

Spectrotemporal sensitivities in rat auditory cortical neurons

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Abstract

Studies in several mammalian species have demonstrated that auditory cortical neurons respond strongly to single frequency-modulated (FM) sweeps, and that most responses are selective for sweep direction and/or rate. In the present study, we used extracellular recordings to examine how neurons in the auditory cortices of anesthetized rats respond to continuous, periodic trains of FM sweeps (described previously by deCharms et al., *Science* 280 (1998) pp. 1439–1444, as moving auditory gratings). Consistent with previous observations in owl monkeys, we found that the majority of cortical neurons responded selectively to trains of either up-sweeps or down-sweeps; selectivity for down-sweeps was most common. Periodic responses were typically evoked only by sweep trains with repetition rates less than 12 sweeps per second. Directional differences in responses were dependent on repetition rate. Our results support the proposal that a combination of both spectral and temporal acoustic features determines the responses of auditory cortical neurons to sound, and add to the growing body of evidence indicating that the traditional view of the auditory cortex as a frequency analyzer is not sufficient to explain how the mammalian brain represents complex sounds. © 2001 Published by Elsevier Science B.V.

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1. Introduction

Natural sounds, including those used by humans and other animals to communicate, are generally complex acoustic signals comprised of several frequency components and characterized by time-varying amplitude and frequency modulations. Given the great relevance of complex sound features for auditory processing, a complete understanding of neural auditory processing must account for how such complex sound features are represented in the brain. Increasing evidence suggests that much of the neural processing of dynamic acoustic features takes place at the level of the auditory cortex (for review, see Schreiner et al., 2000). In the present study, we characterize neuronal responses to trains of frequency-modulated (FM) sweeps in the auditory cortex of the anesthetized rat (*Rattus norvegicus*), in order to

better understand how complex acoustic features are represented in the auditory cortex.

Many studies of auditory cortical processing have involved measurements of neuronal responses to acoustically simple sounds such as short duration pure tones. The logic behind this approach stems from the classic portrayal of auditory processing (including cortical processing) as spectral decomposition. Accordingly, it is well known that tonotopic ‘maps’ exist in every mammalian auditory cortex studied to date (for review, see Merzenich and Schreiner, 1992). Within these maps, neurons are ‘tuned’ to particular sound frequencies organized from low to high across the cortex, preserving the topography observed in the cochlea. More recent findings suggest, however, that auditory cortical sensitivities are more complex than is suggested by neuronal responses to pure tones (deCharms et al., 1998; Depireux et al., 2001; Klein et al., 2000; Theunissen et al., 2000). In particular, cortical responses to spectral features appear to be highly dependent on factors such as the order and rate of frequency presentation (Brosch et al., 1999; Cotillon et al., 2000; Kilgard and Merzenich,

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1999; Wang et al., 1995), as well as the co-occurrence of other tones (Brosch et al., 1999; Horikawa et al., 1997; Schulze and Langner, 1999).

Evidence for complex acoustic processing by the auditory cortex has come from both behavioral and electrophysiological studies. For example, although gerbils with total bilateral ablation of the auditory cortex can discriminate pure tones differing in frequency as accurately as intact gerbils, lesioned gerbils cannot discriminate FM sounds that differ in the direction of modulation (Ohl et al., 1999; Wetsel et al., 1998). Further processing by the auditory cortex thus appears to be necessary for the encoding and representation of dynamic changes in spectral features, but not for differentiating spectral cues per se.

Electrophysiological studies have revealed that auditory cortical cells are sensitive to several time-varying stimulus features such as amplitude and frequency modulation. Auditory cortical cells in several species respond strongly to linear or sinusoidal FM stimuli (monkeys: deCharms et al., 1998; cats: Mendelson et al., 1993; gerbils: Ohl et al., 2000; Schulze et al., 1997; rats: Ricketts et al., 1998; ferrets: Shamma et al., 1993). Moreover, most FM-responsive cells show selectivity for stimulus parameters such as direction and speed of frequency modulation (deCharms et al., 1998; Depireux et al., 2001; Nelken and Versnel, 2000). In the same vein, auditory cortical cells in marmosets respond strongly to recordings of species-specific vocalizations, which are characterized by their dynamic properties (Wang, 2000; Wang et al., 1995). Cortical responses in marmosets are highly specific to particular calls, becoming significantly reduced when recorded vocalizations are presented in reversed, compressed or expanded form.

