THE ORGANISATION OF POLYGENIC ACTIVITY WITHIN A CHROMOSOME IN *DROSOPHILA*

II. VIABILITY

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1. INTRODUCTION

IN an earlier paper (Breese and Mather, 1957) we have described an investigation into the distribution, along chromosome III of *Drosophila melanogaster*, of genetic activity affecting the numbers of abdominal and sternopleural chaetae. The starting material comprised chromosomes III from two lines, H and L, selected respectively for high and low numbers of abdominal chaetae. From these were constructed a variety of recombinant chromosomes, each of which included known combinations of segments from the H and L chromosomes III. This was achieved by the use of the so-called "rucuca" marker stock, but as finally produced the recombinant chromosomes themselves contained no marker genes, though they may have contained short segments of material from between the marker genes of the "rucuca" chromosome. The chromosomes built up and the segments of which they were constructed are listed in table 1 and fig. 1 respectively, which are reproduced from the earlier paper. The legends to table and figure provide further information about the recombinant chromosomes, and a full account of the technique of construction is to be found in the earlier paper.

Once constructed, a recombinant chromosome was maintained against *Me Sb* in the male line, and was thus protected from disruption by further recombination and also in large measure from the action of selection. It could, of course, accumulate variation by mutation during its maintenance, and we have evidence that this in fact occurred.

The recombinant chromosomes were tested for their effects chiefly in diallel sets of crosses. The crosses used were always of the types

$\frac{I}{Me\ Sb} \times \frac{J}{H}$ where I and J indicate any two of the recombinant chromosomes. The *Me Sb* chromosome largely reduces, even if it does not wholly suppress, recombination in the mothers so that the identity of chromosome I is in the main preserved. A cross of this kind yields

four types of progeny: $\frac{Me\ Sb}{H}$; $\frac{J}{Me\ Sb}$; $\frac{I}{H}$; $\frac{I}{J}$. The last class is of

course wild type and provides the material for assessing the joint effect

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of I and J on the chaeta characters. It will be observed, however, that the first class is constant over all crosses and so may be used as a

TABLE 1

The recombinant wild-type chromosomes constructed and used in the experiments. Capital and small letters indicate segments derived from chromosome III of the H and L lines respectively. The limits of the segments denoted by A-a, B-b, etc. are shown in fig. 1. In Group (c) the constitution in respect of segment D-d is not fully certain as the gene ca was omitted from the marked chromosome used in the process of construction

Group	(a)	(b)	(c)
Parental chromosomes	(1) ABCD (2) abcd	= APQRD = apqrd	= AXYZRD = axyzrd
Recombinant chromosomes	(3) aBCD (4) abCD (5) abcD (6) ABCd (7) ABcd (8) Abcd	(9) APqrd (10) APQRd (11) apQRD (12) apqRD	(13) AxyZR(D) (14) AxYZR(D) (15) AXyZr(D) (16) AXyzR(D) (17) AxyzR(D) (18) axyZr(d) (19) axYZr(d) (20) zXYZr(d) (21) aXYzr(d) (22) aXyzr(d)

basis for comparing the effects of the recombinant chromosomes on the viabilities of their carriers. The crosses which provided the information about chaeta number described in the earlier paper, also yielded

FIG. 1.—The genes used in constructing the wild-type chromosomes and the segments of which, in consequence, these chromosomes were constructed (see in the text).

The extent of each segment is indicated by the arrows, the limits being shown in their average positions. Apart, however, from the left of A and the right of D, the limits might fall by the vagaries of recombination anywhere between the straddling genes (e.g. the right limit of A might come anywhere between *h* and *st*) the average position being midway between them on the genetical map. This variation in position of recombination could also lead to a small piece of the marked chromosome being inserted in the region of the limit.

The average positions of all the limits are indicated in relation to the genetical map (above) and some of them also in relation to the mitotic cytological map (below). The general position of the centromere (Cent.) is shown on the mitotic map, though it may well be nearer to the left limit of region Y than is indicated. All positions on this map are very approximate.

From Breese and Mather (1957).

the data on viability now to be described. The various sets of crosses and experiments will be referred to in this paper in the same way as in the earlier report.

2. THE MEASURE OF VIABILITY

In all crosses, the parents were mated for 2-3 days in tubes and then transferred to half-pint milk bottles in which their progeny were raised for counting and recording.

In the first set of crosses made (M_1 in the first experiment) the parents remained in the bottles until their early offspring began to emerge. The result was numbers of flies too large for complete classification to be undertaken. Samples of 130-150 were therefore classified from these cultures. In all later crosses, the parents were restricted to 48-60 hours in the bottle, and all the progeny emerging were classified.

At first, in the M_1 and M_2 sets of crosses in the first experiment, no regard was paid to sex in estimating viability, which was measured as $100 \left[\frac{I}{J} \right] / \left[\left[\frac{I}{J} \right] + \left[\frac{Me\ Sb}{H} \right] \right]$ where $\left[\frac{I}{J} \right]$ is the number of wild-type flies of both sexes and $\left[\frac{Me\ Sb}{H} \right]$ the number of flies of both sexes carrying the two marked chromosomes. Equal viabilities of the two classes will then be indicated by a value of 50 per cent. The H and $Me\ Sb$ flies were disregarded. These classes could affect the viability as we measured it by affecting the level and outcome of competition among the four classes within the bottle, but any such effect would seem unlikely to be great in the experiments as conducted and its consequences negligible.

