NWO Computational Life Sciences Program

Computational Analysis of Spatio-temporal Patterns of Activity in Neuronal Networks

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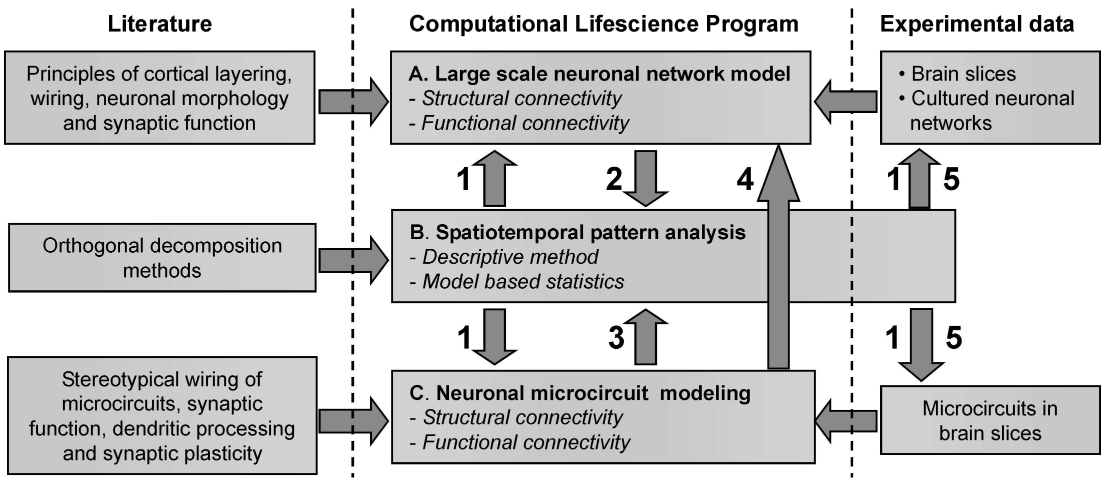
Information processing in the brain, in particular in the cortex, is based on spatio-temporal patterns of electrical activity in neuronal networks. Recently introduced experimental techniques allow the monitoring of these patterns in great detail by simultaneously recording of neuronal activity from a large number of locations in the network. High-speed photodiode array monitoring of voltage sensitive dye activity allows the study of the impact of alterations in functional synaptic connectivity on the spatio-temporal patterns of neuronal activity in cortical brain slices. With planar multi-electrode arrays, action potentials can now be recorded simultaneously from 60 sites in developing dissociated rat neocortical networks for up to 50 days in vitro.

To be able to analyse and interpret the flood of data these new techniques produce, we will develop (i) mathematical and statistical methods for analysing spatio-temporal patterns of neuronal activity, and (ii) computational models of neuronal networks to simulate these patterns and understand them in relation to structural and functional connectivity within the network. Goals (i) and (ii) will be pursued in close interaction, whereby the computational models are used to help to develop statistical methods, and the statistical methods in turn are used to test whether the model can capture the characteristics of the experimentally observed patterns. An essential part of (ii) is the development of a stochastic model for the generation of network connectivity and its variation.

The methods and models will be validated with the extensive data we have on spatio-temporal patterns in cortical brain slices and cultured neuronal networks. Ultimately, these methods and models are indispensable in the search for key genetic regulators of network development, network activity and animal behaviour. In particular, the data on spatio-temporal activity in brain slices obtained from normal (wild type) versus mutant mice (with a known genetic mutation) will be compared. The research goals will be executed in three subprojects (see Figure):



A. Development of a macroscopic neuronal network model with realistic functional and structural connectivity to simulate neuronal activity in cortical brain slices and cultured neuronal networks.
B. Development of statistical methods for analysis and comparison of experimentally observed spatio-temporal activity patterns.
C. Development of a neuronal microcircuit model composed of neurons with full morphological complexity to investigate how the fine structure of synaptic connectivity contributes to the dynamics of neuronal activity.