Contrary to what one would expect if frequency decomposition were the primary encoding mechanism of auditory cortex, pure tones are not the best stimuli for evoking responses from cortical neurons. FM stimuli and combinations of pure tones often drive cat auditory cortical cells more effectively than pure tones (Whitfield and Evans, 1965; Nelken et al., 1994, respectively). Whitfield and Evans (1965) found that 10% of the neurons that respond to FM stimuli do not respond at all when stimulated with pure tones. Similar observations were recently reported by deCharms et al. (1998). Using reverse correlation techniques, deCharms et al. designed optimized stimuli for auditory cortical cells in awake owl monkeys. A subset of these stimuli, consisting of trains of FM sweeps (described as moving auditory gratings) evoked much higher firing rates than best-frequency pure tones (deCharms et al., 1998). The responses observed in owl monkey cortex were highly selective for the direction and rate of frequency modulation in moving auditory gratings. Cortical response

selectivity for this kind of FM stimuli has also been observed in anesthetized ferrets (Depireux et al., 2001, 1998). Collectively, these results provide strong evidence that it is not primarily the overall spectral content of a sound that drives auditory cortical responses. Spectro-temporal features of sound appear to more strongly determine responses in auditory cortex.

In the present study, we measured response properties to moving auditory gratings in the rat auditory cortex. Our goal was to assess how temporal properties of these stimuli affected spectral sensitivities, in order to better understand how complex sounds are represented in the brain.

2. Materials and methods

2.1. Subjects

Microelectrode recordings were collected from four adult female Sprague–Dawley rats.

2.2. Surgical preparation, acoustic stimulation and recording procedure

The surgical procedure we used for electrophysiological recordings has been previously described in detail (e.g., see Kilgard and Merzenich, 1999). Animals were anesthetized with sodium pentobarbital (50 mg/kg intraperitoneal). A state of areflexia was maintained throughout surgery and recordings through supplemental doses of pentobarbital (8 mg/kg). Because barbiturate anesthesia is likely to produce hypothermia, a feedback-controlled heating pad was used to maintain body temperature at $\sim 37^{\circ}\text{C}$. Once the animal was anesthetized, its skull was supported in a head holder. A tracheotomy was performed in order to facilitate breathing, and the cisterna magna was drained to prevent cerebral edema. The temporal muscle was removed and a craniotomy was performed to expose the right auditory cortex. The dura was removed and the exposed auditory cortex was covered by silicon oil in order to keep it moist.

Electrophysiological recordings took place in an electrically shielded, sound-attenuated chamber. Extracellular responses were recorded using tungsten microelectrodes (1–4 M Ω) lowered tangentially into the cortex to variable depths (~ 250 – 1300 μm). Most responses described in this study represented the spike activity of several neurons. Previous studies have indicated no general differences between the response properties of single units and multi-unit clusters in the auditory cortex (Brosch and Schreiner, 2000; Gaese and Ostwald, 1995; Kilgard and Merzenich, 1999); activity from single units was thus not separated in the present study. The

