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BIOPHYSICAL CONSIDERATIONS IN ELECTRICAL STIMULATION OF THE AUDITORY NERVOUS SYSTEM[a]

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A considerable body of both theoretical and experimental data exists regarding the electrical activation of nervous tissue. Over the past decade, the increasing use of this technique as both a quantitative research tool and a prosthetic approach to restoration of function has spurred attempts to develop general descriptions of the relevant physical processes so that models and experimental results pertaining to widely different circumstances could be compared. The emerging picture has generally been that of an orderly, well-behaved system in good agreement with the properties of the Hodgkin–Huxley model of the excitable nerve membrane.[1] However, a rather large number of variables must be accurately specified to obtain useful predictions from such models, and the relevant data are frequently either unavailable or impractical to obtain for the complicated circumstances pertaining to many clinical devices. Therefore, it is important to develop an efficient set of empirical descriptors of each system which can be used to relate clinical and animal experiments to each other and to the operating curves of such models.

It is not our purpose to present a detailed model of the electrical activation of the auditory nerve. Too little is known about the electrical and physical properties of this system and too many technical variations of prosthetic electrodes and waveforms have been employed for this to be either feasible or useful (see the review by Eddington[2]). Rather, we here point out at least the general effects of the relevant factors and suggest some simplifying assumptions and insights that appear to account for most clinical results and that might guide future development. There appears to be a general consensus that the scala tympani affords the best-distributed access to the auditory nerve. Therefore, we have limited the ranges of many variables to those found in this setting to try to draw as many hard conclusions as possible, at the expense of generalizability to other situations.

There are four general considerations in the electrical activation of neural tissue. First, the electrically excitable target elements must be defined and

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their physical dimensions and structural details described sufficiently to make reasonable guesses about their electrical cable properties.[1] Second, the stimulating electrical waveforms and physical arrangement of the electrodes must be specified so that the resultant electrical fields may be calculated. Third, special circumstances in the transmission medium, usually assumed to be a homogeneous volume conductor, must be noted and their effects on the fields experienced by the target elements estimated. Finally, and this is potentially quite important in an auditory prosthesis, the investigator must consider secondary factors such as the response of higher-order neurons to the fine spatiotemporal details of the resultant first-order recruitment.

The Target

From the time that electrical stimulation was first employed in neurophysiology, it was noted that there were systematic differences in the responsiveness of neural elements, depending on their size, shape, and composition.

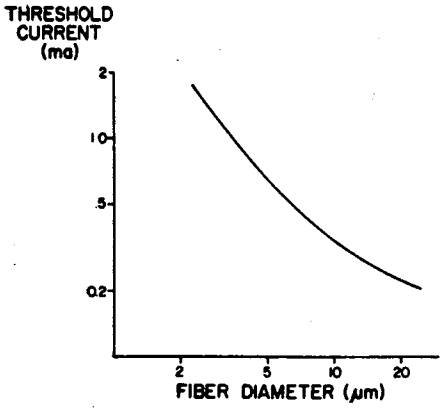

FIGURE 1. Theoretical relationship between the threshold current of a 100-μsec duration monopolar cathodal pulse delivered 1 mm above a node of Ranvier and the diameter of the myelinated nerve fiber. (From McNeal[4] [based on the Frankenhaeuser and Huxley[1] model of the electrical cable properties of such fibers]. Reprinted by permission.)

From such experiments, two properties emerged that continue to be used to categorize their sensitivity: threshold and chronaxie.[3] To a first approximation, threshold can be related both theoretically and empirically to the physical dimensions of the target structure, and chronaxie (defined later) to the electrical properties of its membranes.

