Current developments in the genetics of livestock improvement

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There is a character in a play of Molière who was pleased and surprised to be informed that he had been speaking prose all his life. Most livestock producers are in somewhat the same position: without being aware of the fine body of genetic theory which exists, they have nevertheless been steadily putting it into practice for many centuries. What then has the science of genetics to add to the efforts of practical livestock breeders?

In the first place, it provides a rational basis for their activities and observations. Hence breeders need not speculate about whether the stallion or the mare has the greater genetic influence on the offspring — the genetic mechanism ensures that their contributions are approximately equal. Cattle breeders need not devote a generation of activity to stamping out an undesirable recessive gene — its recessiveness guarantees its persistence, though at low frequency. The decline in fertility and viability which often accompanies inbreeding can be explained largely as the effect of increasing homozygosity in exposing such recessive genes.

Secondly, it provides a verifiable starting point for the development of the complex breeding operations that many populations now require, and that are as far removed from simple selection as the motor car is from the bicycle. Examples are the large and complicated breeding and selection programmes that produce modern egg-laying chicken strains, or the large investment which is currently made in testing and selection of dairy cattle for use through AI. Inevitably, much of the contribution of genetics is simply to provide the hard physical base on which investment appraisal can be carried out, and one of the more active areas in the genetics of livestock improvement is precisely this region, where genetic events meet their economic consequences.

How adequate is genetic theory, as it now stands, for this role? Where are the major deficiencies? How can it be made more useful as a basis for the practical decision-making that constitutes an animal improvement programme?

How adequate is the theory?

The theory of inheritance has grown steadily for over a century by the regular progression of hypothesis construction, experimental testing, and extension, to the point

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where it is now quite remarkably coherent and comprehensive. The physical nature of
the genetic mechanism is beyond dispute. The varied uses and refinements of this
basic mechanism in different species are thoroughly mapped. A single body of theory
has proved sufficient to relate the great diversity found in living organisms back to
its physical origin in DNA molecules. The extent to which our present knowledge of
genetics provides a satisfactory account of heredity is well stated by Lewontin (1974):
'What we know as the science of genetics is meant to explain two apparently anti-
thetical observations — that organisms resemble their parents and differ from their
parents. That is, genetics deals with both the problem of heredity and the problem of
variation. It is in fact the triumph of genetics that a single theory, down to the molecular
level, explains in one synthesis both the constancy of inheritance and its variation.'

Apart from its general utility as an account of the hereditary mechanism, how
adequate is genetic theory as a basis for practical breeding programmes? Almost all
characters of substantial economic interest in farm livestock depend on the activity
of genes at a large number of loci. This is to be expected since
1) most growth and production traits are influenced by many aspects of the animal’s
physiology, and
2) traits involving few genes are likely to have been selected to homozygosity in the past.
Thus, most traits of interest are by definition 'quantitative' traits. How many genes at
a minimum are involved in a quantitative trait? We have no estimates in farm animals,
but figures of the order of 10-20 have been estimated for mice and Drosophila (Com-
stock, 1974). Even with this number of genes (and in practice the number is likely to be
considerably higher) individual gene effects will not be measurable, and the genetic
model on which a breeding programme is based will need to be the same as that for an
indefinitely large number of genes.

This model, which is in effect Fisher’s (1918) statistical version of the Mendelian
theory, says that genes can act in three ways:
1) singly (giving additive gene effects);
2) in intra-locus pairs (giving dominance effects);
3) in inter-locus combinations of two or more (giving epistatic effects).
This model omits only one major element of the physical reality which it represents:
it ignores the fact that genes are grouped in chromosomes and that loci are therefore
physically linked. How important is this deviation from reality? The evidence has been
reviewed by Comstock (1974), taking as a measure the degree to which linkage affects
the limits obtainable by selection. The question is complex, but has been clarified some-
what by simulation studies. The drag which linkage imposes on selection response
depends on many factors, but most heavily on recombination frequency (c) and
effective population size (N). For reasonable values of c, he found that with N equal
to at least 60, there was minimal interference with selection. The general conclusion
is that for fairly large populations ignoring linkage makes little difference to the pre-
diction of genetic change.

