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The following Progress Report describes the results of the majority of our AFOSR-supported research for Year 3 of the project entitled "A Systems Theoretic Investigation of Neuronal Network Properties of the Hippocampal Formation." The Progress Report is divided into six sections: a brief statement of the research objectives, an overview of general experimental and analytical procedures; research characterizing nonlinear response properties of the in vivo dentate gyrus; the extension of this research to the in vitro hippocampal slice; computer simulations of nonlinear response properties of the dentate based on the experimental work; and a listing of publications during the past year of support.

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The following Progress Report describes the results of the majority of our AFOSR-supported research for Year 3 of the project entitled "A Systems Theoretic Investigation of Neuronal Network Properties of the Hippocampal Formation." The Progress Report is divided into six sections: a brief statement of the research objectives, an overview of general experimental and analytical procedures; research characterizing nonlinear response properties of the *in vivo* dentate gyrus; the extension of this research to the *in vitro* hippocampal slice; computer simulations of nonlinear response properties of the dentate based on the experimental work; and a listing of publications during the past year of support.

OBJECTIVES

The goals of our research are to develop a mathematical model and computer simulation of the functional network properties of the hippocampal formation, a brain system essential for the formation of memory. The hippocampal formation is typical of neuronal systems in the mammalian brain in that it is composed of many populations of neurons which are heterogeneous with respect to neurotransmitter and biophysical membrane properties, and which are interconnected through feedforward and feedback pathways into a complex network structure. These factors greatly increase the difficulty of i) determining dynamic properties of the global network, and ii) distinguishing between response dynamics that are intrinsic to a given cell population and response dynamics that derive from other neuronal populations through network connections. We have developed and applied a combined theoretical and experimental approach based on nonlinear systems theory that we believe overcomes some of these difficulties.

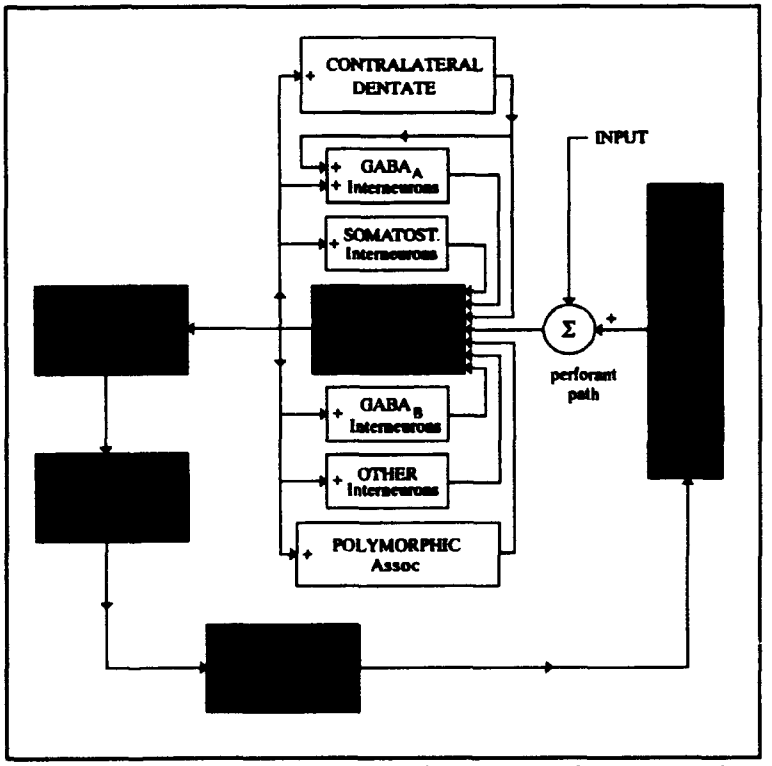

Figure 1. Schematic diagram of the five subsystems of the hippocampal formation and the major feedforward and feedback pathways within the dentate gyrus

In general terms, our strategy has been the following. The nonlinear response properties of each subsystem are assessed experimentally by applying a random interval train of electrical impulses to the fiber pathway which connects that subsystem to the remaining network. For example, the majority of our studies to date have utilized stimulation of the

perforant path, which arises from the entorhinal cortex and terminates within the dentate gyrus. Throughout random train delivery, evoked activity is recorded from the projection neurons of the stimulated subsystem; in the case of perforant path stimulation, evoked activity is recorded from granule cells of the dentate gyrus. Nonlinear input/output properties of the subsystem are defined as the kernels of a functional power series expansion, and computed as the relationship between inter-impulse intervals of the input signal and magnitude of projection cell output.

Such an analysis is completed for the intact hippocampal formation, when each subsystem is embedded in the larger network, and for experimentally reduced preparations in which feedback from other subsystems and/or from intrinsic interneurons is eliminated. Through systematic "decomposition" of the network, the contribution of each feedback loop can be assessed quantitatively, and an open-loop characterization of the projection neuron population ultimately can be obtained.

