# SELECTION FOR AN INVARIANT CHARACTER, VIBRISSA NUMBER, IN THE HOUSE MOUSE

## III. CORRELATED RESPONSES

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*Summary*

Selection for increased and decreased total number of secondary vibrissae has been practised on the mutant mice of a stock in which the tabby gene is segregating. Five separate groups of vibrissae contribute to the total number and differences were found in the response of individual groups of vibrissae to selection. These differences occur both in the main selection experiment and in subsidiary experiments based on rare non-tabby mice with abnormal scores which occur with very low frequency in ordinary mouse stocks.

Other aspects of hair growth, the primary (mystacial) vibrissae and main coat, have also been observed and correlations between these and the secondary vibrissae are described. A model to represent the relationship between all these elements as a canalization surface is proposed.

## I. Introduction

The number of secondary vibrissae in + strains of laboratory mice is almost invariant. Mice with more or less than the standard number of these vibrissae are rare (Dun 1958). The near constancy of vibrissa number in + mice contrasts with the marked variability of the number of secondary vibrissae in mice carrying the tabby gene (Dun 1959*a*). Tabby is a sex-linked partial dominant which mimics the effects of the crinkled gene (see Falconer, Fraser, and King 1951; Falconer 1953). The tabby gene causes a decrease in the number of secondary vibrissae, and a marked increase in the variability of vibrissa number. This increased variability could be due (1) to the tabby gene causing an increased sensitivity to environmental fluctuations, or (2) to the expression of segregating genes in the presence of the tabby gene, whose actions are not normally manifested in + mice. A selection experiment to distinguish between these alternative explanations was initiated in this Laboratory (see Dun and Fraser 1958, 1959; Fraser and Kindred 1960). In this experiment the *Ta* and + genes were maintained in segregation, and selection for either increased or decreased number of secondary vibrissae was practised on the tabby segregants; no selection was practised on the + segregants. The mean number of secondary vibrissae is shown plotted against generation of selection for the three genotypes (+, *Ta*+, and *Ta*·) in Figure 1.

The results shown in this figure demonstrate (1) that the variability of vibrissa number in tabby mice is largely genetic, and (2) that selection of this genetic variability results, if it is continued long enough, in variation of the normally constant vibrissa number of the + segregants. These results have been interpreted

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on the basis of a canalization of genetic variation which occurs at the normal number of secondary vibrissae. The term canalization is used in the sense that the effect of a genetic substitution at a locus affecting vibrissa number is correlated with the mean genetic value of all the loci affecting vibrissa number; a genetic substitution producing a detectable effect at abnormally high or low vibrissa numbers, produces only a small, or negligible effect when the vibrissa number is normal. On this hypothesis, some aspect of the genotype causes a reduction of the manifestation of substitutions at loci controlling the vibrissa number, when the vibrissa number is normal. This hypothesis can be tested by selecting a line of $Ta+$ mice such that

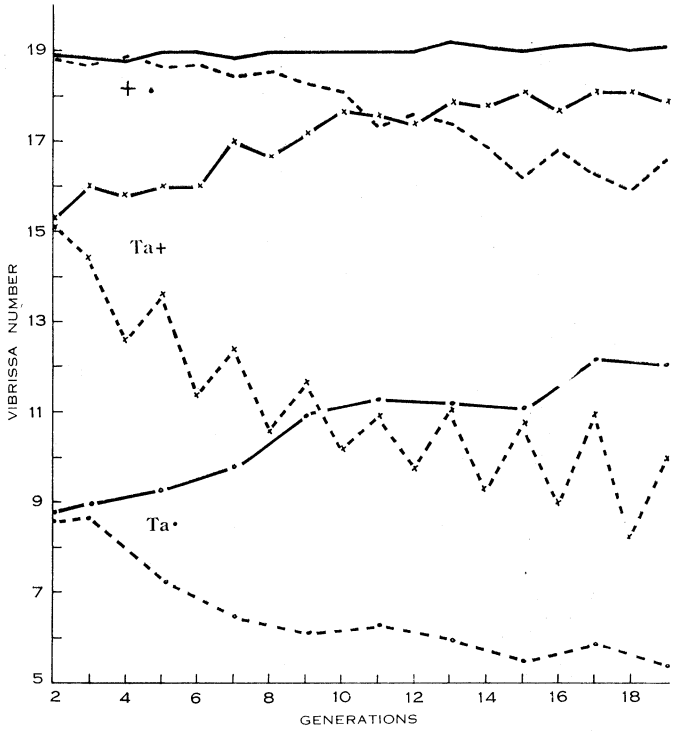


Fig. 1.—Mean vibrissa number at three levels of expression plotted against generation for the tabby selection experiment.

the number of secondary vibrissae approaches the normal value. In such a line, as the mean approaches the normal number, the variability should decrease. Conversely, in the low selection line, as the mean number of secondary vibrissae in + segregants deviates from the normal value, then the variability of vibrissa number should increase. Fraser and Kindred (1960) found the expected decrease of variation in $Ta+$ mice of the high selection line as the mean vibrissa number approached the normal number, and the expected increase of variation in + mice of the low selection line as the mean vibrissa number became less than the normal number. This is illustrated in Figure 2.

The data and analyses presented in the previous papers of this series seem sufficient to justify the conclusion that vibrissa number is a canalized character, with a very marked canalization located at the normal number of 19 vibrissae. A secondary, and less marked canalization occurs at 4–5 vibrissae. Vibrissa number has been considered as a single character, with the separate vibrissae ranking

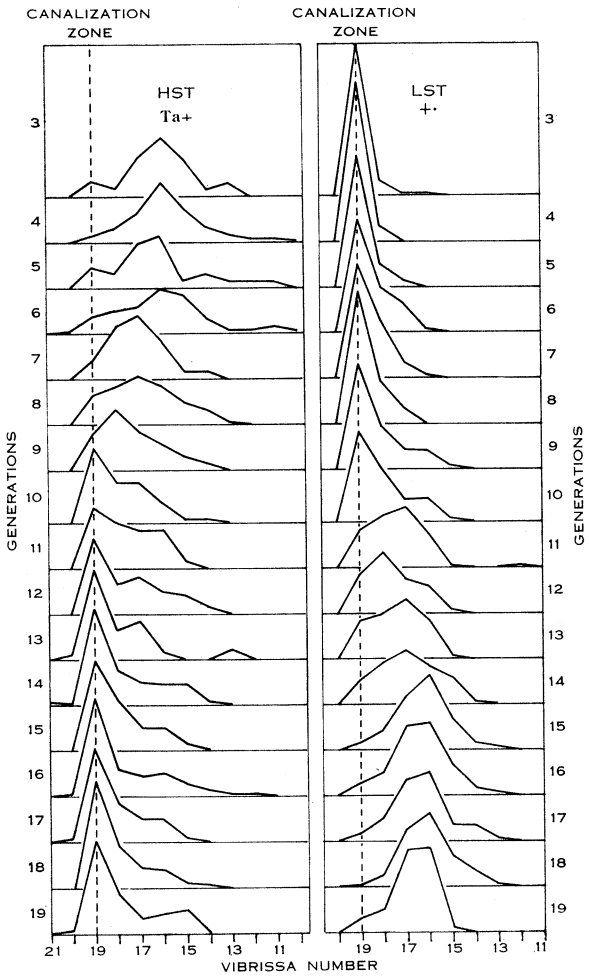


Fig. 2.—Effects of canalization on the variability of selection lines.

