Genetic Improvement in Beef Cattle for Feed Efficiency: Increasing our Understanding of the Biological Basis

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Introduction

The basis of feed utilization has been instigating the curiosity of researchers for many years. In 1859, Charles Darwin pointed out initial insights about the variation of animals under domestication. He mentioned that 'the nature of the organism' and 'the nature of conditions' account for utilization of food by the organism, such as colour from the nature of the food or size from the amount of food. For almost one and a half centuries, geneticists; physiologists; nutritionists and researchers from other disciplines have been working hard in this broad topic: feed efficiency in farm animals; and a number of important advances were made. Crop scientists developed efficient varieties of diverse grains and forages, which are adapted to the different environments around the world that can be economically used to feed farm animals. On the other hand, animal scientists developed breeds and strains, which produce goods that are essential to meet the demand of humankind for animal products. For all livestock production systems feed is a major expense, ranging from 60 to 80% of the total costs across the most common farm animals species. There are also environmental issues associated with livestock production (e.g. greenhouse gases emission, land degradation, loss of biodiversity, water shortage and pollution), which are related to the type of husbandry system, to the compounds of the diet and to the quantity of feed necessary to supply the animals' needs for growing and production. To date, the livestock sector generates more greenhouse gases than transport activities, being responsible for 18% of total greenhouse gases emissions from human activity (FAO, 2006). Therefore, improvements in the efficiency of feed utilization by farm animals could bring economical benefits for the livestock industry and also could be more environmentally sustainable.

Some of the feed efficiency measurements have their theoretical roots on feed evaluation systems. The conceptual framework and initial determinations of the variables used in the two most popular models for representation of nutrient utilization by animals (metabolic - ME and net energy systems – NE) were suggested early in the 20th century (e.g. Armsby, 1917). Based on these models, multiple approaches to measuring and reporting feed efficiency utilization where developed in the last 50 years, such as: maintenance efficiency (Ferrell & Jenkins, 1985), partial efficiency of growth (Archer et al. 1999), Kleiber ratio (Arthur at al. 2001), and residual feed intake (RFI) (Koch et al. 1963). Among these, RFI is the only measure independent from production traits. As a result, RFI probably reflects more variation in basic metabolic processes (maintenance requirements) (Nkrumah et al. 2006) than variation due to differences in level of production. Moreover, there is a known genetic variation in RFI in all livestock species (Pitchford, 2004), making the selection for RFI possible. However, the biological basis associated with this variation has not been completely elucidated either in small animals (e.g. poultry, mice) or in large animals such as beef cattle. A better understanding of the biological basis associated with RFI might result in the following benefits: prediction of correlated response to selection; identification of traits that are less expensive to measure than feed intake and efficiency and; it might suggest alternative, non-genetic methods, which might be used to manipulate metabolism in beef cattle.

The biological basis associated with RFI in beef cattle have been intensively investigated in the last few years (Johnston et al. 2002; Richardson et al. 2004; Herd et al. 2004; Richardson & Herd, 2004, Kolath et al. 2006a,b, Nkrumah et al. 2006, Hegarty et al. 2007). It is recognised that progress is being made in this area. Some plausible explanations for variation in RFI and identification of physiological markers as predictors for RFI have been developed. As well, technologies such as infrared thermography (Schaefer et al. 2005, Montanholi et al. 2006) and indirect calorimetry (Nkrumah et al. 2006, Castro Bulle et al. 2006) has been applied as a predictive tool for the animal's RFI. There is no shortage of approaches that, singularly or in combination, might contribute to genetic variation in energy utilization in ruminants. Therefore, a challenge for the future is to unravel the mechanisms responsible for the remaining unexplained variation in RFI and to validate the proportional contribution of the already known mechanisms, which might result in new predictors for RFI that could be applied as selection criteria for feed efficiency in beef cattle. The objectives of this paper include: i) to contextualize and define the concept of RFI and to present some of its genetic parameters; ii) to review some of the studies conducted to evaluate the biological basis of RFI and to suggest possible 'new-candidates' for RFI bio-markers; and iii) to highlight some of the potential implications and opportunities for beef cattle breeding on the biological basis of feed efficiency.

Review of literature

Like in other livestock production sectors, the beef sector aims for high productivity and profit to be a successful enterprise. A significant portion of this success is due to the objectives of the breeding program applied. An objective of breeding programs is to increase the efficiency of production, and irrespective of how efficiency is defined, the efficiency of nutrient utilization will form a major component of the breeding program objective (Pitchford, 2004). Feed costs are the main portion of total expenses in cattle feeding operations. The cost of feeding beef cows may account for 60–65% of the total cost of production in a cow-calf operation (Kaliel & Kotowich, 2002). In the feedlot operation these costs may represent more than 70% of the total expenses of production (Taylor & Field, 1999). Thompson & Barlow (1986) modelled the effect of changes in feeding and growth parameters on the efficiency of the cow-calf unit and they concluded that one of the most promising avenues for increasing the biological efficiency of the total production system would be to decrease the maintenance feed costs of breeding cows. To date, approximately 24 million metric tonnes of feed dry matter are fed to an estimated 6.5 million growing calves destined for slaughter in Canada. An improvement in feed utilization of only 1% would result in an estimated savings of over $31 million annually in feed costs to the beef industry alone. It also could result in a reduction of over 242,000 metric tonnes of manure dry matter per year and minimize the greenhouse gases emissions which could have a large impact on reducing the environmental impact of cattle feeding operations. Therefore, improvements in the efficiency of feed utilization will go a long way in reducing the cost of production and will also result in important environmental benefits.

Feed efficiency traits have been incorporated in selection objectives and selection criteria in poultry (Fairfull & Chambers, 1984) and pig breeding programs (De Vries & Kanis 1992). In dairy (Persaud et al. 1991) and beef cattle (Barwick et al. 1994) breeding programs, selection objectives have generally focused on outputs (e.g. fertility and carcass traits), which have not included feed efficiency traits. This approach has been used in cattle due to the difficulty in recording feed inputs. Indeed, the establishment of nucleus breeding herds in dairy and beef presents the opportunity to include feed efficiency traits in the selection objectives and also the opportunity to identify biological predictors of the feed efficiency traits. Besides the myriad of feed efficiency measures described in the literature herein special emphasis will be given to RFI, which has emerged as one of the key parameters for assessing feed efficiency in all livestock species in the last two decades. Especially in the case of beef cattle, there has been increased interest in using RFI as a selection criterion in animal breeding programs. Actually, the Australian beef genetic improvement scheme, BREEDPLAN, started providing estimated breeding values for RFI on animals from 2002 (Arthur & Herd, 2005).

