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Towards a biological basis for predicting nutrient partitioning: the dairy cow as an example

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Prediction of nutrient partitioning is a long-standing problem of animal nutrition that has still not been solved. Another substantial problem for nutritional science is how to incorporate genetic differences into nutritional models. These two problems are linked as their biological basis lies in the relative priorities of different life functions (growth, reproduction, health, etc.) and how they change both through time and in response to genetic selection. This paper presents recent developments in describing this biological basis and evidence in support of the concepts involved as they relate to nutrient partitioning. There is ample evidence that at different stages of the reproductive cycle various metabolic pathways, such as lipolysis and lipogenesis, are up or down regulated. The net result of such changes is that nutrients are channelled to differing extents to different organs, life functions and end-products. This occurs not as a homeostatic function of changing nutritional environment but rather as a homeorhetic function caused by the changing expression of genes for processes such as milk production through time. In other words, the animal has genetic drives and there is an aspect of nutrient partitioning that is genetically driven. Evidence for genetic drives other than milk production is available and is discussed. Genetic drives for other life functions than just milk imply that nutrient partitioning will change through lactation and according to genotype – i.e. it cannot be predicted from feed properties alone. Progress in describing genetic drives and homeorhetic controls is reviewed. There is currently a lack of good genetic measures of physiological parameters. The unprecedented level of detail and amounts of data generated by the advent of microarray biotechnology and the fields of genomics, proteomics, etc. should in the long-term provide the necessary information to make the link between genetic drives and metabolism. However, gene expression, protein synthesis etc, have all been shown to be environmentally sensitive. Thus, a major challenge in realising the potential afforded by this new technology is to be able to be able to distinguish genetically driven and environmentally driven effects on expression. To do this we need a better understanding of the basis for the interactions between genotypes and environments. The biological limitations of traditional evaluation of genotype × environment interactions and plasticity are discussed and the benefits of considering these in terms of trade-offs between life functions is put forward. Trade-offs place partitioning explicitly at the centre of the resource allocation problem and allow consideration of the effects of management and selection on multiple traits and on nutrient partitioning.

Keywords: cattle, genotype environment interaction, nutrient partitioning, plasticity

Introduction

In its broadest sense, the term 'nutrient partitioning' refers to the processes by which available nutrients are channelled, in varying proportions, to different metabolic functions. A narrower definition commonly applied in dairy nutrition refers specifically to the partition of nutrients between milk outputs and body reserves. This paper deals with both the general principles and the specific application to dairy cows. As the accompanying review by Dijkstra and co-workers (2007) deals in detail with rumen function and digestion, we focus in this paper on post-absorption nutrition.

Prediction of nutrient partitioning is a long-standing problem of animal nutrition (Kellner, 1926) that has still not been solved (Hanigan *et al.*, 2005). The substantial variation that can exist between individuals in their response to the same change in feeding is well documented (Kellner, 1926; Broster *et al.*, 1969; Kirkland and Gordon, 2001a).

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At present it is still not possible to predict which cows will be economically worth supplementing. This variation between individuals in nutrient partitioning also impinges on the issue of how to intervene nutritionally to redress metabolic imbalances that cause costly health, reproduction, and welfare problems. The effectiveness of such supplements depends on them being designed to fit with the cows' particular partitioning of nutrients.

Another substantial problem for nutritional science is how to incorporate genetic differences into nutritional models (McNamara and Baldwin, 2000; Bryant *et al*., 2005). These two problems are linked as their biological basis lies in the relative priorities to the animal of different life functions (growth, reproduction, health, etc.) and how they change both through time within the animal's life and in response to genetic selection. The purpose of this paper is to present recent developments in describing this biological basis and evidence in support of the concepts involved as they relate to nutrient partitioning. The reproductive dairy cow is used as an example species because the literature concerning nutrient partitioning is relatively well developed for the dairy cow, because there are pronounced changes in nutrient partitioning associated with changing reproductive status (pregnancy, lactation, return to oestrus cycling etc), and because the dairy cow has undergone strong selection for one aspect of this cycle, lactation.

Why has the problem of understanding and predicting nutrient partitioning resisted the best efforts of researchers for so long? It is our belief that this is in part due to the pervasive, and in our opinion myopic, view of the animal as a passive (bio)chemical converter of feed into useful products. Consequent on this view, the major question of research has been: '*How* do animals partition nutrients?' This is a valuable question particularly if we want to make metabolic interventions. However, when the goal is to understand and predict partitioning, we will argue that a more important question is: '*Why* do animals partition nutrients (in the way they do)?' We believe that tackling this question will allow substantial progress to be made.

Why do animals partition nutrients?

