Parallel Session

Physiology VI

THE IMPACT OF GEOMETRY ON EFFECTIVE MODELS OF NUTRIENT UPTAKE BY ROOT HAIRS

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Keywords: Nutrient, Uptake, Geometry, Homogenisation, Hairs.

Full-geometry numerical simulations of nutrient uptake by plant roots covered with root hairs can be computationally challenging and time-consuming. Multiscale methods such as homogenisation offer a desirable alternative, allowing for the determination of effective macroscopic equations which capture microscale geometric details but are substantially easier to analyse. Here, we will show how to extend homogenisation of the root hair uptake problem to the limit of very sparse root hairs, and then consider the effects of the root hair length on sink terms representing the nutrient uptake in the effective equation. Finally, we demonstrate the validity of these asymptotic results by comparing them with the corresponding full-geometry numerical simulations.

Acknowledgements: I would like to acknowledge and thank The University of Nottingham and European Research Council for co-funding FUTUREROOTS project, which gave rise to this work.

Parallel Session

Physiology VI

ENGINEERING COMPARTMENTALISATION IN BIOCHEMICAL PATHWAYS - ANALYSIS AND DESIGN

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Keyword: Compartmentalisation.

Compartmentalisation is a fundamental aspect of the functioning of biological systems at multiple levels. With the advent of imaging techniques that give spatial resolution of sub-cellular processes, the spatial organisation of biochemical pathways is being increasingly appreciated. Compartmentalisation of biochemical pathways at the intracellular level plays a critical role in many cellular contexts, including signal transduction and the regulation of metabolic processes. Compartmentalisation is also being used in bottom-up approaches to building functional pathways, in synthetic and chemical biology. There is also significant interest in manipulating the natural compartmentalization within cells, for example to engineer metabolic pathways.

In trying to understand the role of compartments and attempting to design compartmentalized systems, a number of questions arise. These involve the effects of compartmentalising certain components of a pathway, the complexities associated with using compartmentalisation to manipulate more complex pathways, and the modelling framework to be used, so as to give reliable predictions for analysis and design. In this talk we present a dedicated modelling/systems framework [1, 2], which involves the dissection of basic building blocks of pathways, more complex extensions of these, and the effects of compartmentalisation. We use this framework to show (i) how compartmentalisation affects the basic building blocks of pathways, such as modification cascades, (ii) how various trade-offs emerge in engineering the compartmentalisation of more complex signalling and metabolic pathways, and (iii) our analysis of compartmental ODE models (by comparison with detailed PDE models), shows when they are reliable, and where they fall short. Following this, we discuss basic design principles for spatial organisation in compartmentalised nucleic acid based circuits including transcription-translation systems.

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Parallel Session

Physiology VI

MULTICELLULAR AGING AS A NONEQUILIBRIUM PHASE TRANSITION

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Keywords: Regeneration, Wound healing, Reaction-diffusion, Cell cycle arrest.

Aging seems elusive but inevitable for all of us. Reductionist approaches to pinpointing the underlying mechanisms have revealed overwhelming complexities associated with multiple factors on multiple scales. Nevertheless, our previous experimental study of time-delayed wound healing assays shows that biological aging at the multicellular level may resemble the physical aging in glass-like materials in the sense that the wound healing, as a biological analogue to the relaxation processes, exhibits dynamical scaling as relaxation does in non-equilibrium physical systems [1]. The scaling exponent characterizes the aging rate of the cells at the multicellular level. The slowdown of healing in relation to the waiting time before wound creation was further studied with an asymmetric reaction-diffusion model and a cell-based model in parallel for searching the control parameter in analogous to those (e.g. temperature) in physical systems. By scrutinizing the critical behaviors of two models, we find that the broken symmetry associated with cell cycle regulation could be the most viable control parameter of the aging at the multicellular level. Like the physical particles trapped in a local potential well imposed by self-surrounding interactions, cells imposed by strong intercellular interactions may also be trapped in a local biochemical potential well and the detailed balance with respect to the cell cycle state is then violated, yielding a nonequilibrium phase transition of the system at the multicellular level. This theory proposes a non-reductionist approach to multicellular aging that brings new thinking to the regenerative medicine of tissue, the anti-aging therapy and the longevity of life.

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Parallel Session

Physiology VI

MATHEMATICAL MODELLING OF CELLULAR RESPONSE PATHWAYS FOR OXIDATIVE STRESS

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Keywords: Stress response pathways, Dose-response, Mathematical modelling with ordinary differential equations, Data-based model.

Cells regulate enzyme activities to modulate their metabolic flux. This is especially important for reducing detrimental influences caused by stress. A possible carcinogenic stressor is 3-nitrobenzanthrone (3–NBA). The polycyclic aromatic hydrocarbon is known for enhancing reactive oxygen species (ROS) within cells. High ROS levels lead to DNA damage and induce apoptosis.

Here, a mathematical modelling approach is presented for investigating the impact of 3–NBA on ROS generation and their metabolisation by the corresponding stress response pathways.

In the modelled metabolic network, glycolysis, the pentose phosphate pathway and the glutathione redox cycle are included as cellular pathways which are deeply involved into ROS degradation. The gluconate shunt which is controversially discussed in mammalian cells is also incorporated. The model consists of ordinary differential equations. It is based on multispecies enzymatic reactions and corresponding regulatory mechanisms.

Parameterisation was achieved via both literature values and data-fitting to experimental data obtained from RT4 cells exposed to seventeen 3–NBA levels.

The simulated dose-response curve is in good agreement with experimental data of intracellular relative ROS levels after 24 hours of exposure to 3–NBA.

Our investigation is an important step towards establishing safety limits for 3–NBA which is contained in diesel engine exhaust. However, this model can be employed for responses to other oxidative stressors.

Acknowledgements: DS acknowledges the support within the DFG project 'Modellierung der konzentrationsabhängigen Änderungen im Energiestoffwechsel von Urothelzellen nach Exposition gegen 3-Nitrobenzanthron', SCHM1207/5-1.

Parallel Session

Physiology VI

MATHEMATICAL MODEL TO RELATE TELOMERASE ACTIVITY AND TELOMERE LENGTH WITH THE HUMAN FOLLICULAR AGING

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Keywords: Follicle, Granulosa cell, Telomere, Telomerase, Aging.

The aim of this work is to study the aging rate at which human follicles reach the preovulatory state as a function of Telomerase-activity. A human preantral follicle takes approximately 85 days to achieve the preovulatory size, going through several stages (Gougeon, 1996). The lengths of the telomeres of granulosa cells (GCs) of each class of follicles, during folliculogenesis, are modelled using a chemical master equation formalism similar to the one in (Wesch el al., 2016). Seven differential ordinary systems of equations, corresponding to seven stages of the follicule maturation, concatenated in time, are considered. The influence of different Telomerase-activity rates and the telomere shortening of the preovulatory follicle is studied.

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