

# SIMULATION OF GENETIC SYSTEMS BY AUTOMATIC DIGITAL COMPUTERS

## VII. EFFECTS OF REPRODUCTIVE RATE, AND INTENSITY OF SELECTION, ON GENETIC STRUCTURE

By A. S. FRASER\*

[*Manuscript received March 4, 1960*]

### *Summary*

Simulation by Monte Carlo methods of the effect of selection against phenotypic extremes has shown that selection can produce a degree of genetic canalization which is more restrictive than that indicated by the limits of selection, showing that canalization of a rigid degree can be caused by loose selection.

### I. INTRODUCTION

This paper is a direct extension of Part VI of this series (Fraser 1960), describing further runs of the "epistasis" programme. In the initial runs of this programme the rate of reproduction was maintained constant at 50 progeny per mating, and the criteria of selection was similarly maintained constant at  $\pm 1.0$ . In these previous runs, variations of the structure of the genetic system, and of the number of parents, were compared, showing that selection against phenotypic extremes would lead to the fixation of a simple additive genetic system at an extremely slow rate in all but very small populations. With the epistatic systems defined by this programme such selection operated to modify the relation of genotype to phenotype, which in this particular system became an S-shaped function. The efficiency of selection in these runs was independent of population size.

In the further runs of this programme described below, two aspects have been examined. These are (i) the effect of variation of the number of progeny per mating, and (ii) the effect of variation of the intensity of selection.

### II. PARAMETERS

Although the epistasis programme has been constructed to minimize the number of parameters maintained constant during a run, some must be specified. These are:

- (1) The type of mating—self-fertilization or random mating.
- (2) The number of parents—this has been set to 160 per generation for all the present runs.
- (3) The reproductive rate—this has been set at 10, 20, 30, 40, and 50 progeny per mating, in two independent sets of runs, which are termed the "reproductive rate" set.

\* Division of Animal Genetics, C.S.I.R.O., University of Sydney.

- (4) The maximum and minimum limits of eligible phenotypes—these have been set at  $\pm 1.0$ ,  $\pm 2.0$ ,  $\pm 3.0$ ,  $\pm 4.0$ ,  $\pm 5.0$  respectively, in two independent sets of runs, termed the "selection intensity" set.
- (5) The vectors of coefficients of dominance and interaction—these have been set at the ranges used in the previous runs (see Fraser 1960), allowing considerable potential variation of both dominance and epistasis.