GENERAL EXPERIMENTAL AND ANALYTICAL PROCEDURES

Preparations. All experiments are conducted using the hippocampus of male, New Zealand white rabbits. For experiments conducted both *in vivo* and *in vitro*, fibers of the perforant path were stimulated electrically and the evoked response of granule cells of the ipsilateral dentate gyrus were recorded from the cell body layer. Recordings of extracellular population spike and epsp responses are used to monitor global activity of populations of granule cells; intracellular recordings are used to monitor the activity of single neurons.

Random Impulse Train Stimulation. A random interval train of electrical impulses was used to stimulate perforant path fibers. The train consisted of a series of 4064 impulses with inter-impulse intervals drawn from a Poisson distribution. For most experiments conducted to date, the mean inter-event interval (λ) of the random train has been 500 ms and the range of inter-event intervals has been 1-5000 ms.

Analytical Procedures. Nonlinear input/output properties of the dentate are defined as the kernels of a functional power series expansion:

$$y(t) = G_0 + G_1[h_1,x(t)] + G_2[h_2,x(t)] + G_3[h_3,x(t)] + E \qquad (1)$$

where y(t) is the output of dentate granule cells, (G_i) is a set of mutually orthogonal functionals, (h_i) is a set of symmetric kernels which characterize the relationship between the input and output, and E is an error term due to truncation. The train of discrete input events defined by x(t) is a set of δ-functions representing the stimulus train. The first four kernels of the series are obtained by the process of orthogonalization using cross-correlation techniques applied to point process events.

Interpretation of the Kernel Functions. The first order kernel, $h_1(\tau)$, is the average of all evoked dentate population spike responses (with a latency of τ) occurring during train stimulation. The second order kernel, $h_2(\tau, \Delta)$, represents the modulatory effect of a preceding stimulus occurring Δ ms earlier on the number of granule cells activated (with a latency of τ)

by the most current stimulation impulse, irrespective of any other impulses which may occur during that interstimulus interval. The third order kernel, $h_3(\tau, \Delta_1, \Delta_2)$, represents the modulatory effect of any two preceding stimuli occurring Δ_1 ms and Δ_2 ms earlier on the number of granule cells activated by the most current stimulation impulse, irrespective of any other impulses which may occur during either interval. In a more general sense, the kernel functions provide a complete characterization of the functional properties resulting from the interaction among whatever system of neural elements is studied (the elements comprising the system may be conductances, single neurons, populations of neurons) studied. As a result, the kernels provide a basis for predicting the activity of those elements in response to any arbitrarily selected stimulus condition.

NONLINEAR SYSTEMS ANALYSIS of the *in vivo* HIPPOCAMPAL DENTATE GYRUS

In experiments conducted previously, we characterized nonlinear response properties of granule cells recorded *in vivo*. When a relatively low stimulus intensity was used for random impulse train stimulation (one that evoked a population spike amplitude approximately 10% of maximum when the perforant path was stimulated using single impulses delivered at 0.5 Hz), first order kernels showed that the average population spike amplitude was 2.2 ± 0.3 mV (Figure 2, upper panel).

Second order kernels indicated that granule cell output exhibited prominent nonlinearities in response to several ranges of interstimulus intervals: population spike amplitude was almost completely suppressed when preceding impulses occurred within 10-30 ms (Figure 2, middle panel), and there was a marked facilitation of spike amplitude when preceding impulses occurred within 50-400 ms. Maximum facilitation was exhibited when Δ=90-100 ms. Intervals greater than 1000 ms induced no consistent change in spike amplitude.

Prominent third order nonlinearities were expressed when the intervals separating any pair of preceding intervals was ≤200-300 ms. In response to these stimulus patterns, granule cell output was reduced by an average maximum of approximately 60% of the first order kernel, with the magnitude of suppression inversely related to interval length (Figure 2, bottom panel).

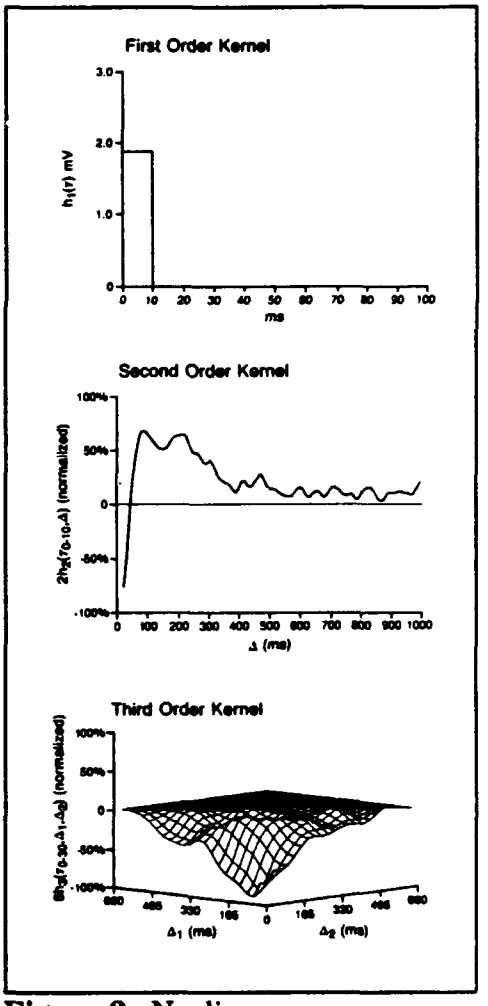

Figure 2. Nonlinear response properties of dentate granule cells: medial perforant path input

