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Progress Report

**Office of Naval Research
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"Cortical Adaptive Filtering in
Bioacoustic Signal Classification"**

Period: November 1, 1992- April 30, 1993

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Goals

Frequency receptive fields (RF) in the auditory cortex are systematically altered as a result of a brief training experience. Responses to training signals (conditioned stimulus, CS) are increased whereas responses to other frequencies, including the pretraining best frequency (BF) are decreased. These changes can be sufficiently large so that the frequency of the CS becomes the new BF.

Frequency RFs describe the frequency filtering characteristics of auditory system neurons. Systematic changes of these RF may then be seen to indicate *adaptive filtering*; i.e., adaptive filtering may be said to have occurred when training with a selected acoustic signal results in plasticity of the receptive field that is highly specific to that signal.

The goal of this project is to determine the underlying processes of adaptive filtering both neurophysiologically and computationally. Of particular interest, we are applying findings from olfactory (paleo) cortex and training rules derived from the hippocampus (archicortex) to the architecture of the thalamo-neocortical auditory system to determine computational implications for bioacoustic signal classification. An initial stage of this project has been to determine fundamental characteristics of adaptive filtering which are essential for computational analysis. These findings provide a basis for experiments to test predictions which have been generated by the computational work.

An unanticipated benefit of the computational analysis of the functional thalamo-cortical architecture has been the realization that it provides for the training and cue-retrieval of temporal sequences of spectrally-complex acoustic stimuli with high accuracy and high capacity.

Dr. Richard H. Granger has provided essential assistance in computational neurobiology.

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Summary of Previous Findings

Our previous reports on this project summarized the properties and several computational aspects of adaptive filtering. Briefly, adaptive filtering in the auditory cortex --

- is highly frequency specific
- develops very rapidly (as soon as five training trials)
- is very long lasting (tested to eight weeks)
- is discriminative across levels of task difficulty
- develops in instrumental as well as classical conditioning
- is associative
- can reject predictable sounds, as in habituation
- is a property of single cells in the auditory cortex
- is found in supra as well as infragranular lamina
- is not simply projected from the auditory thalamus
- likely involves a neuromodulatory mechanism
- can be explained by modified Hebbian Rules
- alternatively might be explained by network properties
- arises from an extension of paleocortical architecture
- has architectural features consistent with the storage and accurate retrieval of complex acoustic sequences

The physiological characteristics, found in the behaving subject, are fundamentally the same as those of synapse-specific long term facilitation, previously studied both neurophysiologically and computationally in the hippocampus and olfactory cortex. This similarity supports the extension of computational approaches from the archicortex and paleocortex to the auditory neocortex and suggests that findings from long term potentiation may help elucidate adaptive filtering in the auditory cortex.

Progress, November 1, 1992 - April 30, 1993

Laminar Analysis of Adaptive Filtering in the Auditory Cortex

The simultaneous determination of intracortical mechanisms in adaptive filtering by simultaneous recording of cells in the several lamina of the auditory cortex constitutes an extremely difficult technical problem, compensated by its importance. Although we have extended our findings to all layers, it has proven impossible to construct an electrode array of 6-10

wires to record within the same frequency column at all depths. Thus, the best frequencies of cells in the several lamina cannot be identical within a given subject. Therefore, in cooperation with the Center for Integrated Sensors and Circuits at the University of Michigan (supported by Neural Prosthesis Program, NINDS, NIH) we have been testing their thin-film multichannel recording arrays, all of whose recording probes are contained on a substrate $\approx 15\text{-}30\mu$ thick. This has enabled simultaneous recordings within different layers of the same isofrequency column of the auditory cortex. While several technical details need to be worked out to achieve routine success, we have been able to use a modification of their design for chronic implantation.

Optical Imaging of Adaptive Filtering Across the Frequency Representation of the Auditory Cortex

Laminar analysis provides for an important insight into adaptive filtering. The other critical cortical dimension concerns adaptive filtering across, rather than within, the frequency representation of the auditory cortex. We have previously predicted that adaptive filtering should increase the representation to important frequencies at the expense of less important frequencies. While we have used standard multiple microelectrode penetrations to determine how adaptive filtering, during the last six months we have started a collaboration with Dr. Ron Frostig of UCI in optical imaging of the functioning auditory cortex. Dr. Frostig was a major contributor to the development of imaging using the intrinsic signal, while at Torsten Weisel's laboratory at Rockefeller University. We have already achieved the first successful images of frequency bands and done so through the intact (thinned) skull. We expect to be able to determine how adaptive filtering may modify the frequency representation of the auditory cortex later this year.