Threshold

All other things being equal, large-diameter fibers have a lower action-potential *threshold* than do small diameter fibers, and large-diameter cell bodies have lower thresholds than small ones, for extracellularly applied electrical currents. For nerve fibers, a fairly good theoretical understanding of the size effect is possible and is in good agreement with empirical results.[4] The relationship for myelinated fibers is shown in FIGURE 1. The fiber diameter of the human auditory nerve myelinated fibers falls generally in the midportion of this curve (3–10 μm),[5] where the threshold current is nearly a linear

inverse of the fiber diameter. Unmyelinated fibers have very high thresholds, and any unmyelinated portion of the spiral ganglion cell's apical dendrite that might survive in a deaf cochlea is unlikely to be the site of spike initiation, even if it lies closer to the stimulating electrode than do the other parts of the cell. Similarly, the small-diameter myelinated and unmyelinated fibers present in the nerve probably do not contribute to the percepts of auditory prosthesis patients unless they are being stimulated at levels far above the large-fiber threshold, and thus far above perceptual threshold. However, if there has been a selective and nearly complete loss of the large-diameter fibers, the psychophysical threshold may be sufficiently elevated that modest increments in stimulation current over this will, in fact, recruit small fibers whose normal perceptual roles are not understood.

The effect of the cell body is very much harder to model accurately. The depolarization of a neuron to the point of threshold requires a fairly extended spatial distribution of current flow through elongated processes attached to the cell body; a spherical cell body without processes is virtually inexcitable extracellularly.[6] The fact that the spiral ganglion cell is a moderately sized and spindle-shaped (20×30 μm) bipolar cell with its own myelin sheath suggests that its presence does little to alter the electrical excitability of the overall structure.

Chronaxie

Chronaxie is the classical measure of the responsiveness of the target neuron to temporal as opposed to spatial features of the electrical stimulation field. Operationally, it is determined by the threshold duration of a monopolar, monophasic electrical stimulation pulse whose current amplitude is twice that of the minimum activating current needed by an infinite duration pulse.[3] The standard linear plot of threshold current strength (y-axis) versus stimulus duration (x-axis) for single monophasic square pulses has a hyperbolic shape from which a horizontal asymptote is readily estimated (FIG. 2). Only a few points on the curve are needed to obtain a fairly reliable interpolation of the pulse duration at twice this level. This time relates both theoretically and empirically to the time constant of the target cell membrane, which is the product of the membrane capacitance and resistance per unit area. Conceptually, it can be appreciated as the degree to which the capacitance in the cell membrane slows its ability to follow a quickly changing applied extracellular field.

The chronaxies of myelinated nerve fibers are generally independent of their diameter. Most measurements cluster around 100 μsec, with a range of 20 to 200 μsec, in agreement with models of such fibers. This probably relates to the relatively low membrane capacitance imparted by the myelin sheath, and is in reasonable agreement with estimates of the membrane time constant made from intracellular recordings (time constant should be about 1.4 times chronaxie). The chronaxie of unmyelinated nerve fibers and cell bodies is generally much larger, on the order of 500–6000 μsec. This is probably related to the much larger amount of exposed, high-capacitance membrane. However, the effect of cell bodies is impossible to separate from their attached processes, which may be myelinated (output axons) or un-

myelinated, but made of membranes whose electrical properties are not directly measurable (dendrites). In such complex geometries, the chronaxie actually observed depends complexly on the orientation of the target neuron to the stimulating electric field and the actual site of spike initiation (see Ranck [6] for a review of preceding points).

In the case of the auditory nerve, the presence of myelin over all three structures—apical dendrite, soma, and output axon—suggests that the chronaxies should be relatively short.[7] In preparing this discussion, we discovered that no estimate of chronaxie using the classical paradigm seems to have been made for auditory nerve fibers activated via intracochlear electrodes. This is presumably because of the recent emphasis on biphasic waveforms for safety, bipolar electrodes for selectivity, and continuous frequency trains for psychophysical relevance. We, therefore, undertook a simple experiment to relate the classical measurement to the more commonly used waveforms.