The concept of RFI was first described in 1963 by Koch et al. These authors examined various indices for calculating feed efficiency and suggested that feed intake could be adjusted for liveweight and weight gain, effectively partitioning feed intake into two components: (1) the feed intake expected for the given level of production; and (2) a residual portion. The residual portion (RFI) can be used to identify those animals that deviate from their expected level of feed intake, and they can be classified as high efficiency (negative residual intake) or low efficiency (positive residual intake). The units of RFI are in amount of feed eaten adjusted to mean production rather than feed per unit production, which is common for other efficiency measures. The residual portion is related to true metabolic efficiency which would be comparable across beef industry segments. This feature not only overcomes the limited insight into efficiency of the entire production system, which occurs when using others measures of feed efficiency, but also overcomes the problem of the high correlation with production traits that is characteristic of other feed efficiency traits.

The computation of RFI requires the estimation of expected feed intake. This can be predicted from production data by using feeding standards formulae (e.g. National Research Council, 1996), by using individual feed intake prediction models (e.g. Cornell Value Discovery System, 2004) or by phenotypic or genetic regression using actual feed test data (Kennedy et al. 1993). Calculation of RFI, as reported in several recent studies which used the phenotypic regression approach (Archer et al. 1997; Arthur et al. 2001a,b; Crews et al. 2003), can generally be summarized as:

$$\mathbf{y = \beta_0 + \beta_1(ADG) + \beta_2(WT) + RFI}$$

Where $\mathbf{y}$ is daily feed intake, $\boldsymbol{\beta_0}$ is the regression intercept, $\boldsymbol{\beta_1}$ is the partial regression of daily intake on average daily gain (ADG), and $\boldsymbol{\beta_2}$ is the partial regression of daily intake on body weight (WT). Note that the above equation was designed for young and growing cattle; although the concept of RFI is not so limited, it is possible to adapt equations for other beef cattle categories as well such as pregnant beef cows (Montanholi et al. 2006).

All reviews (e.g. Kelley, 2006) and major studies highlight the existence of genetic variation in feed efficiency and the fact that most feed efficiency traits are moderately heritable, hence the potential for genetic improvement (Arthur & Herd, 2005). Pitchford (2004) calculated the mean heritability of 0.25 for RFI from 35 estimates across seven species/types. Specific heritability estimates of RFI in beef cattle include 0.39 to 0.43 (Arthur et al. 2001a); 0.26 to 0.30 (Crews et al. 2003) and 0.38 (Schenkel et al. 2004). There are no estimates for heterosis associated with RFI in cattle but, negligible values (around 3%) were found in Japanese quail (Pitchford, 2004). From the genetic point of view, RFI owns an extra advantage in comparison to other traits of feed efficiency. It presents a high genetic correlation between the trait measured in the young animal and that measured in the adult, while for other feed efficiency traits, such as feed conversion ratio, this correlation is low (Archer et al. 2002). This indicates that RFI probably reflects more variation in basic metabolic processes (maintenance requirements) than variation due to differences in level of production or growth rate.

Although RFI offers the possibility to select on the proportion of feed intake, which is due to the metabolic processes, in some respects quantitative genetics has been based on a 'black box' approach. This philosophy has been useful, and during the past few decades the discipline of Genetics has been very successful in delivering tools and outcomes to improve animal production (Arthur & Herd, 2005). However, this approach does not make use of the knowledge of physiological processes of animal production. The better understanding and application of the biological basis involved in RFI differences can be very useful for a number of disciplines. The biological basis associated with RFI might work as a tool in Animal Breeding, as well as a bridge between Nutrition, Physiology and Genetics research. Especially in the case of Genetics, a comprehensive understanding of the biological basis of RFI might be helpful for prediction or assessment of correlated responses to selection, supporting quantitative geneticists and also by giving some hints to molecular geneticists about possible metabolic pathways, which might be controlled by certain major genes.

Some studies have been conducted on the biological basis of RFI in beef cattle, mainly by Australian, American and Canadian researchers (Johnston et al. 2002; Richardson et al. 2002 and 2004; Herd et al. 2004a; Richardson & Herd, 2004, Kolath et al. 2006a,b, Nkrumah et al. 2006, Hegarty et al. 2007). Richardson et al. (2002), by looking at the blood cell profiles in animals selected for and against RFI, concluded that it is doubtful that blood cells parameters could be used as predictors for RFI. In a more comprehensive study, Richardson et al. (2004) looked at a number of physiological parameters through key metabolites in beef steers from weaning through to slaughter (Table 1). These researchers found phenotypic correlations between RFI and concentrations of: β-hydroxy butyrate (r = 0.55 at weaning); aspartate aminotransferase (r = 0.34 at weaning; r = 0.43 at feedlot phase); plasma urea (r = 0.26 at weaning); total blood protein (r = 0.26 at weaning); plasma levels of glucose (r = 0.40 at feedlot phase); creatinine (r = -0.45 at feedlot phase); insulin (r = 0.43 over the experiment); blood plasma cortisol (r = -0.40 over the experiment) and leptin (r = 0.31 over the experiment). The concentrations of urea, triglycerides, insulin, and cortisol tended to be correlated with sire estimated breeding values, providing evidence for genetic associations with RFI. Johnston et al. (2002) demonstrated that plasma IGF-1 levels are correlated to RFI (r = 0.56) and its adequacy as a selection criterion for RFI was suggested (Wood et al. 2004). Currently, IGF-1 is used as a marker in a two-stage selection for RFI in Australian breeding programs and since 2004, IGF-1 information was also included in the generation of EBVs for RFI (Arthur & Herd 2005).

