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Reassessing methods to improve quantitative traits used in breeding programmes in the light of information from molecular biology

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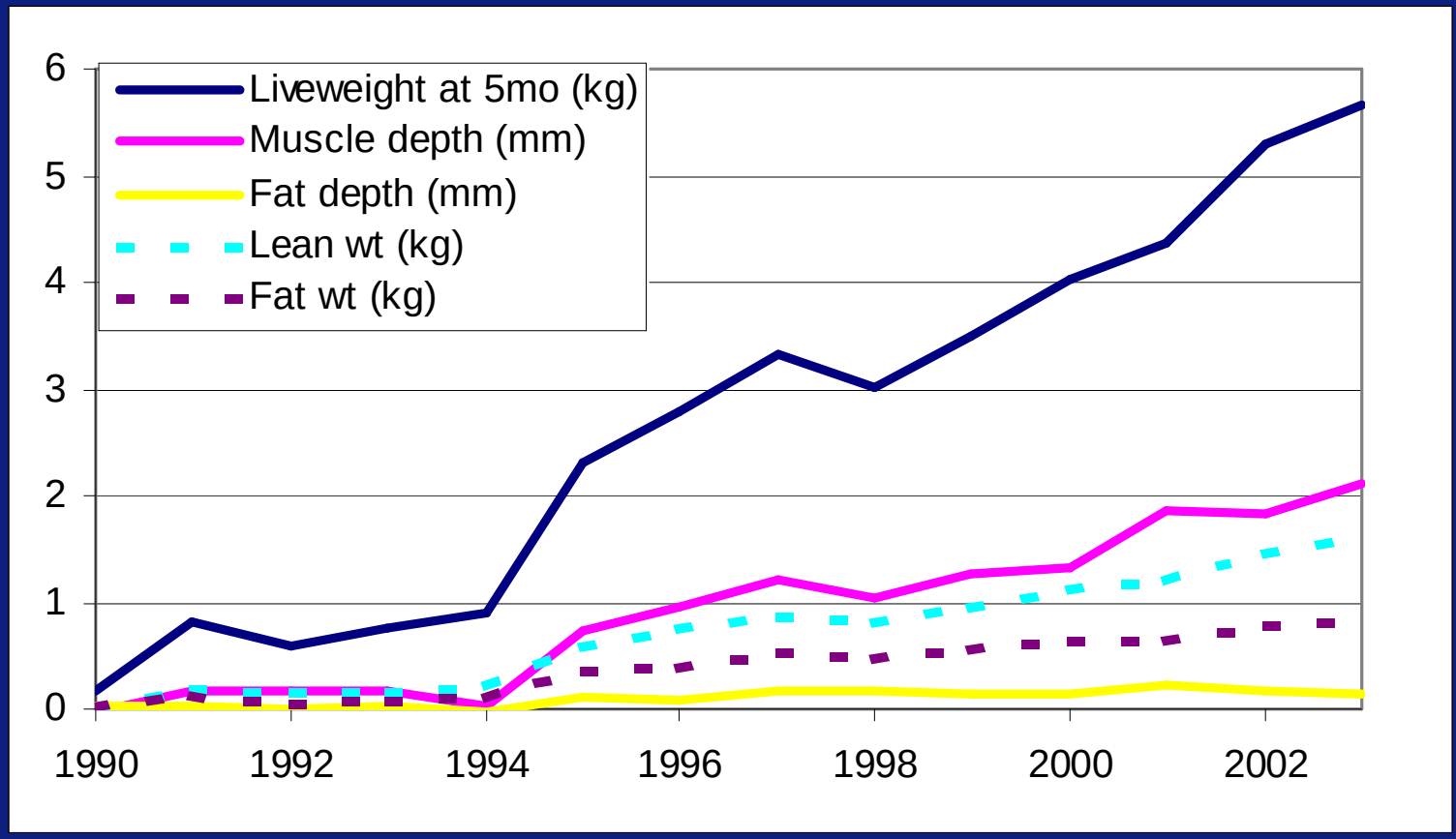
Introduction

- Current quantitative genetic tools have been very successful at changing characteristics of selected populations

