

behavioral data, we elected to employ on the neural level the same test procedures used in human psychophysics. That is, we isolated responses of single auditory nerve fibers, presented single trials of tones in a two-alternative forced-choice (2AFC) paradigm and used transformed up-down decision rules to make fibers track preselected performance levels. Performing the experiments this way allowed us to construct psychometric functions and analyze the data using criterion-free approaches similar to those developed in signal detection theory.

For rate coding of frequency, the decision process was based on the numbers of spikes elicited by the two trials. For example, for frequency DLs obtained at CF the algorithm merely selected the trial that elicited more spikes. Our data (Javel et al., 1988) indicate that frequency DLs determined this way depend only on fiber tuning properties, and that the size of the DL is accurately estimated by examinations of response areas. Also, slopes of psychometric functions obtained from single fibers in cats were considerably shallower than those obtained behaviorally in humans but were relatively close those reported by Costalupes (1988) for cats.

For temporal-based analyses, the decision process, which was implemented in software, utilized phase-locked ISIs elicited by the two tones. The algorithm assumed that the fiber "knew" the frequency at which discrimination performance was being examined. ISIs were assigned to appropriate modal values of ISI histograms, and a running sum of deviations between expected and obtained ISIs was computed for each tone presentation. As an answer the algorithm selected the tone with the higher average frequency, defined as the reciprocal of the sum of the deviations and the test frequency. This response, of course, is either correct or incorrect. If incorrect, the frequencies of the tones were stepped apart, and if correct the frequencies were either unchanged or stepped closer together, depending upon the performance level being converged upon. We found that adaptive frequency discrimination tracks were quite stable and reliable, and that temporal-based DLs at frequencies < 1000 Hz ranged between 2 and 5 Hz (Javel et al., 1988; Javel, 1989a). Thus, the absolute performance of single fibers closely matched behavioral performance. However, above 1 kHz fiber performance deteriorated rapidly, and reliable DLs could not be obtained above 2 kHz. This is due in part to the decline in phase-locking with frequency. The decline in performance, however, is more rapid than that predicted by Goldstein and Srulovicz's (1977) temporal model.

An analytically powerful feature of single-cell experiments is the ability to investigate independently the contributions of various response parameters to the decision process. For example, we could examine temporal integration effects (Goldstein and Srulovicz, 1977) by limiting the length of the longest ISI allowed to enter the decision process. In concurrence with predictions of temporal models, we found that the magnitude of the frequency DL increases as the length of the longest allowable ISI increases.

We also developed what we believe to be an accurate excitation pattern model that predicts auditory nerve fiber responses on a cell-by-cell basis, and we applied it to the question of rate-place analyses of frequency discrimination performance (Javel, 1989b). We found that population-based responses generate psychometric functions that approximate the cat behavioral data relatively well. Also, population measures accounted nicely for the size of the frequency DL at low (< 2 kHz) frequencies, but they overestimated frequency DLs at higher frequencies. Based on the good fit to behavioral data provided by rate-based single-cell and population responses, we concluded that temporal-based theories of frequency discriminability are not needed to account for behavioral performance.

Use of Models to Integrate Behavioral and Single-Cell Electrophysiological Data. The following example illustrates how models may be used to guide neurophysiological and behavioral experiments. It also illustrates how models may be compared. In this example, we used the neural and behavioral models illustrated in figure 1 to predict: (1) behavioral dynamic ranges, and (2) temporal integration functions at threshold and uncomfortable loudness (UCL). In these simulations we tested both monopolar and bipolar electrode geometries to determine their effect on dynamic range and temporal integration.

The Model. The right portion of figure 1 contains a simple spike counting behavioral threshold model. Neural activity is summed equally across all fibers over a 100 ms time interval. We assume that behavioral threshold is reached when the stimulus elicits a pre-defined number of discharges, denoted by N_{thr} . Likewise, we assume that uncomfortable loudness has been reached when the stimulus elicits a larger number of discharges, denoted by N_{ucl} . For this set of simulations, we set $N_{thr} = 3$ and $N_{ucl} = 1500$. Other simulations, using quite different values of N_{thr} and N_{ucl} , resulted in very similar types of model behavior.

The left part of figure 1 contains a simple cochlear neural model. An electrode, located 15 mm into a cochlea of length 30 mm, delivers stimulus current, I_{stim} . The current is attenuated by pairs of resistors before it enters each fiber. Guided by Merzenich and White's (1977) data, we estimated that attenuation increased with distance from the electrode at a rate of 0.5 dB/mm for a monopolar electrode (see figure 2B) and at a rate of 4 dB/mm for a bipolar electrode (figure 3B). The attenuated stimulus then drives the input of a fiber model. For simplicity, all fibers in this set of simulations are identical and behave in a simple manner. Using rate-intensity functions from Javel's data for 200pps pulse trains (e.g., figure 6 in project 3), we approximated the fiber input-output function using 3 straight-line segments. Figures 2a and 3a contain identical plots of this fiber input-output function. From Hinojosa and Marion's (1983) data we estimated the number of excitable fibers (N_{fibers}) at 10,000.

Simulation Results. Simulation results are illustrated in figure 2 for the monopolar electrode and in figure 3 for the bipolar electrode. Figures 2C and 3C represent the total spike rate in the whole cochlea, plotted as a function of stimulus intensity. Figures 2E and 3E are identical to 2C and 3C except that the vertical axis is scaled logarithmically. Figures 2D and 3D indicate how behavioral threshold and UCL vary with stimulus duration, and figures 2F and 3F contains the same behavioral threshold function, but with an expanded vertical scale.

Dynamic Ranges. At all stimulus durations, dynamic range for bipolar stimulation (i.e., UCL minus threshold) is at least 3 times larger than that for monopolar stimulation. In contrast, dynamic ranges in humans are minimally dependent on electrode configuration (see figures 4 & 5). Equally disturbing, the model's dynamic ranges are extremely small compared to those observed in humans. No remotely reasonable modifications of model parameters can correct these inadequacies.

Threshold Temporal Integration Functions. We used the model to determine threshold as stimulus duration increases. These temporal integration functions were obtained by determining the intensity at which N_{thr} spikes occurred and plotting that value as a function signal duration. In contrast to the data from humans illustrated in figures 8 (monopolar) and 9 (bipolar), the slopes of the model's threshold temporal integration functions depend strongly on the type of electrode used. Furthermore, the slopes of the model temporal integration functions are very shallow compared to the human data.

A Modified Model We determined that a small modification in the fiber input-output function can dramatically improve the correspondence between model predictions and the human psychophysical data in every response category. In a duplicate set of simulations, illustrated in figures 6 and 7, we used an integrated Gaussian function to approximate rate-intensity functions, instead of 3 linear segments (compare figures 6A and 7A to figures 2A and 3A). The modified model predicts dynamic range and temporal integration functions that are remarkably consistent with behavioral data.

Absolute Thresholds. The modified model also offers a possible reason why behavioral thresholds are much lower than those measured in single fibers (Pfungst, 1990). For both bipolar and particularly for monopolar stimulation, absolute thresholds predicted by the modified model (figures 6D and 7D) are considerably lower than those predicted by the original model (figures 2D and 3D).

There appears to be little difference between the cochlear input-output functions illustrated in plots 2C and 6C for monopolar stimulation, or between plots 3C and 7C for bipolar stimulation. However, the predicted psychophysical responses are dramatically different for the two descriptions of fiber input-output functions. On first inspection, it is hard to believe that such a small change in the form of the input-output function could make such a large difference in predicted psychophysical responses. However, by comparing the cochlear input-output functions illustrated in plots 2E and 6E (or 3E and 7E), it becomes apparent that there are indeed large differences in the cochlear input-output functions, particularly at low intensities.

This example illustrates the potential value of models. The results described above indicate that because of integration in the CNS, it may be very important to collect sufficient neurophysiological data at lower intensities than has previously been considered worthwhile. In particular, an accurate estimate of the shape of fiber input-output functions over a wide range of stimulus intensities may be necessary for understanding behavioral responses.

Further Comparisons between Model and Data. The analysis described above is extended in the following examples.

Example 1: Javel's data (personal communication) indicate that at low pulse rates stimulus amplitude must be increased by 1-6 dB, depending on the fiber, to increase discharge probability from 0.1 to 0.9, or a factor of 9:1. Psychophysical temporal integration functions from 4 human subjects are illustrated in Fig. 8 for monopolar stimulation and in Fig. 9 for stimulation using closely-spaced bipolar electrodes. Thresholds were measured using a modified Bekesy tracking technique. The plots show that threshold decreases monotonically with the number of pulses, indicating temporal summation of the signals. The function appears to have about the same shape and slope for either monopolar or bipolar stimulation. Fig. 10 shows these same eight psychophysical functions normalized and replotted (solid lines) along with plots (dashed lines) of predicted temporal integration functions using the spike-counting model. The dashed line labeled "2 dB" represents a model cochlea with fibers whose discharge probability increases from 0.1 to 0.9 in only 2 dB. The second dashed line, labeled "4 dB", represents a cochlea where fiber discharge probability increases from 0.1 to 0.9 in about 4 dB. These values are well within Javel's published 1-6 dB dynamic ranges for fibers.

Example 2: In this example, we modified the model illustrated in figure 1 to predict psychometric and intensity discrimination functions that are obtained using a 2AFC procedure. Two modifications of the model were necessary: (1) A stochastic model of the fiber's rate-intensity function was substituted for the deterministic version. Fig. 11 contains a diagram of the simple stochastic fiber model that we used. The ratio of membrane noise voltage (V_{gaus}) to the average threshold voltage (V_{thr}), which we denote by R , is inversely related to the slope of the fiber's rate-intensity function. As we have seen in the previous examples, this slope may play a crucial role in determining behavioral threshold. (2) The spike counts elicited in the two observation intervals of the 2AFC

task are compared in order to determine which of the two stimuli was more likely to be larger in amplitude.

We used the modified model to predict psychometric functions obtained with behavioral threshold measurements using a 2AFC paradigm. Figure 12 contains plots of data collected from a subject at UCSF by White. Figure 13 is a replot of the same data after normalization. Figure 14 illustrates the "extremes" of model predictions produced using a range of model parameters thought to be appropriate for this subject, namely 200-20000 fibers, a monopolar attenuation function, and an R ratio of 0.132 to 0.142, where R was estimated from the slopes of the subject's temporal integration data. The slopes of the model simulations and the behavioral data are similar, even though we assumed no variability in structures central to the auditory nerve. Thus, it is possible that the variability in auditory-nerve discharges is primarily responsible for the observed behavior.

Although these comparisons of model performance to behavioral data are much too cursory to draw any conclusions, we believe these examples illustrate the potential value of such modeling approaches for data analysis and experimental design. In the studies described below, we will develop and apply model approaches to the data in manners similar to those described above.

D. EXPERIMENTAL DESIGN AND METHODS

Studies to be performed in this project are aimed at obtaining behavioral data on specific auditory detection and discrimination tasks in cats, and correlating those findings with physiological and anatomic data obtained from the same animals that provided the behavioral data. Lastly, all these data will form inputs to mathematical models whose goal is to account for perceptual performance and predict auditory behavior for arbitrary experimental conditions.

Experimental Techniques

Only the behavioral testing procedures and the modeling work are described below. To conserve space and avoid redundancy, only brief descriptions of the physiological and anatomic techniques are given. Complete details of procedures used in those studies are provided in the Methods section of Project III.

Subjects. The cat was chosen as an experimental animal for these studies was made for several reasons. First, because our intention is to develop an animal model of cochlear implant function that allows collection of both behavioral and electrophysiological data from the same subject, the animal must be amenable for study with both methods. As a physiological model, the current electrophysiological literature on cochlear implants is almost exclusively from the cat (c.f., Hartmann et al., 1984; Javel et al., 1987; van den Honert and Stypulkowski, 1984, 1987). Furthermore, the ubiquity of the cat as subject in acoustic studies of auditory physiological function provides a vast database for comparison.

