THIRTY YEARS OF AAABG

Ian Franklin

CSIRO Livestock Industries, Belair, SA

SUMMARY

AAABG was founded to stimulate animal breeding research and its adoption by the various livestock industries. To this extent, it has been successful; since the inaugural conference 30 years ago, over 2000 papers, both invited and contributed, cover most the major issues. This paper presents a brief and personal overview of issues and successes, most of which were resolved during the first fifteen years, and of the challenges ahead.

INTRODUCTION

> In many ways the lot of the theoretical population geneticist … is a most unhappy one. For he is employed, and has been employed for the last 30 years, in polishing with finer and finer grades of jeweller's rouge, those three colossal monuments of mathematical biology, *The causes of evolution*, *The genetical theory of natural selection* and *Evolution in Mendelian populations*. (Lewontin, 1964)

Lewontin, of course, was talking about the contributions of Haldane, Fisher and Wright to population genetics theory. Equally, the reference could apply to quantitative genetics. Fisher, and to a lesser degree Wright, laid the foundations of quantitative genetics: Fisher in his 1918 and many subsequent papers on design and analysis of experiments, and Wright for his work on genetic relationships, the effects of small population size and his influence on J. Lush. However, in contrast to population genetics, quantitative genetics always had a strong empirical foundation, and clear commercial applications.

Population genetics is concerned with changes in the frequency of genes in populations and the mechanisms underlying the maintenance of the standing variation. Quantitative genetics, on the other hand, focuses on genetic and phenotypic means and variances of traits in populations. Clearly, the two disciplines are related. By concentrating only on the mathematical and statistical aspects, however, both run the risk of ignoring the underlying biology. In recent years, molecular genetics has reinvigorated population genetics; quantitative genetics is approaching a similar renaissance. I shall return to this later.

For much of the 20th century, animal breeding research concentrated on refining the statistical methodology for estimating components of variance and developing breeding programs based on these components. By the 1970s, despite years of effort by researchers, extension officers and some producers, penetration of modern animal breeding technology to the extensive industries of Australia was still poor. Advances were evident in the pig and poultry industries, and in dairy, as most states had developed dairy herd improvement programs. Nevertheless, even in these industries, estimates of rates of realised genetic progress were rare. In the extensive industries, there were none. BLUP methodology, now incorporating the inverse genetic relationship matrix, offers a means to estimate realised progress, given accurate estimates of genetic parameters.

It was clear that an effective means to present an already well established animal breeding theory to extension officers and, especially, to producers, was desirable. Neither the Genetics Society nor the Australian Society of Animal Production was an adequate forum for this.

1979 -- THE INAUGURAL MEETING

Stuart Barker opened the inaugural conference with an historical account of animal breeding research in Australia, the motivation for establishing the Association, and established the

groundwork for future meetings. Paddy Cunningham delivered a summary of the current understanding of quantitative genetics (in many respects just as relevant today), and its relation to animal breeding. In this, and in almost meetings that followed, special sessions were devoted to the current status of breeding programs for each of the most commercially significant species.

This conference, and most of those that followed, had a theme (Table 1). Here, the theme was measurement. Of course, animal improvement is possible without objective measurement, and some degree of visual appraisal continues to this day, but the introduction of objective measurement (and reliable pedigrees) to the various extensive industries had in the past been a major stumbling block to the application of quantitative genetics theory.

