VARIATION OF SCUTELLAR BRISTLES IN DROSOPHILA XV. SYSTEMS OF MODIFIERS[1]

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QUANTAL differences (key characters) have played a major role in systematics, and, although there has been a great deal of discussion of the role of such quantal characters in speciation, there have been very few attempts to analyze the genetic basis of phenotypic constancy. The assumption that such phenotypic constancy is diagnostic of genetic constancy has been shown to be invalid for a range of characters (see WADDINGTON 1953, 1962; BATEMAN 1959a,b; DUN and FRASER 1958; RENDEL 1959; MILKMAN 1965; FRASER 1963). It is now apparent that phenotypic constancy may mask the existence of a variable underlying genotype that can only result in expression of deviations from the constant norm if considerable selection pressure is applied.

The number of scutellar bristles in Drosophila being four in the majority of individuals, with rare individuals having more or less than this number, has been a useful character in systematic differentiation. PAYNE (1918) showed by selection for increased number of scutellar bristles that the mean number could be increased to such a degree that individuals with the norm of four were extremely rare. A considerable effort has been devoted to the analysis of the effects of selection for scutellar bristles in Drosophila. DUN and FRASER (1958), and FRASER, NAY and KINDRED (1959) have shown that introduction of an oligogene with a major effect on a constant norm (secondary vibrissae in the mouse) resulted in variation of the character such that selection was effective in producing major differences of the mutant expression. Substitution of the normal allele in such selection lines showed deviations from the norm, i.e. the variable underlying genotype had been modified by selection to such a degree that the differences were too great to be masked by the mechanism of constancy operative in wild type. RENDEL (1959) used the same approach in his work on number of scutellar bristles, showing that selection for increased number of bristles in scute leads to a small increase of the number of bristles in non-scute. FRASER (1966) repeated this experiment obtaining essentially the same results. The minimal hypothesis to explain these results is that a multigenic genotype determining the number of scutellar bristles is normally suppressed in its phenotypic expression by developmental canalization of scutellar bristle development at a norm of 4. The effect of substituting sc^1 for sc^+ is to reduce the effectiveness of the multigenic genotype such that the average number of bristles is below the norm, and the full variability

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of the multigenic genotype is then expressed. Selection on the basis of this exposed variability can then result in modification of the expression of the genotype, which normally only rarely exceeds the limits of canalization, producing rare deviants. However, selection of such rare deviants, as practiced by Payne, can alter the effectiveness of the genotype resulting in an increased number of bristles. The phrase "underlying genotype" is frequently used for the multigenic genotype. The minimal hypothesis of a single, homogenous, underlying genotype has been discussed extensively by RENDEL and his colleagues (RENDEL 1959; RENDEL and SHELDON 1960). FRASER (1963) repeated the experiments of PAYNE (1918) selecting for increased number of bristles in sc^+ stocks. He found essentially the same phenomena: marked heterogeneity of response both between different lines and between generations within lines. MATHER (1943) and SISMANIDIS (1942) interpreted these phenomena in terms of the underlying genotype consisting of linked complexes in relational balance. REEVES and ROBERTSON (1953) have suggested that such phenomena could be due to selection of modifiers resulting in the modification of isoalleles into oligogenes. FRASER (1963) showed the validity of this suggestion in a selection line for decreased number of scutellars in *D. simulans*. A gene, Bare, segregated as a dominant in this line. Backcrossing to unselected lines resulted in the progressive weakening of the penetrance and expressivity of this gene until eventually it was not phenotypically detectable. L. ERWAY (personal communication) has found essentially the same phenomena for a gene, extra verticals, in *D. melanogaster* that causes a marked increase of the number of scutellar bristles. The penetrance and expressivity of this gene are markedly decreased by backcrossing to unselected lines. FRASER *et al.* (1965) extended the original selection lines of FRASER (1963) developing a set of selection lines that have been the basis for an increasingly detailed genetic analysis aimed at identifying the cause of the heterogeneity of selection response. FRASER (1965b) showed that the selection lines could be separated into two groups on the basis of their different behavior in crosses. ERWAY (personal communication) has shown that the explanation lies in some lines being homozygous for the gene, extra-verticles (*x-vert*), which is a 3rd-chromosome recessive. This gene does not occur in other lines. FRASER, ERWAY and BRENTON (1967) describe the expression of *x-vert* and *x-vert*$^+$ lines.

A test of the minimal hypothesis of a single underlying genotype can be made by substituting sc^1 for sc^+ in lines selected for increased scutellar number. The selection response in sc^1 should be analogous to that found in sc^+. This test was made by FRASER and GREEN (1964) and MILLER and FRASER (1967). The substitution of sc^1 or sc^5 for sc^+ suppresses the x-vert gene, and its modifiers, which are termed the β modifiers. The same substitutions do not suppress the scutellar modifiers that act in the presence of *x-vert*$^+$, these being termed the α modifiers. It is evident that the hypothesis of a single, homogenous underlying genotype is not tenable. The genetic control of number of bristles is divided into one set of genes (the β set) which is not expressed when the level of bristle formation is below the norm, and another set (the α set) which is expressed when the level of bristle formation is above or below the norm. MILLER and FRASER's (1967) results

suggest that the α genotype is not expressed in *sc*$^+$; *x-vert*. The working hypothesis we have adopted is shown below.

Switch loci	α system	β system
sc$^+$; *x-vert*	suppressed	active
sc$^+$; *x-vert*$^+$	active	suppressed
sc; (*x-vert* or *x-vert*$^+$)	enhanced	suppressed

This hypothesis is examined in detail in the present paper.

