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## Mechanistic modeling based on meta-analysis : prediction of the net hepatic fluxes of energetic nutrients in ruminants

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### ► To cite this version:

Lahlou Bahloul, Daniel Sauvant, Jean Vernet, H el ene Lapierre, Pierre Noziere, et al.. Mechanistic modeling based on meta-analysis : prediction of the net hepatic fluxes of energetic nutrients in ruminants. Annual ADSA-ASAS Meeting, 2012, Phoenix, United States. 1 p., 2012, Annual ADSA-ASAS Meeting. hal-01356564

**HAL Id: hal-01356564**

**<https://hal.science/hal-01356564>**

Submitted on 3 Jun 2020

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# Summaries of Communications

## Proceedings of the 2012 Meeting of the Animal Science Modelling Group

Edited by  
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This group meets yearly for one-day meetings. The 2012 meeting was sponsored by Nutreco Canada, Inc., Guelph, ON, Canada; ADM, Decatur, IL, USA; Cargill Animal Nutrition, Veldriel, the Netherlands; Agri-King, Inc., Fulton, IL, USA; Adisseo, Alpharetta, GA, USA; and Evonik Industries AG, Hanau, Germany. It was held on July 14 at the Hyatt Regency Phoenix, 122 North 2nd Street, Phoenix, Arizona, USA, prior to the ADSA/ASAS Joint Annual Meeting. Summaries of the papers presented follow. Each summary has been peer reviewed and edited for clarity. The person who presented the paper is identified with an e-mail address.

**Prediction of methane production in beef cattle within a mechanistic digestion model.** J. L. Ellis<sup>1,2</sup>, J. Dijkstra<sup>2</sup>, A. Bannink<sup>3</sup>, E. Kebreab<sup>4</sup>, S. Archibeque<sup>5</sup>, and J. France<sup>1</sup>. <sup>1</sup>Centre for Nutrition Modelling, Department of Animal and Poultry Science, University of Guelph, Guelph, ON, Canada, jellis@uoguelph.ca; <sup>2</sup>Animal Nutrition Group, Wageningen University, Wageningen, The Netherlands; <sup>3</sup>Wageningen UR Livestock Research, Lelystad, The Netherlands; <sup>4</sup>Department of Animal Science, University of California, Davis, CA, USA; <sup>5</sup>Animal Sciences, Colorado State University, Fort Collins, CO, USA.

Previous evaluations of the Dijkstra et al. (1992) model revealed the model performed well in terms of methane (CH<sub>4</sub>) emissions on dairy cow data, but less so on high grain fed beef cattle data (Kebreab et al. 2008). Prediction of the rumen volatile fatty acid (VFA) profile is central to accurate CH<sub>4</sub> prediction within mechanistic models. The purpose of this study was therefore to evaluate prediction of CH<sub>4</sub> emissions from high grain fed beef cattle using the Dijkstra model with pH-independent (Bannink et al. 2006; Murphy et al. 1982)

and alternative pH-dependent (Bannink et al. 2008; Murphy et al. 1982 as adjusted by Argyle and Baldwin 1988) VFA stoichiometries, as well as with a new VFA stoichiometry which adjusts for the use of monensin (Ellis et al. 2012), to see if prediction improvements could be made. To adapt the model itself for use with beef cattle, revised equations to predict fluid volume and fractional rate of passage in the rumen and the hindgut, alterations to the fractional passage rate of protozoa from the rumen, as well as adjustment to the kinetics of fibre fermentation in the hindgut were implemented. The database used for independent evaluation of CH<sub>4</sub> predictions consisted of 104 data points from 6 studies on high grain fed beef cattle, where the average body-weight was 426 ± 68 kg, DMI was 7.99 ± 2.05 kg d<sup>-1</sup> and roughage% was 11.8 ± 5.5. Analysis revealed improvements in CH<sub>4</sub> (MJ d<sup>-1</sup>) predictions when the pH-dependent versus the pH-independent VFA stoichiometries were used in terms of root mean square prediction error (RMSPE) (45.8 to 40.9% and 35.1 to 32.1% for the Bannink and Murphy/Argyle lines of stoichiometry, respectively), and that further reductions were made when the effect of monensin on the VFA stoichiometry was accounted for (to 37.5 and 31.5%, respectively). However, the concordance correlation coefficient (CCC) statistic was reduced with the inclusion of pH due to a decrease in predicted variation (0.363 to 0.347 and 0.493 to 0.365 for the Bannink and Murphy/Argyle lines of stoichiometry, respectively), but was improved with inclusion of monensin (to 0.401 and 0.395, respectively). All VFA stoichiometries tended to over-predict low observed CH<sub>4</sub> (MJ d<sup>-1</sup>) values. Results indicate that further improvement in the representation of VFA stoichiometry, and likely the effects and prediction of pH, are required for mechanistic modelling of CH<sub>4</sub> emissions from high grain fed beef cattle, but that inclusion of monensin leads to prediction improvements.

**Key words:** Beef cattle, mechanistic modelling, methane, volatile fatty acid stoichiometry

**Argyle, J. L. and Baldwin, R. L. 1988.** Modeling of rumen water kinetics and effects of rumen pH changes. *J. Dairy Sci.* **71**: 1178–1188.

**Bannink, A., France, J., Lopez, S., Gerrits, W. J. J., Kebreab, E., Tamminga, S. and Dijkstra, J. 2008.** Modelling the implications of feeding strategy on rumen

fermentation and functioning of the rumen wall. *Anim. Feed Sci. Technol.* **143**: 3–26.

**Bannink, A., Kogut, J., Dijkstra, J., France, J., Kebreab, E., Van Vuuren, A. M. and Tamminga, S. 2006.** Estimation of the stoichiometry of volatile fatty acid production in the rumen of lactating cows. *J. Theor. Biol.* **238**: 36–51.

**Dijkstra, J., Neal, H. D. StC., Beever, D. E. and France, J. 1992.** Simulation of nutrient digestion, absorption and outflow in the rumen: model description. *J. Nutr.* **122**: 2239–2255.

**Ellis, J. L., Dijkstra, J., Bannink, A., Kebreab, E., Hook, S. E., Archibeque, S. and France, J. 2012.** Quantifying the effect of monensin dose on the rumen volatile fatty acid profile in high grain fed beef cattle. *J. Anim. Sci.* doi:10.2527/jas.2012–3966.

**Kebreab, E., Johnson, K. A., Archibeque, S. L., Pape, D. and Wirth, T. 2008.** Model for estimating enteric methane emissions from United States dairy and feedlot cattle. *J. Anim. Sci.* **86**: 2738–2748.

**Murphy, M. R., Baldwin, R. L. and Koong, L. J. 1982.** Estimation of stoichiometric parameters for rumen fermentation of roughage and concentrate diets. *J. Anim. Sci.* **55**: 279–296.

**Prediction of volatile fatty acid production rates by the Molly cow model.** S. Ghimire<sup>1</sup>, P. Gregorini<sup>2</sup>, and M. D. Hanigan<sup>1</sup>. <sup>1</sup>Department of Dairy Science, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061, USA, sand72@vt.edu; <sup>2</sup>DairyNZ, Hamilton 3240, New Zealand.

Predicting ruminal production of volatile fatty acids (VFA) is important, as they supply energy to the animal and also dictate methane production. We evaluated the VFA production submodel in the Molly cow model (Baldwin et al. 1995; with modifications by Hanigan et al. 2009) using data from eight publications that reported VFA production rates for cattle. Evaluations were conducted with ruminal water balance predictions enabled and the ruminal VFA stoichiometry coefficients (Argyle and Baldwin 1988) set either to mixed for all diets, or to mixed when forage represented between 20 and 80% of the diet, to concentrate when <20% forage, and to forage when >80% forage. Predictions appeared relatively insensitive to change in VFA coefficients by diet type. Root mean square prediction errors (RMSPE) were 63, 63, and 49% for acetate, propionate, and butyrate production rates, respectively. A large proportion of the error was slope bias for acetate and butyrate, and a modest proportion was for propionate. Because interconversions between acetate and propionate represent as much as 15% of the observed variation in net production rates (Sutton et al. 2003), lack of such consideration in the model may contribute to model prediction errors. We used the following thermodynamic equations with two of the studies (Seal and Parker 1994; Sutton et al. 2003) to assess the potential

of applying such an approach within Molly to reduce VFA prediction errors:

$$V_{A \rightarrow P} = K_{A \rightarrow P} [\text{Acetate}] [\text{CO}_2] P_{\text{H}_2}^3 ([\text{ADP}] [\text{P}_i] [\text{H}^+])^{0.6}$$

$$V_{P \rightarrow A} = K_{P \rightarrow A} [\text{Propionate}] [\text{H}_2\text{O}]^2 ([\text{ATP}] [\text{H}_2\text{O}])^{0.6}$$

Observed pH and ruminal VFA concentrations were used with standard constant hydrogen pressure ( $P_{\text{H}_2}$ ), and concentrations of  $\text{CO}_2$ ,  $\text{H}_2\text{O}$ , ADP, ATP, and  $\text{P}_i$  (Ungerfeld and Kohn 2006). Rate constants for acetate to propionate ( $K_{A \rightarrow P}$ ) and propionate to acetate ( $K_{P \rightarrow A}$ ) were derived independently from the control treatments and used to predict the fluxes for the other treatment. The observed changes in VFA concentrations and pH explained the observed changes in acetate to propionate, but over predicted the change in propionate to acetate flux in the study of Sutton et al. (2003). When applied to the Seal and Parker (1994) data, the equations predicted the increase in propionate to acetate flux, but failed to predict the observed reduction in acetate to propionate flux. The inability to predict all responses might be due to lack of data for controlling factors other than pH and VFA concentrations. A more thorough evaluation of the effects of thermodynamics on VFA interconversion and incorporation into Molly might provide improved predictions of VFA production.