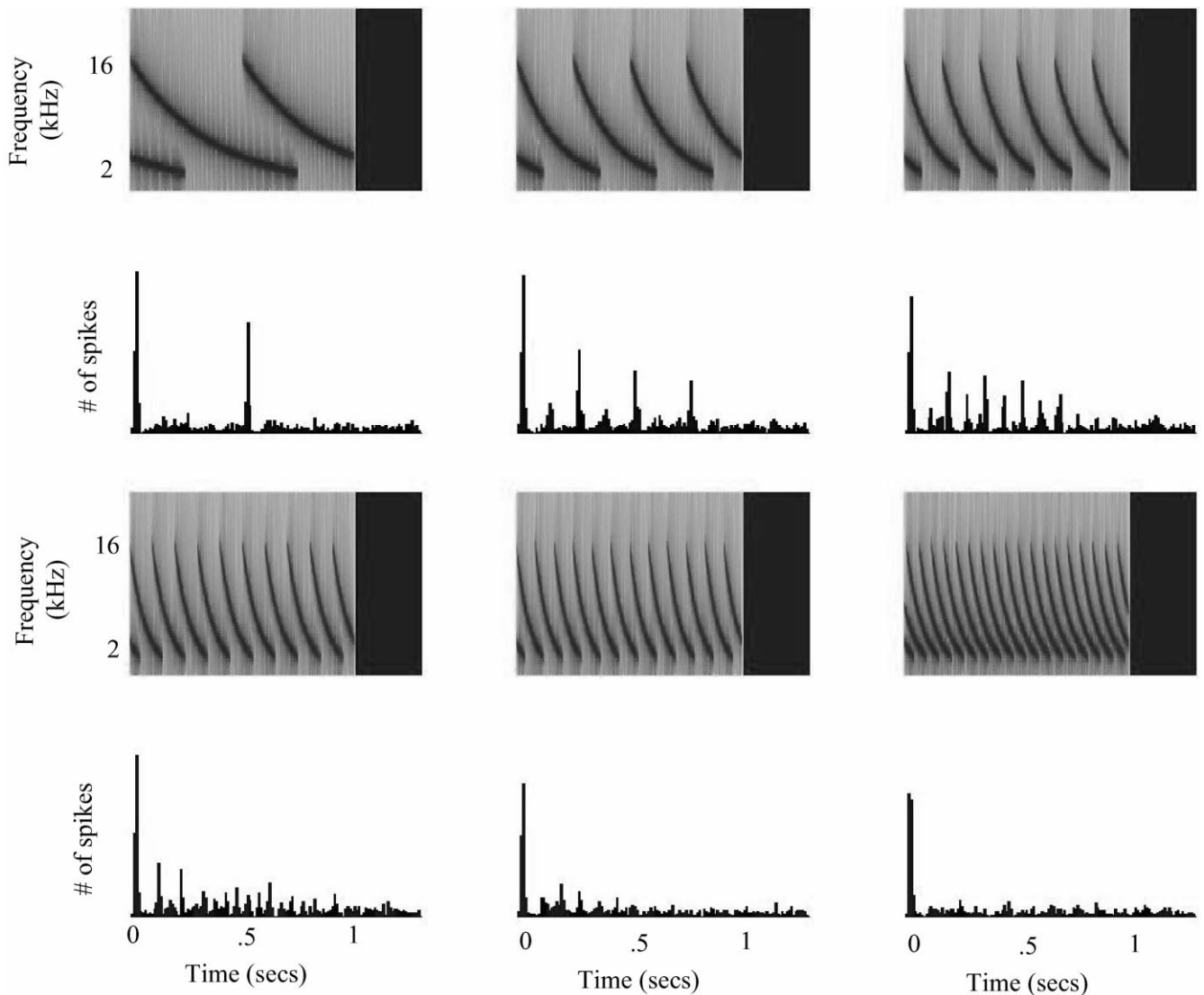


Fig. 1. Global post-stimulus time histogram showing responses from all the recorded units to six sweep trains differing in repetition rate. Periodic responses are clearly apparent for low repetition rates (upper panel: two, four, and six sweeps/s), whereas they are greatly reduced at faster rates (lower panel: 10, 12 and 18 sweeps/s). Note also the reduction in response amplitude as repetition rate increases.

word unit as used in this report refers to the functional unit recorded at a particular penetration site, whether it included one or more neurons. Stimuli were delivered monaurally to the left ear via an earphone positioned inside the rat's pinna. For recordings at each penetration site, rats were initially stimulated with tonal stimuli ranging from 0.5 to 30 kHz (25 ms duration with a 3 ms rise/fall time, 300 ms period) spanning 3–4 octaves from the center of the approximate best frequency of the unit. Stimuli were presented in a pseudorandom sequence of frequency–intensity combinations selected from 45 frequency values and 10 intensity levels to determine the unit's frequency–response tuning curve.

Following this, the unit's responses to FM stimuli were evaluated. Stimuli consisted of 16 trains of FM sweeps; eight trains were upward-directed, sweeping

from 2 to 16 kHz, and eight trains were downward-directed, sweeping from 16 to 2 kHz. There was a 2-octave spacing between frequencies. The repetition rate within a train ranged from 2 to 24 sweeps per second (sweeps/s) with rate of frequency modulation ranging from 4 to 24 octaves/s. Stimulus duration was 1 s. Both upward- and downward-modulated sweep trains were presented, so that responses to otherwise identical sweeps (i.e., differing only in direction of frequency modulation) could be directly compared. For recordings at each penetration site, four series of all 16 stimuli were presented in a pseudorandom order. Neuronal responses were recorded from stimulus onset to 300 ms after the end of the stimulus. The interstimulus interval was 2 s. Each sound was presented at ~ 70 –80 dB sound pressure level. Precise calibration was not possi-

ble for our FM stimuli because of amplitude changes intrinsic to their structure, and limitations in the signal generating system. Sound generation was calibrated for pure tones, however, and the system exhibited relatively flat responses for the frequencies included in the sweep trains (i.e., 2–16 kHz). These sounds are identical in form to those described by deCharms et al. (1998) as moving auditory gratings. Time–frequency representations of a subset of these sounds are shown in Fig. 1.

