National Animal Nutrition Program (NANP) Nutrition Models Workshop

6   Purposes and types of models. M. D. Hanigan*, *Virginia Tech, Blacksburg, VA.*

The principles of mathematical modeling in agricultural sciences are well described by France and Thornley (1984). They categorized models as static or dynamic, empirical or mechanistic, and deterministic or stochastic, although, in practice, they can fall somewhere in the middle of each. In general, our nutrient requirement models are static, empirical, and deterministic; they provide snapshots in time, do not describe the mechanisms underlying responses, and do not consider the inherent variance intrinsic to biological systems. These models are generally easier to derive, and have served the community very well for more than a century. The Molly cow model is dynamic, mechanistic, and deterministic; it predicts responses through time, is based on the underlying driving elements of digestion and metabolism, but does not represent the biological variation underlying predictions. Dynamic models are very useful when one needs to predict changes over time as compared with representing only the new state after the system is given sufficient time to reach steady state. For example, growth and lactation models are typically dynamic, empirical, and deterministic. They capture the effects of slightly greater growth rates on body weight at any point in the growth cycle, or the effect of greater persistency on overall lactational yield. Static nutrient response models only provide the new rate of growth or milk yield after the animal has consumed the diet long enough to reach a new steady state. They cannot predict full lactation yields. Mechanistic models are often used to represent the effects of underlying behavior on higher level performance, e.g., the effects of passage rate on ruminal digestion or the effects of enzymatic activity of a tissue on metabolism. Such representations may provide more precise predictions of higher level performance, although that generally requires that the mechanisms are well defined and provide unbiased estimates. The models are also very useful to assess the relative importance of more basic information. Addition of stochastic elements to mechanistic models can accommodate known variance in the underlying mechanisms and thus provide confidence intervals for predictions.

Key Words: mathematical model, type, review

7   Dynamic deterministic models. T. Hackmann*, *University of Florida, Gainesville, FL.*

This lesson will demonstrate how to construct dynamic deterministic models, which are popular for mechanistic modeling in nutrition research. This type of model represents a biological system as a set of state variables and simulates how these variables change over time. For example, it can represent the rumen system using state variables for fiber, protein, and starch; subsequently, it can simulate the size of these nutrient pools over a feeding cycle. The model is written formally using differential equations, but it can be drawn first as a compartmental model diagram. In this diagram, each state variable is represented by a rectangle (a pool). Arrows leading to and from a pool represents input and output of material. For the rumen, these arrows commonly represent nutrient intake, digestion, and passage. The diagram is then translated into a set of differential equations. These equations define the change of state variables (pools) over time as the difference between inputs and outputs [i.e., d(*state variable*)/dt = *inputs* − *outputs*]. These inputs and outputs, in turn, are functions of parameters (e.g., digestion and passage rates) and other state variables. After defining values of parameters, the model is solved and used to generate predictions. A simple model may have an analytical solution, but a more complex model must be solved numerically (e.g., with Euler's method and difference equations). During a demonstration exercise, the speaker will show how to construct a simple (one-pool) model of rumen fermentation by coding difference equations into an Excel spreadsheet. During a hands-on exercise, participants will construct their own, multi-pool model.

Key Words: mathematical model, state variable, differential equation

8   Estimation of parameter values in nutrition models. L. Moraes*, *The Ohio State University, Columbus, OH.*

The use of modeling techniques in animal nutrition relies on the construction of mathematical models determined by a set of parameters. In practice, parameter true values are unknown. Estimators must be obtained with data from designed experiments, observational studies, meta-analysis or another appropriate data generating mechanism. For virtually any type of model, parameter estimates have to be optimal in some sense. For example, linear regression least squares estimates are the minimizers of the squared differences between observations and predictions. In this setting, if model errors are assumed to independent, identically and normally distributed, least squares estimators coincide with maximum likelihood estimators. Maximum likelihood is the standard estimation method for more complex models used in animal nutrition. It seeks parameter values that maximize the likelihood function: a function constructed with the probability density of the observations but as a function of parameters while fixing the data. Nonlinear models are regularly used in the development of mechanistic models as these allow the relationship between variables to be specified by a function that is nonlinear with respect to the parameters. The flexibility of specifying nonlinear functional forms comes with a cost: the function to be optimized is often complex and an analytical solution to the problem is many times not available. Further, several of the mechanistic models used in animal nutrition rely on the use of differential equations that require numerical integration. Parameter estimation in these cases is usually approached by algorithmic optimization of either a likelihood function or a nonlinear least squares cost function. Recently, Bayesian methods have been proposed as estimation approaches for nutrition models as they naturally describe multilevel structures and incorporate prior information in the analysis. This lesson will cover parameter estimation in a variety of models frequently used in animal nutrition as well as demonstration exercises. During a hands-on exercise, workshop participants will estimate parameters in different models using the freely available software R.

