CHANGES IN GENE FREQUENCY DUE TO SELECTION

SP Simpson

AFRC Institute of Animal Physiology and Genetics Research, Edinburgh Research Station, Roslin, Midlothian EH25 9PS, UK

SUMMARY

A mathematical model is given which describes changes in gene frequency when there is directional selection on a trait under the control of a major gene and polygenes. It is used to show the effects of halothane testing and selection for leanness on the frequency of the halothane gene in pig stocks.

INTRODUCTION

Much of the theory used to explain the consequences of selection assumes that the quantitative trait under consideration is under the genetic control of many genes with small effects, or under the control of a single major gene with different levels of fitness associated with each genotype. Some quantitative traits are under the control of both polygenes and a major gene affecting fitness. For example, leanness in pigs is under the control of a major gene, the halothane gene, in addition to polygenes. Although the major gene improves leanness, it has adverse effects on meat quality and survival. A diagnostic test for the gene, the halothane test, has been devised (Webb and Jordan, 1978) which enables most homozygotes and some heterozygotes carrying the gene to be removed from the breeding stock (Southwood *et al.*, 1988a). A mathematical model is given here which can be used to predict changes in gene frequency when directional selection acts on a quantitative trait which is under the control of polygenes and a major gene affecting fitness.

METHODS AND RESULTS

Assumptions: A single major gene affecting a quantitative trait is segregating in an infinitely large population. There are different levels of fitness associated with each genotype. A fixed proportion of the population is selected on the basis of the quantitative trait, eg. by index selection.

At generation t, p_t^2, $2p_tq_t$ and q_t^2 are the genotype frequencies for genotypes *aa*, *aA* and *AA* respectively. The probability of being selected given genotype i and given the gene frequency at generation t is S_i, where i=1,2,3 corresponds to *aa*, *aA* and *AA* respectively. Directional

selection is used to select a proportion α for breeding stock, thus $p_t^2S_1+2p_tq_tS_2+q_t^2S_3=\alpha$. The threshold used for selection depends on the genotype means, μ_i, which may differ from generation to generation. After selection the genotype frequencies are $p_t^2S_1$, $2p_tq_tS_2$ and $q_t^2S_3$. After mating the gene frequency in the offspring can be expressed as follows:

$$p_{t+1} = \frac{p_t^2S_1+p_tq_tS_2}{p_t^2S_1+2p_tq_tS_2+q_t^2S_3}$$

If there is a heterozygote advantage, ie. $(S_1,S_3)\leq S_2$, the gene frequency converges to a stable equilibrium. For all other situations the gene frequency converges to zero or one. When there is a heterozygote disadvantage, ie. $(S_1,S_3)\geq S_2$, an unstable equilibrium exists. At the equilibria, $p=(S_3-S_2)/(S_1-2S_2+S_3)$.

When there is directional selection, individuals above a threshold, z, are selected. S_i is the proportion within each genotype above the threshold satisfying $p_t^2S_1+2p_tq_tS_2+q_t^2S_3=\alpha$. Furthermore, $S_i=F_i^*(1-\Phi((\mu_i-z)/\sigma))$, where σ is the within genotype standard deviation and Φ is the standardised normal distribution function, and F_i is the genotype specific fitness.

If the heritability of the polygenic component of the trait is zero, the genotype means are fixed. The S_i depend on the gene frequency. The equilibrium gene frequency is found by solving $p=(S_3-S_2)/(S_1-2S_2+S_3)$ and $p^2S_1+2pqS_2+q^2S_3=\alpha$ for p and the threshold, z. When the heritability of the polygenic component is not zero, μ_i in addition to S_i may vary. There is a directional change attributable to selection. However, when a major gene is present, in the initial generations this change is not constant for each genotype. The equilibrium gene frequency can be found by calculating p_{t+1} recursively from p_t, appropriately adjusting μ_i at each generation.

