Representation of Spectral and Temporal Sound Features in Three Cortical Fields of the Cat. Similarities Outweigh Differences

JOS J. EGGERMONT
Departments of Physiology and Biophysics, and Psychology, The University of Calgary, Calgary, Alberta T2N 1N4, Canada

Eggermont, Jos J. Representation of spectral and temporal sound features in three cortical fields of the cat. Similarities outweigh differences. J. Neurophysiol. 80: 2743–2764, 1998. This study investigates the degree of similarity of three different auditory cortical areas with respect to the coding of periodic stimuli. Simultaneous single- and multunit recordings in response to periodic stimuli were made from primary auditory cortex (AI), anterior auditory field (AAF), and secondary auditory cortex (AII) in the cat to address the following questions: Is there, within each cortical area, a difference in the temporal coding of periodic click trains, amplitude-modulated (AM) noise bursts, and AM tone bursts? Is there a difference in this coding between the three cortical fields? Is the coding based on the temporal modulation transfer function (tMTF) and on the all-order interspike-interval (ISI) histogram the same? Is the perceptual distinction between rhythm and roughness for AM stimuli related to a temporal versus spatial representation of AM frequency in auditory cortex? Are interarea differences in temporal response properties related to differences in frequency tuning? The results showed that: 1) AM stimuli produce much higher best modulation frequencies (BMFs) and limiting rates than periodic click trains. 2) For periodic click trains and AM noise, the BMFs and limiting rates were not significantly different for the three areas. However, for AM tones the BMFs and limiting rates were about a factor 2 lower in AAF compared with the other areas. 3) The representation of stimulus periodicity in ISIs resulted in significantly lower mean BMFs and limiting rates compared with those estimated from the tMTFs. The difference was relatively small for periodic click trains but quite large for both AM stimuli, especially in AI and AII. 4) Modulation frequencies <20 Hz were represented in the ISIs, suggesting that rhythm is coded in auditory cortex in temporal fashion. 5) In general only a modest interdependence of spectral- and temporal-response properties in AI and AII was found. The BMFs were correlated positively with characteristic frequency in AAF. The limiting rate was positively correlated with the frequency-tuning curve bandwidth in AI and AII but not in AAF. Only in AAF was a correlation between BMF and minimum latency found. Thus whereas differences were found in the frequency-tuning curve bandwidth and minimum response latencies among the three areas, the coding of periodic stimuli in these areas was fairly similar with the exception of the very poor representation of AM tones in AII. This suggests a strong parallel processing organization in auditory cortex.

INTRODUCTION

Differences and similarities in the representation of both spectral and temporal aspects of sound have been demonstrated in about half a dozen auditory cortical areas. Differences support the idea that auditory cortex is organized functionally in a segregated manner, i.e., where different areas respond to different aspects of sound. As a result of such differences, two segregated pathways, similar to the “what” and “where” pathways in the visual system, have been proposed for monkey auditory cortex (Rauschecker 1997). Similarities emphasize that multiple cortical representations of certain stimulus properties are preserved thereby allowing a synthesis of spatially distributed responses. In addition, local integration of the property that is preserved in each area with other sound attributes that are mapped differently in these areas can be performed independently.

Spectral stimulus properties

In the cat, the primary auditory cortex (AI) and the anterior auditory field (AAF) show very similar single-unit frequency tuning (Knight 1977; Phillips and Irvine 1982). In contrast, the depth-recorded local field potential in AI of the cat was more sharply tuned than in AAF (Knight 1977). In AI and AAF, the percentages of monotonic and nonmonotonic units was also very similar (Kowalski et al. 1995; Phillips and Irvine 1982) but AAF featured multipeaked frequency response areas that rarely were observed in the central and ventral parts of AI but frequently were seen in the dorsal part (Knight 1977; Sutter and Schreiner 1991; Tian and Rauschecker 1994). In the ferret, the single-unit frequency-tuning curve bandwidth at 20 dB above threshold in AAF (mean 2.5 octaves) was approximately twice as large as that in AI (mean 1.3 octaves) (Kowalski et al. 1995). In the Mongolian gerbil, no differences were found in the responses to tone bursts and slow FM sweeps in AI and AAF (Schulze et al. 1997).

Secondary auditory cortex (AII) in cat appeared not as well organized tonotopically as AI, and the units showed broader frequency-tuning and higher thresholds to tone-burst stimulation than in AI. In parts of AII, responses were more sustained than in AI and latencies could be >100 ms; however, phasic responses with relatively short latencies (<50 ms) were also common (Schreiner and Cynader 1984). Recently a double representation of the cochlea within the classical boundaries of AII in cat was demonstrated (Volkov and Galazyuk 1998). One tonotopic representation was found in the dorsocaudal region (2.6–3.2 mm long) with a spatial orientation similar to that described in AI (low frequencies caudal, high frequencies rostral), the second ventrorostral region was smaller (1.4–2.5 mm) and had the opposite tonotopic orientation (i.e., as in AAF). The dorsocaudal region
may be close to the transition zone between AI and AII as defined by Schreiner and Cynader (1988). Thus AII, not unlike AI, may consist of several specialized subregions.

Latencies

Conflicting reports exist about the minimum latencies in AI and AAF. Whereas Knight (1977) and Phillips and Irvine (1982) found the same latencies in the cat, Kowalski et al. (1995) reported a mean AAF latency of 16.8 ms that was substantially shorter than the mean latency in AI of 19.4 ms. These latencies were, however, several milliseconds longer than found in cat AI (mean 12.5 ms) by Raggio and Schreiner (1994) and Mendelson et al. (1997) but comparable with those (mean 17.7 ms) reported for free-field studies by Eggermont (1996). In cat, AI and AAF receive different anatomic projections from the auditory thalamus: AI receives the heavier projections from the ventral medial geniculate body (MGB), whereas AAF receives the heavier projections from the posterior group of thalamic nuclei, PO (Morel and Imig 1987). All receives its input largely from the caudal dorsal nucleus of the MGB (Andersen et al. 1980) and is part of the extra lemniscal pathway. AI, AAF, and AII also receive input in layer I from the nontopographical organized medial part of the MGB (Winer 1992). This different innervation may in part be responsible for the observed differences in latencies and frequency tuning.

Temporal stimulus properties

Periodic amplitude modulated (AM) sounds such as sine- or square-wave modulated tone bursts also are represented differently in separate cortical fields in cat (Schreiner and Urbas 1988). The average best modulation frequency (BMF) in AAF of the paralyzed and lightly barbiturate anesthetized cat was higher than in AI. This was largely the result of higher BMFs (\( \approx 100 \) Hz) for units with characteristic frequencies (CFs) \( >10 \) kHz, whereas for lower CFs, all BMFs were \( <20 \) Hz and similar to those in AI. In AII, a range of “normal” BMFs close to 10 Hz was found but supplemented by a large group of BMFs with values \( <5 \) Hz. Such low BMFs were found less frequently in AI or AAF (Schreiner and Urbas 1988).

Comparison of the effect of various periodic stimuli such as sinusoidal AM and rectangular AM of tones at the CF (Schreiner and Urbas 1986, 1988) with periodic click trains (Eggermont 1991, 1993; Schreiner and Raggio 1996) in cat AI suggests that the BMFs are highest for sinusoidal modulation than for rectangular modulation and lowest for periodic click trains. Phillips et al. (1989) used continuous repetitive tone pips and analyzed them in terms of the response per tone pip, i.e., in terms of entrainment. Eggermont (1991) showed a similar analysis for periodic click stimulation and Schreiner and Raggio (1996) also presented their data in this alternative format in addition to using the temporal modulation transfer function (tMTFs). These entrainment functions are low-pass functions of click (tone pip) repetition rate and were very similar in these three studies (Eggermont 1997).

Internal neural representations

Regardless of whether entrainment functions or tMTFs are used, these measures are constructed on basis of full knowledge of the stimulus presented to the animal. The stimulus is, of course, unknown to the animal, and its nervous system cannot extract temporal information from aspects such as the stimulus onset and repetition rate. As a consequence, period histograms, as used in the construction of the tMTFs, cannot be computed by the nervous system. However, information similar to that in period histograms is available in the interspike interval (ISI) histograms (Horst et al. 1986) or autocorrelograms (Cariani and Delgutte 1996a). These internal neural representations can be used to extract stimulus periodicity information and may even be preferred. As Cariani and Delgutte (1996b) remarked “period histograms or their derived measures (synchronization and modulation indexes), for example, detect only stimulus-locked time patterns, and will miss more subtle, asynchronous codes . . . . Until better methods are used to study responses to complex stimuli in more central auditory stations, complex temporal pattern codes cannot be ruled out.” In response to harmonic stimuli, the most frequent ISI present in a population of auditory nerve fibers appears to correspond to the perceived pitch (Cariani and Delgutte 1996a). This ISI calculation can be done for individual neurons and then pooled across the entire population or across a local group of neurons recorded on the same electrode. A direct comparison between tMTFs and ISI histograms for cortical coding of periodic stimuli has so far not been made. It is one of the purposes of this study to compare this for three sets of stimuli: periodic click trains, amplitude-modulated noise bursts (AM noise), and amplitude-modulated tone bursts (AM tone) in three areas: AI, AAF, and AII.

