User approach of expanded MAGENTC for animals; parsimonious modelling trials

Anca Melintescu PhD

“Horia Hulubei” National Institute for Physics and Nuclear Engineering, Bucharest-Magurele, ROMANIA
ancameli@ifin.nipne.ro, melianca@yahoo.com

3rd Meeting of the EMRAS II Working Group 7, “Tritium”, IAEA Headquarters Vienna, Austria, 25–29 January 2010

WG7 - robust assessment for Human dose after accidental tritium releases

Committed dose depends on time integrated intake and not on details about dynamics → Time integrated concentration in animal products

Animals of interest - cow (meat and milk), sheep (meat and milk), beef, goat (meat and milk), pig, chicken

cow milk after HTO intake	**good**
cow milk after OBT intake	**1 exp**
goat milk after OBT intake	**moderate**
goat milk after HTO intake	**no exp**
sheep milk after HTO intake	**no exp**
sheep milk after OBT intake	**no exp**
broiler meat after HTO intake	**no exp**
broiler meat after OBT intake	**no exp**
egg after HTO intake	**Russian data**
egg after OBT intake	**no exp**
beef meat after HTO intake	**2 exp(?)**
beef meat after OBT intake	**no exp**
veal after OBT intake	**Poor**
pig after OBT intake	**Poor**
piglets after OBT or HTO intakes	**Medium**
sheep after OBT intake	**Partial**

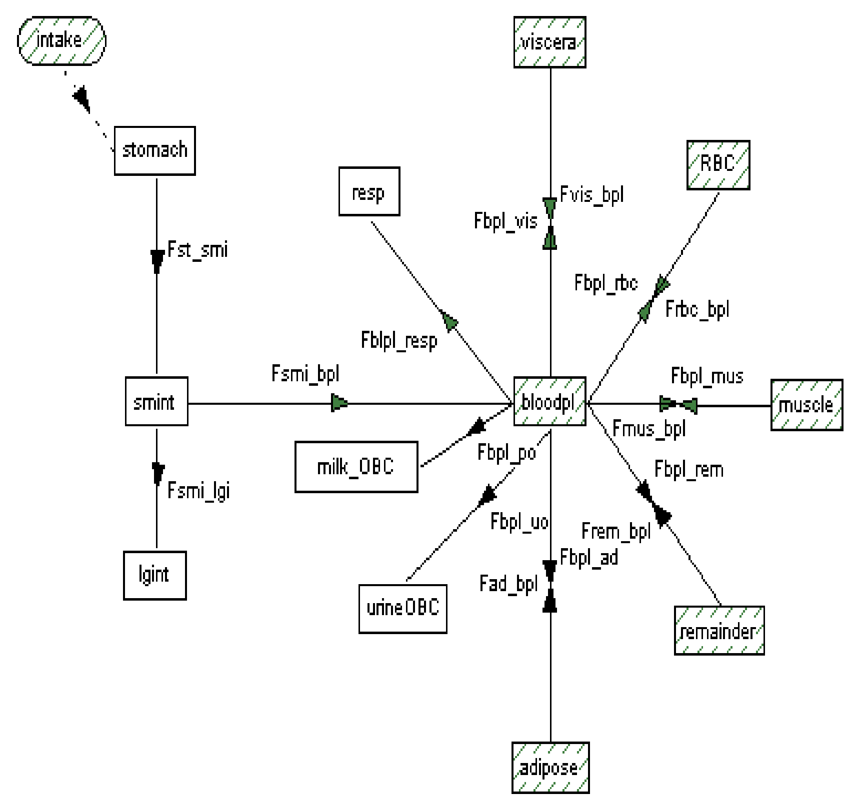
Experimental data base very sparse → generic model → Common process for all farm animals and particularization

MAGENTC - MAmmal **GEN**eral **T**ritium and **C**arbon transfer

- Complex dynamic model for H-3 and C-14 transfer in mammals
- full description given in:

D. Galeriu, A. Melintescu, N. A. Beresford, H. Takeda, N.M.J. Crout, “The Dynamic transfer of 3H and 14C in mammals – a proposed generic model”, *Radiat. Environ. Biophys.*, (2009) 48:29–45

- 6 organic compartments;
- distinguishes between organs with high transfer and metabolic rate (viscera), storage and very low metabolic rate (adipose tissue), and ‘muscle’ with intermediate metabolic and transfer rates;
- Liver, kidney, heart, GIT, stomach content, small intestine – high metabolic rates → “viscera” compartment
- Blood - separated into RBC and plasma (plasma is the vector of metabolites in the body and also as a convenient bioassay media);
-The remaining tissues - bulked into “remainder”;
- All model compartments have a single component (no fast-slow distinction)



Steps for MAGENTC

- Step 1: Collect relevant experimental data;
- Step 2: Basic understanding of metabolism and nutrition; Reviews of the past experience (STAR, TRIF, OURSON, UFOTRI, PSA etc);
- Step 3: Formulate basic working hypothesis;
- Step 4: Using the rat (very good experimental data base thanks to H. Takeda, NIRS Japan) for exercise;
- Step 5: Understanding the animal nutrition from literature and make a standardization;
- Step 6: Developing the conceptual and mathematical model;
- Step 7: Test the model with experimental data;
- Step 8: Make prediction for the cases without experimental data;
- Step 9: Trials for simplify without losing the predictive power.

Working material (IFIN-HH, Romania)

1. **Experimental data (Revision prepared by A. Melintescu, 2000)**

   - Cows and mini goats
   - Pig and piglets
   - HTO and OBT intake
   - Old data, experimental conditions poorly reported.
   - Available in English as an internal document and can be incorporated as an annex in WG7 (maybe as a Tecdoc!?)

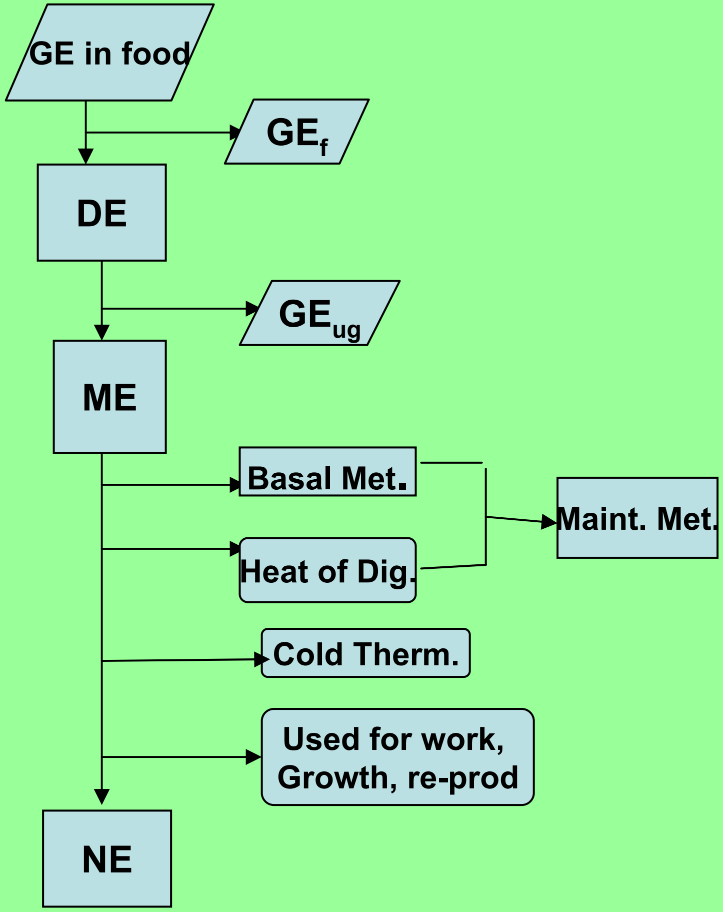
Working material (IFIN-HH, Romania)

2. **Feed intake of farm animals, a briefing for environmental transfer models**

Efficiency of energy transfer (k) = the ratio between net energy utilized and metabolisable energy consumed

k factor	**Efficiency of utilization**
k_m	maintenance
k_p	protein deposition
k_f	fat deposition
k_g (or k_{pf})	growth in general
k_l	milk production (lactation)
k_c	fetal growth (the conceptus)
k_w	work (e.g. in draught animals)
k_{wool}	wool growth

Energy flow



Ruminants

Efficiencies → metabolizability, q_m = the ratio between ME and GE

We used the following relationships:

