Molly and other dynamic models

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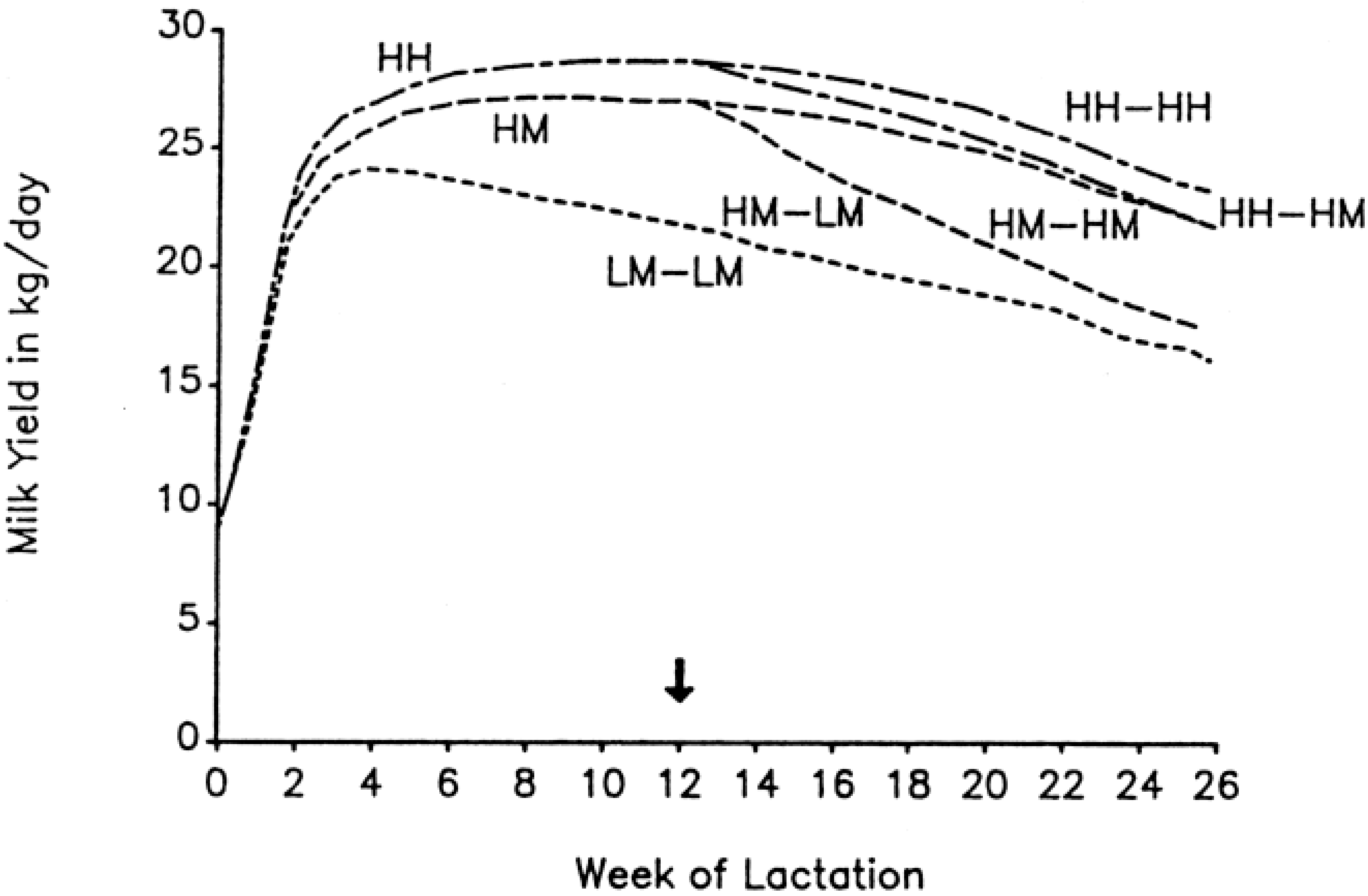
Why use dynamic, mechanistic models?

Table 6. Estimated marginal means ± SE from monthly herd recording data for the effects of enzyme treatment[1] by dairy

	Dairy 1		Dairy 2		Dairy 3	
Outcome	Control	Enzyme	Control	Enzyme	Control	Enzyme
Milk yield (kg/d)	37.6 ± 0.84	38.2 ± 0.84	37.9 ± 0.82	41.5 ± 0.82	43.5 ± 0.57	43.7 ± 0.57
ECM (kg/d)	42.4 ± 0.76	41.6 ± 0.76	36.8 ± 0.75	41.0 ± 0.76	46.1 ± 0.51	46.2 ± 0.51
Fat (%)	4.56 ± 0.07	4.46 ± 0.07	3.80 ± 0.07	3.86 ± 0.07	4.03 ± 0.05	4.02 ± 0.05
Fat yield (kg/d)	1.73 ± 0.04	1.68 ± 0.04	1.35 ± 0.04	1.54 ± 0.04	1.77 ± 0.03	1.78 ± 0.03
Protein (%)	2.91 ± 0.03	2.92 ± 0.03	2.94 ± 0.03	2.91 ± 0.03	2.95 ± 0.01	2.92 ± 0.01
Protein yield (kg/d)	1.10 ± 0.02	1.09 ± 0.02	1.06 ± 0.02	1.16 ± 0.02	1.29 ± 0.02	1.28 ± 0.02
Log_{10} SCC	4.42 ± 0.06	4.34 ± 0.06	3.68 ± 0.06	3.87 ± 0.06	4.12 ± 0.04	4.09 ± 0.04
BW (kg)	654 ± 9.25	656 ± 9.25	564 ± 9.35	565 ± 9.44	635 ± 6.46	637 ± 6.42