Anesthesia, cortical rhythms, and temporal coding

Recently, we (Kenmochi and Eggermont 1997) reported a strong correlation between the dominant oscillation (spindle) frequency in the spontaneous local field potential (LFP) and the BMF for periodic click train stimulation in primary auditory cortex. The mean spontaneous rhythm was generally in the frequency range of 8–14 Hz but could be as high as 30 Hz, and one expects this LFP rhythm to be similar in other auditory cortical fields. This suggests that the BMFs in AI, AAF, and AII will be very similar when recorded under identical anesthesia levels. Spontaneous EEG rhythms are strongly dependent on the level of arousal or drowsiness, thus one expects the tMTFs to be similarly affected by changes in anesthesia level. However, Schulze and Langner (1997) did not find substantial effects of anesthesia on coding of AM tones in AI in the gerbil.

In awake squirrel monkeys, Bieser and Müller-Preuss (1996) investigated periodicity coding for AM sounds in eight auditory cortical areas and found a broad range of BMFs ranging from 2 to 128 Hz. Low modulation frequencies (2–64 Hz) produced mostly phase-locked neural responses whereas higher AM (128–512 Hz) sounds showed only a distinct in overall-spike-rate variations. For instance in field Pi, the highest firing rates were found for modulations of 128 Hz, whereas in field T1 they were highest for 256 Hz. Specifically in fields AI, Pi, and T1 the sensitivity to AM frequency was large enough to encode envelope fluctuations (modulation rates between 4 and 64 Hz) found in monkey calls. Steinschneider et al. (1980, 1982) found...
phase-locked activity in the depth-recorded local field potentials in auditory cortex of awake macaques up to 250 Hz and for multiunit spike activity =100 Hz.

For periodic click trains, Eggermont (1993) found for ketamine-anesthetized cats a best repetition rate of 7.9 ± 2.1 (SD) Hz, and in barbiturate-anesthetized cats Schreiner and Raggio (1996) obtained a similar value of 6.5 ± 3.8 Hz. A comparison of BMFs for AM sound in cat (Eggermont 1994, 1997; Schreiner and Urbas 1988) with those from awake squirrel monkeys (Bieser and Müller-Preuss 1996) and awake macaques (Steinschneider et al. 1980, 1982) suggests that anesthesia affects the BMF. This conclusion also was drawn by Goldstein et al. (1959) and Eggermont and Smith (1995a) on the basis of evoked potential (EP) studies. Under barbiturate anesthesia the limiting rate (50% of maximum EP amplitude) in cats was 6–8 Hz, down from 15–20 Hz in awake cats (Goldstein et al. 1959), whereas for light ketamine anesthesia the limiting rate was only slightly <15 Hz (Eggermont and Smith 1995a).

Comparing the results in awake and anesthetized animals suggests that level and type of anesthesia are likely having an effect, potentially by influencing the frequency range of the dominant autonomous cortical rhythms. It is thus desirable to eliminate potential effects of differences in anesthesia level between recordings when comparing spectral and temporal coding properties in various cortical fields. For this purpose, simultaneous recordings were made from AI, AAF, and AII in lightly ketamine-anesthetized cats.

Perceptual attributes of periodic sounds

Amplitude-modulated tones or noise produce various hearing sensations depending on the modulation frequency. These are rhythm and fluctuation strength for AM frequencies below ~20 Hz, and roughness and pitch for AM frequencies >20 Hz. The sensation of roughness disappears >300 Hz and is strongest at 70 Hz, whereas pitch related to periodicity in the stimulus envelope loses much of its perceptual strength >3 kHz (Zwicker and Fastl 1990). The click repetition rates and AM frequencies used in this study straddle the boundary between rhythm and roughness, and the limiting rate of phase-locked cortical responses may be related to that perceptual boundary. All results obtained for AM stimuli in auditory cortex so far point to a potential temporal code up to frequencies of ~20–30 Hz (Schulze and Langner 1997). However, no direct evidence for an internal temporal code based on ISIs so far has been demonstrated in auditory cortex nor has its AM frequency range been determined.

This study addresses the following questions: 1) Is there, within each cortical area, a difference in the temporal coding of periodic click trains, AM noise bursts, and AM tone bursts? 2) Is there a difference in this coding among the three cortical fields? 3) Is the repetition rate range of temporal coding as inferred from stimulus referenced measures such as the tMTF and internal neural representations such as the all-order ISI histogram the same? 4) Is the perceptual distinction between rhythm and roughness for AM stimuli related to the upper limit of a temporal representation of AM frequency in auditory cortex? And 5) are interarea differences in temporal response properties related to differences in frequency tuning and response latencies?

METHODS

The care and the use of animals reported on in this study was approved (No. P88095) by the Life and Environmental Sciences Animal Care Committee of the University of Calgary.

Animal preparation

Cats were premedicated with 0.25 ml/kg body wt of a mixture of 0.1 ml acepromazine (0.25 mg/ml) and 0.9 ml of atropine methyl nitrate (5 mg/ml) subcutaneously. After ~0.5 h, they received an intramuscular injection of 25 mg/kg of ketamine (100 mg/ml) and 20 mg/kg of pentobarbital sodium (65 mg/ml). Ducravin (20 mg/ml) was injected subcutaneously and rubbed in gently, then a skin flap was removed and the skull cleared from overlying muscle tissue. A large screw was cemented upside down on the skull with dental acrylic. An 8-mm-diam hole was trephined over the right temporal cortex so as to expose parts of AI and AII. A 4-mm hole was drilled over the AAF. The dura was left intact, and the brain was covered with light mineral oil. Then the cat was placed in a sound-treated room on a vibration isolation frame and the head secured with the screw. Additional acepromazine/atropine mixture was administered every 2 h. Light anesthesia was maintained with intramuscular injections of 2–5 mg · kg⁻¹ · h⁻¹ of ketamine. The wound margins were infused every 2 h with durocain, and also every 2 h new mineral oil was added if needed. The temperature of the cat was maintained at 37°C. At the end of the experiment the animals were killed with an overdose of pentobarbital sodium.

Acoustic stimulus presentation

Acoustic stimuli were presented in an anechoic room from a speaker placed 55 cm in front of the cat’s head. The sound-treated room was made anechoic for frequencies >625 Hz by covering walls and ceiling with acoustic wedges (Sonex 3") and by covering exposed parts of the vibration isolation frame, equipment, and floor with wedge material as well. Calibration and monitoring of the sound field was done using a B&K (type 4134) microphone placed above the animal’s head and facing the loudspeaker. A search stimulus consisting of random-frequency tone pips, noise bursts, and clicks was used to locate units. Characteristic frequency (CF) and tuning curve of the individual neurons were determined with 50-ms-duration, gamma-shape-envelope, tone pips presented randomly in frequency once per second (Eggermont 1996). The 81 different frequencies used were equally spaced logarithmically between 625 Hz and 20 kHz (or between 1.25 and 40 kHz) so that 16 frequencies were present per octave. After the frequency-tuning properties of the cells at each electrode were determined, periodic click trains (1-s duration followed by 2 s of silence) and amplitude-modulated noise or tone bursts (0.5-s duration followed by 2.5 s of silence) were presented once per 3 s. The modulation frequencies were between 1 and 32 (click trains) or 2 and 64 Hz (AM sounds) at logarithmically equal distance with four values per octave and were presented randomly. The AM wave form was an exponentially transformed sine wave (Epping and Eggermont 1986) with a maximum modulation depth of 17.4 dB so that the envelope, when expressed in dB, was sinusoidally modulated. The sequences of 21 click trains or 21 AM noise or AM tone bursts were repeated 10 times resulting in a total stimulus ensemble duration of 630 s per stimulus type. The click trains and AM sounds were presented at peak intensities of 35, 55, and 75 dB SPL, and results for the intensity where the firing rate was the highest are presented. Clicks consisted of single polarity electric pulses 0.1 ms in duration.
Recording and spike separation procedure

Three tungsten micro electrodes (Micro Probe) with impedances between 1.5 and 2.5 MΩ were advanced independently perpendicularly to the AI, AAF, and AII surfaces using remotely controlled motorized hydraulic microdrives (Trent-Wells Mark III). The electrode signals were amplified using extracellular preamplifiers (Dagan 2400) and filtered between 200 Hz (Kemo VBFS, high-pass, 24 dB/oct) and 3 kHz (6 dB/oct, Dagan roll-off) to remove local field potentials. The signals were sampled through 12 bit A/D converters (Data Translation, DT 2752) into a PDP 11/53 microcomputer, together with timing signals from three Schmitt-triggers. In general the recorded signal on each electrode contained activity of two to four neural units. The PDP was programmed to separate these multiunit spike trains into single-unit spike trains using a maximum variance algorithm (Eggermont 1992). The spikes from well-separated wave-form classes, each assumed to represent a particular neuron, were stored and coded for display. The multiunit data presented in this paper represent only well-separated single units that, because of their regular spike wave form, likely are dominantly from pyramidal cells (Eggermont 1996). Thus contrary to the common use of the term multiunit as a cluster of not well separable units, in this analysis the separable single-unit spike trains extracted from the multiunit recording were added again to form a multiunit spike train with better statistics and that likely consists of contributions from only one type of neurons.