Herd et al. (2004) and Richardson & Herd (2004) utilized data from the above studies along with scientific information about feed utilization to estimate the percentage contribution of different physiological events to variation in RFI. Herd et al. (2004) reviewed and summarized five plausible mechanisms by which the variation in the efficiency of nutrient use may occur, Figure 1. Together, these mechanisms may be responsible for about one-third of the variation in RFI, with the remaining two-thirds likely to be associated with heat loss due to variation in other processes, such as protein turnover, ion transport and proton leakage. The study conducted by Richardson & Herd (2004) was slightly different from the previously discussed. Herein, the contribution of 'protein turnover, tissue metabolism and stress' was computed by using a multi-trait prediction equation, without any direct measurement of actual 'protein turnover', Figure 2. The traits selected for this multi-trait equation were: Aspartate amino transferase (AST), beta-hydroxy butyrate (BOH), creatinine (CRE), dry matter digestibility (DMD), leptin (LEP), cortisol (COR), blood viscosity (VIS) and ultrasound measurements (rib (RIB), rump (RUM) and eye-muscle area (EMA). These traits were used to identify differences in body composition (BOH, LEP, CRE, RIB, RUM, EMA); tissue turnover and metabolism (AST and BOH); stress responsiveness (COR) and; any difference in digestibility (DMD). This multiple-trait equation explained 0.52 of the observed variation in RFI.

These two studies discussed above imply that protein turnover might be a meaningful source of variation for RFI. Thus, more specific studies in this area might improve our understanding on the biological basis of RFI. Besides protein turnover, another two physiological processes also have major contributions to the total maintenance energy requirements; these are ion pumping and proton leakage (Rolfe et al. 1999). It is important to be reminded that the basic premise behind the concept of RFI is that the variation in feed efficiency is the result of variation in the basic biological processes, which are mainly represented by these three processes.

Ion pumping is a cellular metabolic process where ions are moved across cell membrane against their concentration gradient. Such transport is highly demanding in energy. In the field of Energy Metabolism one particular kind of ion pumping deserves special emphasis, the Na^+/K^+ pump that accounts for 20 to 30% of the total maintenance energy requirements (Baldwin et al. 1980). The electrical and concentration gradient established by the Na^+/K^+ pump supports the cell resting potential. The exportation of sodium from the cell provides the driving force for several facilitated transporters, and also the translocation of sodium from one side of an epithelium to the other side creates an osmotic gradient that drives the absorption of water. The function of this pump is controlled by the enzyme Na^+/K^+-ATPase, which is located in the cell membrane of every animal cell (Reece & Dukes, 2004). Although it has been suggested that ion pumping is an important source of variation to explain the differences associated with RFI (Richardson & Herd, 2004), there is a lack of studies demonstrating a genetic variation on this physiological event. However, there are some studies that identified a genetic component of ion pumping. For instance, the hyperkalemic periodic paralysis in some lines of Quarter horses is associated with a genetic dysfunction of the Na^+/K^+ pump (Pickar et al. 1991). Similarly, in certain human families one of the forms of migraine headaches is associated with mutations in a gene that encodes a subunit of the Na^+/K^+-ATPase (Wessman et al. 2004).

The proton leakage (H^+) across the mitochondrial membrane is partially catalyzed by uncoupling proteins (UCPs). These proteins have an important role in the total heat production in mammals, representing around 20% of the maintenance energy requirements (Rolfe et al. 1999). The respiration chain across the inner membrane of the mitochondria provides an efficient conversion of energy from a membrane gradient to ATP, through the conversion of ADP + ~P using an electrochemical gradient generated by H^+ concentration (mitochondrial matrix: lower H^+ concentration, mitochondrial intermembrane space high H^+ concentration). When this gradient results in the production of ATP, the system is defined as 'coupled'. However, if the energy is directed away from ATP production toward heat production, due to the activation of a given uncoupler (e.g.: weak acids or UCPs) that dissipates the H^+ electrochemical gradient, less energy is available for ATP production and the system is 'uncoupled' (Jezek et al. 1998). In this situation, energy efficiency is decreased because energy is lost as heat rather than used as an energy source by the cells. The UCPs are located in the mitochondrial inner membrane and promote the pumping of protons from the mitochondrial intermembrane space (H^+) back to the mitochondrial matrix, avoiding the generation of an electrochemical gradient, and thus impairing the ATP formation (Garlid et al. 2000). Kolath et al. (2006b) observed that high and low-RFI beef steers had similar expression of the two most popular UCPs (2 and 3). However, in a previous study these authors (Kolath et al. 2006a) found out that the mitochondrial function was not different between high and low-RFI steers but rather the rate of mitochondrial respiration is increased in low-RFI compared to high-RFI steers, suggesting a better efficiency of electron transfer in low-RFI steers.

Protein turnover involves the continual synthesis and breakdown of body proteins. These processes greatly exceed those of either protein intake or protein deposition (Reeds & Fuller, 1983). Although protein turnover has an important role in helping to ensure homeothermy in mammals, its role in 'tissue plasticity' is also vital (Lobley, 2003). Continual, extensive remodeling of tissue proteins to alter tissue structure, metabolism or activity occurs as part of normal physiological mechanisms. Depending on the physiological condition, increases and decreases in both cell number and size within specific tissues can occur (Lobley, 2003); as well protein synthesis and degradation within cells can be changed (McBride & Kelly, 1990). These changes in metabolism are associated with maintenance energy requirements, which might be reflected on variation in RFI. Around 20% of the maintenance energy requirements are due solely to whole body protein synthesis (Rolfe et al. 1999). There are some divergent information about relationships between protein turnover and RFI. Tatham et al. (2000) found a positive relationship between RFI and plasma creatinine:urea ratio, which is indicative of higher turnover of creatine phosphate in the muscle of high-RFI bulls. Conversely, Castro Bulle et al. (2006) did not find any difference between high and low-RFI beef steers in terms of myofibrillar protein metabolism. These two studies looked at metabolites derived from muscle metabolism which represents 50% of the whole body protein but accounts for only 15-20% of the whole body protein synthesis. However, there has been no investigation done in the protein turnover of more metabolic active organs such as gut, which accounts for only 5-7% of the body mass and represents 32-45% of the whole body protein synthesis.

