The Sense of Flutter-Vibration: Comparison of the Human Capacity With Response Patterns of Mechanoreceptive Afferents From the Monkey Hand[1]

WILLIAM H. TALBOT, IAN DARIAN-SMITH,[2] HANS H. KORNHUBER,[3] AND VERNON B. MOUNTCASTLE

Department of Physiology, The Johns Hopkins University School of Medicine, Baltimore, Maryland

IT WAS OUR PURPOSE in the studies described in this paper to combine two experimental designs which differ remarkably in method, and in their historical and conceptual development, but which in a larger context have as a common aim the understanding of sensory performance and its relevant neural mechanisms (30). Electrophysiological studies, particularly with the method of single-unit analysis, can now provide precise measures of the neural encoding in first-order nerve fibers of the parameters of peripheral stimuli, and of the successive relay and transformation of that neural replication from periphery to cerebral cortex. They have so far provided little understanding of those cerebral mechanisms which, operating upon the transformed replication of the peripheral event in the primary receiving areas of the cerebral cortex, are thought to lead to subjective sensory experience and its overt behavioral counterparts. Psychophysical studies, on the other hand, seek to establish lawful relations between those experiences and certain physical aspects of the stimuli which evoke them. The results of these quantitative measures of the sensory performance of the intact, behaving organism are therefore of the first importance for sensory neurophysiology, for they establish: *1*) the dynamic range required of the input on the afferent side of the system to account for the output—the measured sensory capacities; *2*) the information about the stimulus which must be preserved in the initial encoding to account for the over-all information transmitting capacity of the nervous system in a particular sensory sphere; and *3*) a basis for determining which of the many codes available to the pulse-operated input system may be of functional significance in the sensory performance measured. It is thought that a continued correlation of the results of these two types of studies will set the limits and establish some of the parameters to be expected of that higher order neural mechanism intervening between initial cortical display and sensory experience, referred to above.

Ideally, the two types of observation should be made in the same organism at the same time. Given the demands of the single-unit method when applied in its quantitative form, and particularly the desired level of control of stimulus parameters, this is not yet possible for somesthesis. For the present we have made the assumption that what monkeys and humans feel with their hands is in principle the same, and that neurophysiological observations made in the one may with some validity be correlated with psychophysical measures in the other, given a precise identity of experimental design in the two cases.

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[2] Visiting Lecturer in Physiology, 1966, from the School of Physiology, University of New South Wales, New South Wales, Australia.

[3] Foreign Fellow of the Public Health Service, 1965–1966, from the University of Freiburg im Breisgau, Germany.

We have chosen to study vibratory sensibility, which has so often engaged the attention of experimental psychologists (5, 9, 18, 24, 27; for older literature see 4). Vibratory sensibility is a derived form of mechanoreception which depends for its unique and readily identifiable character upon the time-varying property of stimuli adequate to evoke it. It thus opens for study the problem of neural coding in the temporal as well as the spatial and intensive domains. We have delivered regularly oscillating mechanical stimuli to the glabrous skin of the hands of human subjects, and measured the frequency-intensity threshold function, and the subjective magnitude estimation of the intensity of the oscillation. In an exactly similar design we have examined the neural activity evoked in large myelinated mechanoreceptive afferent nerve fibers innervating the glabrous skin and some deep tissues of the hands of monkeys. In that which follows, these results are presented and relevant correlations put forward which we believe explain the behavioral capacity of the first in terms of the dynamic encoding properties of the latter.

METHODS

Stimulation

The mechanical stimulator used in these experiments controls the axial movement of small Lucite probes, of diameters 0.5–3 mm, having a contact surface ground to approximately 1/3 of a sphere. The basic stimulator, described elsewhere (12, 29), includes power amplifiers and feedback circuitry to make the axial displacement of the probe tip reproduce accurately the time course of an input waveform. This displacement is independent of the mechanical resistance encountered over the experimental range. Rack-and-pinion and universal-joint devices allow orientation of the probe normal to the curving surface of the fingers and hand over a ±45° range from the vertical.

Input waveforms to the stimulator were derived from two sources. The first was a step generator constructed so that its output voltage increased linearly at controlled rates of rise to a preset level, and was held constant for a preset duration. The second input source was a function generator whose sinusoidal output was algebraically summed with the step-generator output at the input to the stimulator. The amplitude of each source could be adjusted before summing.

The stimulus pattern which was used for all experiments, both on monkey and on man, is shown diagrammatically in Fig. 1. A sinusoidal displacement was superimposed on a stepwise indentation of the skin. The step's rise time was 30 msec—more rapid indentations led to tissue damage. Its amplitude was 930 μ, and its duration typically 1,400 msec. The rest position of the probe was approximately 370 μ away from the surface of the skin so that the first part of the movement was in air, and the skin was indented by about 560 μ. The rest position in relation to the surface of the skin was checked frequently and adjusted when necessary so that stimulus conditions would be constant throughout the study of a fiber, which for many lasted 3 hr. A 370 μ step of short duration was used as a check stimulus. The rest position was adjusted, when necessary, so that the check stimulus just evoked one impulse in the fiber being studied. This proved to be a more precise control than visual observation of contact point. In any event, random variations in the rest position rarely exceeded 10 μ. This proved inconsequential, for tests showed that variations of the total step indentation by 50–100 μ had no effect upon the responses to the superimposed sinusoids, although larger changes did so. In the human experiments rest position was checked by adjusting the check stimulus to evoke a barely perceptible sense of contact. When, in the animal experiments, more than one point in the receptive field was being studied the one-spike test was inadequate, and the rest position for each point was adjusted under microscopic control (16×) so that the check stimulus appeared just to touch the skin.

Sinusoidal stimulation always began 200 msec after the onset of the step movement; its frequency and amplitude were experimental variables. The duration of the period of sinusoidal stimulation varied somewhat with sine-wave frequency. The function generator was gated on for a period of 930 msec, at the end of which it completed the cycle then in progress. Thus the period of sinusoidal stimulation could be longer by nearly one cycle than the gating period. At low frequencies (e.g., 2 cycles/sec) this caused the period of actual sinusoidal stimulation to exceed the standard step duration of 1,400 msec; for these it was lengthened to 1,800 msec.

Although the output of the mechanical stimulator is linearly related to input voltage at low frequencies, there is severe attenuation at high ones. The estimates of sine-wave amplitudes expressed in microns are based upon repeated optical calibrations of the entire system at each frequency used, over the whole intensity range of stimuli delivered.

The initial phase of sinusoidal movement was always the one shown in Fig. 1, a withdrawal from the skin. This constancy of the initial phase is important in the analysis of the data. The movement of the stimulus probe tip lagged behind the driving voltage; it represented a significant fraction of one cycle only at frequencies above 50 cycles/sec. The

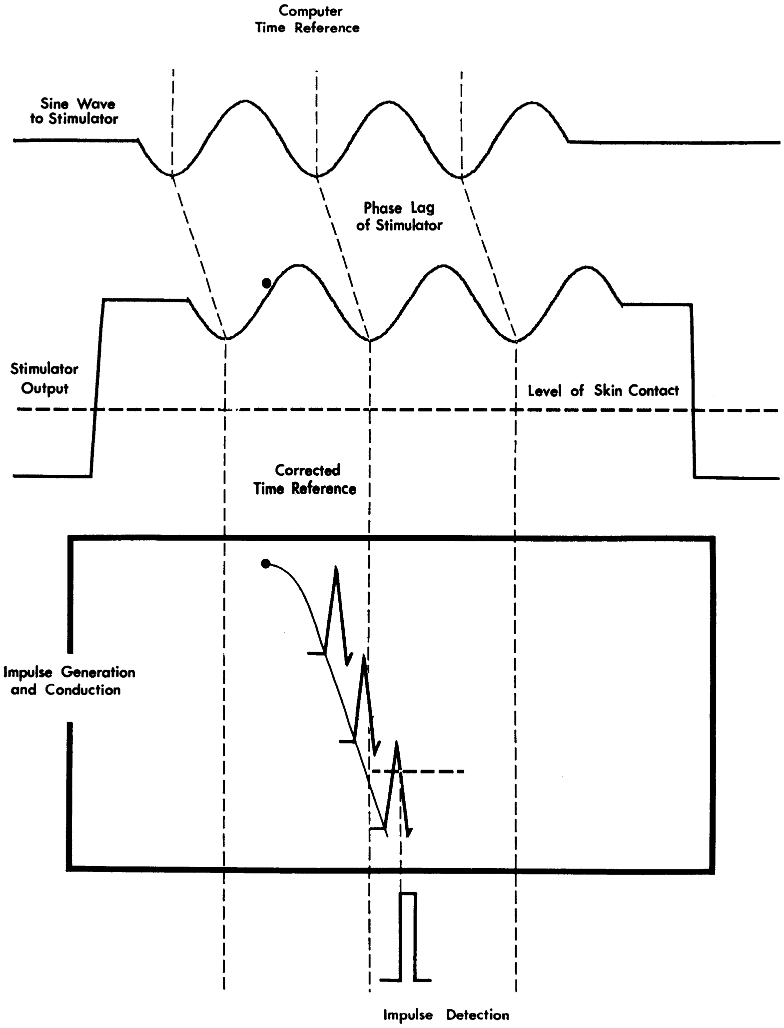


FIG. 1. Diagram showing factors producing phase lag between skin stimulation and recorded nerve impulses. All data recorded in the series of experiments described in this paper have been corrected for the initial phase lag between the source sine wave and movement of the mechanical stimulator, but not for any other sources shown here. Black dots represent an arbitrary instant, chosen for illustration, when a generator potential might be initiated in the nerve ending. Computer recognition of a response would occur only after an action potential is generated, conducted to the recording electrode, and detected by the differential amplitude discriminator. At high frequencies of the stimulating sine wave this delay may be long enough to cause an impulse to be analyzed with respect to a stimulus cycle later than the one which caused its generation. None of the observations or interpretations of this paper depend upon knowledge of the precise relation between impulse and that specific generating sine wave.

lag was measured at each frequency so that corrections could be made in data analysis. It is important to note, however, that there are other sources of phase lag between the stimulus and the recorded response which cannot be readily corrected for (see Fig. 1) and which make it difficult to derive valid inferences from the observed phase relations between stimulus and response. None of the analyses described or the conclusions reached in that which follows depend in any way upon the phase relations between stimulus and response.

Animal experiments

Fifty-two median nerve preparations in monkeys, *Macaca mulatta*, weighing 2.8–3.5 kg were used. Anesthesia at the level of areflexia was induced and maintained by intravenous sodium pentobarbital. Rectal temperatures were maintained at 38 ± 1 C, palmar and forearm skin temperature was usually at 30–34 C, but in some experiments was maintained at 36–38 C. The forearm was fixed by an ulnar clamp, with the hand positioned palm upward in a bed of Plasticine. A skin-flap pool in the middle of the forearm was first filled with Krebs solution, and the palmaris longus muscle removed to expose the median nerve. The nerve was freed from surrounding tissue and placed over a dissecting plate. Its attached connective tissue was removed and the perineural sheath opened by microdissection, thus freeing the natural bundles of nerve fibers. The Krebs solution was replaced by Fisher's C.P. mineral oil. Individual bundles were severed proximally and small filaments further divided until the action potentials of a single fiber were unquestionably identified. Filaments were lifted onto a silver-wire electrode: the second electrode was placed on adjacent grounded tissue. Conventional a-c amplifiers were used. For measurements of conduction velocity the nerve dissection was made in the upper arm, fibers isolated and identified using physiological stimuli to their receptive fields, and the nerve stimulated electrically at the wrist.

Upon isolating a single mechanoreceptive fiber, its receptive field was determined using small glass probes to deliver gentle stimuli, under 16× microscopic observation. For many the fields were mapped onto photographs of the hand, previously prepared, in which each dermal ridge was clearly identifiable. The response properties of each, the basis for classification of the mechanoreceptive afferents innervating the glabrous skin, were determined using the stimulator described above, for hand-delivered stimuli frequently gave equivocal results concerning discharge properties, though with them one could identify with certainty the field of cutaneous termination of a fiber. Fibers selected for detailed quantitative studies had fields located on the glabrous skin, but not extending to the margin of the nail bed, nor overlying skin creases at the interphalangeal joints, nor in a region difficult to immobilize, such as the finger webs. The receptive fields had to be accessible to a normal approach by the probe tip descending from above. Fibers rejected for quantitative study by reason of field location differed in no other property from those accepted. For each fiber studied the 2-mm probe tip was oriented to cover symmetrically the cutaneous receptive field, which as the data of Table 3 show were usually less than 2 mm in diameter, on the fingers. For Pacinian afferents the skin site was chosen at which a high-frequency stimulus entrained the discharge of the fiber, at lowest intensity.

Both the animal and the frame carrying the stimulator were fixed upon a heavy table mechanically isolated from the surround, and particular attention was paid to maintaining a stable spatial relation between probe tip and hand.

Data collection

Once a fiber was isolated, its field determined, and its functional class established, a rapid survey was made of its response at different intensities, for a number of frequencies. For this preliminary "tuning curve" no permanent records of the neural responses were made. By visual inspection of the record displayed on a storage oscilloscope, trace synchronized with onset of each sine wave, the amplitude of the sine wave required to elicit 1 impulse/cycle was determined. Comparison of these results with the more precise determination described below proved that this could be done with considerable accuracy, though the observer usually accepted "perfect following" at a criterion later shown to correspond with probabilities slightly less than 1.0 that an impulse did in fact occur for every stimulus cycle. Such tuning curves were determined by visual inspection alone for a total of 103 fibers. For 30 of these, more detailed studies of the frequency-intensity neural-response relations were made by converting the experimental data to digital form at the time of collection, using a LINC computer. The laboratory interface used with the computer included a differential amplitude discriminator (13), Schmitt triggers for detecting transitions on lines transmitting electrical signs of stimulation, storage registers for preserving the detected information until read by the computer, and a timing system for measuring the intervals between events.

In these experiments data collection was broken into series of 16 or more replications of the standard stimulus pattern, for any selected frequency and intensity of the sinusoidal component. Four kinds of data event reached the computer via three transmission lines: nerve impulses, the initial and terminal transitions of the step stimulus, and positive-going zero crossings of the square-wave output of the function generator. These last gave a reliable synchronization signal in fixed phase relation to each cycle of the sine-wave stimulus (see Fig. 1). A code for every event which occurred between the onset of step stimulation and its ending was recorded, together with the interval of time between it and the immediately preceding event. Time intervals were measured with a resolution of 125 μsec.

The data collected during each stimulus were stored on magnetic tape during the rest period between stimuli (typically 3.6 sec) so that almost the full capacity of the computer's memory was available for storing the response to each stimulus. Since the stimulus waveform was stereotyped and the response consisted exclusively of a series of discrete events, the data stored on magnetic tape constitute a complete description of the experimental results. Analogue tape records of the data were occasionally made to preserve a description of the quality of the nerve impulse being studied, and the certainty of its isolation from other signals: isolation was continually monitored throughout all data collection periods by visual inspection.

In order to provide an immediate basis for modifying experimental plans, interval histograms or cycle time histograms (see below) were often plotted immediately after each set of stimuli. Most analyses were, however, performed later.

Data analysis

All of the digitalized data from the monkey experiments were screened by two simple graphic analyses: an interval histogram and the cycle time histogram. For each, only that part of the neural response which occurred between the first and the last minima of the source sine wave (Fig. 1) was analyzed. Usually data for a series of 16 replications of the stimulus pattern were lumped together for analysis. When the sine-wave frequency was high, however, analyses were cut short at the point of arithmetic overflow in the LINC computer.

Both of these analyses were intended to show the relation between the neural response and the sinusoidal component of the stimulus. The interval histogram, which shows the frequency distribution of the interspike intervals of various durations, permits the recognition in the response of multiples and submultiples of the stimulus frequency. The cycle time histogram, which shows the frequency distribution of occurrence times of nerve impulses with respect to the "start" of the sine-wave cycle reveals the degree of phase-locking even when the over-all nerve impulse firing frequency is below the sine-wave frequency.

The cycle time histogram is similar to the "folded" histogram of Rose et al. (15). The extensive coding of the sinusoidal stimuli and our data lists made the generation of this histogram simple. The list was examined until the first sine-wave cycle code was encountered. The times of occurrence of nerve impulses occurring between that cycle code and the next one were plotted with respect to the time when the first code was recorded, impulses occurring between the second and the third code were entered with respect to the second code, etc.

Neither of these screening analyses provides any information about the time course of the responses throughout the period of sinusoidal stimulation. This information was obtained: *1*) from conventional impulse occurrence time histograms (commonly called poststimulus time histograms) the abscissas of which spanned the entire period of the step stimulation and *2*) from graphs of the instantaneous frequency function. Since the independent variable, time, of the instantaneous frequency function is expressed in discrete uniform increments, it is possible to derive the mean value for each specific time period in a number of replications, thus generating the average time course of the changes in nerve impulse frequency for all responses to a particular kind of stimulation.