We have tended to see nutrient partitioning as a mechanism for accommodating discrepancies between the composition of the feed and the composition of products (milk) with 'overflow' being dumped in body reserves, i.e. partition as a homeostatic mechanism in response to environmental changes (Figure 1a). This aspect of partition undoubtedly exists and is typically seen when looking at the differences between feeds at one time-point (Chilliard *et al*., 1998b; Oba and Allen, 2000; Nielsen *et al*., 2006). However, it does not on its own provide a sufficient answer to the question 'why do animals partition nutrients?' This becomes apparent if we extend the question to include the time dimension, i.e. 'Why does partition change with time?' It is well documented that partition changes with stage of lactation (Kirkland and Gordon, 2001b) and there is ample evidence that at different stages of the reproductive cycle various metabolic pathways, such as lipolysis and lipogenesis, are up or down regulated (e.g. Chilliard *et al*., 2000; Theilgaard *et al*., 2002) and that endocrine profiles also change (Bauman, 2000). The net result of such changes is that nutrients are channelled to differing extents to different organs, life functions and end-products. This occurs not as a function of changing nutritional environment but rather as a function of (physiological) time. This is partition as a homeorhetic, or teleophoretic, mechanism (Chilliard (1999) for definitions see Bauman (2000)). The onset of lactation provides the classic example of this with the uncoupling of GH and IGF and the resulting channelling of nutrients to the mammary gland (Bauman, 2000).

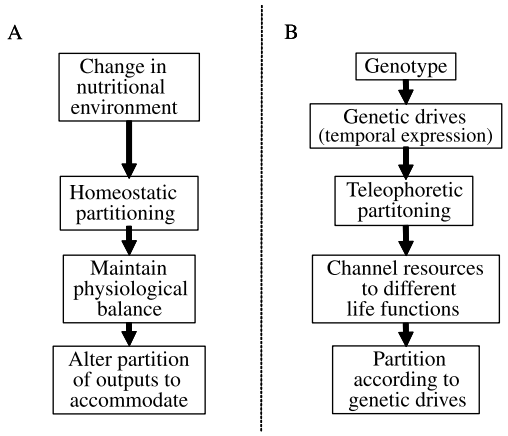

Figure 1 A schematic representation of the two types of nutrient partitioning, homeostatic and teleophoretic.

The concept of teleophoresis/homeorhesis has been around for some time (Waddington, 1957; Monod, 1970; Bauman and Currie, 1980; Chilliard, 1986). The implication behind this concept is that the animal has genetic drives – the expression of genes for functions such as milk production through time. These drives can only be fulfilled if the necessary resources are channelled, or partitioned, to them (Figure 1b). In other words, there is an aspect of nutrient partitioning that is genetically driven. Although genetic drives are implicit in teleophoresis, they are with the exception of milk production, largely overlooked both in our nutritional models, and in our thinking. '*Negative*' energy balance, insulin '*resistance*' and reproductive '*failure*' are all expressions that imply that the machine, i.e. the cow, is malfunctioning. However, these can all be seen as positive attributes, natural adaptations that have evolved to allow the animal to maximise her chances of (evolutionary) success. The cow, despite domestication, has drives that relate to functions other than milk production, functions such as safeguarding reproduction, maintaining disease resistance etc (Houdijk *et al*., 2001; Friggens, 2003; Friggens *et al*., 2004). It is becoming increasingly clear that lack of progress in predicting nutrient partitioning is in

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large part due to the failure to consider the cow as an active biological entity with her own 'agenda' i.e., her genetic drives. (We refer to this aspect of nutrient partitioning as teleophoretic rather than homeorhetic because is in the service of genetic drives, or goals.)

Evidence for a genetic drive for use of body reserves

An example of this neglecting of drives relates to use of body reserves in early lactation. The traditional view is that intake is limited in early lactation and *therefore* cows mobilise to make good the difference. The equivalent view in nutritional modelling is that of body lipid as an overflow for energy, a passive store that continuously increases when the energy input exceeds the predicted energy output. However, there is mounting evidence that mobilisation is not always a passive response.

Attempts to abolish body lipid mobilisation in early lactation by feeding energy rich diets are in general not successful (Gagliostro and Chilliard, 1991; Grummer *et al.*, 1995; Andersen *et al.*, 2003; Ruppert *et al.*, 2003). By itself, this does not constitute evidence that genetically driven body lipid mobilisation exists in early lactation. Given that rumen digestibility can be depressed when the energy content of the diet being offered is increased, it is difficult to ascertain with complete certainty that this type of experiment has truly overcome limitations to intake and thus that the observed lipid mobilisation is not due to inadequate intake levels i.e., that it is not environmentally driven. If, alternatively, it is assumed that all observed body lipid mobilisation is environmentally driven – that genetically driven mobilisation does not exist – then a number of expectations arise that can be tested: If mobilisation is environmentally driven then it has arisen because intake is limited, and in most cases this limitation is related to the bulkiness of the feed. Thus, under these assumptions, it would be expected that intake is related to live weight (Mertens, 1987; National Research Council, 2001).

