# A dynamic mathematical model to study the flexibility of energy reserves in adipose and muscle cells

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INRA SCIENCE & IMPACT

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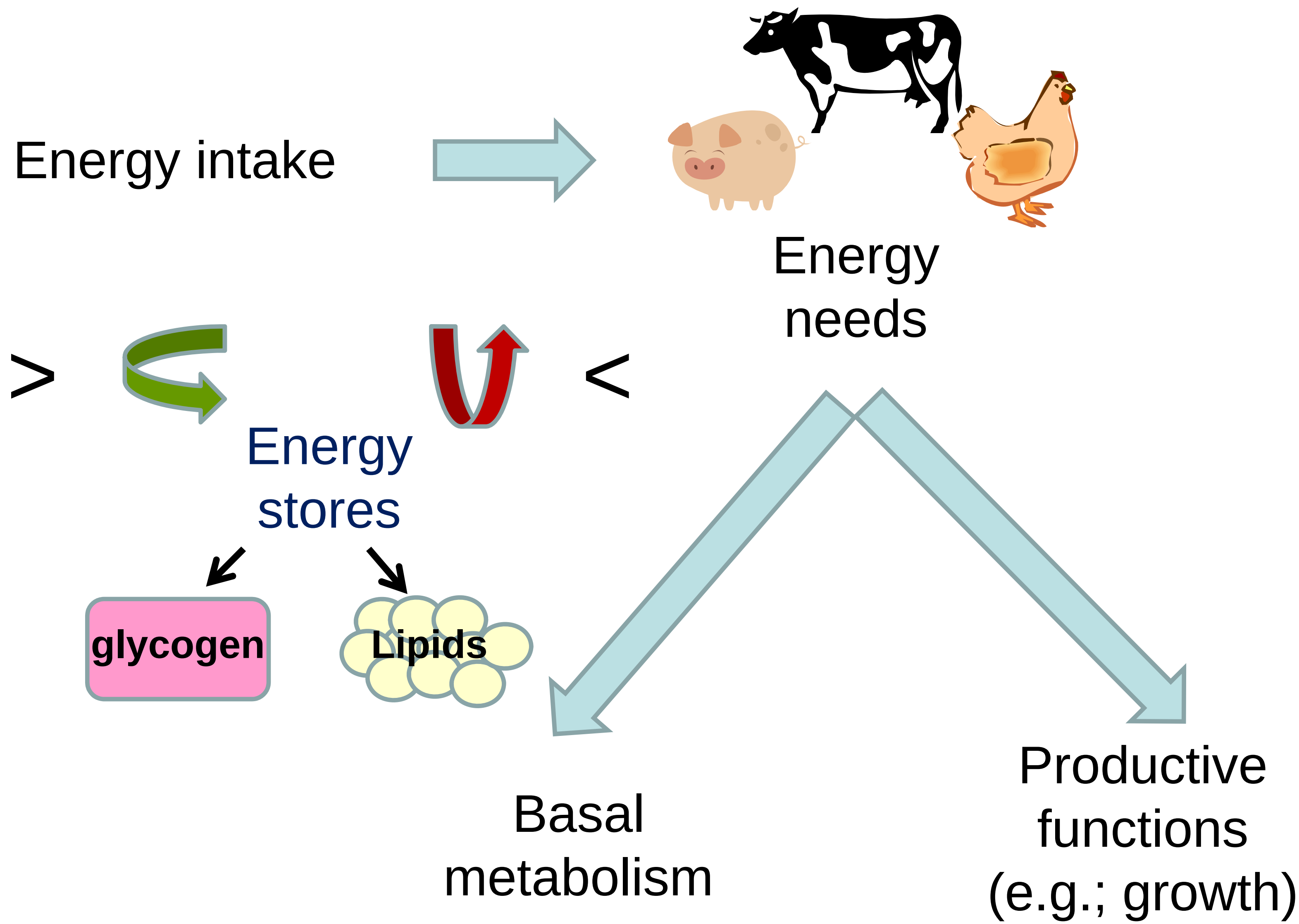
AGRO CAMPUS OUEST