In addition, the electrode signals were band-pass filtered between 10 and 100 Hz to obtain spike-free signals of ongoing local field potentials (LFP). These signals also were passed through Schmitt triggers set at ∼2 SD (i.e., at about −100 μV) below the mean value of the ongoing signal during silence. The ‘‘spikes’’ of these LFPs were processed in the same way as single-unit spike data. We have shown previously that these level crossings represent most of the temporal (Eggermont and Smith 1995a) and spectral (Eggermont 1996) response properties of the single units recorded at the same electrode.

The boundary between AI and AAF was explored by taking a series of LFP and multiunit measures (with the high-pass filter set at 10 Hz with 6 dB/oct) from caudal to rostral and assuring that there was a gradual increase in CF, which reversed in direction when advancing to the AAF. The AII was identified anatomically and electrophysiologically based on the broader tuning curves and different response patterns compared with those in the central and ventral parts of AI. Recordings in AII were generally made from the ventrostral part. Recording electrode positions in the three cortical areas were chosen such that recordings with approximately similar best frequencies (within 0.5 octave) at 50–70 dB SPL were obtained. Recordings were made between 600 and 1,200 μm below the cortex surface.

Data analysis

The number of action potentials in the first 100 ms after each tone-pip presentation were counted for each intensity. The counts for three adjacent frequencies were combined to reduce variability and divided by number of stimuli and presented as a firing rate per stimulus. This resulted in 27 frequencies covering 5 octaves so that the final resolution was ∼0.2 octaves. The results per stimulus intensity were combined into a rate-frequency-intensity profile from which tuning curves, rate-intensity functions, and iso-intensity-rate contours could be derived (Eggermont 1996). The frequency-tuning curve was defined for a firing rate at 25% of the maximum firing rate. The threshold was determined as 2.5 dB below the intensity that produced visible time locked responses to the tone pip, i.e., midway between the stimulus that produced a response and the one that did not. The tuning curve bandwidth was measured at 20 dB above threshold and expressed in octaves.

Latency measures were corrected for the acoustic travel time from the speaker to the cat’s ears by subtracting 1.6 ms (speaker distance 550 mm divided by the speed of sound 340 mm/ms).

The following capacity of the neurons for click repetition rate and AM frequency was estimated from the temporal modulation transfer functions and ISI histograms. The temporal modulation transfer functions were obtained by Fourier transformation of the period histograms (Eggermont 1991). Each modulation period was divided into 16 bins, and only recordings with at least five counts in the maximum bin per 10 stimulus presentations at a rate of 8 Hz were analyzed further. The rate-tMTF was defined as the number of spikes per 10 presentations of the 1-s duration click train or 0.5-s-duration modulated noise or tone burst, as a function of click repetition rate or modulation frequency. The synchronization-tMTF was defined as the amplitude of the first harmonic of the period histogram, as a function of the click-repetition rate or AM frequency. The BMF was defined as the click or AM rate for which the synchronization-tMTF was maximal. The limiting rate was defined as the highest rate at which the response was 50% of that at the BMF. The significance of the vector strength for each modulation frequency (defined as $P < 0.005$) was calculated using the Raleigh test (Mardia 1972).

ISI histograms and autocorrelograms for lags up to three periods were constructed with 16 bins per stimulus period for each individual click rate or AM frequency. The accuracy was thus proportional to the stimulus period, and the capacity to represent click repetition rates or AM rates in an interval code is reflected in a peak in the same position in the histograms regardless of the click repetition rate or AM frequency. Population autocorrelograms and interval histograms were obtained by adding all the individual single-unit ones. Multiunit (MU) autocorrelograms per recording site were also calculated, they reflect both single-unit autocorrelograms as well as cross-correlograms between units on the same electrode. The autocorrelograms is formally identical to the all-order ISI histogram, i.e., formed by adding the interval histogram for adjacent spikes, for one but adjacent spikes, etc., (Cariani and Delgutte 1996a) and I use the terms interchangeably.

All statistical analyses were performed using Statview 4.5. Illustrations were made with Horizon and Powerpoint Software.

RESULTS

Results presented for periodic click trains are from 62 simultaneous recordings with an electrode in each of AI, AAF, and AII in 14 cats, resulting in 186 MU records and the same number of LFP records. The MU records could be separated into 552 single-unit (SU) spike trains of which 250 had large enough firing rates to permit analysis of the tMTF (as defined in METHODS). In nine of these cats, responses also were obtained for AM noise and AM tones for a total of 102 MU records (separable into 156 SU spike trains with sufficient firing rates). We also made 23 simultaneous recordings for click train stimulation with two electrodes in AI and one in AAF resulting in 69 MU records (88 single units with sufficient firing rates) and 69 LFP recordings in seven additional cats. In 27 of these recordings, we also stimulated with AM noise and AM tones (27 MU records resulting in 33 single-unit spike trains with sufficient firing rates). The total number of single units presented in this study is 338 (of 740 single units recorded from) in 21 cats. In the MU data, all units with well-defined spike wave form were included regardless of their firing rate.

Representative examples for periodicity coding

Figure 1 shows dot displays from electrode sites in AI (left), AAF (middle), and AII (right) with similar CF of ∼5 kHz in
response to periodic click trains (top), AM noise bursts (center row), and AM tone bursts (carrier 5 kHz; bottom). Click repetition rates were between 1 and 32 Hz, whereas AM frequencies were between 2 and 64 Hz. Both LFP triggers (orange dots) and single units (green, blue, or black dots) are shown for a time base of 600 ms after stimulus onset. As a consequence only the response to the first half of the click train is shown. The recording site in AI did not show strong single-unit responses to click trains (and is therefore not representative of our sample of AI units) but good following for the LFP. For AM stimuli, however, three single units were responding up to AM rates of 16 Hz, with the stronger responses for AM noise. No onset unit responses coinciding with the LFP triggers were noted for AM noise bursts and unit onset responses were limited to modulation frequencies between 8 and 32 Hz for AM tone bursts. For AAF, the LFP triggers showed similar following as in AI, whereas the unit activity was much more pronounced especially for the AM stimuli. The best following was found for AM tone bursts (≤32 Hz) albeit that the more vigorous responses were obtained for AM noise burst stimulation. A pronounced off response is noted for noise with AM frequencies of 16–64 Hz. In AII, LFP activity showed weak following as did most unit activity, and the strong long latency unit activity for noise bursts was largely independent of AM rates and likely a rebound response after initial suppression of firing.

The second example (Fig. 2) from recording sites, with an AM frequency of ~2.5 kHz in AI and AAF and 3–7 kHz (broadly tuned) in AII, illustrates preferential locking of the unit firing to the modulation frequency for AM sounds in AI, to the broadband sounds (click train and AM noise) in AAF and to the AM tones (2.5 kHz) for AII. The LFP triggers in AI and AAF are found to follow repetition rates for clicks up to ~10 Hz and with skipping one period ≤16 Hz. AM rate following was slightly higher: up to ~16 and 20 Hz with skipping one period. Off responses again were noted for AM noise stimulation but this time in AI.

From these dot displays the next step is to generate period histograms and from these the rate tMTF (mean number of spikes per 10 stimuli), the vector strength (Goldberg and Brown 1969), and the synchronization tMTF [the product of rate and vector strength (VS)]. Figure 3 presents this for three MU conditions shown in Fig. 2. Figure 3A presents results for the AAF recording in response to click trains, the period histogram (the 1st 2 panels show this twice, useful to track peak phase changes that exceed 1 period as in Fig. 3C) illustrates the gradual shift of the peak response in its relative position in the click-repetition period (i.e., its phase). The third panel shows the rate tMTF, and an abrupt drop in the response is noted >9.56 Hz. The VS (4th panel) appears significant for all repetition rates except at 11.3 and 32 Hz. Finally, the synchrony tMTF peaks at 4.76 Hz (its BMF) although it is only marginally larger than at 8 Hz. The limiting rate (50% of the value at BMF) is found for 9.52 Hz and coincides with the abrupt drop in firing rate. Figure 3B shows the same analysis for AM noise in the AI recording. The nearly constant phase of the peak response in the period histograms for AM frequencies <8 Hz forms a clear exception to the normal monotonic increase of phase. The abrupt drop in mean firing rate at 8 Hz results in both a BMF and limiting rate at 6.72 Hz. Figure 3C shows one of the infrequent instances where a recording in AII showed good locking to the period of AM tones. The mean number of spikes per 10 stimuli decreases monotonically with AM frequency, the VS shows a band-pass dependence on AM frequency, the BMF is 9.52 Hz, and the limiting rate is 11.3 Hz.

