

Mathematical model of the bovine oestrous cycle

HMT Boer^{1,2}, C Stötzel³, S Röblitz³, P Deuflhard³, RF Veerkamp¹, H Woelders¹

¹Animal Breeding and Genomics Centre, Wageningen UR Livestock Research, Lelystad, Netherlands, ²Adaptation Physiology Group, Department of Animal Sciences, Wageningen University, Wageningen, Netherlands, ³Zuse Institute Berlin, Department of Numerical Analysis and Modeling, Research Group Computational Drug Design, Berlin, Germany
Email: marike.boer@wur.nl

Introduction Systems biology aims at understanding how the various components of a biological system function together, rather than investigating individual parts. One approach is the translation of a conceptual biological model into a set of mathematical equations that represent dynamic relations between system components. The purpose of building such mathematical models is to interpret and predict dynamics of complex biological systems, and to identify new research questions. One example of a dynamic biological system is the bovine oestrous cycle. Regulation of the cycle is controlled by numerous factors, interacting through feedback loops. Therefore, it is hard to obtain insight in the dynamics of the system by describing isolated parts. Mathematical modelling of the involved mechanisms is expected to improve insight in biological processes underlying female reproduction, and could thereby help to find causes of declined fertility in dairy cows (Boer *et al.*, 2009). Such a model is recently developed for the human menstrual cycle (Reinecke and Deuflhard, 2007). The objective of this work was to develop a mechanistic model that simulates the dynamics of the bovine oestrous cycle at individual cow level.

Material and methods The model was constructed by first defining a number of key components of the system and their interactions, which were represented in a flow chart. Subsequently, a set of differential equations were derived to describe the relations mathematically. Time delays were incorporated when appropriate, to capture the time needed for factors to influence each other. Hill functions were used for modelling of inhibitory and stimulatory effects of hormones.

Results The current model comprises a mathematical representation of follicle development and accompanying fluctuations in hormone concentrations in a cycle with three follicular waves. The main organs involved in the regulation of the oestrous cycle are the ovaries, hypothalamus and pituitary. These organs interact via hormones in the blood (Figure 1). Differential equations describe the control of the hormones oestradiol (E2), progesterone (P4), gonadotropin releasing hormone (GnRH), luteinizing hormone (LH), follicle stimulating hormone (FSH), inhibin (Inh) and prostaglandin (PGF2 α) on the growth of follicles and CL. Simulations show that the model is able to describe the system consistent with empirical data for cows (Figure 2).

Conclusions This model could help in understanding the dynamic regulation of the bovine oestrous cycle. It is expected that this model will serve as a basis for more elaborate models and simulations, with the ability to study effects of external manipulations and genomic differences. Possible extensions of the model could be in the field of energy metabolism, stress, and factors affecting the expression of oestrous behaviour. The model can be used to determine the level of control exerted by various system components on the functioning of the system. Further, hypothesised causes of declined fertility in dairy cows could be tested by changing model parameters.

References

Boer HMT, Woelders H, Beerda B and Veerkamp RF. 2009. Estrous behavior in dairy cows: identification of underlying mechanisms and gene functions. *Animal*. Article in press. DOI: 10.1017/S1751731109991169.
Reinecke I and Deuflhard P. 2007. A complex mathematical model of the human menstrual cycle. *Journal of Theoretical Biology* 247, 303-330.

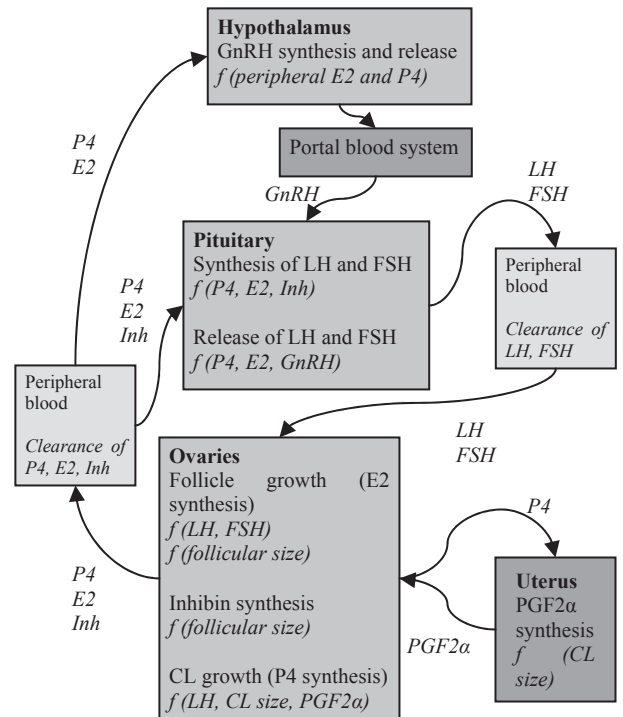


Figure 1 Schematic representation of the dynamic model of the bovine oestrous cycle. Each process is represented by a set of differential equations, indicated by $f(\dots)$.

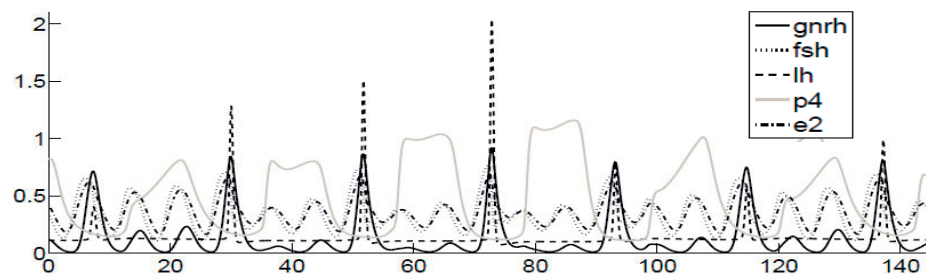


Figure 2 Preliminary simulation result, showing hormone fluctuations in consecutive cycles.