$k_m = 0.35q_m + 0.503$

$k_g = 0.78q_m + 0.006$

$k_l = 0.35q_m + 0.420$

Ruminants’ standardized feed

Feed	Dry mater	Protein digestibility	Digestible protein (g/kg fw)	Digestible fat (g/kg fw)	Digestible cellulose (g/kg fw)	Digestible SEN (g/kg fw)	Organic matter digestibility	Metabolisable energy (kJ/kg fw)	q	K_m	K_l	K_g
hay	0.86	0.61	70	12	141	247	0.592	7160	0.45	0.66	0.577	0.357
concentrates	0.88	0.79	110	27	17	518	0.815	10690	0.64	0.74	0.657	0.528
grain	0.88	0.77	83	15	14	626	0.87	11528	0.715	0.75	0.667	0.564
straw	0.88	0.07	14	3.6	3.8	122	0.84	1147	0.302	0.60	0.525	0.241
pasture	0.215	0.71	22.2	4.24	36	78	0.72	2181	0.56	0.7	0.617	0.443
upland pasture	0.376	0.6	20.3	9.4	90	190	0.51	2200	0.344	0.65		

Metabolisable energy intake = maintenance + production

$ME_{Intake} = ME_m + ME_{pd}$

$$ME_m = M * KK * S * \frac{0.26 * LBW^{0.75} * \max(0.84, \exp(-\frac{0.03 * t}{365}))}{K_m} + 0.1 * ME_{pd}$$

$$M = \max(1, 1 + 0.26 * \frac{t_{wstop} - t}{t_{wstop} - t_{wstart}})$$ - Correction for suckling mammals

KK - animal type

S – gender differentiation

S	Gender
1.15	male
1	female and castrate

KK	Animal type
1.4	*Bos Taurus*
1.2	*Bos Indicus*
1.25	Dairy goat
1.17	Angora goat
1.05	Other goats
1	Sheep

ENERGY REQUIREMENT FOR ACTIVITY

- minimal activity for survival: standing, eating etc, and the estimates depend on animal weight

- We introduced this minimal activity in the maintenance needs and then we approximated the activity needs for grazing animals in various conditions (plain, hill, good or low quality pasture)
- We deduce the following equation for activity allowance:

$$ME_{activity}=(F_p * F_q)*a_2*ME_{stable}$$

W – animal weight (kg);
a_2 – fraction of maintenance;
F_p – time fraction on the pasture;
F_q – index of pasture quality

Animal type	**a_2**	**F_q**
Sheep	0.12	1 – good pasture 1.5 – average pasture 2.5 – uplands
Goat	0.15	1 – good pasture 1.5 – average pasture 2.5 – uplands
Cow	0.1	1 – good pasture 2 – scarce pasture

- For pig and hen - we did not split minimal activity from maintenance
- For wild animals - activity is 50-60 % from maintenance

ENERGY REQUIREMENT FOR WOOL PRODUCTION

-Wool production for sheep and goat - considered at a generic level of 4 kg/y with a need of ME 125 kJ/kg

ENERGY REQUIREMENT FOR LACTATION

-we considered the body mass constant
-the lactation energy need depends on animal type and fat content.
-The metabolic energy need, per litter of milk:

$$ME\ (kJ/L) = b + c\ FP$$

FP - the fat percentage
b, c - constants

specie	b	c
cow	2470	672
sheep	3630	556
goat	3200	447

ENERGY REQUIREMENT FOR EGG PRODUCTION

-The metabolizable energy need for egg production is related with mass of egg production per day multiplied by metabolizable energy need per unit mass of egg.
-Average production of a laying hen - 250 eggs per year
-average mass of egg - 62 g
-For each g of egg are necessary 10.2 kJ and the composition of egg is few variable among breeds.

WATER INTAKE

- Sources of water:
  - drinking water;
  - water in food;
  - metabolic water;
  - respiration;
  - skin absorption.
- Water content of the body depends strongly on fat content → protein content is quite constant with age and breed.
- body composition
- water content

} are known

- If the water turn over half-times are experimentally known
- water balance - known

} we deduce the water intake

Water intake depends on animal type:

- body mass;
- dry matter intake;
- lactation stage (if it is necessary);
- ambient temperature;
- management practice.

There are various empirical formulas of assessing drinking water, but in practice, there is a quite large natural variability.

- Metabolic Water - MW can be easy assessed knowing the feed composition:
  - digestible proteins, DP;
  - digestible fats, DF;
  - digestible carbohydrates, DCH

$$MW=0.42*DP+1.07*DF+0.6*DCH$$

- Respiration and skin absorption can be assessed by analogy with humans (Zach 1985) in absence of relevant data
- Respiration rate of standard man is multiplied by the ratio of metabolic energy used.
- For mammals using ME_m and ME_p and knowing k_p, an approximation for inhalation rate is:

$$Inhrate = \frac{ME_m + (1-k_p) * ME_p}{13400 * 23}$$

→ little effect on overall uncertainty, because respiration and skin absorption have a low share in the water input

with energy in kJ and inhalation rate in m^3/d

Drinking water + water from food → recommendation based on milk production (where is the case) and DMI

Water intake – increases with environmental temperature

Water intake – large variability, even for the same animal type

- cow	$WI=DM*2.15+MP*0.73+13.5$	(Voors, 1989)
- cow	$WI=DM*[3.3+0.082*(T_{env}-4)]+0.87*MP$	(ARC 1980)
- sheep	$WI=0.82*MP+DM*[1.26+0.1*(T_{env} -5)]*1.35$	(ARC 1980)
- sheep	$WI= DM*(0.18* T_{env}+1.25)$	(NRC 1985)
- goat	$WI=0.1456*BM^{0.75} + 0.143*MP$	(NRC 1981)
- pig	$WI=DM*3.6+0.03$	
- hen	$WI=\frac{BM}{8}*(1+0.6*\frac{T_{env}-20}{15})+0.68*\frac{EP}{1000}$	

WI – water intake;
DM – dry matter;
MP – milk production;
BM – body mass
T_{env} – environmental temperature;
EP – egg production per day

Body composition (protein, CH, fat) + 4 % ash → body water → body water mass (BWM)

Water turnover half-time:

$$TW = 0.693 * \frac{BMW}{WI}$$

Body water half-times for different mammals

Mammal	**TW (days)**	**Ranges (days)**	**Reference**
Veal	3.4	2.8 - 3.6	Black
Beef	3.4	2.9 - 4.1	Black
Cow non-lactating	4	Single value	Thorn
Cow lactating	3.5	3 - 4.5	Kirchmann
Sheep	3.1	2.5 - 3.5	Crout
Goat lactating	4.1	2.9 - 5.3	Hoeck
Goat non-lactating	8.3	6.7 - 10.4	Hoeck
Pig	3.8	3.3 - 4.3	Kirchman
Saw after weaning	10	Single value	Van Hess, 2000
Broiler	4.9	Single value	Kirchmann

Growth - described in relative units;

- refers to Standard Reference Weight (when skeletal development is complete and fatness is in the middle)
- unified approach, except lean beef