A different — and unexpected — complication was, however, revealed by these early sets of crosses. It became clear that the male and female wild-type flies were showing different effects of the recombinant chromosomes III on their viabilities. In all later crosses, therefore, the viability of the wild-type flies was measured separately for males and females. In each case the measure taken was $100 \left[\frac{I}{J} \right]^* / \left[\left[\frac{I}{J} \right]^* + \left[\frac{Me\ Sb}{H} \right] \right]$ where $\left[\frac{I}{J} \right]^*$ is the number of wild-type males or females, according to which viability was being measured. Males and females were, however, pooled in the $\frac{Me\ Sb}{H}$ class as although there was often a slight shortage of females, in no case was this significant and the ratio borne by the two sexes to one another did not vary significantly over the whole set of experiments. Equal viabilities of the two classes will thus be indicated by a value of $33\frac{1}{3}$ per cent. In every experiment but two where viabilities were measured separately the female proved to vary from cross to cross, as tested by contingency χ^2 's measuring the variation in relative numbers of these females and the marked flies (table 2). Further, there was always a significant shortage of the wild-type females when compared with either the wild-type males or the marked flies. As measured by these

χ^2 's the viability of males on the other hand failed to show any sign of variation in any experiment, and there was no shortage of these males by comparison with the marked flies. Thus genetic differences in chromosome III are revealed by changes in viability of the females; but these same differences failed to produce comparable changes in the viabilities of the males. Further evidence of this difference between

TABLE 2

Contingency χ^2 's testing variation of numbers of wild-type flies relative to Me Sb/H flies in the various experiments. Males and females were not recorded separately in M₁ and M₂ of the first experiment so that the test is of variation in the pooled numbers of the two sexes. In all other cases the test is of variation in the numbers of wild-type males and females separately. In all cases the males and females are pooled in the Me Sb/H class, as the sex ratio did not vary significantly among these flies

Experiment	Variation relative to <i>Me Sb/H</i> class of numbers of wild-type					
1. M ₁ . . M ₂ . .	Females and Males					
	χ^2		N		P (in per cent.)	
	87.9 62.0		48 48		<0.1 8	
1. O ₁ . . O ₂ . . 2. Set 1 . . 2 . . 3. Set 1 . . 2 . . 4. . . Total .	Females			Males		
	χ^2	N	P (in per cent.)	χ^2	N	P (in per cent.)
	106.4	48	0.1	40.3	48	78
	45.1	47	56	35.1	47	90
	80.8	58	3	70.7	58	14
	71.2	46	1.3	51.7	46	32
	58.3	34	0.6	41.0	34	23
	38.9	35	35	43.9	35	17
	55.1	27	0.1	36.7	27	10
	455.8	295	v. small	319.4	295	16

the sexes will be found in the later sections dealing with the individual experiments, though as will be seen it was not so great in the last as in the earlier experiments.

3. THE FIRST EXPERIMENT

In this experiment all the chromosomes (1)-(8) (see table 1), with the exception of (2), were used in a diallel set of crosses, every chromosome being brought from the mother into combination with every chromosome from the father. With 7 chromosomes there were thus 49 combinations including the 7 homozygotes. The 42 heterozygous

combinations fall into 21 pairs, the members of a pair differing only in the way in which the two chromosomes were brought in from the two parents.

The diallel set was made up four times, giving all combinations of two genetic backgrounds (M, the background of the *Me Sb/H* stock, and O, the Oregon background) and the two groups of recombinant chromosomes (1 and 2), these being formally alike but constructed on different occasions so that they may differ as a result of the normal variation in position of crossing-over between the marker genes. One heterozygous combination failed in one of the four replicates. The consequent missing value was replaced by the viability from its reciprocal cross, and the corresponding adjustment made in the degrees of freedom available in the analysis of variance.

In the first two diallel sets (M1 and M2) no distinction was drawn between male and female wild-type flies, but in the O1 and O2 diallel sets of this, and in all later experiments, males and females were counted separated. Pooling males and females in O1 and O2 as well as in M1 and M2, the average viability percentages as defined in section 2 above, were found to be M1-47.4, M2-49.5, O1-46.6 and O2-48.7 in the four diallel sets with a grand average of 48.0, where, of course, 50 per cent. indicates a viability equal to that of the *Me Sb/H* class which was used as the yardstick. When the sexes are taken separately in the O1 and O2 sets $33\frac{1}{3}$ per cent. indicates viability equal to that of the *Me Sb/H* class (see section 2) and the average percentages actually found were O1 females 28.8, O2 females 30.6, O1 males 31.9 and O2 males 33.8. Thus overall viabilities are reasonably high: we are not dealing with sub-lethal combinations of genes. The range of viabilities encountered in the females of the O1 and O2 diallel sets is illustrated in fig. 4.

The viability percentages were all transformed into angles (see Fisher and Yates, 1957) before analysis in this and all the other experiments. These viability results were analysed in two ways, as were the chaeta numbers of the earlier paper. This first analysis was by means of the W/V and W/W' relations of the diallel tables (see Hayman, 1954; Jinks, 1954; and Breese and Mather, 1957). The W/V and W/W' graphs are shown in fig. 2 for the sexes pooled in the combined M and O replicates, and for the sexes separately in the combined O1 and O2 replicates. The corresponding graph for the abdominal chaetae is also repeated from fig. 2 of the earlier paper for comparison. Each point on the various graphs is numbered to show the recurrent chromosome in the diallel array from which that point is derived. This was also done in fig. 2 of the earlier paper, but unfortunately an incorrect set of numbers was assigned to the points in that figure. The error has been rectified in the present fig. 2, which in this respect therefore corrects and replaces the earlier graph.

Several points emerge from these graphs. In the first place, in contrast to the females, the males of O1 and O2 show little more than

FIG. 2.—The W/V (solid circles) and W/W' (open circles) graphs from the diallel analyses of the first experiment for (a) abdominal chaeta number and (b)–(d) viability. For (b) the data are from the combined sexes in the complete experiment, for (c) from females in O₁ and O₂, and for (d) from the corresponding males. The numbers indicate the chromosomes to which the points relate. The straight lines are the best fitting linear regressions, for which the calculated slopes are shown. The dotted curves in (b) and (c) have no special significance, being included only to bring out the curvilinear nature of the W/V relation in these graphs. For the sake of clarity no regression lines are shown in (d), and some of the chromosome numbers are omitted.

Note. (a) is from Breese and Mather (1957) where, however, the points were numbered incorrectly in respect of the chromosomes to which they relate. This numbering is now corrected.

random scatter about the point (O, O) in both W/V and W/W' relations. Completely random scattering round (O, O) would imply a total absence of genetic difference among the seven chromosomes in their effects on viability of the males. The small departure from random scatter shows that this is not fully the case, and indeed we shall see further indications of effects in male viability in other experiments; but the graphs of fig. 2 show that any effect on males is very small as compared with effects on females.