**Key words:** Volatile fatty acids, Molly, thermodynamics

**Argyle, J. L. and Baldwin, R. L. 1988.** Modeling of rumen water kinetics and effects of rumen pH changes. *J. Dairy Sci.* **71**: 1178–1188.

**Baldwin, R. L. 1995.** Modeling ruminant digestion and metabolism. Chapman and Hall, London, UK.

**Hanigan, M. D., Palliser, C. C. and Gregorini, P. 2009.** Altering the representation of hormones and adding consideration of gestational metabolism in a metabolic cow model reduced prediction errors. *J. Dairy Sci.* **92**: 5043–5056.

**Murphy, M. R., Baldwin, R. L. and Koong, L. J. 1982.** Estimation of stoichiometric parameters for rumen fermentation of roughage and concentrate diets. *J. Anim. Sci.* **55**: 411–421.

**Seal, C. J. and Parker, D. S. 1994.** Effect of intraruminal propionic acid infusion on metabolism of mesenteric- and portal-drained viscera in growing steers fed a forage diet .1. Volatile fatty acids, glucose, and lactate. *J. Anim. Sci.* **72**: 1325–1334.

**Sutton, J. D., Dhanoa, M. S., Morant, S. V., France, J., Napper, D. J. and Schuller, E. 2003.** Rates of production of acetate, propionate, and butyrate in the rumen of lactating dairy cows given normal and low-roughage diets. *J. Dairy Sci.* **86**: 3620–3633.

**Ungerfeld, E. M. and Kohn, R. A. 2006.** The role of thermodynamics in the control of ruminal fermentation. Pages 55–86 in K. Sejrsen, T. Hvelplund, and M. O. Nielsen, eds. Ruminant physiology: Digestion, metabolism and impact of nutrition on gene expression,

immunology and stress. Wageningen Academic Publishers, Wageningen, the Netherlands.

**Evaluation and improvement of empirical models to predict ruminal VFA proportions in sheep fed fresh temperate forages.** E. Ollion<sup>1</sup>, D. Pacheco<sup>2</sup>, and R. E. Vibart<sup>3</sup>. <sup>1</sup>Animal Nutrition Group, Wageningen University, The Netherlands and ISARA-Lyon, France; <sup>2</sup>Animal Nutrition, AgResearch, Palmerston North, New Zealand; <sup>3</sup>Land & Environment, AgResearch, Palmerston North, New Zealand, ronaldo.vibart@agresearch.co.nz.

Concentrations of volatile fatty acids (VFA) are widely used to aid in understanding the fermentation processes occurring in the rumen, particularly as these products of fermentation are essentially related to feed conversion efficiency and methane formation (Bannink et al. 2006). The objectives of this modelling exercise were twofold; our first objective was to evaluate existing empirical models of VFA prediction in the rumen of sheep fed fresh temperate forages, typical of New Zealand (NZ) pastoral farming. Our second objective was to develop an improved empirical model of VFA molar proportions of sheep fed fresh temperate forages fed exclusively in NZ. An independent dataset of sheep studies conducted in NZ where fresh forages were fed ( $n=32$  observations, 11 publications) were used for the original evaluation of the existing empirical models (Objective 1, results not shown). Three empirical models were chosen for this purpose: the model by Friggens et al. (1998) (FRIG) developed from sheep fed several supplements and grass silage mixtures; and two models by Nozière et al. (2011) developed from multiple ruminant species and diets (NOZ1 and NOZ2, as presented in Tables 3 and 5 of Nozière et al. 2011). Chemical composition of the diets and VFA proportions were reported in all studies. From this modelling exercise, it was identified that the diurnal dynamic aspects of variation of VFA molar proportions (i.e., sampling time relative to feeding) needed to be accounted in order to improve prediction accuracy. The development of the new model

(Objective 2) from fresh forage diets (NEW) used a subset of the NZ studies ( $n=22$ ). The observations used to develop the NEW model were randomly selected to create new predictive equations; the NEW model accounted for sampling time relative to feeding. The remaining observations ( $n=10$ ) plus the addition of VFA observations by Mbanzamihiho et al. (2002) were used to evaluate the models. Measures of fitness between measured and predicted VFA molar proportions included the relative prediction error (RPE) defined as the square root of the mean squared prediction error (RMSPE) relative to the mean observed value, the percent of variance explained by the model ( $R^2$ ), errors due to mean bias, slope bias and random error (% of MSPE), and concordance correlation coefficient (CCC) analysis. Although the slope bias for acetate and butyrate remained high, the NEW model performed better than FRIG, NOZ1 and NOZ2 when tested with the evaluation dataset (fresh forages,  $n=12$ ; Table 1). Additional modelling work showed that the NEW model did not perform well when evaluated with diets other than fresh forages. In summary, a new model was developed with better predictive ability to describe VFA proportions in the rumen of sheep fed fresh forages. However, the dataset used for evaluation is small, precluding immediate application; further evaluation of the new model is required. Accounting for the effect of sampling time is a novel approach in empirical modelling of VFA, with implications for further modelling and experimental research.

**Key words:** Volatile fatty acids, rumen, forages, sheep

**Bannink, A., Kogut, J., Dijkstra, J., France, J., Kebreab, E., van Vuuren, A. M. and Tamminga, S. 2006.** Estimation of the stoichiometry of volatile fatty acid production in the rumen of lactating cows. *J. Theor. Biol.* **238**: 36–51.

**Friggens, N. C., Oldham, J. D., Dewhurst, R. J. and Horgan, G. 1998.** Proportions of volatile fatty acids in

**Table 1.** Evaluation of the predictive performance of VFA molar proportions using the empirical models of Friggens et al. (1998) (FRIG), Nozière et al. (2011) (NOZ1 and NOZ2) and a newly developed model (NEW). Ac, acetate (mol 100 mol<sup>-1</sup> VFA), Pr, propionate (mol 100 mol<sup>-1</sup> VFA), Bu, butyrate (mol 100 mol<sup>-1</sup> VFA). RPE, relative prediction error (% of observed mean); CCC, concordance correlation coefficient

	FRIG			NOZ1			NOZ2			NEW		
	Ac	Pr	Bu	Ac	Pr	Bu	Ac	Pr	Bu	Ac	Pr	Bu
Measured	67.9	19.0	9.5	67.9	19.0	9.5	67.9	19.0	9.5	67.9	19.0	9.5
Predicted	62.7	23.0	11.3	62.6	21.9	11.8	66.1	17.2	13.3	68.0	18.9	9.6
RPE	23.8	6.1	0.9	28.4	2.4	0.9	15.6	2.9	1.7	8.5	0.3	0.3
$R^2$	0.60	0.03	0.20	0.29	0.44	0.02	0.23	0.36	0.16	0.69	0.64	0.56
Mean bias (%)	77.0	50.4	31.6	68.3	68.0	53.6	14.2	21.0	80.2	0.1	0.3	0.2
Slope bias (%)	4.7	37.6	29.0	4.5	13.9	4.1	32.0	62.2	0.02	59.3	4.2	35.6
Random error (%)	18.3	12.0	39.4	27.2	18.1	42.3	53.8	16.8	19.8	40.6	95.7	64.2
CCC	0.26	-0.07	0.23	0.28	0.37	0.06	0.44	0.41	0.08	0.76	0.80	0.73

relation to the chemical composition of feeds based on grass silage. *J. Dairy Sci.* **81**: 1331–1344.

**Mbanzamihiho, L., Fievez, V., da Costa Gomez, C., Piattoni, F., Carlier, L. and Demeyer, D. 2002.** Methane emissions from the rumen of sheep fed a mixed grass-clover pasture at two fertilisation rates in early and late season. *Can. J. Anim. Sci.* **82**: 69–77.

**Nozière, P., Glasser, F. and Sauvant, D. 2011.** *In vivo* production and molar percentages of volatile fatty acids in the rumen: a quantitative review by an empirical approach. *Animal* **5**: 403–414.

**Limits in modelling CH<sub>4</sub> production from VFA stoichiometry of rumen fermentation.** D. Sauvant<sup>1,2</sup>, A. Serment<sup>1,2</sup>, and S. Giger-Reverdin<sup>1,2</sup>. <sup>1</sup>AgroParisTech, UMR MoSAR, F-75005 Paris, France; <sup>2</sup>INRA UMR 791 MoSAR, F-75005 Paris, France, sauvant@agropar.istech.fr.

Prediction of CH<sub>4</sub> production is a major current challenge in modelling in ruminant nutrition. Numerous empirical equations for prediction of CH<sub>4</sub> production have been proposed. They are based either on animal or dietary items (e.g., NDF) or on measured characteristics of diet utilization (dry matter intake, DMI; organic matter digestibility, OMD). To achieve better accuracy, the principles of fermentation stoichiometry have been proposed to predict CH<sub>4</sub> production from that of volatile fatty acids (VFA) within a mechanistic rumen model (Mills et al. 2001). Recent studies have shown that application of such principles of VFA stoichiometry tended to overestimate measured CH<sub>4</sub> production when this predicted production is in the higher range. It was the case in Alemu et al. (2011) where four methods were compared with four slopes of the regression line “observed CH<sub>4</sub> =  $f(\text{predicted CH}_4)$ ” less than 1. The same type of bias was also observed *in vitro* with simultaneous measured VFA and CH<sub>4</sub> by Navarro-Villa et al. (2011) and in our research unit (Serment et al., unpublished). The present study involved a further evaluation of CH<sub>4</sub> prediction between two *in vivo* databases where experiments dealing with levels of either DMI or % concentrate were selected (Sauvant et al. 2011). In dataset 1 (158 experiments and 450 treatments), CH<sub>4</sub> production was measured and, in dataset 2 (77 exp. and 169 tr.), CH<sub>4</sub> production was predicted from apparent VFA production (calculated from measured apparent OMD in the rumen combined with the measured VFA profile as suggested by Nozière et al. 2010). Evaluation of results revealed a similar bias [mean slope of “observed CH<sub>4</sub> =  $f(\text{predicted CH}_4)$ ” = 0.33] and stressed that over-prediction of CH<sub>4</sub> occurred for diets with a high content of NDF and low DMI, microbial growth efficiency and particle outflow rate. These four studies showed a similar trend of over-estimating CH<sub>4</sub> production in the higher range of CH<sub>4</sub> production rates. This could reveal a limit to the application of currently used principles of stoichiometry

of fermentation, which possibly is caused by increased influence of H<sub>2</sub> concurrent sinks with high CH<sub>4</sub> production rates.