Finally, several simple numerical analyses were performed to answer specific questions about the data. These will be described in the text. Most of the analyses discussed were carried out on the LINC computer. Occasionally data were transferred to an IBM 7094 for further analysis.

Many of the illustrations for this report are direct products of the LINC computer, graphs, particularly histograms, being more accurately drawn using the Calcomp plotter than would be possible manually.

Psychophysical experiments

All the subjects were healthy adults, five male and five female, not recently engaged in manual work. Each was seated comfortably, right hand and fingers embedded in a large block of Plasticine. Stimuli were delivered to the pads of the distal phalanges of index or middle fingers, except for the experiments with cutaneous anesthesia, when the thenar eminence was chosen. We found local iontophoretic cocainization to be much more effective here than on the finger pads. A 1,000 cycles/sec signal delivered through earphones masked the faint hum of the mechanical stimulator.

Estimates of threshold for recognizing movement

METHOD I. The step indentation of the skin was maintained constantly for 30–60 sec, as the intensity of the superimposed sine wave was raised smoothly through and above threshold, and then decreased to and below threshold. Five upgoing and five downgoing passes were made during each indentation and threshold determined, for each frequency (7). The subjects were asked not to make estimates of pitch and to ignore the pitch change with intensity (26). Downgoing thresholds were regularly slightly lower than upgoing, and the former appear on the graphs of Fig. 2.

METHOD II. The step indentation and the duration of the sine wave were identical with those used in the animal experiments, 1,410 and 930 msec, respectively. For each step indentation the subject was asked to answer, yes or no, whether he felt an oscillatory component in addition to the step indentation. Successive stimuli were delivered at 6/min or 12/min and the intensity of the sine wave increased or decreased step by step from one stimulus to the next. With this method we noted no differences in threshold depending upon the direction of change in intensity in a series of stimuli. The stimulus frequencies examined in each subject were 2, 5, 10, 20, 40, 60, 100, 150, 200, and 300 cycles/sec.

The iontophoretic method used for anesthetizing the dermis and epidermis of the skin selectively was similar to that described by Rein (14). A 2% solution of cocaine in 80% alcohol was the anesthetic agent. A few drops of 1/1,000 adrenaline HCl were added to each 100 ml of the solution.

The back of the hand rested in a small bath of Ringer solution, which served as one electrode. The second, a small rectangle of gauze, soaked with cocaine solution, was held firmly on the thenar eminence. A current of 0.2–0.5 ma/cm^2 gauze was passed for 8–12 min, and was progressively increased as anesthetization of the skin developed. Our criterion for dermal anesthesia was the inability to appreciate light tactile stimuli, or pinpricks. Anesthesia lasted for about 1 hr.

Estimate of magnitude of the sinusoidal stimulus

Two series of experiments were carried out on five and four subjects respectively, all of whom were familiar with the stimulus paradigm and the imposed task. Each observer had sufficient preliminary training to identify the sinusoidal component of the stimulus separately from the step indentation. Each was asked to rate the relative amplitudes of the sine-wave components in each of a series of 80 stimuli, presented at intervals of 10 sec, and arranged in a nearly random order as regards sine-wave amplitude. At the commencement of the series each subject was presented with three stimuli with an amplitude roughly in the middle of the amplitude range to be covered, and each was so informed. The subject called a number after each stimulus indicating his subjective estimate of the relative intensity of the sine-wave component. Most subjects used scales ranging from 0 to 15–20; no directions concerning scaling were given. Intensity sequences were examined at 40 cycles/sec and at 250 cycles/sec which, it will be seen, approximate the frequencies of maximal sensitivity for the two mechanoreceptive afferents responsive to sinusoidal stimulation. At 40 cycles/sec the intensity range was from 0 to 385 μ; at 250 cycles/sec from 0 to 120 μ. These ranges were limited by the power characteristics of the function generator. In each series 16 equal intensity steps were presented on 5 occasions each.

EXPERIMENTAL OBSERVATIONS

I. *Human sense of flutter-vibration*

THRESHOLD INTENSITY-FREQUENCY FUNCTION. In these experiments we wished to compare the results of psychophysical experiments in man with those of neurophysiological ones in monkeys. It was therefore necessary that the two sets of experiments be made under as exactly similar circumstances as possible. This was especially so for the threshold intensity-frequency function, which has been shown to vary with the locus and area of the skin stimulated (17, 31), skin temperature (28), the age of the subject, the duration of the stimulus (21), contactor size, and the presence or absence of free surround (19, 20, 22), etc. We have therefore repeated this measurement in our own experimental paradigm, and held conditions and parameters identical in the human and the monkey experiments. In our first experiment stimuli were delivered to the glabrous skin of the thenar eminence; step indentations of the skin of long duration were delivered, and the amplitude of a superimposed sine wave slowly increased and decreased until five upgoing and five downgoing threshold estimates had been made for each subject, for each frequency tested (METHOD I, p. 305). Downgoing thresholds were routinely slightly lower than were upgoing ones, and they are plotted by the lower curves of Fig. 2. The results for a single subject are given to the right, the means for 10 to the left. The function is not monotonic with regard to frequency; in the log-log coordinates of Fig. 2 it is fitted adequately by 2 straight lines of different slopes. The variation in the identification of threshold was always much less for a single subject than for all considered together. We did not test frequencies above 300 cycles/sec extensively; the threshold function is known to rise again steeply for higher frequencies, a fact which we have confirmed.

The double-limbed functions shown in Fig. 2 are paralleled by the subjective experiences of our subjects. That is, each reported and we ourselves confirmed that as the frequency shifts through the range from 40 to 80 cycles/sec, at comparable intensities relative to threshold for each frequency tested, there is a remarkable change in the sensation experienced. For the range 5–40 cycles/sec the stimulus is felt as a light flutter of the skin which can be localized accurately. As the frequency of stimulation shifts from 60 to 80 cycles/sec, and above, the sensation changes to one of vibratory hum, seems to shift deep within the hand, and is less accurately localized. For this reason we suggest that this quality of somesthesis be designated flutter-vibration, rather than vibration.

This duality of the sensory experience and the double-sloped functions of Fig. 2 suggested that the sense of flutter-vibration might be served by two sets of afferent fibers, one innervating the glabrous skin and sensitive in the low range of frequency, the second terminating in deep tissues and sensitive in the high range. That this may indeed be the

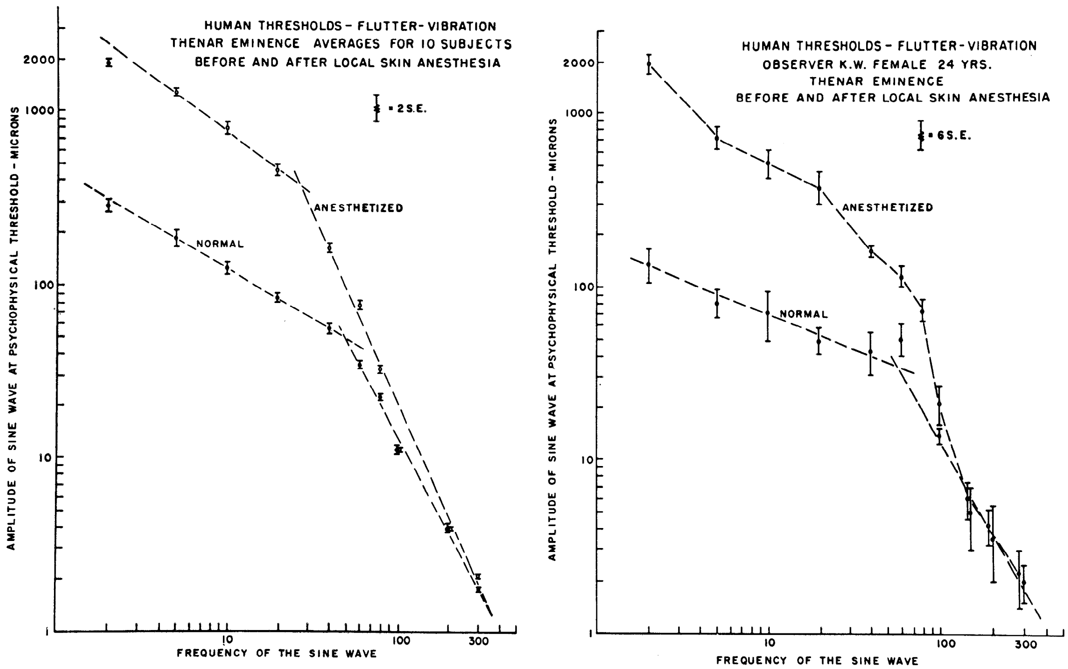


FIG. 2. Relation between the amplitude of a sine-wave oscillatory movement of the skin and the human threshold for the perception of movement, at a series of different frequencies, measured by METHOD I. Stimuli delivered to the glabrous skin of the thenar eminence of the hand. Points on the graphs to the left are the means for 10 observers, those to the right for a single one. Cutaneous anesthesia by cocaine iontophoresis elevated the thresholds for perception of low-frequency stimuli (2–40 cycles/sec) by factors of 5 to 10; sensitivity to high-frequency oscillation was little affected by skin anesthesia. The SE bars on the graphs to the left refer to the total dispersion of all observations by all subjects. Dissociation by cutaneous anesthesia of the double limbed threshold function suggests that the sense of flutter-vibration on the hand is served by two sets of primary afferents, one terminating in the glabrous skin, the other in deeper tissues.

case is indicated by the fact that these two qualities can be dissociated by local anesthesia of the skin. The experiment described above was repeated after cocaine iontophoresis had rendered the glabrous skin insensitive to light mechanical stimuli and to pinpricks. The results are given by the upper curves of Fig. 2, which show that skin anesthesia had no effect on sensitivity to high-frequency stimuli, but elevated the thresholds in the low-frequency range by factors of 5–10.

An alternative interpretation of the result of this experiment is that no dissociation is produced, but that high frequency vibration is more efficiently transmitted from anesthetized to sensitive skin than is low, and that both flutter and vibration sensed on the palmar skin surface of the hand are served by sets of afferents terminating in the glabrous skin. Indeed, the natural period of the skin—the region of the lowest merchanical impedance—is about 200 cycles/sec, although the impedance curve is broadly tuned (17). However, several facts support the interpretation given above, some of which will be documented in later sections of this paper: *1*) no afferents terminating in the glabrous skin are sensitive to high frequency oscillation in the range of intensities required to match the human threshold function curve; *2*) deep tissues bared of skin are sensitive to high frequency vibration; *3*) an afferent fiber type ending in deep tissue is exquisitely sensitive to high frequency vibration; and *4*) there is a subjective shift from superficial to deep in the perceived location of the stimulus with upward shift in stimulus frequency.

A large number of the mechanoreceptive afferents from the glabrous skin which we observed innervated the finger pads. In order to obtain a more direct comparison with neurophysiological findings, we repeated the experiment in humans, this time delivering stimuli to the finger pads, using METHOD II (p. 305), the stimulus pattern illustrated in Fig. 1, which was also used in all animal experiments. The results obtained are shown by the middle curve of Fig. 3, in which the curve for the thenar eminence is also reproduced (upper) for comparison.

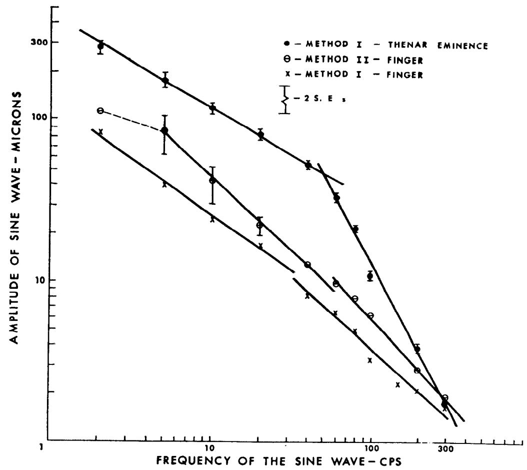


FIG. 3. Comparison of different frequency-intensity threshold functions for the perception of oscillatory movement. The upper curve is reproduced from Fig. 2, for stimuli delivered to the thenar eminence, and was determined using METHOD I (see METHODS section of text). Lower curve plots the results of measurements made with this same method, but with stimuli delivered to the distal pad of the middle finger (5 subjects), while the middle curve indicates the results obtained on the finger with METHOD II (9 subjects). The difference in sensitivity and in the degree of break between the high- and low-frequency limbs of the functions are largely due to differences in the position of the stimulus on the hand. The difference due to method is significant, but small.

The thresholds on the finger are somewhat lower than on the thenar eminence, and the break between the two halves of the threshold function less marked, although the dual subjective impression is similar. It is this function for the finger tip which is reproduced in other figures for comparison with neurophysiological findings. The difference between the two curves obtained is thought to be due to location and not to the difference in method, as the lower curve of Fig. 3, obtained with METHOD I, attests.

SUBJECTIVE MAGNITUDE ESTIMATION. In these experiments a slowly repeated stimulus of the type shown in Fig. 1 was delivered to the finger pad of each subject, and the amplitude of the superimposed sine wave varied from one stimulus to the next in a nearly random order, during a given series. The subjects, who were familiar with the stimulus pattern, were asked to rate the amplitudes of the superimposed sine waves by assigning numbers to them. They recognized and were instructed to ignore the change in subjective pitch which occurs with increasing intensity. Two frequencies, 40 and 250 cycles/sec, were chosen for detailed study, for they are close to the "best tuning frequencies" of the two types of afferents which are thought to serve flutter and vibration, and which are described in some detail later. The subjective magnitude estimations are shown in Figs. 4 and 5. The data have been fitted with straight lines without any consideration of threshold phenomena. The figures of Table 1 show that the results are just as well described by power functions with exponents (n's) close to unity. Our observations are therefore wholly compatible with those of Stevens (18) who, using a different stimulus pattern, found magnitude estimation functions for 60 and 120 cycles/sec to be adequately described by power functions with exponents of 0.95 and 0.83, respectively.

With these observations on the threshold and magnitude estimation functions in hand, we next turned to studies of the first-order mechanoreceptive afferents innervating the hand of the monkey, with these principal questions in mind: *1*) which afferents can account by their sensitivities and dynamic properties for the double-limbed threshold

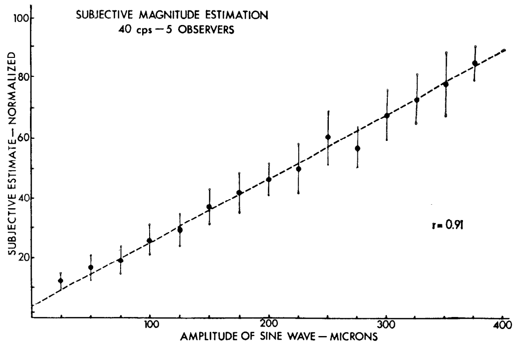


FIG. 4. Relation between the amplitude of oscillatory stimuli at 40 cycles/sec delivered to the distal pad of the middle finger (METHOD II) and human observers' subjective magnitude estimation of the intensity of the flutter. Original subjective scales differed slightly between subjects: they have been normalized for the ordinate of this graph. Points are means of 25 observations, 5 for each of 5 observers. Vertical lines = 6 × SE, for each of these populations of 25 numbers, after normalization. Straight line was fitted without the requirement that it pass through the origin, and no consideration has been given to the shape of this function in the range of very weak stimuli. r = partial regression coefficient; see Table 1.

function curve for flutter-vibration; *2*) what neural code—which aspect of the internal structure of the neural discharge—appears to be pertinent for the perception of movement; *3*) which aspect of the neural discharges could form a basis for frequency discrimination; and *4*) what changes in neural discharge with increasing intensity could provide a basis for the linear magnitude estimation functions shown in Figs. 4 and 5.

II. *General properties of large myelinated mechanoreceptive afferent fibers innervating the monkey hand*

The population of afferent fibers innervating the monkey hand which we studied is restricted both by intent and isolation technique to the 5- to 12-μ band of myelinated afferents, which is known to project into the lemniscal system directly, via the dorsal columns. The dynamic response properties of the smaller myelinated mechanoreceptive fibers are unknown, but their virtual exclusion from the dorsal columns suggests that they play no direct role in the sense of flutter-vibration. Of the former there are three classes which are identifiable, each by a unique combination of the tissue it innervates, its receptive field pattern, its rate of adaptation, and its dynamic response properties. These are indicated briefly in Table 2; each must be considered a candidate to serve the sense of flutter-vibration. They are: *1*) the quickly adapting "movement detectors" which end in the dermal ridges of the glabrous skin: *2*) the slowly adapting "movement and intensity detectors" which also end in the dermal ridges; and *3*) a third set innervating subcutaneous tissues, which are thought to terminate in Pacinian corpuscles.

