

XIII. COMMUNICATIONS BIOPHYSICS*

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A. EVOKED CORTICAL RESPONSES AS A FUNCTION OF "STATE" VARIABLES

Electrical responses evoked by sensory stimuli and recorded with gross electrodes placed in different locations of the nervous system have been of great interest to electrophysiologists for many years. The use of implanted electrodes for recording the electrical activity from unanesthetized preparations has made possible parallel electrophysiological and behavioral studies. A recent report¹ has stated that in unanesthetized cats the evoked cortical response to an acoustic click consists of several components. One of these components, termed ER₁, corresponds to the evoked response from the classical barbiturate-anesthetized preparation. The data reported here are part of a study in which it is attempted to relate the components of the evoked response complex (ERC) to that which may be loosely termed the "state" variables of the organism.

Electrodes (nichrome steel of approximately 100 mu, encased in Teflon) were implanted through small holes drilled in the skull over AI (left side), in the frontal sinus, and in the neck muscle. The electrode in the frontal sinus provided a reference for the electrode in AI, from which the evoked responses were recorded. The neck electrode, also referred to frontal sinus (or to another neck electrode), provided a monitor of the

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electric activity in the neck muscle.

During the recording sessions the animal was mildly restrained by putting him into a loosely fitting bag with a drawstring at each end. The animal's head and tail protruded and the width of the bag was such that although he could not stand, he could lie comfortably in a V-shaped trough. The animal usually remained quiet, appeared to be comfortable, and did not struggle to get free from the bag.

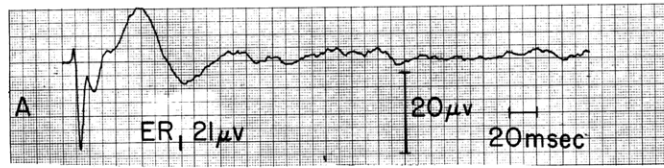
Light flexible leads were soldered to the electrodes, and the leads were then connected to the preamplifiers. The output of the amplifiers was recorded on magnetic tape and was also continuously monitored during the course of the experiment with two dual-beam oscilloscopes. Auditory stimuli were delivered through a loud-speaker directly in front of the animal's head, approximately 8 inches from his nose. For the data reported here, clicks were generated by delivering a 0.1-msec square pulse to the loud-speaker.

During a recording session one can detect changes in state by observing the various electrophysiological responses. When the animal is "awake," the voltage on the neck lead is relatively high and the cortical record (ECG) shows low-voltage, fast activity. In "deep sleep" the voltage from the neck muscle drops below the noise level of the amplifiers and one sees only small twitches^{2, 3} occurring irregularly. The ECG also shows low-voltage, fast activity in this state. There is an intermediate state in which the voltage from the neck muscle is moderately high and in which slow waves predominate in the ECG. This intermediate state may be called "light sleep."

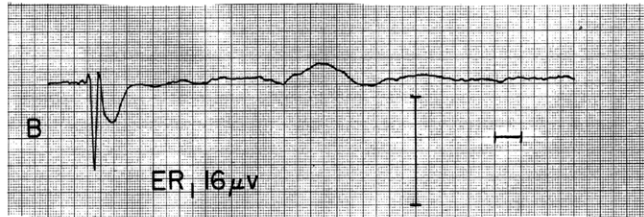
Since the waveforms of the responses differ with the "state" of the animal, indiscriminate averaging of responses is not meaningful. After each recording session, the tape records are played back into an Offner Dynagraph. Sections of this monitor record are then selected for homogeneity. Evoked responses are then averaged over these homogeneous sections of the monitor-record. Within these sections, which are considered homogeneous from the monitor records, the single evoked responses are similar. That is, homogeneity with respect to the neck muscle activity and the on-going cortical activity correlates well with homogeneity of evoked responses when they are considered in more detail and on a shorter time scale.

Figure XIII-1A shows an average of 64 cortical responses computed for the beginning of a recording session. Figure XIII-2A shows a section of the monitor, the ink-written record, from the AI and also from the neck, both referred to the frontal electrode. The averaged response has an initial surface-positive peak, a second smaller positivity, followed by a longer-lasting negative deflection. Since the AI/frontal recording for this "state" is relatively free of background activity, this waveform is visible, even in single traces on the oscilloscope.

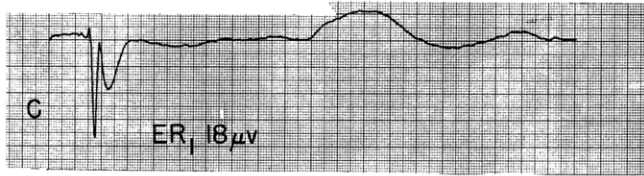
At present, a further partitioning and definition of "state" variables requires a specification of duration of exposure to the stimulus. Some investigators⁴ have reported



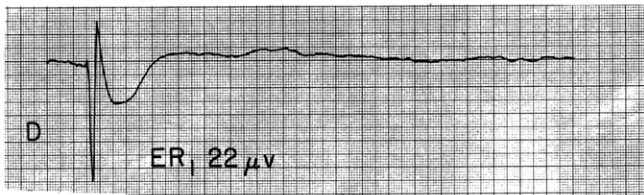
AWAKE
NAIVE



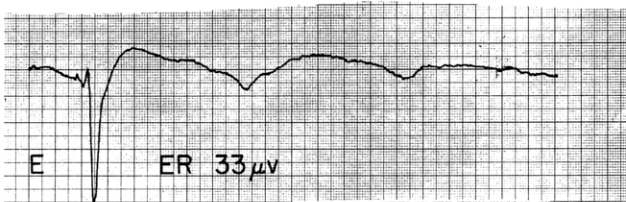
AWAKE
HABITUATED



LIGHT
SLEEP



DEEP
SLEEP



NEMBUTAL

Fig. XIII-1. Averaged evoked responses (N=64) to an acoustic click recorded from auditory cortex (A₁). Reference electrode is in the frontal sinus. Note the changes in form of the averaged response as a function of "state." Stimulus rate, 1/sec.

