14th Quarterly Progress Report

January 1, 2006 to March 31, 2006

Neural Prosthesis Program Contract N01-DC-02-1006

The Neurophysiological Effects of Simulated Auditory Prosthesis Stimulation

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This report describes our progress during the 14th quarter of contract NIH-NIDCD-DC-02-1006 (January 1, 2006 - March 31, 2006). During this quarter, we conducted sixteen physiology experiments that continued and extended our investigations of interactions between cochlear implant channels. These experiments, as well as other work completed during the quarter, are described briefly in the next section. (An appendix describes interesting data from one recent experimental series describing physiological aspects of current steering – a topic that has been discussed at length in recent scientific colloquia.) The final section of this report briefly describes the work we plan for the next quarter.

Summary description of work over the last quarter

During the previous quarter we completed sixteen neurophysiology experiments investigating responses to stimulation of single and multiple auditory information channels. These studies used acoustic stimulation of the cochlea by pure-tone bursts delivered by a calibrated speaker, and electrical stimulation of the cochlea by modulated and unmodulated biphasic current pulse trains delivered by a cochlear implant. The extent of cochlear activation during stimulus presentation was determined by observation of neuronal activity along the tonotopic axis of the inferior colliculus (IC). The experiments completed during the this quarter included initiation or continuation of:

- Acoustic forward masking studies with multichannel silicon recording probes (NeuroNexus Technologies) and standard tungsten wire microelectrodes (FHC). The latter were used in these experiments specifically to record activity of single neurons in the inferior colliculus to these acoustic stimuli. We now have a database of single- and multi-unit responses that is sufficient to complete a manuscript describing the responses in the inferior colliculus to sequential acoustic tone stimuli (current in preparation).
- Electrical forward masking studies at UCSF and at the University of Michigan with John Middlebrooks. These experiments are analogous to our acoustic forward masking experiments, but use electrical stimulation rather than acoustic stimulation of the cochlea to elicit responses in the auditory nervous system. During this quarter, we also finished acquisition and compilation of data sufficient to complete a manuscript, currently in preparation, describing forward masking using electrical stimulation.
- Experiments exploring the effects of changing the remote current fraction (RCF – described in detail in QPR #8). During this quarter, we completed one experiment for this series. At the termination of the experiment, the cochlear implant electrode was fixed in place and the cochlea was harvested for histological study. This cochlea joins two others implanted in the previous quarter, and will be used to verify exact radial and longitudinal location (i.e., along the cochlear spiral) of stimulating sites in these experiments.

- Experiments describing responses to sinusoidally amplitude modulated (SAM) electrical pulse trains. Experiments in this series, in particular examine effects of modulation depth and stimulus level. These experiments were conducted using 250 and 1000 pps pulse trains.
- Experiments describing the effects of envelope phase/frequency differences on responses to interleaved SAM pulse trains presented on two distinct cochlear implant channels. These experiments used pulse trains of 250 and 1000 pps, within the range of contemporary implant processors, and envelope modulation frequencies between 15 and 30 Hz, within the range of modulation frequencies characteristic of speech.
- Experiments investigating physiological effects of stimulation by "virtual electrodes" using current steering, or appropriate division of stimulating current between two physical implant channels. These experiments are designed to examine the physiological correlates of stimulation by virtual electrodes -- a topic of psychophysical research that has been reported only recently at cochlear implant and auditory neuroscience meetings. The previously reported studies of stimulation by virtual electrodes have used commercial implant processors in human implant subjects. In the studies we have undertaken, we examine auditory neural activity along the tonotopic axis, measured in the inferior colliculus, to identify the location along the cochlea of the virtual stimulating electrode. We include as Appendix I four figures describing the results of one recent experiment using this paradigm.

In addition to the above, we have also continued analysis of experimental data acquired during this and previous quarters, and have continued preparation of several manuscripts for publication (described briefly in QPR #13 and below).

Travel

R. Snyder traveled to the University of Michigan to work with J. Middlebrooks to complete collection of data for our study of electrical forward masking.

