Lessons from established breeding programs: Terrestrial and aquatic animals

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Abstract

Some relevant components of selection program theory and implementation are reviewed. This includes pedigree recording, genetic evaluation, balancing genetic gains and genetic diversity and tactical integration of key issues. Lessons learned are briefly described – illustrating how existing method and tools can be useful when launching a program in a novel species, and yet highlighting the importance of proper understanding and custom application according to the biology and environments of that species.

Introduction

Livestock breeding programs have a long and continuing record of success at making useful genetic change in commercially important traits. However, in many cases there remains a challenge to make genetic change that is relevant to the target production system(s), and to make effective dissemination of the resulting genetic material.

Where to go?

In its most basic form this is a question about what type of animals we want to generate through genetic change. It is important to specify the environment(s) and productions system(s) in which we want the developed stock to perform Genotype by Environment Interaction can be important. Specifically, the environment in which we conduct breeding programs is often higher quality, more controlled and less stressful than those in which the bulk of production takes place.

We can define breeding directions by specifying rationally derived economic weightings for each trait of importance, or we can use a desired gains approach to explore the range of possible outcomes. A combination of these two is often the best route.

How to get there?

This is all about how to make genetic change in the desired directions. The main tools for animal breeders have been selection and crossbreeding, but there is a wide range of issues to be accommodated when implementing these. New systems to integrate these issues in an implementation framework are now being used in progressive breeding programs. Molecular genetic technologies are now being implemented–but they still act as a supplement to more classical methods.

This brief paper will review established and emerging selection systems for making genetic change, with some reference to both terrestrial and aquatic animal industries.

Genetic evaluation – a refresher

Background

The phenotype, or trait values, of an animal is influenced by the genes that determine an animal's predisposition to perform within the prevailing environment. The environment itself affects the way in which genes are expressed. A breeding program aims to improve the average phenotype of a population by improving the average genetic merit in successive generations. When evaluating candidate parents for selection, an animal's superiority is therefore measured in terms of its genetic merit, in particular, the component of its own genetic merit that can be transmitted to its offspring. This heritable component is known as an animal's breeding value, and is the value of an animal's genes to its progeny. For a particular trait, the variation between breeding values as a proportion of the phenotypic variation is known as the trait's heritability.

As true breeding values are difficult to measure, predictions of their value are used to rank animals as candidate parents. Different criteria exist for predicting true breeding values, and these differ in their accuracy and associated costs. In some cases, an animal's own phenotypic record is an efficient predictor of its breeding value. Alternatively, criteria can be used which incorporate records from individuals and their relatives. The genetic component of an animal's phenotype includes a fraction of genes that are

identical, by descent, to related individuals. The size of this fraction is proportional to the degree of relationship, e.g. animals with common parents (full-sibs) share, on average, half of their genes. The requirement to record an animal's pedigree increases the cost of selection, but knowledge of the proportion of shared genes between individuals, and records on their phenotype, increases the accuracy of prediction for the individuals involved.

Selection methods

Once a decision is made to initiate a selective breeding program to exploit a population's genetic variation and increase productivity, the type of selection program to best serve the needs of the industry and give the best results must be chosen. In the current context, there are four basic methods of selection:

Individual selection (or mass selection)

Individual selection is based solely on phenotypic records. It is simple and low cost, as this method does not require specialized systems for recording identity and pedigree. Difficulty in recording identity in aquatic species has made individual selection popular, however, the traits for which selection can be applied are limited to those that can be directly measured on the live individual (e.g. not really suitable for carcass quality and disease resistance traits). The accuracy of prediction is determined by the heritability, such that for a highly variable environment, individual phenotype is a poor estimate of breeding value. Thus it is only really effective when the heritability is at least moderately high. The absence of family information in a proper mate selection program increases the risk of deleterious inbreeding - but selecting a large number of parents may offset this.