A pair of closely spaced microelectrodes was passed dorsoventrally and caudorostrally along the parasagittal plane through the cochlear nucleus of an anesthetized cat. Acoustic stimuli were used to map the structure, identifying the responses typical of the dorsal and ventral cochlear nuclei and, in particular, the low-frequency, large spherical cell region lying deep in the anteroventral cochlear nucleus (see FIGURE 4 and related text in the section THE EFFECTS). The latter cells have been described as "primary-like" in that they appear to follow one-for-one the action potentials of their input auditory nerve fibers.[8] The round window of the ipsilateral cochlea was then exposed, opened,

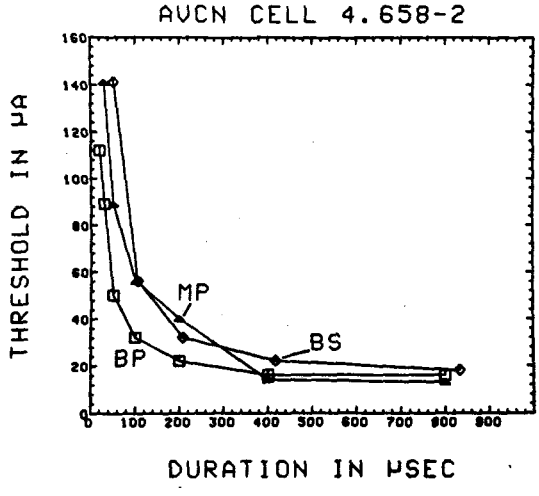

FIGURE 2. Classical strength/duration curve for a presumed "primary-like" large spherical cell recorded in the anteroventral cochlear nucleus of an acutely neomycin-deafened cat. Curve MP indicates monopolar, monophasic cathodal stimulation (single pulses at 8 pps) from a scala tympani electrode; BP indicates bipolar, monophasic cathodal stimulation from the electrode used for MP referenced to another similar contact located 0.7 mm more basal along the basilar membrane; BS indicates bipolar, biphasic stimulation using a continuous sinusoidal waveform whose half-cycle duration is plotted on the x-axis.

TABLE 1

RESPONSE PROPERTIES OF AVCN CELLS TO INTRACOCHLEAR ELECTRICAL STIMULATION

Cell No.	Depth in Track (μm)	Threshold—100 μsec Cathodal (μA)	Chronaxie—Cathodal (μsec)
1	4155	100	380
2	4175	112	650
3	4313	89	200
4	4658	56	310
5	4122	126	850

and 0.1 cc of 5% neomycin infused over a 20-min period, without losing the stereotaxic orientation of the skull. This treatment has been shown to lead to an immediate destruction of the mechanosensitivity of the hair cells, leaving the spiral ganglion cells and their apical dendrites at least temporarily intact and excitable.[9] An appropriately scaled-down version of the human scala tympani electrode array was then introduced through the round window opening so that its four longitudinally spaced electrodes were positioned about halfway around the first turn and lying up against the organ of Corti. The microelectrode pair was reintroduced along approximately the same track originally mapped, and single units encountered at various depths were characterized by their responsiveness to various locations, orientations, and waveforms of electrical stimulation in the scala tympani. Lesions were made at the ends of the tracks to verify histologically the location of the recorded units.

Chronaxie was estimated for five cells which were located in the large spherical cell region of the anteroventral cochlear nucleus. They were distributed over a range of 200 to 850 μsec (mean 478 μsec) (TABLE 1). Theshold currents varied by a factor of two, presumably as a result of different distances between the origination point of each cell's input from the basilar membrane and the distance to the nearest available stimulation electrode. However, it is not clear from this small sample size whether the large range of chronaxies may represent some heterogeneously distributed property of the spiral ganglion cells, possibly correlated with their thresholds.

One cell (FIG. 2) was tested for the effects of pulse duration with both monopolar (MP) and longitudinal bipolar (BP; 0.7-mm separation) cathodal pulses (AC coupled to minimize damage but with a time constant of 100 msec to approximate the classical monophasic condition). Monopolar chronaxie of 310 μsec was reduced to about 100 μsec bipolar. This same cell was also tested with continuous sinusoids (BS; same bipolar pair) in which the pulse duration was taken to be the duration of each half-cycle. "Chronaxie" estimated in this manner was 200 μsec. This cell had the lowest threshold of any tested, suggesting that its input came from a region of the basilar membrane closest to a stimulating electrode, and thus most likely to represent the threshold phenomena reported psychophysically by patients [10] or found behaviorally in monkeys.[11]

