

The Center for Neurogenomics and Cognitive Research in Amsterdam (CNCR, see www.cncr.nl) and the Swammerdam Institute for Life Sciences (SILS, see www.science.uva.nl/sils) are seeking applications for

2 PhD-students (proteomics and computational science) fixed term, each 1+3 years

Systems Biology of the Synapse

Synapses are the fundamental processing elements that form the basis for the unsurpassed computational power of our brain. At the same time, synapses are in itself rather simple, well-defined structures of +/- 1 μm^3 with probably a maximum of 2 thousand different types of proteins present. We will apply a systems biology approach to identify protein networks underlying synapse function and to translate this into a realistic dynamical model for synaptic signalling. The project contains a "wet" proteomics research line and a "dry" network modelling research line for which two PhD positions are available. Researchers on both research lines will collaborate intensively. This project is supported by and embedded in the Netherlands Institute for Systems Biology (NISB, see www.sysbio.nl).

Research project A (Proteomics)

The project consists of three phases. First, brain fractionation techniques will be optimized to obtain synaptic fractions enriched for either pre- or postsynaptic proteins (6 months). Second, synaptic proteins will be immunoprecipitated from a synaptic fraction and analyzed using mass spectrometry. These data will be used to build a synaptic interactome. This phase also includes testing of new antibodies (custom generated). Approximately 50 synaptic protein complexes will be analyzed (18 months). Third, similar immunoprecipitations will be performed upon several challenges: genetic deletions in vivo (knock-out mice, all already available), pharmacological challenges (activation of synaptic receptors, depolarization), and other behavioral challenges. In addition, the protein profile of the synaptic membrane fraction will be compared quantitatively (total phase 3: 18 months). The choice of the antigens for immunoprecipitations and the selection of knock-out mice to test will be inspired by the model prediction in project 2 (see below).

Research project B (Network Modeling)

The project consists of two phases. First the network of interaction between synaptic proteins (interactome) has to be established from prior knowledge, existing data and the data generated in the adjoin project. The important proteins that play a role in the functioning of the synapse could then be identified in the network. The tools to be used in this research are primarily from network theory, statistics and computer science. In the second phase of the project the dynamic interactions of the proteins that form core-hubs in the synaptic interactome will be modeled using coupled linear differential equations. Model parameters are fitted from experimental data on synaptic signaling in hippocampal neurons. Model predictions will be experimentally tested in the adjoin project.

Suitable candidates:

For research project A we are looking for candidates with a master degree in Biology or Chemistry with some experience with protein chemistry and an interest in neuroscience

For research project B we are looking for candidates with a master degree in Mathematics, Statistics, (Bio)physics, or Computerscience and an interest in neuroscience

For both candidates a strong motivation to pursue a career in science, an interest in working as a team and the ability to work across disciplines are required.

Applications and more info

Please send CV and cover letter to Els Borghols at els.borghols@cncr.vu.nl with position 32A or B in the subject line **before August 15th, 2008**. More info can be obtained from Matthijs Verhage (project coordinator) at matthijs.verhage@cncr.vu.nl or specifically for project A: Guus Smit at guus.smit@cncr.vu.nl or for project B: Niels Cornelisse at niels.cornelisse@cncr.vu.nl.