Energy intake
Energy needs
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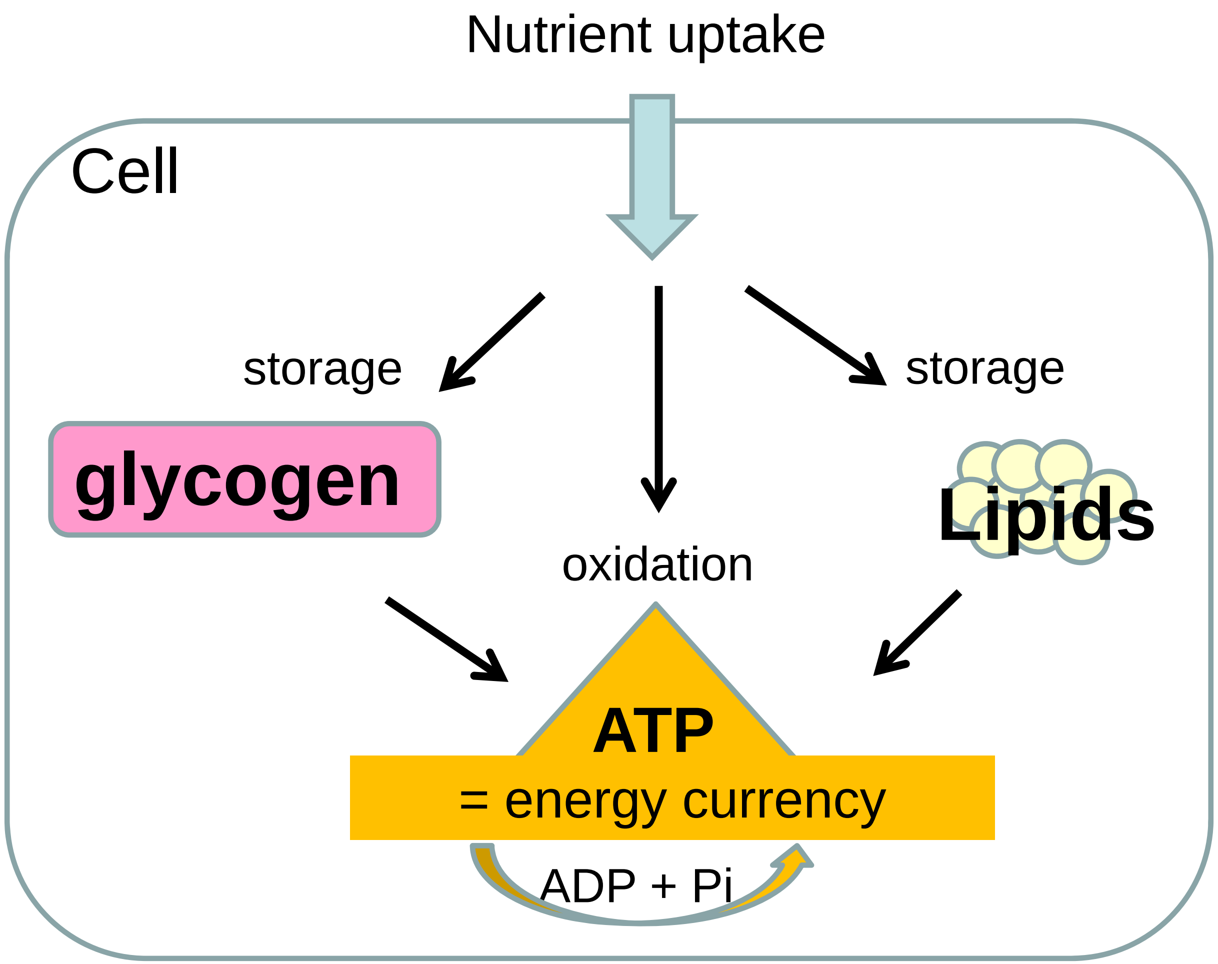
Energy stores
glycogen
Lipids
Basal metabolism
Productive functions (e.g.; growth)


- Context

# Flexibility of energy reserves: a key for animal production




Cellular (metabolic) efficiency

Tissue composition (production quality)

- Context

# Flexibility of energy reserves is controlled by a complex biochemical network

Difficult to be simply unraveled by mind

- **Inter-connections** between glucose and fatty acid pathways
- Nutrients, enzyme equipment and intracellular/extracellular signals influence the **reaction rates**
- **Time** after each nutrient load (meal) is likely important for the type & amount of cell energy stores

- Aim

Developing a **dynamic** mathematical **model** to investigate and predict the **plasticity of energy stores** into **animal cells** (adipose cells and muscle fibers)

