17th Quarterly Progress Report

October 1, 2006 to December 31, 2006

Neural Prosthesis Program Contract N01-DC-02-1006

The Neurophysiological Effects of Simulated Auditory Prosthesis Stimulation

Submitted by:
Russell L. Snyder, Ph.D.
Steve Rebscher, M.A.
Ben Bonham, Ph.D.

University of California, San Francisco

Department of Otolaryngology – Head and Neck Surgery

Epstein Hearing Research Laboratory

533 Parnassus Avenue, Room U490E

San Francisco, CA 94143-0526

This report describes our progress during the 17th quarter of contract NIH-NIDCD-DC-02-1006 (October 1, 2006 - December 31, 2006). During this quarter, we continued work on several manuscripts describing results of experiments conducted under this contract. We also conducted four additional physiology experiments that continued and extended our investigations of 1) interactions between cochlear implant channels in the ICC and 2) temporal response properties if ICC neurons to SAM tones and SAM pulse trains.. These experiments, as well as other work completed during the quarter, are described briefly in the next section. The following section identifies two manuscripts submitted for publication. 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 work on two manuscripts which have been submitted for publication in peer-reviewed journals. In addition, we completed four neurophysiology experiments that continue our investigation of responses to stimulation of single and multiple auditory information channels. These experiments used acoustic stimulation of the cochlea by pure and SAM tones delivered by a calibrated speaker, as well as electrical stimulation of the cochlea by modulated and unmodulated biphasic and pseudomonophasic current pulse trains delivered by a cochlear implant. The extent of cochlear activation during stimulus presentation was determined by using a multichannel silicon recording probe (NeuroNexus Technologies) to observe neuronal activity along the tonotopic axis of the inferior colliculus (IC). No new experimental series were initiated during this quarter. Instead, experiments during this quarter continued our ongoing studies of central auditory response to stimulation using:

- Unmodulated single-tone stimuli
- Sinusoidally amplitude modulated (SAM) single-tone stimuli
- Single (isolated) biphasic and pseudomonophasic electrical pulses delivered via a cochlear implant
- Multiple isolated pulses delivered via the same and different channels of a cochlear implant
- Unmodulated single- and two-channel pulse trains
- Single-channel SAM pulse trains using a range of modulation depths and stimulus levels

The immediate goals of these experiments were to 1) selectively activate lower frequency regions of the cochlea by building electrodes that extended further into to the cochlea, 2) determine the limits of neural coding of SAM signals by stimulating the cochlea with SAM pulse trains that varied systematically in modulation depth, modulation frequency and spectral spread, 3) identify the physiological basis for creation of virtual cochlear implant channels by current steering.

Stimulation of more apical regions of the cochlea: We have adopted two strategies to selectively activate the low frequency region of the cochlea. The first strategy is to build intracochlear electrodes that incorporate stimulation sites at the most apical locations possible given the constraints of our current mold. Our progress in this regard is illustrated in the attached Figures 1 & 2

Figure 1 is an image of one of our 8 contact guinea pig electrode array used in previous experiments. This array has 8 stimulating electrode contacts embedded in a silicone elastomer carrier. The contacts are numbered with #1 being the most apical and #8 the most basal contact. The contacts have a diameter of

about 125 microns and a center-to-center spacing of ~500 microns. Upon insertion, the round window will be located at approximately the location of the red dashed line. Upper inset shows a cast of the guinea pig scala tympani with the approximate locations of the contacts after insertion. The most apical contact (#1) sits at about the 6-8kHz region. The most basal contact sits at the 25-30kHz region.

Figure 2 is an image of a 12 contact electrode array used in the current series of experiments.. The contacts are numbered as in Figure 1 with contact #12 being the most basal contact.. The inset shows a cast of the guinea pig scala tympani with the approximate locations of the contacts after insertion. The most apical contact (#1) sits at about the 4kHz region; the most basal contact sits at about the 25kHz region. Thus using this electrode we are able to selectively stimulate the basal (high frequency) half of the guinea pig auditory nerve array, which is tuned to a range of CFs from 4 to 25kHz. This range represents the approximate maximum possible range over which we can *selectively* stimulate with our current electrode design. We can activate lower frequency regions, but only by stimulating more basal regions at higher intensities. This limitation arises both from the design of the carrier mold and the size of the guinea pig scala tympani. At approximately the middle of the second turn, the guinea pig scala becomes too small for the cross-sectional area of our current carrier. The electrode fills the scala and cannot be inserted further without damage to the organ of Corti.

Although this range (4 – 25kHz) represents almost 3 octaves, it does not include the speech frequencies, which we would choose to selectively stimulate for some experiments. Therefore, we have been led to explore additional electrode placement strategies including insertion of visually placed ball electrodes into fenestrations of the lateral wall of the cochlea along the 2nd and 3rd turns. These strategies will allow us to activate at least two arbitrarily low frequency regions of the cochlea in addition to the middle and high frequency regions activated by our carrier array.

We have also updated our analysis software to facilitate analysis of the temporal response properties of ICC neurons.

Manuscripts submitted

Rebscher, S.J., Hetherington, A., Snyder, R.L., Leake, P.A., and Bonham, B.H. (submitted). Design and fabrication of multichannel cochlear implants for animal research. *J. Neurosci. Methods.*

Snyder, R.L., Middlebrooks, J.C., and Bonham, B.H. (submitted). Cochlear implant electrode configuration effects on activation threshold and tonotopic selectivity. *Hearing Res.*

Work planned for next quarter

During the next and final quarterly period of this contract, R. Snyder and B. Bonham will travel to Denver to present results from contract work at the annual midwinter meeting of the Association for Research in Otolaryngology in Denver.