equally. This assumption was always regarded with suspicion, since the secondary vibrissae are clearly separated into several groups, distinguishable on their location. This is illustrated in Figure 3.

Fraser, Nay, and Kindred (1959) have examined the variation of secondary vibrissae in various crosses between random-bred *Ta* and *cr* stocks, with the aim of determining whether any interaction occurred between these two mutant genes in their effects on vibrissae. No such interaction could be detected, but the comparisons between the various crosses lead to the conclusion that the genetic

control of the number of secondary vibrissae is separated into a number of distinct genetic systems which are to varying extents autonomous for specific groups of vibrissae. Consequently, it was pertinent to re-examine and extend the genetic analysis of secondary vibrissa number. In the first part of this paper, this has been done (*a*) for the main selection experiment in which secondary vibrissa number has been considered as a single character; (*b*) for comparisons between inbred lines into which the tabby gene has been backcrossed; and (*c*) for selection experiments in which selection was practised only on a specific group of secondary vibrissae.

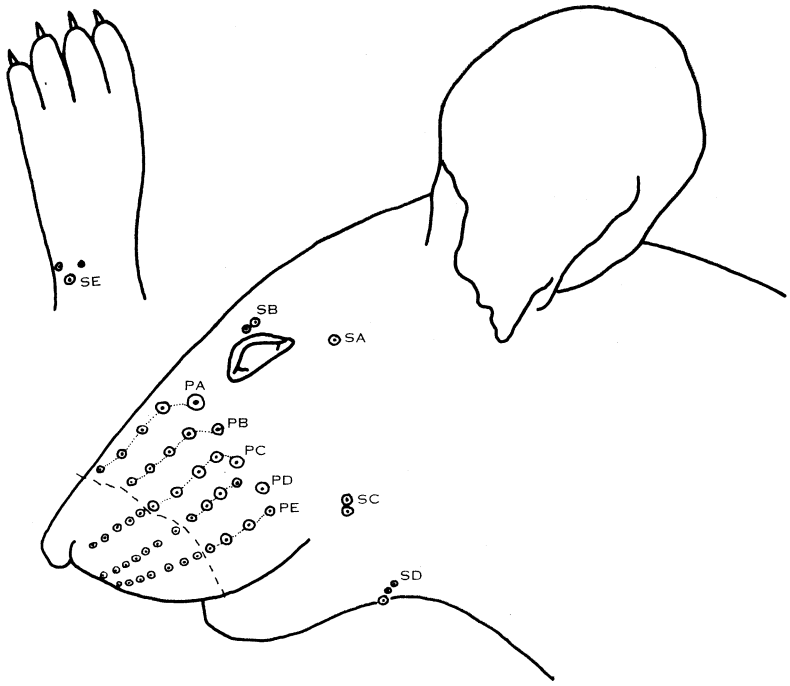


Fig. 3.—Head and distal part of right fore limb of the mouse showing distribution of vibrissae.

In the second part of the paper, the analysis is extended to include the hairs of the main coat, and the primary vibrissae. These are morphologically related to the secondary vibrissae, and the manifold effects of the tabby, crinkled, and ragged genes on all three types of hairs indicate that the three types of hairs are not independent developmental entities. The tabby and crinkled genes have only slight effects on the primary vibrissae, whereas the ragged gene has a marked effect. Therefore, the ragged gene has been backcrossed into the main selection lines to expose variation of the primary vibrissae, in the same way that the tabby gene was used to expose variation of the secondary vibrissae.

## II. Methods and Materials

The locations of the vibrissae are illustrated in Figure 3. The scoring of secondary vibrissae has been described in previous papers of this series. The primary vibrissae are arranged in five rows in which the posterior vibrissae are large, whereas

the anterior vibrissae are small. Only the posterior vibrissae have been scored: five in rows A–D, four in row E. There is a marked difference in size between these and the small anterior vibrissae which were not scored.

The main selection experiment of our programme has been described fully in previous papers (see Dun and Fraser 1959; Fraser and Kindred 1960). The high and low lines of this experiment are termed the HST and LST lines respectively. Three genotypes, +, *Ta*+, and *Ta*·, occur in each line, since segregation is maintained at the +/*Ta* locus.

Two sub-lines have been formed from the HST/LST lines by crossing + mice from these lines with *Ra*+ mice. This has been continued for several generations, resulting in the *Ra* gene being backcrossed onto HST and LST. These sub-lines are termed the HST–*Ra* and LST–*Ra* lines. The same procedure, involving the *cr* gene, has produced the crinkled backcross lines, which are termed HST–*cr* and LST–*cr* respectively.

Two further selection experiments have been maintained in which selection was based on a specific group of secondary vibrissae. Earlier studies on these lines have been described by Dun (1959*b*), and Fraser, Nay, and Kindred (1959). In the HB/LB lines selection has been maintained on the number of B vibrissae. In the HD/LD lines selection has been maintained on the number of D vibrissae. These lines, both HB/LB and HD/LD, were started with a collection of rare + mice which had less or more than the normal number of B or D vibrissae. After 5–6 generations, the tabby gene was crossed into these lines, but selection was maintained solely on the number of B or D vibrissae, in the + segregants.

In addition to the selection experiments, and their sub-lines, the tabby gene has been backcrossed into a number of inbred lines: CBA, DBA, 101, C57, and A. Six generations of backcrossing have been completed.

## III. Results and Discussion

### (*a*) *Main Selection Experiment*

The results of the main selection experiment (HST/LST) have been shown in Figure 1, for the total number of secondary vibrissae. The data on total number of secondary vibrissae are shown separately for the five groups in Figure 4.

