

Eighth Quarterly Progress Report
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**The Neurophysiological Effects of
Simulated Auditory Prosthesis
Stimulation**

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1 Introduction

The purpose of this contract is to investigate issues involving the transfer of information from implantable auditory prostheses to the central nervous system of individuals using these devices. This investigation is being pursued along multiple parallel tracks and include the use of animal experiments and computer model simulations to:

- Characterize fundamental spatial and temporal properties of intra-cochlear stimulation of the mammalian auditory nerve.
- Evaluate the use of novel stimuli and electrode arrays.
- Evaluate proposed enhancements in animals with a partially degenerated auditory nerve.

In this Eighth Quarterly Progress Report, we focus primarily on the first half of the second of these three aims. Our computer simulations have suggested a novel speech processing strategy for cochlear implants which may dramatically increase temporal information coding and dynamic range with a cochlear implant. While we have not as yet proven that the simulations are correct, preliminary experiments on animals in our laboratory and humans at RTI produce results consistent with the model predictions. This work draws heavily on the material presented in the Fifth Quarterly Progress Report where the underlying theory was described.

2 Activities of the Eighth Quarter

- Completed off-line analysis of single-fiber data obtained from all previous cats.
- Submitted a manuscript for publication in *Hearing Research* that summarizes the single-fiber data obtained on this contract.
- Presented data at the 1st International Symposium and Workshop on Objective Measures in Cochlear Implantation in Nottingham, England. Two podium and one poster presentation were given.
- Begun work on a manuscript describing relationships between single-fiber measures and the compound action potential from electrically stimulated cat cochleae.

- A manuscript describing the results reported in the fifth QPR, the nature of “pseudospontaneous activity,” was revised and accepted by Hearing Research[7]. This was authored in collaboration with the RTI group.
- One cat has been deafened using the UCSF-Melbourne kanamycin-ethacrynic acid protocol. This animal has been deaf for four months and will undergo implantation and single-unit/EAP recordings in the next quarter.
- Several guinea pigs were used in a series of deafening procedures using the UCSF-Melbourne kanamycin-ethacrynic acid protocol. However, a poor survival rate was obtained with this procedure. This has prompted us to propose the use of a noise exposure protocol for deafening. This procedure has the advantage of allowing us to obtain differing cochleotopic patterns of secondary neuronal degeneration through the use of high-pass and low-pass filtered noise as the exposure stimulus. A request for amendment to our existing animal use protocol has been submitted to the University of Iowa Animal Care Unit. We anticipate approval of this amendment.

3 Pseudospontaneous Activity

3.1 Background

A major difference between the deaf and hearing ears is the relative absence of spontaneous activity in the deafened cochlea[3, 6]. This has implicated the inner hair cell synapse as the source of spontaneous activity[10] although recently it has been suggested that elimination of spontaneous activity with ototoxic deafening is not as complete as might be suspected[11]. We expect that restoration of physiologic levels of spontaneous activity to the deafened cochlea would be a productive approach to speech processor design for a number of reasons:

- The normal auditory nerve is spontaneously active in quiet[5]. Sound produces a slowly progressive within and across fiber synchronization as intensity is increased[9]. Replication of this phenomenon should allow greater dynamic range and more orderly loudness growth.
- Studies of “stochastic resonance” demonstrate increased temporal resolution in sensory systems when independent noise is present in a set

of parallel detectors[1]. The spiral ganglion is quite comparable to such parallel detectors and spontaneous activity in each fiber is a form of independent noise[2].

- Loss of spontaneous activity is one proposed mechanism for tinnitus[3] and its restoration may potentially improve tinnitus suppression by cochlear implants.

In the Fifth QPR we demonstrated that it may be possible to restore physiologic levels of “pseudospontaneous” activity to the deafferented auditory nerve through the appropriate application of unmodulated high-rate (eg. 5 kHz) pulse trains. This Eighth QPR investigates the consequences of mixing sinusoidal “data” stimuli with these high-rate “conditioning” stimuli. Due to the difficulties with stimulus artifact using these stimuli, we have as yet no single-unit data to support or refute these predictions. Preliminary EAP data is consistent with the predictions however.