As a behavioral subject the cat has an undeserved reputation as an irascible and uncooperative worker. However, quite unlike its house-dwelling relations, the behaviorally trained cat has proved to be a worthy psychophysical subject using either positive reinforcement or aversive stimulation and avoidance techniques. The extant psychoacoustic literature from the cat includes behavioral data on absolute detection threshold functions to steady and pulsed tones (Gerken and Sandlin, 1977; Neff and Hind, 1955); frequency DLs (e.g., Elliott et al., 1960; Thompson, 1960; Costalupes, 1988) and intensity DLs (e.g., Elliot and McGee, 1965; Raab and Ades, 1946); psychophysical tuning curves (Pickles, 1979); temporal summation (Costalupes, 1983; Cranford and Igarashi, 1977); and critical bandwidth (Pickles, 1979; Nienhuys and Clark, 1979). The cat has also served previously as a behavioral model of electrically induced hearing (Black, Steel, and Clark, 1983).

The P.I., Dr. Smith, has extensive experience in applying psychophysical methods identical to those proposed here to investigations of both normal and pathological hearing in guinea pigs, rats, chinchillas (Smith, Brown, Moody, Stebbins, and Nuttall, 1987), monkeys (Smith, Moody, and Stebbins, 1987; Smith, Moody, Stebbins, and Norat, 1987), and now in cats (see Preliminary Studies). The planned experiments will utilize established behavioral techniques, with only slight modifications to allow for use of electrical stimuli delivered through implanted electrodes. We anticipate no problems in adapting procedures we already know to behavioral studies of cochlear implant function in cats.

Healthy young adult cats (approximately 9-12 months of age), which exhibit no indication of middle ear infection, will be maintained on a restricted food diet to facilitate the use of food as a reward for subsequent behavioral training and testing.

Apparatus. Behavioral testing will be conducted in 60 x 60 x 60 cm test boxes constructed from 3/4 inch plywood. The boxes are electrically shielded, ventilated, and have a two-way mirror observation panel. The cats are held in a plexiglass restraint stand with an adjustable collarpiece. The stand has been designed to restrict movement relative to the test equipment and thereby minimize the chance of damage to the implant connector (Fig. D-1). The stand permits some freedom of movement to allow the animal to either stand or sit. Mounted on the

threshold procedure, or bursts of standard and comparison stimuli in a discrimination paradigm). Figure D3 shows a schematic diagram of the test paradigm timing intervals for the different test procedures. The subject is required to release the key during the test-signal period to indicate detection of the target stimulus. All correct releases of the key during presentation of the test signal are followed by delivery of a small volume of pureed cat food through the feeder tube. Following a 3 S inter-trial interval (ITI), during which the cue light remains off, the light begins flashing again to signal the start of another trial sequence. A missed response (holding through the test-signal interval) results in a subsequent variable hold and test-signal presentation.

Release of the key at any other time within the trial sequence, except during the test-signal period, causes the cue light to be extinguished and a time-out period to begin. During this the subject is required to wait before initiating a subsequent trial sequence. A response during the time-out period results in the initiation of another time out. The time out is mildly aversive and serves to decrease inappropriate responding. To assess the subject's guess rate, 20% of all test-tone trials are "catch" trials where all experimental parameters are identical to test-tone trials, except the test signal is withheld. Responses during catch trials result in a 5 S time out. Holding through a catch trial, i.e., a correct response, results in a subsequent variable hold and test-signal interval. Data from sessions with >20% responses to catch-trials are not used in subsequent data analyses.

Daily experimental sessions last from 45 minutes to 1.5 hours, depending upon the particular task during that session. In general, while considerable variability exists across animals in the length of training time necessary to produce reliable behavioral measures, it may require as long as 8-12 months to produce reliable behavioral data (this also depends on the complexity of the hearing task). Sessions will be conducted 5 days a week.

Experiment 1: Measurements of Absolute Threshold

Overview: Our goal in this set of experiments is to understand what aspects of neural response determine behavioral threshold, and how electrode configuration, variable degrees of nerve survival, and stimulus waveshape affect this relation. By using the same chronic cat preparations for both neural and behavioral measures, we can largely eliminate the difficult problems associated with comparisons across animals. Detection threshold data will be collected as a function of electrode arrangement, stimulus waveform type, and extent of histopathology. Comparisons of both data types will be made on two levels, namely (1) direct comparisons of measures of threshold (e.g., behavioral detection and rate or synchrony threshold) to provide an understanding of how stimulus and anatomical variations influence the behavioral and physiological representation of electrical signals, and (2) models relating neural responses in populations of cochlear fibers to behavioral threshold.

Behavioral Measurements. A tracking procedure will be used that varies the level of the test tone from trial to trial. In a tracking procedure the initial level of the stimulus is typically set at some level above threshold. Since neither thresholds or dynamic range estimates for electrical stimuli have been measured in the cat for electrical stimuli, these values must first be determined empirically.

Correct detection of the test signal results in a decrease in signal level for the subsequent trial. This decrease in intensity continues until the animal fails to report the presence of the test stimulus. At this point, the level of the electrical signal will be increased for the next trial presentation. Attenuation step sizes as small as 0.1 dB will be used. In any given session, measurements will continue until seven transitions or intensity reversals have been obtained at each frequency. Threshold will be defined as the average stimulus intensity over the last 5 transitions. Infrequently, animals show some difficulty in behavioral control under tracking procedures. While less efficient, it is generally sufficient to re-establish stimulus control by simply switching the animal to a constant stimulus procedure, where stimulus intensity is varied randomly from trial to trial. Following determination of threshold at a given frequency, the frequency (or pulse rate) is switched digitally, and another track is obtained, until the desired number of signals has been tested.

Stimulating Conditions and Anatomic State. Thresholds will be determined daily for 9-18 logarithmically-spaced frequencies from 0.02-20 kHz. Thresholds will be obtained at several frequencies for sinusoids presented continuously (to determine the existence of tone decay) and as bursts and for single pulses and trains of biphasic stimulus pulses presented at different rates. Detection thresholds will be compared under several conditions. First, the effects of varying local current fields will be ascertained by measuring thresholds as electrode source and sink location are varied. Based on our prior experience, we are confident that animals will quickly (i.e., within 2 sessions) accommodate to changes in the signal they listen to. Second, the effects of variations in the neural density and distribution relative to the stimulating electrodes will be assessed by comparing behavioral threshold data with histological findings from animals' having different degrees and patterns of neural degeneration.

Interpretation of Data and Evaluation of Neural-Behavioral Models. Following collection of behavioral data, the animal will be shipped to Duke University, where Dr. Javel will record responses of bushy cells in and anteroventral cochlear nucleus (AVCN) using stimuli and test procedures similar to those employed in behavioral testing. Use of identical techniques facilitates direct comparisons of behavioral and electrophysiological data in the same animal. Techniques used in the electrophysiological stage of the study are described in Project III. Also

presented there is a rationale for recording from AVCN, as well as a discussion of the types of responses we expect to see and techniques for determining tuning properties of neurons in deafened ears.

Two data sets will be acquired for each neuron. To provide information for modeling work, a dense (0.2 dB steps) rate-intensity function will be obtained for intensities that bracket the behavioral thresholds provided by that animal, i.e., from 3 dB below the most sensitive behavioral threshold to 3 dB above the least sensitive threshold. Signal duration, waveshape, signal timing, and stimulating electrode configuration will be the same as those used in collecting the behavioral data. Signals will be repeated until the mean spike count per trial exceeds the variance. This value, of course, depends on discharge rate. The threshold-related manipulation is performed next. It consists of using the same tracking algorithm employed behaviorally, but this time to force neurons to track their own thresholds using four different criteria (1, 5, 10, 20 spikes/S) above the spontaneous rate. We have already conducted similar studies using adaptive tracking techniques on the single-cell level (Javel et al., 1988; Javel, 1989a,b; see Preliminary Studies). Attempts will be made to record from cells connected to a variety of points along the cochlear duct.

Physiological data analysis will focus on determining which subset of neurons responds at intensities corresponding to behavioral threshold, and to what degree. Plots of response magnitude as a function of cochlear locus of the neuron will be constructed, and the physiological data will form inputs to CNS processing models that attempt to predict threshold.

Modeling Behavioral Threshold. Spike counting models (White, 1984), timing models (Luce and Green, 1974) and models with central mechanisms that are sensitive to synchronization of interfiber discharge (Loeb, White and Merzenich, 1983; see Project IV) are examples of types of models that will be evaluated. Given estimates of the point of cochlear origin for cells recorded and the degree of neural survival at each cochlear locus, we can determine how neural activity spreads across the cochlea with increasing stimulus intensity. The electrophysiological and neuroanatomical measures will be incorporated into candidate neural-behavioral models to determine each model's ability to predict behavioral threshold functions. The predictions will be compared to the behavioral measurements to determine which models are most plausible. Detailed examples of ways such models are used to compare neurophysiological and behavioral threshold data are provided in the Preliminary Studies.

In the normal cochlea, because spontaneous activity is at such a high level, it is possible that a greater increase in spike activity is required to achieve sensation than in the deafened cochlea. The deaf cochlea may be more sensitive to electrical stimuli simply because the fibers are no longer driven by the "noisy" release of transmitter from the inner hair cells. The spontaneous activity level of fibers in the deaf cochlea is far less than that of a normal cochlea (van den Honert and Stypulkowski, 1987). In the Preliminary Studies section our model simulations suggested that behavioral thresholds can be quite low due to the summation of inputs from many fibers, each of which is weakly driven and therefore has a relatively low probability of discharge. Presumably such sensitivity would not be possible if significant levels of spontaneous activity were present to interfere with the detection process.

Absolute thresholds are usually considerably lower for monopolar than for bipolar electrodes. This is consistent with a behavioral model that sums activity over a large region of the cochlea. However, the difference in absolute thresholds could also result from inefficient shunting of stimulus current by poorly located bipolar electrodes. Direct neural and behavioral measurements in the same animals and with the same electrodes should help us identify those mechanisms important in defining absolute threshold. For example, if behavioral threshold occurs at stimulus levels so low that recorded neural activity in the most sensitive fibers is only rarely evoked over the entire duration of the stimulus, we can be certain that some form of spatial summation is occurring.

Interestingly, most models of nerve excitation only exhibit threshold changes of 2-6 dB/octave as sinusoidal stimulus frequency is varied from 100 Hz to 1000 Hz. This value is substantially different than the 9-15 dB/octave slopes observed behaviorally (Pfungst et al., 1981). However, several nerve membrane models have been proposed that may account for such steep slopes (see White's Modeling Studies in Project III's Preliminary Studies; White, 1984; Rubinstein and Spelman, in press; Motz and Rattay, 1986). After determining in Project III which description of single fiber response-intensity behavior is most accurate in this stimulus-response domain, that description will be used in the neural-behavioral model illustrated in figure 1. We will then determine the accuracy of this neural-behavioral model in predicting behavioral threshold as a function of sinusoidal stimulus frequency and modify the neural-behavioral model accordingly. As an example of how we might modify such a model, consider how we modified the original model in the Preliminary Studies section by changing the shape of the fiber's rate-intensity function to an integrated Gaussian. Another possible model modification would reduce the region of the cochlea over which we sum activity.

