Sixth Quarterly Progress Report

November 1, 1996 through January 31, 1997

NIH Project N01-DC-5-2103

Speech Processors for Auditory Prostheses

Prepared by

Charles Finley, Blake Wilson, Chris van den Honert and Dewey Lawson

Center for Auditory Prosthesis Research

Research Triangle Institute

Research Triangle Park, NC 27709

Contents

I. Introduction

One of the principal objectives of this project is to design, develop, and evaluate speech processors for implantable auditory prostheses. Ideally, the processors will represent the information content of speech in a way that can be perceived by implant patients. Another principal objective is to develop new test materials for the evaluation of speech processors, given the growing number of cochlear implant subjects enjoying levels of performance too high to be sensitively measured by existing tests.

Work in the present quarter included:

- Continued studies with Ineraid subject SR2, to record intracochlear evoked potentials for pulses presented at high rates, up to 10000/s. The stimuli used in this quarter included sinusoidally amplitude modulated trains of pulses and the modulated pulse trains produced by a single-channel speech processor.
- Speech reception and evoked potential studies with new Ineraid subject SR16 (week of November 11). Studies included comparisons of performance with his clinical *compressed analog* (CA) processor and *continuous interleaved sampling* (CIS) processors with various choices of values for the processor parameters. This subject enjoyed a quite large increase in performance with CIS processors and is a candidate for field studies with a research portable processor (the Innsbruck/RTI processor), to evaluate possible further improvements in performance with continued and daily use of the CIS strategy.
- Additional studies with Ineraid subject SR14, previously studied by us in 1994. The principal purpose of this visit was to compare performance and fitting procedures for the new COMBI-40 speech processor and our laboratory implementation of CIS processors. Aaron Parkinson, of the University of Iowa, participated as a visiting investigator in the studies with SR14 (week of November 18).
- Initiation of field studies with Nucleus percutaneous subject NP2, using the Geneva/MEEI/RTI portable processor, to evaluate possible learning effects with sustained use of a CIS processor (January 31).

- Development of DSP software for programming the Geneva/MEEI/RTI processor with an RTI implementation of CIS processors. This development was directed by Marian Zerbi; she was ably assisted by Phillip Loizou, a visiting investigator from the University of Arkansas at Little Rock.
- Further development of an interface system for control of the implanted receivers in subjects with bilateral Nucleus implants. The further development enables high-speed control of both sides for studies of speech processor designs.
- Further development of the evoked potentials laboratory, including development of new high-speed stimulus sources that can disconnect after delivery of stimulus pulses to improve the signal-to-noise ratio of recordings; incorporation of low-noise, high-bandwidth optical isolators in both the stimulating and recording sides of the system; and development of new low-noise amplifiers for the recording head stage. Laboratory studies were conducted both *in vitro* and with two human subjects to evaluate and refine various elements of the stimulating and recording systems.
- Continued development of new speech test materials, designed to increase the sensitivity of testing for subjects at the high end of the performance scale.
- Completion of a course on multirate sampling and processing by Zerbi (course conducted at UCLA; Zerbi's participation supported by RTI internal funds).
- Continued analysis of speech reception and evoked potential data from prior studies, especially analysis of results from open set speech tests for the first five subjects in the Nucleus percutaneous series (NP1-5) and analysis of evoked potential data involving pairs of pulses, where the stimuli included pairs of identical pulses with various interpulse intervals or pairs of pulses with fixed interpulse intervals and various amplitudes for the first pulse (the fixed amplitude of the second pulse was equal to the greatest amplitude for the first pulse).
- Continued preparation of manuscripts for publication

In this report we present results from evoked potential studies using pairs of pulses with identical pulse amplitudes and various interpulse intervals. Results from other studies and activities indicated above will be presented in future reports.

II. Intracochlear Evoked Potentials in response to Pairs of Pulses: Effects of Pulse Amplitude and Interpulse Interval

A crucial factor in the performance of speech processing strategies for cochlear implants is the peripheral electrode/neuron interface. The behavior of this interface is influenced by many interrelated factors including electrode design and placement, stimulus level and duration, and neuronal survival and physiology. To better understand these relationships we have recorded intracochlear evoked potentials (EPs) from unstimulated electrodes within the implanted cochlea in response to applied electrical stimulation. Through these measures it is possible to observe the aggregate behavior of a population of neurons in response to stimulation, and infer how well stimulus information is represented in the neural response.

In previous reports we have described recordings of intracochlear EPs for a variety of pulse train stimuli (Quarterly Progress Reports 7, 9 and 11, NIH Contract N01-DC-2401, 1994 and 1995). A consistent observation of all of these studies is that the auditory nerve is limited in its ability to respond to rapidly changing electrical stimulation, most likely because of the refractory behavior of individual neurons. These observations may be related to observed deficits in the perception of high frequency temporal information. In addition, these recordings may provide some indication of the physiological and anatomical state of the implanted cochlea. Consequently, they may help identify more effective ways to stimulate the cochlea and advance our understanding of the sources of patient variability. An ultimate objective is to apply these methods as a preliminary step in the design and fitting of optimized speech processors for individual subjects.

Recently we have been examining EP responses to pairs of pulses. The simplicity of such stimuli allows data analysis in terms of well known neural mechanisms. While several other types of pulse-pair protocols also have been recorded, the present report will deal only with presentation of two equal-amplitude, biphasic pulses separated in time by varying interpulse intervals (IPI). While holding pulse amplitude constant and equal for both pulses, masking and facilitation effects of the first pulse on the response to the second may be explored by varying IPI and recording the amplitude of the response to the second pulse. Electrical stimulus artifact is minimized in the recordings by averaging equal numbers of both positive- and negative-leading, biphasic pulse pairs.

Methods

Stimulus Presentation and Recording

Charge-balanced, biphasic current pulses (32.8 µsec/phase duration) were presented to a single monopolar electrode referenced to a remote return electrode in *m. temporalis*. Studies were conducted with implant patients having percutaneous access to their intracochlear electrodes. These included subjects using either the Ineraid device or a research version of the Nucleus device in which the electrode array was accessed via a percutaneous connector. Stimulus pulses were delivered by a custom-built, electrically-isolated current source. Stimuli were generated under software control by a digital signal processor (DSP) subsystem (Spectrum Signal Processing, TMS320C25 System Card) installed in a personal computer (PC) system. Stimulus pulses were delivered in bursts of fourteen pairs. A new burst was initiated every 1.5 seconds. Within a burst the first pulse of each pair followed the last pulse of the preceding pair by 66 msec. Stimulus pair IPIs (from the beginning of the first pulse to the beginning of the second) varied from 0.32 to 32.0 msec, increasing in 13 approximately equal logarithmic steps within each presentation burst. Stimuli were presented repeatedly for response averaging as either positive- or negative-leading pulses. Typically, responses to 200 presentations of each stimulus polarity were averaged, although in cases producing smaller EPs up to 800 trials were averaged. Pulses within any pair always shared the same initial polarity.

Potentials evoked by the electrical stimuli were recorded from a neighboring unstimulated electrode in the implanted cochlea. In the case of the Ineraid array an adjacent electrode was used for recording; whereas, with the Nucleus array an electrode located three bands away from the stimulating electrode was selected to provide equivalent spacing between stimulating and recording electrodes across all subjects. In all cases, potentials were recorded differentially with respect to a surface paste electrode placed on the ipsilateral mastoid. The recording system was isolated electrically from the stimulation system and used a wrist band, rather than the stimulus return electrode, as a ground reference connection to the subject. Signals were buffered and amplified (x 1000) using a custom-built, electrically-isolated amplifier with fast saturation recovery and high bandwidth (70 kHz, single pole cutoff) characteristics. Data were sampled (16.4 µsec sampling period) and synchronously averaged on a burst-by-burst basis in the same DSP subsystem used to generate the stimuli. Data were passed to the host PC system for display, storage and subsequent analysis.