Table 1. Location and themes of each AAABG conference over 30 years

Year	Volume	Site	Theme
1979	1	Armidale	Measurement and recording
1981	2	Melbourne	Selection and mating programs
1982	3	Brisbane	Efficiency
1984	4	Adelaide	Implementation
1985	5	Sydney	Various
1987	6	Perth	Various (breeding objectives)
1988	7	Armidale	Economics
1990	8	Hamilton, NZ	Technology transfer
1991	9	Melbourne	Profit and Prophets
1992	10	Rockhampton	International trade
1995	11	Roseworthy	Quality and profit
1997	12	Dubbo	Responding to client needs
1999	13	Mandurah	Breeding for 21st century
2001	14	Queenstown, NZ	Biotechnology
2003	15	Melbourne	50 Years of DNA
2005	16	Noosa Lakes	New Genetic Technologies
2007	17	Armidale	Making it happen
2009	18	Barossa Valley	Matching genetics and environment

Over the next 15 years, most of the major issues were resolved. Statistical methods and algorithms to take advantage of rapid changes in computer technology were developed and made available to researchers, and to the industries, for estimating genetic parameters, or for managing and implementing breeding programs. A National Dairy Herd Improvement Scheme was established (Jones 1991), programs such as Breedplan (Nicol *et al*. 1985), Woolplan (Brien 1990) and Lambplan (Banks 1990) were in place. Sire evaluation programs were created for sheep and cattle and made available to producers (James 1979; Roberts 1979). These were crucial for improving productivity and quality in these species.

The following years saw discussion of some of the finer points of implementation, the status of emerging industries, trade and the potential for the new DNA based technologies. Clearly, I cannot discuss in any detail the 2000 odd papers presented over the 30 years of AAABG. In any case, to many of these I can add no worthwhile opinion. Rather I restrict myself to a subset of issues; those that I believe represent the essential elements of any breeding program. I can do no better than quote Bill Hill at the 1981 meeting:

> With *well defined* breeding objectives, *reliable* estimates of genetic parameters such as heritabilities and genetic correlations and an *adequate* knowledge of the biology of the species, it is not difficult to construct a feasible breeding program *predicted* to have near-optimal rates of progress over a *few* generations.

Readers may note that I have inserted an emphasis of my own.

WELL DEFINED BREEDING OBJECTIVES

The first of these is the most problematic, and numerous AAABG sessions have been devoted to this topic. Many authors have discussed the complexities of this issue (eg Barlow 1987). However, since considerable progress can be achieved with an objective not based on detailed economic analysis, it is not a precondition for beginning a breeding program. Indeed, it may be the last element to be put in place. The primary goal of the commercial livestock producers is to improve enterprise efficiency. Each suffers from a deteriorating environment, as they have to compete for market share not only with members of their own industry but also with other products, with pressure from retailers and with the changing demands from consumers. In other words, producers need, like the Red Queen, to run as hard as they can to stay in the one place. Often, the major benefit accrues to the retailers and the consumers.

Ideally, one needs to develop an economic model for each industry - one that allows inputs for each circumstance and helps to define the variables that are critical for economic survival. In practise, a truly predictive model is almost certainly non-linear and probably impossible, as it is difficult to predict vicissitudes in consumer demand (*e.g.* changing fashions for egg colour or egg size), in ethical attitudes and of course, the weather. The model needs, therefore, to accommodate risk management (see Anderson 1988). Then, this economic model needs to be linearised at the current status of the enterprise, or at some future goal. It is no wonder that breeders and their advisors often choose to adopt a desired gains model, or more dangerously, choose a set of traits that they believe covers their needs. In practise, then, the breeding objective is commonly defined as a linear sum of traits that we wish to improve, each weighted by a set of economic values.

The greatest dangers arise when all relevant traits (including those not easily measurable) are not included in the objective (Hill 1981), or when the objective is based on individual performance rather than the enterprise (Cartwright 1982). Finally Smith (1988), following Smith *et al.* (1986), argues that, "genetic improvement should not be used to correct inefficiencies in the system". It seems that bounds need to be set on this principle. Some issues, such as stocking rates, are clearly managerial decisions. Others are less clear. Should we, for example, assume optimal parasite control when the relationship between resistance and cost of control is a step function? Also, consider a flock producing fibre of a diameter that markedly mismatches market demand for apparel wool. It could be argued cogently that this is an example of a managerial inefficiency, and that the producer should engage in breed substitution (or upgrading) rather than waste valuable selection differential on reducing fibre diameter.

