



Mathematical Modelling of Bovine Fertility and Metabolism



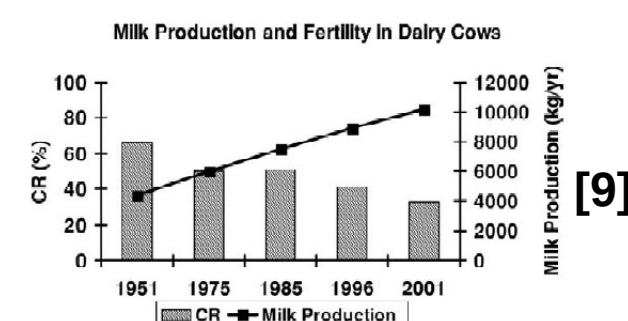
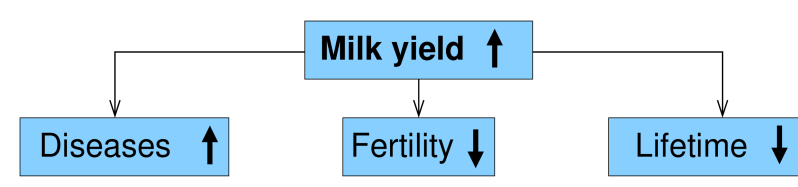
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Motivation

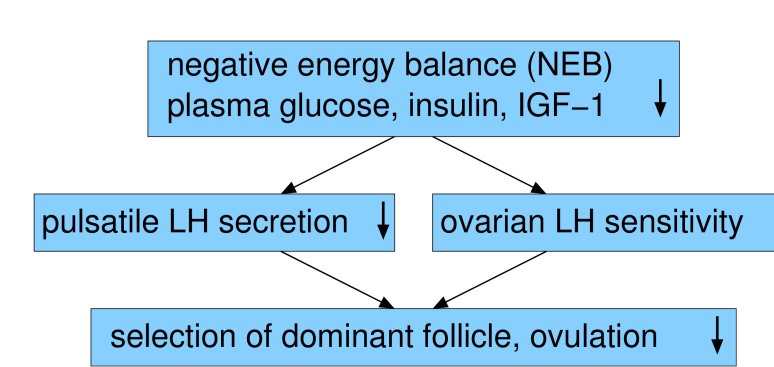
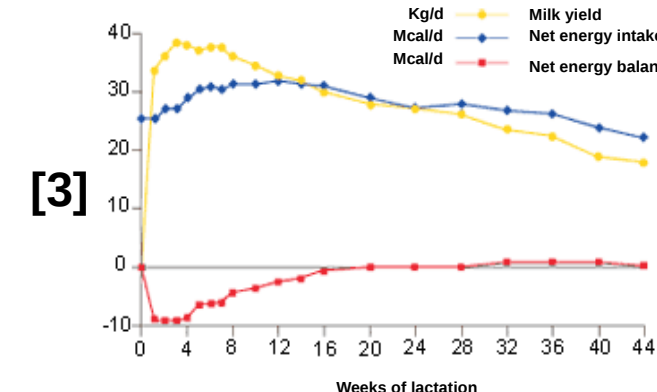
Milk yield and Fertility in Dairy Cows

Over the past 50 years, dairy industry has successfully improved milk production by increasing the milk yield of individual cows. However, increased capacity for milk production in dairy cows has been associated with a decline in fertility, an increase in metabolic problems and disease incidence [9]. The reasons for the decline in fertility are complex and not completely understood.



Metabolism and Fertility

Energy balance has been shown to be one of the most important factor that influences fertility in dairy cows. Nutritional requirements increase rapidly with milk production, resulting in a negative energy balance. This is strongly associated with the length of anovulatory period through an attenuation of the LH pulse frequency and lower levels of blood glucose, insulin and IGF-I [9].



