# THE UTILISATION OF GENETIC VARIATION

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## SUMMARY

Underlying the considerable effort by national governments and international organisations to conserve the global diversity of our domestic animals is the notion that among the four thousand or so breeds and strains lies a valuable repository of germplasm, a fund of unique genes that we need to draw upon to meet our future needs. There has been little justification for this view. In this paper I examine some of the evidence, and conclude that the argument is overstated.

**Keywords**: Genetic variation, germplasm, utilisation

## INTRODUCTION

The United Nations Convention on Biological Diversity, ratified in 1992, includes specific references to conserving genetic diversity in domestic livestock, using this diversity in a sustainable manner and sharing the benefits of this use. Consequently, there has been increasing national and international effort directed at identifying, characterising and conserving endangered breeds. This effort raises a number of important questions. What is the purpose? What kind of genetic variation do we need to conserve, and what is its nature? The last question is important; for without an understanding of the resource available to us, it is difficult to specify how to exploit it. I find it surprising that, to some, the course seems clear. The FAO's global strategy for conserving animal genetic resources has been described as follows:

> Identify and understand those unique genetic resources which collectively comprise the global gene pools for each of the 40+ species domesticated and used to provide food and agriculture.
>
> Develop and properly utilise the associated diversity, to increase production and productivity, achieve sustainable agricultural systems and meet demands for specific product types.
>
> Monitor particularly those resources which are currently represented by small populations of animals; or which are otherwise being displaced by one or other breed displacement strategies.
>
> Preserve the unique resources which are currently not in demand.
>
> Train and involve people in management of these resources, including their best use and development, and in the maintenance of diversity.
>
> Communicate to the world community the importance of our domesticate animal genetic resources and of the associated diversity, its current exposure to loss and its irreplaceability.

Hammond (1994) p. 427.

Clearly, such a program is expensive and time consuming. It is important to note that, unlike most programs in conservation biology the primary aim is not to save species from extinction; none of our domesticated species is in danger. Rather, the aim is to conserve breeds and strains of those species assumed important for our future needs and for continued genetic improvement.

The 'imperatives' outlined above carry at least two implicit assumptions. The first is that there are a large number of endangered breeds that carry genes important for future genetic progress or for a sustainable agricultural system. The second is that we know how to identify those breeds, to exploit their diversity and to train individuals to employ appropriate conservation measures.

## THE PURPOSE

Genetic variation is necessary for genetic change; one of the most important principles in population genetics is that the rate of change for any trait is proportional to the amount of genetic variation for that trait. It is generally accepted that genetic variation is important for the survival of the species. This is a poorly understood principle because the advantage seems to be to the species rather than to the individual. Nevertheless, the maintenance of genetic variation seems to be necessary for the long term survival of most taxonomic groups but, as I have already indicated, extinction of domesticated species is not an issue.

The term 'utilisation' relates to human needs. For species in general, the important issue is that we are part of a global ecosystem, and our own survival depends on the maintenance of that ecosystem. The important issue here, however, is our direct use of a subset of species to meet our practical and aesthetic needs. We nurture other species of plants and animals because of their direct importance, as companions, as decoration or to supply food, clothing, fuel, cosmetics and other things. It is generally accepted that domestic animal (and plant) diversity must be maintained to meet our short and longer term requirements (see Hammond 1994). I have no quarrel with this. The principles that underlie the movement to conserve a wide range of breeds for each domesticated species, which I find less obvious, are (1) that breeds are repositories of important genetic diversity, (2) that this diversity is unique and (3) that we know how to exploit this diversity. My aim, in this paper, is to examine these propositions more carefully.