Differences between Nonlinearities of Granule Cells Expressed in Response to Medial and Lateral Perforant Path Input

We recently have begun an analysis of the lateral perforant path as well. The two pathways can be distinguished easily using established criteria (McNaughton and Barnes, 1977). Our initial results have revealed that, in marked contrast to the medial perforant path, second order kernels for the lateral perforant path display inhibition for almost all inter-impulse intervals within the range of 10-1000 ms. In some preparations, a slight facilitation (10-20%) of population spike amplitude is seen in response to intervals of 50-100 ms. In further contrast to the medial perforant path, third order kernel values are almost exclusively positive, indicating facilitative interactions.

The medial and lateral perforant paths transmit information from associational neocortical and olfactory brain regions, respectively (Wilson and Steward, 1978), and terminate onto spatially restricted, non-overlapping regions of granule cell dendrites (Steward, 1976). The contrasting nonlinear response properties of the two components of the perforant path indicate that functional characteristics of the dentate gyrus (and thus, the entire hippocampus) may be determined by the modality of stimuli being processed. Neural representations associated with non-olfactory stimuli would be subject to the transformations characteristic of the medial perforant path, whereas those associated with olfactory stimuli would be subject to the transformations characteristic of the lateral path. More interestingly, associations of non-olfactory and olfactory cues (e.g., Staubli et al., 1984; Eichenbaum et al., 1988) would involve a cross-modulation of the activities propagated along the medial and lateral perforant paths, respectively. Such an interaction between the input/output properties of two pathways can be studied readily within the context of a systems analysis approach by using asynchronous random train stimulation of both inputs simultaneously (Sclabassi and Noreen, 1981). "Self-kernels" and "cross-kernels" computed for the two afferents would reveal, for example, the extent to which granule cell response to a medial perforant path impulse depends on the time since a prior medial perforant path impulse (self-kernel), and the time since a prior lateral perforant path impulse (cross-kernel).

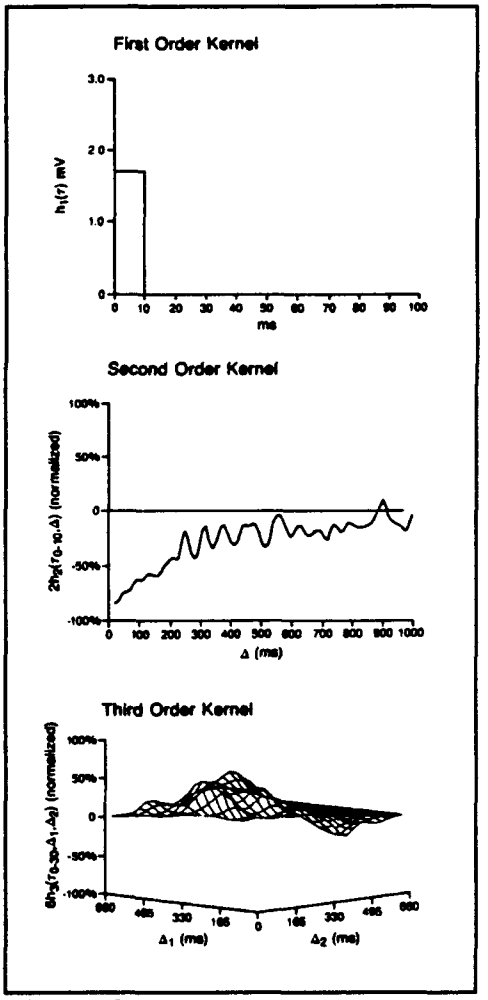

Figure 3. Nonlinear response properties of dentate granule cells: lateral perforant path input

Importantly, the identical dual input procedures can be extended to asynchronous activation of subcomponents of the medial or lateral perforant path (i.e., subcomponents of a homogeneous pathway), so that synchronous discharge of target neurons is not the only condition used for evaluating network function.