Representative Data and General Analysis

Figure 1 shows representative data recorded from electrode #4 of Ineraid patient SR14. Stimuli were pairs of equal amplitude, biphasic current pulses applied to monopolar electrode #3. IPIs were varied from approximately 10 to 1 msec. For large IPIs (>3 msec) each stimulus pair produced a pair of responses (EP_1 and EP_2) identical to one another. Each consisted of an initial negative-going peak (N_1), followed by a smaller positive-going peak (P_1), which then decayed slowly back to a constant baseline. Prior to each N_1 response is a brief, large magnitude transient which is residual stimulus artifact not canceled out by the averaging process. This residual is highly repeatable and is independent of stimulus IPI. For this experiment the pulse pairs were generated by zeroing all but the first two pulses of a pulse train. Consequently, the brief positive-going spikes repeated at different constant intervals for each record are digital-to-analogconverter glitches passed through the current source and injected in to the tissue during zero amplitude pulses.

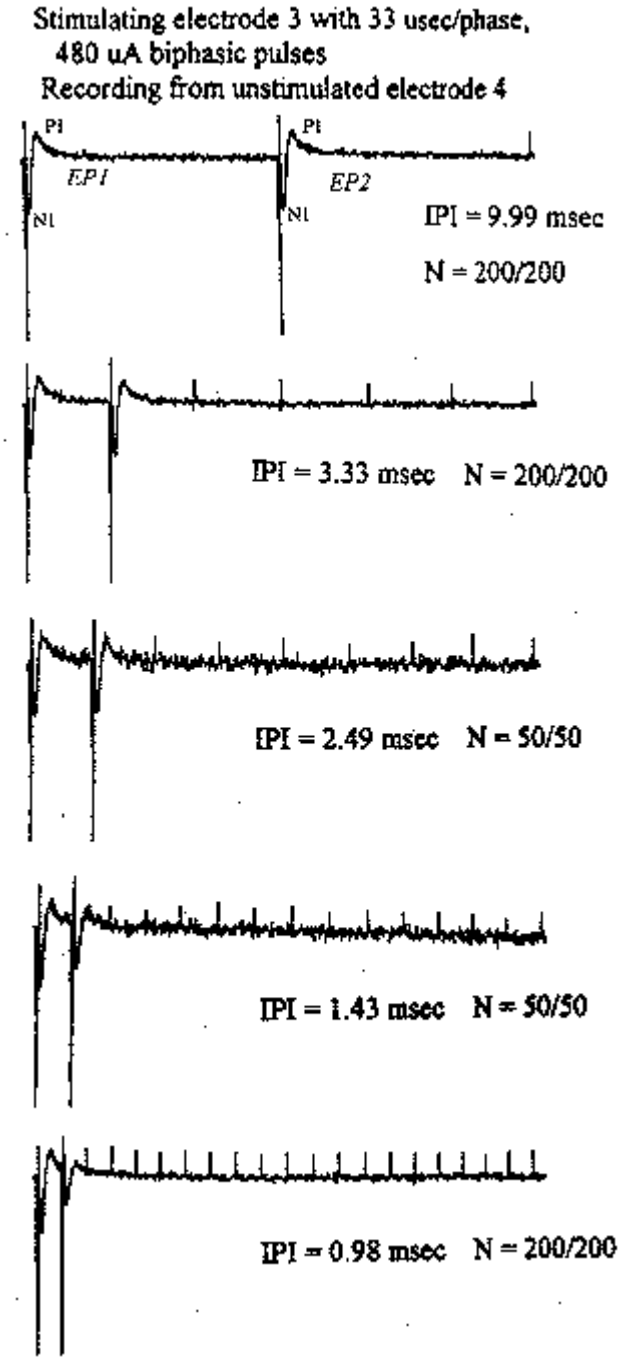

Figure 1. EP responses to pulse pair stimulation with varying IPI.

As the IPI is reduced below 3 msec, the EP_2 response to the second pulse of the stimulus pair reduces in magnitude. This is clearly evident for the conditions where the IPI is <1.43 msec and is generally attributed to neurons still being in the refractory state due to the first pulse depolarization as the second pulse occurs. As the IPI is reduced still further (< 1 msec), the magnitude of EP_2 continues to decrease. In addition, the EP_2 response, along with its preceding artifact component, overlaps components of the EP_1 response to the first pulse. The combined effect greatly complicates estimation of EP_2 magnitudes.

Figure 2 illustrates a subtractive analysis procedure for alleviating this complication. An underlying assumption is that the evoked electrical fields that produce EP_1 and EP_2 and their associated artifact components are primarily additive (*e.g.* they sum linearly to produce the aggregate response). If this is the case, the individual responses may be resolved by subtracting an independent measure of EP_1 alone from the aggregate response, thus leaving the EP_2 response to the

second pulse. Figure 2(a) shows an aggregate EP_1+EP_2 response for subject SR3 to a stimulus pulse pair with an IPI of 1 msec. Note that EP_2 is superimposed on the trailing part of the P1 component of EP_1. Figure 2(b) shows an independent estimate of EP_1 obtained by averaging responses to single isolated stimuli. Generally this estimate will be based on a large number of trials, resulting in a lower overall noise level in the record as is evident in the figure. Figure 2(c) shows the resulting subtracted record with a clean estimate of the EP_2 response. Note that the EP_1 response has been completely eliminated with only a small residual artifact remaining. Note also that the flat baseline in Figure 2(c) supports our assumption of linear superposition.

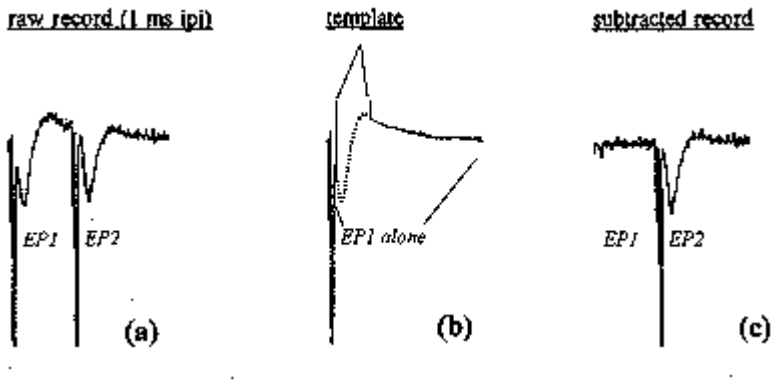

Figure 2. Template selection and record subtraction for an EP response pair.

To have a uniform and robust method for measuring latency and magnitude of EP responses, we have developed an analysis procedure that minimizes the need for experienced judgment in scoring individual records, especially small or noisy responses. Additionally, it provides an objective measure of the confidence that may be placed in the data, and it may be automated for bulk processing of large amounts of data. Figure 3 illustrates typical data derived from analysis of EP responses to paired pulses using this method. The procedure is as follows:

1. Derive a waveform template from a measure of EP_1 alone. The intermediate part of the EP waveform in Figure 2(b) indicated by dots is a section of the EP response referred to as a *template.* This template spans EP_1data samples 13-60 counting from the stimulus onset. With sampling intervals of 16.4 µsec this region begins 213 µsec into the record at which point the electrical artifact residual is over but the rising phase of the N_1 component is beginning. The template ends at 984 usec and includes the P_1 component but ignores much of the low magnitude decline back to baseline. Experience has shown that these parameters may be used for a wide range of recording conditions. The most important consideration in selecting this template is to ensure that the onset of the template does not include residual electrical artifact.