While not entirely resolved, the debate over this issue during the early life of AAABG, has certainly had an effect – compare, for example, Ponzoni (1979) with Ponzoni (1988).

RELIABLE ESTIMATES OF GENETIC COMPONENTS

Perhaps this is the area where we have seen the greatest advance over the last 30 years. Initially, genetic variances and covariances were estimated using carefully designed experiments (*eg* half sib families) and the analysis of variance. Now we have an armoury of statistical and computing tools, using maximum likelihood, Monte Carlo, and other optimisation algorithms, to estimate more directly the desired genetic components. Most readers will be aware of packages such as ASREML and WOMBAT. I do not wish to imply here that design is irrelevant – any estimation procedure works better with well-designed data sets.

AN ADEQUATE KNOWLEDGE OF THE BIOLOGY OF THE SPECIES

It is a common practise in statistics to avoid drawing conclusions about within population relationships from between population comparisons. To do so even further isolates quantitative geneticists from the functional relationships inherent in the underlying biology. The components

of wool weight provide a good example of such functional relationships. For example, the well described inverse relationship between density and fibre diameter ($N \propto D^{-2}$) reveals an underlying functional relationship, related to the developmental events leading to the initiation and formation of the follicle. Similarly, the inverse relationship between length growth rate and diameter, such that the ratio L/D^2 is approximately constant within the animal, has been much trumpeted by nutritional scientists as genetic (and indeed it has a high heritability). Finally, the supply of nutrients to the follicle, and to the fibre (reflected in the product LD^2) is a consequence of a complex set of processes that reflect feed intake, feed efficiency and partition of nutrients and energy between various components of body growth. The fact that the quantities above are ratios should deter no one; I have already argued that all of these variables should be log transformed. Whether these components prove useful as selection criteria is a moot point, but they may help to improve our understanding of physiological changes underlying gains. Similar functional relationships exist, I am sure, for other complex traits in diverse species.

At a deeper level, many animal scientists have searched, often in vain, for reliable physiological indicators of production traits (see Blair *et al*. 1990). However, one appears very promising as an indicator of growth rate and feed efficiency. The IGFs, and in particular IGF1, were first suggested by Salmon and Daughaday (1957) as mediators of growth. IGF1 is expressed throughout the organism, and its receptors are ubiquitous. It has now been shown to correlate well with body size in a variety of species, and with feed efficiency in cattle and pigs.

PREDICTED PROGRESS OVER A FEW GENERATIONS

It is well known from single trait selection experiments that, in populations of reasonable size, response is undiminished and approximately linear over tens or even hundreds of generations. Loss of genetic variation is usually not a problem. However, we have few data on the stability of genetic correlations over long periods; this is potentially important since most practical breeding programs depend on multivariate selection indices. This is, perhaps, another reason for choosing criteria that are, as much as is possible, functionally unrelated.

It is as important as ever to monitor realised progress. A departure from that predicted indicates something is seriously amiss, taking into account, of course, the fact that there may be considerable variation between replicate lines.

A DIGRESSION ON SCALING

Despite the fact that most statistical packages available to the breeder offer the option to transform the observed data, I have seen little evidence that such transformations are common. The topic is rarely discussed; the one exception is a note by James (2007). Since many important commercial traits involve growth processes, logarithmic transforms are often appropriate. Such transformations have the additional benefit of removing the irksome problem of ratios in objectives and selection criteria. We accept the need to transform data such as faecal egg counts, but not fibre diameter, and use measurements such as the coefficient of variation, which is an explicit admission that a logarithmic scale is appropriate.