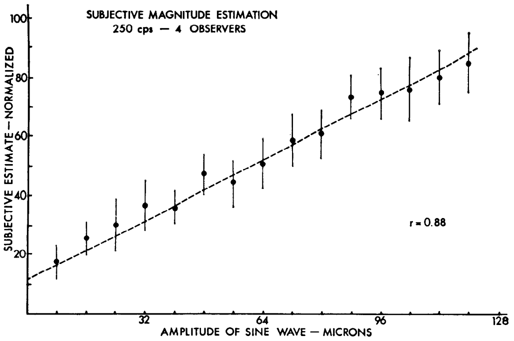


FIG. 5. Relation between the amplitude of oscillatory stimuli at 250 cycles/sec delivered to the distal pad of the middle finger (METHOD II), and the human observers' subjective magnitude estimation of the intensity of the vibration. Original subjective scales differed slightly between subjects: they have been normalized for the ordinate of this graph. Points are the means of 20 observations, 5 for each of 4 observers. Vertical lines = 6 × SE of these populations of 20 numbers, after normalization. Straight line was fitted without the requirement that it pass through the origin, and no consideration has been given to the shape of the function in the range of very weak stimuli. r = partial regression coefficient; see Table 1.

GENERAL OBSERVATIONS. In 53 median nerve preparations we isolated a total of 523 fibers for study. They were chosen from the very much larger sample observed by reason of the isolation and long-term stability of their impulse discharges. Of these, 260 were quickly and 213 were slowly adapting afferents innervating the glabrous skin of the monkey hand, and 50 were Pacinian afferents. Classification was made on the criteria described in the following paragraphs. These numbers give no true measure of the proportions which actually exist in the monkey median nerve, for in different parts of the series we concentrated upon study of one

TABLE 1. *Regression fits: human subjective estimation of the intensity of sine-wave stimuli delivered to the skin*

	40 cycles/sec		250 cycles/sec	
	Log-log	Linear	Log-log	Linear
Partial correlation coef	0.914	0.911	0.911	0.88
Regression coef (n)	0.95	0.211*	1.16	0.637*
SE of reg coef	0.022	0.005	0.03	0.02

* Differences in regression coefficient for linear fits due to fact that dependent variables were normalized while independent ones were not (see Figs. 4 and 5).

TABLE 2. *Properties of large myelinated mechanoreceptive afferents innervating the monkey hand**

Class	Size, μ	Peripheral Termination	Receptive Field	Adaptive Properties	Dynamic Sensitivity
Quickly adapting movement detectors	5–12	Dermal ridges of glabrous skin	Small, continuous graded. Activation by traveling waves limited to 5-mm surround	QA on-off type response to steady stimuli. Require liminal slope for activation†	Exquisitely sensitive to oscillating stimuli in low-frequency range. Best tuning points ca. 30 cycles/sec
Slowly adapting movement and intensity detectors	5–12	Dermal ridges of glabrous skin	Small, continuous, graded. Precise detectors of variations of intensity	Onset transient a function of slope. Succeeding periodic discharge a function of intensity	Steady periodic discharge frequency modulated by sinusoidal stimuli in 2–10 cycles/sec range
Pacinian afferents movement detectors	5–12	Single or small cluster of Pacinian corpuscles, subdermal and deep tissues	Point of greatest sensitivity, but field is unlimited. Activated by traveling waves from great distances	QA on-off type response to step stimuli. Require liminal slope for activation	Exquisitely sensitive to oscillating stimuli in the high-frequency range. Best tuning points ca. 250 cycles/sec

* Mechanoreceptors ending in joint capsules and ligaments, periosteum and deep tissue, and in muscle, not considered in this table. † A small proportion of the movement detectors behave differently as slope changes. They are described in the text, and this response property illustrated in Fig. 6.

or another type, and selected it preferentially. What is certain, from all our observations, is that the quickly adapting afferents outnumber those adapting slowly by a considerable factor. It is equally clear that the Pacinian afferents are far less numerous than either type which ends in the glabrous skin. In our dissections we occasionally isolated joint or muscle spindle afferents; these were readily identified by their distinctive functional properties. Neither is suited to serve the sense of flutter-vibration, and will not be considered further here.

ADAPTIVE PROPERTIES. The glabrous skin mechanoreceptive afferents are readily classified by the presence or absence of a continuing discharge during steady indentation of the skin with the mechanical stimulator. There is no group distributed along a continuum between these two extremes, as regards this property. The large majority of the quickly adapting afferents display the classical behavior—they discharge one or two impulses with the onset of a steady stimulus, are silent thereafter, and again discharge one or two impulses upon its removal; a liminal slope is required for excitation (Fig. 6, left). A small number of this class, which like the larger majority is silent during steadily maintained skin indentation, behaves quite differently as regards the rate of indentation at stimulus onset. As the records of Fig. 6 (right) show, they continue to discharge so long as the stimulus is moving through a segment of space vertical to the skin surface, and with very slow rates of indentation may discharge long trains of impulses. We have not observed that these relatively rare fibers differ from the majority of quickly adapting afferents, as regards their receptive fields or their dynamic sensitivities. The "steady-state" fibers, which discharge nearly regular trains of impulses during steady indentation of the skin, also provide signals which vary with the rate of stimulus application, for the onset transient discharge is sensitively determined by the stimulus onset slope.

As regards adaptation, the Pacinian afferents display properties similar to those of the majority of quickly adapting glabrous skin afferents. As is well known, they discharge one or two impulses at "on" and "off," of a skin indentation, and none during its steady maintenance. A more rapid rate of stimulus application is required as a liminal slope for excitation than is the case for the glabrous skin quickly adapting fibers.

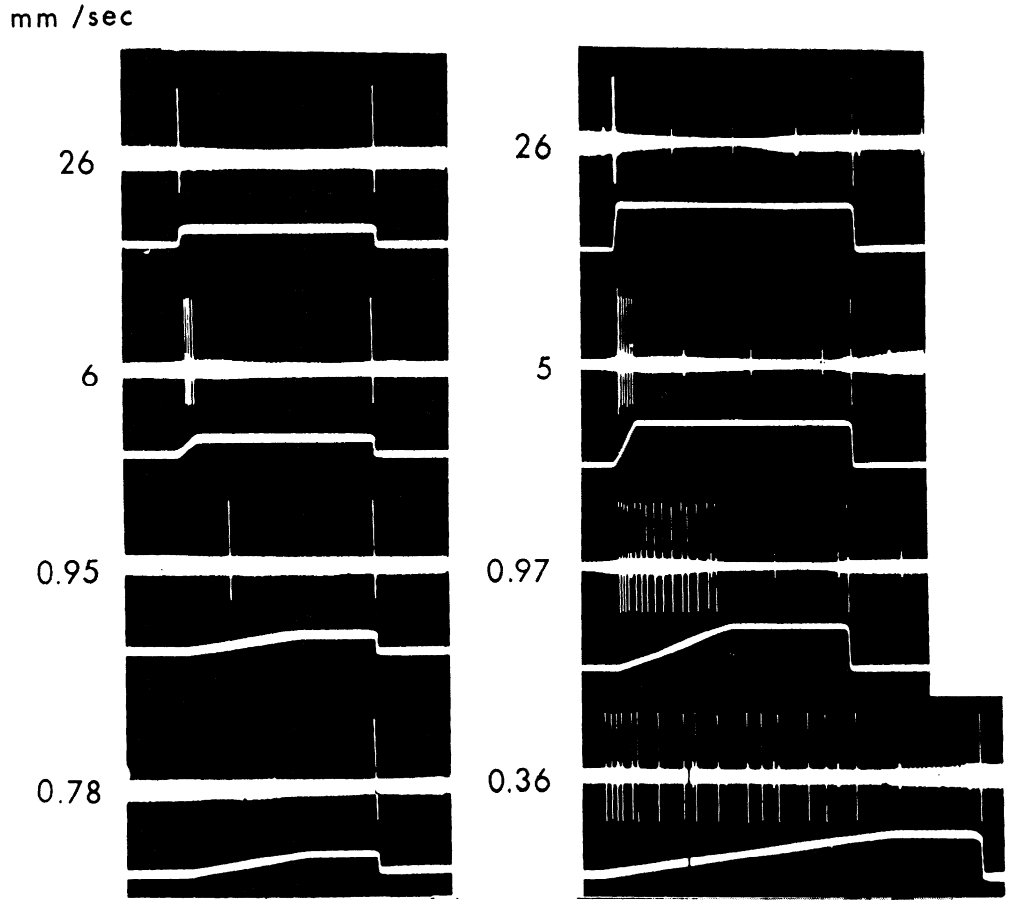


FIG. 6. Records which illustrate the two different discharge patterns observed in quickly adapting mechanoreceptive afferents innervating the glabrous skin of the monkey hand. Fibers of the type whose records are shown to the left display classical on-off behavior, and require a minimal rate of skin indentation at discharge threshold. Those of the type illustrated to the right continue to discharge so long as movement continues, at least over the range of several seconds tested experimentally. The different discharge patterns are not determined by stimulus intensity, which is here supramaximal for each fiber. *Left:* fiber-innervated receptive field on distal pad of thumb. Stimulus duration 610 msec; total skin indentation 320 μ. Stimulus slopes as indicated in mm/sec; critical slope was about 0.80 mm/sec. *Right:* fiber-innervated receptive field on the thenar eminence. Stimulus duration 780 msec; total skin indentation 850 μ. Fibers isolated for study by microdissection of median nerves.

RECEPTIVE FIELD CHARACTERISTICS. Since the hands of monkeys vary in size, which may introduce an error if observations made in different animals are combined, an effort was made to measure as many receptive fields as possible in one animal. Both median nerves were used. After the first experiment the arm wound was cleaned and sutured, a broad spectrum antibiotic given, and the animal allowed to recover from anesthetic. The second and final experiment was done the following day. A total of 104 mechanoreceptive afferents innervating the glabrous skin of the hands was isolated, and their adaptive properties determined using the mechanical stimulator. Receptive fields were outlined using fine glass probes as stimulators, and drawn onto enlarged photographs of the hands. They are thought to be accurate to about one dermal ridge interval, 0.2–0.3 mm. They were all later redrawn onto photographs of the right hand, and are shown in Fig. 7; those of slowly adapting afferents to the left, of the quickly adapting ones to the right. Of the 104 fields, 66 could be projected onto planes tangent to the skin surface without serious distortion; they were measured planimetrically at 800–1,000×areal magnification. The 38 not measured differed in no other way from those measured. The results are given in Table 3. The fields of the two types do not differ significantly in size.

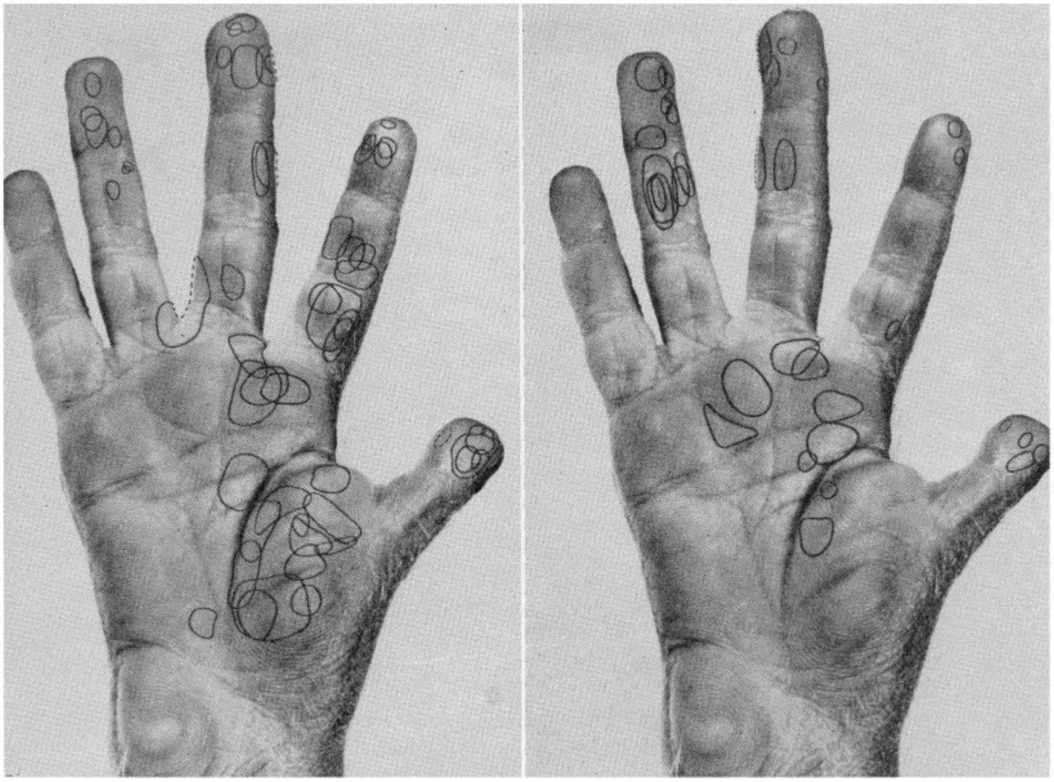


FIG. 7. Photographs of the receptive fields of large myelinated mechanoreceptive afferents innervating the glabrous skin of the monkey hand. All fibers were isolated from the two median nerves of a single monkey (see text). Receptive fields determined as those areas within which local punctate stimulation of dermal ridges elicited nerve impulses in the fiber under study. Fields were outlined for 104 fibers; of these, 91 appear above. Sixty-four were sufficiently planar for accurate areal measurements, which are given in Table 3. The hands of the monkey were photographed before the experiment, and the fields plotted onto large prints; edges were determined under 16× microscopic view. Fields of cutaneous quickly adapting fibers to the left, of slowly adapting ones to the right.

A typical field for either is about 2 mm in diameter if it lies on a finger pad, and about 4 mm on the palmar skin.

The fields shown in Fig. 7 were determined by successive trials of single weak punctate stimuli delivered to individual dermal ridges. The results illustrated in Fig. 8 show that quite a different "receptive field" will be mapped for a quickly adapting mechanoreceptive afferent of the glabrous skin if a stimulus oscillating at its best tuning frequency (30–40 cycles/sec) is used as a testing stimulus. Such a field is many times larger than that determined by punctate stimulation; presumably the receptors are confined to the latter, but are activated by traveling waves propagated across the skin surface. Nevertheless, as shown by Fig. 8, even a stimulus of 400 μ sine-wave amplitude must be within 5 mm of the edge of the field determined by punctate stimulation, to excite the afferent. Making a reciprocal interpretation, such a stimulus will activate these glabrous skin afferents within an area of that radius, and weaker stimuli those in successively smaller areas.

The Pacinian afferents display a quite different sensitivity. As many investigators

TABLE 3. *Receptive field areas*

	Rapidly Adapting Cutaneous Receptors		Slowly Adapting Cutaneous Receptors	
	Distal phalanx	Palm	Distal phalanx	Palm
n	23	18	17	8
Mean, mm^2	3.71	10.47	3.84	12.49
SE of mean	±0.75	±1.83	±0.64	±2.35

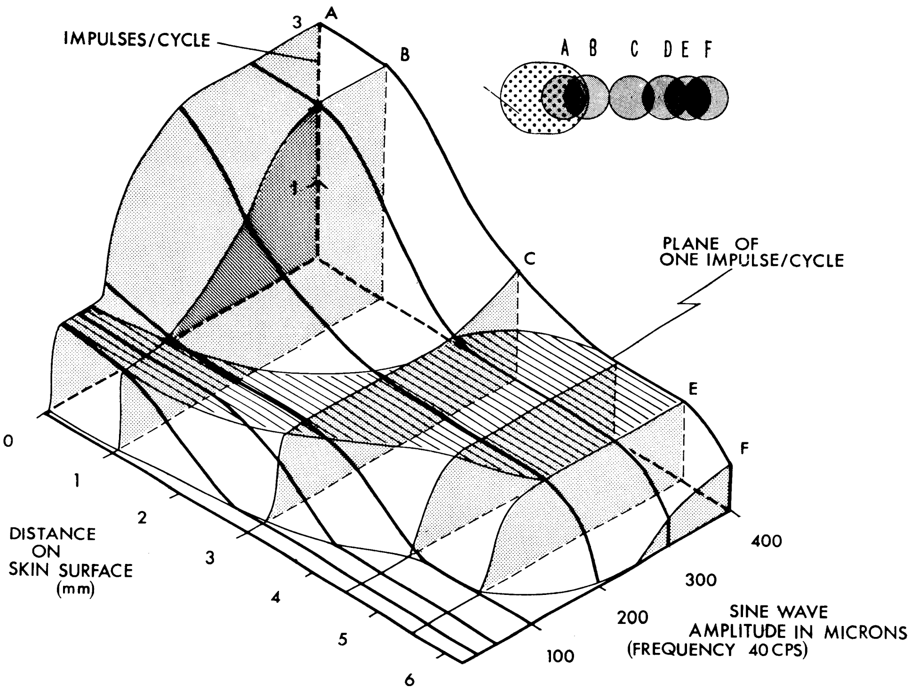


FIG. 8. Results of a study aimed at a reconstruction of the profile of activity set up in a population of quickly adapting mechanoreceptive afferent fibers innervating the glabrous skin of the monkey hand. A single fiber, observed under constant conditions for a long time, is made to occupy a series of positions in the imaginary reconstructed population by delivering stimuli to a series of different positions within and adjacent to its peripheral receptive field. The fiber used for the study, the results of which are shown above, innervated a 6 x 4 mm peripheral receptive field located on the ventral surface of the index finger (dotted area, inset). Intensity series were run at 40 cycles/sec, at each of positions A–F; stimulus probe tip 2 mm. Results are plotted in three coordinates: distance along the skin surface, and hence by reciprocal interpretation position within the neural population; intensity of the sine-wave stimulus; and the response as impulses per cycle. The heavy black lines running from left above to right below thus outline approximately one-half the profile of the evoked neural activity in the population of fibers affected by a stimulus at or near the center of the peripheral receptive field. At 25 μ and 50 μ sine-wave amplitude a population of fibers perfectly entrained is surrounded by a narrow fringe of those failing to follow perfectly. As intensity rises further the discharge in the center of the population becomes disorganized, and fibers there discharge 2 and then 3 impulses/cycle, on the average. With this increase in intensity the active population spreads laterally, and the central zone is surrounded by an expanded belt of fibers which are perfectly entrained, the "plane of 1 impulse/cycle."

have emphasized (8, 10, 16), they are extraordinarily sensitive to transient mechanical stimulation. They are not located in the skin itself, but beneath it. Using brief, quick punctate stimuli one can usually locate on the surface of a finger or the palm a "best point" for their excitation, but beyond that a receptive field in the usual sense cannot be mapped, for if sufficiently strong and quickly moving a stimulus delivered at any locus in a very wide area is adequate. Indeed, if a stimulus probe oscillating at the best tuning frequency for the Pacinian afferents (250 cycles/sec) and of only 5–20 μ amplitude is placed anywhere on the palmar skin it will drive such an afferent which ends in the hand; for one ending in the finger it will do so from any spot on the surface of the finger. This is not thought to be due to activation of widely branched terminals of the single afferent fiber, for Pacinian afferents commonly terminate peripherally in a single corpuscle, or by short branches in a few which are clustered together.