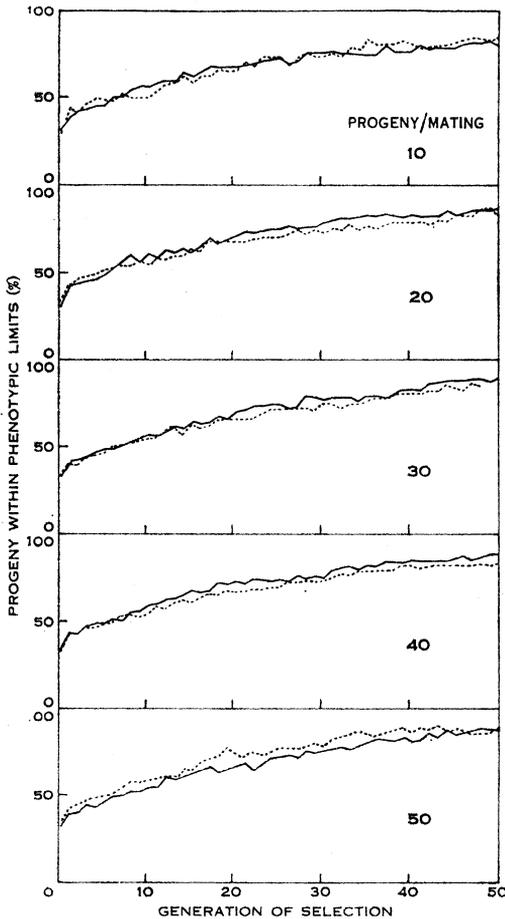


Fig. 1

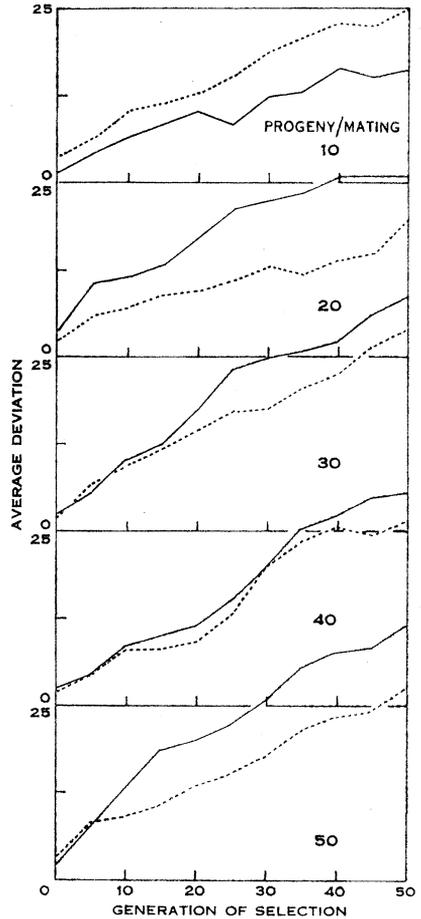


Fig. 2

Fig. 1.—Percentage of progeny with phenotypes within selection limits plotted against generation of selection, for the reproductive rate set of runs.

Fig. 2.—Average deviation of the gene frequencies of the basic loci from the initial value of 0.5 at which the runs were started.

The two sets of runs involving different numbers of progeny per mating were all made with the same criteria of selection, namely  $\pm 1.0$ . The two sets of runs involving different criteria of selection were all made at a reproductive rate of 10 progeny per mating.

III. RESULTS AND DISCUSSION

(a) Reproductive Rate

The results from the reproductive rate set of runs are illustrated in Figures 1 and 2. Figure 1 shows the percentage of progeny which had phenotypes within the selection limits plotted against generation of selection. This measures the efficiency of selection. Any differences between runs made at different numbers of progeny

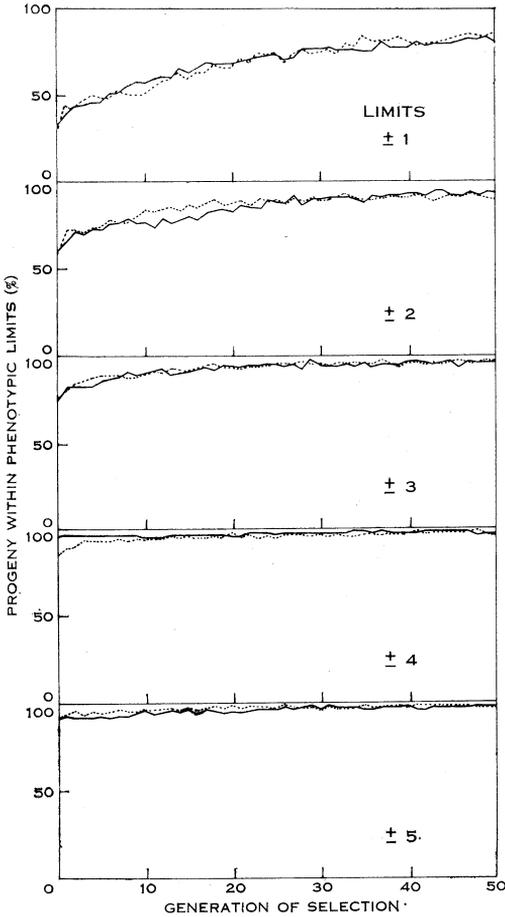


Fig. 3

Fig. 3.—As for Figure 1, for the selection intensity set of runs.