A suitable scale of measurement is not merely desirable to ensure the independence of variances upon the mean, as we know linear analysis is quite robust to such deviations. The importance, I argue, is to ensure an appropriate genetic scale. Failure to choose one can lead to apparent dominance and non-linearity of response, if measured inappropriately, and may be particularly important in interpreting genetic crosses. QTL analyses, in particular, often involve crosses between divergent species, and it seems prudent to remove apparent effects that are merely a consequence of choosing an inappropriate scale.

ON THE NATURE OF QUANTITATIVE VARIATION

At the core of contemporary animal breeding theory is the nature of quantitative inheritance. In general, most traits of interest to the breeder appear approximately additive. For heritability at least, this assumption is well justified by experiments in drosophila, mice, corn and other species; the behaviour of genetic correlations is less clear. Furthermore, genetic variation is not limiting; it seems that new variation is generated at such a rate (by mutation or recombination) that progress can continue almost indefinitely. These observations provide a strong empirical foundation for applying the theory to livestock improvement. However, if we wish to understand the genetic basis of this variation, we enter difficult territory – one that requires that we reconcile the above observations with our increasing awareness of the complexity of gene action.

Through much of the 20th century, deep divisions beset population genetics over the origin and maintenance of the standing variation in gene frequencies. One, the "classical" view, maintains that most variation is either deleterious and maintained by recurrent mutation, or neutral and maintained by drift. Hence, phenomena such as inbreeding, and its converse, heterosis, are due the covering or uncovering of these harmful mutations. The alternative "balanced" view is more mystical, full of terms such as co-adapted gene complexes, assumes widespread epistasis and that variation can be maintained by over-dominance. Undoubtedly, the truth lies somewhere in between, but I tend to sit in the latter camp; one of the so-called "naïve pan-selectionists". The classical view still dominates population genetics, and adherents tend to treat genes as entities, not imbedded in a complex interacting system. Concepts of the "the Selfish Gene" and terms such as junk DNA have arisen from such thinking. I suggest that those who see value in identifying genes of large effect that can improve selection response for commercial traits also reflect the "bean bag genetics" approach, as Mayr disparagingly called single gene selection models.

I am much encouraged by the revelations of molecular genetics, which support the notion that even simple phenotypes are a consequence of a complex interactions at all levels of gene expression. The mammalian genome has roughly 20,000 genes, not much more than that found in far less complex organisms. Complexity in development arises, I believe, through greater interaction between genes and between their gene products.

The observable properties of quantitative variation, together with the very high rates of generation of new variation each generation, despite the underlying interactions, are then a paradox that can only be resolved, I believe, by concluding that many genes can affect each trait, and that each of these genes contribute, on average, a small affect.

BIOTECHNOLOGY AND THE FUTURE

In recent years, and especially in the three meetings spanning 2001-5, attention has focused on biotechnology, and particularly on marker assisted selection (MAS). For the reasons alluded to above, I have always been sceptical of the promises of MAS, as I was earlier of claims by some genetic engineers that large changes in productivity could be achieved benignly. I do not imply that genes of large effect cannot be found, or that identifying such genes is unimportant. In populations undergoing intense selection, rare alleles or new mutations that have a large effect on the trait will increase in frequency, despite the fact that they may be deleterious in other respects. Also, false positives are common in QTL screens with small data sets leading the researchers (and their funding bodies) to the conclusion that a significant fraction of the variation for a trait can be attributed to a few genes. The current state of MAS in cattle was recently summarised by Van Tassell *et al*. (2007), who concluded that the application of QTL has been, as yet, limited. What disturbs me is not the search for QTL, nor for the genes that affect livestock in useful or adverse ways. Rather, it is the promise to funding agencies, and the diversion of research funds from other important research areas that is problematic.

DNA technology's first important application was to identify parentage, initially using microsatellites, now being replaced by SNPs. Accurate pedigrees are an important part of modern animal breeding technology, but DNA sampling is an enabling technology for other genetic tests, such as testing for carriers of deleterious genes. Pedigrees define genetic relationships, but with a wide SNP coverage of the genome, it is possible to estimate these relationships directly. Since these would be realised rather than expected relationships, they will be more accurate.

