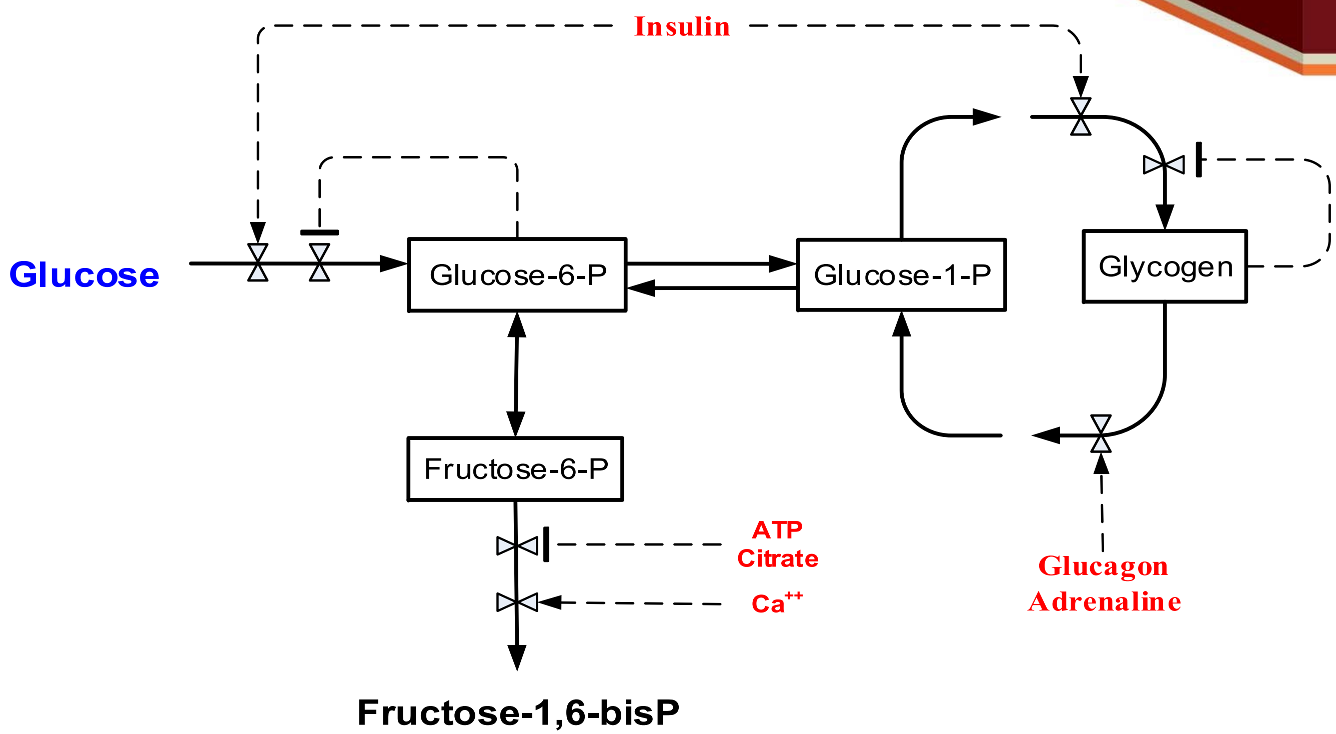
Introduction to Modeling

Mark D. Hanigan

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



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

$$\text{is } \overline{HF} < \overline{LF} \text{ given observed variance}$$

