

Reproduction during lactation of dairy cattle: Integrating nutritional aspects of reproductive control in a systems research approach



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Implications

- Reproduction in mammals is a highly complex system that is affected by many genetic and environmental components.
- There is no simple way to describe control of reproduction, such as “increased body fat improves fertility”; there are too many variables.
- A systems research approach involving cooperative and integrated study design, hypothesis setting, data sharing, and mathematical modeling can speed improvement in reproductive success
- Reproduction in dairy cattle is a multivariate process that is under control of heritable and constitutive genetic traits, nutrient profiles and intake, season, housing, and climate. To more rapidly improve practical reproduction such as pregnancy rate, a fully systems biology approach to research and application must be taken. We have improved management, housing, nutrition, and breeding, but we must now fully integrate our efforts to identify those primary genetic and nutritional controls. A bio-mathematical systems model that can contribute to this task is proposed.

Key words: lactation, mechanistic models, reproduction, systems biology

Introduction

Reproductive success in any mammalian species, including highly selected dairy cattle, is a result of dynamic, interacting genetic and environmental factors. These include the genetic background or genome of the animal and the nutrient composition, and intake; a complex of interaction between hormonal and neural processes; and environmental factors such housing, temperature, and season of year. Although few would argue with this generic summary, it is a primary premise of this review that to improve dairy cattle reproductive success, the research and application communities including university scientists, breeding organizations, bull studs, nutrition companies, and pharmaceutical firms must fully accept the

complexity of the process and adapt accordingly. That said, we have had a tremendous increase in both basic and applied, “on-farm” knowledge about reproductive management. Because of the increase in basic knowledge and improved method to apply it practically, attitudes about research funding and practical management are changing rapidly. There is in the past few years a significant increase in more complex (systems biology) approaches to reproductive improvement and recognition that this is truly the only way to move forward.

We hope to encapsulate recent research findings that demonstrate the complexity of the situation and provide one or two examples of how the dairy science research and application communities are moving forward, which should speed improvement in reproductive success. The primary goal is to stimulate an increase in coordinated, systems-based research and analysis in the animal agriculture community worldwide. This is meant to be a general review, not an in-depth reiteration of detail, which can be found in the references. In addition, the primary goal is to stimulate discussion and thought from, perhaps, a little different perspective compared with traditional approaches and also to encourage the audience of younger scientists and students to pursue new approaches in their careers.

As an example of a systems approach in describing complex biological relationships, in the decision process for a title of this paper, the phrase “how lactation competes with resources for subsequent reproduction” was suggested. Additionally, phrases such as “negative energy balance reduces reproduction” or “high-producing cows are less fertile,” or “genetics does not affect reproduction” have been used many times in teaching and in research reviews. However, in fact, these are all simplifications that can be misleading, especially to students. Thus, in this review we hope to encapsulate recent research findings that demonstrate the complexity of the situation and provide one or two examples of how the dairy science research communities, both basic and applied, are moving forward and can speed improvement in reproductive success. Hopefully, we can seize opportunities to solve what in effect is actually a quite simple problem: how to feed everyone in the world a highly nutritious diet that includes animal products. Our call and challenge as animal scientists is no less than this: how do we ensure a safe and sustainable high quality protein food supply worldwide for future generations?



A Systems Approach to Reproduction

Systems biology means different things to different people. But at a minimum, it is 1) at least the recognition that each piece of the system (e.g., gene, enzyme, pathway, cell, organ, animal, and herd) has a specific function related to the outcome of the entire system and is not limited to any one subsystem; and 2) a fully systems approach in research and application is the best way forward. For example, synthesis of ATP from the TCA cycle and electron transport chain in the liver provides immediate support to anabolic reactions in a liver cell, but the protein synthesized is exported into the blood to serve other needs of the system. When the work in metabolic control of pathway flux evolved into study of gene transcription and protein translation, and when sophisticated techniques were developed to study those processes, systems biology was taken by some to be relevant only to genomic, transcriptomic, or proteomic work. However, the genome, transcriptome and proteome exist only to serve the needs of the entire system. The fields of genomics and transcriptomics have provided a wealth of knowledge, but in large part, this information has not been fully integrated into our biological models and decision-making systems. Measuring transcripts of mRNA or defining QTL and SNP tell us about part of the system, but knowledge at those levels needs to be integrated into control of metabolic, endocrine, and cell-signaling pathways and then into animal-level nutritional, genetic, and reproductive management. Given that, where do we move forward in the system of research in control of animal production?