Another apparently crude aspect of the quantitative model is the way in which it
defines the additive effect of a gene:

\[ \text{pd} + (1 - \text{p}) \text{h}, \]

where \( p \) is the frequency of the gene, \( d \) is the genotypic value of its homozygotes and \( h \) the value of a heterozygote, both measured from the population mean. This is a shifting definition, changing with gene frequency and with the population mean, and taking no account of the chemical pathways that the gene activates. In fact, it is a statistical abstraction. It has parallels in quantum mechanics. Apart from its statistical convenience, all we can say for it is that it appears to work. Models of larger effects (for example, heritability) constructed using it as the basic element, can be, and have been verified experimentally. I should, however, add that where epistatic gene effects are concerned, the basic model is less satisfactory (Barker, 1974).

It seems to me unlikely that better or more useful algebraic representations of the Mendelian mechanism are going to be found. The application of genetics to the improvement of livestock is therefore going to be mediated by these rather simple models, and by the armoury of descriptive and manipulative statistics to which they give rise: gene frequencies and gene effects; components of genetic variance and covariance; heritability; genetic correlations; measures of population size and structure; reproductive rate; coefficients of additive and dominance relationship between individuals; inbreeding coefficient; heterozygostity index.

**Strategic framework of livestock improvement**

In order to consider systematically the points at which this body of theory can be applied to the improvement of a population of livestock, I have arranged the sequence of operations involved in the form of a flow-chart (Fig. 1). This is adapted from a previous publication (Cunningham, 1974a).

The construction of a breeding scheme requires answers to a logical series of questions. The first of these concerns the breeding goal. This must first be defined, and techniques for measuring it must be established. Definition and measurement of breeding goal is self-evident in some cases (e.g. litter size in pigs, milk yield in cows) but very difficult in others (e.g. carcass merit in cattle, meat quality in all species). The difficulty may be simply that there is no general agreement among producers on what is desirable, or that the trait is technically rather difficult to measure precisely. There is the additional consideration that the breeding objective may need to change substantially with the passage of time. Many breeding programmes have in the past been seriously hampered by problems at this initial stage. A lot of the early stimulus for work in blood groups in fact derived from the prospect that cheap indirect indicators could be developed for traits of particular breeding interest. A recent review is given by Spooner (1974).

The second phase is to ask if the differences measurable in the declared breeding goal are heritable. This question must be asked at two levels. Initially we must know if there are large additive genetic differences between available populations. If the ans-
Define breeding goals
Devise techniques for measuring them

Are there large additive differences between available populations?

Are goals heritable within chosen population?

Highly

Moderately

Poorly

Are responses favourable?

Is there heterosis?

SELECTION

CROSSING SYSTEMS

Choose crosses + system to maximize heterosis

Optimize selection programme

Evaluate lines, Optimize selection within lines

Move to best available population

NO

NO

NO

Fig. 1. General strategy of livestock improvement.
wer is yes, then the conclusion is that one must acquire the best of these available populations. Population substitution has undoubtedly been the main mechanism for genetic improvement of livestock in the past. In Ireland, for example, we are now in the final stages of a 25-year transition from a Shorthorn to a Friesian cow population. Where population substitution can be made quickly and easily (for example in poultry) then a small advantage is sufficient to justify the change. In larger animals, population substitution is usually carried out by continuous top crossing with introduced males, and is a longer and more expensive process. The genetic difference required to justify the change is then much larger. I have estimated that it should be at least 20% in the case of dairy cattle (Cunningham, 1974b).

At the second level, that is, within the chosen population, we must again ask how heritable are the observed differences. If heritability is moderate to high, we can use selection theory to construct an improvement scheme, and to predict its outcome. If heritability is low, then one must look for non-additive genetic variations to exploit. In practical terms, this means a search for heterosis effects of economic value. Since the measurement of heritability is such a cardinal point in the development of a breeding programme, it is not surprising that it has occupied a central place in research in animal breeding. Is too much effort devoted to this single task? Probably yes. The heritability of most important traits in most developed populations is now fairly well established. It seems to me that for the future, its estimation and reporting (together with other structural and genetic statistics of the population) will increasingly be a matter of routine. For example, in dairy cattle populations served by AI, the annual evaluation of bulls for selection is now often done in a sophisticated analysis that can yield estimates of variance components as a by-product. Thus the annual report of such an organisation could simply contain a section headed 'annual review of genetic parameters'. These could then be used for periodic revision or servicing of the selection programme.

If the heritability level indicates that selection will be effective, the next stage is to see if there are internal antagonisms within the selection goal. The basic measure of this is the genetic correlation. If the correlations are favourable, then it simply remains to combine the traits to be improved and the information available in an optimum way. This is achieved by the use of a selection index. Programmes of this kind are found, for example, in pig populations served by an organised testing scheme.