Key Words: least squares, likelihood, Bayesian

9   Model evaluation. E. Kebreab*, *University of California, Davis, Davis, CA.*

Statistical measures of model performance commonly compare predictions with observations judged to be reliable. Model evaluation indicates the level of accuracy and precision of model predictions by assessing the credibility or reliability of a model in comparison to real-world observations. Quantitative statistical model evaluation methods can be classified into 3 types including (1) standard regression statistics, which determines strength of linear relationship, (2) error index, which quantifies deviation in observed units, and (3) relative model evaluation that are dimensionless. Within the first category, analysis of residuals

involves regressing residuals against predicted or other model variables. In this method, the model is unbiased if residuals are not correlated with predictions and the slope is not significantly different from zero. Predicted values can also be centered making the slope and intercept estimates in the regression orthogonal and thus, independent. This allows for mean biases to be assessed using the intercepts of the regression equations, and the slopes to determine the presence of linear biases. Mean square error of prediction (MSEP) and its square root (RMSEP) are commonly used methods of evaluation. In general RMSEP values less than half of observed SD may be considered having a good performance. The MSEP can be decomposed into error due to 1) overall bias of prediction, 2) deviation of the regression slope from unity, and 3) disturbance. Examples of the third category include concordance correlation coefficient (CCC), and the Nash-Sutcliffe index (NSE). The CCC can be represented as a product of 2 components (range from 0 to 1 and 1 indicates perfect fit): a correlation coefficient estimate that measures precision and a bias correction factor that indicates how far the regression line deviates from the line of unity. The NSE is a normalized statistic that determines relative magnitude of residual variance compared with observed data variance. During model evaluation, a combination of the methods described above should be used to gain insight on model performance. The hands-on excercises include coding a function to calculate RMSEP, NSE and CCC for a set of data, which will be provided to participants.

Key Words: model performance, modeling, prediction accuracy

10   Example models for ruminant digestion and metabolism .
H. A. Rossow*, *Veterinary Medicine Teaching and Research Center, University of California Davis, Tulare, CA.*

Mathematical models are a tool to examine existing theories, find gaps in knowledge and explain phenomena of nutrient digestion and metabolism. The model can then produce simulation data to examine model behavior and determine if predictions from such models make biological 'sense'. The objective of this session is to explore how concepts or theories of nutrient digestion, metabolism and lactation physiology are translated into mechanistic mathematical equations and combined into a whole animal model using the Molly model. Molly is a mechanistic model of a dairy cow composed of a digestive element and an animal element. The digestive element converts chemical composition of the diet to volatile fatty acids, microbial growth and absorbed nutrients using physical attributes of the diet such as proportions of large and small particles and water passage. The animal element converts products from the digestive element into tissues (protein), waste products, heat production or secreted products (milk, milk fat, etc.). In this session, representations of digesta passage, protein synthesis and milk production in Molly will be examined beginning with a conceptual diagram. Then differential equations representing these processes will be described. Finally, because Molly predicts changes in production processes over time, full lactation simulations will be demonstrated to show examples of how passage, protein accretion and milk synthesis change over time.

Based on these examples, participants will conduct a simulation exercise which uses concepts of milk synthesis in Molly that were explored previously to predict lactation performance. A compiled version of the Molly program which operates only in the Windows environment is available for download at http://www.vmtrc.ucdavis.edu/laboratories/metabolic/molly.cfm and will be used in the simulation exercise. In the exercise, participants will observe effects of altering milk production processes on production of the dairy cow to understand how metabolic processes can be represented by mathematical equations to provide a conceptual framework that improves our understanding of animal biology.

Key Words: computer simulation model, dairy cow, metabolism

11   Meta-regression analysis of animal nutrition literature. R. R. White*, *Department of Animal and Poultry Sciences, Virginia Tech, Blacksburg, VA.*

Quantitative literature summary (meta-analysis) is often used to generate a more comprehensive understanding of system behavior than can be obtained from individual experiments. Although every data set is unique and often requires some individualized analysis, most meta-analytical data can be evaluated using weighted, mixed effect, regression in a 9-part procedure, described as follows. 1) Search criteria should be clearly defined. 2) The literature should be searched and all response variables, their standard errors, and all explanatory variables should be recorded. 3) Data should be evaluated for transcription errors and outliers. 4) Missing standard errors should be estimated by error propagation, where possible. 5) Standard errors from fixed-effect regression and mixed-effect regression should be standardized to remove statistical analysis effects, and weights should be calculated from these standardized standard errors. 6) Backward, stepwise regression should be performed, using fixed effects for all explanatory variables of interest, and random effects for study, laboratory, or location, as needed. 7) After a model is identified where all variables included are below a significance cutoff defined by the researchers, the parameters removed from the model should be iteratively re-tested for significance in the final model. This step helps ensure variables were removed for non-significance rather than accidently removed due to model instability. 8) Parameter estimate correlation should be evaluated using variance inflation factors. Variance inflation factors above 10 are acceptable for parameters correlated by calculation but all other parameters should have variance inflation factors below 10. If parameter estimates have excessive correlation, the parameter with the highest variance inflation factor should be removed. 9) Researchers should iterate through steps 6 to 8 until a model is identified where all parameters are statistically significant and have acceptable covariation. Although this procedure might require adjustment for some applications, it provides a general framework for performing meta-regression analysis of animal nutrition literature. The workshop associated with this abstract will walk through this process using an example data set.

Key Words: meta-analysis, regression, methods