Phase-locking of auditory-nerve discharges to sinusoidal electric stimulation of the cochlea

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(Received 28 May 1991; accepted 2 October 1991)

The activity of auditory-nerve fibers was recorded in anesthetized cats in response to sinusoidal electric stimuli applied through a bipolar electrode pair inserted about 5 mm into the cochlea through the round window. The synchronization index was calculated from period histograms for frequencies ranging from 0.2 to over 10 kHz. The stimulus artifact was largely eliminated through the use of differential micropipettes and an adaptive digital filter. Measured synchronization indices were many times larger than the indices that could be attributed to the residual stimulus artifact. Synchronization indices at each stimulus frequency varied considerably from fiber to fiber, even in the same animal. The dependence of synchrony on stimulus frequency was also variable, decreasing monotonically in some fibers and nonmonotonically in others. The average electric synchronization index for all fibers did not fall as steeply with frequency as does the average synchrony for acoustic stimuli. The finding of significant phase locking to electric stimuli well above 1 kHz suggests that the poor frequency discrimination of cochlear-implant recipients for single-channel stimulation above this frequency may be due to the inability of the central processor to make effective use of the available phase-locking information for monaural stimulation.

Introduction

Studies of auditory-nerve fiber responses to electric stimulation are fundamental to the design of improved stimulation schemes for cochlear implants. They help identify basic limitations on the patterns of activity that can be elicited in the auditory nerve by a cochlear implant. They also describe how responses to electrical stimulation differ from those to acoustic stimulation. Such information may suggest changes in the stimulation scheme that would make responses for electric stimuli more similar to those for acoustic stimuli and perhaps processed more naturally by the central nervous system (Kiang et al., 1979).

One response property of particular interest is the phase locking of the discharges of auditory-nerve fibers to the stimulus waveform (Rose et al., 1967; Johnson, 1980). Phase locking is relevant not only for cochlear implants, but also for models of central auditory processing of fine temporal information. The highest stimulation frequency to which discharges can phase lock sets an upper bound on the bandwidth of any signal that can be encoded over a nerve fiber. Phase locking of auditory-nerve discharges to the formant frequencies of speech may be an important cue for speech discrimination under some circumstances (Young and Sachs, 1979). Phase locking is also likely to be an important cue for frequency discrimination by cochlear-implant recipients, particularly for single-channel stimulation where place cues are unavailable. Psychophysical experiments show that cochlear implant patients poorly discriminate the frequency of sinusoidal signals and pulse trains applied through a single electrode when the frequency of stimulation exceeds 300-1000 Hz (Adington et al., 1978; Shannon, 1983; Hochmair-Desoyer et al., 1983; Tong et al., 1982; Townshend et al., 1987). It is not known whether this poor performance is because auditory-nerve fibers lack phase locking to electric stimuli, or because the central processor cannot make use of the available information.

Previous studies of the temporal patterns of discharge in response to sinusoidal electric stimulation have been mostly concerned with frequencies below 1 kHz (Kiang and Moxon, 1972; Hartmann et al., 1984; Hartmann and Klinke, 1990; Van den Honert and Stypulkowski, 1987b; Parkins, 1989; Javel et al., 1987; Javel, 1990). These studies have established that discharges of auditory-nerve fibers are precisely phase-locked to sinusoidal or pulse-train stimuli for these frequencies. For higher frequencies, the interpretation...
of the data is confounded by the possibility that the stimulus artifact (the component of the recorded potential due to stimulus current flowing between the recording electrodes) can exaggerate phase locking (Johnson, 1978). The few existing reports of phase locking at frequencies above 1 kHz (Glass, 1984; Hartmann and Klinke, 1987, 1990) did not adequately address this artifact problem. This paper reports systematic measurements of the phase locking of auditory-nerve discharges in anesthetized cats in response to sinusoidal electric stimuli applied through intracochlear electrodes. Great care was taken in reducing the stimulus artifact to a minimum, and in quantitatively assessing the effect of any remaining artifact on measurements of phase locking. A preliminary report of these results has been presented (Dynes and Delgutte, 1989).