Between-family selection

Between-family selection predicts the mean breeding value of each family from its phenotypic mean. Families are treated as homogeneous groups so that each family member has the same estimated breeding value. Families are selected as whole groups and so individuals used as parents are chosen at random from the superior families. In general, the rate of response is slow when selecting on family means. However, when the heritability and common environmental variation are low, rates of response are much higher than individual selection. This method also allows for the selection of traits that may only be measured on slaughtered animals, e.g. flesh colour or fat percent. The mean of records taken on slaughtered animals can be used to estimate breeding values for the remaining family members. There are similar advantages for disease resistance traits.

Within-family selection

Within-family selection predicts the breeding value of an individual by the deviation of its phenotype from its family mean. Animals that exceed their family mean by a certain amount would be selected as parents. This method has the greatest value when environmental effects are common to members of a family but different between families, e.g. families kept in separate tanks or pens. Without need to replicate family tanks, this method reduces the size of a facility required to run a breeding program, and with particular mating strategies, can help lower the rate of inbreeding.

Combined selection

Combined selection is a method of evaluation that can incorporate information on an animal's breeding value from several sources. The simplest example is the weighted sum of within- and between-family records, where weights are derived from the heritability and the degree of relationship of individuals within- and between-families. This concept can be extended to include records from more distantly related individuals where each new source of information is appropriately weighted. Increasing the number of records from different relatives increases the accuracy of prediction above that of other methods. The general method used to predict breeding values from the information of many different relatives is known as BLUP (Best Linear Unbiased Prediction). In addition to the use of information from different relatives, the accuracy of prediction is increased by the capacity of BLUP to correct for environmental effects. Therefore, the ranking of candidate parents on EBVs (Estimated Breeding Values) permits selections to be made from a common base across different families, environments and year-classes or cohorts.

BLUP EBVs are the criterion of choice for ranking candidate parents. However, their efficient estimation relies on accurate pedigree records. The cost of keeping such records is marginally different to that of family selection, but the higher accuracy, control of inbreeding and ability to monitor genetic trends makes BLUP selection much better than individual selection. Furthermore, the cost of DNA pedigree recording continues to drop.

The importance of pedigree data

Probably the most fundamental question to ask when designing an aquatic breeding program is whether to record pedigree. This is sufficiently important that it deserves further comment.

Recording the identity of parents of fish in a breeding

operation is neither cheap nor easy. There are costs involved in either maintaining family tanks or in DNA fingerprinting, and fish marking and in data management. There are also potential compromises in production efficiency within the breeding program stock.

Given this, some real benefits from pedigree recording would be expected if it is to be worthwhile. Such benefits include:

Higher selection accuracy

Knowledge of pedigree, especially sire pedigree, has classically been seen as important information to provide to seedstock buyers in terrestrial species. This has not been for any rigorous technical reason, so much as a feeling that good sires leave good progeny - that like begets like. This was recognised by Charles Darwin in 1852 who stated that:

" ... the importance of the principle of selection in regard to Merino sheep is so fully recognised, that men follow it as a trade. The sheep are placed on a table and are studied, like a picture by a connoisseur; this is done three times at intervals of months, and the sheep are each time marked and classed, so that the very best may ultimately be selected for breeding."

Modern geneticists are luckier than Darwin because they know about genes and how they are transmitted. This means that information from relatives can be used to help evaluate individuals for their breeding value.

It is desirable to select the fish with the best genes because they will leave the best progeny. Relatives share some of their genes – for example full sibs (which share the same father and mother) share half their genes in common (see Figure 1). This means that how well a fish's relatives perform tells us something about the quality of that fish's own genes. Modern genetic evaluation analyses manage to balance the information from relatives to make the best estimates of breeding value (EBV). This results in faster genetic gains, most especially for traits with a low heritability - typical of disease resistance traits.

Pedigree information is also needed to estimate heritabilities and genetic correlations. These parameters can be used to help design more effective breeding programs and give more accurate EBVs.

