt pk cn. Fourteen chromosomes were tested and 13 had k's of about 0.55 over cn bw and 0.58 - 0.84 over b pr lt pk cn. One chromosome had a high k over both cn bw and b pr lt pk cn. For reasons to be presented later, it is assumed that this b pr chromosome was not the result of a single exchange between pr and lt. If one disregards this anomaly, then all of the b pr recombinants had reduced k's. This result is in agreement with the proposition that there is a component of SD located between b and pr. Before examining more carefully the properties of this component, I shall present the distorting abilities of some of the other recombinants.

Table III shows the abilities of some of these recombinants to distort cn bw and b pr lt pk cn. The k values of R(SD-5) b pr lt - 1, R(SD-5) b pr lt pk - 1, and R(SD-5) b pr lt pk - 2 are quite variable but they tend to be near 0.5 over both cn bw and b pr lt pk cn. These chromosomes would be expected to have k values near 0.5, since they should not have either the SD component between b and pr or the component near lt. The pr lt double recombinant also has a value near 0.5. The two pr SD-5 chromosomes that were tested both had high k values.

It was rather peculiar that these pr SD chromosomes should have high k's. It was also rather peculiar that such a high frequency of pr "double crossovers" were obtained from SD-5/b pr lt pk cn females. Because I could not

TABLE I

The distorting abilities of the b SD-5 recombinants.

Recombinant	Cross*	Number of males tested	Total progeny	Mean k	95% confidence limits of k
b-20	1	5	348	.99	-
	2	12	729	.98	
b-8	1	4	344	.96	-
	2	11	664	1.00	
b-14	1	5	494	.99	-
	2	10	426	1.00	
b-7	1	5	350	1.00	-
	2	12	765	1.00	
b-13	1	5	481	1.00	-
	2	12	1077	1.00	
b-5	1	4	325	.97	-
	2	12	835	1.00	
b-10	1	5	424	.98	-
	2	12	778	.98	
b-2	1	5	443	1.00	-
	2	11	890	1.00	
b-1	1	5	484	1.00	-
	2	12	1123	1.00	
b-3	1	5	487	1.00	-
	2	11	889	1.00	
b-6	1	5	546	1.00	-
	2	12	1018	1.00	
b-12	1	11	1153	.56	.53 - .59
	2	21	1553	.79 **	.72 - .85 **
b-4	1	11	1119	.54	.50 - .58
	2	22	1490	.82 **	.75 - .88 **
b-11	1	10	973	.54	.50 - .58
	2	20	1618	.80 **	.74 - .86 **
b-9	1	6	538	.55	.50 - .60
	2	19	1288	.79 **	.72 - .85 **

TABLE I (Continued)

* 1. $\frac{R(SD\text{-}5)b\text{-}x}{cn\ bw}$ male mated to $\frac{cn\ bw}{cn\ bw}$ females.

2. $\frac{R(SD\text{-}5)b\text{-}x}{b\ pr\ lt\ pk\ cn}$ male mated to $\frac{b\ pr\ lt\ pk\ cn}{b\ pr\ lt\ pk\ cn}$ females.

** Calculated from arc sin $\sqrt{k}$.

Note: None of these k values have been corrected for relative viability of SD and SD^{+} progeny.

TABLE II

The distorting abilities of the b pr SD-5 recombinants.

Recombinant	Cross*	Number of males tested	Total progeny	Mean k**	95% confidence limits of k**
b pr-8	1	5	330	1.00	-
	2	10	412	.97	-
b pr-7	1	11	866	.51	.47 - .55
	2	24	2136	.70	.66 - .74
b pr-1	1	11	958	.54	.50 - .58
	2	16	1185	.66	.59 - .73
b pr-9	1	10	687	.55	.48 - .62
	2	14	1147	.70	.64 - .76
b pr-4	1	11	1003	.59	.55 - .63
	2	19	1833	.81	.75 - .86
b pr-12	1	10	971	.57	.53 - .61
	2	23	2299	.65	.61 - .67
b pr-10	1	10	739	.54	.49 - .59
	2	21	1701	.78	.71 - .84
b pr-15	1	11	956	.57	.53 - .61
	2	23	2184	.58	.53 - .63
b pr-3	1	10	856	.54	.50 - .58
	2	19	1256	.79	.70 - .87
b pr-14	1	11	1215	.55	.52 - .58
	2	22	2221	.71	.65 - .76
b pr-5	1	9	836	.60	.53 - .67
	2	18	1479	.75	.70 - .80
b pr-2	1	11	1062	.54	.51 - .57
	2	23	2047	.71	.64 - .78
b pr-16	1	11	1023	.58	.55 - .61
	2	24	2321	.71	.68 - .74
b pr-6	1	10	742	.56	.50 - .62
	2	16	1371	.84	.76 - .90

TABLE II (Continued)

* 1. $\frac{R(SD\text{-}5)b\ pr\text{-}x}{cn\ bw}$ male mated to $\frac{cn\ bw}{cn\ bw}$ females.

