Particle-based transport modeling: Applications to calcium puffs and filopodia

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The modeling of spatially inhomogeneous intracellular transport processes often requires the simulation of detailed particle trajectories. I will present two applications of this particle-based modeling approach.

The first part of the talk is concerned with filopodia, finger-like cell membrane protrusions that are used to probe and interact with the environment in many eukaryotic cell types. Polymerization dynamics of actin filaments, comprising the structural core of filopodia, largely determine their instantaneous lengths and overall lifetimes and require the transport of G-actin monomers along the membrane tube. Using a particle-based stochastic simulation approach, we discovered that excluded volume interactions in this crowded environment result in partial and then full collapse of central filaments in the bundle, leading to a hollowed-out structure. This work demonstrates that excluded volume effects in the context of reaction-diffusion processes may lead to unexpected geometric growth patterns and complicated, history-dependent dynamics of intermediate meta-stable configurations.

The second part of the talk will be about the release of calcium ions from intracellular stores via inositol-4,5-triphosphate receptor channels. The calcium ion concentration dynamics are highly diverse, lead to local calcium “puffs” as well as global waves propagating through cells. Local fluctuations in the number of calcium ions play a crucial role in the onset of these features, hence accurate modeling requires the simulation of detailed particle trajectories. However, tracking of individual ions is computationally difficult due to the scale separation in the ion concentration when channels are in the open or closed states. Using a spatial multi-scale model we extract calcium puff statistics and identify the regime in which puffs can be found and develop a mean-field theory to extract the boundary of this regime.