**Key words:** Methane, rumen, stoichiometry, modelling

**Alemu, A. W., Dijkstra, J., Bannink, A., France, J. and Kebreab, E. 2011.** Rumen stoichiometric models and their contribution and challenges in predicting enteric methane production. *Anim. Feed Sci. Technol.* **166–167**: 761–778.

**Mills, J. A. N., Dijkstra, J., Bannink, A., Cammell, S. B., Kebreab, E. and France, J. 2001.** A mechanistic model of whole-tract digestion and methanogenesis in the lactating dairy cow: model development, evaluation and application. *J. Anim. Sci.* **79**: 1584–1597.

**Navarro-Villa, A., O'Brien, M., Lopez, S., Boland, T. M. and O'Kiely, P. O. 2011.** Modifications of a gas production technique for assessing *in vitro* rumen methane production from feedstuffs. *Anim. Feed Sci. Technol.* **166–167**: 163–174.

**Nozière, P., Glasser, F. and Sauvant D. 2010.** *In vivo* production and molar percentages of volatile fatty acids in the rumen: a quantitative review. *Animal* **4**: 1057–1074.

**Sauvant, D., Giger-Reverdin, S., Serment, A. and Broudicou, L. 2011.** Influences of diet and rumen fermentation on methane production by ruminants (in French). *INRA-Prod. Anim.* **24**: 433–446.

**Estimating optimal smoothing parameters for the daily feed intake and weight forecasts required to implement sustainable precision farming systems for swine.** J. Rivest<sup>1,2</sup>, C. Pomar<sup>2</sup>, J. Pomar<sup>3</sup>, and L. Hauschild<sup>4</sup>. <sup>1</sup>Centre de Développement du Porc du Québec inc., Sainte-Foy, Québec, G1V 4M7, Canada; <sup>2</sup>Agriculture et Agroalimentaire Canada, Sherbrooke, Québec J1M 1Z3, Canada, candido.pomar@agr.gc.ca; <sup>3</sup>Department of Agricultural Engineering, Universitat de Lleida, 25198 Lleida, Spain; <sup>4</sup>Faculdade de Ciências Agrárias e Veterinárias, Universidade Estadual Paulista, Jaboticabal, São Paulo, 14883–262, Brazil.

Feeding growing pigs individually with daily tailored diets, whose formulation is based on their own real-time patterns of feed intake and growth, is a key element in the development of sustainable precision swine farms (Pomar and Pomar 2012). Daily feed intake (DFI) has been proposed to be estimated at time  $t$ ,  $m$ -period-ahead, based on individual pig information collected in real-time using a double exponential smoothing forecasting time series method ( $DFI_{t+m} = b_{0,t} + m \cdot b_{1,t}$ ) where  $b_{0,t}$  and  $b_{1,t}$  are the intercept and the slope of forecasting (Hauschild et al. 2012). A similar equation was used to estimate  $BW_{t+m}$ . Two smoothing functions ( $S_t = \alpha \cdot y_t + (1 - \alpha) \cdot S_{t-1}$  and  $S'_t = \alpha \cdot S_t + (1 - \alpha) \cdot S'_{t-1}$ ) were used to update daily  $b_{0,t}$  and  $b_{1,t}$ , where  $y_t$  is the observation of the DFI or BW and  $\alpha$  [ $0 \leq \alpha < 1$ ] is the

smoothing constant used to weigh current and past observations. The  $S_t$  and  $S'_t$  are respectively the single and double exponential smoothing values from which  $b_{0,t}$  and  $b_{1,t}$  are estimated ( $b_{1,t} = \alpha \cdot (S_t - S'_t) / (1 - \alpha)$ ;  $b_{0,t} = 2S_t - S'_t$ ). The objective of this study was to identify optimal  $\alpha$  values minimizing the mean absolute percentage error (MAPE) while balancing the smoothing and responsiveness effects. Feed intake was studied using individual DFI data collected from nine performance tests (2406 pigs) at the CDPQ Experimental Station in Deschambault (Québec, Canada). The MAPE was evaluated for each pig for different  $\alpha$  values. Datasets with frequent weights are scarce and therefore, BW forecast was studied in one test data in which 119 pigs were weighed five times over a period of 19 wk. Because the forecast method was intended for pigs undergoing weekly weighing, weekly BW estimates were obtained by linear interpolation including random errors (CV = 1%). DFI and BW forecasts were obtained on a daily basis as required by precision feeding systems. High  $\alpha$  values gave more weight to recent observations and increased forecast responsiveness to DFI or BW pattern changes while low  $\alpha$  values smoothed off the forecasts. Increasing  $\alpha$  values reduced the delay in the response to DFI or BW pattern changes. Forecasts in pigs with small changes in DFI or BW patterns were less sensitive to changes in  $\alpha$  values while optimal individual MAPE was affected by DFI or BW pattern changes. In the studied datasets, minimal MAPE for DFI forecasts was observed between 13.8 and 18.2, which were obtained for  $\alpha$  values between 0.12 and 0.26 (Fig. 1).

Minimal MAPE observed for BW forecasts was of 1.57 at 0.32  $\alpha$  value. It is suggested to use  $\alpha$  values of 0.17 for DFI and 0.32 for BW when implementing precision feeding in pig farms.

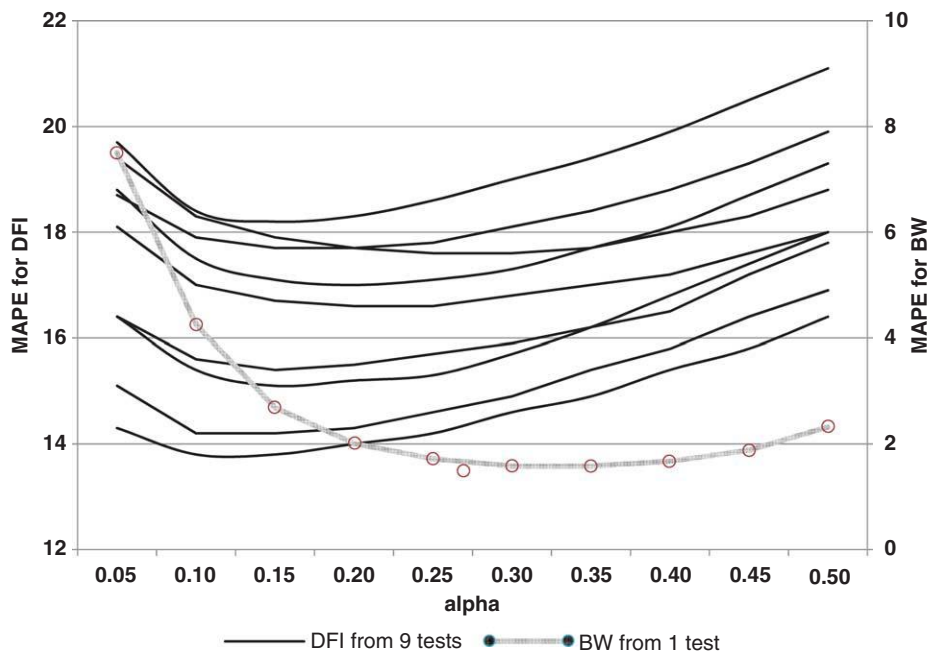
**Key words:** Individual pigs, nutrient requirements, precision feeding, forecast

**Hauschild, L., Lovatto, P. A., Pomar, J. and Pomar, C. 2012.** Development of sustainable precision farming systems for swine: estimating real-time individual energy and nutrient requirements in growing-finishing pigs. *J. Anim. Sci.* (in press).

**Pomar, C. and Pomar, J. 2012.** Sustainable precision livestock farming: a vision for the future of the Canadian swine industry. *Adv. Pork Prod.* **23**: 207–213.

**Beefbox: a dynamic simulator of growth for young bull production.** F. Garcia-Launay<sup>1</sup>, A. Ferard<sup>2</sup>, T. Delcros<sup>1</sup>, D. Bastien<sup>3</sup>, G. Cabon<sup>2</sup>, D. Micol<sup>1</sup>, and J. Agabriel<sup>1</sup>. <sup>1</sup>INRA, UMR1213 Herbivores, Theix, F-63122 Saint-Genès-Champanelle, France, florence.garcia-launay@rennes.inra.fr; <sup>2</sup>ARVALIS-Institut du végétal, Station Expérimentale de la Jaillière, 44370 La Chapelle Saint-Sauveur, France; <sup>3</sup>IDELE-Monvoisin – BP 852 25 – 35652 Le Rheu Cedex, France.