Feedforward Projections of Perforant Path Afferents to Hippocampal Pyramidal Neurons: Electrophysiological Studies

Functional characterizations of the hippocampus have been based primarily on its intrinsic trisynaptic circuitry, formed by successive excitatory projections from the entorhinal cortex to the dentate gyrus, from dentate granule cells to CA3 pyramidal cells, and finally from CA3 pyramidal cells to CA1 pyramidal cells. Despite anatomical evidence for additional monosynaptic projections from entorhinal to CA3 and CA1, few *in vivo* electrophysiological studies of the direct pathway have been conducted to test the validity of the cascade model of the hippocampus. We stimulated axons of entorhinal cortical neurons *in vivo* and recorded evoked single and population spike responses in the dentate, CA3 and CA1 of hippocampus. to determine if pyramidal cells are driven primarily via monosynaptic or trisynaptic pathways. Results of our earlier studies showed that neurons within the three subfields of the hippocampus discharge simultaneously in response to input from a given subpopulation of entorhinal cortical neurons, and that the initial monosynaptic excitation of pyramidal cells then is followed by weaker excitatory volleys transmitted through the trisynaptic pathway. In addition, we found that responses of CA3 pyramidal cells often precede those of dentate granule cells, and that excitation of CA3 and CA1 pyramidal cells can occur in the absence of dentate granule cell excitation.

During the previous year, we demonstrated that the direct entorhinal input to CA3 pyramidal neurons can express LTP that is homosynaptic (pathway specific) and NMDA-receptor dependent; this contrasts with LTP of granule cell input to CA3 (the disynaptic component), which is heterosynaptic (enhanced efficacy to all inputs) and does not depend on activation of NMDA receptors. In addition, we investigated the optimal stimulus parameters for the induction of LTP and found that LTP of granule cell input occurs preferentially in response to frequencies < 50 Hz, whereas LTP of perforant path input occurs preferentially to 400 Hz.

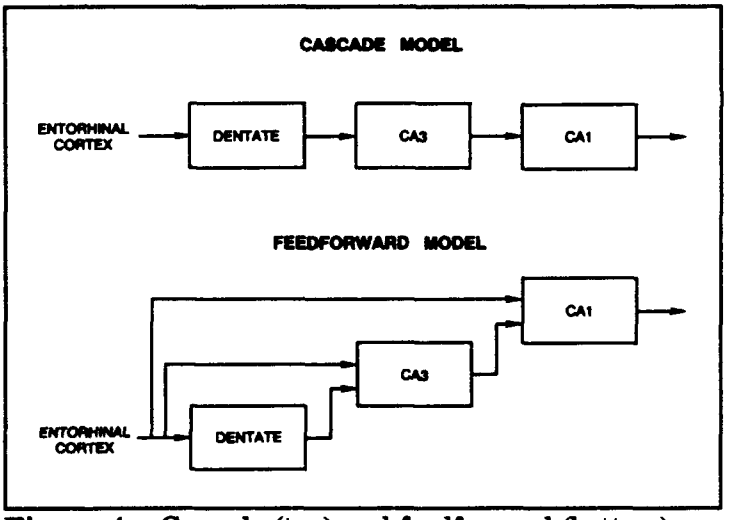

Figure 4. Cascade (top) and feedforward (bottom) models of the hippocampal formation

In total, these results argue that instead of the traditionally assumed cascade relationship between the three subsystems of the hippocampus, excitatory input from the entorhinal cortex initiates a two-stage feedforward excitation of pyramidal cells, with the dentate gyrus providing feedforward excitation of CA3, and with both the dentate and CA3 providing feedforward excitation of CA1. As a direct consequence of these studies, we are developing the higher-order Laplace transform expressions for such an excitatory feedforward system. Using the Laplace transforms for this case, experimentally determined first, second, and third order kernels for the dentate, CA3 and CA1 may be combined to realize an input/output model of the functional dynamics of the hippocampus.

The existence of a significant NMDA-mediated component of transmission through this pathway suggests that the feedforward connection could contribute significantly to nonlinearities in the input/output properties of CA3 pyramidal cells because of the prominent voltage-dependent blockade of the NMDA channel by Mg^{++} ions. Finally, because it appears that the optimal induction parameters may differ for these pathways, the possibility exists that different patterns of afferent activity could lead to the selective induction of homosynaptic or heterosynaptic LTP (in different pathways), and thus have fundamentally different consequences for global functional properties of the hippocampal system.

GABAergic Modulation of NMDA-Dependent Synaptic Responses *in vivo*

The voltage-dependence the Mg^{++} blockade of the NMDA channel suggests that the magnitude of the NMDA receptor-mediated excitation of dentate granule cells will be dependent on the level of depolarization, and thus, the level of GABAergic inhibition. During this past year, we investigated this possibility through experiments that examined the NMDA receptor-mediated synaptic responses of granule cells *in vivo* in the presence of CNQX (50 μM), an antagonist for the glutamatergic AMPA receptor. Results showed that the specific NMDA receptor antagonist, APV, reduced the CNQX-resistant EPSP by approximately 12% in response to low intensity stimulation, and 27% of baseline in response to high intensity stimulation. However, when the $GABA_A$ receptor antagonist, bicuculline, was infused concurrently, a larger NMDA-mediated component of the EPSP was observed: APV reduced the area of the EPSP evoked using low intensity stimulation by 22%, and using high intensity stimulation by 40% of the respective pre-drug baselines (Figure 5). These data indicate that local inhibitory mechanisms *in vivo* interact with convergent excitatory afferents to determine the nonlinear intensity-response properties of the NMDA receptor channel.

