New traits for dairy cattle breeding.

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Abstract

Phenomics is the discipline of deriving methods to accurately describe the characteristics of an animal. Being able to routinely and accurately measure, and predict, the (future) performance of an animal (and therefore system) is useful both in day-to-day farm management but also in optimising genetic gain. Animal characteristics, often termed phenotypes, can be broadly classified into: 1) producer scored – mastitis, lameness, milking speed, temperament, 2) professionally scored/recorded – linear type classification, veterinary surgeons, artificial insemination technicians, 3) technological – mid-infrared spectroscopy of milk, reproductive tract ultrasound, video image analysis, 4) statistical – herd-level solutions from genetic evaluations after accounting for genetic and selected non-genetic effects, 5) genomics – contribution to personalised management and risk assessment, 6) "next generation" – transcriptomics (i.e., expression profile for genes at a given time period), and 7) experimental – extensive phenotyping (e.g., immunological challenge) of a smaller number of animals divergent for a characteristic under investigation (e.g., genetic merit). The collation of all data sources into a useable format that can be relayed back, in an easy-to-use format, to the producer via a decision support tool, will require a concerted, multi-disciplinary, and multi-national effort.

Keywords: phenotype, breeding, genetic, dairy

Introduction

Most commentary in dairy cattle breeding nowadays relates to genomic selection. However routine access to accurate phenotypes, on a large population of animals, is still necessary for accurate and up-to-date relevant “genomic keys” or estimates of genetic marker effects. Furthermore, genetic gain is expected to be at least 50% greater with current genomic selection approaches (McHugh et al., 2011; Pryce et al., 2010; Lillehammer et al., 2011). This is mainly achievable through the greater use of younger males rather than previously where only proven bulls, following progeny test, were used widespread. Increased genetic gain, especially if not undertaken concomitant with a detailed phenotyping strategy, can reduce the opportunity to purge out deleterious effects, especially if not identified in the phenotyping strategy. For example, sub-clinical measures of disease are often not recorded (or sometimes not even recognised by the producer) but may be early warning signs of unfavourable correlated responses to selection. Moreover, the consumers in the near future are likely to demand more diverse breeding goals which include traits such as animal welfare, animal disease, product quality (i.e., nutritional quality and consistency), and environmental footprint. To-date phenotypes for many of these traits are generally lacking.

Phenotypes, a term often used to describe characteristics of an individual (e.g., an animal), can be broadly classified into: 1) producer scored, 2) professionally scored/recorded, 3) technological, 4) statistical, 5) genomics, 6) “next generation”, and 7) experimental (monitoring). Here we describe each of these strategies. Although, most phenotyping exercises and discussions on phenotyping in dairy cattle focus on the mature animal, cognisance must also be given to the nulliparous animal. The critical importance of phenotypes in Irish dairy cattle breeding is testified by the number of co-authors on this article, all heavily involved in phenotyping of cattle in Ireland.

Producer scored

Producers are consistently interacting with their livestock and therefore provide an excellent source of “on-the-ground” data. Biasing herd average performances can of course easily occur with producer scored traits, consciously or not, by under-recording. However, because modern genetic evaluations are based on contemporary comparisons, systematic under- or over-recording of incidence data or manipulating mean performance will not greatly affect genetic evaluations. However, preferential treatment bias, where all but a few (or one) animal are scored poorly (or managed differently) can influence genetic evaluations and is currently a source of concern in bias of genomic evaluations.

Examples of producer scored traits include calving difficulty, mastitis, lameness, other health events, farmer satisfaction/workability, temperament, and milking speed; less commonly recorded phenotypes include body condition score. Direct calving difficulty (Purfield et al., 2012) and farmer satisfaction/workability (Berry et al., 2007; Visscher & Goddard 1995., Cue et al., 1996) are low to moderately heritable while farmer scored health events tend to be even more lowly heritable (Berry et al., 2010; Pryce et al., 1998). However, health and fertility traits tend, on average, to be lowly heritable irrespective of the data source (Berry et al., 2011b), which could in part be due to the genetic architecture but may also be due to greater inaccuracies of recording. In beef cattle, docility at weaning and calf quality at weaning age, both measured by Irish beef farmers at weaning are moderate to highly heritable (Pabiou et al., 2012; Crowley et al., 2011) and in the case of calf quality are moderate to strongly genetically correlated with carcass quality and value (Pabiou et al., 2012).

