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## Prediction of net hepatic release of glucose using a 'hybrid' mechanistic model in ruminants applied to positive energy balance

L. Bahloul<sup>1</sup>, I. Ortigues-Marty<sup>1</sup>, J. Vernet<sup>1</sup>, H. Lapierre<sup>3</sup>, P. Nozière<sup>1</sup> and D. Sauvant<sup>2</sup>

<sup>1</sup>INRA, Unité Mixte de Recherches sur les Herbivores, 63122 St Genès Champanelle, France

<sup>2</sup>UMR, Modélisation Systémique Appliquée aux Ruminants, AgroParisTech, 75005 Paris, France; [sauvant@agroparistech.fr](mailto:sauvant@agroparistech.fr)

<sup>3</sup>Agriculture and Agri-Food Canada, Sherbrooke, QC J1M0C8, Canada

### Introduction

Ruminants depend on hepatic gluconeogenesis to meet most of their metabolic demand for glucose which relies on availability of precursors from diet supply and animal requirements (Loncke *et al.*, 2010). Several mechanistic models of the metabolic fate of nutrients across the liver exist that have been parameterized for dairy cows. They cannot be directly used to predict hepatic gluconeogenesis in all types of ruminants in different physiological status. A hybrid mechanistic model of nutrient fluxes across the liver is presently being developed (Bahloul *et al.*, 2012), that is calibrated empirically based on meta-analysis (Sauvant and Mertens, 2008) to be applicable to all types of ruminants in different physiological status and to usual nutritional practices. The objectives of the present work were to test the hybrid liver model in its present state of development to simulate the net hepatic release of glucose when the glucogenic/ketogenic/nitrogenous nutrient profile entering the liver varies. This first application of the model was limited to ruminants in positive calculated energy balance, in which the nutrient fate across the liver is mostly directed by mass action laws.

### Material and methods

Net veno-arterial fluxes of nutrients correspond to the inputs (net portal appearance, NPA) and outputs (net splanchnic release, NSR) of the mechanistic model. Nutrients considered are: acetate (C2), propionate (C3), butyrate (C4), glucose, lactate,  $\beta$ -hydroxybutyrate (BHB), total amino acids (TAA), urea,  $\text{NH}_3$ ,  $\text{O}_2$ ,  $\text{CO}_2$  and the absorbed fatty acids. Their flows are expressed in mmol of C/h/BW except for  $\text{NH}_3$ , expressed in mmol of N/h/BW. Ten hepatic compartments are included: C2, C3, C4, BHB, glycogen, protein, glucose, lactate, TAA and  $\text{CO}_2$ . Conversion fluxes between compartments, including metabolic compartments summarizing the Krebs cycle, represent the main hepatic metabolic pathways. The model based on mass action laws is adjusted on empirical relationships of the net hepatic transfer of nutrients derived by meta-analysis (Loncke, 2009) from FLORA database, allowing estimation of NSR of nutrients. The empirical equation used to predict glucose NSR was based on the sum of the NPA of precursors (Loncke *et al.*, 2010), modified to take into account all AA potentially convertible to glucose. Indeed, if only the NPA of glucogenic AA is considered, a deficit of carbon is calculated to meet glucose output. Sets of experimental data, representative of nutritional practices representing different combinations of ketogenic, glucogenic and nitrogen nutrient inputs, were used to adjust parameters of the conversion fluxes, in cattle and sheep, only in calculated positive energy balance. Nutritional status ranged from 1 to  $5 \times \text{ME}$  and 1.4 to  $6.7 \times$  metabolizable protein maintenance requirements. Parameters were adjusted so that the simulated model outputs converge at best with the values predicted by empirical relationships. The model was evaluated by: (1) calculating the full C balance across the liver; and (2) by comparing outputs (NSR) of glucose simulated by the model with values predicted by the empirical relationships.