Protein turnover, ion pumping and proton leakage account for around 60 to 70% of the total energy requirements for maintenance, which basically represent the animals' energetic inefficiency. Therefore, not only are investigations on these individual physiological events desirable, but also studies looking at the total 'heat' output are needed and sometimes easier to conduct than punctual investigations. Animal calorimetry studies have been carried on beef steers separated in low and high RFI groups. Nkrumah et al. (2005) found that more efficient beef steers (low-RFI) had lower heat production than medium or high-RFI steers. Similar results were presented by Castro Bulle et al. (2006). These results indicate that RFI may be negatively correlated with maintenance energy requirements. However, from the practical point of view the assessment of animals' heat production is too laborious and expensive to be performed on a large scale (e.g. testing a contemporary group of bulls). Thus, more reliable alternatives are required. The principal route for energy loss in ruminants is evaporative heat loss (through heat exchange in the lungs and nasal turbinates) (Blaxter, 1967). However, part of the energy loss happens through the skin. This tissue is responsible for 11% of the total heat production of the animal's body (Webster, 1983). Heat is dissipated through the skin by radiation, convection, conduction, or evaporation (Turner, 2001). A possible way to introduce this 'heat' information in breeding programs could be through infrared images (IRI). The infrared camera measures and images the emitted infrared radiation from an object. The fact that radiation is a function of object surface temperature makes it possible for the camera to calculate and display its estimated temperature (Turner, 2001).

Infrared thermography has been applied to assess a number of different aspects of animal production. The surface temperature of the animal's body could be related to several pathological and physiological mechanisms and production aspects. IRI may have potential as a technique for early detection of illness in cattle (Hurnik et al. 1984; Berry et al. 2003; Schaefer et al. 2004). IRI appears to have limited usefulness for routine detection of estrus in dairy cows, but the technique may have potential as a research tool for the study of skin temperature patterns (Hurnik et al. 1985). IRI could be used prior to slaughter to detect poor quality beef and pork (Tong et al. 1995; Schaefer et al, 1989). IRI also may have applications in the field of Animal Nutrition: Caldwell (2007) noticed that bulls fed a high energy diet had higher foot temperatures than bulls fed a low energy diet. Schaefer et al. (2005) demonstrated some preliminary results that IRI may be useful in the assessment of feed efficiency in cattle. Thermal image technology is a potential tool to be applied in large scale animal production systems, because it is a non-invasive, quickly and easily obtained measurement. Moreover, Montanholi et al. (2007) have some preliminary information demonstrating, for the first time, a positive correlation (r = 0.43) between infrared thermography and indirect calorimetry (heat production measured through gas exchange) in cows.

Another approach to look at the maintenance requirements is to consider the individual organs metabolic rate. The gastrointestinal tract (GIT) and liver are the main contributors to the maintenance energy requirements, relative to their contributions to total body mass (less than 10%) in ruminants (Lobley, 2003). Around 50% of the maintenance energy requirements are due to GIT (16 to 29%) and liver (20 to 26%) metabolism (Johnson et al. 1990). Unfortunately, there is limited information in the scientific literature relating RFI and the metabolism of the GIT and liver. However, the literature is rich in information about maintenance energy requirements and visceral tissue changes. There are demonstrated differences in efficiency of energy use for maintenance between animals, within species and at similar physiological states. There is also evidence that the maintenance energy requirement is associated with genetic variation in RFI (Herd et al. 2004).

Liver and GIT weights appear to increase or decrease in direct proportion to dietary intake within and across physiological stages of maintenance, growth, fattening or lactation (Johnson et al. 1990). There are also changes in visceral organ weights according to the plane of nutrition (Sainz & Bentley, 1997; Swanson et al. 1999). Changes in tissue mass are the net result of rates of cellular proliferation, cellular losses, as well as changes in cellular size (Alberts et al. 2002). The intestine has a remarkable capacity to adapt to changing conditions of alimentation. Starvation or protein deficiency results in atrophy (shrinkage of a tissue or organ due to a reduction in the size or number of cells). On the other hand, refeeding or feed intake above the normal levels results in hyperplasia (increment in the size of a tissue or organ due to the increment in the number of cells) (Fawcett, 1994). Compared to other organs that are constantly being renewed, the hepatic parenchyma is a rather stable cell population; cells in division are seldom seen in the normal liver (Fawcett, 1994). This implies that changes in the liver weight are mainly due to hypertrophy (increment in the size of a tissue or organ due to the enlargement of existing cells).

Measurements of DNA, RNA and protein content in tissue samples can be used as indirect parameters of cell proliferation and cell size (Burrin et al. 1988; Sainz & Bentley, 1997; Swanson et al. 1999; Baldwin et al. 2004). The amount of DNA in the tissue sample is associated with the number of cells, because DNA is one of the components of the cell nucleus. DNA content between cells is quite constant within a specific cell type. The net content of protein and RNA within a cell or tissue is a result of the balance between synthesis and degradation. The relationship between estimates of actual rates of protein synthesis and ratios of cellular constituents is commonly used to indicate protein synthetic capacity of a tissue. Research has been conducted on the quantification of these nucleic acids and its quantitative relationships in liver and intestine of cattle relative to nutritional treatments (Swanson et al. 1999; Baldwin et al. 2004). However, these determinations were not well characterized between animals of different breed types or in animals ranked according to their RFI values. In the same way, direct measurements through tissue morphological studies of the patterns of cell proliferation and cell size changes may display a complementary role to the indirect measurements described above (or vice-versa). As well, patterns of natural cell death (apoptosis) might be observed through light microscopy.

Still related to the source of variation ‘protein turnover, tissue metabolism and stress’ discussed above (Figure 2), the stress component seems to display an important role in the variation of RFI in beef cattle. Stress in beef cattle is a non-specific response of the body to any demand from the environment (Frazer et al. 1975). Cattle in an intensive husbandry system are potentially subjected to an increased abundance of stressors (Fox, 1985). These stressors may end up requiring some extra activation of the animals’ immune system, which might result in a lower performance or a poorer feed efficiency (Klasing & Leshchinsky, 2000). There are some indications that in the main domestic species the high genetic pressure applied for growth has contributed to the development of lines in which nutrients are more directed to the growth of muscle at the expense of the immune system (Rauw et al. 1998). One of the consequences of chronic stress in farm animals is a suppression of the body defense barriers resulting in a lower resistance to pathogens, which certainly will result in an activation of the immune system beyond the basal level. Cortisol, a glucorticoid hormone, synthesized and released by the adrenal gland, is a key component of the physiological response to stress (Palme et al. 2005). Richardson et al. (2004) noticed that beef steers with a genetic propensity for low-RFI have a lower cortisol concentration in the blood following stress than steers with high-RFI (8.51 vs 19.84 ng/ml) and the correlation between RFI and concentration of plasma cortisol was -0.40. Thus, cortisol levels might be a good candidate as a bio-marker for RFI.