The main advantage of farmer scored traits is that they are inexpensive to record as long as the necessary systems for ease of recording and uploading of data to national databases exist. The main disadvantage of farmer scored traits is that they are subjectively recorded and this can contribute to a reduced heritability due to the introduction of residual variation into the phenotypic variation. However, if all producers score these traits then large progeny group sizes will be achievable and thus high accuracy of selection will prevail, even with low heritability. Although many dairy bulls now used are genomically tested without any phenotypic information, access to accurate traditional breeding values is still required for accurate genomic predictions.

Phenotypes that are not commonly recorded by producers in many countries but that should possibly be considered include calf viability as well as traits such as the intensity and duration of oestrus. Technological advances may help reduce the necessity for producers to record a plethora of phenotypes and are discussed in a later section. For example, electronic milk recording that records the initiation and completion of milking, may supplement farmer scored milking speed and similarly milking temperament could also be scored by milk recording meters that can identify when milk clusters are kicked off. The heritability of actual recorded milking speed is greater than that of farmer scored milking speed (Rensing and Ruten, 2005). Furthermore, automated body condition score (Roche et al., 2009) may replace (or supplement) farmer scored body condition score.

Professionally scored

Many professionally scored phenotypes exist in dairy cattle and probably the most well known is linear type classification scored by trained classifiers. Linear type traits describe different morphological characteristics of an animal including body size, feet and legs, and structure of the mammary system (Coyne et al., 2012). Other professionally recorded traits include health/disease diagnosed by veterinarians (Emanuelson et al., 1988), feet and leg ailments recorded by professional hoof trimmers (Buch et al., 2011; Van der Waaij et al., 2005; Van der Linde et al., 2010) and cow insemination information recorded by AI technicians (Berry et al., 2012b).

Professionally scored traits, although probably scored with greater accuracy (at least consistency) across herds generally incur a cost of recording. Key to minimising the cost of recording many of these data, without the requirement for legislation, is to: 1) provide feedback, in a useful and understandable format for the recorder to improve the profitability of their business, or 2) remove the necessity of duplicate recording or transcribing such as may be required for receipt and payment. In the case of providing information for use in a business model, veterinarians, for example, may be given access to herd summary (and individual cow information) for all their clients. These phenotypic measures may be adjusted for genetic merit effects and therefore may better reflect management (see section on statistical phenotypes). Herds performing poorly relative to contemporaries may therefore be easily identified and remedial or prophylactic action can be taken. Problem animals within these poorly performing herds may also be easily identified. Furthermore, herd temporal trends may be easily identifiable and action taken early. Linking these data to animal movement information and the herds the purchased animals originated from, can provide very useful information especially on likely disease status. This type of information can be very useful for veterinarians but can only be accomplished if veterinarians (and producers) accurately record the data. Accurate recording of data is likely to be an iterative process at the beginning with the observable benefit from herd reports prompting greater, more accurate and more complete recording.

Given the cost of some professional recording systems, 1) the usefulness of the gathered information, and 2) alternative methods of recording to reduce costs must be constantly investigated. For example, one of the main objectives in collecting linear type classification information was its apparent association with cow functionality and longevity. However, health traits such as mastitis and lameness are now routinely recorded in most countries, as is animal longevity. Although the heritability of these traits tend to be low (Berry et al., 2011b), the improvement in accuracy of selection from inclusion of linear type traits in multi-trait genetic evaluation for these functional traits is generally low, in Ireland at least, because of the low level of recording of linear type trait information. Nonetheless, linear type trait information also provides clear information of the morphological structure of the animal including its mammary system and can be used in assortative mating programmes to rectify or improve any unfavourable cow characteristics such as poor teat placement. The routine use of such information by dairy farmers, however, should be quantified and a cost: benefit analysis on the recording of linear type trait information undertaken. Coincidently, a similar conclusion is evident for linear type classification in beef; access to serial live-weight measurements and carcass information questions the requirement for costly linear type classification although the latter does provide an early indication of the performance of an individual (McHugh et al., 2012; Pabiou et al., 2012) where no progeny information is available. However, has a cost: benefit analysis ever been undertaken?

Alternative methods to professional recording of traits also exist and are discussed in greater detail in the section “Technological phenotypes”. In Ireland do-it-yourself milk recording (Berry et al., 2006) is used in 25% of herds that milk record. Although this method still requires a professional to distribute the milk meters to farms, there is no requirement (and therefore no cost) of a professional to be present during the milk recording process, although extra labour requirement (either from the farmer or a family member) is still necessary. The labour requirement is however reduced by the requirement for only one milk sample (either AM or PM milking) for compositional analysis and prediction equations applied to convert to a 24-hour equivalent (Berry et al., 2006).

Future research on phenotyping needs to adopt a multi-disciplinary approach among different professional disciplines, to quantify the ability of information and communication technologies, amongst others, to reduce the cost of recording of phenotypes with little or no compromise in accuracy – greater accuracy of recording is also possible.