Consider first the responses to selection found in the *Ta*+ segregants. There is a clear separation into two patterns of response. The A, B, and E groups show very little response to selection for an increased number, which contrasts with the quite marked response to selection for a decreased number. The C and D groups have an opposite pattern of response, showing very little response to selection for a decreased number which contrasts with the quite marked response to selection for an increased number. This difference of symmetry of response between the A, B, and E groups compared with the C and D groups could be due to their being controlled by two or more independent systems. Alternatively, these results can be explained by the numbers of vibrissae in the different groups all being determined by a single genetic system, *if* the five groups of secondary vibrissae differ in their sensitivity to the effect of the *Ta* substitution, and *if* there is an upper limit to vari-

ation at the normal number, and a lower limit to variation which affects only the B, D, and E groups. The existence of upper and lower limits to variation has been demonstrated in previous analyses (see Fraser and Kindred 1960). The different groups certainly differ in their sensitivity to the *Ta* substitution. The substitution

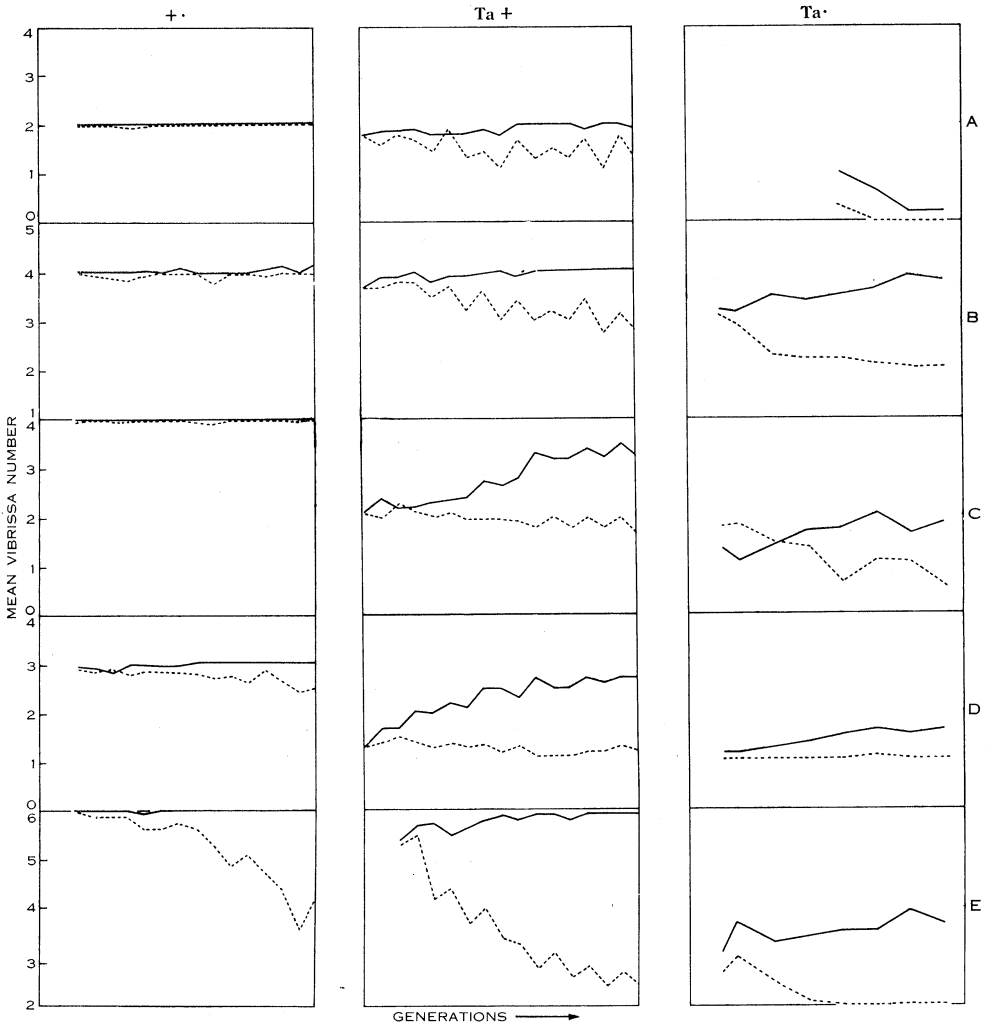


Fig. 4.—Mean vibrissa number at separate secondary sites plotted against generation for the tabby selection experiment.

of a *Ta* for a + gene to produce *Ta*+ causes a reduction of the number of secondary vibrissae from 19 to approximately 15. The greater part of this reduction occurs in the C and D groups. The number of C and D vibrissae is approximately halved in *Ta*+ compared to +. It is, therefore, quite plausible to postulate that the differences in response found between the A, B, and E versus the C and D groups

is not due to their being determined by different genetic systems, but rather to their having a different sensitivity to the effect of the *Ta* gene: the C and D groups being markedly sensitive, whereas A, B, and E groups are relatively insensitive. In *Ta*+ the reduction in number of the A, B, and E vibrissae is only sufficient to move the mean expression out of the upper canalization zone. This allows the expression of genetic variability on which selection for a decreased number can be effective, but selection for an increased number is ineffective due to proximity to the canalization zone. Conversely, the reduction in number of C and D vibrissae in *Ta*+ is marked, moving the mean expression well below the upper canalization zone, and bringing it close to the lower canalization zone. This reduces the effectiveness of selection for a decreased number. The hypothesis is illustrated in Figure 5.

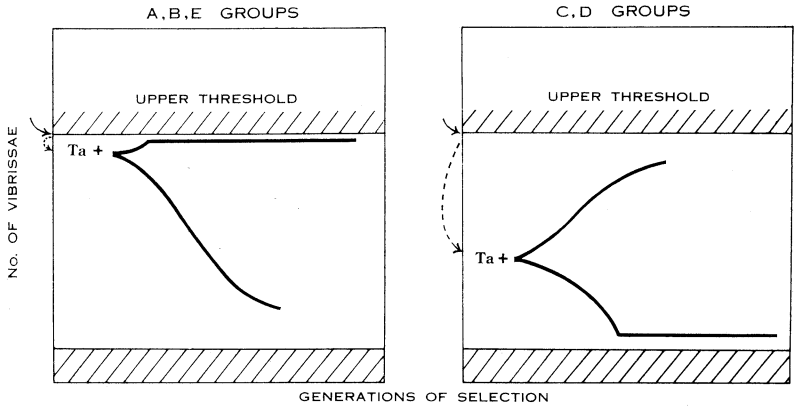


Fig. 5.—Limitation of vibrissa advance for individual secondary vibrissa groups by thresholds.