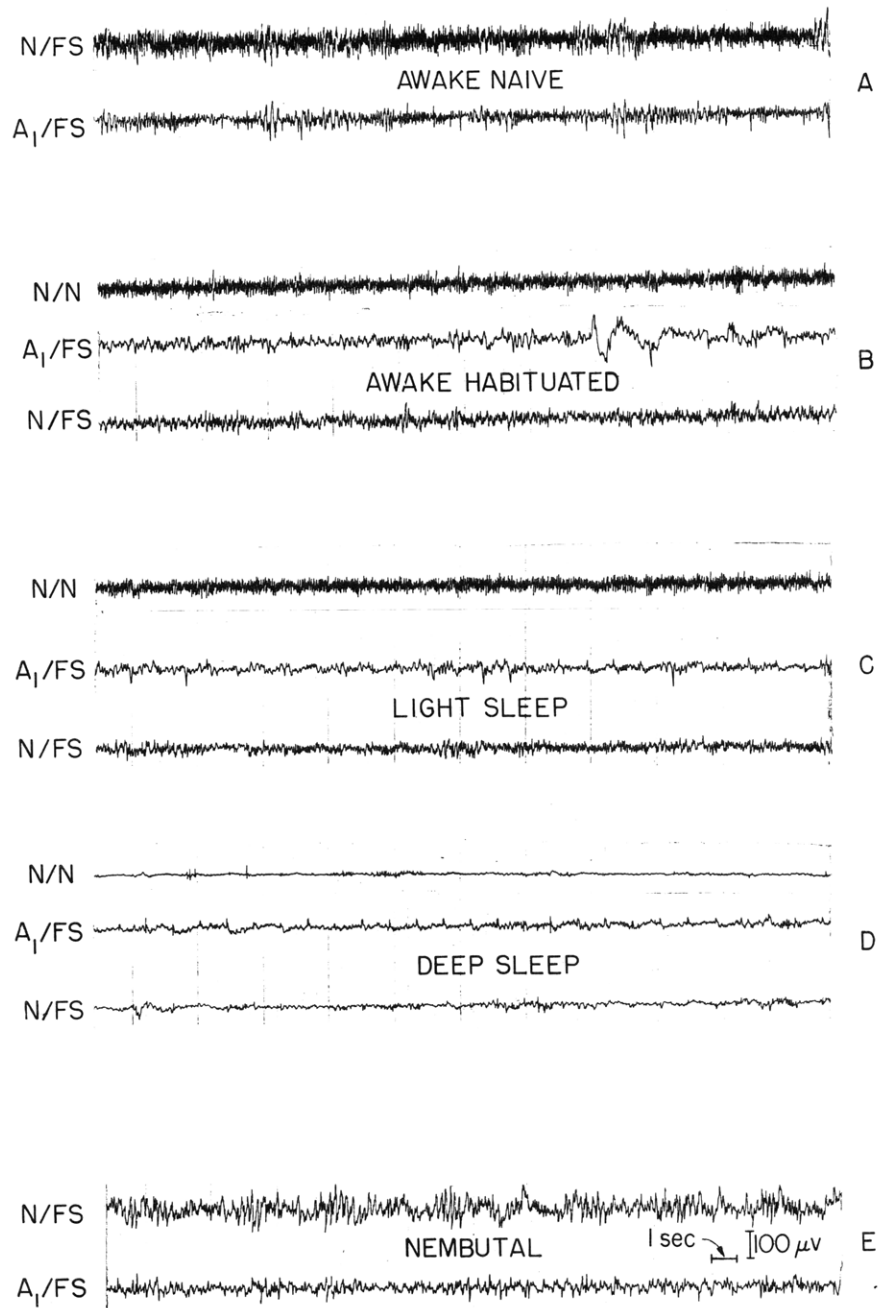


Fig. XIII-2. Samples from monitor records. (N/FS, neck with respect to frontal sinus; N/N, neck with respect to another electrode also in the neck muscle; A₁/FS, auditory cortex (A₁) with respect to frontal sinus.) Notice the quiet base line for N/N in sample labeled "sleep." The samples are selected from the section of tape over which the respective averages are taken.

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a high degree of lability of the evoked response from the unanesthetized animal. After prolonged, unchanging stimulation, the evoked response is said to decline in magnitude and even to disappear entirely. After behavioral arousal, brought about by a change in the stimulus, or by some other alteration in the animal's immediate environment, the response is said to reappear. This "state" is referred to as "habituated." Our animal was exposed to a click stimulus at a rate of 1/sec for a period of more than 24 hours. During the 24 hours, preceding the beginning of recording, the animal was able to move freely in the soundproof room, that is, he was not "wired-in" to the amplifiers. Following this initial 24-hour period, he was placed in the canvas bag, the electrodes were connected, and responses were recorded for approximately 12 hours.

Figure XIII-1B shows an average of 64 cortical responses after the prolonged exposure. Figure XIII-2B shows a section of the monitor record. For this "state" the long-lasting negativity is no longer present in the response, and neither is it present in the single traces viewed on the oscilloscope. During this recording session the negativity did not return when either wideband noise or light was introduced, nor did the entrance of the experimenter into the room, with resultant arousal, lead to the reappearance of the negative component. On the other hand, the presence of an ER_1 of comparable magnitude to that shown in Fig. XIII-1A suggests that the changes in the waveform are probably not a result of changes in the acoustic stimulus or middle-ear muscle activity.

Figure XIII-1C shows the average of 64 evoked responses for the "state" referred to as "light sleep." Figure XIII-2C shows a section of the monitor record for this average. The response in this state differs slightly from the "habituated" state, except for the presence of a very late negativity with a latency of approximately 170 msec.