In practice the proportions selected from each sex may differ. The genotype means or the genotype specific fitness may also be sex dependent. In addition, more replacement females than males are usually needed. After selection the genotype frequencies in males and females will differ. The changes in gene frequency can be written:

$$p_{t+1}{}^m = \frac{p_t{}^m p_t{}^f S_1{}^m+(p_t{}^m q_t{}^f+p_t{}^f q_t{}^m)S_2{}^m/2}{p_t{}^m p_t{}^f S_1{}^m+(p_t{}^m q_t{}^f+p_t{}^f q_t{}^m)S_2{}^m+q_t{}^m q_t{}^f S_3{}^m}$$

and

$$p_{t+1}^{f} = \frac{p_t^m p_t^f S_1^f + (p_t^m q_t^f + p_t^f q_t^m) S_2^f / 2}{p_t^m p_t^f S_1^f + (p_t^m q_t^f + p_t^f q_t^m) S_2^f + q_t^m q_t^f S_3^f}$$

where m and f denote maternally and paternally derived alleles. These equations are subject to the constraints $p_t^m p_t^f S_1^m + (p_t^m q_t^f + p_t^f q_t^m) S_2^m + q_t^m q_t^f S_3^m = \alpha^m$ and $p_t^m p_t^f S_1^f + (p_t^m q_t^f + p_t^f q_t^m) S_2^f + q_t^m q_t^f S_3^f = \alpha^f$, where α^m and α^f are the proportions of males and females to be selected. The equations do not yield a simple general expression for the equilibrium gene frequency, but can be solved iteratively.

APPLICATION

The techniques presented here can be used to study the effects of directional selection and halothane testing in pigs. Figure 1 shows the changes in gene frequency when males and females are halothane tested with 0.85 homozygotes and 0.02 heterozygotes reacting and an initial gene frequency of 0.33. These values are consistent with the findings of Southwood *et al.* (1988b). The figure shows the change in gene frequency when there is directional selection for an additive trait with a standardised difference between the homozygote means of 0.5 and a heritability of 0.3 for the polygenic component. These values were chosen because Webb and Simpson (1986) found the difference between homozygotes in the lean proportion of joints averaged 0.5 standard deviations. Furthermore, Simpson and Webb (1989) found that the halothane gene appeared additive for many traits. The figure gives the changes in gene frequency when there is halothane testing of males and females prior to index selection. When halothane testing alone is used, the gene frequency decreases very slowly when the gene frequency is low, illustrating that this is not an efficient technique for eliminating the gene. However, if halothane testing is suspended in a herd where the gene is present the gene frequency would rapidly increase. If both halothane testing and index selection are used, the gene is maintained in the population at an equilibrium frequency of 0.274. The equilibrium value is similar to the present gene frequency in British Landrace nucleus stocks (Southwood *et al.*, 1988b). The practice of halothane testing and index selection may maintain the gene in the populations.

DISCUSSION

Changes in gene frequency and the equilibrium gene frequency, when it exists, can be estimated quite easily when the genotype means are fixed. When there is a large polygenic component, several factors affect the genotype means and hence the equilibrium gene frequency. In

a randomly mating population that has not been subjected to selection the polygenes will evenly distributed amongst the genotypes. Selection redistributes the polygenes and alters the genotype means. Selection also reduces polygenic variation and consequently heritability (Bulmer, 1971). The reduction in variance and change in genotype means, and consequently gene frequency, can be calculated at each generation if we assume that the polygenes are evenly distributed amongst the genotypes in the base population. In practice the population may have already been subjected to selection, in which case we may not know whether the limiting values of the variance and heritability have been reached, or how the the polygenes are distributed amongst the genotypes. Under these conditions changes in gene frequency cannot be predicted as accurately. Changes in variance have a large effect on changes in the gene frequency but redistribution of polygenes has relatively little effect. Despite these limitations, the model can be used to study the dynamics of major genes in populations subject to selection.

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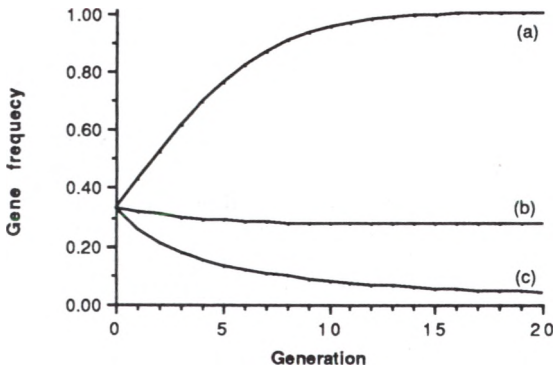

Figure 1. Change in gene frequency due to (a) index selection alone, (b) halothane testing and index selection and (c) halothane testing alone.