Quantitative modeling of 'decision-making' going on within neurons

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Learning and memory formation in the brain, as well as the compensatory adjustments during development, ageing and brain disorders, rely on sculpturing of connectivity strengths between neurons together with control of the neuron's membrane properties. This in turn is intricately controlled through the activation of receptor induced chemical signaling cascades within neurons. Synaptic plasticity, such as long term potentiation (LTP - a long-lasting increase in the synaptic strength) and long-term depression (LTD - a long-lasting weakening of the synapse), has been characterized experimentally in several brain regions. To understand the numerous and non-linear interactions within the nerve cell leading to a 'decision' whether e.g. LTP or LTD should result in a certain situation is indeed a challenge. Computer modeling and simulations are necessary to synthesize the information gained from experimental measurements, and to further investigate and pinpoint underlying mechanisms which are critical. When searching for a mechanistic understanding how plastic changes in the nervous system are controlled it is also useful to build multi-scale models, where interactions between the neural networks electrical signaling and the subcellular chemical signaling are integrated and allowed to influence each other.

The student(s) working with a project along these lines should ideally have knowledge in biochemistry in addition to computer programming experience. The study time will be spent in both Stockholm and Bangalore, and should in addition include a visit for 6 months in total to Edinburgh or Freiburg.

Work along these lines by the supervisors are exemplified in the following references [1-5].

1. Ajay SM, Bhalla US (2007) A propagating ERKII switch forms zones of elevated dendritic activation correlated with plasticity, HFSP J. 1(1):49-66.

2. Bhalla US (2011) Multiscale interactions between chemical and electric signaling in LTP induction, LTP reversal and dendritic excitability, Neural Netw. 24(9):943-9.

3. Kotaleski JH, Blackwell KT (2010) 'Modelling the molecular mechanisms of synaptic plasticity using systems biology approaches', Nat Rev Neurosci. 2010 Apr;11(4):239-51. Review.

4. Lindskog M, Kim M, Wikström MA, Blackwell KT, Kotaleski JH (2006) Transient calcium and dopamine increase PKA activity and DARPP-32 phosphorylation, PLoS Comput Biol. 2006 Sep 8;2(9):e119.

5. Rajasethupathy P, Vayttaden SJ, Bhalla US (2005) Systems modeling: a pathway to drug discovery, Curr Opin Chem Biol. 9(4):400-6. Review.