Impact of selection on effective population size: a commentary on 'Inbreeding in artificial selection programmes' by Alan Robertson

W I L L I A M G. H I L L*

Institute of Evolutionary Biology, School of Biological Sciences, University of Edinburgh, West Mains Road, Edinburgh EH9 3JT, UK

In a closed population of finite size, parents become increasingly related over generations and therefore inbreeding accumulates, heterozygosity decreases and random genetic drift of gene frequencies increases due to sampling. Under idealized conditions of random mating, discrete generations, constant population size, equal opportunities of leaving offspring and equal numbers of male and female parents, both the inbreeding coefficient and the genetic drift variance will increase in proportion to $1/2N$ if there are N parents. To deal with unequal numbers of male and female parents and variable family size, Wright (1931) defined the effective population size N_e, such that the increment in inbreeding is in general $1/2N_e$. If the variance of family size, the number of offspring becoming parents in the next generation, is σ_n^2 with pair mating, then $N_e = 4N/(2 + \sigma_n^2)$ (Wright, 1938). So, if family sizes differ only by chance about the mean of 2, i.e. are Poisson-distributed, then $\sigma_n^2 = 2$ and $N_e = N$ (some second order terms have been left out of these formulae). Further complexity includes accounting for different numbers of males and females and variation in numbers of sons per sire, daughters per sire, etc. (Gowe *et al.*, 1959). In his classic paper, Robertson (1961) points out that, in a population under selection for a quantitative trait, relatives of a selected individual in this and subsequent generations are also more likely to be selected, because relatives resemble each other. The variance in numbers of progeny, grand progeny and so on therefore rises progressively, N_e is reduced, and the rate of inbreeding and the increment of drift variance are increased. This has implications for the design of breeding programmes, selection experiments and conservation programmes.

There are a number of steps in Robertson's prediction of the magnitude of the effect that selection has on N_e. In addition to the random component, N_e depends on the variance in expected numbers of selected offspring per family, which is, in turn, a function of the variance in full-sib family 'selective advantages' s_i, such that $\sigma_n^2 = 2 + \text{var}(2s_i)$. He further argued that the selective advantage will be transmitted across generations, halving each time, to a limiting value of $2s_i$, so the total variance in selective advantage is $\text{var}(4s_i)$ and $N_e = N/(1 + 4\sigma_s^2)$. Robertson (1961) found 'by trial and error' that for mass selection an expression for the variance is $\sigma_s^2 = i^2\sigma_b^2/(\sigma_b^2 + \sigma_w^2) = i^2 t$, where i is the selection intensity, σ_b^2 is the variance between families, σ_w^2 the variance within families and t the corresponding sib correlation for the quantitative trait under selection. (I am surprised that he needed trial and error, because it can be derived by the method he used to predict the heritability of a threshold trait (Robertson & Lerner, 1949).) This led to the result (from eqn 2 in Robertson (1961)), $N_e = N/(1 + 4i^2 t)$.

Robertson (1961) has noted that the phenotypic and therefore the genetic variance among members of the selected group is less than that of random individuals, so the variation between the offspring families will be reduced. Hence, a correction is needed to the above equation, reducing the impact of selection on N_e. These comments were more important than then realized. Firstly, heritability estimates from between family variances are biased in selected populations, as Robertson (1977) elaborated later; secondly, this reduction in variation among families and consequent generation of gametic disequilibrium (Bulmer, 1971) have an impact on selection response and has become known as the 'Bulmer effect'. A further and important point Robertson (1961) made was that if selection was based on an index in which information on relatives is included, the correlation of index values of relatives and consequently family selective values would be increased. Then the reduction in N_e is greatest for lowly heritable traits (when t is small) as most weight is put on family mean.

Taking the relevant factors into account, Robertson (1961) predicted inbreeding rates for two *Drosophila* experimental populations. The prediction, $N_e = N/2 \cdot 5$, was 'in fair agreement' for one experiment, but the prediction for the other was poorer.

* Tel: +44-131-650 5705. Fax: +44-131-650 6564. e-mail: w.g.hill@ed.ac.uk

Robertson's formulae were used by Nei & Murata (1966) to predict the impact of correlation of fertility in natural populations on effective population size. Otherwise the paper's initial impact was not large. But animal breeders were aware of the problems he raised and some took steps to limit the numbers of offspring selected from extreme individuals. It was 30 years before the formal analysis was much further developed, stimulated by the increasing refinements made in breeding programme design and the aim of balancing selection intensity against reduction in N_e, a subject Robertson (1960) himself had initiated. The influence of the paper as judged by the science literature took a while to grow: it was cited only three times by 1963, the citation index window, a further 15 by 1970, then 32, 57 and 90 times in the following decades to 2000, and 40 times since then, 237 to date in all.