MATERIALS AND METHODS

The basic material consists of two sets of selection lines of *D. melanogaster* that have been described previously (FRASER *et al.* 1965). These are termed the A and B sets of lines. Lines A1, A9 and A18 are *x-vert;* line A4 is polymorphic for *x-vert/x-vert*$^+$, and all of the other A and B lines are *x-vert*$^+$. Unless otherwise stated all of the A and B lines are *sc*$^+$. A number of lines have been derived from the *x-vert* lines (A1, A9, A18). A single line selected for increased number of bristles was formed from a mixture of the A1, A9 and A18 lines and selection was maintained for 17 generations. Two lines were then formed in which selection was maintained until the 90th generation when the lines were maintained as unselected mass cultures. These are termed the AH1 and AH2 lines. The selection history of lines A1, A9, A18 and AH1, AH2 are shown in Figure 1.

Another set of lines were derived from the AH1 line. Selection in these lines was maintained for a fixed number of bristles in each line. These are termed the AS set of lines. The AS10 line was based on the selection of females with 10 bristles, the AS9 line was based on selection of females with 9 bristles and so on. The aim was to derive a set of *x-vert* lines with a wide range of bristle numbers. The selection history of these lines is shown in Figure 2.

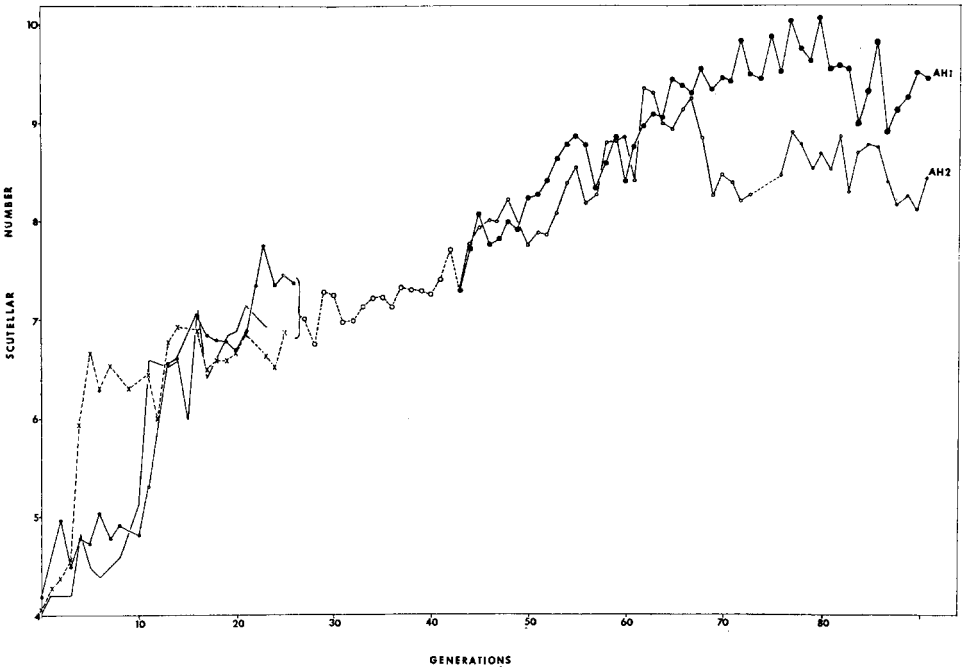

FIGURE 1.—Mean scutellar number of females from selection lines A1, 9, 18 and the derived lines AH1 and 2.

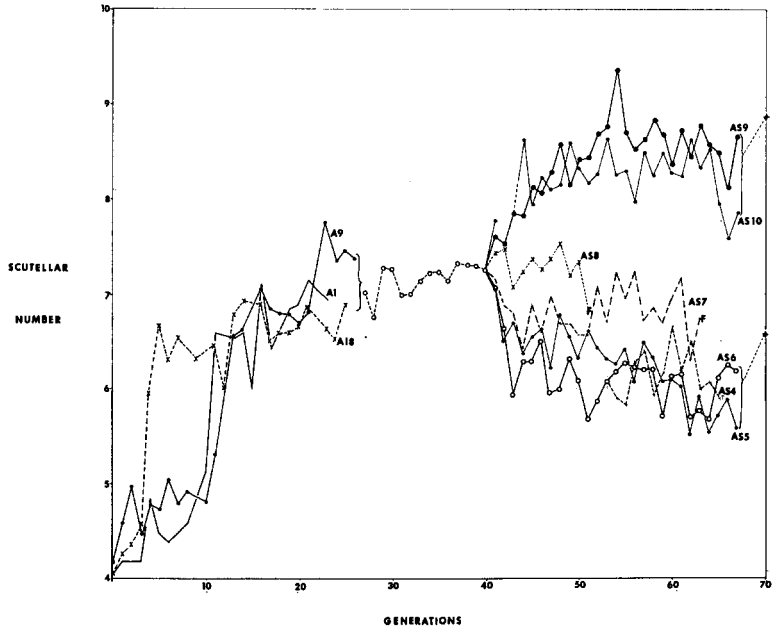

FIGURE 2.—Mean scutellar number of females from selection lines A1, 9, 18 and the derived lines AS4, 5, 6, 7, 8, 9, 10.

A feature of the AS set of lines was the occurrence of an apparent lower limit to selection at about a mean of six bristles. A further set of reverse selection lines was established to check this possibility. Selection for decreased number of scutellar bristles was practiced in stocks derived by crossing A1 × A9, A1 × A18, and A9 × A18. The results are shown in Figure 3. It is clear that there is not a limit to selection at six bristles.

A series of crosses were made between the lines to produce F_1 and F_2 progenies. The crosses were of 4 males with 4 females in ¼ pint creamers on standard cornmeal-agar medium. Fifty females were scored after 14 days.

RESULTS

A set of crosses were made between the AH1 and AH2 lines. The results are given in Table 1, showing some dominance of the lower (AH2) over the higher (AH1) level of response. Another set of crosses were made between the AS set of lines. The results are given in Table 2. There is a reasonable agreement between reciprocals. These values are plotted against the midparent values in Figure 4 showing that the genetic basis of differences between the AS set of lines is essentially additive.