## THE NATURE OF GENETIC VARIATION.

Underlying all genetic variability is the variation that we can now identify at the molecular level. In many mammals, approximately one in a hundred nucleotide sites is polymorphic, in other words there are of the order of $10^7$ polymorphic sites for each species. In addition, there are numerous insertions, deletions and re-arrangements of DNA sequence. It is impossible to envisage conserving genetic variation at this level and, in any case, since the majority is neutral, or nearly so, there is little point in attempting to do so. Of the remainder, many will be deleterious, and these are of little relevance to the issues here. For example, metabolic disorders can often be traced to single gene differences but we do not wish to conserve strains that carry unique metabolic disorders.

We observe, also, variation at the chromosomal level - genic and chromosomal rearrangements that are common in evolutionary lineages but are probably irrelevant here since, again, most are deleterious. Hence, in this discussion, the only important genetic differences are those that affect production efficiency, product quality or fitness *i.e.* that have measurable phenotypic effects.

Phenotypic variation can be divided into two classes: continuous and discontinuous. The genetic component of discontinuous variation is sometimes a single gene, but often is not. Colour patterns in mammals are influenced by forty or more known genes, although many of these exhibit undesirable pleiotropic effects. Even the presence or absence of horns in sheep and cattle, often described in text books as a simple Mendelian trait, is more complex than it seems. One can be misled, when observing a meristic trait, or a simple presence or absence, by threshold effects. For example, Wright (1968) describes crosses between two guinea-pig strains, one with three toes, the other with four. Despite segregations in $F_2$ and backcross generations that resembled Mendelian ratios, further analysis revealed that at least four factors were involved in the difference.

While there are thousands of examples of conspicuous polymorphisms in a wide range of plant and animal species they are, nevertheless, relatively rare. Most are probably adaptive, but are of little significance in commercial species. I do not mean to imply that conspicuous polymorphisms are absent - quite the contrary. There are many genetic variants that have been consciously selected by man during domestication, such as colour patterns or conformational traits having little to do either with productivity, reproduction or survival, whatever their aesthetic appeal. An important challenge for governmental conservation programs, therefore, is to look beyond overt differences among strains, such as the distinctive patterning of the Belted Galloway, the lop ears of the Anglo Nubian or feather barring in the Plymouth rock and decide what variations are of real significance for production efficiency, product quality or adaptation.

Of greater importance are those polymorphisms that we might call inconspicuous. These are genetic differences that have effects on fertility, production or survival that are not immediately apparent, because they have no obvious phenotypic effect, and are often seen only in response to environmental stress. One of the best known of these examples is the Booroola fecundity gene (*Fec*$_B$), which for years remained unidentified in a high fecundity selection line. Perhaps even more important are disease resistance or stress resistance genes, now relatively well known in plants but unidentified in commercially significant animals. One of the best known examples is a genetic resistance to lymphoid leucosis in chickens (Crittenden 1975). From time to time we see reports of major genes contributing to parasite resistance or tolerance, or to production efficiency, but such examples rarely stand up to detailed scrutiny. If there were such genes, conservation and utilisation issues would be resolved, for what we need to do is identify such genes in breeds and strains and introgress them into our important commercial strains.

However, overwhelmingly, most important genetic differences for production quality and adaptation are polygenic, and under these circumstances the arguments for conservation and the means to use such variation are much more problematic. Just as we tend to over-apply Occam's razor and assume simple Mendelian inheritance for apparently discrete phenotypic differences, it has become fashionable in recent times to assume that, while many genes potentially contribute to genetic variation, only a few genes are important in genetic response. This view, I believe, ignores much of a long history of attempts to understand the nature of quantitative variation.

## QUANTITATIVE VARIATION

Despite the enormous effort invested in plant and animal breeding, and the huge pay-offs, we know almost nothing about the genetics of quantitative traits. In the early days following the rediscovery of Mendel, Johannsen, Nilsson-Eale, East and others proposed simple models, namely that quantitative traits are simply ones controlled by a number of genes each of small and approximately additive effect; such models provided a bridge between the Mendelians and the Biometricians, and Fisher finally put an end to the division between the two groups in his 1918 paper, laying the foundation for quantitative genetics. Little has changed since then. Most quantitative geneticists still subscribe to the view that quantitative traits are controlled by a large number of genes, each of small effect, interacting additively. Some, on the other hand, deny that there are a large number of loci, and suppose that there are but a few, with perhaps two or three loci contributing the bulk of the genetic variance. The latter view is the driving force behind the search for QTL and their application in marker assisted selection.