Figure XIII-1D shows an average of 64 responses for the state described as "deep sleep." Figure XIII-2D shows a section from the monitor record for this average. The neck activity has all but disappeared and one sees only occasional irregular twitches. The evoked responses are now easily seen on the cortical monitor, but the averaged response shows that the magnitude is slightly greater and that there is a sharp negativity that follows the ER_1 very closely. The second positivity, seen in the previous averages, is now broader and slightly larger in magnitude.

Finally, Fig. XIII-1E shows the average of 64 responses after nembutal (0.06 mgm/kgm) was injected into the peritoneal cavity. Figure XIII-2E shows the monitor record, a pattern typical of activity during light anesthesia. The averaged response is also typical of a lightly anesthetized animal, showing only an ER_1 with subsequent repetitive activity.

Our results may be summarized as follows. In the awake "naive" state the full range of components shown by Kiang, Neame, and Clark¹ is present. In the "habituated" and "light sleep" states the long-lasting negative component drops out, leaving the earlier components relatively unchanged. In the "deep sleep" state the ER_1 becomes somewhat

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larger and is followed by a sharp negativity. Finally, under barbiturate anesthesia, all components drop out except the ER₁ which is not distinguishable from the ER₁ in an awake, habituated, or lightly sleeping animal. Although these data are preliminary in that they represent a detailed analysis for only one preparation, corroborative evidence has been seen in other animals.

D. C. Teas, N. Y-S. Kiang

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B. JOINT PROBABILITIES IN FIRING PATTERNS OF A SINGLE NEURON

The nervous system often exhibits electrical activity during complete absence of externally controlled stimuli. During presentation of discrete stimuli at slow rates, the on-going electrical activity in a sensory system seems perturbed for several hundred milliseconds after stimulus presentation, and then returns to a "spontaneous" level.

In the past, in examining these phenomena at the level of the firing pattern of a single neuron, we have used several different measurements that essentially determine the probability of firing at a particular time relative to the stimulus, or relative to the previous action potential.^{1,2} We report here on some new measurements that serve to examine the effects of two earlier events (either stimulus and action potential, or two action potentials) on the probability of firing.

Data from single units are obtained with microelectrodes, and recorded on magnetic tape for subsequent processing with the TX-0 digital computer. In the examples shown below, tungsten microelectrodes were used to isolate neurons in the auditory cortex (AI) of lightly anesthetized (nembutal) cats.

Two simple joint probability measurements are schematically indicated in Fig. XIII-3. In each case the indicated measurement is made for a large number of action potentials. Joint probability relationships are demonstrated with the use of a

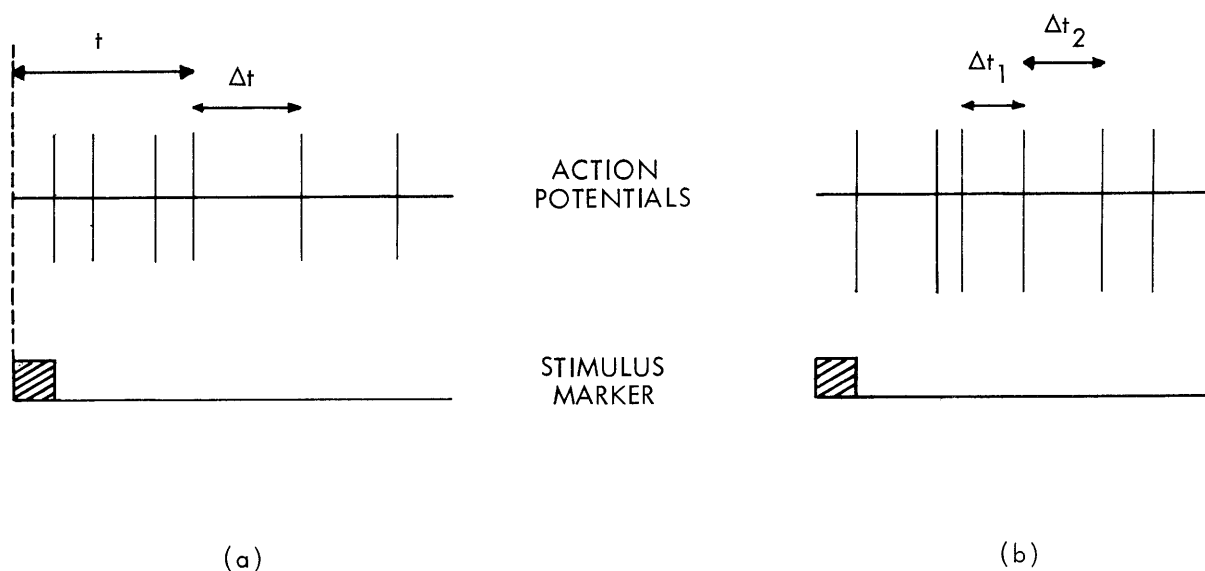


Fig. XIII-3. Diagram of the two joint probability measurements discussed here.

two-dimensional plot on which a particular pair of measurements represents a single point. Thus we can plot either: (a) Δt vs t , or (b) Δt_2 vs Δt_1 . In the first case we examine the correlation between Δt , the interval between two successive spikes, and t , the time since the most recent stimulus. In the second case we examine the correlation between Δt_2 , the second of two successive intervals, and Δt_1 , the first interval. (The restriction to successive intervals is arbitrary. We would expect departures from independence only for a relatively short time span. If two well-separated intervals were examined in this way we would expect complete independence.)

The actual form that a joint probability display takes is shown in Fig. XIII-4. The plot consists of a raster of 64×64 points, whose intensity indicates the number of measurements falling into that particular category. Arbitrary arrangements of the numbers 0-8 are displayed on a field of "1"'s in Fig. XIII-4. As in our other processing arrangements, the time resolution (or bin width) is under control of the operator.