Genetic trends in the Wye Suffolk lamb crop



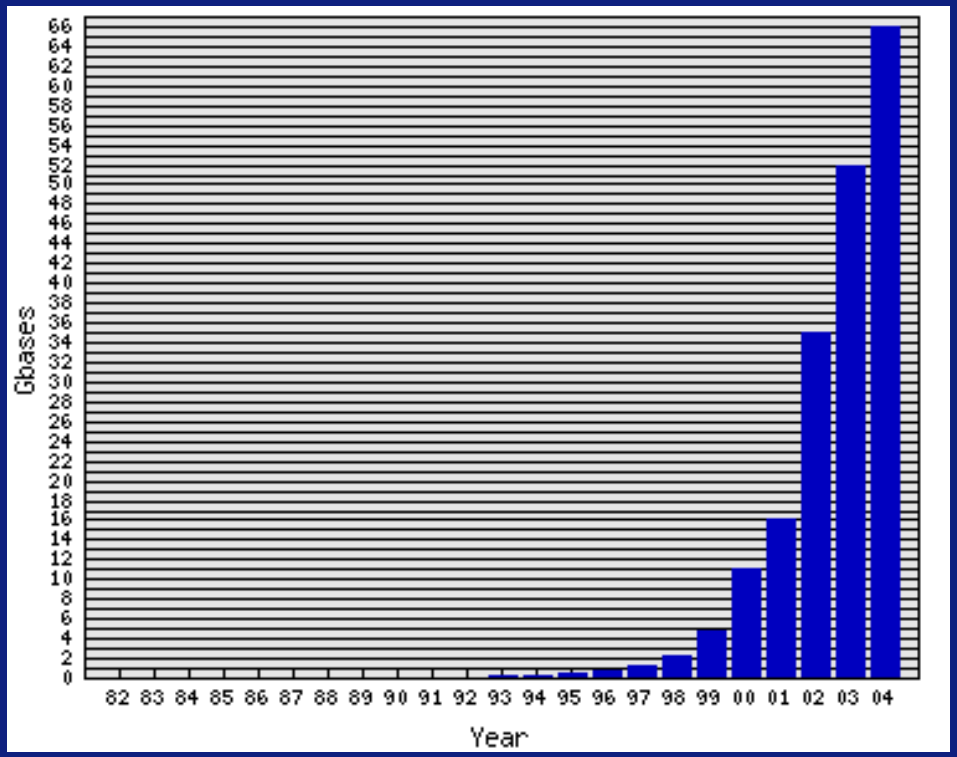
Source: Routine records from Wye Suffolk flock

Mean phenotypic values: 35kg (LWT), 28mm (MD), 3mm (FD)

Introduction

- Current quantitative genetic tools have been very successful at changing characteristics of selected populations e.g. Terminal sire breeds in UK
- Over the last 10 years the application of molecular biology has generated vast quantities of genetic data publicly available on the web

Growth of nucleotide sequences in EMBL database



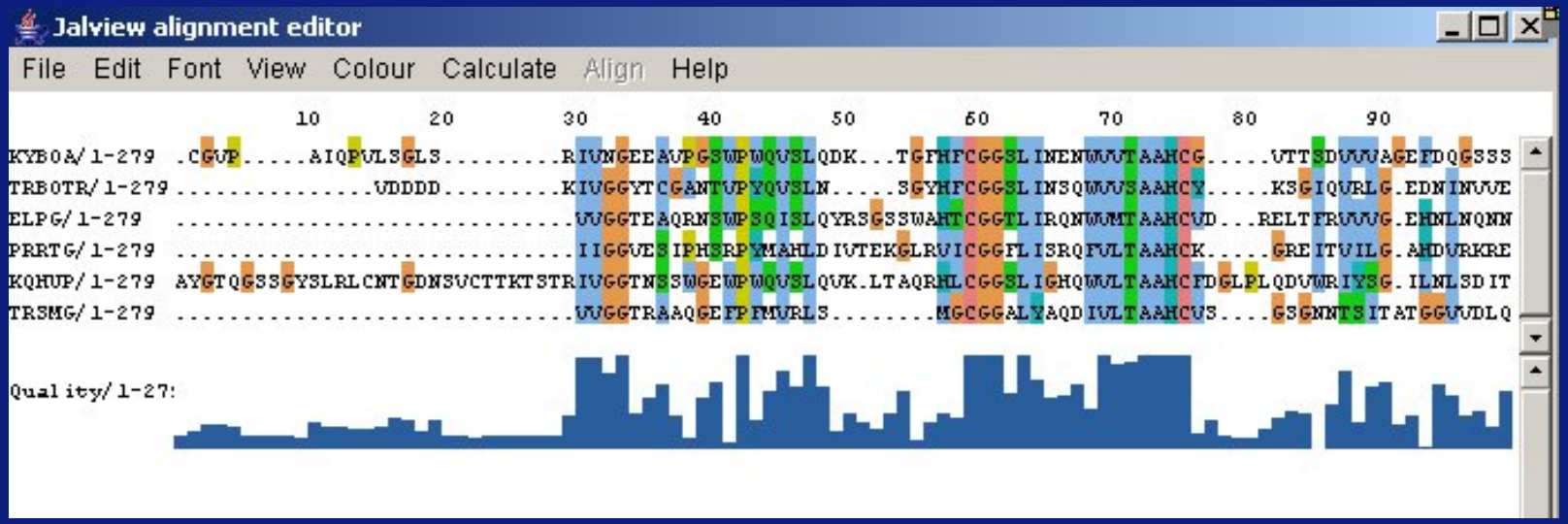
Many other databases available:

