Stewart, B. and J.R. Merriam. University of California, Los Angeles. Segmental aneuploidy of the X-chromosome.

Aneuploidy, the condition of genetic imbalance, appears to be detrimental in animals, and, when the aneuploid region is sufficiently large, lethal. These deleterious effects of aneuploidy may be thought of as arising from two sources; a relatively small number of genes each, when aneuploid, with a large detrimental effect, or a number of loci, each with a small effect, which cumulatively result in the ill effects of aneuploidy. It should, by examining a series of aneuploids, be possible to distinguish these two possible causes. A gene with a large aneuploid effect should be mappable, where the cumulative effect of many genes will map to a region rather than to a specific locus. It has recently been shown by Lindsley and Sandler et al. (1972) that the latter is the case for the major autosomes of Drosophila melanogaster. The present study was initiated to observe the effects of aneuploidy on the X-chromosome. The X may potentially be different from the autosomes in its tolerance to aneuploidy, as it is itself present in different numbers in the two sexes, and is subject to the regulation imposed by dosage compensation. Furthermore, a series of deficiencies covering the entire X provide a valuable tool for the mapping of mutants and of the structural genes of enzymes.

In order to generate such a series of aneuploids, translocations involving a y-marked X and the $B^{S}Yy^{+}$ were isolated. y females were mated to $y/B^{S}Yy^{+}$ males. Among the progeny of this cross was a $y/y/B^{S}Yy^{+}$ female, which was back crossed to a $y/B^{S}Yy^{+}$ male to establish a stock. From this stock, $y/y/B^{S}Yy^{+}$ females were collected and mated to FM7/Y males. $y/B^{S}Yy^{+}/Y$ males were isolated from this cross, irradiated with X-rays, and mated to either FM7a (a female fertile variant of FM7) females or $\overline{XX}$ females. The $y^{+}B^{S}$ female progeny of the cross of FM7a females to irradiated males were individually mated to FM7a males. From the cross of $\overline{XX}$ females by irradiated males, $y^{+}B^{S}$ males were individually mated to $\overline{XX}$ females. The progeny of both sets of crosses were scored for the presence of translocations involving the X and the $B^{S}Yy^{+}$.

Using these procedures, 75 X;Y translocations were recovered. Information concerning their X and Y breakpoints, male viability and fertility, and aneuploids observed in $\overline{XX}$ stocks is listed in the tables below. Only a minority of the translocations listed could be used in the crosses described below. They were mostly lines with a single break each in the X and Y chromosomes and that could be maintained with viable and fertile males in a $\overline{XX}$ stock.

By crossing two of these translocations with displaced X breakpoints and Y breaks involving different arms, it is possible to recover among the F_1 progeny individuals aneuploid for the region between the two X breakpoints. Duplication-bearing males and females and deficiency-bearing females are generated in each cross, and can be genetically distinguished from each other and from euploid progeny. The results obtained from crossing the X;Y translocations pairwise to generate X chromosome aneuploids are shown in the figure below. Each cross was set up using 15 parents of each sex. Crosses were done reciprocally where possible, and at least in duplicate.

In all cases, hyperploid females were viable and fertile. These duplication-bearing females often had the phenotypic changes associated with hyperploidy, such as smaller size, misshapen wings, and abnormal abdomens.

Males bearing duplications for all the regions of the X-chromosome were recovered with the exception of the two regions, 3A - 3E and 11D - 12E. Males with a duplication of the former region can be generated in other ways; the failure of the duplication-bearing males to survive in this case is thought to be due to lethal genes in the translocation stocks used. The region 11D - 12E most probably does not survive due to the large size of the region.

Hypoploidy of the X-chromosome is less well tolerated than is hyperploidy. Using the translocation stocks, deficiencies uncovering about one third of the X have been generated. In the rest of the chromosome, the X breakpoints of the translocations are farther apart than the four lettered subunits set by Lindsley and Sandler et al. (1972) as the standard for testing a region for deficiencies. One haplo-lethal locus, 7B - 7C (B5 x B17), has been identified.