However, there are some concerns associated with the measurement of stress hormone levels, especially in blood samples, as done by Richardson et al. (2004). Because secretion of glucorticoids occurs in a pulsatile fashion, blood hormone concentration can change by a factor of 10 or more within minutes (Palme et al. 2005). Therefore, interpretation (on the individual level) of most endocrine parameters based on a single (blood) sample might be misleading. In addition, stress experienced during the sampling procedure imposes an important limitation. Fortunately, stressful sample collection can be avoided by using alternative sample matrices such as: saliva (Negrão et al. 2004), urine (Gwinup & Johnson, 1975), feces (Mooring et al. 2006), and hair (Davenport et al. 2006). Like blood samples, saliva is a ‘point’ sample strongly affected by time of day, food intake, and any environmental disturbance that may have occurred shortly before sampling. On the other hand, cortisol values obtained from urine, feces and hair samples reflect somewhat longer periods of hypothalamic-pituitary-adrenocortical activity, thereby providing a true basal hormonal ‘phenotype’ for each individual subject (Davenport et al. 2006). Palme et al. (2003) found that fecal concentrations of cortisol metabolites in cattle reflected the total amount excreted and therefore reflected cortisol secretory patterns better than did blood concentrations, which changed quickly. In addition, because only the free cortisol fraction from the blood is available for metabolism and excretion, fecal cortisol metabolite concentration may more accurately reflect the biologically active portion of the hormone. Therefore, it might be worthwhile to examine the possible relationship between RFI and cortisol levels in different tissues matrices (e.g. feces) rather than blood plasma.

Conclusions and Implications to Genetic Improvement of Beef Cattle

Feed efficiency measurements constitute one of the key approaches to study animal bioenergetics and metabolism, which represent ‘undiscovered’ niches of potential traits for beef cattle breeding programs. Recently residual feed intake has re-emerged as one of the potential tools to verify the potential differences in feed efficiency among different animals. This trait likely reflects variation in basic metabolic processes more than variation due to differences in the level of production. Therefore, primary research on the most basal energy demanding processes of the organism might result in quite reliable indicators of animals’ performance, which might constitute potential tools for beef breeding.

Research conducted by diverse research groups worldwide have begun to emerge in the last few years. However, reasonable explanations for differences in feed efficiency and accurate predictors are still lacking and there are many of hypotheses yet to be tested. Besides information on increasing our understanding of the biological basis associated with feed efficiency, new bio-markers for feed efficiency will likely be proposed. There is clearly a need for more easily-obtainable indicators of the animals’ residual feed intake than that obtained through the feed record per se.

In this paper, a few potential possibilities of physiological explanations for distinct residual feed intakes were suggested; certainly many other approaches are possible to apply in the searching for biological differences among animals in respect to feed efficiency. For instance, one of the most promising technologies to ‘scan’ the animal’s tissues for potential bio-markers is proteomics; however, the costs associated with this technology are still prohibitive on a large scale. On the other hand, some of the above suggested topics such as cellular studies, infrared thermography and hormonal determinations might be examined using technologies that are more affordable and easily accomplished. Therefore an interesting scenario of testing new traits and looking for key-controlling genes will make the life of Animal Geneticists more fascinating in the near future.

Moreover, the fact that different disciplines are being combined to study feed efficiency, one might expect more biological meaningful models to explore the variation that exists in feed efficiency, as well as a greater interconnection among researchers with different expertise. This interdisciplinary approach is beneficial for ‘Beef Science’ as a whole.

Finally, the economical and environmental benefits associated with selection for more feed efficient animals are strong arguments for a long life of research on this subject. One might suggest that a new era of more and more fine tuned and comprehensive investigations in feed efficiency has emerged with the 're-discovery' of residual feed intake, which certainly will have important repercussions on Beef Breeding in the next decades.

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References

Alberts B, Johnson A, Lewis J, et al. Molecular Biology of the Cell. 4th ed. New York: Garland Publishing; 2002. 1462p.

Archer JA, Arthur PF, Herd RM, et al. Optimum postweaning test for measurement of growth rate, feed intake and feed efficiency in British breed cattle. *Journal of Animal Science*. 1997;75:2024-2032.

Archer JA, Reverter A, Herd RM, et al. Genetic variation in feed intake and efficiency of mature beef cows and relationships with postweaning measurements. In: 'Proceedings of the 7th world congress on genetics applied to livestock production'. (Institut Nacional de la Recherche Agronomique, France:Montpellier) 2002;31:221-224.

Archer JA, Richardson EC, Herd RM, et al. Potential for selection to improve efficiency of feed use in beef cattle: A review. *Australian Journal of Agricultural Research*. 1999;50:147-161.

Arthur PF, Renand G, Krauss D. Genetic and phenotypic relationships among different measures of growth and efficiency in young Charolais bulls. *Livestock Production Science*. 2001a;68:131-139.

Arthur PF, Archer JA, Johnston DJ, et al. Genetic and phenotypic variance and covariance components for feed intake, feed efficiency, and other postweaning traits in Angus cattle. *Journal of Animal Science*. 2001b;79:2805-2811.

Arthur PF, Herd RM. Efficiency of feed utilization by livestock – Implications and benefits of genetic improvement. *Canadian Journal of Animal Science*. 2005;85:281-290.

Baldwin RL, Smith NE, Taylor J, et al. Manipulating metabolic parameters to improve growth rate and milk secretion. *Journal of Animal Science*. 1980;51:1416-1428.

Baldwin RL, McLeod KR, Capuco AV. Visceral tissue growth and proliferation during the bovine lactation cycle. *Journal of Dairy Science*. 2004;87:2977-2986.

Barwick SA, Henzell AL, Graser HU. Developments in the construction and use of selection indexes for genetic evaluation of beef cattle in Australia. In: 'Proceedings of the 5th world congress on genetics applied to livestock production'. (University of Guelph:Guelph) 1994;18:227-230.

Berry RJ, Kennedy AD, Scott SL, et al. Daily variation in the udder surface temperature of dairy cows measured by infrared thermography: Potential for mastitis detection. *Canadian Journal of Animal Science*. 2003;83:687-693.

Blaxter KL.The Energy Metabolism of Ruminants. 2nd ed. (revised). Hutchinson Scientific and Technical : London, UK; 1967. 332p.