French production accounts for 15% of EU young bull production and this market is still increasing (+10% between 2005 and 2010). The French beef industry is subject to strong variations in beef and cereals quotas



**Fig. 1.** Mean absolute percentage error (MAPE) for daily feed intake (DFI) and body weight (BW) at different  $\alpha$  values. The lowest MAPE values were obtained for  $\alpha$  values between 0.12 and 0.26 for DFI and of 0.32 for BW.

and consequently needs references and tools to conduct young bull finishing. The aim of the Beefbox program is to construct a dynamic simulator of young bulls' finishing period, coupling intake, growth and body composition in order to estimate, carcass weight and some characteristics of interest at slaughter for various diets. The simulator Beefbox is based on a dynamic growth model (Hoch and Agabriel 2004) predicting each day body composition, carcass and body weight from metabolizable energy intake. It is completed with a dry matter intake (DMI) ( $\text{kg d}^{-1}$ ) equation fitted with monthly intakes and weights of 374 pens, and a set of equations predicting retail meat yield, three beef cut weights and fat depots (kidney and trimmed fat) fitted with a slaughterhouse database and a beef cut database (Table 2). All the equations were fitted with the experiment as random effect (on slope and intercept) with SAS PROC MIXED. The evolution of DMI with body weight follows an allometry with a coefficient 0.59 that corresponds to the reduced increase of DMI before slaughter. The set of equations for slaughter characteristics (Table 2) gives precise estimates because it relies on the best predictive variables, which are available in the outputs of the growth model. The parameters  $\alpha C$ ,  $\alpha NC$  and  $\alpha MW$  related to protein synthesis in carcass and non-carcass and to efficiency of energy utilization in the growth model were fitted in the whole simulator for the Charolais breed ( $n=176$ ) by minimizing the weighted sum of squares between simulated and observed values of body weight and cold carcass weight (CCW). Simulations were evaluated with the data according to Garcia et al. (2008). Beefbox simulated the slaughter weight with a root standard deviation (RSD) of 15.7 kg and the cold carcass weight with a RSD of 8.7 kg ( $R^2=0.75$ ). Finishing duration was estimated considering the time of simulation to reach observed CCW and predicted with a RSD of 13.2 days ( $R^2=0.89$ ). Estimated and observed average carcass yields were 58.2% and 58.4%, respectively, but the simulator poorly predicted carcass yields ( $R^2=0.0056$ ). This first evaluation highlighted the consistent behaviour of the model. The Beefbox model will be calibrated and evaluated for

other breeds available in the database before incorporation into a decision support system.

**Key words:** Young bull, model coupling, slaughter characteristics

**Hoch, T. and Agabriel, J. 2004.** A mechanistic dynamic model to estimate beef cattle growth and body composition: 1. Model description. *Agric. Systems* **81**: 1–15.

**Garcia F., Sainz R. D., Agabriel J., Barioni L. G. and Oltjen J. W. 2008.** Comparative analysis of two dynamic mechanistic models of beef cattle growth. *Anim. Feed Sci. Technol.* **143**: 220–241.

**Integrating mechanistic models of nutritional and reproductive processes to study reproductive efficiency in dairy cattle.** S. L. Shields<sup>1</sup>, H. Woelders<sup>2</sup>, M. Boer<sup>2,3</sup>, C. Stötzel<sup>4</sup>, S. Röeblitz<sup>4</sup>, J. Plöntzke<sup>4</sup>, and J. P. McNamara<sup>1</sup>. <sup>1</sup>Department of Animal Sciences, Washington State University, Pullman WA, USA, shannon.shields@email.wsu.edu; <sup>2</sup>Animal Breeding and Genomics Centre, Wageningen UR Livestock Research, Lelystad, the Netherlands; <sup>3</sup>Adaptation Physiology Group, Department of Animal Sciences, Wageningen University, Wageningen, the Netherlands; <sup>4</sup>Computational Systems Biology Group, Zuse Institute Berlin, Berlin, Germany.

The objective was to integrate two existing mechanistic, dynamic models of nutritional and reproductive processes in the dairy cow. The objective of this research model is to be suitable for evaluation of data, concepts, and hypotheses regarding underlying genetic, nutritional, and physiological control of reproduction. A model of metabolism in the cow (Molly, UC Davis), published and evaluated in literature (Baldwin et al. 1987) and describing metabolism of glucose, amino acids, and fatty acids in tissues at an aggregated metabolic pathway level, was designed to help improve understanding of control of the metabolic transactions in organs. The model of reproductive processes that

**Table 2. Predictive equations for daily dry matter intake (DMI,  $\text{kg d}^{-1}$ ), kidney fat (KFat), trimmed fat (TFat), total retail meat yield (RMY), chuck (CHW), tenderloin (TEW) and eye of round (ERW) weights. NCFat corresponds to non-carcass fat, CFat to carcass fat and CCW to cold carcass weight**

Equation	Numbers		<i>P</i> value for breed adjustment <sup>z</sup>		<i>R</i> <sup>2</sup>	RMSE
	Nexp	Ngroups	intercept	slope		
DMI = 0.229 BW <sup>0.59</sup>	112	374	0.006	0.004	0.78	0.88
KFat = -1.02 + 0.36 NCFat	31	177	0.0001	0.0001	0.98	0.41
TFat = 0.0013 (CFat + 1) <sup>1.91</sup>	33	186	0.0001	ns	0.92	1.06
RMY = 0.454 CCW <sup>1.09</sup>	3	17	–	–	0.99	3.01
CHW = -1.83 + 0.021 RMY	4	23	–	–	0.98	0.38
TEW = -0.23 + 0.01 RMY	4	23	–	–	0.56	0.26
ERW = 0.04 + 0.04 RMY	4	23	–	–	0.90	0.33

<sup>z</sup>RMY, CHW, TEW and ERW were fitted only for the Charolais breed.

was used describes growth and decay of the follicles and corpus luteum, gonadotropin releasing hormone, follicle stimulating hormone, luteinizing hormone, progesterone, oestrogen, oxytocin, and prostaglandin F<sub>2α</sub> over time (Stötzel et al. 2011). The two models were integrated using ACSLX (however other software can be used). The nutritional and reproductive processes were integrated at key regulatory control points including: how glucose affects energy, body fat, LH pulsatility, initiation of cycling (Start Cycling = 37 DIM - 0.15016 × kg Body Fat at 21 DIM); that higher DMI is associated with high leptin concentrations; that leptin ng mL<sup>-1</sup> (as a function of adipose mass) affects first postpartum LH surge (LH pulses/8h = 0.591 + 0.0015 (ng mL<sup>-1</sup>)<sup>5</sup> - 0.025(ng mL<sup>-1</sup>)<sup>4</sup> + 0.144(ng mL<sup>-1</sup>)<sup>3</sup> - 0.319(ng mL<sup>-1</sup>)<sup>2</sup> + 0.237(ng mL<sup>-1</sup>) R<sup>2</sup> = 0.65); and that metabolic rate (sum of all metabolic transactions) as a function of DMI and milk production increases the degradation of progesterone and oestrogen [clearance rate of progesterone, ng μL<sup>-1</sup> = 2.6455 - 0.1606 (DMI)<sup>2</sup> - 0.5896(DMI) R<sup>2</sup> = 0.9964; clearance rate of oestrogen, ng mL<sup>-1</sup> = atadv (formation of ADP in the visceral tissue) × 0.0009]. Changing energy intake or milk production caused a pattern and direction of response in reproductive processes consistent with available data. Increased metabolic rate decreases oestrogen and progesterone concentration, reduces the ovulatory surge and decreases embryo survival. This research model should be useful to frame specific hypotheses on control of reproductive processes by genetic and nutritional driven mechanisms.

**Key words:** Systems biology, reproduction, nutrition, research model

**Baldwin, R. L., France, J. and Gill, M. 1987.** Metabolism of the lactating cow. I. Animal elements of a mechanistic model. *J. Dairy Res.* **54**: 77–105.

**Stötzel, C., Plöntzke, J. and Röebnitz, S. 2011.** Advances in modelling of the bovine oestrous cycle: Administration of PGF<sub>2α</sub>. ZIB-report 11–17, Zuse Institute, Berlin, Germany.

**A bovine reproductive physiology model to predict interactions between nutritional status and reproductive management.** O. Martin<sup>1</sup>, F. Blanc<sup>2</sup>, J. Agabriel<sup>3</sup>, C. Disenhaus<sup>4</sup>, J. Dupont<sup>5</sup>, C. Ponsart<sup>6</sup>, P. Paccard<sup>7</sup>, J. Pires<sup>2</sup>, S. Fréret<sup>5</sup>, S. Elis<sup>5</sup>, J.Gatien<sup>6</sup>, P. Salvetti<sup>6</sup>, and N. C. Friggens<sup>1</sup>. <sup>1</sup>INRA, UMR 791 Modélisation Systémique Appliquée aux Ruminants, F-75005 Paris, France, nicolas.friggens@agroparistech.fr; <sup>2</sup>Clermont Université, VetAgroSup, F-63370 Lempdes, France; <sup>3</sup>INRA, UMR 1213 Herbivores, F-63122 Saint-Gènes-Champagnelle, France; <sup>4</sup>AGROCAMPUS OUEST, UMR 1348 Physiologie, Environnement et Génétique pour l'Animal et les Systèmes d'Élevage, F-35590 Saint-Gilles, France; <sup>5</sup>INRA, UMR 85 Physiologie de la Reproduction et des Comportements, F-37380 Nouzilly, France; <sup>6</sup>UNCEIA,

Department R&D, F-94704 Maisons-Alfort, France; <sup>7</sup>Institut de l'Élevage, 9 allée Pierre de Fermat, 63170 Aubière, France.

This model has been developed within a multi-disciplinary project bringing together physiologists, veterinarians, modellers, and breeding industry experts with the aim to develop a realistic representation of bovine reproductive physiology able to accommodate the effects of known nutritional factors on reproduction. Three related modules have been developed. The first represents the axis of reproductive biology structures namely the hypothalamus, pituitary gland, ovary (follicle, oocyte and corpus luteum), and uterus together with the associated dynamic patterns of the major hormonal signals (GnRH, FSH, LH, oestrogen, progesterone, prostaglandins, and interferon tau). This model successfully recreates hormonal profiles through the different reproductive stages (postpartum anoestrus, oestrus cycling, and pregnancy). An example of an LH profile simulated by the model through two successive oestrus cycles is presented in Fig. 2, relative to an observed profile. This module also simulates follicular waves with selection and ovulation (or not) of the dominant follicle. It also models the cross talk between the corpus luteum and uterus with respect to length of the luteal phase and embryonic loss (early or late) or maintenance of pregnancy. In the second module, oestrus expression behaviour is simulated. This is based on the hormonal profiles from the first module (mainly oestrogen) and incorporating other factors such as number of herd mates in oestrus. The third module represents reproductive management. In this module a wide range of reproductive management strategies can be represented in terms of their temporal structure both within day as time windows of oestrus observation and across lactation or calendar time as time windows of different reproductive actions. This module is designed to allow the impact of different reproductive management strategies on herd reproductive performance to be tested. At present, the reproductive physiology model has been shown to provide a realistic representation of hormonal profiles, follicle and corpus luteum dynamics, and hence normal reproductive performance measures. The next phase of this work (which will be carried out in a European Union funded project) will use the model to improve reproductive management tools that are urgently needed by the cattle industry.