The results for the + and *Ta*· genotypes agree in general with this model of selection being limited by proximity to the upper or lower thresholds. In the E group of secondary vibrissae the initial success of selection for a decreased number decreases as the mean approaches the lower limit of 2; this lower limit is also apparent in the *Ta*+ genotype.

It is, therefore, reasonable to postulate that the different responses between the various groups of secondary vibrissae are due to the existence of canalization zones and to the different sensitivities of the various groups to the substitution of the *Ta* for the + gene. These data from the main selection experiment cannot therefore be taken as confirming or rebutting the existence of separate genetic systems controlling the numbers of vibrissae in the different groups.

### (*b*) Ta/*Inbred Backcross*

Another approach to this problem has been made using inbred lines of mice. This has been done for the + genotype by Dun (1958) who found that the occurrence of deviations from the normal number was of the order of 0·2% in the A, B, C, and E groups. Variation of the number of D vibrissae was much more frequent: approximately 15%. Considering only the A, B, D, and E groups there were no correlations

between groups in the occurrence of deviant numbers of secondary vibrissae. Dun (1958) states "that the incidence of variation increased through CBA, C3H, C57, and DBA to a peak in the A strain". The A strain also showed the greatest number of

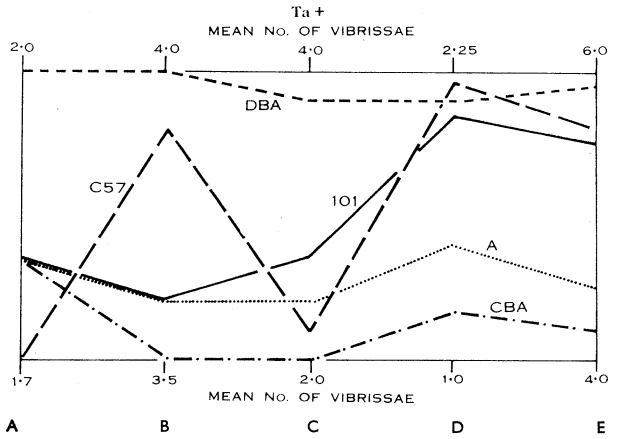


Fig. 6.—Mean numbers of different groups of secondary vibrissae in the five lines of Ta/inbreds for *Ta*+ mice .

animals with deviant numbers of B, C, and E vibrissae. It appears that any correlation between the different secondary groups is small.

An extension of Dun's survey has been made by backcrossing *Ta* into the same set of inbred lines, allowing their comparison at non-canalized levels of expression.

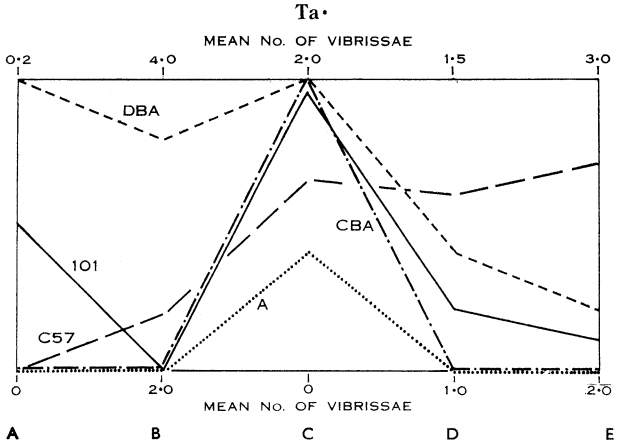


Fig. 7.—Mean numbers of different groups of secondary vibrissae in the five lines of Ta/inbreds for *Ta*· mice.

The mean numbers of vibrissae in the various secondary groups of the different inbred lines for the *Ta*+ and *Ta*· genotypes are shown in Figures 6 and 7.

In *Ta*+ mice of the inbred lines, the DBA, A, and CBA lines show a definite correlation between the five groups: DBA has consistently high numbers of vibrissae,

whereas A and CBA have consistently low numbers. The C57 and 101 lines do not show this correlation. Considering only the *Ta*+ genotype, these data show that there is a correlation between the various secondary groups, which is fairly easily disrupted. The data from *Ta*· indicate that any such correlation must be very slight, or, more probably, that proximity of the mean number to the lower canalization zone confounds the correlation.

### (*c*) *Individual Group Selection*

A third approach to the problem of genetic correlations between the different groups of secondary vibrissae has been made by maintaining selection on the number of vibrissae in a specific group. Two such selection experiments have been continued

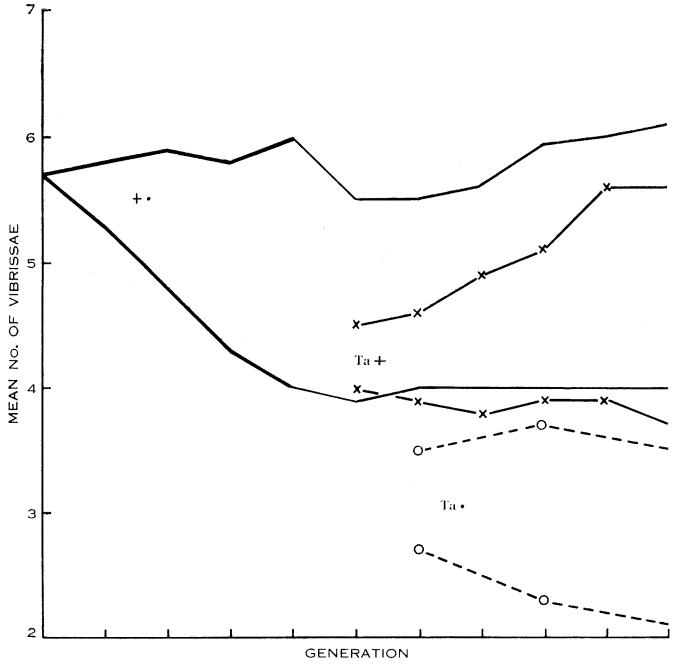


Fig. 8.—Mean vibrissa number plotted against generation for the B selection experiment.

from the stocks constructed by Dun (1959*b*). In one, selection is maintained on the number of B vibrissae; in the other, selection is maintained on the number of D vibrissae. These experiments were primarily intended as investigations of rare + mice which differed from normal in their number of B or D vibrissae (see Dun 1958). After it had been established that these rare deviants were genetically determined, selection was initiated to allow investigation of correlated responses in the other groups of secondary vibrissae, to this selection on a single group (see Dun and Fraser 1959; Fraser, Nay, and Kindred 1959). The stocks, initially, were solely of the + genotype. After several generations of selection, *Ta* was introduced into all four selection lines, and segregation was then maintained for the +/*Ta* genes. Selection was still

restricted to + mice; the *Ta* gene was introduced so that the effects of selection on + mice could be compared with those mainfested in *Ta*+ and *Ta*· mice.