Work planned for next quarter

J. Middlebrooks will visit UCSF to complete a manuscript describing our experiments of forward masking during electrical stimulation. In addition, we plan to complete and submit several manuscripts that are currently in various stages of preparation. Topics of these manuscripts, and primary authors, include: Acoustic forward masking (B. Bonham), Effects of changing the remote current fraction (B. Bonham), Effects of electrode placement within cochlea (R. Snyder), and Development and fabrication of the UCSF-type cochlear implant for the guinea pig (S. Rebscher). We will continue histological processing and examination of cochleas with embedded implants harvested during the previous quarter (described in QPR #13) as well as the cochlea embedded during this quarter. We will collaborate with D. Sinex of Utah State University in a series of experiments that investigate and compare responses to acoustic speech, presented via a loudspeaker, with responses to electrically processed speech presented via a cochlear implant.

Appendix I – Current steering experimental results

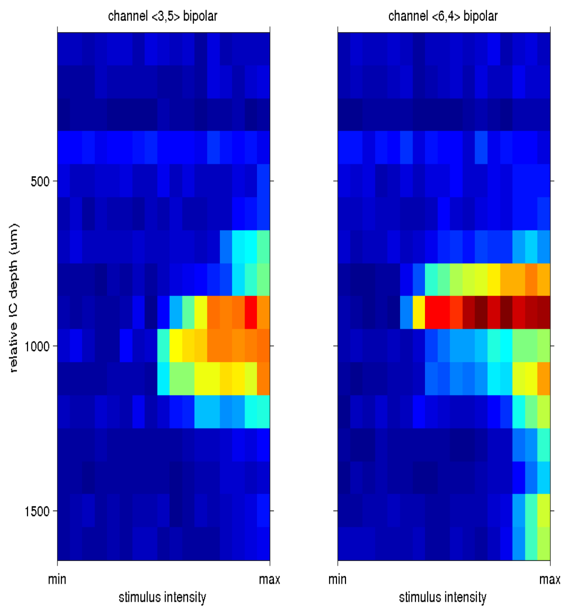

Figure 1: Spatial tuning curves for two bipolar channels. Shown are spatial tuning curves resulting from stimulation of two bipolar channels. Red pixels indicate strong response, and blue pixels indicate little or no response. The left panel describes the spread of activity in the inferior colliculus (ordinate) as a function of current level (abscissa) delivered to bipolar pair <3,5>. The right panel describes the spread of activity when current is applied instead to the interdigitated bipolar pair <6,4>. Increments along the abscissa are 1 dB. Spread of activation at levels several dB above the minimum threshold is relatively restricted.