Technological phenotypes

Technological phenotypes here refer to data that are (or could be) automatically captured, although the information may not always be translated into useful phenotypes for herd management and animal breeding. Arguably one of the greatest technological advances for phenotyping in dairy cattle was electronic milk recording. Although currently the milk samples taken are used predominantly for the analysis of milk fat, protein, and lactose composition through exploitation of mid-infrared (MIR) spectroscopy analysis of the milk samples, the MIR spectrum can also be used in quantification of other phenotypes. Mid-infrared spectroscopy is the method of shining light through individual cow and bulk milk tank samples, measuring the absorbance pattern of the light in the mid-infrared region, and using the wavelength absorption patterns to predict different milk quality characteristics. Evidence exists documenting the ability of MIR analysis of milk to predict different milk quality attributes (Soyeurt et al., 2011, 2012; Dal Zotto et al., 2008; De Marchi et al., 2009) as well as other performance traits such as energy balance (McParland et al., 2011) and methane emissions (Dehareng et al., 2012). Because MIR is undertaken on all milk samples from milk recorded cows (as well as herd bulk milk tank samples), once the prediction equations are developed, the derived phenotypes are available at no extra cost. Research on other phenotypes that can be derived from the milk MIR are also underway (http://www.optiMIR.eu). Milk, because available daily for all lactating animals, is an excellent source of information. Other phenotypes derived from milk samples include milk electroconductivity and its association with udder health (Norberg, 2005), progesterone profiling for detection of ovulation and pregnancy, and serial measures of serological response to *Mycobacterium avium paratuberculosis* (MAP) as an indictor of presence of MAP in the herd.

Other technological advances, not associated with milk sampling, but of huge importance in dairy production are pedometers (Roelofs et al., 2005) and their association with oestrus (and possible health), video image analysis of carcasses as a predictor of meat yield (Pabiou et al., 2010), near infrared spectroscopy or Raman spectroscopy as predictors of meat quality (Prieto et al., 2009), and many more.

The main advantage of technological phenotypes is the generally low running cost once the initial capital investment of purchasing and calibrating the technology is overcome; an additional advantage is the objectivity associated with the recording of the data assuming it is correctly calibrated. Technology is rapidly advancing and greater collaborations between animal scientists and technologists and engineers must be encouraged. For example, putting in place a system that includes: 1) pedometers, 2) in-line milk monitoring, and on exiting the milking parlour, 3) automatic weighing and while weighing cameras (possibly infra-red based) take video/still images of the 4) lumbar processes, 5) udder and 6) hooves to quantify and detect BCS, mastitis, and lameness, respectively while 7) pressure pads in the weighing crate also measure lameness. Based on decision rules set up, the cow can automatically be drafted for later inspection.

The main disadvantage of technological phenotypes is the cost of development and where necessary the calibration on a sufficiently sized sample population representing the variation likely to be present in the population.

Of increasing interest internationally is feed efficiency (Berry and Crowley, 2012). Although gross feed efficiency is (indirectly) included in many national dairy cattle breeding goals, including Ireland (Berry et al., 2007), net feed efficiency ideally requires measures of feed intake (and energy sinks) or some indicator traits of net feed efficiency directly. Feed intake is related to feeding duration (Basarab et al., 2011) and because most cows are electronically identified during milking, positioning sensors above the feed face can potentially be a very useful method to quantify the duration of feeding and therefore predicting feed intake; not measured here is feeding rate although instruments (yet still cumbersome) are available to measure bite rate (Prendiville et al., 2010). In grazing animals, algorithms based on information generated by pedometers can be used to predict duration of grazing and therefore feed intake. Information can be downloaded from the pedometers on entry to the milking parlour. Many other possible technological advances exist such as monitoring of rumen conditions by using sensor and communication technology in rumen boluses or monitoring of congregation of cows (or bulls with cows) through the use of GPS technology to identify cows in oestrus.

Statistical phenotypes

Genetic evaluations use best linear unbiased prediction (BLUP) which is a procedure to estimate genetic merit (and other random effects) of animals while simultaneously adjusting for systematic environmental effects. Likewise, this method estimates fixed effects (BLUEs) while simultaneously adjusting for differences in genetic merit. Although some fixed effects (e.g., parity) are routinely monitored for biological plausibility, other fixed effects like contemporary group, are discarded. However, effects like herd-year (i.e., contemporary group) can provide useful benchmarking statistics for producers since they are adjusted for genetic effects. Such information is already used in the evaluation of male fertility and performance of AI technicians in Ireland (Berry et al., 2011a).