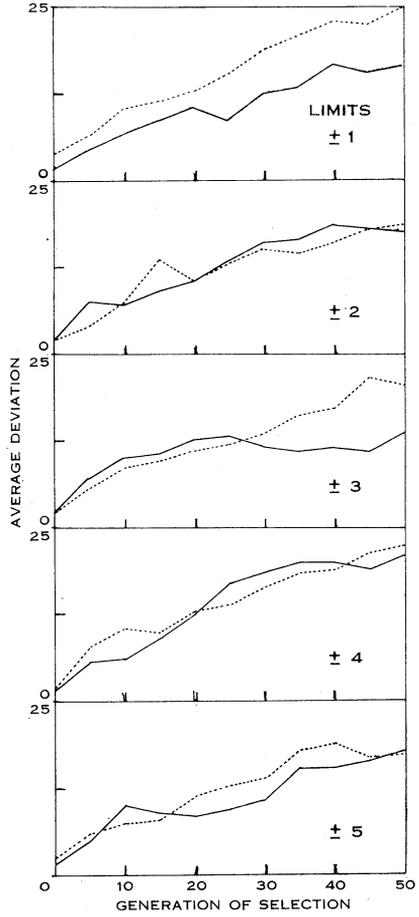


Fig. 4

Fig. 4.—As for Figure 2, for the selection intensity set of runs.

are small, and justify the conclusion that selection against phenotypic extremes is not markedly affected by population size, where there is available variation of the epistatic component of genetic variation.

Figure 2 shows the average deviation of the gene frequencies of the basic loci from the initial frequency of 0.5, at which the runs were started (Fraser 1960).

Again, the differences between runs are small, apart from those made at 10 progeny per mating, which show a markedly slower rate of increase of deviations from the initial gene frequency. Since one of the most interesting features of selection against extremes is its effect on the distribution of gene frequencies of the "basic" additive loci, it follows that the parameters should be set to minimize the effects of population size, reproductive rate, etc. Therefore, in the selection intensity set of runs the reproductive rate has been set at 10; the population size has been set at 160, the maximum possible for this programme.

(b) *Selection Intensity*

The results from the selection intensity set of runs are shown in Figures 3-7. Figure 3 shows the percentage of progeny which had the phenotypes within the selection limits plotted against generation of selection.

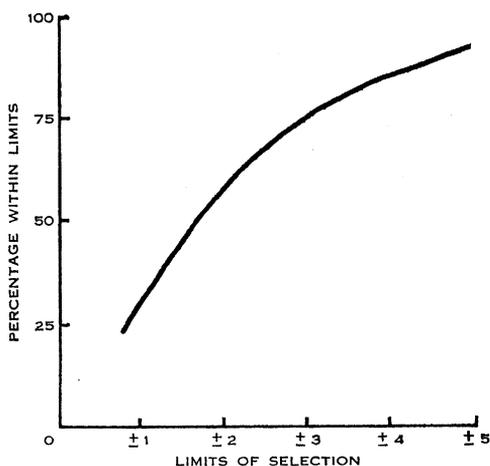


Fig. 5.—Percentage of progeny with phenotypes within limits plotted against selection limits, for the first generation, prior to selection.

It is clear, as would be expected, that the efficiency of selection, as measured by the percentage of progeny with phenotypes within the selection limits, is positively correlated with the intensity of selection, this being low for wide selection limits, high for narrow selection limits. The percentage of progeny in the first generation of selection which are within the selection limits is plotted against selection limit in Figure 5.

In the previous paper the conclusion was drawn that selection against extremes is a minor contributor to the incidence of genetic fixation of a complex epistatic genetic system. This conclusion is verified in the present set of runs. Figure 4 shows the average deviation of gene frequencies from the original value of 0.5 plotted against generation of selection for the selection intensity set of runs.

There are no marked differences between the runs at different selection limits in the rate of increase of deviations from the original gene frequencies. Consequently,

it is safe to conclude that the trend towards genetic fixation is predominantly controlled by the population parameters of reproductive rate and number of parents.