Burrin DG, Britton RA, Ferrel CL. Visceral organ size and hepatocyte metabolic activity in fed and fasted rats. *Journal of Nutrition*. 1988;118:1547-1552.

Caldwell TR. Dietary energy and breed Effects on growth, health and body composition of yearling beef bulls. Master Science Thesis. Department of Animal & Poultry Science - University of Guelph, Guelph, ON, Canada. 182p. 2007.

Castro Bulle FC, Paulino PV, Sanches AC, et al. Growth, carcass quality, protein and energy metabolism in beef cattle with different growth potentials and residual feed intakes. *Journal of Animal Science*. 2006 Dec 18; [Epub ahead of print].

Cornell Value Discovery System CVDS: CVDS version 1.0.6 User's Guide. 1st ed. Department of Animal Science, Cornell University, Ithaca, NY. 2004. 33p.

Crews DH Jr, Shannon NH, Genswein BMA, et al. Genetic parameters for net feed efficiency of beef cattle measured during postweaning growing versus finishing periods. In: 'Proceedings, Western Section, American Society of Animal Science' (Phoenix). 2003;54:125-128.

Darwin C. The Origin of Species. (1st ed. 1859). Random House of Canada Limited : Toronto, ON; 1998. 689p.

Davenport MD, Tiefenbacher S, Lutz CK, et al. Analysis of endogenous cortisol concentrations in the hair of rhesus macaques. *General and Comparative Endocrinology*. 2006;147:255-261.

De Vries AG, Kanis E. A growth model to estimate economic values for food intake capacity in pigs. *Animal Production*. 1992;55:241-246.

Fairfull RW, Chambers JR. Breeding for feed efficiency: poultry. *Canadian Journal of Animal Science*. 1984;64:513-537.

Fawcett DW. A Textbook of Histology. 12th ed. Chapman & Hall : New York, NY. 1994. 964p.

Ferrell CL., Jenkins TG. Body composition and energy utilization by steers of diverse genotypes fed a high-concentrate diet during the finishing period: II. Angus, Boran, Brahman, Hereford, and Tuli sires. *Journal of Animal Science*. 1998;76:647-657.

Frazer DJ, Ritchie JSD, Frazer AF. The term 'stress' in a veterinary context. *The British Veterinary Journal*. 1975;131:653-658.

Fox MW. Philosophies and ethics in ethology. In: 'Ethology of farm animals: A comprehensive study of the behavioural features of the common farm animals.' AF Fraser (editor). Elsevier : Amsterdam, 1985:29-32.

Gwinup G, Johnson B. Clinical testing of hypothalamic-pituitary-adrenocortical system in states of hypo- and hypercortisolism. *Metabolism*. 1975;24:777-791.

Hegarty RS, Goopy JP, Herd RM, et al. Cattle selected for lower residual feed intake have reduced daily methane production. *Journal of Animal Science*. 2007 Feb 12; [Epub ahead of print]

Herd RM, Oddy VH, Richardson EC. Biological basis for variation in residual feed intake in beef cattle. 1. Review of potential mechanisms. *Australian Journal of Experimental Agriculture*. 2004;44:423-430.

Hurnick JF, DeBoer S, Webster AB. Detection of health disorders in dairy cattle utilizing a thermal infrared scanning technique. *Canadian Journal of Animal Science*. 1984;64:1071-1073.

Hurnick J F, Webster AB, DeBoer S. An investigation of skin temperature differentials in relation to estrus in dairy cattle using a thermal infrared scanning technique. *Journal of Animal Science*. 1985;61:1095-1102.

Jezek P, Garlid KD. Mammalian mitochondrial uncoupling proteins. *International Journal of Biochemistry & Cell Biology*. 1998;30:1163-1168.

Johnson DE, Johnson KA, Baldwin RL. Changes in liver and gastrointestinal tract energy demands in response to physiological workload in ruminants. *Journal of Nutrition*. 1990;120:649-655.

Johnston DJ, Herd RM, Kadel MJ, et al. Evidence of IGF1 as a genetic indicator of feed efficiency traits in beef cattle. In: 'Proceedings of the 7th world congress on genetics applied to livestock production'. (Institut Nacional de la Recherche Agronomique, France:Montpellier) 2002; CD ROM Communication. No. 10-16.

Kaliel D, Kotowich J. Economic evaluation of cow wintering systems — Provincial swath grazing survey analysis. Alberta Production Economics Branch, Alberta Agriculture Food and Rural Development, Edmonton, AB.2002.

Kelley AL. The relationship of genetics and nutrition and their influence on animal performance. In: 'Proceedings of the Beef Improvement Federation - 38th Annual Research Symposium and Annual Meeting' (Pearl River Resort, Choctaw, Mississippi) 2006; p.84-90.

Kennedy BW, Van der Werf JHJ, Meuwissen THE. Genetic and Statistical properties of residual feed intake. *Journal of Animal Science*. 1993;71:3239-3250.

Klasing KC, Leshchinsky TV. Interactions between nutrition and immunity. Lessons from animal agriculture. In: *Nutrition and immunology: Principles and practice*. Editors: Gershwin JB, Germanand. Keen CL. Elsevier : Amsterdan. P. 363-373. 2000

Koch RM, Swiger LA, Chambers D, et al. Efficiency of feed use in beef cattle. *Journal of Animal Science*. 1963;22:486-494.

Kolath WH, Kerley MS, Golden JW, et al. The relationship between mitochondrial function and residual feed intake in Angus steers. *Journal of Animal Science*. 2006a;84:861-865.

Kolath WH, Kerley MS, Golden JW, et al. The relationships among mitochondrial uncoupling protein 2 and 3 expression, mitochondrial deoxyribonucleic acid single nucleotide polymorphisms, and residual feed intake in Angus steers. *Journal of Animal Science*. 2006b;84:1761-1766.

Lobley GE. Protein turnover – what does it mean for animal production. *Canadian Journal of Animal Science*. 2003;83:327-340.

McBride BW, Kelly JM. Energy cost of absorption and metabolism in the ruminant gastrointestinal tract and liver: a review. *Journal of Animal Science*. 1990;68:2997-3010.