The second point to emerge from the graphs is not only that the females (and, of course, correspondingly the pooled sexes) show striking genetic differences among the seven chromosomes, but also that the genes responsible display both dominance and interaction among themselves. The action of dominance is revealed by the spacing of the array points along the lines in the graphs; and the action of interaction by the curvilinearity of the W/V relation and also by the departure of the W/W' line from a slope of 2. Slight departures of both kinds were detected in the graphs from chaeta numbers and were ascribed in the earlier paper to causes other than genic interaction. Those in the viability graphs are, however, so much larger and more striking as to leave no doubt that interaction is present and is, to say the least, a much more important feature of the gene system in chromosome III affecting viability than of that affecting chaeta number. We may note, too, that, in so far as the intercept of the best fitting W/V line on the y-axis can still be used to measure dominance where the relation is basically curvilinear, its proximity to the origin indicates complete or virtually complete dominance of the operative combinations of genes for viability as compared with the partial dominance indicated in the case of the chaeta. We shall see further evidence of high dominance later.

The third and last feature to be noted about these graphs is that the seriation of the points relating to the seven individual chromosomes is different in the case of viability from that shown with the chaeta numbers. The place of a point in this seriation reflects the overall dominance, or potence, of the combination of genes carried by the chromosome it represents, the farther down towards the left of the line the greater being the potence. In the case of chaeta number, the main division of the points is between (4), (5) and (8) carrying the more dominant b segment and (1), (3), (6) and (7) carrying the more recessive B segment. The wholly H chromosome, (1), is the most recessive. With viability, however, the B-b segment is no longer outstanding in determining the potence properties and the most recessive and most dominant chromosomes are (6), ABCd, and (4), abCD, respectively. The significance of this observation will be examined in more detail later: the point to note for the moment is that in respect of their contributions to dominance and potence the segments do not behave in the same way for viability as for chaeta number.

The second analysis of the data was by fitting constants to represent

the contribution of the various segments to the additive and dominance variation in viability, just as was done for chaeta number. These constants can be used as the basis for arriving at an analysis of variance which allows the contributions of the different possible sources of variation in viability to be tested for significance (see Breese and Mather, *loc. cit.*). If all four diallel sets are to be brought into a single analysis, the results from the pooled sexes must be used as only these

TABLE 3
Analyses of variance of results of first experiment

Item	N	Mean squares		
		All sets— sexes pooled	O ₁ and O ₂	
			Females	Males
Additive effects (A) . . .	4	120.12*	145.50*	9.89
Dominance (D) . . .	4	108.85*	122.26*	33.36†
Res. interaction (I) . . .	19	17.56	28.16*	7.99
Backgrounds (B) . . .	1	10.42	...	...
Groups (G) . . .	1	72.01*	33.39	29.96
B × A }	8	20.79	...	...
B × D }				
B × I	19	9.16	...	...
G × A	4	15.54	2.55	15.89
G × D	4	34.58†	22.00	7.79
G × I	19	13.16	15.21	15.91
Remaining interactions . . .	28	7.13	...	...
Reciprocals	84/41‡	12.77	11.27	8.81
Theoretical error	...	11.47	12.01	11.76

* $P < 0.01$.

† $0.05 > P > 0.01$.

‡ 84 for "All sets" and 41 for the two "O₁ and O₂" columns. Note that both these values are reduced by 1 owing to a missing cross.

All tests of significance were carried out by means of χ^2 's as described in the text.

are available from M₁ and M₂. For O₁ and O₂, however, the sexes may be analysed separately. The three analyses of variance, for pooled sexes over all four diallel sets and for the females and males respectively in O₁ and O₂, are given in table 3 and the average value of the eight constants, a "d" measuring the additive contribution and an "h" measuring the dominance contribution from each segment, are given again for the three different sets of data in table 4.

In contrast with the earlier analyses of chaeta number, no items appear for the sex difference and its interactions in the present analyses. The sexes were not separately recorded in M₁ and M₂ so that the sex difference cannot be introduced into the analysis of the complete experiment, and where it could be introduced in the analysis of O₁ and O₂ the position is in fact made clearer by dealing with the sexes quite separately. A slightly different break-down has further been

adopted for a number of items in the present analyses in order to bring out certain special features of the viability results. The tests of significance were also carried out differently. With the chaeta numbers these had to be based on comparisons with error variances estimated from the reciprocal differences and high order interactions. A different possibility is open with the viabilities since these are measured as proportions. When transformed into angles, proportions have a theoretical variance of $\frac{820.7}{n}$ (Fisher and Yates, 1957), where n is the total number of individuals from which the proportion is estimated. This number varies, though not too widely, from culture to culture, but a theoretical variance can still be found for use in the analysis by

TABLE 4

The constants measuring the additive and dominance contributions of the four regions in the first experiment. For d a positive value indicates higher viability given by the H segment, and a negative sign higher viability given by the L segment. For h a positive sign indicates dominance in the direction of higher viability

	d _a	d _b	d _c	d _d	h _a	h _b	h _c	h _d	s.e.
All sets—sexes pooled	-0.53	-1.21	-0.48	0.86	1.85*	0.45	0.50	1.38†	0.64
O ₁ and O ₂									
Females .	-0.74	-1.39	-0.16	2.04†	2.17†	2.16†	-0.05	2.12†	} 0.82
Males .	1.13	-0.89	0.37	0.77	1.62	1.17	-0.08	0.47	

* $P < 0.01$.

† $0.05 > P > 0.01$.

taking the harmonic mean of the different numbers of individuals counted in the various crosses and using this as the value for n in the formula. The error variances so obtained are given in the bottom line of table 3. Where such a theoretical variance is available, the ratio borne by any sum of squares in the analysis to the theoretical error is distributed as a χ^2 for the number of degrees of freedom appropriate to the sum of squares. All the tests of significance of table 3 have been carried out in this way.