CONDUCTION VELOCITIES. In order to obtain accurate measures of conduction velocities of the different types of fibers identified, a special experiment was performed. The median nerve was exposed for microdissection in the upper arm, and for stimulation in continuity at the wrist. A total of 103

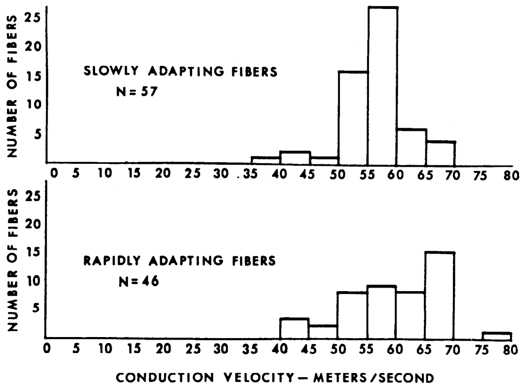


FIG. 9. Histograms of conduction velocities of the two types of myelinated mechanoreceptive afferent fibers innervating the glabrous skin of the monkey hand. All measurements were made in a single experiment. Single fibers were isolated by microdissection of the median nerve in the upper arm, and identified by mechanical stimulation of the skin of the hand. The median nerve was then stimulated at the wrist, where it had been exposed and placed on stimulating electrodes, to obtain the conduction time for each fiber isolated.

single fibers was isolated, identified as to type, and their conduction velocities measured between the wrist and upper arm. We thus avoided the factor introduced by the slight dwindling in axon diameter, and hence slowing in conduction velocity, which occurs in the digital nerves (1). The results obtained are given in Fig. 9. They show that the first-order afferents from the glabrous skin which we have studied fall into the beta distribution (called by some the alpha cutaneous group). Whenever measured, Pacinian afferents have fallen into the same conduction velocity range.

III. *Responses of rapidly adapting mechanoreceptive afferents innervating the monkey hand to sinusoidal mechanical stimulation of the skin surface*

1. GENERAL PROPERTIES OF RESPONSE TO SINUSOIDAL STIMULATION. The general property of the glabrous skin (QAs) and the Pacinian (PCs) quickly adapting afferents which we wish to describe is that for a given frequency of sinusoidal stimulation there is a range of intensities of the sinusoid over which the fiber will discharge in a periodic fashion, one impulse for each cycle of the sine wave. This range of intensities we term the tuning plateau, and its low intensity edge the tuning point. This relation is, however, not indiscriminate; for each fiber the intensity required for entrainment at the tuning point varies in a regular fashion with frequency. A plot of these tuning point intensities versus frequency we term a tuning curve. The position of the tuning curves along the frequency scale is different for the two types of quickly adapting fibers. The cutaneous afferents are sensitive in the low range, with best frequencies at about 30 cycles/sec. The Pacinian afferents are sensitive over the higher range, with best frequencies at about 250 cycles/sec. Sample records of this entrainment for each of the two types are given in Fig. 10. A number of tuning curves are illustrated in a later section, and correlated with the human frequency-intensity threshold function, which they are thought to explain (see Figs. 21, 22, and 24). We wish first to describe certain aspects of the discharge, both at sub- and supratuning intensities, which we believe to be important in a more general consideration of the neural mechanisms in the sense of flutter-vibration.

2. CHANGES IN DISCHARGE PATTERNS OF QUICKLY ADAPTING AFFERENTS AS AMPLITUDE OF THE SINUSOID INCREASES, AT BEST FREQUENCIES. *a. Cutaneous quickly adapting fibers.* The typical changes which occur in the discharge pattern of a cutaneous rapidly adapting fiber, produced by increasing the amplitude of the driving sinusoid, are defined by analyses such as those shown in Fig. 11. The fiber innervated a field 4 mm in diameter; the stimuli were delivered by a 2-mm probe tip located in its center. Thirteen different intensities were studied at the fiber's best frequency of 40 cycles/sec. A sinusoid of 8 μ amplitude evoked only an occasional discharge, smaller ones none at all. When one of 10 μ was delivered, the over-all frequency of discharge was about 16 impulses/sec. These impulses did not occur randomly, but were strictly ordered in time, as the lowermost interval histogram to the left of Fig. 11 attests. They appeared occasionally at intervals equal to the period of the driving stimulus, more commonly at intervals twice or three times as long. The cycle histogram for this same population of responses to the 10 μ stimulus (lower right, Fig. 11) shows that the impulses are narrowly clustered around a

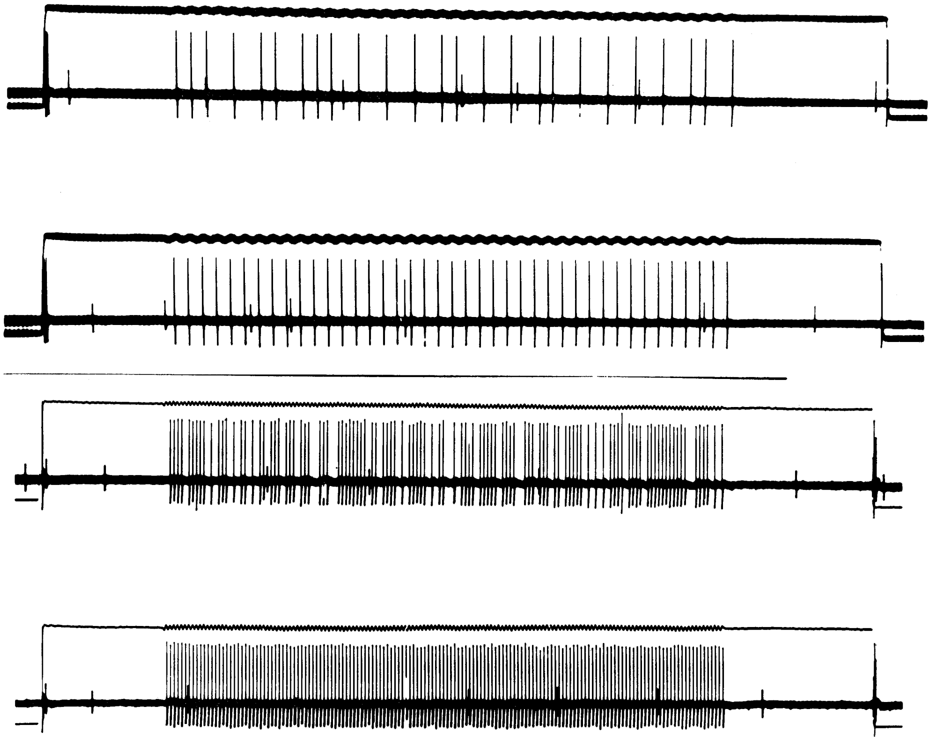
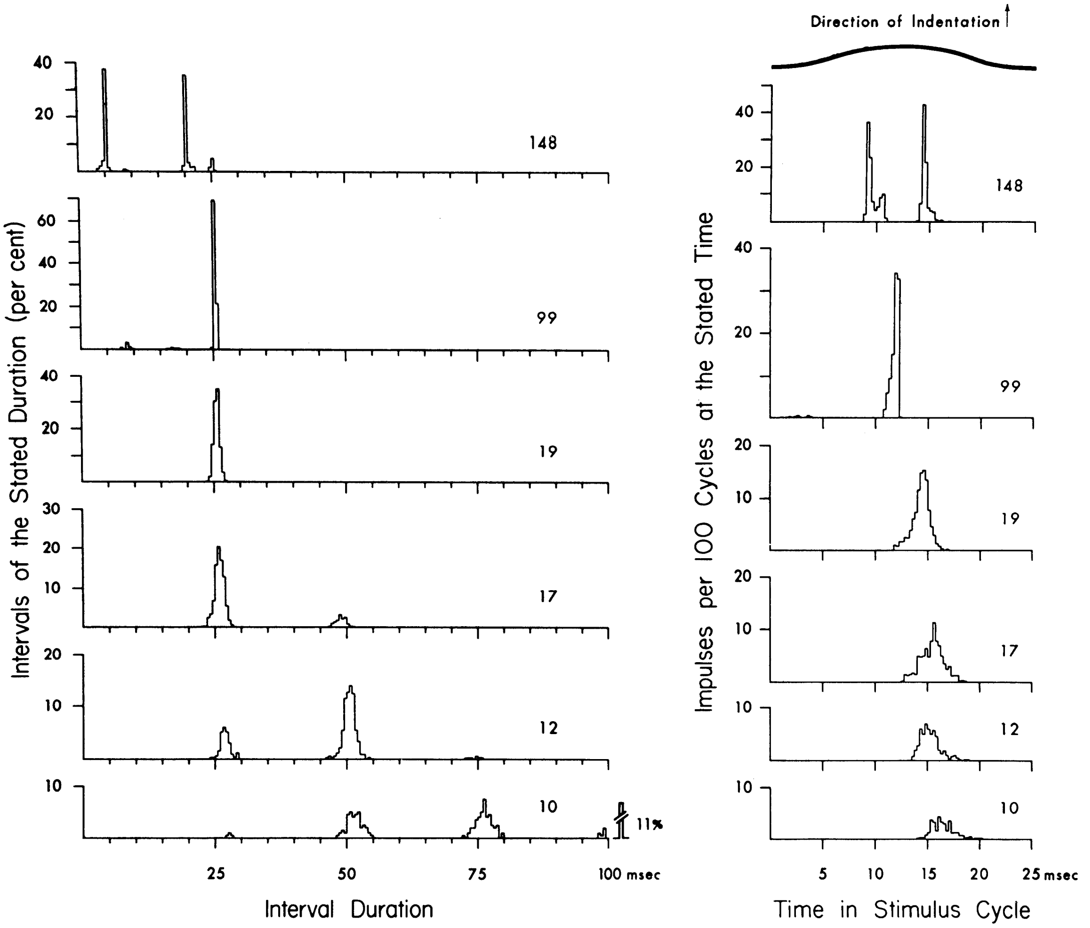


FIG. 10. Recordings of nerve impulses in the two types of quickly adapting, large mechanoreceptive afferent fibers innervating the hand of the monkey, described in the text. For each set of records the upper trace is the electrical analogue signal of the position and movement of the 2-mm-diameter stimulating probe tip. The lower trace is a recording of the electrical signs of nerve impulses in a fiber isolated by microdissection of the median nerve. For each set the step indentation of the skin was 550 μ. The two upper sets illustrate the responses of a cutaneous quickly adapting afferent to a superimposed sine wave of 40 cycles/sec, at 14μ and 18μ amplitude, respectively—just below and just above the tuning point for the fiber. Its receptive field lay in the glabrous skin of the distal pad of the middle finger. The two lower sets of records were obtained, in a similar way, from a Pacinian afferent from the hand. Stimuli were delivered to palmar surface. Frequency, 150 cycles/sec; amplitude of the sine wave 16 μ and 19 μ for the third and fourth sets, respectively. Many other Pacinian afferents had tuning points much lower in amplitude (see Fig. 16). Brief bursts of impulses at on and off of the step indentation barely visible, but present in all records.

given instant in time, relative to the stimulus cycle—a natural concomitant of periodic ordering. This time of occurrence appears here, artifactually, to be just at the peak of the indentation phase of the stimulus; utilization and conduction times have not been accounted for in construction of this graph. They would shift the occurrence to an earlier time on the indentation phase of the stimulus cycle.

With further increases in stimulus intensity the proportion of intervals equal to the stimulus period increased, and those at multiples of it decreased, until with a further small increase in stimulus strength, from 17 to 19 μ, the discharge locked in perfect synchrony, following beat for beat with the stimulus period. This is the tuning point for the fiber, and the range of stimuli between it and those too weak to evoke any response is defined as the zone of demultiplication. The tuning point can also be determined accurately by visual inspection of the response (see METHODS), and tuning curves determined in each of these two ways, by visual and by machine analysis, are presented in later figures.

The table of Fig. 11 shows that with further increases in intensity from 19 μ through 99 μ there was no change in response in terms of the total number of impulses which occurred. That this constancy obtained also for the sequential ordering of the impulses in time was shown by the interval histograms of the responses at 24, 29, 39, 51, and 99 μ, only the last of which is displayed in Fig. 11. This is the zone of the tuning plateau, which is also



Sine Wave Amplitude (in Microns)	148	99	51	39	29	24	19	17	16	12	10	8
Number of Cycles	598	608	606	592	593	592	593	608	605	593	605	607
Number of Impulses	1119	625	606	592	593	592	593	531	425	328	248	87

FIG. 11. Interval and cycle histograms for responses of a rapidly adapting fiber innervating the glabrous skin of the monkey hand. Stimuli delivered at 40 cycles/sec via a 2-mm probe tip oriented in the center of the peripheral receptive field, in the pattern illustrated in Fig. 1. Each histogram is labeled with the amplitude in microns of the sine wave evoking the response. Histograms were generated using the technique described in the METHODS section with 0.5-msec bins for the interval histograms (*left*) and 0.25-msec bins for the cycle histograms (*right*). Note that for stimuli weaker than that which produced nearly perfect tuning the impulses which do occur are phase-locked to the stimulus and appear at nearly integral multiples of the stimulus period.

illustrated by the impulse/cycle vs. sine-wave amplitude graphs of Fig. 12, for two other fibers, and for nine additional ones in Fig. 13. These indicate that the tuning plateau is reached at weaker intensities the closer the frequency of the driving sinusoid to the best frequency of the fiber. There is, however, one further change in response which occurs as intensity is raised through the zone of response demultiplication and across the tuning plateau. As the ascending series of cycle histograms to the right of Fig. 11 shows, with increasing stimulus strengths the occurrence time of the impulse gradually shifts to an earlier position in time relative to the stimulus cycle, even though there is no change in the sequential ordering of impulses in time. We attribute this to two factors which we cannot separate: the more rapid rates of indentation of the skin which accompany increasingly stronger stimuli, and a shortening of the utilization times at the fiber endings. Certainly most of the 5-msec shift relative to stimulus phase, shown in Fig. 11 to occur between 10-μ and 99-μ stimulus intensity, is due to the first factor.

The ratio of the tuning point threshold to that of the demultiplied response, i.e., to the absolute threshold for any response, was measured for a number of fibers at 40 cycles/sec. The ratio is 2.26 (range 1.37–4.00, n = 12), which is 7 db. The position and the extent of this zone suggests that it may account for the "atonal interval" observed in psychophysical experiments, a subject for later discussion.

When even stronger stimulus intensities are used there occurs for most fibers a disruption of the perfect periodicity so characteristic of responses to stimuli of tuning plateau strength. The uppermost histograms of Fig. 11, for the responses to stimuli of 148 μ amplitude, indicate that this is characterized by a doubling of discharge, two impulses occurring with many stimulus cycles. When this doubling occurs irregularly from cycle to cycle a disorganization of the sequential ordering of impulses is obvious. For some fibers there is a range of strong stimuli within this zone of breakdown of periodicity for which a new regularity of 2–1 following supervenes, as shown in Fig. 11. This regularity is, however, not periodic when all impulses are considered, for the intervals between first and second impulses evoked by one stimulus cycle and the first evoked by the next may be markedly unequal at the stimulus frequencies to which these fibers are sensitive. This zone of breakdown of periodicity is illustrated for a number of quickly adapting fibers by the graphs of Fig. 13. The role it may play in the drop of perceived pitch produced by increasing stimulus intensity is discussed in a later section.