The results from the crosses of the AH and AS set of lines indicate that, as a first approximation, the variation of expression of the gene extra-verticals (*x-vert*) can be taken as additive. FRASER (1965b) and MILLER and FRASER (1967) came to the same conclusion for the A1, A9 and A18 lines. The AH, AS lines and lines A1, A9 and A18 are all *x-vert/x-vert*. The modifiers of *x-vert* expression can be considered as essentially additive.

Analyses of variation between *x-vert*$^+$ lines are confounded by proximity to

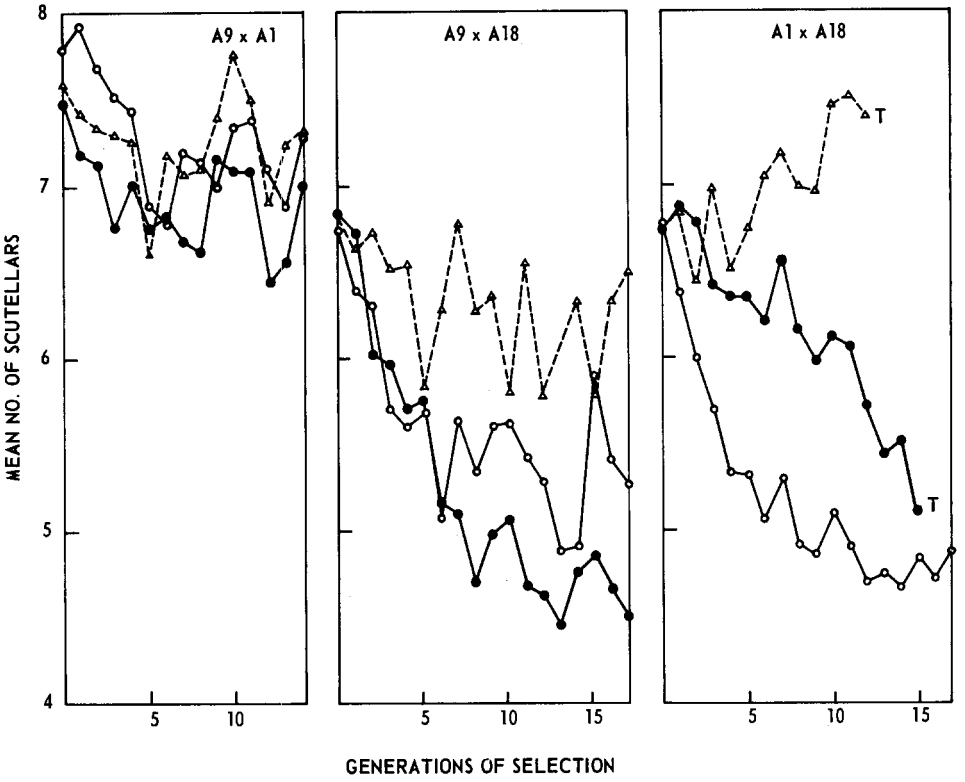

FIGURE 3.—Mean scutellar number of *down* selection lines from crosses of A9×A1, A9×A18, and A1×18. Broken lines are for unselected controls.

TABLE 1

Mean scutellar bristle numbers for the AH1 and AH2 lines and crosses between them

A. Mean bristle number

	Male parent			
	Females		Males	
Female parent	AH1	AH2	AH1	AH2
AH1	9.92	8.50	8.10	7.56
	9.00	8.56	7.88	7.92
	8.72	8.80	7.72	7.52
AH2	8.28	8.52	7.60	7.68
	8.40	8.30	7.88	7.64
	. . .	8.34	. . .	7.48

B. Averages over replicates and reciprocals

	AH1	AH1 × AH2	AH2
Females	9.21	8.48	8.39
Males	7.95	7.70	7.60
Females and males	8.58	8.09	7.99

Three cultures were scored for each cross. The averages over replicates and reciprocals are given.

TABLE 2

Results for female F_1 progeny of a diallelic set of crosses between the AS set of lines

Male parent	Sex of progeny	Female parent					
		AS4	AS5	AS6	AS7	AS9	AS10
AS4	♀	6.05	5.90	5.70	6.95	6.85	7.25
	♂	5.60	5.56	5.15	6.10	6.45	6.20
AS5	♀	5.85	6.20	5.75	6.95	6.90	7.30
	♂	5.35	5.00	5.37	6.00	6.50	6.10
AS6	♀	6.35	6.30	6.15	6.80	6.80	7.10
	♂	5.40	5.20	5.35	5.95	6.00	6.45
AS7	♀	6.60	6.00	6.35	7.21	7.85	7.80
	♂	5.95	5.35	5.15	7.00	7.00	7.15
AS9	♀	7.66	7.70	7.09	7.45	8.85	8.30
	♂	6.92	6.35	6.08	6.90	7.64	7.25
AS10	♀	7.25	7.35	7.23	7.47	8.55	7.95
	♂	6.62	6.22	6.60	7.30	8.32	6.75

the 4 zone, such that there is a marked regression of F_1 values towards the norm (FRASER 1963, 1965b). RENDEL (1959) used a probit transformation to correct for proximity to the 4 zone, concluding that variation of bristle number is essentially additive after such correction has been made. It is reasonable to conclude that RENDEL's lines were *x-vert*$^+$ since he found a correlation between *sc*$^+$ and *sc*^{1} expression. MILLER and FRASER (1967) studying the effects of substitution of *sc*^{1} and *sc*^{5} for *sc*$^+$ in the A set of lines found that F_1 values were predicted by mid-parent values in scute genotypes, i.e. the α genetic system is essentially additive at the scute levels of expression.