It is encouraging to see in table 3 that the differences between reciprocal crosses and the high order interactions nowhere significantly exceed the theoretical sampling variation and indeed in most cases are slightly, though again not significantly, sub-normal. Evidently there is no unexpected or unaccounted major source of variation in the experiments. Taking first the analysis of the complete experiment, there is no doubt of the genetic effect of chromosome III on viability in respect of both additive and dominance components. The effect of residual non-allelic interactions among the segments is not fully significant. The probability for this item is, however, very little above 5 per cent. ($\chi^2_{[19]} = 29.09$ as compared with $\chi^2_{[19]} = 30.14$ at $P = 0.05$)

and taking this in conjunction with the graphs of fig. 2, there can be little doubt that interactions are having their effects. The difference between backgrounds (M *versus* O) appears to be without importance but the differences between the formally similar recombinant chromosomes of the two groups, 1 and 2, are significant. Evidently the precise positions of the points of recombination are important in respect of viability. Furthermore there is an indication that the effect on dominance varies differently with groups, though that of the additive components does not.

The female viabilities in sets O₁ and O₂ can obviously give no information about the effects of background or its interactions. In other respects, however, these females not only test the same effects but confirm the complete analysis in a remarkable way. The residual genetic interactions now emerge as fully significant, and while the effects of groups and the G × D interaction are sub-significant their mean squares are both large and, again in conformity with the full analysis, that for G × A is small.

The male viabilities are in striking contrast. No item is significant except for the dominance effects and that has a probability higher than 2 per cent. With eight items tested it would not be unduly surprising to find one of them showing by chance a probability of just below 5 per cent. Thus no great weight can be placed on this single significant item. Indeed if we sum the χ^2 's for all eight items in this male analysis we find $\chi^2_{[98]} = 94.04$ with a probability of 0.48. The sex difference in the expression of the genetic effects of chromosome III on viability in this experiment is clear from the analysis of variance which completely confirms the conclusion reached from the diallel graphs of fig. 2, *c* and *d*.

One further point remains to be noted about the genetic interactions among the segments as shown by the analysis of females. This gives a mean square of 28.16 as compared with 145.50 for additive effects—

a ratio of $\frac{1}{5.17}$ or $\frac{1}{8.27}$ if both mean squares are reduced by the theoretical error variance. This compares with corresponding ratios of $\frac{1}{225}$ and $\frac{1}{310}$ for abdominal chaeta. Relative to additive effects interactions loom larger in respect of their contribution to the variation in viability than they do in respect of variability in chaeta number, as indeed does dominance also.

The importance of dominance emerges also from the eight constants, the four d's and four h's attributable to the four segments, shown in table 4. Here again the males of O₁ and O₂ show no significant genetic effects. Tested against their empirical standard error, by no means all of the constants are individually significant in the O₁ and O₂ females or the pooled sexes of all four diallel sets. There can be little doubt of the additive effect exerted by segment D-d (constant d_d)

and it will be observed that in both sets of results this is of sign opposite to d_a , d_b and d_c . The D segment from the H line evidently makes for higher viability than does its counterpart from the L line, whereas in all the other three segments the L line appears to make for a higher viability than does the H. Significant dominance is indicated by h_a , h_b and h_d in three of the four segments, it being in every case in the direction of dominance for higher viability. Furthermore the h 's are on the whole higher in value than the d 's suggesting what, for want of a better term, might be described as "over-dominance" in these three segments; though we must note that even where demonstrated such "over-dominance" of a segment carries no implication of over-dominance at any single gene locus in the chromosome.

These findings about the distribution of the additive effects between H and L chromosomes and about dominance again agree, at least broadly, with the conclusions to be drawn from the diallel graphs in fig. 2 *b* and *c*. The chromosome ABCd (No. 6) is farthest up to the right in both diallel graphs, showing that it is the most recessive of the seven. This is to be expected since dominance is for high viability and the A, B and C segments from the H line and the d segment from the L line all give lower viabilities than do their counterparts. Similarly the chromosome abcD (No. 5) is at the other end of the line as would be expected. It is more difficult to sort out the effects of the individual segments from the remaining points in the figure as the structure of the diallel sets is not orthogonal in respect of the segments, but so far as can be judged they are in full agreement with the expectations from table 4.

4. THE REMAINING EXPERIMENTS

The remaining three experiments undertaken for the analysis of the control of chaeta number are less informative than the first one about viability. The fourth experiment is of a different type and as we shall see yields somewhat disparate results. The second experiment ran into such difficulties from missing cultures that its full analysis was impossible even in respect of chaeta number, while both it and the third experiment were undertaken to analyse further the B-b segment which had proved to be of prime importance in the mediation of chaeta number but is of less dominating significance for viability.

(i) The chromosomes used in the second experiment were (3), (5), (6), (8), (9), (10), (11) and (12) of table 1. They confound the effects of segments A-a and D-d, A always being present with d and a with D. At the same time they break segments B-b and C-c down into three new segments P-p, Q-q and R-r (fig. 1). The diallel set of crosses among the eight chromosomes was attempted twice, different groups of recombinant chromosomes being used on the two occasions. As we have noted, so many combinations failed as to make diallel analysis impossible. A partial analysis of variance was, however, attempted from each set of crosses, by fitting constants. The results

are shown in table 5, which sets out the analyses of variance, and table 6, which sets out the constants themselves and compares these with the corresponding groups of constants obtained from the first

TABLE 5

Analyses of variance of results of second experiment. The entries under "Females" and "Males" in the body of the table are mean squares

Item	1st diallel			2nd diallel		
	N	Females	Males	N	Females	Males
Components . .	8	43.8*	15.2	8	38.4*	17.9
Res. Interaction .	26	12.3	9.7	18	18.4	16.8
Reciprocals . .	24	8.3	19.1*	20	11.3	13.9
Theoretical error .	...	10.7	10.7	...	12.2	11.9

* $P < 0.01$.

† $0.05 > P > 0.01$.

experiment. The d and h components were not fitted separately in these analyses, so that in table 5 the item for components covers both additive and dominance effects.

TABLE 6

A. *Additive and dominance components of variation in the second experiment. The figures given are averages over the two diallels*

	d_{a-d}	d_p	d_q	d_r	h_{a+d}	h_p	h_q	h_r	s.e.
Females .	-0.95	0.02	-2.23†	0.66	2.32†	-0.12	0.61	0.16	} 0.84
Males .	0.23	0.72	-0.04	-0.74	1.32	0.31	0.28	-1.37	

† $0.01 < P < 0.05$.