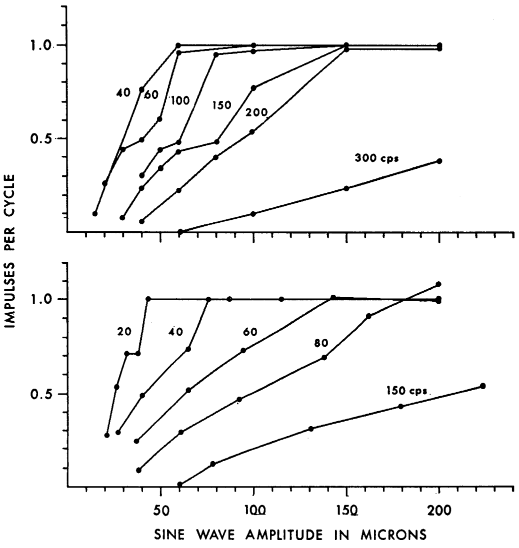


FIG. 12. Families of intensity-response relationships for two cutaneous quickly adapting fibers which innervated the glabrous skin of the monkey hand. Stimuli delivered via 2-mm-diameter probe tips positioned at the centers of peripheral receptive fields. Each point determined by counting the number of impulses and the number of stimulus cycles occurring in the 5th 100-msec period in each of 16 trials delivered as shown in Fig. 1. All data points are shown save on the 1 impulse/cycle plateau, where occasional superimpositions have been omitted. Lines connect points for each frequency of sinusoidal stimulation. Graphs illustrate the decreasing slopes of the intensity functions as the stimulus frequency is displaced from the best frequency of the fibers.

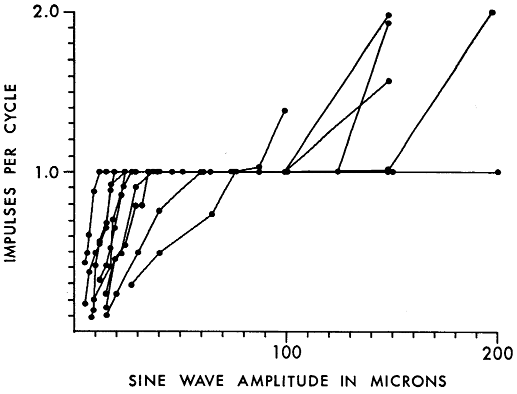


FIG. 13. Superimposed intensity-response relationships for 9 rapidly adapting fibers innervating the glabrous skin of the monkey hand. For each the 4-mm probe tip was oriented at the center of its peripheral receptive field. All stimuli 40 cycles/sec. Each point determined by counting the number of impulses and the number of stimulus cycles occurring during the 5th 100-msec period in each of 16 trials. Stimuli delivered as in Fig. 1. Every data point is shown except on the 1 impulse/cycle plateau, where numerous superimpositions have been omitted. Graphs illustrate the variation in the slopes of the functions for fibers of this class near their best frequency, the tuning plateau which follows the tuning point along the intensity continuum, and the disorganized response at more than 1 impulse/cycle which occurs in some fibers when very strong stimuli are delivered.

We emphasize that the response patterns described for this particular cutaneous fiber are typical of our detailed studies of 12 with machine analysis, and visual inspection of the responses of a large number of others. Fibers do differ in the range of stimulus strengths over which these changes occur: some are more sensitive than others. For all, in the order of increasing stimulus strengths at best frequencies of 30 or 40 cycles/sec, the zone of demultiplication of response is terminated at the tuning point; successively stronger stimuli over a considerable range then produce no further change save a phase shift relative to the stimulus cycle; this is the tuning plateau. With relatively intense stimuli there is a breakdown of periodicity when multiple discharges per cycle occur. Some fibers at some intensity may discharge regularly at 2 impulses/stimulus, resulting in a regular but not periodic pattern of discharge. Only one exception to this pattern was observed. Tuning points for this fiber could be established at several frequencies: but further even small increases in stimulus strength elicited multiple firing with each stimulus cycle, and disorganization of the response: no tuning plateau occurred.

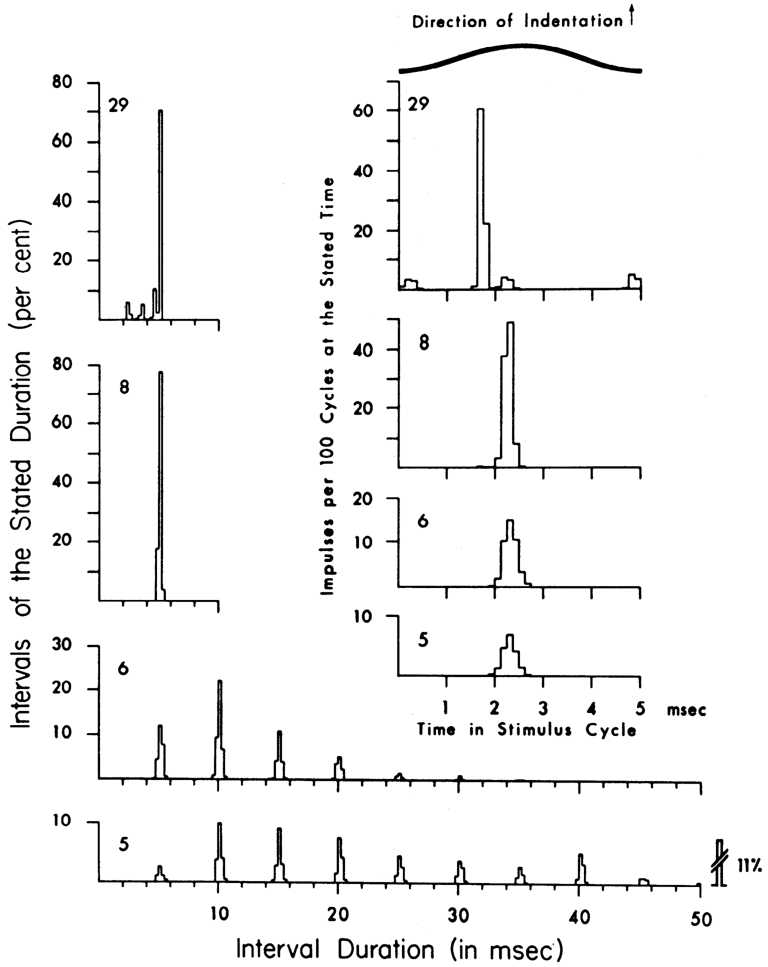
b. The Pacinian afferents. The afferents thought to terminate peripherally in Pacinian corpuscles of the subcutaneous tissue differ in several ways from the cutaneous QAs just described. They are an order of magnitude more sensitive to sinusoidal stimuli delivered to the skin, at their best frequencies, even though they may be located up to several millimeters beneath its surface. Their best frequencies are an order of magnitude higher, in the range of 200–300 cycles/sec, as against 30–40 for the cutaneous QAs. These facts are documented in a later section. Here we wish to show that in spite of these differences the changes in the discharge patterns which occur with increases in the amplitude of the driving sinusoid in general follow the same sequence as those produced in the QA pattern of discharge, as stimulus amplitude grows.

The detailed analyses for the discharge pattern of a Pacinian afferent under sinusoidal drive at 200 cycles/sec are shown in Fig. 14. Stimuli at an amplitude of 4 μ or less produced only occasional discharges. A sine wave at 5 μ evoked trains of impulses with a marked degree of demultiplication: when impulses did occur they were always locked to the stimulus cycle, at 1, 2, . . . 7 times the stimulus period. Occasionally, interimpulse intervals of up to 10 or 11 times the stimulus period occurred in the same locked temporal position relative to the sine-wave cycle. The ascending series of interval histograms to the left of Fig. 14 illustrates the fact that for Pacinian afferents only very slight further increases of intensity produce a discharge locked one-for-one to the stimulus cycle. The tuning point was at 8 μ amplitude; more than one hour later it was determined to be 7 μ in another series by visual inspection of the phase-locked response on the oscilloscope face. A large number of such parallel observations give validity to the tuning curves determined by visual inspection alone, which are described below. The mean ratio of the tuning point intensity to the threshold of the demultiplied response for the five Pacinian afferents studied with machine analysis at 100, 200, and 300 cycles/sec is 1.13 (range 1.00–1.50) or 2.2 db. Thus one further difference between cutaneous and Pacinian quickly adapting afferents is the narrow zone of the demultiplied response for the latter, 2.2 db compared to 7.0 db for the former.

The ascending series of cycle histograms to the right of Fig. 14 indicates that with increases of stimulus strength from the absolute threshold to the tuning point there was little or no change in the position of the impulse in time, relative to the stimulus cycle.

With further increase in the intensity at 200 cycles/sec, for the fiber whose responses are analyzed in Fig. 14, there was no further change until a sine wave of 29 μ amplitude was delivered. It evoked the occasional doubling and tripling of impulses for each sine-wave cycle characteristic of the disorganized response produced by strong stimuli in the cutaneous QAs, described above. The graphs of Fig. 15, to which further reference will be made in another connection, show (upper) that 300 cycles/sec was a slightly "better" frequency for this fiber than was 200, and that for 300 cycles/sec the tuning plateau extended from less than 5 μ to at least 85 μ, the strongest stimulus tested.

The fiber of Fig. 14 was in the middle range of Pacinian afferents, as regards sensitivity. Some of the analyses made of the responses of the most sensitive Pacinian afferent we studied are given in Fig. 16. The lowest pair of histograms characterize the response pattern to a 0.6-μ sine wave, at 300 cycles/sec, which was at or very close to the absolute threshold for any response. An increase to



Sine Wave Amplitude (in Microns)	29	8	6	5
Number of Cycles	3104	3104	3104	3104
Number of Impulses	3372	3100	1316	600

FIG. 14. Interval and cycle histograms for responses of a fiber of the Pacinian type innervating subcutaneous tissue of the monkey hand. Stimuli at 200 cycles/sec delivered via a 2-mm probe tip oriented at the "best spot" on the surface of the skin in the pattern illustrated in Fig. 1. Each histogram is labeled with the amplitude in microns of the sine wave evoking the response. Data collection and analysis described in METHODS: interval histograms (*left*) were made on 0.25-msec bins, the cycle histograms (*right*) on 0.125-msec bins. Note that for intensities below the tuning point all impulses which do occur are phase-locked to the stimulus, and appear at integral multiples of the stimulus period.

0.9 μ evoked the one-for-one phase-locked response characteristic of the tuning point.

3. CHANGES IN DISCHARGE PATTERNS OF QUICKLY ADAPTING AFFERENTS AS AMPLITUDE OF THE SINUSOID INCREASES, AT OTHER THAN BEST FREQUENCIES. *a. The cutaneous quickly adapting afferents.* The differences in the response patterns of the QA fibers to sine-wave stimuli at frequencies other than those in the zone of best frequencies, as stimulus amplitude is increased, can be summarized briefly. First, as the impulse per cycle versus amplitude graphs of Fig. 12 show for two fibers, the zone of demultiplication is greatly broadened by the increasingly slower slopes of the func-

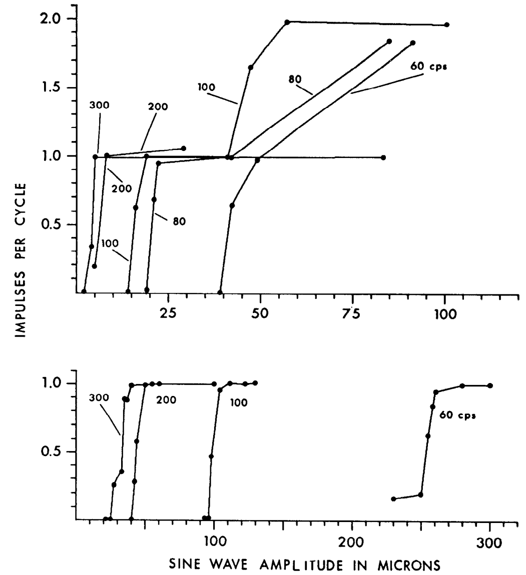


FIG. 15. Families of intensity-response relationships for two Pacinian afferents terminating in subcutaneous tissues of the monkey hand. Stimuli were delivered via 2-mm probe tips positioned over the "best spot" on the skin surface, in the manner illustrated in Fig. 1. Each data point was determined by counting the number of impulses and the number of stimulus cycles occurring in the 5th 100-msec period, in each of 16 trials. All data points are shown save on the 1 impulse /cycle plateau, where occasional superimpositions have been omitted. Lines connect points for each frequency of stimulation. Graphs illustrate the very narrow range between the threshold for any response at all and the tuning points, a characteristic of Pacinian afferents, and the fact that these slopes change only slightly as frequency is shifted away from the best frequencies for the fibers. The graphs above illustrate response disorganization for some frequencies, when very strong stimuli are delivered.

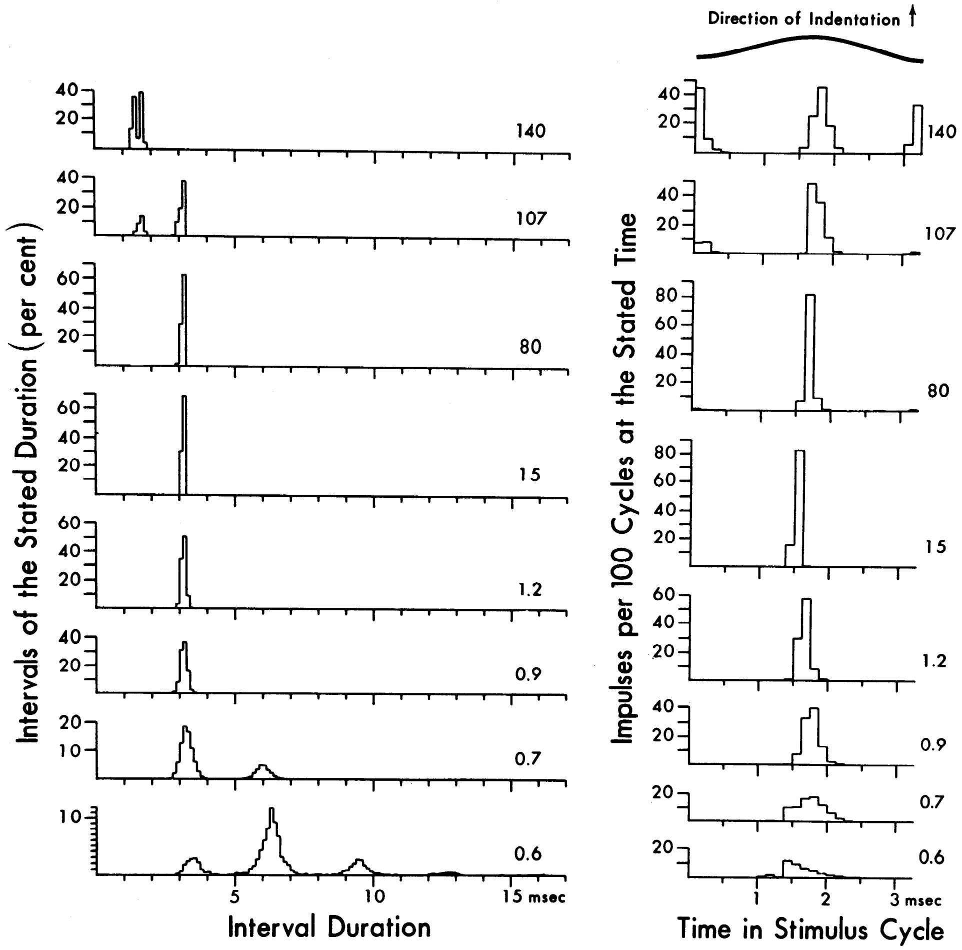
tions as the frequency is shifted from the range of 20–40 cycles/sec up to 150–300 cycles/sec. Second, for low frequencies (2, 5, and 10 cycles/sec) increases in intensity may produce doubling of discharge for some cycles without any one-for-one point at all. The zone of demultiplication merges directly into the zone of disorganization of response with no tuning point or plateau. For many QAs this occurs also when stimuli in the 150–300 cycles/sec range are made sufficiently strong.

b. The Pacinian afferents. The graphs of Fig. 15 show one difference in the response properties of the PCs. That is, even though the position of the impulse per cycle versus intensity function is shifted to the right along the intensity coordinate, as the frequency moves farther away from the best frequency, there is little change in the slopes of the functions. The demultiplication zone occupies nearly as narrow an intensity range for some off-frequencies as it does at the best frequency. The graphs for the fiber in the upper half of Fig. 15 show that for PCs, just as for the cutaneous QA fibers, strong stimuli may produce disorganization of the response even at the best frequencies for the fibers; at off-frequencies—in this case those in the low range—this disruption of the regular patterns may supervene without any clearly defined tuning point.