Since the slope of the threshold vs. frequency curve may be largely a function of fiber and node dimensions (see White and Finley's Modeling Studies in Project III's Preliminary Studies), differences in observed threshold vs. frequency functions may reflect selective damage to a part of the ganglion cell (Pfungst, 1990). Pfingst and colleagues (1981, 1983) have shown that a strong relationship exists between threshold vs. frequency functions and

degree of neural degeneration. However, other than what we propose here, no one has attempted to correlate differences in the slope of this behavioral frequency response function with electrophysiological function and survival of specific segments of auditory neurons. After determining in Project III which single fiber model most accurately represents single fiber responses for different sinusoidal frequencies and different survival patterns, that model will be used in the neural-behavioral model of figure 1 to predict behavioral thresholds as a function of sinusoidal stimulus frequency in animals with different degrees and types of neural degeneration. After optimizing the model's parameters to obtain the best fit to the behavioral data, we will determine its accuracy and then modify the model to improve its performance.

Experiment 2: Measures of Growth of Loudness and Dynamic Range

Overview. Our goal in these studies is to understand what characteristics of peripheral neural responses are related to loudness and dynamic range. Neural and behavioral measures in the same preparations will again be made on two levels: Direct comparisons of the two types of data will be made, and specific models for estimating behavioral dynamic range and loudness from neural responses will be developed and evaluated using behavioral, physiological and anatomic data provided from the same animal. Data on growth of loudness and dynamic range will be collected in animals with differing degrees of histopathology. As was the case in Experiment 1, different current field geometries will be employed during behavioral training to ascertain whether performance depends on stimulus-related factors. Insofar as possible, the "measurement, model simulation, comparison, and modification" process will be replicated for animals with different, documented degrees of nerve survival.

Behavioral Measurements. The growth of loudness and dynamic range will be determined using reaction time (RT) measures. Reaction time, i.e., the interval between the onset of the target stimulus and the release of the lever indicating signal detection (see Fig. D3), has been shown to be a reliable index of perceptual loudness (Gerken and Sandlin, 1977; Pfingst, 1984; Stebbins and Miller, 1964; also, see Preliminary Studies) and is easily measured in the basic behavioral procedure discussed above. These studies have demonstrated an orderly relationship between stimulus intensity and reaction time. In general, the more intense the stimulus is, the shorter is the reaction time. By plotting decreases in response latency against stimulus intensity it is possible to estimate the growth of loudness at least over a 20-30 dB acoustic or a 5-10 dB electrical intensity range. Furthermore, RT indices provide information about the perceptual representation of suprathreshold stimuli absent in simple detection tasks. Since equal latency implies equal loudness comparisons of different stimuli with equivalent RT, across frequency for example, allows us to construct equal-loudness contours.

In using the tracking method described above to determine thresholds, a range of signal intensities must necessarily be presented. Measurement of RT is fully automated and is accomplished as a matter of course in the threshold experiments. Therefore, no additional effort is required to obtain information concerning the perception of suprathreshold stimuli. These data will be gathered under the stimulus and electrode conditions described in Experiment 1.

Single-Cell Recordings. There is no physiological experiment we can perform that directly investigates loudness, which is a perceptual phenomenon. To provide related data we will obtain rate-intensity functions over each neuron's entire dynamic range (i.e., spike probability of 0 to 1.0) in fine (0.1 dB) intensity steps, using the same stimuli that had been used to collect behavioral data. If any overlap exists between the neural and behavioral dynamic ranges, responses at and below those intensities will be studied especially carefully by obtaining neural data for a larger number of trials. Rate-intensity functions will be fitted with cumulative normal functions. The fits obtained at a variety of neural CFs will be used to construct plots of response magnitude as a function of cochlear locus. Using the reaction time measures, correlations will be determined between loudness growth determined behaviorally and neural response growth at various cochlear positions.

Interpretation of Data and Evaluation of Neural-Behavioral Models. The rate-intensity and fiber-origin data obtained in the physiological studies will allow us to determine how neural activity spreads across the cochlea with increasing stimulus intensity for each electrode configuration. The histological data obtained from these same animals allows us to estimate the distribution and anatomical state of excitable elements. These neurophysiological and neuroanatomical measures will be incorporated into candidate neural population models which will drive candidate behavioral models like the one illustrated in figure 1. Detailed examples of the application of this model for estimating uncomfortable loudness levels (UCL) and thresholds are given in the Preliminary Studies. In those preliminary studies we compared two models that were nearly identical except for the assumed shape of fiber rate-intensity functions. We discovered that model predictions of UCL and threshold were highly sensitive to seemingly small differences in fiber rate-intensity functions. As a consequence of this and other modeling work, some of our proposed electrophysiological experiments have been modified to obtain more refined estimates of fiber rate-intensity functions. This illustrates how such simulation studies can be useful in the design of electrophysiological studies and correlative behavioral studies. Simulation studies can point-out which features of electrophysiological responses are most likely to be strongly related to a particular behavioral

response.

To develop candidate behavioral models of loudness, we must first consider how stimulus intensity may be encoded. The most popular hypotheses for electrical intensity encoding are similar to those proposed for the encoding of acoustic intensity. According to these notions, stimulus intensity is encoded either by the number of fibers excited or by the firing rates of the excited fibers. Other models incorporating information about the relative synchronization of discharges between fibers will also be evaluated. Implicit in many of these models is some form of spatial and temporal summation of neural activity, followed by a monotonic nonlinearity that translates the summed activity into loudness (or reaction time in the case of our animal studies).

Recruitment models presume that loudness and dynamic range are a function of the number of nerve fibers driven by a particular stimulus. [The model illustrated in figure 1 becomes a simple recruitment model if we use a simple step function to model each fiber's input-output function.] Such models predict large differences in growth of loudness for different electrode configurations. However, behavioral dynamic ranges are, at most, only weakly related to stimulating electrode type (see figures 4 and 5; Pfingst et al., 1981; Pfingst and Sutton, 1983; Shannon, 1983b). In fact, in some cases behavioral dynamic ranges can be greater for monopolar than for bipolar electrodes. These data suggest that intensity coding involves more than just simple recruitment. Since firing rate (and probability of discharge) grows with stimulus intensity (Javel et al., 1987), discharge rate may be the additional component needed for a good theory of intensity coding. By extending the simple recruitment model to include rate-intensity functions, we have found that it is possible to obtain behavioral dynamic ranges that are little affected by electrode spacing (see Preliminary Studies). In fact, depending on the exact shape of the fiber input-output functions, it is even possible to obtain smaller dynamic ranges for bipolar stimulation than for monopolar.

Each model will be evaluated according to its ability to account for behavioral findings regarding loudness and dynamic range for each of the electrode configurations. For any single electrode configuration, it may be possible to accurately predict some loudness (reaction times) functions using the simple model in figure 1. However, it may be impossible to obtain accurate predictions across all electrode configurations, even if we supply the model with an accurate estimate of the cochlear attenuation function for the different electrode types. For example, we may need to extend the model in figure 1 to include a mechanism for loudness summation (Shannon, 1985; White, 1984). Presumably, in loudness summation, loudness increases as the number of excited neurons becomes distributed over a greater cochlear length, even though the total amount of cochlear nerve activity remains constant. If the simpler models prove inadequate, the model shown in figure 1 will be extended to incorporate a mechanism for loudness summation. In one such model extension, activity from a group of nearby fibers is summed and passed through a compressive nonlinearity to generate a channel's output. In this manner, the model cochlea is divided into channels. All the channel outputs are then summed. In the model, loudness and reaction times are simple monotonic functions of this final sum. The parameters of this model will be varied to provide the best fits to reaction time vs intensity data across all electrode configurations. Such loudness models should be particularly useful in accurately predicting loudness functions for very different electrode configurations, and in understanding loudness functions for multi-channel stimulation.

Experiment 3: Frequency Difference Limens

Overview. DLs for frequency have been shown to be good predictors of subsequent performance on speech perception tasks in humans. Comparatively few animal behavioral data exist for frequency discrimination tasks. Consequently, the stimulus, electrode and neural conditions that contribute to the discrimination of frequency are poorly understood. While neural responses to electrical stimuli show excellent phase-locking at frequencies > 10 kHz, psychophysical frequency discrimination for cochlear implants deteriorates rapidly above 300 Hz. The proposed studies are aimed at illuminating those mechanisms which underlie frequency discrimination with electrical stimuli, and to determine whether electrode or stimulus parameters might be optimized to improve DLs, and hence speech perception.

Behavioral Measurements. By varying slightly the basic behavioral procedure it is possible to test other, more complex, aspects of hearing function. The testing paradigm for the measurement of DLs, either of frequency or intensity, is the same as that used to determine absolute thresholds. Here, however, the animal is not asked to discriminate the absence of a stimulus from its presence. Rather, the animal is required to discriminate between two stimuli which are different in either frequency or intensity (See Fig. D-3). For example, in the threshold procedure described earlier, initiation of a trial sequence requires that the animal hold through fixed and variable holds until the stimulus condition changes from the absence of a stimulus to its presence. Again, the discrimination paradigm differs from the detection threshold tasks in that the initial hold response produces a pulsed standard stimulus. If contact with the manipulandum is maintained through the hold intervals, the tone is modulated sinusoidally at a 4 Hz rate. In a frequency modulation task, the tone is modulated in frequency. In intensity discriminations, it is modulated in amplitude. As with the absolute threshold procedures, the animal is reinforced with food reward for releasing during the presentation of the test signal interval. Initial discrimination trials begin with the difference

threshold will be defined as the average signal intensity difference over the last five transitions.

Single-Cell Studies. Similar to that described in the threshold studies, adaptive tracking procedures using the same stimulus paradigms employed in behavioral data collection will be used on the single cell level to obtain DLs. As shown in Preliminary Studies, we have already collected acoustic data using these procedures. Signals will be identical to those utilized in the behavioral phase of the studies. For intensity discrimination tasks, the decision process will operate solely on spike counts elicited by the signals. Psychometric functions will be determined by forcing the fiber to track various performance levels (i.e., 50%, 70.7%, 87.1%, and 93%), and plotting the resulting DL against percent correct. An important aspect of the physiological studies is that our data collection process allows every spike train to be reconstructed, if the companion modeling work requires knowledge of temporal aspects of the neural response.

Interpretation of Data and Evaluation of Neural-Behavioral Models. One type of intensity discrimination model is described in Example 2 of the Preliminary Studies section. The model is a simple extension of the model illustrated in figure 1. It is a spike counting model in which the spike-counts from two observation intervals are compared to determine which stimulus was larger. The two intervals correspond to the two intervals in a 2AFC intensity discrimination task. This Preliminary Studies example also illustrates how we were able to make a "first-order" estimate of threshold psychometric functions using a simple neural model combined with a commonly used behavioral model. In that study we were estimating the ability of the CNS to discriminate between a zero intensity stimulus and a low intensity stimulus (i.e. intensity discrimination at threshold). The simulations indicated that intensity discrimination at threshold levels may be largely limited by the variability in peripheral nerve discharges. We believe the model does not have to be modified to accommodate the modulation detection task.

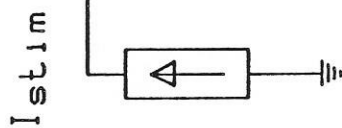
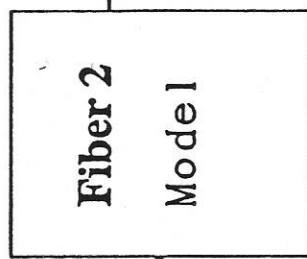
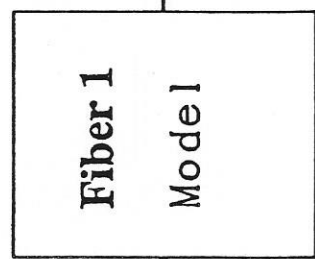
In the model described in *Example 2 of Preliminary Studies*, there are three peripheral nerve response features that could directly affect intensity discrimination. These are the slope of the neural rate-intensity function, the variability of the firing rate, and the attenuation vs. cochlear-place function. The proposed physiological studies will provide us with good estimates of all three. If inter-fiber synchronization of discharges is used by the CNS for intensity discrimination, other response features and models will be used to predict intensity discrimination functions. Among these response features are changes in discharge latency with intensity and variability of discharge latency. Again, the proposed physiological studies will provide us with good estimates of these variables.