Using data from a large-scale trial with 400 cow lactations we have examined this relationship. The key feature of this experiment was that environmental conditions were kept as stable as possible throughout and cows were offered the same total mixed ration throughout lactation (described in full by Nielsen *et al.* (2003)) i.e. the cows and their digestive systems were fully adapted to the feed. The cows were in substantial negative energy balance at 14 days after calving (Friggens *et al.*, 2007). For all cows, intake and live weight at this time are plotted in Figure 2. There was no significant relationship between intake and live weight, thus intake was not constrained by any size-related factor. Further, two other known constraints on intake, competition for feed and heat stress, are not relevant in this experiment as the cows were individually housed (in tie stalls), had unlimited access to feed and water, and were under Northern European climatic conditions (latitude 55.43N). At 14 days post calving, close to the time-point of greatest mobilisation of body lipid, intake was, on average, only 80% of the maximum intake

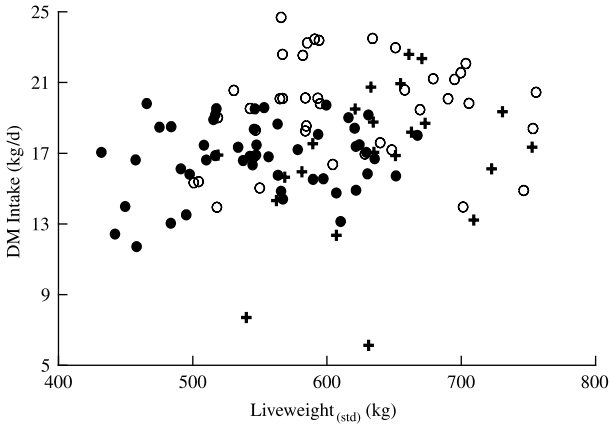

Figure 2 Dry-matter (DM) intake relative to live weight on day 14 of lactation for Holstein Friesian cows in first (●), second (+) and third (○) lactation. Live weight has been adjusted to a standard condition score according to Friggens *et al.* (2007).

attained in the same lactation. It is therefore difficult to argue, given that these cows were on the same feed throughout their productive life, that intake was constrained when there was substantial energy mobilisation. Thus, in this case it seems unlikely that there was any significant amount of environmentally driven mobilisation and that the observed mobilisation in early lactation was largely genetically driven. There are also many examples (see Broster and Broster (1998)) where cows offered the same diet and producing the same amount of milk have markedly different degrees of body lipid mobilisation strongly suggesting that other, animal related, causes of mobilisation exist.

There are good evolutionary arguments for changing levels of body fat reserves throughout the reproductive cycle (Pond, 1984), and strong evidence for coordinated endocrine control of body fatness relative to reproductive stage (Vernon *et al.*, 2001). Further, genetic correlations between body condition scores at different time points in lactation have been reported (Coffey *et al.*, 2001; Pryce *et al.*, 2002). Taken together, all this provides compelling evidence for genetically driven body lipid change. What has this to do with nutrient partitioning? Well, genetic drives for other life functions than just milk imply that partitioning will change through lactation and according to genotype – i.e. it cannot be predicted from feed properties alone.

Defining genetic drives for life functions

There already exists a strong basis for defining genetic drives for a number of life functions such as growth (Emmans, 1997; Knap, 1999), milk yield (Dijkstra *et al.*, 1997, Vetharaniam *et al.*, 2003b), and body lipid reserves. For other life functions such as reproduction, immune function, and processes in support of longevity there is rather less information available (in agricultural research) although these functions are increasingly being explored in terms of their animal-intrinsic components and in terms

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of nutrient partitioning (Elsasser *et al*., 2000; Houdijk *et al*., 2005; Stubbs and Tolkamp, 2006). Thus, in our opinion, developing descriptions of the different genetic drives sufficient for inclusion in nutritional models is a feasible task (see also the accompanying review of Sandberg and co-workers (2007)). However, it requires that the two key dimensions, genotype and time, can be combined in such a way as to adequately describe the changing balance of life functions, and thus the expected teleophoretic nutrient partitioning in support of them. For example, there are clear differences between breeds in their partition of energy between milk and body reserves that change with stage of lactation and also with parity (Dillon *et al*., 2003; Yan *et al*., 2006). Likewise, reproductive state affects drives, for instance pregnancy depresses milk production (Coulon *et al*., 1995; Coulon and Pérochon, 1998) and up regulates lipid deposition (Koenen *et al*., 2001). These types of interaction need to be described quantitatively.