Trt = …

Animal	Trt_1	Trt_2
1	1	0
2	1	0
3	0	1
4	0	1

  - $Milk_{ij} = \mu + \beta_i (Trt_i) + \varepsilon_{ij}$

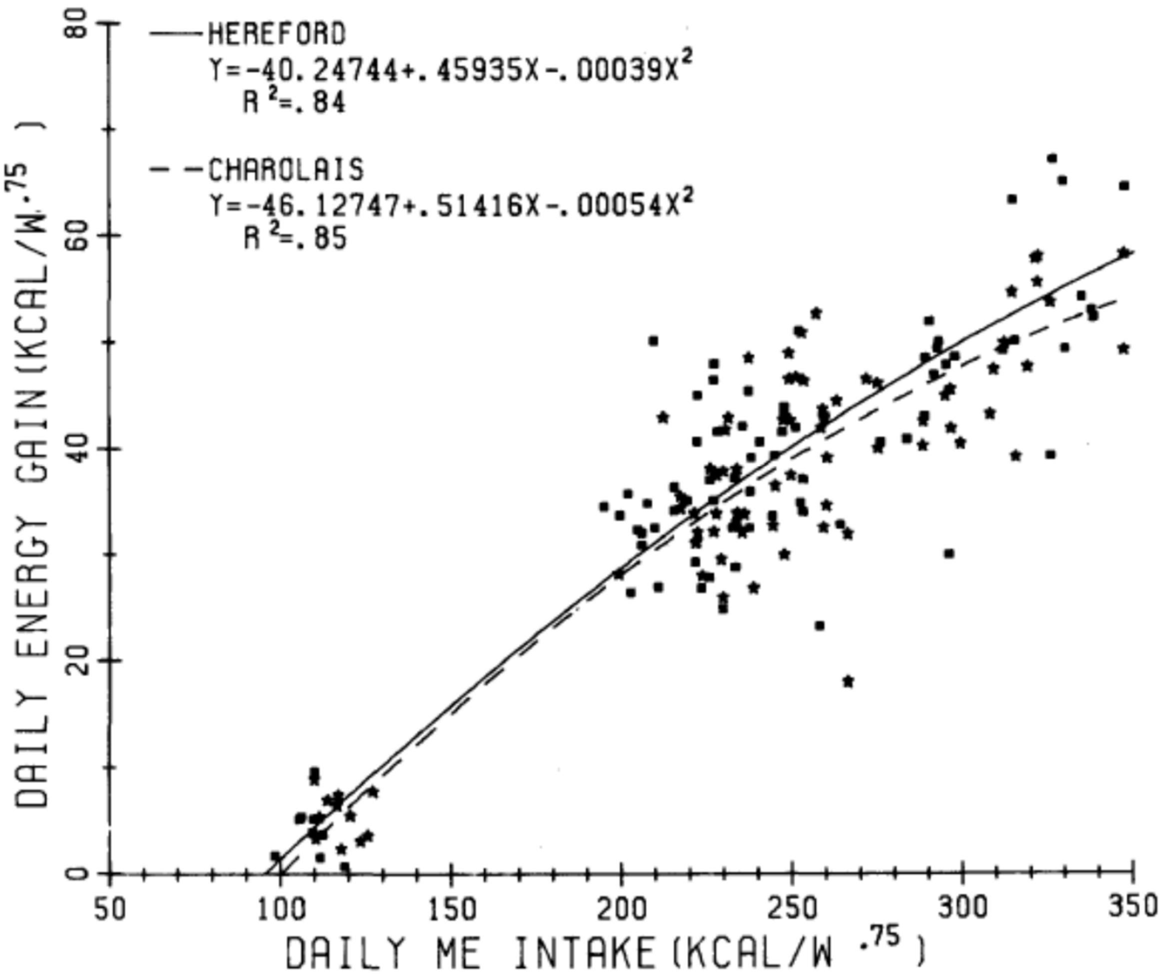
    where i = 1 to # of Trt and j = 1 to # of animals