Our Goal

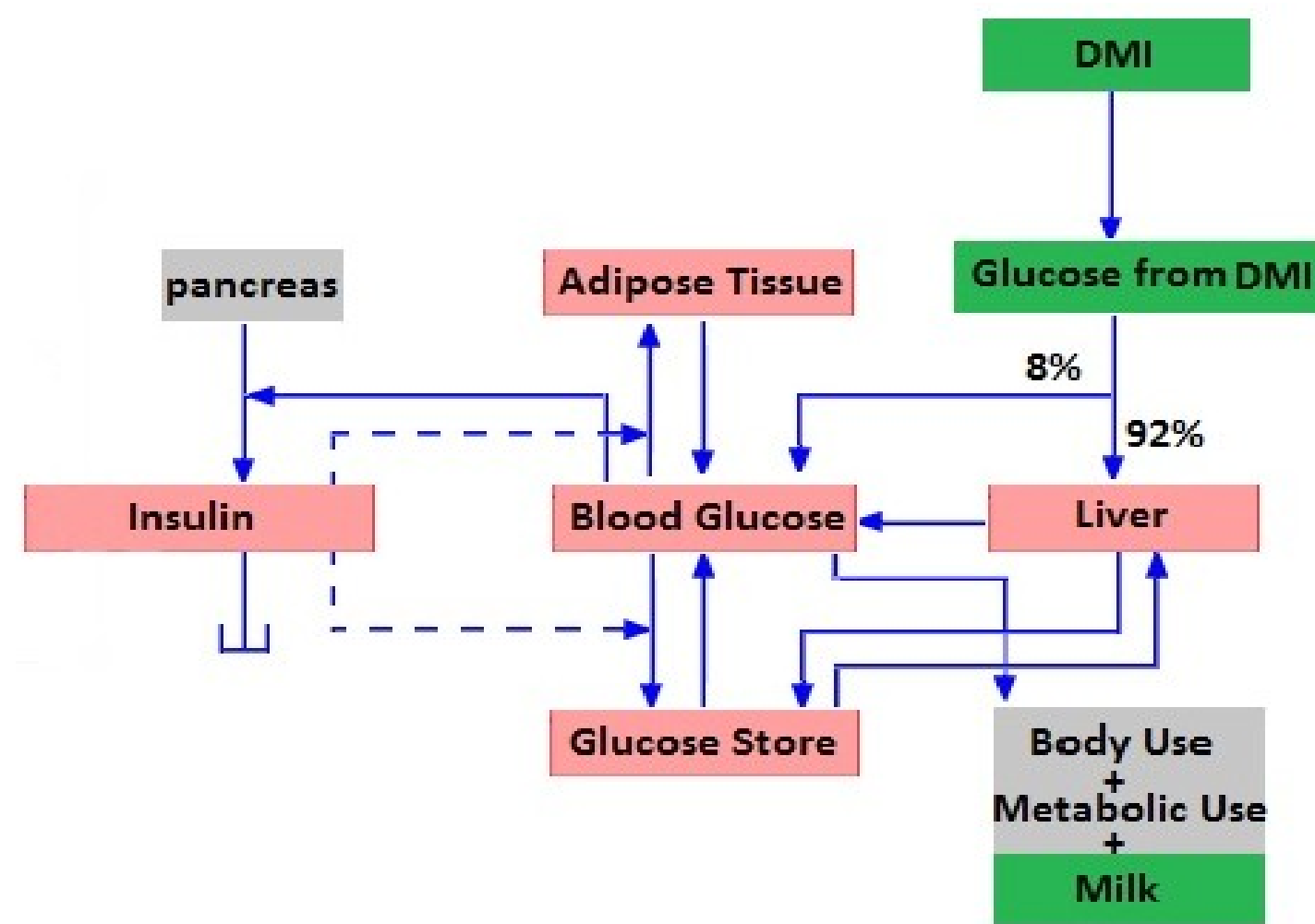
Formulating a mechanistic mathematical model that takes into account interactions between:

- nutrition,
 - milk yield,
 - fertility
- in lactating dairy cows to understand the underlying physiological/biological processes that contribute to low fertility and develop strategies to improve fertility.