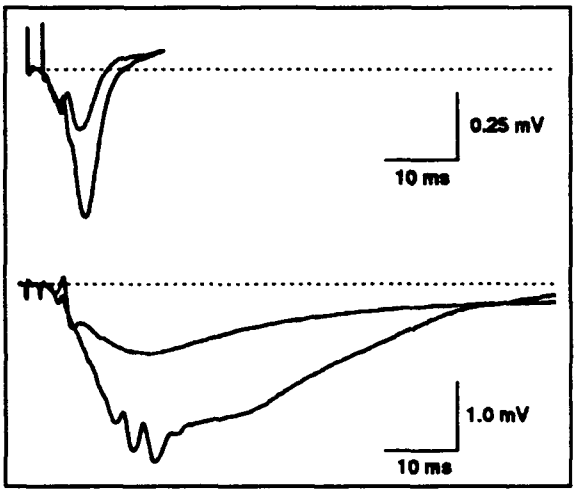

Figure 5. Magnitude of the NMDA receptor-mediated component of population EPSPs recorded in the absence (top) and the presence (bottom) of the $GABA_A$ receptor antagonist, bicuculline.

Other Investigations of the Dentate Gyrus and Hippocampus *in vivo*

In addition to the studies outlined above, there are several other projects currently in progress that are investigating the nonlinear response characteristics of the hippocampus, or fundamental anatomical and electrophysiological properties that are relevant to those nonlinear characteristics. These other studies include: i) changes in nonlinearities observed after the induction of LTP; ii) anatomical investigations of the topography of the monosynaptic and disynaptic inputs to CA3; iii) simultaneous multiple electrode recording from different anatomical locations throughout the hippocampal formation; iv) a comparison of nonlinearities expressed by granule cells of dorsal and ventral hippocampal slices.

NONLINEAR SYSTEMS ANALYSIS of the *in vitro* HIPPOCAMPAL DENTATE GYRUS

We are making extensive use of the *in vitro* hippocampal slice as a preparation that eliminates virtually all feedback to the dentate from other subfields of the hippocampus, allowing an identification of granule cell response dynamics that originate from intrinsic mechanisms only. As we reported last year, nonlinearities expressed by granule cells *in vitro* are significantly different from those expressed by the same cell population *in vivo*. For example, second order nonlinearities of the *in vitro* slice (Figure 6, left panel) were equally prominent, but were qualitatively different than those exhibited by *in vivo* preparations. Instead of suppression of granule cell output in response to short inter-impulse intervals, a robust facilitation was observed. The facilitation was greater in magnitude (with respect to normalized kernel values, 241 ± 27%), occurred maximally in response to shorter intervals (10-20 ms) compared to data from *in vivo* preparations, and was expressed only in response to intervals less than 100-150 ms, a much narrower range than observed *in vivo*. In addition, data from slices consistently exhibited suppression to intervals of 150-800 ms; interstimulus intervals within the same range produced facilitation or no effect for *in vivo* preparations. Third order kernels from slices revealed suppression of a larger magnitude (normalized values, average maximum of 90%), and in response to a much narrower range of intervals (< 90 ms) than was observed for the *in vivo* dentate gyrus (Figure 6, right panel). Third order nonlinearities for *in vitro* slices also included a robust facilitation in response to input patterns defined approximately by Δ_1=100-200 ms and Δ_2=300-400 ms, which was not observed *in vivo*.

Open-Loop Characteristics of Dentate Granule Cells

Isolation of the Dentate Gyrus. In order to study the contribution of intrinsic mechanisms to granule cell nonlinear response properties, it is first necessary to achieve an open-loop condition for granule cells by experimentally eliminating any feedback or feedforward connections to granule cells through interneurons. Several experimental protocols have been developed to eliminate the possibility that other cell populations may contribute to *in vitro* granule cell input/output properties during stimulation of the perforant path. The first protocol involved physically separating a portion of the dentate gyrus from the rest of the slice preparation to ensure that the other main cell layers of the hippocampus (i.e., CA1 and CA3) were not influencing granule cell responses. The separation procedure results in a reduced slice preparation that contains about half of the dentate gyrus (both cell body and