The benefits of doing this may not be immediately obvious but consideration of genetic drives can help resolve a number of nutritional problems. A general problem of mechanistic models is that seemingly insignificant systematic biases in the model parameters can rapidly accumulate across model time-steps into sizeable errors (see also Ellis *et al.* (2006a)). Given that body lipid is usually modelled as an energy buffer, these types of error are seen as the model animal becoming excessively - and unrealistically – fat or thin (McNamara, 2004). One consequence of incorporating additional genetic drives and the implied targets for e.g., body fatness, is that quantities such as body fat are bounded within limits set by the genetic drive and reproductive state. The implication of this is that in order to achieve conservation of energy and mass, intake can become a response. This is radically different from the standard view of intake in the context of energy balance. Traditionally, energy balance i.e. the change in body energy stores, is seen as the response and intake as a given. This thinking is also largely reflected in nutritional models, the majority of which require intake as an input i.e. intake is fixed within a model simulation and is input on the basis of a physical fill calculation. In a review of experiments that compared lipogenic or glucogenic feeding with controls, there was a decrease in intake as a result of the change in feed composition in more than half of the experiments (Van Knegsel *et al*., 2005). It is clearly desirable for nutritional models to be able to predict intake.

Systems that predict intake on the basis of physical fill usually invoke some association between intake capacity and level of milk production or stage of lactation in order to account for changes in intake with days in milk (see Ingvartsen (1994)). However, it has been shown that intake of a high forage feed is independent of milk production level through lactation (Friggens *et al*., 1998) and that the dip in intake around parturition can, at least in part, be accounted for by allowing intake to be a response i.e., incorporating genetically driven body lipid mobilisation in early lactation (Petruzzi *et al*., 2004; Petruzzi and Danfær, 2004). Further, Ellis and co-workers (2006b) have recently shown empirically that adjusting intake prediction equations according to the size of body energy reserves significantly improved the accuracy of predicted intakes. Thus, defining these genetic drives for body reserve change provides an important component for predicting intake.

One substantial challenge to incorporating genetic drives into models of nutrient partitioning is to create a genetic description of animals relevant to partitioning. Traditional breeding values are not so useful, in part because they ignore the time component. This situation is changing with the advent of genetic parameters for shapes of e.g. the lactation curve (Swalve, 1995), and with the use of test day model types of analysis (Veerkamp *et al*., 2001) but there is still a gap between current genetic and metabolic descriptions of animals.

Linking genetic drives to metabolic coefficients

The control systems for metabolism are complex with many levels: neural, paracrine, endocrine, etc., and with a high degree of interaction and overlap (e.g. Vernon and Houseknecht, 2000). Reproducing such a system within a metabolic model is a daunting task, one that has received relatively little attention relative to the effort expended on describing the biochemical aspects of metabolism. The task does not get easier – some might say it becomes impossible - if one is seeking to trace back the temporal expression of such a system to the level of genes. However, it is pertinent to ask the question: 'Why are these control systems so complex?' There appears to be a relatively high degree of failsafe and back-up built into these control systems. This may be of great value in the real world but can be to a substantial degree simplified in the stable milieu of a nutritional model – we don't expect our model processes to develop ailments, be attacked by viruses or senesce. Further, the nature of evolutionary design is such that control systems that have been superseded are not necessarily 'deleted', these remnants can also give the illusion of complexity. (The same is sometimes also true of model software.)

Given these considerations, and the need for a link between genetic drives and metabolic coefficients, a first step would be to create a genetic component to some 'meta-hormones' in nutritional models. A number of examples of the use of meta-hormones to describe teleophoretic changes in nutritional models exist. The model of Neal and Thornley (1983) includes a lactation hormone that affected mammary cell numbers as a function only of time. The models of Baldwin and co-workers include anabolic and catabolic hormones (see Baldwin (1995)). However, and perhaps reflecting their focus on the mechanics of cell metabolism, this aspect of their models appears to have received little attention and is not clearly described. Danfær (1990) uses growth hormone and insulin explicitly to alter nutrient uptake of the mammary gland, muscle and adipose, with these hormones being affected by days in milk and also by milk yield and live weight.

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The model of Sauvant (1994) takes the important step of making teleophoretic control explicit in his model architecture and implements this regulation using catabolic and anabolic meta-hormones. This approach provides a useful platform for including genotype but none of the above models have actually incorporated genetic input parameters. An attempt to examine how such models would cope with different genotypes was carried out by McNamara and Baldwin (2000) who simulated high and low genetic merit cows by altering the lactose synthetic capacity constant within their model and comparing this with observed data for such cows. Their model did not simulate observed rates of body lipid changes adequately, resulting in significant accumulated errors over the lactation. This is not surprising since the model does not explicitly recognise genetic drives other than for milk. As indicated above, the incorporation of genetic drives for body energy change would prevent the accumulated errors. It would also force the description of genotype to include a life function other than milk. The review of Bryant and co-workers (2005) draws attention to the serious limitation of nutritional models not being able to accommodate genotype. In a further study, Bryant and co-workers (2007) show one possible approach to estimating and incorporating genotype effects at the physiological level. Their study explicitly examines the effects of genotype (breeding values for milk) on the coefficients of a metabolic model, the mammary gland model of Vetharaniam and co-workers (2003a).

