Sebastian Jähne

The Anatomy of the Average Hippocampal Neuron

Neurons are the basic unit of our nervous system, and provide the means to execute all behavior, both simple and complex. Knowing the physical parameters of these cells, as well as their molecular composition, will further our understanding of the organization and function of the brain.

Some efforts have been made to carry out compositional studies of subcellular compartments, which have lead to molecular 3D models of the average synaptic vesicle and of the average presynaptic bouton. These studies have provided valuable mechanistic insights. They showed, for example, how proteins with similar function are quantitatively correlated in the synapse, and they identified proteins that are bottlenecks for exo- and endocytosis. Moreover, they have generated, for the first time, a molecular picture of the actual density and structure of membranes and cytosol.

At present, no studies have tackled larger structures, such as the entire neuron. Studies that investigate cells and tissues utilize only genomic or proteomic approaches. In such cases little can be said about the organization of the cells. The numbers and the positions of proteins and lipids within the studied structures are ignored: only the presence of particular genes or proteins is analysed.

Our ultimate goal is to produce a molecular model of a neuron, based on the cultured pyramidal hippocampal neuron. We will generate a model that depicts all of the organelles and the compartments of this cell, both in their accurate locations and including the majority of the proteins of the cell.

The focus of this master thesis is to carry out the initial steps towards such a model, by determining the physical parameters of the neuron, and by finding a way to accurately fit the major compartments and organelles into this scaffold.

In order to achieve this, I have established an appropriate cell culture system to provide a homogeneous set of neurons that can be used both for biochemical analysis and imaging experiments. I further established a membrane staining protocol using the lipophilic carbocyanine dye DiO, which can be employed in conjunction with conventional immunostaining protocols, and permits studying the cellular outline and structure. Finally, I investigated ways to image entire nerve cells in an efficient time scale, at high resolution.