- Aim

**Metabolism within a cell is a succession of reactions,** including mass transfers and enzyme activities regulating reaction rates

$$GLC + \overset{v_{HK}}{HK} \rightarrow G6P + \overset{v_{PGI}}{PGI} \leftrightarrow F6P + \overset{v_{PFK}}{PFK} \rightarrow G3P + \overset{v_{PK}}{PK} \rightarrow PYR$$

glucose pyruvate

**Variables in the model are the concentrations of the different metabolites**

GLC, G6P, F6P, G3P, PYR…

**Mathematical laws are ordinary differential equations** (dx(t)/dt) to represent Michaëlis-Menten kinetics

**Initial conditions are defined** GLC (t0), GLYCOGEN (t0)…

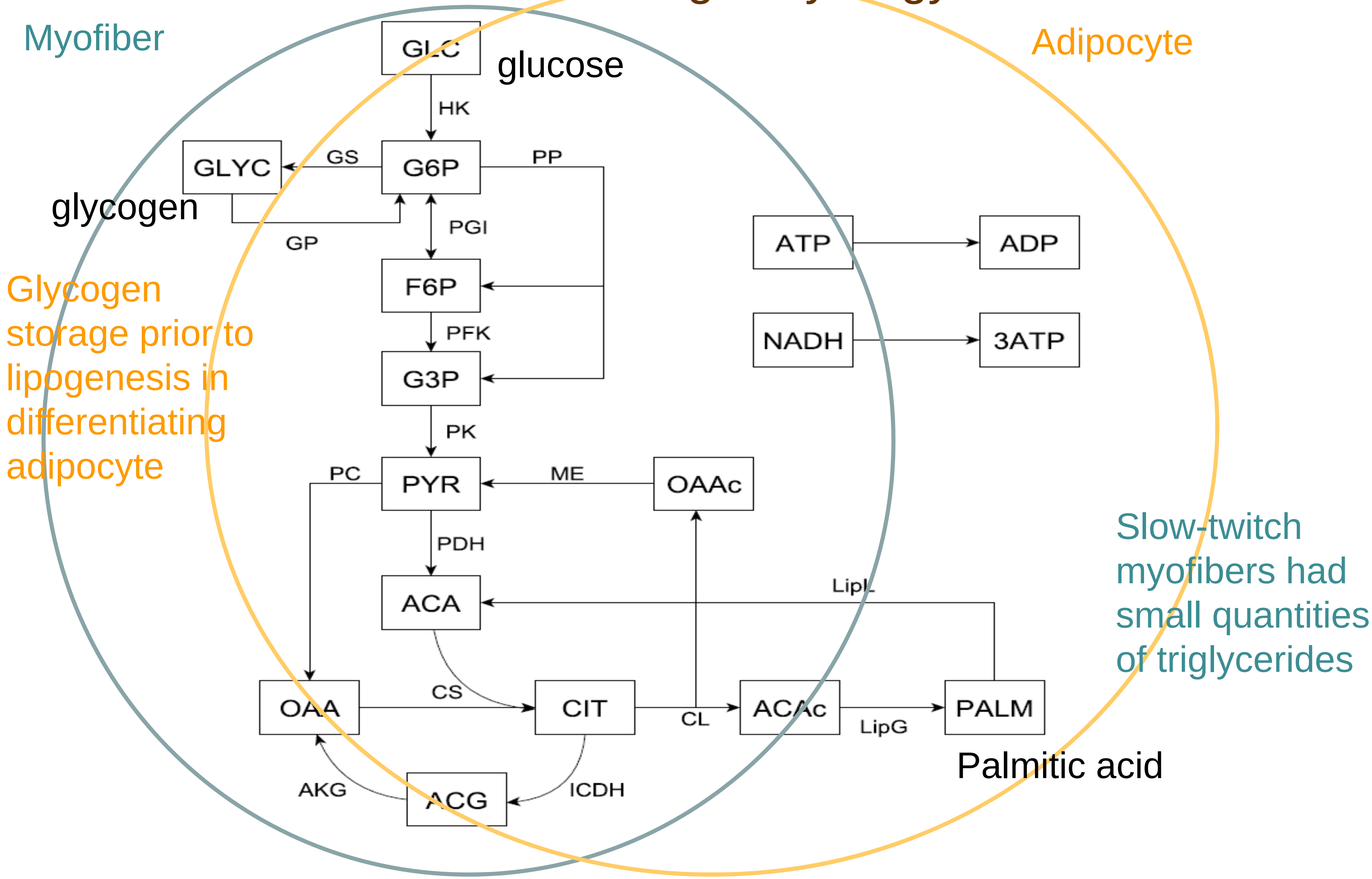
**There are also constants in the model** Glycogen_max,…