2.3. Data analysis

Analyses were performed using programs developed in Matlab 5.3. Spike events were cumulated in 10 ms intervals. In order to minimize variability introduced by spontaneous activity, spikes were considered for data analysis only when cells responded consistently to at least three out of the four presentations of each stimulus. Spikes were considered to be evoked by the onset of a stimulus if they occurred within 50 ms of stimulus onset, and were considered to be evoked by stimulus offset if they occurred within 100 ms of stimulus offset (i.e., 100 ms after the end of each sweep train). The best frequency, defined as the frequency that evoked the greatest response at a moderate intensity, was calculated for each unit based on its responses to tonal stimuli. Best repetition rates were calculated for each unit and were defined as the rate of repetition that evoked the maximal number of spikes from the unit. Selectivity for sweep direction was determined based on firing rate. Cells were considered to be directionally selective if, for the two sweep trains that produced maximal responding, (1) both of these sweeps were modulated in the same direction, and (2) the number of spikes evoked by stimuli modulated in the non-preferred direction was less than 80% of the number of spikes evoked by

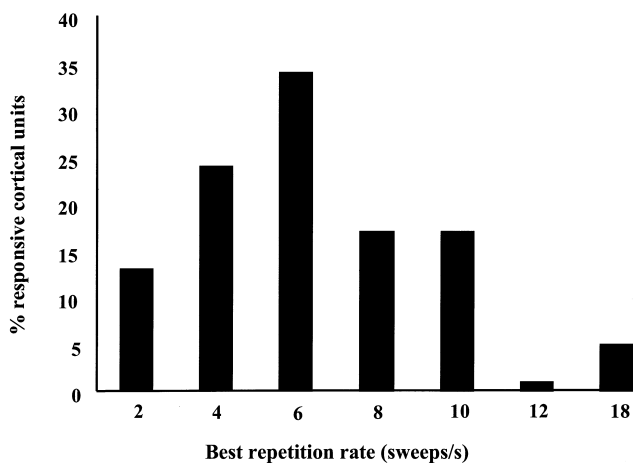


Fig. 2. Percentage of units responding maximally to each repetition rate. Best repetition rates were defined as the rate that elicits the strongest response from the unit.

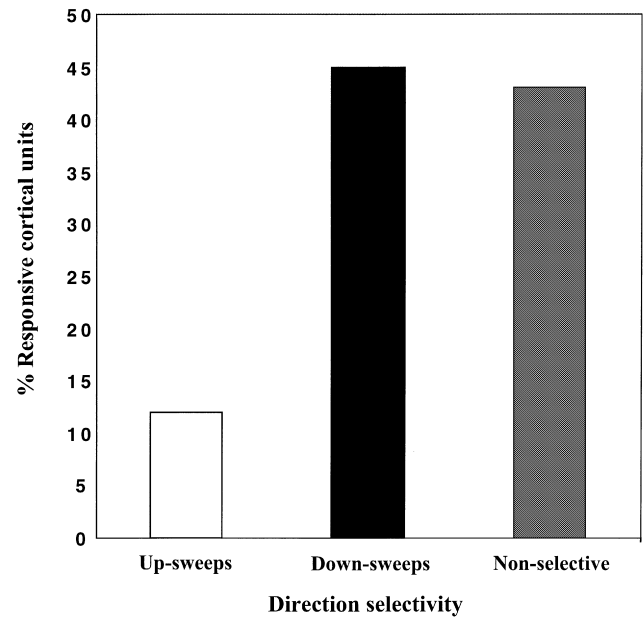


Fig. 3. Percentage of units responding selectively to up-sweeps or down-sweeps. Non-selective refers to the percentage of units that did not exhibit direction selectivity according to the criterion used in this study (see Section 2).

sounds modulated in the preferred direction. Cells with responses that did not meet these criteria were classified as non-selective units. Because the values for calculating direction selectivity were based on responses to those stimuli that evoked the strongest response (i.e., reflecting the preferred repetition rate of the cell), this measure of direction selectivity has the advantage of being insensitive to the overall firing rate of the unit, thus focusing on differential responses related to the direction of frequency modulation.

