

Parallel Session**Cell and Intra-Cell Dynamics VI****COMPUTATIONAL MODELLING OF WHEAT LEAF EPIDERMAL MORPHOGENESIS BASED ON LARGE-SCALE LSM DATA**

ULYANA S. ZUBAIROVA

ulyanochka@bionet.nsc.ru

Laboratory of Evolutionary Bioinformatics and Theoretical Genetics, Institute of Cytology and Genetics SB RAS, Novosibirsk, Prospekt Lavrentyeva 10, Russia

Joint work with Alexey V. Doroshkov (Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia and Novosibirsk State University, Novosibirsk, Russia).

Keywords: Computational modelling, Image processing, Confocal laser scanning microscopy, Wheat leaf epidermis, Morphogenesis.

Computational modelling became one of the main methods of theoretical study of the mechanisms underlying the regulation of the dynamics of spatial patterns in developing tissues. The main stages of modern biological research using computer modelling are the following ones. (1) Accumulation and analysis of large-scales of heterogeneous experimental data; (2) construction of mathematical models and simulations in order to identify new knowledge and the formation of new scientific hypotheses, and, finally, (3) planning and conducting of new experiments to test these hypotheses and refine the mathematical model. In this work, we present these stages by an example of wheat leaf epidermal morphogenesis.

The leaf epidermis of a monocotyledonous plant is a widely used model system for studying morphogenesis. The epidermis of cereals (wheat, barley, rice) leaf is a complex tissue consisting of different cell types organizing in parallel cell rows. For such leaves, a unidirectional growth occurring for a long time enables to observe a series of successive morphogenetic stages at one snapshot. In this work, we propose the concept for using a growing wheat leaf to study dynamical changes in morphogenesis, including stress-induced changes. Linear leaf of a wheat, during its formation for a long time, maintains a phase of steady growth. Therefore, it is possible to observe a series of successive events of morphogenesis fixed in the cellular architecture of a mature leaf.

High-resolution 3D LSM-images allow extracting quantitative characteristics describing the cellular structure of leaf epidermis. However, to obtain a large amount of statistical data methods of high throughput computer based image segmentation should be used. We developed a workflow for detection of structural properties of leaf epidermis from 3D images obtained from confocal laser scanning microscopy. The workflow includes the protocol of sample preparation, image processing ImageJ-plugin and data extraction algorithms. The data on the cellular architecture further will act as a basis for the elaboration and verification of spatial models accounting for structural features of leaves.

Cell-based modelling is a widely used technique for studying the geometric, topological and morphological features of plant tissue during growth. For the leaf epidermis of cereals, a brickwork-like pattern combined with unidirectional growth allows to reduce the dimension and use a quasi-one-dimensional representation of the cellular ensemble in the model. This idea was realized in the model [1] growth of a linear leaf blade. The model allows for fitting of the visible cell length using the experimental cell length distribution along the longitudinal axis of a leaf epidermis. In this work, we assume a unidirectional growing cell ensemble starting from a meristem-like layer of generative cells and then generating parallel cell rows from every cell of the initial layer. We considered the growth zone of the leaf includes division and elongation zones; in addition, the division zone includes a zone of asymmetric divisions forming specialized cells (trichomes and stomata). The model was verified on qualitative and quantitative data on cold stress induced disturbances of morphogenesis in the epidermis of wheat leaf.

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QUALITATIVE CONTROL FOR A GENETIC NEGATIVE FEEDBACK LOOP

LUCIE CHAMBON

lucie.chambon@inria.fr

BIOCORE, INRIA, 2004 Route des Lucioles, BP 93, 06902 Sophia Antipolis, France

Joint work with Jean-Luc Gouzé (BIOCORE, INRIA, 2004 Route des Lucioles, BP 93, 06902 Sophia Antipolis, France).

Keywords: Quantized control, Genetic networks, Negative feedback loop.

