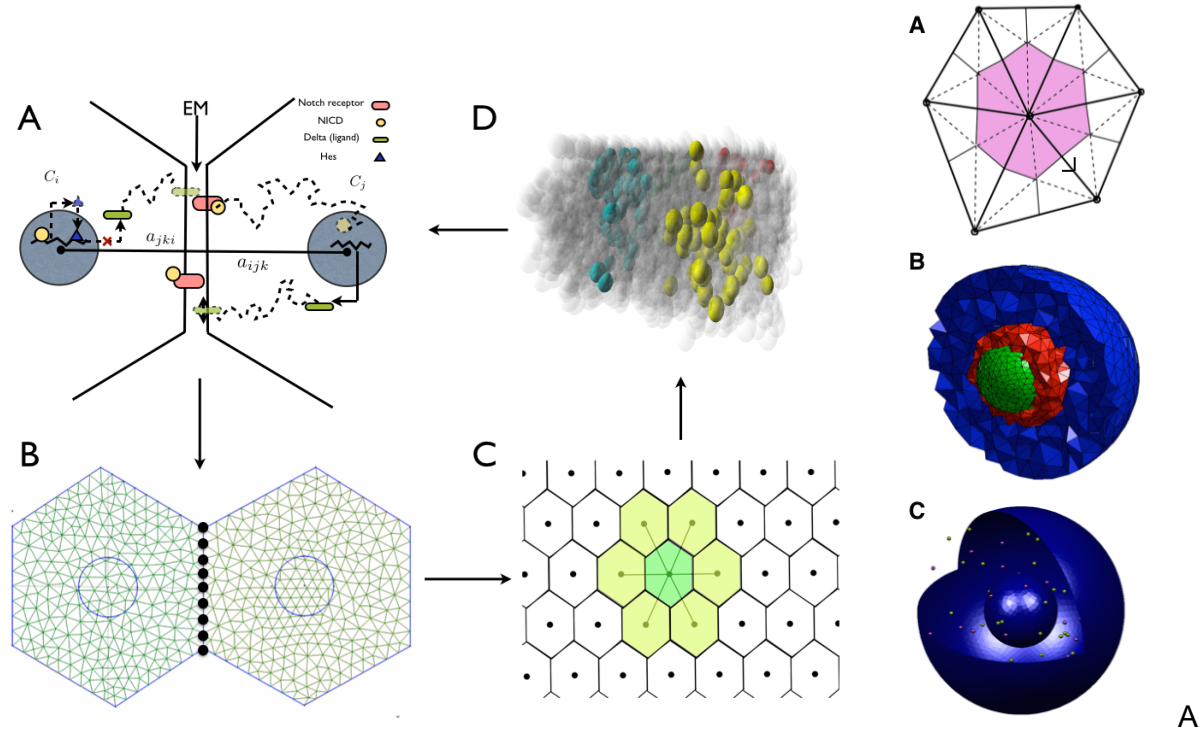
From Single Cells to Tumors - Multiscale Simulation of Stochastic (multi)cellular Systems



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A main aim of systems biology is to understand the biological phenomena observed on a cellular, tissue, and organism level, through an understanding of the molecular interactions that occur inside individual cells. In contrast to many other biological fields, systems biology has embraced mathematical modeling and simulation as a major tool to achieve those goals. With algorithms and software for computer simulation of the biochemistry of cells and aggregations of them, it is possible to understand and predict their quantitative behavior and to suggest new hypotheses and new experiments.

Many modeling levels are used to study cellular regulatory processes. On a fine level, stochastic reaction-diffusion models based on the Reaction-Diffusion Master Equation (RDME) is common. Here, individual cells are discretized using an unstructured mesh and molecular diffusion is treated explicitly in the model. On cell-cell interaction level, many different modeling frameworks are used, such as stochastic cellular automatons.

Consider the involved timescales if we were to simulate a multicellular system while using the detailed level to model stochastic intracellular processes:

- 1e-8 – 1e-5 seconds: Individual diffusion events in the RDME.
- Seconds – minutes: Mean binding time between two diffusing proteins in the cell.
- Hours – days: Cell division, cell death and cell migration.
- Months – years: Time from the transformation of a normal cell to a cancerous cell to a 1 cm solid tumor.

If we were to use spatial reaction-diffusion models of the internal chemical processes of each of the individual cells, we could with state-of-the-art methods simulate a few cells (10-1000 depending on the model complexity) to the timescale of one cell division event on a high-end workstation or small cluster using a few hours of wall clock time. Clearly, tumor scale simulations are out of the question on this level of detail.

The aim of this project is to develop a new stochastic, multiscale and multilevel approximation framework that will allow for an unprecedented level of biochemical realism in simulation of multicellular systems, at manageable computational cost. This will be approached in a systematic way, going from fine scale spatial stochastic models up to coarse-grained models, such that the connection between fundamental biophysical parameters and simulated behavior remain apparent.

The group engages in scientific software development such as pyURDME (www.pyurdme.org) and StochSS (www.stochss.org). We take an interest in distributed and cloud computing.

In this project you will:

- Develop new multiscale approximation for stochastic reaction-diffusion kinetics in single cells
- Develop multiscale approximations for cell-cell communication and interaction
- Participate in scientific software development

I think that you have a strong background in computational mathematics/scientific computing. The project will be technically involved on the programming side, so proficiency in programming (ideally in C and Python) is a requirement . A documented interest to model and simulate biological systems is considered a merit.

Contact me for more information:

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