The evidence that the expression of both the α and the β systems is essentially additive suggested a method to examine the hypothesis that in *sc*$^+$ the α genetic system is only expressed in *x-vert*$^+$ and that the β system is only expressed in *x-vert*. Crosses of *x-vert* with *x-vert*$^+$ lines will produce *x-vert/x-vert*$^+$ F_1 pro-

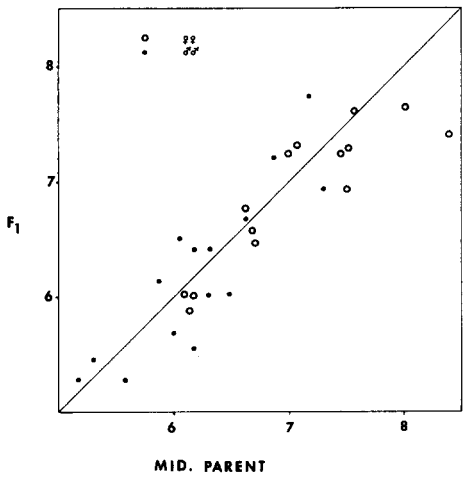

FIGURE 4.—Mean scutellar numbers of F_1 progenies plotted against mid-parent expectation for crosses of the AS set of lines.

genies, and segregation in the F_2 will produce "*x-vert*" and "non-*x-vert*" classes. The parent to F_1 and F_2 relationships should give information on the validity of the hypothesis that the expression of the α and β systems is dependent on the status of the *x-vert* locus. A series of crosses were made between the AH1, AH2, AS10, AS9, AS6, AS5 and AS4 lines (*x-vert/x-vert*) which range in mean number of scutellar bristles from 5.8 to 8.6, and the A6, A21, B7.1, B7.2, B7.3, B11.1, B11.2 and B11.3 lines ($x\text{-}vert^+/x\text{-}vert^+$) which range in mean number of scutellar bristles from 4.3 to 7.0. The F_1s were mass mated to produce F_2 cultures. The F_2 progeny were separated into "*x-vert*" and "non-*x-vert*" classes on the basis of occurrence of extra vertical bristles, since the occurrence of extra verticals is diagnostic of *x-vert/x-vert*, and 50 females of each class were scored. The occurrence of extra verticals is rare in $x\text{-}vert^+/x\text{-}vert^+$ (see FRASER, ERWAY and BRENTON 1967), and in $x\text{-}vert/x\text{-}vert^+$ (ERWAY, personal communication). The diagnosis of *x-vert/x-vert* from the occurrence of extra verticals is, however, not complete, i.e. the penetrance of *x-vert/x-vert* is not complete. The penetrance of *x-vert/x-vert* decreases markedly in F_2s of crosses with unselected base stocks, to values of the order of 40 to 60%. The F_2 data given in Table 4 should be considered in terms (a) of the "x-vert" class including about 50% of the *x-vert/x-vert* individuals, and (b) of the "non-*x-vert*" class including about 50% of the *x-vert/x-vert* individuals which were impenetrant for extra verticals. This raises the question of the scutellar expression of *x-vert/x-vert* individuals which are impenetrant for extra verticals. The scutellar expression of the non-*x-vert* class in F_2 progenies will include a component due to *x-vert/x-vert* individuals that are impenetrant for extra verticals, but may be penetrant for the effect on scutellars. The data from the crosses are given in Tables 3 and 4.

TABLE 3

Results for F_1 female progeny of crosses between the extra-verticals lines (AH and AS lines) and the x-vert$^+$ *lines (A6, 21 and the B lines)*

		x-vert$^+$ lines							
		A21	A6	B7.1	B7.2	B7.3	B11.1	B11.2	B11.3
Parental means		4.80	4.98	5.20	5.66	6.50	7.04	4.30	4.48
High *x-vert* lines									
AH1	8.60	5.63	5.32	5.69	5.54	6.08	6.08	4.91	5.27
AH2	8.58	5.68	5.42	5.60	5.61	6.20	5.80	5.41	5.24
AS9	8.60	5.18	5.83	6.10	5.76	5.93	5.76	5.11	5.21
AS10	8.56	4.88	5.59	5.54	5.78	5.96	5.75	5.01	5.17
High *x-vert* means		5.34	5.54	5.73	5.67	6.04	5.84	5.11	5.22
Low *x-vert* lines									
AS6	5.46	4.38	4.81	5.14	4.98	4.90	5.00	4.30	4.43
TS5	6.38	4.35	4.54	5.04	4.61	4.73	4.81	4.27	4.37
AS4	6.20	4.62	4.70	4.69	4.95	4.83	4.89	4.42	4.32
Low *x-vert* means		4.45	4.68	4.96	4.84	4.82	4.90	4.33	4.37
Overall means		4.95	5.17	5.40	5.31	5.51	5.43	4.77	4.85

Data are averages over reciprocal crosses. Averages are given over the high *x-vert* lines, over the low *x-vert* lines and over all *x-vert* lines.

TABLE 4

The mean scutellar bristle numbers of x-vert *and* x-vert$^+$ *F_2 progeny from the crosses of* x-vert *lines (AH and AS) with* x-vert$^+$ *lines (A6, 21, B7.1,2,3 and B11.1,2,3)*