B. *Comparison of components from first and second experiments*

	d_{a-d}	h_{a+d}	$d_b + d_c^*$	$h_b + h_c$
Females				
1st experiment .	-2.78	4.29	-1.55	2.10
2nd experiment .	0.95	2.32	1.55	0.65
Males				
1st experiment .	0.37	2.10	-0.52	1.09
2nd experiment .	0.23	1.32	-0.06	-0.78

* Regions B+C in first experiment = $P+Q+R$ in second experiment.

Results are presented separately for males and females in both tables. The analyses of variance for the males reveal no item significant against the theoretical error variance except that for reciprocal

differences in the first diallel. This could easily be due to the vagaries of sampling, and indeed if we take all four "reciprocals" mean squares together there is little to suggest anything beyond sampling variation. The main effects for components are significant in females in both diallels. In this they differ from the males just as in the first experiment. No good evidence of residual interaction appears from either set of crosses.

Again in conformity with the first experiment, the only significant constants in table 6A are from the females, though the high standard errors (denoted s.e. in the table) render their individual values rather uninformative. The components are compared for the two experiments in table 6B, where the summed actions of regions B and C are set against those of P, Q and R to which they correspond when taken together.

TABLE 7

Analysis of variance of third experiment. The entries in the main body of the table are mean squares

Item	N	Females	Males
Components (C) . .	6	85.2*	13.2
Res. interactions (I) . .	14	15.2	37.6*
Diallels (D)	1	26.6	90.0*
D × C	6	49.3*	25.8
D × I	14	14.3	18.4
Reciprocals	29	11.9	19.1
Theoretical error . .	...	16.2	15.8

* $P < 0.01$.

Again agreement is as good as could be expected in view of the large standard errors attaching to all entries in the table.

(ii) The third experiment consisted of two diallels, one including chromosomes (1) and (13)-(17) and the other chromosomes (2) and (18)-(20) of table 1. Both of them provide information about the effects of regions X-x, Y-y and Z-z into which regions P-p and Q-q have been jointly broken down (see fig. 1). The two diallels differ, however, in the ways they incorporate the effects of regions A-a, D-d and R-r, so that their overall contrast with one another cannot be interpreted unambiguously. Two combinations (one for each sex) which failed to yield results in this experiment have been given the value of their reciprocals. The numbers of degrees of freedom (N) have been correspondingly adjusted. Four other cultures also failed but were replaced by corresponding cultures raised on a later occasion. The analysis of variance and values of the components are shown for the sexes separately in tables 7 and 8.

The analysis of variance shows the contributions of the three regions, X, Y and Z, to be significant in females and their effects would appear to vary between the two diallels. There is no significant

evidence of interaction in this sex. Curiously enough, however, the item for interaction is significant in the males as is also that for the difference between the diallels. The interpretation of especially the former item is not, however, obvious in the absence of any significant effect of components.

No single component is significant in table 8A. This is not surprising in view of the large standard error attaching to the estimates and in view of the restricted range of the segments under examination as compared with those of the first experiment. Nevertheless, so far as they go, the components of variation set out in table 6A agree with

TABLE 8

A. *Additive and dominance components of variation in the third experiment.*
The figures given are averages over the two diallels

	d_x	d_y	d_z	h_x	h_y	h_z	s.e.
Females .	-2.34	-1.56	-1.04	1.15	1.99	0.77	} 1.56
Males .	0.41	0.06	0.58	-0.05	1.50	-1.15	

B. *Comparison of components from second and third experiments*

	d_{p+q}	h_{p+q}	d_{x+y+z}	h_{x+y+z}
Females . . .	-2.21	0.49	-4.94	3.91
Males . . .	0.68	0.59	-0.11	-0.15

Regions P+Q in 2nd experiment = X+Y+Z in 3rd experiment.

expectation. The female components are in general larger and more consistent than the male. Thus all the female d components are negative and all the h's positive. Furthermore the results from this third experiment agree as well as might be expected with those from the second experiment (table 8B).

(iii) The fourth experiment was of a different kind from the second and third. Eight homozygotes were raised and compared, the eight comprising every combination of the compound regions A-a, PQ-pq and RD-rd. The experiment was carried out in quadruplicate but a few cultures failed in some replicates, none, however, failing in all replicates. This is reflected in the degrees of freedom for variation between like cultures being fewer than the basis design of the experiment would lead one to expect. Since all genic combinations were homozygous in this experiment, no h components are involved—only d components and interactions between these additive components. The four replicates or groups were carried out at the same time and were randomised together. There is thus no point in taking out an item

for gross group or "block" effects. The groups differed in carrying similar but not identical recombinant chromosomes so that the variation of components and interactions over groups (item "replicates $\times$ (C+I)") is of prospective interest.

The results are set out in tables 9 and 10. The most striking feature of table 9 is that, for the first time in these experiments, the effects of

TABLE 9
Analysis of variance of the fourth experiment. The entries in the body of the table are mean squares

Item	N	Females	Males
Components (C) . .	3	63.2†	96.0*
Res. interactions (I) . .	4	9.8	26.5
Replicates $\times$ (C+I) . .	6	90.8*	55.8*
Between cultures of like genotype	14	35.6†	11.7
Theoretical error . .	...	19.9	18.9

* $P < 0.01$.

† $0.01 < P < 0.05$.

the segments are as significant in males as in females. There is no clear evidence of interaction from either sex, but the components vary from group to group in both. The empirical error variance, measured by variation between replicates of the genotypes, is significantly higher than the theoretical error in the females but not in males. The individual components of variation set out in table 10 are uninformative,

TABLE 10
Additive components of variation in the fourth experiment. The figures given are averages over the four replicates

	d_a	d_{p+q}	d_{r+d}	s.e.
Females . . .	-1.16	0.37	-0.06	1.68
Males . . .	-0.98	-0.33	-1.09	1.32
Mean . . .	-1.07	0.02	-0.57	1.49

except for their being of much the same size in both sexes, thus confirming the analysis of variance of table 9.