The transition cow is an example of a complex system of many parts focused on the dominant physiological state of lactation, with a multifactorial goal of feeding the present generation while also initiating the next one. However, the primary research approach has been reductionistic, focusing on specific disciplines such as nutrition, genetics, reproduction, and others. This research has provided a significant amount of understanding and improvement in the field, but until recently, most of the scientists in these disciplines did not interact and test more integrated hypotheses. For example, high milk production and fertility were not thought to be compatible for inclusion together in a study or the thinking was that reproductive traits have low heritability compared with milk production, so the focus was on milk production. Newer, more integrated approaches now have shown clearly the interconnectedness of genetics, nutrition, and reproduction in dairy cattle and other species (Bello et al., 2012; Butler, 2003; Roche, 2006; Chagas et al., 2007; Vazquez et al., 2010; Lean et al., 2011). Great strides in appli-

cations of research in genetics, nutrition, and reproduction have resulted in increased production within the dairy industry. But a full systems approach could improve all of these simultaneously, and even faster.

Overview of metabolism and reproduction

A simple summation of reproductive processes in the lactating dairy cow could be: the hypothalamus provides GnRH, which stimulates LH and FSH release. These hormones affect the ovary to initiate and maintain waves of follicular growth, eventually leading to a dominant follicle that could be ovulated. The follicles secrete estrogen, which has both stimulatory and negative effects on its own synthesis as well as that of LH and FSH. Eventually a follicle is ovulated and a viable egg is presented to the fallopian tubes. The circulating estrogen provides for visible signs of estrus, which, hopefully, are noticed, and leads to the timely insemination of the animal. The fertilized egg begins to develop, and the new developing corpus luteum begins to secrete progesterone. Circulating estrogen levels decline and the increasing progesterone results in a series of adaptations in the uterus that allow for acceptance and implantation of the developing embryo. Each of these processes involves several intracellular and intercellular systems including endocrine and neural signaling, gene transcription, translation, protein linking such as receptor binding and second messengers, enzyme catalysis, and many chemical interactions, all requiring energy. Almost every one of these steps has a genetic component of variable heritability, and many of them can be affected by environmental characteristics such as nutrient composition and quantity, housing, social interactions, season, and climate. For example there are genetic variations in the expression of the FSH receptor and in progesterone-induced gene transcription as well as variations in the receptors and enzymes controlling body fat metabolism, which lead to differences in body fat content, IGF1 signaling, and leptin production (McNamara, 2012). The inclusion of daughter pregnancy rate in bull proofs is “proof enough” that reproduction is heritable; the remaining questions deal with the specific mechanisms and heritabilities.

Nevertheless, the fetus develops over time, and a healthy female calf is born, which goes on to produce copious amounts of milk over several lactations. There are obviously several mechanistic links herein, but this previous discourse sums up the process in general. The good news is that we have a lot of knowledge and detail on these processes and an adequate systems model to direct detailed and integrated research. We will now provide some of the relevant detail needed to integrate nutrition and reproduction.



Body fat and reproduction

The role of body fat and nutritional status in reproductive fertility was recognized early in human history. Ancient or historical texts, drawings, and writings speak to traditions and perceptions of body fatness, shape, and size in human fertility. Likewise, domesticated animals were fattened to become fertile and sleek, and fat cattle were desired for their fertility. It was noted that gross or even moderate stunting of growth delayed sexual maturity in most females. Even when outward signs of fertility were seen; a number of situations in which actual fertility was delayed or reduced were noted, including insufficient total food or the lack of certain food components. Some amount of adipose tissue was necessary for a successful reproductive cycle of ovulation, fertilization, implantation, and pregnancy.