32617
33849

Impact of diet changes on milk yield



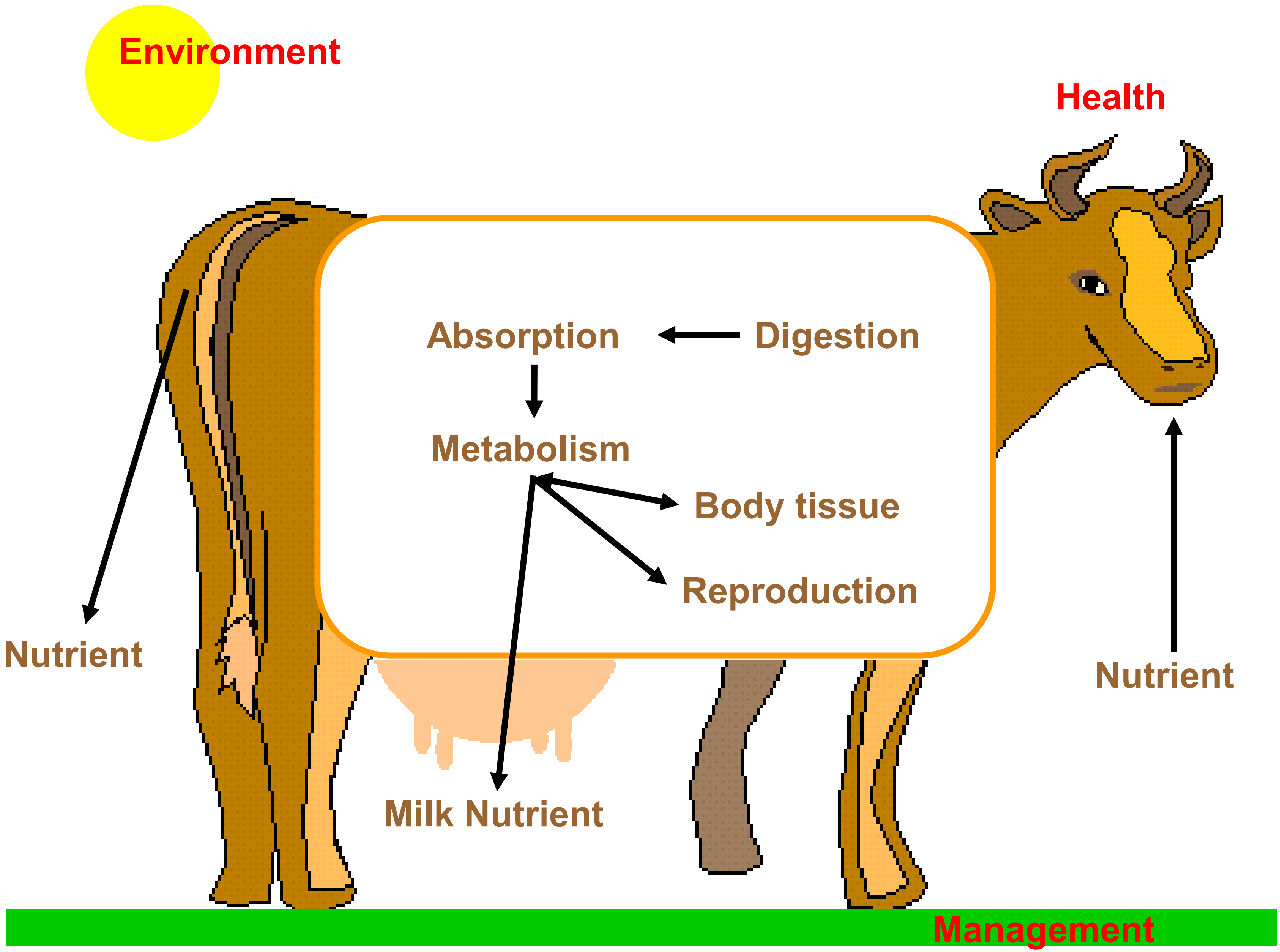
How to represent mechanisms in mathematical equations