Method

Animal preparation

Surgical techniques for accessing the auditory-nerve by a dorsal approach in cats anesthetized with Dial in urethane were as described by Kiang et al. (1965) and Liberman (1978). In addition, the middle-ear muscles were cut in both ears. In 11 animals, a bipolar pair of stimulating electrodes was inserted 4–5 mm into scala tympani through the round window, and cemented in place with dental acrylic. Each electrode was a teflon-coated platinum wire terminated by a ball 0.25 mm in diameter. The tips of the electrodes in the bipolar pair were separated by 2–3 mm along the axis of scala tympani. In one animal, an electrode was placed on the round-window membrane and the other on the perioticum near the apex of the cochlea in order to study responses from an intact cochlea. After surgery, the animal was placed in a sound-proof, electrically-shielded chamber. An acoustic cavity containing a Brüel and Kjær 1-inch condenser microphone and a calibrated probe microphone was sealed into the auditory meatus. (Kiang et al. 1965)

Stimuli

Electric stimuli were bursts of sinusoidal current generated by means of an oscillator and an electronic switch providing a linear rise-fall of 2.5 ms. The stimuli were delivered to the electrodes by an isolated voltage-to-current converter with a bandwidth of 30 kHz. The current was calibrated by means of a known resistor placed in series with the stimulating electrodes. Harmonic distortion products in the current waveform were always at least 40–50 dB below the fundamental. Acoustic stimuli were tone bursts generated in the same manner as electric current bursts. These tones were swept in frequency at the maximum level produced by the sound source (105–110 dB SPL) to determine whether auditory-nerve fibers responded to acoustic stimuli.

Cancellation of the stimulus artifact

In these experiments, it was essential to minimize stimulus artifact in order to obtain accurate measurements of the phase locking of spikes to sinusoidal stimuli. This was accomplished by a combination of techniques. First, spike activity was measured by means of special glass micropipettes that record differentially between their 2 M-KCl-filled lumen and a cylindrical gold conductor located about 50 µm from the tip (Van den Honert and Stypulkowski, 1984). Stimulus artifact for these electrodes was typically 20–35 dB smaller than for conventional micropipettes. Further reduction in stimulus artifact was achieved first by subtracting the stimulus waveform scaled to best match the stimulus artifact from the microelectrode signal, then by processing the subtracted signal through an adaptive digital filter (Widrow et al., 1975) implemented on a Texas Instruments TMS320C25 chip with sampling rates of 20–50 kHz. The adaptive filter had two taps in quadrature phases and an adaptation time constant of 1–5 ms. This adaptive technique enables the cancellation to be effective even when the artifact waveform changes as for example with electrode motion. The root-mean-square (r.m.s.) amplitude of the final stimulus artifact was usually 40–60 dB below peak spike amplitudes.

Assessment of the effect of stimulus artifact

A model developed by Johnson (1978) was used to assess the effect of the remaining stimulus artifact on measurements of synchronization indices (Goldberg and Brown, 1969) to the electric stimuli. According to this model, the synchronization index SI due to the artifact is

$$ SI = \sqrt{\gamma f / \tau} $$

assuming a randomly-distributed spike train contaminated by an additive sine wave at frequency $f$ and where gamma is the ratio of r.m.s. stimulus artifact amplitude to peak spike amplitude, and $\tau$ is the rise time of the spikes. It is difficult to obtain artifact-free measurements of phase locking at high frequencies because the artificial synchrony increases linearly with frequency. For every recording of spikes in response to an electrical stimulus, Equation (1) was used to compute a synchrony floor below which synchrony might be artificial. The rise time $\tau$ was assumed to be 200 µs as indicated by actual measurements, and the ratio $\gamma$ was calculated from measurements of spike amplitude and artifact amplitude during stimulation. Only data for which the measured synchronization...
I calculated kHz

Fig. 1. Artificial synchronization index versus ratio of r.m.s. stimulus amplitude to peak spike amplitude for two stimulus frequencies. Measured synchrony is from a recording of spontaneous activity corrupted by an additive sinusoid; calculated synchrony is from Johnson's (1978) model.

The applicability of Johnson's model was verified by control experiments. Sine waves of known amplitude were electronically added to a recording of spontaneous activity from an auditory-nerve fiber, and the synchronization index to the sine-wave frequency was measured from a period histogram for the contaminated recording. Figure 1 shows both the measured synchronization index and the synchrony floor calculated from Johnson's model as a function of the artifact-to-spike ratio gamma for two frequencies. The measured synchrony is always less than the calculated synchrony floor, except at low levels where both values are within measurement error. The small departure from Johnson's predictions might be due to inaccuracies in measuring the spike rise time, or to a small amount of additive random noise in the spike train (Johnson, 1978). The important point is that the synchrony floor computed from Johnson's model constitutes a conservative estimate of the effect that stimulus artifacts have on measurements of the synchronization index.

Stimulation paradigms

When an auditory-nerve fiber was contacted, electric thresholds for spike discharges were measured for 50–200 ms sinusoidal current bursts by a tracking algorithm (Kiang et al., 1970; Liberman, 1978), using a criterion of 10 spikes/s above spontaneous rate. An attempt was then made to stimulate the fiber acoustically using tone bursts as intense as 105–110 dB SPL.