The mean number of vibrissae in the HB/LB lines are shown plotted against generation of selection for the +, *Ta*+, and *Ta*· genotypes in Figure 8.

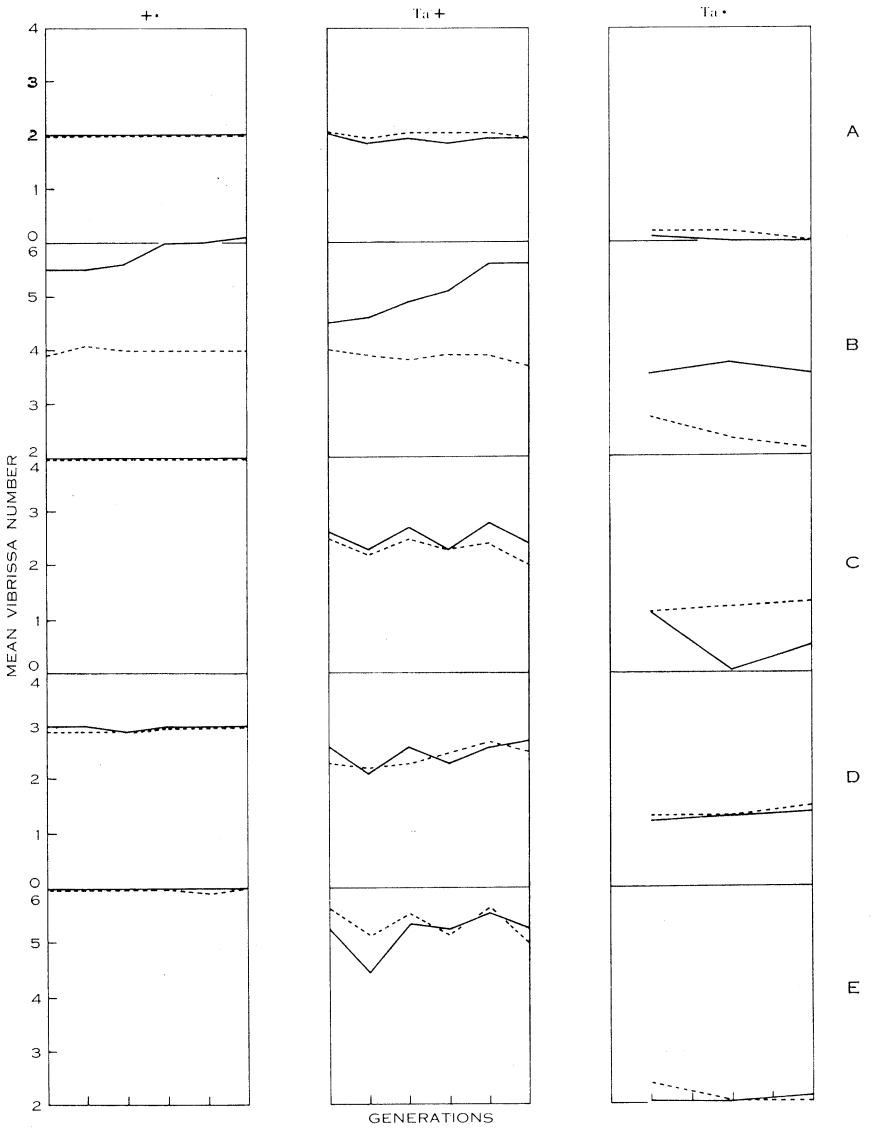


Fig. 9.—Mean vibrissa number at separate sites for the B selection experiment.

During the first phase of the experiment, before *Ta* was introduced, selection for a decreased number was markedly more successful than that for an increased number. This must be considered in reference to the number of B vibrissae at the beginning of selection. The initial population consisted of a group of + mice with

more than the normal number of B vibrissae. These had been found during a survey of vibrissa numbers involving several thousand + mice. The selection on these mice with a greater than normal number of B vibrissae produced a marked response to selection for a decreased number, until the line had been selected back to the normal number of 4, at which no further advance is expected, since the canalization of vibrissa number occurs for the B vibrissae at this number. During the second phase of this experiment, after the *Ta* gene had been introduced, selection was continued on the + segregants, but there has been no response in the low line. Selection for an increased number has averaged a response of approximately 0·1 vibrissa per generation throughout the experiment, with no indication of an upper threshold. The difference between HB and LB is approximately 2 vibrissae, which is greater than the difference in the number of B vibrissae between the high and low lines

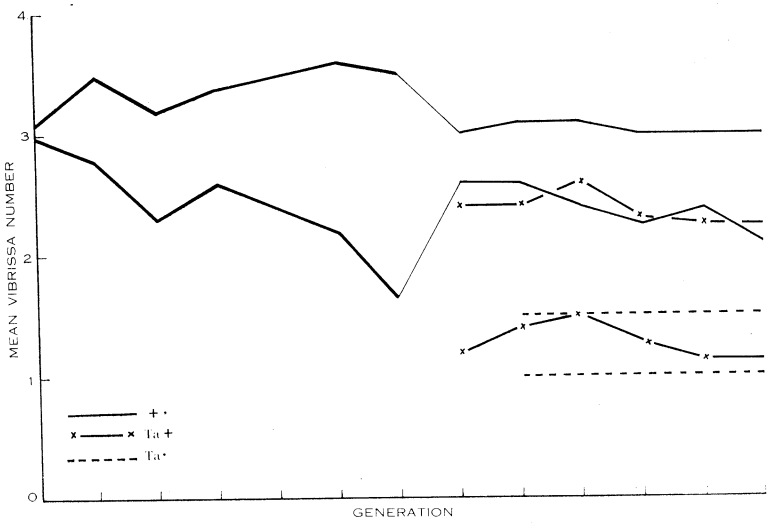


Fig. 10.—Mean vibrissa number plotted against generation for the D selection experiment.

of the main selection experiment; between HST and LST. Consequently, if the different groups of secondary vibrissae have a common genetic basis, then the selection on the number of B vibrissae in the HB/LB lines, should have produced marked correlated responses in the numbers of A, C, D, and E vibrissae. No such responses were found; a few + mice occurred with more or less than the normal numbers of vibrissae in the other groups, but these were rare, and in the same order of frequency as the occurrence of such deviants in unselected stocks. Fraser, Nay, and Kindred (1959) suggested that such correlated responses would be more easily detected in *Ta*+ and *Ta*·, since substitution of the *Ta* gene would, by reducing the mean number of vibrissae, reduce or remove the masking effect of canalization. The mean numbers of vibrissae in the various groups are shown plotted against generation of selection in Figure 9. Only the second phase is shown since no *Ta*+ or *Ta*· mice occurred in the first phase.