1. Central nutrient pools and hormones
2. Compartment equations
3. Equation types
4. Modeling exercise

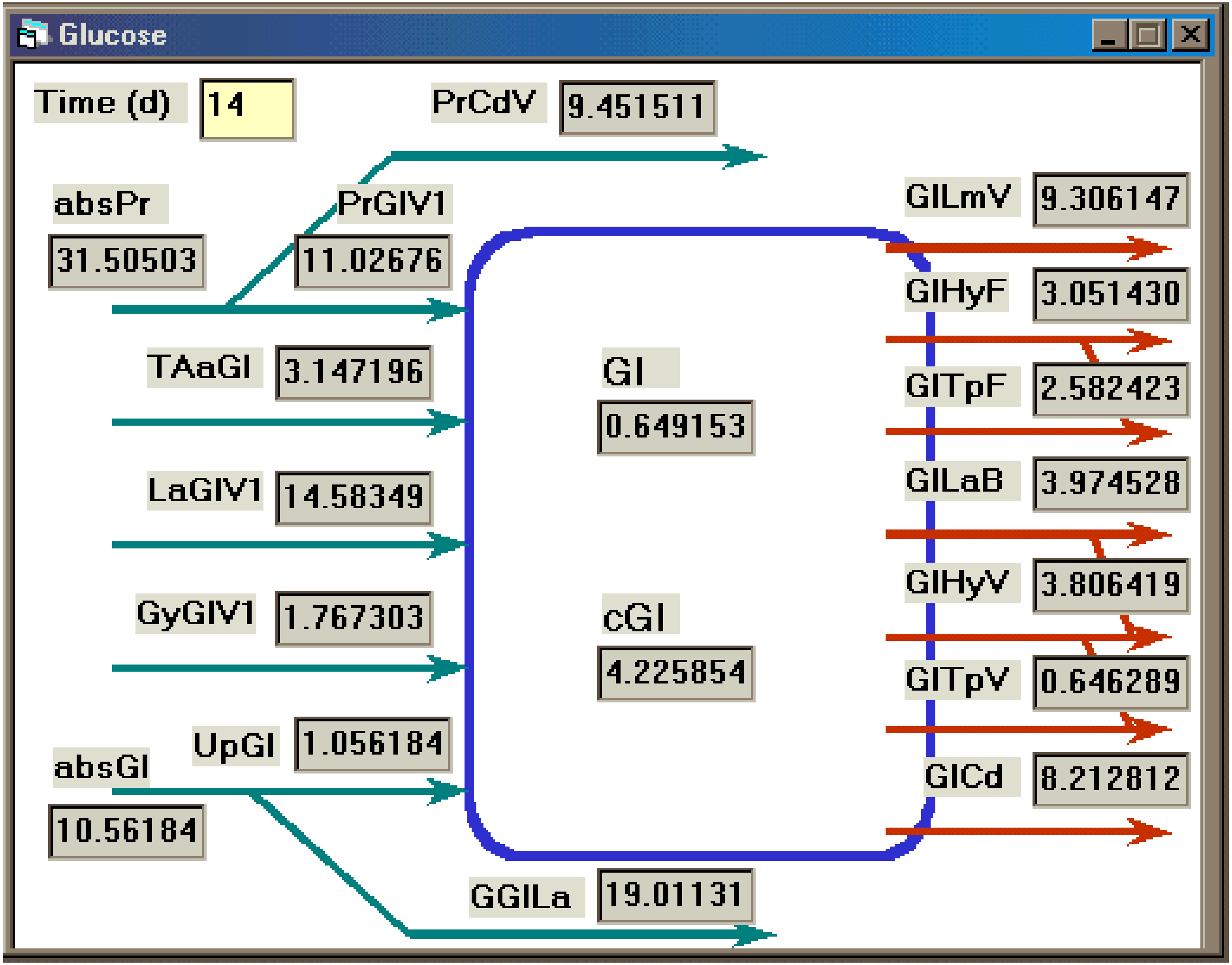
MECHANISTIC

LEVEL	DESCRIPTION OF LEVEL
	...
i + 1	collection of animals
i	animal
i - I	organs
i - II	tissues
i - III	cells
i - IV	organelles
i - V	macromolecules
	...

1. CENTRAL NUTRIENT POOLS and HORMONES


Environment
Health
Absorption
Digestion
Metabolism
Body tissue
Reproduction
Nutrient
Nutrient
Milk Nutrient
Management

Glucose


Glucose
Time (d)
14
PrCdV
9.451511
absPr
31.50503
PrGlV1
11.02676
TAaGl
3.147196
LaGlV1
14.58349
GyGlV1
1.767303
UpGl
1.056184
absGl
10.56184
Gl
0.649153
cGl
4.225854
GGlLa
19.01131
GlLmV
9.306147
GlHyF
3.051430
GlTpF
2.582423
GlLaB
3.974528
GlHyV
3.806419
GlTpV
0.646289
GlCd
8.212812

“Blood” concentrations of nutrients

Units = m/L = glucose / volume
cGl should approximate blood levels
cGl = all glucose in body or tissue pool
/ distribution volume

Distribution volume could be

1. all body fluid or 70% body weight
(blood volume +interstitial fluid)
2. Rumen volume

3. Empty body weight

Hormones

Anabolic

Ahor = current [glucose] / ref [glucose]

= 0.0036 / 0.003

Catabolic

Chor = ref [glucose] / current [glucose]

= 0.003 / 0.0036

Examples:

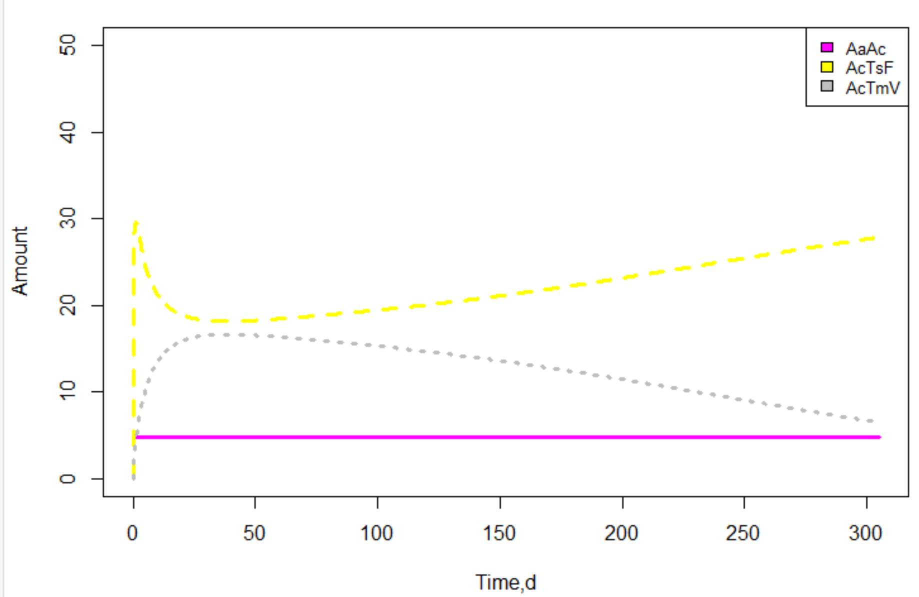
Acetate $\longrightarrow$ Body Fat * Ahor