Fertility and postpartum anestrus vary among species or even breeds, and can be attenuated or exacerbated by nutritional status; and while a certain amount of body fat might correlate with improved fertility, too much may be detrimental. Beef and dairy cattle are the same species but were selected for different functions and, thus, vary in their postpartum anestrus and fertility. This is a general, but valid, indication of at least some role of genetics in reproductive success. Today, we realize that, in fact, there is more to fertility than just fatness—some animals alter fertility after increases or decreases in body fatness (Wade and Schneider, 1992). It is not simply the amount of body fat but flux of glucose or other nutrients such as vitamins and minerals that alter fertility or gestational and lactational success (Wade and Schneider, 1992; Wade and Jones, 2004). In addition, there are hormones such as IGFI and leptin that are released by the adipose tissue and have some role in reproductive processes. There have been several excellent reviews and papers on these topics, which summarize their integrated nature with nutrition genetics and reproduction (Wade and Schneider, 1992; Butler, 2003; Wade and Jones, 2004; Jamrozik et al., 2005; LeBlanc et al., 2005; McNamara, 2005; Lean and Rabiee, 2006; Vinsky et al., 2006; Chagas et al., 2007; Diskin and Morris, 2008; Morris and Diskin, 2008; Lucy et al., 2009; Chapinal et al., 2012; Thatcher et al., 2012). The existence of a relationship between a positive energy balance and reproductive success is clear (Wade and Schneider, 1992; Butler, 2003). This understanding led to a more specific hypothesis: “How can reproductive organs monitor and respond to the amount of body fat, or vice

versa”? A corollary and related line of research asked similar questions in relation to maintenance of body fat: “How does the body monitor and maintain a fairly constant body fat percentage, and what are the situations in which this system can fail and obesity (or extreme thinness) or reproductive problems ensue”? As much work as has been done in genetics, nutrition and reproduction and the clear connections, one might think that a serious systems model approach was already happening, nevertheless, this approach is being embraced now.

One major outcome of this research effort was that the amount of body fat alone did not account for even a small majority of the variation in fertility. Large variations in the amount of body fat and associated rates of change during different stages in reproductively successful females precluded body fat content as being the ultimate driving force (Butler and Smith, 1989; Wade and Schneider, 1992). In a general sense, it is true that body fat is directly related to reproduction; however, the preponderance of evidence is that, although body fat is a key part of the system, it is the nutrient flux involving glucose, fatty acid, and amino acids that is the mechanistic cause of changes in reproductive status and its relative success.

Metabolic flux and the role of glucose in reproduction

One of the subsequent areas of research focused on glucose. Many studies were done to ask the questions of “How does glucose status relate to reproductive success”? Glucose supply and flux is a major driver of reproductive success (Butler, 2003; Wade and Jones, 2004; Chagas et al., 2007). Glucose flux into many cell types, including brain, adipose, liver, muscle, and ovary initiates many cascading signals that direct metabolic flux, including fat and protein synthesis. In addition to generation of energy for anabolic reactions, glucose also is used at multiple sites during gene expression. The multivariate role of glucose in regulation of metabolism occurs immediately via increases in ATP and NADPH concentrations for enzyme activation as well as over several days or weeks through changes in mRNA transcription and translation to make the enzymes that catalyze many synthetic reactions. Several of these effects relate directly or indirectly to reproductive processes.

The role of glucose in reproduction is integrally related to endocrine activity. Glucose elicits specific responses such as insulin and IGFI, and these systems cannot easily be separated. We cannot fully explain the connections between nutrient flux and reproduction without introducing the endocrine aspects. There are well-established relationships among traditional reproductive hormones such as estrogen, testosterone, progesterone, gonadotropins, oxytocin, and relaxin. However, insulin, somatotropin, insulin-like growth factor, thyroid hormone, and corticosteroids are all involved in reproductive processes, both indirectly by regulating cell division and tissue growth and directly via regulation of glucose entry into the ovary; follicular growth; and fetal and mammary gland differentiation, growth, and metabolism. Recent studies also suggest roles for cytokines and inflammatory molecules (Chagas et al., 2007; Mazzatti et al., 2012). These findings have come out of the integration of many different studies on many different aspects of nutrition and reproduction. Yet even though all these hormones have a role in various reproductive functions, the majority respond to or affect the glucose flux in the body.