2. $\frac{R(SD\text{-}5)b\ pr\text{-}x}{b\ pr\ lt\ pk\ cn}$ males mated to $\frac{b\ pr\ lt\ pk\ cn}{b\ pr\ lt\ pk\ cn}$ females.

** Calculated from arc sin $\sqrt{k}$.

Note: None of these k values have been corrected for relative viability of SD and SD^{+} progeny.

TABLE III

The distorting abilities of miscellaneous SD-5 recombinants.

Recombinant	Cross*	Number of males tested	Total progeny	Unweighted Mean k	95% confidence limits of $\bar{k}$
b pr lt-1	1	11	1046	.48	.46 - .51
	2	17	1162	.38	.33 - .42
b pr lt pk-1	1	11	1121	.56	.52 - .60
	2	11	941	.48	.44 - .52
b pr lt pk-2	1	11	1107	.50	.47 - .53
	2	13	1011	.39	.31 - .48
pr lt-1	1	11	995	.49	.45 - .52
	2	18	1127	.55	.52 - .57
pr-3	1	5	445	.99	-
	2	10	578	1.00	-
pr-6	1	4	369	1.00	-
	2	11	583	1.00	-

* 1. $\frac{\text{R(SD-5)-x}}{\text{cn bw}}$ male mated to $\frac{\text{cn bw}}{\text{cn bw}}$ females.

2. $\frac{\text{R(SD-5)-x}}{\text{b pr lt pk cn}}$ male mated to $\frac{\text{b pr lt pk cn}}{\text{b pr lt pk cn}}$ females.

Note: None of these k values have been corrected for relative viability of SD and SD^+ progeny.

phenotypically distinguish pr lt pk cn and lt pk cn progeny, from the above cross, I cannot calculate exactly what the observed frequency of recombination was between b and pr and pr and lt. However, since there were 554 b's, 46 b pr's, 467 pr lt pk cn's or lt pk cn's, and 17 pr's, I can approximate these frequencies of exchange as:

$$b - pr = \frac{554 + 18 + \left[\left(\frac{554}{554+46}\right) 467\right]}{14{,}870} \times 100 = 6.750\%$$

and

$$pr - lt = \frac{46 + 18 + \left[\left(\frac{46}{554+46}\right) 467\right]}{14{,}870} \times 100 = 0.67\%$$

The number of observed double exchanges between b and pr and pr and lt should have been approximately equal to the product of 0.0675, 0.0067, and 14,870, which is 6.74. Thus I should have recovered about four pr's, when in fact 18 were recovered. Moreover, although the numbers were small, four females produced one pr each, one female produced two pr's, and four females produced three pr's each, and these pr's appeared to be recovered as clusters. Because of the high frequency of observed pr's and the indication of clustering, it is quite possible that these pr's were not the result of a double exchange, instead they might have been the result of mutation. This would also explain why the two pr's tested for their ability to distort cn bw had high k's. This hypothesis also provides a reasonable explanation for the observation that R(SD-5) b pr -8/cn bw males had high k values. Perhaps R(SD-5) b pr - 8 was the result of a single exchange between b and pr, along with a mutation at pr. If this were the case, then it would be quite likely that R(SD)-5 b pr - 8 would still be capable of strongly distorting cn bw.

In order to further characterize the component of SD between b and pr, I examined the segregational properties of the pr lt pk cn, lt pk cn, and pk cn recombinants when heterozygous with SM1. Hartl (1975) had shown that

In(2L + 2R)Cy carried Rsp, and since SM1 was derived from In(2L + 2R)Cy (Lindsley and Grell 1968), I felt that it was reasonable to assume that SM1 might also have Rsp. The results of the experiment are shown in Table IV. All of the pr lt pk cn recombinants had k values near 0.5. However, both the lt pk cn recombinants had k's of about 0.3. This suggests that the sperm bearing R(SD-5) lt pk cn were dysfunctioning. It is most reasonable to assume that this is because the R(SD-5) lt pk cn chromosomes have the component of SD between b and pr, but they also must have Rsp^+, i.e. they have the genotype $Sd\ Rsp^+$ and SM1 is $Sd^+\ Rsp$, which together is a "suicide combination" (Hartl 1974). This indicates that the component between b and pr can operate in cis and trans to cause distortion, providing one chromosome has Rsp and the other has Rsp^+.

I have avoided calling the component between b and pr, Sd, and the component near lt E(SD) because the loci I have examined do not appear to behave in exactly the same manner as the loci described by Ganetzky (1977). The difference resides in the properties of E(SD). When Ganetzky (1977) deletes Sd, which is located between b and pr, the deleted SD chromosome is no longer capable of distorting cn bw. However, when I replaced the Sd site with a wild type region from the b pr lt pk cn chromosome, the resulting R(SD-5) b pr chromosomes still appeared to have a slight capacity for distorting cn bw (see Table II).

In order to test more carefully for any residual distortion in the b pr recombinants, I performed the crosses shown in Table V. Since it would have required too much work to test all of the recombinants, I selected only one recombinant, R(SD-5) b pr-5, for extensive examination. When k is close to 0.5, it is important to correct for relative viability of the two progeny classes, if one wishes to demonstrate a significant amount of distortion in

TABLE IV

The distorting abilities of R(SD-5)-x/SM1 males mated to homozygous cn bw females.