Genetic links between different grow-out sites

In order to identify the best genes it is necessary to separate the merit due to favourable environment, nutrition and management from the merit due to good genes. Comparing the same genes at different sites can do this. But this does not mean having to raise

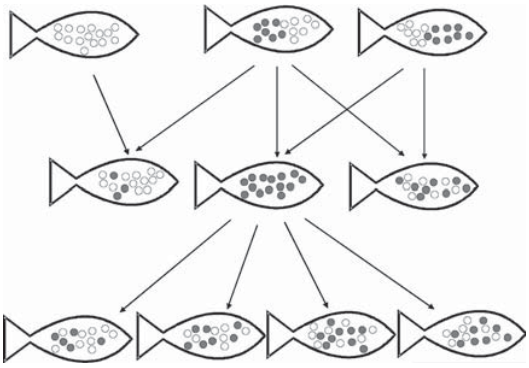


Figure 1. The fish in the middle of this pedigree shares his genes with his relatives (shaded circles represent the genes that this fish carries). So the performance of these relatives helps us to estimate the value of this fish's genes. The more distant the relationship, the lower the proportion of genes shared.

the same individual fish at different sites. Looking at Figure 1, it can be seen that the same genes exist in fish that are related. So if the performances of two half-brothers (same cock, different hens as parents), one at each of two grow-out sites, are compared, this gives a basis to separate genetic differences from environmental differences.

The tool to do this is BLUP genetic evaluation. It accounts for factors such as the fact that one of the brothers might have had a better quality mother. Of course more linkages than that provided by just two brothers are needed. But given this, BLUP will result in EBV's across farm sites which have taken account of the differences between sites in these confounding effects of environment, nutrition and management schedule.

This connection across sites requires pedigree recording - so that relatedness of fish in the breeding program at different sites is known. However, this gives a rational approach to exploiting breeding stock and lines across the whole industry.

A related benefit is the highly relevant and potentially accurate evaluation of outside stock that may possibly come to be imported. This also requires pedigree recording.

Helps guard against inbreeding

Development of accurate genetic evaluation systems giving EBV's across sites, could lead to the excessive use of excellent individual fish and their close relatives. This has been seen in domestic land animals - as breeders put more faith in EBV figures. Cases have been seen where most sires in a breeding population are the sons of one top sire - whose semen is also being used widely!

If pedigree recording is not available, inbreeding can only be avoided by reducing selection intensities. However, with pedigree recording, there is considerable power to ensure fast genetic gains while keeping inbreeding levels and rates at a low level, as described later. This also ensures maintenance of the genetic variability to give sustained genetic gains well into the future.

Enables selection on traits not measurable on live fish

Pedigree recorded fish that have carcass traits measured or are involved in disease resistance tests provide data to estimate EBVs on their live relatives that are candidates as seedstock.

Pedigree recording

There are two main options for recording pedigree:

"Family tanks": The classic option for pedigree recording in aquatic animals that are difficult to tag is to keep full-sib families of fish in separate tanks until they can be tagged. The number of families is limited by facilities, typically between 50 and 500 families are bred per year.

"DNA pedigreeing": The newer option is to use DNA fingerprinting. Over time, costs will reduce. The technology is being used in a number of aquatic breeding brograms.

DNA pedigreeing has some technical advantages over family tank designs:

(i) Fish can be mixed at any time, even as newly fertilized eggs. If possible, it is even permissable to mix sperm (or eggs) from different fish before fertilization, although this leads to some loss of control of selection pressure and design. This early mixing avoids confounding of family genetic merit with tank effects, which can be considerable. The result is more accurate selection, especially for family-based measures such as disease resistance and carcass traits. (Estimated 10 percent to 20 percent gain)

(ii) Cross-classified mating means that many more families can be generated. With 100 parents of each sex, up to 10,000 families can be generated. This gives a richer pedigree design (individuals have maternal half-sibs as well as paternal half-sibs), leading to more accurate EBVs and more gains. It also gives more information on non-additive (or 'nicking') effects, and more power to estimate parameters such as heritability from data on the resulting progeny. (Estimated 5 percent to 10 percent gain)

(iii) It may also allow a more commercially-typical rearing environment for fish in the breeding program, making the measurements taken more relevant and useful. (Estimated 10 percent gain)

Considering the cost of tissue sampling and genotyping progeny, family sizes will be reduced and this will constitute a component disadvantage (estimated 5 percent). However, there are some clever designs that help to manage costs while achieving a good response.