What then do we know about the genetics of quantitative characteristics? We can make a number of observations:

1. For any species, there are perhaps thousands of quantitative traits. For example, in *Drosophila* alone, selection experiments have been carried out on a wide range of characteristics, such as bristle patterns, body size, egg size, developmental time, mating behaviour, maze-running, alcohol tolerance, tolerance to heat or cold, DDT resistance, wing shape and wing tip height -- all respond to selection.
2. Selection response continues almost unabated for many, perhaps hundreds of generations, and, depending on population size, response remains linear for many generations (eg Jones *et al.* 1968; Yoo 1980; Weber 1996).
3. Many loci are involved in the response. Shrimpton and Robertson (1988) established that at least 17 loci on just the third chromosome had contributed to a selection response for sternopleural bristles. This was an underestimate, as detection was limited to effects of 0.6 of a standard deviation.
4. There are often large interactions between loci involved in the response. For example, Shrimpton and Robertson found an effect that could be detected only by its interaction with other chromosome segments. Modern QTL studies are now constantly uncovering epistatic interactions.
5. The primary response is for the trait selected, indicating that there is variation specific for

that trait. Correlated responses are observed, but are not the rule. Even the commonly observed decline in fitness, thought to be an inevitable by-product of long-term selection, disappears if population sizes are large enough (Weber 1996).

The reason for continued response over many generations is now clear. Quantitative variation is

$$V_m = \sum_i^n \mu_i \alpha_i^2$$
$$\approx n \, \bar{\mu} \, \bar{\alpha}^2$$

renewed at quite a staggering rate, of the order $10^{-2}V_e$ to $10^{3}$ $V_e$ per generation (Lynch 1988), where $V_e$ is the environmental variance. In a moderately large population, this is ample to maintain selection response indefinitely (Franklin 1982; Hill 1983). However, the high mutational variance makes a nonsense of the notion that quantitative traits are oligogenic. The mutational variance is where $n$ is the number of loci, $\mu$ is the mutation rate and $\alpha$ the average effect of the new mutation. If the per locus mutation rate is say, $10^{-5}$, a mutational variance of $10^{-3}$ $V_e$ requires either a large average effect of each new mutation (*i.e.* $\alpha^2 >> V_e$) or a large number of loci contributing to the variance. Only the latter is consistent with observations on most traits. A similar conclusion is reached if we reflect on the generation of new variation by insertional mutagenesis; for each trait there must be many loci that are capable of affecting the phenotype.

The observations described above do not support a simple additive oligogenic model for quantitative inheritance. However, there are a number of difficulties. If there are, for example, only a thousand different quantitative traits, each controlled by 20 loci, we have accounted for a third of the mammalian genome and more loci than exist in *Drosophila.* Another difficulty is the apparent independence of response, for one way of getting around the problem of too many genes is to assume that the same subset of genes controls a whole range of traits. A third problem is the apparent additivity of quantitative variation, for this flies in the face of much of what we know about gene action and developmental biology. Indeed, where genes of large effect are found, interaction is becoming the rule rather than the exception (Frankel and Schork, 1996).

So what is the point, and what is its relevance to conserving breeds and strains? I believe that we fool ourselves if we believe that we understand the true nature of quantitative variation, and make policy decisions, or worse, promises to funding agencies, on the assumption that we do. For example, one of the arguments for maintaining a large number of breeds and strains of livestock species, many of which cannot compete economically, is that they may contain valuable genes that one day we may need to introduce into our commercial strains in order to advance beyond some physiological constraint or environmental threat. An alternative view, and one consistent with experimental evidence, is that ample variation exists, *and is constantly being generated*, within our commercial livestock to meet any challenge. In other words, there may be no need to keep a wide range of obscure breeds as an insurance policy. This does not, necessarily, imply that rare breed conservation is otiose.