    Trt is coded as a matix with a column for each Trt

    0 if the animal was not on the treatment and 1 if it was

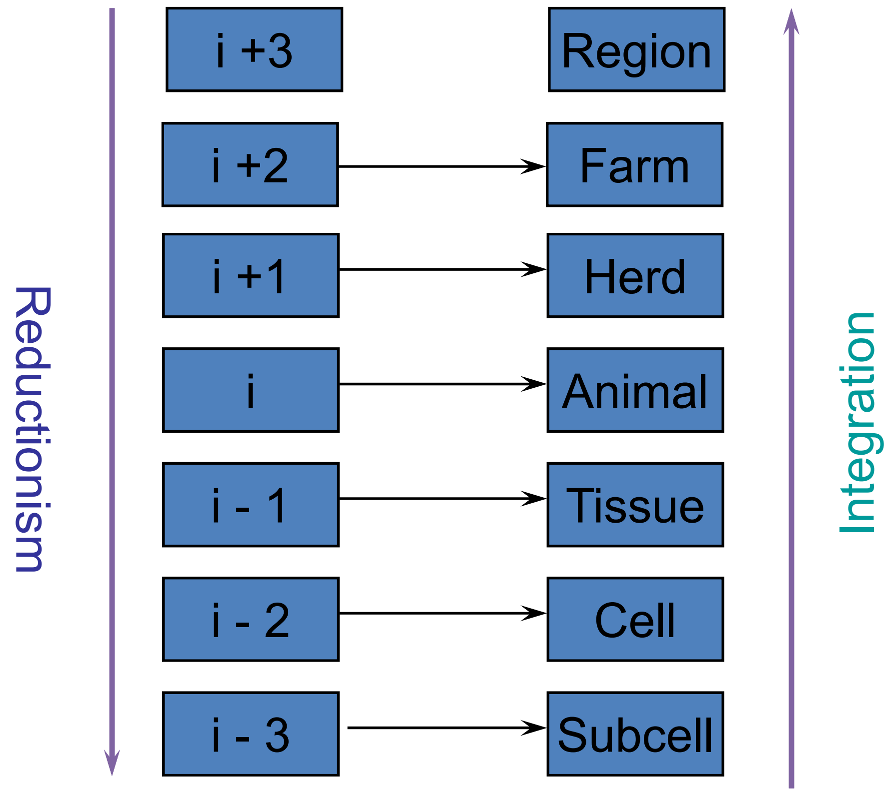
  - Is there some larger question implicit in H?