The marked reduction of phenotypic variation produced by selection in these runs is due to a change of the relation of genotype–phenotype from a linear (additive) function to an S-shaped (epistatic) function. This change is measured, in this programme, by the  $Q$  and  $C$  subgenotypes, which determine the values of the coefficients of the function relating genotype to phenotype. This function is

$$P = x + qx^2 + cx^3,$$

where  $P$  is the phenotype, and  $x$  is the additive + dominance component of the genotype.

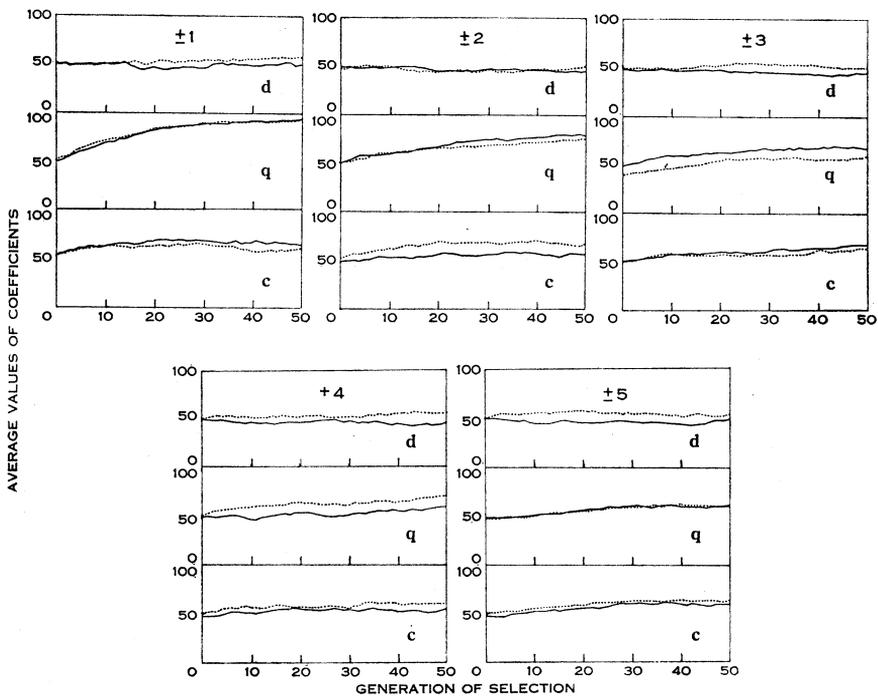


Fig. 6.—Average values of the  $d$ ,  $q$ , and  $c$  coefficients plotted against generations of selection, for the selection intensity set of runs.

The effects of selection on  $q$  and  $c$  are shown in Figure 6, where the average values of these coefficients are plotted against generation of selection. These coefficients can be used to calculate the genotype–phenotype relationships. These are shown in Figure 7, calculated from the values of  $q$  and  $c$  at the 50th generation of selection.

An interesting feature of these results is that selection against phenotypic extremes produces a greater reduction of the phenotypic variance than is indicated from the limits of selection. This is particularly evident from the comparisons of

the genotype-phenotype relation produced by selection at limits of  $\pm 2.0$ , with those produced by selection at limits of  $\pm 3.0$ ,  $\pm 4.0$ , and  $\pm 5.0$  respectively. The latter determine a lesser phenotypic variance even though produced by less intense selection.

A reason for this apparently exaggerated response to selection can be found in the determination of  $q$  and  $c$ . These are each determined by segregating subgenotypes. Consequently, the specific values of the genotype-phenotype relation shown in Figure 7 are mean values, with ranges given by the segregation of the  $Q$  and  $C$  subgenotypes. Selection will operate against the extreme values of the  $q$  and  $c$  coefficients, causing a greater degree of "canalization" than is expected from measurements of reproductive fitness.