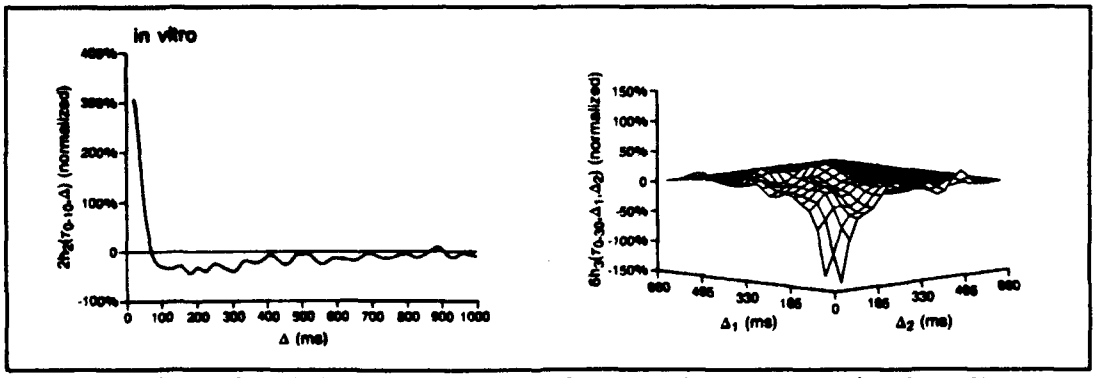

Figure 6. Second and third order kernels for granule cells of an *in vitro* slice.

molecular layers), a small portion of the hilus close to the granule cell body layer and the hippocampal fissure where perforant path fibers enter the dentate molecular layer (Figure 7). When population spike amplitudes were compared before and after the separation protocol (Figure 8), average second order kernels revealed no significant changes in the nonlinear response properties of the remaining population of granule cells. Like the intact slices, when exposed to the $GABA_A$ antagonist bicuculline (10 μM), the "reduced" slice preparations showed an increase in the facilitation observed for intervals of 10-100 ms.

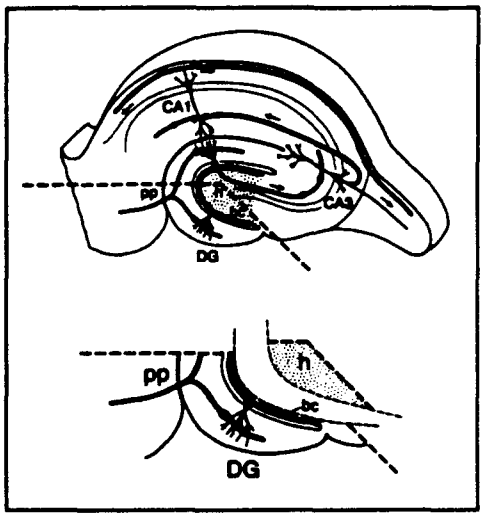

Figure 7. Schematic of the "mini-slice" preparation for isolation of the dentate; pp = perforant path; h = hilus; b = region of GABAergic basket cells which provide feedforward and feedback inhibition to dentate granule cells.

Depletion of Somatostatin. One of the most prominent neurotransmitter candidates for hilar interneurons is the peptide, somatostatin, not only because hilar cell bodies are labeled by somatostatin antibodies, but also because of the dense terminal and fiber labelling observed in the outer 2/3 of the dentate molecular layer. In order to reduce the possible contribution of feedback or feedforward influences mediated by somatostatin, we compared the nonlinear response properties of granule cell population spikes in control animals and animals depleted of somatostation with cysteamine. As determined by radioimmunoassay, cysteamine injected 16 hours before slice preparation (300 mg/kg, subcutaneous) produced a 66.3% depletion of somatostatin. Despite the level of depletion, there were no consistent differences in nonlinear response properties for slices from cysteamine- and saline-treated animals. These results suggest that, in the *in vitro* preparation, feedback and/or feedforward connectivity involving somatostatin as the neurotransmitter does not contribute to the nonlinear response properties of granule cells.

Reduction of Slice Thickness. In addition to dentate isolation and somatostatin depletion, we also have sought to reduce the influence of other cell populations by decreasing the thickness of slices, from 600 μm to 300 μm. Some interneuron populations, most notably GABAergic interneurons, are thought to project parallel to the longitudinal axis of the hippocampus (and thus perpendicular to the plane of section of transverse slices). By decreasing the thickness of transverse slices, the influence of these cell populations should be reduced. To determine whether the influence of GABAergic interneurons was affected, the nonlinear response properties of granule cells were examined for both 600 and 300 μm slices in the absence and presence of bicuculline (10 μM). As demonstrated in Figure 9, right panels), bicuculline had the expected effect on granule cell population spike amplitude in 600 μm slices (i.e., an increase in facilitation for intervals of 10-100 ms), whereas there was no significant effect of bicuculline on the second order response properties of granule cells in 300 μm slices, thus suggesting that the influence of interneurons mediated through $GABA_A$ receptors is eliminated in the thinner slices.