Group data

DISTRIBUTION OF BEST MODULATION FREQUENCIES AND LIMITING RATES FOR PERIODIC CLICK TRAINS. The BMFs for multunit responses to periodic click train stimulation were approximately normally distributed (Fig. 4A). No significant effect of area was noted (Table 1, paired t-test, P >
0.08). For individual single units, the distribution of BMFs generally was comparable with that for the MU data (Fig. 4B) but there were relatively more values in the 2- to 3-Hz range. There were no significant differences between the BMF values for single units with those for the MU data (Table 1). The BMF value for the tMTF based on LFP triggers (Table 1) was significantly larger (paired t-test, $P = 0.008$) than that for MU spikes in AI and also in AII (paired t-test, $P = 0.04$) but not in AAF. The BMFs for LFP triggers and MU spikes were correlated positively ($R = 0.205$; Fisher’s $r$ to $z$ test, $P = 0.0025$).

The distribution for the limiting rates for multiunit is shown in Fig. 5A. No effect of area was found on the mean values (Table 1, paired t-test, $P > 0.5$). For single units, the distribution of limiting rates was generally more predominant in the 9- to 12-Hz range than for the MU data (Fig. 5B). Again higher mean values were found for LFP triggers but these were not significantly different between areas. For all areas, the limiting rates were higher for the LFPs than for the corresponding MUs (paired t-test, $P < 0.05$). The limiting rates for both measures were correlated positively ($R = 0.139$; Fisher’s $r$ to $z$ test, $P = 0.034$).

Besides taking all LFP triggers, a separate analysis was run on only the first LFP trigger after a click (LFP1) to avoid effects of secondary LFP triggers (within 50 ms of the first, as shown in Fig. 2) that are never accompanied by spikes. The BMFs for these LFP1 triggers were not different from those where all triggers were used, however, the limiting rate for LFP1 triggers was significantly higher in AI (19.3 vs. 17.2 Hz; paired t-test, $P < 0.0001$).

**DISTRIBUTION OF BEST MODULATION FREQUENCIES AND LIMITING RATES FOR AM STIMULI.** Best modulation frequencies and limiting rates for MU recordings were not significantly different for AM noise and AM tone stimulation (Table 1; analysis of variance with post hoc Scheffe test, at the $P < 0.05$ level) and therefore the data were combined in the frequency distributions shown in Fig. 6. Most BMFs (Fig. 6A) were found for AM frequencies $<20$ Hz in all three areas but in contrast to click train stimulation, BMFs $>20$ Hz were found as well. As a result, the standard deviation in the BMFs is very large and the modal BMFs are significantly smaller than the mean (Table 1). Limiting rates (Fig. 6B) were relatively uniformly distributed between 2 and 64 Hz.

As shown in Table 1, in each cortical area, the BMFs obtained for LFP triggers were generally similar to those for MU spikes, and the only significant difference was that the LFP measure was significantly higher than that for MUs in AAF for AM tone stimulation (paired t-test, $P < 0.05$). The limiting rates were significantly higher for LFP triggers than for MU spikes for AAF (both AM noise and AM tone, $P < 0.05$) and AII (AM noise only, $P < 0.05$). In AAF the BMFs and limiting rates were significantly ($P < 0.05$) lower than those for AI and AII, whereas there was no difference between AI and AII.

Limiting rates between AM stimuli were not significantly different within a cortical area, but for both AM stimuli they were significantly ($P < 0.0001$) higher than for click train stimulation. This was found for all cortical areas, both for MU spikes and LFP triggers. The BMFs for LFP triggers were significantly higher for AM stimuli than for clicks in AI and AII but not in AAF. For MU spikes, the BMFs were significantly higher for AM stimuli than for clicks in AI and AII, but again not in AAF.

**MEAN TEMPORAL MODULATION TRANSFER FUNCTIONS FOR PERIODIC CLICK TRAINS.** Across all recordings, the mean number of spikes during the click trains was computed for LFP triggers, LFP1 triggers, and MU spikes and shown in Fig. 7. This figure thus represents the rate-tMTFs. The LFP triggers show a weak band-pass dependence on click rate, the LFP1 triggers show a high-pass dependence (as a consequence of only taking at most 1 trigger per click) and the MU spike rate is also weakly band-pass. The highest number of spikes per click train on average was obtained in AAF.

The mean VS for the three response measures is shown in Fig. 7. Dot displays for simultaneous LFP and SU activity in AI, AAF, and AII in response to periodic click trains, and amplitude-modulated noise and tone bursts (2.5 kHz). Format is similar to Fig. 1. CFs of the recording sites were $\sim 2.5$ kHz in AI and AAF and $3-7$ kHz in AII (broadly tuned).
FIG. 4. Distributions of the BMFs for multiunit (MU) and SU activity in response to periodic click trains in the 3 areas. A: BMFs are very similarly distributed for MUs. B: same for single units.

FIG. 3. A: period histograms, rate modulation transfer function, vector strength, and synchrony modulation transfer function for the response to clicks in AAF as shown in Fig. 2. Period histogram is shown twice. Preferred phase of the response shifts from the beginning to little over half of the period for increasing click rates. Rate temporal modulation transfer function (tMTF, middle panel) shows an abrupt reduction at a click rate of 11.28 Hz. Vector strength (VS) is relatively strong throughout the entire range of click rates. Synchrony tMTF peaked at 4.76 and at 8 Hz, the best modulation frequencies (BMF) was estimated at 8 Hz. Limiting rate, at 50% of the value at the BMF, was at 11.28 Hz. B: following the same format, the result for AM noise in AI, for data shown in Fig. 2, is presented. Note that AM rates now are between 2 and 64 Hz. Firing rate and VS as well as number of synchronized spikes drops substantially at 8 Hz (limiting rate) for a BMF of 6.72 Hz. C: again in the same format, shows results for AM tone stimulation in AII (data same as in Fig. 2). Number of spikes per tone burst is a slowly decreasing function of AM frequency, the VS is high only between 6.72 Hz and 9.52 Hz. BMF is 9.52 Hz, and the limiting rate is 11.28 Hz.
LFP1 triggers approaches the VS values for all the LFP-trigger conditions and for MU spikes. This suggests that the jitter in both LFP triggering and spike firing is limiting the VS at high click rates. In AI, the VS for MU spikes was equal to that for the LFP triggers <4 Hz and >16 Hz but was higher in between. In AAF, the VS was very similar for MU spikes and LFP triggers. For AII, the VS for MU spikes was slightly higher than for LFP triggers at all click rates. The highest VSs for MU recordings was obtained in AI for click rates of 8 and 9.56 Hz.

The product of the number of spikes per click train and the VS results in the synchronization tMTF (Fig. 9). All the tMTFs were band-pass with the BMF at 8 or 9.52 Hz regardless of cortical area or response measure. The maximum number of synchronized spikes or LFP triggers per click train was highest in AI.

The ratio of the number of MU spikes and the number of LFP triggers was largely independent of click rate (Fig. 10A), whereas the ratio for the synchronized rate dropped somewhat >10 Hz (Fig. 10B). This again suggests that LFP triggers can be used to predict the unit response to periodic click trains up to a scaling factor depending likely somewhat on the setting of the trigger level.

Averaging across all units to obtain mean tMTFs such as shown in Fig. 9 inevitably is dominated by units with the highest firing rates. Thus we also normalized each single-unit tMTF on its value at the BMF and then averaged. The so-obtained mean normalized-tMTF did not differ essentially from the normalized mean-tMTF for AI but was slightly different for AAF and AII (Fig. 11). The differences suggest that in AAF and AII, units with BMFs <8 Hz and >16 Hz had on average lower firing rates than units with BMFs in between.

The VS and tMTF curves averaged across the single units were similar to those for the MU data. The BMF of the mean SU tMTFs was 9.52 Hz for AI and AII and 8 Hz for AAF.