In setting these results into relation with those of the earlier experiments we must bear in mind that earlier the comparisons were chiefly among at least partly heterozygous combinations whereas this time they are among homozygotes. It may be therefore that the sex difference is mainly to be found in the behaviour of heterozygotes, variation among homozygotes showing up in one sex as much as the other. Comparisons among the viabilities of the homozygous males of the first experiment, however, reveals no expression of the differences which

are detectable between their sisters, and so lends no support to this possibility. It is possible, too, that the contrast with earlier experiments springs in part from variation, newly arisen by mutation during the time the chromosomes were stored between their construction and their use in this last experiment. That mutation had occurred is testified by the appearance of lethal homozygotes in this last experiment though obviously no lethals could have been present when the recombinant chromosomes were first made up. Whatever the cause of the contrast, the different structure of the experiment or mutation, it is clear that this last experiment adds little to our earlier evidence, especially to that from the first experiment.

5. THE GENETICAL ARCHITECTURE OF VIABILITY

Our information about the genetical architecture of viability must come chiefly from the first experiment: failure of cultures, differences in design and the narrower range of genetic differences followed, combine to make the second, third and fourth experiments less informative. So far as they go, however, they agree with the first one in the results they give except that none of them reveals genic interaction in an unambiguous way and the fourth shows differences in viabilities among males where no such differences appeared from any other experiment. The failure of interaction to appear clearly in the later experiments should not be regarded too seriously. There is a hint of its occurrence in the second experiment, where the mean squares depending on it exceed error in the females of both diallels (table 5). The third experiment is concerned with genetic differences confined to a very narrow region of the chromosome, and the fourth experiment again gives a hint of interaction among the males which here are revealing the effects of genic differences even more strongly than the females. The appearance of differences in viability among the males of the fourth experiment is a more positive disagreement with the earlier results. The reason for this occurrence is, however, obscure and it need not prevent us from discussing the genetical properties of the differences among the females upon which the first experiment throws most light.

Perhaps the most striking result of the experiment is this difference in the extent to which the sexes reveal the effects of genes mediating viability. This would be worthy of further study as a problem in its own right. It is not, however, our chief concern at present. Rather we wish to consider the genetical causation and structure of the character as we have found it. The first experiment (table 4) gives evidence of genetical activity of every segment of chromosome III, except segment C-c, in determining the viability of females. Furthermore segment D-d would appear to be acting in the opposite direction to its fellows in the sense that higher viability is associated with D, derived from the H chromosome, whereas with the other segments it is

associated with a, b and c from the L chromosome. Dominance is clear and, it would appear, complete. Also it is unidirectional towards high viability. Interaction occurs between the genes of different segments and the diallel analysis points to it being of a kind analogous to the "duplicate genes" of classical genetics with the dominant high viability genes of one segment tending to suppress, or at least reduce, the effects of low viability genes in the other segments.

One further point is made clear by this first experiment. The flies vary in the length of chromosome for which they are heterozygous. Some are homozygous for all of the four segments. Others are heterozygous for one segment, still others for two, three and even all four segments. The average viabilities of the different type of female are plotted against the number of segments for which they are heterozygous in fig. 4, the figures being obtained from the O₁ and O₂ diallels of the first experiment, in which the sexes were recorded separately. There is a tendency for viability to show a general rise as the number of heterozygous segments increases from one to three. But the flies heterozygous for all segments by no means show the greatest viability, nor do all the homozygous combinations show viabilities poorer than those of the majority of heterozygotes. In other words viability cannot be simply related to heterozygosity: gene content is the important consideration and not heterozygosity *per se*.

Now the genetical architecture of viability stands in sharp contrast to that of chaeta number as revealed by these same flies (Breese and Mather, 1957). Dominance was detectable in respect of chaeta number, but it was not so strong as with viability. Also it was ambidirectional and not unidirectional as with viability. There was evidence of interaction between the genes of different segments affecting chaeta number but again it was quite trivial in its effects as compared with the interaction of the genes affecting viability (fig. 2). The contrast of the additive or d, effects of the segments on chaeta number and viability is less instructive, since the uniformly greater chaeta producing activity of the H segments as compared with the L is to be attributed to the artificial selection applied for this character especially to the ancestors of the H line. We may note, however, that the relative magnitude of effect of the four segments are not the same for the two characters (fig. 3). Also it is perhaps significant, in view of the correlated response of fertility to selection for chaeta number observed by earlier authors (*e.g.* Mather and Harrison, 1949) that the segments from the L line gives higher viability in more cases than do segments from the H line which is descended from ancestors more heavily selected for chaeta number.

This contrast between the genetical architectures of chaeta number and viability is of interest in two respects. In the first place it shows us that the effects on the two characters cannot be attributed to any simple pleiotropic action of the same set of genes. The relative magnitudes and directions of the additive effects of the segments differ

for the two characters, as do their properties in dominance and interaction. To take the analysis further we have investigated the correlation between chaeta number and viability among the 28 genetic combinations in the females of diallels O₁ and O₂. The linear regression of viability (measured in angles) on abdominal chaeta number is -0.235 which has a probability of almost exactly 0.05. It is thus of marginal significance. It accounts for 14 per cent. of the overall variation in viability; and if we use differences between the reciprocals

FIG. 3.—The contributions made by the four segments A-D (see fig. 1) to the additive (d) and dominance (h) variation in abdominal chaeta number and viability. All data are from the first experiment, those for chaetae being from the combined sexes in the whole experiment and those for viability from females in O₁ and O₂ only. The units of measurement are chaetae in the one case and angularly transformed percentage viabilities in the other.

of the crosses from which the 21 heterozygous combinations are derived as a measure of non-heritable variation, so arriving at an estimate of the heritable variation among the 28 genotypes we find that the correlation of chaeta number and viability still accounts for no more than 18.5 per cent. of the heritable variation in the latter. Thus even if we ascribe the whole of this relation between the characters to pleiotropic action of individual genes—an assumption which is by no means necessarily valid—we still have over $\frac{4}{5}$ of the heritable

variability in viability to account for by reference to further genes. Evidently simple pleiotropy is of but little help to us in understanding the relations between the genetic control of characters such as chaeta number and viability.