Fertility of the duplication-bearing males and females carrying heterozygous deficiencies appears to be a function of the size of the aneuploid region. Flies with smaller aneuploid regions are more likely to be fertile than those aneuploid for a larger region. This size relationship is not constant over the entire chromosome, however; some areas of the X seem able to tolerate more aneuploidy than others.

A number of phenotypic effects were associated with the aneuploids. Males hyperploid for the region 8F - 11A (B52 x B53) had curled wings; females hypoploid for this region had out-

stretched wings. Aneuploidy of the region 8C - 11A (J8 x B53) gave the same phenotypes, but duplications or deficiencies of smaller portions of this region did not. The phenotypes were variable; not all of the flies aneuploid for the region displayed abnormal wings. Of the seven Minutes reported on the X, five occur in regions not expected to survive as heterozygous deficiencies because of the large size of the region. No evidence was found for the existence of Minute 1(k); heterozygous deficiencies of the reported location of Minute 1(k) were not associated with a Minute phenotype. A Minute phenotype appeared in deficiencies of the region 14F - 15D/E (B25 x B10, B35 x B10, B35 x B18), which corresponds to the location of Minute 1(o).

From the results of the viability and fertility of aneuploids of the X-chromosome, it would appear that the detrimental effects of aneuploidy result from the cumulative effects of many genes rather than from a few genes with relatively large effects, since aneuploidy is tolerated in almost all regions of the X-chromosome if the region is small enough. The X-chromosome is thus similar to the major autosomes in this respect.

Additional X;Y translocations are currently being recovered and analyzed. With the X-chromosome breakpoints closer together, it should be possible to complete the study of the effects of aneuploidy on the X-chromosome, and to generate a series of overlapping deficiencies uncovering the entire X to be used for mapping new mutants.