For certain classes of stimuli, intensity DLs decrease with intensity (White, 1984). For the model described in the Preliminary Studies section, this could be due to an increase in the slope of fiber rate-intensity functions as intensity is increased. In fact, there is evidence that is consistent with this hypothesis (see White's multi-node model in Project IIP's Preliminary Studies). For this reason, it is important that the physiological studies determine which part of the rate-intensity function units operate on at the levels used in collecting the behavioral data. At the same time, however, there are alternative and possibly complementary explanations: (1) The standard deviation of the spike counts, relative to the change in the mean spike count for a given increment in the stimulus, may decrease with intensity. (2) The shape of the cochlear attenuation function may cause increasing numbers of fibers to be excited (i.e. recruited) as stimulus intensity is increased. By developing a neural-behavioral model that accurately predicts intensity DLs over a wide stimulus domain, we will be able to estimate the relative importance of these features of neural response for intensity discrimination. In behavioral experiments, stimuli will be selected to sample from several values of intensity, pulse-width, pulse-rate, and pulse-train duration. Corresponding electrophysiological experiments will provide data on: (1) the slopes of the rate-intensity functions, (2) the variability in discharge rate, and (3) the cochlear attenuation function. This data can be directly "plugged into" models like the behavioral model described in Preliminary Studies, and compared with behavioral data to estimate model parameters.

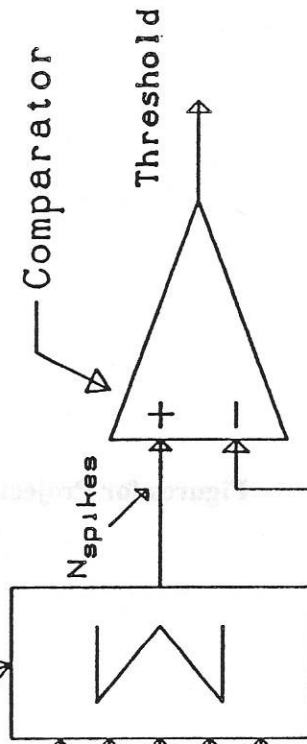
As indicated in the Preliminary Studies, we anticipate that variability in peripheral nerve fiber responses may largely account for the relatively poor performance typically observed at low intensities. However, as intensity is increased, more central factors may limit intensity discrimination. The intensity discrimination model described in the Preliminary Studies section will be extended to include a central noise source. We can further extend this model by adding a compressive nonlinearity immediately after the point where activity is summed and prior to the point where the "central" noise is added. Of particular interest in this regard is elucidating the effects of variable spiral ganglion cell loss on behavioral and model performance. When significant cell loss exists, at least two factors may come into play: (1) fewer fibers will be available to convey information about stimulus intensity and (2) the slope of rate-intensity functions may change because: (a) central nodes are excited because peripheral nodes have degenerated or (b) the operating point on existing fiber rate-intensity functions will have moved upward. The interaction of these factors in determining intensity DLs with the use of the proposed neural-behavioral models.

E. HUMAN SUBJECTS

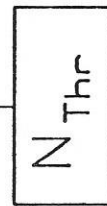
Different Fiber Models
 Represent the Diversity of
 Nodes in the Auditory Nerve



Spike Counter
 $\tau = 100 \text{ msec}$



Threshold
 is evoked if
 $N_{spikes} \geq N_{Thr}$

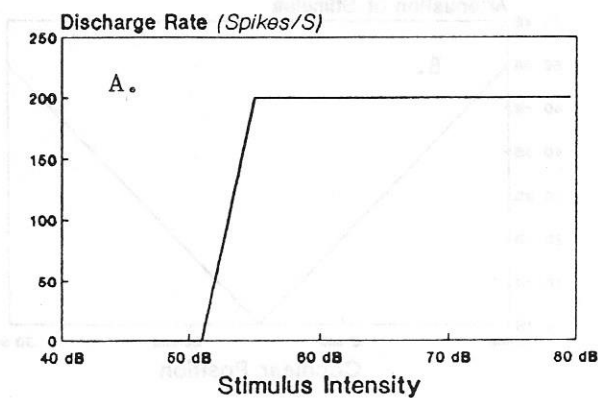


**Behavioral Threshold
 Model**

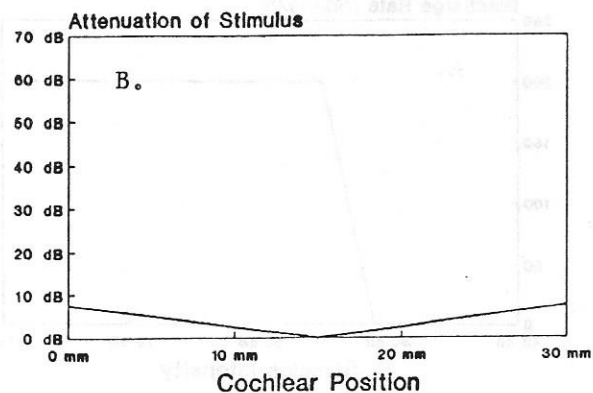
Nfibers

Figure 1. Cochlear Neural Model and Behavioral Threshold Model

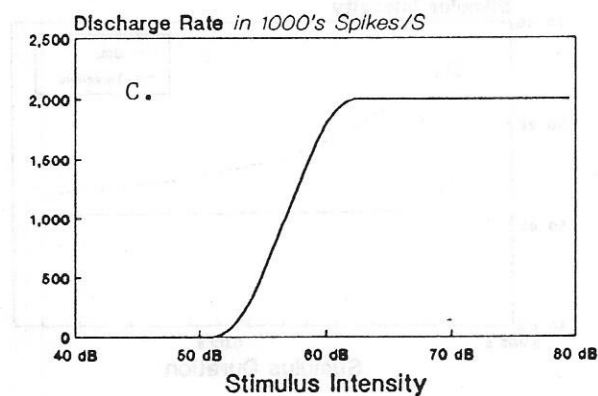
Fiber Input-Output Function



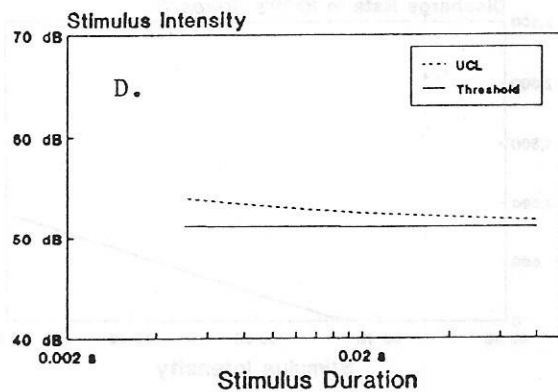
Attenuation Across Cochlea



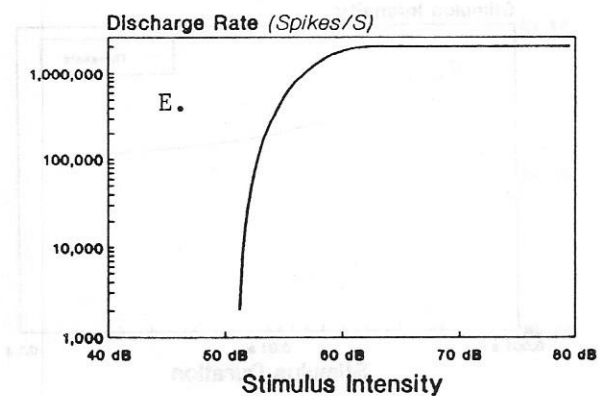
Cochlear Input-Output Function



Temporal Integration



Cochlear Input-Output Function



Temporal Integration

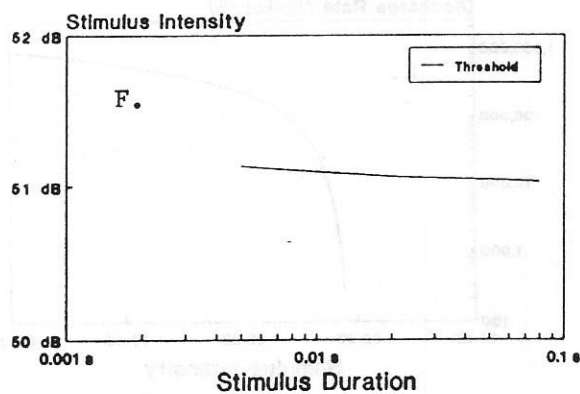
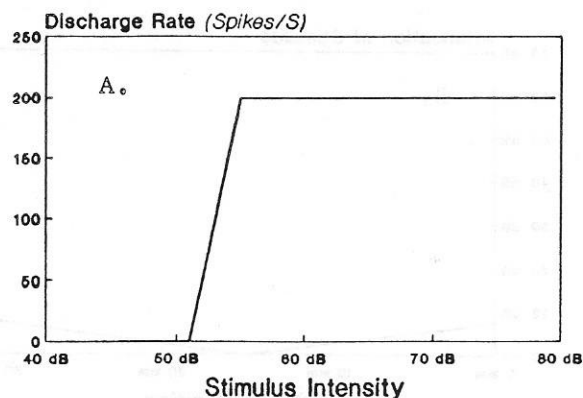
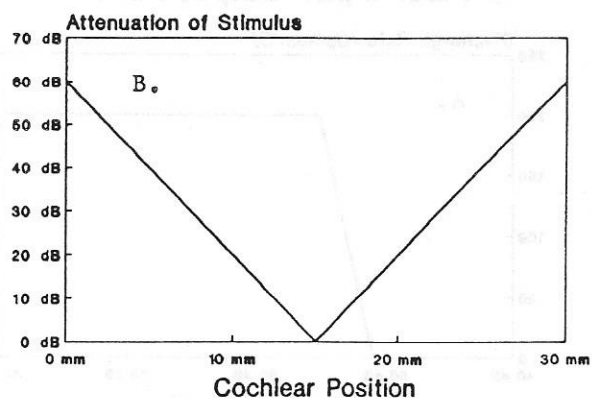


Figure 2. Simulation of Model: Results for Monopolar Electrode and "3-line" Fiber Input-Output Model