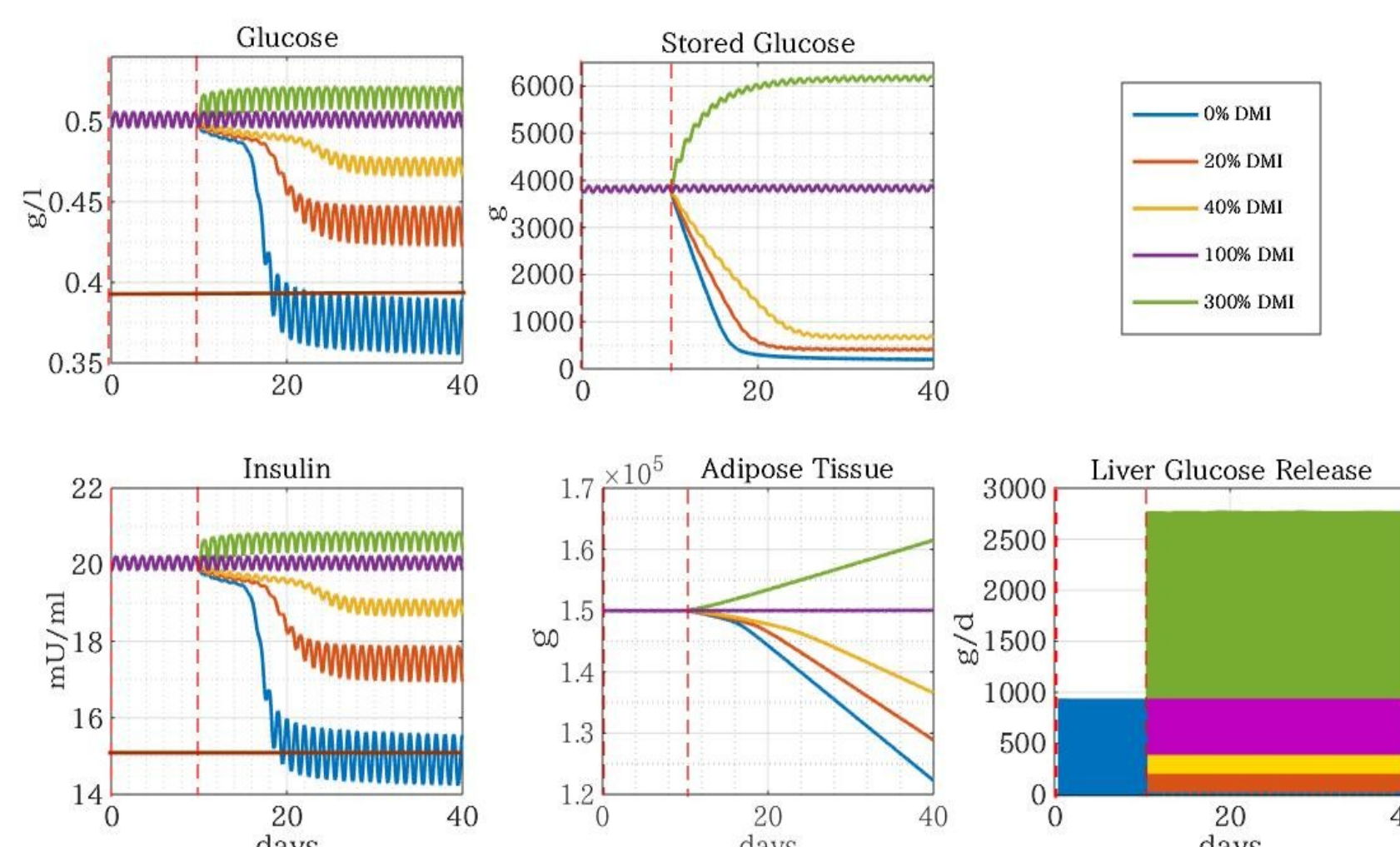
Metabolism

Glucose-Insulin Metabolism in Bovine model [4]

- 5 state variables (red boxes): 5 ODEs with 25 parameters.
- Model input (green boxes): Dry matter intake 'DMI' and milk yield.