3.2 Results

The stochastic axonal model and the stimulation paradigm has been described in detail elsewhere[7]. A simulation of a single axon is performed for 8 seconds of real time with a stimulating electrode located 0.5 mm preperpendicularly from the third node of Ranvier counted from the distal terminal. Post-stimulus time (PST) and period histograms are constructed from simulated single-unit recordings at the fourth node of Ranvier from the central terminal. The stimuli consist of a 1 kHz sinusoid starting at $t = 28ms$ in association with a 5 kHz monophasic pulse train beginning at $t = 0$. The sinusoid is called the “speech” or “data” signal and the pulse train is called the “conditioner” as it is conditioning the fiber by making it produce pseudospontaneous activity. Period histograms are constructed following onset of the sinusoid and spike rate is computed at varying intensities of both sinusoid and conditioner.

Figure 1 demonstrates rate-level functions for the simulated fiber when the sinusoid is presented with and without an associated conditioner of 319 μA . This level of conditioning produces a pseudospontaneous rate of 16 spikes/s in the absence of the sinusoid[7]. Note that without the conditioner, there is an extremely limited dynamic range of approximately 1 dB – a well described limitation of electrical stimulation. In the presence of the conditioner however, the dynamic range is expanded to approximately 25 dB – similar to that seen with acoustic stimulation[8].

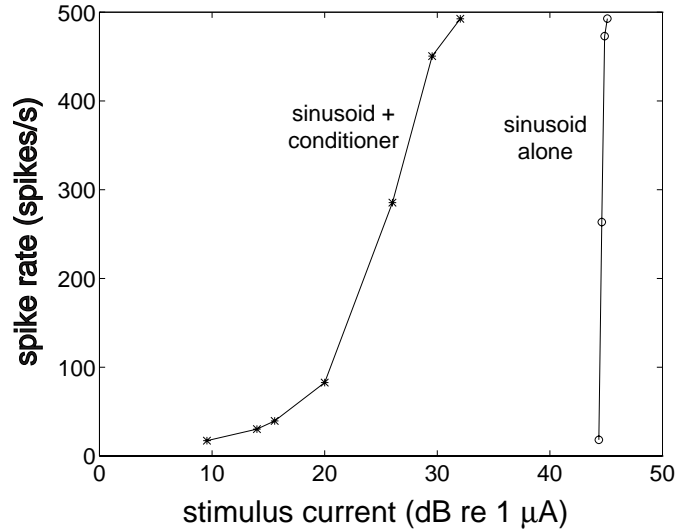


Figure 1: Rate-level functions with and without a 5 kHz conditioner. The conditioner level is 319 μA .

Another well-known limitation of electrical stimulation is the high levels of synchrony produced by such a stimulus[4]. This synchrony produces a loss of temporal resolution in that multiple fibers code the timing of the peak of a stimulus rather than its entire waveform. Figure 2 illustrates this limitation with a period histogram showing the response of a simulated fiber to four periods of a 1 kHz, 264 μA sinusoid. No conditioner is present and it is clear that the fiber can only code the timing of the peaks of the signal.

When a 20 μA sinusoid is preceded and accompanied by a 325 μA conditioner, a rather different period histogram results as seen in Figure 3. This conditioner in the absence of the sinusoid produces a pseudospontaneous rate of 116 spikes/s. It dramatically improves the temporal resolution of the simulated fiber and allows it to code most of the attributes of the waveform in a manner quite similar to acoustic stimulation.