If acoustic responses were detected, an acoustic tuning curve was measured using the same tracking algorithm and rate criterion as for electric thresholds.

In the initial series of experiments, average discharge rate and synchronization index were measured as a function of level in steps of 0.25 dB, usually starting at 0.5 dB above threshold. Stimulus level was increased until it was judged that the synchronization index had saturated. Typically, a 3-dB range of levels was used. For a few fibers, level series were continued well above saturation in order to examine behavior at very high discharge rates. The stimuli used in these level series were 1-s bursts of sinusoidal currents presented every 2 s. Because the adaptive filter used for artifact cancellation took time to reach full effectiveness, the first 200 ms of each current burst recording was discarded in data processing. The stimuli were presented in groups of 12 until a sufficient spike count (usually 1000) was reached. If the discharge rate was very low, fewer spikes were collected in order to save time for other measurements. Measurements of synchronization indices were based on period histograms computed with at least 20 bins.

In later experiments, a single synchrony measurement was made for each frequency in an attempt to cover a broader frequency range. For each stimulus frequency, the tracking algorithm used in threshold measurements (Kiang et al., 1970) was used to determine the stimulus level that produced a discharge rate of 200 spikes/s. The synchronization index was then measured for this stimulus level.

Results

General observations

This report is based on recordings from 140 auditory-nerve fibers in 12 cats. In 7 cats, insertion of the electrodes into the cochlea resulted in loss of acoustic sensitivity. All but a few of the fibers showed no spontaneous activity, and did not respond to acoustic tones at 105–110 dB SPL for any frequency. In 5 cats, including the one in which the stimulating electrodes were at the round window, most fibers showed spontaneous activity and well-defined acoustic tuning curves in the early stages of the experiment. In these cats, fibers for which electrophonic responses were detected were excluded from further analysis. Electrophonic responses were easily identified by lower threshold currents and much shallower rate-level functions than for other fibers in the same animal (Moxon, 1971). Unless specifically noted otherwise, phase-locked responses of auditory-nerve fibers were similar in deafened and hearing cats, so that data from both types of animals were pooled in this report.
Figure 2 shows electric thresholds as a function of frequency for 7 auditory-nerve fibers for which thresholds were measured over a broad range of frequencies. None of these fibers responded to acoustic stimuli. For all fibers, threshold increases monotonically with frequency. Threshold variations among fibers exceed 10 dB for all frequencies, consistent with other reports (Van den Honert and Stypulkowski, 1984, 1987a; Hartmann and Klinke, 1990). For 5 of these fibers, the frequency dependence of threshold is approximately 3 dB/octave. The growth of threshold with frequency appears somewhat steeper than 3 dB/octave for the two fibers identified by open circles and crosses. Although these two fibers were from the same animal, another fiber from this animal (identified by stars in Fig. 2), showed a frequency dependence of threshold more consistent with 3 dB/octave. These threshold data resemble those shown in previous reports for cat auditory-nerve fibers (Kiang and Moxon, 1972; Hartmann and Klinke, 1990).

Figure 3 shows PST histograms for 3 auditory-nerve fibers from the same cat in response to 1-s bursts of sinusoidal current at 7 kHz. For the fiber shown on the left, the discharge rate is approximately constant throughout the duration of the stimulus. The middle fiber shows some decay in discharge rate for 200 ms followed by a steady plateau. The right fiber shows considerable decay extending to the end of the stimulus. The shape of these PST histograms can be characterized by a decaying exponential superposed on a baseline discharge rate. For a given fiber, increasing the stimulus intensity caused an increase in the baseline rate, but no change in the time constant of the exponential. Changing the stimulus frequency did not change the character of the PST histogram for the frequencies used. A measure of the adaptation was formed by taking the ratio of the decrease in discharge rate over the course of the PST histogram to the initial discharge rate. Among the histograms measured, 25% showed less than 30% adaptation, as for the left fiber, 50% showed from 30 to 80% adaptation, as for the middle fiber, and 25% showed more than 80% adaptation, as for the left fiber. These results extend to high-frequency stimuli previous reports of a form of adaptation in response to low-frequency electric stimuli (Moxon, 1967; Van den Honert and Stypulkowski, 1987b; Javel et al., 1987; Parkins, 1989; Javel, 1990). The results further show that there is considerable inter-fiber variability in the time course of adaptation. Because large adaptation in response to electric stimuli is not found consistently for all auditory-nerve fibers, it seems unlikely that such adaptation would be important in psychophysical forward masking with electric stimuli (Dent and Townsend, 1987; Shannon, 1990).