Using simulation, I had found that his formulae overpredicted the effect of mass selection on N_e, but (annoyingly) did not realize why. Wray & Thompson (1990) identified the key point that, as selection increases the population mean in the next generation, the selective advantage transmitted to offspring of selected individuals is less than one-half, because their competitors are also better. They developed an analysis in terms of means and variances, or simply mean squares, of genetic contributions of Mendelian sampling terms to later generations, a methodology subsequently widely followed in this and other applications. Wray & Thompson (1990) considered mass selection and cases of different numbers of male and female parents, and showed that inbreeding rates could be increased by about 75% over that in unselected populations. Results for mass selection were initially further developed by Woolliams et al. (1993) and Santiago & Caballero (1995) and subsequently generalized to include overlapping generations, selection on index and on best linear unbiased prediction (BLUP) (Bijma & Woolliams, 2000), and linkage (Santiago & Caballero, 1998).

Emphasis has now turned from predicting the effective population size in terms of numbers of selected individuals to breeding schemes in which family size is allowed to vary, selecting the most offspring from the best families, less from the next best and so on (Toro & Nieto, 1984). The objective is then to maximize predicted response for a specified rate of inbreeding without prior specification of family sizes or matings. Dynamic systems have been developed taking account of the predicted breeding value of each selection candidate and its relationship to all others (e.g. Meuwissen, 1997; Grundy et al., 1998), and to control contributions across generations (Sánchez et al.,

2003). Other major developments have been to incorporate inbreeding rates in the design of breeding programmes to utilize single genes, a few quantitative trait locus (QTL) linked to markers, and full genotype selection using multiple markers. In these the ideas, if not the methods, of Robertson's (1961) paper have persisted.

References

Bijma, P. & Woolliams, J. A. (2000). Prediction of rates of inbreeding in populations selected on best linear unbiased prediction of breeding value. *Genetics* **156**, 361–373.

Bulmer, M. G. (1971). The effect of selection on genetic variability. *American Naturalist* **105**, 201–211.

Gowe, R. S., Robertson, A. & Latter, B. D. H. (1959). Environment and poultry breeding problems. 5. The design of poultry control strains. *Poultry Science* **38**, 462–471.

Grundy, B., Villanueva, B. & Woolliams, J. A. (1998). Dynamic selection procedures for constrained inbreeding and their consequences for pedigree development. *Genetical Research* **72**, 159–168.

Meuwissen, T. H. E. (1997). Maximising the response of selection with a predefined rate of inbreeding. *Journal of Animal Science* **75**, 934–940.

Nei, M. & Murata, M. (1966). Effective population size when fertility is inherited. *Genetical Research* **8**, 257–260.

Robertson, A. (1960). A theory of limits in artificial selection. *Proceedings of the Royal Society of London, Series B* **153**, 234–249.

Robertson, A. (1961). Inbreeding in artificial selection programmes. *Genetical Research* **2**, 189–194.

Robertson, A. (1977). The effect of selection on the estimation of genetic parameters. *Journal of Animal Breeding and Genetics* **94**, 131–135.

Robertson, A. & Lerner, I. M. (1949). The heritability of all-or-none traits: viability of poultry. *Genetics* **34**, 395–411.

Sánchez, L., Bijma, P. & Woolliams, J. A. (2003). Minimizing inbreeding by managing genetic contributions across generations. *Genetics* **164**, 1589–1595.

Santiago, E. & Caballero, A. (1995). Effective size of populations under selection. *Genetics* **139**, 1013–1030.

Santiago, E. & Caballero, A. (1998). Effective size and polymorphism of linked neutral loci in populations under directional selection. *Genetics* **149**, 2105–2117.

Toro, M. A. & Nieto, B. M. (1984). A simple method for increasing the response to artificial selection. Optimisation of selection response under restricted inbreeding. *Genetical Research* **44**, 347–349.

Woolliams, J. A., Wray, N. R. & Thompson, R. (1993). Prediction of long-term contributions and inbreeding in populations undergoing mass selection. *Genetical Research* **62**, 231–242.

Wray, N. R. & Thompson, R. (1990). Prediction of rates of inbreeding in selected populations. *Genetical Research* **55**, 41–54.

Wright, S. (1931). Evolution in Mendelian populations. *Genetics* **16**, 97–159.

Wright, S. (1938). Size of population and breeding structure of populations in relation to evolution. *Science* **87**, 430–431.