4. TIME TRENDS IN THE RESPONSE OF QUICKLY ADAPTING MECHANORECEPTIVE AFFERENTS TO SINUSOIDAL STIMULI. For the analyses described above the tuning point was defined as that amplitude of the sine-wave stimulus which evoked 1 impulse/cycle, and maintained this relation throughout the 930-msec stimulus. At and around the best frequencies for both types of quickly adapting afferents there is no discernible time trend in the responses, which change from the zone of demultiplication of response into perfect tuning symmetrically in time over the stimulus duration. At other than best frequencies, and especially for the cutaneous QAs, a time trend does appear. As stimulus strength is increased from below threshold for any response tuning first occurs early in the response, and further increases are required to evoked tuning throughout. This phemonenon contributes to the increasingly slower slopes of the impulse per cycle functions of Fig. 12, for higher than best frequencies. Its virtual absence for the Pacinian afferents accounts for the nearly equal slopes of their impulse per cycle functions shown in Fig. 15, at different frequencies.

IV. *Response of slowly adapting mechanoreceptive afferents innervating the monkey hand to sinusoidal mechanical stimulation of the skin surface*

The general properties of the slowly adapting afferents which terminate in the ridges of the glabrous skin were described in SECTION II, and the way in which they signal the intensity of mechanical stimuli has been detailed in an earlier paper (12). The stimulus-response function is linear, and is thought to account for a similarly linear relation



Sine Wave Amplitude (in Microns)	0.6	0.7	0.9	1.2	15	80	107	140
Number of Cycles	4766	4758	4768	3509	2464	2493	4166	4416
Number of Impulses	2233	3838	4708	3498	2455	2571	4920	8752

FIG. 16. Interval and cycle histograms for the responses of the most sensitive Pacinian afferent observed, to 300 cycles/sec sinusoidal stimulation of the skin of the palm of the hand. Histograms were constructed in the manner described in the METHODS section; each is labeled with the sine-wave amplitude, in microns. The sine waves were superimposed upon a step indentation of about 550 μ, as shown in Fig. 1. *Left:* interval histograms constructed on 0.125-msec bins. *Right:* cycle histograms constructed on 0.125-msec bins. Phase correction described in Fig. 1 has been applied to the cycle histogram. Interval histogram for the responses at 0.9 μ amplitude indicates that nearly perfect tuning was elicited by a stimulus of that amplitude. The slight phase lag for strong intensities, shown in the cycle histograms, is attributed to slightly slowed conduction in fibers conducting at 300 impulses/sec.

between the intensity of brief nonoscillating skin indentations and the human subjective magnitude estimations of those intensities (11). It it our purpose here to examine the possibility that afferents of this class may contribute also to the sense of flutter-vibration. Our conclusion, held tentatively, is that they do not, for reasons detailed in that which follows.

1. RESPONSE PROPERTIES OF SLOWLY ADAPTING AFFERENTS, AT LOW FREQUENCIES (2–10 CYCLES/SEC). The records of Fig. 17 illustrate the pattern of response of these afferents to low-frequency oscillations. The uppermost record, obtained with a steady skin indentation of about 550 μ with no superimposed oscillation, illustrates the slowly adapting pattern of discharge. It evolves from the high

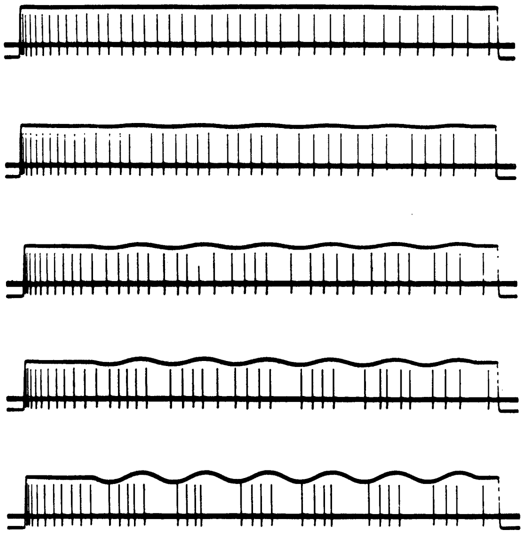


FIG. 17. Records of the impulse discharges of a slowly adapting primary afferent mechanoreceptive fiber to a steadily maintained skin indentation of 55 μ (upper set of records), and when a 5 cycles/sec oscillating stimulus is superimposed on that step, at sine-wave amplitudes of 23 μ, 46 μ, 72 μ, and 114 μ, for the second, third, fourth, and fifth sets of records, respectively. In each set the upper trace is the analogue electrical signal of the position and movement of the 2-mm probe tip, lower is record of the action potentials in the nerve fiber, recorded after its isolation by microdissection from the median nerve of a monkey. The receptive field of the fiber lay in the glabrous skin of the palm. Topmost record shows the onset transient and the slowly declining quasi-steady-state discharge characteristic of the slowly adapting afferents. Frequency modulation in phase with the sine wave is visible when its amplitude is only 23 μ, which is less than one-eighth the human threshold at 5 cycles/sec. Duration of the step stimulus, 1400 msec; of the superimposed sine wave, 930 msec.

frequency onset transient to the "early steady state" of nearly constant (slowly declining) frequency. The successively lower records of Fig. 17 show that a superimposed sine wave of 5 cycles/sec elicits a frequency modulation in synchrony with the stimulus, and that this is discernible at very low sine-wave amplitudes. This entrainment by frequency modulation is further illustrated by the interval histograms for another fiber, under 5 cycles/sec sine-wave drive, given in Fig. 18. The frequency modulation is apparent at 12 μ sine-wave amplitude, and highly significant at all higher intensities. This clear encoding of frequency at the first-order level occurs at intensities well below the human threshold for the perception of movement at 5 cycles/sec (see Figs. 2 and 3). This is true no matter which method of measuring the human threshold is used for comparison. Indeed, it is a startling experience when, as a subject, one looks at the stimulating tip; at intensities below threshold one can see the movement at 2, 5, and 10 cycles/sec, but one cannot feel it! We conclude that at least at these frequencies the slowly adapting afferents do not contribute to the sense of flutter. The observation described affords an example, we believe, of a neural code which can be impressed upon the first-order fibers experimentally, but which has no meaning in terms of sensation. At least that is the conclusion suggested by the facts currently available.

2. RESPONSE PROPERTIES OF SLOWLY ADAPTING AFFERENTS, AT HIGHER FREQUENCIES (20–200 CYCLES/SEC). Response of slowly adapting afferents is quite different when the frequency of sine-wave oscillation is raised to match or nearly match the steady discharge frequency itself. An example is given by the interval histograms shown to the left of Fig. 19. The lowermost interval histogram shows that the mean frequency of discharge evoked by the step indentation alone was about 30/sec, with considerable spread. The next histogram above shows a marked entrainment of the fiber's discharge at the stimulus frequency of 40 cycles/sec, one which is nearly one-to-one at higher intensities. This very low entrainment threshold nearly matches the human threshold, as comparison with the curve for METHOD II in Fig. 3 will show. The important fact, however, is that this low-threshold entrainment is the result of the coincidence of two variables: the frequency of the steady-state discharge and the frequency of the stimulus. Further studies revealed that the entrainment threshold rises rapidly if the steady-state frequency is changed, by changing step indentation amplitude, to produce a mismatch with stimulus frequency. A similar mismatch results when the stimulus frequency is raised well above any possible steady-state discharge. Such a result is shown for the same fiber by the histograms to the right of Fig. 19. At a stimulus frequency of 100 cycles/sec, entrainment resulted only at sine-wave amplitude of 170 μ. This is to be compared with human thresholds of 6–10 μ at 100 cycles/sec.

We conclude therefore that the slowly

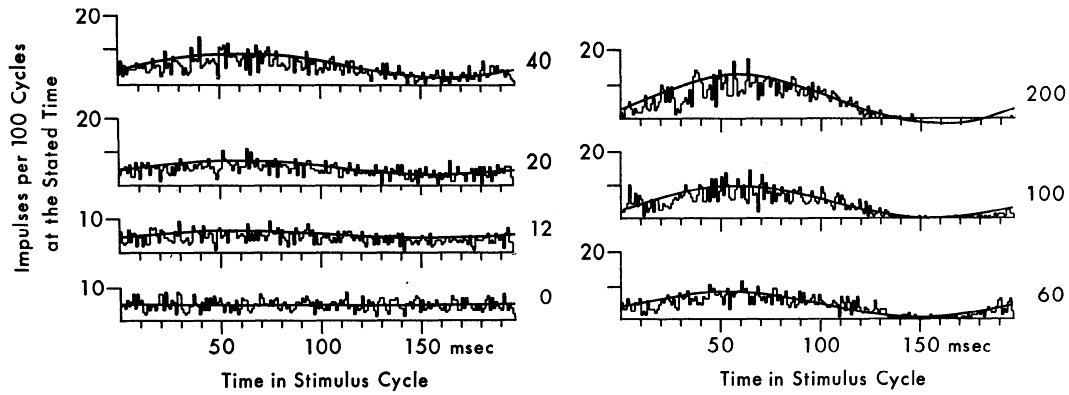
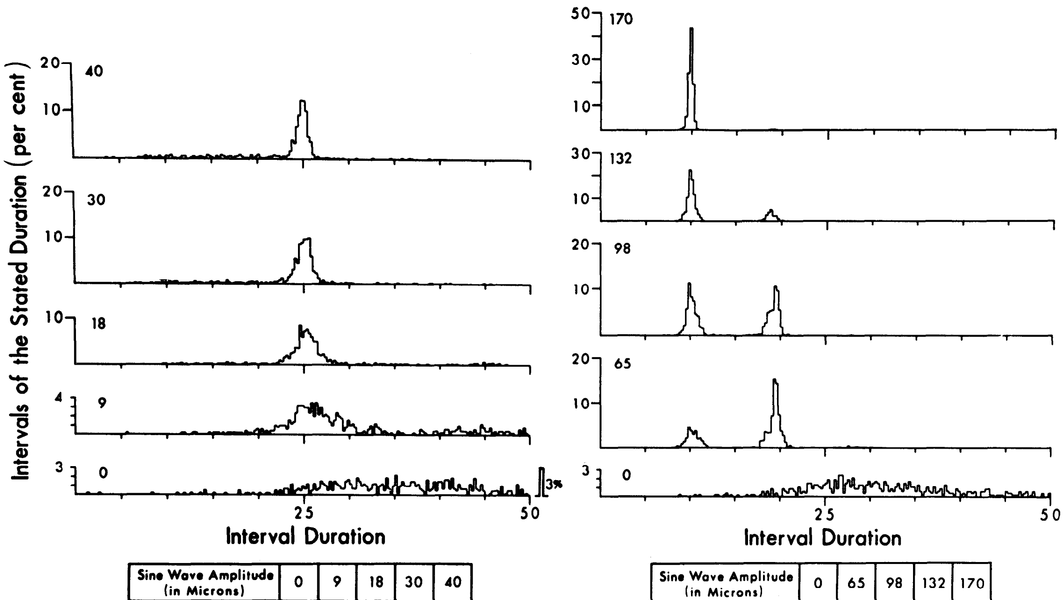


FIG. 18. Cycle histograms for the responses of a slowly adapting fiber innervating the glabrous skin of the monkey hand. Stimuli at 5 cycles/sec delivered via a 2-mm probe tip oriented at the center of the peripheral receptive field for the fiber, in the pattern shown in Fig. 1. Sine waves superimposed on the histograms have been fitted by the method of least mean squares. Each histogram is labeled with the amplitude in microns of the sine wave eliciting the response. Histograms were constructed with technique described in the METHODS section, using a bin size of 1 msec. Graphs show that a frequency modulation appears at a stimulus amplitude of 12 μ, and is clear for all higher intensities.

adapting afferents play no essential role in the sense of flutter-vibration. At low frequencies they discharge in frequency modulation at intensities far below the human threshold. At intermediate frequencies (20–40/sec) they may entrain at very low sine-wave amplitudes, if the discharge elicited by the steady indentation is comparable to the



Sine Wave Amplitude (in Microns)	0	9	18	30	40
Number of Cycles	—	592	592	592	592
Number of Impulses	413	492	554	603	636

40 cps Stimulation

Sine Wave Amplitude (in Microns)	0	65	98	132	170
Number of Cycles	—	1488	1488	1488	1488
Number of Impulses	467	861	996	1255	1485

100 cps Stimulation

FIG. 19. Interval histograms for the responses of a slowly adapting fiber innervating the glabrous skin of the monkey hand. Stimuli at 40 cycles/sec (*left*) and at 100 cycles/sec (*right*) were delivered via a 2-mm probe tip oriented at the center of the peripheral receptive field of the fiber, in the pattern shown in Fig. 1. Responses of the fiber to step indentations without a superimposed sine wave are shown by the two histograms labeled "0". Note that the mean frequency of firing to the step alone is about 30 impulses/sec, and that much lower intensities are required to elicit nearly one-to-one firing when the sine wave is 40 cycles/sec than when it is 100 cycles/sec.

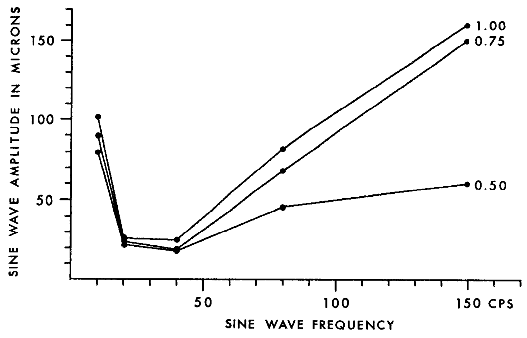


FIG. 20. Tuning curves for a quickly adapting afferent innervating the glabrous skin of the monkey hand, isolated by microdissection of the median nerve. The three curves plot the amplitude of the sine wave, at a series of frqeuencies, required to raise the probability to the levels indicated that an impulse will be evoked by each cycle of the stimulus.

stimulus frequency, but require strong stimuli for entrainment when this is not the case. Yet human thresholds are not markedly different for differences in step indentation known to produce markedly different rates of discharge in these fibers, in the early steady state. Finally, when stimulus frequencies are higher than any possible during the early steady state, entrainment thresholds are one or more orders of magnitude higher than the human thresholds.

V. *Further analysis of frequency functions: tuning curves for first-order fibers, and their relation to human threshold function for flutter-vibration*

It is apparent from the evidence presented in earlier sections that the tuning point for a first-order fiber can be defined with precision, and that tuning points for a number of frequencies through the sensitive range compose a tuning curve for the fiber. This measurement is similar to that in which the human threshold-frequency function is determined. In the first case the datum of interest is that stimulus intensity required to produce phasic entrainment of the fiber's discharge at the stimulus frequency, at some selected probability; in the second the end point is the human observer's report of a sensation of movement, at threshold. In this section we wish to compare the results of these two sets of experiments, while making the "cross-species" assumption that the sensations experienced by man and monkey are similar, at least at the first level of analysis.

1. CUTANEOUS QUICKLY ADAPTING AFFERENTS. Tuning curves for these fibers have been determined in the two ways described on p. 305. One determined by machine analysis is shown in Fig. 20. It is typical of those measured in this way and of those established by visual inspection of the responses of 66 other fibers of this class. The frequencies which entrain a one-to-one discharge at lowest amplitude (the best frequencies) are between 20 and 40 cycles/sec in this population (mean 30.5 ± 1.5 cycles/sec), and for either lower or higher frequencies stronger stimuli are required for phasic entrainment. The tuning curves for different fibers differ in their position on the intensity scale; some fibers are more sensitive than others over the frequency range tested, though their tuning curves are nearly parallel. Of the 67 fibers, 32 had minima at their best frequencies below 30 μ; the remaining 35 curves are distributed continuously along the intensity continuum, as regards their minimal tuning points. This is shown by Fig. 21 which displays tuning curves for 12 fibers studied in a single experiment, and by Fig. 22 in which the tuning points for all 67 fibers studied are given.

The heavy line in Figs. 21 and 22 is the human threshold-frequency function, determined at the human finger tip using METHOD II (see p. 305 and Fig. 3). The low-frequency limb of this function is blanketed by the tuning points for the more sensitive quickly adapting fibers. The conclusion we draw is that a comparable class of fibers innervating the human hand could account for the low-frequency end of the human flutter-vibration curve, and we have observed no other myelinated mechanoreceptive afferent innervating the glabrous skin of the primate hand which could do so. It is equally obvious that this class of fibers cannot account for the high-frequency limb of the human sensitivity curve. This conclusion is based on the assumption that what is required for the human decision that a stimulus is moving versus it being steady is the appearance of a periodic signal in the relevant first-order fibers, a proposition which will be subject to later discussion.