Monopolarly measured classical chronaxies thus appear to be distinctly longer for these cells than for other myelinated axons, where theory and intra-

and extracellular measurements all converge around 50–150 μsec. The values reported here are typical of those of grey-matter chronaxies, which have been presumed to result from the complex product of unmyelinated soma/dendrite components and myelinated axons. However, the architecture of the heavily myelinated spiral ganglion cells is clearly not like that of most CNS nuclei. If unmyelinated membrane capacitance is not a factor, then it seems likely that the increased time constant of the cells implicit in this measurement comes from higher than usual resistivity, perhaps from an unusually thick or resistive myelination or smaller nodes of Ranvier. This may have implications for the interaction of multiple stimuli that are close to each other in time and space, since the residual intracellular effects of one subliminal stimulus may persist considerably beyond its actual current duration. Attempts to estimate these neuronal time constants using bipolar and/or biphasic stimuli appear to underestimate them by a considerable factor.

Efficiency

One reason for measuring strength/duration relationships is that it provides useful information regarding the optimal design of stimulation equipment. The critical variable in the damage of tissue and electrodes by electrolytic reactions is the charge density per phase, expressed in microcoulombs per real square centimeter of exposed metal ("real" refers to accessible surface area including roughening effects). The actual limit depends complexly on the composition of the metal, its electrical history, and the composition of the electrolyte, particularly including trace additives of proteins and amino acids.[12, 13] For platinum alloy electrodes, the safe limit below which electrolytic reactions are entirely avoided is likely to be around several hundred $\mu C/cm^2$. Translated to cochlear electrode dimensions, this is several $\mu C/mm^2$. A disk electrode 0.3 mm in diameter has about 0.1 mm^2 area (using geometric rather than real area for simplicity), so the maximum charge per pulse should be kept to considerably less than 1 μC, or 1 mA × 1 msec. For single-pulse stimuli, the product of the threshold current amplitude and the pulse duration can be used as a measure of the stimulus efficiency. In this experiment, it is interesting to note that this threshold charge is slowly but steadily decreasing for progressively narrower pulses, even those requiring very high current levels (FIG. 3). For pulses longer than chronaxie, efficiency becomes rapidly poorer. Of course, it may be impractical to build stimulation circuits capable of the high driving voltages and fast slewing rates that are needed for very short pulses.

It should be noted that this fast-pulse efficacy does not hold for continuous waveforms, such as the bipolar sinusoid, whose effects are plotted in FIGURE 3 (curve BS frequency scale is plotted at x-axis positions where pulse duration and half-cycle time are approximately equal). This probably pertains also to symmetrical biphasic pulses, since the efficiency reversal probably occurs at the point at which the electrical response of the voltage-dependent gates in the neuron membrane cannot keep up with rapidly reversing fields. This effect is distinct from and in addition to the time constants inherent in the axon membranes, which affect monophasic and biphasic pulses equally. Stimulation at frequencies in excess of about 5 kHz occurs primarily by successive

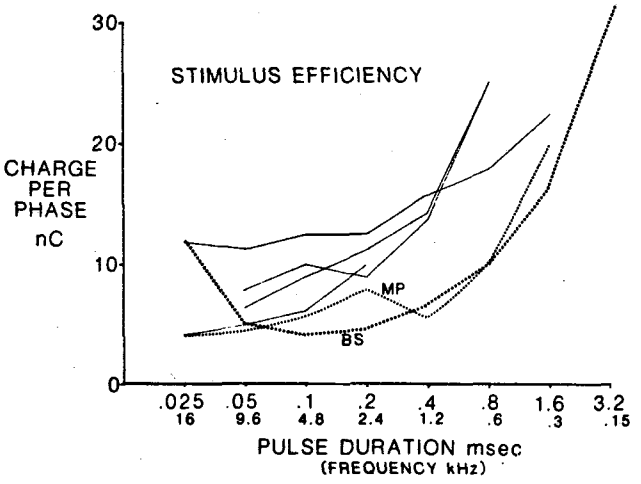

FIGURE 3. The charge per phase (area of the waveform) is plotted for intracochlear activation of five different AVCN cells at threshold amplitude for various pulse durations. Curves marked MP and BS are from same cell as in FIGURE 2; the frequency of the sinusoidal stimulus for curve BS is plotted at the single pulse duration corresponding closest to a half-cycle duration. The four unmarked fine lines represent four other cells activated by monopolar, monophasic cathodal pulses delivered through the scala tympani electrode with the lowest threshold for the unit (which was the apical-most electrode for all five units shown here).

summation of only partially rectified membrane currents from each successive stimulus cycle, resulting in progressive loss of efficiency. The actual current level required to reach threshold for the 16-kHz point shown in curve BS of FIGURE 3 was 560μA, far off the scale of FIG. 2, despite the more similar chronaxies of these curves.