On balance, considerably more response to selection is likely to be achieved using the DNA pedigreeing approach.

For simple illustration, three options for a breeding program design are to be considered:

- Individual or mass selection (no pedigree)
- Family tanks
- DNA pedigree

The three options have different cost profiles, as shown in Figure 2.. These diagrams are not drawn to scale - it is the pattern that is important here. The time scale is probably about 4 or 5 generations, and returns will likely be generally much higher than indicated when integrated across an industry. Capital costs are incurred early and returns come late, which makes the profiles less favourable when discounting future dollars is undertaken. Ongoing costs for DNA pedigreeing are assumed to decrease in real terms over the next several years.

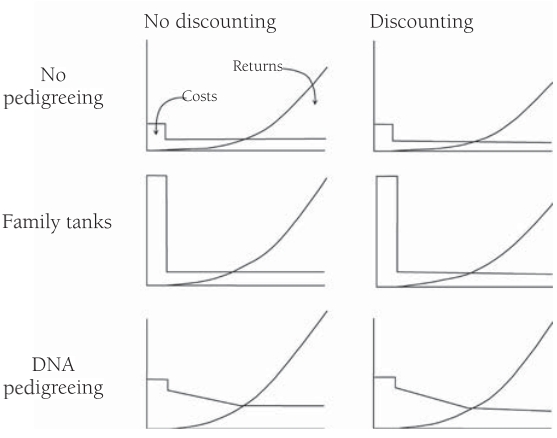


Figure 2. Three options for a breeding program design.

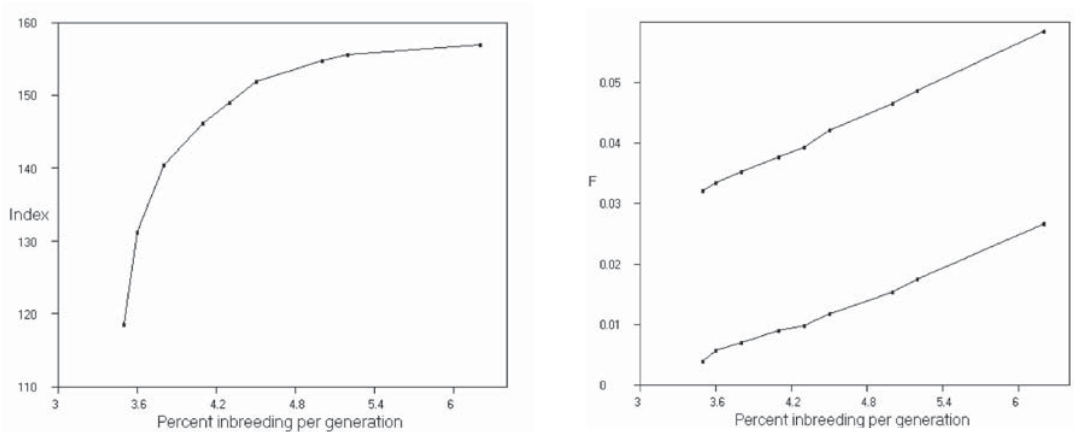


Figure 3. An example of the balance among genetic gain (Index), inbreeding rate per generation, and inbreeding level in progeny (F).

Maintaining diversity

The left pane of Figure 3 shows the range of options for a breeding program at the stage of making selection and mating decisions. 'Index' is a single score covering all traits. The connected points in the figure are possible outcomes predicted for progeny generated from the selections and matings made. Maximum gain reflects emphasis on selection of fewer parents chosen from the best few families – and this gives the highest long-term inbreeding risk (on the horizontal scale).

On the other hand, avoiding inbreeding by selecting across families also leads to lower gains. We want high index values but low inbreeding values, and the curve in the left pane of the figure is the frontier of optimal outcomes, given differing emphasis on genetic gain and long-term inbreeding. A key task is to decide where on this frontier we want to.

Long-term inbreeding is effectively the same issue as genetic diversity. Using more parents and/or less related parents gives more diversity and less inbreeding in the longer term. We can also avoid inbreeding in the short-term by minimizing the relationship between fish that are mated to each other. The right pane of the figure shows how the level of inbreeding in progeny conceived (F) can be reduced from the upper line (random mate allocation) to the lower line (minimum relationship mating, using full pedigree information). Results are lower to the left of the graph, as more sires are used giving more opportunity to avoid mating relatives.