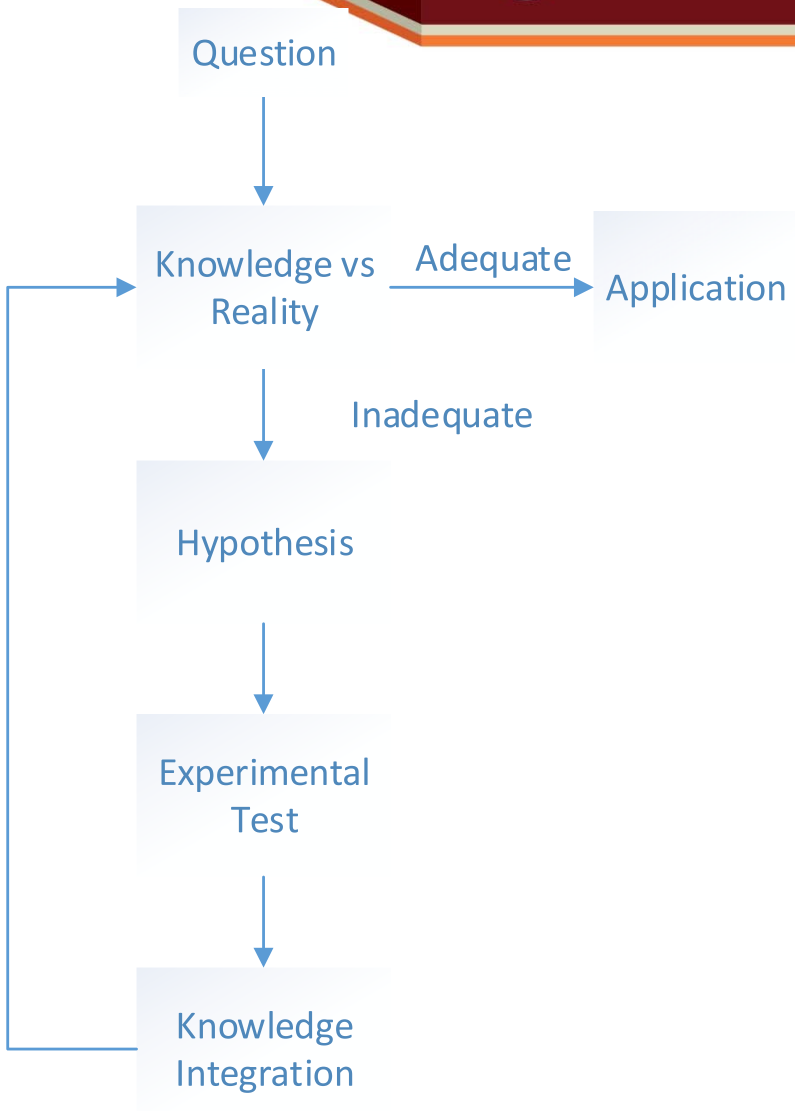
Input: Output Relationships



Old and Garrett, 1987

The Scientific Process



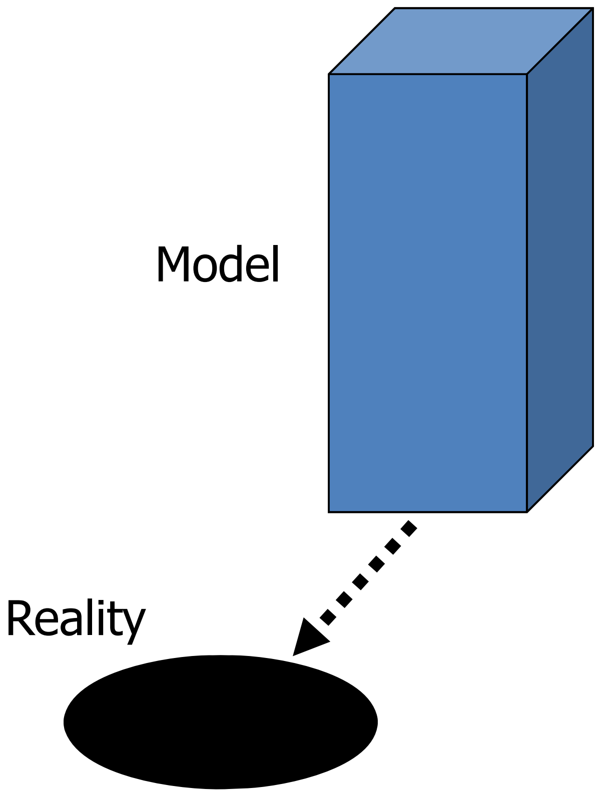


The Model Development Process

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

Model Development Loop

- Doesn't have to be perfect
- ALL MODELS ARE WRONG, but some are useful
- Development cycle
  - Construct
  - Test
  - Improve
  - Test
  - Improve
  - Test
  - Improve
  - Test
  - …



Goals and Objectives

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?
  - $(MEI – NEm) / Eff_{ME\ to\ NE}$?
  - If simple fails, perhaps add complexity

Appropriate Model 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.

Editorial, *J. Am. Med. Ass.*

Model classification

Dynamic OR Static

Deterministic OR Stochastic

Mechanistic OR Empirical

France, J. and J. H. M. Thornley. 1984. Mathematical models in agriculture. Butterworths, Sevenoaks, Kent.