THE STIMULI

The sequence of events by which an applied electrical signal gives rise to a conducted action potential involves a series of electrical processes, some of which are best characterized by their voltages and others by their current, but all of which are related by Ohm's law:

If a voltage is applied between two electrodes (one of which may be a remotely located common or reference electrode), a current will flow whose amplitude depends inversely on the vector sum of three impedances: the resistance of the saline solution between the two electrodes and the impedance of the metal/electrolyte interface of each electrode. At the frequencies and dimensions of cochlear prostheses, the latter two are by far the larger and dominant factor. Once there is current flow through the medium, it gives rise to changes in the relative potentials at various locations in the extracellular fluids. The distribution of such potentials can be determined from a knowledge of the possibly heterogeneous impedances of the medium (discussed later). This, in turn, gives rise to fluxes of current into and out of nerve membranes

which span these voltage gradients. This process depends on the orientation of these membranes with respect to the fields and their intrinsic time constants, as discussed earlier. Finally, these transmembrane currents produce changes in the normal resting potential which the cells maintain between the inside and the outside. When any local area of membrane becomes depolarized by about 20 mV from its usual resting potential of about 80 mV (inside negative), this initiates a series of rapid changes in the conductance of that patch of the membrane to sodium and potassium ions. This gives rise to the neural action currents which propagate the local depolarization rapidly throughout the neuron as an action potential.

Waveform

In the final analysis, the variable that gives the investigator the best control over the situation is the waveform of the current that flows through the electrodes. Normally, this is controlled by a constant-current stimulator. However, several circumstances may cause the stimulus generation apparatus to have control of voltage only. Telemetry devices relying on simple inductive coupling of an amplitude-modulated carrier provide essentially only voltage control of their outputs. More sophisticated metering of current or charge requires much more sophisticated circuitry.[14] If several sets of electrodes are connected in parallel, even a current-regulated circuit cannot guarantee any particular distribution of current through any particular electrode. If the impedance of each electrode were constant and known, then the current distribution could be calculated from Ohm's law. However, metal/electrolyte interfaces are complex impedances whose resistive and capacitive terms are nonlinear, time-dependent functions of frequency, current density, polarization voltage, and total charge flow. The most obvious nonlinearity occurs when the voltage drop across the junction passes the 1–2 VDC required to drive the electrolysis reactions of water. In a typical intracochlear electrode with a nominal impedance of 10 kilohms at 1 kHz, this potential would be reached (assuming linear behavior) with 100 μA of current, right in the middle of the operating range of most such devices. Thus, whenever possible, current should be controlled or at least monitored.

For continuous waveforms such as sinusoids, the stimulus is obviously biphasic. However, when pulses are employed, the question arises as to whether a monophasic pulse of anodal current (electrode-positive) or cathodal current (electrode-negative) should be used, or whether the stimulus will be a biphasic pulse, in which case there arises the question of which phase will be first and whether they will be symmetrical in shape. It is now generally recognized that the stimulation should cause equal and opposite amounts of charge to flow in each phase of the biphasic waveform so that no net DC current results.[15] This minimizes the various electrolytic reactions of both the medium (saline solution) and the electrodes (usually oxidizable metals), which otherwise give rise to products that are highly damaging to both the tissue and the electrodes themselves. It seems reasonable that initially cathodal pulses will have somewhat lower thresholds since this current tends to depolarize the portions of the cell membrane that are closest to the electrode, where the current density is highest. However, the effect depends complexly on the target geometry, the distances involved, the position of the other

electrode of a bipolar pair, and the pulse durations and their symmetry. In the human cochlea, the activation threshold is unlikely to be more than a factor of two higher for anode-first pulse pairs, although there may be considerable differences in the fine details of the spatial and temporal distribution of fibers actually producing action potentials. In our study in cats of monopolar, monophasic 100 μsec pulses, anodal thresholds averaged twice cathodal thresholds, probably a worst-case situation.