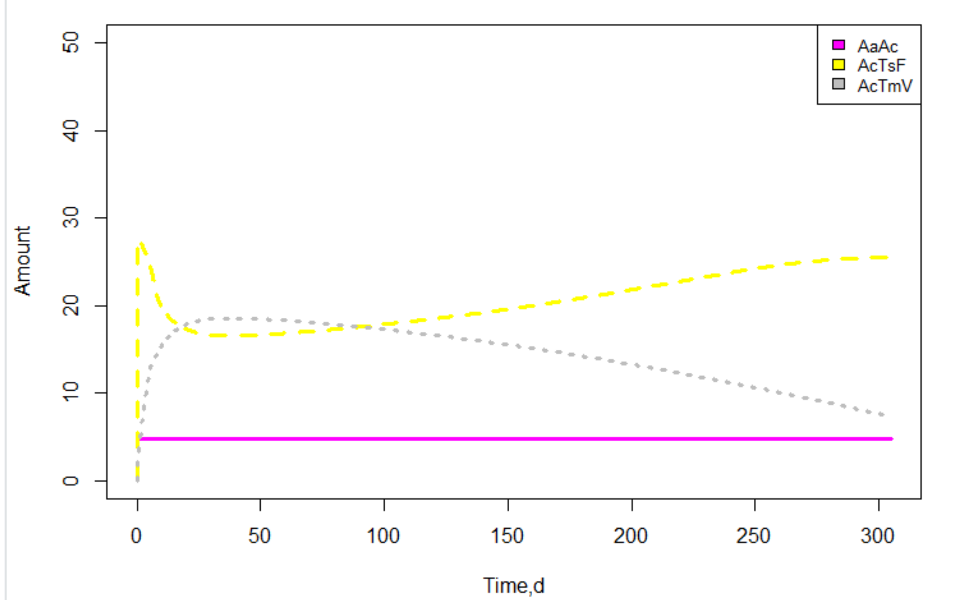
Body Fat $\longleftarrow$ Acetate * Chor

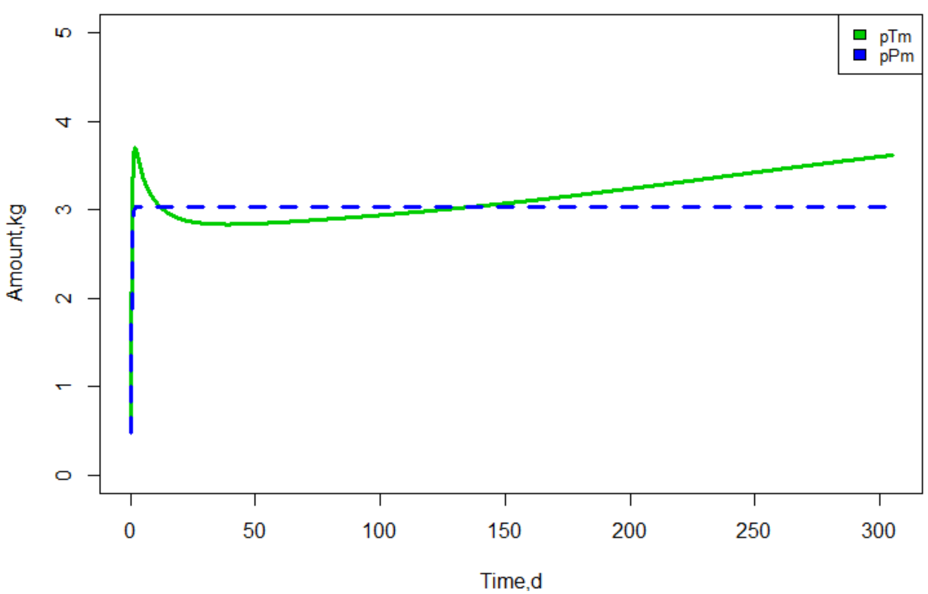
EXAMPLE: Molly cAc.r

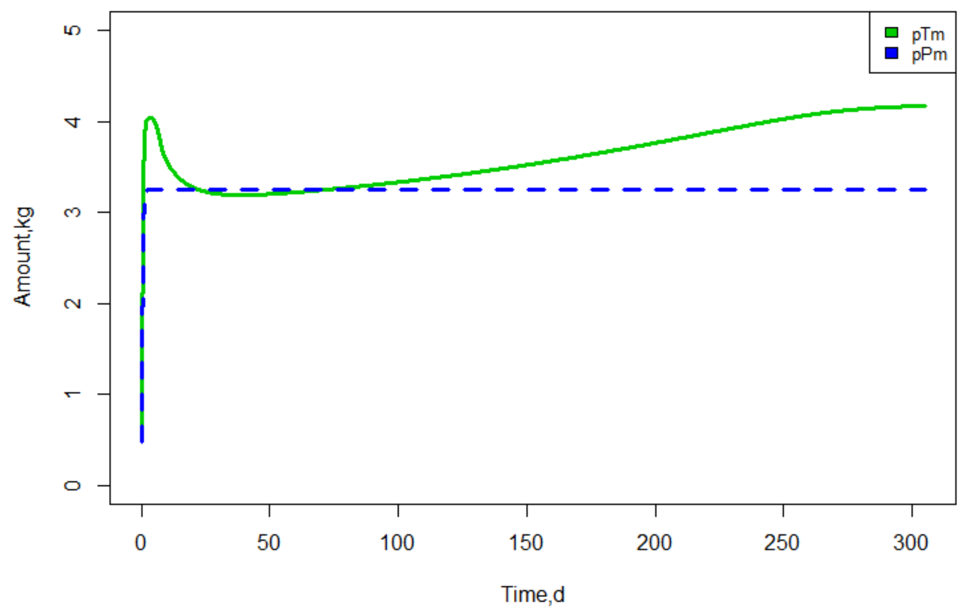
1. Default: Ref GI = 0.003
   cGI = 0.0036
   Ahor = 1.2