Hebbian Rules/Network Properties of Adaptive Filtering

The computational work of Dr. Granger has shown that adaptive filtering could arise either via Hebbian Rules, which include synaptic weakening of unimportant frequencies during training, or reduced response to such frequencies due to network properties. As explained in our Report for the period ending October 30, 1992, we proposed to address this issue. In a

study still in its early stages, we have been able to accomplish juxtacellular recordings (spike amplitudes $\approx$ 5-10 mV) that permits direct manipulation of the postsynaptic excitability of the target (presumably pyramidal) cell (i.e., increase or decrease excitability by injection of positive or negative current) while a single tone that drives the cell is presented. Hebbian analysis predicts that responses to the paired frequency will be increased with increased postsynaptic excitability and decreased with decreased postsynaptic excitability. We obtain receptive fields before and after pairing, to determine the degree of specificity of the treatment. Studies to date have been directed to synaptic strengthening, because it is easier to perfect techniques under this condition. Positive results have been obtained in several cases and adaptive filtering that is specific to the paired frequency has been found (Figures 1,2,3). Studies will be extended to the negative case, to determine if Hebbian synaptic weakening can produce adaptive filtering.

Long Term Potentiation in the Auditory Cortex: Homosynaptic

As explained above, it is important to determine the extent to which LTP develops in the thalamocortical auditory system. In an ongoing series of studies, LTP is being studied in anesthetized subjects. Single pulse stimuli are applied to the magnocellular medial geniculate body (MGBm), eliciting a field potential whose laminar profile had been mapped, before and following one or more high frequency trains to this same site. LTP was obtained in several cases, for 1-2 hours. This experiment is in progress.

Long Term Potentiation in the Auditory Cortex: Sensory Heterosynaptic

The operation of an LTP mechanism within the architecture of the thalamocortical auditory system is most important for its potential effect on auditory information. Therefore, we have extended the homosynaptic study to a heterosynaptic study of the effects of a high frequency train to the MGBm on click evoked field potentials in the auditory cortex. Intensity functions to click are first determined and a click intensity that is submaximal is used for the baseline response. Following a 15 minute period of stable click EPs (0.2 Hz), high frequency trains are applied to the MGBm, with clicks continuing thereafter. An immediate transient depression generally is elicited, followed

in some cases by a facilitation that lasts for as long as recordings have been obtained, e.g., at least one hour. This experiment is in its early stages.

Long Term Potentiation in the Auditory Cortex: Induction of Frequency-Specific Adaptive Filtering

The homosynaptic and sensory heterosynaptic studies lead naturally to the critical question of the extent to which an LTP mechanism can produce adaptive filtering. We have just begun to obtain data from waking animals bearing chronically implanted electrodes. A standard behavioral training paradigm is used, although there is no behavioral conditioned response. The CS is a tone (100 ms) of non-best frequency and the US is a brief (50 ms) train of high frequency (200 Hz) stimulation of the MGBm at CS offset. Frequency receptive fields are obtained before and after training (average ITI = one minute). We have obtained a CS specific shift of tuning. The CS frequency became the new best frequency. This adaptive filtering was maintained for 40 minutes, the retention period used in this subject (Fig. 4). This experiment is still in its early stages.

Conclusions

Research is progressing along the lines previously delineated. Guided by Granger's computational work, we are proceeding to investigate physiologically the rules by which adaptive filtering operates in the auditory cortex. The approach is to study LTP-like processes in the thalamocortical auditory system, specifically, in the pathway from the Magnocellular Medial Geniculate to the Primary Auditory Cortex of the guinea pig. Two complementary approaches are being used: LTP-based, in which homosynaptic, sensory heterosynaptic and specific modification of frequency receptive fields are under investigation, and direct tests of the means by which synaptic strengths are modified in the cortex. We are also continuing to determine the domain of adaptive filtering both by depth (laminar) studies and frequency representation studies, the latter using the powerful new technology of optical recording. All of these related experiments, in progress, have yielded positive results to date and so will be continued to successful conclusion.