Phase locking

Figure 4 shows interval and period histograms for one auditory-nerve fiber in response to sinusoidal currents at 3 different frequencies. For all 3 frequencies, the period histograms have roughly a sinusoidal shape, indicating that discharges are moderately phase-locked to the stimulus. This contrasts with period histograms for low-frequency stimuli, which show a sharp peak restricted to a small fraction of the stimulus cycle (Kiang and Moxon, 1972; Hartmann et al., 1984; Van den Honert and Stypulkowski, 1987b; Javel et al., 1987; Parkins, 1989). The interval histograms show a peak at about 5–6 ms, which corresponds to the reciprocal of the average discharge rate for all 3 frequencies. This indicates that the fiber is discharging regularly in response to these high-frequency sine waves, much as it does for low-frequency stimuli (Hartmann et al., 1984; Van den Honert and Stypulkowski, 1987b; Javel et al.,
Fig. 4. Period histograms (left) and interval histograms (middle) for an auditory-nerve fiber at three frequencies. Stimuli were sinusoidal currents that produced a discharge rate of about 200 spikes/s. The right panels show details of the interval histograms in the middle column using smaller bin widths. The ticks at the top of each panel represent multiples of the stimulus period.

1987; Javel, 1990; Parkins, 1989). Despite this regularity, variations in interspike intervals correspond to many stimulus cycles: At 5 kHz, for example, there are usually between 20 and 32 stimulus cycles between successive spikes. Examination of the interval histograms in the region of the mode shows definite peaks at intervals equal to the period of the stimulus, confirming the phase locking of discharges. Note that

Fig. 5. Synchronization index (top) and average discharge (bottom) as a function of stimulus level for two auditory-nerve fibers from the same cat. The stimulus was a 5-kHz sinusoidal current. The top panel shows both the measured synchrony (triangle) and the synchrony floor (circle) calculated from measurement of stimulus artifact by means of Johnson's (1978) model.
phase locking is more apparent for the 8-kHz stimulus than for the two lower frequencies, a point to which we will return later.

Figure 5 shows the average discharge rate, the synchronization index, and the synchrony floor as a function of stimulus level for two auditory-nerve fibers in response to 5-kHz sinusoidal currents. For both fibers, the synchrony floor calculated from Johnson's model is a small fraction of the measured synchrony, showing that these measurements do represent a phase-locked response rather than an effect of the stimulus artifact. These two fibers were from the same cat, were contacted within minutes of one another, and did not respond to acoustic stimuli. For both fibers, discharge rate grew by 400–500 spikes/s over a 3–4 dB stimulus increase, yet the synchronization index for the left fiber is much lower than that for the right fiber. Such inter-fiber variability was not unusual in our data.

Figure 6 shows the average discharge rate and the synchronization index as a function of current level for 4 fibers using 8-kHz sinusoidal stimuli, and for 3 fibers using 5-kHz stimuli. These fibers were selected because measurements were available over a particularly large range of stimulus levels. For all fibers, discharge rate grew with level, with the exception of a few levels where decreases occurred. Discharge rate can reach values in excess of 400 spikes/s when stimulus level exceeds threshold by a few dB. These rates are much higher than those achieved with acoustic stimuli of the same duration (Moxon, 1967; Javel et al., 1987). Although the slopes of the rate-level functions appear to be somewhat steeper for the 8-kHz stimulus than for the 5-kHz stimulus, this observation does not hold for all fibers. In contrast to discharge rate, the synchronization index does not vary greatly with stimulus level, except for two fibers at very low discharge rates, where measurement errors can be very large due to the small number of spikes collected. This constancy of the synchronization index is consistent with previous reports for fibers that have no spontaneous activity (Johnson, 1980; Hartmann et al., 1984). For fibers that do show spontaneous activity, electric synchrony grows over a range of stimulus levels, although most of this range is below the discharge rate threshold (Hartmann and Klinke, 1990).

Because the synchronization index does not vary greatly with stimulus level, the median synchronization index across all stimulus levels was used to characterize the phase locking for each fiber and each frequency. In some experiments, the synchronization index was obtained only for the stimulus level that produced a discharge rate of 200 spikes/s in an effort to obtain data for many frequencies. Figure 7 shows the median synchronization index as a function of frequency for 6 auditory-nerve fibers for which data were available for many frequencies. Three of these fibers show a nearly monotonic decrease in synchronization index with frequency, while the frequency dependence of synchrony is clearly nonmonotonic for 3 fibers. For monotonic fibers, the frequency at which the synchronization begins to fall rapidly also varies appreciably. Thus, there is considerable variability among fibers, not only in the

![Figure 6](image_url)
Fig. 7. Median synchronization index against the frequency of sinusoidal electric stimuli for 6 auditory-nerve fibers from 4 cats. Each symbol represents data for one fiber. None of these fibers responded to acoustic stimuli.