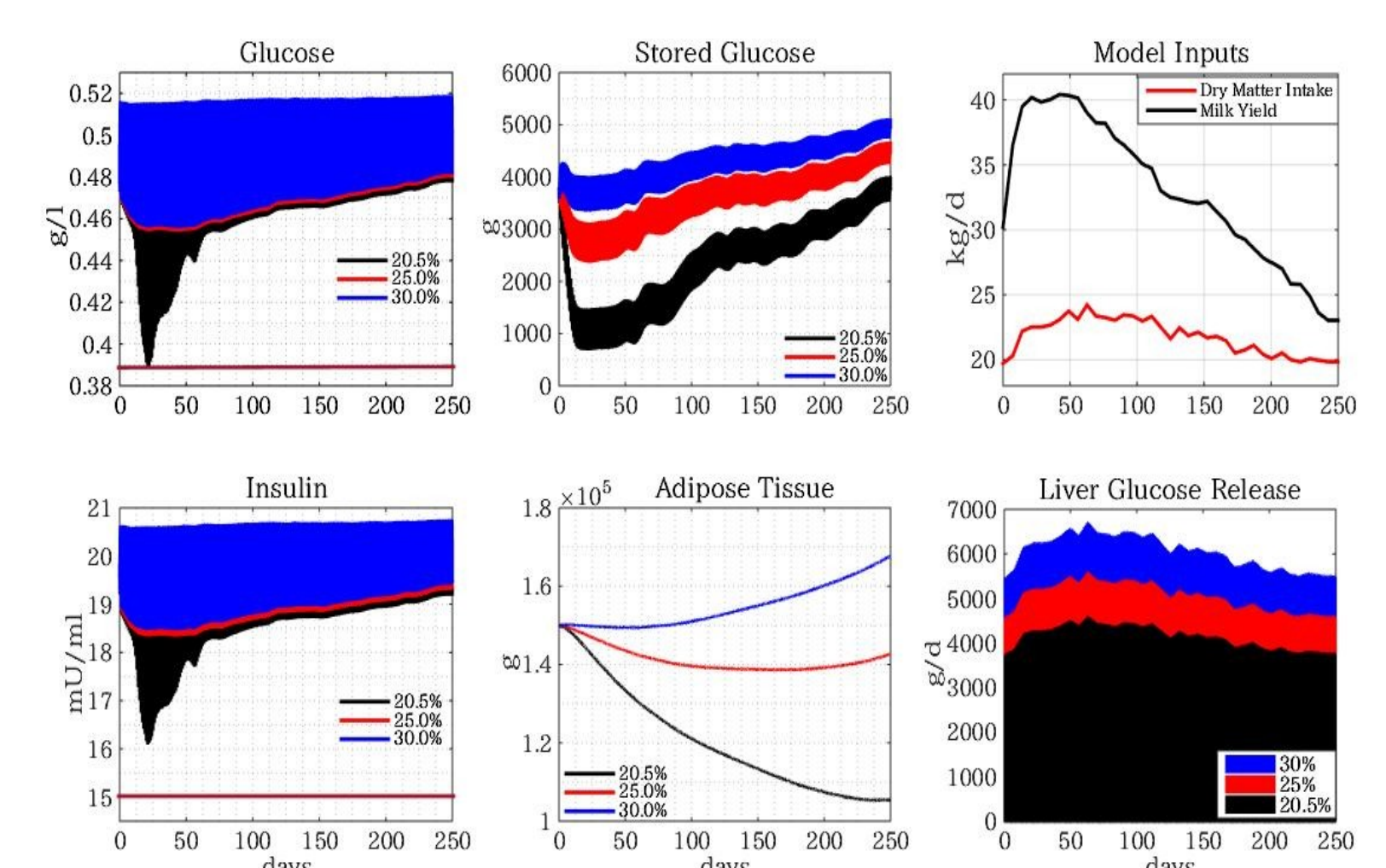


Non-lactating Cows



Glucose-insulin dynamics with different dry matter intake 'DMI' fractions. First 10 days (between two red dashed line) is the standard feeding, i.e. 100% DMI. Lower bound of glucose and insulin concentration is depicted by the brown horizontal line.