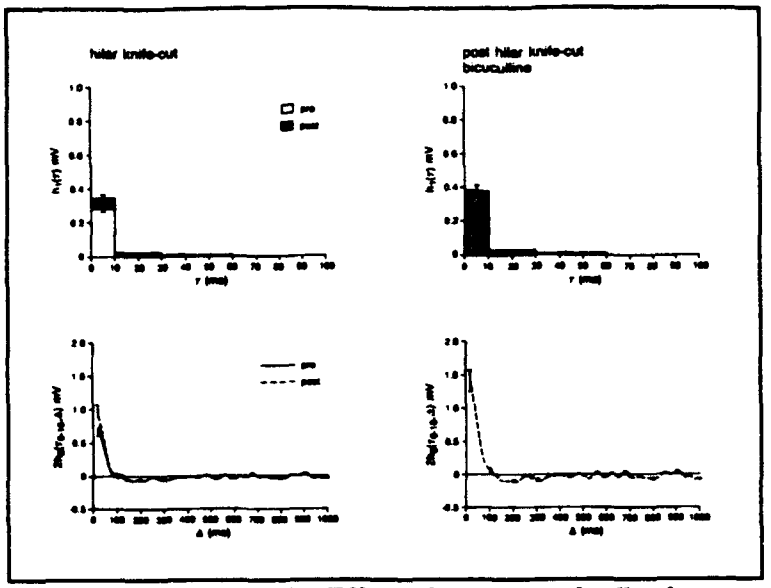

Figure 8. *Left panels: Effect of removing feedback to* granule cells from the hilar region of the dentate on first and second order kernels. Right panels: Effect of bicuculline on granule cell nonlinearities of a mini-slice preparation.

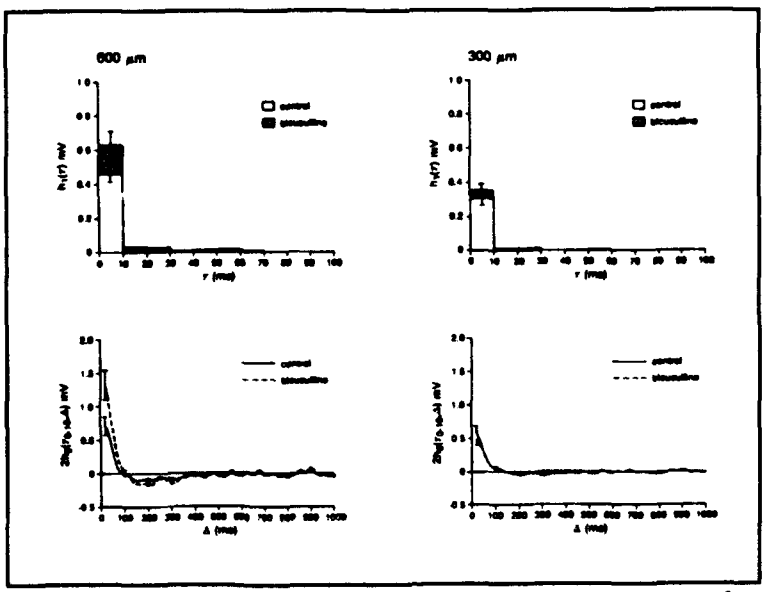

Figure 9. Effect of bicuculline nonlinearities of granule cells recorded from 300 μm and 600 μm thick slices

Contribution of $GABA_B$ Receptor Activation. The preceding experiments confirm that $GABA_A$ receptor activation can contribute to *in vitro* granule cell nonlinear response properties, although this influence is reduced relative to *in vivo* preparations. However, it is also likely that $GABA_B$ receptors are activated, contributing to granule cell nonlinear response properties. To test this hypothesis, granule cell population spike response properties were analyzed in 600 μm slices before and after the addition of the $GABA_B$ antagonist saclofen (500 μM). Saclofen produced a small but significant reduction in the suppression of granule cell responses that occurs for intervals of 150-800 ms.

These findings suggest that orthodromic activation of granule cells activates $GABA_B$ receptors, which contributes to, but is not solely responsible for, suppression of granule cell responses observed in second order kernels for longer interstimulus intervals. In order to provide further support for this conclusion, intracellular recording methods were use to observe the effect of saclofen on granule cell postsynaptic potentials. In 600 μm slices (N=8) that were incubated in bicuculline (10 μM), the response of granule cells to orthodromic stimulation included an epsp with one or more action potentials, and a hyperpolarizing after-potential with a latency to peak of 175 ± 20 ms, and a duration of 800-2000 ms. For granule cells held at a depolarized membrane potential (-50 to -55 mV), the hyperpolarizing response increased with increasing intensity, reaching an average maximum value of 11.4 ± 3.1 mV. With maximal stimulus intensity, the amplitude of responses decreased as cell membrane potentials were hyperpolarized. The amplitude of the response decreased to zero when membrane potentials were -90 to -100 mV, suggesting that the response is mediated by potassium.