Genes, RNA, proteins, SNP,EST etc. with both raw sequences and annotated with a wide range of information.

Introduction

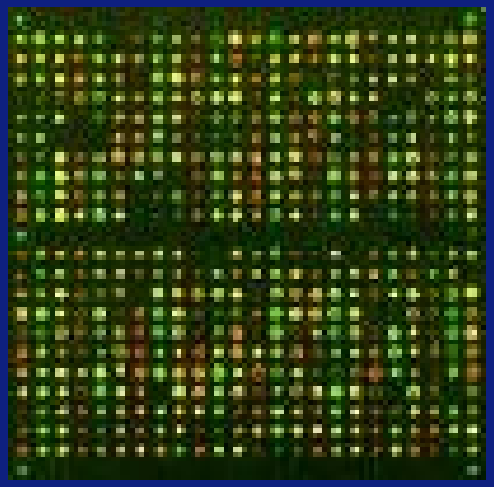
- Current quantitative genetic tools have been very successful at changing characteristics of selected populations e.g. Terminal sire breeds in UK
- Over the last 10 years the application of molecular biology has generated vast quantities of data publicly available on the web
- Molecular biology has created many new methodologies and tools

Methodologies



Some examples

- Sequence alignment
- Phylogenic analysis
- Microarrays



Largely unused in animal breeding schemes

Current quantitative genetic theory

Infinitesimal model

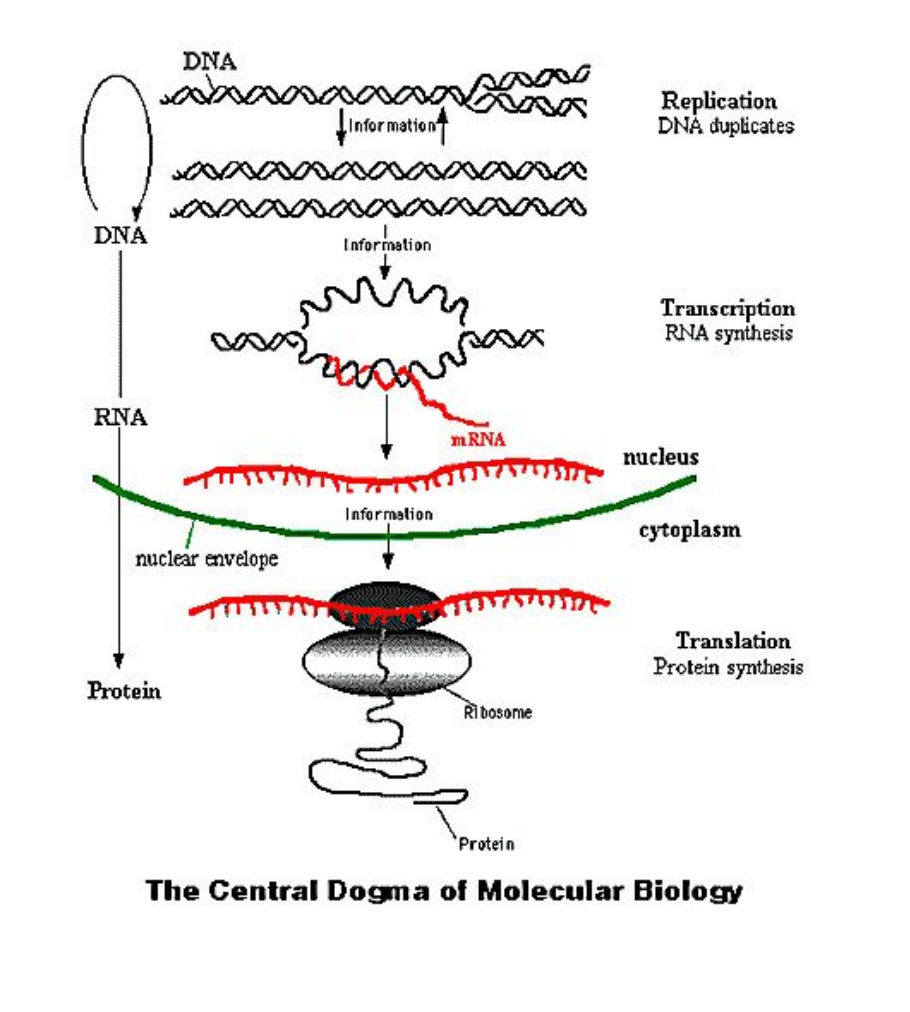
P = A + D + I + E + GxE + error (residual) + others