2. Change cGI = 0.003
   Ahor = 1

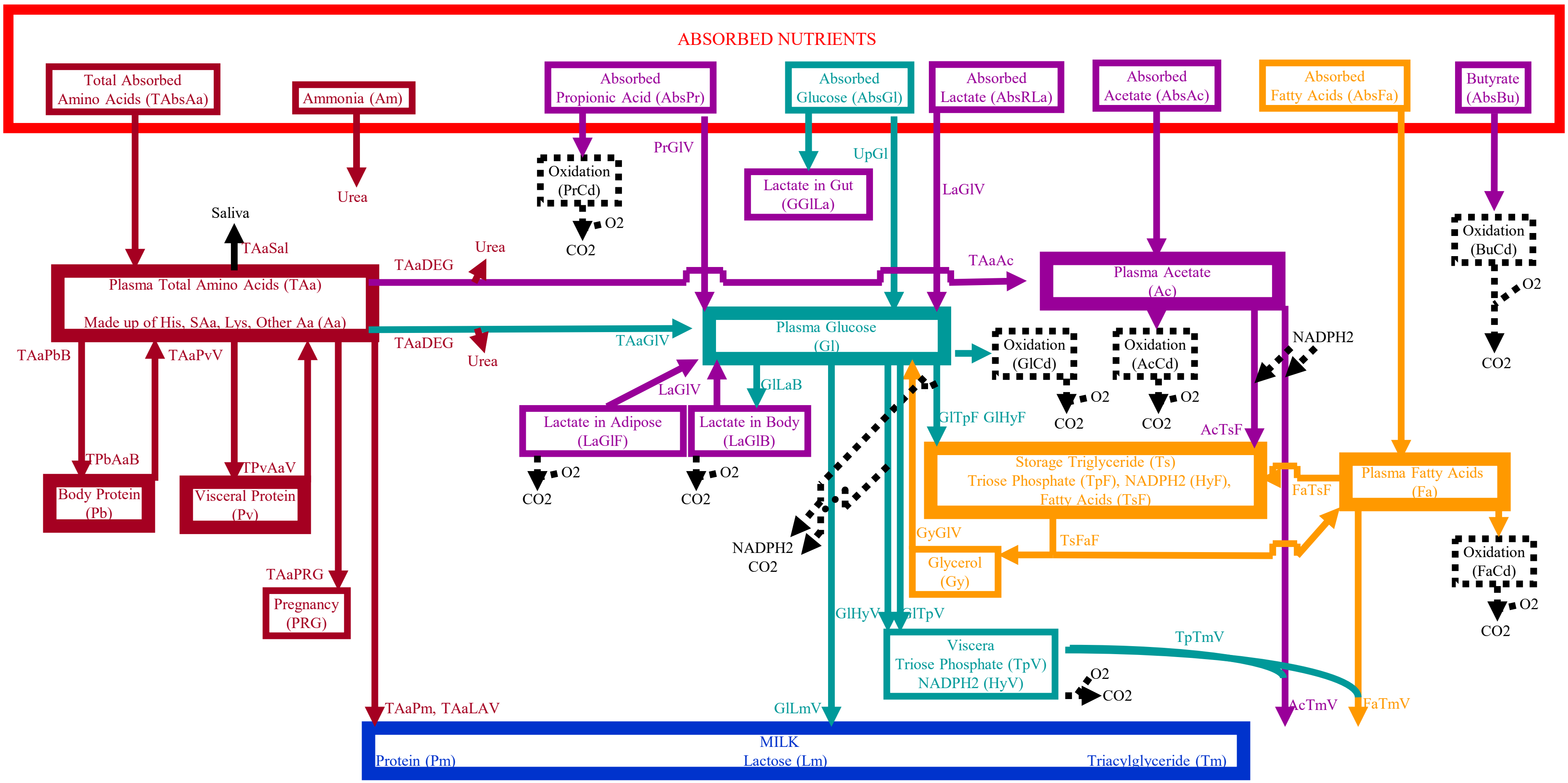

AaAc
AcTsF
AcTmV
Amount
Time,d


AaAc
AcTsF
AcTmV
Amount
Time,d


pTm
pPm
Amount,kg
Time,d

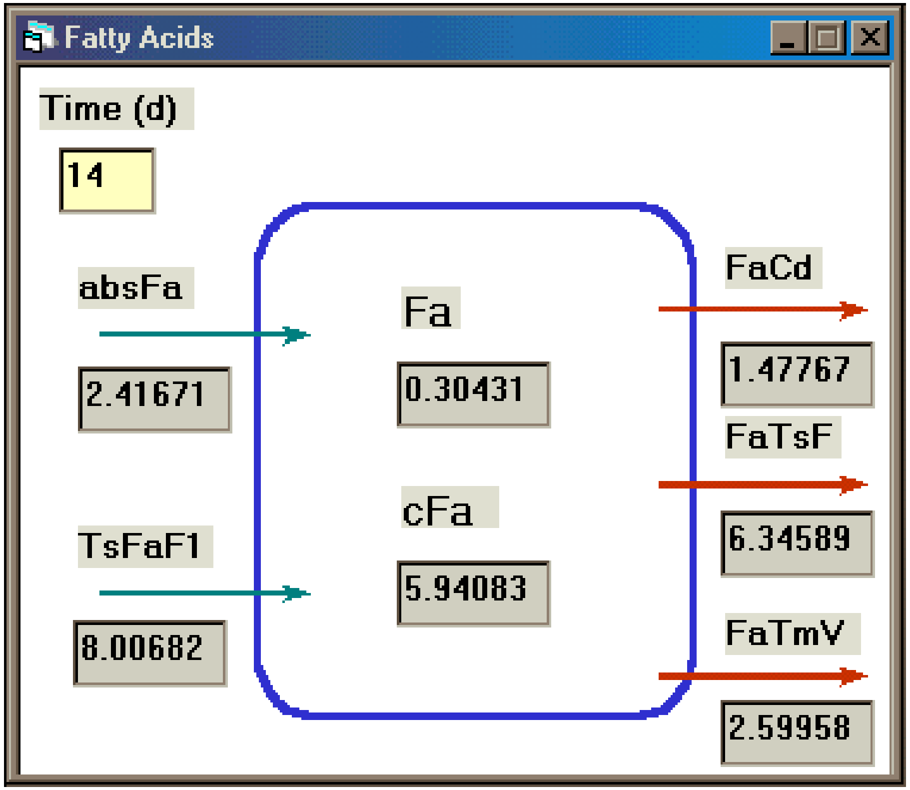

pTm
pPm
Amount,kg
Time,d

2. COMPARTMENT EQUATIONS


ABSORBED NUTRIENTS
Total Absorbed Amino Acids (TAbsAa)
Ammonia (Am)
Absorbed Propionic Acid (AbsPr)
Absorbed Glucose (AbsGl)
Absorbed Lactate (AbsRLa)
Absorbed Acetate (AbsAc)
Absorbed Fatty Acids (AbsFa)
Butyrate (AbsBu)
Urea
Oxidation (PrCd)
O2
CO2
PrGlV
UpGl
Lactate in Gut (GGlLa)
LaGlV
Oxidation (BuCd)
Saliva
TAaSal
Urea
TAaDEG
TAaAc
Plasma Total Amino Acids (TAa)
Made up of His, SAa, Lys, Other Aa (Aa)
Plasma Acetate (Ac)
Plasma Glucose (Gl)
TAaGlV
TAaDEG
Urea
TAaPbB
TAaPvV
Oxidation (GlCd)
Oxidation (AcCd)
NADPH2
LaGlV
GlLaB
Lactate in Adipose (LaGlF)