		x-vert$^+$ line.																	
		A21		A6		B7.1		B7.2		B7.3		B11.1		B11.2		B11.3		Overall means	
x-vert line		vt	vt$^+$	vt	vt$^+$	vt	vt$^+$	vt	vt$^+$	vt	vt$^+$	vt	vt$^+$	vt	vt$^+$	vt	vt$^+$	vt	vt$^+$
High *x-vert* lines																			
AH1	I	7.74	5.34	7.28	4.96	7.65	5.20	7.89	5.60	7.84	5.58	7.46	6.44	7.67	5.00	7.41	5.60	7.55	5.66
	II	7.69	5.64	6.80	5.46	8.00	6.22	7.18	5.54	8.00	6.34	7.67	6.62	7.73	5.56	6.84	5.48		
AH2	I	7.47	5.50	6.69	5.38	7.28	5.66	7.52	5.54	7.27	5.66	7.43	6.50	6.90	5.38	7.00	5.10	7.30	5.71
	II	6.84	5.46	7.11	5.24	7.84	6.26	7.35	6.20	7.94	6.30	7.42	6.12	7.30	5.48	7.45	5.70		
AS9	I	6.45	5.18	6.33	5.16	7.78	5.66	7.45	5.72	7.19	5.40	7.54	6.12	7.46	5.16	7.37	5.04	7.23	5.55
	II	7.12	5.78	6.40	5.60	7.30	5.48	7.64	5.86	7.70	6.14	7.36	6.30	7.48	5.12	7.24	5.02		
AS10	I	6.85	4.66	7.16	5.00	7.26	5.92	7.54	5.30	7.69	5.76	7.12	5.52	6.94	5.52	7.37	5.26	7.26	5.44
	II	6.39	5.64	7.00	4.82	7.36	5.51	7.63	5.60	7.82	5.94	7.58	6.70	7.03	4.96	7.50	4.90		
High *x-vert* means		7.06	5.40	6.84	5.20	7.55	5.74	7.53	5.67	7.56	5.89	7.45	6.29	7.31	5.27	7.27	5.26		
Low *x-vert* lines																			
AS6	I	5.25	4.70	5.76	4.48	5.80	4.72	6.10	4.92	6.12	5.14	6.48	5.40	6.75	4.56	5.84	4.48	6.09	4.84
	II	5.60	4.70	5.50	4.62	6.41	5.00	6.74	5.12	6.58	5.10	6.36	5.48	6.06	4.54	6.11	4.58		
AS5	I	6.22	4.78	5.76	4.80	6.62	4.96	6.48	5.28	6.52	4.94	6.27	5.26	6.05	4.36	6.13	4.70	6.16	4.84
	II	5.94	4.88	6.19	4.80	6.11	4.78	6.42	5.04	5.91	4.76	6.30	5.26	5.70	4.50	6.00	4.52		
AS4	I	6.02	4.52	5.92	4.50	6.75	5.04	6.62	4.94	6.07	5.28	6.10	5.42	6.00	4.66	6.07	4.50	6.17	4.84
	II	5.98	4.73	5.98	4.67	6.18	4.80	6.22	5.11	6.39	4.88	6.26	5.60	5.89	4.26	6.34	4.58		
Low *x-vert* means		5.81	4.70	5.83	4.63	6.29	4.86	6.40	5.05	6.24	5.00	6.27	5.38	6.05	4.46	6.06	4.54		
Overall means		6.53	5.10	6.41	4.96	7.02	5.37	7.05	5.41	7.07	5.51	6.95	5.90	6.78	4.93	6.76	4.96		

The reciprocal crosses are given as I (*x-vert*, female parent) and II (*x-vert*$^+$, female parent).

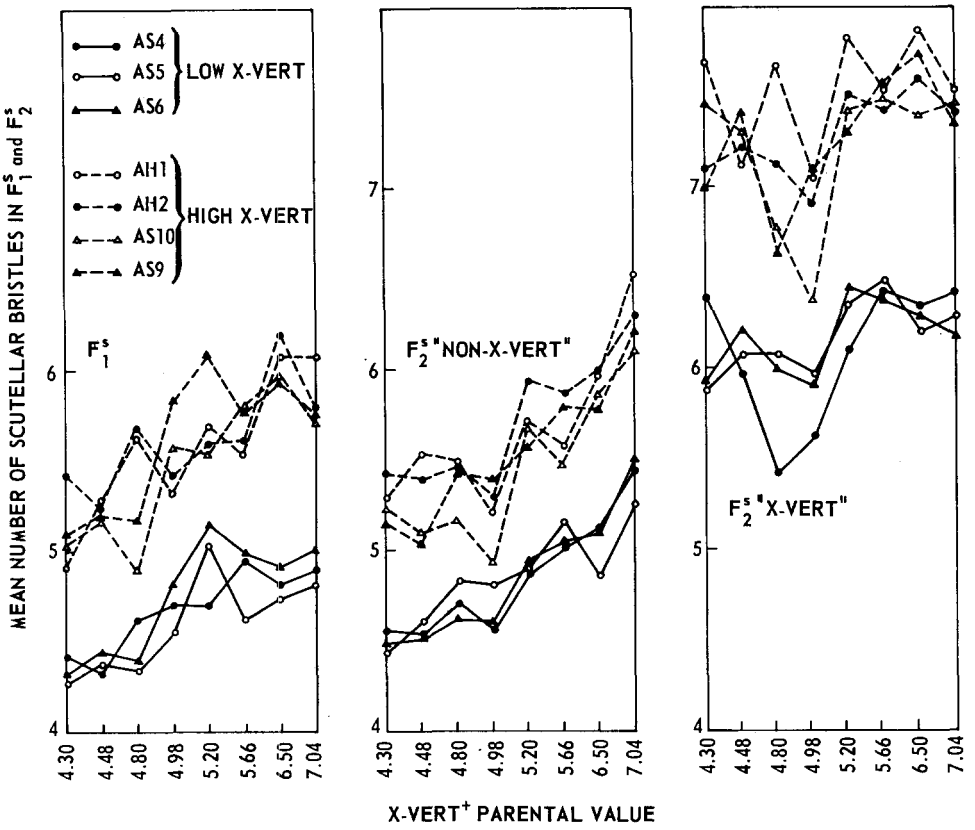

FIGURE 5.—Mean scutellar numbers of F_1 and F_2 from crosses of AS, AH *x-vert* lines with A and B *x-vert*$^+$ lines. Data are of F_1 and F_2 value plotted against *x-vert*$^+$ parental value, separately for each *x-vert* parent.

