STOCHASTIC SIMULATION OF REACTION-DIFFUSION MODELS OF LIVING CELLS

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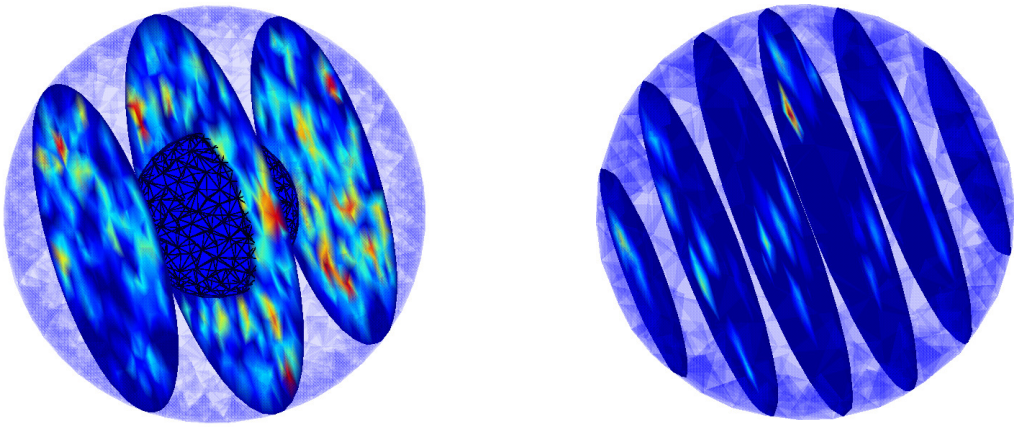
Background



This research is concerned with *approximation properties* and *improved algorithms and applications* for models of processes taking place inside living cells.

According to classical macroscopic chemistry, the concentrations of reacting substances generally obey rate-diffusion laws. Inside living cells, however, the number of molecules of the chemically active molecules is often small and reactions between the molecules are more accurately described by a *random* process. One then pictures the molecules as diffusing more or less freely inside the cell by random Brownian motion and reactions are scheduled as random events.

A good approach for simulation of such *reaction-diffusion* models is to partition the cell into subcells or compartments. The molecules in a subcell can react with each other or move to an adjacent subcell with a certain probability. A realization of the process is advanced in time by updating the number of molecules in the subcells after a reaction or a diffusion event. To the left in the figure above, the distribution of a chemical species in a cell is shown and to the right, another species is shown in the nucleus. Blue corresponds to a low number and red to a high number of molecules.

A code for simulation of models of living cells URDME is freely available from urdme.org. The code uses parts of *Comsol Multiphysics* to generate meshes and certain data needed by the algorithm. The mathematics behind the method is described in detail in [1].

In this research we collaborate actively with Johan Elf at the Department of Cell and Molecular Biology and the Centre for Interdisciplinary Mathematics at Uppsala University.

Project 1: Accuracy and model reduction

There are a number of open problems related to the numerical method: The accuracy of the method depends on the mesh quality and the size of the subcells but it is not known exactly how. The time stepping is simplified by a fractional step method but how large errors are incurred by this procedure? The cells are not rigid and a computational method is needed for moving parts. The model can be simplified in certain regions but how can these regions be determined automatically? Some molecules are actively transported in a cell. How can different types of molecular transport be included in the stochastic model?

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Project 2: Algorithms and applications

There are also several interesting research questions within the URDME software. The algorithm used is event-based and therefore of general interest in computational physics, how can it be implemented using modern multicore architectures efficiently? There is ongoing work on the simulation of microscopic models, how can they be incorporated within the event-based framework in URDME?

In many applications, molecular movement is confined to a membrane or occur in very crowded areas, how should this be modeled? When studying *populations* of bacteria, similar models with adjusted transport- and diffusion mechanisms are valid. A visual example of signalling bacteria is found here displaying a very rich and complicated macroscopic behavior. The current numerical techniques used are very simplistic and call for improvements (see the full article at *Nature*, 463(7279):326–330, 2010, doi:10.1038/nature08753).

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References

[1] S. Engblom, L. Ferm, A. Hellander, and P. Lötstedt. Simulation of stochastic reaction-diffusion processes on unstructured meshes. *SIAM J. Sci. Comput.*, 31(3):1774–1797, 2009. doi:10.1137/080721388.

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