Lactate in Body (LaGlB)
GlTpF GlHyF
AcTsF
TPbAaB
TPvAaV
Body Protein (Pb)
Visceral Protein (Pv)
Storage Triglyceride (Ts)
Triose Phosphate (TpF), NADPH2 (HyF),
Fatty Acids (TsF)
Plasma Fatty Acids (Fa)
FaTsF
GyGlV
TsFaF
Glycerol (Gy)
Oxidation (FaCd)
NADPH2
CO2
TAaPRG
Pregnancy (PRG)
GlHyV
GlTpV
TpTmV
Viscera
Triose Phosphate (TpV)
NADPH2 (HyV)
TAaPm, TAaLAV
GlLmV
AcTmV
FaTmV
MILK
Protein (Pm)
Lactose (Lm)
Triacylglyceride (Tm)

Differential Equation for fatty acids

Units: mole/L per day



dFa/dt = absFa + TsFaF1 - FaTsF - FaTmV - FaCd

3. EQUATION FORMS

1. Michaelis Menton
2. First order (Percentage,dH)
3. Restrictive maximums (Kminh)

1. Michaelis Menton

$$V = Vm / (1 + Km/cS)$$

Vm = maximal velocity moles/d
Km = rate constant at half maximal velocity
= moles/L
cS = concentration of substrate moles/L

