Stochastic spatio-temporal systems in biology: Focus problems

Focus Problem 1: Introducing nonlinear reaction and diffusion phenomena into stochastic spatio-temporal models

Leaders: André Leier & Tatiana Marquez-Lago

We present two focus problems revolving around nonlinear effects in spatiotemporal stochastic systems in biology and how to introduce these accurately into stochastic modelling and simulation frameworks. The first problem is nonlinear diffusion in spatial stochastic simulations. In the classical diffusion equation, nonlinearity is introduced by a concentration-dependent diffusion coefficient. Similarly, nonlinear diffusion can be introduced into the framework of random walks by introducing jump probabilities that depend on walker concentrations or fractions of walkers (i.e. molecules) at a site, yielding generalized random walks. Walker-density dependent jump probabilities can be transformed into nonlinear reaction (diffusion) kinetics in the context of a Master Equation. We will present the ansatz, apply this strategy to develop a stochastic nonlinear diffusion model of epigenetic control in 1D, and pose a couple of interesting questions for future investigation. The second problem is about modeling nonlinear interactions between species, i.e. particles of interest such as receptors or lipid-anchored molecules and different solvent species such as lipids. The nature of this problem is not only nonlinear but also multi-scaled. This question is driven by a number of biological observations regarding lipid organization and clustering of receptors and membrane-anchored molecules in plasma membranes. We will discuss a possible ansatz and the challenges in using it for an accurate stochastic reaction-diffusion model.

Presentation: 9am Monday 16th July

Break-outs:
11.30-12:30 Monday 16th July
16.00-17:00 Wednesday 18th July
14.00-15.30 Thursday 19th July

Focus Problem 2: Multi-resolution methods for spatio-temporal modelling of intracellular processes

Leader: Radek Erban

Classical molecular dynamics (MD) is a widely used computational approach in biochemical research, which describes molecules as groups of atoms which interact with each other according to the rules of classical mechanics. In applications, MD has been used to study how complex biomolecules move, transform and interact over time. Unfortunately, MD simulations of molecules in aqueous solutions are usually limited to modelling processes in relatively small domains containing (only) several thousands of water molecules over relatively short times (say, a nanosecond). Even with state-of-the-art computers, it is an impossible task to use all-atom molecular mechanics simulations to model whole-cell dynamics, because such a simulation would have to include simultaneous computation of trajectories of trillions of atoms. In particular, biological processes which include transport of molecules between different parts of the cell are usually not described with atomistic-level of detail, even when the molecular structure and function are known for some components of the studied system. A question relevant to this workshop is how we can use such information when we build our stochastic spatio-temporal models of intracellular processes. In particular, we will discuss multi-resolution methods for spatio-temporal modelling of intracellular processes which would bridge the gap between all-atom molecular dynamics simulations and stochastic reaction-diffusion models in the macroscopic limit.

Presentation: 10am Monday 16th July

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Focus Problem 3: Criticality and adaptivity in enzymatic networks

Leader: Ruth Williams

In this focus problem we will be addressing a number of questions associated with how the adaptation works, especially on what parameter regime it holds in. This is based on the work presented in the following paper:
https://www.sciencedirect.com/science/article/pii/S0006349516306166

We will be aiming to seek an explanation involving multiscaling, but in our discussions we may also develop other directions and questions. Behaviour with time dependent inputs is another direction that has interesting experimental results and worth exploring if this suits the participants of this question.

Presentation: 2pm Monday 16th July

Break-outs:
15.30-17:00 Monday 16th July
11.30-12:30 Tuesday 17th July

Focus Problem 4: Stochastic analysis of reaction-diffusion processes

Leader: Hans Othmer

Reaction and diffusion (RD) processes are used to model chemical and biological processes over a wide range of spatial and temporal scales. A standard description is the chemical master equation (CME), which is easy to formulate but which can be computationally prohibitive to simulate for large systems. Moreover, there are still basic questions as to how diffusion should be treated in different contexts. One question is how the 'correct' computational cell size is determined, and how much one has to know about the RD dynamics in making that choice. Examples show that a 'one size fits all' approach is often inappropriate. Another question concerns the effect of hindered diffusion in the intracellular medium, and whether it should be described by the classical 'MSD proportional to t' or some other law. We discuss one estimator for the appropriate compartment size for simulating RD systems, we introduce a suitable measure of fluctuations in a discretized system, and we consider multi-scale descriptions of stochastic RD processes. We describe several examples that illustrate the issues that have to be addressed in general systems.

Presentation: 9am Tuesday 17th July

Break-outs:
14.00-15:30 Wednesday 18th July
14.00-15.30 Thursday 19th July

Focus Problem 5: Improved particle-based reaction algorithms

Leader: Steve Andrews

Particle-based simulation methods are valuable for modeling the diffusion and chemical reactions of individual molecules, including especially biomolecules. Here, each molecule of interest is represented by an individual spherical particle. These spheres diffuse, interact with surfaces, and undergo chemical reactions with each other. Existing simulation algorithms are either computationally efficient or very accurate but not both, leading to the question of whether better algorithms can be developed. In this talk, I will introduce the analytical models for diffusion-influenced reactions (Smoluchowski, Collins and Kimball, and Doi), the current algorithms (short time steps, Green's Function Reaction Dynamics, Andrews-Bray, and lambda-rho), and then two proposals for improved algorithms. In the "RDF-matching" algorithm, reactants diffuse, reflect off of each other, and are then selected to react based on their final separations, with reaction probabilities chosen to produce the correct steady-state radial distribution function. In the "Green's function with fixed time steps" algorithm, reactants diffuse, and then either react or reflect based upon their starting and ending positions. Both proposed algorithms should be able to account for long-range interactions, such as soft repulsion and electrostatic forces. Challenges will be to complete these algorithm descriptions and make them computationally efficient, and/or to come up with better algorithm ideas.

Presentation: 10am Tuesday 17th July

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