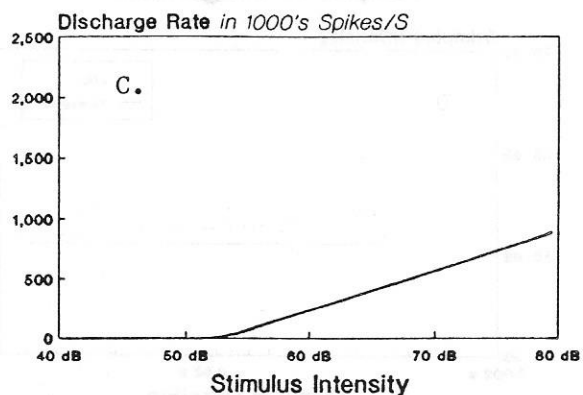
Fiber Input-Output Function



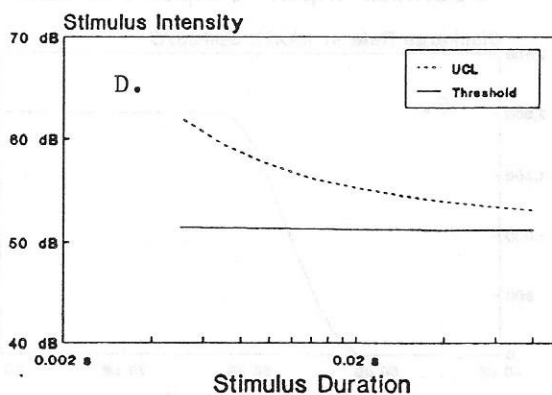
Attenuation Across Cochlea



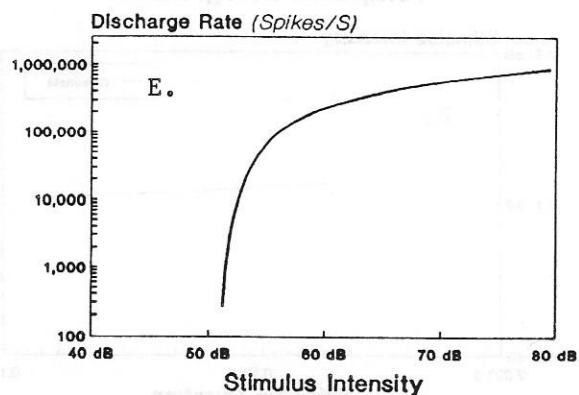
Cochlear Input-Output Function



Temporal Integration



Cochlear Input-Output Function



Temporal Integration

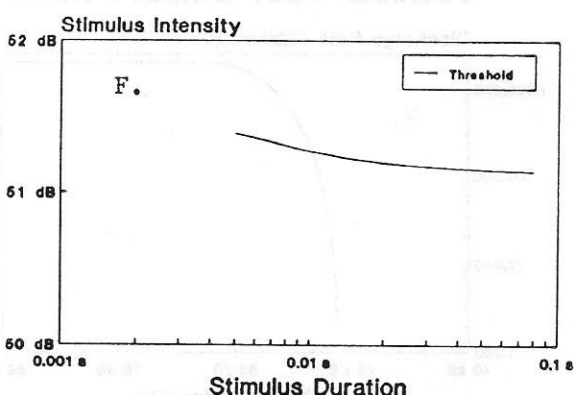
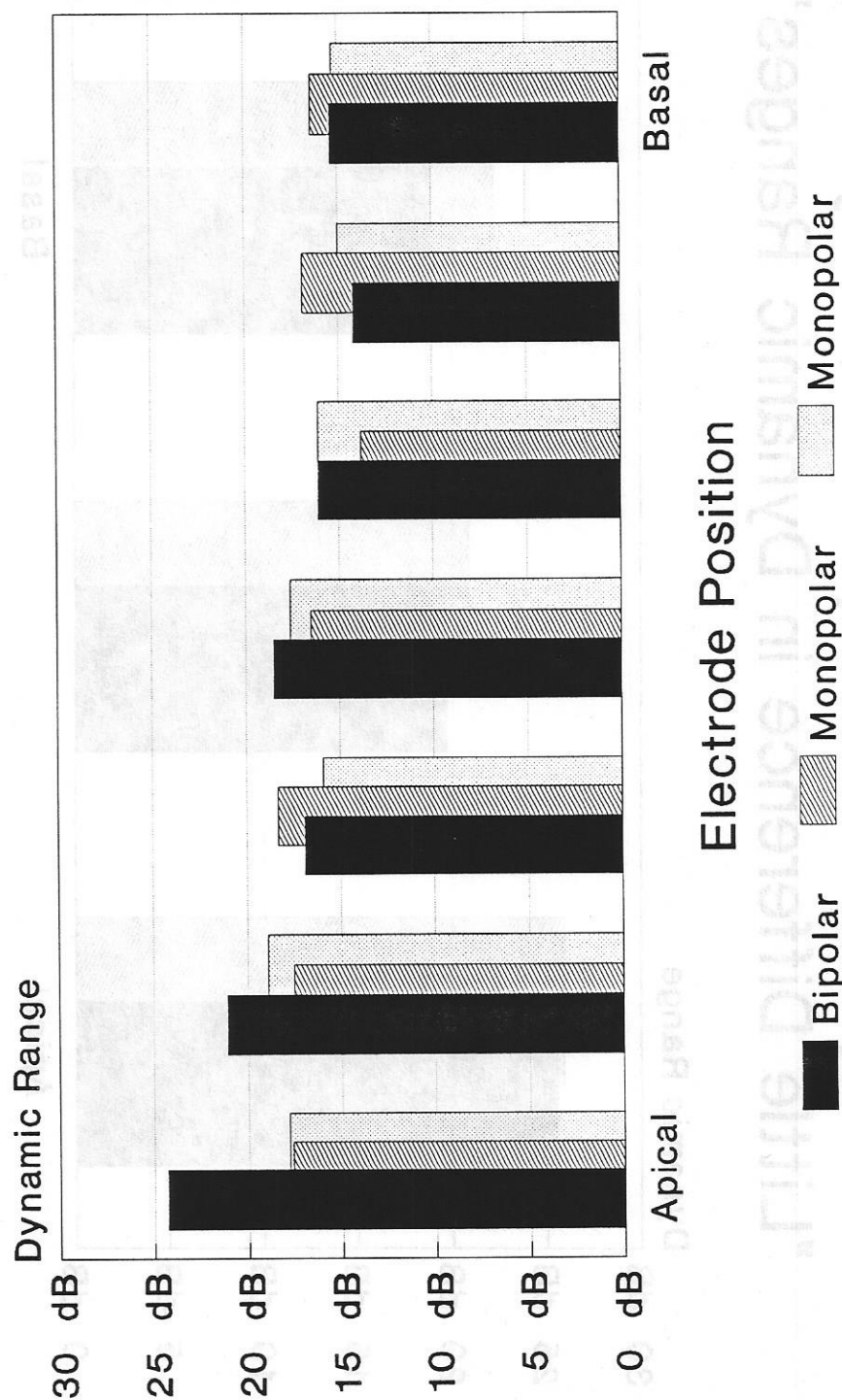


Figure 3. Simulation of Model: Results for Bipolar Electrode and "3-line" Fiber Input-Output Model

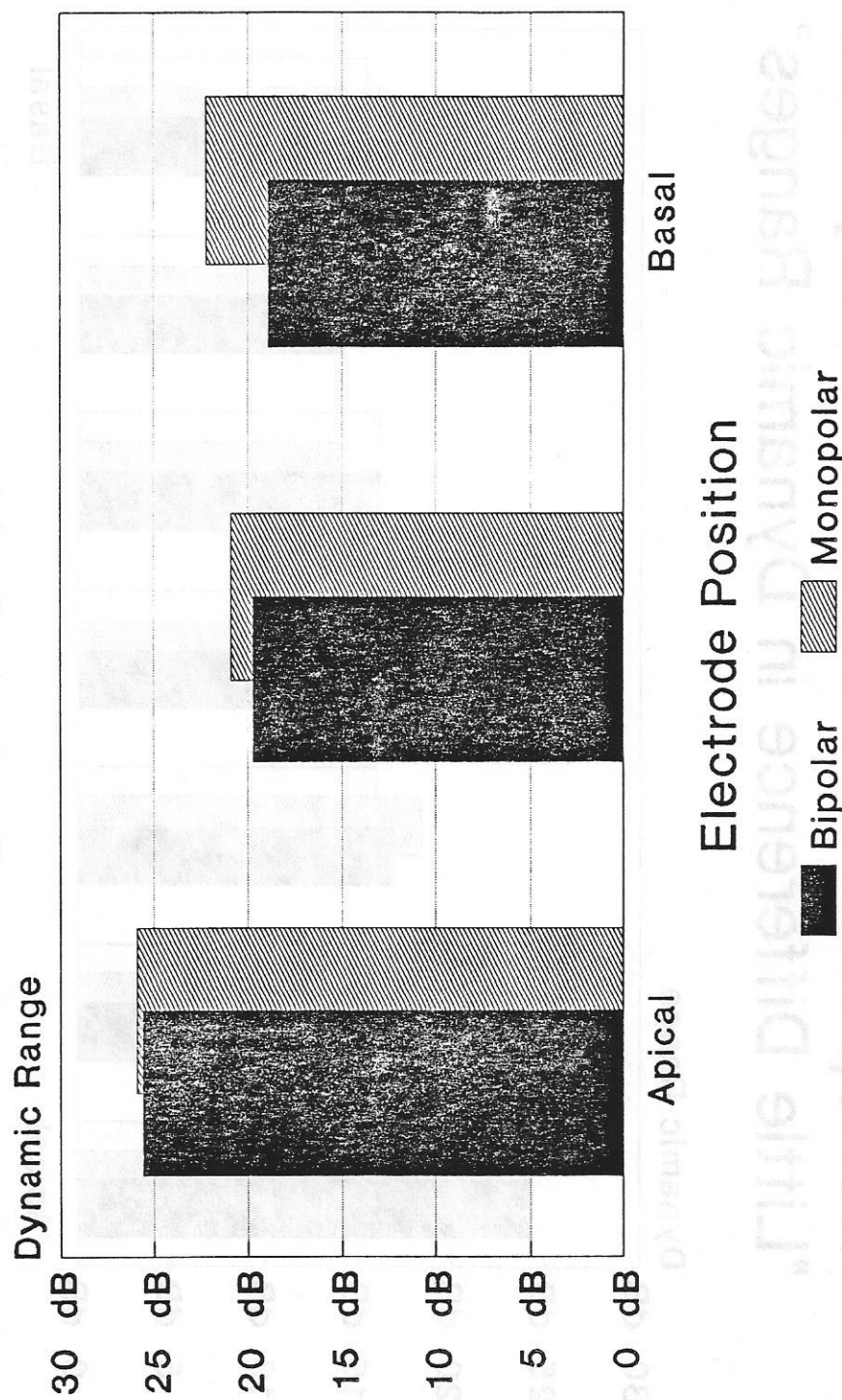
Monopolar vs. Bipolar (subj. CE) "Little Difference in Dynamic Ranges"



Data From Shannon (Hearing Res. 1984)

Figure 4. Dynamic Ranges for Bipolar and Monopolar Electrodes

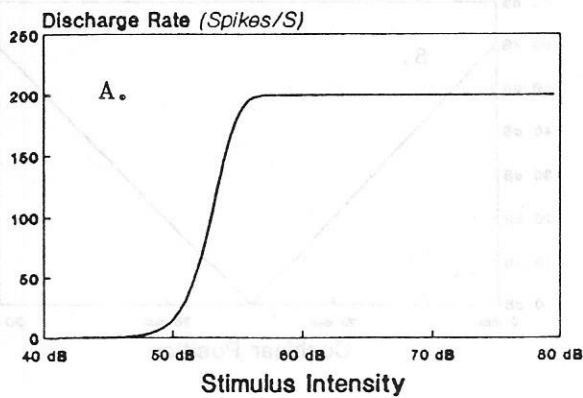
Monopolar vs. Bipolar (subj. CB) "Little Difference in Dynamic Ranges"



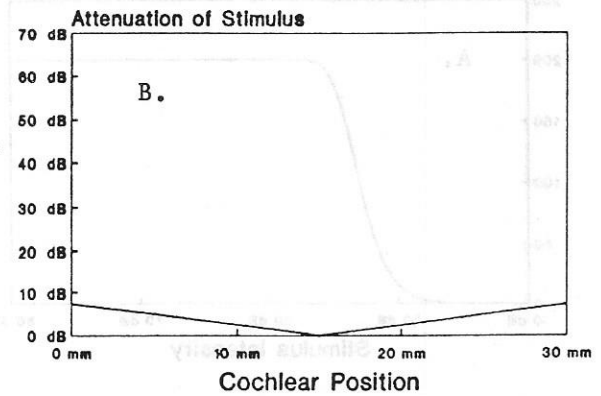
Data From Shannon (Hearing Res. 1984)