2. Cross-correlate the template with the EP_2 response to estimate the latency of the EP_2 response. An estimate of the response latency of EP_2 is determined by finding the latency at which correlation between template and EP waveform is maximized. The template is time shifted ±10 data samples and cross-correlated on a point by point basis with the EP_2 waveform. When shifting negatively (i.e. back in time), portions of the template that overlap with residual artifact in the target waveform are not included in the correlation measure. The latency shift at which the maximal correlation occurs, as measured from the onset of the second stimulus, is chosen as the latency of the EP_2 response.

3. Use the correlation coefficient as a measure of goodness-of-fit. The maximal correlation coefficient from the latency measure is used as an indicator of the goodness-of-fit of the template correlation. As such, it provides an objective measure of the overall quality of the EP data. Correlation coefficients that drop below 0.5 indicate that responses are contaminated with extraneous artifact and/or recording noise

4. Determine EP_2 magnitude using template fit. EP_2 magnitude is estimated by multiplying the slope of the regression line (derived in the cross-correlation of the template with the target waveform at the chosen latency) by the peak-to-

peak magnitude of the template. The template generally is based on many averaged samples and thus represents an accurate measure of EP magnitude. The magnitude of the template is measured as the peak-to-peak difference between its N1 and P1 components.

5. Calculate recovery functions. Recovery functions are calculated by normalizing EP_2 magnitudes to the template magnitude. Results are plotted as a function of IPI. Two recovery function plots are shown in Figure 3 with IPI plotted on linear and logarithmic scales, respectively.

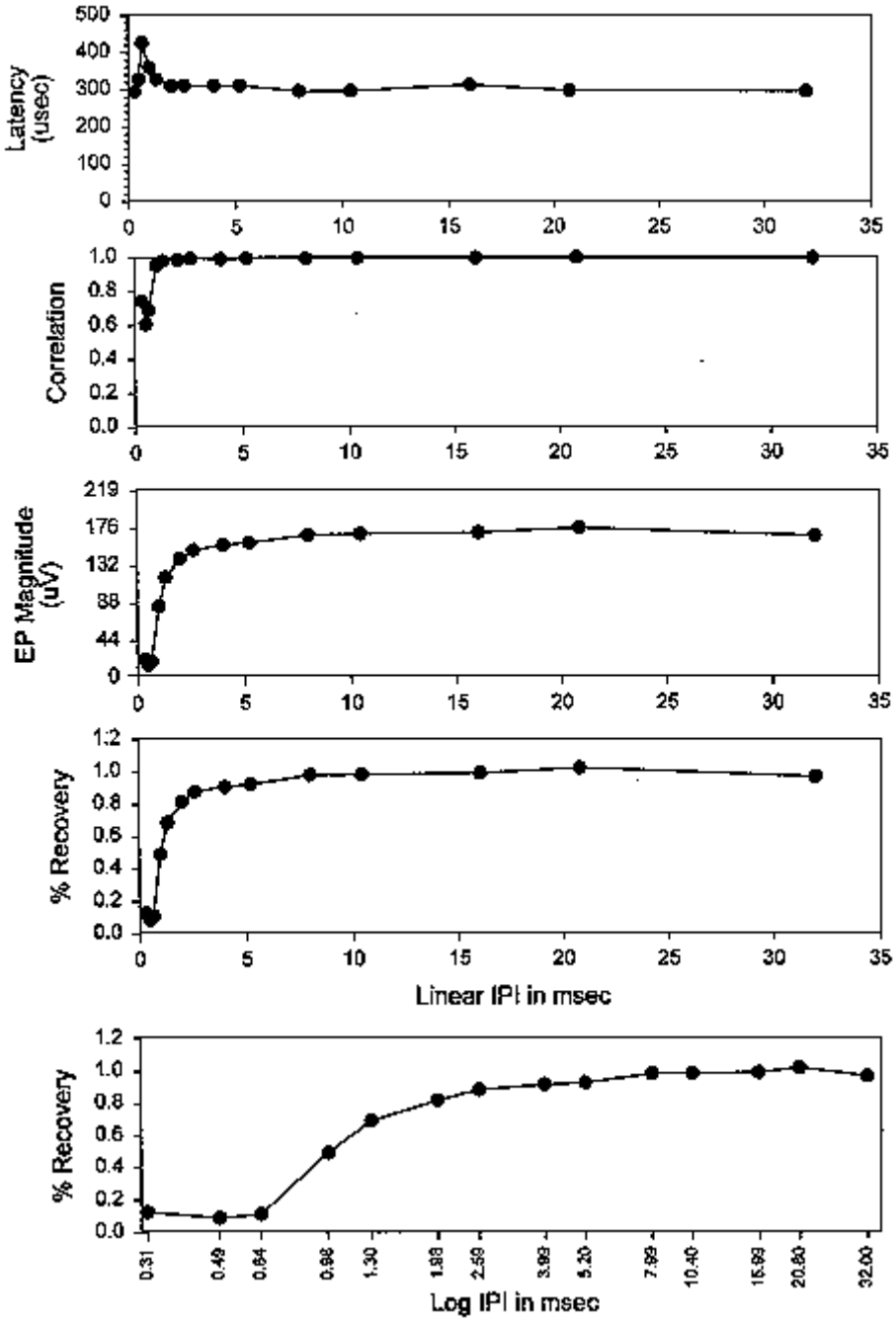

Figure 3. EP analysis method -- Examples of latency, correlation, EP magnitude, and percent recovery measures as a function of IPI.

The present report summarizes data collected for the seven subjects studied to date. Four subjects were implanted with the Ineraid device and three with the percutaneous research version of the Nucleus device. Subjects ranged from excellent (98% maximum NU6 monosyllabic word identification score for a wide variety of CIS processors) to poor (14% maximum NU6 score) in terms of their speech reception performance with open-set test materials.

Results

Figure 4 shows recovery of the EP_2 response as a function of interpulse interval in Ineraid subject SR2. Multiple curves are presented, each recorded for a fixed stimulus level applied to monopolar electrode #3 with respect to a remote temporalis return. In most cases, data for two separate trials are presented to indicate repeatability of the measure. In all cases, the EP responses are recorded from the adjacent more basal electrode #4 referenced to the ipsilateral mastoid. The general recovery pattern is that at small IPIs (<0.5 msec) the response to the second pulse is substantially diminished. As IPI increases, EP_2 magnitude increases and approaches full recovery at IPIs greater than 5 msec. All recovery curves are normalized to the magnitude of the template and are plotted in terms of percentage recovery.

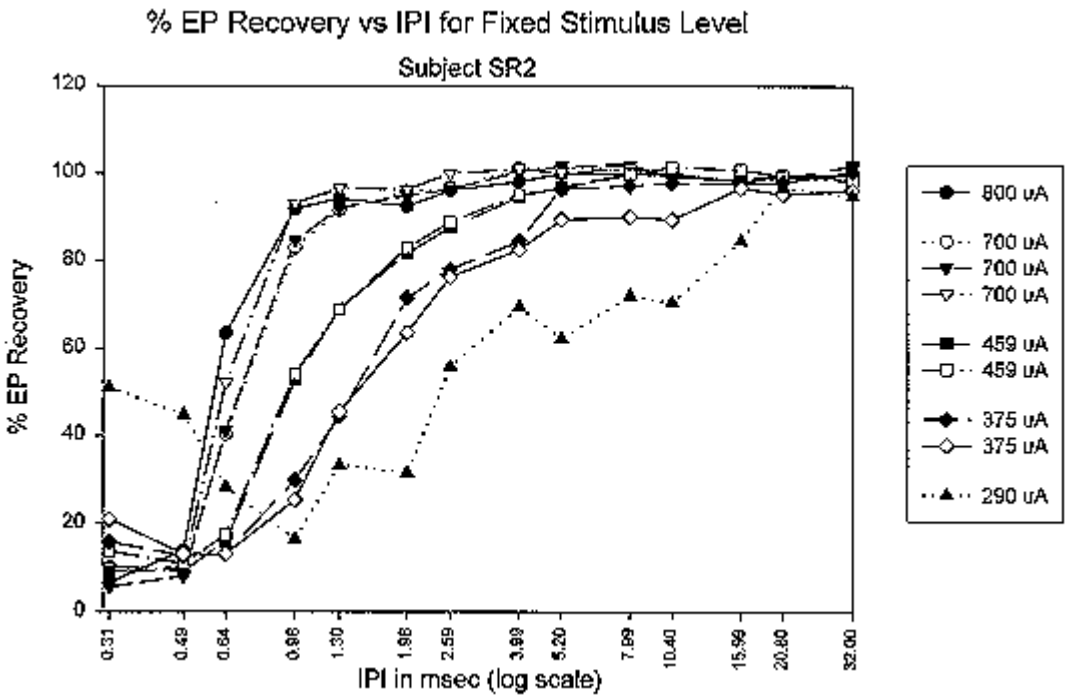

Figure 4. Recovery functions from subject SR2 for different stimulus levels.