Fig. 8. Synchronization index against the time at which the measurement was taken for one auditory-nerve fiber in response to electric sinusoids at 4 frequencies. This fiber did not respond to acoustic stimuli.

Fig. 9. Median synchronization index against the frequency of sinusoidal electric stimuli for 120 fibers from 11 cats stimulated with bipolar, intracochlear electrodes. The filled boxes represent the mean value of the medians at each frequency.

overall strength of phase locking, but also in the shape of the frequency dependence of synchrony. The nonmonotonic frequency dependence of synchrony was verified by repeated measurements in several fibers. For example, Fig. 8 shows the experimental history of the fiber of Fig. 4. The synchronization index is plotted as a function of the time that the measurement was taken. Measurements were made for 4 frequencies in different orders. For each frequency, stimulus level was adjusted to obtain a discharge rate of 200 spikes/s. The synchronization index for 8 kHz is always greater than that for 5 kHz, and, with one exception, than that for 4 kHz. These data confirm that nonmonotonicities in the frequency dependence of synchrony are reliable.

Figure 9 shows the median synchronization index as a function of sinusoidal stimulus frequency for 120 fibers from the 11 cats in which bipolar intracochlear electrodes were used. Interfiber variability is considerable and is largest for frequencies above 3 kHz. For low frequencies, the synchronization index is very close to 1, consistent with previous reports for both sinusoidal and pulsatile stimuli (Hartmann et al., 1984; Javel et al., 1987; Van den Honert and Stypulkowski, 1987b). For frequencies above 2 kHz, the mean synchronization index decreases with increasing frequency at a rate of approximately 6 dB/octave. Despite this trend, for most fibers there remains considerable phase locking at 10 kHz.

Discussion

Comparison with other physiological studies

Most studies of temporal response patterns of auditory-nerve fibers to electric stimuli have used low-frequency sinusoids or pulse trains (Hartmann et al., 1984; Javel et al., 1987; Javel, 1990; Van den Honert and Stypulkowski, 1987b; Parkins and Colombo, 1987; Parkins, 1989). With one exception (Hartmann and Klinke, 1987, 1990), reliable data have not been available for stimuli with frequencies above 1–2 kHz because, as some authors have pointed out, stimulus artifact confounds the interpretation of phase-locking data at high frequencies. In the present study, special care was taken to reduce the stimulus artifact in order to study rigorously the temporal patterns of response to high-frequency electric stimuli. Specifically, for every data record, a synchrony floor representing the effect of stimulus artifact was calculated and compared to the measured synchronization index. Only those data for which the synchrony floor was less than 1/3 of the measured synchrony were included in this study. Care was also taken to avoid complicating effects of electrophonic responses by testing each fiber for acoustic responses.

Previous reports have emphasized the regularity of auditory-nerve fiber discharges in response to low-
frequency sinusoidal or pulse-train stimuli. For stimulus levels a few dB above threshold, discharges tend to occur once for every stimulus cycle in a precisely phase-locked manner (Hartmann et al., 1984; Van den Honert and Stypulkowski, 1987b; Parkins, 1989; Javel, 1990). The present results, as well as those of Parkins (1989), show that this tendency for regular discharges is, to some extent, maintained at higher frequencies in that interval histograms show a pronounced peak at the reciprocal of the average discharge rate. This pattern contrasts with responses to acoustic tones, which are much more irregular (Rose et al., 1967). Nevertheless, responses to high-frequency electric stimuli are not as regular as those to low-frequency electric stimuli in that the number of stimulus cycles between successive spikes is variable because even small variations in interspike intervals correspond to many stimulus cycles. In this respect, responses to high-frequency electric stimuli resemble responses to high-frequency tones more than they do responses to low-frequency, electric stimuli. In view of these findings, Javel's (1990) statement that "at sufficiently high intensities, what one fiber does, they all do" is not likely to hold for high-frequency electric stimuli. Rather, the regularity of auditory-nerve fiber discharges depends on both frequency and mode of stimulation, with responses to low-frequency electric stimuli being the most regular, responses to high-frequency acoustic stimuli the least regular, and responses to high-frequency electric stimuli in between.