**Table 1. Mean BMF and limiting rates for three stimuli and three cortical areas**

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>Measure</th>
<th>AI</th>
<th>AAF</th>
<th>AII</th>
</tr>
</thead>
<tbody>
<tr>
<td>Click trains</td>
<td>LFP</td>
<td>12.5</td>
<td>9.6</td>
<td>8.1</td>
</tr>
<tr>
<td></td>
<td>MU</td>
<td>8.6</td>
<td>6.7</td>
<td>8.5</td>
</tr>
<tr>
<td></td>
<td>SU</td>
<td>8.1</td>
<td>7.3</td>
<td>7.4</td>
</tr>
<tr>
<td></td>
<td>ISI histogram</td>
<td>6.3</td>
<td>6.1</td>
<td>7.0</td>
</tr>
<tr>
<td>AM noise</td>
<td>LFP</td>
<td>16.5</td>
<td>10.2</td>
<td>17.5</td>
</tr>
<tr>
<td></td>
<td>MU</td>
<td>15.7</td>
<td>11.9</td>
<td>15.3</td>
</tr>
<tr>
<td></td>
<td>ISI histogram</td>
<td>10.2</td>
<td>8.5</td>
<td>9.4</td>
</tr>
<tr>
<td>AM tone</td>
<td>LFP</td>
<td>17.2</td>
<td>14.5</td>
<td>19.0</td>
</tr>
<tr>
<td></td>
<td>MU</td>
<td>20.6</td>
<td>8.9</td>
<td>15.7</td>
</tr>
<tr>
<td></td>
<td>ISI histogram</td>
<td>8.6</td>
<td>8.3</td>
<td>9.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BMF, Hz</th>
<th>Limiting rate, Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>AI</td>
<td></td>
</tr>
<tr>
<td>LFP</td>
<td>12.5 ± 8.1</td>
</tr>
<tr>
<td>MU</td>
<td>8.6 ± 3.8</td>
</tr>
<tr>
<td>SU</td>
<td>8.1 ± 2.6</td>
</tr>
<tr>
<td>ISI</td>
<td>6.3 ± 2.3</td>
</tr>
<tr>
<td>AAF</td>
<td></td>
</tr>
<tr>
<td>LFP</td>
<td>16.5 ± 12.0</td>
</tr>
<tr>
<td>MU</td>
<td>15.7 ± 16.9</td>
</tr>
<tr>
<td>ISI</td>
<td>10.2 ± 2.3</td>
</tr>
<tr>
<td>AII</td>
<td></td>
</tr>
<tr>
<td>LFP</td>
<td>17.2 ± 13.0</td>
</tr>
<tr>
<td>MU</td>
<td>20.6 ± 17.7</td>
</tr>
<tr>
<td>ISI</td>
<td>8.6 ± 2.2</td>
</tr>
</tbody>
</table>

Values are means ± SD. BMF, best modulation frequency; AI, primary auditory cortex; AAF, anterior auditory field; AII, secondary auditory cortex; LFP, long field potential; MU, multiunit; SU, single unit; ISI, interspike interval.

**ISI and autocorrelogram representation**

Periodic click trains. First-order ISI histograms and autocorrelograms (all-order ISI histograms) were calculated for all SU and separately for all MU spike trains. As an example, we show the period histograms (triggered with reference to the clicks and the basis for the tMTFs) and all-
terspike intervals equal to one click period are for click repetition rates of 13.44 Hz (AI) and potentially for 16 Hz in both AAF and AII. Evidence for intervals equal to two periods of the stimulus is found at 19.04 Hz for all three areas. Considering only first-order ISIs (Fig. 14B) also shows that, especially for “optimal” click rates such as between 8 and 11.28 Hz, ISIs equal to twice the click period frequently occur. Such firings contribute to the tMTF at those repetition rates but not to the “correct” ISI. This suggests that the period histogram method resulting in tMTFs sets the upper limit for a temporal representation of periodicity.

The mean values of the BMF and limiting rate calculated for the all-order ISI histogram representation for single units are very similar to corresponding values obtained from the temporal modulation transfer functions (Table 1). For those single-unit recordings where the all-order interval histogram showed visible peaks at lag times equal to one stimulus period (in 178 of the 338 units for which a tMTF was calculated), scattergram plots of BMFs and limiting rates from tMTFs and population ISI histograms and autocorrelograms (all-order ISI histograms) for simultaneous MU recordings in the three areas with all CFs ~5 kHz. In Fig. 13A, the period histograms show visible click following ~32 Hz with the largest amplitudes in the 4- to 8-Hz range in each area. In contrast, the all-order ISI histograms (Fig. 13B) show preferred activity at ISIs equal to one period of the click repetition rate only up to 9.52 Hz, possibly to 11.28 Hz with an absence of ISIs for higher click rates. This suggests that the firings locked to the clicks at these rates were isolated spikes or spike pairs that were at least more than three click periods apart. Note that the peak width at the one- and two-period marks are the same relative to the period duration, suggesting an accuracy of firing that is proportional to the time interval between clicks.

Population ISI histograms and autocorrelograms (all-order ISI histograms) were constructed by adding the 338 individual SU ISI histograms and autocorrelograms. For the entire population, the pooled all-order ISI histogram is shown in Fig. 14A. The highest detectable preferred in-

**FIG. 5.** Distributions of the limiting rates for MU and SU activity in response to periodic click trains. A: limiting rates for MU data are very similar for the 3 cortical areas. B: same for SU data.

order ISI histograms for simultaneous MU recordings in the three areas with all CFs ~5 kHz. In Fig. 13A, the period histograms show visible click following ~32 Hz with the largest amplitudes in the 4- to 8-Hz range in each area. In contrast, the all-order ISI histograms (Fig. 13B) show preferred activity at ISIs equal to one period of the click repetition rate only up to 9.52 Hz, possibly to 11.28 Hz with an absence of ISIs for higher click rates. This suggests that the firings locked to the clicks at these rates were isolated spikes or spike pairs that were at least more than three click periods apart. Note that the peak width at the one- and two-period marks are the same relative to the period duration, suggesting an accuracy of firing that is proportional to the time interval between clicks.

Population ISI histograms and autocorrelograms (all-order ISI histograms) were constructed by adding the 338 individual SU ISI histograms and autocorrelograms. For the entire population, the pooled all-order ISI histogram is shown in Fig. 14A. The highest detectable preferred in-

**FIG. 6.** Distribution of BMFs and limiting rates for MU responses to AM stimuli in 3 areas. A: most frequent BMF values found are ~10 Hz but the range of values is much wider than for click stimulation (cf. Figs. 4 and 5), thus the mean value is considerably larger than the mode. B: fairly uniform distribution of limiting rates for AM stimuli in all areas.
Similar for the three cortical areas, clear interareal differences are found for AM noise and AM tone stimulation. Figure 16A shows the population results for AM noise based on individual SU all-order ISI histograms; in Al, ISIs equal to the AM period are found for rates \( \leq 38 \) Hz, whereas for AAF and All, this is at most \( \leq 16 \) Hz. For AM tones (Fig. 16B), in Al ISIs equal to the AM period are again found \( \leq 32–38 \) Hz and in AAF at most \( \leq 16 \) Hz, whereas in All hardly any preferred intervals are seen. This does not mean that no single units can be found that show ISIs equal to a stimulus period; in fact the mean and SD shown in Table 1 clearly indicates this presence. The difference is that only from all-order ISI histograms (Fig. 15, A and B) show that these measures are positively correlated in all three areas (\( P < 0.05 \)). The regression lines are labeled with the area name. For this subgroup of single units, the BMF for the all-order interval histogram was significantly lower (\( \sim 1.7 \) Hz; \( P < 0.0005 \)) than the BMF from the tMTF in all areas. A paired \( t \)-test showed no significant differences in the limiting-rate measures in either of the three cortical areas. Thus the mean values for BMF and limiting rate obtained with the tMTF and the all-order ISI histograms are very similar.

**AM STIMULI** Whereas the all-order population ISI histograms for click train stimulation (cf. Fig. 14A) are very

![Figure 7](http://jn.physiology.org/content/114/10/2752/F7)

**FIG. 7.** Comparison of mean rate modulation transfer functions in the 3 areas. **Top:** results based on LFP triggers. tMTF is a weakly band-pass function of click rate and very similar for the three areas. **Middle:** same but only taking the 1st LFP trigger per click into account. Three functions are now high-pass functions of click rate. **Bottom:** results for MU data, again a weakly band-pass function is obtained. AAF on average shows the largest firing rates across all click rates.

![Figure 8](http://jn.physiology.org/content/114/10/2752/F8)

**FIG. 8.** Comparison of the mean VS as a function of click rate in the paired \( t \)-test showed no significant differences in the limiting-rate measures in either of the three cortical areas. Thus the mean values for BMF and limiting rate obtained with the tMTF and the all-order ISI histograms are very similar.