Saclofen (10-500 μM) caused a dose dependent decrease in the amplitude of the hyperpolarizing potential. The maximum reduction was 80% and occurred with a concentration of 500 μM. In most cases, a hyperpolarizing response of 1-3 mV remained in the presence of the highest concentration of saclofen, although it had a shorter latency to peak (80-120 ms). Experiments are in progress to determine if this remaining hyperpolarization is due to intrinsic voltage-dependent membrane currents activated by cell depolarization (such as an AHP). These results demonstrate that granule cells exhibit a $GABA_B$-mediated slow IPSP following synaptic stimulation, and that this response contributes to nonlinear response properties in a 600 μm slice. Thus, an open-loop preparation for granule cells will have to include the elimination of this influence. Studies are now underway to determine if, like $GABA_A$-mediated processes, this influence is absent in 300 μm slices. Once the optimal open-loop preparation has been determined, further paired intra- and extracellular recordings will be performed and the contribution of intrinsic membrane properties studied in depth.

Use-Dependent Changes in Synaptic Efficacy of the NMDA Receptor Mediated EPSP

We also have examined use-dependent long-lasting changes in the glutamatergic, N-methyl-D-aspartate (NMDA) receptor-complex using intracellular recordings from hippocampal dentate granule cells *in vitro*. To isolate and enhance the NMDA receptor-mediated responses, slices were treated with the AMPA receptor antagonist 6-cyano-2,3-dihydroxy-7-nitroquinaxaline (CNQX, 10 μM) and maintained in 0.1 mM magnesium. Brief high frequency (50-Hz) tetanic stimulation of glutamatergic afferents resulted in long-term potentiation (LTP) of NMDA receptor-mediated EPSPs. Preventing the postsynaptic neuron from depolarizing during high frequency synaptic activation reversibly blocked the induction of

LTP, indicating that simultaneous activation of pre- and postsynaptic elements is a prerequisite for potentiation of NMDA receptor-mediated synaptic transmission. We also found that hyperpolarizing the granule cell cell during delivery of a 10-Hz tetanus to the perforant path induced LTD of NMDA receptor-mediated EPSPs. We also have studied the role of $[Ca^{2+}]_i$ in the induction of LTP and LTD of NMDA receptor-mediated synaptic responses. Prior to tetanization, $[Ca^{2+}]_i$ was buffered by iontophoretic injections of BAPTA. BAPTA completely blocked the induction of LTP (3 ± 5%, N=13) and partially blocked LTD (-14.8 ± 6%, N=10). The magnitude of LTD expressed by BAPTA-loaded cells was significantly smaller than that expressed by control cells ($p < 0.05$). These findings provide the first evidence for the induction of both LTP and LTD of NMDA receptor-mediated synaptic transmission and demonstrate that the level of postsynaptic depolarization can determine which of the two forms of synaptic plasticity is expressed in response to an identical input. Furthermore, our results strongly suggest that postsynaptic Ca^{2+} influx is essential not only for induction of LTP but also for induction of LTD of NMDA receptor/channel function.

THEORETICAL STUDIES AND COMPUTER SIMULATIONS

During this past year we have continued developing a transputer network of parallel processors for use as a simulation tool. We also have continued progress on defining higher order Laplace transforms of the experimentally determined kernels necessary for combining characterizations of individual components of the hippocampus to simulate functional properties of the global system. In addition, however, we have initiated a new project which involves an application of an *n*-level field theory. The goal of this research is to complement the non-parametric model of the hippocampus, represented by the kernels, with a parametric model in which the dynamics of the system are represented explicitly in terms of the underlying biological mechanisms. The completeness of the parametric model can be evaluated by comparing its behavior with the results of simulations using the non-parametric model. The non-parametric model based on the kernels is experimentally determined (and thus, biologically constrained), and constitutes a complete characterization of the system. Through a complementary application of both the nonlinear systems and field theory approaches, a more complete model of the hippocampus can be realized. During this past year, we made excellent progress in developing a model of perforant path input to a population of dentate granule cells which incorporated the fundamental electrical properties and anatomical characteristics of both the pre- and postsynaptic elements (these elements constitute those contained in the "thin" and "mini" hippocampal slice preparation -- see above). The model successfully predicted the amplitude-time course of the extracellular field potential generated granule cells in response to an afferent volley from perforant path afferents.

PUBLICATIONS DURING YEAR 3 OF AFOSR SUPPORT

Journals and Book Chapters:

Berger, T.W., and Yeckel, M.F. Long-term potentiation of entorhinal afferents to the hippocampus: Enhanced propagation of activity through the trisynaptic pathway. In M. Baudry and J. Davis (Eds.), Long-Term Potentiation: A Debate of Current Issues. Cambridge, MA: MIT Press, 1991, pp. 327-356.

Robinson, G.B., Sclabassi, R.J., and Berger, T.W. Kindling-induced potentiation of excitatory and inhibitory inputs to hippocampal dentate granule cells. I. Effects on linear and nonlinear response characteristics. Brain Research, 1991, 562, 17-25.

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