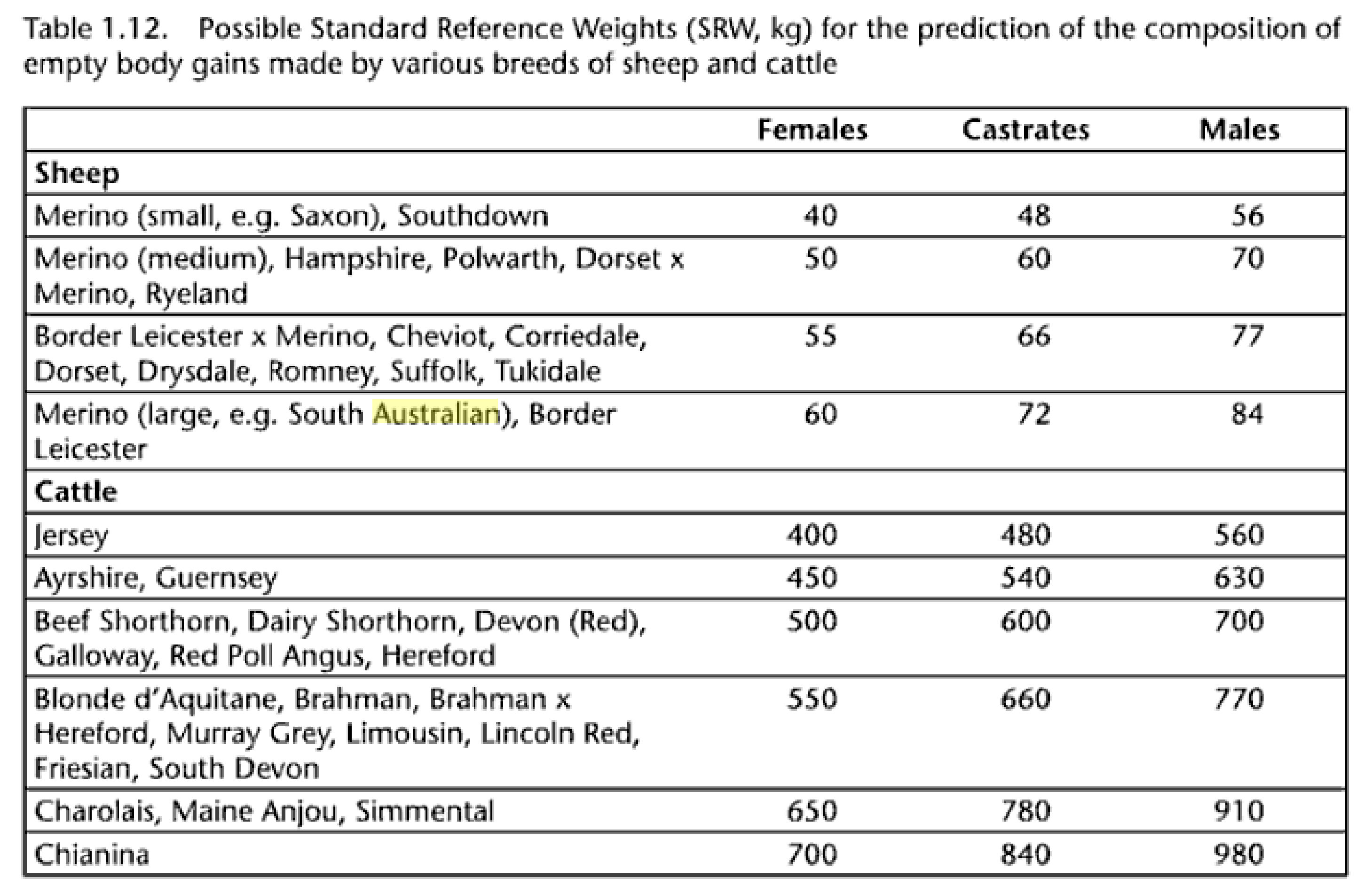


Table 1.12. Possible Standard Reference Weights (SRW, kg) for the prediction of the composition of empty body gains made by various breeds of sheep and cattle

	Females	Castrates	Males
Sheep			
Merino (small, e.g. Saxon), Southdown	40	48	56
Merino (medium), Hampshire, Polwarth, Dorset x Merino, Ryeland	50	60	70
Border Leicester x Merino, Cheviot, Corriedale, Dorset, Drysdale, Romney, Suffolk, Tukidale	55	66	77
Merino (large, e.g. South Australian), Border Leicester	60	72	84
Cattle			
Jersey	400	480	560
Ayrshire, Guernsey	450	540	630
Beef Shorthorn, Dairy Shorthorn, Devon (Red), Galloway, Red Poll Angus, Hereford	500	600	700
Blonde d'Aquitane, Brahman, Brahman x Hereford, Murray Grey, Limousin, Lincoln Red, Friesian, South Devon	550	660	770
Charolais, Maine Anjou, Simmental	650	780	910
Chianina	700	840	980

Mass dependence (relative units) for viscera mass fraction, specific metabolic rates – SMR ((MJ $kg^{-1}day^{-1}$) and partition fractions for maintenance metabolic energy

Relative body weight (EBW/SRW)	Viscera mass fraction normalized to EBW	Specific metabolic rate (MJ $kg^{-1}day^{-1}$)				Partition fraction maintenance metabolism			
		liver	PDV	HQ	Liver+PDV	Adipose	viscera	muscle	remainder
0.07	0.09	1.5	0.77	0.24	0.98	0.006	0.47	0.42	0.104
0.2	0.11	NA	NA	NA	NA	0.023	0.61	0.27	0.097
0.3	0.12	NA	NA	NA	NA	0.04	0.61	0.31	0.04
0.41	NA*	NA	NA	NA	NA	0.068	0.61	0.27	0.052
0.48	NA	2.9	0.47	0.1	0.83	0.094	0.6	0.27	0.036
0.64	NA	2.6	0.36	0.088	0.66	0.13	0.55	0.29	0.042
0.77	NA	2.4	0.3	0.084	0.55	0.15	0.5	0.31	0.04
1	0.08	NA	NA	NA	NA	0.19	0.47	0.3	0.04

Animal Products in Human Diets

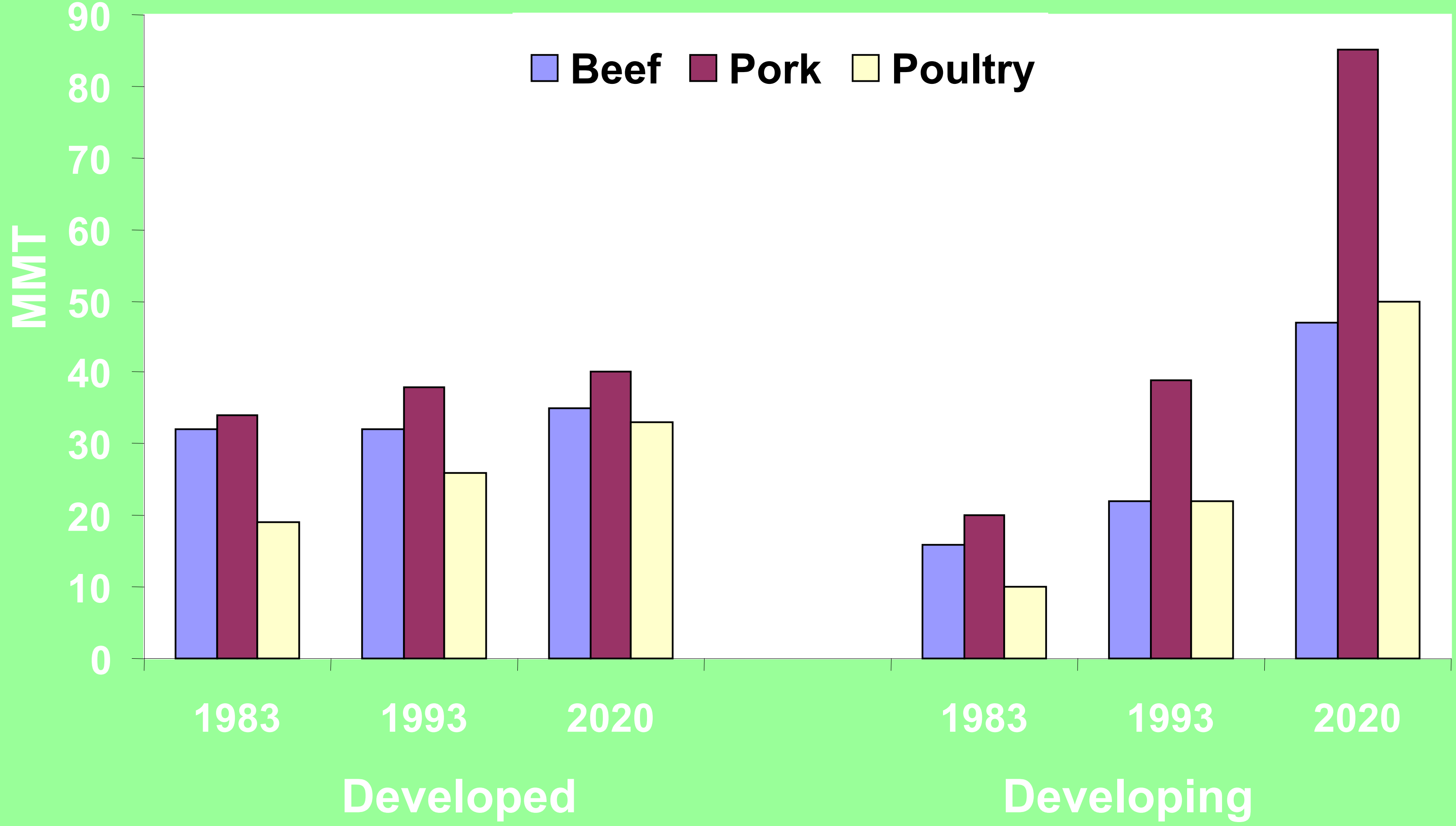
Meat, milk, eggs and fish supply:

- **16 % of human food energy**
- **36 % of human food protein**

Large variations among countries and regions.