Constants can be changed before each simulation, according to the type of cell considered:

e.g.; **Glycogen_Max**: 8% for liver; 4% for muscle, 0.6% for adipose tissue

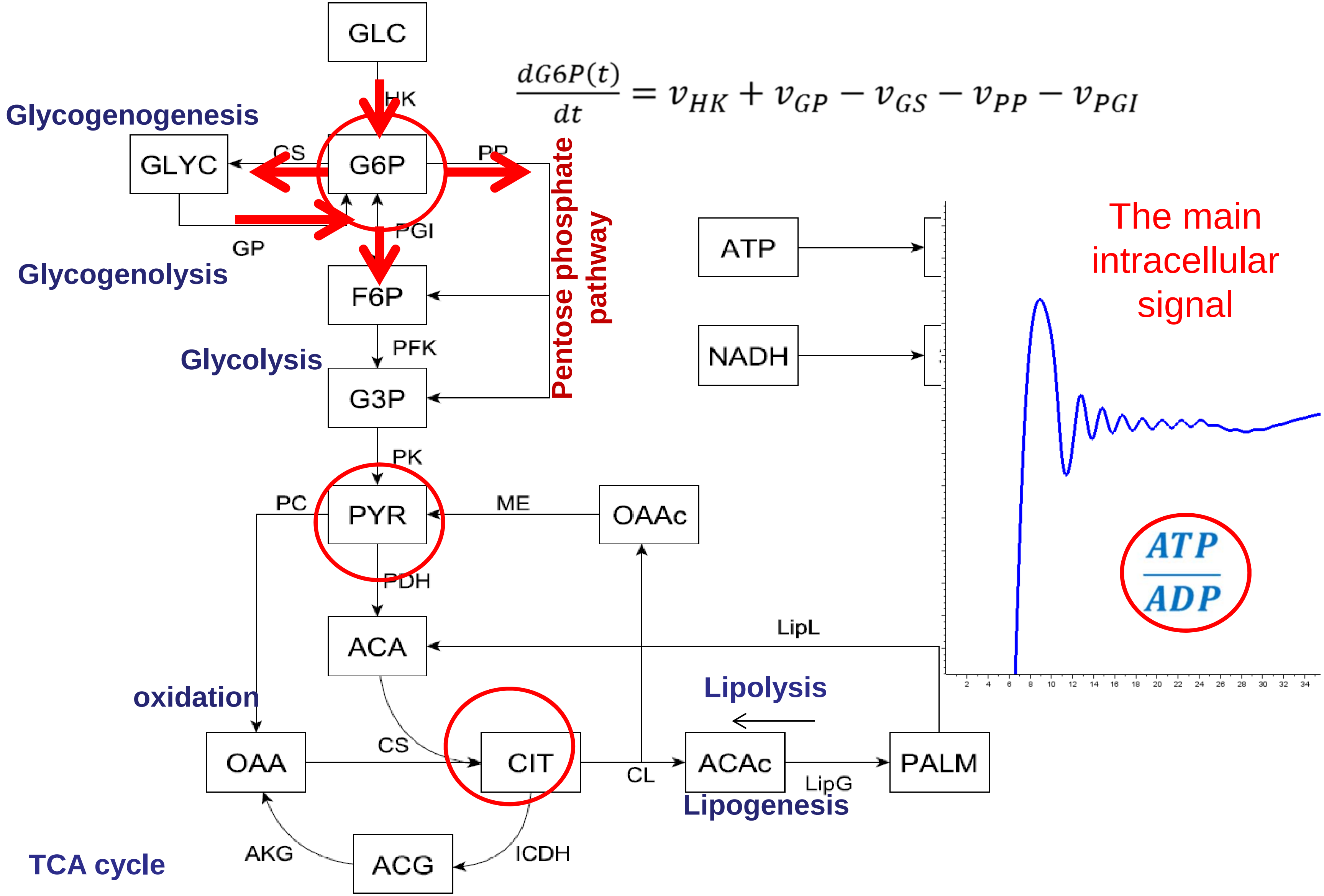