Lactating Cows



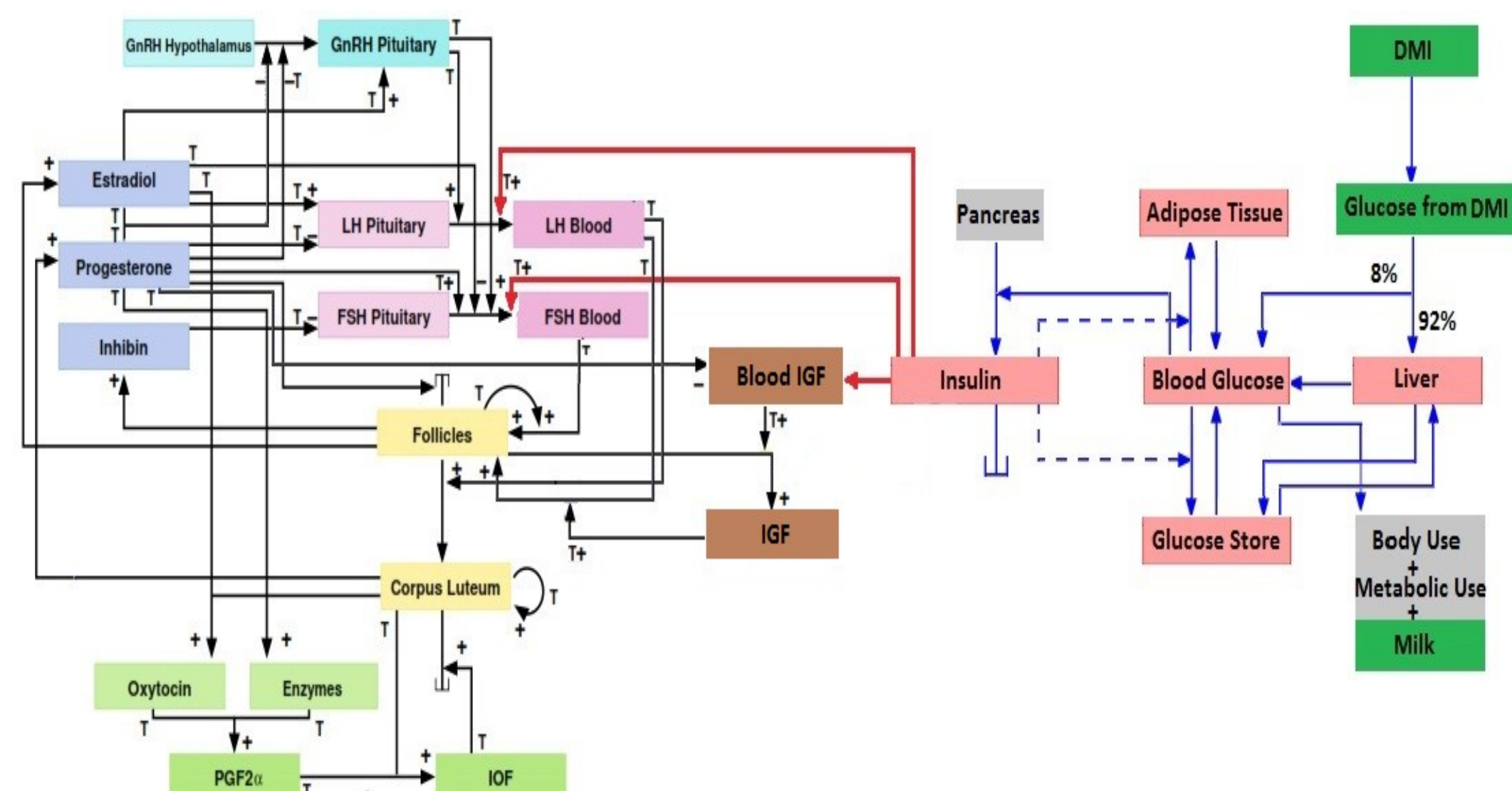
Glucose insulin dynamics throughout the lactation period. Percentages indicate different fractions of glucose content in the dry matter intake 'DMI'. Lower glucose content leads to negative energy balance due to high milk production.

Fertility

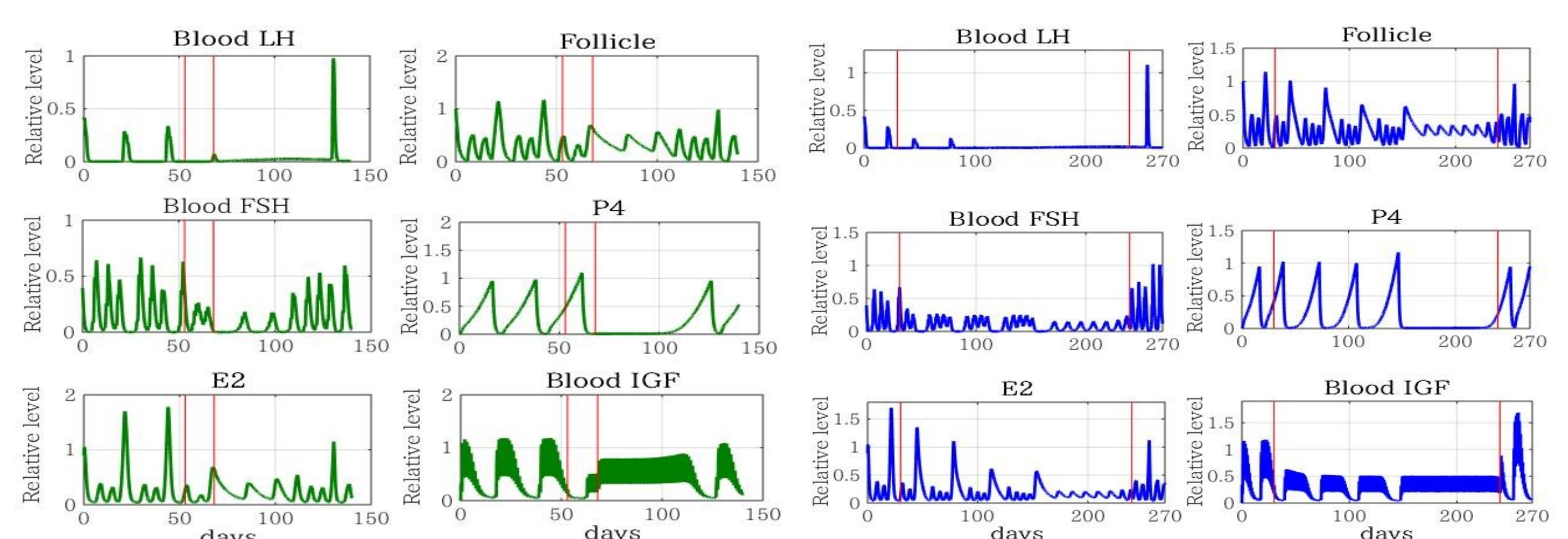
BovSys Model: metabolism model coupled with estrous cycle model [2],[5]