Figure 5. Dynamic Ranges for Bipolar and Monopolar Electrodes

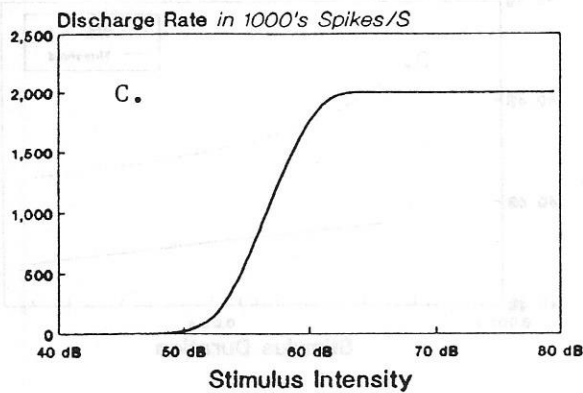
Fiber Input-Output Function



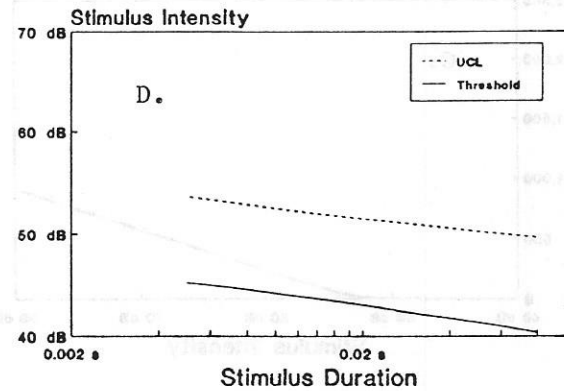
Attenuation Across Cochlea



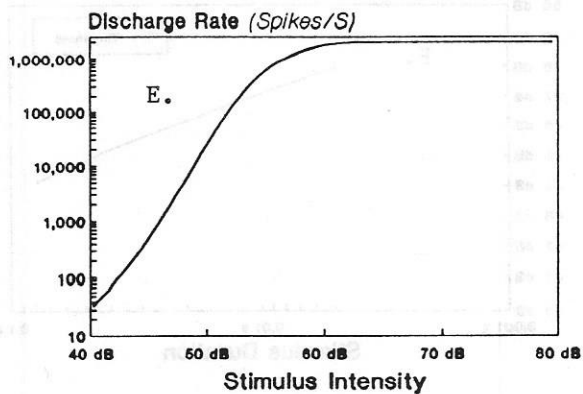
Cochlear Input-Output Function



Temporal Integration



Cochlear Input-Output Function



Temporal Integration

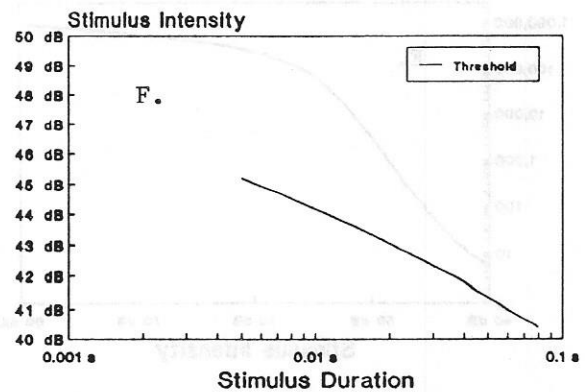
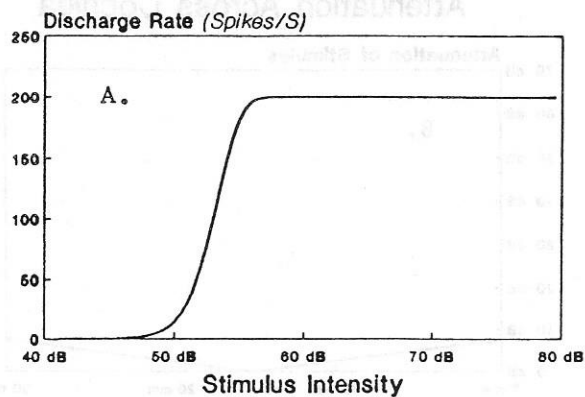
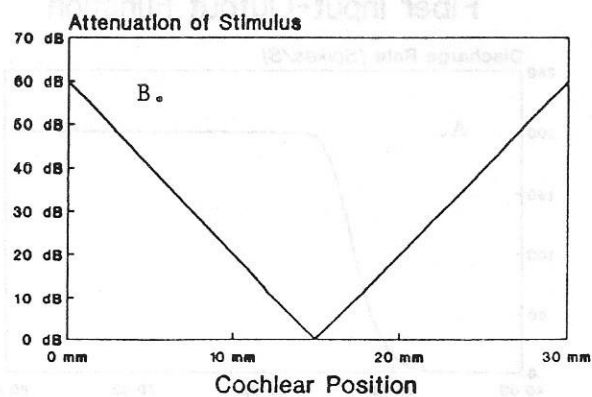


Figure 6. Simulation of Model: Results for Monopolar Electrode and Integrated Gaussian model of Fiber's Input-Output Function

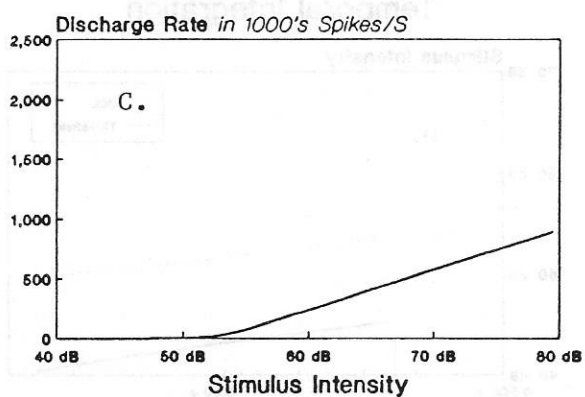
Fiber Input-Output Function



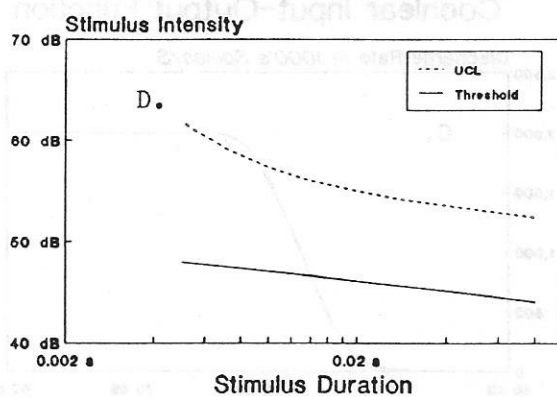
Attenuation Across Cochlea



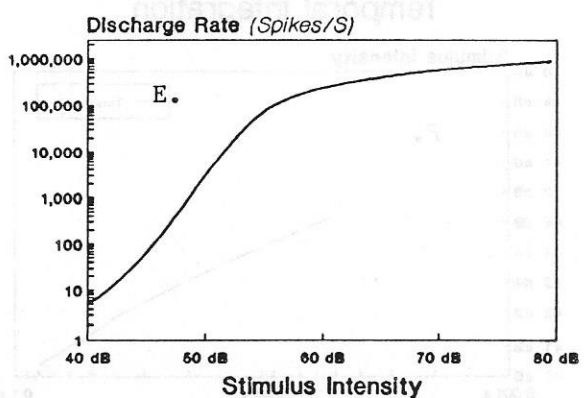
Cochlear Input-Output Function



Temporal Integration



Cochlear Input-Output Function



Temporal Integration

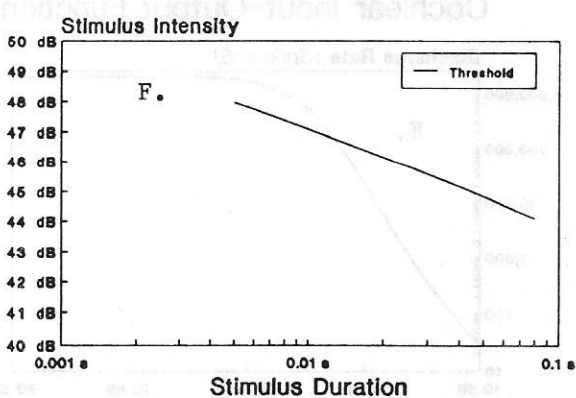


Figure 7. Simulation of Model: Results for Bipolar Electrode and Integrated Gaussian Model of Fiber's Input-Output Function