	$\bar{k}_m$	n_m	$\bar{k}_f$	n_f	$E(k_c)$	95% confidence limits of $\bar{k}_c$
pr lt pk cn-14	.50	12	.50	12	.50	.46 - .55
pr lt pk cn-15	.50	12	.56	12	.43	.38 - .49
pr lt pk cn-16	.50	12	.54	12	.46	.40 - .52
pr lt pk cn-17	.48	12	.54	12	.44	.41 - .47
pr lt pk cn-18	.51	12	.55	12	.47	.41 - .53
pr lt pk cn-19	.47	11	.50	12	.47	.42 - .53
pr lt pk cn-20	.53	12	.54	10	.49	.43 - .55
pr lt pk cn-22	.48	11	.55	10	.48	.43 - .52
pr lt pk cn-23	.49	12	.57	10	.42	.36 - .49
pr lt pk cn-24	.51	11	.52	12	.49	.43 - .55
lt pk cn-1	.29	12	.53	11	.26	.18 - .35
lt pk cn-2	.26	12	.48	10	.28	.19 - .37
pk cn-1	.46	12	.49	12	.47	.42 - .52

TABLE V

The distorting abilities of R(SD-5) b pr-5 under various circumstances.

Experiment	k_m	n_m	k_f	n_f	$E(k_c)$	95% confidence limits of $E(k_c)$
b pr-5 / cn bw x cn bw	.560	49	.508	48	.551	.518 - .584
b pr-5 / cn bw x b pr lt pk cn / b pr lt pk cn	.530	49	.473	48	.555	.526 - .584
b pr-5 / b pr lt pk cn x cn bw / cn bw	.637	48	.506	49	.630	.586 - .674
b pr-5 / b pr lt pk cn x b pr lt pk cn / b pr lt pk cn	.794	45	.608	45	.715	.666 - .764

the segregation ratio. As I described at the beginning of Chapter I, I feel that the best way of doing this is by executing a reciprocal cross. However, I noted there that one drawback to this technique is that conceivably there could be viability maternal effects associated with one of the progeny classes. In order to check if such a problem might be occurring, R(SD-5) b pr-5 was made heterozygous both with cn bw and with b pr lt pk cn and then both classes of heterozygous males and females were mated with homozygous cn bw and with homozygous b pr lt pk cn males or females, as shown in Table V. When R(SD-5) b pr-5 was heterozygous with cn bw, $E(k_c)$ was essentially the same, with both cn bw and b pr lt pk cn homozygous parents (0.551 and 0.555 respectively). However, when R(SD-5) b pr-5 was heterozygous with b pr lt pk cn, $E(k_c)$ was 0.630 with cn bw as the homozygous parent and 0.715 with b pr lt pk cn as the homozygous parent. This large difference in $E(k_c)$ must be due either to a viability maternal effect, or to a female genotype effect on the ability of different sperm classes to function during fertilization. Without further experiments it is impossible to say what causes this difference. This result demonstrates that one must not forget the drawbacks of this type of a viability control.

In Chapter I, I described the results of a large scale experiment with R(SD-5) b pr-5/cn bw males mated to homozygous cn bw; Ki p^p bx sr e^s females. The mean k value of the experiment was 0.506, from 825 males tested. The standard deviation of k was 0.064. In order to check for any viability problems the reciprocal cross of R(SD-5) b pr-5/cn bw females mated to homozygous cn bw; Ki p^p bx sr e^s males was performed. In this experiment, from 31 females tested, $\bar{k}_f$ was 0.478 with a standard deviation of 0.047. It would appear that one reason why $\bar{k}_m$ was below 0.55 was because of reduced viability of progeny with both the R(SD-5) b pr-5 chromosome and the Ki p^p bx sr e^s chromosome. After correcting for viability, $E(k_c)$ equaled 0.529 and the 95

per cent confidence interval of the mean was 0.509 to 0.546. Even after corrections for viability $E(k_c)$ was slightly less than 0.55, although it was significantly greater than 0.5. Perhaps $E(k_c)$ was slightly less than 0.55 because of a maternal viability effect.

Although there does appear to be a problem with either maternal effects or female genotype effects, the fact that all four experiments shown in Table V have $E(k_c)$ greater than 0.5 should certainly be taken as reasonable evidence that segregation distortion is still occurring with R(SD-5) b pr-5. This chromosome has replaced Ganetzky's (1977) Sd site, located between b and pr, with the wild type site from b pr lt pk cn. However, when Ganetzky (1977) deleted this site on his SD-5 chromosome, there was no evidence for residual distortion. The difference is that I used recombination, while Ganetzky (1977) used deletions. One possibility which might account for this difference is that the Sd^+ site on b pr lt pk cn could be semiactive.