However, the issue of creating a genetic description of animals relevant to partitioning remains. Breeding values for physiological parameters are not, in general, available. Although heritabilities for some physiological traits have been reported (Darwash *et al.*, 1999; Lovendahl and Klemetsdal, 2004) they do not show a promising degree of consistency, nor are they highly correlated with production traits (Baumgard *et al.*, 2002). In the past, the choice of traits for which to estimate breeding values has been governed by economic value and ease of measurement. Breeding values for 305-day milk yield were supplemented by breeding values for milk fat and protein as the economic value of these components became apparent. Likewise, fertility traits and proxies for them (e.g. condition score, persistency) have become increasing common as the negative associations between milk production and health and reproduction have begun to have economic consequences. There is no *a priori* relation between the traits measured and the genetic drives we wish to model. We need, now, to clearly identify the biologically meaningful components of genetic drives for which we would like breeding values. This does not necessarily imply that we need genetic evaluations at the level of deep physiology. Indeed, the lack of consistency in existing genetic measures of physiological parameters together with the inherent complexity and multifaceted roles of most hormones and metabolites (Brameld *et al.*, 1999) suggests that, for the time being, we are likely to find useful measures of genetic drives at a higher level of organisation. Identifying the biologically meaningful components of genetic drives can be done, in part, by careful evaluation of existing data for repeatable phenomena regarding the time trends we wish to include. For example, it has been found across many trials that a major influence on the rate of body mobilisation in early lactation is the size of body reserves at calving (Martin and Sauvant, 2002). This suggests that the description of curve shapes for body reserves can be simplified to body fatness at calving coupled with an estimate of body fatness the cow is driven to obtain at the time of the nadir in body fatness. If existing descriptions of the heritability of body energy curves (e.g. Coffey *et al.*, 2002) can be couched in these terms then we have a basis for starting to incorporate genotypes into our nutritional models (Friggens and Badsberg, 2007).

The process of extracting phenomena from existing data requires a clear idea of the biological processes that one is seeking to characterise and, in particular, of the current and permanent environmental effects on them. This is especially important with respect to characterising genetic drives. There are a large number of proposed functions for describing lactation curves of milk yield (Rook *et al.*, 1993) of which relatively few can be described as being biologically meaningful (Friggens *et al.*, 1999; Pollott, 2000). This biological meaningfulness comes not from fit statistics to data but rather from consideration of, in the case of milk, mammary cell proliferation and death (Vetharaniam *et al.*, 2003a) relative to the animals underlying priorities with respect to her offspring.

We can gain insight of how the cow functions as an active biological entity from other fields such as life history biology. Life history biology is concerned with those traits, or life functions, that contribute directly to fitness and this discipline has been studying the interplay between different life functions at the genetic and phenotypic level for some time (Stearns, 1992; Roff, 2002). It provides both the necessary concepts, for example how to optimise combinations of life functions, and some experimental evidence that together with established scaling rules will allow the development of appropriate descriptions (e.g. Roff *et al.*, 2002; Worley *et al.*, 2003). The context for life history biology is natural selection and evolution, which may at first sight seem somewhat removed from the problems of nutrient partitioning in dairy cows. However, the difference in perspective is valuable. The question 'why do animals partition nutrients?' only makes sense in the context of overall fitness and this approach is increasingly yielding valuable concepts for agricultural science (Yearsley *et al.*, 2001; Tolkamp *et al.*, 2002; Van der Waaij, 2004). Given that the role of the environment in shaping both the expression of genotype and selection is made explicit in life history biology, it also provides a broader framework within which to rationalise new evidence linking genetic drives to metabolism.

Until recently we have been faced with a paucity of data concerning a genetic description at the level of metabolism

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and the temporal changes in expression of genes, proteins and other downstream molecules. This is rapidly changing with the advent of microarray biotechnology and the fields of genomics, transcriptomics, proteomics etc. The unprecedented level of detail and amounts of data (e.g. Allan *et al.*, 2005) generated by these techniques should provide the necessary information to make the link between genetic drives and metabolism. However, a major challenge in the use of *–omics* data is that gene expression, protein synthesis etc, have all been shown to be environmentally sensitive (e.g. Rhoads *et al.*, 2005). Thus, studies carried out under different conditions will identify different candidates for allegedly the same biological function. For example, the gene expression of reproductive hormones is sensitive to both stage of reproductive cycle and nutritional status (Moore *et al.*, 2004). Heat stress has also been shown to affect gene expression (Schwimmer *et al.*, 2006). A major challenge in realising the potential afforded by this new technology is to be able to distinguish genetically driven and environmentally driven effects on expression. To do this we need a better understanding of the biological basis for the interactions between genotypes and environments.

Genotype environment interactions and plasticity

So far, this paper has placed emphasis on genetic drives and the teleophoretic aspects of nutrient partitioning. This is not because the homeostatic aspects are unimportant but simply because we see the oversight of the teleophoretic aspect as the current rate-limiting step in development of improved nutrient partitioning models. Clearly, we expect these two aspects to be acting in concert. Combining the genetically derived teleophoretic aspects and the environmentally affected homeostatic aspects is the crucial step for the next significant advance in models of nutrient partitioning, and this requires consideration of genotype environment interactions. Genotype-environment interactions (G × E) occur when the size of the animal's response to a change in environment (e.g. a reduction in feed availability) is different for different genotypes. The term G × E is frequently used to describe an interaction in the statistical models used for genetic evaluation. As such, and in common with a widely held view of 'statistical' interactions, G × E has been considered a nuisance to be ignored if possible. However, when considered in biological terms it quickly becomes apparent that the underlying processes are of great importance and thus G × E should not be ignored.