Static

Does not represent the system through time

- Steady state representation, e.g. digestion coefficient

$$Feces = Intake - \left(a \times Intake + b \right)$$

- 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

Dynamic

Time is an element in the equation or model

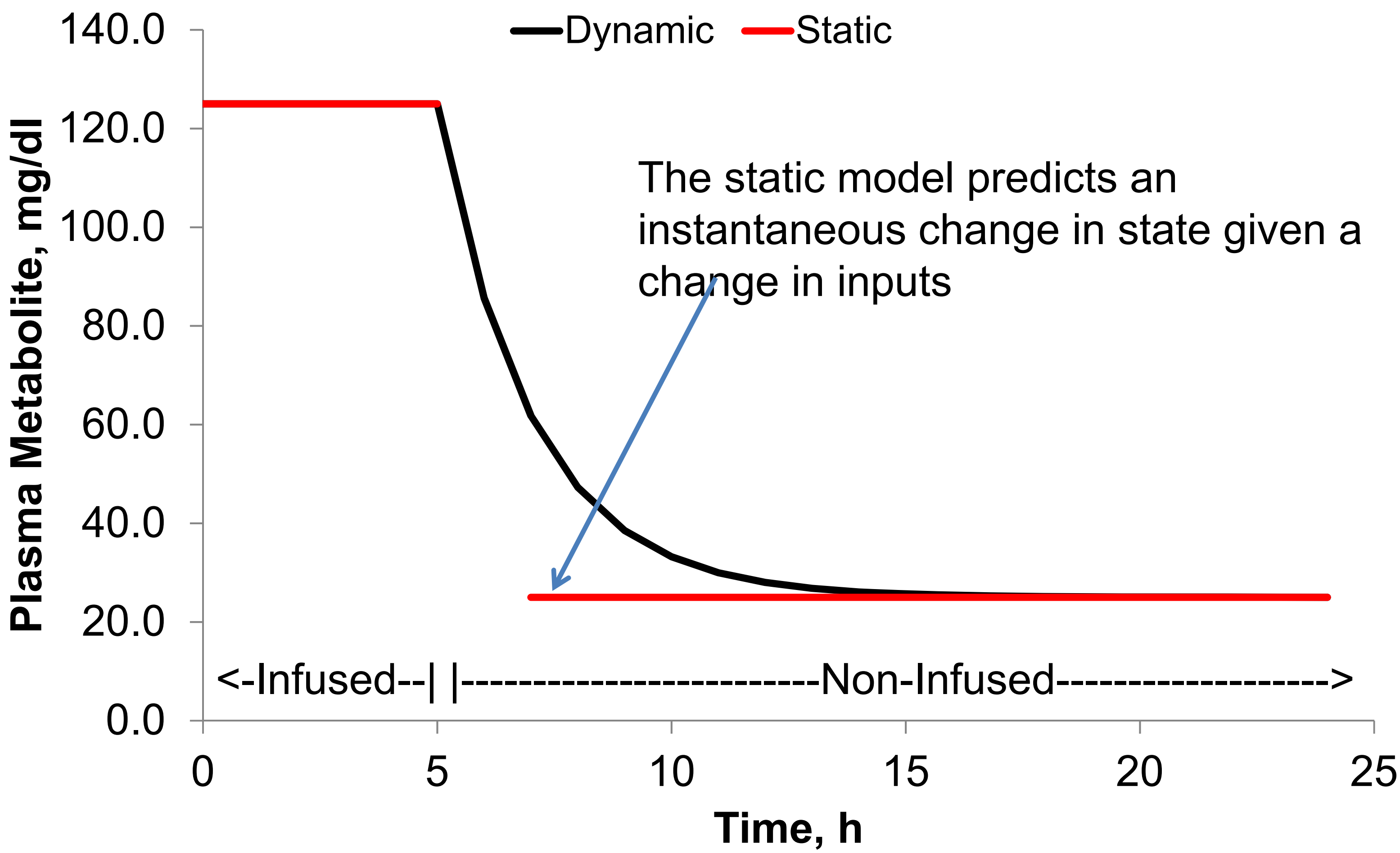
- Generally capable of non-steady state predictions, e.g. drug or metabolite clearance from blood

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

- 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.