- M&M

# The model can be viewed as the superposition of two cells functioning in synergy



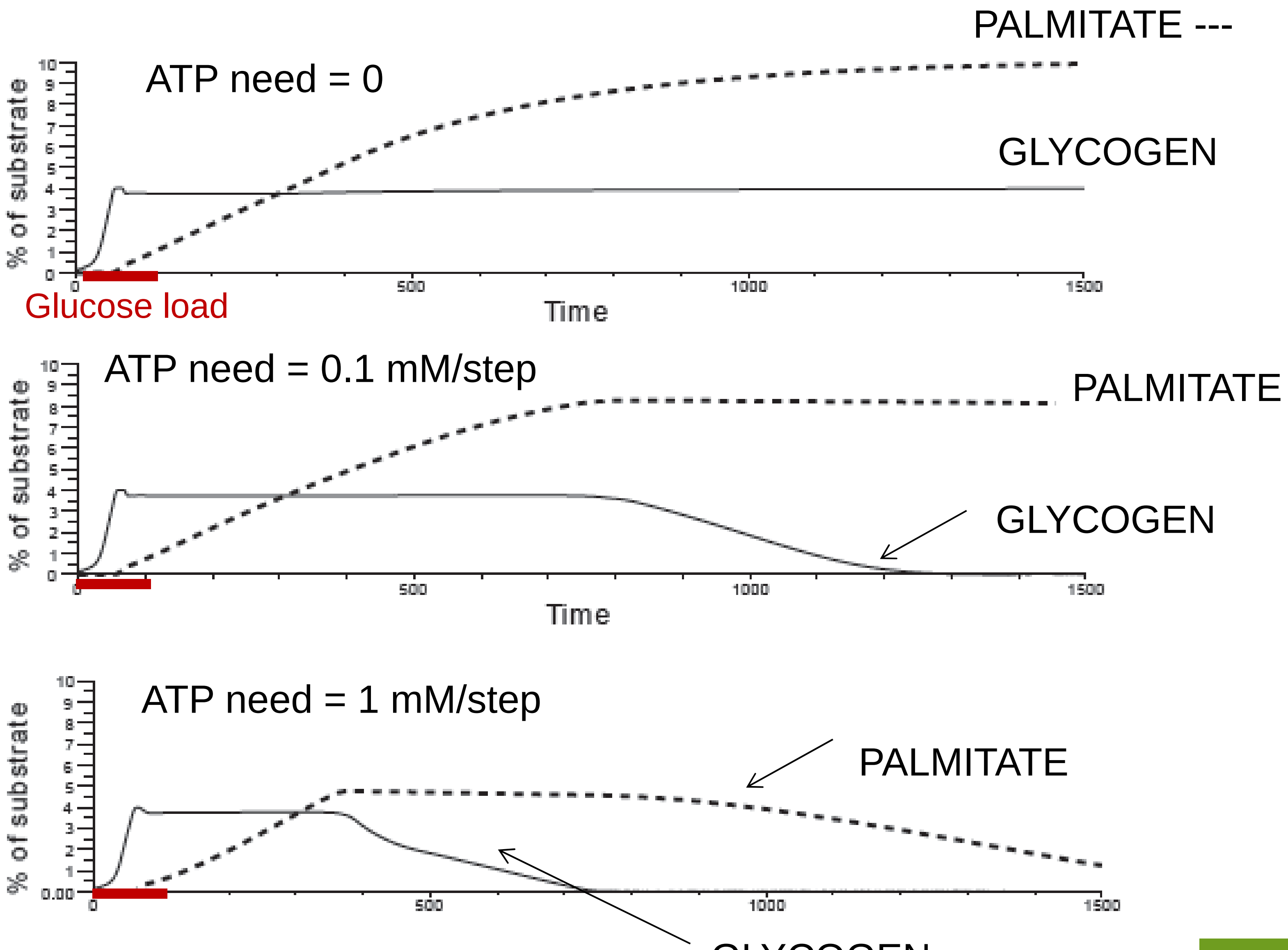

- M&M

$$\frac{dG6P(t)}{dt} = v_{HK} + v_{GP} - v_{GS} - v_{PP} - v_{PGI}$$