### Results and discussion

The full C balance across the liver simulated by the model (Figure 1) indicates a tight agreement between C outputs and inputs, with a small deficit averaging 0.0021 mol C/d. Comparison between the model simulated and the empirically predicted NSR of glucose (Figure 2) shows a good (93%)



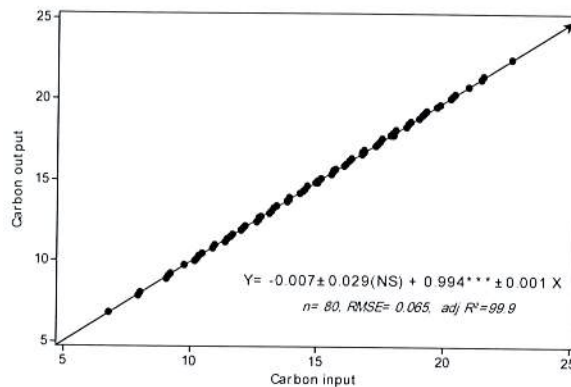


Figure 1. Relationship between the carbon output (Y) simulated by the model and the carbon input (X) in mmol of C/h/BW, \*\*\*P<0.001.

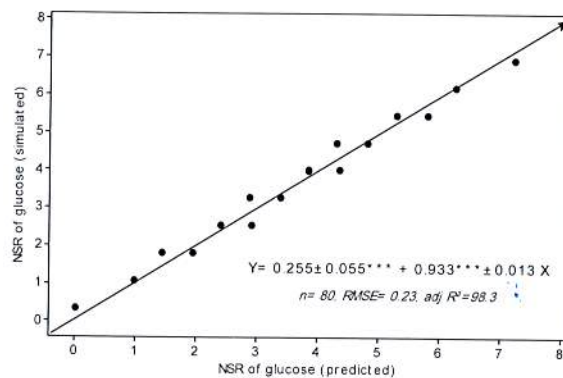


Figure 2. Relationship between the NSR of glucose (Y) simulated by the model and predicted by structural relationship (X) in mmol of C/h/BW, \*\*\*P<0.001.

simulation. For C3 and TAA, the major glucogenic nutrients, the simulated outputs compare well with the values predicted by the structural relationship. Parameters of mass action laws obtained by model adjustment show that 93%/h and 173%/h of intrahepatic pool of TAA and C3 is metabolized to oxaloacetate (OA) respectively; 124% of intrahepatic pool of OA is converted to glucose. Almost, all TAA up taken by the liver (73%) appeared used for neoglucogenesis. The hepatic uptake of C3 (91%) seems to be converted completely to glucose, only 19%/h and 0.8%/h of intrahepatic pool of C3 are released and converted to pyruvate respectively. A strength of the approach is to identify situations responsible for poor adjustments: an underestimation (0.34 mmol of C/h/BW) of the simulated NSR glucose is observed at elevated TAA NPA (>3 mmol of C/h/BW).

The hybrid model based strictly on mass action laws simulates well the prediction of hepatic release of glucose for ruminants in positive energy balance. The model was found to be stable in term of C balance, with a small negligible deficit in C. The next step consists on the application of the model to ruminants in negative energy balance. If necessary, regulations representing hepatic metabolism will be introduced to take account interaction between nutrients and tissues (nutrient requirements).

### Acknowledgements

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## References

- Bahloul, L., D. Sauvant, J. Vernet, H. Lapierre, P. Nozière and I. Ortigues-Marty, 2012. Mechanistic modeling based on meta-analysis : prediction of the net hepatic fluxes of energetic nutrients in ruminant. *Can. J. Anim. Sci.* 92, 559-560.
- Loncke, C., 2009. Modélisation des relations entre l'alimentation et les flux splanchniques de nutriments énergétiques chez le ruminant. Thèse de doctorat, AgroParisTech. France.
- Loncke, C., P. Nozière, S. Lemosquet, J. Vernet, H. Lapierre, D. Sauvant and I. Ortigues-Marty, 2010. Splanchnic release of glucose in relation to dietary supply and animal performances. *Renc. Rech. Ruminants* 17, 317.
- Sauvant, D. and D. Mertens, 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.

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Ermias Kebreab

Hélène Lapierre



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