Initial Report of 3rd year dissertation on Effect of Synaptic Plasticity on CA1/CA3 pyramidal neurons

Introduction

The human brain is the most complex, sophisticated, and powerful information-processing device known. The mechanism behind the cognitive functions of the human brain remains enigmatic. Investigating the brain under a computational point of view has the difficulty that three in general hard questions have to be answered at the same time: 1) What information is processed? 2) How is the information coded in the spatio-temporal structure of neuronal activity? 3) What computational operations are performed by cortical networks? We're building computational models as a way to bridge the gap between these levels of description and to integrate information from multiple sources into a coherent picture.

One of the vital players in cognitive functions is the human memory system which is interconnected with the learning paradigm as well. We begin our exploration of this plasticity in this proposed work, by modelling in the neuronal level. As of yet we know of two memory structures in human brain mainly the cortex and the hippocampus. The hippocampus and the related structures are specialized for rapid arbitrary learning, while the cortex slowly accumulates semantic representation based on many experiences. This work will feature memory and learning rules which are mainly localised in hippocampus.

Hippocampal memories are broadly divided into *episodic* (having information about episodes or events), *declarative* (representing explicitly available information) and *spatial* (representation in space). This work intends to see the effect of learning and memory on CA1 and CA3 pyramidal neurons present in the hippocampus. It will be carried out in a variety of simulation environment, like *NEURON* (based on cable theory), *PDP++* and *GENESIS* (based on compartment) so that the result could be equally justified in all the models.

Here we will use an approach based on Hebbian learning that achieves model learning objective of developing an internal model of the important structural features of the environment (i.e., things are strongly correlated). We would look into the biological mechanism of learning through the associative nature of LTP/D in terms of two requirements for opening of the NMDA receptor: presynaptic neural activity and postsynaptic activity.

Specification

This will be carried through the simulation on the CA1/CA3 pyramidal neuron model, and observing the effect of hebbian plasticity, in the form of *long-term potentiation (LTP)* and *depression (LTD)* which is the basis of most models of learning and memory, as well as the development of response selectivity and cortical maps. Hebb originally conjectured that synapses effective at evoking a response should grow stronger, but over time Hebbian plasticity has come to mean any long-lasting form of synaptic modification (strengthening or weakening) that is synapse specific and depends on correlations between pre- and postsynaptic firing. This work endeavours to explore this effect along with unravelling few facts like Hebbian plasticity gains great power by acting independently at each synapse but in the same time acquires stability problems as well. We will be concentrating on Hippocampus as it serves as one of the major memory architecture beside the neo-cortex. Hippocampus is relatively more important for spatial representation and hence important to this work.

It will look into the issue of the modification of synapse during learning and memory. The project would briefly touch the mechanism of synaptic scaling, spike-time dependent plasticity (STDP) and synaptic redistribution.

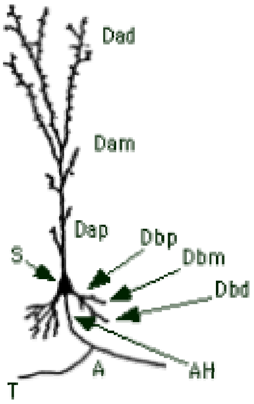

Figure 1 CA1 pyramidal neuron

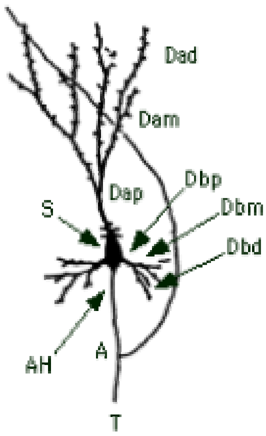

Figure 2 CA3 pyramidal neuron

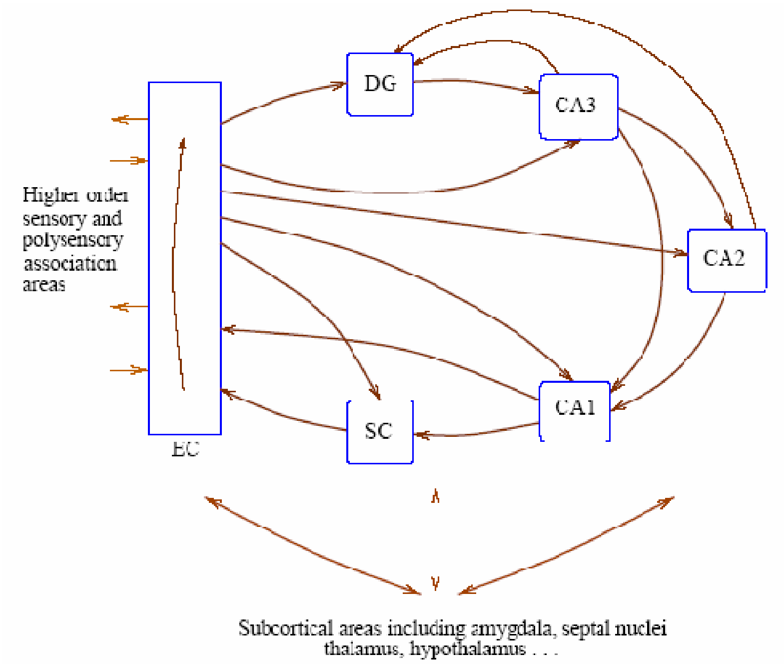

Figure 3 Summary of major pathways interconnecting the components of the hippocampal system. Note the multiple pathways from EC to CA1, CA2, CA3, and SC. Also note the back projections from CA1 and SC to EC. The HS also receives a wide array of sub cortical inputs (not shown). The subicular complex (SC) has been depicted as a single monolithic component for simplicity. Abbreviations: HS, hippocampal system; DG, dentate gyrus; EC, entorhinal cortex; SC, subicular complex.