3. Results

Responses from a total of 111 units were recorded in this study. Units responding to stimulus onsets were prevalent (66%), whereas units rarely responded to stimulus offsets (0.4%). Most recorded units exhibited a period of inhibition following onset responses. Such inhibition was independent of the sound to which the unit responded. Following the onset response, units were silent for a period of approximately 90 ms. Similar inhibitory periods have been previously reported in auditory cortical responses to tone pips in rats (Sally and Kelly, 1988) and cats (Eggermont, 1992).

3.1. Selectivity for repetition rate

Figure 1 shows a post-stimulus time histogram representing the pooled response pattern from all the re-

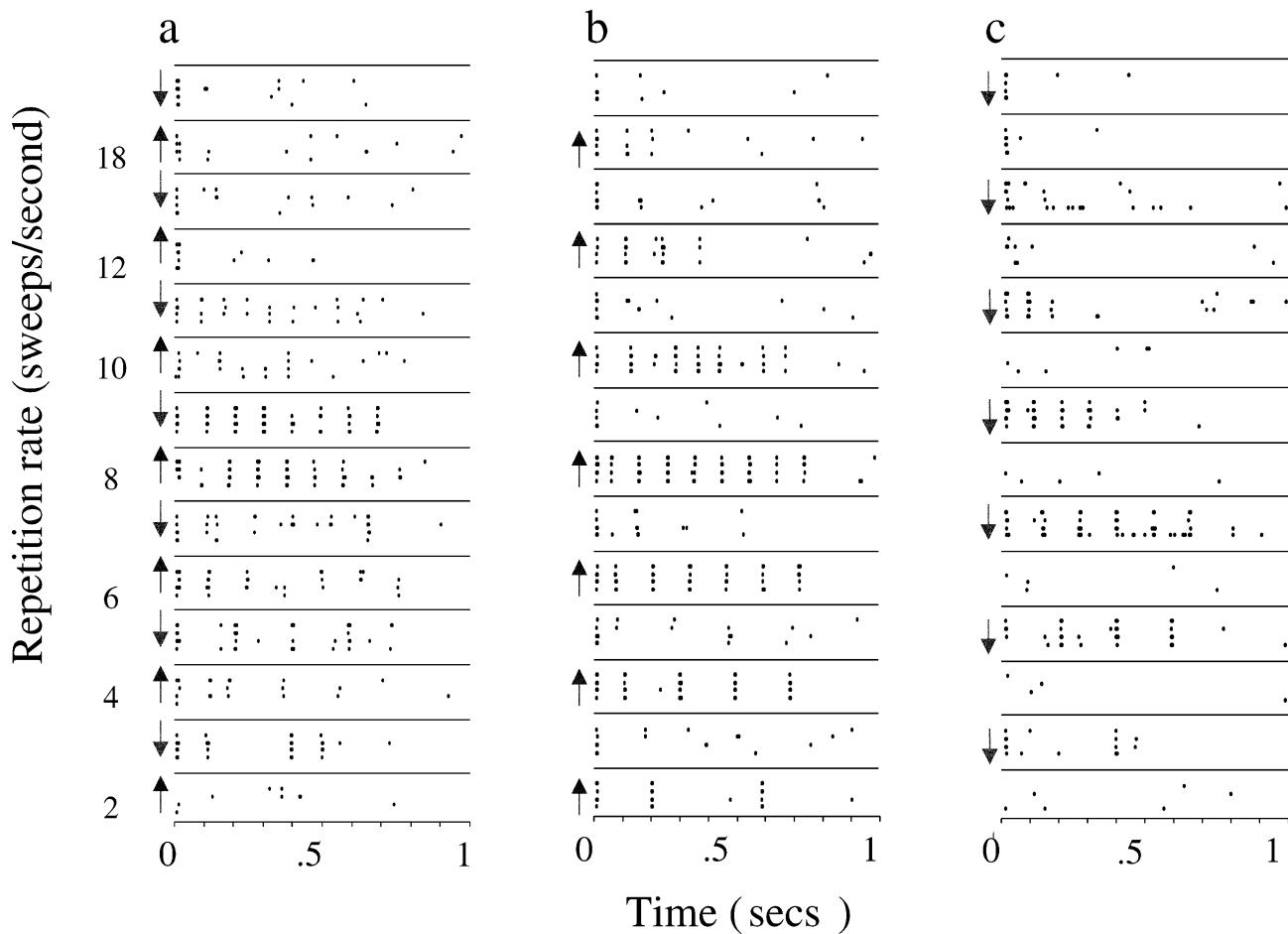


Fig. 4. Raster plots illustrating response patterns to each of the stimuli used in this study from three units that differ in their selectivity for direction. Direction of frequency modulation alternates for each repetition rate, as indicated by the left-side arrows. (a) Non-selective unit: responses were similarly evoked by either direction of frequency modulation; (b) Up-sweep-selective unit: strong, consistent responses occurred only in response to upward-directed sweep trains; (c) Down-sweep-selective unit: consistent responses were restricted to downward-directed sweep trains; notice the lack of onset responses to the non-preferred direction. Note also that responses are highly temporally coordinated for each stimulus presentation and follow closely the period of the stimulus.

corded units to stimuli differing in repetition rate. Because only units exhibiting similar response properties contribute to the overall response pattern, pooled responses highlight regularities in how units respond throughout the duration of the sweep stimuli, as well as how their responses change as a function of repetition rate. At low and medium repetition rates (two to 10 sweeps/s), units exhibited periodic responses that were closely correlated with the period of the sweep train. At these rates, the period of the responses was the same as the period of the stimulus, and each response occurred shortly after the onset of each sweep within the train. As the repetition rate increased, however, the responses of the units to individual sweeps within the train diminished. At high repetition rates, only onset responses were observed, and the unit remained mostly silent throughout stimulus presentation.