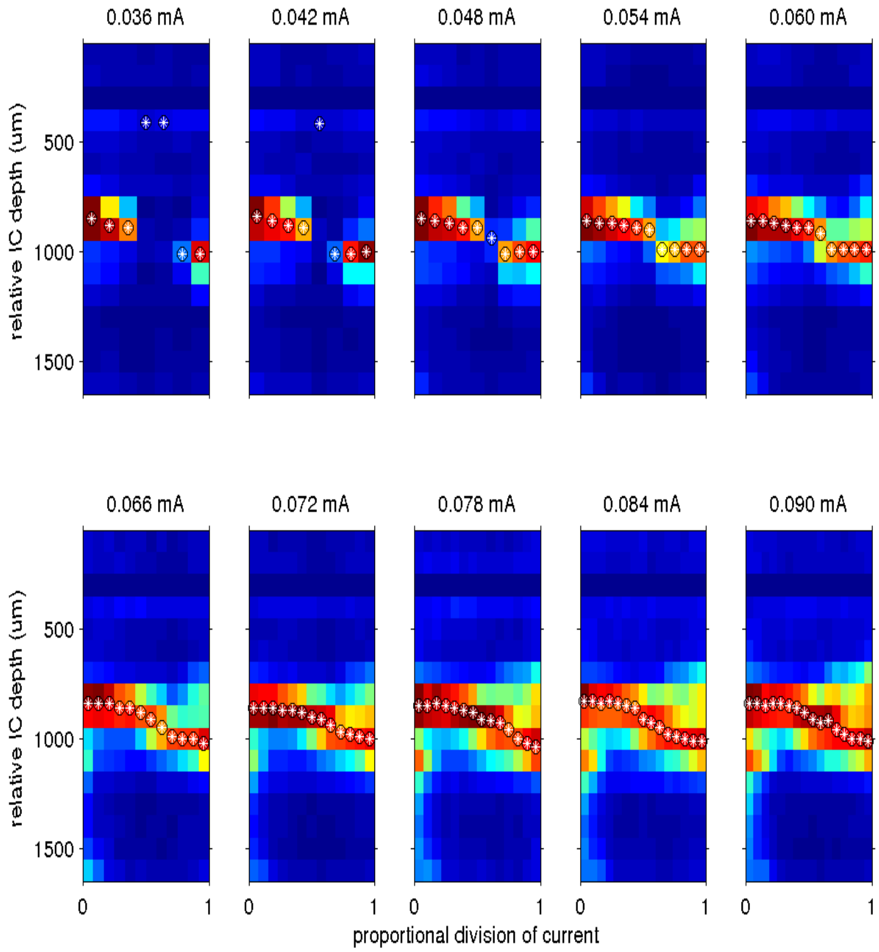

Figure 2: Bipolar current steering -- creation of virtual electrodes. Total stimulating current was held constant for each panel of this figure (indicated at top of panel). The proportion of the total current delivered to electrode pair <3,5> is indicated along the abscissa of each panel; the remainder of the stimulating current was delivered to electrode pair <6,4>. For example, in the top-left panel, the total current applied to the cochlea was 0.036 mA. The leftmost column of this panel depicts the neural activity along the tonotopic axis of the IC when all the current was applied to electrode pair <6,4>. The rightmost column in this panel depicts neural activity when all the current was applied to electrode pair <3,5>. Intermediate columns depict activity when the total current was divided between these two bipolar electrode pairs. When the current was divided equally (center column), no pixels were colored red, indicating that current delivered to each implant channel (<3,5> and <6,4>) was below minimum threshold. The white point in each column indicates the location of the peak of the measured activity, determined by a spline-fit to the data. As the total applied current is increased in successive panels, the sub-threshold gap in the center columns decreases in width and is eventually eliminated. The region over which activity is observed (i.e., spread of activation) also increases. Initially, the activity peak determined by the spline fit exhibits a relatively sudden jump from a superficial to deeper location (900 um to 1000 um) as the current is shifted from pair <6,4> to pair <3,5>, but as the overall current level is increased, this peak shift becomes more gradual. This might suggest that at low stimulus levels the number of virtual channels between physical electrodes is smaller than at higher stimulus levels.

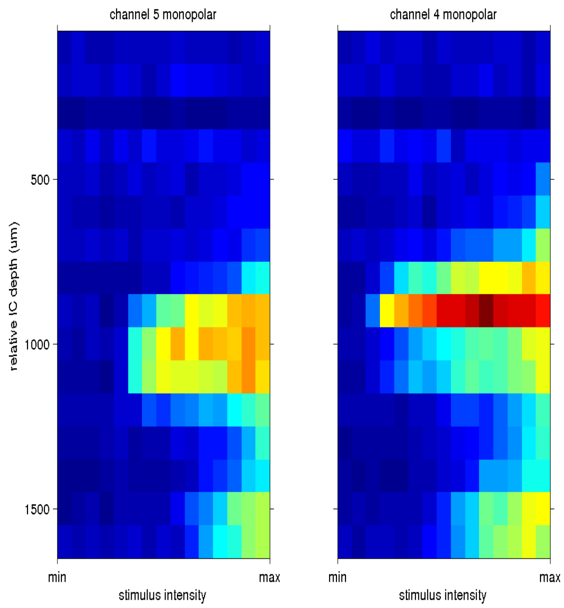

Figure 3: Monopolar spatial tuning curves. This particular experiment was fortuitous in that the monopolar spatial tuning curves were more restricted than those in nearly all our neurophysiological studies. Shown here are monopolar spatial tuning curves for stimulation of monopolar channels <5M> (left panel) and <4M> (right panel). The shape and location of responses to these monopolar stimuli is similar to responses to the bipolar stimuli shown in Figure 1 at stimulus levels a few dB above minimum threshold. However, as stimulus current is increased, a second, ectopic, region of activation becomes apparent near 1550 um.