Aside from this activity, we plan exclusively to continue work on the several manuscripts resulting from contract work that are currently in various stages of preparation. Topics of these manuscripts, and primary authors, include: Responses to interleaved pulse trains (S. Bierer), Acoustic forward masking (B.

Bonham), Effects of changing the remote current fraction (B. Bonham), Electrical forward masking (J. Middlebrooks), and Response to sinusoidally amplitude modulated (SAM) current pulse trains (R.Snyder).

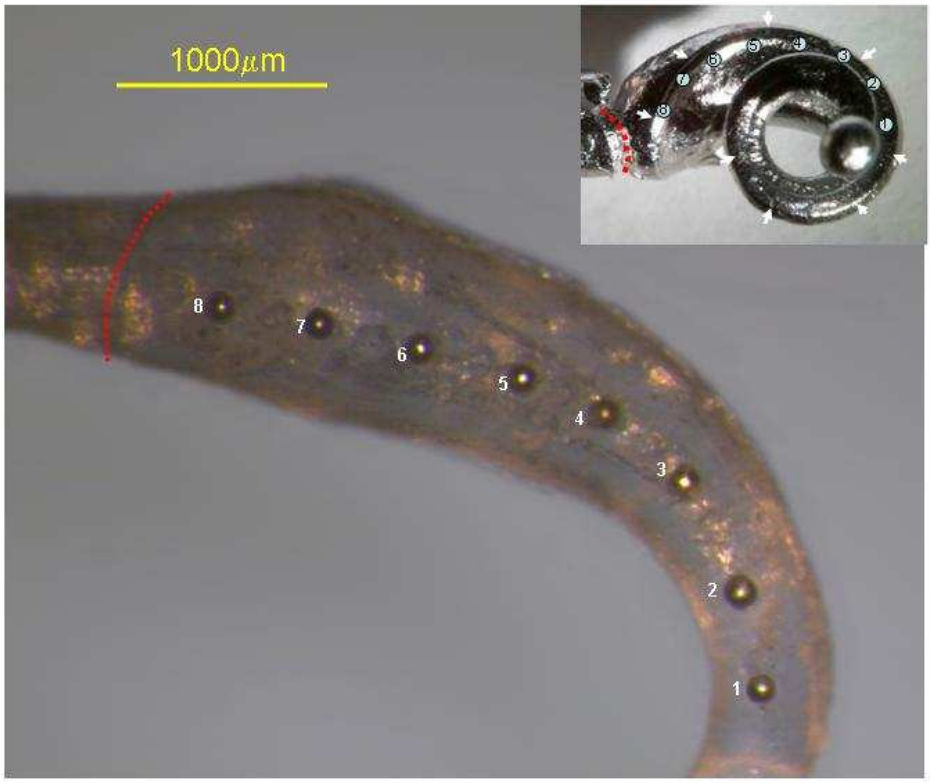
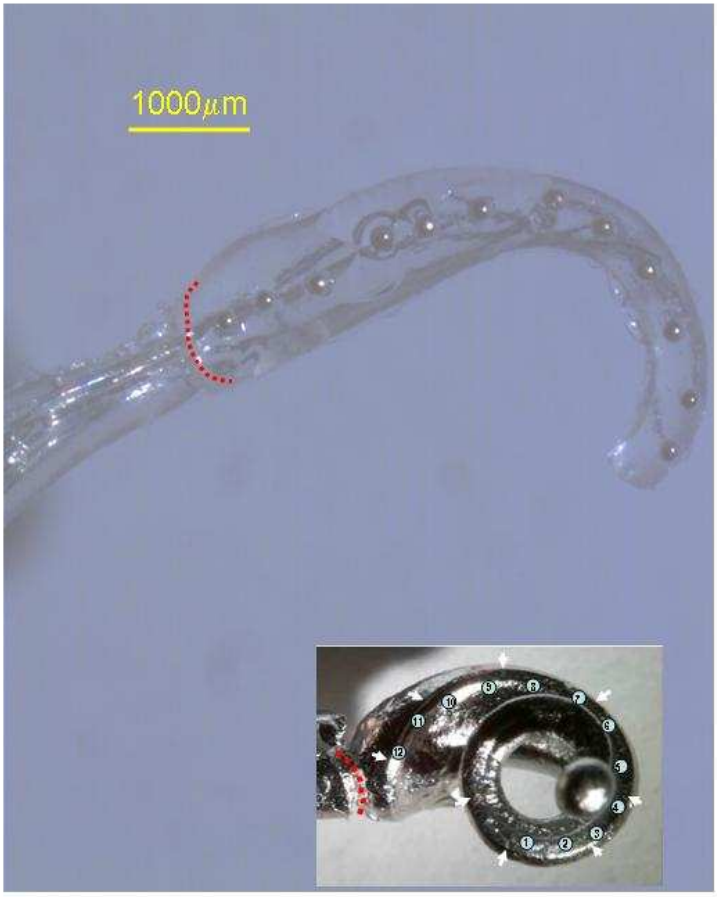


Figure 1


1000μm