Glucose is known to have a direct effect on the hypothalamus, which causes the release of GnRH, which in turn causes LH release from the pituitary (Wade and Jones, 2004). In addition, glucose elicits increases in circulating insulin and IGFI, which have positive effects on follicular

growth. Although there appears to be a wide range of effective glucose flux rates to allow these effects, they are still critical. This is one reason that in most cases, fertility is not affected negatively until a serious deficit in glucose occurs. In lactating sows and cattle, return to estrus after parturition also is closely connected with adequate glucose flux. Many cows that are producing large quantities of milk are losing large quantities of body fat; nevertheless, they show signs of estrus, conceive, and eventually calve. This indicates the genetic and environmental variation in all the various subsystems needed for successful reproduction. The role of glucose in stimulating insulin and IGFI is also important in the return to ovulation of viable oocytes (Butler, 2003). Thus, there is not necessarily a “competition for resources” but a “genetic variation in animal response to milk production and nutrient supply in reproductive success.”

The role of fatty acids

Certain classes of fatty acids, primarily the omega-3 series and omega-6 series and their metabolites have also been identified as positive controllers of reproduction (Ambrose et al., 2006; Bilby et al., 2006a,b). Some intriguing results have been reported in practical use of omega-3 and omega-6 fatty acids in improving fertility in lactating dairy cattle (Bilby et al., 2006a,b), yet molecular mechanisms are not yet understood. However, possibilities include control of basic cell development and membrane function, and in reduction of inflammation that may hinder oocyte development (Armstrong et al., 2003). There is ample evidence that specific fatty acids can alter gene expression in many tissues (Al-Hasani and Joost, 2005 and many references therein). Fatty acids may play a role in oocyte development and viability (Bilby et al., 2006a, b; Chagas et al., 2007). However, we still are limited in our techniques to measure characteristics such as ‘oocyte quality.’ Here is where a systems approach can help: we can use tools such as bio-mathematical models based on sound experimental data to quantify and measure the other aspects of the system to the point that a specific proportion of the remaining undefined variation in reproduction may be due to oocyte quality and development.” Once this occurs, two things are possible: 1) it allows us to more effectively focus limited research resources and 2) through proven modeling statistics we can make

a quantitative hypothesis as to the actual percentage of reproductive success due to oocyte quality which, in turn, should facilitate identification of specific nutrigenomic mechanisms for the effects fatty acids have on reproduction.

The role of amino acids

In addition to glucose and fatty acids, amino acid metabolism also affects reproduction. Results from earlier work originally suggested that excess amino acids caused increases in blood urine nitrogen and, perhaps, concentrations of urea or ammonia in the uterus, which may affect embryo survival (Butler, 1998). However, these early findings have not been fully supported. Yet the dogma of “don’t feed excess protein because it reduces fertility” is constantly repeated. A recent meta-analysis of many dairy studies showed that, at the most, in animals fed very high protein diets (19 to 21%), there may be a reduction in pregnancy of about 10% (Lean et al., 2011). This is important and not to be ignored, yet it demonstrates again that amino acid nutrition is one piece of the system that we need to specifically quantify and probably is not as quantitatively important as glucose flux and metabolic rate.

In addition to the contribution of amino acid metabolism, there is likely a subtle interaction among amino acids, gene transcription, and endocrine regulation. Genomic studies have suggested a connection between variants in the myostatin and calpastatin genes and fertility in the cow (Garcia et al., 2006; Chagas et al., 2007; Szyda and Komisarek, 2007). These intriguing studies may provide evidence for a mechanistic link among protein metabolism, gene expression, and reproduction.

The role of metabolic rate

It is clear that the visible signs of estrus in lactating dairy cattle are evident for a short length of time. Instead of 18 to 24 hours, it is often only 6 to 10. In addition, heifers have a longer visible estrus than lactating cows. These observations have led to hypotheses and research, which in summary, has demonstrated that lactating animals consuming large amounts of feed and making large amounts of milk have a faster metabolic rate and