We have begun a systematic investigation of the effects of different conditioner levels on rate-level functions for sinusoidal stimulation. Figure 4 shows the rate-level functions for a 1 kHz sinusoid at varying conditioner levels. These calculations show that threshold and pseudospontaneous rate are related. Conditioners resulting in higher pseudospontaneous rates also result in lower thresholds. Conditioners yielding lower spontaneous rates

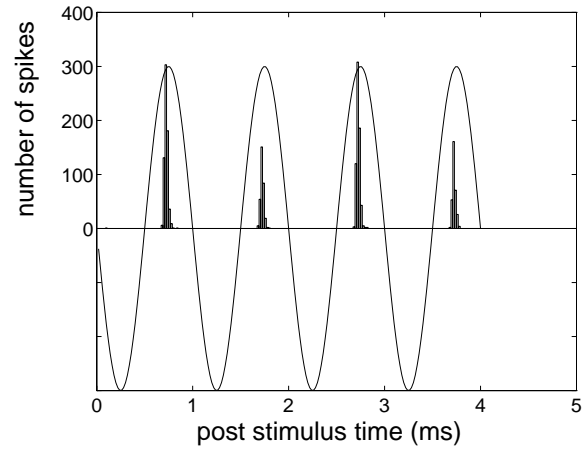


Figure 2: Period histogram (four periods) with a 1 kHz sinusoidal stimulus. The histogram has been offset by 0.6 ms to correct for the spike latency.

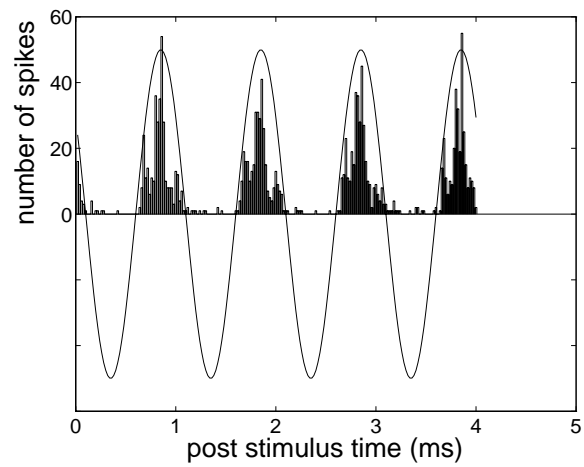


Figure 3: Period histogram (four periods) with a 1 kHz sinusoidal stimulus mixed with a 5 kHz conditioner of $325 \mu A$. The histogram has been offset by 0.6 ms to correct for the spike latency.

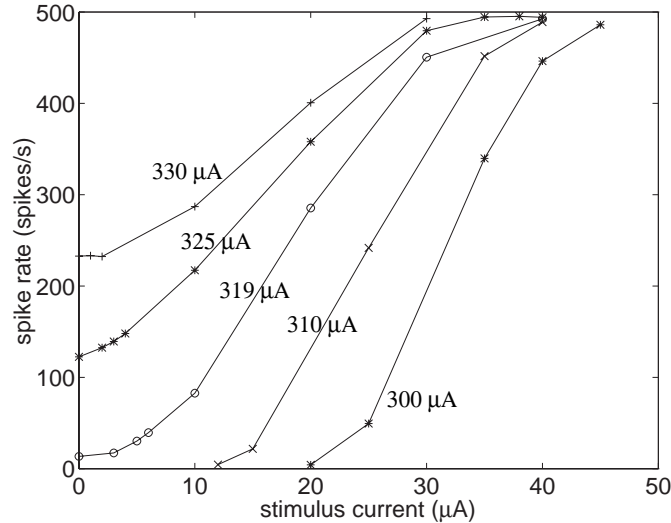


Figure 4: Rate-level functions for a 1 kHz sinusoid with different conditioner levels. Linear units.

produce higher thresholds. This relationship is similar to that seen in the normal cochlea where high-spontaneous rate units are lower threshold than low-spontaneous rate units[5]. At the higher conditioning levels, a pseudospontaneous rate is present for sinusoidal currents of zero. It is clear, however, that pseudospontaneous spike activity is not necessary for broadening the dynamic range. The dynamic range effect is greatest for conditioners producing pseudospontaneous spikes but is quite obvious for conditioner levels which do not produce any spike activity.

