Introduction to Modeling

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What is a Model

- Merriam-Webster Dictionary:
  - structural design, e.g. a home on the model of an old farmhouse
  - a usually miniature representation of something; *also*: a pattern of something to be made
  - an example for imitation or emulation
  - a person or thing that serves as a pattern for an artist; *especially*: one who poses for an artist
  - an organism whose appearance a mimic imitates
  - one who is employed to display clothes or other merchandise
  - a type or design of clothing or a product (as a car)
  - a description or analogy used to help visualize something (as an atom) that cannot be directly observed
  - a system of postulates, data, and inferences presented as a mathematical description of an entity or state of affairs; *also*: a computer simulation based on such a system, e.g. climate models
Visual Model of Muscle Glycogen Metabolism

- **Glucose**
- **Fructose-6-P**
- **Glucose-6-P**
- **Glucose-1-P**
- **Glycogen**
- **Fructose-1,6-bisP**
- **ATP**
- **Citrate**
- **Ca++**
- **Glucagon**
- **Adrenaline**

**Glycogen**
- A pool (g, L, mol)
- A flux (g/min)

**Glucose**
- External input or output (g/d, g/L)
- Activation or stimulation (??)
- Inhibition (??)
A Statistical Model

• Hypothesis: High Forage > Low Forage
  – Experimental Objective
  – Is milk less from HF than LF
    
    \[ \text{is } \overline{HF} < \overline{LF} \text{ given observed variance} \]

    \[ \text{Milk}_{ij} = \mu + \beta_i (\text{Trt}_i) + \varepsilon_{ij} \]
    
    where \( i = 1 \) to # of Trt and \( j = 1 \) to # of animals
    Trt is coded as a matrix with a column for each Trt
    0 if the animal was not on the treatment and 1 if it was

  – Is there some larger question implicit in H?

<table>
<thead>
<tr>
<th>Animal</th>
<th>Trt(_1)</th>
<th>Trt(_2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
The Model Development Process

1. What is the question?
2. Define goals and objectives
3. Review the literature: concepts and data
4. Develop a visual representation
5. Construct an appropriate mathematical representation
6. Transform the mathematics to computer code
7. Select or derive model parameters
8. Evaluate and assess vs the objectives
• Doesn’t have to be perfect

• ALL MODELS ARE WRONG, but some are useful

• Development cycle
  – Construct
  – Test
  – Improve
  – Test
  – Improve
  – Test
  – ...
  – ...
Objectives and goals are critical

- Objective: predict body weight change over time with an error less than 20%

- Model Scope
  - Subatomic particle behavior?
  - Cellular function in all the cells?
  - Tissue responses in all the tissues?
  - \( \frac{(\text{MEI} - \text{NEm})}{\text{Eff}_{\text{ME to NE}}} \)?
  - If simple fails, perhaps add complexity
"entities must not be multiplied beyond necessity" which is also expressed as *lex parsimoniae* in Latin which translates to the “law of parsimony” or the “law of economy”

William of Ockham, 14th century

‘A model like a map cannot show everything. If it did it would not be a model but a duplicate. Thus the classic definition of art as the *purgation of superfluities* also applies to models. And the model-maker’s problem is to distinguish between the superfluous and the essential.

Model classification

Dynamic OR Static

Deterministic OR Stochastic

Mechanistic OR Empirical

Static

Does not represent the system through time

- Steady state representation, e.g. digestion coefficient

\[ Feces = Intake - (a \times Intake + b) \]

- There is no element of time represented in the above equation
- Generally will not accurately represent the system as it changes from one state to another
- Should accurately represent the system in steady state before and after the change assuming the equation is appropriate
Time is an element in the equation or model

- Generally capable of non-steady state predictions, e.g. drug or metabolite clearance from blood

\[
Metabolite(t) = Metabolite_{Initial} \times e^{(-k \times t)}
\]

- Time is explicitly defined in the above model of metabolite clearance

- The model predicts the amount of the metabolite present in the blood pool at any point in time given an initial dose \((Metabolite_{Initial})\) and a rate of metabolite clearance from blood \((k)\) per unit of time.
The static model predicts an instantaneous change in state given a change in inputs.
Deterministic

- Assumes a single true answer and deviations reflect measurement error or some other stochastic process.
  - Model predicts the true answer.
  - Inputs, parameters, and observed responses all deterministic

- Many biological models are deterministic
  - Standard curves
  - Most clearance and digestion models are deterministic
  - Requirement models
  - Growth models

- Easier to parameterize
Stochastic

- Explicitly accommodate variance in inputs, outputs, parameters

\[
Metabolite(t) = \left[ Metabolite_{\text{Init}} \pm \sigma_{\text{MeasureInit}} \right] \times e^{[-k \pm \sigma_k] \times [t \pm \sigma_t]} + \sigma_{\text{MeasureConc}}
\]

- \( \sigma_{\text{MeasureInit}}, \sigma_k, \sigma_t, \) and \( \sigma_{\text{MeasureConc}} \) represent variance in initial concentration, \( k \), time, and the metabolite concentration, respectively.