## USING GENETIC VARIATION

The three main options are within-breed selection, crossbreeding and introgression.

**Within breed selection.** This is, and will remain, the dominant mode of animal improvement. In time, and especially as rates of genetic gain increase, the gap between the highly improved breeds and the less common breeds will increase. While I am not a strong supporter of such market-driven developments, and regret the marginalisation of many breeds (such as the Jersey), this course seems inevitable. And, since I have argued the `unique germplasm' notion, my reservations are more aesthetic than economic.

Rather, the dangers lie in poor definition of breeding objectives and the marketing of breeds designed for one environment (such as intensive production systems for temperate regions) as well suited for alternative environments (such as small holders in the humid tropics). Thus, cultural imperialism is a far greater danger, in my opinion, than the loss of rare breeds already marginalised in their own environments.

**Crossbreeding.** The exploitation of heterosis in breed crosses is often advocated and commonly used to achieve short-term gains. In some species, such as poultry, crossbreeding is widely employed more to protect seed-stock than to achieve maximum gains in production efficiency. In fact, crossbreeding may impede progress, and even its benefit to corn-breeding is debatable.

In large-animal production systems, such as sheep and cattle, the exploitation of heterosis suffers from two conflicting requirements. On the one hand, the greater the genetic distance, the greater the heterosis expected. On the other hand, in order to achieve a sustainable industry, both breeds need to be commercially acceptable in their own right. Maintaining two or more equivalent breeds, while maintaining sufficient genetic distance to ensure significant heterosis may require a difficult balancing act. Australia's fat lamb industry may be the exception rather than the rule.

Similarly, crossbreeding involving highly productive but unadapted breeds and less productive, adapted breeds can be seen only as a short-term solution. In these cases, where there is a very substantial difference between the breeds, the aim is not so much to capture heterosis but to combine the important features of the two breeds. Under these circumstances intercrossing may lead to substantial breakdown of those characteristics, and a selection program following on from a crossbred base may be the best option.

**Introgression.** Introgression is the transfer of one characteristic from one breed to another that lacks that trait. A scenario often envisaged is the transfer of disease resistance from an exotic breed to a susceptible commercial strain. Undoubtedly, such circumstances will arise, but such an application can be envisaged only if the trait is controlled by preferably one, but at most two or three genes. The effect should also be additive. Introgression, as a strategy, will be made much easier by the availability of genetic markers, but given the rarity of genetic differences of this kind, maintaining a large number of rare breeds for such a circumstance may be a costly gamble.

## CONCLUSIONS

Genetic improvement of our important commercial species will, in my view, continue to be driven by selection within our existing commercially important breeds, and introgression of genes from other, non-commercial breeds will play an unimportant role. I do not wish to imply that there is no case for breed conservation. Clearly the array of breeds that dominate production in the highly developed countries are unsuited to many of the more stressful environments of the emerging nations, and animal production industries must be built upon the breeds already adapted to these environments. Again, however, it is unlikely that new improved strains will be built upon the presently endangered breeds in these environments; it is much more likely that breeding programs will be aimed at improving production efficiency and product quality in those breeds that are most successful in that environment.

The likelihood of environmental changes driving new breeding objectives presents, I believe, a much stronger case for conservation. There may be increasing pressure for a more extensive agriculture, despite the trends of the last twenty or thirty years, not only on moral and aesthetic grounds, but on arguments for energy efficiency as well. The pressures for changed husbandry are well illustrated by the very strong moves in Europe towards outdoor pig production. The large white breeds are quite unsuited to this trend, and breeders have had to go back to more traditional strains. Similar pressures are bound to increase in the poultry industry as pressure for more humane conditions intensifies.

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