Geometry

The most significant variable in the *selective* activation of subpopulations of neurons, such as desired for multichannel prostheses, is the physical arrangement of the stimulating electrodes with respect to the target fibers. The current density in a volume-conducting medium is highest at the surface of the current sources and sinks (electrodes), and drops off rapidly in the intervening fluid. For monopolar electrodes (large remote reference sink), threshold current has been found to vary almost linearly with distance over the range of 100 to 1000 μm.[6] Depending on fiber or cell diameter, the threshold current for a 200-μsec duration cathodal pulse tends to be 5–20 μA at 100-μm distance; and 50–200 μA at 1000-μm distance. This is in general agreement with both the thresholds and the limited dynamic ranges reported for intracochlear monopolar electrodes.[10] Once the current density in the modiolus reaches threshold, virtually all remaining auditory nerve fibers will be activated, regardless of their distance from the electrode.[16] The best selectivity and largest dynamic range will be achieved when the electrode is closest to the target subpopulation, since this maximizes the relative distance to the remainder of the population. The loss of apical dendrites has a pronounced effect on the excitability of spiral ganglion cells, primarily because it removes their closest excitable membrane from the immediate vicinity of a scala tympani electrode.[17] This will affect selectivity as well as threshold, no matter what design of intracochlear electrode is chosen.

The use of bipolar electrodes is often advocated to improve the selectivity by confining the spread of current to a limited volume of fluid "between the two electrodes." Of course, current flow in a volume conductor is not like sparks across an air gap. The degree to which current flow can be controlled depends on the actual spacing between the electrodes; the degree to which an advantage is so obtained depends on the relative spacing to the target subpopulation. If the electrodes are too far apart, they act simply as two local monopolar electrodes which happen to be out of phase. If the targets are too far away, the high-current density gradient in the immediate vicinity of the pair is of no use, as the neurons are actually being activated by the much more homogeneous current densities obtaining at that distance.

The electrical field gradients surrounding monopole and dipole antennas are mathematically well defined and well understood by radio engineers. The field strength around a monopole varies inversely with distance ($1/r$) and around a dipole with distance squared ($1/r^2$). While the situation is more complex in biological preparations, some useful general rules arise. To a first approximation, the optimal spacing between the bipolar elements should be of the same order as the distance to the presumed target elements. In this range, the function of threshold versus distance approaches distance

squared, significantly improving selectivity over the linear function for monopolar stimulus spread. Since the object of electrical stimulation is to generate longitudinal gradients along elongated neural elements, the orientation should be parallel to the fibers, further enhancing the selectivity.[17] Again, the closer the target, the better the selectivity.

Occasionally it is stated that electrode surface areas must be kept small to improve selectivity or reduce shunting in bipolar pairs. The former consideration applies only when the effective diameter of the exposed electrode disc begins to approach the distance between the electrode and the target, since the current from the perimeter areas then has less selective effect on the targets closest to the center. The latter consideration applies only when the resistance of the intervening saline medium in a bipolar pair is equal to or greater than the metal/electrolyte contact impedance; otherwise current density is uniform over the surface of each contact so that their shape has no effect on shunting. For the frequencies and surface geometries available to cochlear prostheses, this condition simply never arises, and the current is always distributed almost uniformly rather than selectively concentrated at adjacent edges. Bipolar electrode contacts should therefore be as large as the distance between them permits, stopping only when danger of physical shorting arises. This decreases their impedance, which lowers the necessary driving voltages, linearizes their behavior, reduces the danger of elctrolytic reactions, and reduces the shunting effects of any small electrical leaks along leads and connectors.[18]