Taken from James W. Oltjen
Dept. Animal Science University of California, Davis

Past and projected total consumption of various meats



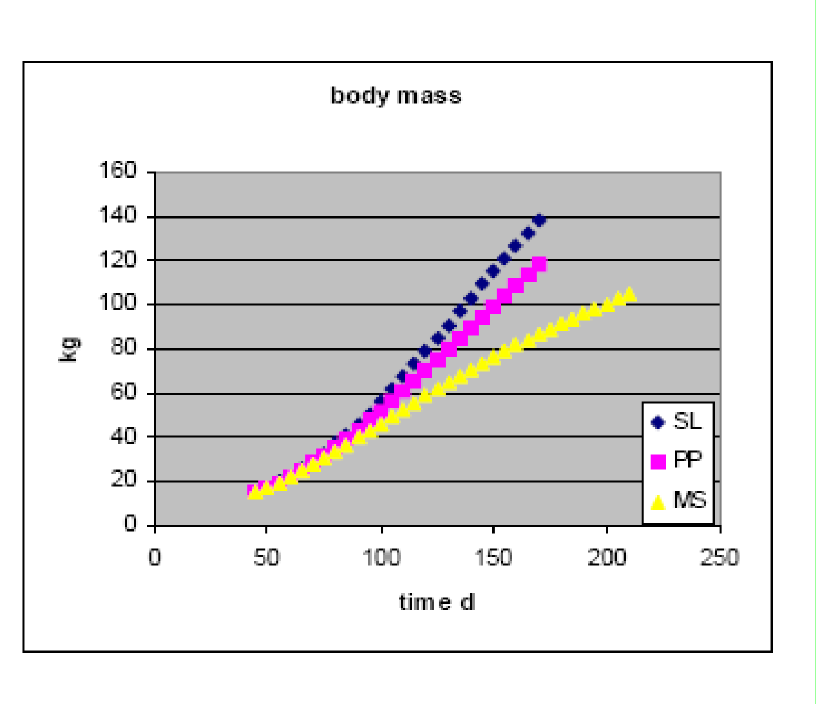
Taken from James W. Oltjen
Dept. Animal Science University of California, Davis

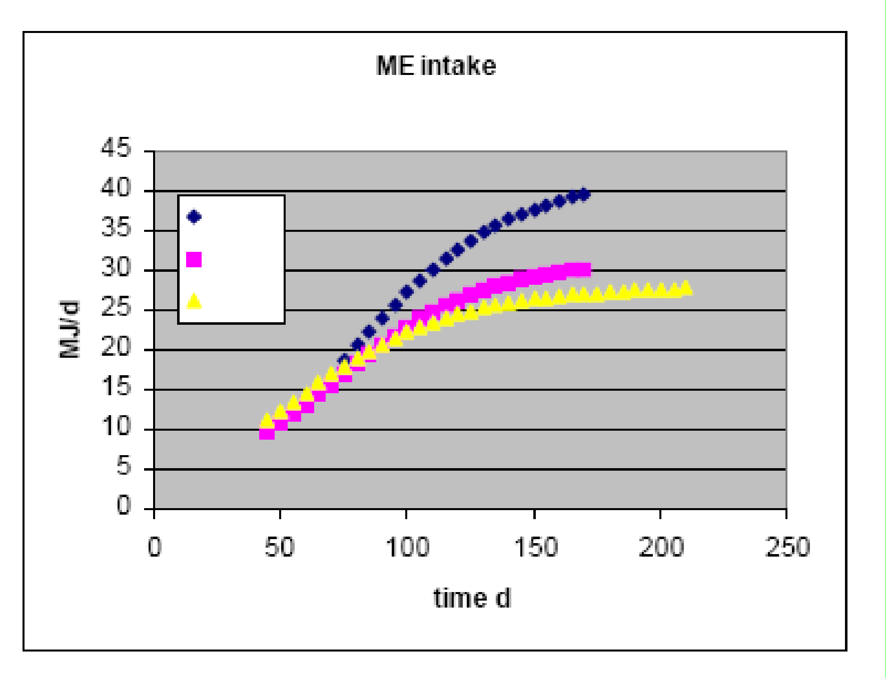
PIGS

- Model developed for pig growth – adapted from INRA France (Noblet and Van Milgen);

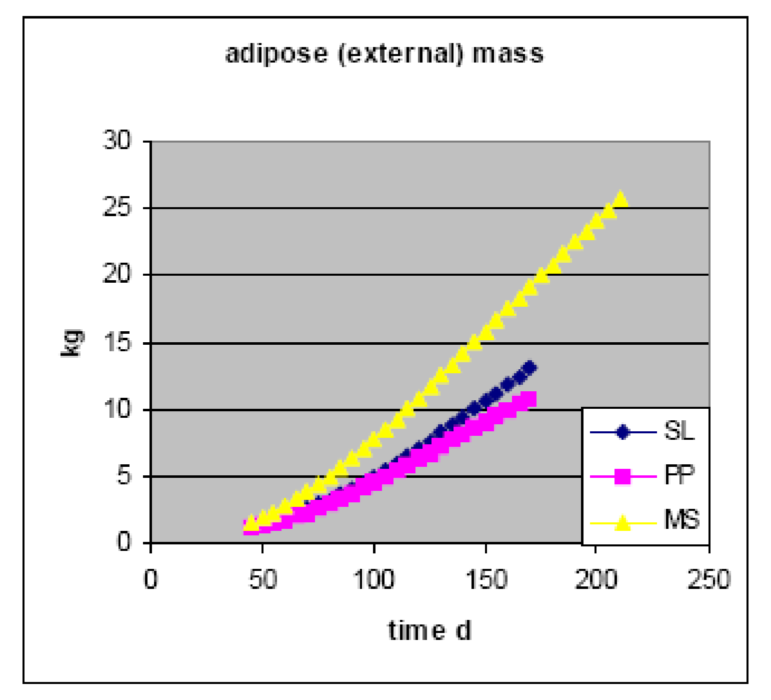
- 3 contrasting genotypes analyzed:
  - Synthetic Line (SL) - 'conventional' genotype;
  - Pietrain (PP) - lean genotype with low visceral mass;
  - Meishan (MS) - fat genotype

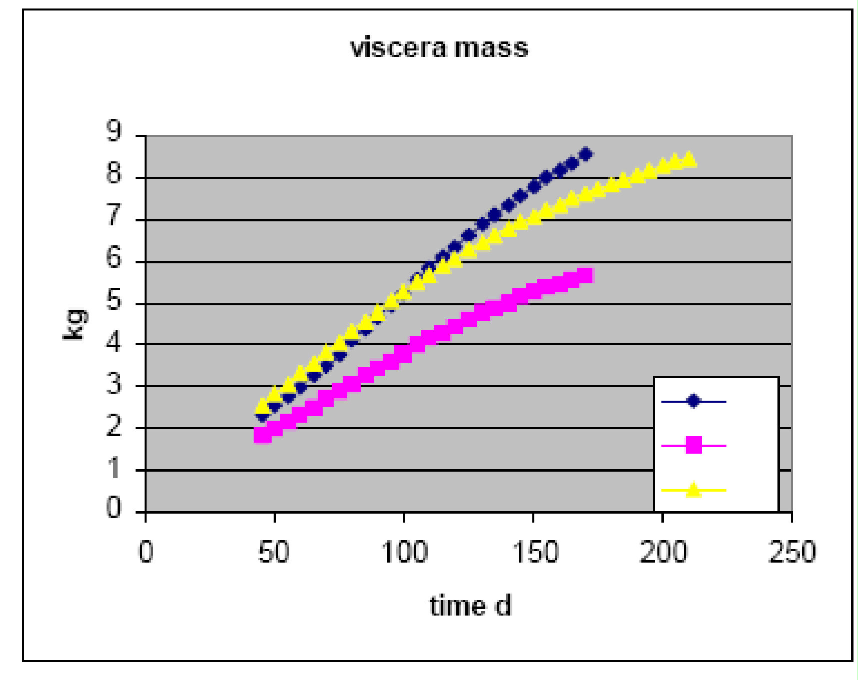
Dynamics of pig body mass and MEI intake for different pig genotypes