**Key words:** Reproductive physiology, follicular waves, oestrus cycle, dynamic model

**A mechanistic and dynamic model to simulate diurnal patterns of herbage intake, grazing behaviour and nutrient supply of a dairy cow, MINDY: Brief model description.** P. Gregorini<sup>1</sup> and M. D. Hanigan<sup>2</sup>. <sup>1</sup>DairyNZ, Feed and farm systems, Modelling team, Hamilton 3240, New Zealand, pablo.gregorini@dairynz.co.nz; <sup>2</sup>Department of Dairy Science, Virginia



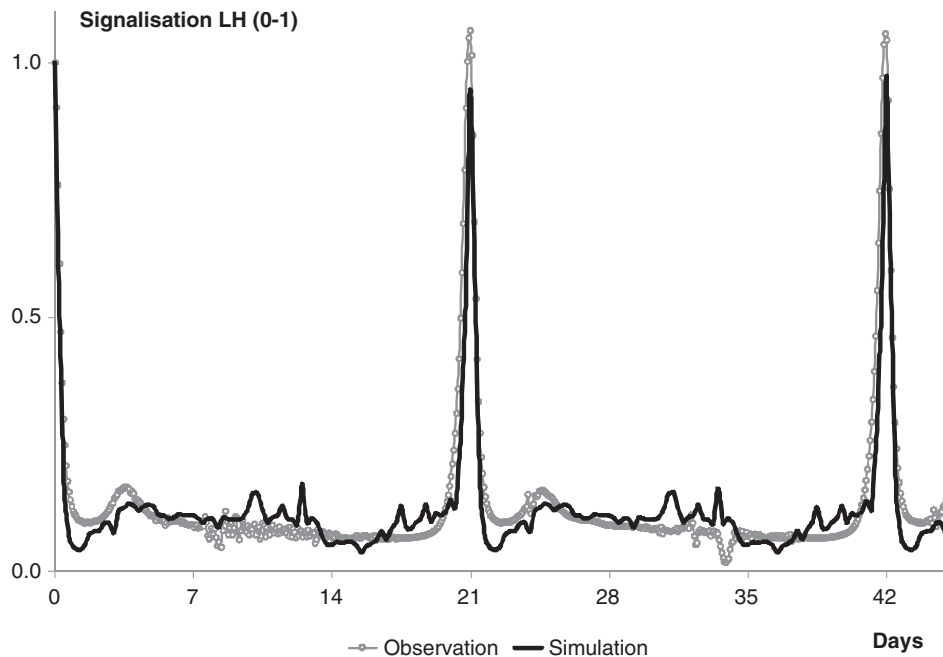


Fig. 2. Model generated and observed LH profiles (scaled to lie between 0 and 1) through 2 successive ovarian cycles.

Polytechnic Institute and State University, Blacksburg, VA 24061, USA.

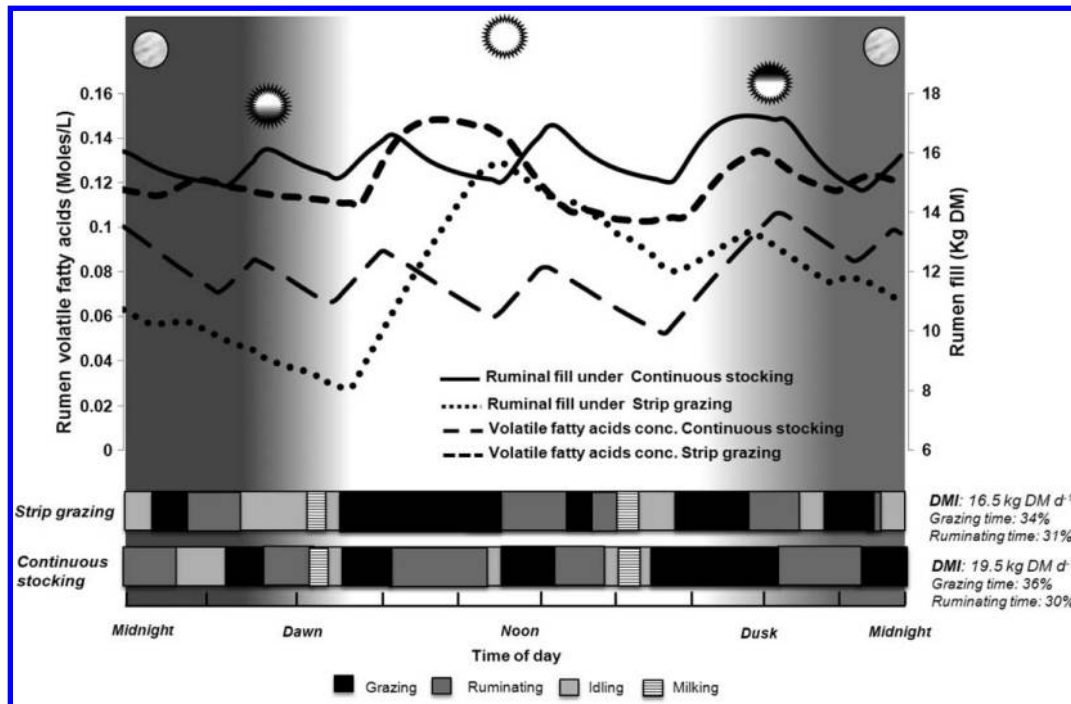
The complexity of the grazing process has been largely recognized, and research knowledge has accumulated from a simple bite to long-term digestive constraints. Because herbage intake is the most important variable affecting animal production, prediction and description of the grazing process are critical for management decisions. Past modelling efforts have focused on the mechanics and quantification of the grazing process. None of them have integrated within meal, diurnal and daily changes of animal internal state with spatio-temporal fluctuations of sward structure and quality in a grazing dairy cow. This communication briefly describes MINDY, a mathematical, mechanistic and dynamic simulation model of the diurnal grazing pattern of a dairy cow. MINDY is based on a cluster of three models: (1) Molly (Hanigan et al. 2009); (2) a model representing diurnal fluctuations of the internal state of the animal motivating feeding behaviour, hunger; and (3) a sward structure, herbage quality and grazing behaviour model. MINDY's objective is to describe the diurnal patterns of ingestive and digestive (including rumination) behaviours, herbage intake, and nutrient supply to the animal in response to the animal internal state and grazing environment. MINDY provides results at different foraging spatio-temporal scales (from a bite to a cluster of meals and to lactation). MINDY also predicts locomotion (i.e., steps taken while eating and searching) and sward defoliation dynamics. Due to Molly, MINDY is able to simulate detailed diurnal fluctuations of digestion and metabolism. MINDY's

code, development and simulations use ACSLXtreme (Aegis Technologies Group, Austin, TX) with a maximum integration interval of 1 min. Key parameters were subjected to a sensitivity analysis and then parameterized using two datasets from mid-lactation Friesian (Gibb et al. 1998) and late lactation Holstein (Taweel et al. 2004) dairy cows grazed. Assuming a relatively homogeneous sward, MINDY requires the same external inputs as Molly (feed quality and cow features) plus the height and mass of herbage, as well as the area offered to be run. For illustrative purpose, some of MINDY's outputs are presented using a high genetic merit Holstein–Friesian cow in mid-lactation grazed under continuous and strip-grazing methods on a *Lolium perenne* dominated sward (Fig. 3). In summary, MINDY provides an integrative and quantitative representation of the diurnal grazing pattern as described by Gregorini (2012). Once tested thoroughly against independent data MINDY will be used to predict and explain changes in daily herbage intake, and nutrient supply as a response to grazing management.

**Key words:** Modelling, herbage intake, grazing behaviour, dairy cow

**Gibb, M. J., Huckle, C. A. and Nuthall, R. 1998.** Effect of time of day on grazing behaviour by lactating dairy cows. *Grass Forage Sci.* **53**: 41–46.

**Gregorini, P. 2012.** Stobbs Memorial Lecture: Diurnal grazing pattern: its physiological basis and strategic management. *Anim. Prod. Sci.* <http://dx.doi.org/10.1071/AN11250>



**Fig. 3.** Predicted diurnal patterns of grazing, rumination and idling, ruminal fill and rumen volatile fatty acids concentration, plus daily eating and rumination time and herbage dry matter intake (DMI) of a high genetic merit New Zealand Holstein-Friesian dairy cow grazed under continuous stocking and strip-grazing (7 am new daily strip allocation) methods.

**Hanigan, M. H., Palliser, C. C. and Gregorini, P. 2009.** Altering the representation of hormones and adding consideration of gestational metabolism in a metabolic cow model reduced prediction errors. *J. Dairy Sci.* **92**: 5043–5056.

**Taweel, H. Z., Tas, B. M., Dijkstra, J. and Tamminga, S. 2004.** Intake regulation and grazing behavior of dairy cows under continuous stocking. *J. Dairy Sci.* **87**: 3417–3427.