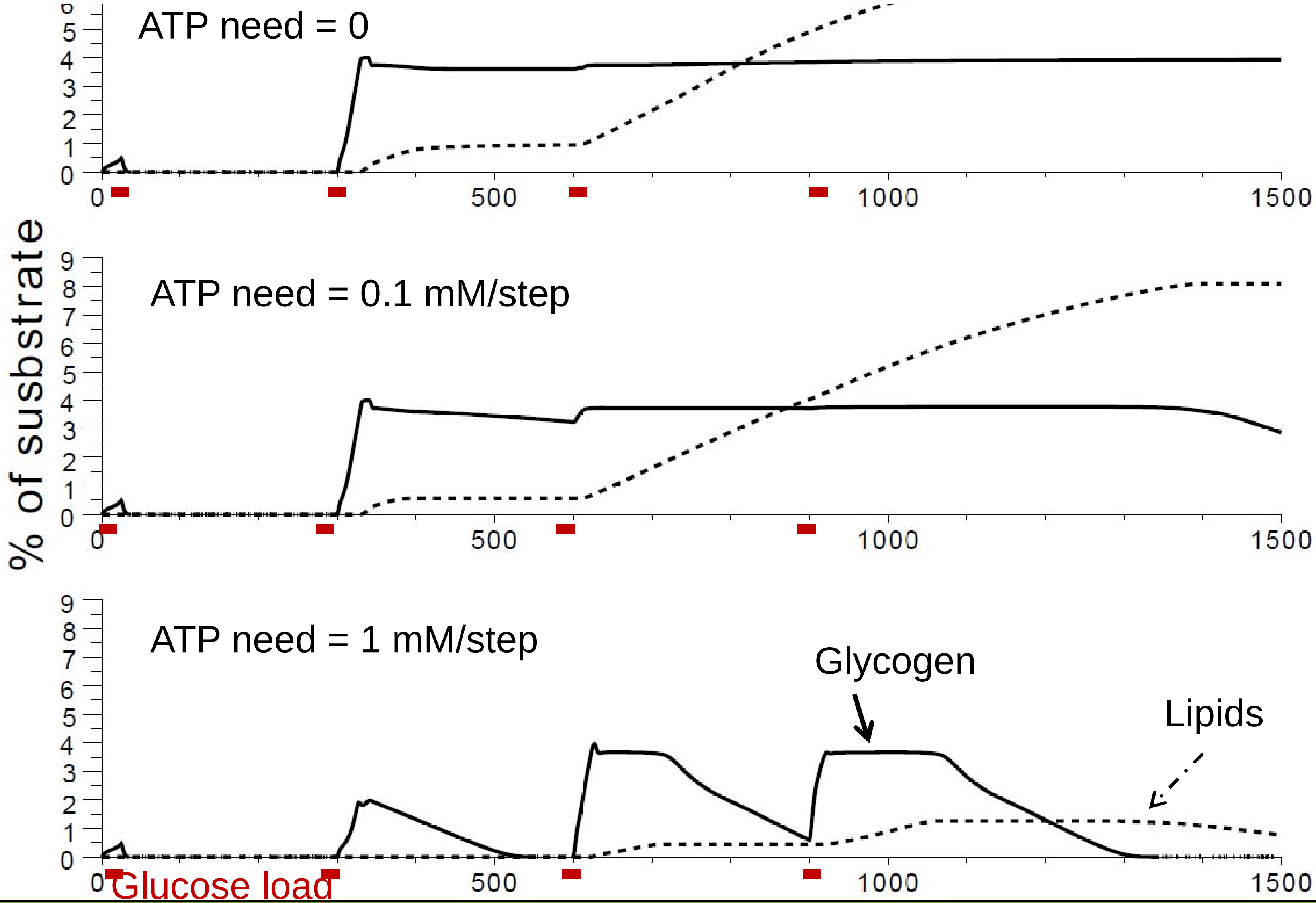

- M&M

Considering a single input of glucose during the first 100 steps (total =100 units per simulation). Simulation lasts 1500 steps