Temporal analysis of fixed effects can be used to: 1) identify possible deteriorations in performance over-time, and 2) plan for future herd management such as feed budgeting given futuristic milk production and therefore dietary energy requirements. Test-day models provide a useful tool in herd management (Bastin et al., 2009) especially where longitudinal data, such as milk yield and composition as well as heifer growth rates, exist. Herd-level longitudinal profiles across a given trajectory can be modelled as random components in the random regression mixed models. As well as providing information on systematic trends across lactation they can also be used to detect aberrant test-days which may be indicative of, for example, weather conditions at the time but could also be due to short-term changes in management such as deterioration in feed quality. The ability to predict futuristic performance, as well as being useful for the individual producers in herd management, also provides useful information for milk processors and beef abattoirs in predicting upcoming supply patterns.

The advantage of statistical phenotypes is that they are already generated during genetic evaluations and are therefore freely available. More detailed statistical modelling of data may have to be undertaken, especially for serial data, to maximise its usefulness, but an investment in these models is also likely to improve the genetic evaluations. Moreover, investment will be needed to develop the appropriate presentation methods of the model solutions to producers and explaining how these data can be used in day-to-day herd management.

Genomic phenotypes

Animals are generally managed based on the information available at that time. For example, cows not detected in oestrus after a voluntary waiting period post-calving, may be inspected. Similarly mastitis and lameness will be treated when observed or cows may be fed according to production. Individual animal genomic information will undoubtedly soon become an additional phenotype exploited in day-to-day herd management; genomic information through direct genomic values already contributes to herd breeding strategies. Such personalised management (also commonly termed personalised medicine) based on individual genomic information is already being discussed in the human population. For example mutations in BRCA1 and BRCA2 genes in humans are implicated in certain forms of cancer in humans (King et al, 2003) and knowledge of the sequence of both genes in individuals can be exploited in more closer and frequent monitoring of individuals or the use prophylactics treatments. Similarly, knowledge of the genome sequence of individual animals can be used to potentially alter the decision rules implemented in the computer algorithms for detection of diseases placing more stringent rules on animals with greater genomic risk of infection. Furthermore animals with a poor genomic sequence for natural return to oestrus may be intervened earlier post-calving.

Genomic sequence information obviously has a considerable impact on selection of animals for parents of the next generation.

In the future pharmacogenetics (impact of genetic variation to response to medication) may be used to tailor the treatment of disease, or even the vaccination strategy based on information on the animal genome. Furthermore, crossbreeding is increasing in interest in some dairy cattle populations, primarily because of the exploitation of heterosis due to the suppression of undesirable deleterious recessive alleles because of the presence of a dominant allele (dominant hypothesis) and/or the advantage of a heterozygote due to overdominance (overdominance hypothesis). Irrespective, knowledge of the genome sequence of an individual animal may be used to generate measures of its general combining ability, and for individual matings where genomic information is also available on the potential mate, a measure of the specific combining ability (and an associated probability distribution function) can be generated to guide selection and mating decisions to maximise heterosis and additive genetic merit.

The main disadvantage with the use of genomic information as a phenotypic tool is the cost of identifying and quantifying the relevant functional mutations. The necessity for very large datasets, even for high heritability traits like stature, is clearly evident in the human literature (Visscher, 2008), although population structure in humans differ to dairy cattle. Nonetheless, large populations are still required and international collaboration, where genotype by environment interactions are few, will arguably be the best strategy to achieving the end goal.

“Next generation” phenotypes

Transcriptomics is the study of gene expression while metabolomics and proteomics are the study of metabolites and protein, respectively. DNA in all cells are identical but different complements of genes are expressed in different cells; for example the eye colour gene(s) is not likely to be expressed in the genes in the feet of an individual. Similarly, although an animal may have a favourable allele complement of, for example, polymorphisms in fertility genes, they may not be transcribed (i.e., turned on) or may be lowly transcribed (i.e., lowly turned on). The transcript abundance or the measure of how “active” a gene is can be determined by measuring the quantity of the relevant mRNA (or metabolome or proteome) present in the particular cell. Up until recently this was performed using microarrays for global gene expression or by RT-PCR for individual gene expression profiles. However, next generation sequencing technologies overcome some of the limitations of previous methods with the added advantage of lower cost; the cost of sequencing will continue to reduce as newer generation sequencing technologies develop.

Knowledge of the transcriptome, metabolome or proteome abundance within cells, if accurately quantified, may result in greater heritability because of a potentially lower contribution of residual variation (e.g., herd management such as voluntary waiting periods for the derivation of fertility traits). Heritability estimates for traits such as commencement of luteal activity (Berry et al., 2012a; Veerkamp et al., 2000) tend to be greater than traditional estimates of heritability because of the likely lower contribution of residual variation to the overall phenotypic variation.