Figure 4 also shows the effects of stimulus magnitude on the shape of the recovery curve. For this subject and electrode, 700 µA corresponded to most comfortable loudness (MCL) for the burst of paired pulses, whereas 375 µA was the upper limit of stimulation on this electrode employed in typical CIS processors. Recovery curves for 800 and 700 µA stimulation are essentially the same, both showing rapid recovery beginning at 0.5 msec IPI. As stimulus level is reduced to 459, 375, and 290 µA, recovery rates decrease progressively. As stimulus levels are decreased, the IPI at which recovery begins after the first pulse increases. For the lowest stimulus level (290 µA), the recovery curve shows an initially large component of EP recovery at short IPIs that declines as IPI increases, reaches a minimum and then begins a slow climb back to full recovery at very long IPIs. This pattern of EP recovery to low amplitude stimuli also is observed in other subjects and across stimulus/recording electrode sites. As stimulus level is reduced, absolute EP magnitudes diminish, thus requiring more trials (1600 in this case) to record successfully the very small averaged potentials evoked with small IPIs. Even then, these low level records are quite noisy, as is evident in the non monotonic slow recovery phase for the 290 µA level curve in Figure 4.

Figure 5 presents further examples of these patterns of recovery in NP2, one of the subjects implanted with a Nucleus electrode array. Three curves are presented. One was recorded with the 500 µA stimulus level that corresponded to MCL for this subject when the burst of pulse pairs was presented, while the other two are repeated trials recorded at a lower stimulus level of 375 µA. Again the recovery curves recorded with the lower stimulus level demonstrate the high initial recovery that declines to a minimum at longer IPIs followed by a slow gradual rise approaching full recovery at very long IPIs.

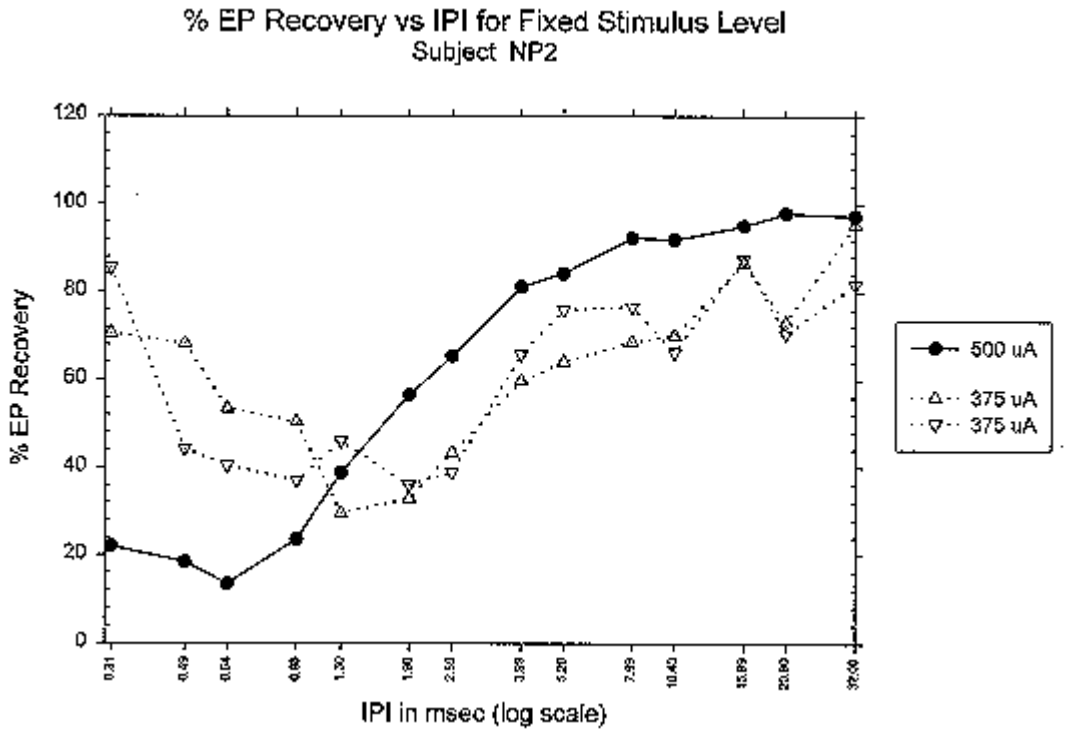

Figure 5. Recovery functions from subject NP2 for different stimulus levels.

Both the qualitative and quantitative effects of stimulus amplitude on recovery are significant. Figure 6 replots the data presented in Figure 4 to show better the relationship between EP recovery and stimulus level for fixed IPI. If EP recovery were independent of stimulus level, the curves for constant IPIs would lie parallel to the abscissa. This independence is observed only for either very short (0.31 and 0.49 msec) or very long (>3.98 msec) IPIs at stimulus levels above 400 µA. For stimulus levels below 400 µA, independence is observed only for an extremely long IPI. While amplitude independence at long IPIs is an assumed condition for recovery functions, it is evident that increasingly longer IPIs are necessary to achieve full recovery as stimulus levels decrease. Overall, the data in Figure 6 indicate that only EP responses corresponding to a small region of the stimulus parametric space are independent of stimulus level.

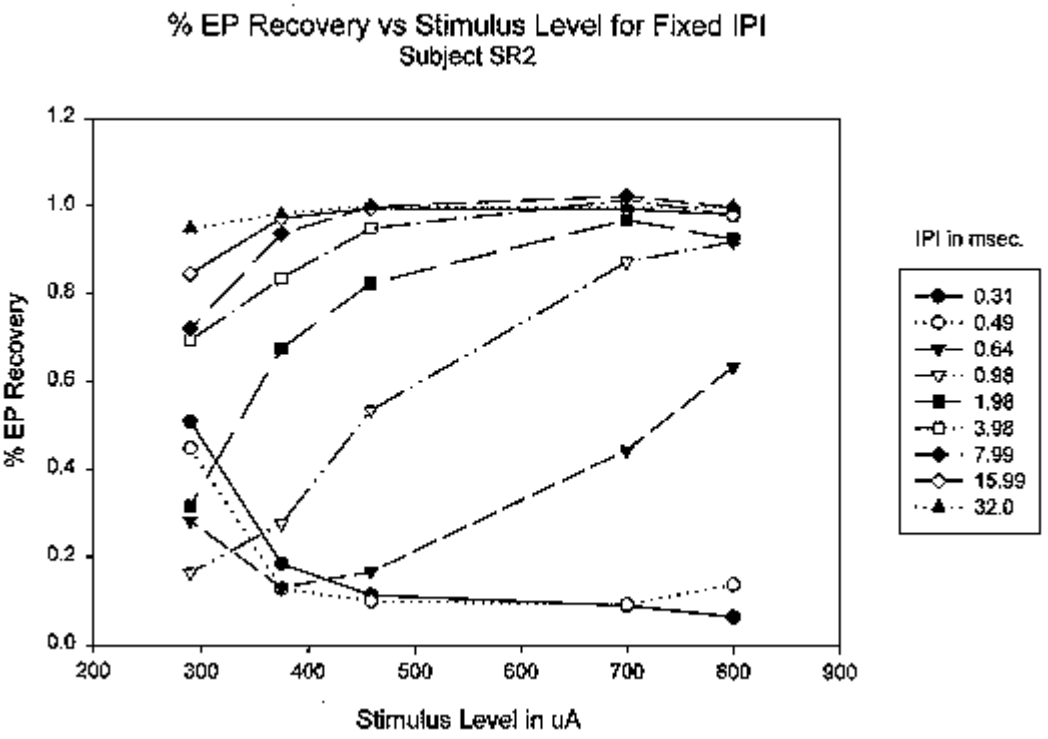

Figure 6. Recovery percentage for subject SR2 *vs*. stimulus level for fixed IPIs.