The key underlying process is called plasticity. In agricultural science, a rather limited definition of plasticity is usually invoked: the rate of change in the level of a single trait when measured across different environments (see Figure 3). This narrow definition of plasticity is often referred to as environmental sensitivity. When defined like this, plasticity is a double-edged sword. On the one hand, it could be argued that we should select for animals that have low plasticity for milk production (cow type A in Figure 3). Such cows would maintain high levels of milk production across a relatively wide range of environments. On the other hand, it could be argued that low plasticity for milk production means that the gains that can be expected from improvements in the environment (i.e. the slope in Figure 3) will be less than for cows with high plasticity (cow type B in Figure 3).

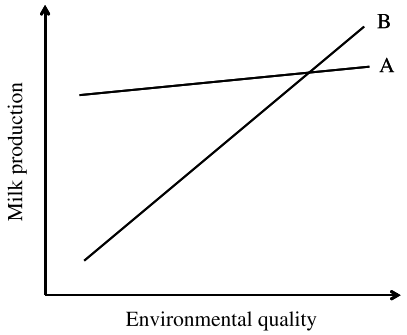

Figure 3 A schematic representation of plasticity in a single trait (e.g. milk production). When the trait is measured across different environments for a given genotype the resulting line/trajectory is called a reaction norm. Plasticity in that trait is shown by the slope of the reaction norm. In this example, genotypes A and B have different slopes and thus differ in their plasticity. When, as in this case, the slopes of the reaction norms for different genotypes are not parallel then there is evidence of a genotype environment interaction.

G × E interactions are increasingly being reported in dairy cows (Raffrenato *et al.*, 2003; Kolmodin *et al.*, 2004; Petersson *et al.*, 2005; Calus, 2006) and lend support to the idea that genetic selection for production will tend to produce animals of type B (Figure 3), very high producing in ideal environments but increasingly sensitive to the environment (Beilharz and Mitpaiboon, 1994). There is also physiological evidence that the modern dairy cow shows a high degree of plasticity in milk production, and is very well able to adapt to a range of environments (Collier *et al.*, 2005). However, if we only consider plasticity in a single trait it is difficult to assess the associated consequences of this and to place it in the context of nutrient partitioning.

If nutrient partition remained constant as nutrient supply decreased then all life functions would be depressed in equal proportion. We know this is not the case. There are clear examples at the level of the whole animal, organ/tissue, and metabolism of nutrient partition being modulated in response to environmental pressure (Manning and Bronson, 1990; Chilliard *et al.*, 1998a; Tolkamp *et al.*, 2006; Loor *et al.*, 2006). Clearly, when nutrient availability is decreased there is plasticity in nutrient partitioning such that certain genetic drives are prioritised over others. Supplying the resources for one genetic drive means that the resources supplied to one or more other genetic drives will be correspondingly reduced. Thus, an animal with low plasticity for milk production is an animal that maintains milk production at the expense of other life functions. It could be, for instance, that the cow coped by reducing body fat levels or by reducing disease resistance. Clearly, the consequences of this trade-off will depend upon which of the other life functions are negatively affected.

Plasticity and G × E, although often discussed in terms of one trait only, have limited biological meaning unless

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they are interpreted in the context of the total fitness of the animal. In other words, a broader definition of plasticity than that usually used in agricultural science is necessary. Plasticity can be defined, in biological terms, as the combined physiological mechanisms by which the animal copes with environmental challenge.

Trade-offs and G × E in multiple traits

By considering the G × E problem in terms of trade-offs between life functions we place partitioning explicitly at the centre. This notion of trade-offs underpins the view that continued selection solely for production will lead to unacceptable compromises in other life functions. The partitioning of resources is illustrated in a simplified form in Figure 4. Only two life functions are considered: production (R_{Prod}) and 'other' (R_{Other}). Any one of the stippled lines downwards sloping from left to right indicates, for a constant total amount of resources obtained by the animal (R_{Obt}), all possible combinations of resource allocation between R_{Prod} and R_{Other}. Each of these lines represents a different level of total resources, increasing with distance from the origin. The solid line indicates a constant resource partition (c). The situation illustrated graphically in Figure 4 is shown as a flow diagram in Figure 5, with one extension. The extension makes explicit the fact that the resources obtained by an animal (R_{Obt}) are a function of the resource availability in the environment (R_{Env}) and of the animal's genetic capacity to uptake resources (R_{Cap}). If the animal can increase R_{Obt}, i.e. it can move to a higher level of total resources obtained, then production (R_{Prod}) can increase without altering the partition between life functions indicated by c in Figure 4. Thus, if the resource