There remains one further stage, which has not received sufficient attention in the past. That is, the integration of the genetic selection programme with its economic costs and consequences. Essentially this means arranging that those paying for the genetic improvement get the best value possible for their money. It is usually the case that the genetically optimum scheme is not that which is economically optimum. This area of study, that is, the cost-effectiveness of breeding programmes, is one in which we have a particular interest, and which needs much further development both in terms of technique and application.

In the absence of sufficient additive variation to justify a selection programme, one often finds considerable heterosis. The standard evolutionary explanation for this seems
to me quite satisfactory. That is, that for any character of importance in 'fitness', natural selection will have exhausted additive variation long before we assumed responsibility for the evolution of the population. These characters are therefore the ones for which different populations or strains are likely to carry gene complements consistent within the strain, but different from one strain to another. This enhances the probability of heterozygosis, and hence of overdominance, when the strains are crossed. In general, the experience with different species bears this out: heterosis is observed most strongly for fertility and viability traits, for which the heritability is in general low. Thus, evolution has produced the fortunate general pattern that traits which cannot be improved by selection, can be improved by judicious crossbreeding. In passing, one should note the important difference between these two avenues of genetic improvement — that selection is cumulative through the generations, whereas the exploitation of heterosis is a one-step gain which must be recreated in each generation.

The systematic development of crossbreeding systems has for many years been the basis of corn and poultry breeding. Operationally, this consists of a search for strains which cross well, and systems (2-way, 4-way, cyclical etc.) which maximize the overall gain.

A combination of selection and crossbreeding is often profitable. This is most likely to be useful if it is possible to divide the selection goal into a part which is highly heritable, and a part which is highly heterotic. It is particularly valuable if these two parts are to some degree antagonistic but can be dealt with separately in sire and dam lines. The most active current area in farm livestock for the development of such systems is in pigs, where it is profitable to concentrate selection for post-weaning growth, efficiency and carcass traits in a male line, and to supply the females from a crossbreeding system designed for ease of operation and maximum heterosis for maternal traits.

This catalogue exhausts the major options which genetic theory offers in the area of livestock improvement.

Two examples

In a paper read before this Society, Alan Robertson (1966) gave the opinion that the development of a certain phase of the genetics of quantitative traits had come to an end. In a sense, I agreed with him when I suggested that the basic models we use in the dissection of quantitative variation are unlikely to be improved on. Since then, the emphasis has shifted considerably in the direction of efficient application of these models, I would like to mention two results from our own research group which illustrate this changed emphasis.

One of the major difficulties in cattle selection, particularly in Europe, has been that of defining a meaningful balance between milk and beef in the selection goal and in the resulting breeding programme. We attempted to force this problem into the standard model for a selection index, that is, to define the balance of these traits simply in relation...
to their marginal economic value to the producer. It quickly became apparent that the standard model was inadequate for this case. The individual selected is the bull. The bull is neither milked nor, in a commercial sense, reared for beef. His genotype is not therefore exploited in himself, but in his offspring. So we pursued the consequences of an insemination in an attempt to define in which animals, in which generations, at what times, and with what probabilities his genotype was, in fact, giving rise to improved production for the farmer. It emerged that quite a complicated network of probabilities was needed to link the insemination to its consequences. In the end, it proved possible to define these probabilities as functions of the population net reproductive rate, the rate of cow replacement, and the extent of crossing with beef bulls. To express all future consequences on a common basis, we then weighted each possible lactation or beef animal among his descendants by

1) the probability of their existence (a function of the three population parameters mentioned above);
2) a discount factor to allow for their dispersion through time;
3) a generation discount factor to allow for the dilution of his genotype as the generations proceed.

Because it has some features in common with discounted cash flow, we called it the discounted gene flow method (McClintock & Cunningham, 1974). It has proved very useful in probing the dependance of the selection scheme on the population structure. For example, it emerged that the amount of beef crossing practised had a major bearing on the balance of beef and dairy traits in the selection goal, and therefore on the relative value of expenditure on testing for beef and dairy traits.

In pig breeding, it has been established that Landrace × Large White F₁ females show about 10% advantage in overall productivity over purebreds of either breed. In Ireland, only 11% of the sow population is crossbred. There is therefore a large gain to be made by promoting the greater use of crossbreeding. The standard formula for this is to establish a structure to supply F₁ females to commercial producers. This, however, has the disadvantage of higher costs for replacement females and constant exposure of the breeding herd to introduced disease. A two breed reciprocal backcrossing system could provide home-produced females with minimal exposure of the herd, since only males would need to come from outside.