Hypothesis:

- Insulin serves as a metabolic signal influencing LH release by the anterior pituitary [7].
- Insulin and IGF-I can act at the level of the hypothalamus to stimulate GnRH secretion and therefore control the release of LH and FSH [6].
- IGF-I are positively correlated with the level of feed intake [1].
- Loss of appetite and decreased feed intake reduce blood insulin and IGF-I [6].
- IGF-I enhances the follicular cell responsiveness to LH [8].
- Plasma IGF concentration increases transiently during the follicular phase and decrease during the luteal phase of the ovarian cycle [1].



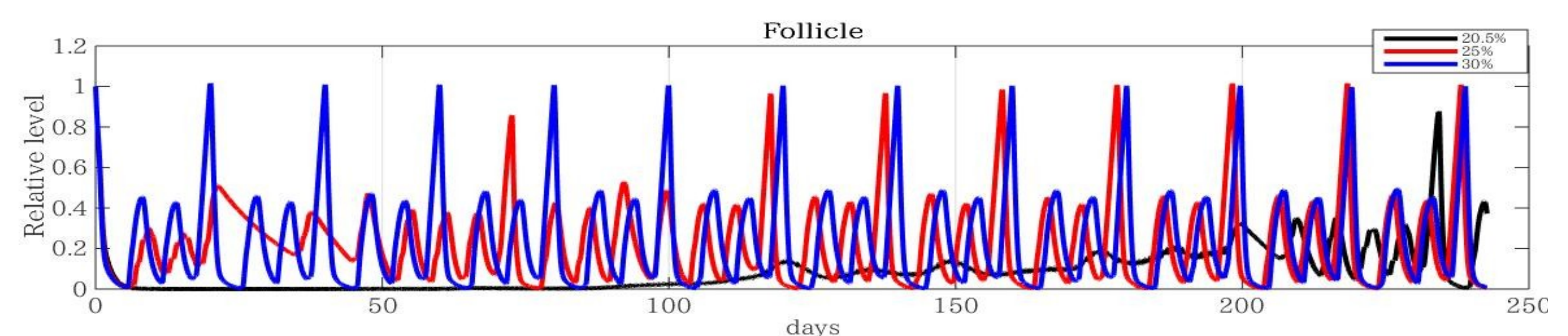
Non-lactating Cows



Effect of acute dietary restriction, i.e. 40% of DMI within 15 days on the estrous cycle. Restriction period is bounded between the two red lines. Immediate failure of the follicle to ovulate after 15 days of acute dietary restriction.

Effect of chronic dietary restriction, i.e. 70% of DMI within 30 weeks on the estrous cycle. Restriction period bounded between the two red lines. Cow becomes anestrus after a long term dietary restriction.

Lactating Cows



Follicular waves corresponding to different fractions of glucose content in DMI throughout the lactation period. Lower glucose content results in a prolonged anovulatory anestrus.

Outlook

- Pharmacological treatment: Implementing a PK/PD model to evaluate different scenarios of hormonal elevation by the administration of: Insulin, IGF.
- A bifurcation approach to analyse the follicular waves period.
- Development of new mathematical algorithm for efficient parameter identification from experimental data in periodic systems.

References

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