It is interesting to note some properties of such a joint probability matrix. For example, the conditional measurement of Δt vs t can be simply related to the Post Stimulus Time (PST) and Interval histograms with which we previously characterized unit firing patterns. (For definitions of these terms see Gerstein and Kiang¹ and also Fig. XIII-1 of a previous quarterly report.³) If the matrix Δt vs t is added column by column, the resulting set of 64 numbers form the

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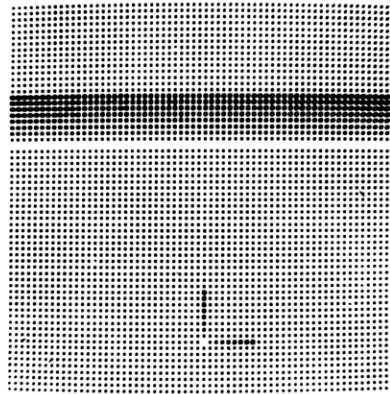


Fig. XIII-4. Display used for joint probabilities. Field of "1"'s, arbitrary arrangements of 0-8.

PST histogram of the data. Similarly, if the matrix is added row by row, the resulting set of 64 numbers form the interval histogram of the data. These properties are useful in interpreting the joint distribution.

The matrix of Δt_2 vs Δt_1 has somewhat different properties. In this case either addition by rows or by columns must result in the same set of 64 numbers that form the interval histogram. If a new (symmetric and suitably normalized) matrix is generated from these two sets (x_i, y_j) of 64 numbers $(a_{ij} = x_i y_j)$, we obtain the matrix that would occur if Δt_1 and Δt_2 were completely independent. Comparison of this constructed matrix and the experimental matrix thus allows a rapid check for systematic departures from independence.

Furthermore, if independence of Δt_1 and Δt_2 is assumed, it can be shown that summations of the matrix elements along the two diagonals are related to: (a) the autocorrelation function of the interval histogram, and (b) the convolution of the interval histogram with itself. The extent to which these relationships are fulfilled can be used conversely to investigate the degree of statistical independence.

Joint probability analyses of two units from the auditory cortex of anesthetized cats are shown in Figs. XIII-5 and XIII-6. In each case the data taken during the presentation of 1/sec clicks can be compared with spontaneous activity.

The PST and interval histograms for unit 106-1 have been shown previously.¹ In the nomenclature previously used,³ it is a (-) unit, with a dip in the PST histogram for approximately 100 msec after the stimulus. The dependence of Δt on t for this unit is shown in Fig. XIII-5. The features that correspond to the PST and interval histograms can readily be picked out: There are few events in the columns following the stimulus, there are many events in the rows representing small intervals. In this case, not much more useful information can be obtained.

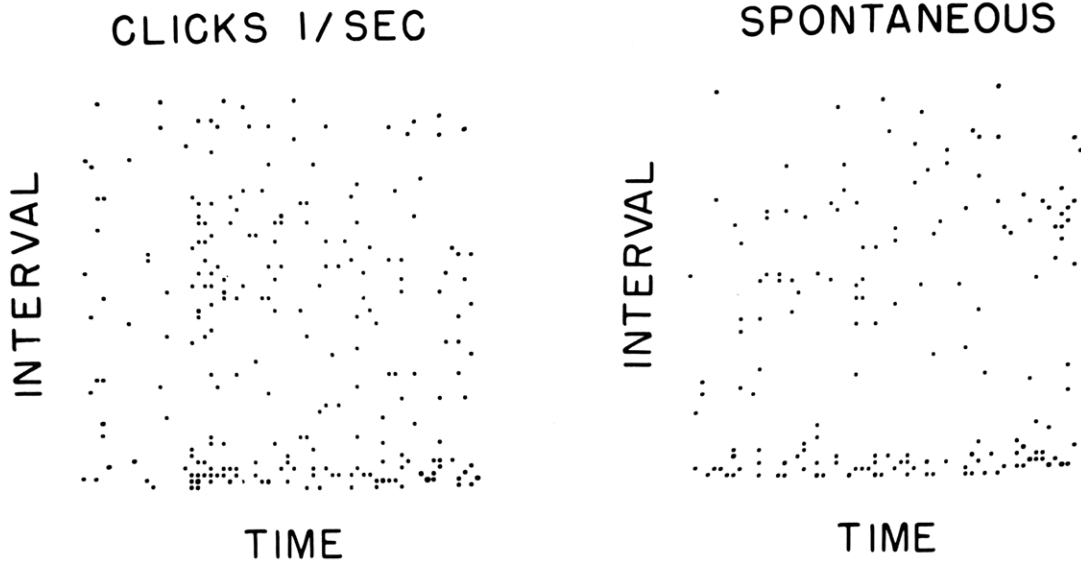


Fig. XIII-5. Joint $\Delta t, t$ distribution for unit 106-1.
(Bin width, 8 msec.)

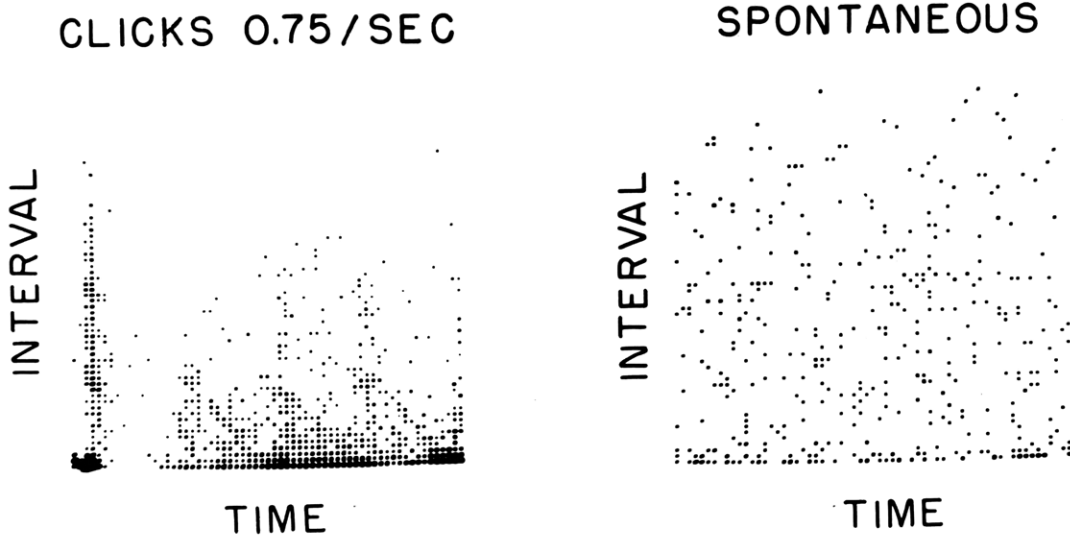


Fig. XIII-6. Joint $\Delta t, t$ distribution for unit 116-1.
(Bin width, 8 msec.)