Figure 5 illustrates this point by using a logarithmic scale for the sinusoidal current and the normalized spike rate transformation proposed by Sachs and Abbas for acoustic stimulation of the intact cochlea[8]. This transformation subtracts out the spontaneous rate and then normalizes to the maximal rate yielding a normalized rate between zero and one. With this transformation it is clear that conditioning levels higher than that producing a pseudospontaneous rate of 116 spikes/s do not yield further increases in dynamic range. It is tempting to speculate that the normal mammalian auditory system uses spontaneous activity as a means to increase dynamic range. If this is true, the highest rates might be fixed by that which results in maximal dynamic range. There would be no need for higher spontaneous rates as they would yield no further advantage and would be metabolically

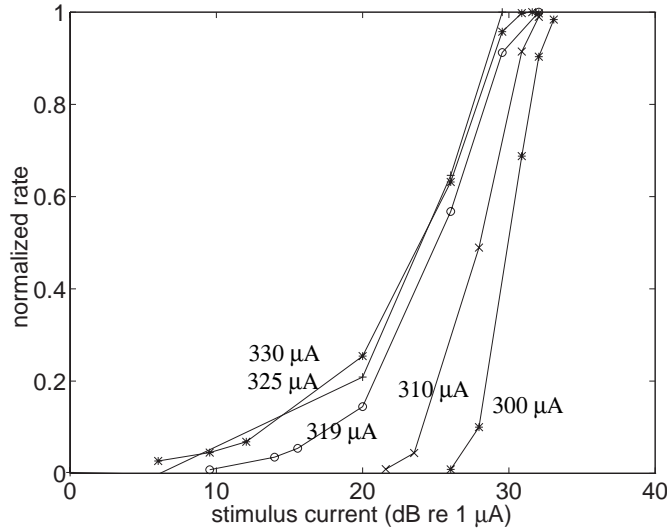


Figure 5: Rate-level functions using log units and the Sachs-Abbas spike rate normalization.

costly.

To investigate the effects of stimulus level on the temporal representation of conditioned stimulus, period histograms are presented at four levels in Figure 6. These responses closely resemble those seen for acoustic stimulation. At low levels, the spontaneous activity phase locks to the stimulus without increasing rate. At higher levels, the response appears like a half-wave rectified version of the stimulus as rate increases. At these high levels, some refractory-related distortion becomes evident in the histograms (compare responses $20 \mu A$ and $30 \mu A$). At still higher stimulus levels the rate saturates but the pattern of response degenerates to highly synchronous representations of the stimulus peak with an alternating pattern resembling that seen in the absence of a conditioner.

Given these theoretical findings using sinusoids, we were interested in assessing the effects of a conditioning stimulus on neural representations of an amplitude modulated pulse train. In Figure 7, data obtained by Wilson and Finley at RTI from an Ineraid subject is displayed. A speech token is presented to the subject and amplitudes of the stimulus pulses presented are plotted alongside measures of the EAP. Different amplitudes of a conditioning stimulus are presented prior to the onset of the speech token. The figure

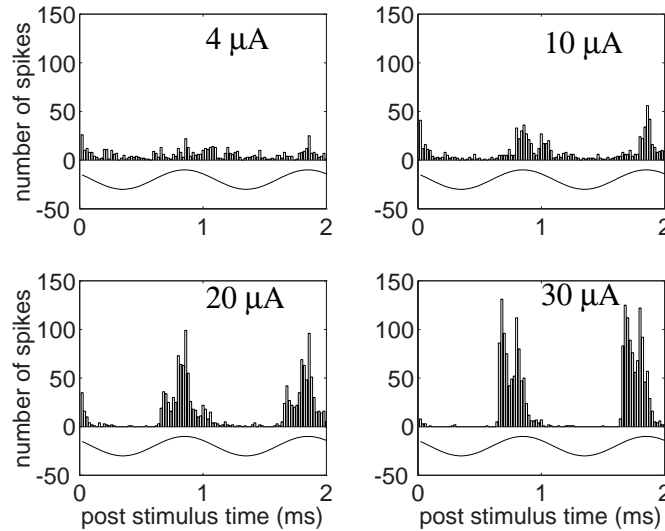


Figure 6: Period histograms for a 1 kHz sinusoid and 5 kHz conditioner at $325 \mu A$. Current level for the sinusoid is given in each panel.

demonstrates that the conditioner improves the temporal representation of the pulse train by the EAP through decreases in refractory-related distortion. It is not known whether such “improved” temporal representation will improve speech reception but such studies are underway at RTI.

