

Modelling axonal growth

Date : 23/4/2010

Laboratory

Theoretical Modeling of Cellular Physiology
UMR 8542
Ecole Normale Supérieure
46 rue d'Ulm 75005 Paris
Director : Alain Prochiantz

PhD Supervisor

David Holcman
email : holcman@biologie.ens.fr
phone : +33 144322377

Subjects / Tools-Methodologies

- 1 : Neuroscience/Computational modelling
- 2 : Biophysics/Statistical physics
- 3 : Applied mathematics/Stochastic analysis

Summary of lab's interests

The main interest of our group is to study the function of cellular microstructures in cellular biology and to develop related modeling tools. Our goal is to identify principles underlying cellular and network function in normal and pathological conditions. For that purpose, in collaboration with experimental groups, we aim to answer basic questions in cellular biology such as what defines trafficking in cells, how cells respond to stimuli, what makes virus particles optimal. We are currently working on the nucleus organization, cytoplasmic viral trafficking and synapses. Recently using asymptotic analysis and Brownian simulations, we estimated the synaptic current at excitatory synapses and study the effect of the cleft geometry, receptor trafficking and other factors. Other projects concern sensor cells, such as photoreceptors, where we work on building a complete model to better understand noise in cones and simulate the effect of drugs such as viagra which affects the the PDE enzyme activity. We dedicate a large effort to develop physical and mathematical models to study cellular properties from the molecular level. We mainly develop approaches inspired from statistical physics, partial differential equations, stochastic dynamical systems and simulations. In the past, by using asymptotic analysis, we computed the expansion of the mean time for a Brownian molecule to escape through a small hole located on a piece of a cell membrane. This computation defined the forward binding rate of chemical reactions occurring in microdomains.

Summary of project

Neuronal growth and guidance are crucial for brain development, wiring, and regeneration. Although regulators of axonal growth and guidance have largely been identified, we are still missing the molecular principles integrating these signals within the neuronal cell. Recent progresses in quantifying protein-protein interactions in vitro and in vivo, and dynamics of molecules, organelles, cytoskeletons, and cell morphogenesis combined with mathematical modeling now allow to address this complexity. We will start with a working hypothesis that membrane morphogenesis requires interplay between cytoskeletal dynamics and vesicular trafficking. We propose in this PhD to integrate various signaling pathways such as the Rab family and cellular mechanisms involving cytoskeletal and vesicular elements to study changes of neurite shape, and construct a physical models and mathematical analysis to estimate the motion of the vesicle and to predict the neurite dynamics. We propose to integrate guidance signaling that can modulate the neurite growth and its direction. The model should reveal the amount of changes in specific parameters mediating specific neuronal membrane remodeling and guidance. All together, this PhD proposal will lead to an integrated picture of the cellular biology

underlying axonal and dendritic growths in response to external signals.