The differences between HB/LB of the number of A, C, D, and E vibrissae in *Ta*+ and *Ta*· are small, and it is probable that these are due more to random drift than to a correlated response to the selection on the number of B vibrissae.

The HD/LD experiment is analogous to the HB/LB experiment, except that it is based on selection of the number of D vibrissae. The initial population consisted of + mice with more or less than the "normal" number of D vibrissae. These were found by Dun (1958) during his survey of the variation of vibrissae in + mice. The frequency of + mice with less than the normal number of D vibrissae is much greater than that of mice with less than the normal number of B vibrissae. The mean number of D vibrissae in the HD/LD experiment is shown plotted against generation of selection in Figure 10. The *Ta* gene was crossed into the stock at the 7th–8th generation, but selection was still restricted to + mice.

The primary phase of the HD/LD experiment, before *Ta* was introduced, showed a slow response to selection for an increased number: approximately 1 vibrissa in 8 generations. Response to selection for a decreased number was more marked: approximately 2·5 vibrissae. Differences from the normal number in the A, B, C, and E vibrissae were very rare, being no more frequent than the occurrence of mice with abnormal vibrissa numbers in unrelated + stocks.

When the HD/LD stocks were crossed to a *Ta* stock to introduce the *Ta* gene, there was a very marked regression towards the normal number of D vibrissae, which was more marked in the HD than in the LD lines. Although selection has been maintained on the + segregants after this cross, there has been no response in the HD line, and only a very slight response in the LD line. There is a greater difference of the number of D vibrissae between HD and LD in the *Ta*+ genotype than in either the + or *Ta*· genotypes. This can be explained by the existence of a zone of canalization at 3 vibrissae, and a secondary zone at 1 vibrissa. The effect of a single substitution of *Ta* for + moves the mean away from the upper zone of canalization; the complete substitution in *Ta*· moves the mean into the lower zone of canalization.

The numbers of A, B, C, D, and E vibrissae are shown in Figure 11 plotted against generation of selection for the second phase of the experiment. In this phase differences occurred in all of the other vibrissae. In the + genotype, a small but consistent difference occurred in the number of E vibrissae. In the *Ta*+ genotype differences occurred in all the other groups; the difference in the mean number of E vibrissae was approximately equal to the difference in the number of D vibrissae which had been produced by selection.

In one aspect these data are confusing. Selection during the first phase; prior to the introduction of the *Ta* gene, had produced a difference of approximately 3·5 D vibrissae, but no differences occurred in the number of A, B, C, or E vibrissae. In the second phase, after the introduction of the *Ta* gene, the difference of the number of D vibrissae between HD and LD has been reduced to approximately 1 vibrissa, yet a correlated difference has been found in the number of E vibrissae. It would appear that the cross to introduce the *Ta* gene has changed the genetic composition of the populations.

### (d) *Primaries and Main Coat*

In general, the various data on the numbers of secondary vibrissae indicate that correlations between the various groups are small or non-existent. However,

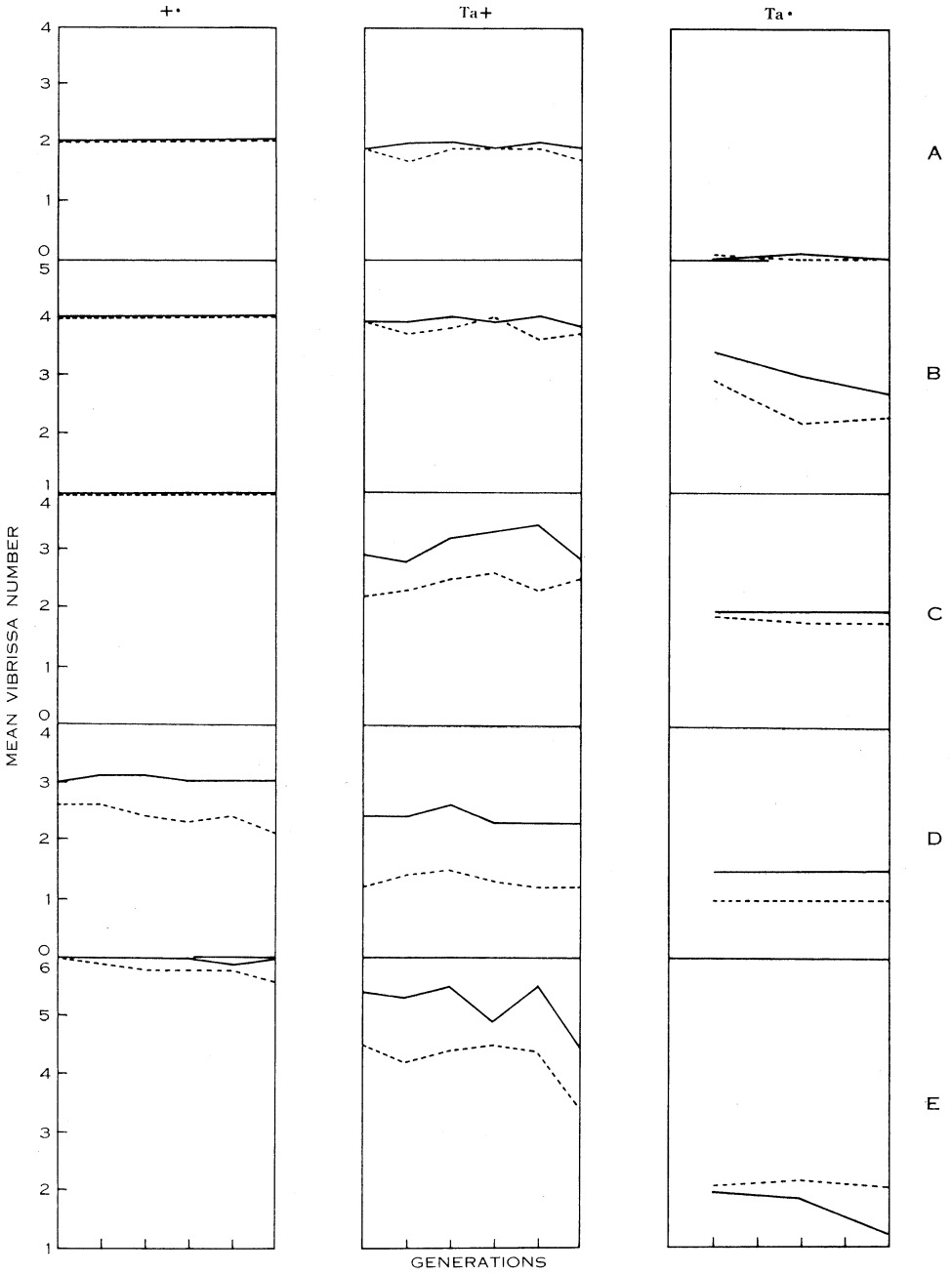


Fig. 11.—Mean vibrissa number at separate sites for the D selection experiment.

the effect of substitution of the *Ta*, *Ra*, and *cr* genes on all five groups of secondary vibrissae demonstrates that the different vibrissae are related. These mutants also affect the primary vibrissae and the hairs of the main coat, and, consequently, it is pertinent to examine the effects on the primary vibrissae and the main coat, of selection on the number of secondary vibrissae.