2. THE PACINIAN AFFERENTS. A typical tuning curve for a fiber which we classify as a Pacinian afferent is shown in Fig. 23. The

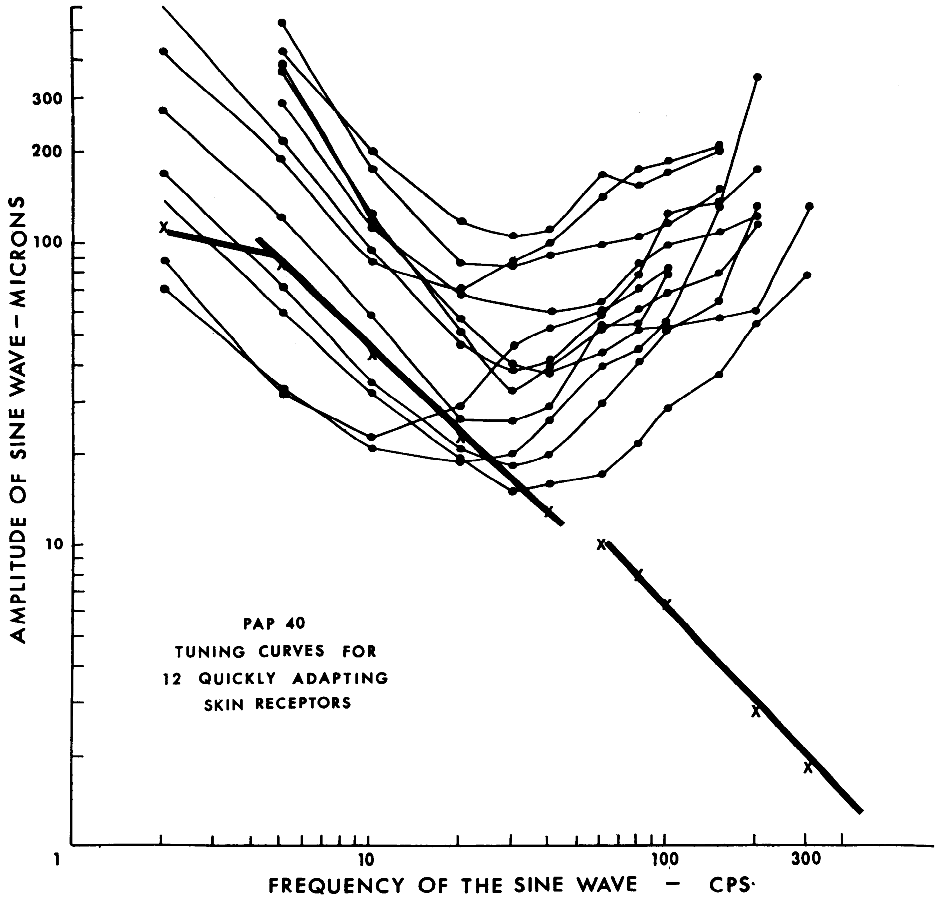


FIG. 21. The light lines are tuning curves for a dozen quickly adapting afferent fibers innervating the glabrous skin of the monkey hand. Each fiber was isolated for study by microdissection of the median nerve, and the tuning curves constructed by determining the tuning points for each fiber, at a series of frequencies, as described in the text. The heavy black line replots the human frequency-intensity threshold function for the fingertip, illustrated in Fig. 2.

best frequency for this fiber was about 250 cycles/sec. For higher frequencies the entrainment thresholds, like the human functions, rise rapidly; they are not shown because our control of amplitudes at higher frequencies was imprecise. With decreases in frequency the tuning curve for this fiber inscribes a nearly hyperbolic course until, below 40 cycles/sec, entrainment could not be produced by any intensity. At these low frequencies, as intensity is increased, the pattern of discharge may pass from demultiplication to disorganization without a perfect tuning point or a tuning plateau. For those frequencies within the tuning range, tuning occurred after only very small increases in intensity beyond that required to elicit any response at all, as shown by the very narrow range between the 0.5, 0.75, and 1.0 impulse/cycle curves of Fig. 23. This is another measure of the very narrow zone of demultiplication for Pacinian afferents shown in Figs. 14 and 16. The tuning curves for 14 other Pacinian afferents are shown in Fig. 24. It is apparent that the Pacinian afferents can account for the human sensitivity in the high-frequency range, and we have observed no other class of fibers innervating the hand of the monkey which could do so.

The second tuning curve shown in Fig. 23 is that of the only Pacinian afferent which differed in any way from the description given above. Its tuning curve extended further into the low-frequency range, by a considerable margin, than that of any other Pacinian studied.

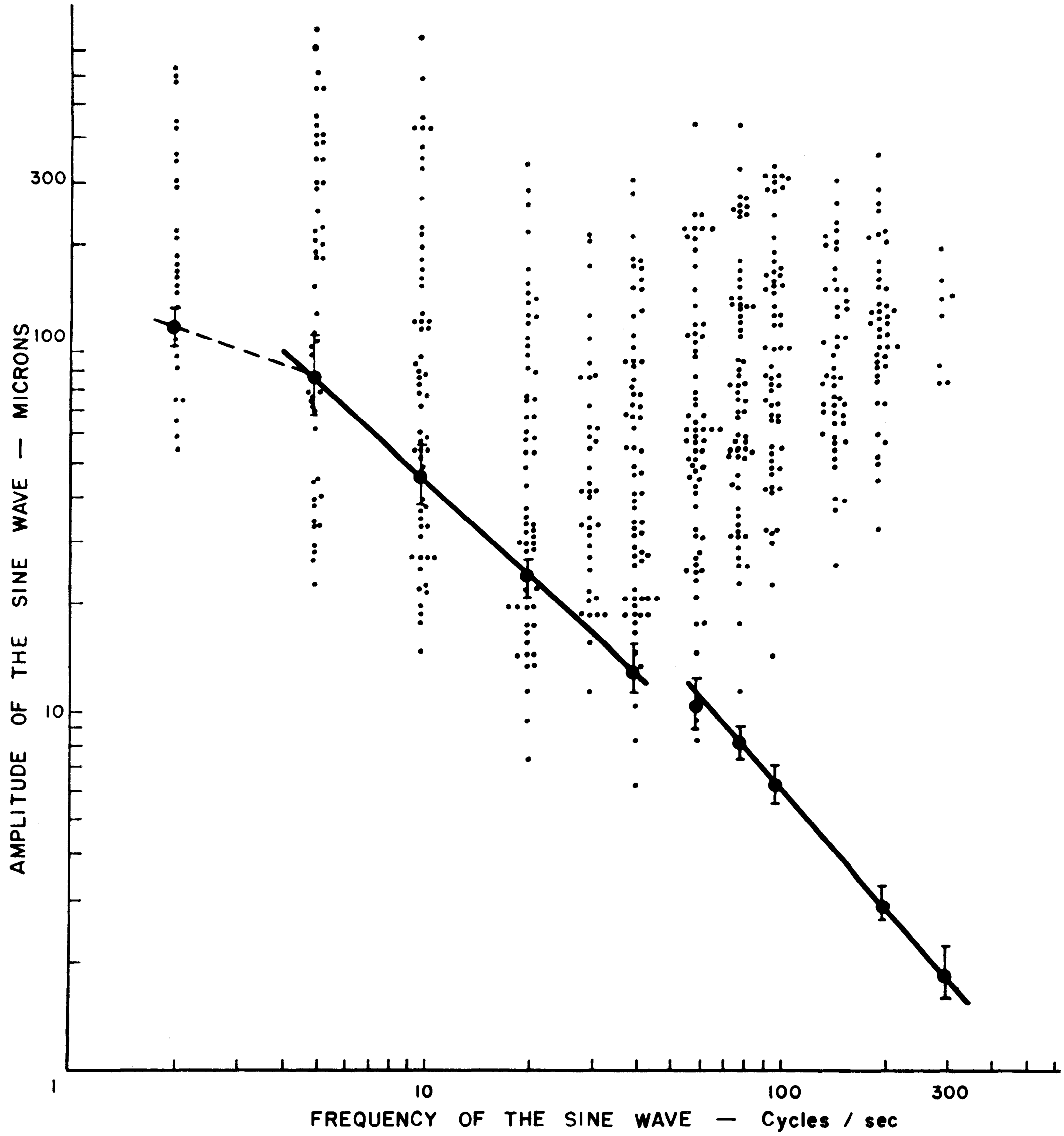


FIG. 22. Tuning points for 67 quickly adapting afferent fibers innervating the glabrous skin of the monkey hand. Each fiber was isolated for recording by microdissection of the median nerve, and tuning points determined at a series of frequencies, as described in the text. When the points for any one fiber are connected, a tuning curve such as those illustrated in Fig. 21 results. Heavy black line replots the human frequency-intensity threshold function for the fingertip illustrated in Fig. 2. Data displayed illustrate the range of sensitivity of the population of quickly adapting cutaneous afferents to oscillating stimuli, and that the most sensitive edge of this range overlaps the low-frequency limb of the human function, but not the high-frequency limb.

3. WHAT PROPORTION OF THE AFFERENTS ENGAGED AT A GIVEN FREQUENCY DISCHARGE PERIODICALLY AT THE HUMAN THRESHOLD? Figures 22 and 24 show that at any given frequency only a portion of the total population of afferents of one or the other type will be driven periodically at intensities equal to the human threshold for the perception of movement. Those proportions are given in Table 4; they suggest that some 10–20% of the available afferents are required to be entrained to evoke the human sense of movement. This conclusion, however, places a severe requirement upon our cross-species assumption, which will be considered in later discussion.

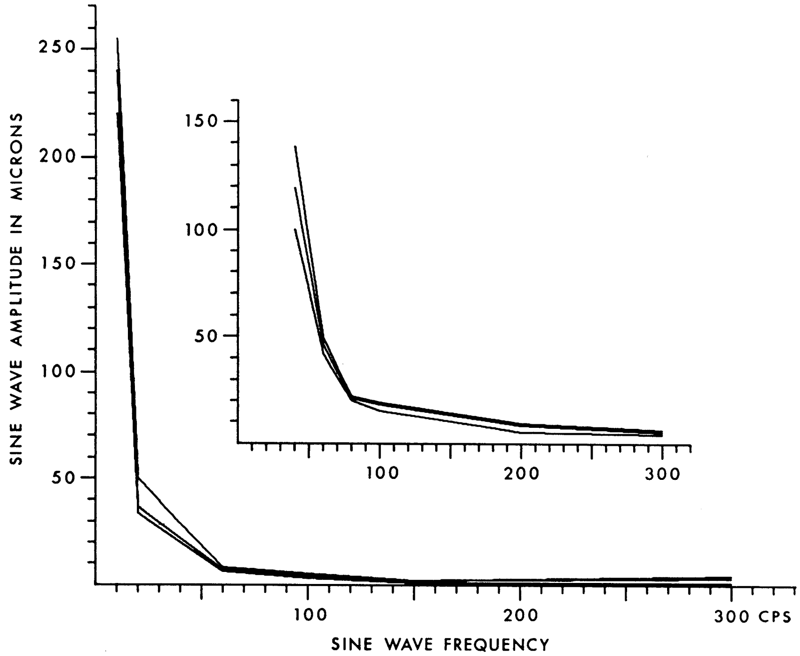


FIG. 23. Tuning curves for two Pacinian afferents terminating in deep tissues of the monkey hand, each isolated separately by microdissection of the median nerve. Stimuli were delivered to palmar skin. The three curves in each plot, from upper to lower, the amplitude required to raise the probability to 1.0, 0.75, and 0.50 respectively that an impulse will be evoked by each cycle of the stimulus. Inset curves are typical of Pacinian afferents; the other curves are those for the Pacinian with the widest frequency sensitivity observed. It was unique in this respect.

VI. *Further consideration of intensity functions, and their relation to human subjective magnitude estimation of the intensity of a sinusoidal stimulus*

The last question to be considered is that posed by the observations illustrated in Figs. 4 and 5. They show that at or near the best frequencies of the two sets of fibers thought to account for the sense of flutter-vibration, the human subjective estimation of the intensity of oscillatory movement is a linear function of the stimulus amplitude. Perusal of the intensity functions of the cutaneous QA fibers and of the Pacinian afferents, illustrated in various forms in Figs. 11 through 16, yields no simple explanation of that human function. At its best frequency each fiber locks in one-to-one synchrony with the stimulus, at the tuning point; there is little further change in response over a wide range of increasing stimulus intensity. Throughout this tuning plateau these fibers provide no neural signal of increasing intensity, yet, over this same range the sensation evoked is judged by human observers to be increasing linearly with sine-wave amplitude. Upon what change in first-order neural input does that change in sensation depend?

The linearity of the magnitude functions of Figs. 4 and 5 suggested at once that the

TABLE 4. *Percentages of populations of quickly adapting afferents innervating the monkey hand which are entrained at intensities equaling human thresholds for the perception of oscillatory movement, at different frequencies*

Frequency, cycles/sec	2	5	10	20	40	60	80	100	150	200	300
% Cut. QA fibers entrained, n = 67	10	27	27	34	7	3	0	0	0	0	0
% Pacinian fibers entrained, n = 20	0	0	0	0	10	20	40	25	20	15	10

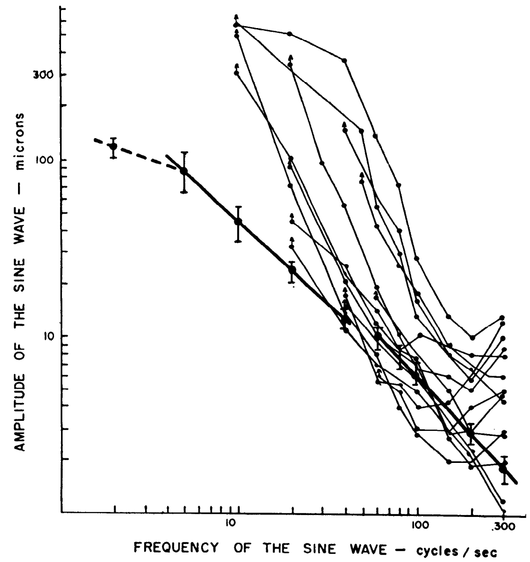


FIG. 24. Tuning curves for 14 Pacinian afferents innervating the monkey hand. Each point indicates the amplitude of the sine-wave stimulus required to produce an approximate one-to-one entrainment of the fiber, at the given frequency. Upwardly directed arrows at the left end of each tuning curve mean that entrainment could not be produced by any lower frequency, no matter what the sine-wave amplitude. Stimuli delivered as shown in Fig. 1, and described in the METHODS section. Heavy black lines reproduce the human frequency-intensity threshold function from Fig. 3. The overlap of the tuning curves with only the high frequency end of the human function suggests that the Pacinian afferents could account for sensitivity in the high but not the low range of frequencies.

slowly adapting afferents might play a role, for they respond in a linear fashion to increases in the intensity of a nonoscillating stimulus (12). They might provide a similar increase in neural signal in parallel with increases in sine-wave amplitude—even though they can provide no unequivocal signal of the frequency of that sine wave. Studies of the over-all frequency of discharge of these afferents as a function of sine-wave amplitude suggests, however, that this is not the case. In the low range of stimulus frequency, for example, increasing amplitudes of a superimposed sine wave may simply increase the degree of frequency modulation. The temporal order of discharge may be shaped by the sine wave by a repositioning of impulses in time with no regular change in the total number of impulses per unit time. At higher frequencies these fibers provide an even more equivocal signal of sine-wave amplitude, for the degree of entrainment and the over-all rate of discharge are determined by the interactions of three variables: the discharge rate produced by the degree of step indentation, the frequency of the sine wave, and its amplitude.

The last possibility we considered is that the intensity of oscillation might be derived (by a central neural mechanism) through a spatial integration of the activity in the entire population of neurons engaged by the stimulus. The results of an experiment aimed at testing this possibility are given in Fig. 8. The single fiber under study is made to occupy a series of different positions from the center to the edge, in the succession of slightly serially shifted, neural populations engaged by the stimulus, when the latter is delivered to a series of several sites shifted across and outside of the peripheral receptive field of the fiber. Such a reconstruction depends of course upon a constancy of conditions, one thought to have been achieved in these experiments upon first-order fibers. The spatial integration performed resulted in a monotonic but slightly negatively accelerating function. Some differential weighting in the integration might have brought this to linearity, but obviously the difficult problem of how the afferents responsible for the sense of flutter-vibration can signal both frequency and intensity requires further study.