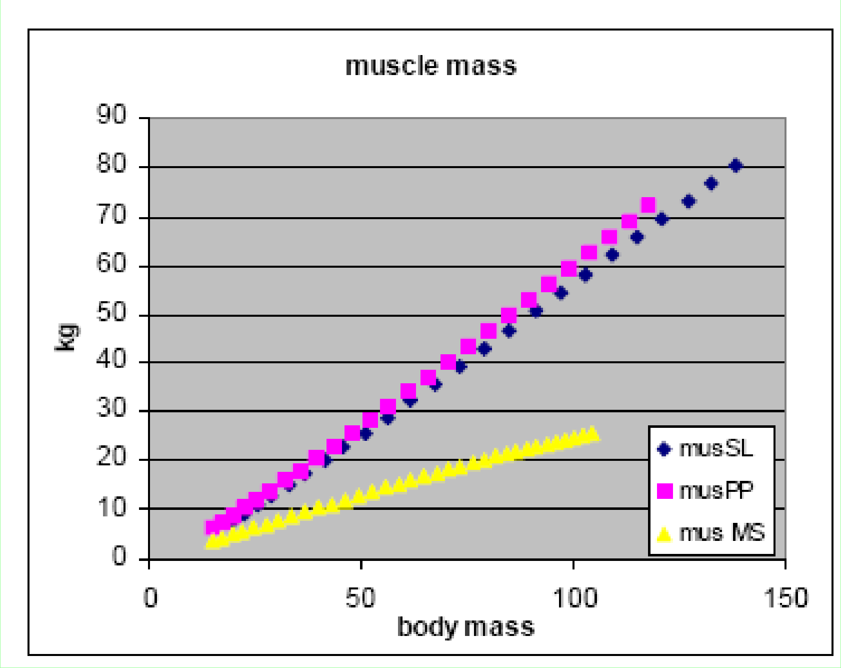


Dynamics of adipose and viscera mass for different pig genotypes

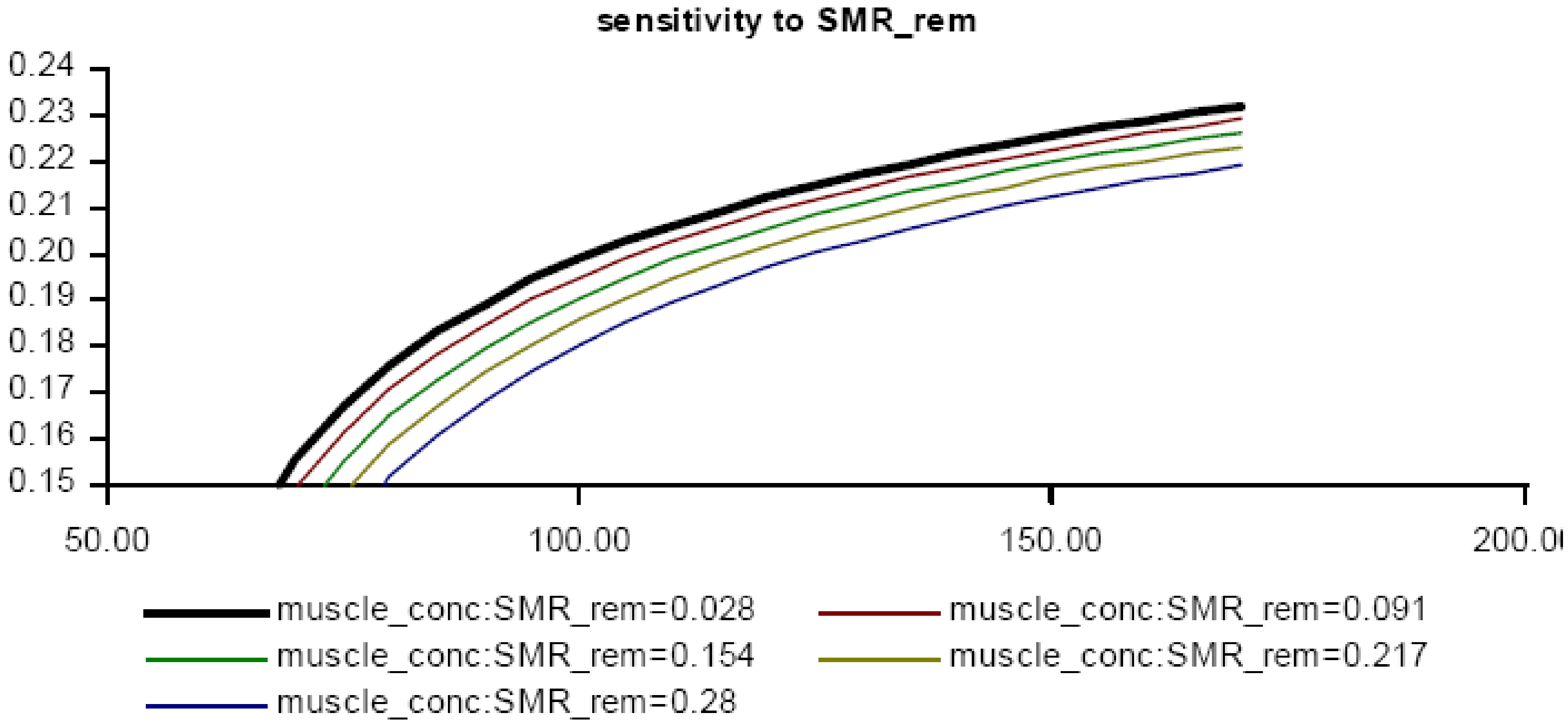




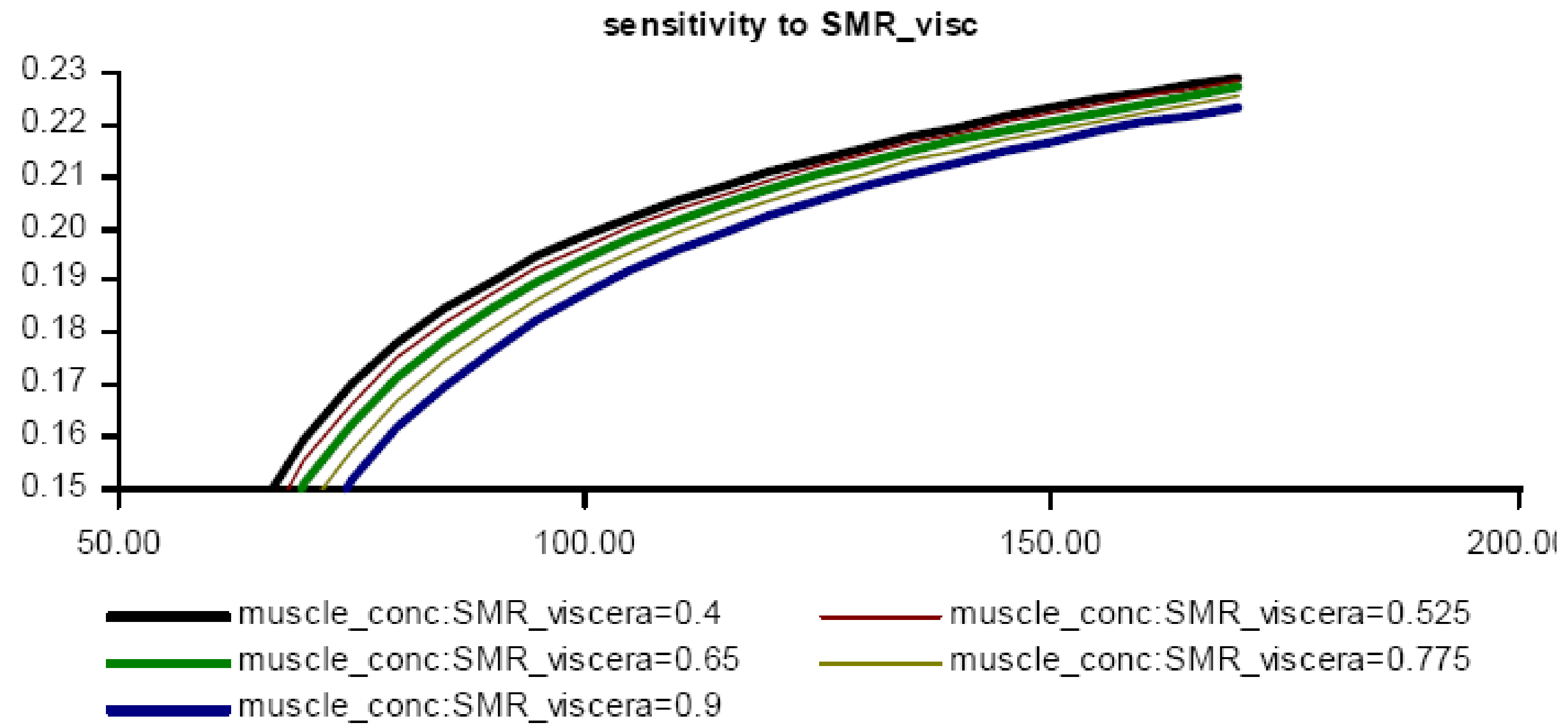
Muscle mass as a function of body mass for different pig genotypes