Static vs Dynamic



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

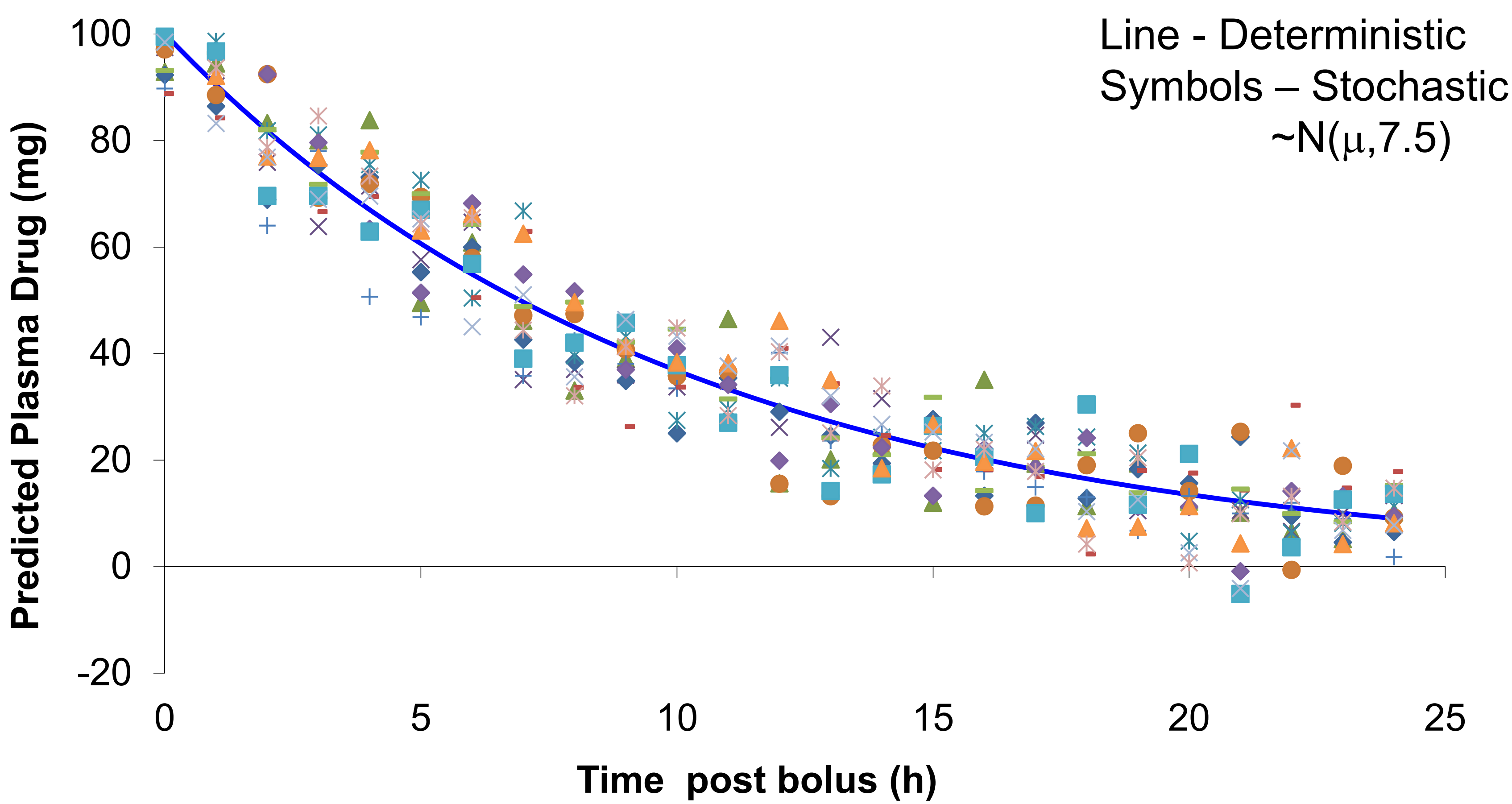
Stochastic

- Explicitly accommodate variance in inputs, outputs, parameters

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

- $\sigma_{MeasureInit}$, σ_k, σ_t, and $\sigma_{MeasureConc}$ represent variance in initial concentration, k, time, and the metabolite concentration, respectively.
- σ generally ~N(0, σ) 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



