AKB 8 Cell Motility: Neuronal Growth

Time: Tuesday 10:15–11:00 Room: ZEU 260

AKB 8.1 Tue 10:15 ZEU 260

Optical Neuron Guidance and Growth Cone Motility — •Daniel Koch, Timo Betz, Allen Ehrlicher, Michael Gögler, Björn Stuhrmann, and Josef Käs — Institut for Soft Matter Physics, University of Leipzig, Linnestr. 5, 04103 Leipzig, Germany

Understanding and controlling neuronal growth is a main research focus in the life sciences. All molecular stimuli for neuronal growth eventually address the polymeric cytoskeleton of the growth cone, a highly motile structure at the tip of an advancing neurite. However, the detailed molecular mechanisms underlying growth cone motility still need to be resolved. We have shown that optical forces induced by a highly focused infrared laser beam influence the motility of a growth cone by biasing the polymerization-driven intracellular machinery. In actively extending growth cones, a laser spot placed at specific areas of the neurite's leading edge affects the direction taken by a growth cone. In an optical tweezers setup simultaneous phase contrast and fluorescence imaging, real-time shape detection, and automated laser irradiation are combined to control growth cone motility. Additionally we use high resolution edge detection in combination with a cross-correlation algorithm to extract the actin cytoskeletal dynamics in a growth cone in order to shed light on the mechanisms underlying optical neuron guidance. These novel techniques allow the investigation and manipulation of a natural biological process, the cytoskeleton driven morphological changes in a growth cone, with potential applications in the formation of neuronal networks and in understanding growth cone motility.

AKB 8.2 Tue 10:30 ZEU 260

Filopodia orientation determines neurite turning — •Allen Ehrlicher, Timo Betz, Michael Gögler, Daniel Koch, Björn Stuhrmann, and Josef Käs — University of Leipzig, Linnéstr. 5 Abt PWM 04103 Leipzig Germany

Neurons must migrate through a complex array of tissues, chemical signals, and mechanical stimuli to form the connections necessary for life. At the leading edge of neuronal extensions are highly dynamic structures called growth cones, which navigate through the body, interpreting the myriad of signals into appropriate attractive or repulsive responses. Extending beyond the growth cone are spike-like bundles of actin known as filopodia, which communicate many of these environmental cues to the cell, and probe the immediate area of the cell for the best path. We have observed that the orientation of these filopodia strongly predicts growth cone turn behavior. Furthermore, using optical tweezers we directly manipulate the position and orientation of filopodia, and thus are able to induce growth cone turning. All of a cell's movements are generated by its polymeric cytoskeleton, which is composed principally by actin, microtubules, and motor proteins such as myosin, though the relevance of each constituent is yet unclear. Our observations strengthen the hypothesis that microtubule extension into the growth cone's peripheral region along filopodia is the dominating factor for neurite turning, and not asymmetry in the polymerizing actin meshwork.

AKB 8.3 Tue 10:45 ZEU 260

Quantifying the Dynamic Actin Gel and its Active Forces in Neuronal Growth — •Timo Betz, Daniel Koch, Daryl Lim, Miriam Wisehart, Allen Ehrlicher, and Josef Käs — Institut for Soft Matter Physics, University of Leipzig, Linnestr. 5, 04103 Leipzig, Germany

The neuronal wiring of a developing organism is performed by the highly motile structures at the tips of growing neurites, called growth cones. The locomotion of these structures is largely driven by the dynamics of an active actin gel in the lamellipodium, similar to other motile cells. We developed an experimental assay to measure the neuronal actin dynamics by tracking prominent structures in the lamellipodium of GFP-actin transfected neuronal cells. This is used to quantify the active movement of the actin gel in the neuronal growth cones, a process called retrograde flow. It is currently believed that the growth cone exerts forces onto the substrate by coupling the retrograde flow of the active actin gel to the substrate. To further investigate this, we additionally measure the substrate forces directly by detecting the deformation of an elastic substrate, allowing us to correlate retrograde flow with traction forces. With this assay we have established a method to simultaneously measure all the forces and dynamics necessary to test recently proposed theoretical models for cell motility. We present a detailed analysis of the actin dynamics, substrate forces and local friction constants used by neuronal growth cones as they migrate through the body to correctly wire complex neuronal networks during development.