ONR Supported Publications

11/92-4/93

- Edeline, J-M. and Weinberger, N.M. Receptive field plasticity in the auditory cortex during frequency discrimination training: Selective retuning independent of task difficulty. Behavioral Neuroscience, 1993, 107, 82-103.
- Weinberger, N.M., Ashe, J. H. and Edeline, J-M Learning-induced receptive field plasticity in the auditory cortex: Specificity of information storage . In: Neural Bases of Learning and Memory, J. Delacour (Ed.), World Scientific Publishing: Singapore, In Press.
- Cruikshank, S.J. and Weinberger, N.M. Induction of auditory cortical receptive field plasticity: Hebb rules? Society for Neuroscience Abstracts, 1993, In press.
- Bakin, J.S., Kwon, M.C., Masino, S.A., Weinberger, N.M. and Frostig, R.D. Tonotopic organization of guinea pig auditory cortex demonstrated by intrinsic signal optical imaging through the skull. Society for Neuroscience Abstracts, 1993, In press.
- Weinberger, N.M., Javid, R. and Lapan, B. Long-term retention of learning-induced receptive field plasticity in the auditory cortex. Proceedings of the National Academy of Science (U.S.A.), 1993, 90, 2394-2398..
- Edeline, J-M., Pham, P. and Weinberger, N.M. Rapid development of learning-induced receptive field plasticity in the auditory cortex. Behavioral Neuroscience, In press.
- Weinberger, N.M. Learning-induced changes of auditory receptive fields. Current Opinion in Neurobiology, In press.
- Weinberger, N.M. Fear conditioning produces enduring receptive field plasticity in the auditory cortex. In: The Cognitive Neurosciences, M.S. Gazzaniga (Ed), The MIT Press, Cambridge, Mass. In press.

Figure Legends

Figure 1. Basic experimental set-up for juxtacellular recording, to control the post-synaptic state of auditory cortical neurons while also recording their response to acoustic stimuli.

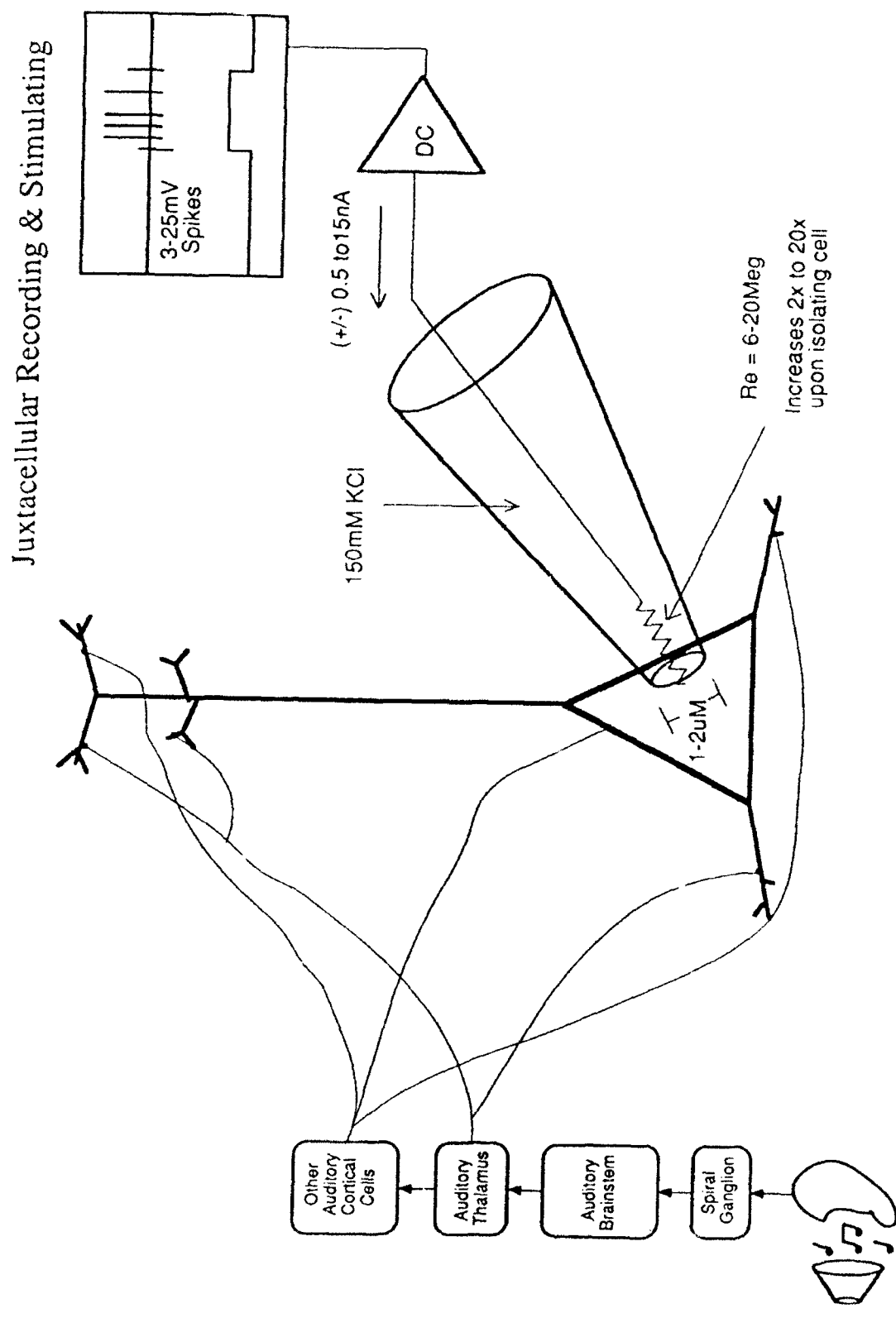
Figure 2. An example of facilitation of response to a tone caused by the presence of the tone during increased post-synaptic excitability, produced by positive current. Note that increased response to the tone is maintained after the current is shut off (compare "Tone Alone" with "Tone Alone After Treatment").