The relationship of parental to F_1 values is shown in Figure 5. The mean scutellar numbers of F_1 females are shown plotted against the values for the *x-vert*$^+$ parent. The F_1 values for crosses involving a particular *x-vert* line, e.g. AS4, are connected. These data demonstrate a consistent difference between F_1s from the high *x-vert* lines (AH1, AH2, AS10, AS9) and those from the low *x-vert* lines (AS6, AS5, AS4) which is of the order of 0.6–0.9. A similar consistent difference can be seen between F_1s from high and low *x-vert*$^+$ lines; the F_1 values show a regression on *x-vert*$^+$ parent value with a difference of 0.6 from the low *x-vert*$^+$ parent (B11.2) to the high *x-vert*$^+$ parent (B11.1). If the variation between the parent lines is essentially additive, then half of the differences are expected to be recovered in the F_1s. This expectation is not realized for either type of parent. The parental difference between high and low *x-vert* lines is approximately 2.6 bristles. The analogous difference between F_1s is 0.6–0.9 contrasting with the expected value of 1.3. The parental range for high and low *x-vert*$^+$ lines is 2.74 bristles. The analogous range in F_1s is 0.6 contrasting with the expected value of 1.4. There appear to be only slight differences in the recovery of parental differ-

ences in the F_1s between the *x-vert* and *x-vert*$^+$ parents; 0.6–0.9/1.3 and 0.6/1.4 respectively. All of the F_1 progeny are *x-vert/x-vert*$^+$ and it is apparent that genes modifying the expression of *x-vert/x-vert*, and *x-vert*$^+$*/x-vert*$^+$ are expressed in *x-vert* heterozygotes. In terms of our model, both the α and β multigenic systems are expressed in *x-vert* heterozygotes.

A feature of the expression of the β system in *x-vert/x-vert*$^+$ is that the expression of this system involves only the number of scutellars in *x-vert/x-vert*$^+$, whereas it affects the numbers of scutellars, dorso-centrals and verticals in *x-vert/x-vert* heterozygotes. In terms of our model, both the α and β multigenic systems range of effects of the genes of the β system.

The relationship of parental to F_2 values is similarly shown in Figure 5, separately for the "*x-vert*" and "non-*x-vert*" classes. Considering first the "non-*x-vert*" values, there is a close similarity to the values found for the F_1s. The recovery of parental differences in the F_2s comparing the high and low *x-vert* lines is of the order of 0.75–0.85, and that for *x-vert*$^+$ differences is of the order of 0.9–1.0. The recovery of *x-vert* differences has not increased between F_1s and "non-*x-vert*" F_2s, (0.6–0.9 in F_1s compared to 0.75–0.85 in F_2s) whereas the recovery of *x-vert*$^+$ differences has increased from 0.6 in F_1s to 0.9–1.0 in "non-*x-vert*" F_2s.

The "non-*x-vert*" class includes *x-vert*$^+$*/x-vert*$^+$, *x-vert/x-vert*$^+$ and *x-vert/x-vert* (impenetrant for extra-verticals). The increased recovery of *x-vert*$^+$ differences in the "non-*x-vert*" class of the F_2s over that found in F_1s could be due to the genes responsible for these differences; the α system, having an increased expression in *x-vert*$^+$*/x-vert*$^+$ over that in *x-vert/x-vert*$^+$, since the F_1s consist solely of *x-vert* heterozygotes, whereas the "non-*x-vert*" class of the F_2s consists of $\frac{2}{3}$ or less of *x-vert* heterozygotes, and $\frac{1}{3}$ of *x-vert*$^+$*/x-vert*$^+$. On this hypothesis the expression of *x-vert*$^+$ differences in *x-vert*$^+$*/x-vert*$^+$ would be of the order of 1.3–1.8 which is fairly close to the expectation of 1.4 on the assumption of the α system being essentially additive. The hypothesis that the expression of a difference of the α system is affected by the status of the *x-vert* locus will be further considered below.

The relationship of parental to F_2 values for the "*x-vert*" class are similarly shown in Figure 5. There is a marked difference between the results from the F_1s and the results from the "non-*x-vert*" class of the F_2s, in that the regression of F_2 "*x-vert*" value on *x-vert*$^+$ parental value is very much less, having a maximum value of 0.3. Conversely, the difference between the high and low *x-vert* lines in F_2 "*x-vert*" values is of the order of 1.2, which is a marked increase over the equivalent value in F_1s and the "non-*x-vert*" class of F_2s.

The presentation of the data has been simplified in Figure 6 by averaging the data for the high *x-vert* lines (AH1, AH2, AS10, AS9) and for the low *x-vert* lines (AS6, AS5, AS4). The data are also shown averaged over all *x-vert* parents. The agreement between the F_1 and "non-*x-vert*" F_2 values is clear, emphasizing the lack of agreement with the "*x-vert*" F_2 values, in which the regression on *x-vert*$^+$ parental value is clearly less. The individual points shown in Figure 6 involve eight cultures with 400 flies scored for the high *x-vert* crosses, and six