This is not to say that the pleiotropic action of genes is never of significance in determining the relations between characters or their correlated responses to selection. Where characters are related developmentally in a reasonably simple way we must expect pleiotropic

FIG. 4.—Viabilities of females in families from O₁ and O₂ of the first experiment plotted against the number of segments for which the flies were heterozygous. The segments for which the family was heterozygous are shown by unbracketed capital letters against each point and the homozygous segments by bracketed capital or small letters according to whether they came from H or L. All viabilities are in percentages, the horizontal line at 33 1/3 per cent. marking the level at which the wild-type flies have a viability equal to their *Me Sb/H* sibs.

relations between them. Even in such cases, however, the pleiotropic tie may have far from simple consequences, as has been shown by Cocks (1954) in respect of the obviously relatable characters, abdominal and sternopleural chaeta numbers. When, therefore, we turn to such disparate characters as chaeta number and viability it is no surprise to find that pleiotropy of gene action is of little help in understanding their relations. Linkage of the members of the relevant polygenic systems is then the key to the determination of covariation within

related groups and correlated responses to selection. Such linkage will ensure that chromosome segments, or effective factors to use the term of Mather (1949), will show pleiotropic action even where the individual genes do not; but it will be a stable pleiotropy only so long as the chromosome segment is unbroken by crossing-over, for recombination will result in a redistribution of the linked associations and hence in a reassociation of the characters themselves. This conclusion is not new. The significance of linkage as opposed to genic pleiotropy, and the distinction between the apparent and resolvable pleiotropy of a segment or effective factor, which springs from linkage, and the unresolvable basic pleiotropy of single genes, have often been discussed and emphasised (*e.g.* by Mather and Harrison, 1949). The subject is raised yet again only because the present results hammer home so firmly the distinction between genes and segment and the insufficiencies of genic pleiotropy as an explanation of the relations observable between characters in genetical experiments.

6. GENETICAL ARCHITECTURE AND NATURAL SELECTION

The second respect in which the contrast between chaeta number and viability is of interest lies in the relation it reveals between the genetical architecture of a character and the forces of natural selection to which that character has been subjected (Mather, 1960). Now chaeta number and viability must be acted on differently by natural selection. Chaeta number would appear to have a central optimum with both extremes at a disadvantage relative to the more central values. In other words selection will be essentially stabilising. Viability on the other hand will obviously be subject more to directional selection, the advantage lying with the higher expression of the character.

It has been pointed out by Fisher (1930) that natural selection will tend to modify the phenotypic expression of heterozygotes towards closer resemblance to that of homozygotes carrying the more favourable allele. With unconditional advantage of one allele over another, such as would generally be the case where selection is essentially directional, this will mean unidirectional dominance as we have found with the viability genes. With stabilising selection, however, the more common allele will in the long run be the more favourable irrespective of the direction in which it pulls the character. Dominance should then tend to become ambidirectional (Fisher, *loc. cit.*) as is the case with the genes governing chaeta number. Thus the difference between the polygenic systems giving viability and chaeta number in respect of their properties of dominance is relatable to the difference in the impact of natural selection upon them.

The same difference might also be expected to arise in respect of non-allelic interaction. Directional selection would be expected to favour any interaction which tended to conceal the shortcomings in

action of the individual genes, and this is achieved by a duplicate system of interaction where dominance and interaction pull together, as we find it in the case of viability. With stabilising selection towards a central optimum the advantage of a given type and direction of interaction would vary with the combination of genes, so that there would be a lower and less persistent pressure of selection towards interaction and even such as evolved would tend to be ambidirectional and self-cancelling. Interaction should thus be a less striking feature of the gene systems governing a character of this type, and indeed in the case of chaeta number they appear to be so.

Studies in *Drosophila pseudoobscura*, *persimilis* and *prosaltans* have shown that interaction is as much a feature of the genetical architecture of viability in these species as in *D. melanogaster* (Spiess, 1958). And indeed we should expect it to be so as natural selection must be directional in its impact on viability in one species as much as in another. Spiess goes on further to point out the relation of the occurrence of so-called synthetic lethals to genic interactions. Such recombinational lethals would be expected with a duplicate type of interaction of the kind we have found, though we may note that complementary interactions, where homozygosity for one recessive gene produces the effect irrespective of the constitution at other loci, would not give them. This complementary relation is characteristic of the classical point mutation lethals, which serves again to emphasise the distinction between lethality springing from mutational and balance effects. Both types of lethal have been found in chromosome II of *D. melanogaster* (Misro, 1949), but surprisingly enough Hildreth (1956) has not been able to obtain evidence of synthetic or balance lethals in chromosome III. Spiess seeks to relate this to a difference in the properties of interaction in the polygenic systems of the two chromosomes as they affect viability, citing our own evidence that interaction of the genes in chromosome III is of little significance in the control of chaeta number. Even leaving aside the problem then raised of why the properties in interaction should differ between the gene systems of the two chromosomes, it is now clear that the difference in interaction is a feature not of the two chromosomes but of the two characters. Indeed certain of our observations positively suggest that such balance lethals do arise. In building up stocks for experiment 3 some 23 chromosomes were selected as showing recombination between *st* and *p^b* and 19 as showing recombination between *p^b* and *cu*. Two chromosomes for each set proved to be lethal when homozygous and, what is more, the lethals in the two *st*—*p^b* recombinants appeared to be allelic as did the two in the *p^b*—*cu* recombinants. The suggestion of a link between recombination and the appearance of lethals is clear. Our present data thus suggest that synthetic lethals are capable of production by recombination in chromosome III. So Hildreth's results are still unexplained and it would indeed appear worthwhile to repeat his experiments with other examples of chromosome III to discover whether his findings

were characteristic of this chromosome in general or merely specific to the sample of it that he happened to employ.