In the context of gene regulatory networks, a negative feedback loop is modelled by N -coupled ordinary differential equations, highly non-linear due to Hill functions. This classic dynamical system properly captures the two main biological behaviours arising from this type of recurrent network motif: homeostasis under global stability of the unique fixed point, and biochemical oscillations otherwise. Various diseases may appear in case of homeostasis disruption. In this context, a quantized control strategy is designed in order to remove the undesirable oscillations emerging from such a disorder. For this purpose, the expression of one gene is either amplified or reduced in the controlled system [1]. The piecewise constant nature of the control law is adapted to control techniques commonly used in biotechnology [3] and biological constraints such as qualitative nature of the measurements. Under appropriate conditions on the control law, global convergence towards the fixed point is achieved through successive repulsive regions of the state space and a final sliding mode. In case of uncertain and more realistic measurements, the control strategy is slightly modified in order to highlight an adjustable zone of convergence around the fixed point. These two results are illustrated with a specific synthetic biological oscillator: the Repressilator [2].

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**CYTOSKELETON SELF-ORGANIZATION IS ROBUST
AND DEPENDS ON CELL GEOMETRY ALONE**

LYUBOV CHUMAKOVA

Lyuba.Chumakova@ed.ac.uk

U. Edinburgh

Joint work with A. Plochocka (U. Edinburgh), A. M. Davie (U. Edinburgh) and N. A. Bulgakova (U. Sheffield).

Keywords: Cytoskeleton, Microtubule, Self-organization.

Cytoskeleton organization is essential for the correct cellular, and therefore organism, function. It is along the cytoskeleton that cellular components are transported to their biologically relevant positions, and perturbations of the cytoskeleton networks result in pathologies. *In vitro* studies suggest that both environment (e.g temperature) and genetics (e.g amounts of cytoskeleton components in cells) interfere with cytoskeleton properties. However, organisms are exposed to different environmental parameters, which additionally change during the lifespan of an individual. Furthermore, the genetics also varies between organisms. How then, despite all these varying parameter regimes, do cellular components reach relevant positions in correct amounts, enabling normal cell function and tissues be structurally stable?

We demonstrate that in *Drosophila* embryo epithelial cells the microtubule cytoskeleton self-organizes and this organization depends on the cell geometry alone [1]. Using *in vivo* studies, stochastic simulations, and analysis of a probabilistic model, we show that microtubule organization is robust on the tissue scale, namely it converges to the same cell-shape-dependent steady state independently of cytoskeleton properties and behavior.

References

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WHY COUSINS ARE MORE SIMILAR THAN MOTHER-DAUGHTERS: IMPLICATIONS FOR CIRCADIAN-CONTROLLED CELL FATE

SHAON CHAKRABARTI

shaon@jimmy.harvard.edu

Harvard University, Dana Farber Cancer Institute

Joint work with Andrew Paek (University of Arizona), Jose Reyes (Harvard University), Galit Lahav (Harvard University) and Franziska Michor (Harvard University, Dana Farber Cancer Institute).

Keywords: Single-cell, Circadian, Cell-fate, Heterogeneity, Lineage-correlations.

Understanding the fundamental principles of cell fate control is a central goal of cell biology and cancer research. Correlations in intermitotic times of single cells are thought to arise from control processes like the circadian clock, but the underlying principles are poorly understood. In this talk, I will show results from single cell lineage-tracking experiments we performed to uncover correlation structures in the surprisingly heterogeneous intermitotic and apoptosis times (IMT and AT respectively) of a colon cancer cell line, in response to the chemotherapeutic agent cisplatin. The real heterogeneity in the IMT is “hidden” due to stochastic competition between cell division and death, and I will present a statistical algorithm we developed to infer the correct shapes of both the IMT and AT distributions. In addition, we found that cell fates were correlated in sister cells regardless of whether they divided before or after cisplatin treatment, suggesting the presence of a cellular state determining fate outcomes early in a cell’s lifetime. Based on this finding, we developed a unified theory explaining how such complex correlation structures and heterogeneities can arise as a consequence of circadian-controlled cell fate decisions. Our work suggests an important role of the circadian clock in controlling times to cellular fates both in the presence and absence of drugs.