Montanholi YR, Ko M, Mader C, et al. Relationships among residual feed intake, plasma urea nitrogen concentration and infrared images in beef cows. In: 'Proceedings of the Joint Colloquium of the Canadian Society of Animal Science, Canadian Society of Agronomy and Canadian Society of Horticultural Science' (Nova Scotia Agricultural College, Truro). 2006;P42:103.

Montanholi YR, Odongo NE, Swanson KC, et al. Usefulness of infrared imaging as a predictor of heat loss and methane production in dairy cows. In: 'Proceedings of the American Society of Animal Science Annual Meeting. San Antonio, TX. United States. 2007. [*in press*].

Mooring MS, Patton ML, Lance VA, et al. Glucorticoids of bison bulls in relation to social status. *Hormones and Behavior*. 2006;49:369-375.

National Research Council: Nutrient requirements for beef cattle. 7th revised ed. National Academic Press, National Academy of Science, Washington, DC. 1996. 232p.

Negrão JA, Porcionato MA, De Passillé AM, et al. Cortisol in saliva and plasma of cattle after ACTH administration and milking. *Journal of Dairy Science*. 2004;87:1713-1718.

Nkrumah JD, Okine EK, Mathison GW, et al. Relationships of feedlot feed efficiency, performance, and feeding behavior with metabolic rate, methane production, and energy partitioning in beef cattle. *Journal of Animal Science*. 2006;84:145-153.

Palme R, Wetscher F, Winckler C. Measuring feacal cortisol metabolites: a non-invasive tool to assess animal welfare in cattle? In: 'Proceedings of the IVth Central European Buiatric Congress'. (Lovran, Croatia) 2003; pp. 145-150.

Palme R, Rettenbacher S, Touma C, et al. Stress hormones in mammals and birds: Comparative aspects regarding metabolism, excretion, and noninvasive measurement in fecal samples. *Annals New York Academy of Sciences*. 2005;1040:162-171.

Persaud P, Simm G, Hill WG. Genetic and phenotypic parameters for yield, food intake and efficiency of dairy cows fed ad libitum. 1. Estimates for 'total' lactation measures and their relationship with live-weights traits. *Animal Production*. 1991;52:435-444.

Pickar JG, Spier SJ, Snyder JR, et al. Altered ionic permeability in skeletal muscle from horses with hyperkalemic periodic paralysis. *American Journal of Physiology*. 1991;260:C926-933.

Pitchford WS. Genetic improvement of feed efficiency of beef cattle: what lessons can be learnt from other species? *Australian Journal of Experimental Agriculture*. 2004;44:371-382.

Rauw WN, Kanis E, Noordhuizen EN, et al. Undesirable side effects of selection for high production efficiency in farm animals: a review. *Livestock Production Science*. 1998;56:15-33.

Reece WO, Dukes HH. Dukes' Physiology of Domestic Animals. 12th ed. Cornell University Press : Ithaca, US; 2004. 999p.

Reeds PJ, Fuller MF. Nutrient intake and protein turnover. *Proccedings of Nutrition Society*. 1983;42:463-471.

Richardson EC, Herd RM, Golditz IG, et al. Blood cell profiles of steer progeny from parents selected for and against residual feed intake. *Australian Journal of Experimental Agriculture*. 2002;42:901-908.

Richardson EC, Herd RM, Archer JA, et al. Metabolic differences in Angus steers divergently selected for residual feed intake. *Australian Journal of Experimental Agriculture*. 2004;44:431-440.

Richardson EC, Herd RM. Biological basis for variation in residual feed intake in beef cattle. 2. Synthesis of results following divergent selection. *Australian Journal of Experimental Agriculture*. 2004;44:431-440.

Rolfe DF, Newman JM, Buckingham JA, et al. Contribution of mitochondrial proton leak to respiration rate in working skeletal muscle and liver and to SMR. *American Journal of Physiology*. 1999;276:C692-699.

Sainz RD, Bentley BE. Visceral organ mass and cellularity in growth-restricted and refed beef steers. *Journal of Animal Science*. 1997;75:1229-1236.

Schaefer AL, Jones SD, Murray AP, et al. Infrared thermography of pigs with known genotypes for stress susceptibility in relation to pork quality. *Canadian Journal of Animal Science*. 1989;69:491-495.

Schaefer AL, Cook N, Tessaro SV, et al. Early detection and prediction of infection using infrared thermography. *Canadian Journal of Animal Science*. 2004;84:73-80.

Schaefer AL, Basarab J, Scott S, Colyn J, et al. The relationship between infrared thermography and residual feed intake in cows. *Journal of Animal Science*. 2005;83:Supl.1/J, 263. *Journal of Dairy Science*. 2005;88:Supl.1, 263.

Schenkel FS, Miller SP, Wilton JW. Genetic parameters and breed differences for feed efficiency, growth, and body composition traits of young beef bulls. *Canadian Journal of Animal Science*. 2004;84:177-185.

Swanson KC, Redmer DA, Reynolds LP, et al. Ruminally undegraded intake protein in sheep feed low-quality forage: effect on weight, growth, cell proliferation, and morphology of visceral organs. *Journal of Animal Science*. 1999;77:198-205.

Taylor RE, Field TG. Beef Production and Management Decisions. 3rd ed. Prentice Hall : Upper Saddle River, NJ. 1999. 714p.

Tatham BG, Davis JJ, Ferrier GR. Commercial application of net fed intake assessment, biochemical relationships and economic implications of using tested Angus bulls. *Asian-Australian Journal of Animal Science*. 2000;13:327-330.

Thompson JM, Barlow R. The relationship between feeding and growth parameters and biological efficiency in cattle and sheep. In: 'Proceedings of the 3rd word congress on genetics applied to livestock production'. (University of Nebraska:Lincoln) 1986;11:271-282.

Tong AKW, Schaefer AL, Jones SDM. Detection of poor quality beef with infrared thermography. *Meat Focus International*. 1995;4:443-445.

Turner TA. Diagnostic thermography. *Veterinary Clinics of North America: Equine Practice*. 2001;17:95-113.

United Nations Food and Agriculture Organization. (Livestock's long shadow – Environmental Issues). http://www.fao.org/newsroom/en/news/2006/1000448/index.html. Accessed in December 1st 2006.

Webster AJF. Energetics of maintenance and growth. In: *Mammalian Thermogenesis*. Girardier L, Stock M. (editors). 1st ed. New York: Chapman and Hall Ltd; 1983. 359p.