Just as the progression of Moore's Law had, perhaps, the largest impact on animal breeding technology over the last 30 years, DNA technology is progressing at a similar rate. For example, the human genome project cost millions of man-hours and billions of dollars to complete; the task has recently been repeated for less than $50,000. Complete DNA sequencing is now within the reach of all species. We can analyse the whole transcriptosome, or identify transcripts in a selected chromosomal region, and profile expression patterns for each. SNP chips containing 100,000 or more polymorphic bases are now available for many species.

While advances are made in annotating the known genes (identifying their protein product and possible function), we are still far from interpreting the complex interactions and predicting the phenotypic consequences of gene substitutions, alone or in combination. We are still ignorant of the developmental genetics of body size, or even of organelles such as the wool follicle or the mammary gland, but the rate of gain in our knowledge is truly staggering. Comparative genomics offers us a chance to ask, for example, why some species are susceptible to parasites, but closely related ones are not. The challenge to the modern quantitative geneticist is to capture this new knowledge to identify pathways and genes that can be used to improve productivity.

REFERENCES

Anderson, J.R. (1988) *Proc. Aust. Assoc. Anim. Breed. Genet.* **7**:32
Banks, R. (1990) *Proc. Aust. Assoc. Anim. Breed. Genet.* **8**:237
Barlow, R. (1987) *Proc. Aust. Assoc. Anim. Breed. Genet.* **6**:162
Barker, J.S.F. (1979) *Proc. Aust. Assoc. Anim. Breed. Genet.* **1**:2
Blair, H.T., McCutcheon, S.N. and Mackenzie, D.D.S. (1990) *Proc. Aust. Assoc. Anim. Breed. Genet.* **8**:133
Brien, F.D. (1990) *Proc. Aust. Assoc. Anim. Breed. Genet.* **8**:241
Cartwright, T.C. (1982) *Proc. Aust. Assoc. Anim. Breed. Genet.* **3**:5
Cunningham, E.P. (1979) *Proc. Aust. Assoc. Anim. Breed. Genet.* **1**:8
Cunningham, E.P. (1979) *Proc. Aust. Assoc. Anim. Breed. Genet.* **1**:18
Hill, W.G. (1981) *Proc. Aust. Assoc. Anim. Breed. Genet.* **2**:3
James, J.W. (1979) *Proc. Aust. Assoc. Anim. Breed. Genet.* **1**:47
James, J.W. (2007) *Proc. Assoc. Advmt. Anim. Breed. Genet.* **17**:150
Jones, L.P. (1991) *Proc. Aust. Assoc. Anim. Breed. Genet.* **9**:9
Lewontin, R.C. (1964) *Proc. XI Int. Congr. Genetics* Oxford, Pergamon Press *p571*
Nicol, D.C., Graser, H.-U., Tier, B. and Hammond, K. (1985) *Proc. Assoc. Advmt. Anim. Breed. Genet.* **5**:151
Ponzoni, R.W. (1979) *Proc. Aust. Assoc. Anim. Breed. Genet.* **1**:320
Ponzoni, R.W. (1988) *Proc. Aust. Assoc. Anim. Breed. Genet.* **7**:55
Roberts, E.M. (1979) *Proc. Aust. Assoc. Anim. Breed. Genet.* **1**:48
Salmon, W.D and Daughaday, W.H. (1957) *J. Lab. Clin. Med.* **49**: 825.
Smith, C., James, J.W. aand Brascamp, E.W. (1986) *Anim. Prod*. 43: 545
Smith, C. (1988) *Proc. Aust. Assoc. Anim. Breed. Genet.* **7**:42
Van Tassell, C.P. Sostegard, T.S. Liu, G. and Matukmalli L.K. (2007) *Proc. Assoc. Advmt. Anim. Breed. Genet.* **17**:461.