Sensitivity of muscle concentration to SMR in remainder organs



Sensitivity of muscle concentration to SMR in viscera



- Constant OBT and HTO concentration in food (intensive farming);
- Tested with experimental data and inter-compared with other models (MCT – Japan, STAR, PRISM – UK, OURSON – France, ETMOD – Canada);

Predicted-to-observed ratios for HTO in organs (84 days after start of contamination)

Organ	MCT	FSA	IFIN	PRISMDG	STAR-H3(DG)	EDF
Heart	0.54	33.4	2.17	1.31	0.81	0.19
Lungs	0.56	11.7	2.25	1.36	0.84	0.20
Liver	0.51	5.39	2.07	1.25	0.77	0.18
Jejunum	0.54	11.2	2.17	1.31	0.81	0.19
Ileum	0.56	38.4	2.27	1.37	0.85	0.20
Colon	0.58	5.89	2.35	1.42	0.88	0.21
Kidney	0.52	29.2	2.09	1.26	0.78	0.18
Muscle	0.53	0.42	2.13	1.29	0.80	0.19
Brain	0.53	7.70	2.15	1.30	0.80	0.19
Blood	0.62	2456	2.51	1.52	0.94	0.22

Predicted-to-observed ratios for OBT in organs (84 days after start of contamination)

Organ	MCT	FSA	IFIN	PRISMDG	STAR-H3(DG)	EDF
Heart	2.05	9.89	1.40	1.51	1.29	1.29
Lungs	2.79	4.11	1.90	2.06	0.13	1.30
Liver	1.92	1.04	1.11	1.20	0.08	0.84
Jejunum	3.00	3.23	1.73	1.88	0.12	1.09
Ileum	2.24	13.0	1.53	1.65	0.10	0.96
Colon	3.28	2.23	2.24	2.42	0.15	1.40
Kidney	2.17	8.46	1.48	1.60	0.10	1.17
Muscle	4.44	0.23	1.90	3.65	0.23	3.11
Brain	3.91	4.69	-	3.17	0.20	1.65
Blood	3.04	970	1.27	1.92	0.12	1.22

Tests with growing pigs and veal

Few experiments

1. Pigs of 8 weeks old fed for 28 days with HTO:
    Muscle P/O ~ 1
    Viscera P/O ~1

2. Pigs of 8 weeks old fed for 28 days with milk powder contaminated with OBT:
    Muscle P/O ~ 3
    Viscera P/O ~ 2

3. Pigs of 8 weeks old fed for 21 days with boiled potatoes contaminated with OBT:
    Muscle P/O ~ 0.2
    Viscera P/O ~ 0.3

    } Not quite sure about these values → Potential explanation: old and insufficiently reported experimental data

4. Two calves of 18 and 40 days old, respectively fed for 28 days with milk powder contaminated with OBT:
    Muscle P/O ~ 1
    Viscera P/O ~ 2.5

CONCLUSIONS

- The model is apparently research grade, but it is tested with experimental data without calibration;
- It is continuously improved in parallel with literature search on animal nutrition and metabolism;
- Input parameters need only a basic understanding of metabolism and nutrition and the recommended values can be provided;
- Results (not shown) give arguments for distinction between subsistence and intensive farming (observed also for Cs-137 post-Chernobyl);
- Model provides robust results for all intake scenarios of interest

PARSIMONIOUS APPROACH

Parsimonious model = a model with as few parameters as possible for a given quality of a model

- Models of complex environmental processes and systems - widely used as tools to assist the development of research, and to support decision making at a number of levels (e.g. international, national government, corporate);
- Many models become unwieldy, over-parameterised and difficult to test as they seek to capture the temporal and spatial dynamics of relevant processes. The performance of most models is usually assessed through some kind of 'test' against observed data → this testing is commonly a simple comparison between a given model and a given set of observed data.
- Invariably there are many plausible model representations of particular processes and the influence of these alternatives on model performance is rarely investigated.

  We believe that models should be parsimonious, i.e. as simple as possible, but no simpler.

Many thanks to Prof Neil Crout (Univ. of Nottingham, UK), because he taught me what “Parsimonious” is and made enjoyable this type of “games”.

Approach

- create families of related models which vary in their level of detail, structure and parameterisation;
- 'measure' model performance, in particular predictive capability;
- to compare this performance between members of the model families to either:
  - (a) allow the selection of the 'best' model
  - (b) facilitate the averaging of predictions by different models.

Model selection

- There are many statistical approaches to model selection. Broadly, these fall into two types:
  - (i) those in which the "best" model is chosen according to some criterion;
  - (ii) those in which some kind of averaging takes place over a possible class of models.
- Approaches of type (i) → frequentist
- Approaches of type (ii) → Bayesian

- A typical approach of type (i) can be described as follows:

1. Explicitly identify the class of models to be considered, including if possible a "minimal" model and a "maximal" model.

Potential problem: time consuming

2. Use the data to select the "best" model, basing the selection on a suitable model choice criterion.

Potential problem: too many candidate models which fit the data → unable to identify a single best model

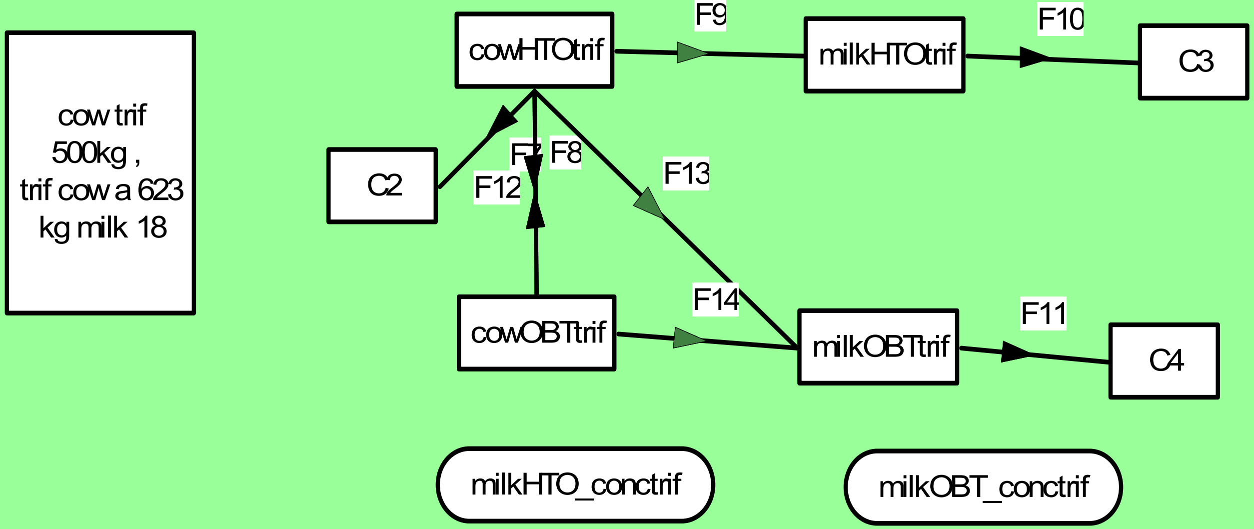
3. Proceed as if the selected model is correct.