These observations are particularly important in interpreting EP findings in terms of stimulus levels applied in speech processors. Due to loudness recruitment with trains of pulses, typical stimulus levels in pulsatile speech processors are well below the upper range of stimulation tolerated with isolated pulse pairs. For instance, subject SR2's MCL for a wide variety of CIS processors corresponds to a 375 µA stimulus amplitude on electrode #3. At this level of stimulation, time constants of two-pulse, refractory recovery are roughly 2 msec, well in excess of the 833 µsec IPI typically used in his CIS processors. At lower mapped stimulation levels during processor operation, even longer recovery times would be expected. These effects would be combined with temporal integration effects that occur at yet lower levels, thus producing complex temporal interactions between individual stimulus pulses in pulse trains. Examples of this behavior are presented later in Figure 9.

Examination of data from Ineraid subject SR3 illustrates how recovery functions recorded from different regions of the cochlea within the same subject can appear highly similar or quite different depending on stimulus level. Figure 7 shows recovery functions recorded from three different cochlear regions at several stimulus levels. Test conditions include:

1) stimulating apical-most electrode #1 at 1000, 750 and 500 µA while recording from electrode #2;

2) stimulating mid position electrode #3 at 1000 and 520 µA while recording from electrode #4; and,

3) stimulating basal electrode #5 at 1000, 500 and 400 µA while again recording from electrode #4.

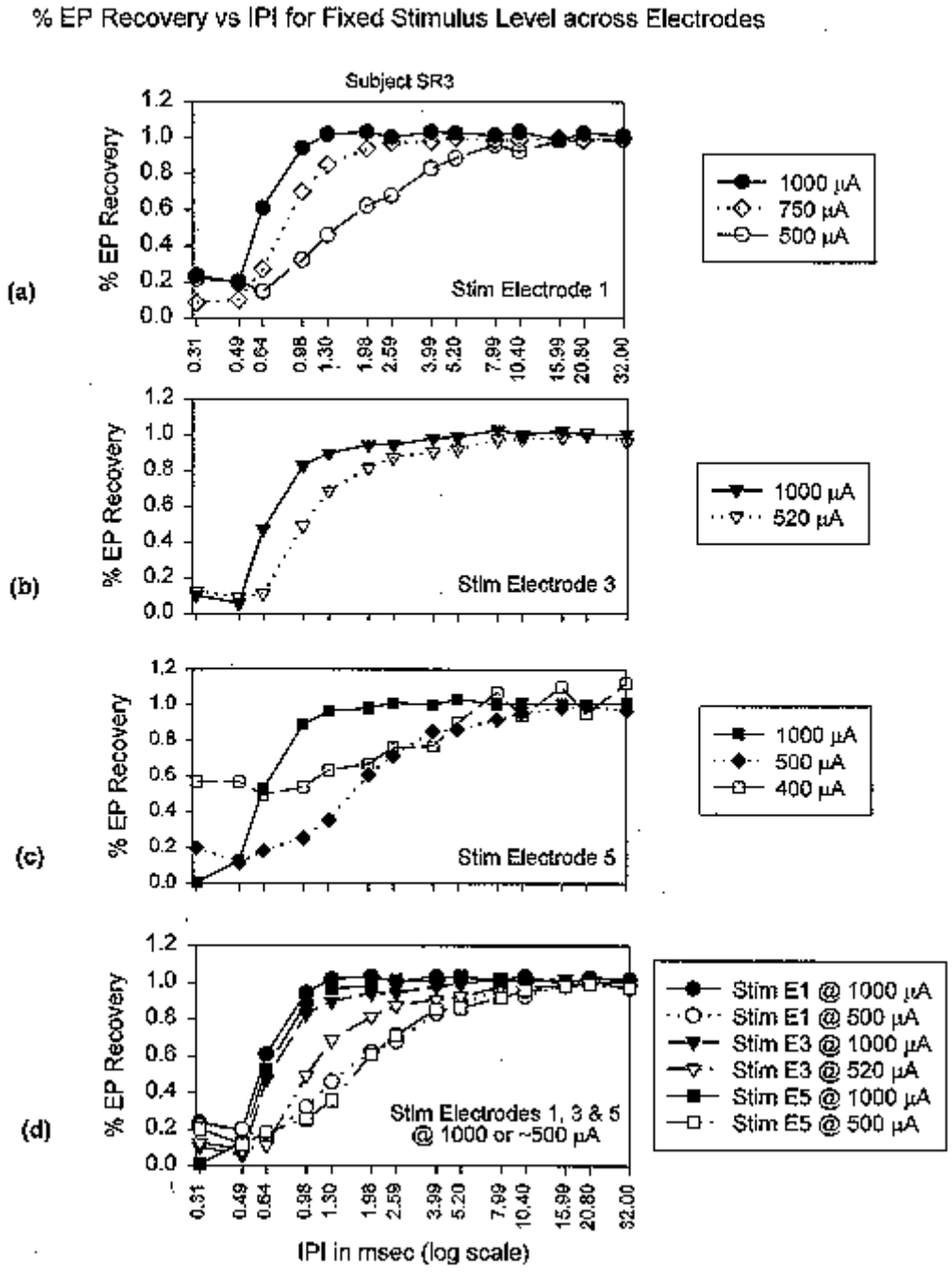

Figure 7. Recovery functions from subject SR3 -- variation across electrodes as a function of stimulus level.

Several response patterns are evident in the data. First, in panels 7(a) through 7(c) each individual electrode site demonstrates the amplitude-dependent pattern of recovery described earlier. In particular, for electrode #5 where the stimuli span the greatest range of amplitude, the full pattern is observed including substantial integration for small IPIs. Second, all three electrodes have very similar fast recovery when stimulated at 1000 µA. In contrast, when the stimulus level is reduced to approximately 500 µA for each electrode site, the EP recovery response changes. As shown in panel 7(d), EPs recover in a very similar fashion for stimulation on electrode #1 and #5; however, the recovery response at electrode #3 is clearly more rapid, although beginning its assent at the same IPI as electrodes #1 and #5.