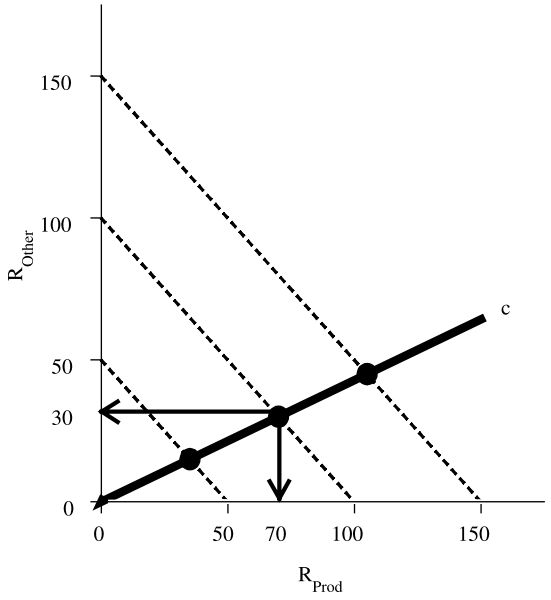

Figure 4 Possible combinations of resource allocation to two different life functions; production (R_{Prod}) and all other functions (R_{Other}) for three different levels of total resources (50, 100, and 150 arbitrary units indicated by stippled lines). The solid line (c) indicates a constant resource partition between life functions such that, in this example, 0.7 of total resources is always allocated to production.

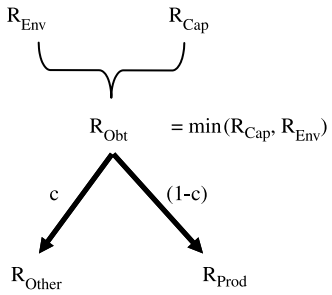

Figure 5 A simple trade-off model for resource allocation between two different life functions; production (R_{Prod}) and all other functions (R_{Other}) with partition explicitly included as coefficient 'c'. The resources that the animal has obtained (R_{Obt}), and that are thus available for allocation, are assumed to be the lesser of the environmentally determined availability (R_{Env}) and the animals capacity to acquire resources (R_{Cap}). It is worth noting just how much this trade-off model of resources resembles traditional nutrient flow models.

availability from the environment (R_{Env}) is not limiting then it should be possible to increase production without engendering a (change in) trade-off. However, if the resources available to the animal are fixed, i.e. R_{Obt} is constant, then the only way to increase one life function e.g., production, is at the expense of other life functions. This trade-off requires a change in c, the partition of resources. Within these two extremes, what is predicted to happen when we select for increased production?

To answer this question we can start by considering a likely trajectory of selection within this highly simplified trade-off view, depicted in Figure 6. Assuming that we can provide a non-limiting environment ($R_{Cap} < R_{Env}$), then increasing production without altering partition, c, will result in an increasing amount of resources going to the non-production life function (R_{Other}). However, there must be some upper level of resource allocation to other functions (U_{Other}) above which no further fitness benefit accrues. For example, if one considers survivability in energetic terms, once requirements for activity, thermoregulation,

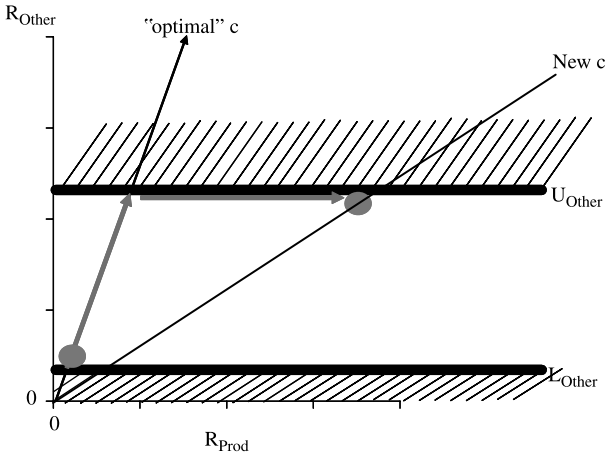

Figure 6 A likely trajectory of change in resource partitioning (c) due to selection for production within a non-limiting environment (see text for details).

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metabolic turn-over and cellular repair have been covered little benefit of further energy allocation to survival is expected. If R_{Cap} (and thus R_{Obt}) is such that resources supplied to fitness are in excess of the upper limit, i.e. R_{Obt}*c $> U_{other}$ then further gains in production are likely to be achieved by decreasing c (Figure 6). This is because, under these conditions, an animal that has decreased c (From "optimal to New") so that R_{Obt}*c $= U_{other}$ will produce more than an animal that has exactly the same R_{Obt} and has not altered c. Thus, genetic changes in nutrient partitioning towards production and away from other life functions are expected. Studies in dairy cows support this (Dechow *et al*., 2002; Berry *et al*., 2003).