**AM STIMULI** Whereas the all-order population ISI histograms for click train stimulation (cf. Fig. 14A) are very similar for the three cortical areas, clear interareal differences are found for AM noise and AM tone stimulation. Figure 16A shows the population results for AM noise based on individual SU all-order ISI histograms; in Al, ISIs equal to the AM period are found for rates \( \leq 38 \) Hz, whereas for AAF and All, this is at most \( \leq 16 \) Hz. For AM tones (Fig. 16B), in Al ISIs equal to the AM period are again found \( \leq 32–38 \) Hz and in AAF at most \( \leq 16 \) Hz, whereas in All hardly any preferred intervals are seen. This does not mean that no single units can be found that show ISIs equal to a stimulus period; in fact the mean and SD shown in Table 1 clearly indicates this presence. The difference is that only
All-order ISIs compared for clicks and AM stimuli. An illustration of the dependence of all-order interval histograms on stimulus type for three selected SU recordings is shown in Fig. 17, A–C. For primary auditory cortex (Fig. 17A), the results for click trains (click rates from 1 to 32 Hz) show that rates between 1 and 11.3 Hz produce preferred ISIs equal to the click interval, whereas for AM noise and AM tones (AM rates from 2 to 64 Hz) this range is shifted upward from ~5–8 to 32 Hz. Clearly low AM rates for noise and tones are not effective in generating a temporal representation of the AM period. In contrast to high click rates, high AM rates are much more effective likely because AM stimuli do not induce the strong postactivation suppression that is commonly found for clicks (cf. Fig. 2). For AAF (Fig. 17B), the picture is somewhat different. For clicks, preferred ISIs equal to the interclick interval are again found up to 11.3 Hz, but for AM noise and AM tones, the upper boundary is only slightly higher at ~16–19 Hz. Again a strong band-pass dependency is found for AM noise, but less so for AM tones. In AII (Fig. 17C), one of the limited number of examples for which AM tones produced some clear ISIs in single-unit activity at the AM period (mostly between 8 and 16 Hz), the result was not overly clear for the other stimuli: for AM noise and for click trains only rates ~8 Hz were effective.

To construct an analogue to the tMTF based on ISIs, the maximum in the three bins surrounding and including the AM period for the all-order ISI population histograms was calculated. The results are illustrated in Fig. 9A. For LFP triggers, the number of synchronized triggers at low and high click rates is very similar in the 3 areas, but the peak number of synchronized triggers is largest in AI and about the same in AAF and AII. Taking only 1st triggers for the LFP shows basically the same result with AII slightly better than AAF. For MU spikes (bottom), again the results are qualitatively the same in the three areas but with AI producing more synchronized spikes than AAF and AII. Note that the average number of spikes per stimulus was highest in AAF (cf. Fig. 7).

10% of the units in AII showed detectable periodic ISIs for AM tones, whereas nearly all did for AM noise. The mean BMFs and limiting rates calculated from the individual all-order ISI histograms (Table 1) are strikingly lower than for the values obtained from the tMTFs (except the BMFs for AAF), but somewhat similar to those obtained from the population ISI histogram. As can be seen, the SDs for the limiting rates for AM stimuli are much larger (and also relative to the mean) than for click stimulation.
The number of ISIs is highest at 9.52 Hz and its subharmonic of 4.76 Hz (for AI and AII), and slightly lower at 8 and 4 Hz for AAF. This dip might be related to an interaction between depression periods in ongoing spindle activity and the activation introduced by the clicks with rates between 4 and 9 Hz (Eggermont and Smith 1995a).

For AM noise stimulation, the elicited maximum number of periodic ISIs is largest in AAF than in AI and smallest in AII. There is a rapid drop in the number of ISIs at >11.3 Hz for AAF and AII, whereas in AI the number only slowly decreases for higher AM rates. Again a dip in the number of ISIs is noted, this time at 4.76 Hz; however, there is no indication of a harmonic structure in the dependency on modulation rate. AM tone stimulation only produces significant numbers of periodic ISIs in AAF with very few intervals >13 Hz, whereas AI and AII both stay close to the background level. Thus with the exception of AM noise in AI, the highest AM rate for a significant number of ISIs is ~13 Hz. Comparison of, for instance, Figs. 11 and 12 (see also Table 1) shows that the BMFs and the limiting rates are generally higher for the tMTF-based characterization. This suggests that individual stimulus-locked spikes are evoked for rates >13 Hz and are distributed across stimulus duration but that there are no doublets with an ISI equal to the AM period generated for these higher AM rates.

**TEMPORAL MODULATION TRANSFER FUNCTIONS AND LATENCY.** For single units, the first-click latencies obtained at peak equivalent SPL levels of 75 dB were correlated positively with the minimum latency for tone pips (significant in all 3 areas, \( P < 0.001 \)) and were on average 1.3 ms longer than the minimum latency for pips (which typically was found also at 75 dB SPL, the highest intensity used). First-click latencies were shortest (\( P < 0.0001 \)) in AAF and about equal in AI and in AII (Table 3). Minimum tone pip latencies were also shortest (\( P < 0.0005 \)) in AAF and again about equal in AI and AII. The BMF for single units in response to periodic click trains was correlated positively with the first-click latency (Fig. 19A). The regression lines are labeled with the area name. This correlation was significant for AAF but not for AI and AII. The limiting rate was correlated positively with first-click latency for AI and AAF but not for AII (Fig. 19B).

**CORRELATION OF SPECTRAL AND TEMPORAL PROPERTIES.** For all recording sites, the LFP trigger and multiunit intensity-frequency response areas were measured. Multipeaked response areas for MU recordings were found in 8% of recording sites in AI, for 26% of recording sites in AAF, and for 9% of recording sites in AII. The CF and bandwidth (BW) at 20 dB above threshold at CF was determined for both LFP and MU recordings. At the same recording sites, the CF values were, with some exceptions, very similar for LFP and MU (Fig. 20A). In 10 cases the differences in CF were >1 octave. However, the 20 dB BW was significantly larger in AI and AAF for frequency tuning of LFP triggers than for MU spikes recorded on the same electrode (Table 2, Fig. 20B). This amounted to 0.4 octaves (\( P < 0.01 \)) for AI and to 0.8 octaves (\( P < 0.0001 \)) in AAF. In all the bandwidths were not significantly different for LFP-trigger- and MU-spike-based tuning curves. Between cortical areas, the MU tuning curve bandwidth in AAF and AII was not

---

**FIG. 11.** Comparison of a normalized mean tMTF for MU data with the mean of normalized MU tMTFs. For the normalized mean tMTFs, the same graphs shown in Fig. 9 were normalized to a peak level of 1. In the 2nd case, all individual MU tMTFs first were normalized, then averaged, and then the peak value again was adjusted to 1. For AI, the 2 curves are identical; for AAF and AII, some differences are noted both at low and high click rates.
FIG. 12. Comparison of LFP trigger and MU-spike based tMTFs for 3 stimulus types in 3 cortical areas. A: in all 3 areas, click trains evoke ≈3 times more LFP triggers per stimulus (or half the stimulus in case of the click trains) for modulation rates <30 Hz. No noticeable difference was found between the 2 AM stimuli. For MU spikes, the difference in response size was smaller (B). Also in this case the click stimuli produce considerably larger responses than the AM stimuli, especially in AI and AAF. In AII, the mean number of synchronized spikes per AM tone was <0.5 across the AM frequency range. In AI, the response to AM noise was also very low.

This was largely the result of several high BMF values for recording sites with CFs >10 kHz. The limiting rates for MU recordings were independent of CF in all three areas (Fig. 21B). The limiting rates for MU recordings, however, were correlated positively with tuning curve BW in AI and AII (P < 0.0005) and independent of BW in AAF (Fig. 21C).

**DISCUSSION**

In answer to the research questions posited in the introduction, we found the following:

- Significantly different (P = 0.8). The BW in AAF was slightly higher by 0.3 octaves than in AI (P = 0.3). In contrast, the BW in AII was ~1 octave higher than in AI (P < 0.001). For the LFP measure, the tuning curve BW for AAF and AII were the same. The BWs in AAF and AII were 0.7 octaves higher than in AI (P < 0.0005).

- The BMFs and limiting rates for LFP recordings were independent of the CF and BW in all three areas. The BMF for MU recordings was independent of CF in AI and AII but was correlated positively with CF for AAF (P < 0.05; Fig. 21A).
TABLE 2. CF range and tuning curve bandwidths in three areas

<table>
<thead>
<tr>
<th>Measure</th>
<th>LFP</th>
<th>MU</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF range, kHz</td>
<td>1.0–17.0</td>
<td>1.0–15.5</td>
</tr>
<tr>
<td>BW, octaves</td>
<td>1.9 ± 0.8</td>
<td>1.5 ± 0.8</td>
</tr>
</tbody>
</table>

Values are means ± SD. CF, characteristic frequency; BW, bandwidth.

1 The mean BMFs for the temporal modulation transfer functions in AI and AII were about a factor 2 higher for AM stimuli than for periodic click trains, and limiting rates were a factor 4 higher. In AAF, the mean BMFs for the AM stimuli were ~1.5 times larger than for periodic click trains and the limiting rates were about a factor 3 larger. For all three areas, the mean BMFs based on the all-order ISIs for AM stimuli were ~1.5 times those for clicks and limiting rates were less than a factor 2 higher. Thus AM stimuli in general produce much higher BMFs and limiting rates than periodic click trains.

2 Temporal modulation transfer functions for periodic click stimulation were very similar in the three cortical areas, hence the BMFs and limiting rates were not significantly different. For AM noise, the BMFs and limiting rates were also similar across areas, whereas for AM tones the BMF and limiting rates were about a factor 2 lower in AAF compared with the other areas. However, the firing rates for AM tones were by far the highest in AAF.