This approach gives power to monitor and control the balance between genetic gain and genetic diversity.

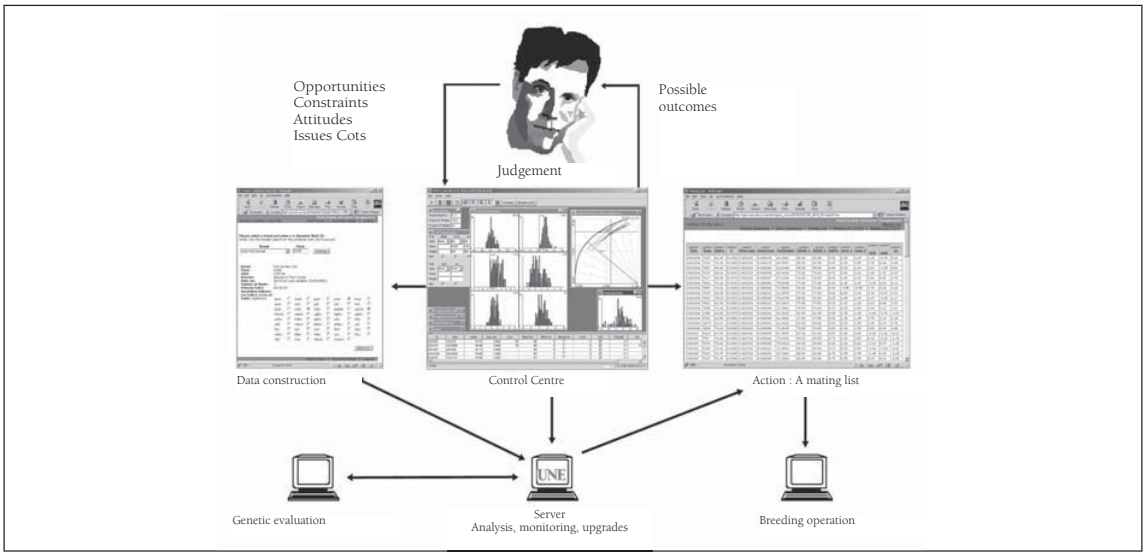


Figure 4. A mate selection system that allows dynamic viewing and choice of outcomes – Total Genetic Resource Management (see www.xprime.com.au).

Table 1. Some Animal Breeding issues.

Selection on EBV	Connection between sub-pops.
Genetic diversity	Corrective mating / trait distribution
Optimal contributions	Multiple objectives / line splitting
Progeny inbreeding	Scheduling to meet demand
Limits on reproduction	Seedstock dissemination
Logistical constraints	Quarantine barriers
Marker Assisted Selection	Other health management issues
Multi-stage selection	Use of reproductive technologies
Breeding population size	Costs
Crossbreeding	Funding limits

Mate selection - an integrating approach

Breeding program design can be pre-determined and implemented through sets of rules, or it can emerge as a consequence of decisions made at the level of individual matings. This latter is the tactical approach, with decisions made tactically in the face of prevailing animals and other resources. It has recently been taken up in the running of progressive breeding programs in sheep, beef, dairy, pig, poultry and some aquatic breeding programs (TGRM, illustrated in the Figure 4).

Tactical implementation of breeding programs provides a practical means to integrate technical, logistical and cost issues facing animal breeders. Moreover, tactical implementation benefits from opportunistically optimal use of prevailing animals and other resources, resulting in better outcomes.

In any breeding operation, there is an almost infinite range of actions – selections and matings, or "mate selection sets" - that can be made, involving decisions on issues such as those shown in Table 1.

Each mate selection set is predicted to have a given utility to the breeder - based on outcomes for these various issues. The tactical approach works by searching across these possible routes ahead, and finding one that is predicted to suit the breeder's needs, either the very best solution, or something sufficiently close to it. This has only recently become possible because of the development of efficient computing algorithms that mimic evolutionary processes to approach the best solution.