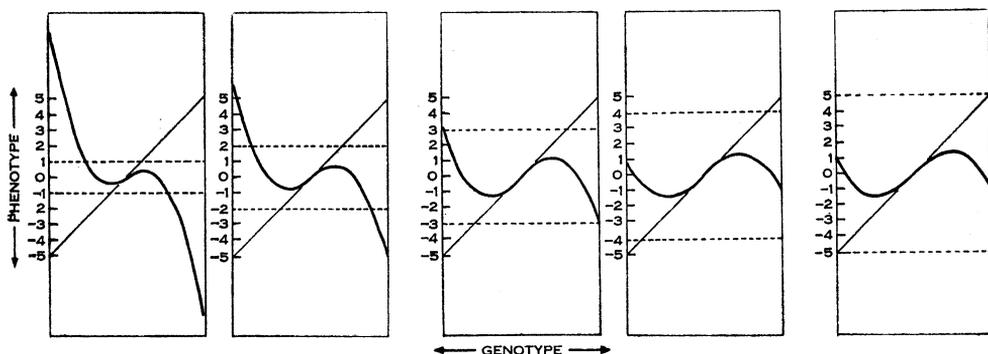


Fig. 7.—Relationship of genotype-phenotype determined by the values of the  $Q$  and  $C$  subgenotypes, at the 50th generation of selection.

These results from simulated genetic systems are analogous to those obtained in analyses of vibrissa number in mice (Fraser and Kindred 1960). This character is fairly strongly canalized at a vibrissa number of 18–19. Mice have been produced in selection experiments with numbers both above and below this value. On the assumption that the canalization is an effect of selection against extreme vibrissa numbers, measurements were made of various components of reproductive fitness on a wide range of mice with different vibrissa numbers. Only mice with very low or very high vibrissa numbers showed a decreased fitness. This indicated that direct selection on vibrissa number was not very intense, although it is possible that vibrissa number has effects on aspects of reproductive fitness which were not measured in these experiments, i.e. the number of vibrissae is an important characteristic under conditions which, because they do not occur in an experimental mouse colony, are not measured. Conversely, Rendel (personal communication) considers that the most probable reason for canalization of an external character is that due to the necessity for maintenance of a specific pattern of development of the tissue concerned, i.e. number of vibrissae is maintained constant at 18–19 as a secondary consequence of the regularity of development of all epithelium. Selection against such irregularities would be intense. These hypotheses both provide a possible explanation of the apparent lack of intense selection against extremes of

a "canalized" character, one on the direct effects of the character on some unmeasured aspect of fitness, the other on a "pleiotropic" relationship of the character to other more important characters which are under intense selection. The results obtained in the selection intensity set of runs show that neither explanation is necessary, since selection operative at limits far removed from a "canalization zone" can cause a sufficient reduction of phenotypic variance.

An interesting feature of the form of the genotype-phenotype relation is that selection against extremes has modified this from the linear additive form to a sigmoid form which has an inverse direction to that of the linear form. Genetic substitution would, in the presence of the sigmoid function, produce an effect opposite to that produced by the same genetic substitution in the presence of the linear function. This is due to the genetic model being based on a cubic equation determining the form of the genotype-phenotype relation. It is possible, but not certain, that a model based on a higher-order equation would not show this unexpected divergence between additive and epistatic systems. An experimental test is possible where the basic genetic system has pleiotropic effects on a canalized and on a non-canalized character. Response to selection should then be negatively correlated between the two characters.

#### IV. ACKNOWLEDGMENT

The author is indebted to Miss C. Jones for her help in preparing the diagrams.

#### V. REFERENCES

- FRASER, A. S. (1960).—Simulation of genetic systems by automatic digital computers. VI. Epistasis. *Aust. J. Biol. Sci.* **13**(2): 150.
- FRASER, A. S., and KINDRED, B. M. (1960).—Selection for an invariant character, vibrissa number, in the house mouse. II. Limits to variability. *Aust. J. Biol. Sci.* **13**(1): 48.