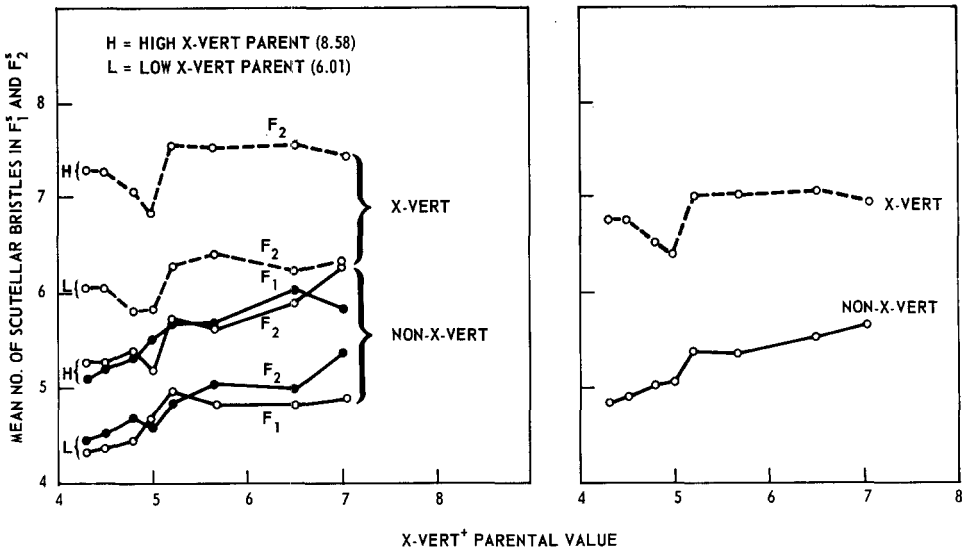

FIGURE 6.—As in Figure 5, averaged over *x-vert* high and *x-vert* low parents, and averaged over all *x-vert* parents.

cultures with 300 flies scored for the low *x-vert* crosses. Each point is, therefore, an estimate of considerable accuracy, but it should be emphasized that the regression of progeny on the *x-vert*$^+$ parental values involves only eight lines, and, therefore, it is possible that the apparent slight regression of F_2 "*x-vert*" data on *x-vert*$^+$ parental values may be a sampling artefact; the expression of the α system may be completely suppressed in *x-vert/x-vert*.

A test of the suppression of α in *x-vert/x-vert*, and of β in *sc/sc* can be envisaged since MILLER and FRASER (1967) have shown that scute suppresses *x-vert*. Stocks could be constructed that are *x-vert/x-vert* and segregating for scute/scute$^+$.

$$sc/sc^+;\ x\text{-}vert/x\text{-}vert \times sc/\mathrm{Y};\ x\text{-}vert/x\text{-}vert$$

producing

$sc/sc^+;\ x\text{-}vert/x\text{-}vert$ $\qquad$ $sc/sc;\ x\text{-}vert/x\text{-}vert$ females

and

$sc^+/\mathrm{Y};\ x\text{-}vert/x\text{-}vert$ $\qquad$ $sc/\mathrm{Y};\ x\text{-}vert/x\text{-}vert$ males

Selection on sc^+/Y; *x-vert/x-vert* should involve the β system and not the α system, and selection on the *sc*/Y; *x-vert/x-vert* should involve the α system and not the β system. Such an experiment should allow formation of lines for extra scutellar bristles involving response of one or other of the α and β systems.

A feature of the selection lines used in this study is that the *x-vert/x-vert* lines are primarily characterized by differences of the β system, whereas the *x-vert*$^+$/*x-vert*$^+$ lines are characterized by differences of the α system. An explanation can be based on the α system having a greater heritability than the β system in *x-vert*$^+$/*x-vert*$^+$, and the converse occurring in *x-vert/x-vert*. Selection would, therefore, result in differences of the α system in lines in which *x-vert* was absent,

at a low frequency or impenetrant. Conversely, in lines in which *x-vert* is frequent, selection would result in differences of the β system. The frequency of *x-vert* was not measured in the initial stocks from which our lines were derived at the time of their derivation. Tests made of these stocks several years later have not shown them to contain *x-vert*. The gene could be present at a low frequency. Either *x-vert* has always been rare in these stocks, or natural selection has acted to reduce its frequency. There is some evidence that the latter is true. A more complex version of this explanation includes the impenetrance of *x-vert/x-vert* in unselected backgrounds. The β system is expressed in *x-vert/x-vert*$^+$ to a lesser degree than in *x-vert/x-vert*, and, consequently, it is reasonable that the β system would be similarly expressed in impenetrant *x-vert/x-vert*. It is possible that *x-vert* could have occurred at a moderate to high frequency in base populations, but with a low penetrance such that it could not be easily detected. The establishment of our selection lines from single fertilized females would result in *x-vert* having a frequency of 0.25 or more in a few of these lines. The high frequency of *x-vert* in these lines would bias the selection response towards the β system, resulting in an increased penetrance and expressivity of *x-vert*, such that selection would also favor increasing the frequency of *x-vert*. This can account for the pattern of response to selection found in the *x-vert* lines; A1, A9, A18 (see FRASER *et al.* 1965). A period of slow advance was followed by a period of extremely fast advance, followed by a period of slow advance. The initial period of slow advance can be considered as involving the α and β system, and the increasing penetrance of *x-vert*. The period of fast advance can then be envisaged as increasing the frequency of *x-vert* to fixation. The second period of slow advance can be considered as involving the β system.

A further complexity has been demonstrated by ERWAY (personal communication) who found that the decreased penetrance of *x-vert* that occurs on repeated backcrossing to unselected lines, is markedly reduced by suppression of recombination of the 3rd chromosome. Clearly, the penetrance of *x-vert* is largely determined by genes located on the 3rd chromosome; *x-vert* and its penetrance modifiers form a linked complex. This explains the results of NASSAR and FRASER (1965) who found that selection involving the 3rd chromosome alone was far more effective than selection involving all three chromosomes. It appears that selection primarily involved the *x-vert* linkage complex in the lines that were variable only for the 3rd chromosome, whereas selection over all three chromosomes involved primarily the α system.

DISCUSSION

The great majority of analyses of quantitative variation are premised on the genetic basis consisting of a homogenous multigenic system, in which individual alleles cannot be identified. A remarkably detailed and sophisticated biometrical methodology has been developed (see LERNER 1950 and FALCONER 1960) aimed at increasing the efficiency of selection for increased yield in economic crops and animals. In this context the naive genetic model has proved extremely useful.