Lessons learned

Genus has a long history in many countries of running progressive breeding programs in pigs (through the Pig Improvement Company, PIC). The systems and know-how built up have formed a basis to develop both classical and novel approaches to breeding programs in shrimp (through SyAqua, in Hawaii, Mexico, Brasil, Thailand and recently in Kentucky). Genus also has R&D programs for genetic improvement in other species.

What lessons have been learned?

- Breeding programs have many elements in common across species, including:
    - Every animal has a father and a mother, with few exceptions.
    - The genetic information systems outlined in the appendix can be the same or similar across species.
    - All breeding programs need to define target directions/outcomes for genetic change, and achieve an optimal balance of fast genetic gains and conserved genetic diversity.
    - Many aspects of optimizing breeding program design are common across species. The best designs can be very different, but the underlying design methods and tools can be the same or similar.
    - The task of discovering genetic markers and mutations that are useful in breeding programs is very similar across species. The building of a "gene discovery pipeline" has given dramatic improvements in speed and cost-effectiveness across four key species, to date.
    - Designs for testing carcass and disease resistance traits have many aspects in common.
- Breeding programs have many key elements that differ across species, including:
    - Reproductive systems, levels, and behaviour can differ considerably across species, affecting ability to control and synchronize matings, manage mating ratios, preserve gametes, boost reproduction, generate polyploidy etc.
    - Other aspects of life-cycle differ, affecting the optimal timing and pattern of mating events and the optimal population structure.
    - Ease of tagging individuals can differ considerably, affecting the optimal balance, in both pattern and extent, of use of DNA pedigreeing, family containment and other pedigreeing/family evaluation strategies used.

- o Production environments can differ dramatically, especially for aquatic species, so that we must pay specific attention to development of performance under a range of conditions.

When launching breeding programs in novel species we have the double task of exploiting existing tools and know-how, while having a good understanding of those factors that make this species require custom systems and breeding management. With the ongoing emergence of aquaculture, a number of organizations are gaining experience in this double task. It can be achieved in a sufficiently large organization with an R&D chain that comprises connected teams in groupings such as:

1. Development of fundamental quantitative and molecular methods and core tools across all species

2. Development of applicable components that are as species-specific as required: databases, genetic evaluation, mate selection, etc. (see Appendix).

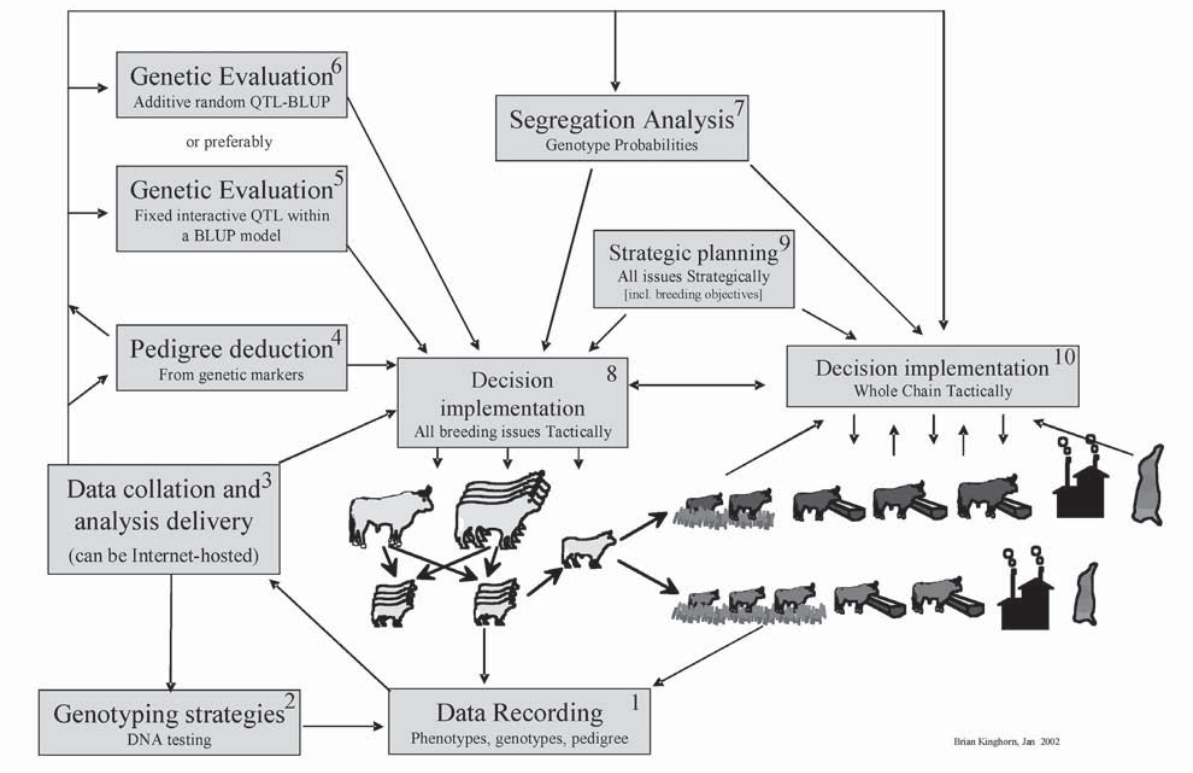
3. Implementation of breeding programs in teams dedicated to one or a few species, using tools and support from all parts of the chain.

