

final report

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Compartmental analysis of energy expenditure and glucose/insulin fluxes in sheep

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Abstract

A workshop led by Dr Ray Boston who is Professor of Applied Biomathematics at the University of Pennsylvania on '**Compartmental analysis of energy expenditure and glucose/insulin fluxes in sheep**' was held at the University of New England from 16th – 26th July 2012. This was a follow-up to a previous workshop held in March 2007. The main purpose of this workshop was to enable UNE and NSW DPI staff to work through modelling issues that had arisen since the 2007 workshop.

At the current workshop, sessions were focussed on various modelling challenges that were posed by the participants and had become apparent since the 2007 meeting. The topics and datasets investigated were derived from current research programs or teaching practicums. All of the research topics and datasets were chosen because they could readily be developed into research publications with joint authorships between the University of New England and the University of Pennsylvania.

At the end of the 8-day workshop, Dr Boston delivered a public seminar to the School of Environmental and Rural Science on the topic "A New Model of Non-Esterified Fatty Acid Metabolism: Lessons From the Glucose Minimal Model". This lecture exemplified the power of the modelling techniques that he had been imparting to our research and teaching staff over the course of his visit.

The workshop has helped consolidate the modelling group in Armidale. Some of the projects will lead to further collaborations between our two Universities, and to further joint publications, e.g. the animal-based studies of glucose challenge and insulin response led by Drs Jim McFarlane and Ian Godwin. Draft papers developed in connection with the recent workshop with Professor Boston as a co-author included: 'A model of bicarbonate carbon movements through body compartments of sheep', 'A compartmental modelling method for determining the production and inter-conversions of volatile fatty acids in the rumen', 'A model of leptin kinetics in sheep', 'A model of the kinetics of nitrate reduction and use in the rumen of sheep' and 'A model describing the kinetics of passage of fluid phase and particulate digesta through the gut of sheep'.

Executive summary

A workshop led by Dr Ray Boston, Professor of Applied Biomathematics at the University of Pennsylvania, on 'Compartmental analysis of energy expenditure and glucose/insulin fluxes in sheep' was held at the University of New England from 16th – 26th July 2012. This was a follow-up to a previous workshop held in March 2007. Dr Ray Boston is an internationally recognised modeller. His major expertise is in the use of compartmental analysis to model pathways of animal and human metabolism. He has developed several major industry modelling software packages such as WinSAAM and MinMod, and has played a major part in the development of the CPM Dairy software in the USA.

The main purpose of this workshop was to enable UNE and NSW DPI staff to work through modelling issues that had arisen since the 2007 workshop. At the current workshop, tutorials were focussed on various modelling challenges that had been experienced by the participants and had become apparent since the 2007 meeting. The topics and datasets investigated were derived from current research programs or teaching practicums. The research topics and datasets were chosen because they could readily be developed into research publications with joint authorships between the University of New England and the University of Pennsylvania.

At the end of the 8-day workshop, Dr Boston delivered a public seminar to the School of Environmental and Rural Science on the topic "A New Model of Non-Esterified Fatty Acid Metabolism: Lessons From the Glucose Minimal Model". This lecture exemplified the power of the techniques that he had been imparting to our research and teaching staff over the course of his visit.

The workshop contributed to a developing modelling group in Armidale and will help reverse the decline in expertise in modelling expertise in Australia in recent years. Some of the projects, including the animal-based studies of glucose challenge and insulin response led by Drs Jim McFarlane, Ian Godwin and Robin Dobos and the studies of rumen volatile fatty acid production led by Prof John Nolan will lead to further collaborations between our two Universities and to further joint publications.

Conclusions

The workshop enhanced modelling expertise in the Armidale modelling group. Draft papers developed in connection with the recent workshop with Professor Boston as a co-author included: 'A model of bicarbonate carbon movements through body compartments of sheep', 'A modelling method for determining the production and inter-conversion of volatile fatty acids in the rumen', 'A model of leptin kinetics in sheep', 'A model of the kinetics of nitrate reduction and use in the rumen of sheep' and 'A model describing the kinetics of passage of fluid phase and particulate digesta through the gut of sheep'.

Recommendations

That the MLA continue to encourage and support the activities of modellers and thereby maintain and develop a nucleus of compartmental modelling expertise in Australia, especially modelling aimed at providing a better description of energy metabolism and the environmental consequences of feeding management strategies.

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1. Background

Dr Ray Boston is Professor of Applied Biomathematics at the University of Pennsylvania and is an internationally recognised modeller. He has developed many models and improved our understanding of ruminant nutrition and more recently human health. His major expertise is in the use of compartmental analysis to model biochemical pathways. He has developed several major industry modelling software packages, WinSAAM, MinMod and played a major part in the development of CPM Dairy software. (The software, MinMod was developed to understand the relationship between insulin and glucose using data collected from glucose tolerance tests either in animal or human experiments and is used in hospitals worldwide.)

