DYNAMIC MODEL OF STOMATAL DEVELOPMENT AND PATTERNING WITH AUXIN REGULATION

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Keywords: Stomatal development, Cell-based modeling, Cell division, Auxin.

Stomata are specialized pores localized in the epidermis of leaves, stems and other plant organs. Their role is to control the gas exchange between the plant and the environment as well as to regulate plant transpiration. The stomatal pore is surrounded by two kidney-shaped guard cells which are the result of a symmetric cell division and differentiation event following one or more asymmetric cell divisions that are required to achieve proper spacing of the stomata. The main developmental question is what triggers the cell division and differentiation steps that lead to the formation of guard cells and the distribution of stomata in the plant epidermis. Experimental results in *Arabidopsis thaliana* suggest that the phytohormone auxin is involved in the regulation of the stomatal lineage pathway [1]. In order to gain a better understanding of the influence of auxin during stomatal development, we have set up mathematical models that link auxin activity with that of bHLH transcription factors known to be involved in cell division and differentiation during stomatal patterning. Using appropriate auxin thresholds, which control the cell differentiation transitions, we generated stomatal patterns qualitatively similar to the ones seen in wild-type *Arabidopsis* and some mutant alleles. Statistical analyses on the model outcomes allowed us to determine the patterns' robustness to parameter changes. In order to compare the simulated stomatal patterns with those in the real leaves, we described the set of stomata using Delaunay triangulations and then analysed the distribution of triangle sides. This approach enables the study of length scales given by distances between stomata. The interplay between the mathematical model and supporting experimental evidence shows that auxin plays a central role as decision maker within the stomatal lineage as well as regulator of specific bHLH genes dynamics.

References

[1] J. Le et al. (2014). *Auxin transport and activity regulate stomatal patterning and development,* Nature Communications 5, 3090.

<u>Parallel Session</u>

Physiology III

ANALYSIS OF DIFFERENT BURSTING MODES IN THE INTEGRATED OSCILLATOR MODEL FOR PANCREATIC β-CELLS

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Keywords: Pancreatic β-cells, Bursting modes, Bifurcation Analysis.

Intracellular Ca^{2+} oscillations and pulsatile insulin secretion are results of bursts of electrical impulses produced by insulin-secreting β-cells of pancreatic islets of Langerhans. Recently, mathematical modelling have been focused on the mechanism for this bursting activity and, as new data are acquired, old models are modified and new models are developed. Comprehensive models must now account for the various modes of bursting observed in islet β-cells (fast bursting, slow bursting, and compound bursting). The Integrated Oscillator Model (IOM) is one such model. In this model, β-cell electrical activity, intracellular Ca^{2+}, and glucose metabolism interact via numerous feedforward and feedback pathways, and produce metabolic oscillations with sawtooth or pulsatile time course, reflecting very different oscillation mechanisms. In this study, favourable conditions are determined to one type of oscillations or the other; the transitions between modes of bursting and the relationship of the transitions to the patterns of metabolic oscillations are analysed. Importantly, this work suggests pathways through which oscillations of one type can be converted to oscillations of another type and clarifies what can be expected in experimental measurements of β-cell oscillatory activity.

BILE FLUX QUANTIFICATION BY *INTRA-VITAL* MICROSCOPY

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Keywords: Quantitative microscopy, Bayesian model selection.

One of the main functions of the liver is bile production, excretion and its re-uptake from the blood. Bile acids are secreted into the bile canaliculi network (BCN) where they flow toward bile ducts and, eventually, to the gallbladder. Since the bile canaliculi are formed by the apical membranes of adjacent hepatocytes and have a diameter $< 1\mu m$, the direct measurement of bile velocity and pressure distribution in the BCN is impossible. We have previously shown that speed and bile pressure of bile can be inferred from *intra-vital* microscopy (IVM) measurements by fitting the bile flow model to quantitative experimental data. A major challenge in quantitative IVM is posed by high sensitivity of hepatocytes to phototoxic damage. In order to decrease phototoxicity, the images have to be acquired with low illumination, thus decreasing the signal-to-noise ratio. Off-the-shelf segmentation algorithms failed to properly analyze such images. To address this problem, we developed a new probabilistic method for segmenting hepatocytes and BCN visualized by IVM [implemented in http://motiontracking.mpi-cbg.de]. The proposed segmentation method was applied to the analysis of adult mouse liver by IVM under control and chemically perturbed conditions [1]. The results of the quantification were consistent between multiple mice and had a relatively small confidence interval, which allowed us to perform Bayesian selection of the bile propagation model, quantitative estimation of model parameters and their uncertainty.