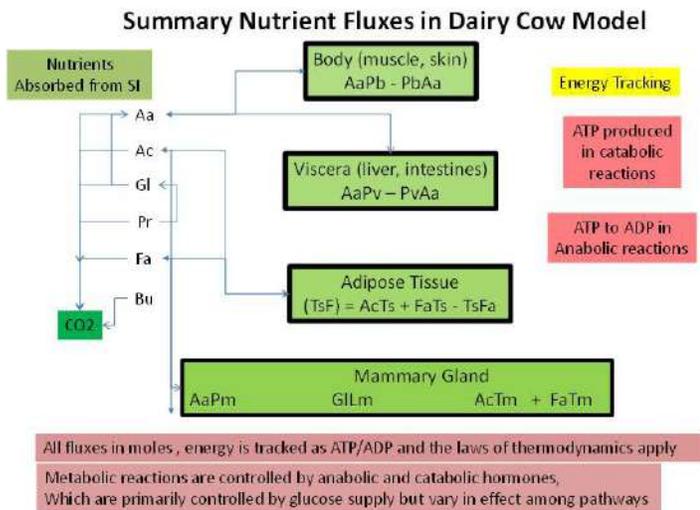
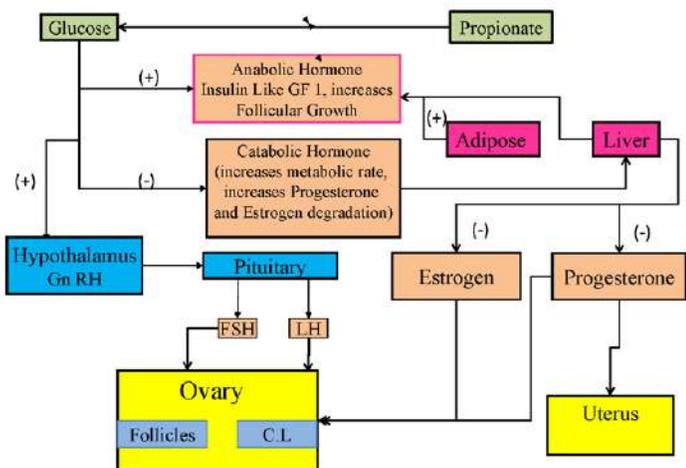


Figure 1. Brief flow diagram of the Molly model of nutritional fluxes in the dairy cow. The model tracks moles or kilograms of nutrients and metabolites and tracks energy use as ATP/ADP stoichiometrically from known biochemistry. Details are available in Baldwin, 1995.

resultant blood flow through the liver (Sangsrivong et al., 2002; Lopez et al., 2004; Chagas et al., 2007; Morris and Diskin, 2008). This increased blood flow has a secondary effect on the degradation of estrogen and progesterone to increase their clearance rate. This most likely explains the majority of the change in visible estrus. This sometimes has been simplified as “higher producing cows are infertile,” but that is only a piece of the story, and the majority of the cows are still able to conceive. Nevertheless, reduced amounts of circulating estrogen can have positive and negative effects on reproductive processes from the hypothalamus to the uterus. We are just beginning to seriously quantify such effects.

Figure 2. Summary flow diagram of Jenny, an integrated model of nutritional and metabolic (Molly, Baldwin, 1995) and reproductive (Stotzel model, 2010) processes in the dairy cow.



Similarly, the increased blood flow increases liver clearance of progesterone. Progesterone is required for the initial acceptance of the embryo by the uterus and subsequent pregnancy that ensues. In brief, it is likely that increased degradation of progesterone plays a role in diminished conception rate; however, we also likely do not possess sufficient quantitative data on peripheral and local progesterone concentrations to accurately estimate the magnitude of this effect. There has been excellent work on this issue conducted by the research group at Sydney Australia (Lean and Rabiee, 2002; Rabiee et al., 2002). In the model below, we show one example of how this knowledge can be applied and explored further.

A Mechanistic, Dynamic, Bio-mathematical Systems Model of Reproduction in the Dairy Cow

So with that brief description, how do we move forward? How do we systematically and quantitatively integrate these physiological systems into a coherent research approach? One proven way is with a bio-mathematical systems model. This approach has been successfully used in physics, chemistry, and biology for many years (Baldwin et al., 1987 a, b; Baldwin, 1995; Cornish-Bowden, 2005; Cornish-Bowden et al., 2007) and is not even new to dairy science; there have been several models for nutritional and reproductive responses in dairy cattle. The Dairy NRC (2001) is a classic example, and there have been several recent advancements in modeling a quantitative description of the estrous cycle in dairy cattle. Some of the first described follicular development and estrus cycling (Soboleva et al., 2000, 2004). A systems modeling approach to reproduction is not new, either. There have been several attempts (Blanc et al., 2001; Boer et al., 2010, 2011; Vetharanim et al., 2010) as well as the general recognition of nutrigenomics and fertility (Dawson, 2006). One such model described different progesterone profiles built from observed data (Meier et al., 2009). Both groups noted that these models could be used as a framework for studying nutritional and physiological effects on estrus cyclicity. Martin et al. (2012) proposed the framework for a nutrition and reproduction model in the cow, whereas others have described models for pregnancy recognition (Shorten et al., 2010) and steroid synthesis in the placenta (Nguyen et al., 2012). The most sophisticated one for estrus cyclicity to date has been published in various forms as an integrated model of the bovine estrous cycle (Boer et al., 2011, 2012; Stotzel et al., 2011). It clearly, concisely, and elegantly details the cyclical interactions among GnRH, FSH, LH, follicular growth, E2, P4, corpus luteum, inhibin, and oxytocin. However, even though several of these authors refer to the importance of genetic and nutritional control of reproductive processes, none of these models include such control. In addition to our work described here, another approach to modelling nutritional effects on reproduction is also ongoing (Martin et al., 2012) and promises to be quite useful.