WinSAAM is computer software that allows the user to develop models using either compartmental or non-compartmental approaches (Stefanovski et al., 2003). The software has been developed by Dr Ray Boston and others from its origins developed by Mons Berman in the 1960s. WinSAAM now runs in Windows. It is freely available at no cost to the user and is a powerful tool for use in biological and animal production studies.

In March 2007, Dr Boston visited UNE to conduct a workshop on linear modelling using WinSAAM. As a result of this visit he has developed a collaborative relationship with Professor Nolan and Dr Dobos and a nucleus group of modellers has developed in Armidale. Dr Boston began analysing data from experiments supported by MLA that measured CO₂ kinetics (and methane production) in ruminants as a measure of energy expenditure using isotope tracers. Professor Boston introduced UNE staff and students to the power of compartmental models, and the use of the WinSAAM software as a means of describing and interpreting research data. Topics covered in 2007 included:

- Fitting Tracer Kinetic Data using WinSAAM
- Representing data in WinSAAM and data weighting schemes
- Fitting regression models in WinSAAM
- Fitting Compartmental Models in WinSAAM
- Understanding the differences between Linear and Non-linear Biological Systems

Since 2007, UNE and DPI modellers have been applying the techniques learned at the initial meeting with Dr Boston. Inevitably, challenges and problems have become apparent.

2. Project objectives

The aim of the current workshop was to use Dr Boston's expertise to assist active modellers to solve a series of modelling problems, issues and questions that have arisen during the last 4-5 years.

3. Workshop activities

The tutorials conducted by Dr Ray Boston were focussed on resolving various modelling challenges that were posed by the participants and had become apparent since the 2007 meeting. The topics and datasets investigated were derived from current research programs or teaching practicums. All of the research topics and datasets were chosen because they could readily be developed into research publications with joint authorships between the University of New England and the University of Pennsylvania.

Over 8 days, Dr Boston gave a series of 'one-on-one', 'hands-on' tutorials to UNE staff. The main interactions are listed below.

- Dr Robin Dobos raised issues concerning the development of a model of bicarbonate kinetics that he is developing to enable energy expenditure in grazing animals to be determined by improving the 'CO₂ entry rate technique'. He also interacted with Dr Boston in relation to a model of leptin kinetics he is developing with Dr Jim MacFarlane.
- Professor Nolan worked on a model of 'Nitrate Kinetics in Sheep' that is relevant to the use of dietary nitrate for mitigating methane emissions in ruminants and also on a model for determining volatile fatty acid production (VFA) rates in sheep. The VFA model is being prepared for publication in the International Modelling Conference to be held in Australia in 2014.
- Dr Mark Barnett worked with Dr Boston to develop a model for describing the kinetics of digesta flow through the gut of ruminants. The model is based on patterns of faecal excretion of non-digestible markers of the liquid and particulate components of digesta after intra-ruminal administration of the markers.
- Dr Ian Godwin also used the interaction with Dr Boston to upgrade some of the methods used to determine of blood and extracellular volumes in animals that are included in third year undergraduate physiology teaching units at UNE.

Public lecture

At the end of the 8 day workshop, Dr Boston delivered a public seminar to the School of Environmental and Rural Science on the topic "A New Model of Non-Esterified Fatty Acid Metabolism: Lessons From the Glucose Minimal Model".

This lecture exemplified the power of the modelling techniques that he has been imparting to our research and teaching staff over the course of his visit.

Implications and future activities

Expertise in modelling techniques has been declining in Australia in recent years.

The support of MLA for this workshop has helped to develop modelling expertise in Armidale and Australia and has helped facilitate a number of modelling studies that will be published in the near future.

Some of the projects worked on, including the animal-based studies of glucose challenge and insulin response led by Drs Jim McFarlane and Ian Godwin will lead to further collaborations between our two Universities and to further joint publications.

Draft papers developed in connection with the recent workshop with Professor Boston as a co-author included:

- 'A model of the kinetics of passage of fluid phase and particulate digesta through the gut of sheep';
- 'A model of bicarbonate C movements through body compartments of sheep'
- 'A modelling method for determining the production and inter-conversion of volatile fatty acids in the rumen';
- 'A model of leptin kinetics in sheep';
- 'A model of the kinetics of nitrate reduction and use in the rumen of sheep'.

4. Reference

Stefanovski D, Moate PJ, Boston RC (2003) WinSAAM: a windows-based compartmental modeling system. *Metabolism* **52**, 1153-1166.