References

[1] K. Meyer, O. Ostrenko, G. Bourantas, H. Morales-Navarrete, N. Porat-Shliom, F. Segovia-Miranda, H. Nonaka, A. Ghaemi, J.-M.Verbavatz, L. Brusch, I. Sbalzarini, Y. Kalaidzidis, R. Weigert, M. Zerial. (2017). *A Predictive 3D Multi-Scale Model of Biliary Fluid Dynamics in the Liver Lobule*, Cell Systems 4(3), pp277-pp290.

Parallel Session
Physiology III

EFFECT OF DEEP INSPIRATIONS ON AIRWAY SMOOTH MUSCLE CELL-MATRIX ADHESIONS

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Keywords: Integrins, Cell–matrix adhesion, Hysteresis.

Contraction of airway smooth muscle (ASM) cells leads to bronchoconstriction, a narrowing of the airways characteristic of asthma. Cell–matrix adhesion (mediated by integrins) plays an important role in bronchoconstriction, since integrins regulate how contractile forces generated within the cells are transmitted to the airway tissue. It is not yet known how cell—matrix adhesions are affected by environmental fluctuations due to tidal breathing in the intact airway, and here we use two models to investigate the effect of oscillatory loading (representing tidal breathing) on the adhesion dynamics. Firstly we use an individual-based discrete model, and then introduce a multiscale continuum model which is able to replicate the results. We observe two qualitatively different adhesion states in which either adhesion rupture or adhesion formation dominate, depending on the amplitude of the oscillatory loading. For intermediate loading we observe a region of bistability and hysteresis due to shared loading between existing bonds; the level of adhesion depends on the loading history. Due to the bistability, we show that perturbations mimicking deep inspirations (DIs) could induce a switch between high and low adhesion states. This result could help to explain experimental observations on the possible bronchodilatory effect of DIs.

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A MATHEMATICAL MODEL OF BOVINE PROGESTERONE BASED ON CORPUS LUTEUM MEASUREMENT

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Keywords: Estrus cycle, Progesterone, Reproduction, Corpus luteum.

In [1], a mathematical model of progesterone levels in bovines is given by the following differential equation $\frac{dP4}{dt} = \alpha CL - \beta P4$. Here P4 is the progesterone concentration, CL is the size of the corpus luteum, t is time, α is the (constant) production rate and β is the (constant) clearance rate. In [1], optimal values for the parameters α and β are found. Since the progesterone produced by corpus luteum may depend on the state of the CL (growing, static or regressing), we propose a new model $\frac{dP4}{dt} = \alpha + \sum_{i=1}^{3} \alpha_i CL_i - \beta P4$. Here α is the baseline P4 level, CL_1 is the size of the growing CL, CL_2 is the size of the static CL, CL_3 is the size of the regressing CL, α_i are the P4 production rates of the CL and β is the clearance rate. This new model allows for the possibility that a growing and regressing CL are present at the same time. A bifurcation analysis is performed for this model. The parameters of this new model are optimised. A sensitivity analysis is also performed on these parameters. The P4 production rates of the growing, static and regressing states of CL are found. The [1] model and our new model are used to predict the data and the results are compared. Furthermore, our new model is trained on a training data and tested on new (unseen) data.

References

[1] *Boer, H.M.T., Stötzel, C., Röblitz, S., Deuflhard, P., Veerkamp, R.F. and Woelders, H.* (2011) *A simple mathematical model of the bovine estrous cycle: follicle development and endocrine interactions.* Journal of theoretical biology, 278(1), pp.20-31.