![Figure 13](http://jn.physiology.org/)

**Figure 13.** Examples of period histograms and all-order interspike-interval (ISI) histograms for simultaneous MU recordings in AI, AAF, and AII. CFs of the 3 recording sites were ~5 kHz. A: period histograms with clear synchronized responses ~32 Hz in all areas. B: ISIs equal to the click repetition period cease to exist for click rates >9.52 Hz.

![Figure 14](http://jn.physiology.org/)

**Figure 14.** Population ISI histogram for click train stimulation obtained by adding SU ISI histograms. A: all-order ISI histograms; intervals with periodicity equal to the click period are found in all 3 areas ~14.33 Hz. Evidence for intervals equal to 2 periods of the stimulus is found ~19.04 Hz for all 3 areas. B: 1st-order ISIs only. It is clear that even at “optimum” click rates, a substantial portion of ISIs is equal to twice the click period.
dent of CF in AI and AII and positively correlated with CF in AAF. The limiting rate for MU data were independent of CF in all three areas. The limiting rate, however, was correlated positively with the frequency-tuning curve BW in AI and AII but not in AAF. So in general there is only a modest interdependence of spectral- and temporal-response properties in AI and AII. The BMF for single units in response to periodic click trains was correlated positively with the first-click latency in AAF. The limiting rate was correlated positively with first-click latency for AI and AAF but not for AII. In AAF, a strong correlation between temporal response properties and latency was found.

Synchronized firing combines firing rate and stimulus synchrony

In the present study, as in previous ones from our lab (Eggermont 1991; Eggermont and Smith 1995a), temporal

3 The representation of stimulus periodicity in ISIs showed significantly lower estimates of mean BMFs and limiting rates in all three areas compared with those estimated from the temporal modulation transfer functions. The difference was relatively small for periodic click trains in all three areas and largest for AM stimuli in AI and AII.

4 Modulation frequencies <20 Hz were represented strongly in the ISIs. This is the repetition-rate and AM-frequency range where the sensation of rhythm prevails over that of roughness. Thus rhythm may be coded in auditory cortex in temporal fashion in the all-order ISIs of single units across the entire CF range.

5 Frequency tuning for MU spikes is sharpest in AI followed by AAF and broadest in AII. Single-unit latencies to high-intensity clicks are shortest in AAF and ~4 ms longer in both AI and AII. The BMFs for MU data were indepen-
modulation transfer functions based on firing rate, VS, and synchronized firing were calculated. Rate tMTFs were generally nondistinctive and mostly low-pass functions of click repetition rate or AM frequency. As a consequence, the synchronized firing tMTF, from which all our BMF and limiting-rate measures were obtained, to some extent represents the dependence of the VS on AM frequency. The synchronized rate is preferred above the VS because low-firing-rate neurons, which fire at most a single spike to a click or AM peak, tend to have higher VSs than units that fire spike clusters; yet for the nervous system, the latter may have more impact in being able to fire other neurons. Furthermore the VS is an idealization that requires the evaluation of relative timing and correction for overall firing rate. These stimulus aspects are available to the experimenter but not to the animal, so this calculation is not likely to happen in the nervous system. Consequently, synchronized firing rate is a more appropriate measure to use than VS.

**LFPs versus spike activity**

This work demonstrates that LFP triggers and single- or multiunit spikes result in similar estimates of the CF of a recording site, thereby corroborating and extending the conclusions of an earlier study that was confined to AI (Eggermont 1996). The 20-dB bandwidth of the frequency-tuning curves for LFP triggers was substantially higher than those for MU spikes in AI and AAF, whereas there was no difference in AII. The difference in AI and AAF can be explained on the assumption that the postsynaptic potential contributions to the LFP can be recorded from a larger volume surrounding the electrode tip than action potentials. This would require a larger dipole field for synaptic potentials than for action potentials, and this is not unreasonable to assume (Mitzdorf 1985). The similarities in AII for LFP tuning and MU tuning in AII then must be explained by an extensive convergence of units with a broader range of CFs to a single AII unit or to its projection site, the dorsal part of the MGB. However, if this larger summing volume idea is correct and the cell density and dipole orientation is the same in AI and AAF, one would expect the BW for LFP tuning curves to be more similar in AI and AAF because the MU tuning curve bandwidths are also close in value. This is not what is observed; hence to explain the difference in LFP and MU bandwidths, other factors such as an effect of inhibitory activity on spike initiation should be considered.

Because the depth-negative LFP component from which the triggers are obtained represents dominantly excitatory postsynaptic events (Mitzdorf 1985) and single-unit firing also is determined by inhibitory mechanisms, the sharper tuning observed for single- and multiunit activity might be the result of such inhibitory activity. Under this assumption, the simi-
TABLE 3. Click and tonepip latencies

<table>
<thead>
<tr>
<th></th>
<th>AI, ms</th>
<th>AAF, ms</th>
<th>AII, ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>75 dB SPL clicks</td>
<td>17.5 ± 4.1</td>
<td>13.5 ± 3.3</td>
<td>17.6 ± 3.8</td>
</tr>
<tr>
<td>Minimum pip latency</td>
<td>15.8 ± 4.1</td>
<td>12.4 ± 1.7</td>
<td>16.4 ± 5.1</td>
</tr>
</tbody>
</table>

Values are means ± SD.

BMF for clicks trains and AM stimuli, thereby extending Eggermont and Smith’s (1995a) findings, which were limited to click trains in AI. Because for click stimulation, BMFs were in the 8- to 14-Hz range for LFP and MU and strongly correlated with the autonomous cortical rhythms (Kenmochi and Eggermont 1997), this was expected. Cortical oscillations in the 7- to 14-Hz range have been suggested previously to play a role in the magnitude and timing of cortical evoked activity and behavioral responses. For in-
higher for the LFP than for the MU estimate, whereas for click train stimulation, there were no differences. The VS of the synchronized response was significantly lower for AM stimuli than for click stimulation, especially the "resonance" around 9 Hz was much reduced. This has the immediate consequence that the limiting rate, a relative measure equal to the repetition rate at 50% of the strength of the response at the BMF, will be higher for AM stimuli. The use of such a relative measure therefore is more useful to capture the shape of the tMTF than to estimate the upper bound of phase locking to AM frequency. For the ISI measure, the limiting rate was estimated from the visibility of interval peaks, so that measure poses a strict limit to interval

stance, Ahissar et al. (1997) found that in the somatosensory cortex of urethan-anesthetized rats and guinea pigs, ~25% of units in layer IV/V exhibited spontaneous oscillations in the neighborhood of preferred whisking frequencies (~10 Hz). They suggested that such independent neural oscillators with intrinsic frequencies that match the rhythm of sensory events can participate in decoding temporal sensory information through phase-locked thalamocortical loops. Combined with our present and previous findings, this suggests that synaptic and action potential activity in the cortex depends as much on ongoing LFP rhythms as it does on stimulus-induced rhythmicity. Under certain conditions, the one can entrain the other. We have shown previously that synchrony in the firing of distant neurons within AI could be explained largely by such global cortical activity (Eggermont and Smith 1995b).

For AM stimuli, the limiting rates of the tMTFs were...
coding. The finding that these limiting rates were generally smaller than for the corresponding measure based on tMTFs suggests that either the tMTF measure overestimates the capacity for repetition rate coding or that the tMTF for high AM rates is based only on an average of preferred firing times of isolated spikes or on a combination of these two factors.

**Similarities and differences between areas and comparison with other studies**

**SPECTRAL RESPONSE PROPERTIES.** The observation that the frequency-tuning curve bandwidth for LFP triggers was much higher in AAF than in AI confirms the earlier observation by Knight (1977). For MU data, the bandwidth was lowest in AI and largest in AII with that for AAF midway between the others. The finding that the MU frequency-tuning curve bandwidth in AII is much higher than in AI also agrees with previous findings (Schreiner and Cynader 1984). The MU bandwidth in AAF was somewhat higher than that in AI but not as high as reported for the ferret (Kowalski et al. 1995), which showed a 20-DB bandwidth in AAF that was comparable with what I found in AII. Knight (1977) had found that the frequency response characteristics of single units in AAF and AI in the cat were strikingly similar. The findings of broader single-unit tuning curves in AAF may be related to the percentage of multipeaked tuning curves found in this area. Tian and Rauschecker (1994) found a substantial number of them, and I did encounter such tuning curves in 26% of the recordings in AAF. In contrast, Knight (1977) found them only in a few penetrations.