The implication of G × E is that there is genetic variation in plasticity i.e. some genotypes are better suited to meeting environmental challenges than others. It is well documented that European breeds can have severely compromised performance in tropical conditions (Stanton *et al*., 1991; Chagunda *et al*., 2004). It has also been found, within temperate environments, that different breeds and different bulls within breed (Jones *et al*., 1999) have different propensities to e.g. mobilise body reserves. The key question is: how will selection affect plasticity? In practical terms, what happens when resources become limiting?

What we have done by placing plasticity in the context of trade-offs is to expand its definition from being the slope of a reaction norm (Figure 3) to being the change in allocation of resources between life functions *that contribute to fitness*. In this context, a high degree of plasticity, that is an ability to change partitioning to preserve fitness, is a positive attribute. If genetically speaking the partition coefficient c is reduced by selection but the animal retains the plasticity to increase c in response to resource limitations then we have both higher producing and more robust animals (see Figure 7; Robust, (details in Figure legend)). This scenario has been put forward by some as being the situation in modern dairy cows (Collier *et al*., 2005). Unfortunately, in the long term, this seems to be an unlikely outcome for a number of reasons. Simulation studies (Kolmodin *et al*., 2003) and considerations of the costs of plasticity (West-Eberhard, 2003), i.e. maintaining plasticity is itself a life function and thus subject to trade-off, suggest that selection for increased production will reduce plasticity. Thus, it is likely that if the partition coefficient c is reduced by selection then the animal loses the plasticity to increase c in response to resource limitations and is thus less robust (see Figure 7; Selected).

Also, the higher the level of production and thus the higher the level of intake, the more likely it is that any given food is limiting (Kronfeld, 1976). Not only is the plasticity of selected animals likely to decrease but also the likelihood of them encountering a limiting environment will increase. Thus, maintaining plasticity must be an important consideration. Although dairy cows currently show a substantial ability to cope (Collier *et al*., 2005), they do so at the expense of other life functions such as reproduction (Royal *et al*., 2002) and health (Windig *et al*., 2005). There is now also evidence

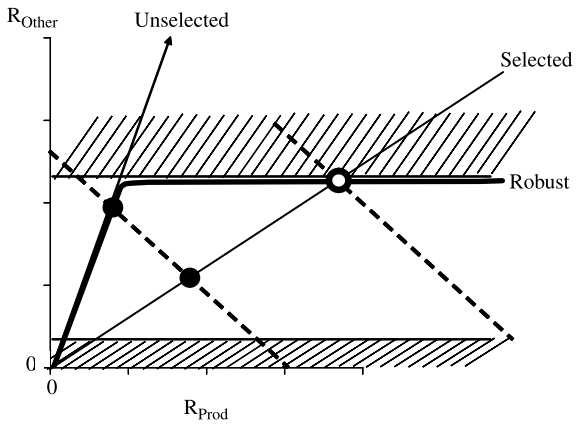

Figure 7 Possible consequences on plasticity of selection for production. If selection has occurred in an abundant environment (upper limit indicated by the stippled line furthest from the origin) then the partition of the selected animals in that environment is indicated by the open circle. If the environment now becomes poorer (indicated by the stippled line closest to the origin) then two extremes of partition are possible: no change in partition indicating low plasticity (solid circle on the line 'Selected'), and a complete reversion to the partition of the unselected animal indicating high plasticity (solid circle on the line 'Robust'). Given that the partition of the unselected animal reflects the optimum fitness, it can be seen that the cost of selection for increased production in the low plasticity, Selected, animal is a substantial reduction in fitness when placed in a limiting environment.

of emerging G × E interactions for traits such as fertility, health and longevity (Mark, 2004; Calus, 2006; Windig *et al*., 2006). Further, if one considers intensively selected species such as the broiler chicken, there is clear evidence that these animals ability to cope with suboptimal environments is severely limited (De Greef *et al*., 2001; Yalcin *et al*., 2001). We should not be complacent about this eventuality in dairy cows and should certainly aim to include plasticity in our nutritional models if we wish to predict how best to manage future generations of dairy cows.

Perspectives

Clearly, a number of important issues need to be incorporated into this conceptual framework if it is to be able to make useful predictions both at the level of managing and selecting high yielding dairy cows. This review has only briefly touched on the issue of time. The issue of the benefits and costs of plasticity can only really be evaluated in the context of within lifetime temporal patterns. There is a need to extend and evaluate concepts for modelling G × E effects on nutrient partitioning as the animal moves through different physiological stages of life (Humphries *et al*., 2003). It is our view that our models for nutrient partitioning should be extended to: (1) include genetic drives for other life functions than milk, (2) include the temporal changes in partitioning expected from these genetic drives, and (3) take account of consequences of trade-offs on fitness. If we can achieve this, we have the basis for greatly extending our existing nutrient models to allow better prediction of differences between individuals and the interactions between genotype and environment.

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