Mini-symposium on "Position-jump models of biological processes on irregular lattices"

Organised by Dr Christian Yates and Dr Ruth Baker as part of the 9th European Conference on Mathematical and Theoretical Biology 15-19 June 2014

Date: Sunday 15th June. Time: 16:00-19:00. Place: Valdemar Room.

Timetable:

The schedule is as follows:
16:00-16:45 Christian Yates (University of Oxford) **– "Relevance of the Voronoi domain partition for position-jump reaction-diffusion processes on nonuniform rectilinear lattices".**

16:45-17:30 Basil Bayati (Intellectual Ventures) - **"Multi-resolution stochastic reaction-diffusion and fractional-diffusion methods with applications to pattern formation, brain tumor growth, and epidemics".**

17:30-18:15 Stefan Engblom (University of Uppsala) – **"Mesoscopic Stochastic Modeling and the Diffusion Operator".**

18:15-19:00 Lina Meinecke (University of Uppsala) – **"Stochastic simulation of diffusion on unstructured meshes via first exit times".**

The plan is for the talks to last 35 minutes leaving 5-10 minutes for questions and changing speakers.

Talks will start on time as scheduled.

Abstract for the mini-symposium as a whole:

Spatial reaction-diffusion models have been employed to describe many emergent phenomena in biological systems, including spatial ecology, animal coat patterning, limb/digit formation and tumour growth.

The predominant modelling technique for reaction-diffusion systems, due to its analytical tractability and ease of simulation, has been the use of partial differential equations (PDEs). However, due to recent advances in computational power, the simulation, and therefore postulation, of computationally intensive individual-based models (with individuals representing animals, cells, molecules, particles *etc.*, depending on the context of the model) has become a popular way to investigate the effects of intrinsic noise in reaction-diffusion systems.

Position-jump processes are used for the mathematical modelling of spatially extended chemical and biological systems with increasing frequency. Traditionally, computational domains have been divided into regular voxels. Molecules are assumed well-mixed within each of these voxels and are allowed to react with other molecules within the same voxel or to jump to neighbouring voxels with predefined transition rates.

For a variety of reasons implementing position-jump processes on irregular grids is becoming increasingly important. For example, in one dimension, when incorporating the evolution (i.e. growth/shrinkage) of the underlying domain into these individual-based models, an irregular domain partition is naturally engendered. In higher dimensions irregular domain partitions may be used to represent the underlying structure of the tissue cells over which a morphogen is diffusing. Irregular domain partitions may also be used to avoid the inherent anisotropy caused by regular lattices or to implement adaptive meshing regimes for systems with significant spatial gradients.

Although irregular lattices are being used with increasing frequency, it is not immediately clear what form an appropriate irregular partition of the domain should take. Nor is it obvious, once the domain has been specified, how to go about determining the appropriate transition rates. This mini-symposium will bring together a range of experts who are interested in the modelling of stochastic reaction-diffusion processes on irregular domain partitions.

Speakers abstracts:

Christian Yates: Position-jump processes are used for the mathematical modelling of spatially extended chemical and biological systems with increasing frequency. A large subset of the literature concerning such processes is concerned with modelling the effect of stochasticity on reaction-diffusion systems. Traditionally, computational domains have been divided into regular voxels. Molecules are assumed well mixed within each of these voxels and are allowed to react with other molecules within the same voxel or to jump to neighbouring voxels with predefined transition rates.

For a variety of reasons implementing position-jump processes on irregular grids is becoming increasingly important. However, it is not immediately clear what form an appropriate irregular partition of the domain should take if it is to allow the derivation of mean molecular concentrations that agree with a given partial differential equation for molecular concentrations. I will demonstrate that the Voronoi domain partition is the appropriate method with which to divide the computational domain, under the assumption of a fixed functional form for the transition rates.

In this talk, I will investigate theoretically the propriety of the Voronoi domain partition as an appropriate method to partition domains for position-jump models and provide simulations of diffusion processes in order to corroborate our results.

Basil Bayati: A method is presented for adaptive mesh refinement applied to stochastic simulations of spatially evolving reaction-diffusion processes. The propensities for the diffusion process are derived for meshes that are adaptive, locally refined, and structured. Convergence of the diffusion process is presented and the fluctuations of the stochastic process are verified. Furthermore, a refinement criterion is proposed for the evolution of the adaptive mesh. The method is applied to pattern formation problems. Additionally, a three-dimensional inhomogeneous, stochastic reaction-

diffusion equation is used as a model for the simulation of the growth of a glioma in a human brain. The inhomogeneity of the white and grey matter of the brain is taken into account by a discontinuous diffusion coefficient. A multi-resolution wavelet-based framework is used to solve the three-dimensional Langevin equation. Simulations are shown for the spread of the tumor over the duration of years. Lastly, a numerical method is proposed for the simulation of stochastic reaction-diffusion processes subject to heavy-tailed diffusion. The method is based on operator splitting of the diffusion and reaction terms in the master equation. The diffusion term follows a multinomial distribution governed by a kernel that is the discretized solution of the fractional diffusion equation. Simulations of a nationwide influenza epidemic are shown.

Stefan Engblom: In this talk I will consider computational modeling of diffusion-controlled reactions with applications mainly in molecular cell biology. I will give a brief overview of the modeling involved, in the non-spatial as well as in the fully spatial setting, and I shall also mention some different means by which such models can be simulated.

In the main part of the talk I will discuss convergence. Conditions for the validity of spatial mesocopic modeling in general and of the diffusion operator in particular will be emphasized. Defining the mesoscopic Laplacian from a discrete Finite Element Method has its definite advantages, but there are also some limitations. It has been suggested that these are partially solved when switching to the Finite Volume Method and a critical discussion of this idea will be offered.

I will finish by briefly discussing some problems were spatial modeling truly changes the dynamics when compared to the well-stirred case. Here we can expect an accurate description of the molecular transport mechanism to be important.

Lina Meinecke: In molecular biology it is of interest, besides reactions, to also simulate spatial phenomena in the cell, that is diffusion. Biochemical systems in cell biology often only contain very low copy numbers of certain species. As a result the reaction-diffusion equation, a macroscopic or deterministic partial differential equation describing the concentrations, is inaccurate and does not reproduce experimental data. Hence, a stochastic and individual-based description is needed. The diffusion of the molecules is then given by Brownian dynamics and the reactions between them occur with certain probabilities.

For stochastic simulation of the diffusion, the cell is partitioned into compartments or voxels in a mesoscopic model. The number of molecules in a voxel is recorded and the molecules can jump between neighbouring voxels to model diffusion. In order to accurately represent the geometry of the cell including outer and inner curved boundaries it is helpful to use unstructured grids, meaning triangulations, for the voxels. The probabilities to jump between the voxels are given in [2] by a discretization of the Laplacian with the finite element method (FEM) on the mesh. Solutions of the diffusion equation with FEM can encounter problems on unstructured grids of poor quality. The maximum principle may not be satisfied by the FEM solution and the derived jump coefficients may be negative, which no longer allows for an interpretation as jump propensities. Ignoring the negative coefficients and setting them to zero leads to an incorrect diffusion speed.

Presenting the speed of diffusion correctly from the inner part of the cell to the outer boundary can be of importance for example in signaling, where a signal is released in the nucleus and propagates to the cell membrane. We therefore derive the jump coefficients from the theory of first exit times. In order to demonstrate the method of global first exit times (GFET) we will show results on skewed unstructured meshes in 2D and compare with analytical results. Then the method is applied to diffusion on truly irregular grids in 3D.