In order to check if this was the case, I examined a wild-type recombinant recovered from a cross of R(SD-5) b pr-5/cn bw females mated to b pr lt pk cn males. This recombinant I will call R(SD-5) b^+ pr^+-5. It will likely be genotypically the same as R(SD-5) b pr-5, except it will have most of euchromatic 2L from b pr lt pk cn replaced with euchromatic 2L from cn bw. As shown in Table VI, R(SD-5) b^+ pr^+-5 appears to distort cn bw, giving $E(k_c)$ equal to 0.543. Since this recombinant can also distort cn bw, it must be either because Sd^+ on both cn bw and b pr lt pk cn are semi-active, or because the Sd site between b and pr is not the only Sd site on the particular SD-5 chromosome used in this study. If the Sd site between b and pr is not the only Sd site, then I feel that the component near lt is a likely candidate for the other Sd site. Henceforth I shall refer to the site between b and pr as Sd_1 and the site near lt as Sd_2. Each of these sites alone provides a certain

TABLE VI

Tests to determine if Sd$^+$, on b pr lt pk cn is semi-active.

Experiment	k_m	n_m	k_f	n_f	$E(k_c)$	95% confidence limits of $E(k_c)$
$\frac{RR(SD\text{-}5)b^+ pr^+\text{-}5}{cn\ bw}$ x cn bw	.515	50	.472	40	.543	.520 - .567
$\frac{R(SD\text{-}5)\ b\ pr\ lt}{b\ pr\ lt\ pk\ cn}$ x b pr lt pk cn	.337	43	.370	43	.464	.407 - .522
$\frac{b\ pr\ lt\ pk\ cn}{SM1}$ x b pr lt pk cn	.424	45	.355	49	.572	.547 - .597

capacity to distort, while both together enable maximal distortion.

It is now necessary to decide whether or not $\underline{Sd_1^+}$, on b pr lt pk cn is semi-active ($\underline{Sd_1^s}$). A good test would be to observe the segregation ratio of $\underline{Sd_1^s\ Rsp/Sd_1^s\ Rsp^+}$. This should have a k greater than 0.5. The chromosome R(SD-5) b pr lt-1 (see Table III) is $\underline{Sd_1^s\ Rsp}$. That it carries Rsp will be discussed later. The chromosome b pr lt pk cn is $\underline{Sd_1^s\ Rsp^+}$. Accordingly, I determined $E(k_c)$ for R(SD-5) b pr lt-1/b pr lt pk cn. It was 0.464 and the 95 per cent confidence limits of this mean were 0.407 - 0.522 (see Table VI). The test did not show any significant distortion and accordingly suggests that $\underline{Sd_1^+}$, on b pr lt pk cn is not semi-active ($\underline{Sd_1^s}$). Furthermore, it is very unlikely that the crossover which produced R(SD-5) b pr lt-1 would have occurred between lt and $\underline{Sd_2}$. If this were the case, then the genotype of R(SD-5) b pr lt-1 could have been $\underline{SD_1^+\ Sd_2^+\ Rsp}$. Since it did not show distortion when heterozygous with b pr lt pk cn, it is reasonable to attribute the residual distortion of R(SD-5) b pr-5 to $\underline{Sd_2}$ and not to some other site in 2R of SD-5.

As another approach to determine if $\underline{Sd_1^+}$, on the b pr lt pk cn chromosome, is semi-active, I examined the segregation ratio of b pr lt pk cn/SM1 when mated to b pr lt pk cn homozygotes. The heterozygote could be symbolized as $\underline{Sd_1^s\ Sd_2^+\ Rsp^+/Sd_1^+\ Sd_2^+\ Rsp}$. If $\underline{Sd_1^s}$ is truly semi-active, then one would expect that $E(k_c)$ would be less than 0.5. As shown in Table VI, $E(k_c)$ was 0.572 and the 95 per cent confidence limits of the mean did not overlap 0.5. Since k_c was not less than 0.5 this evidence also suggests that $\underline{Sd_1^+}$, on b pr lt pk cn is not active. It is peculiar, however, that $E(k_c)$ was greater than 0.5. I feel that it is quite reasonable to attribute this to a maternal viability effect. It might be that progeny which are homozygous b pr lt pk cn are less viable if the female parent is homozygous for b pr lt pk cn rather

than if the female parent is heterozygous for b pr lt pk cn. This hypothesis is also in agreement with the observation that $E(k_c)$ for R(SD-5) b pr lt-1/ b pr lt pk cn mated to b pr lt pk cn/b pr lt pk cn was slightly less than 0.5 and also with the observation that $E(k_c)$ for R(SD-5) b pr-5/b pr lt pk cn mated to b pr lt pk cn/b pr lt pk cn was greater than $E(k_c)$ for R(SD-5) b pr-5/ b pr lt pk cn mated to cn bw/cn bw.

The evidence presented here suggests that both Sd_1 and Sd_2 are capable of inducing a certain amount of distortion, providing one chromosome has Rsp and the other has Rsp^+. On the other hand, Ganetzky (1977) has presented evidence suggesting that only Sd_1 can operate on its own to induce distortion. His results lead him to call Sd_2 an enhancer of SD, E(SD). There are two obvious possibilities that could explain this discrepancy. Firstly, it is possible that the SD-5 chromosome used by Ganetzky (1977) had a Sd_2 allele that could not distort alone. Secondly, perhaps an SD chromosome that has had Sd_1 deleted behaves differently than an SD chromosome that has had Sd_1 replaced with Sd_1^+ by recombination.