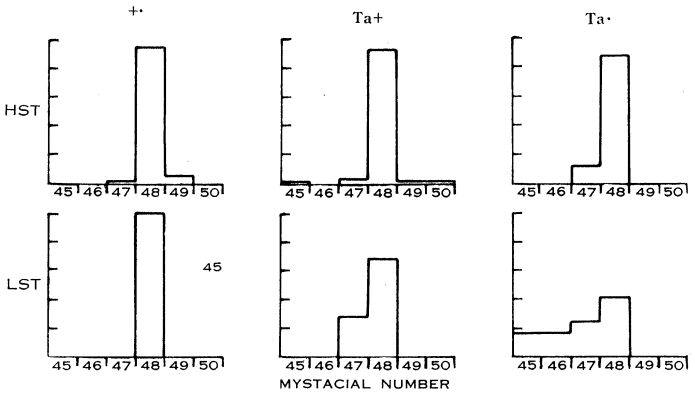


Fig. 12.—Frequency histogram of mystacial number of HST and LST, generation 16.

The HST/LST selection lines, in which selection was on the number of secondary vibrissae in *Ta*+ and *Ta*·, were scored for the number of primary vibrissae. The results are shown in Figure 12 as frequency histograms at the 16th generation of selection in the three genotypes. There has been a definite response in the primary vibrissae to the selection practised solely on the secondary vibrissae. This indicates

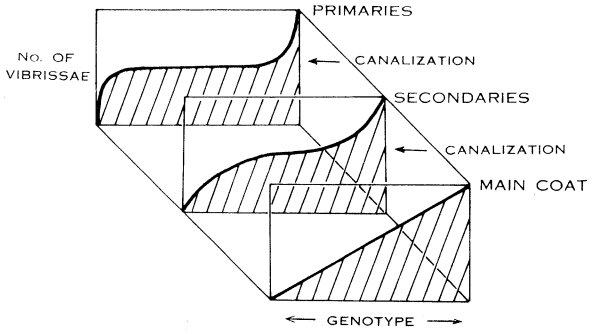


Fig. 13.—Canalization diagram for primary and secondary vibrissae.

that there is a common genetic determination of primary and secondary vibrissae. The much lower response to selection which occurs in the primaries can be explained by their being more strongly canalized. This is illustrated in Figure 13, which shows a hypothetical relationship of genotype to phenotype (number of primary vibrissae).

The *Ta* gene does not have any effect on the number of primary vibrissae in unselected stocks; the effects on primaries are only manifested in the HST and

LST selection lines. Another mutant, *Ra*, causes a very marked reduction of both primary and secondary vibrissae in homozygotes (Dun 1959*a*). Consequently, the *Ra* gene can be used to expose genetic variation of the primary vibrissae, in the same way that *Ta* has been used to expose genetic variation of the secondary vibrissae. The *Ra* gene has been backcrossed onto the HST/LST selection lines to allow comparison between the numbers of primaries and secondaries at the *RaRa* level of expression with that at the *Ta·* level. The mean numbers of primary and secondary vibrissae in *RaRa* and *Ta·* mice at the 16th generation of selection are shown in Figure 14.

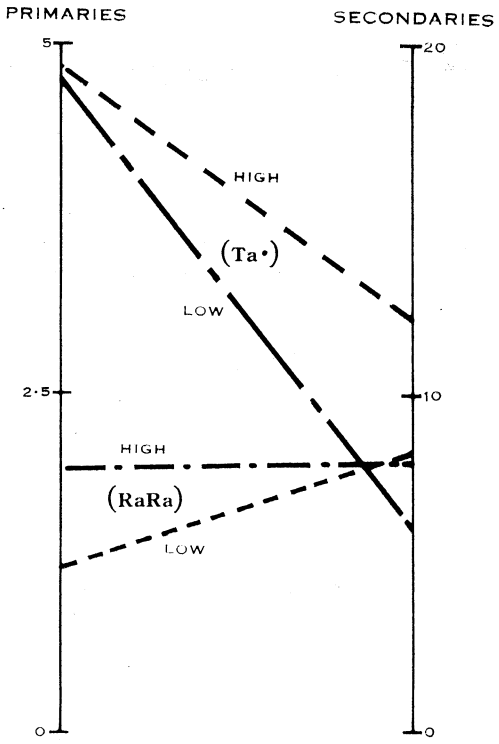


Fig. 14.—Relationship between mean numbers of primary and secondary vibrissae in *Ta·* and *RaRa* mice.

These results are surprising in the lack of difference between HST–*Ra* and LST–*Ra* in the number of secondaries, since there is a difference between them in their number of primary vibrissae. It would appear that the selection on the number of secondaries in *Ta* mice which has been maintained in the HST/LST lines, has produced a genetic difference which in the presence of *Ra* has no effect on secondaries, but has a marked effect on the primaries.

Dun (1959) in a comparison of the effects of *Ra* and *Ta* concluded that *Ra* has a closely timed action, affecting follicles initiated after $12\frac{1}{2}$ days foetal age, whereas *Ta* does not have a precisely timed action. It is, therefore, feasible to suggest that the lack of difference between HST–*Ra* and LST–*Ra* in the number of secondaries

is due (1) to the selection which has been practised affecting the later initiated secondaries, and (2) to the *RaRa* mice lacking these later initiated follicles. This hypothesis has the advantage of rationally explaining a puzzling interaction, but considerable further work will be needed to determine its validity.

The relationship between primaries and secondaries, i.e. a positive genetic correlation, contrasts with the absence of genetic correlations between the various groups of secondaries.