The Medium

The bony spiral lamina and soft tissue membranes of the cochlea can be expected to cause electrical currents to flow differently than they would in perilymph alone, which is electrically similar to normal saline solution, that is, a homogeneous, isotropic volume conductor with a specific resistivity of 65 ohm-cm. On the other hand, these boundaries are electrically unlike simple plastic tubes. While the different conductivities of membranes, scar tissue, axon bundles, and bone have been much studied in isolation, the most salient point to keep in mind is that they are all only moderately less conductive than saline solution, a fairly poor conductor. Even bone requires for its metabolic sustenance an intricate system of blood vessels and cytoplasmic channels which are fluid-filled and contribute to its conductivity. Probably no element present in either the normal or the pathologic cochlea has a conductivity more than an order of magnitude poorer than that of saline solution or perilymph, and probably all are isotropic within a factor of two.[19] In particular, scar tissue is likely to have no more than two or three times the resistivity of perilymph, which is consistent with the relatively unchanged electrode impedances, psychophysical thresholds, and percepts obtained during the first few weeks of implant function when such encapsulation is developing (unpublished results from two most recent patients implanted at UCSF with 16-contact electrode arrays fabricated in the Coleman Laboratory). Larger fluctuations in electrode impedances measured at low current densities have been noted both *in vitro* and *in vivo*. These have been ascribed to contamination of metal surfaces by silicone oil, oxide build-up, and other debris which are removed by current flow at normal levels of use.[20]

In volume-conducting situations, such inhomogeneities have surprisingly little effect on the distribution of current density, particularly when compared with the large, predictable effects of physical distance from a bipolar electrode. Several attempts have been made to measure the actual distribution of fields inside the cochlea during intracochlear stimulation by using the inactive electrodes either as probes or distributed common electrodes.[21, 22] So far this has not been particularly useful, stemming from limitations of technique and interpretability. In fact, the best detector of current distribution in the cochlea still appears to be the array of nerve fibers themselves, whose output may be inferred, albeit indirectly, by carefully designed psychophysical studies. This is particularly the case in elucidating complex interactions such as those between adjacent electrodes.

The Effects

The spatiotemporal patterns of activity resulting from electrical activation of any ensemble of nerve fibers will be quite unlike their normal physiological activation patterns. In some systems, the effect of stimulation is more or less in proportion to the total amount of activity elicited without regard to such details. In the auditory nervous system, there is reason to believe that the central processor is exquisitely sensitive to the details, perhaps even to the active exclusion of "noise-like" patterns lacking spatial or temporal detail.

We have already addressed the limitations in spatial selectivity encountered by various electrode configurations. The enhanced detection of spatial gradients and a concomitant insensitivity to poorly differentiated activity levels is a common second-order property in neural perceptual systems. It is usually accomplished by sets of concentrically arranged inhibitory fields surrounding the excitatory field of a given second-order neuron. Such inhibitory action has been noted in the dorsal cochlear nucleus,[23] and might be expected to limit the sensitivity of these neurons to poorly localized electrical stimulation of the first-order neurons.

AVCN versus DCN

Figure 4 shows the distribution of thresholds to electrical stimulation as a function of the depth in the cochlear nuclei at which each unit was encountered in our experiment. This is superimposed on the frequency mapping of this depth axis by the acoustically tuned penetration made prior to acute neomycin treatment. The tracks pass through two tonotopically organized structures which presumably correspond to first the dorsal (DCN) and then anteroventral (AVCN) cochlear nuclei. A poorly responsive region presumably devoid of large cells was noted in the second area (broken hatched line), and was followed by large, sharply tuned, strictly excitatory responses typical of the large spherical cells of the AVCN. The estimated location of the four stimulating electrodes (based on insertion depth) is shown translated into best frequency position (right side ordinate) on the basilar membrane, with A for apical-most and B for basal-most contact. The capital letters refer to the thresholds for evoking single unit action potentials with a latency of 0.9–1.4 msec for a 100-μsec duration monopolar, monophasic search stimulus

at the electrode that gave the lowest threshold. The lowercase letters indicate responses at latencies of 1.5–4.0 msec, which were possibly polysynaptic. Capital letters in parentheses refer to thresholds for evoking short-latency field potentials which were clearly not unitary and presumed to be from terminal arborizations of primary afferents. It is noteworthy that DCN units required stimulation currents an order of magnitude greater than AVCN units, even though this region appeared to be receiving low-threshold afferent input and was equally sensitive to acoustic stimuli. This suggests that the normal inhibitory mechanisms of the DCN may virtually eliminate it from contributing to the perceptual effects of intracochlear prostheses, which would then have to be conveyed to higher centers via the AVCN relay.