The nutritional flux model of Baldwin (1995) included a very rudimentary empirical model of fetal growth based on an exponential equation that converted to energy requirements and amino acid requirements, but there were no mechanistic elements. Fetal growth was not a major focus of that model, but it did clearly recognize the quantitative importance of fetal growth on lactation, especially during later stages of lactation. Hanigan et al. (2009) elaborated on this approach and constructed a more mechanistic model that can be used to test hypotheses on nutritional and hormonal effects on fetal growth and then resultant effects on the total maternal energy

Reproduction Model Stötzel et al., 2011

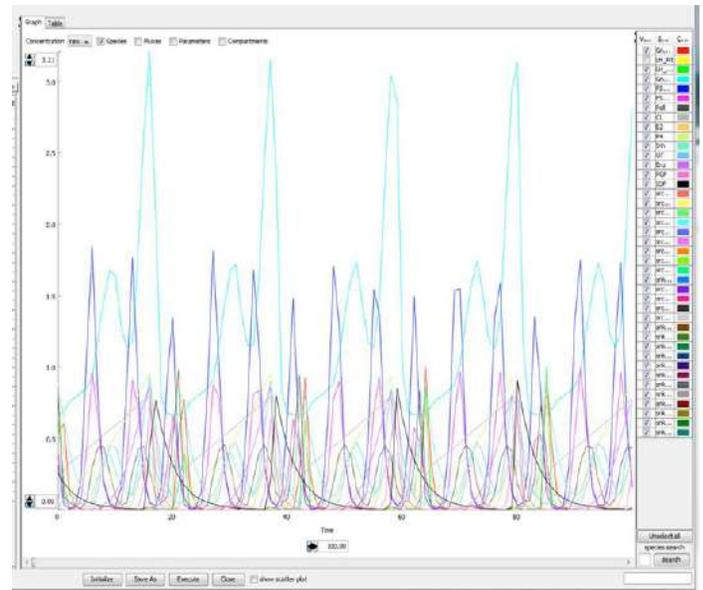
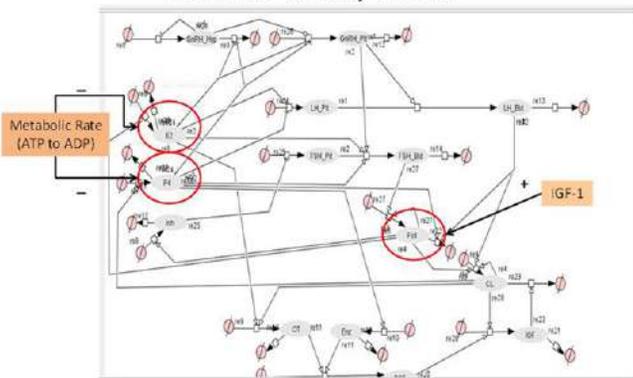


Figure 3. Schematic and general results from a model of reproductive fluxes in the dairy cow. Figure 3a (above) shows the flux diagram, overlaid with the three points of integration with the metabolic model. Figure 3b (right) is the screen shot of default output fluxes including GnRH, LH, FSH, follicles, E₂, P₄, and oxytocin.

and nitrogen requirements. These efforts in modeling have been useful, but each is limited to only one facet or set of processes of the entire system.