Figure 3. An example of frequency specific adaptive filtering induced by pairing a non-best frequency with positive current. Pre-pairing, the best frequency was 20.0 kHz; the paired frequency was 18.0 kHz. Following pairing (in the absence of current), responses to the paired frequency had increased while responses to the best frequency, and particularly higher frequencies, decreased (see "Post minus Pre").

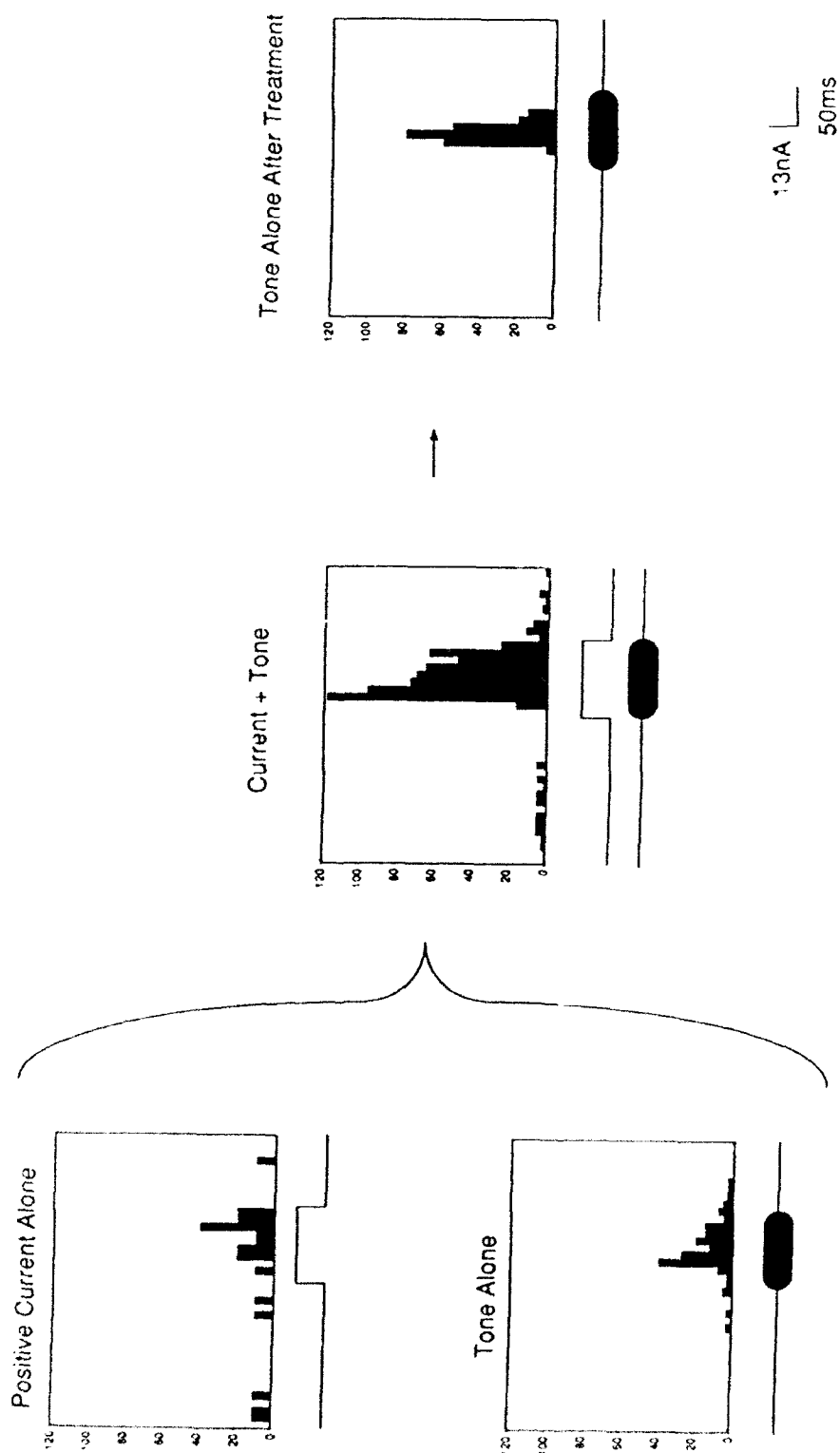
Figure 4. Long term frequency specific adaptive filtering induced by using a behavioral paradigm with brief stimulation of the magnocellular medial geniculate body as the "LTP"-like induction train. Receptive fields were obtained from the auditory cortex before, immediately after and 30 minutes after 60 training trials (6.0 kHz tone = 100 ms, MGm training (50 ms) at tone offset). Pretraining, the best frequency was 8.0 kHz. After training, tuning shifted to the frequency of the training tone, 6.0 kHz. Moreover, this adaptive