Population variances

Selection

Genes with large effects and QTL positioning – marker assisted selection

Central dogma of molecular biology and the ‘omics – the links between a gene and a trait



The Central Dogma of Molecular Biology

Genomics

Transcriptomics

Proteomics

Metabolomics

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Questions to address

1. Does new molecular information change the basic model used in quantitative genetics?

2. What will be the situation in, say, 10 years time?

3. Do we need new tools to improve QT?

4. What new information should be collected routinely on farms to prepare for the introduction of new methods?

Does new molecular information change the basic model used in quantitative genetics?

Central Dogma, additive and environmental effects

Additive effects

- Large amount of additive effect remains
- DNA does not always determine trait breeding value directly
- Not all DNA/RNA/Proteome effects are additive – e.g. transcription factors in promoter regions can have multiplicative effect
- Error term contains “genetic” effects

Environmental effects

- Environment only affects the animal via its downstream metabolic pathways
- All have a genetic basis, modified by a range of post genomic factors
- Some pathways largely inviolate; some very responsive to environmental changes
- Individual animal GxE effects lost in error term

What will be the situation in 10 years time?

Future scenario

- Amount of information will continue to grow and be available to all (in research community?)
- Computers will become faster, larger, cheaper
- DNA, RNA, Protein extraction, sequencing and analysis will become cheaper
- What is now experimental will become routine
- Move away from population evaluations to individual evaluation based on knowledge of genome etc.

Future knowledge

- Know which DNA sequences determine a QT
- mRNA/cDNA profile of these sequences
- Proteins coded by these mRNA, their functions and levels of expression
- Tissue and time specific mRNA etc.
- SNP profile of individual animals
- Complete genome to phenotype pathways

Do we need new tools to improve QT?

Possible new methods

- Tracing and analysing SNP in a closed herd – analogous to sequence alignment with proteins
- Link patterns of SNP to trait value/level of expression - SNP to QTL to performance differences
- Pattern scoring system – relative values linked to genome models and modified by environment
- Link genes with level of expression in quantified environmental factors - Under what conditions are genes expressed, level of expression, what other genes required to influence this?
- Model a trait from genome, through proteome and metabolome to phenotype as a prediction tool

Future work with quantitative traits

- Define a trait in terms of its metabolome, proteome and hence genome. Use as the basis for evaluation.
- Identify all (majority of) QTL affecting a trait – use human/other mammalian genomes by homology if neccessary
- Timing and positioning of samples from gene expression sites will be crucial – welfare considerations
- Real effect of the environment on gene expression and QT value
- Move towards evaluating an animal as an individual rather than as a member of a population – this animal has these genes which influence this trait in this environment

What new information should be collected routinely on farms to prepare for the development of new methods?

New information

- Collect and store useable DNA samples from all performance recorded animals – Minimum scenario – Start now
- Build within-herd databases of SNP information
- Environmental measures appropriate for QT in a DNA context – Minimum scenario – Start now
- Appropriate mRNA/cDNA for gene expression in particular tissues – Strategy for welfare-friendly collection required
- Whole genome SNP for QT critical sites – Some way off but critical

Conclusions

- Current theory produces results so why change it?
- The inherited portion of trait values modified at all levels post-transcription
- New methods needed to utilise vast pool of new data
- Still more data required – within herd variation – SNP
- Start collecting new data now

Thanks for listening