Using GFRD to Study Pattern Formation due to the Interplay of Active and Passive Transport

Thomas Sokolowski and Pieter Rein ten Wolde

***Short Abstract* — Biological cells exploit the interplay of active transport along cytoskeletal tracks and cytosolic passive diffusion to establish a wide range of spatial patterns of functional proteins, mRNA and specialized organelles (among others). Extending the well-established Green's function reaction dynamics (GFRD) chemical simulation scheme based on analytical solutions of the Smoluchowski equation we develop a framework which allows for an event-driven spatio-temporal simulation of both transport modes in different 3D geometries with a significantly higher efficiency as compared to usual Brownian dynamics schemes.**

***Keywords* — active transport, diffusion, Green's function reaction dynamics, Smoluchowski equation, cytoskeleton.**

I. Purpose

ACTIVE transport of intracellular cargo on cytoskeletal tracks via ATP-driven motor proteins plays a key role in establishing well-defined spatial patterns of functional intracellular components, ranging from proteins to organelles. It is the interplay between active transport, cytosolic diffusion and cellular geometry that finally determines spatial patterns of the transported cargo. We aim at understanding the principles of these pattern formation mechanisms by simulating particle movement and interactions at the individual level. For that purpose we extend the Green's function reaction dynamics algorithm [1,2] to include active transport phenomena.

II. Green's Function Reaction Dynamics

Green's function reaction dynamics (GFRD) is an event-driven algorithm which makes it possible to simulate individual chemical reactions at the particle level in space and time [1,2]. The key idea is to sample if possible only the time points at which interactions of particles will occur. For that purpose, the simulation space is separated into protective domains in such a way, that a given domain contains at most two interacting particles. These domains isolate every particle or particle pair from any influence outside the domain and provide the distribution of next-event times by reducing the set of possible next events.

The Green's function of the particles inside a domain can be obtained analytically by solving the Smoluchowski equation (or Einstein diffusion equation in the one-particle case) with properly chosen boundary conditions. Potential particle reactions are represented by radiative boundaries.

Once the Green's function is found, it can be used to calculate survival probabilities and propensity functions, from which one can draw next-event times. For the smallest next-event time a new configuration is then generated for the involved particles according to the calculated Green's function and new protective domains are defined around them, starting the scheme over again for the updated objects.

For low enough copy numbers the scheme is up to five orders of magnitude faster than usual Brownian dynamics algorithms, only being slowed down by rare events of more than two particles getting very close to each other. In such a case, the GFRD simulation algorithm automatically switches to a reaction Brownian dynamics sampling scheme which accounts for detailed balance [3].

III. Including Active Transport

As active transport on cytoskeletal tracks is a stochastic process with a directional bias, the scheme can be adapted naturally to simulate also this type of transport. Our recent work introduces new shapes apart from the spherical domains used up to now (plains for membranes, cylinders for cytoskeletal filaments) and aims at solving the Smoluchowski equation for the resulting geometries.

We will make use of the extended simulation framework to address the principles of pattern emergence by modeling the polarized growth of fission yeast (*S. pombe*). In this system, active transport of regulatory factors (such as *tea1* and *tip1*) towards the cell tips on microtubule bundles causes the cell growth polarity [4] and interestingly also has been shown to affect the dynamics of the bundles themselves [5].

References

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Biochemical Networks Group, FOM Institute AMOLF, Science Park 113, 1098 XG Amsterdam, The Netherlands. E-mail: sokolowski@amolf.nl