Empirical

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

Mechanistic vs Empirical

Empirical

$$Protein_{Milk} = \alpha EI + \beta NI + \chi EI^2 + \delta NI^2 + \varepsilon\left(EI \times NI\right)$$

Mechanistic

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

- 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

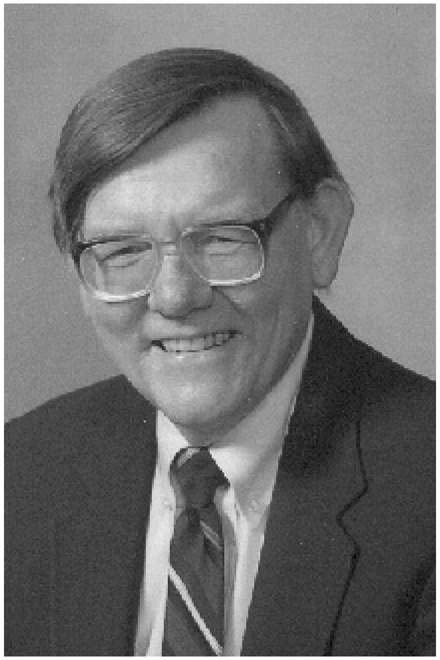
Models Used in Animal Nutrition

- 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
- Doeschl-Wilson (2007) Pig Growth Genetics Model
  - 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