**Mechanistic modelling based on meta-analysis: Prediction of the net hepatic fluxes of energetic nutrients in the ruminant.** L. Bahloul<sup>1</sup>, D. Sauvant<sup>2</sup>, J. Vernet<sup>1</sup>, H. Lapierre<sup>3</sup>, P. Nozière<sup>1</sup>, and I. Ortigues-Marty<sup>1</sup>. <sup>1</sup>INRA, 1213-Unité Mixte de Recherches sur les Herbivores, F63122 St Genès Champanelle, France, lahlou.bahloul@clermont.inra.fr; <sup>2</sup>UMR, 791-Physiologie de la Nutrition et Alimentation, AgroParisTech, 75231 Paris, France; <sup>3</sup>Dairy and Swine Research and Development Centre, Agriculture and Agri-Food Canada, Sherbrooke, Quebec, Canada J1M 1Z3.

Several mechanistic research models on hepatic metabolism have been established. They have been mostly parameterized for the dairy cow, and cannot be directly used for all types of ruminants in different physiological states. The study's originality is to use a modelling approach which associates meta-analysis with mechanistic modelling, as promulgated by Sauvant and Mertens

(2008). The objective is to set up a mechanistic model of liver metabolism that will predict the net splanchnic release (NSR) of all energetic nutrients in ruminants while being simple and robust enough to be used in feeding systems. This paper presents the initial development of this model, primarily calibrated for animals presenting a positive energy balance. Inputs and outputs of the model are based on net arterio-venous nutrient fluxes. The inputs correspond to the net portal appearance (NPA) of nutrients [acetate (C<sub>2</sub>), propionate (C<sub>3</sub>), butyrate (C<sub>4</sub>), glucose, lactate, B-hydroxybutyrate (BOHB), fatty acids, total amino acids (TAA), and oxygen (O<sub>2</sub>)]. The outputs correspond to the NSR of the same nutrients. The structure of the model consists of robust empirical equations (structural relationships) of the hepatic conversion of nutrients derived by meta-analysis (Loncke 2009) using the FLORA database (Vernet and Ortigues-Marty 2006), which collates more than 250 publications. These structural relationships predict the NSR of nutrients according to their NPA or to the NPA of their main precursors. The model includes the following hepatic compartments: C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, BOHB, Krebs cycle, storage (glycogen, protein), glucose, lactate and TAA. Conversion fluxes between compartments are included to establish the links between the different structural relationships. They represent the main hepatic metabolic pathways, and are implemented as mass action laws. Sets of experimental data (experimental designs) representing combinations

of nutrient inputs representative of nutritional practices were used to adjust parameters of the conversion fluxes. Parameters are adjusted so that the outputs of the model converge at best with the values calculated by structural relationships. Two steps are being carried out to evaluate the model: comparison of outputs predicted by the model with values predicted by the structural relationships (preliminary results cf. Table 3) and calculation of the carbon balance between outputs and inputs of the model. The first results of the adjustment of the net splanchnic fluxes predicted by the model are encouraging. The combination of empirical equations which consider net fluxes of individual nutrients across the liver with adjusted conversion fluxes across nutrients will contribute to develop a simple hepatic metabolism model of energetic nutrients compatible with the empirical structure of the INRA feeding system for ruminants.

**Key words:** Dynamic model, hepatic metabolism, ruminants

**Loncke, C. 2009.** Modelisation des relations entre l'alimentation et le flux splanchnique des nutriments energetiques chez le ruminant. Thèse de doctorat, AgroParisTech. France.

**Sauvant, D. and Mertens, D. R. 2008.** Use of meta-analysis to build a mechanistic model of responses of rumen digestion to dietary fibre in cattle. *Can. J. Anim. Sci.* **88**: 730.

**Vernet, J. and Ortigues-Marty, I. 2006.** Conception and development of a bibliographic database of blood nutrient fluxes across organs and tissues in ruminants: data gathering and management prior to meta-analysis. *Reprod. Nutr. Dev.* **46**: 527–546.

**Representation of protein synthesis regulation in mammary epithelial cells.** S. I. Arriola Apelo<sup>1</sup>, J. A. D. R. N. Appuhamy<sup>2</sup>, and M. D. Hanigan<sup>1</sup>. <sup>1</sup>Department of Dairy Science, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061, USA, sebuy@vt.edu; <sup>2</sup>Department of Animal Sciences, University of California, Davis, CA 95616, USA.

The initiation of mRNA translation is regulated by the mammalian target of rapamycin (mTOR) pathway that

**Table 3. Relationship between empirically predicted (X) and simulated (Y) NSR of C in C<sub>2</sub>, C<sub>4</sub>, BOH and glucose (mmol h<sup>-1</sup> kg<sup>-1</sup> BW)**

	Mean (SD) of X	Intercept	Slope	RMSE
C-C <sub>2</sub>	4.21 (1.38)	0.33*	0.87*	0.1
C-C <sub>4</sub>	0.12 (0.03)	0.03*	0.87*	0.001
C-BOH	1.82 (0.24)	-1.04*	1.55*	0.01
C-glucose	3.14 (0.53)	-0.74	1.26	0.4

\*Significantly different from 1 (slope) and 0 (intercept).

senses cellular nutrient status and hormonal signals (Dennis et al. 2011). Appuhamy and Hanigan (2010) presented a model of regulation of mTOR phosphorylation by essential AA (EAA) and insulin. The objective of the present work was to extend that model to represent the individual EAA effect on mTOR phosphorylation and fractional protein synthesis rate ( $SR_{(Pr)}$ ) in the mammary gland. Data to estimate model parameters were obtained from Appuhamy et al. (2012). The model was fitted against mTOR phospho:total ratios standardized to the observed mean of the complete Dubelcco Modified Eagle Medium treatment ( $Q_{P(mTOR)}$ ) and  $SR_{(Pr)}$  (% h<sup>-1</sup>). The Nelder-Mead algorithm was used to maximize the log likelihood function in ACSLX (Aegis Tech, Huntsville, AL, USA). The EAA term driving mTOR phosphorylation ( $F_{U,P(mTOR)}$ ) was substituted by a representation of individual EAA. The Akt term was set to 1 because there was no variation in insulin concentration and this was maintained close to reference values. The solution for mTOR phosphorylation mass action rate constants ( $k_{P(AA)}$ ) for all the EAA, but Leu, were several-fold greater than the mean intracellular AA concentrations and standard deviations were greater than estimates. Hence, Leu ( $C_{Leu}$ ) was the only AA driving mTOR phosphorylation as stated in the equation:

$$F_{U,P(mTOR)} = Q_{U(mTOR)} * k_{U,P(mTOR)} * \left( 1 + \frac{C_{Leu}}{k_{P(Leu)}} \right)$$

where  $k_{U,P(mTOR)}$  represented the rate constant for the reaction previously estimated by Appuhamy and Hanigan (2010). Protein synthesis was represented by a Michaelis Menten function of Ile and Met. Other EAA ( $K_{SR(AA)}$ ) showed no substrate effect on protein synthesis. Also, a  $Q_{P(mTOR)}$  term initially included to adjust the maximum rate of synthesis ( $Vmax_{SR(Pr)}$ ) had a standard deviation greater than its final estimate indicating over-parameterization. Therefore,  $SR_{(Pr)}$  was represented as a function of intracellular Ile and Met concentrations:

$$SR_{(Pr)} = \frac{Vmax_{SR(Pr)}}{\left( 1 + \frac{k_{SR(Ile)}}{C_{Ile}} + \frac{k_{SR(Met)}}{C_{Met}} \right)}$$

Final parameter values, observed means and prediction errors are presented in Table 4. Intracellular Leu concentration explained 67% of the variation observed in mTOR phosphorylation. No mean or slope bias was observed for  $Q_{P(mTOR)}$  predictions. Intracellular concentrations of Ile and Met together explained 63% of the variation observed in protein synthesis with no mean or slope bias. Regression of  $SR_{(Pr)}$  residuals on intracellular Leu concentration and  $Q_{P(mTOR)}$  showed no remaining effect explained by these two variables. Concluding, the model indicated that protein synthesis was inhibited when the cell sensed a shortage of Ile and

**Table 4. Observed means and prediction errors for model variables, and estimates and standard deviation of parameters related to these variables<sup>2</sup>**

Variable	N	Mean	RMSPE	Parameter	Estimate	SD
$Q_{P(mTOR)}$	47	0.715	0.236	$K_{P(Leu)}$	29.37	0.156
$SR_{(Pr)}$	40	0.914	0.387	$Vmax_{SR(Pr)}$	1.586	0.024
				$K_{SR(Ile)}$	95.84	5.435
				$K_{SR(Met)}$	3.498	1.264

<sup>2</sup>Pool of phosphorylated mTOR ( $Q_{P(mTOR)}$ , arbitrary units), mass action rate constant of Leu effect on mTOR phosphorylation ( $K_{P(Leu)}$ , mM), phosphorylated mTOR reference scalar ( $Ref\_Q_{P(mTOR)}$ ), fractional protein synthesis rate ( $SR_{(Pr)}$ , % h<sup>-1</sup>), maximum rate of protein synthesis ( $Vmax_{SR(Pr)}$ , % h<sup>-1</sup>) of individual AA concentration at half of  $Vmax$  ( $K_{SR(AA)}$ , mM).

Met to avoid malfunction of the translational machinery and to reduce energy expenditure, but this signal was not through the mTOR pathway.

**Key words:** Amino acids, mTOR, protein synthesis, modelling

**Appuhamy, J. A. D. R. N. and Hanigan, M. D. 2010.** Modeling the effects of insulin and amino acids on the phosphorylation of mTOR, Akt, and 4ebp1 in mammary cells. Page 225–232 in D. Sauvante, J. V. Milgen, P. Faverdin, and N. Friggens eds. Modelling nutrient digestion and utilisation in farm animals. Wageningen Academic Publishers, Wageningen, the Netherlands.