Approach

As a starting point, a neuronal lattice is to be created which is full of neurons found in the CA1 and CA3 areas of the hippocampus. The exact parameters of these neurons will be obtained from the Neuron database maintained in Yale University's *Sense Lab*. The neuronal lattice thus obtained will be trained using Leabra algorithm that combines error-driven and Hebbian learning with k-Winners-Take-All inhibitory competition (available in PDP++) or as an alternate measure we can use the *hebbsynchan* object in the GENESIS environment, which works exactly like the standard synaptic object, except that the weight value of the synapses are adjusted based on a product of the pre- and postsynaptic activities. Then the effect of this synaptic plasticity will be observed on the single neuron and subsequently the whole lattice will be taken into consideration to see what level of plasticity propagates from the input receptor to the n X n matrix of neuron. To generate realistic results, in the proposed neuronal lattice, synapse-specific Hebbian forms of plasticity, such as long-term potentiation and depression, must be augmented by global processes that regulate overall levels of neuronal and network activity as regulatory processes are often as important as the more intensively studies Hebbian processes in determining the consequences of synaptic plasticity for network function.

We know that during learning the NMDA channel allows calcium ions (Ca^{++}) to enter the synapse, which triggers a complex sequence of chemical events that ultimately results in the modification of synaptic efficacy (weight). Hence, this model will allow us to see the effect of the learning and memory on the output transmitters like NO and Glutamate.

Model learning is difficult as we are presented with a large amount of low quality information from our cognitive senses. The appropriate *a priori* biases are hence important to supplement and organize our experiences. As detailed earlier, the main objective of this work is to see the effect of plasticity on the far end of a group of interconnected neuron, when learning is induced in one end and allowed to propagate. The usefulness of the simulation environment has not yet been tested, so if need be custom software may also have to be written.

Timetable

The total time available for this project is around seven months i.e., from November 2003 to May 2004. The most important objective of this work is to understand the neural coding used in learning through the use of spike-time dependent rules. Since most of work presented here would be influenced by Gerstner's book, I plan to go through the whole book in depth so as to have a clear understanding of the problem. The main stages involved for proper execution of this project are:

1. *Literature survey*
2. *Constructing models of the neurons on the specified simulation environment*
3. *Inducing synaptic plasticity in the form of Hebb learning*
4. *Observing the effects on the neuron and the synapses*
5. *Collecting results and writing the dissertation*

NOV	DEC	JAN	FEB	MAR	APR	MAY
1	1					
	2	2				
			3			
			4	4		
				5	5	5

The month of May is in a way a contingency period, though a lot of time is envisaged in choosing the proper simulation environment and carrying out the simulations.

Current Research

A lot of work is going around the world studying the synaptic plasticity property of the neuron and to search for techniques to model them exactly as their biological counterparts. Apart from the study of the purely phenomenological model for spike time dependent synaptic plasticity, researchers have come out with kinetic models based on the NMDA receptors and calcium control hypothesis.

Recently a lot of interest has been focussed on episodic memory. Episodic memory (Tulving, 1995) refers to our ability to remember events and situations in our daily lives and acquire memories of specific events by reading a newspaper or watching a newscast. There is a broad consensus that the hippocampal system (HS) consisting of the hippocampal formation and neighbouring cortical areas in the medial temporal lobe plays a critical role in the encoding and retrieval of episodic memories (Squire, 1992; Cohen & Eichenbaum, 1995; Nadel & Moscovitch, 1997). But how the HS sub serves this mnemonic function in concert with cortical circuits is not fully understood. The firing pattern of plasticity is also an interesting realm of ongoing research.

References

- Abbott, L.F. (2000). *Synaptic plasticity – taming the beast*. Nature Neurosci., 3:1178-1183
- Shastri, L. (1988) *Semantic Networks: An evidential formalization and its connectionist realization*, (MorganKaufamnn)
- Gerstner, W and Kistler, W. (2002) *Spiking Neuron Models* (CUP)
- C.O'Reilly, R and Munakata, Y (2000) *Computational Explorations in Cognitive Neuroscience* (MIT Press)
- Mira, J., and Alvarez, J. R., (Eds.) (2003), *Computational Methods in Neural Modelling*, Proceedings IWANN 2003, LNCS 2686, Springer, Berlin
- Schwartz, J.H et al (2000). *Principles of Neural Science* (McGraw-Hill)