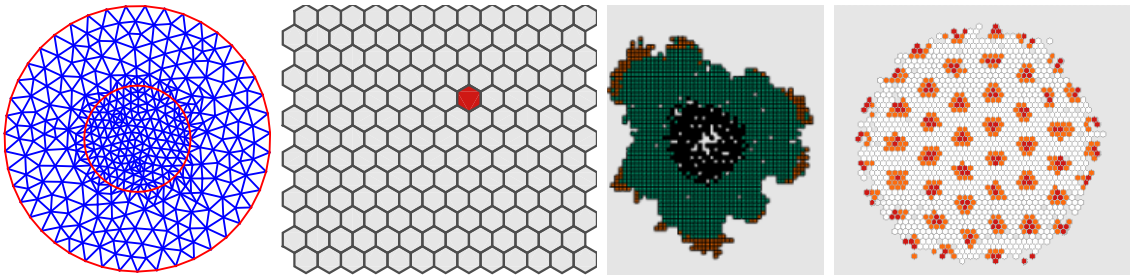
COMPUTATIONAL CELL POPULATION MODELS: MULTISCALE AND MULTIPHYSICS MODELING

STEFAN ENGBLOM



Effective summary

This line of research is concerned with *novel and improved algorithms* as well as *new applications* for models of processes taking place inside living cells and all the way up to a large population of interacting cells. The research is centered around the numerical software "URDME"[1], freely available under the GPL-license. In essence, URDME is a flexible simulator of chemical reaction networks in arbitrary geometries and is being extended with models of living cells in a population. Applications of current interest include studies in tumor modeling, neuroscience, wound healing, and embryo developmental processes.

There are several possible directions for interesting and challenging projects. For examples, *new applications of and new types of computational cell population models*, but also improving the *simulation efficiency and flexibility*. Research of a more theoretical character include questions in *numerical stochastic analysis* as well as gaining a *better understanding of certain mathematical properties* of the models involved. Precise suggestions for projects suitable to MSc/BSc-theses can be formulated upon request.

Interested candidates with a background in one or more of computer science, software engineering, computational physics, scientific computing, or molecular systems biology are more than welcome to contact me for a further discussion.

[1] http://www.urdme.org

Background

A golden standard in *reaction-diffusion* modeling at the scale of a single cell is to partition the biological cell into smaller sub-volumes and formulate a stochastic model over this discretization. The molecules (e.g., proteins, mRNA/DNA) in a sub-volume can react or move to an adjacent sub-volume according to certain probabilistic laws. A realization of the process is simulated in time by keeping track of the number of molecules whenever such a reaction- or diffusion events happen.

It is often of interest to understand the *emergent behavior* of cells: if a certain rule is followed by a single cell, what is the observed collective behavior at the population level? Across millions of cells? This is a true *multiscale challenge* and to solve it models at the single cell need to be consistently coupled with a model of the cell population which takes care of the mechanics of the whole population.

Project suggestions

The software URDME simulates event-based stochastic models and relies on *Comsol Multiphysics* to generate the required discretization. As a result of this setup, URDME is the leading software capable of simulating these models in non-Cartesian geometries. It has lately been equipped with a modeling workflow to handle also cell population models and models for single firing neurons. We are now interested in expanding on this line of research by tackling the multiscale challenge.

Ideas for further discussions include:

High-performance computing: The computational algorithm at the population level is an interesting target for efficient implementation, including also interesting issues of parallelism. There exists also the possibility of implementing approximate fast algorithms.

Advanced modeling: Cases of particular interest include models where there is a presence of signaling between cells: directly via cell-cell junctional contacts, or via cellular protrusions, and/or via chemical substances. Interesting applications include tumor growth models, angiogenesis, morphogenesis, wound healing, and embryo development processes. Another track is first-principle based models for firing neurons. There is also the possibility of performing a mathematical analysis around a subset of these models.

URL: www.stefanengblom.org
E-mail address: stefane@it.uu.se