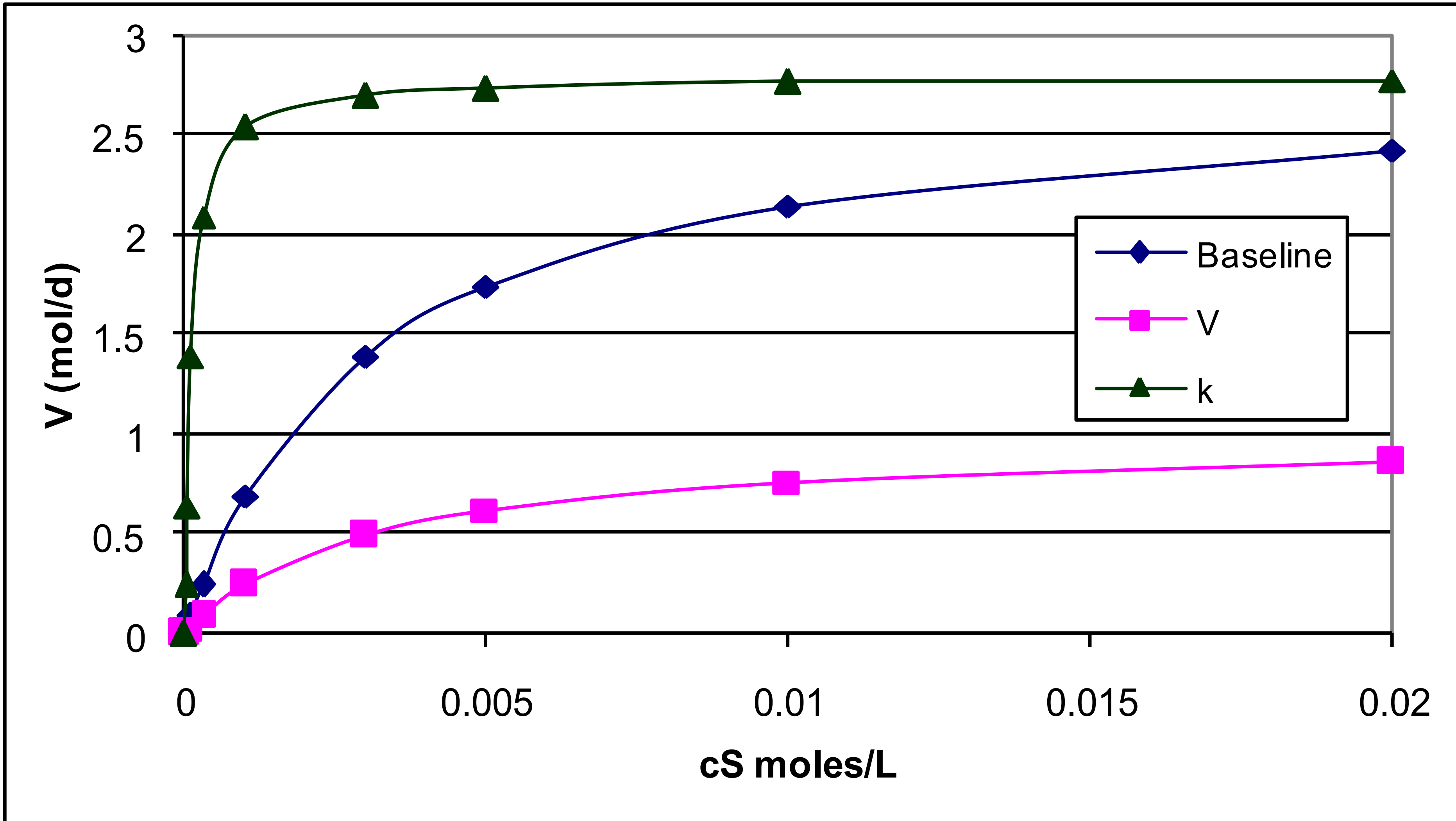
Affinity increases $V = k_{Gl} / cGl$

Inhibition decreases $V = cGl / k_{Gl}$

Example $TsFaF = V_{TsFaF} * EBW^{0.75} * Chor /$

$$(1 + (cFa/k_{TsFa}) + (k_{TsFaF}/cTs)^5)$$

V = Vm / (1 + Km/cS)



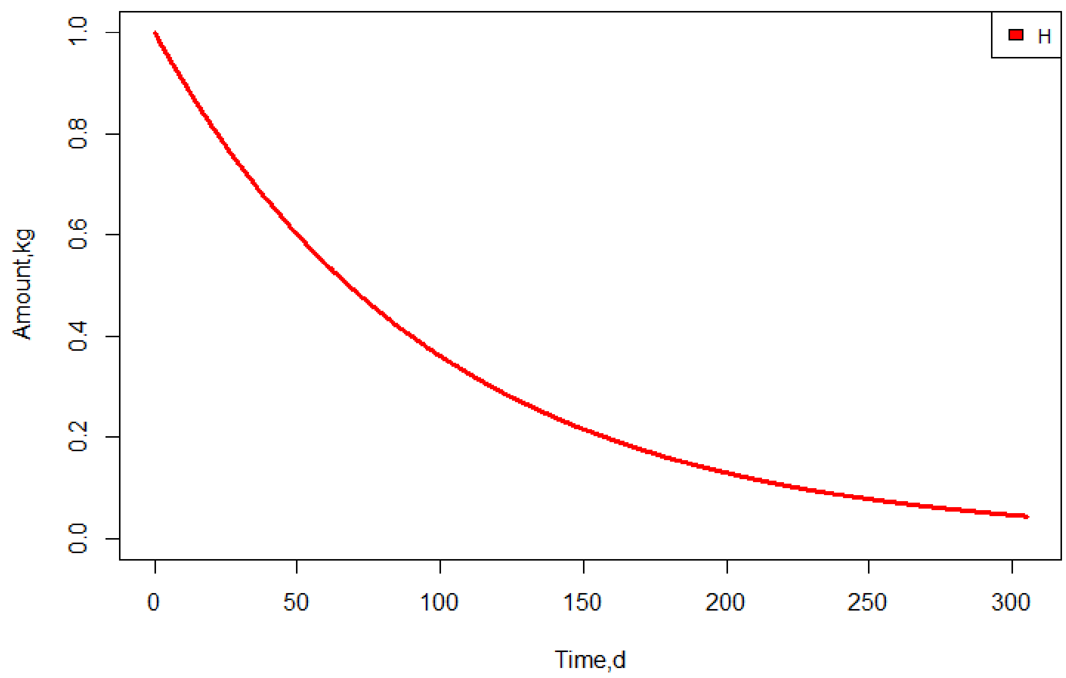
2. First Order (Percentage)