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A more interesting situation is shown in Fig. XIII-6. The PST histogram of unit 116-1 has been shown previously²; it is a (+) unit, with an increase of activity immediately after the stimulus, and two or three later peaks of activity. These peaks are also visible as columnar structure in Fig. XIII-6. Also, there seems to be diagonal structure (rising towards the left) associated with each peak. This implies that in a certain number of instances, the second action potential is well time-locked to the stimulus, while the first action potential can occur at various times.

Although no figure is shown, several units have been examined for the dependence of Δt_2 on Δt_1 . In the small number of units that have been processed there appears to be approximate statistical independence between the values of successive spike intervals. Considerably more work is required in order to become familiar with various spike patterns that have been processed in this way.

G. L. Gerstein

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C. SHORT-TIME AFTEREFFECTS OF NOISE ON AUDITORY NERVE RESPONSES

Acoustic stimuli produce effects in the periphery of the auditory nervous system which outlast both the stimulus and the evoked neural response that is recorded with gross electrodes. Previous studies have demonstrated that the amplitude of the auditory nerve response to a click (N_1) (recorded with gross electrodes) is reduced, if the click is preceded by either another click,¹ a burst of noise,² or a burst of high-frequency tone.³⁻⁵ The response amplitude increases monotonically with increasing time interval, T , between the first stimulus and the test click; response amplitude decreases monotonically with increasing intensity or duration of the first stimulus. If the first stimulus is a low-frequency tone, the response has a supernormal amplitude for certain values of T .⁴⁻⁶ All of these earlier workers report that the cochlear microphonic potential, CM, in response to the test click is unchanged by the preceding stimulus as long as very high intensity stimuli are not used. More recent reports confirm this finding.^{7,8} In the work reported here we have attempted to describe the aftereffects of low and moderate intensity wideband noise as a function of several stimulus parameters. The intensity and duration of the noise bursts have been limited so as to produce aftereffects lasting

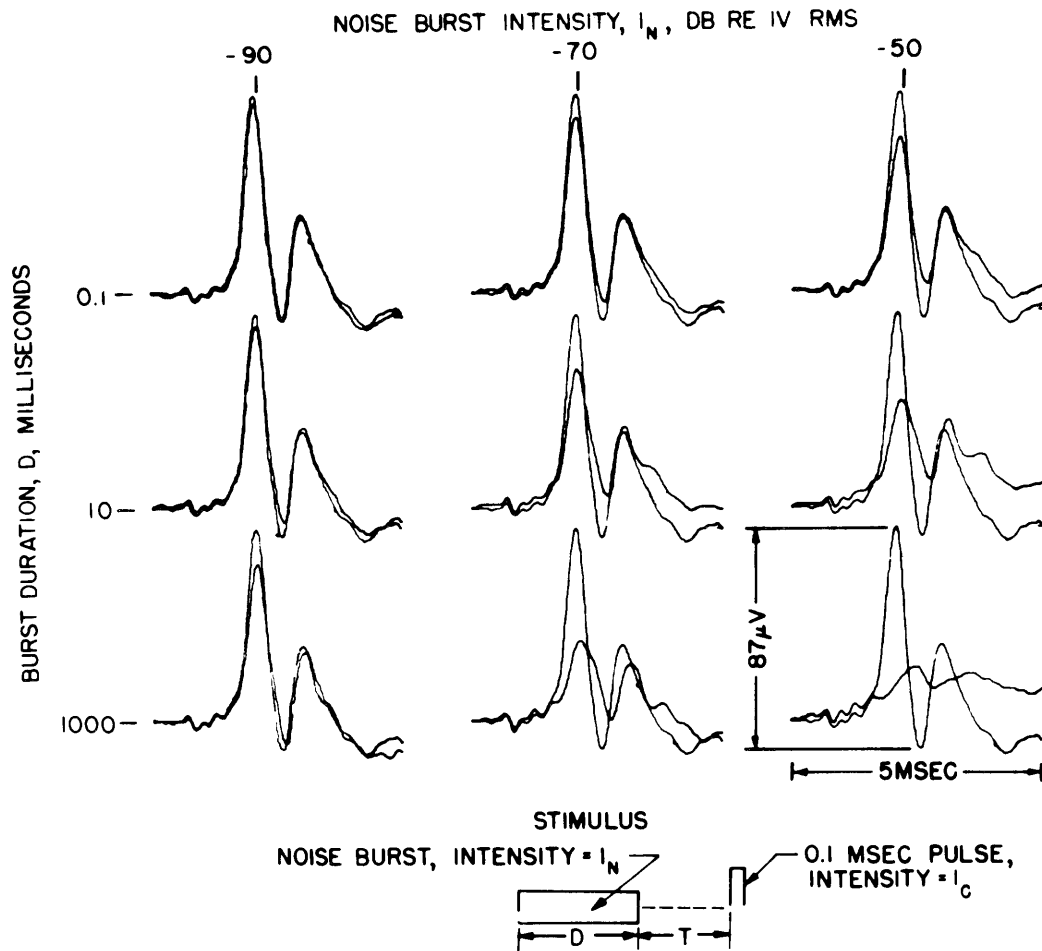


Fig. XIII-7. Averaged responses to clicks with and without a preceding noise burst for various values of burst intensity and duration. The larger trace in each case is the control response. Number of responses averaged for each trace, 32; T and I_C constant, with $T = 10$ msec; $I_C = -80$ db re 3.9 volts; $V_{DL} = -100$ db. (Cat O.)

less than 10 seconds.