For low-frequency, large-amplitude sinusoidal electric stimuli, auditory-nerve fibers can discharge during opposite phases of the stimulus cycle, and can even show multiple discharges during one half cycle (Hartmann et al., 1984; Van den Honert and Stypulkowski, 1987b; Parkins, 1989). Responses to opposite phases are thought to originate from different sites of excitation along the stimulated fiber (Van den Honert and Stypulkowski, 1987b). Among the 140 fibers that we studied, bimodal period histograms were seen only for 7 fibers, 6 of them from the same cat. These bimodal responses were only found when the stimulus level was raised more than 3 dB above threshold. Restriction to low stimulus levels cannot entirely explain the low proportion of bimodal histograms because in several cats we failed to find bimodal period histograms even at high stimulus levels. Apparently, responses to opposite phases of the stimulus cycle are less common at high frequencies than at low frequencies. The origin of this effect is unclear.

Figure 10 compares our results on the phase locking of auditory-nerve fibers to sinusoidal electric stimulation with both electric synchrony data from Hartmann and Klinke (1987, 1990), and acoustic synchrony data from our laboratory (Johnson, 1980). For all frequencies, the synchronization index is somewhat lower in our data than those of Hartmann and Klinke, although the variability is similar in both data sets. The Hartmann and Klinke data were obtained using round-window stimulation in cats acutely deafened by neomycin injection into the cochlea. Ours were from ears intact prior to insertion of the bipolar electrodes into the cochlea. In addition, Hartmann and Klinke used a different technique for artifact rejection based on running crosscorrelation (matched filtering). They did not obtain a measure of the effect of the stimulus artifact on synchrony. For both sets of electric synchrony data, the variability in the measurements is considerably greater than that for acoustic synchrony, an observation also made by Parkins (1989). In addition, the mean electric synchronization indices for both data sets are well above those for acoustic stimulation for frequencies above 3-4 kHz, with the difference increasing with frequency. At 1 and 2 kHz, however, our electric synchrony data are somewhat below acoustic synchrony. Parkins (1989) has also reported that acoustic synchrony is somewhat greater than electric synchrony for frequencies near 1-2 kHz in deafened squirrel monkeys.

The finding that acoustic synchrony falls faster with frequency than does electric synchrony is consistent with ideas of Weiss and Rose (1988) on the origin of the frequency dependence of synchrony. By comparing the responses of hair cells and auditory-nerve fibers in two species, Weiss and Rose concluded that the degradation in acoustic synchrony is due to a cascade of at least three lowpass filter processes. One process which might contribute to the degradation in synchrony for both acoustic and electric stimulation is random jitter.
in spike conduction times (Anderson, 1973; Verveen and Derksen, 1968). The fact that acoustic synchrony degrades faster with frequency than does electric synchrony suggests that spike jitter is not the major factor in the degradation of acoustic synchrony. Rather, the degradation in acoustic synchrony is probably due largely to low-pass filtering at the level of hair cells and synapses, which are bypassed in electric stimulation (Weiss and Rose, 1988). A further argument against jitter in spike conduction times being the major factor in synchrony degradation comes from fibers with a nonmonotonic frequency dependence of electric synchrony, because this would require frequency-dependent jitter. Interestingly, no such nonmonotonic frequency dependence has been demonstrated for acoustic stimulation (Johnson, 1980). Either the processes responsible for these nonmonotonicities are specific to electric stimulation, or their effects are masked in acoustic stimulation due to the severe degradation in timing that occurs at more peripheral stages of processing.

Mechanisms of electric stimulation

Intriguing findings of this study are the large interfiber variability in synchronization indices and the nonmonotonicities in the frequency dependence of electric synchrony. This variability was not obviously correlated with electric thresholds, slopes of the rate-level functions, and, in cats with acoustic sensitivity, with CF or spontaneous discharge rates. We cannot rule out that interfiber variability might be due in part to differential damage to the hair cells or the nerve fibers due to insertion of the stimulating electrodes into the cochlea. However, our results from one cat and those of Hartmann and Klinke (1987, 1990) show that comparable variability in synchronization indices is seen with round window stimulation, suggesting that damage caused by electrode insertion is not the major factor. Another possibility is that low-synchrony responses might be due to synaptically-mediated nerve responses resulting from electrical excitation of the hair cells. There is some evidence that synaptic transmission can be elicited by direct electric stimulation of fish electroreceptors, an organ for which synaptic transmission is thought to be similar to that in hair cells (Steinbach and Bennett, 1971). Further, Van den Honert and Stypulkowski (1984) have shown that certain auditory-nerve fibers respond to monophasic electric pulses with long latencies and large jitter. They have suggested that this "delta" response, which is distinct from the electrophonic effect, might result from direct depolarization of the hair-cell membrane. The delta response might be the basis of the low synchronization indices measured in some auditory-nerve fibers, although low-synchrony fibers are also found for animals in which hair cells were presumably destroyed by ototoxic drugs (Parkins, 1989; Hartmann and Klinke, 1990).