Potential problem: underestimation of the true uncertainty

Case Study Models

TRIF Model (NRPB, UK, 1996)

- simple, compartmental
- predicts H-3 transfer in cows (meet and milk) and sheep (meet and milk)
- comparisons with the experiments are not successful



cow trif
500kg ,
trif cow a 623
kg milk 18

cowHTOtrif

F9

milkHTOtrif

F10

C3

C2

F7 F8

F12

F13

cowOBTtrif

F14

milkOBTtrif

F11

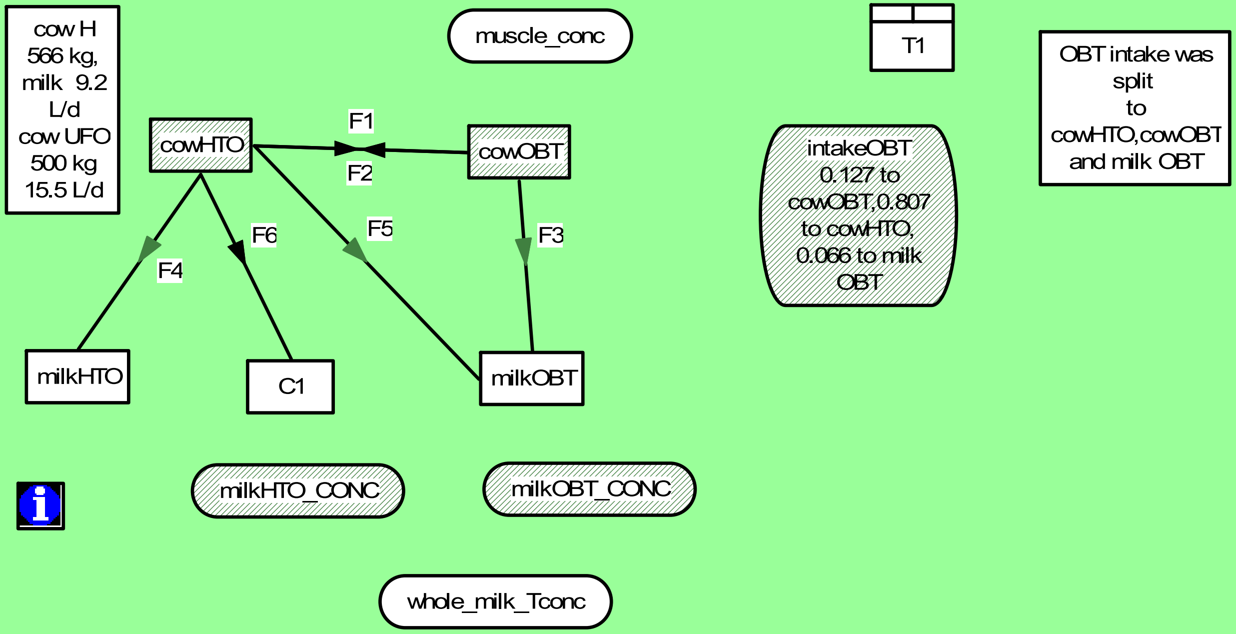
C4

milkHTO_conctrif

milkOBT_conctrif

UFOTRI (W. Raskob, FZK, Germany)

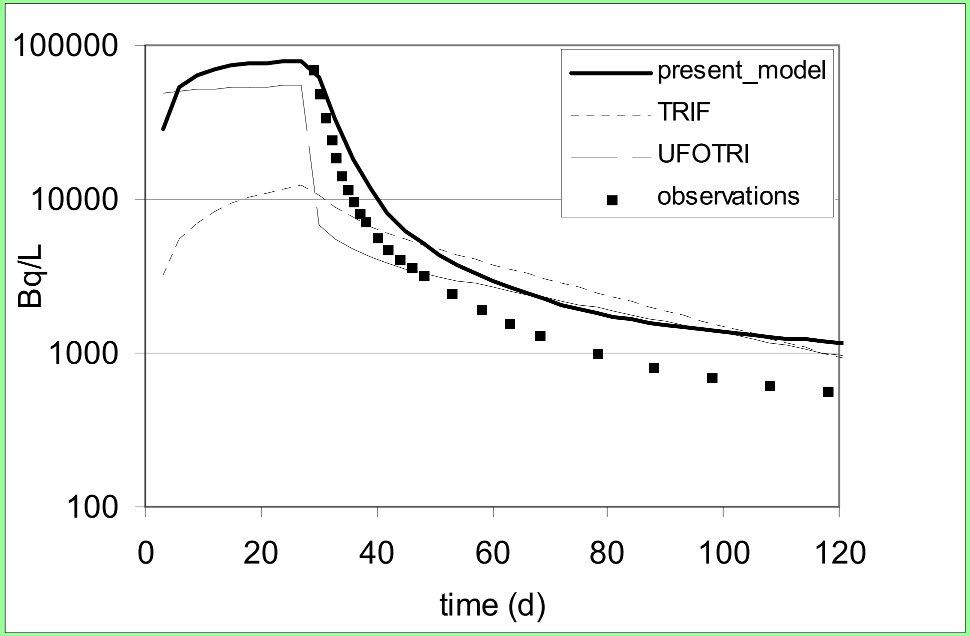
- simple, compartmental
- predicts H-3 transfer in cows (meet and milk)
- direct transfer from grass OBT to cow HTO, cow OBT, milk OBT
- comparisons with the experiments are good
- OBT partition intake is justified in MAGENTC
- this model can applied for other lactating animals



MAGENTC (IFIN-HH, Romania)

- complex, dynamic
- predicts H-3 and C-14 transfer in various growing mammals, biota and birds
- comparisons with the experiments are good

Inter-comparison between TRIF, UFOTRI, MAGENTC for OBT in milk after an OBT intake



Using complex models to get to simple models for dairy farm animals

Compartments:

1. Animal (EBW) water: Free Hydrogen or HTO in body water
2. Animal OBH (OBT)
3. Milk water (Free Hydrogen or HTO)
4. Milk OBH (OBT)
5. Intake water (FH, HTO)
6. Intake OBH (OBT)
7. fh Intake fraction of OBH going to body FH
8. fo Intake fraction of OBH going to body OBH

Transfers:

K11	water loss to environment
K12	transfer body FH to body OBH
K13	body FH to milk FH
K14	body FH to milk OBH
K21	body OBH to body FH
K24	body OBH to milk OBH

Model inputs:

MP milk production
Milk OBH content per liter Milk OH (Moh)
Milk water (Mfh)
Milk FH content per liter
Animal composition, depends on body condition – taken as average
Animal FH (Afh), Animal OH (Aoh), Milk FH (Mfh) and Milk OH (Moh) – known

***Select water halftime from existed Tables*:**

$(k11+k12+k13+k14)=0.693/Tw$ [1]

Excretion of FH and OH in milk:

$MP*Mobh=k24*Aoh+k14*Afh+Iobh*(1-fo-fh)$ [2]
$MP*Mfh=k13*Afh$ → k13 (body FH to milk FH)

Equilibrium of Afh and Aoh →

$Afh*0.693/Tw=Ifh+Ioh*fh+k21*Aoh$ [3]
$Aoh*(k21+k24)=Ioh*fo+Afh*k12$ [4]

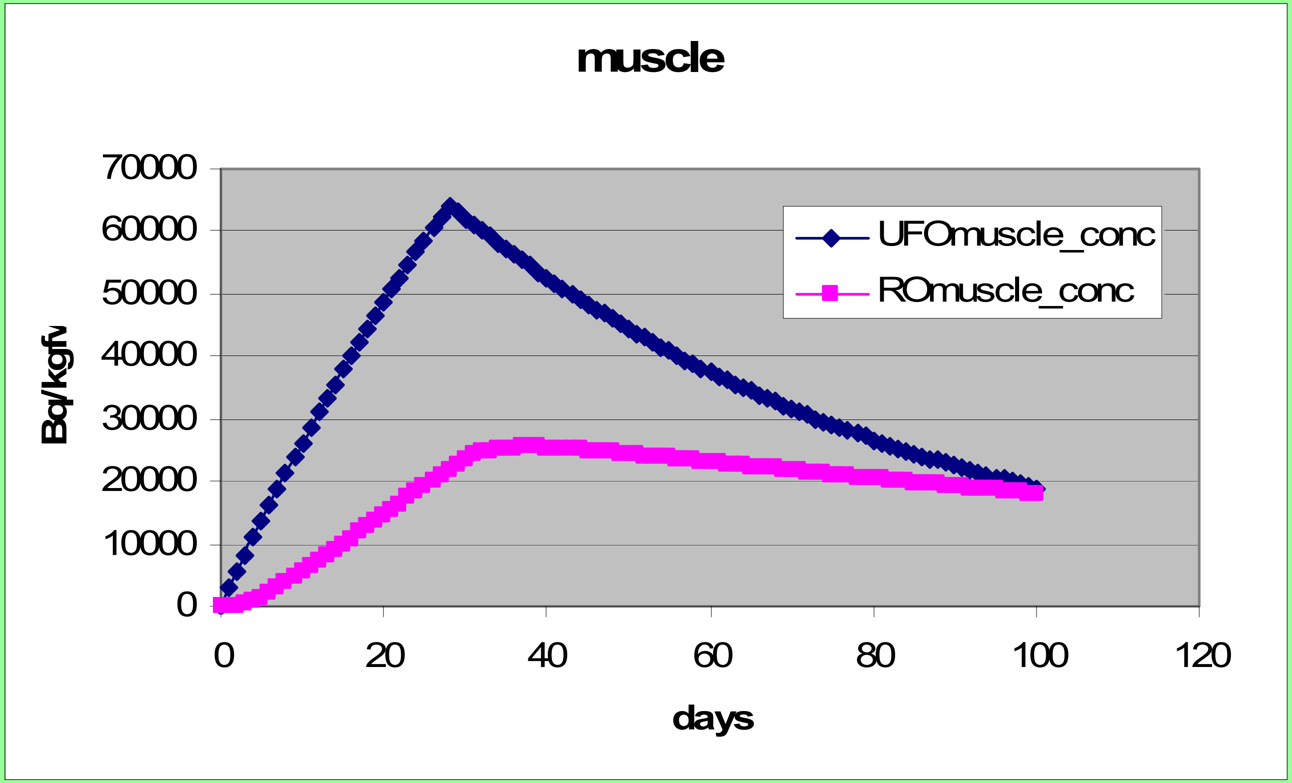
***Take K21 from MAGENTC* (**body OBH to body FH)

