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Altering the representation of hormones and adding consideration of gestational metabolism in a metabolic cow model reduced prediction errors

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ABSTRACT

The model of R. L. Baldwin predicts various aspects of digestion and metabolism in the cow including nutrient partitioning between milk and body stores. However, prediction bias has been observed for body weight (BW) and body condition score (BCS) when diets of differing energy density are simulated over long periods. Originally, the model overpredicted BW loss in early lactation and gain in late lactation. This bias was reversed and limited to early lactation when a better representation of milk synthesis capacity was introduced into the model. It was hypothesized that a better representation of the effects of energy status on anabolic and catabolic hormones and a more complete representation of metabolic demands and growth associated with pregnancy would help in improving predictions of body tissue mobilization in early lactation. Providing independent glucose reference points and independent sensitivity scalars for the 3 hormones driven by glucose concentrations improved overall model precision. These improvements were primarily realized through reductions in prediction errors for blood glucose concentrations and BCS. In both cases, slope bias associated with the predictions was reduced, indicating that the changes in representation were beneficial although BCS bias was not completely removed. Milk component yields were predicted with slightly greater mean and slope bias. The addition of enhanced pregnancy calculations did not provide apparent additional benefit relative to model prediction errors. However, the data used for the assessments did not include observations from the last 60 d of gestation, where BW gain and metabolic demand associated with pregnancy would be expected to be greater. Improvements in BCS were not observed when the revised model was tested using an independent data set. Predictions of blood fatty acids, the rate of BCS and BW loss, and milk fat yields in early lactation were still inappropriate and require further work. The results could be caused by inaccurate early lactation intakes, the aggregated representation of blood fatty acids, or an inadequate representation of peripheral insulin resistance during early lactation.
Key words: model, lactation, milk composition, body weight

INTRODUCTION

The metabolic cow model of Baldwin et al. (1987a,b,c; referred to as Molly) predicts various aspects of digestion and metabolism in the cow including nutrient partitioning between milk and body stores. The model has been updated several times (Baldwin, 1995; Palliser et al., 2001; Beukes et al., 2004, 2005; Hanigan et al., 2006, 2007) including alterations in the representation of milk synthesis enzymatic activity to address systematic bias in predicting milk yield and composition. These updates have improved prediction accuracy; however, challenges remain with predicting BW and body composition changes over the course of a lactation and in response to nutrient supply (Hanigan et al., 2007).

It was observed that the model generally overpredicted BW loss approaching peak lactation and BW gain in later lactation (McNamara and Baldwin, 2000). Additionally, predicted changes in milk yield were under-responsive to changes in dietary nutrients, which magnified the weight gain problem (Hanigan et al., 2008). As these simulations were run using the observed DMI and diet composition, the problem was not related to inappropriate DMI predictions. Attempts to address the issue by adjusting the basal energy expenditures were only partially successful (McNamara, 2004). However, systematic bias in predictions of milk yield and composition was a contributor to the BW problem. Redefining the representation of mammary cells and regulation of their activity to achieve improvements in predictions of milk yield and composition changed the nature of the problem, resulting in underprediction of

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BW and BCS loss and milk fat yield during the first 50 to 100 d of lactation (Hanigan et al., 2007). Because the model predicts partitioning of absorbed energy between maintenance, milk production, and body stores (for a full description of the scheme, see Baldwin, 1995), the observed prediction errors could result from inappropriate predictions of energy partitioning, although biased intake predictions cannot be ruled out.

Molly has been found to underpredict total-tract fiber and protein digestion and overpredict fat digestion when compared with a large set of literature data (Hanigan et al., 2006). However, digestion parameters were adjusted to remove the observed mean bias before the evaluations reported by Hanigan et al. (2007). It is possible that predictions of fiber digestion from herbage were still biased, because such observations were not present in the literature data set. Because digestibility evaluations were not conducted by Kolver et al. (2007), this hypothesis could not be tested. However, it seems unlikely that such bias would explain the observed bias as the problem would be present throughout lactation.

Because milk fat yield and blood fatty acid concentrations were both underpredicted in early lactation (Hanigan et al., 2007), it is possible that the early lactation problem results from inadequate responses to hormonal signals controlling body fat mobilization causing underprediction of blood fatty acids and milk fat output. Of course, this problem could result from very subtle errors in glucose concentrations that may drive greater errors in anabolic and catabolic hormones given the sensitivity of these hormones to blood glucose.

The original description of Molly did not include a representation of gestational gain or metabolic requirements to support that gain (Baldwin et al., 1987a,b). Energetic and AA demands to support gestation, but not gestational weight gain, were subsequently addressed (Baldwin, 1995). Although a representation of gestational gain would not appear to be linked to inadequate weight loss in early lactation, it would increase weight gain in late lactation that would allow an offsetting increase in the setting for basal energy requirements, which in turn would enhance weight loss in early lactation as demonstrated by McNamara (2004), thus helping to address the observed temporal bias.

It was hypothesized that the observed bias in predicting BW and BCS over the course of a lactation was due to 1) a combination of inadequate representation of the effects of glucose on hormonal concentrations and 2) an inadequate representation of gestational gain in late lactation. Thus, the objectives of this work were to 1) revise the representation of hormonal concentrations in Molly, 2) revise the representation of nutrient demands and BW gain associated with pregnancy in Molly, and 3) evaluate these revisions.

MATERIALS AND METHODS

The base model used for this work was that described by Baldwin (1995) with modifications as described by Hanigan et al. (2006, 2007). The digestive parameter settings listed in Table 1 were used for all simulations. These parameters were derived by fitting the model to the literature data set described by Hanigan et al. (2006) with no accommodation for experimental bias. Adoption of these digestion parameter settings reduced the root mean square prediction errors (**RMSPE**) for all ruminal and total-tract digestibility predictions by 10 percentage units or more, except for total-tract starch digestion, which had no change. Predictions of ruminal VFA and their molar percentages were also dramatically improved. Mean and slope bias were greatly reduced compared with values reported by Hanigan et al. (2006), which should ensure more accurate predictions of absorbed nutrients for the work described herein. The model with the above changes will be referred to as Molly2007. The revised model described herein will be referred to as Molly2008 (Molly2007 plus changes in hormonal and gestational representation).

Model coding changes were undertaken in ACSL (Ver. 11.8, Aegis Technologies Group, Austin, TX). Simulations and parameter estimations were conducted using ACSL Optimize (Ver. 2.5.4, Aegis Technologies Group) using a variable step, second-order Runge-Kutta-Fehlberg numerical integrator. The maximum integration interval was set to 0.01 d. Parameters were estimated using a Nelder-Mead Simplex optimization algorithm to maximize a log-likelihood function. Residual errors were assumed to be homogeneous.

Revisions undertaken in Molly2008 are described below. A decision was made to start with the representation of hormonal control of tissue deposition and mobilization because the combination of errors in predicting fatty acids, milk fat, and body fat as well as sensitivity analyses offered strong evidence that this area of the model required attention.

Tissue Responsiveness to Endocrines

Two anabolic ($\boldsymbol{H_{Anab1}}$ and $\boldsymbol{H_{Anab2}}$) and one catabolic ($\boldsymbol{H_{Catab1}}$) hormones are represented as functions of the concentration of glucose in blood ($\boldsymbol{C_{Gl}}$, mol/L) in Molly2007 with exponents to adjust sensitivity. A second catabolic hormone is defined in the model and was used in the 1995 version of the model as a positive effector of the conversion of AA to glucose. However, it was