**Appuhamy, J. A. D. R. N., Knoebel, N. A., Nayananjalie, W. A. D., Escobar, J. and Hanigan, M. D. 2012.** Isoleucine and leucine independently regulate mTOR signaling and protein synthesis in mac-t cells and bovine mammary tissue slices. *J. Nutr.* **142**: 484–491.

**Dennis, M. D., Baum, J. I., Kimball, S. R. and Jefferson, L. S. 2011.** Mechanisms involved in the coordinate regulation of mTORc1 by insulin and amino acids. *J. Biol. Chem.* **286**: 8287–8296.

**Prediction of nitrogen excretion from lactating cattle using a cross-classified mixed model.** K. F. Reed<sup>1</sup>, L. E. Moraes<sup>1</sup>, D. P. Casper<sup>2</sup>, and E. Kebreab<sup>1</sup>. <sup>1</sup>Department of Animal Science, University of California, Davis, CA 95616, USA, kfreed@ucdavis.edu; <sup>2</sup>Department of Dairy Science, South Dakota State University, Brookings, SD 57007, USA.

Nitrogen (N) utilization by cattle is below 40%, but the amount and form in which it is excreted is dependent on various parameters including N intake ( $N_i$ ) (Kebreab et al. 2002). In particular, urinary N excreted (UN) contains urea, which is hydrolyzed to ammonia by urease found in feces. Ammonia emissions and nitrogenous run-off from livestock operations present serious health and environmental concerns. Among livestock, dairy cattle and, especially, lactating dairy cows are the largest contributors (Vitousek et al. 1997). Predicting N

excretion of lactating dairy cattle based on dietary and animal variables has the potential to improve the understanding of N utilization in cattle and alleviate environmental impacts. Most published prediction equations for N excretion are based on only  $N_i$ . The study objective was to develop UN and faecal N (FN) prediction equations based on dietary and animal variables that might play a significant role in influencing N excretion. The data used for model development consisted of 1094 observations on lactating dairy cows from 40 energy-balance studies conducted at the USDA Energy and Metabolism Laboratory from 1962 to 1995. A meta-analytical mixed model approach was taken, in which study and animal were used as cross-classified random effects. Independent covariates or variables tested included: total  $N_i$ , digestible energy (DE), neutral detergent fibre (NDF), ether extract (EE), age, and body weight (BW). The statistical model was implemented in R using S4 classes package for fitting linear mixed-effects models (lme4). A likelihood ratio comparison test of models demonstrated that the significant variables are  $N_i$ , DE, NDF, EE and BW for UN;  $N_i$ , DE, and EE for FN; and  $N_i$ , DE, NDF, and BW for total excretion (UN + FN) of manure nitrogen (MN). The following models were selected based on Akaike Information Criteria:

UN (g d<sup>-1</sup>)

$$= -204.4 (19.65) + 0.32 (0.099) N_i (\text{g d}^{-1}) \\ + 52.0 (4.93) \text{ DE (Mcal kg}^{-1} \text{ DM)} \\ + 0.6124 (0.18) \text{ NDF (\%)} - 5.63(1.81) \text{ EE(\%)} \\ + 0.11(0.015) \text{ BW (kg)}$$

FN (g d<sup>-1</sup>)

$$= [14.87(0.32) + 0.013 (0.00020) N_i (\text{g d}^{-1}) \\ - 2.99(0.098) \text{ DE (Mcal kg}^{-1} \text{ DM)} \\ + 0.16(0.025) \text{ EE (\%)}]^2$$

MN (g d<sup>-1</sup>)

$$= 0.38(17.36) + 0.63 (0.0089) N_i (\text{g d}^{-1}) \\ - 17.75(4.43) \text{ DE (Mcal kg}^{-1} \text{ DM)} \\ + 0.56 (0.17) \text{ NDF (\%)} + 0.11(0.013) \text{ BW (kg)}$$

A K-fold cross-validation technique was used for model evaluation, in which the data were folded by study to yield 40 folds. This method is based on a procedure in which data are iteratively divided into training and testing sets so that the predictive ability of the model is estimated at each iteration by the mean square prediction error (MSPE). The error on predictions is estimated by the average MSPE from all iterations and the uncertainty in the error of prediction is estimated by the MSPE variance. Initial model diagnostics yielded a root MSPE as a percentage of the observed mean of 20.6% for UN, 6.04% for FN, and 9.37% for MN.

**Key words:** Meta-analysis, nitrogen metabolism, dairy cattle

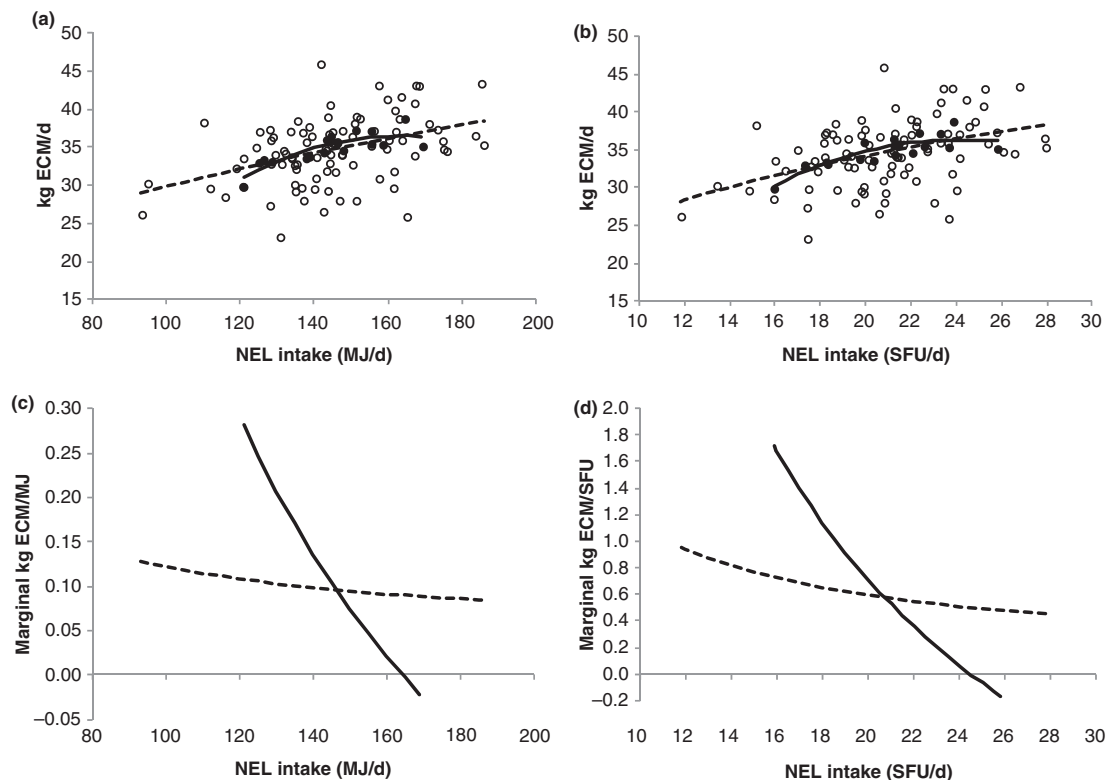
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**Evaluation of individual versus group level observations and different feed ration evaluation systems for estimating milk yield responses.** C. Jensen<sup>1,2</sup>, M. R. Weisbjerg<sup>1</sup>, and S. Østergaard<sup>1</sup>. <sup>1</sup>Department of Animal Science, Aarhus University, Blichers Allé 20, 8830 Tjele, Denmark, charlotte.jensen@agrsci.dk; <sup>2</sup>Knowledge Centre of Agriculture, Cattle, Agro Food Park 15, 8200 Aarhus, Denmark.

Milk production response functions are needed for the economic optimization of energy level in feed rations

based on NorFor (Volden 2011), a non-additive net energy (NEL) system. Previous production responses were based on additive Scandinavian feed units (SFU). The objectives were to compare response functions based on: (1) individual cow observations versus treatment means; (2) NEL versus SFU. Data used were from two block experiments; each lasted from 3 to 15 wk after parturition and included 90 multiparous Danish Holstein cows. Treatments were three types of roughages combined with three levels of concentrates as TMR rations. Datasets were 90 individual (idv) or 18 group (grp, treatment means) level observations. A mixed linear effects model with random effect of experiments was used for analyses of energy corrected milk (kg, ECM) response; explanatory variables were energy intake as both a linear effect and transformed by natural logarithm. A declining marginal milk yield response (MR) was found for all scenarios (Fig. 4). At 10, 50 and 90 percentiles of NEL intake the MR were (idv/grp): 0.11/0.24, 0.10/0.11 and 0.09/0.02 kg ECM per MJ, respectively; with SFU the MR were (idv/grp): 0.67/1.15, 0.57/0.48 and 0.50/0.10 kg ECM per SFU, respectively. This shows that at both low and high levels of energy intake, there is a significant difference between using idv versus grp data. To compare MR from NEL and SFU system,



**Fig. 4.** (a) and (b) The milk production response in kilograms energy corrected milk per day ( $\text{kg ECM d}^{-1}$ ) to increased net energy intake according to NorFor ( $\text{MJ d}^{-1}$ ) and Scandinavian feed unit ( $\text{SFU d}^{-1}$ ). Observations on individual level ( $\circ$ ) and on group level ( $\bullet$ ). Predicted responses on individual level (---) and on group level (—). (c) and (d) The marginal milk production response (marginal kg ECM per energy unit) to increased net energy intake according to NorFor ( $\text{MJ d}^{-1}$ ) and Scandinavian feed unit ( $\text{SFU d}^{-1}$ ).

we converted ECM per SFU to ECM per NEL by the factor 0.144 SFU per MJ, which was the calculated mean from idv data. At 10, 50 and 90 percentiles of SFU intake the converted MR (idv/grp) were: 0.10/0.17, 0.08/0.07 and 0.07/0.01 kg ECM per MJ, respectively. This shows a larger MR for the NEL system than the SFU system, though the differences are small. These results demonstrate that different outcomes can be obtained when modelling responses from individual and group-based data, which is particularly important in models such as those targeting optimal feeding levels.