Continuous reciprocal backcrossing stabilises quickly to give females with 67% as much heterozygosity as the F₁. The question was: will they show 67% as much heterosis as the F₁? Or more? Or less? The literature was uninformative, so an experiment was set up with mice to investigate the relationship between heterosis and heterozygosity. Almost 1000 litters were produced, from dams with 0, 25, 50, 75 and 100% of the heterozygosity of the F₁. The results (McGlouglin, 1976) showed a clear and linear increase in performance as heterozygosity increased. The results are being checked in field data with pigs, but meantime confirm the original supposition that most of the benefits of crossbreeding can be obtained by a simple self-contained breeding system.

E. P. CUNNINGHAM

Blood groups and biochemical polymorphisms

In his paper in 1966, Alan Robertson was, I think, somewhat uncertain about the ways in which research on blood groups and biochemical polymorphisms would be found useful in livestock improvement. The early promise was built on the possibility of finding marker genes which could significantly speed up selection. That promise has in general not been fulfilled. In my opinion, that was largely to be expected. If particular alleles at any locus are strongly tied (either by direct action or by linkage) to an important production trait, then crude selection for that trait will tend to have done the easy initial work of changing the frequencies at that locus. The loci which remain markedly polymorphic are likely to be those whose alleles are little related to the trait. The corollary of this is that one might expect to find useful associations with traits that have not been subject to much selection, either because they were not of much economic interest until recently (like meat quality), not easy to include in a selection programme (like disease resistance), or simply not observed by producers (like components of fertility).

Of course other applications of blood group techniques have developed. Parentage testing is now an accepted routine. More recently, the development of indices of heterozygosity based on biochemical markers has been a useful guide to population structure, and indeed to the explanation of variation in performance, particularly in fertility. The use of blood groups for historical research on the origin of breeds, has also been very productive.

The literature in several of these areas has been reviewed: cattle (Stormont, 1967), genealogy (Rendel, 1967), horses (Sandberg, 1974). I would like, as a specialist from a contingent field, to comment briefly on some recent papers that I found of particular interest.

There is considerable genetic variation both between (King et al., 1975) and within (McLoughlin & McGloughlin, 1975; Jensen, 1974) breeds of pigs in meat colour, post-mortem muscle pH and associated traits. Two recent reports, from Denmark (Jensen et al, 1976) and the USA (Rasmusen & Christian, 1976), show parallel associations between the H red cell antigen system and this syndrome. The Danish results, based on very extensive data, showed a doubling of the frequency of PSE muscle in pigs with the Ha factor over those without it. Less striking, but nonetheless potentially useful, links have also been reported between H-system alleles and reproductive performance (Rasmusen & Hagen, 1975) and between transferrin genotype and litter size (Imlah, 1970).

Any population of animals lies somewhere on the scale that goes from complete homozygosity to complete heterozygosity. For most populations, we have no idea where on this scale they fall. Blood group genes enable us to attempt to measure the position of the population and of individuals within it. For the same reasons which give rise to heterosis, one might expect performance for some traits to improve with the degree of heterozygosity of individuals within a population. This indeed has been

found to be the case for bull breeding values for milk production (Schleger & Stur, 1976), and for cow fertility (Pirchner, 1974; Hierl, 1976).

In sheep, haemoglobin type has been found to have an effect on survival of hill lambs (Purser & Hall, 1974) and on the response to induced ovulation (Pant & Pandey, 1975). A range of blood group and enzyme marker genes have been found to be related to performance in racehorses (Osterhoff et al., 1971). Blood typing has been used to confirm the suspected pattern of coat colour inheritance in horses (Trommershausen-Smith et al., 1976). Blood typing has been found a useful indicator of genetic distance between strains of pigs, and consequently has been a guide in predicting heterosis in crosses (Verhorst et al., 1974). Statistical methods are being developed to facilitate the measurement of marker gene contribution to quantitative traits (Geldermann, 1975) and their use in historical research on breed origins (Kidd & Cavalli-Sforza, 1974).

My impression is that, in common with quantitative genetics, the genetics of blood groups and biochemical polymorphisms has moved closer to the real needs of improving livestock populations in recent years. Adapt or perish is the rule of evolution. It applies to fields of science just as it does to species of animals.

References


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