This last possibility would appear to be the case with respect to Sd_2. This was demonstrated by replacing Sd_2 with Sd_2^+ from b pr lt pk cn. Females of the genotype R(SD-5) b pr lt/R(SD-5) pk cn were mated to b pr lt pk cn males and recombinants that were lt and pr lt were retained. These were called RR(SD-5) lt and RR(SD-5) pr lt. Since R(SD-5) b pr lt is Sd_1^+ Sd_2^+ Rsp and R(SD-5) pk cn is Sd_1 Sd_2 Rsp, the lt recombinant would be Sd_1 Sd_2^+ Rsp and the pr lt recombinant would be Sd_1^+ Sd_2^+ Rsp. As shown in Chapter I the distribution of 1,145 RR(SD-5) pr lt/cn bw males mated to cn bw; Ki p^p bx sr e^s females gave a mean k of 0.463 and a standard deviation of .076. A reciprocal cross involving 33 females gave a mean k of 0.467 and a standard deviation of 0.063. These results give an $E(k_c)$ of .504 with 95 per cent confidence limits of .481

to .528. This chromosome does not distort, as one would expect. RR(SD-5) lt/ cn bw males, on the other hand, had a mean k of 0.713 and a standard deviation of 0.118 (the sample size was equal to 1,142). A reciprocal cross had a k_f of 0.47. Since only 17 females were examined, I will not calculate k_c. The mean k_m of 0.713 was far greater than one would expect from the results with deletions of Sd_2, which had k_c's of about 0.6. Since the deletion of Sd_2 had a different k than the recombinant that replaced Sd_2 with Sd_2^+, it is apparent that, with respect to SD, a deletion does not necessarily behave the same as an allelic substitution through recombination.

The reason that it is of some importance to know whether or not Sd_2 is capable of operating without Sd_1 is that Holm (personal communication) has observed that compound 2R chromosomes constructed from SD-72/cn bw are capable of distorting compound 2L chromosomes from the lt stw strain. SD-72 has a pericentric inversion with break points at 39-40 and 42A (Lewis 1962) and because of this, a compound 2R chromosome constructed from SD-72 has a fairly good chance of having Sd_2, but it could not have Sd_1, since Sd_1 is distal to the left break point of the inversion. Since an SD-72 compound 2R can distort a compound 2L, it would be most reasonable to assume that it is Sd_2 that is operating in the compound 2R, especially in view of the evidence that has been presented here.

Some SD-72 compound 2R's can cause almost total elimination of certain compound 2L's (Holm, personal communication). This observation demonstrates that some loci in 2R or proximal 2L of SD-72 are capable of inducing a high level of distortion under certain conditions. This suggests that it should be possible to exchange most of 2L on SD-72 without appreciably affecting the k of the recombinant. In order to test this I obtained b pr recombinants from SD-72/b pr lt pk cn females. Five of these recombinants were retained and tested for their ability to distort cn bw. The results are shown in Table VII.

TABLE VII

The distorting abilities of R(SD-72) b pr-x/cn bw males mated to cn bw/cn bw females.

Recombinant	k_m	n_m	k_f	n_f	$E(k_c)$	95% confidence limits of $\bar{k}_c$
b pr-1	.493	48	.507	43	.489	.462 - .512
b pr-2	.513	49	.499	47	.514	.490 - .538
b pr-3	.503	49	.505	43	.498	.477 - .518
b pr-4	.497	50	.499	49	.498	.476 - .520
b pr-5	.504	50	.500	45	.504	.478 - .530

In all five cases $E(k_c)$ was close to 0.5 and the 95 per cent confidence interval of the mean included 0.5. There was absolutely no evidence for distortion. This result clearly presents a paradox. If a compound 2R constructed from SD-72 can distort a compound 2L, then why can't R(SD-72) b pr distort cn bw? My results have shown that under certain circumstances Sd_2 alone can cause a residual amount of distortion in the SD-5 chromosome studied here. In order to resolve the previously mentioned paradox one must determine what the circumstances are that allow segregation distortion to operate in SD-72 compound 2R's. The results presented here suggest that Sd_2 is a likely site on which to initiate this study.

Another site of interest is Rsp. As mentioned in the introduction to this chapter, Ganetzky (1977) has presented evidence which suggests that Rsp is located near what Hilliker and Holm (1975) have called Group II, in the proximal heterochromatin of 2R. However, Ganetzky (1977) realizes that such a placement is inconsistent with the sensitivity of a large heterochromatic deletion such as $Df(2R)\ M\text{-}S2^{10}$. Ganetzky (1977) concludes by inferring that it is most likely that Rsp is located proximal to Group I and that his deficiency mapping of the site was somewhat misleading because of possible multiple hit events.