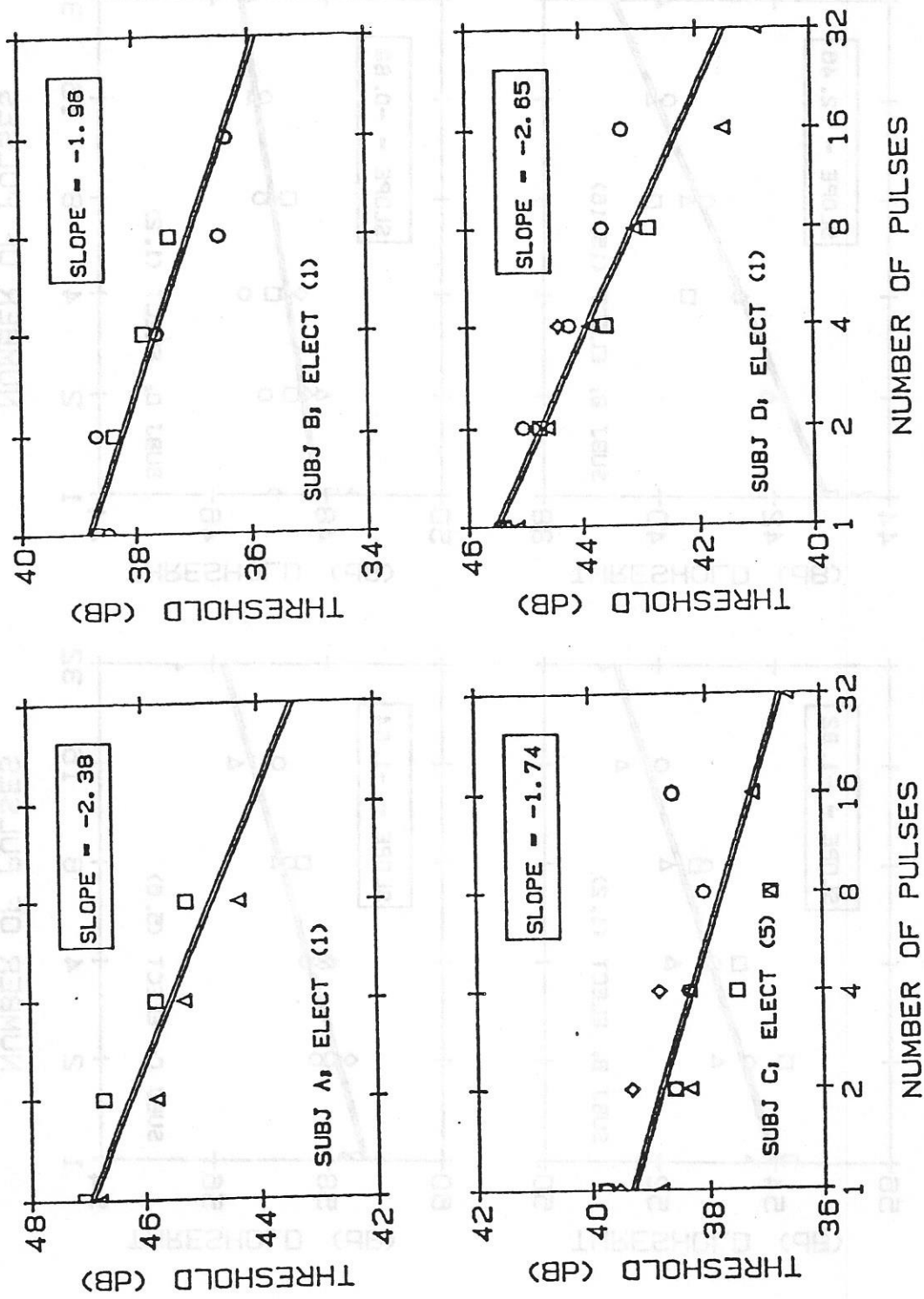


Figure 8. Patient Temporal Integration Functions for Monopolar Stimulation

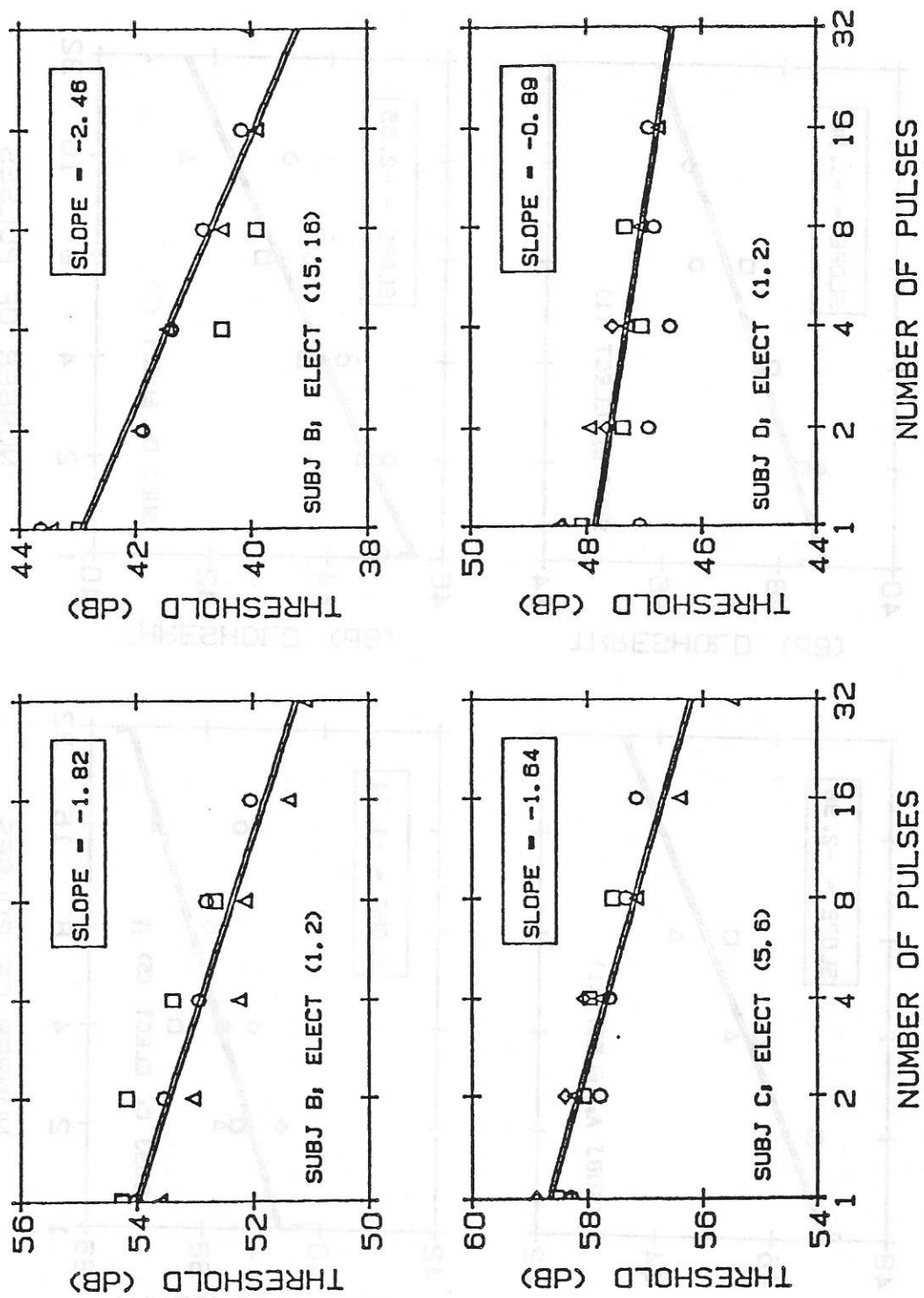


Figure 9. Patient Temporal Integration Functions for Bipolar Stimulation

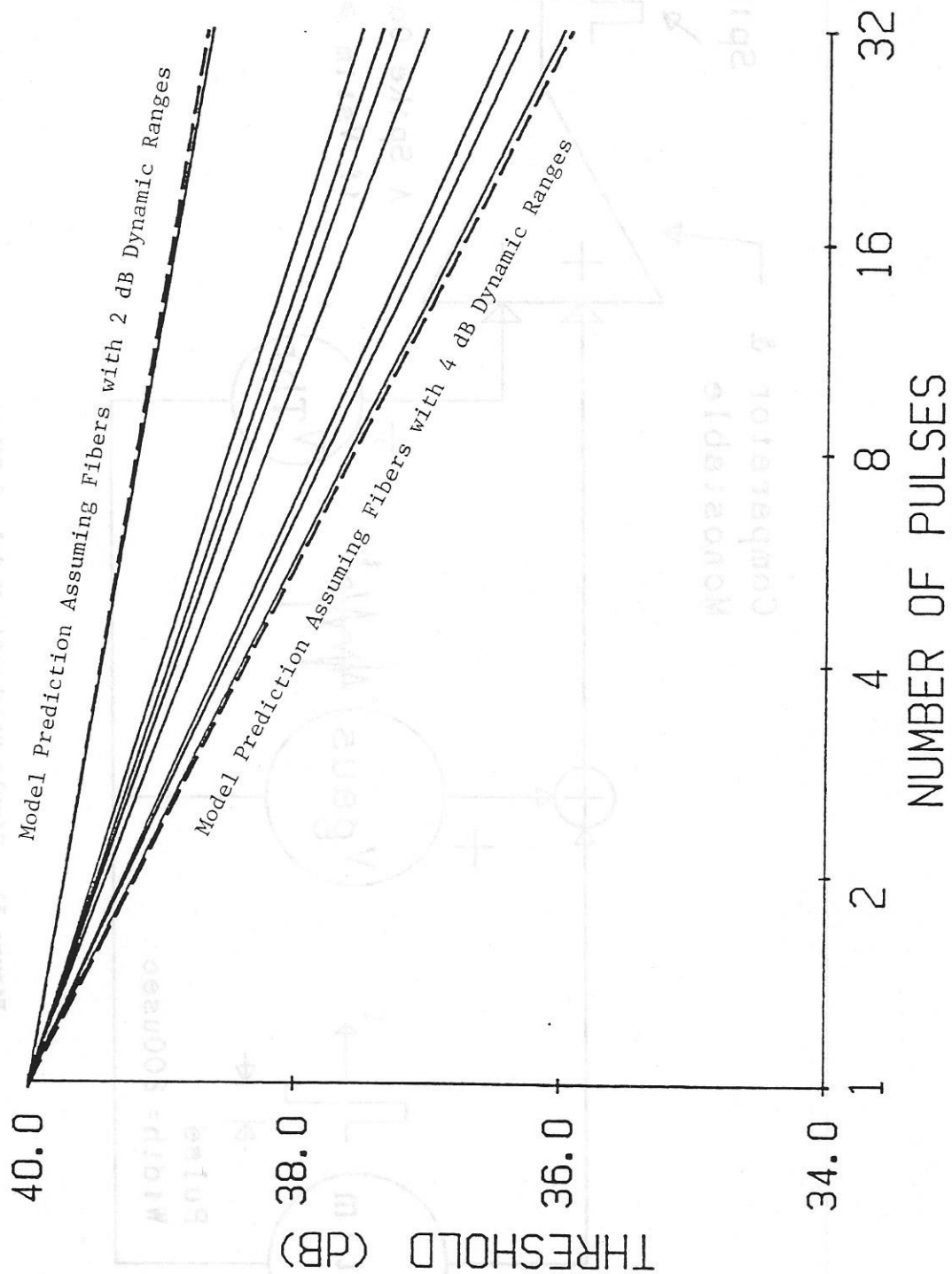


Figure 10. Comparison of Model Predictions With Temporal Integration Data From Humans