The *Ta*, *Ra*, and *cr* genes also have effects on the structure of the main coat—these effects are the main diagnostic features on which identification of the mutants is based. In *Ta* and *cr* homozygotes, and *Ta* hemizygotes, the main coat lacks any of the guard hairs or zigzags, being comprised solely of medium-length straight hairs. In *Ta* heterozygotes the loss of guard hairs and zigzags is not complete, being localized to a varying number of stripes. Crinkled heterozygotes do not detectably differ from normal mice. The *Ra* gene similarly causes a partial loss of guard hairs and zigzags in heterozygotes, which is irregularly expressed. *Ra* homozygotes show a greater degree of hair loss. Homozygous mice, which survive to an age when the

TABLE 1

MEAN RELATIVE FREQUENCIES OF THE FOUR TYPES OF COAT HAIRS OF THE HST AND LST LINES OF NORMAL MICE AT THE 16TH GENERATION OF SELECTION

| Selection Line | Guard Hairs | Awls | Auchenes | Zigzags |
|---|---|---|---|---|
| HST | $1 \cdot 30 \pm 0 \cdot 68$ | $11 \cdot 80 \pm 3 \cdot 42$ | $7 \cdot 74 \pm 3 \cdot 10$ | $79 \cdot 13 \pm 3 \cdot 67$ |
| LST | $1 \cdot 39 \pm 0 \cdot 74$ | $20 \cdot 73 \pm 7 \cdot 73$ | $3 \cdot 83 \pm 2 \cdot 61$ | $74 \cdot 05 \pm 8 \cdot 96$ |

main coat develops, are nearly naked with sparse abnormal hairs. A qualitative appraisal of the effects of these mutants ranks *Ra* as being more drastic than *Ta* or *cr*, and the main coat hairs as being more sensitive to the actions of these mutants than the secondary vibrissae, which are more sensitive to these actions than the primary vibrissae. It would be expected from this conclusion that selection on the number of secondary vibrissae should have correlated effects on the primary vibrissae, and on the main coat, if the genes which are being selected act similarly to the *Ta*, *cr*, and *Ra* mutants. These correlated effects should be less extreme for the primaries; more extreme for the main coat hairs. Dun (1959*b*) found that the degree of striping of the main coat in *Ta*+ mice is strongly correlated with the effect of selection.

Fraser (1951) has shown that there is considerable variation of the structure of the main coat in + mice. The frequencies of the four distinguishable types of hairs varied considerably both between different strains, and between mice of the same strain. Counts were made, for this study, of the relative frequencies of the types of coat hairs in + mice of the HST/LST lines at the 16th generation of selection. The mean frequencies are given in Table 1.

These data show that the relative frequency of awls has increased in the LST and decreased in the HST lines. The auchenes have increased in HST and decreased in LST. This difference is very marked, to the extent that it is possible to classify + mice as HST or LST on the basis of their frequency of auchenes with only a slight degree of misclassification. It appears that the selection on secondaries which has been practised on HST/LST has produced a more marked effect on the main coat than it has on the number of secondaries. This can be explained by the canalization of the main coat being less intense than that of the secondary vibrissae. This is illustrated in Figure 13.

### (*e*) *Conclusion*

These data indicate that the three aspects of hair growth which have been studied differ in their degree of developmental canalization. There appears to be very little canalization of the structure of the main coat, a marked canalization

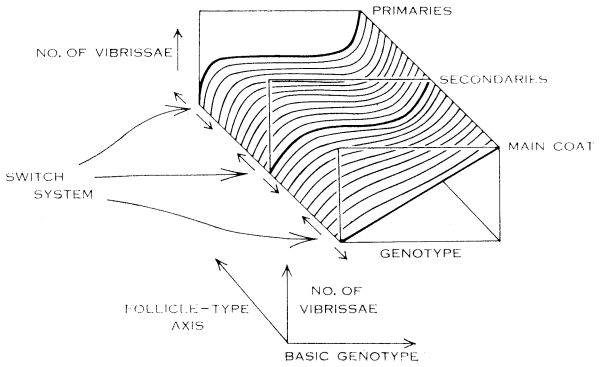


Fig. 15.—Canalization surface for primary and secondary vibrissae and main coat.

of the number of secondary vibrissae, and a very strong canalization of the number of primary vibrissae. This conclusion can be drawn both from the comparison of the effects of the *Ta*, *cr*, and *Ra* genes on these three aspects of hair growth, and from the correlated effects of selection found in the main selection experiment, where selection on the total number of secondaries produced a more marked response on the structure of the main coat, and a less marked response on the number of primaries, than it did on the number of secondaries. This conclusion can be restated on the basis of a correlation surface which defines the relationship of the "basic genotype" to the phenotype. Such a surface would be near linear for the intersect defining the structure of the main coat, moderately inflected for the intersect defining the number of secondary vibrissae, and markedly inflected for the intersect defining the number of primary vibrissae. This model is based on the assumptions (1) that the differences between the primary, secondary, and main coat follicles can be expressed by position along the axis termed "follicle-type axis", and (2) that the "basic-genotype axis" measures the primary effect of the *Ta*, *cr*, and *Ra* mutant genes, and of the genes selected in the main selection experiment. A shift along the basic-genotype axis would cause a simultaneous change in all three phases of hair growth; the extent

to which this change would be manifested in an observable difference would depend on the inflexion of the canalization surface, e.g. any shift away from the mid-point along the basic genotype axis results in a change of the structure of the main coat, whereas only a very large shift from the mid-point along this axis results in a change of the number of primary vibrissae.

Variation of the basic genotype cannot be the only possible path of genetic variation. This is shown by the lack of genetic correlation between the various groups of secondaries found in the HB/LB and HD/LD selection experiments. This model, to be sufficient, must include the possibility of genetic variation whose effects are manifested only on one specific group of hair follicles. Variation of position along the follicle-type axis will explain such genetic variation, i.e. genetic variation of the developmental system which differentiates one path of development of hair follicles from another. The model still includes one further possibility of genetic variation: that determining the shape of the canalization surface. It is feasible to postulate that the shape of the surface is under genetic control.* This model is illustrated in Figure 15.

This model can clearly only be regarded as a working hypothesis, but there are grounds for considering that the variability on which selection was based in the HB/LB experiment was different from that selected in the HST/LST experiment. The initial population on which HB/LB was based was derived from rare deviants in + mice, whereas the variation on which selection was based in HST/LST was that exposed by substitution of *Ta*. This variation was largely additive and appeared to be normally distributed. This suggests that the rare phenotypic deviants found in + mice of unselected strains are determined by a different genetic system to that which determines the variation of vibrissa number in *Ta*, *cr*, or *Ra* mice. This leads to the conclusion that + mice can deviate from the normal canalized vibrissa number because of variation in two different genetic systems, and, therefore, that the next phase of our researches should be directed at differentiating between + deviants caused by these two separate systems.

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