I had planned to determine the sensitivities of the SD-5 recombinants that I recovered, but this proved difficult to do because of a peculiar type of semi-sterility in males of the genotype SD-5/SD-72. Many of the SD-5 recombinants also showed this semi-sterility in combination with SD-72 and consequently insufficient progeny were recovered to warrant reporting the results. Although I shall not report the sensitivities of all of the SD-5 recombinants, I shall discuss two particular recombinants. R(SD-5) pr lt-1/SD-72 males mated to b pr lt pk cn females gave a mean k of 1.0. Ten males were tested

and 680 progeny recovered. On the other hand R(SD-5) b pr lt-1/SD-72 males mated to b pr lt pk cn females gave a mean k of 0.593 with a 95 per cent confidence interval from 0.529 to 0.657. Eleven males were tested and 842 progeny were recovered. Although, for some reason, the latter k was significantly greater than 0.5, it is apparent that R(SD-5) b pr lt-1 was essentially insensitive to SD-72, while R(SD-5) pr lt-1 was very sensitive to SD-72. Since Ganetzky (1977) has shown by recombination that Rsp lies between pr and cn, it is unlikely that the difference in the sensitivities of these two recombinants could be a result of an exchange distal to pr. It is most reasonable to attribute the sensitivity difference to differences in the site of exchange between lt and pk, i.e. this data suggests that Rsp lies between lt and pk. Furthermore, since the frequency of exchange in the centromeric heterochromatin of 2R is very low (Hilliker 1975), the result suggests that Rsp lies in the euchromatin of 2R proximal to pk.

I found this result extremely perplexing in view of the observation that a compound 2R constructed from SD-72 can distort certain compound 2L's (Holm, personal communication). If SD compound autosomes behave the same as standard SD autosomes, then C(2R)SD should have Rsp and C(2L) should have Rsp^+. Since compound autosomes rarely have duplications or deficiencies of proximal euchromatic regions (Hilliker and Holm 1975), if Rsp and Rsp^+ are located in the proximal euchromatin of 2R, it is very unlikely that a compound 2L could have Rsp^+. On the other hand, if Rsp^+ were located in the centromeric heterochromatin of 2R, it would be quite likely that a compound 2L could have Rsp^+.

In order to more carefully examine the location of Rsp, I sought a chromosome that was free of inversions, but carried Rsp. The chromosome b pr rl cn appeared to be insensitive to SD-72, since Sd-72/b pr rl cn males mated to cn bw females gave a mean k of 0.5 with the 95 per cent confidence interval

of the mean being 0.46-0.54. Eleven males were tested and 719 progeny were recovered. If b pr rl cn was insensitive because it carried Rsp, then it should be able to induce self-distortion of R(SD-5) lt pk cn, which is Sd_1 Sd_2^+ Rsp^+. In the cross R(SD-5) lt pk cn-1/b pr rl cn mated to b pr rl cn, $E(k_c)$ was 0.266 and the 95 per cent confidence interval of this mean extended from 0.222 to 0.309. The mean k of the male cross was 0.250 (25 males tested) and the mean k of the female cross was 0.480 (25 females tested). Clearly b pr rl cn can induce self-distortion of R(SD-5) lt pk cn-1. Because of this, it is quite likely that b pr rl cn carried Rsp.

If b pr rl cn carried Rsp, then it was a suitable chromosome to use to map Rsp, since I have observed that b pr rl cn does not have any inversions. Accordingly, b pr rl cn was recombined with a sensitive second chromosome from the wild-type Oregon-R stock. Six separate recombinants of every genotype resulting from a single exchange were retained and tested for sensitivity to an SD chromosome. All recombinants that did not have cn were tested for sensitivity to R(SD-5) pk cn. The results are shown in Table VIII. All of the b and b pr recombinants were more or less sensitive, since they all had mean k's significantly greater than 0.5. On the other hand, all of the b pr rl recombinants had mean k's whose 95 per cent confidence intervals included 0.5. The reciprocal recombinants of those shown in Table VIII were tested for their sensitivity to R(SD-5) b-8. The results are shown in Table IX. The cn recombinants had high mean k's of about 0.97. All but one of the rl cn and pr rl cn recombinants had mean k's whose 95 per cent confidence intervals included 0.5. The one exception was rl cn-2 and it had a mean k of 0.43. Although I do not know why it had a mean k significantly less than 0.5, it certainly did not show any evidence of sensitivity.

These results suggest that Rsp is tightly linked to rl on the b pr rl cn

TABLE VIII

The sensitivities of b-bearing recombinants, from Or - R/b pr rl cn females, when heterozygous with R(SD-5) pk cn.

