Parallel Session

Mathematical Methods in Biology III

A NEW LATTICE-GAS CELLULAR AUTOMATON MODEL FOR CELL AGGREGATION

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Keywords: Cell adhesion, Cellular Automaton, Linear stability analysis, Partial differential equation approximation.

The ability of individual cells to assemble and organize themselves into very diverse and highly distinctive patterns via cell adhesion is crucial for tissue development [1]. Pattern formation and cell aggregation have been studied with continuous models [2] and by multiple individual-based models [3]. While the continuous approaches use generic equations to describe population dynamics, the individual-based models usually associate energies and/or forces with cell interactions that govern the dynamics of individual cells. In this view, cells resemble physical particles that are moved passively, not taking into account the ability of cells to regulate their biophysical properties. We here propose a new model for cell aggregation based on a lattice-gas cellular automaton [4] whose rules are motivated by the decision-making process of individual cells that constantly try to optimize the number of neighboring cells. We analyze this model by means of a linear stability analysis, derive a critical wave length of the observed aggregation pattern and provide a partial-differential equation approximation of the system near the onset of aggregation.

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THE EFFECT OF NUTRIENT-LIMITED GROWTH ON FLORAL PATTERN FORMATION IN YEAST BIOFILMS

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Keywords: Yeast biofilm, Reaction-diffusion system, Travelling wave solution, Linear stability analysis.

Yeast species have important impacts on human life, and in many applications it would be advantageous to control their growth. For example, yeasts are used extensively in food and drink production and in biotechnology, but are also a leading cause of persistent hospital-acquired infections. It is therefore of interest to understand the fundamental mechanisms that determine colony morphology. Yeast biofilms are complex systems in which growth is influenced by nutrient consumption, flow of extracellular fluid, and mechanical forces. In this work, we investigate the hypothesis that nutrient-limited growth is the mechanism by which patterns form. Analysis of experimental images shows that biofilms expand radially at a roughly constant speed, and undergo a transition from circular to floral morphology, which is characterised by the formation of finger-like 'petals'. We use this data to parametrise a reaction-diffusion model with non-linear degenerate cell diffusion. In doing this, we show that two-dimensional travelling wave solutions to our model are linearly unstable to transverse perturbations for experimentally feasible parameters. There is good agreement between experimental floral patterns and predictions using the range of unstable wave numbers. Our model, which incorporates nutrient-limited growth alone, therefore provides a potential explanation for petal formation in yeast biofilms.

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Mathematical Methods in Biology III

DETERMINING THE PROBABILITY FLUX FROM A BROWNIAN SOURCE TO SMALL ABSORBING WINDOWS VIA A MIXED ANALYTICAL-STOCHASTIC SIMULATION METHOD

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Keywords: Biophysical models, Computational biophysics, Cell sensing.

How can a cell reconstruct the position of a chemotactic source releasing Brownian particles from information gathered by receptors? To answer this pressing question in cell biology, we developed an efficient numerical procedure to extract the steady-state flux to absorbing windows located on the boundary of a domain without having to simulate Brownian trajectories in the entire domain. Furthermore, we calculate these fluxes analytically for absorbing windows located on the boundary of half-space as well as a disk in two-dimensional space using matched asymptotics. We find good agreement with our stochastic simulations and also show that knowledge of these fluxes allows the reconstruction of the source position when three or more windows are present.

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Parallel Session

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AN INTUITIVE AND EFFICIENT APPROACH FOR TESTING PARAMETER IDENTIFIABILITY

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Keywords: Dynamic models, Ordinary differential equations, Parameter estimation, Identifiability, Uncertainty.

The feasibility of uniquely estimating parameters of dynamical systems from observations is a widely discussed aspect of mathematical modelling. Several approaches have been published for analyzing this so-called identifiability of model parameters. However, they are typically computationally demanding, difficult to perform and/or not applicable in many application settings.

Here, an approach is presented which enables quickly testing of parameter identifiability. Numerical optimization with a penalty in radial direction enforcing displacement of the parameters is used to check whether estimated parameters are unique, or whether the parameters can be altered without loss of agreement with the data indicating non-identifiability. This so-called "Identifiability-Test by Radial Penalization" (ITRP) can be employed for every model where optimization-based parameter estimation like least-squares or maximum likelihood is feasible and is therefore applicable for all typical deterministic models in mathematical biology. The approach is illustrated and tested using 11 ordinary differential equation (ODE) models.

The presented approach [1] can be implemented without great efforts in any modelling framework. It is available within the free Matlab-based modelling toolbox Data2Dynamics. Source code is available at https://github.com/Data2Dynamics.

Acknowledgements: This work was supported by the German Ministry of Education and Research by grant *EA:Sys [FKZ 031L0080]*.

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Parallel Session

Mathematical Methods in Biology III

REDUCTION OF METABOLIC NETWORKS KEEPING CORE DYNAMICS

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Keywords: Metabolic networks, Reduction, Dynamical systems.

Metabolic modeling has proved to be a very powerful tool to get a better insight into the metabolism of an organism. For organisms such as microalgae and cyanobacteria, periodic fluctuation of light induces instationarity of their metabolisms, with accumulation of metabolites (especially lipids and carbohydrates). Therefore, such metabolisms are never at steady state.

However, most of the approaches dedicated to metabolism analysis assume balanced growth (i.e. systems at steady state), which leads to rough approximations. Furthermore, metabolic models are of high dimension, which makes their mathematical analysis and parameter identification complex. Identifying conditions to maximize productivity by a rigorous mathematical analysis is generally not possible.

We propose a method to reduce the dimension of a dynamical metabolic system, which is appropriate to derive model based control strategies. Contrary to nearly all existing works, the idea is to keep some dynamical components of the model.

A first attempt in this direction was carried out with the DRUM method ([1]). DRUM approach has proven to provide sound results, with very efficient representation of accumulation of lipids and carbohydrates in microalgae submitted to light/dark cycles. However, as almost all methods developed for metabolic analysis, it relies on a series of assumptions whose mathematical bases have not been rigorously established.

The main objective of our work is to provide mathematical foundations for the reduction of metabolic networks to low dimensional dynamical models. For reducing systems accurately, we propose a dynamical approach that relies on time scale separation and Quasi Steady-State Approximation. We prove that concentrations of fast metabolites are one order of magnitude lower than concentrations of metabolites with slow dynamics. Finally, we apply the method to a toy model and we compare the result with DRUM.

References

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