About 10 years ago, we embarked on an effort to develop an integrated nutritional and reproductive model (McNamara, 2010). This attempt has finally come to fruition with the first integrated mechanistic, dynamic, and deterministic model of nutrient flux and reproductive processes in the dairy cow, named “Jenny” (Celo et al., 2010 a, b; Shields et al., 2012). The model is a specific integration of the Molly model (Figure 1) and the Stotzel model (Figure 3), leading to Jenny (Figure 2). The flow diagrams of the model summarize the interconnected nutritional, metabolic, hormonal, and reproductive processes (Figures 1, 2, and 3).

The objective of this model is provide a way to evaluate data, concepts, and hypotheses regarding underlying genetic, nutritional, and physiological control of reproduction. A model of metabolism (Molly, UC Davis), which describes metabolism of glucose, VFA, and amino acids for fat and protein metabolism in the body and milk component production (Baldwin, 1995), was integrated with a model of reproductive estrous cycle processes (Boer et al., 2011, 2012; Stötzel et al., 2011), which describes growth and decay of the follicles and corpus luteum and changes in concentrations of gonadotropin-releasing hormone, FSH, LH, progesterone, estrogen, oxytocin, and prostaglandin F_{2α}.

Initially, we obtained data from the literature on the anabolic connection based on the work of Kawashima et al. (2007), which provided an increase of 1 mm in follicular growth for each 20 ng/L of IGF1. For the catabolic connection, we obtained data on the effects of feed intake and liver blood flow on degradation of estrogen and progesterone (Sangsrivong et al., 2002), which demonstrated that for every increase of 1 kg/day DMI of an average dairy ration, the degradation of E and P increased about 1.6%. It is important to note that quantitative biology requires collection of data over time to estimate dynamic changes that occur over time such as these. Quite often studies are done with a fairly qualitative hypothesis in mind, and true time and concentration dynamic data are not collected. An international consortium of nutritionists and reproductive physiologists are working to address this problem and are developing methods and programs to speed integrative research to solve dairy reproductive problems (Block et al., 2012).

The two models were then integrated at the following three specific points based on the available literature described above:

Glucose and IGF-I affect rates of FSH, LH, and follicular growth according to this equation:

$$\text{follicular_growth } f \{ \text{follicular_rate_constant} = \text{hp_fsh_mod} + [\text{follicular_rate_factor_IGF_1}(0.001833) * (\text{IGF_1} - \text{average_IGF_1})] \}$$

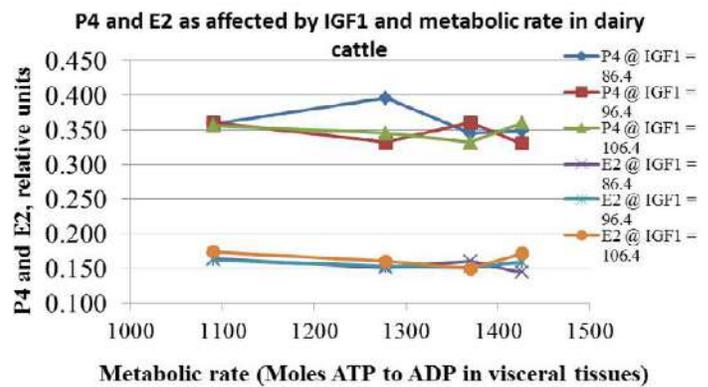
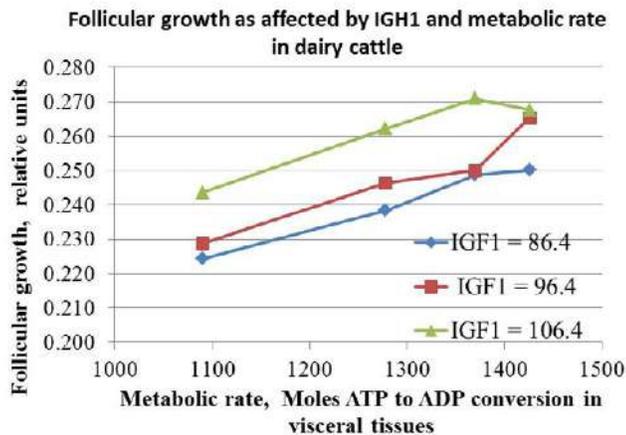
Degradation of estrogen and progesterone is a function of metabolic rate in visceral tissues of Molly (AtAdV):

$$\text{Estrogen degradation } f \{ \text{deg_const_E2} = \text{estrogen degradation factor } [0.00034] + (\text{metab_rate_degradation_factor_E2} * (\text{AtAdV} - \text{avg_AtAdV})) \}$$

$$\text{Progesterone degradation } f \{ \text{deg_const_P4} = \text{progesterone degradation factor } (0.0005669) + (\text{metab_rate_degradation_factor_P4} * (\text{AtAdV} - \text{avg_ATADV})) \}$$