Recombinant	Number of males tested	Total progeny	Mean k	95% confidence limits of mean k
b-1	10	1222	.71	.65 - .77
b-2	10	1272	.70	.64 - .76
b-3	10	1190	.76	.67 - .85
b-4	10	1127	.66	.56 - .76
b-5	10	1191	.71	.67 - .75
b-6	9	1072	.75	.66 - .84
b pr-1	10	848	.80	.72 - .88
b pr-2	10	920	.61	.54 - .68
b pr-3	10	1081	.78	.69 - .87
b pr-4	10	1467	.59	.56 - .62
b pr-5	10	1416	.75	.68 - .82
b pr-6	9	1005	.71	.62 - .80
b pr rl-1	10	1026	.50	.47 - .53
b pr rl-2	9	947	.54	.48 - .60
b pr rl-3	10	1347	.50	.45 - .55
b pr rl-4	10	1053	.52	.50 - .54
b pr rl-5	10	699	.47	.42 - .52
b pr rl-6	9	581	.51	.44 - .58

Note: None of these k values have been corrected for relative viability of SD and SD^+ progeny.

TABLE IX

The sensitivities of cn-bearing recombinants, from Or-R/b pr rl cn, when heterozygous with R(SD-5)b-8.

	Number of males tested	Total progeny	Mean k	95% confidence limits of mean k
cn-1	10	1426	.95	-
cn-2	10	1387	.97	-
cn-3	10	1313	.95	-
cn-4	10	1348	.97	-
cn-5	10	1404	.97	-
cn-6	9	1372	.99	-
rl cn-1	9	1134	.48	.44 - .52
rl cn-2	9	1215	.43	.39 - .47
rl cn-3	10	1612	.49	.47 - .51
rl cn-4	10	1464	.47	.44 - .50
rl cn-5	10	1625	.50	.48 - .52
rl cn-6	10	1625	.47	.44 - .50
pr rl cn-1	10	1297	.51	.47 - .55
pr rl cn-2	10	1763	.49	.45 - .53
pr rl cn-3	10	1593	.48	.46 - .50
pr rl cn-4	10	1600	.50	.46 - .54
pr rl cn-5	10	1639	.49	.46 - .52
pr rl cn-6	10	1334	.49	.45 - .54

Note: None of these k values have been corrected for relative viability of SD and SD^+ progeny.

chromosome. This in turn implies that Rsp could be located in heterochromatin, since exchange between heterochromatic loci is very rare (Hilliker 1975). However, this proposal contradicts the observation that R(SD-5) pr lt-1 was sensitive, while R(SD-5) b pr lt-1 was insensitive. In order to avoid the contradiction one must either assume that Rsp is in fact located in euchromatin and it was only chance that prevented me from separating Rsp from rl in any of the 12 recombinants between rl and cn, or one must assume that R(SD-5) b pr lt-1 was the result of a rare heterochromatic exchange. In view of Holm's (personal communication) observation that a compound 2R constructed from SD-72 can distort a compound 2L, I feel that it would be best to assume that R(SD-5) b pr lt-1 was the result of a rare heterochromatic exchange.

In an attempt to obtain firmer evidence on the location of Rsp, I recovered four γ-ray induced lethal mutations of Group II on cn bw (these mutations were induced in sperm). If any one of these Group II lethals was a deletion that also deleted Rsp^+, and if Rsp^+ was located proximal to Group I, then Group I would necessarily also be deleted. A deletion of Rsp^+ on cn bw should cause cn bw to be insensitive (Ganetzky 1977). The sensitivity of three of the four Group II lethals to SD-5 is shown in Table X. It is apparent that the three chromosomes retained their sensitivity to SD-5. The fourth Group II lethal was sterile with SD-5 in both males and females. This problem was avoided by testing its sensitivity to SD-72. Ten SD-72/(rl)-1-cn bw - 4 males were mated to cn bw females and 1,139 progeny were recovered. The mean k was 1.0. Thus all four lethals of Group II were sensitive and they could not be used to provide any positive information on the location of Rsp. Nevertheless, complementing these lethals with Hilliker's (1976) EMS induced lethals in the heterochromatin of 2R could provide information on where Rsp is not located. The resulting complementation patterns are shown in Figure 11. The chromosome (rl)-1-cn bw-1 appears to be a deletion extending from Group II

TABLE X

The sensitivities of cn bw chromosomes with γ-ray induced lethals on them.