Another mechanism which might explain the variability in synchronization indices is interference between multiple sites of nerve excitation. Both experimental (Javel et al., 1987; Van den Honert and Stypulkowski, 1984, 1987b; Parkins, 1989) and modeling (Colombo and Parkins, 1987; Finley et al., 1990; Rubinstein, 1991) studies suggest that there exist multiple sites for spike initiation in electric stimulation of the auditory nerve, and that the site of excitation can depend on the stimulus waveform and the distance between the stimulated fiber and the stimulating electrode. Specifically, the two opposite phases of low-frequency sinusoidal currents can excite an auditory-nerve fiber at two distinct nodes of Ranvier (Van den Honert and Stypulkowski, 1987b; Parkins, 1989; Hartmann and Klinke, 1990). The situation is even more complicated at high frequencies because the spike conduction time between two adjacent nodes is a significant fraction of the stimulus cycle. For example, assuming an internodal distance of 140 μm (Liberman and Oliver, 1984), and a conduction velocity of 8 m/s, the internodal conduction time corresponds to a phase difference of 30° for a 5-kHz stimulus. Thus, if there were at least two sites of excitation separated by one or more internodal distances, the synchronization index might differ greatly depending on whether spikes initiated at different sites collide or alternate. These effects could vary greatly among fibers because there is considerable variability in internodal distances (Liberman and Oliver, 1984). Also, if the sites of excitation depend on the placement of the neuron in the electric field, we might expect to find some correlation between fiber CF and synchrony-frequency characteristics. Unfortunately, the small number of fibers for which we have both acoustic CF and synchrony data for several frequencies precludes the demonstration of such correlations.

The multiple site of excitation hypothesis is also consistent with nonmonotonicities in the frequency dependence of synchrony because interference between sites must depend on the exact relation between the stimulus period and the internodal conduction time. This hypothesis might also explain why electric synchrony is lower than acoustic synchrony for frequencies near 1–2 kHz. For acoustic stimulation, there may be a unique site of excitation near the synapse, so that interference between multiple sites would not occur. At higher frequencies, acoustic synchrony drops drastically, presumably because of factors peripheral to the site of spike initiation. This multiple site interference hypothesis could be tested by experiments of the type suggested by Parkins (1989) in which both the frequency of periodic stimuli and the waveform of each stimulus cycle are manipulated independently.
Central processing of fine time patterns of discharge

This study was largely motivated by the psychophysical observation that cochlear-implant recipients poorly discriminate the frequency of sinusoidal or pulse-train stimuli presented through a single electrode for frequencies above a few hundred Hz (Eddington et al., 1978; Tong et al., 1982; Shannon, 1983; Hochmair et al., 1983; Townsend et al., 1987). Such discriminations must be based on temporal cues because place cues are likely to be absent with single-electrode stimulation, particularly when care is taken to randomize stimulus levels. Our results clearly demonstrate that the discharges of single fibers in the cat's auditory nerve are phase-locked to sinusoidal electric stimuli up to the highest frequency that was tested (17 kHz in one case). Although the average synchronization index decreases gradually with frequency, there is no obvious break in the 300–1000 Hz range where psychophysical performance degrades rapidly. In comparing human psychophysical with animal physiological data, one must, as always, be cautious about species differences and the possible effects of anesthesia. A further difference is that our cats had normal hearing until insertion of the stimulating electrodes into the cochlea, whereas human cochlear-implant recipients have usually been deaf for many years prior to implantation, so that the patterns of nerve-fiber degeneration and the sites of discharge initiation may differ for the two conditions. Despite these differences, our results suggest that the poor performance of cochlear-implant patients in frequency discrimination is not due to a lack of temporal information in the discharge patterns of auditory-nerve fibers, but to the inability of the central nervous system to make use of the available timing information. Before drawing conclusions about the importance of fine temporal patterns of discharge in frequency discrimination, one needs to examine in detail what temporal cues could be used for frequency discrimination, and whether these cues are available in electrical stimulation for frequencies above 1 kHz. Such a discussion can be placed in the more general context of models for the central processing of auditory spectral information.