Responses were recorded from anesthetized cats with a wire electrode placed on the bone near the round window; a reference electrode was connected to the headholder. Stimuli were delivered with a PDR-10 earphone connected to the external meatus by a plastic tube.

The stimulus configuration is drawn at the bottom of Fig. XIII-7. The noise burst was generated by a General Radio 1390A noise generator (bandwidth 20-20,000 cps) that was gated by an electronic switch. The rise and fall times of the noise burst were approximately $10 \mu\text{sec}$. All noise-intensity measurements are referred to a 0-db level corresponding to 1 volt rms at the terminals of the earphone. (The voltage measurement

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was made at the output of a lowpass (8 kc, 18 db/octave) filter that was inserted to approximate the lowpass properties of the earphone.) This reference level corresponds to a sound pressure of approximately 120 db re $0.0002 \text{ dynes/cm}^2$. The clicks were produced by applying a 0.1-msec rectangular pulse to the earphone. The pulse polarity was chosen so as to produce a condensation click at the earphone.

A control click was often inserted before each burst-click pattern. If the amplitude of the response to this control click was less than that obtained when the noise burst was removed, the stimulus repetition rate was reduced. Hence, the stimulus pattern was repeated at a rate that was slow enough to avoid any overlapping of aftereffects from one noise burst to the next. As a result, the stimulus repetition rate was varied from one per second to one every 20 seconds, the rate depending on the stimulus parameters. Responses were averaged on the ARC-1 computer.⁹

Averaged response waveforms illustrating the effects of changing burst duration, D , and intensity, I_n , are given in Fig. XIII-7. Each pair of responses is a comparison of the click response obtained with and without the preceding noise burst. The larger response for each case was obtained without the noise burst.

Figure XIII-8 illustrates the dependence of N_1 amplitude on noise intensity for six values of burst duration D . For the range of I_n used, it appears that there is little change in the aftereffect when the burst duration is increased above 100 msec.

The data of Fig. XIII-8 can be replotted as in Fig. XIII-9. For a given response amplitude, an I_n vs D curve can be plotted which might be thought of as an equal aftereffect contour. However, these data only insure equality of the amplitude of N_1 . It may be that different noise burst parameters produce equal N_1 amplitudes, but different waveforms. Figure XIII-10a shows that for one set of four "equivalent" I_n - D pairs, the whole click response waveform is nearly the same. The small differences in the later components of the averaged responses waveforms are significant, however, since these differences do not occur if the noise-burst parameters are unchanged (Fig. XIII-10b).

It is also possible that a set of noise-burst parameters which produces "equivalent" aftereffects for one value of T , may not be equivalent for other values. Figure XIII-11 shows that they are not. The data of Fig. XIII-11 were obtained by finding five different pairs of noise duration and intensity values which produce equal aftereffects with T equal to 10 msec. For the chosen I_c , these equal aftereffects reduced the click response to 78 per cent of its control value. If these I_n - D pairs are used at other values of T , we find that response recovery after a short-duration high-intensity burst is more rapid than after an "equivalent," low-intensity, long-duration burst.

In Fig. XIII-12 a comparison is made of N_1 amplitudes for a set of equivalent noise bursts at three click intensities. The equivalent pairs of I_n and D values were determined at T equal to 10 msec and I_c equal to -50 db. The figure shows that N_1 amplitudes to lower intensity clicks are reduced by a larger percentage, and that the "equivalence"

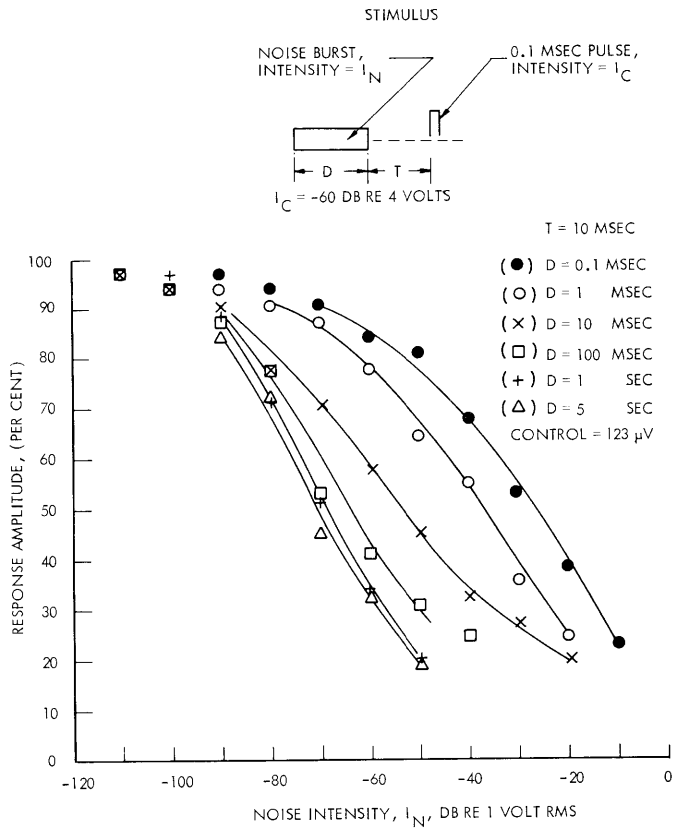


Fig. XIII-8. Peak-to-peak amplitude of N_1 vs burst intensity for several values of burst duration. I_C and T constant; $VDL = -95$ db. (Cat N.)