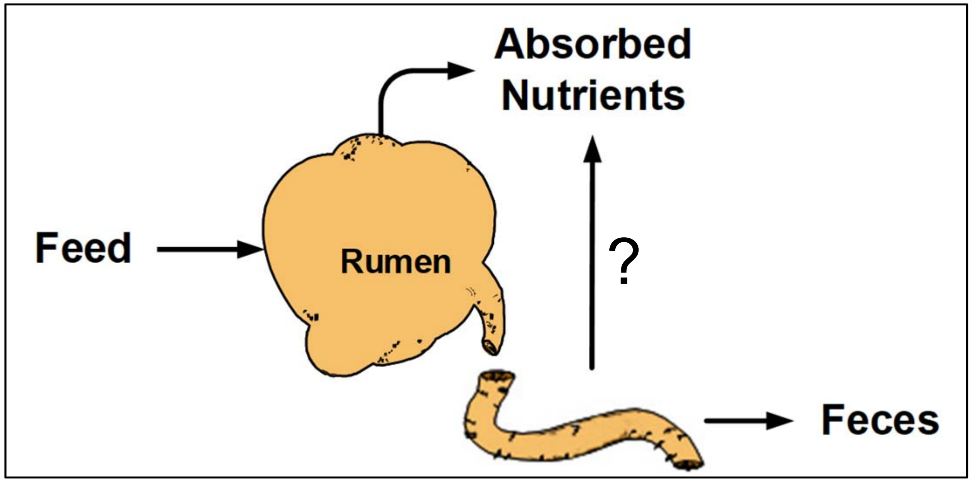
The Model Development Process



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



$$\frac{dQ_{Rum}}{dt} = F_{Intake} - F_{Rum,SI} - F_{Rum,Bld}$$

$$F_{Intake} = DMI \times C_{Nutrient}$$

$$F_{Rum,SI} = Q_{Rum} \times K_{Passage}$$

$$F_{Rum,Bld} = Q_{Rum} \times K_{Degradation}$$

$$Q_{Rum} = \int \frac{dQ_{Rum}}{dt} + iQ_{Rum}$$

$$F_{SI,Bld} = a \times F_{Rum,SI}$$

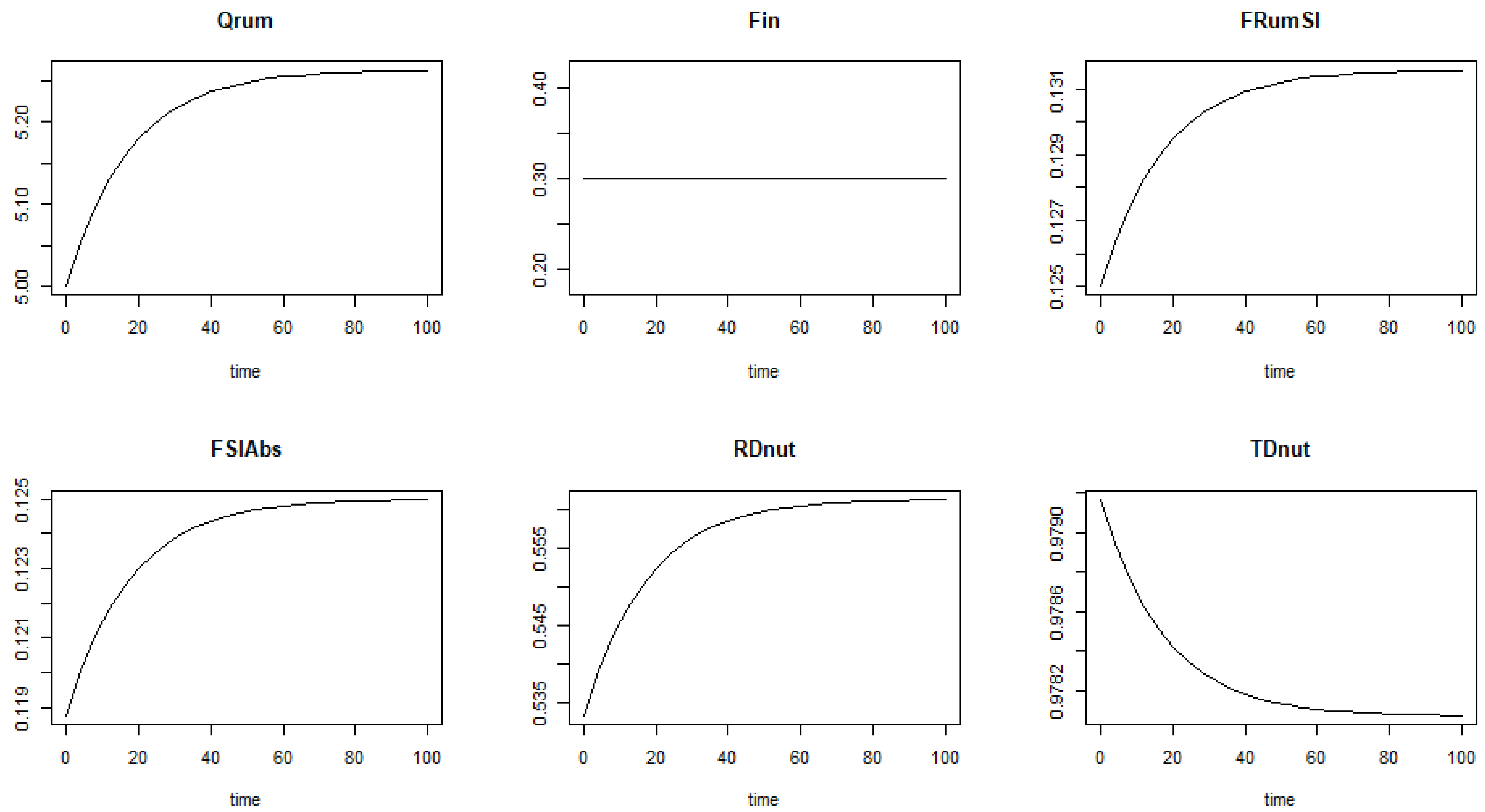
$$F_{Feces} = F_{Rum,SI} - F_{SI,Bld}$$

```
---------------- R Code ----------------
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 * Kpass
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
```

Model Output



DAIRY SCIENCE