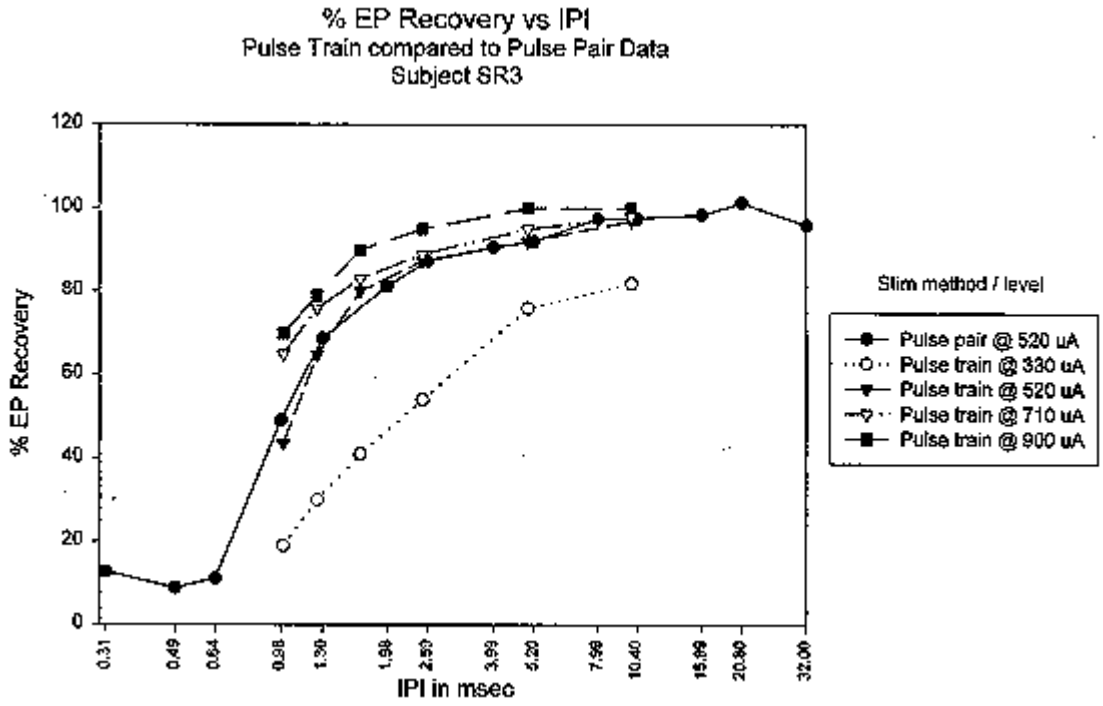

Figure 8. Recovery functions for subject SR2 derived from pulse train data.

These pulse-pair data from subject SR3 may be linked to responses of sustained pulse trains presented in earlier reports. Figure 8 presents recovery curves derived by examining the response magnitude to the second pulse in each of a set of constant-amplitude pulse trains that vary by stimulus amplitude and pulse rate (PPS). Also shown in the figure is the recovery function from Figure 7 that was measured using the paired-pulse procedure for 520 µA pulses. Data sets for the two procedures, although collected months apart, are essentially identical over their common parametric space. Figure 9 shows plots of EP magnitudes corresponding to individual pulses of the first 30 msec of these constant-amplitude pulse trains. Each train was 50 msec or longer. Data are presented for trains of four different amplitudes and three different pulse rates. Of particular interest are the plots of normalized EP magnitudes on the right. Note that (1) the percentage of suppression for the second pulse in each train is greater in response to lower amplitude stimuli, (2) the responses to subsequent pulses in the constant magnitude train tend to vary in an alternating fashion below or near the level of the second pulse response, (3) there is an apparent adaptation over time for the responses to higher stimulus levels, whereas for lower level stimuli they vary about a stable mean, and (4) the degree of variation increases and the specific pattern of alternation changes as the stimulus is decreased. All of these phenomena are examples of the complex, amplitude-dependent, temporal-interaction effects that can occur between individual pulses within pulse trains.

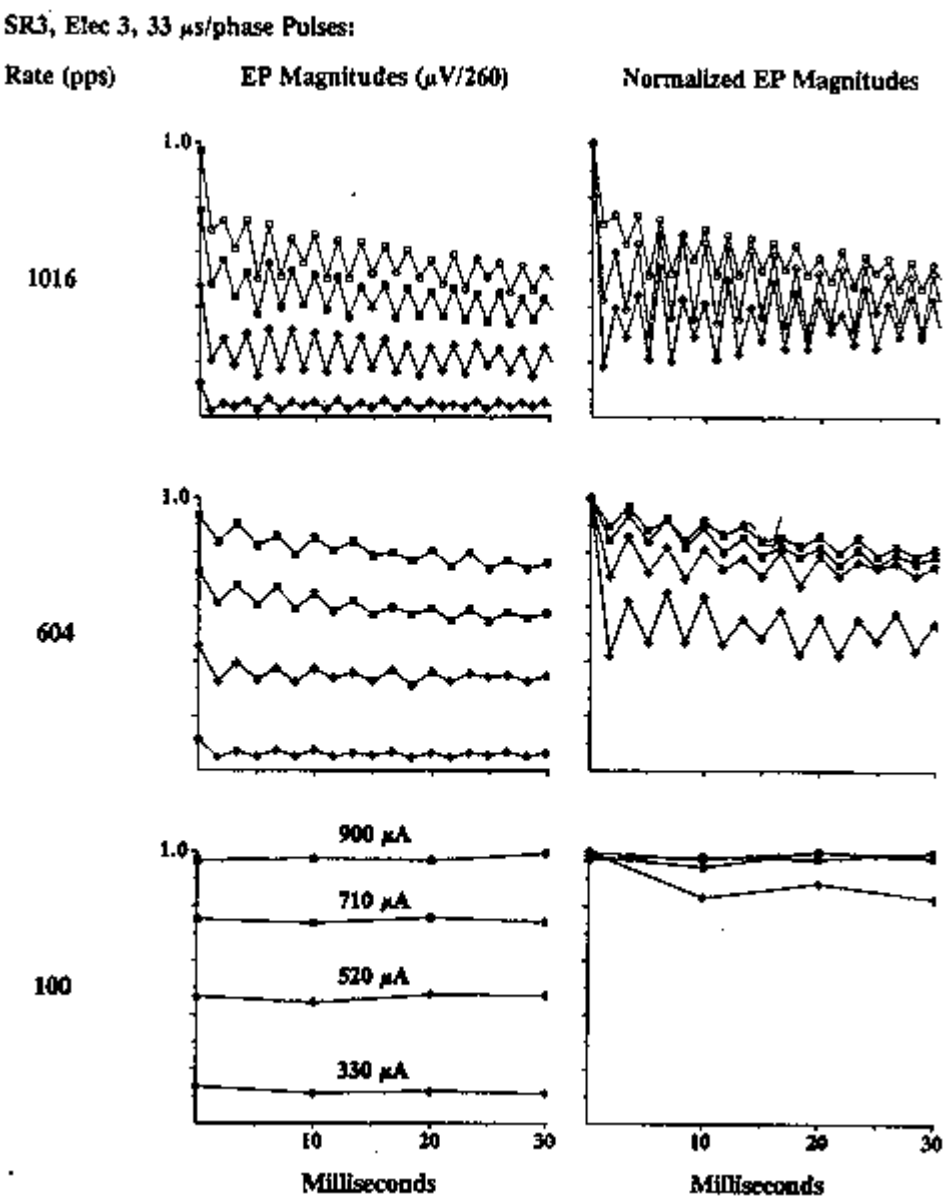

Figure 9. Pulse train response magnitudes for trains of different stimulus amplitudes and pulse rates.

Discussion

The present results show that two-pulse, refractory recovery functions are highly dependent on stimulus amplitude. At high stimulus levels, recovery functions converge to a common, fast recovery curve. At lower levels recovery is slower and begins at longer IPIs after the first stimulus. At the lowest stimulus levels, strong temporal summation is expected prior to a further delayed onset of recovery, followed by yet slower recovery to full response magnitude. These phenomena occur in general, but vary in detail, both across subjects and across electrodes within individual subjects.