After their integration using ACSLX software, we then conducted a behavioral analysis using data from research conducted on our dairy that contained various levels of milk production and feed intake (Figure 4). We provided rates of milk production (UCCELLS in Molly) from 25 to 55 kg/day of milk and feeding rates (FDDMIN in Molly) from 18.8 to 27.3 kg DMI/day through the first 100 days in milk as inputs into the model. This produced a range of metabolic rates in the Molly model from 1,090 to 1,426 M/day and a range of IGF1 from 86.4 to 106.4 ng/L. When the integrated model was run, increasing anabolic signals as represented by IGF1 increased follicular growth (Figure 4a), while increasing metabolic rate increased the degradation of estrogen and progesterone (Figure 4b). However, it was the interaction of these systems that provided an interesting pattern of change in follicular growth and steroid degradation. The effects, using the best data available, were small, subtle, and interactive. This is a first-generation model and is being subjected to vigorous evaluation. However, it demonstrates an example of using existing knowledge of mechanisms and data and suggests some reasons why improvement in the field has not been straightforward. Quite often, looking at one subsystem at the expense of another will lead to a simplified, often linear interpreta-

Figure 4. Figure 4a (*left*) shows the average yield of follicular growth as an effect of changing IGF1 concentrations, and Figure 4b (*right*) shows progesterone and estrogen as a function of metabolic rate (AtAdv) in moles/day in a mathematical model of nutritional and reproductive processes in the dairy cow.



tion. However, when the subsystems are integrated with the recognition, for example, that increased follicular growth increases estrogen, which has positive and negative effects throughout the reproductive system, it opens the door to a more realistic output and demonstrates the need for systems research. It is with this systems approach and a model such as this and others described, that we can speed improvement in dairy cattle reproductive success.

Our ultimate goal would be to create a mathematical, mechanistic, integrated, and dynamic model that describes the “real cow.” To accomplish this, we need a re-invigorated, multi-investigator, multi-disciplinary, integrated approach to solve the present and future problems of reproduction. This research effort will require construction and testing of mechanistic bio-mathematical models and can be facilitated by training students, scientists, and professionals in the importance of using these tools to identify, solve, and prevent reproductive problems.

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About the Authors



John McNamara has been a faculty member at Washington State University since 1983, after earning M.S. and Ph.D. degrees at University of Illinois and Georgia, respectively. He has focused on adipose tissue biology and efficiency of dairy cattle and lactating pigs. In recent years this work has both focused more on the transcriptional regulation of adipose tissue biology and expanded to systems approaches and modeling in genetic and nutritional control of reproduction in the dairy cow. He has given invited lectures in more than 10 countries on these topics and taken three sabbatical leaves to study them. He teaches full systems approaches in his classes as well. Dr. McNamara has received several research and teaching awards and was recently elected Fellow, American Dairy Science Association. He and his wife Sue, who he met at the University of Illinois, are now proud grandparents of a girl and a boy.

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Shannon Shields was raised in Spokane, Washington and after years of working in retail, sales, and customer service, returned to college in 2004 and graduated from the university of Idaho in 2008 with a B.S. in Animal Science/PreVet. She continued at the University of Idaho to earn a M.S. in Animal Sciences with a research emphasis in Dairy Nutrition in 2010 with Dr. Pedram Rezamand. She started a doctoral program at Washington State University in Animal Sciences with Dr. John McNamara and embarked on a novel project to develop a biochemical systems model in genetics, nutrition, and reproduction in dairy cattle. She has presented the first iterations of this model at several regional and national meetings and this project forms part of the basis for international collaboration on systems biology in dairy cattle. She has taken an opportunity to expand her experience and now works for Elanco Animal Health as their Dairy Sales Representative in the Pacific Northwest.