Ninth Workshop Dynamical Systems Applied
to Biology and Natural Sciences DSABNS 2018
Turin, Italy, February 7-9, 2018

GENE AND HORMONE REGULATORY MATRICES AS A TOOL TO DESCRIBE mRNA AND HORMONE CONCENTRATIONS IN PRIMARY CULTURES OF BOVINE GRANULOSA CELLS

Malgorzata J. Wieteska[1]*, Leo Creedon[1], John A. Hession[1],
Katarzyna K. Piotrkowska-Tomala[2], Agnieszka Jonczyk[2],
Pawel Kordowitzki[2] and Dariusz J. Skarzynski[2]

[1]Institute of Technology Sligo, Ireland

[2]Institute of Animal Reproduction and Food Research,
Polish Academy of Sciences in Olsztyn, Poland

algorzata.Wieteska@mail.itsligo.ie (*corresponding author), creedon.leo@itsligo.ie, hession.john@itsli
k.piotrowska-tomala@pan.olsztyn.pl, a.jonczyk@pan.olsztyn.pl, p.kordowitzki@pan.olsztyn.pl,
d.skarzynski@pan.olsztyn.pl

Bovine ovarian follicles contain a layer of granulosa cells which produce two hormones: estradiol (E2) and progesterone (P4). E2 and P4 are the main hormones responsible for regulation of the growth and decay (atresia) of the follicles and for ovulation. The information required for the production of these two hormones is communicated through mRNA concentrations of enzymes involved in the steroidogenesis pathway [4], [5]. We have created models of mRNA and hormone concentrations in the granulosa cells.

The data used to build these models was obtained from *in vitro* primary cultures of bovine granulosa cells with data collected every 8 hours for 24 hours. The cells were stimulated by adding 50ng/ml IGF-1, 25ng/ml FSH or 100ng/ml IGF-1, 25ng/ml FSH and control. The granulosa cells were obtained from follicles of diameter $5-8$mm.

Gene Regulatory Matrices (GRMs) are a well known technique for modelling the interactions (promotion and inhibition) between genes [1], [3], [6]. This assumes that the process is a Markov

 ISBN: 978-989-98750-4-3

process. This technique is used here, but with genes and hormones, to create Gene and Hormone Regulatory Matrices (GHRMs). In addition, a network (a directed weighted graph) is constructed from the underlying interactions of several mRNA coding enzymes and receptors (BCL2, CYP $19A1$, HSD $3B2$, IGF 1rec, BAX, CYP $11A1$, FSHrec, HSD $17B1$, RIPK3, LH-rec, StAR) and two hormones (E2 and P4). Four such matrices/networks are presented, depending on environmental conditions (hormone supplementation regimes).

Apart from differential equations techniques (which require knowledge of rates of decay of proteins and mRNA) there is no existing technique to accurately predict the concentration of proteins based on the concentration of mRNA. This novel approach using GHRMs permits the use of three nodes/variables to accurately model the concentration of the remaining ones over 24 hours. The three nodes used are E2 (or HSD$3B2$), P4 (or CYP$19A1$) and IGF1R. This permits comparison of the strength of the impact of each of the three genes (or hormones) on the concentration of the genes responsible for the atresia of the follicles (BAX, BCL2), the gene directly responsible for progesterone production (HSD $3B2$) and genes directly responsible for estradiol production (HSD $17B1$, CYP $19A1$). This also permits comparison of the impact of each given environmental condition on E2 and P4 production in follicles with diameter $5 - 8$mm. This will also help to understand the role of IGF-1 in twinning since IGF-1 peripheral concentration is about 47% higher in twinning cows compared to control [2].

References

[1] *Defterli, Ozlem and Fügenschuh, A and Weber, Gerhard Wilhelm*. (2010) *New discretization and optimization techniques with results in the dynamics of gene-environment networks*, Conference: 3rd Global Conference on Power Control & Optimization, pp. 2-4.

[2] *Echternkamp, S.E., Spicer, L.J., Gregory, K.E., Canning, S.F. and Hammond, J.M*. (1990) *Concentrations of insulin-like growth factor-I in blood and ovarian follicular fluid of cattle selected for twins*, Biology of Reproduction, 43(1), pp.8-14.

[3] *Gebert, J and Lätsch, M and Pickl, SW and Radde, N and Weber, G-W and Wünschiers, R*. (2004) *Genetic networks and anticipation of gene expression patterns*, AIP Conference Proceedings 718(1), pp.474–485.

[4] *Miller, Walter L and Auchus, Richard J*. (2011) *The molecular biology, biochemistry, and physiology of human steroidogenesis and its disorders*, Endocrine reviews, 32(1), pp.81-151.

[5] *Nguyen, Phuong*. (2012) *Mathematical Modelling of Steroid Synthesis in Steroid-Producing Tissues and Steroid Partitioning in Circulation*, Doctoral dissertation, ResearchSpace@ Auckland.

 ISBN: 978-989-98750-4-3

[6] *Wang, Yong and Joshi, Trupti and Zhang, Xiang-Sun and Xu, Dong and Chen, Luonan*. (2006) *Inferring gene regulatory networks from multiple microarray datasets*, Bioinformatics, 22(19) pp.2413-2420.

 ISBN: 978-989-98750-4-3