Institution: University of Edinburgh and SRUC, Scotland’s Rural College

Unit of Assessment: 6

Title of case study: The development of genomic selection and application through optimal contribution theory in livestock breeding

1. Summary of the impact (indicative maximum 100 words)

Impact: Economic: Genomic selection has revolutionised, and is now standard practice, in the major dairy cattle, pig and chicken breeding programmes, worldwide and provides multiple quantifiable benefits to breeders, producers, consumers and animals.

Significance: Increased food production world-wide
Beneficiaries: Breeding companies, primary producers, consumers, livestock.

Attribution: Work led by Haley and Woolliams (Roslin Institute now part of UoE).

Reach: Methodologies applied worldwide in livestock improvement, and more recently applied in human genetics and plant breeding.

2. Underpinning research (indicative maximum 500 words)

The key insight, first made by Prof. Haley (Group Leader, Roslin Institute and UoE employed 1985-onwards) and senior postdoc Visscher (Roslin institute employed 1995-2007) in 1998 [3.1] was the realisation that dense single nucleotide polymorphism (SNP) arrays could be applied to livestock improvement in several ways. Critically, as well as being used to identify the locations of gene variants affecting phenotypes, SNP arrays can also be used to make whole genome prediction of genetic merit for complex traits (recently exemplified for height in humans [3.2], led by Visscher). Based upon this original work, the application of whole genome prediction to animal breeding was developed further by Meuwissen et al. [3.3] and is now standard in dairy cattle breeding programmes. Further, recent advances led by Prof. Woolliams (Group leader, Roslin Institute and UoE, employed 1977-onwards) [3.4, 3.5] have guided implementation in dairy cattle and more recently in the poultry industry. Pig and beef industries now also implement this technology.

The basic concept of genomic selection is that a dense SNP chip can ‘tag’ every chromosomal ‘segment’ of an individual, and with pre-calibrated data the genetic merit of an animal for any measureable performance trait can be predicted accurately. Potentially this revolutionises breeding practices, allowing identification of genetically superior animals essentially at birth. This makes breeding programmes more efficient, and allows selection for traits that would otherwise pose huge logistical difficulties, e.g. disease resistance, product quality or environmental impact.

The greater the efficiency of a breeding programme, the greater the danger of unintended side effects arising from erosion of genetic variability, genetic bottlenecks and inbreeding. Research at Roslin addressed and solved this problem, and provided the tools to implement the solutions in practice. Specifically, **optimal contribution theory**, developed and published by Prof. Woolliams in 1999 [3.6], provided the theoretical basis to balance genetic selection and conservation of genetic resources (including avoidance of inbreeding). This theory now has now been extended by Woolliams and colleagues to include genomic selection using dense SNP chips.

Through industrial collaboration, Roslin-led research (Woolliams) produced software to evaluate and implement these solutions. All major breeding programmes in the intensive breeding industries (pigs and poultry) are now guided by this theory and its principles.

3. References to the research (indicative maximum of six references)

3.1) Haley, C.S. and Visscher, P. M. (1998) Strategies to utilize marker-QTL associations. Journal of Dairy Science 81: 85-97. http://dx.doi.org/10.3168/jds.S0022-0302(98)70157-2

3.2) Yang J.A., Benyamin, B., McEvoy, B.P., Gordon, S., Henders, A.K., Nyholt. D.R., Madden, P.A., Heath, A.C., Martin, N.G., Montgomery, G.W., Goddard, M.E. and Visscher, P.M.

(2010). Common SNPs explain a large proportion of the heritability for human height. Nature Genetics 42: 565-U131. http://dx.doi.org/10.1038/ng.608

3.3) Meuwissen, T.H.E., Hayes, B.J. and Goddard, M.E. (2001). Prediction of total genetic value using genome-wide dense marker maps. Genetics 157: 1819-1829. http://www.genetics.org/content/157/4/1819.full

3.4) Daetwyler, H.D., Villanueva, B., Bijma, P. and Woolliams, J.A. (2007). Inbreeding in genome-wide selection. Journal of Animal Breeding and Genetics 124: 369-376. http://dx.doi.org/10.1111/j.1439-0388.2007.00693.x

3.5) Daetwyler, H.D., Villanueva, B. and Woolliams, J.A. (2008). Accuracy of Predicting the Genetic Risk of Disease Using a Genome-Wide Approach. PlosONE 3: e3395. http://dx.doi.org/10.1371/journal.pone.0003395

3.6) Woolliams, J.A., Bijma, P. and Villanueva, B. (1999). Expected genetic contributions and their impact on gene flow and genetic gain. Genetics 153: 1009-1020. http://www.genetics.org/content/153/2/1009.full

4. Details of the impact (indicative maximum 750 words)

The concept of genomic selection was first developed by Haley and Roslin/SRUC have remained at the forefront of the development and implementation of genomic selection. Optimal contribution theory (described above), provided the theoretical basis to balance genetic selection and conservation of genetic resources (including avoidance of inbreeding) and has been adopted by breeding companies [5.1]. Applications of genomic selection currently have the greatest quantifiable impact in the dairy cattle breeding, poultry and pig breeding industries.

