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DIRECT ASSESSMENT OF SYNAPTIC MODIFICATION RULES(U)  
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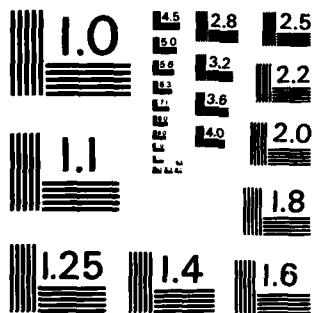
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) <b>Our objectives are to quantify synaptic modification rules and to understand them in a context of simple neural networks capable of pattern recognition and clustering. The experimental work plus considerations of parsimony favors one particular form of the excitatory synaptic modification rule. Modification of the translation of synaptic activation into cell firing may well be governed by a separate rule. Although different than the first rule, simple computer models show these two rules are together compatible and noncontradictory.</b>		

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**AFOSR-TR- 84-1015**

**AFOSR-83-0236  
Annual Scientific Report  
15 June 1984**

**DIRECT ASSESSMENT OF SYNAPTIC MODIFICATION RULES**

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## 2. Research Objectives:

Our objective is to determine the most reasonable form(s) of algebraic equations governing synaptic modification and other neuronal modifications that would allow neural circuits to perform pattern recognition and concept formation. A second objective is to determine in theoretical analyses how these equations affect the performance of simple neural networks.

## 3. Status of the Research:

Recall that our experiments stimulate the monosynaptic excitatory pathway from the entorhinal cortex to the dentate gyrus. In the dentate gyrus extracellular field potentials measure synaptic excitation and sometimes cell firing.

Below we refer to our favored synaptic modification equation

$$\Delta m = \epsilon \cdot f(y) \cdot (x - m)$$

$\epsilon$  is a non-specific, arousal-like term

$f(y)$  is a postsynaptic term related to net excitation. The term  $(x - m)$  is a presynaptic term;  $x$  is presynaptic frequency;  $m$  is the synaptic strength.

Study (1) documents the long-term nature of associatively induced depression. This same study also shows that prior, experimentally induced potentiation is not a requirement for demonstrating the induced depression. The experiments in this study plus considerations of parsimony argue for the absence of a temporal decay term in the excitatory synaptic modification rule.

Study (2) for which the data has been collected but is still undergoing analysis, is the documentation of the asymptotic nature of associative long-term potentiation and depression.

In this study and in many of our future experiments we must be in total control of efferent entorhinal activity. With the large number of repeated high frequency conditioning stimulations given in this experiment, and in the planned perturbation experiments, the likelihood of recirculating and/or endogenous limbic activity through the entorhinal cortex is quite high. Our old method of lesioning the entorhinal cortex increases the tendency for seizures so that many experiments are no good and must be discarded. A new method was developed and documented. This involves placing many small injections of the neural toxin tetrodotoxin in the entorhinal cortex.

After much experimentation we were able to determine concentrations and volumes which allowed our stimulating electrodes in the angular bundle to work but which blocked stimulation of the entorhinal cortex itself. Using the proper injection parameters this block easily lasts several hours longer than the experiments.

With this technique we were able to do the study of asymptotic modification. This study (2) documents onset of these asymptotic synaptic modifications and their long-term nature.

Substantively we were able to infer from this experiment that asymptotes are produced as specific rather than nonspecific processes. This implies that the arousal like term ( $\epsilon$ ) of the synaptic modification equation going to zero is not the prime cause of the asymptote and that the presynaptic term ( $x-m$ ), rather than the postsynaptic term  $f(y)$ , is going to zero to produce the asymptotic condition. This conclusion is totally consistent with the above equation.

As an added by product of this study it was noted that the onset of both potentiation and depression can be seen at least as soon as 980msec after a 17.5msec conditioning train. Although the potentiation may well be nonassociative this is not so likely in the case of depression.

The data of this experiment is currently undergoing extensive analysis. A small portion has been written in abstract form. The entire study may be analyzed and written by next year.

Another study (3) confirms a nonsynaptic modification which appears to obey slightly different rules than the excitatory synaptic modification above. This input-output study looked at the relation between synaptic drive and cell firing-as well as is possible with extracellular field potentials. In this work we confirmed the long-term modifiability and reversibility of this input-output function. We were able to show that the contingency of CA4 stimulation (which is net inhibitory upon the dentate gyrus) is able to produce the input-output shift. This effect predicts a second and different modification equation than the equation shown above. In particular, convergent excitation [ $f(y)$ ] is not required. Simple modelling shows the synaptic rule and the rule for this "nonsynaptic" modification are complementary thus extending the contingencies a neuron can learn. However, this study was done prior to the development of the tetrodotoxin technique and requires replication with this method if results are to receive strong interpretation, and extensive mathematical treatment.

Finally, study (4) identifies morphological changes at synapses which imply a subcellular mechanism of enough specificity to produce the physiological modifications we have observed. This work studied the postsynaptic density of entorhinal-dentate synapses in the region of synapses showing long-term potentiation. These postsynaptic densities increase in size consistent with the idea that potentiation is mediated by stronger synapses.

In the area of neural modelling we constructed a feedback circuit that includes mostly excitatory elements. For this circuit we identified the conditions that will guarantee convergence to a stable value. The actual value varies with the input. This circuit is used to combine probabilistic predictions of neurons receiving different inputs so as to produce predictions of patterns which are consistent among the neurons of the entire network.

We are currently trying to establish the consistency of the experimentally favored synaptic modification rules as the rules governing modification in this circuit. We will ask what type of concept formation (clustering) properties this circuit will have if its synapses are so modifiable.

Our other work will continue to experimentally confirm (or alter) the two types of modification rules discussed above.

#### 4. Publications:

1. Levy, W. B & Burger, B. Long-term depression as a companion of LTP. submitted for publication, Exp. Brain. Res.
2. Burger, B., Dickstein, R. & Levy, W. B Determinants of asymptotic limits of long-term potentiation. Soc. Neurosci. (1984) Abst.
3. Levy, W. B Long-term reversible changes in the translation of synaptic current into cell firing. Soc. Neurosci. (1984) Abst.
4. Desmond, N. L & Levy, W. B LTP-associated changes in postsynaptic density length and the length of the synaptic interface in the dentate gyrus. Soc. Neurosci. (1984) Abst.

#### 5. Personnel:

William B Levy, Ph.D., Research Assistant Professor -50%  
Ruth Dickstein, D.Sci., Research Associate -100%  
Barbara Burger, Graduate Student in Neuroscience -100%

#### 6. Talks:

I gave talks at: Baylor Medical School in Houston, Department of Neuroscience, September 1983; Institute for Cognitive Psychology at UC SAN Diego, July 1983; at AFOSR at Bolling to the Life Science Group, Winter 1984; and at the AFOSR evaluation meeting at Irvine, July 1984.

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