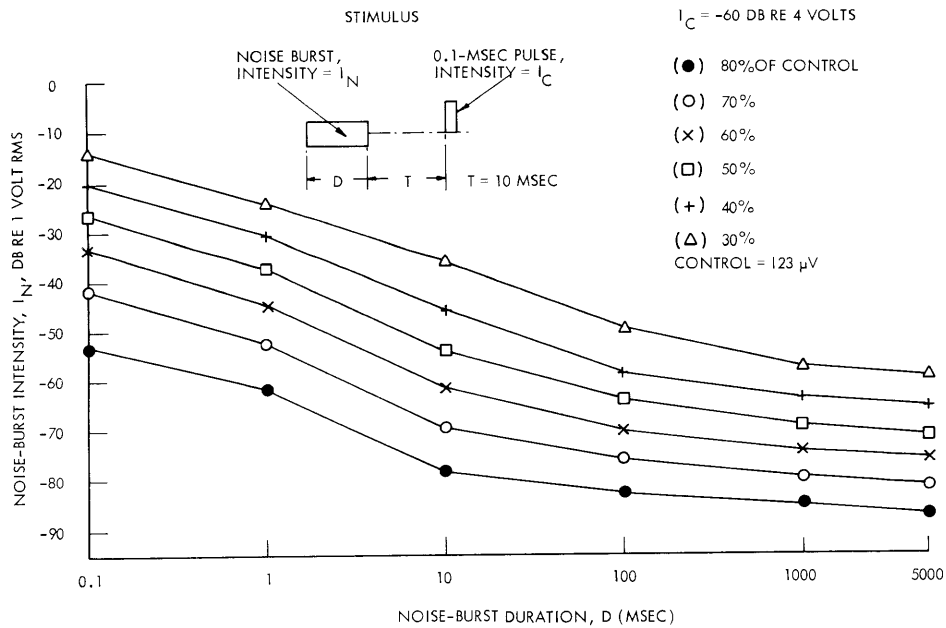


Fig. XIII-9. Equal aftereffect curves obtained from the data of Fig. XIII-8. Several levels of equal aftereffects are shown in the I_N - D plane.

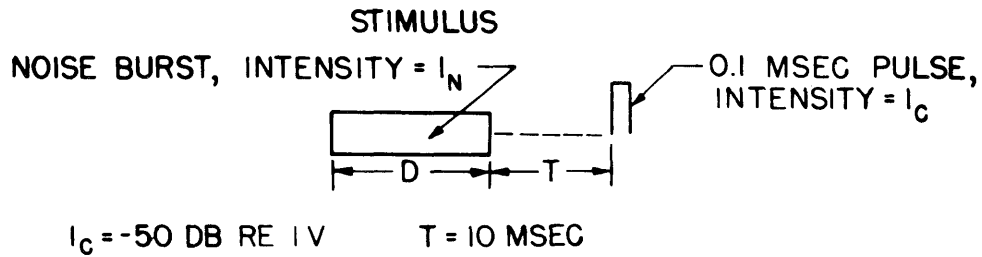
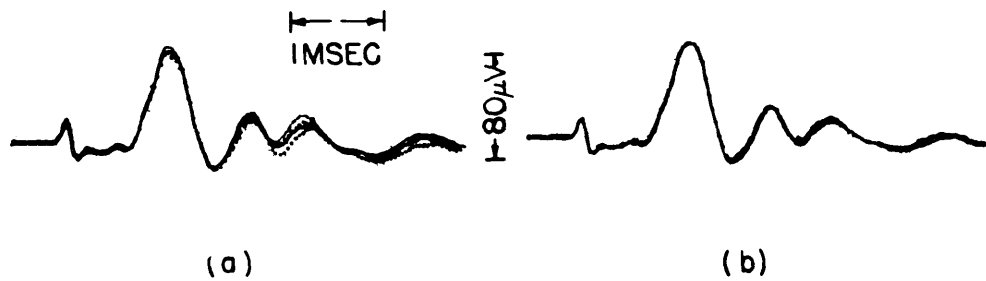


Fig. XIII-10. (a) Superimposed averaged responses for four values of noise-burst parameters which produce equal N_1 amplitudes. Noise parameters ($I_n = -18$ db and $D = 0.1$ msec, -26 db and 1 msec, -55 db and 10 msec, -68 db and 100 msec) produced the effects illustrated in the superimposed traces. N_1 amplitude is 66 per cent of its control value of 140 mv. (b) Four different averaged responses with identical stimulus conditions: $I_n = -55$ db, $D = 10$ msec; number of responses averaged, 32; I_c and T constant; $VDL = -95$ db. (Cat L.)

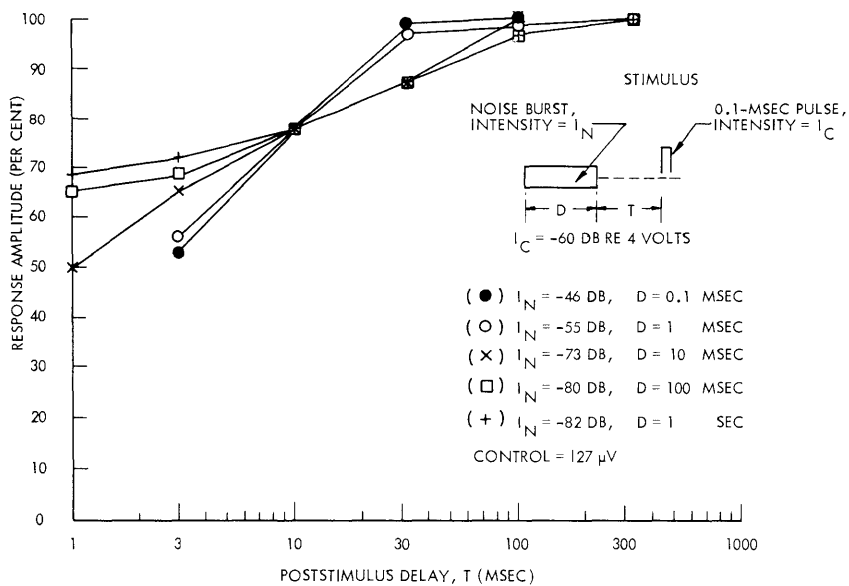


Fig. XIII-11. N_1 amplitude vs T . Pairs of I_n and D values were chosen so as to make the N_1 amplitudes equal at $T = 10$ msec. (Amplitudes are peak-to-peak measurements.) I_c constant; $VDL = -95$ db. (Cat N.)

