Research in QTL Analysis

Searching for QTL in designed experiments

Designed experiments are employed to guarantee linkage disequilibrium between the genetic markers and the QTL, and also to limit the number of possible alleles segregating at a QTL. Many QTL studies in domestic livestock have used wide crosses, involving an economically relevant breed and a distantly related economically irrelevant breed. Alternatively, a number of large paternal half-sib families can be generated from existing outcrossed populations. The latter design carries less risk of producing results that are irrelevant to commercial breeding populations.

The main difference between analysing data from designed experiments and data belonging to "farm" or "complex" pedigrees is the handling of the effects of polygenes. In designed experiments polygenic effects can safely be assumed to be part of the residual error because of the balanced nature of the data. In complex pedigrees the polygenic effect must be fitted explicitly in the model.

To analyse data from designed experiments AGBU has developed a comprehensive suite of software.

Linkage Mapping

Before QTL mapping can proceed it is usual to derive chromosomal linkage maps using the resource population. AGBU has traditionally relied on Phil Green’s CRIMAP software for generating maps, but has developed a suite of accompanying programs to facilitate the process. These programs perform formatting tasks, tests of segregation distortion and removal of unlikely multiple recombinants. AGBU has recently built the Bos Taurus consensus map for chromosome 19, under the auspices of the International Society of Animal Genetics.

QTL Mapping

QTL mapping software developed at AGBU can analyse data on a number of paternal half-sib families.

There is software to perform forward-backward stepwise regression on average transmission probabilities to determine the best fitting model of regressor variables. These regressor variables are included as cofactors when analysing specific QTL. They help to reduce the error variance.

The suite of software developed for QTL mapping can either perform single marker analysis or search for QTL in intervals defined by adjacent pairs of markers (interval mapping). The software has a unix feel and is operated by specifying values for a number of command line switches. The switches allows the user to specify

- single- or multiple-trait analysis
- single- or multiple-family analysis
- use of significant, unlinked regions as cofactors
- use of regression or maximum likelihood to derive solutions
- permutation tests
- tests of pleiotropy
- tests of pleiotropy versus 2 QTL each affecting different traits.

A feature of the software is its versatility. Many types of analysis can be performed on the data. A partial scan can be specified if the
user has no need to perform a full genome scan. Batch jobs can easily be set up using the command line.

The multiple-family analysis uses a recently developed expectation maximization (E-M) algorithm. This algorithm was developed by Richard with the assistance of Professor Geoff McLachlan at the University of Queensland. (A paper is currently in preparation - link to abstract). It has proved to be a more robust method than employing numerical techniques. It can provide posterior probabilities of individual sires segregating for the QTL and of the linkage phase between the marker alleles and the QTL alleles.

Future Developments

Alternative models are being investigated to improve the genetic evaluation of the fertility traits in OVIS. This also requires modification of analysis to better incorporate non-naturally mated animals (eg embryo transfer animals etc).

Addition of new traits into OVIS

Linkage mapping software that can be used in complex pedigrees is planned. CRI-MAP uses the Elston-Stewart algorithm (peeling) to determine genotype probabilities for those individuals in the pedigree that have not been genotyped for a particular locus. This algorithm may produce biased results with marriage or inbreeding loops. This software will be required when complex pedigrees will be used to generate the maps, rather than pedigrees from designed experiments.