Adjust MAGENTC to Tw and constant mass, metabolic needs
Use MAGENTC Ioh as metabolisable oh intake and Ioh

Impose that x ~0.3 from Aoh comes from metabolism of Afh

$X*Aoh*(k21+k24)=Afh*k12$ [5]
[4]+ [5] → $(1-x)\ Afh\ K12=x*fh*Ioh$

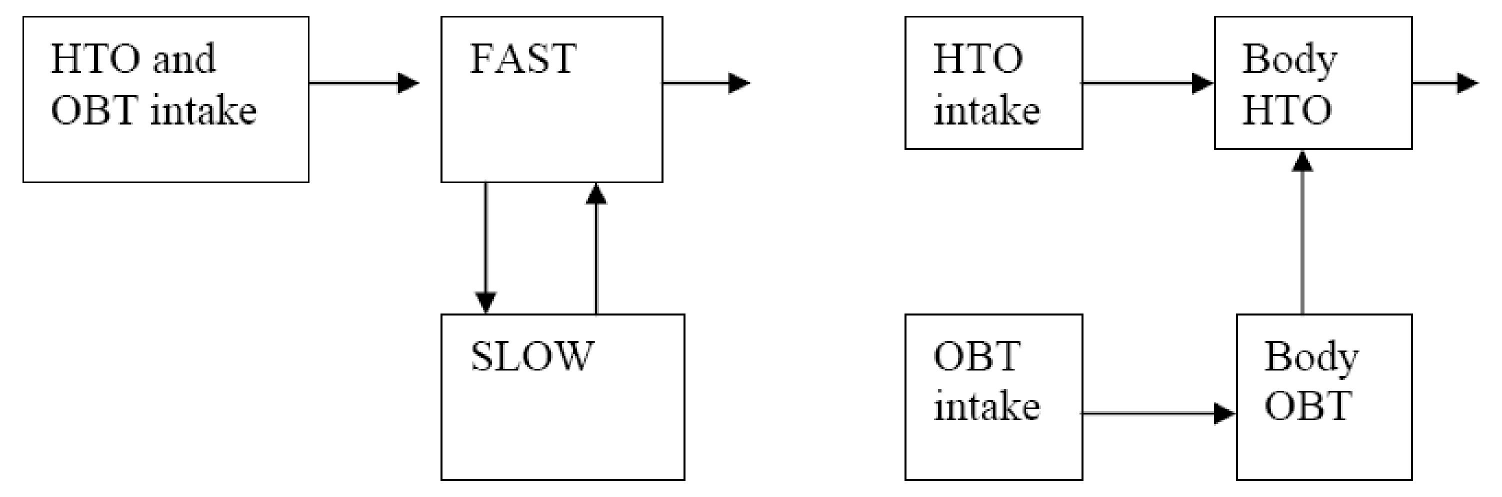
Comparison between UFOTRI and MAGENTC for OBT concentration in muscle



We must follow the previous steps and **hope for the best!!!**

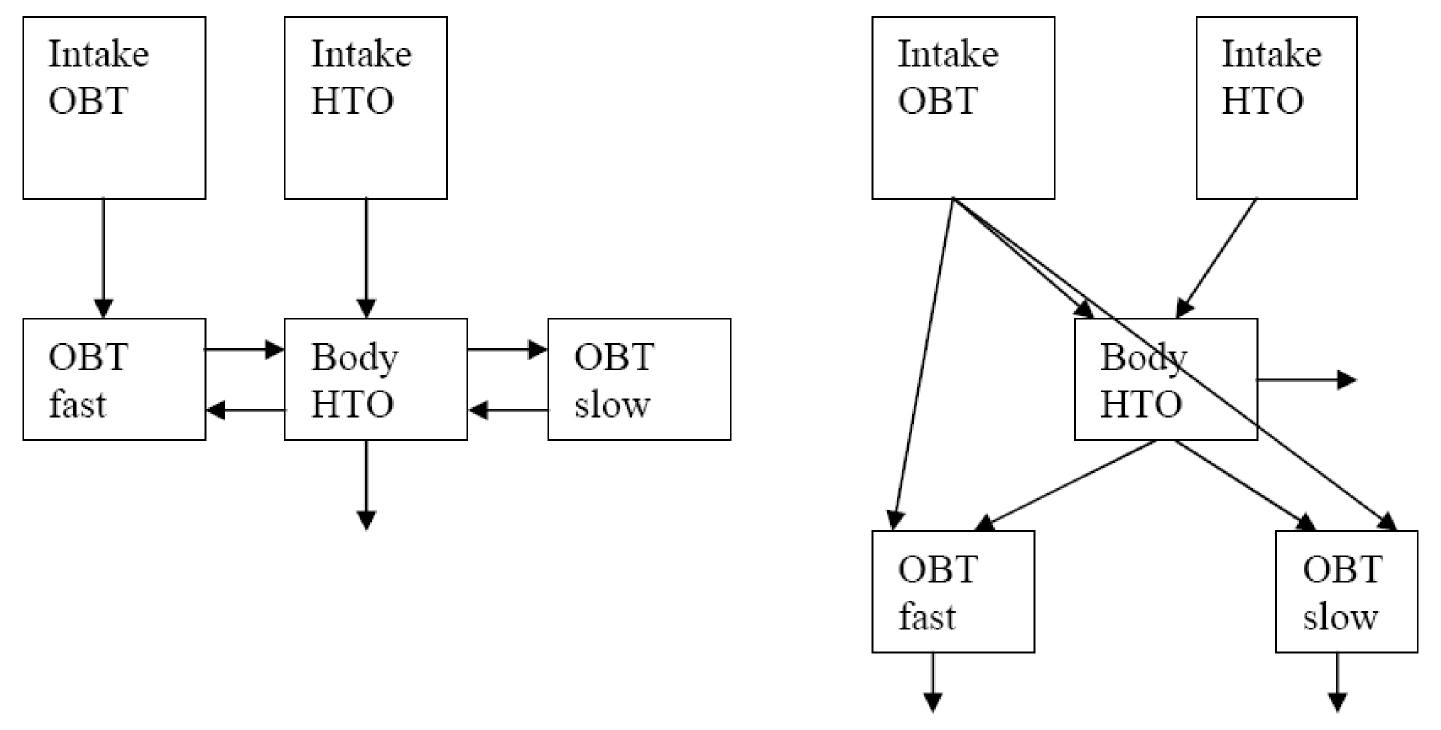
Pig case (EMRAS Scenario)

Flowchart of the simple models STAR (on the left) and OURSON (on the right)



- STAR sends all organic intake to body water → it overpredicts total tritium concentrations in urine and underpredicts OBT concentrations in pig organs.
- OURSON sends all organic intake to the body OBT compartment → it underestimates total tritium concentrations in urine and HTO concentrations in meat, and overestimates OBT concentrations in organs.

Flowchart of the models MCT (on the left) and PRISM (on the right)



- MCT does not consider the fraction of input organic tritium that is directly absorbed in the body OBT → explains the under prediction in urine.
- Both models have fast and slow OBT compartments but:
    - MCT transfers catabolic OBT to body water, whereas
    - PRISM transfers it out of the body, which is perhaps an oversimplification.

CONLUSIONS

- A simple but robust model for dairy farm animals can be developed starting from UFOTRI, but using MAGENTC's data base and results;
- A simple, but robust model for meet production can be developed, but this needs more work and collaboration;
- The experimental data base collected in IFIN is available, because models' tests are mandatory for parsimonious approach.

Thank you!