The present results are readily interpreted in the context of simple neural mechanisms. It is useful to begin by examining the general response of a population of neurons to a pair of stimulus pulses. The occurrence of the first stimulus pulse essentially divides the neural population into two parts, namely those neurons that did fire and those that did not. Subsequently, the neurons that did fire progress through a sequence of absolute and relative refractory states. When in absolute refraction, a neuron cannot by definition be fired under any circumstance. This state is followed by a period of relative refraction in which the neuron may be fired but at an elevated threshold. As time progresses the firing threshold returns to its original level, at which point relative refraction ends. In contrast, neurons that did not initially fire in response to the first pulse remain available to respond to the second at any time and may even have lowered threshold levels due to residual subthreshold depolarization by the first pulse. Depending on the magnitude and timing delay of the second pulse, various subsets of the two initial populations of neurons will respond to it at various times,

thus producing an aggregate EP in response to that pulse. Although the response states for an individual neuron are well well defined, the underlying neural behavior described above may not be easy to recognize in the aggregate EP response. This is because the thresholds and latency of firing of the population of neurons may be quite heterogeneous due to individual physiological and anatomical differences, as is the variation of stimulus level across the population due to electrical field falloff from the stimulating electrode. Consequently, the EP response reflects the predominant trends of the total population behavior as opposed to the behavior of a specific neural element. The true physiological response range and spatial distribution of individual neurons within the neural population remain unknown.

In discussing the present data, we will distinguish between EP responses to relatively high and relatively low level stimuli for a progression of increasing IPIs. For very short IPIs, an initial high level first pulse will fire many neurons in the population, leaving few if any to respond to the second pulse, thus producing a small second EP response. As IPI is extended but remains in the period of absolute refraction, no additional unfired neurons will be recruited and the second EP response remains at its initial low level. At the point where the first pulse is sufficiently large to fire most neurons in the population, there will be little effect on neural recruitment by increasing stimulus level, thus setting the stage for convergence of recovery functions at high stimulus levels. As IPI is extended into the period of relative refraction for the initially fired neurons, more and more neurons will be recruited by the second pulse as the thresholds of these neurons decline, thus producing a gradually increasing second EP magnitude for larger IPIs. Eventually the initially fired neurons fully recover, and the EP returns to its initial level.

In contrast, the first pulse of a low level stimulus pair will stimulate fewer neurons in the population, leaving more unstimulated neurons in a subthreshold depolarization state with temporarily lower effective thresholds. Consequently for small IPIs, when the initial depolarization is not yet fully decayed, more neurons will be stimulated, thus producing larger EPs. As IPI is increased, the initial threshold shift of unfired neurons diminishes, fewer neurons are recruited, and the EP magnitudes fall. The fact that this phenomenon occurs with biphasic pulses indicates that the principal underlying mechanism is related more to nonlinear membrane dynamics and resulting threshold shifts, as opposed to simple integration of charge. After each charge-balanced, biphasic pulse there is no residual charge in the tissue. As IPI is extended into the period of relative refraction for the initially fired neurons, more neurons will be recruited and the EP will grow, just as for higher level stimuli as described above. However, because in this case the level of the second pulse is lower, it takes longer for the neural thresholds to decline sufficiently to be stimulated by the second pulse. The EP magnitudes reflect this, with longer recovery times for lower level stimuli. As with high level stimuli, the initially fired neurons eventually come out of relative refraction, and the EP recovers to its original level.

Brown, Abbas and Gantz (1990) and Brown, Abbas, Borland and Bertschy (1996) have reported a series of EP studies in Ineraid subjects using an alternative forward-masking paradigm to remove electrical artifacts in the records. This method relies on the presentation of a pulse pair referred to as a masker and a probe. At short IPIs the masker puts the nerve in full refraction at which point the probe response consists only of electrical artifact. This artifact signature is then subtracted from the probe alone condition to extract neural EP responses. The principles of this method are entirely consistent with the neural refractory behavior observed in our own data. Usually with the forward-masking method, to ensure that the nerve is in a maximal refractory state, the masker is set at a high level within the top 20% of a patient's dynamic range. These authors have reported EP growth functions and refractory recovery functions for a large number of subjects. A significant observation from their work is that growth and recovery functions vary across and within subjects. These investigators suggest that variations observed in their data may reflect pathophysiological status of the cochlea. Such variations in the data of the present report have been found to be largely stimulus amplitude dependent.

In a separate control study in cat the Iowa group has reported that the time course of recovery from refraction is independent of masker and probe levels as long as the masker is greater than or equal to the probe stimulus (Brown and Abbas, 1990). This observation is generally inconsistent with the stimulus level dependence described in this report. The most likely explanation for this discrepancy is the difference in stimulus level that these studies employed. In both the human and cat studies by Brown and colleagues, high stimulus levels were used for measurement of recovery functions. Results from the present study suggest that as stimulus levels increase, recovery becomes faster and converges to a common recovery function (see Figure 4). This effect is also apparent on close observation of the cat data of Brown and Abbas (1990). For two of the three cats reported, refractory recovery functions tend to be slower at lower probe stimulus levels. With the majority of high probe levels used in the present study, recovery functions converged to a common, fast recovery curve.

Based on the amplitude dependency of recovery functions reported in the present study, it is important to consider the possibility that at least part of the recovery variation observed across and within subjects is attributable to stimulus level directly as opposed to underlying pathophysiology. For instance, does a patient with wide dynamic range and fast recovery appear different from a patient with a narrower dynamic range and slower recovery if both are stimulated at similar levels?

To explore this question we have characterized all of our recovery functions by measuring the time required for each curve to recover to 63% of its final value. (This is roughly equivalent to treating each curve as a simple exponential function characterized by a single time constant. Such functions rise to 63% of their final value within one time constant.) Figure 10 is a scatter plot showing 63% recovery times for all subjects, all electrodes and all stimulus levels plotted with respect to applied stimulus amplitude. Linear regression lines are plotted for all data points common to an individual subject. Compared to recovery times elicited by high level stimuli, recovery times after lower level stimulation spread broadly with a wider range of variation. The general pattern associating shorter recovery times with higher stimulus amplitude is also quite distinct. It is significant that patients who show fast recovery times for high stimulus levels have recovery times for low stimulus levels that do not differ from those of other subjects.

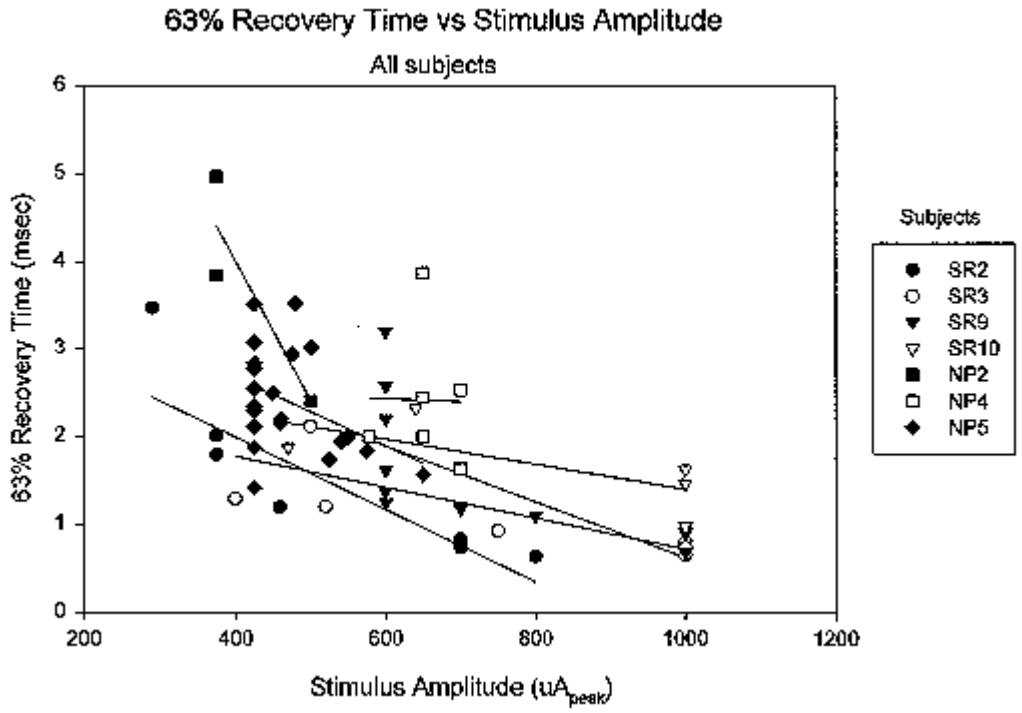

Figure 10. Estimated recovery times *vs*. stimulus amplitude for all subjects, all electrodes, and all stimulus amplitudes.