DISCUSSION

I. *Psychophysics of flutter-vibration*

In general, the threshold flutter-vibration function in humans measured by us is similar to that obtained by the majority of other investigators: it is described by a curve roughly U-shaped in contour, in linear coordinates, with lowest threshold at about 250 cycles/sec. Our quantitative measurements were confined to frequencies of 300 cycles/sec and below, although we did confirm that the threshold rises again very rapidly for frequencies about 300. We found, however, as did Von Békésy (25), that if the frequency range examined is extended down to 5 cycles/sec the results when plotted on logarithmic coordinates are best described by two straight lines, of different slopes. Further, these two limbs are differentially affected by cutaneous anesthesia, which produces a 5- to 10-fold elevation of thresholds for frequencies below

40–50 cycles/sec, while scarcely affecting those for frequencies between 60 and 300. The quite different effects of cutaneous anesthesia upon vibratory sensibility described by different investigators are due, we believe, to the choice of but one frequency for study: if a low frequency is chosen, marked changes in threshold are produced by anesthesia; if high, none (2, 3). These facts, together with the change in the subjective experience with change in frequency across the 40–60 cycles/sec zone, led to this hypothesis: flutter-vibration is served by two sets of first-order fibers, one terminating in the skin itself and sensitive to low frequencies and a second ending in subcutaneous and certain deep tissues, and most sensitive in the range of 100–300 cycles/sec. All of our observations on the response properties of first-order myelinated mechanoreceptive afferents innervating the glabrous skin of the monkey hand are fully consonant with this idea.

These findings and conclusions pertain strictly to studies of the glabrous skin of the hand. This is a point we wish to emphasize, for some studies, now underway, of the hairy skin of the arms of men and monkeys indicate quantitative though not qualitative differences in both the psychophysical and the neurophysiological findings. Indeed, differences are suggested by the anatomical differences in the innervation of glabrous and hairy skin and account, we believe, for many discrepancies in the reports of studies of vibratory sensibility in different parts of the body: differences in sensibility are set by difference in peripheral innervation.

We emphasize also that both our psychophysical and electrophysiological observations were purposely made using a constant stimulus pattern. It is well known, however, that the values for vibration threshold and even the shape of the threshold function curve may be altered by changing any one of a number of parameters, or conditions: contactor area and shape (20, 22), area of free surround (19), angle of axis of oscillatory movement relative to the skin surface, duration of the oscillatory stimulus, skin temperature, the age and sex of the observer—all these and doubtless others not yet studied influence the threshold. We have observed many of these effects, and that in both the human and animal the results—the threshold of the perception of movement in the one case and the tuning points in the other—may be affected to some degree by the amplitude of the step indentation of the skin upon which sine-wave stimuli are superimposed. We chose to hold this parameter constant. In this regard it would be of interest to measure that degree of skin indentation which a subject allowed free movement of the hand would seek in attempting to achieve maximum sensitivity. In our psychophysical experiments this "motor" component of the sensory performance has been eliminated by holding the hand in a steady position. We do know that for the skin QA fibers the step indentation at which tuning thresholds are lowest is somewhat greater than the 500 μ chosen as our constant step indentation.

II. *Encoding in the temporal domain: first-order signals evoked by sine-wave stimuli, and their relation to the perception of periodic motion*

Study of either of the two classes of fibers which we believe account for the sense of flutter-vibration, as the intensity of the sine wave is increased, reveals two "thresholds." The first is that at which a neural discharge is evoked phase-locked to the stimulus, but the fiber is not entrained, during the delivery of the superimposed sine wave. The second is that point along the intensive continuum, often very sharp, at which a nerve impulse occurs with each cycle at a high probability and in a narrowly fixed phase relation to the stimulus (see Figs. 11, 14, and 16). It is our proposition that these two account for two clearly identifiable points on the sensory continuum. As sine-wave amplitude increases subjects first become aware of a roughness which is not the readily recognized flutter or vibration with its identifiable pitch. A second transition to this latter occurs rather abruptly with further increase in sine-wave amplitude. The range between these two transition points is called the atonal interval (25), and corresponds rather precisely with the zone of demultiplication of response in the first-order input trains. It is 2 db at 300 cycles/sec psychophysically and 2.2 db for Pacinian afferents at 100–300 cycles/sec; it is 8–10 db at lower frequencies psychophysically and 7 db at 40 cycles/sec for the cutaneous quickly adapting fibers.

This coincidence of transitions in both subjective experience and the neural signals which evoke them lends some support to our general hypothesis: what is required for the perception of periodic movement is the appearance in some small number of primary afferent fibers of a regularly periodic signal, at some high level of probability. Using the tuning point as estimator we have constructed tuning curves for the two sets of fibers. Comparison of these curves with the human threshold function (Figs. 21, 22, and 24) provides the basis for our statement that these two sets of fibers account for the sense of flutter-vibration.

This statement depends upon the validity of two assumptions. The first is the requirement for periodicity discussed above. The second is the cross-species assumption, i.e., that the sensitivities of the two sets of afferents innervating the hand are about the same in monkey and in man. If the human first-order fibers are considerably more sensitive than are those of the monkey, our hypothesis would be changed only in degree to say that a larger percentage of the available population must be entrained to evoke a sensation of movement than is suggested by the data of Table 4. If the human first-order fibers are by any considerable factor less sensitive than are those of the monkey, the interesting proposition is put that the sensation of periodic movement with identifiable pitch might be evoked at intensity levels below that at which any first-order fiber is entrained to discharge periodically. Such a mechanism is readily imagined. Given that each of two or more first-order fibers converging upon a second-order element possesses supraliminal synaptic security for each impulse, and that the demultiplied but phase-locked trains of impulses evoked in them by weak stimuli are asynchronous, a second-order neuron could be perfectly entrained when no one of its converging inputs is so. Some preliminary results indicate that the discharges evoked by the same oscillating probe in pairs of fibers observed simultaneously need not be synchronous, at weak intensities, so that a study of this question at the level of the dorsal column nuclei becomes an important experimental object. For the present, parsimony suggests that the thresholds for first-order fibers innervating the hands of monkey and man are not strikingly different, and thus our periodicity hypothesis fits the facts available better than any reasonable alternative.

Such a hypothesis, however, is unlikely to apply to all first-order mechanoreceptive afferents which are caused to discharge in a nearly periodic fashion. For example, the steady-state receptors of the glabrous skin discharge very regularly in the early steady state, and the frequency of that discharge provides a sensitive signal of the intensity of the stimulus (12). During the plateau of a 1-sec steady indentation of the skin, for example, only these among the large myelinated first-order afferents will discharge, the quickly adapting ones then being silent. Yet the stimulus is felt as steady, not oscillating. Does this mean that the particular code of a labeled line is a part of the label (11)? Such a label might be given by the over-all time constant of the linked relays from first-order fibers to the cortex. For the QA afferents this appears to be one which emphasizes and preserves impulsive, periodic transmission in spite of whatever convergence there may be of elements whose trains cannot be expected to remain in perfect synchrony. Those cortical cells linked to the slowly adapting afferents might by a long time constant and asynchronous convergence allow a smearing of impulsive events. Our early observations on cortical cells have shown a preservation of impulsive events for those which "adapt quickly" and are thought on this and other grounds to be linked to the quickly adapting afferents of the glabrous skin. Whether those cortical cells which "adapt slowly" discharge as regularly as do the slowly adapting first-order afferents to which they are thought to be linked has not yet been determined.

III. *Encoding in the temporal domain: pitch discrimination and its relation to first-order signals*

The ability of humans to identify the frequency of an oscillating stimulus, i.e., to recognize and to discriminate between pitches, is poor compared with their capacity in the auditory sphere. The most widely quoted study is that of Goff (6), who measured the discriminable frequency increment over the range of 25–200 cycles/sec, using stimuli of equal "loudness" at each frequency, for the cases of 20 and 35 db above thresholds. For the latter level the discriminable increment at 25 cycles/sec is about 4 cycles, but it rises very rapidly as the base frequency rises, so that at 200 cycles/sec the discriminable increment is about 60 cycles/sec and at the intensity level of 20 db above thresholds it is nearly 100 cycles/sec. These findings suggest that whatever discrimination of frequency can be made depends upon signals in the cutaneous quickly adapting fibers, and that were the input confined to the Pacinian afferents (e.g., by skin anesthesia) the discrimination of frequency would be very poor indeed.

Consider then the glabrous skin quickly adapting afferents, which account for the perception of flutter in the range in which frequency discriminations can be made. What are the relevant neural signals? First, it is certain that pitch discrimination on the skin does not depend upon a shift in the members of the accessible population which are entrained, as frequency changes, as is the case in the cochlea and the auditory system. This is so because all the tuning curves of the QA afferents are nearly symmetrical and parallel, differing only in sensitivity level, and have nearly the same best frequencies of 30.5 ± 1.5 cycles/sec. As Von Békésy has pointed out (25), what is "pitch" in the auditory system is "location" in the somesthetic.

A second alternative to be considered is that "cutaneous pitch" varies along an intensive not an extensive continuum, and that a discrimination of the frequency of a stimulus might be made on the basis of the total number of impulses in any given short period of time, such as 1 sec—the discrimination of pitch is not improved by longer inspection times. This appears unlikely because the total number of impulses which occur in response to two slightly different frequencies might be similar in the two cases due to doubling or missing in the two trains, on any given pair of trials.

A third proposition, which we favor, is that a central neural mechanism exists which alters its own activity (which "measures") the dominant period in the input trains of impulses; which is, in the given case, responsive to the difference in the length of the dominant repetitive periods of 40 and 33 msec. There is of course no direct proof that this is so, but if further evidence accrues to support it, it will mark a special but not a general case of the importance of the sequential ordering of impulses in central nervous discriminative mechanisms.

DROP IN PERCEIVED VIBRATORY PITCH WITH INCREASES IN INTENSITY. The sensation of vibratory pitch on the skin changes with increase in the intensity of the sinusoidal stimulus. Von Békésy (25) has shown, for example, that when a stimulus 20 db above threshold (we assume the threshold for the perception of a pitch, i.e., not including the atonal interval) is chosen as a standard, a further increase in intensity to 40 db (from 10 to 100 times threshold) produces a drop in perceived pitch of about half an octave, a change which occurred gradually, with no jumps. The observations were made at 25, 50, and 100 cycles/sec, and thus cover the zone of action of both classes of primary afferent fibers serving flutter-vibration. Below the 20-db level the pitch changes were small. This relative constancy of pitch with increase in intensity from 1 to 10 times the pitch threshold fits the extent of the plateau period of phased-locked discharge which we observed for both the Pacinian and the QA afferents innervating the hand of the monkey. Stronger stimuli produced what we have termed the "disorganization" of response, in which some cycles produce more than one impulse. This appears to correlate, in intensity level, with the "roughness" described by subjects as intensity is increased. Why is this interpreted as a pitch drop and not a rise? One possible explanation is that as intensity rises, 2 impulses/cycle may alternate more or less regularly with 1/cycle. Second- and nth-order neurons of the system will be more intensely excited by the double discharges than by the single. If this more intense activation at one-half the driving frequency should dominate higher order activity one might expect the perceived pitch to drop by exactly 1 octave; but this is not the case. The explanation of the smooth drop in pitch with increase in intensity may be the differing levels of intensity at which different fibers of the active population pass from the plateau period of perfect periodicity to the phase of alternating double and single discharges per cycle, to that of a more marked and irregular disorganization. Why an integration of these signals across that population leads to a smooth drop in perceived pitch is not yet explicable, however, in terms of central neural mechanisms.

IV. *Subjective magnitude estimation of intensity of a sine-wave stimulus, and relevant neural signals*

Here we are faced with the paradox that: *1*) the subjective magnitude estimation is a linear function of the amplitude of the sine wave which evokes it, and *2*) over this same range of intensities the response of the relevant first-order fibers is a discontinuous function of sine-wave amplitude. From the tuning point upward, over a considerable range of rising intensities, while the subjective estimation of magnitude is rising linearly, there is no change whatsoever in the neural input upon which the sensation of movement and the judgement of pitch depends. Reasons have been given for rejecting the initially attractive notion that the slowly adapting afferents, which do increase their rates of discharge as linear functions of the amplitude of steady step indentations of the skin (12), might also provide such a signal of the amplitudes of superimposed sine waves. The possibility that a spatial integration (carried out by a central mechanism) across the population of quickly adapting afferents activated by a sinusoidal stimulus might provide the signal for intensity gained some support from the results illustrated in Fig. 8, but requires further study. This integration might occur in addition to the use of the spatial distribution of activity in a neural population as a signal of the spatial form and extent of the stimulus.

V. *Mechanical impedance of tissue, and tuning curves of primary afferent fibers*

Studies of the mechanical properties of the skin and other soft tissue (17) and of the body skeleton (23) have shown that the conductivity of the tissues is maximal and mechanical impedance minimal in the range of 100–300 cycles/sec, the zone of the highest human sensitivity to vibratory stimuli. The findings of Sato (16) suggest an almost perfect impedance match between these conducting tissues and the relevant receptors in the high-frequency range, for both isolated and in situ Pacinian corpuscles (cat mesentery) were found to have quite similar sensitivity curves. Here we assume that the Pacinian corpuscles of the mesentery and those of other tissues have similar properties. The frequency range in which the cutaneous quickly adapting fibers are most sensitive (30–40 cycles/sec), however, is one at which the mechanical impedance of tissue is very high. Their regions of best sensitivity, and their tuning curves, must therefore be the result of the mechanical properties of the receptors themselves, and not of the transmitting properties of the skin. It is most likely that they respond only to direct pressure, or sheer force. This accounts for the fact, illustrated in Fig. 8, that even a very strong oscillating stimulus at 40 cycles/sec must be within 5 mm of the center of the receptive field of a quickly adapting afferent of the glabrous skin in order to excite these quickly adapting afferents, and the absence of sensation referred to regions of skin in which traveling waves, set up by distant oscillating stimuli, can be observed stroboscopically may not be interpreted to result from central inhibition of activity from that area: no activity exists there which is driven in synchrony with the traveling waves.

SUMMARY

In psychophysical experiments we measured the human thresholds for the perception of oscillatory movement, when sine-wave mechanical stimuli over the range of 5–300 cycles/sec were delivered to the glabrous skin of the hand. The double-limbed nature of the resulting frequency-intensity function, and the elevation of thresholds in the low- but not the high-frequency range by cutaneous anesthesia suggested the duality of what we term the sense of flutter-vibration. These findings also implied that this sense is served by two distinct sets of primary afferent fibers, one terminating in the glabrous skin and most sensitive to frequencies of 5–40 cycles/sec, and a second terminating in the deep tissues and sensitive over the range 60–300 cycles/sec.

The human subjective estimation of the magnitude of an oscillatory stimulus was measured at 40 and 250 cycles/sec, when sine-wave mechanical stimuli were delivered to the glabrous skin of the hand. This estimate is a linear function of sine-wave amplitude; the results are equally well described by power functions with exponents close to 1.

In a similar experimental paradigm the frequency sensitivities of the myelinated mechanoreceptive afferents innervating the monkey hand were determined. Single fibers were isolated by microdissection from the median nerve.

The class of afferents innervating the glabrous skin which adapts slowly to steady skin indentation showed a frequency modulation of that steady discharge when sine-wave stimuli of 2–10 cycles/sec were superimposed upon the indentation. This occurred at intensities far below the human thresholds at those frequencies. At higher frequencies these fibers may be entrained to discharge 1

impulse/cycle of the stimulus, and thus provide a neural signal of stimulus frequency only if the latter closely matches the frequency of the steady-state discharge. On the basis of present evidence we conclude that this set of afferents is not likely to contribute to the sense of flutter-vibration. The frequency modulation at low frequencies is a distinct neural code impressed upon these first-order elements which is apparently of no sensory significance, at least over a reasonable range of intensities.

The quickly adapting afferents which innervate the glabrous skin are sensitive to oscillatory stimuli in the low-frequency range. As the intensity of such a stimulus is increased it first elicits neural discharges at multiples of the stimulus period. Slightly stronger stimuli evoke 1 impulse/stimulus cycle, which we term the tuning point. Measurement of tuning points for a number of frequencies compose a tuning curve. The lower limbs of the tuning curves for these fibers blanket and thus can account for the low-frequency limb of the human threshold function, and no other afferent innervating the monkey hand has been found which could do so.

A quickly adapting afferent ending in subcutaneous tissue, which on indirect evidence and the findings of others we identify as terminating in Pacinian corpuscles, is extraordinarily sensitive to oscillatory stimuli in the high-frequency range, delivered to the surface of the skin. Their tuning curves blanket and can account for the high-frequency limb of the human threshold function, and no other afferent innervating the monkey hand has been observed which could do so.

For both types of quickly adapting afferents increases in intensity of sine-wave stimuli of 5 to 10× that required for tuning produce no further changes in the response; still stronger stimuli produce disorganization of the periodic response. There is therefore no ready explanation of the near linearity of the human subjective magnitude estimation of the intensity of oscillatory stimuli. We suggest this may derive from a central spatial integration of all input set up by the stimulus, but more evidence is required to make this a possibility.

The perception of regular oscillatory movement depends upon the appearance in primary afferents of regularly periodic trains of nerve impulses. Reasons are given for suggesting that the discrimination between different frequencies depends upon a central mechanism sensitive to (which "measures") the length of the periods in the input trains. The drop in perceived pitch which occurs as the intensity of an oscillatory stimulus increases is associated with a disorganization of the periodic signals in first-order fibers.

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