Table 1. X;Y translocation stocks

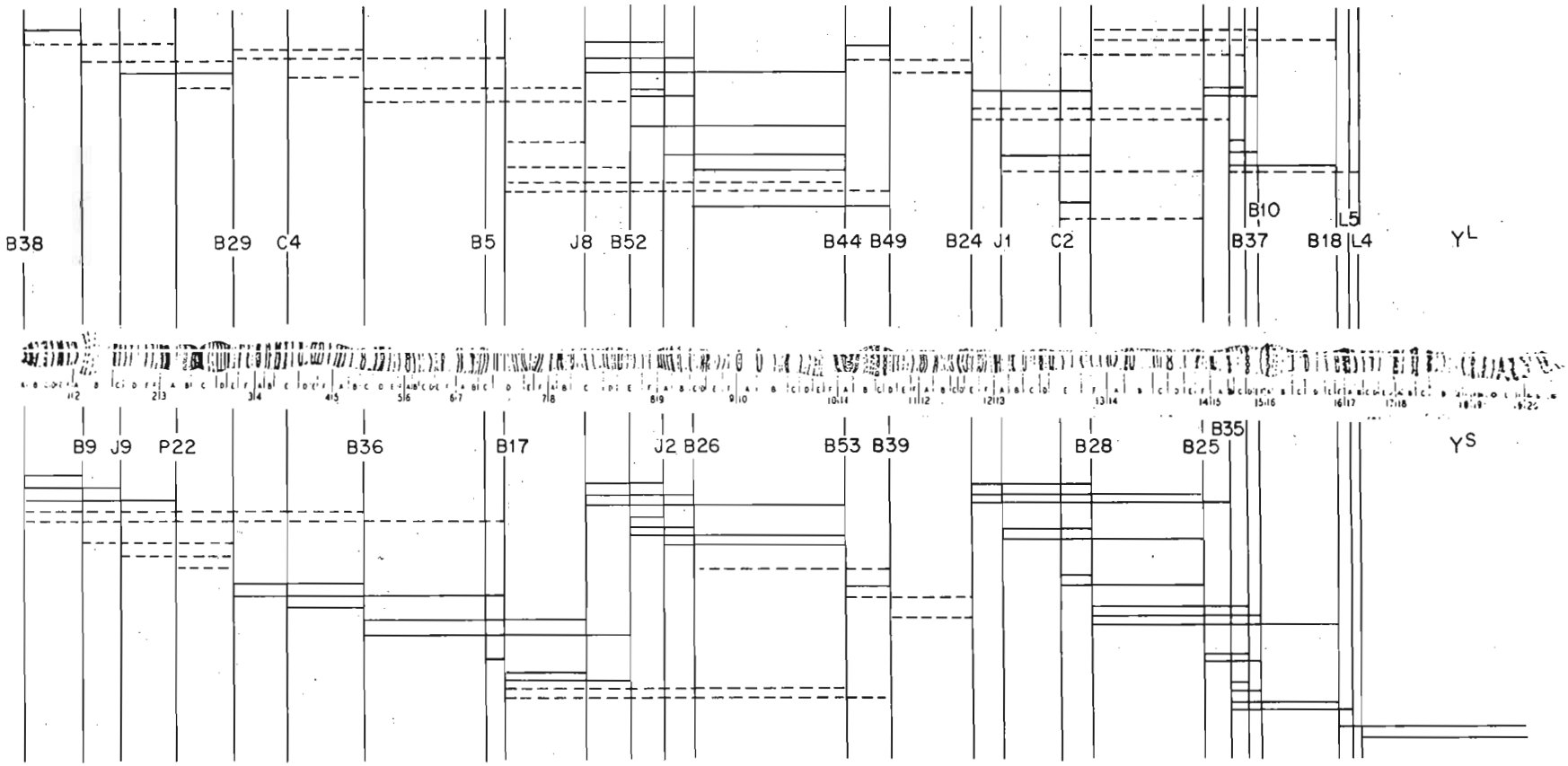
Stock	X Breakpoint	Y Breakpoint	Males	Stocks Kept	Aneuploids in $\overline{XX}$ Stock
B48	tip, 3F	Y^S	viable, fertile	y w f	y w^+ f B^S
B38	tip	Y^L	viable, fertile	y w f/FM7	y^+ w f
B41	tip	Y^S	viable, fertile	y w f	y w f B^S
B11	1B, 4A	insertion	viable, fertile	FM7	-----
J14	1D	?	lethal	FM7	-----
B4	1F, 3C	insertion	viable, fertile	y f	y^+ f B^S
B9	2A	Y^S	lethal	FM7	-----
B27	2B	insertion	viable, fertile	y w f	y^+ w f B^S
J9	2C	Y^S	lethal	FM7	-----
P22	3A	Y^S	lethal	FM7	-----
B33	3A-B, 12E	insertion	viable, fertile	y w f	y^+ w f B^S
P5	3C	?	lethal	FM7	-----
B3	3C2,3	insertion	viable, fertile	y f	y^+ f B^S
B29	3E	Y^L	viable, fertile	y w f/FM7	y^+ w^+ f
C10	3E, 7F	?	viable, fertile	y f/FM7	-----
C4	4C	Y^L	viable (barely)	FM7	-----
B36	5C	Y^S	viable, fertile	y w f/FM7	y w^+ f B^S
B5	7C	Y^L	lethal	FM7	-----
B17	7D	Y^S	viable, fertile	y f/FM7	y f B^S
J8	8C	Y^L	viable, fertile	FM7	-----
B52	8F	Y^L	viable, fertile	y w f/FM7	y w f^+ B^S, y^+ w^+ f
J2	9A	Y^S	viable, fertile	FM7	-----
B26	9C	Y^S	viable, fertile	y w f/FM7	y^+ w f^+, y w^+ f B^S
L3	9C-D	insertion	viable, fertile	y f	y^+ f B^S
P11a	10C	insertion	lethal	lost	-----
P11	10C	insertion	viable, fertile	y f/FM7	-----
B44	11A	Y^L	viable, fertile	y w f/FM7	y w f^+ B^S, y^+ w^+ f
B45	11A	Y^S	viable, fertile	y w f/FM7	y^+ w f^+, y w^+ f B^S
B53	11A	Y^S	viable, fertile	y w f/FM7	y^+ w f^+
J4	T(X;Y;3) 11A, 87	?	lethal	FM7	-----
S15	11B	Y^S	lethal	FM7	-----
B16	11B	Y^S	lethal	FM7	-----
P7	11C-D	?	lethal	FM7	-----
B39	11D	Y^S	viable, fertile	y w f/FM7	y^+ w f^+
B49	11D	Y^L	viable, fertile	y w f/FM7	y^+ w^+ f, y w f^+ B^S
B7	12B-C	?	lethal	lost	-----
L1	12E	Y^L	viable, fertile	FM7	y f^+ B^S