$$V = K * S$$

K = rate constant, units of %, kg/kg, etc /d
S = Amount of substrate (GI), moles

Example NealThornley.r mammary model

$$dH = -Kh * H$$



3. Restrictive maximums

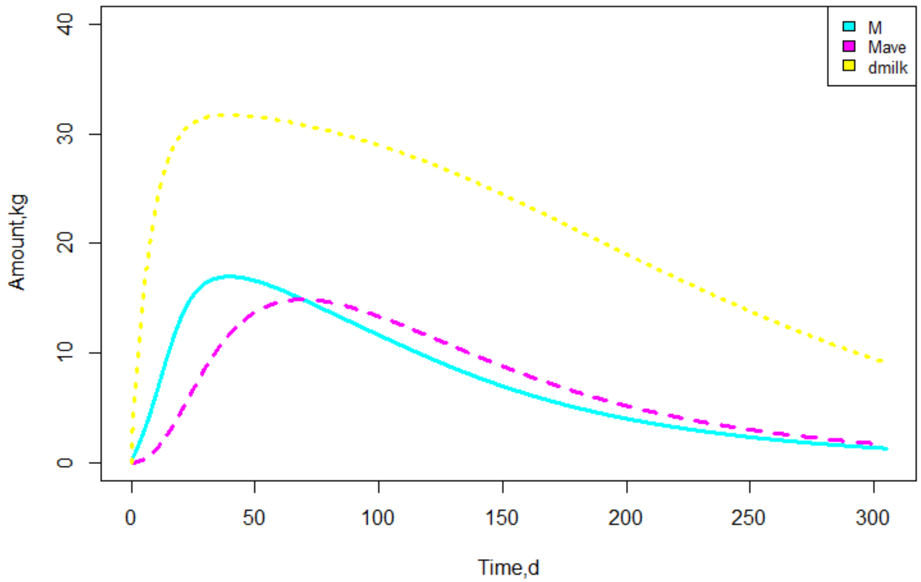
Example NealThornley.r

Milk retention decreases milk secretion

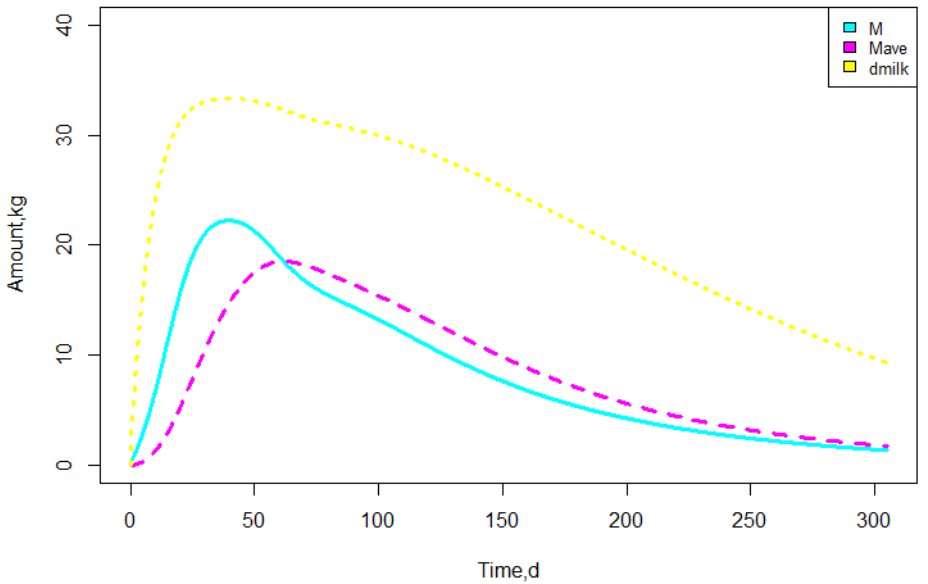
Pm = Km * Cs * Kminh

Kminh = (Mm – M) / (Mm – M + KR)

Mm = 30



Mm = 40



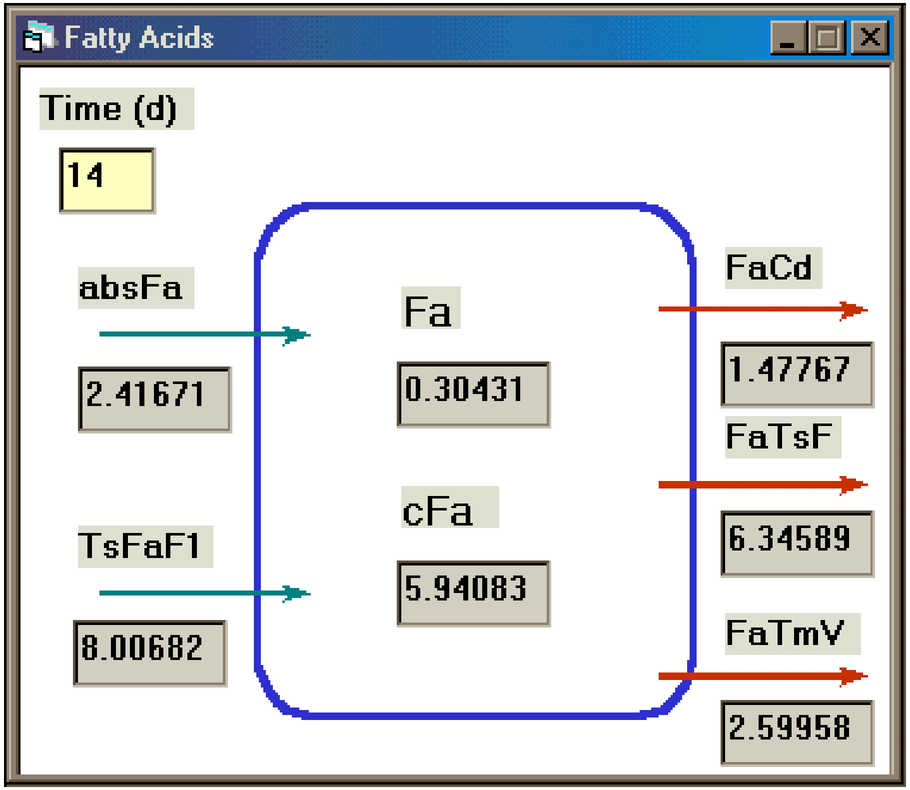
Mechanisms represented within models

NealThornley.r	milk yield based on cell function(Cu, Cs, H, M) milk retention effects (Kminh)
BaldwinLm.r	milk yield based on lactose production (PCLm= 4.8%) Lm dependent on glucose(Gl),amino acids(Aa)
BaldwinPm.r	milk fat (Tm) and protein yield (Pm) added Tm is from fatty acids (Fa) and acetate (Ac) Pm is from Aa
MollycAc.r	anabolic(Ahor) and catabolic(Chor) hormones Ac pool added

4. Modeling Exercise
Mollycac.r

Differential Equation for fatty acids

Units: mole/L per day



dFa = absFa + TsFaF1 - FaTsF - FaTmV - FaCd

parms section

cGl = 0.0032,
#cFa=0.00025,
cTs = 0.25,
vFa = 600,
VFaTmV = 0.0008,
VAcTmV = 0.006,
VTsFaF = 0.1,
KTsFaF = 0.2,
K1TsFa = 0.0005,
VFaTsF = 0.08,
KFaTsF = 0.0005,
K1FaTs = 0.002)

qinit section

Fa = 0.667,

res section

dFa,

Graph cFa

FaTmV, TsFaF1, FaTsF

eqns – Acetate section

absAc = 60

dVAcTs = 10*Ahor-0.35*VAcTs

eqns - Fatty acid section after acetate section

cFa = Fa/vFa

AbsFa = 1

TsFaF = VTsFaF * 121 * Chor /
(1 + (cFa/K1TsFa)^2 + (KTsFaF/cTs)^5)

TsFaF1 = TsFaF * 3

FaTsF = VFaTsF * 121 /
(1 + KFaTsF/cFa + K1FaTs/(Ahor*cGl))

Move FaTmV equation here from milk fat section

Move FaTmV1 equation here from milk fat section

FaCd = 1.2

dFa = AbsFa+TsFaF1-FaTsF-FaTmV-FaCd