Impacting dairy cattle

Dairy cattle breeding is a multi-million dollar international industry and genomic selection has been implemented in large national breeding programmes since 2008 (initially in the US, Canada, Australia, New Zealand, Ireland and The Netherlands). It now has been extended to nearly all major breeding programmes, including the UK (led by SRUC) in 2012. When implemented in dairy cattle breeding, compared to traditional progeny testing, genomic selection double rates of genetic progress whilst, at the same time, reducing costs of the breeding programmes [5.2]. Currently, virtually all bull semen commercially available to dairy farmers comes from bulls evaluated using genomic selection/prediction techniques. However, cows born from genomically-selected bulls have probably been milking for only 2 years in the REF impact window, in countries that were earliest to adopt. Genetic trends for the dairy populations in the US and Canada were analysed recently [5.3]. Attributing only half of the recent additional genetic gains from the use of young bulls to genomic selection – which is likely to be conservative - suggests that genomic selection has contributed at least £200M to these dairy industries in the last 2 years. This will rise rapidly as more of the population descends from genomically-selected parents.

Impacting poultry

Poultry breeding achieves benefit through the extremely rapid multiplication of stock. At Aviagen (an Edinburgh-based poultry breeding company) a single male bird in the breeding nucleus today can be the great-great-grandparent of ~50 million birds in 4 years' time, producing ca. 76,000,000 kg of meat. Thus, small improvements in the precision with which superior birds are identified and utilised in the breeding nucleus scales up to huge benefits at the consumer level, after only four years [5.2]. Conservatively, we may expect a genetic improvement in productivity due to selective breeding of ca. 1% per year (as shown by 5.3), i.e. an extra 760,000 kg from a single male bird after 4 years, with these benefits cumulating across all male birds used in the breeding nucleus, and also cumulating over years with each successful round of selection.

Increased precision of selection further increases these gains: Aviagen implemented genomic selection in 2012 and an improvement of 20% in the identification of genetically superior males would lead to a further 152,000 kg of meat per nucleus male breeding bird per year. Aviagen's activities lead to 50% of the world's marketed chicken and >50% of the world's turkey.

Further, scientists controlling the Aviagen breeding programmes are almost entirely Edinburgh trained, and The Roslin Institute currently advises Aviagen on its breeding strategies and on optimal implementation of genomic selection.

Impacting pigs

Optimal contribution theory has enabled efficient and sustainable breeding programmes to be implemented in many species, and it is the key to efficient long-term exploitation of both traditional and genomic selection. Its current impact is best illustrated through interactions with Genus, formerly PIC, which runs the world's largest pig breeding programme [5.1].

Genus currently has a 36% share of the "technified" (improved genetics) segment of global pork production, which comprises 40% of global pork production. Therefore, Genus contributes the genetics for 14% of total global pork production.

A LINK-funded project "Sustainable use of animal genetic resources" (1999-2002) involving Roslin, SRUC, Genus and two other partners identified optimal contribution theory as the single most potent technology to bring an immediate clear improvement to the breeding system, with a predicted 10-25% increase in genetic gain [5.4]. This extra gain was assessed using software [5.5] developed through a joint Roslin initiative, which is now widely used within the breeding industry. Genus implemented these concepts through placement of a geneticist within the Roslin Institute, from 2002 onwards.

Optimal contribution theory was first implemented into Genus breeding programmes in May 2003, however the major benefits have arisen since its use was scaled up after 2008. The company currently uses optimal contribution theory to optimize selection and matings, on a weekly basis, in 33 GN status lines from 10 farms on 4 continents. The data included in these evaluations stretches back ~25 generations to the early 1980s. Over 13 million records are used in routine genetic evaluations, which are performed weekly. Over 54 million piglets born alive are registered in the Genus database, resulting from application of this technology, contributing substantially to the world supply of pig meat, as indicated by their global share described above.

5. Sources to corroborate the impact (indicative maximum of 10 references)

5.1) David McLaren, Genus PLC. http://tinyurl.com/loqw5z6

5.2) Hayes BJ, Bowman, PJ Chamberlain, AJ Goddard, ME (2009). *Invited review*: Genomic selection in dairy cattle: Progress and challenges. Journal of Dairy Science 92, 433–443. http://dx.doi.org/10.3168/jds.2008-1646

5.3) "The impact of genomic selection on North American dairy cattle breeding organizations", a presentation by J. Chesnais, *et al.* http://tinyurl.com/pg2vofj

5.4) Avendaño, S., Watson, K.A. and Kranis, A. (2010). Genomics in poultry breeding – from utopias to deliverables. Proceedings of the 9th World Congress on Genetics Applied to Livestock Production, 9:49. http://tinyurl.com/nfzayej

5.5) Van der Steen HAM, Prall GFW and Plastow GS (2005). Application of genomics to the pork industry. Journal of Animal Science 83, E1-E8 http://tinyurl.com/oojjjn4

5.6) Rutten, MJM, Bijma P, Woolliams JAM and van Arendonk JAM. (2002). SelAction: Software to Predict Selection Response and Rate of Inbreeding in Livestock Breeding Programs. Journal of Heredity, 93, 456-458. http://dx.doi.org/10.1093/jhered/93.6.456