B24	12E	Y^L	viable, fertile	y w f/FM7	y w f^+ B^S
B32	12E	Y^L	viable, fertile	y w f	y w f^+ B^S
B51	12E	Y^L	viable, fertile	y w f	y w f^+ B^S
C8	T(X;Y;2) 12E, 26	?	lethal	FM7	-----
B46	T(X;Y;2;3) 12E, 2R, 3R	Y^S	viable, fertile	y w f	y^+ w f^+
J1	13A	Y^L	viable, fertile	y f/FM7	y f^+ B^S
C2	13E-F	Y^L	lethal	FM7	-----
P12	13E-F	Y^S	viable, fertile	FM7	-----
B28	13F	Y^S	viable, fertile	y w f/FM7	y^+ w f^+
M1	14A	?	lethal	FM7	-----
B6	14E-F	Y^S	viable (barely)	FM7	-----
B25	14F	Y^S	viable, fertile	y w f/FM7	y^+ w f^+
B35	15B	Y^S	viable, fertile	y w f/FM7	y^+ w f^+
B13	15D	Y^L	viable, fertile	lost	y f^+ B^S
B37	15D-E	Y^L	viable, fertile	y w f/FM7	y w f^+ B^S
B10	15E	Y^L	viable, fertile	y f/FM7	y f B^S
P21	15E	Y^L	viable, fertile	FM7	y f^+ B^S
B47	15E	Y^L	viable, fertile	y w f	y w f^+ B^S
B8	16D	Y^L	lethal	FM7	-----
L5	16F	Y^L	viable, fertile	y f/FM7	y f B^S
B18	16F-17A	Y^L	viable, fertile	y f/FM7	y f B^S
C7	17A5,6	?	viable, sterile	FM7	-----
L4	17B-C	Y^L	viable, fertile	y w f/FM7	y w f B^S
J10	17 D-E (complex)	Y^S	viable, fertile	y f/FM7	y^+ f
P8	18A	?	viable, sterile	FM7	-----
B50	18A	Y^L	viable, fertile	y w f	y w f B^S
P6	18B	Y^L	viable (barely)	FM7	-----
S33	20		viable, fertile	y f/FM7	-----
P3(y)	20		viable, fertile	FM7	-----
J11(y)	20		lethal	FM7	-----
B12(y)	20		viable, fertile	y f/FM7	-----
S23	20		viable, fertile	FM7	-----
J6	20		viable, fertile	y f/FM7	-----
B31	20		viable, fertile	y w f	y^+ w f
B34	20		viable, fertile	y w f	y w f B^S
C1	complex		lethal	FM7	-----
C5	complex		lethal	FM7	-----
B43			viable, fertile	y w f	y^+ w f B^S

Table 2. Summary of the analysis of 75 X;Y translocations.

	Procedure A	Procedure B
Male viable and fertile		
Single X break; Y^L	9	11
Single X break; Y^S	3	9
Double X break; insertion into Y	5	3
Complex	2	2
Other	5	3
Male viable and sterile		
Single X break; Y^L	2	-
Single X break; Y^S	1	-
Other	2	-
Male lethal		
Single X break; Y^L	3	-
Single X break; Y^S	5	-
Double X break; insertion into Y	1	-
Complex	2	-
Other	8	-

Heterozygous deficiencies in females



Duplications in males

—— = *viable*

---- = *nonviable*