The closer to practical application, the more species-specific activities become.

The question can be asked: Should we just run simple programs, such as mass selection, in developing countries where resource and skill levels may be limiting? This is a valid point for many terrestrial species such as cattle, but the high fecundity of most aquatic species means that we can concentrate high-quality breeding effort in relatively small and contained breeding programs, at a relatively low cost. The biggest challenges remaining may then be data recording at field test sites in different environments and dissemination of genetically improved stock to industry.

Appendix : Information system

1. Data Recording. This is a key component. In some cases, special tools and methods are required to make measurements, especially for traits related to carcass quality and disease resistance. Robust and accessible databases are critical to exploitation of progressing approaches such as mate selection.



Some Key information systems in animal breeding.

2. Genotyping Strategies. Genotyping is becoming increasingly widely practiced, with applications using both genetic marker loci and known gene loci. Inferring genotype from the known genotypes of relatives and/or linked loci has the potential to play a useful role in reducing costs of tissue sampling and genotyping. Segregation analysis, described below, can be used for calculating genotype probabilities. These in turn can be used in an iterative genotyping strategy – they are used to help choose which individuals and loci to genotype in each iteration.

3. Data collation and delivery. Our experience is that the Internet facilitates very effective distributed deployment of services using operators located close to end-users/customers. Internet hosting also provides opportunities for technical support, and a simpler path to scaling up operations.

4. Pedigree deduction. Good method and software can be used to solve complex parent-allocation problems – such as to deduce the parents of progeny out of a syndicate mating of tens or hundreds of parents.

5. Genetic Evaluation – Fixed interactive QTL within a BLUP model. Direct or 'diagnostic' markers are simplest to use here, as we can treat them as fixed but interacting effects. For linked markers, we can modify transmission probabilities in segregation analysis to calculate QTL genotype probabilities.

6. Genetic Evaluation – Additive random QTL BLUP. This is increasingly being used for genetic evaluation where genetic marker information is available. It is a relatively simple extension of classical method. However, it aims to more accurately evaluate the average genetic merit of individuals for given traits, and misses the added opportunities to exploit the known mode of action of discovered genes, and the interactions among them that we increasingly find to be important.

7. Segregation analysis. This type of analysis is key to a number of genetic information systems, including items 2, 4, 5 and 8 in this list.

8. Tactical Decision Implementation for breeding. As described above. This integrates technical, logistical and cost issues affecting breeding decisions into a single framework.

9. Strategic Planning tools. Integration of a range of design evaluation and planning tools into a single project-planning framework.

10. Decision Implementation for whole supply chain. Design in animal breeding and production programs is classically implemented through sets of rules to follow. However, a tactical approach uses all prevailing information to develop an action report that dictates management decisions directly.