One of the main difficulties however in the routine implementation of such technologies is the limited availability of suitable biological tissues on which to undertake the analysis. For example, udder biopsies would be required to generate the transcriptome of mammary cells. However, Medrano et al. (2010) reported an almost unity correlation between the transciptome of udder biopsies and mRNA isolated directly from the somatic cells in milk thereby eliminating the requirement of udder tissue biopsies although the milk was collected a short period after milking (Medrano et al., 2010); replication studies are nonetheless, lacking.

An emerging field of phenotyping is metagenomics which in dairy cattle is generally confined to the rumen metagenome. Metagenomic analysis of the rumen microbial populations can provide an inexhaustible insight into the prokaryotic ecosystem within the rumen. Metagenomic approaches are now more feasible with the development of second and third generation sequencing reducing the cost of sequencing. However, their direct usefulness within national breeding strategies is questionable although the information generated from metagenomic analysis can be used in prioritising indicator traits, more amenable to routine recording, for further investigation.

Experimental phenotypes

Precise estimates of genetic parameters such as heritability estimates and genetic correlations with other traits, are necessary to estimate the response to selection for different breeding goals. An alternative approach is to generate two (or more) experimental groups of animals, each with sufficient genetic diversity, but divergent for the breeding goal under investigation. The animals can be deeply phenotyped, especially for traits not amenable to routine collection nationally. Least squares means of the divergent groups of animals can be used to quantify any deleterious consequences of the breeding goal. Unfavourable genetic trends may subsequently be rectified in the breeding goal. Although the trait itself may not be readily recorded nationally (why it was a phenotype of interest in the experiment), indicators of the trait, often referred to by some as "biomarkers" may be identified in the experiment. Often complicated indicators, especially at the omic level, are investigated by scientists. However, simpler possible indictors are often overlooked; for example animal girth may be a good measure of feed intake necessary for the inclusion of net feed efficiency in breeding goals. Caution however must be given to the experimental design (especially decision rules) and statistical analyses used to elucidate the effects in such experiments.

An additional approach, although non amenable to deep phenotyping, is to evaluate the change in a given trait on commercial farms per unit change in genetic merit for that trait. This can be undertaken across environments. However, estimates of genetic merit of the animals in the "test population" must not be derived from their phenotypic information so that no environmental covariance exists within the experimental design. The results can be a very useful tool in convincing stakeholders that genetic evaluations are accurate. Ramsbottom et al. (2012) related mean herd EBI (i.e., the Irish national dairy cattle breeding objective) to annual profit per cow – equivalent to profit per lactation in seasonal calving herds – across 1,131 Irish dairy herds. The EBI is profit per lactation and is expressed on a predicted transmitting ability. Therefore regression of profit per lactation on EBI was expected to be €2; Ramsbottom et al. (2012) reported a regression coefficient of €1.94 (se=0.42) clearly showing that differences in genetic merit for EBI were reflected in differences in profitability in Irish dairy farms. Ramsbottom et al. (2012) also showed that genetic merit for both milk production and fertility were contributing to this profit. Finally, another "experiment" to aid in convincing producers of the benefits of genetics is, during farm visits, to separate approximately 10 cows of the highest and lowest genetic merit for the overall breeding goal. The mean difference in performance among the cows should be obvious, but there will be variation within group and may even be some overlap especially for the low heritability traits. Producers being able to physically see the differences due to genetics can aid in uptake.

Given the increase in genetic gain expected with genomic selection, experimental or sentinel herds are critical to quickly identify possible unfavourable genetic trends in some difficult to measure traits. Moreover, selection indexes assume the response to selection is linear. However, the response to selection may (and more than likely will) differ depending on genetic merit of the animal and how it interacts with the environment. This is especially true in grazed grass based systems of milk production and this hypothesis can be tested in controlled experiments with factorial deigns of genotype by system of production. The main disadvantage of controlled experiments is the cost associated with running the experiments; however, the financial repercussions of not embarking on such an insurance policy can be many multiples greater.

Conclusions

Routine access to low cost, accurate phenotypes across a range of important traits remains key to sustainable genetic gain in dairy cattle. Many different types of phenotypes exist but also many different technologies now exist (some requiring just slight modifications) to record the necessary information. Not covered in this article, but of increasing importance are decision support tools, that combine the plethora of data from the different sources, summarises it into an easily understandable format and provides advice on remedial action to be taken, if necessary, to increase herd performance and profitability.

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