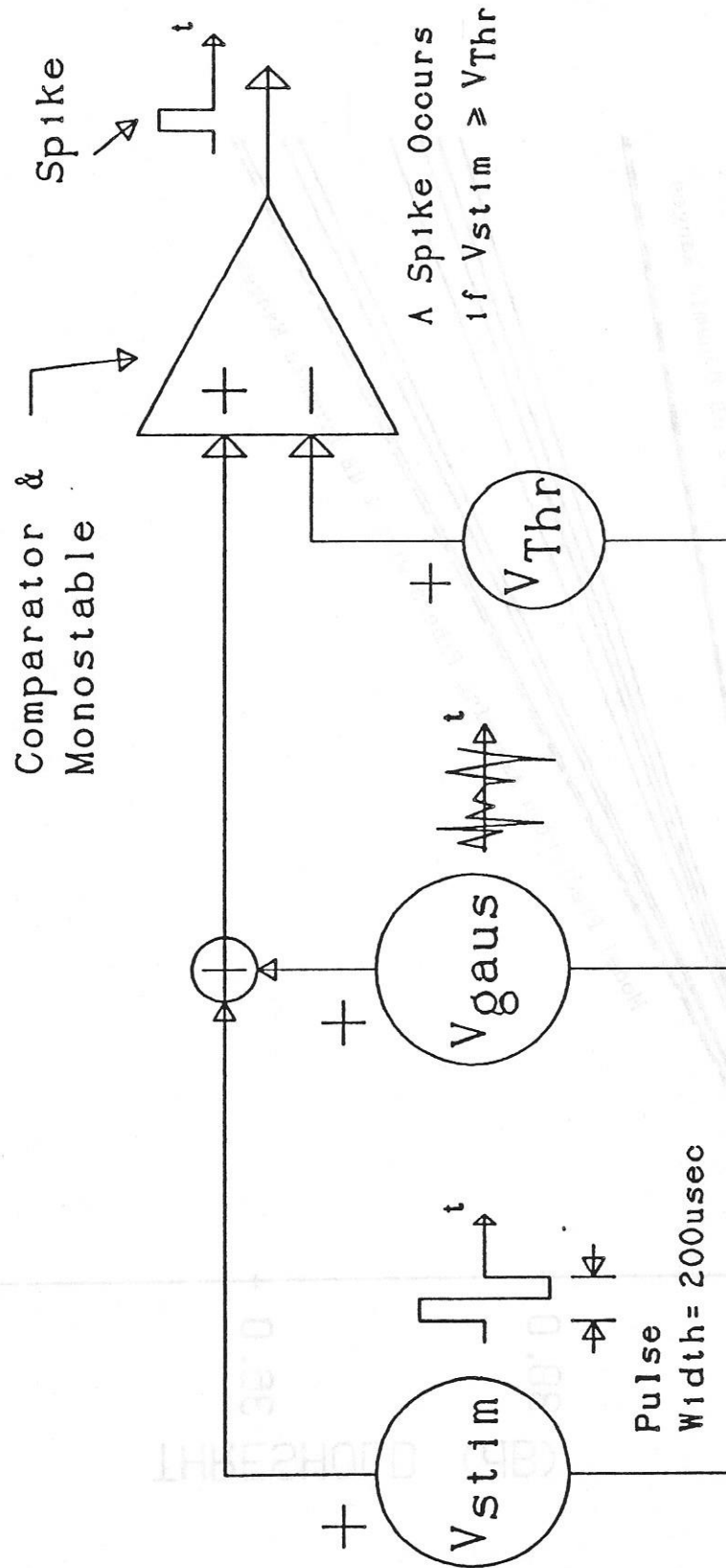


Figure 11. Simple Stochastic Model of Fiber

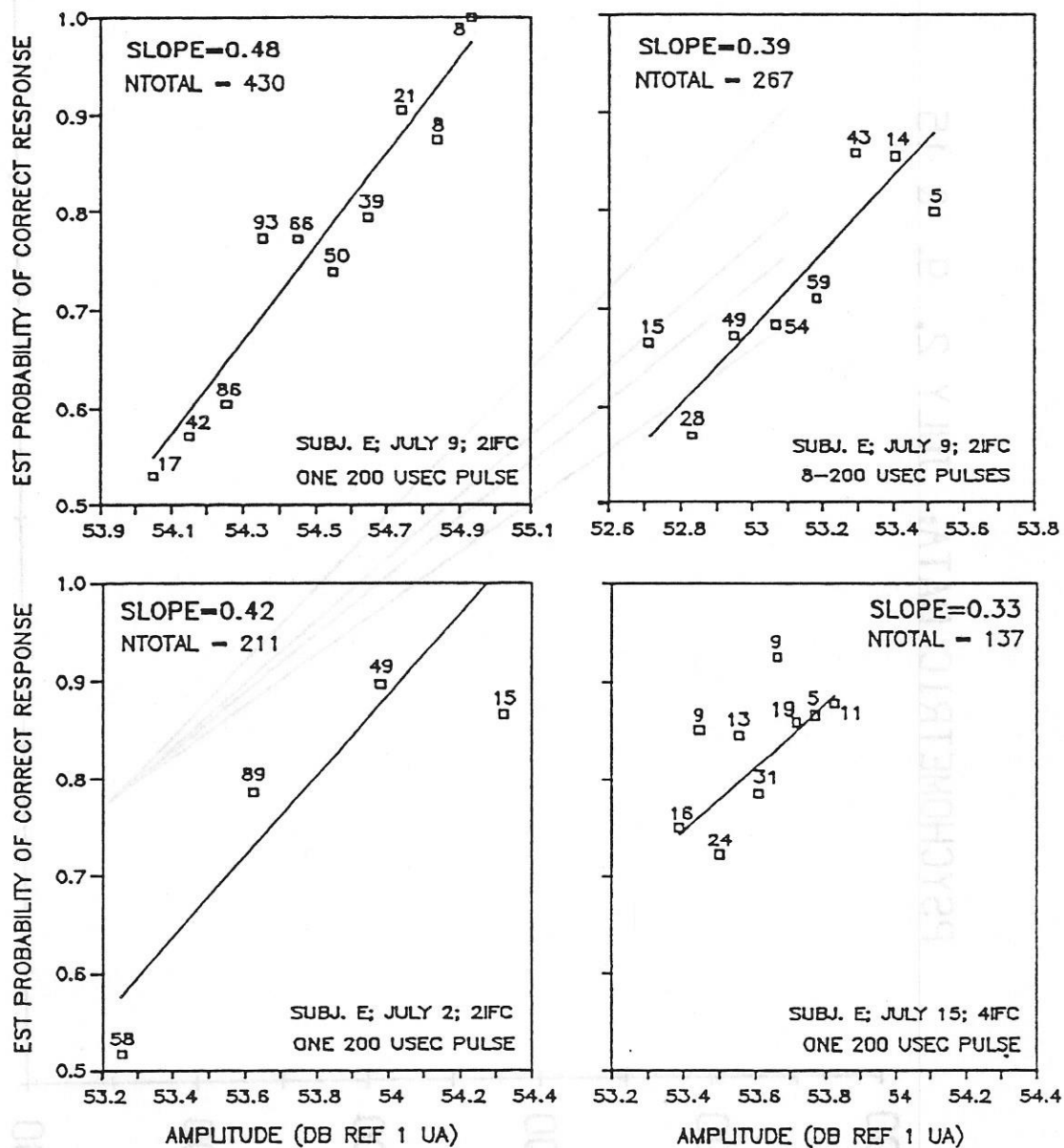


Figure 12. Threshold Psychometric Functions from One Subject

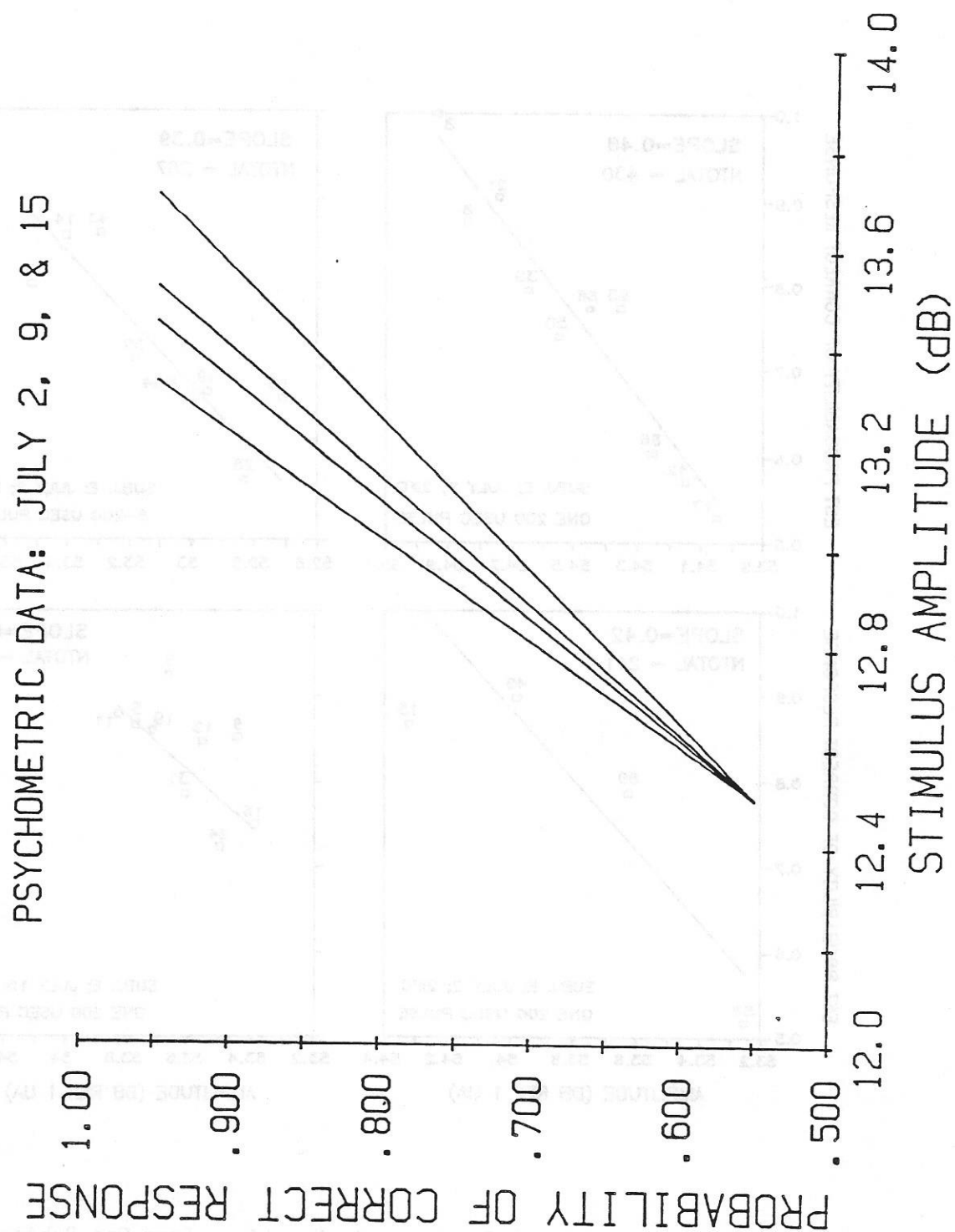


Figure 13. Data From figure 12 Normalized

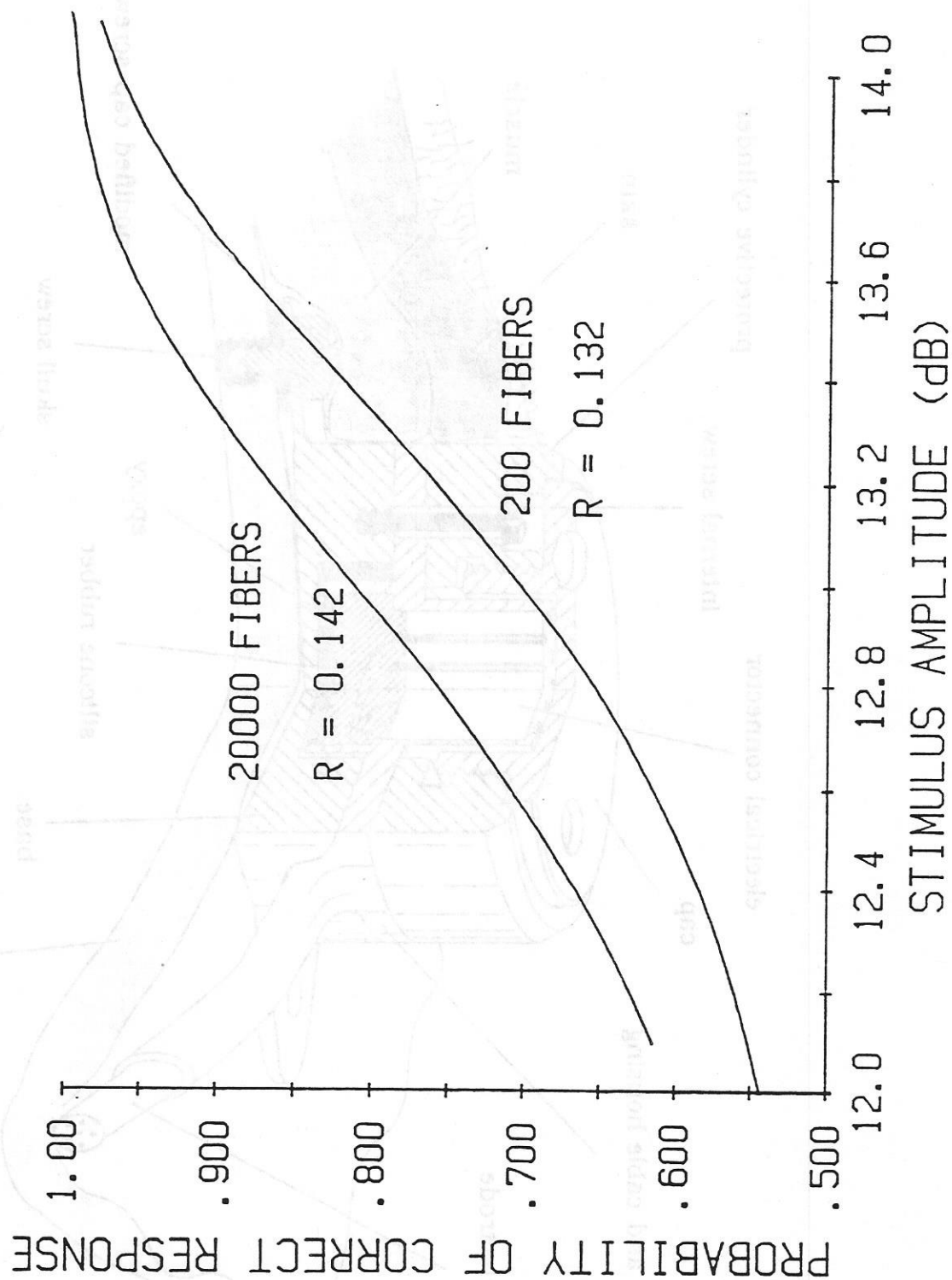


Figure 14. Model Predictions of Psychometric Functions for Extremes of Model Parameters.