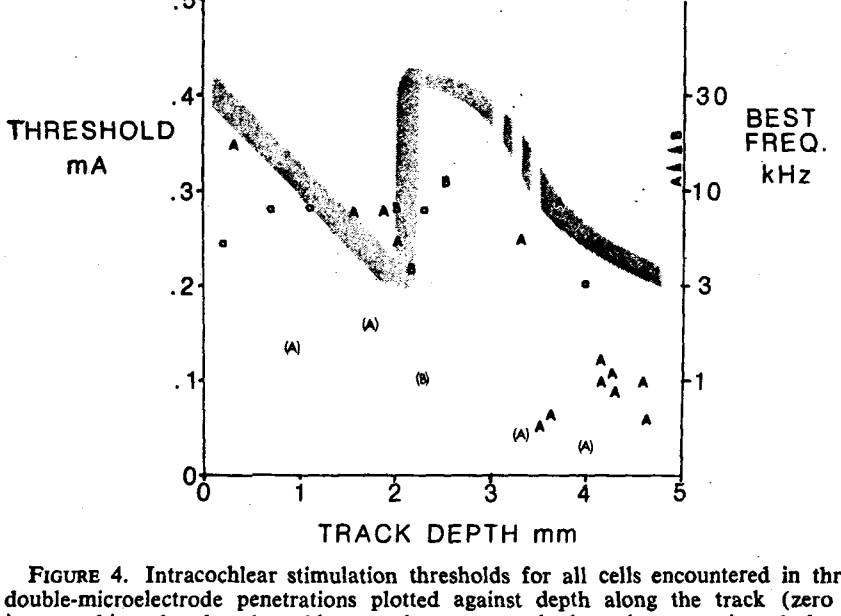

FIGURE 4. Intracochlear stimulation thresholds for all cells encountered in three double-microelectrode penetrations plotted against depth along the track (zero is just touching the dorsal cochlear nucleus; parasagittal tracks are oriented dorsocaudal to ventrorostral at approximately 30° from horizontal stereotaxic coordinates). The *shaded line* indicates the acoustical tuning curves (right ordinate) of cells encountered in a prior penetration along the same axis before acute neomycin deafening. See text for explanation of symbols.

Phase-Locking

Temporal effects are particularly interesting since the normal mechanisms for the interpretation of speech sounds almost certainly rely at least partly on the unique "phase-locking" of afferent activity to stimulus frequencies far above the physiological limit of one-to-one frequency following.[24] We have recently demonstrated that electrical stimuli cause a very similar, perhaps even enhanced, phase-locking effect over the relevant sinusoidal frequencies up to at least 3.2 kHz.[25] This leads to a paradox in the apparent insensitivity

of prosthesis patients to frequency modulation beyond about 300 Hz, which is the subject of a theoretical treatment published elsewhere.[26] Despite the lack of a clear psychophysical pitch correlate of periodicity, such temporal effects may well be responsible for the rather complex sounds that auditory prosthesis patients describe even for the best localized stimuli that can be delivered. Temporal effects probably also relate to the empirical observation that pulse amplitude and duration cannot be traded arbitrarily to achieve similar quality percepts at threshold or at any constant loudness level. Even when equal numbers of neurons are activated, there will be considerably more temporal dispersion in the firing resulting from a long, low-amplitude pulse than from a short, high-level pulse. When complex waveforms such as the polyharmonic spectra of speech are applied directly to multiple intracochlear electrodes, the psychophysical effects are far beyond prediction by even the most sophisticated theories. Thus, it is likely that the continued development of auditory prostheses and speech processors for the encoding of electrical stimuli will have to proceed largely on empirical grounds, with electrophysiological theory able to provide general guidance on electrode design and placement and, perhaps, some *post hoc* rationalization of the results.

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