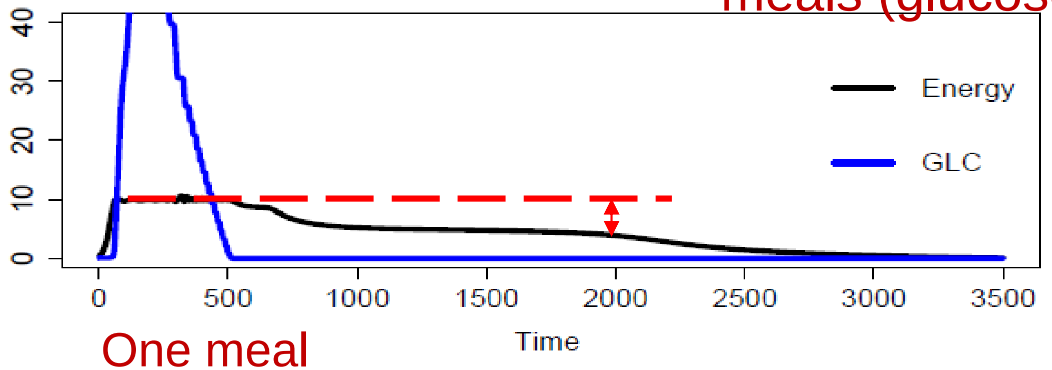

- Results

# Considering a discontinuous uptake of glucose
# (25 units by meal, total 4 meals per simulation = 100 units)



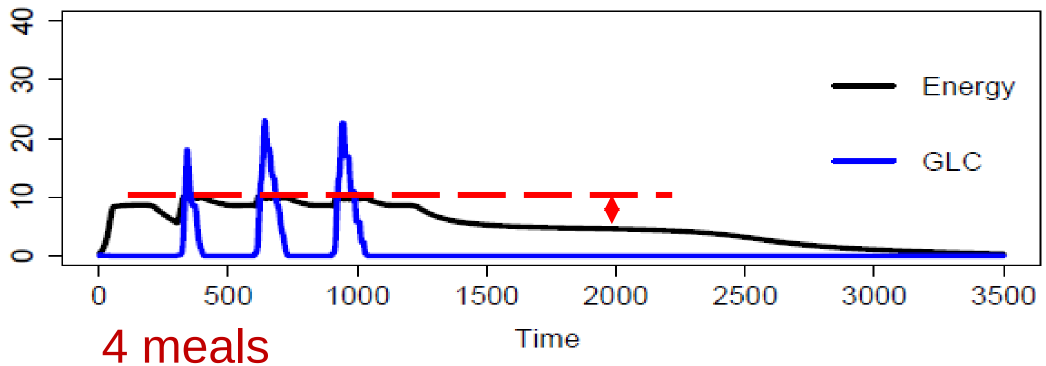

- Results

# Model prediction: availability of energy according to number of meals (glucose) per day




One meal

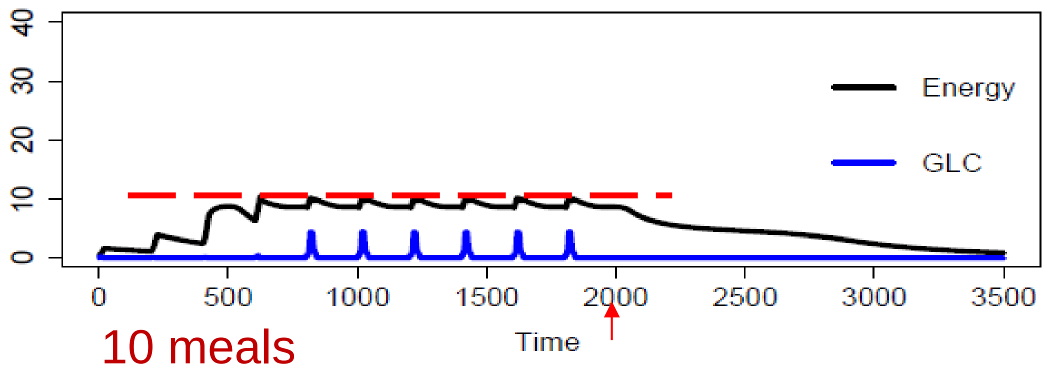
**Available energy was higher with more frequent meals rather than with one daily input**




4 meals

This was due to the fact that storage of lipids is less efficient than storage in glycogen

Nibbling subjects would be theoretically leaner than single-meal eaters




10 meals

❖ The model is generic and phenomenological

❖ It allows understanding and predicting the effects of types (providing different sources of energy: carbohydrates / lipids) and number of meals on energy reserves within cells

❖ Different scales can be considered, so that the model allows investigating different hypotheses in farm animal production:

☺ postprandial metabolism and energy use
(= fast dynamics)