**TEMPORAL RESPONSE PROPERTIES.** For MU responses to periodic click train stimulation, the BMFs and limiting rates of the temporal modulation transfer functions were very similar in AI, AAF, and AII. The BMFs were also similar for AM noise and AM tones in all areas but, especially in AI and AII, significantly higher than the BMFs for click trains. The BMFs in AAF were not very different for AM stimuli and click trains, largely because they were relatively low for the AM stimuli. In general, click trains were much more effective in generating responses with a high VS, and thus a high number of synchronized spikes, than were AM stimuli. In this respect, AM noise was most effective in AAF, then in AII, and least in AI. AM tones were also most effective in AAF, then in AI, and least in AII. This effectiveness may be related to the fact that solely in AAF the BMFs were relatively low, i.e., in the frequency range (8–14 Hz) of the autonomous cortical spindle rhythm. This will enhance the VS at that frequency and also enhance the resonance effect because spikes produced with the \((n + 1)\)th click or AM peak will line up with those in the rebound to the \(n\)th click or AM peak (Eggermont and Smith 1995a). Units with BMFs in the 8- to 10-Hz range invariably had higher firing rates than those with BMF outside this area. The drawback of this strong resonance for click stimulation is that for repetition rates above the resonance frequency, the strong postactivation suppression will limit click following severely. The weaker synchronization and suppression for AM stimuli allows higher limiting rates. I did not observe a lack of responsiveness to clicks for units with CFs \(\sim 10\) kHz (the ‘null’ in the click spectrum), likely because the stimuli were presented at a sufficient high level to allow strong activation of the units.

For click trains, the dominance of BMFs \(\sim 8\) Hz was similar to our earlier findings (Eggermont 1991; Eggermont and Smith 1995a) and those of Schreiner and Raggio (1996). The BMFs for AM tones in AI were also generally similar to those reported by Schreiner and Urbas (1988), but in the present study, the BMFs were distinctly higher in AI and were lower in AAF than reported by Schreiner and Urbas. The difference in the BMF values for AI may be related to our sampling bias, which preferred short latency neurons, and these will have higher BMFs than neurons that respond with very long latencies. For instance, if the latencies are \(\sim 100\) ms, a frequent finding in AII (Schreiner and Cynader 1988) and likely the result of a rebound from inhibition, then one does not expect the units to follow modulation rates \(>10\) Hz. Because long-latency responses are not very punctuate in onset and tend to be tonic, the VS will be very low. Thus in general the BMF will be much lower than 10 Hz for long-latency neurons. In the few instances that we did record from long-latency neurons, the BMF was \(<4\) Hz. Our finding of a much lower mean BMF in AAF was limited to the response to AM tones because for the same units an AM noise stimulus resulted in a much higher BMF. The BMF to AM tones was in the 8- to 14-Hz spindle frequency range. If in Schreiner and Urbas’s (1988) recordings the amount of spindling was reduced or the spindling frequency was higher because of a very light anesthesia (the cats also were paralyzed), it is likely that higher BMFs would be found.

**LATENCIES.** The BMF for single units in response to periodic click trains was correlated positively with the latency of the response to first clicks in AAF but not in AI and AII. Thus whenever a correlation was present, higher BMFs were found in units with longer latencies. The limiting rate was correlated positively with first-click latency for AI and AAF but not for AII. Latencies are determined by conduction delays and as such are sensitive to length and axon diameters differences in major afferent projections. Latencies are also sensitive to effects of inhibition that can delay the first-spike response to a stimulus substantially, and for high AM frequencies or click rates, latencies also are affected by the amount of synaptic depression. The minimum latency in AI was on average 15.8 ms for tone pips, this is similar to the Kowalski et al. (1995) finding of 16.8 ms and somewhat shorter than my previous results of 17.7 ms (Eggermont 1996) but significantly longer than the value of 12.5 ms found by Raggio and Schreiner (1994) and Mendelson et al. (1997). One potential reason for this difference could be the inclusion of more units from the dorsal part of AI, although the small percentage of multipeaked tuning curves in this study argues against that (Heil et al. 1992). Another potential reason may be found in the use of free-field stimulation in the present study with a speaker in the midline, this adds 1–2 ms to the latency for free-field contralateral stimulation, which is more comparable to closed-field contralateral stimulation (Eggermont 1998b). Minimum latencies in AAF were \(\sim 4\) ms shorter than in AI in the present study, and this is in contrast to other studies in cat (Knight
Temporal coding of rhythm in cortex

The amplitude-modulated stimuli and periodic click trains used in this study produce a different hearing sensation below and above \(~16\) Hz. Although they sound clearly rhythmic \(<16\) Hz, a sensation of roughness and pitch starts to dominate for higher modulation frequencies. Psychophysical studies (reviewed in Zwicker and Fastl 1990) have shown that the strongest sensation of rhythm is produced between 2 and 8 Hz with an optimum at 4 Hz, whereas the strongest sensation of roughness is obtained for \(~70\) Hz. The roughness sensation disappears altogether above a modulation frequency of 300 Hz. Above this frequency AM produces a sensation of pitch only.

The boundary frequency between rhythm and roughness may be related to a difference in neural coding above and below that frequency. As demonstrated here, ISIs code periodic stimuli for click rates \(\approx 14\) Hz (from the all-order interspike interval population histogram) and for AM noise rates \(\approx 38\) Hz (in AI). AM tones appear to be producing about three times as many ISIs in AAF than in the other areas but with a limiting rate of at most 16 Hz. Thus a fairly strong temporal representation, residing in the ISIs is found for low-modulation frequencies. This is the repetition rate and AM frequency range where the sensation of rhythm prevails over that of roughness. Thus rhythm may be coded in auditory cortex in temporal fashion in the all-order ISIs of single units, whereas roughness and likely also pitch (Schulze and Langner 1997) may be represented as a rate-place code.

COMPLEX SOUND REPRESENTATION. It is known that steady-state vowel discrimination is preserved in case of lesions in human auditory cortex; however, stop-consonant discrimination, depending largely on precise voice-onset-time (VOT) representation, is impaired (for review: Phillips 1993). Thus auditory cortex is involved and necessary to integrate timing information with spectral information as needed in word perception. The crucial question is whether different cortical areas have different roles in complex sound processing? I have shown previously that VOT is coded similarly in single units in AI (Eggermont 1995a) and in AAF and AII (Eggermont 1998a). Several other neural correlates of precise timing, such as required in gap-detection (Eggermont 1995b, 1998a) and the representation of rhythmicity (this study) also seem to have a similar representation in AI, AAF, and AII.

Some of the auditory primitives considered in psychophysical and model studies to bind components of the same sound object perceptually include common onset and offset of sound, common rates of AM and FM, harmonicity, and common spatial origin (Bregman 1990; Cooke 1993). It is useful for the subsequent discussion to group these auditory primitives in contour and texture components of sound. Contour components are those temporal aspects of sound that covary across frequency and are likely exclusively coded in the temporal domain. Onsets and common rates of slow (<20–30 Hz) amplitude and FM, i.e., the region where rhythm is dominant, are clearly contours that delineate, for instance, sound duration and separation between noise bursts and format transitions. Common higher rates of AM, in the roughness and pitch range, as well as harmonicity are aspects of sound texture. Texture aspects can be further characterized by pitch, timber, and roughness and slow changes therein. These texture aspects of sound thus relate to, constant or slowly changing, spectral representations in a cortical rate-place code. One expects texture and contour components thus to have largely independent neural representations.
in auditory cortex or potentially also in subcortical areas. Binding various sound features that are rate-place coded in different cortical areas is likely done in the time domain and for the auditory system based on the contour aspects of sound.

We found that the temporal representation of rhythm as well as sound onsets was strong in both primary cortical areas, AI and AAF, whereas it was distinctly less punctuate or absent (for AM tones) in ALL. Thus the primary areas may be more suited to represent all the contour aspects of sound. Specifically, because of its strong response to clicks and noise onsets, AI may be specialized in sound transients such as onsets and offsets. In ALL, low-frequency AM of broadband signals, clicks, and AM noise are still effectively represented in temporal code, but slow changes in the AM of pure tones are not represented.

Thus it seems that the neural activity in AI, AAF, and ALL together, but in different proportions and in distinctly different coding strategies, represents contour and texture. If the auditory cortex would be segregated in two streams like the visual system (Rauschecker 1997), then the three areas studied here are likely all part of the “what” stream. This also suggests a more extreme parallelism for the auditory cortex compared with the visual one. The “where” stream dealing with sound localization and movement should then, if it exists in the cat, largely reside outside these areas, for instance, in the anterior ectosylvian sulcus (Middlebrooks et al. 1994). The fact that these latter aspects of sound are computed from input of both ears distinguishes them from the, at least partially, monocular character of the “where” pathway in the visual system.

G. Smith provided valuable suggestions throughout the experiments. K. Ochi and M. Kennnochi assisted with the data collection. This investigation was supported by grants from the Alberta Heritage Foundation for Medical Research and the Natural Sciences and Engineering Research Council of Canada. Address for reprint requests: Dept. of Psychology, The University of Calgary, 2500 University Dr. N.W., Calgary, Alberta T2N 1N4, Canada.

Received 13 May 1998; accepted in final form 31 July 1998.

REFERENCES