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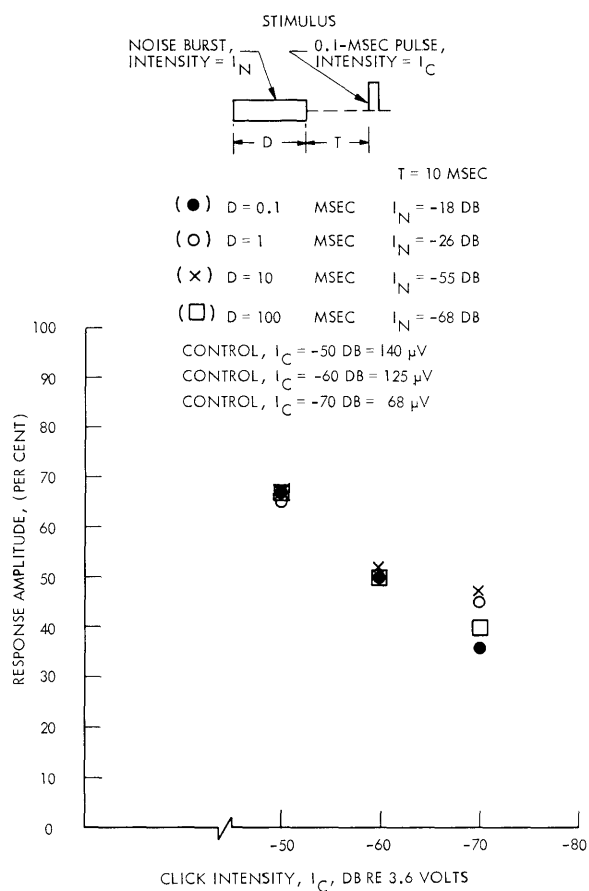


Fig. XIII-12. N_1 amplitude vs click intensity for four pairs of I_N and D . The four noise-burst-duration pairs were chosen to give equal N_1 amplitudes for I_C equal to -50 db. (N_1 amplitudes are peak-to-peak measurements.) T constant; $VDL = -95$ db. (Cat L.)

of the set of bursts is maintained quite well for small changes in click intensity (10 db).

A comparison of equal aftereffect curves in the I_N - D plane is shown in Fig. XIII-13 for two click intensities. Since the sets of curves for the two intensities (differing by 15 db) are roughly parallel (except for the smallest values of D), we can conclude that "equivalence" of a set of I_N - D values holds approximately over this intensity range.

In summary, we have measured the aftereffects produced by a burst of wide-band noise on the response to a click. We have focused our attention on the effects of changing the noise-burst parameters, and on the hypothesis that a set of I_N - D values produces equivalent aftereffects. The data have shown that

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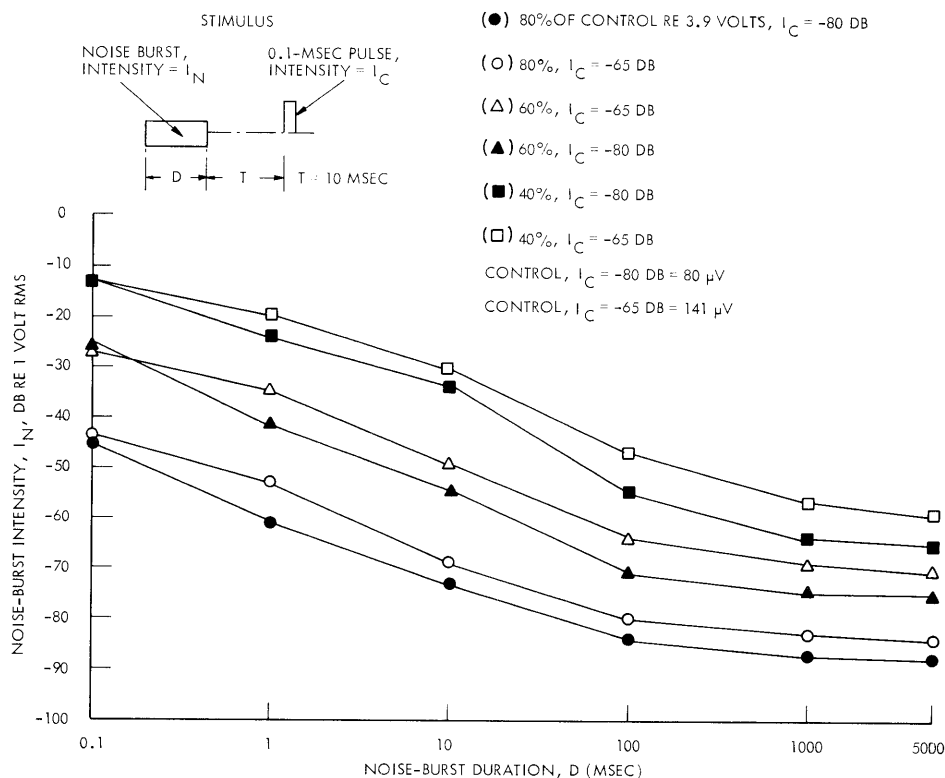


Fig. XIII-13. Equal aftereffect curves for two values of click intensity. (Cat O, VDL = -100 db.)

this hypothesis is not valid when variations in T are permitted, but that it is quite accurate for small variations in click intensity (10-15 db).

J. F. Buoncristiani, W. T. Peake

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