In recent years, a number of models have been proposed for the central representation of the stimulus spectrum on the basis of the discharge patterns of auditory-nerve fibers (Carlson et al., 1975; Delgutte, 1984, 1987; Deng and Geisler, 1987; Ghitza, 1988; Loeb et al., 1983; Meddis and Hewitt, 1991; Seneff, 1988; Shamma, 1985; Srulovicz and Goldstein, 1983; Young and Sachs, 1975). While most of these models were originally formulated for speech stimuli, they are also applicable to sinusoidal stimuli. These models can be organized into four classes. In one familiar class, the stimulus spectrum is represented by the pattern of short-time average discharge rates of auditory neurons as a function of their point of innervation along the cochlea (see Delgutte, 1987, for a formulation that would overcome the small dynamic range of auditory-fibers). These 'rate-place' models are consistent with the poor performance of implant recipients in frequency discrimination above 1 kHz because the required place cues are almost certainly lacking for single-channel stimulation. A second class of models (Loeb et al., 1983; Shamma, 1985; Deng and Geisler, 1987) is based on the coincidence of discharges of auditory-nerve fibers innervating different points along the cochlea. Because such coincidence depends critically on the precise dependence of the response phase on cochlear place (Pfeiffer and Kim, 1975), which must be severely disrupted in single-channel electric stimulation, these 'cross-place coincidence' models are also consistent with the poor frequency discrimination of implant recipients above 1 kHz. In a third class of models, the responses of auditory-nerve fibers tuned to a particular frequency are processed by a filter matched to the response pattern for that frequency (Young and Sachs, 1979; Srulovicz and Goldstein, 1983; Delgutte, 1984; Seneff, 1988). Our results suggest that, in stimulation with a sinusoidal electric stimulus of sufficient intensity, fibers innervating the cochlear place corresponding to the stimulus frequency will respond in a phase-locked manner. Although such phase locking would also occur for other cochlear places, it is the function of the matched filter to ignore these off-place components. Therefore, these 'matched filtering' schemes should remain effective for electrical stimulation, so long as there is a sufficient number of surviving fibers at the stimulus place, and the response patterns for electric stimuli do not differ as much from those for acoustic stimuli as to render the matched filter inoperative. Finally, a fourth class of models for spectral representation detects dominant periodicities in the discharge patterns of fibers innervating the entire cochlea (Carlson and Granstrom, 1975; Delgutte, 1984; Ghitza, 1988; Meddis and Hewitt, 1991). Because essentially all auditory-nerve fibers phase lock to the electric stimulus, these 'dominant periodicities' schemes should also remain effective in electrical stimulation as long as a sufficient complement of fibers is available.

To summarize, the contrast between the precise phase locking of auditory-nerve fibers to electric stimuli and the poor performance of implant recipients in frequency discrimination favors rate-place and cross-place coincidence models of central processing over matched filtering and dominant periodicities models for frequencies above 1 kHz. Clearly, some temporal model is needed to account for frequency discrimination of cochlear-implant patients for low frequencies. Moreover, virtually any temporal model for auditory spectral representation that integrates information across fibers innervating the same cochlear place requires phase coherence in the responses of these fibers.
While such phase coherence is known to exist with great precision in acoustic stimulation (Pfeiffer and Kim, 1975), such data are not available for electric stimulation. A degradation in cross-fiber phase coherence with increasing frequency might explain the poor performance of implant recipients in discriminating high-frequency stimuli.

In conclusion, it would be premature to conclude from the poor frequency discrimination of cochlear-implant recipients that there is no need for the speech processors of implant devices to encode fine temporal aspects of the sound waveform. While our results suggest that there are strong constraints on the type of temporal information that can be used by the brain, this does not mean that fine time patterns of discharge play no role in frequency discrimination, let alone speech reception which is a more complicated task. In fact, Wilson et al. (1990, 1991) have shown that increasing the pulse rate above 1 kHz in a speech processor which presents brief pulses in a non-overlapping sequence to each electrode in an implanted array improves speech reception. This result from continuous interleaved sampling speech processors suggests that fine temporal patterns of discharge might be important in certain situations. Physiological knowledge of the temporal characteristics of the neural response for stimuli produced by interleaved sampling speech processors is needed to elucidate which temporal mechanisms might be responsible for these improvements in speech reception.

Acknowledgements

We thank D.K. Eddington and N.Y.S. Kiang for their valuable advice and comments at many stages of this work, and R.D. Hall and J.T. Rubinstein for helpful comments on the manuscript. We also thank M.F. Bourgeois, D.A. Lecarson, L.W. Dodds, S. Pierce and P. Riley for surgical assistance. This research was supported by NIH grant DC00361.

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