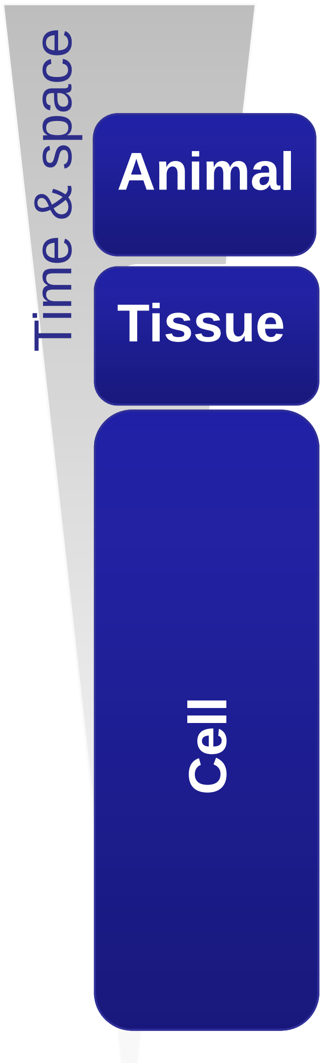
😐 management of energy reserves along animal growth
(= slow dynamics)

By changing ATP requirements and model parameters

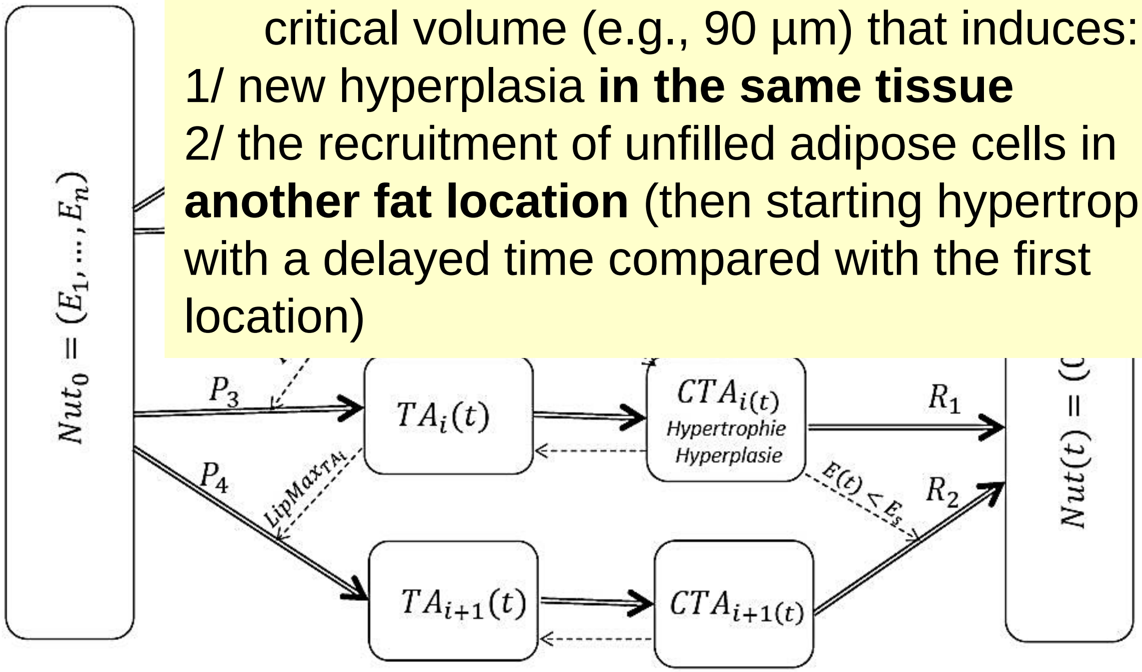
- Conclusion

By partitioning energy between priority tissues, lean and other tissues according to growth stages

(cf existing models such as *BeefBox Mecsic, Agabriel et al; INRA¨Porc in pig)*




By introducing cell hyperplasia and hypertrophia




Storing lipids into cells during simulation leads to hypertrohy of existing adipose cells until a critical volume (e.g., 90 µm) that induces:

1/ new hyperplasia **in the same tissue**

2/ the recruitment of unfilled adipose cells in **another fat location** (then starting hypertrophy with a delayed time compared with the first location)

nb(t + 1) = nb(t)(1 + H(LipmaxC - LipC (t)))

- Further development