However, there is a tendency to extrapolate the validity of what was a necessarily minimum genetic model into a demonstrated theory. This can be seen in the assumption of this model in treatments of quantitative variation given in genetics textbooks. A number of scientists have questioned this tendency, raising, for example, the issues of the effects of linkage (see MATHER 1943) and genetic interaction (see LERNER 1954). GOODALE (1918) suggested that the differentiation of a character into a number of components would allow an increased precision. Essentially, he proposed that the value of a particular quantitative character was determined by the interaction of a number of genetic systems, each acting on some particular aspect of development. FRASER (1953) applied this concept to the variation of type of fleece in sheep. WADDINGTON (1955) working with characters of the crossvein in Drosophila suggested that the amount and type of crossvein was determined by the interaction of a number of genetic systems.

The interest of developmental geneticists such as WADDINGTON in the analysis of quantitative variation lead naturally to a concept of each character being determined by a number of different systems of genes, since the methods and results of developmental genetics involve the separation and identification of different tissue systems. WADDINGTON (1962) working with the homeotic mutant aristapaedia showed that the switching of the development of the arista into a leg-like structure resulted in the suppression of arista-modifying genes, and the expression on the leg-like arista of leg-modifying genes. If development is switched into the arista path one set of genes is expressed, whereas if development is switched into the leg path another set of genes is expressed. JACOBSEN (1966) working with the character, number of extra facial vibrissae in the mouse, has provided a further illustration, basing her work on the results of DUN and FRASER (1958) and FRASER, NAY and KINDRED (1959) who developed selection lines in the mouse for extra facial vibrissae. Reverse selection of these lines was effective indicating that the genes for increased number of vibrissae had not been fixed in the selection line. JACOBSEN showed that the increased number of vibrissae in the high line was due to the development of extra hair follicles, but that the reduction of the number of vibrissae in the reverse selection line had been accomplished not by reduction of the number of follicles, but instead by the suppression of their formation of hairs. Clearly, two genetic systems are involved: one determining the number of follicles, the other determining the formation of hairs by existent follicles. It is clearly possible to discriminate between different genetic systems under circumstances where different aspects of development interact to determine the character. Other methods need to be devised in organisms, such as Drosophila, where developmental analyses are not available. The present paper details the use of major mutants.

MILLER and FRASER (1967) have shown that substitution of scute for scute$^+$ suppresses the expression of *x-vert/x-vert* and the β system. The results detailed above show that substitution of *x-vert* for *x-vert*$^+$ has complementary effects, suppressing the expression of the α system. Although the *x-vert* and scute genes are recessive in their diagnostic effects of addition and deletion of bristles, there is a strong suggestion that their interaction with the α and β systems is partially

expressed in heterozygotes. MILLER and FRASER (1967) have shown that the expression of *x-vert/x-vert* is markedly reduced in scute heterozygotes, with a slight reduction of the expression of the β system. The data in this paper suggest that the expression of the α system is progressively reduced from *x-vert*$^+$/*x-vert*$^+$, though *x-vert/x-vert*$^+$ to *x-vert/x-vert*, whereas the expression of the β system is increased from *x-vert/x-vert*$^+$ to *x-vert/x-vert*.

A discrimination of two multigenic systems involved in the determination of the number of scutellar bristles has been achieved by use of the scute and *x-vert* loci. Our model of the genetic basis of the whole genetic mechanism can be revised and extended as shown below. The term, *suppressed*, is used for the complete or near complete suppression of expression; the term, *repressed*, is used for a marked reduction of expression; *expressed* is used for the degree of expression found in *wild-type*.

Switch loci	α system	β system
sc$^+$/*sc*$^+$; *x-vert/x-vert*	Suppressed	Enhanced, with manifold effects
sc$^+$/*sc*$^+$; *x-vert/x-vert*$^+$	Repressed	Reduced, with little, if any, manifold effects
sc$^+$/*sc*$^+$; *x-vert*$^+$/*x-vert*$^+$	Expressed	(Not known)
sc/sc$^+$; *x-vert/x-vert*	(Not known)	Repressed
sc^5/*sc*^{5}; *x-vert/x-vert* *x-vert*$^+$/*x-vert*$^+$	Expressed	Suppressed
sc^1/*sc*^{1}; *x-vert/x-vert* *x-vert*$^+$/*x-vert*$^+$	Enhanced	Suppressed
sc^1/Y; *x-vert/x-vert* *x-vert*$^+$/*x-vert*$^+$	Enhanced	Suppressed

It is clear from our results that the constancy of number of scutellars at four did not evolve as a fortuitous fixation, but rather involved the development of a complex system of interactions resulting in the stabilization of development at the value of four scutellars. FRASER (1960) using computer simulation of genetic systems to examine the effects of selection for a fixed norm has concluded that such selection is ineffective in the absence of a strong force of random genetic dispersion, i.e. normalizing selection will be ineffective in large populations for multigenic systems of many loci. Analyses of other models in which potential for evolution of systems of canalization was included showed that normalizing selection was more effective in producing phenotypic constancy by the evolution of systems of canalization, than by fixation of a multigenic system (FRASER 1960). Theoretical analyses, and experimental analyses have both lead to the same conclusion, that the evolution of a constant norm involves major genetic changes of considerable complexity. This conclusion gives strong support to the use of quantal key characters in systematics. The characteristics that comprise the constant norm of a species, differentiating it from other species, are unlikely to be the

result of random fixation and more probably are the result of complex systems of genetic interaction determining developmental canalizations.

SUMMARY

The effects of substitution at the locus extra-verticals (*x-vert*) on the expression of genetic differences for extra scutellar bristles have shown that a distinction can be made between two genetic systems: the α system which is suppressed in *x-vert*, non-scute genotypes, enhanced in scute genotypes, and the β system which is enhanced in *x-vert*, non-scute genotypes, suppressed in scute genotypes.

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