filtering was maintained at the 30 minute retention test. The top panel shows the tuning curves; the bottom panel shows the effects of the treatment, in which the pre tuning curve is subtracted from the immediate and 30 minute post functions. Note the maximal increase at the frequency of the paired tone and the sharpening of the effect after 30 minutes.

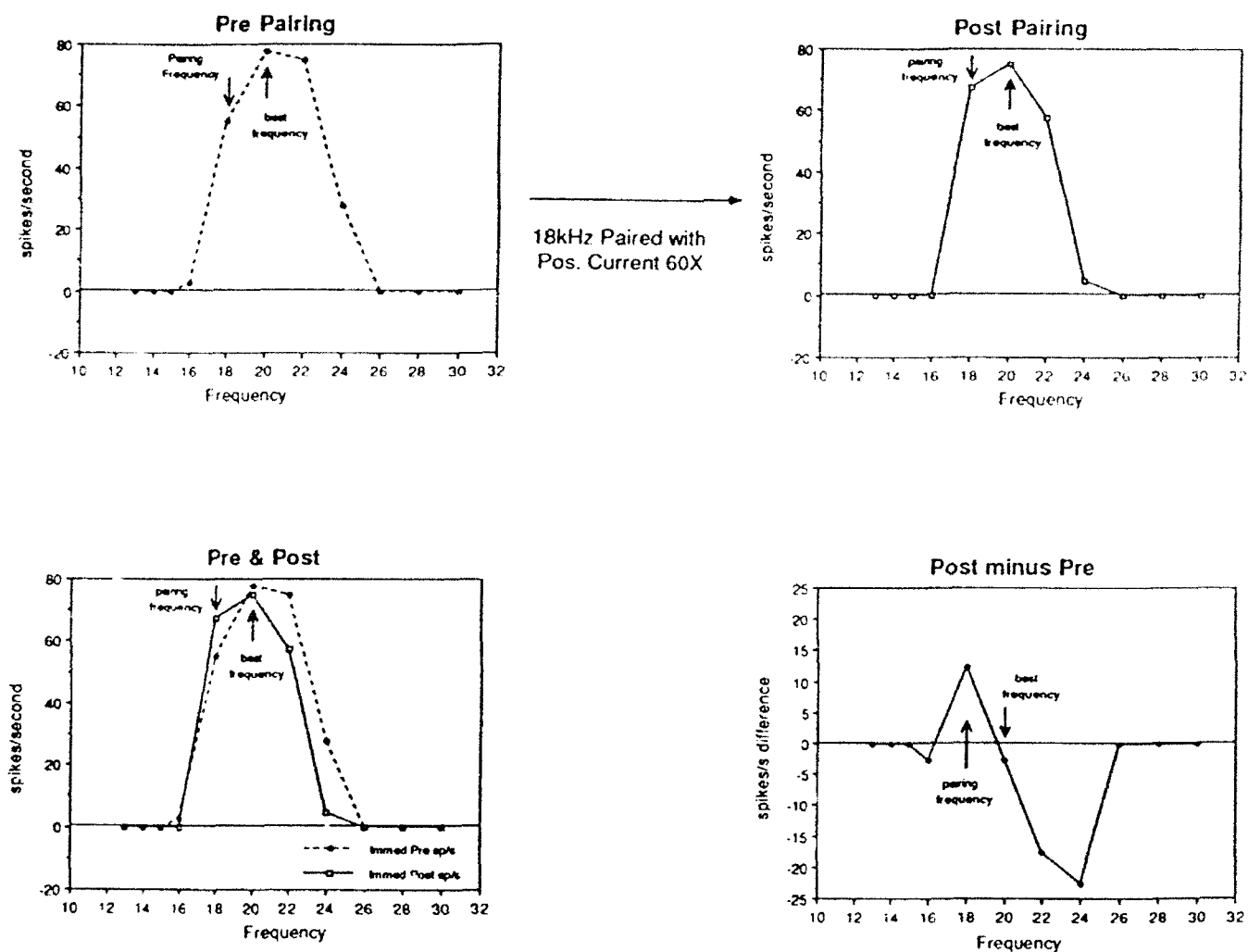
Controlling of Pre & Post Synaptic Activity in the Auditory Cortex:



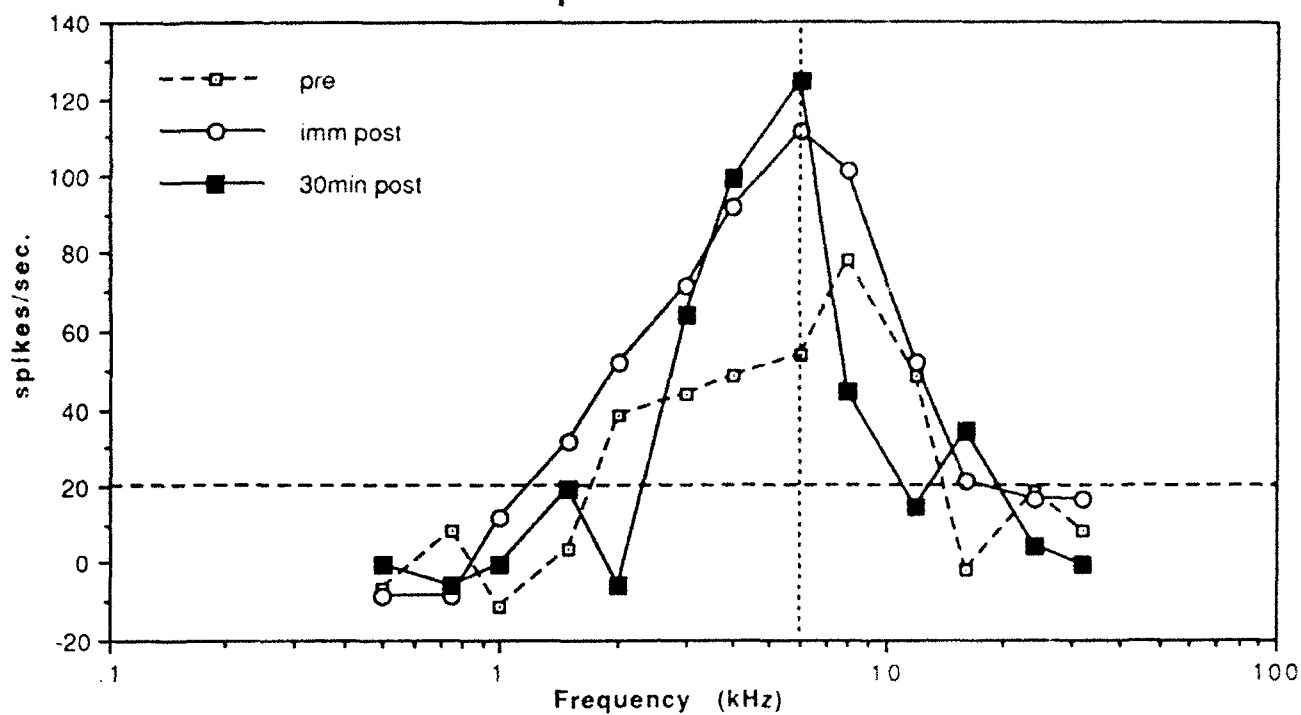
Enhancing Post-Synaptic Response to a Tone Averaged Responses Normalized to Spikes/Second



Current - Stimulated Enhancement of Post-Synaptic Response can Induce Receptive Field Plasticity



Iam29/p4/MGm Stim.



Iam29/p4/MGm Stim.