4 Plans for the Ninth Quarter

The following activities are planned for the ninth quarter (October - December, 1998) of this research project:

- Continue deafening guinea pigs with high-pass and low-pass noise so as to obtain sets of animals with cochlear insults concentrated in either the apical or basal aspects of the cochlea.
- Acute experiments on some of the chronically deafened guinea pigs and the chronically deafened cat will be done toward the end of the next quarter.
- Complete work on a manuscript detailing relationships between electrically evoked single-fiber response properties and the electrically evoked compound action potential.

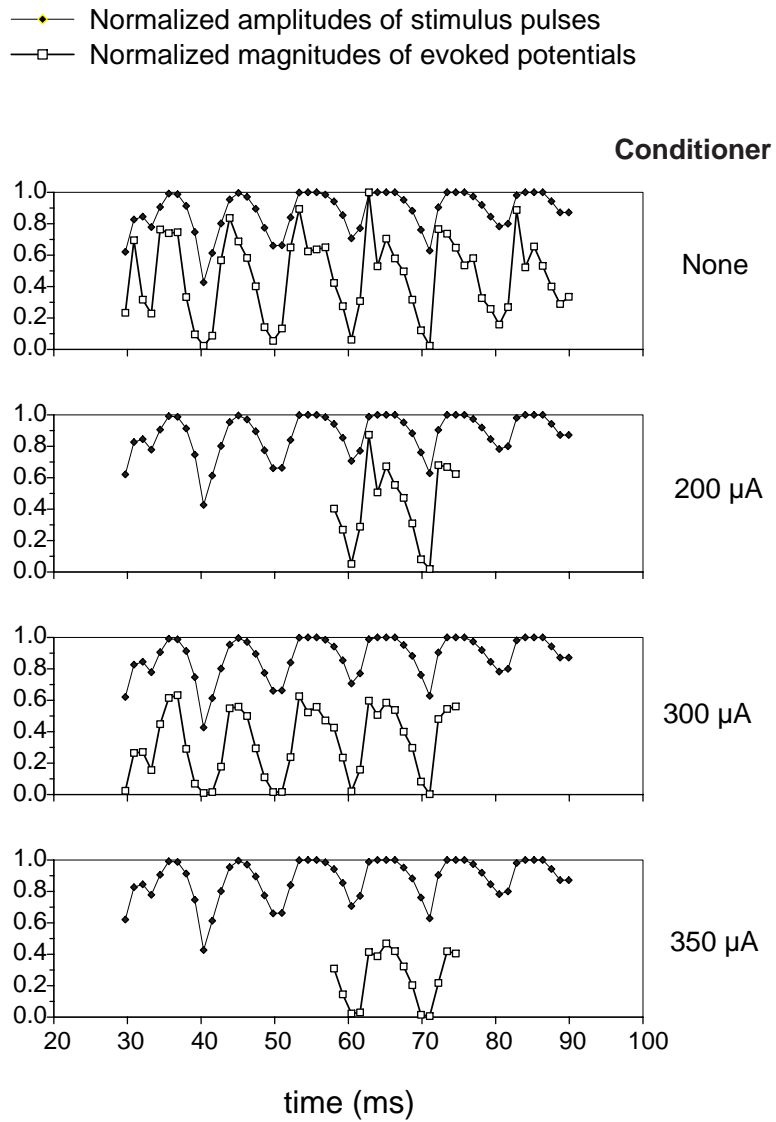


Figure 7: EAP and pulse amplitude with a speech token presented with varying levels of conditioning. This figure is courtesy of Blake Wilson and Charles Finley and was performed under their NPP contract.

- Prepare a manuscript on the material in this QPR.
- Prepare a manuscript comparing stochastic properties of single-unit responses in the cat to those simulated by the model.
- Prepare manuscripts on responses to pulse trains, including amplitude modulated pulse trains, as reported in the 7th QPR.
- Attend Neural Prosthesis workshop.

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