**Key words:** Dairy cows, modelling, response curves

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**The use of linear programming to select diets based on their use in the population and their cost – a goal programming approach.** J. G. Fadel<sup>1</sup>, L. E. Moraes<sup>1</sup>, J. M. Katz<sup>2</sup>, C. K. Winter<sup>2</sup>, and S. E. Buttrey<sup>3</sup>. <sup>1</sup>University of California, Department of Animal Science, One Shields Avenue, Davis, CA 95616, USA, jgfadel@ucdavis.edu; <sup>2</sup>University of California, Department of Food Science and Technology, One Shields Avenue, Davis, CA 95616, USA; <sup>3</sup>Naval Postgraduate School, Operations Research Department, Glasgow Hall 290, Monterey, CA 93943, USA.

The objective of this study was to utilize a linear programming (LP) approach to select feeds that are similar to that observed in an individual or population diet and also minimize the total cost for each diet using a goal programming approach. This approach is applicable in agriculture when you want to vary the diet as little as possible based on diets currently fed. The traditional use of linear programming for formulating diets for humans or animals is typically through the following brief example:

$$\begin{aligned} \min \sum_{j=1}^n c_j x_j; \\ \text{subject to the following constraints (ST):} \\ \sum_{j=1}^n a_{kj} x_j (\leq, =, \geq) b_k, \text{ for } k = 1, 2, \dots, m \end{aligned} \quad (1)$$

where  $c_j$  is the cost of feed  $j$ ,  $x_j$  is the amount of feed  $j$ ,  $a_{kj}$  is the content of nutrient  $k$  in feed  $j$ ,  $b_k$  is the animal's requirement for nutrient  $k$ ;  $n$  and  $m$  represent the number of feeds and constraints respectively. However, if part of the objective is to select feeds that are similar to that observed in an individual or population, then another technique is necessary. The technique of selecting foods that are similar to what an individual is currently consuming or similar

to median food consumed by the population is well established in the literature (Briend et al. 2003; Katz et al. 2012). The objective function for the  $i$ th individual would be:

$$\min \sum_{h=1}^2 w_h (d_{hi}^- + d_{hi}^+), \quad (2)$$

where  $w_h$  and  $d_{hi}^-$  or  $+$  are the weight and the plus or minus deviation respectively for the  $h$ th goal and  $i$ th individual. The model would be run in three steps where the first step would be the LP of the primary goal as in Eq. (3). The second step would be to minimize the cost of the diet as in Eq. (1). The third step would minimize the deviation from the goals with the objective function as in Eq. (2). The primary goal objective function would be:

$$\begin{aligned} \min F_i = \sum_{j \in R_i} \text{abs} \left( \frac{Q_{ij}^{opt} - Q_{ij}^{obs}}{Q_{ij}^{obs}} \right) + \sum_{j \notin R_i} \left( \frac{1 + \frac{1}{NC_j}}{Q_j^{med}} \right) \cdot Q_{ij}^{opt}, \\ \text{ST: } \sum_{j=1}^{n_i} a_{kj} Q_{ij}^{opt} (\leq, =, \geq) b_{ki}, \text{ for } k = 1, 2, \dots, m \end{aligned} \quad (3)$$

where  $F_i$  is the objective function for the  $i$ th individual;  $R_i$  includes all  $j$  feeds currently observed in the  $i$ th individual's diet;  $Q_{ij}^{opt}$  is the decision variable and the optimum quantity of  $j$ th feed, for the  $i$ th individual;  $Q_{ij}^{obs}$  is the reported quantity of  $j$ th feed consumed by the  $i$ th individual,  $NC_j$  is number of individuals consuming  $j$ th food not part of the  $i$ th individual's observed diet,  $Q_j^{med}$  is the population median food intake of the  $j$ th food,  $a_{kj}$  is the content of nutrient  $k$  in feed  $j$ ,  $b_{ki}$  is the  $i$ th individual's requirement for nutrient  $k$ ,  $n_i$  represents the number of feeds for the  $i$ th individual, and  $m$  represents the number of constraints. The third step of the LP requires the weighted objective function described for the  $i$ th individual in Eq. (2), and the constraints are:

$$\begin{aligned} F_i + d_{i1}^- - d_{i1}^+ = \min F_i \\ \sum_{j=1}^{n_i} c_j Q_{ij}^{opt} + d_{2i}^- - d_{2i}^+ = \min C_i \\ \sum_{j=1}^{n_i} a_{kj} Q_{ij}^{opt} (\leq, =, \geq) b_{ki} \\ d_{hi}^-, d_{hi}^+, Q_{ij}^{opt} \geq 0 \end{aligned} \quad (4)$$

If  $w_1 \gg w_2$ , then this formulation will weigh the first goal greater than the second. This LP technique will allow the formulation of diets based on the current

diet programs and the population without imposing additional constraints.

**Key words:** Linear programming, dietary modelling, goal programming

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**Pretty good on average: A rationale for stochastic models for cattle metabolism.** I. J. Lean<sup>1</sup>, H. Golder<sup>1</sup>, and J. P. McNamara<sup>2</sup>. <sup>1</sup>SBScius, Camden, NSW, Australia, ianl@sbscius.com.au; <sup>2</sup>Washington State University, Department of Animal Sciences, Pullman, WA, USA.

Great advances have been made in modelling cattle metabolism and production with deterministic models, both mechanistic and dynamic (Baldwin et al. 1987), semi-mechanistic (Russell et al. 1992) and empirical models. Very similar estimates of energy and protein requirements for dairy cattle have been derived using the semi-mechanistic and empirical models (Lean 2011), indicating considerable consensus for nutritional requirements. However, observations can be made from diverse experiments that indicate limitations of current deterministic approaches to evaluating responses to nutrients. The premise of this communication is that considerable gains may be made in the precision of estimation of responses to diet and productivity enhanced by examining sources of heterogeneity or variability in animal responses to nutrient inputs and by including stochastic elements in future models.

The intent of this communication is to provide a rationale to stimulate interest in and development of stochastic models. Ruminant scientists have inherently understood that ruminants are metagenomic; it has been estimated that 90% of the cells in *Homo sapiens* are microbial, not human, in origin (Turnbaugh et al. 2007). The percentage of microbial organisms for cattle may be expected to be higher. Little is understood about communications between ruminal organisms and the host mammal and there is marked heterogeneity in ruminal populations (Jami and Mizrahi 2012; Golder et al., unpublished). The rumen is not a homogenous environment, with marked differences in moisture, fibre content and redox potential. Aggregations of organisms within microfilms, further compartmentalise the rumen. The implications for the accuracy prediction of responses from this variation in rumen environment are not clear; because it is difficult to capture total rumen output in vivo and concentrations of rumen contents are not definitive. Firkins et al. (1998) reported considerable variance in estimates of microbial N flow to the duodenum derived from net energy intake and ascribed this in part to random variation. Cattle grown on tropical forages have feed intakes far exceeding those predicted from standard models (McLennan 2005). We can hypothesise that these observations support the potential for very different ruminal biomes to exist compared to those established on temperate pastures and potential for substantial heterogeneity in ruminal environments as a function of early exposure and adaptation. In order to assess the variation in ruminal responses to fixed inputs, we examined results of a series of 118 fermenter observations for 30 different diets (Lean et al. 2005). The mean and range of the standard deviations for rumen outputs and measures of efficiency were assessed, within the 30 diets and are presented as variable means, and the mean and range of the SD for the 30 diets, expressed as a percentage of diet mean (Table 5). Even in a tightly controlled system with rumen fluid derived and pooled

**Table 5.** Mean daily production of volatile fatty acids and protein measures, mean and ranges for the standard deviations of 30 different diets tested using in vitro continuous culture fermenters. The raw data used in Lean et al. (2005) were re-analysed to provide the mean and ranges of the dietary standard deviations

Variable (mean)	Mean of SD of diets (% of mean)	Range of SD of diets (% of mean)	Variable (mean)	Mean of SD (% of mean)	Range of SD (% of mean)
Total VFA (375.3 mmol d <sup>-1</sup> )	3.6	0.1 to 10.9	Microbial protein N produced per day per kg DM digested (28.8 g)	8.3	2.0 to 23.2
Acetate (230.3 mmol d <sup>-1</sup> )	4.3	0.3 to 8.4	VFA produced mol kg <sup>-1</sup> CHO digested (10.1 mol kg <sup>-1</sup> )	4.0	0.1 to 11.2
Butyrate (36.6 mmol d <sup>-1</sup> )	10.2	0.3 to 28.4	VFA produced mol kg <sup>-1</sup> microbial N produced (208.8 mol kg <sup>-1</sup> )	9.3	0.9 to 17.5
Propionate (79.9 mmol d <sup>-1</sup> )	9.5	0.7 to 44.8	Crude protein degraded (70.4%)	7.3	1.8 to 15.5
Valerate (9.7 mmol d <sup>-1</sup> )	22.5	0.7 to 53.6	Isovalerate (5.5 mmol d <sup>-1</sup> )	30.1	0.3 to 118.0

from two animals, and no protozoa, there is considerable variation, i.e., 9 to >50% of the mean for the SD of some outcomes. While models and understandings can be improved by characterising components of variation, the reduction in variance remains to be determined. Michaelis–Menten reactions are subject to variance, and Baldwin provided an opportunity for this to be characterised through varying the equilibrium constants and the maximum velocity rates of enzyme equations in the deterministic, dynamic model of cattle metabolism, Molly (Baldwin et al. 1987). Models for the future will capture sources of variance including that intrinsically inherent e.g., genotype and enzymatic reactions, and environmental sources including nutrition, exposures to microbes at the onset of feeding and anti-nutritional factors.

**Key words:** Stochastic, metagenomic, rumen

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