- \( \sigma \) generally \( \sim \text{N}(0, \sigma) \) and randomly sampled

- Predicted \( Metabolite(t) \) should match the observed population if error model matches reality

- More difficult to parameterize and computationally expensive
Deterministic vs Stochastic

Predicted Plasma Drug (mg)

Time post bolus (h)

Line - Deterministic
Symbols – Stochastic
\sim N(\mu, 7.5)
Empirical

- Relates inputs and outputs at the same level of aggregation
  - many feed evaluation models
  - \( DMI = 3(\text{Milk}) + 0.02(\text{BW}^{0.75}) \)

- Advantages
  - simple and quick
  - less detail

- Disadvantages
  - limited ability for extrapolation
  - Don’t utilize underlying system knowledge to improve precision
Mechanistic

- Attempts to explicitly represent the underlying structure of a system
  - Molly cow model from UCDavis

- Advantages
  - May result in more precise prediction: generally assumes a more complex structure
  - May be suitable for extrapolation
  - Aids in understanding the system

- Disadvantages
  - Often more parameters and inputs making it harder to parameterize
  - Can be less precise and accurate if improperly formulated or parameterized
  - Takes a lot of time and effort to develop
Empirical

\[ \text{Protein}_{\text{Milk}} = \alpha EI + \beta NI + \chi EI^2 + \delta NI^2 + \varepsilon (EI \times NI) \]

Mechanistic

\[ \text{Protein}_{\text{Milk}} = \frac{\alpha \text{Cells}_{\text{Mammary}} \times \beta \left( \frac{\text{Ribosomes}}{\text{Cell}} \right) \times \chi [P-eIF2] \times \delta [P-4eBP1]}{1 + \frac{k_{\text{ATP}}}{[\text{ATP}]} + \frac{k_{\text{EAA}}}{[\text{EAA}]} + \frac{k_{\text{mRNA}}}{[\text{mRNA}]} } \]

- \( EI = \) energy intake, \( NI = \) nitrogen intake
- Milk protein output and nutrient intakes are at the same level, i.e. the animal, thus empirical
- Ribosomes, cell signaling proteins, ATP, etc. are lower levels of function than milk protein output and thus mechanistic
Models Used in Animal Nutrition

- NRC Nutrient Requirement Models
  - Static, Deterministic, Empirical
- Particle Passage Models (Pond et al., 1988)
  - Dynamic, Stochastic, Empirical
- Gompertz Growth Model (Winsor, 1932)
  - Dynamic, Deterministic, Empirical
- Oltjen Growth Model (1986)
  - Dynamic, Deterministic, Mechanistic
- Brossard Pig Growth Model (2009)
  - Dynamic, Stochastic, Empirical
  - Dynamic, Stochastic, Mechanistic?
Summary

- Modeling as an integral part of the scientific process
- Modeling process should be followed
- Set Goals carefully and adhere to them
- 3 general model classifications
- Classes are a continuum rather than discrete
- Models can reflect a single level of organization or operate across levels
Ransom Leland Baldwin, V
Professor of Animal Science
University of California, Davis
Member: National Academy of Sciences

Born: September 21, 1935, Meriden, CT
Died: November 30, 2007
Education: Michigan State University (1963)
Books: Simulation of the Effects of Nutritional and Physiological Status on the Growth of Mammalian Tissues: Description and Evaluation of a Computer Program, More
Awards: Guggenheim Fellowship for Natural Sciences, US & Canada
Compartmental Model Example

\[
\frac{dQ_{\text{Rum}}}{dt} = F_{\text{Intake}} - F_{\text{Rum,SI}} - F_{\text{Rum,Bld}}
\]

\[
F_{\text{Intake}} = DMI \times C_{\text{Nutrient}}
\]

\[
F_{\text{Rum,SI}} = Q_{\text{Rum}} \times K_{\text{Passage}}
\]

\[
F_{\text{Rum,Bld}} = Q_{\text{Rum}} \times K_{\text{Degradation}}
\]

\[
Q_{\text{Rum}} = \int \frac{dQ_{\text{Rum}}}{dt} + iQ_{\text{Rum}}
\]

\[
F_{\text{SI,Bld}} = a \times F_{\text{Rum,SI}}
\]

\[
F_{\text{Feces}} = F_{\text{Rum,SI}} - F_{\text{SI,Bld}}
\]

--- R Code ---

```r
DMI <- 1; # kg/h
Cnut <- 0.30; # kg/kg DM
iQrum <- 5.0; # kg
Kdeg <- 0.02; # per hour
Kpas <- 0.04; # per hour

Fin <- DMI * Cnut
FRumSI <- Qrum * Kpas
FRumDeg <- Qrum * Kdeg
dQrum <- Fin - FRumSI - FRumDeg

KSIAbs <- rnorm(1, mean=0.95, sd=0.15)
DCnutr <- 0.80
FSIBld <- FRumSI * DCnutr
FFeces <- FRumSI - FSIBld
```