Differences in the genetical architecture of characters may be expected to show up when crosses are made between individuals from different populations, that is to say when combinations of genes are brought together which do not normally meet and which have therefore not been subjected to co-adaptation by the action of natural selection (Mather, 1943). With a relatively simple genetic system showing ambidirectional dominance such as is to be expected from the past action of stabilising selection and which has been found in the case of chaeta number, the relative unbalance of heterozygous genotypes resulting from crosses between individuals from different populations should show itself merely by increased average departure from the optimum. This departure is as likely to be towards lesser as towards greater manifestation of the character. In other words, inter-population hybrids should show a greater spread round their overall mean which itself need not depart from the mean of intra-population families. This spread must of course be measured as the variance of mean of families raised from inter-population crosses, since the variance within such families will chiefly reflect the degree of heterozygosity of the parents and so is largely irrelevant to the measurement of unbalance.

No data are available for chaeta number in crosses between wild populations of *D. melanogaster*, but the frequency of chiasma formation has been followed in such crosses of the campion plant *Lychnis dioica* by Dr C. W. Lawrence (see Mather, 1959). Chiasma frequency is a character with a central optimum and therefore subject to stabilising selection. Mr Lawrence has found an overall mean number of 14.07 chiasmata in the pollen mother cells of families raised from crosses within populations and an overall mean of 14.22 from crosses between populations. These two averages do not differ significantly. When, however, the variances were calculated among the family means, a figure of 3.6 was found for crosses between populations as against 1.15 for crosses within populations. This difference is in the expected direction and is significant. These figures differ a little from those quoted by Mather (1959) as a result of the addition of further material.

Observations are available on the viability of flies from inter-population crosses in a number of species of *Drosophila* (Vetukhiv, 1954, Wallace and Vetukhiv, 1955). The remarkable fact has emerged that viability is commonly higher in the F_1 of such crosses than in crosses made within populations, though in the F_2 it falls very much below the intra-population level. This result becomes much less surprising, however, when we consider the architecture of viability as we have found it. Dominance is unidirectional towards high viability, and in that it will be selected for in every population where the genes are segregating, we might expect it to be displayed as strongly or virtually as strongly in heterozygotes from crosses between populations as in

those from crosses within. Interactions will be selected only among genes occurring together and we might therefore expect them to be a less marked feature of genotypes obtained by crosses between, as opposed to within, populations. No clear information is available on this point. The mere occurrence of unidirectional dominance will, however, ensure that if the viability is maintained at its normal level by different polygenic combinations in different populations, the F_1 hybrids will enjoy the advantage of the genes from both populations and this will display itself as an even higher manifestation of the character. On this view the inter-population F_1 's should be heterozygous for more viability genes than individuals within populations, and indeed would owe their greater viability to this higher heterozygosity. That they are in fact more highly heterozygous is attested by the great fall of viability in F_2 , where the wider segregation and the lower effect of interaction between genes from different populations in maintaining viability will be making themselves felt.

The problem therefore resolves itself into the question of why populations should differ in the genes which maintain viability at its normal level. We should expect the genes varying and segregating in any one population to be but a sample of the full range of member genes of the polygenic system affecting viability, the rest of the genes being homozygous in that population. We should expect, too, that the genes varying in one population, or to put it the other way, the genes homozygous in one population, not to be the same as those in the other, if only for reasons of sampling. But why should the homozygous genes sometimes be the recessives making for lower viability, which will frequently be covered in inter-population F_1 's, rather than always the dominant genes making for higher viability? The effects of any recessive genes tending to lower viability will of course be mitigated by their interactions, but they cannot have been wholly removed or the population flies would not be of lower viability than the inter-population hybrids. We must suppose, therefore, that even though viability within populations is not the highest that can be achieved, it is nevertheless adequate. While it would seem obviously to be true that higher viability will always have an advantage, it might well be that above a certain level the selective advantage does not rise correspondingly with the increase in viability as measured in experiment. Viability might then be stabilised at a level below the maximum by the operation of other factors within the population. Random fixation, such as must tend to occur within polygenic systems, would tend to result in at least some of the less advantageous genes becoming fixed and if the selective disadvantage were not great it could fail fully to counteract this tendency. In any case one thing is certain: the higher viability of the inter-population hybrids could not itself be stabilised within a population, for we have seen that it breaks down in F_2 as a result of segregation and recombination. High viability in one generation is not itself sufficient: it must be maintainable over

the generations. The behaviour of inter-population hybrids shows us that there can be a conflict between these requirements, for the genetic combination which gives the high expression of the character contains within its wide heterozygosity the seeds of its own breakdown. We must not be surprised, therefore, if we find the expression of a directionally selected character within a population to be not the maximum achievable but the maximum maintainable, and these are by no means necessarily the same thing.

7. SUMMARY

In the experiments described by Breese and Mather (1957) for investigating the distribution along chromosome III of polygenic activity affecting chaeta number, the wild-type flies whose chaeta were counted were obtained as parts of segregating families all of which contained $\frac{Me\ Sb}{H}$ flies. The proportion of wild-type flies relative to this constant marked class provides, therefore, a measure of the effect on viability of the various recombinant chromosomes that the wild-type flies carry.

In all but one of the experiments the females alone showed clear effects of the various recombinant chromosomes III on viability, the males showing little if any variation. For various technical reasons only the first of the experiments provides useful information about the genetical architecture of viability; and this shows dominance to be marked and unidirectional towards high viability. Non-allelic interactions of a kind relatable to the classical "duplicate gene" type are present and strong. Viability is not directly relatable to degree of heterozygosity.

The genetical architecture of viability is markedly different from that of chaeta number as revealed by the same flies in the same experiments. The simultaneous effects of the chromosomes on the two characters cannot be ascribed, except perhaps to a very small extent, to simple pleiotropy in action of the individual genes. Rather the pleiotropic effects of the chromosome segments are due to linkage within them of different polygenic systems affecting the two characters.

The differences in genetical architecture of the two characters are relatable to the different impacts of natural selection on them, selection for chaeta number being stabilising towards a central optimum and that for viability being directional towards an extreme value. The different expressions in inter-population crosses of characters showing the different architectures are reviewed and the occurrence in such F_1 hybrids of viabilities exceeding the levels found within populations is discussed. Viability within populations must be related to the maximum level maintainable which is by no means necessarily the maximum level achievable in any one generation.

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