A. $\frac{\text{SD-5}}{\text{(rl)-l-cn bw-x}}$ ♂ x $\frac{\text{cn bw}}{\text{cn bw}}$ ♀♀

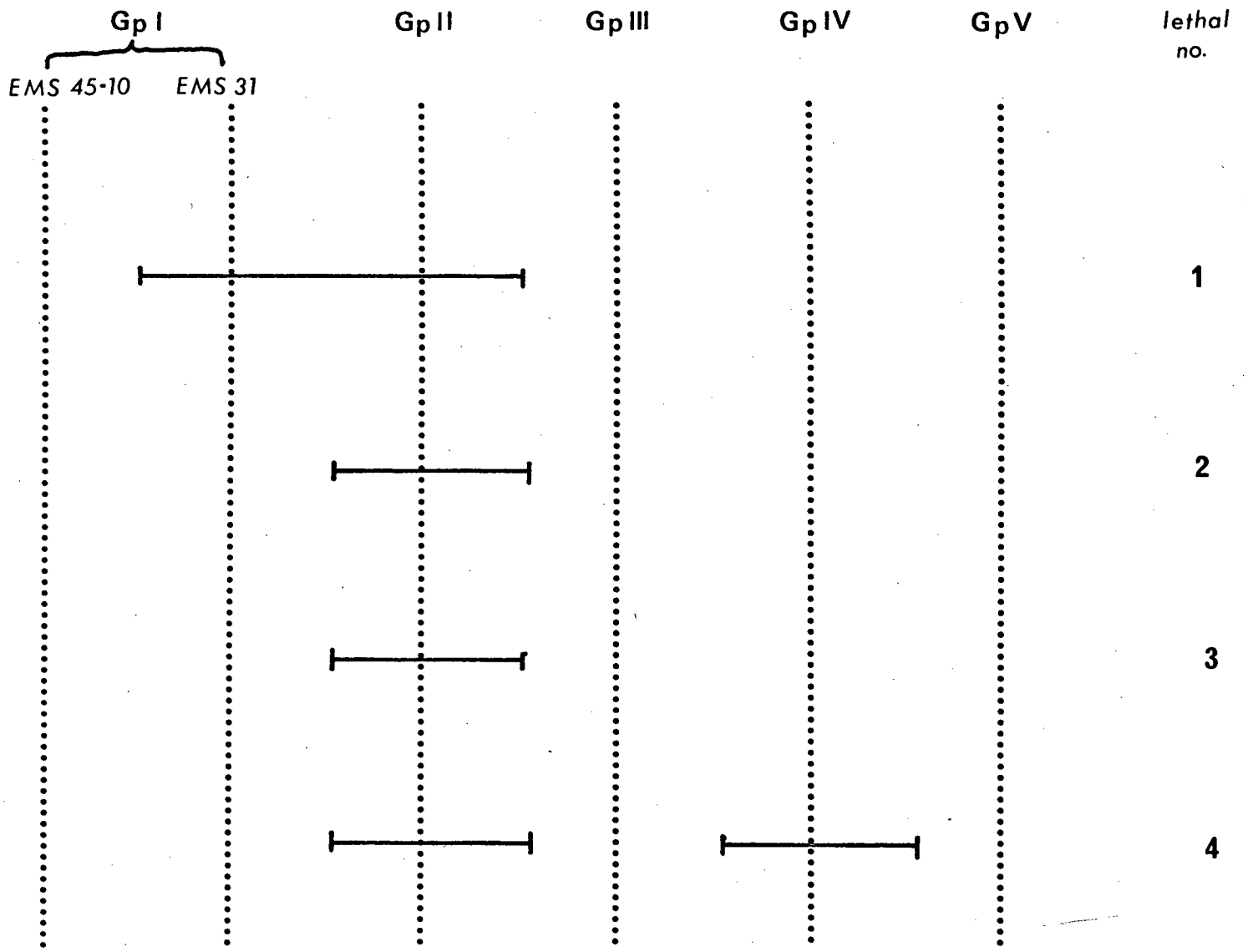
Lethal Number	Number of males tested	Total progeny	Mean k
1	44	2746	.993
2	47	2934	.980
3	42	2773	.982

B. $\frac{\text{SD-5}}{\text{(rl)-l-cn bw-x}}$ ♀ x $\frac{\text{cn bw}}{\text{cn bw}}$ ♂♂

Lethal Number	Number of females tested	Total progeny	Mean k	95% confidence limits of mean k
1	10	1006	.52	.50 - .54
2	10	1044	.52	.49 - .55
3	10	951	.49	.46 - .52

FIGURE 11

The complementation relationships between the cn bw chromosomes bearing putative deficiencies and Hilliker's (1976) groups of lethal mutations in the proximal heterochromatin of 2R. This is to the left of Group I.


Gp I
Gp II
Gp III
Gp IV
Gp V
lethal no.
EMS 45-10
EMS 31
1
2
3
4

to the Group I site specified by EMS 31. It complements with all four of the lethals (EMS 45-10, EMS 45-84, EMS 45-91, and EMS 45-87) in the other site of Group I. Thus Rsp would not appear to be located between Group II and the site specified by EMS 31. This result also demonstrates that the EMS 31 site is distal to the other Group I site specified by EMS 45-10, EMS 45-84, EMS 45-91, and EMS 45-87. The other γ-ray induced lethals on cn bw provide little information of any sort. The chromosome (r1)-1-cn bw-4 was peculiar in that it was the result of a multiple hit event, even though only 2000 rads were used to generate these lethals.

CONCLUSION

This SD mapping study was parallel to Ganetzky's (1977) work in many ways. Both studies have demonstrated the existence of an important component on SD-5 that is located just distal to pr. They also have demonstrated the existence of another component, on SD-5, that is located near lt. Both studies have contributed a meagre amount of evidence in support of the contention that Rsp is located in the proximal heterochromatin of 2R. This agreement serves to increase the credibility of the points agreed upon. The only major difference between our results is that my findings suggest that the component of SD located near lt is capable of inducing distortion in the absence of the SD component located just distal to pr, providing one chromosome has Rsp and the other chromosome has Rsp^{+}. Accordingly, the site that is located just distal to pr, I have called Sd_1 and the site that is located near lt, I have called Sd_2.

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