Wessman M, Kaunisto MA, Kallela M, et al. The molecular genetics of migraine. *Annals of Medicine*. 2004;36:462-473.

Table 1. Metabolic processes evaluated and specific parameters measured to access the some potential bio-marker for RFI in beef cattle

Process	**Parameter** (in blood plasma unless shown otherwise)
Energy substrates	- Glucose, β-hydroxy butyrate (BOH), triglycerides
Skeletal muscle mass	- Creatinine (blood and urine), urea
Protein metabolism	- Creatine kinase, urea, albumin, total plasma protein (TPP), 3-methyl histidine (urine, 3MH), aspartate aminotransferase (AST)
Fat mass and metabolism	- Triglicerides, leptin
Liver function	- Total bilirubin, γ-glutamyl transferase, AST, alkaline phosphatase
Stress	- Cortisol
Oxygen transport efficiency	- Blood viscosity
Digestion	- Dry matter digestibility (DMD)
Rumen microbial protein production	- Allantoin (urine)

Source: Richardson et al. 2004.

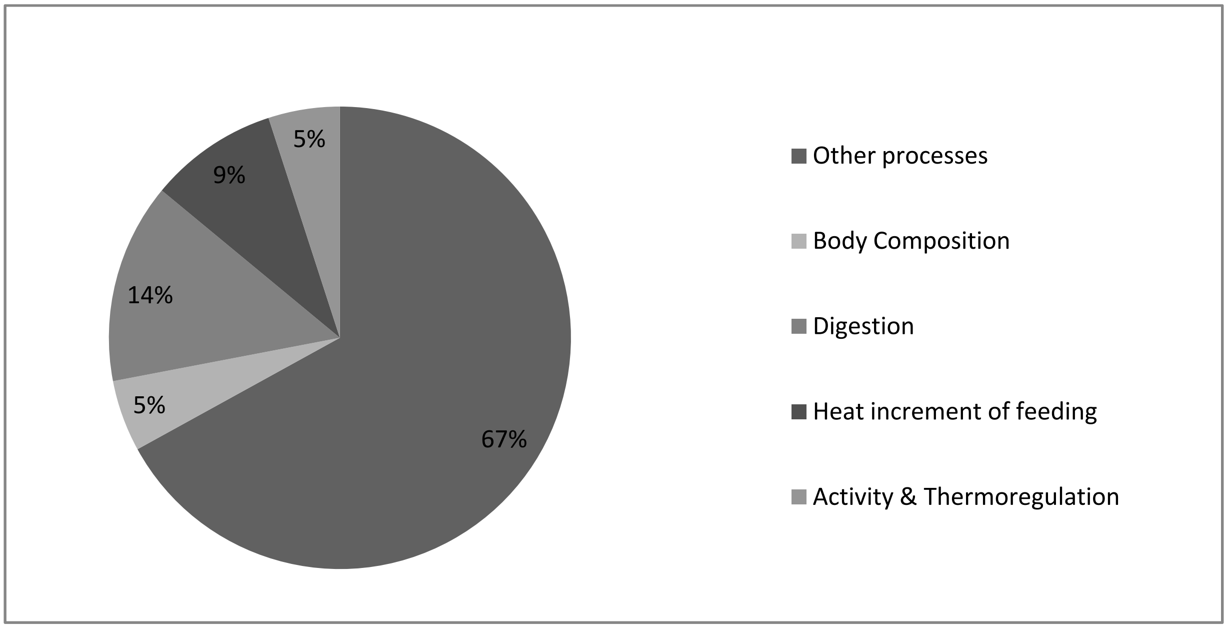

Figure 1. Estimates of the percentage contribution of different mechanisms contributing to the variation in RFI in beef cattle. Source: Herd et al. 2004.

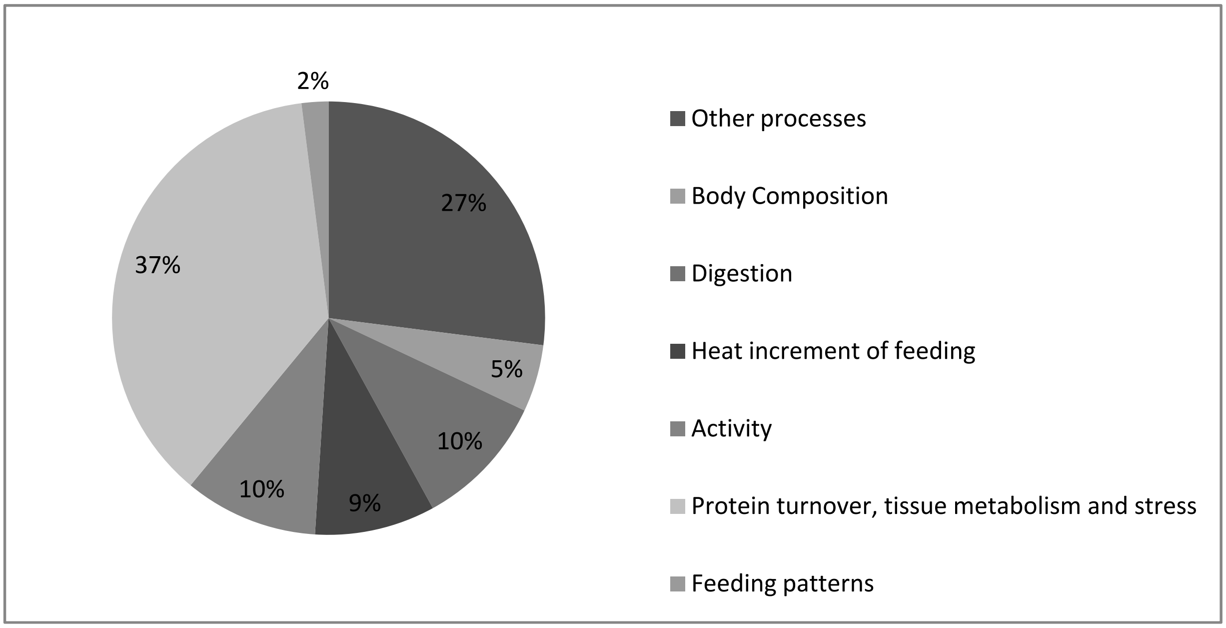

Figure 2. Estimates of the percentage contribution of different mechanisms contributing to the variation in RFI in beef cattle. Source: Richardson & Herd, 2004