In view of the observed influence of stimulation level on recovery rates, in Figure 11 we examine the same 63% recovery times plotted as a function of EP magnitude. Using EP magnitude as a dependent variable links observed variation in recovery times more strongly to the intrinsic response characteristics of the local population. As in Figure 10, linear regression lines are plotted for all electrode and stimulus level conditions for individual subjects. The data indicate a clear inverse relationship between recovery time and EP magnitude with a greater range of recovery times occurring for small EP magnitudes. For small EP levels, there is overlap in recovery times across subjects. In particular, subjects who have the fastest recovery times with high EP magnitudes do not necessarily have the fastest recovery times with low EP magnitudes. The range of variability in recovery times for a fixed EP response level may likely be attributed to differences in the neural populations such as pathophysiology of individual fibers, as well as the density and spatial distribution of target neurons that contribute to the pattern of fiber recruitment and synchrony of firing in the aggregate EP response of the population. In contrast, the range in recovery times as a function of EP magnitude may be due to more intrinsic neural response properties, in turn more dependent on stimulus level. In any case, there is no clear sorting of patients into groups based on recovery times. Similarly, there appears to be no correlation of recovery times with overall performance level. The symbol key for Figure 11 is in order of decreasing maximum monosyllabic word recognition scores (NU6) for each subject using a variety of CIS processors studied in the laboratory. Note that the best performing subject (SR2) and the poorest performer (SR9) have comparable recovery

times for similar EP magnitudes. Interestingly, one of the better performing subjects (NP2) has by far the longest recovery times.

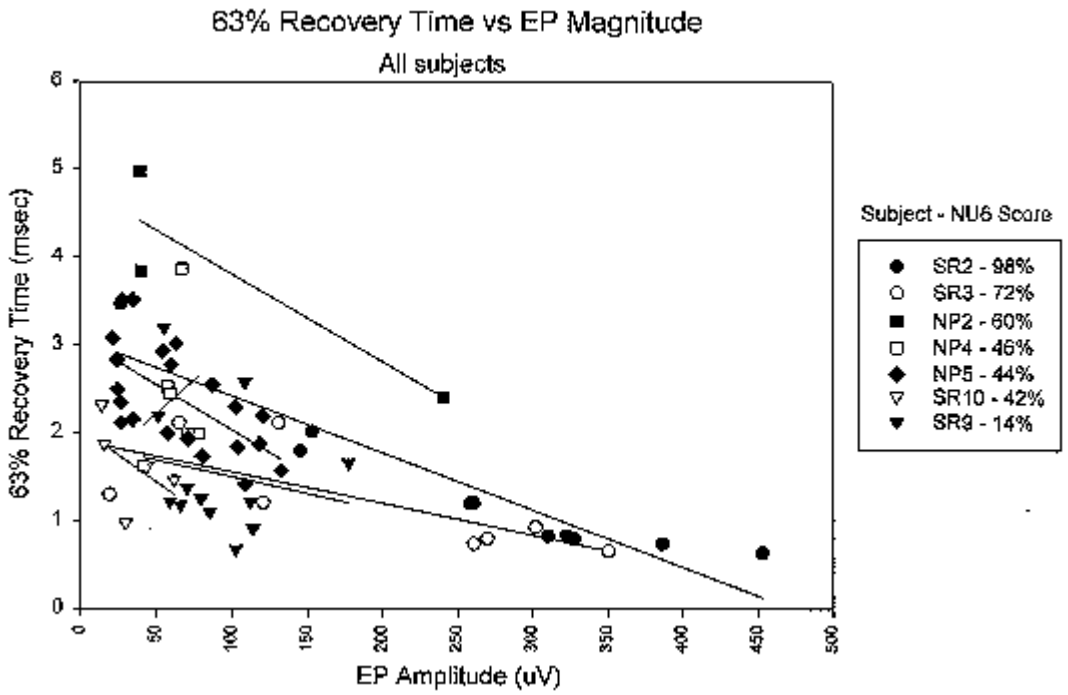

Figure 11. Estimated recovery times *vs.* EP response magnitude for all subjects, all electrodes, and all stimulus amplitudes.

In general the present work showing significant dependence of refractory recovery behavior on stimulus amplitude suggests that it is important to examine observed differences in patient results under conditions that provide controls for such effects. Comparisons based on equal loudness or equal stimulus levels across subjects, while interesting in terms of general EP behavior, may not provide as much insight into underlying mechanisms as originally expected. In addition, because EP measures of refractory recovery are clearly amplitude dependent, it is important to recognize that response measures made at high stimulus levels may not reflect mechanisms active during lower level stimulation with a functioning speech processor.

References

Brown, C.J. and P.J. Abbas (1990) Electrically evoked whole-nerve action potentials: Parametric data from the cat. *Journal of the Acoustical Society of America*, 88, 2205-2210.

Brown, C.J., P.J. Abbas and B. Gantz (1990) Electrically evoked whole-nerve action potentials: Data from human cochlear implant users. *Journal of the Acoustical Society of America*, 88, 1385-1391.

Brown, C.J., P.J. Abbas, J. Borland and M.R. Bertschy (1996) Electrically evoked whole nerve action potentials in Ineraid cochlear implant users: responses to different stimulating electrode configurations and comparison to psychophysical responses. *Journal of Speech and Hearing Research*, 39, 453-467.

III. Plans for the Next Quarter

Our plans for the next quarter include the following:

- Completion of recordings for new speech tests.
- Completion of new stimulating and recording systems for the evoked potentials laboratory.
- A visit by consultant Sig Soli, to review and refine our plans for studies with recipients of bilateral implants. The

discussion will include design of processing strategies for the coordinated stimulation of the two sides and design and use of tests to evaluate possible advantages of such stimulation in environments with multiple speakers and/or directionally distinct noise sources. The visit is scheduled for March 6, 1997.

- Preparation for continued studies with a recipient of standard Nucleus implants on both sides (subject NU4) and for new studies with a recipient of Med El implants on both sides. The latter subject has full insertions of the electrode array on both sides and reportedly enjoys excellent performance with either implant alone, and with simultaneous use of the two implants under the control of separate speech processors. Preparation for studies with the Med El subject will include development of an interface system for laboratory control of receivers in both Med El implants.
- Continued speech reception and evoked potential studies using high pulse rates, up to and including 10000 pulses/s on single channels.
- Fitting of three additional Ineraid subjects with the Innsbruck/RTI processor, to evaluate possible learning effects with sustained use of CIS processors. The subjects include two who are at the low end of the performance spectrum with their clinical CA processors.
- Additional evoked potential and speech reception studies with these subjects during their visits for fitting of the Innsbruck/RTI processor.
- Continued development of a new type of compression function for use in CIS processors, designed to mimic principal features of the noninstantaneous compression found in normal hearing at the synapse between sensory hair cells and adjacent neurons.
- Preparation for psychophysical studies to investigate pitch perception with structured random pulse trains and to investigate effects of pulse polarity, number and rate on the threshold of audibility.
- Continued analysis of speech reception and evoked potential data from prior studies.
- Continued preparation of manuscripts for publication, including one invited editorial and two invited papers.

II. Acknowledgments

We thank subjects SR2, SR14, SR16 and NP2 for their participation in the studies of this quarter. We also are pleased to acknowledge the contributions of visiting investigators Aaron Parkins and Phillip Loizou to the work of the this quarter.