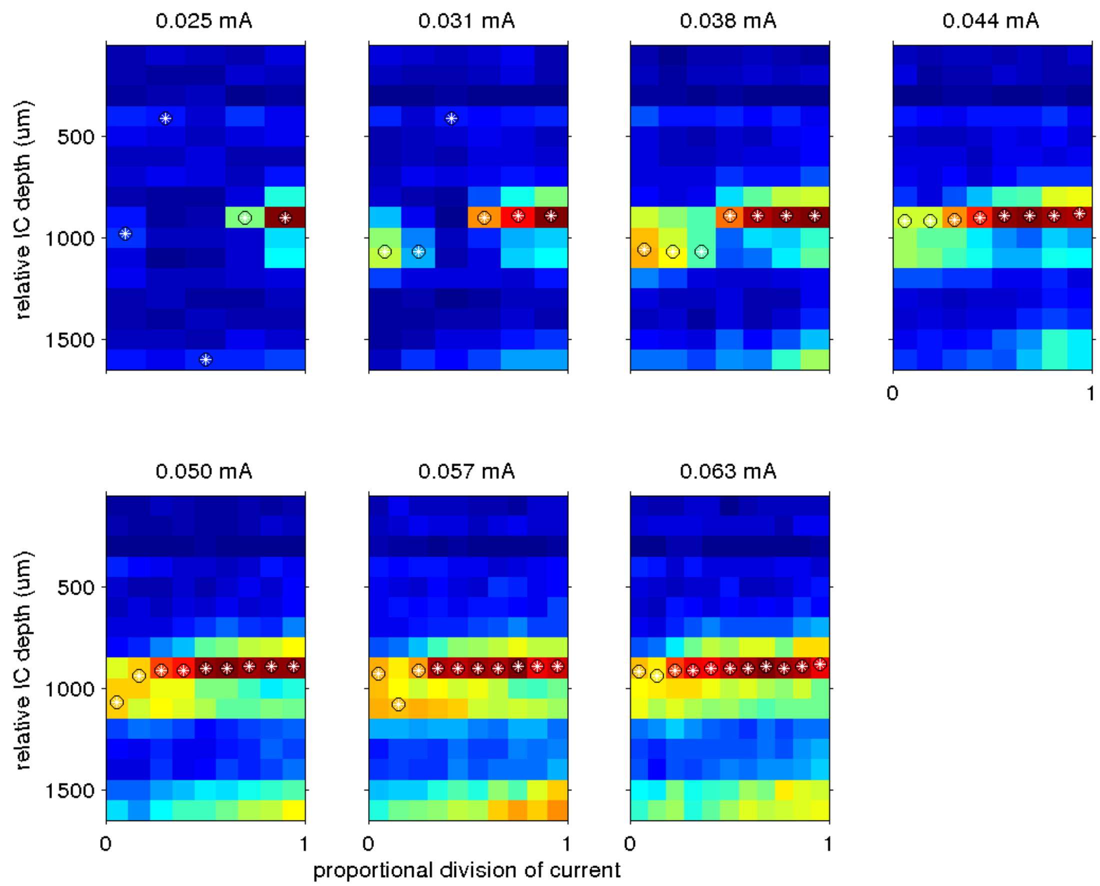

Figure 4: Monopolar current steering – no evidence of virtual channels. As in Figure 2, the total current applied to the cochlear implant is indicated at the top of each panel. The abscissa identifies the proportion of the total current applied to monopolar electrode <4M>; the remainder of the total current is applied to monopolar electrode <5M>. At low total current levels, dividing current between the two monopolar channels produces stimulation on each channel that is below response threshold (blue central columns in first two panels). Increasing the total current eliminates the sub-threshold gap, but there is no evidence here of a gradual shift of activity peak from one tonotopic location to another. It is possible that a gradual shift of the center of activity might be observed by using finer increments along the abscissa than were used in this experiment (e.g., in the third panel). However, comparison of this figure with Figure 2 suggests that in this case, a precise control of current required to create virtual stimulating channels for monopolar stimulation might be relaxed if current is instead divided between bipolar stimulating channels.