UNIVERSITÄT ZU LÜBECK

TECHNISCHE HOCHSCHULE LÜBECK

**Master thesis**

**Topic: A computational model of dynamic memory formation and degradation in neuronal networks**

**Summary:**
Experimental evidence of structural plasticity allows to say that neurons in learning networks rewire their connections after sensory stimulation, due to elimination of existing spines and generation of new ones.
This process cannot be described mathematically in a deterministic way and can be modelled as a Markov process with different transition rates and transition probabilities. This allows for computational random simulations, which can be averaged to obtain the expected connectivity evolution of a network subjected to external stimuli. The same result can be obtained alternatively solving a system of differential equations provided by a mathematical model called "Directed Configuration Model" (DCM).
The DCM was so far studied with additional constraints, which imposed the total sum of possible connections and neuronal terminals (called "synaptic resources" for simplicity) to be constant throughout the entire evolution of the network. These constraints however do not allow the model to be usable in scenarios where the number of possible total connections changes overtime, for example due to a neurodegenerative disease. For this reason, this thesis worked without those constraints, extending the DCM to describe the evolution of a learning network which is slowly destroyed by Alzheimer's disease and subject to compensation mechanisms. The model was also extended to introduce the action of therapeutic non-invasive brain stimulation, more specifically transcranial direct current stimulation (tCDS). The disease and tDCS were modelled with a semi-quantitative approach, using modelling assumptions based on the current literature trying to inform as many parameters as possible from experimental evidence. This was done with the aim of studying how different tDCS stimulation parameters affect positively or negatively the strength of the memories, in the short term (during the tDCS protocol) and long term (after the tDCS protocol). Another goal was to test which of the two proposed modelling assumptions for tDCS agrees the best with the experimental evidence.
Those goals were accomplished by performing several in-silico experiments, studying the expected evolution of a network made of populations of neurons, subject to repeated learning stimuli, tDCS and Alzheimer's disease. For each experiment a different tDCS stimulation parameter was changed to see the positive, negative or absent effects on the memories stored in the network. The simulations were performed solving the differential equations of the extended DCM model, and internal population connectivity was used as measure of the strength of memories.
The results of the experiments showed that: 1) modelling tDCS as a learning stimulation followed by an increase (regeneration) of resources produces improvements matching the

available experimental evidence; 2) Long term improvements after tDCS application are only due to the amount of resources regenerated during the tDCS protol; 3) short term changes in memory strength during the tDCS protocol can be caused by several stimulation parameters, such as timing and intensity of the tDCS stimuli, and amount of regenerated resources.
Agreement was observed between the experimental results and the experimental evidence, observing improvements in memory strength due to the tDCS. This thesis can be used as a starting point for new experimental studies to check if the results of real-life experiments adhere to the in-silico experiments. Additional speculations about homeostatic structural plasticity and tDCS resource growth curves were also made to motivate the design of further studies.

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