Figure 2 shows the distribution of best repetition rates (i.e., the repetition rate that evoked the maximal

number of spikes) among the recorded units. Most units responded preferentially to stimuli of low and medium repetition rates, in particular four and six sweeps/s. Consistent with the response pattern observed in Fig. 1, few units responded preferentially to stimuli with repetition rates higher than 10 sweeps/s.

3.2. Selectivity for direction

Most of the recorded units (57%) were classified as directionally selective (see Fig. 3). Of those, 45% responded preferentially to downward-directed sweep trains, whereas 12% responded preferentially to up-sweeps. Several of the units (43%) did not exhibit any selectivity for direction according to the criterion we used. Figure 4 shows raster plots illustrating each of the three types of direction selectivity observed in this study (i.e., down-sweep-selective, up-sweep-selective and non-selective).

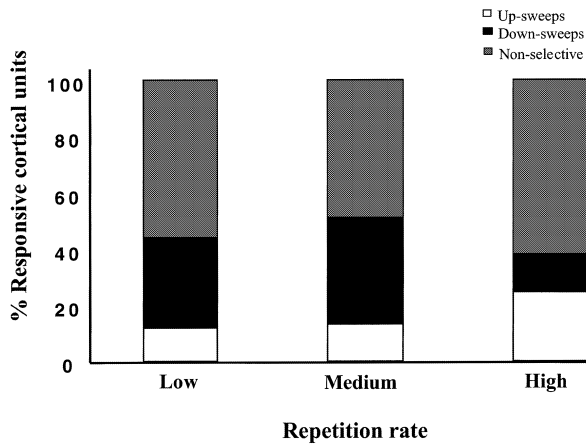


Fig. 5. Percentage of units responding selectively to up-sweeps or down-sweeps as a function of repetition rate. At low and medium repetition rates (at and below 10 sweeps/s), the majority of the selective units responded preferentially to down-sweeps. At high repetition rates (12 and 18 sweeps/s) this selectivity was reversed, with the majority of the selective units now responding to up-sweeps. Notice that the overall percentage of directionally selective units also varies as a function of repetition rate.

3.3. Interactions between direction selectivity and repetition rate

When responses to subsets of the FM stimuli were analyzed, it was found that the percentage of units selective for each direction of FM varied as a function of repetition rate (see Fig. 5). When the repetition rate was low (two and four sweeps/s) and medium (six, eight and 10 sweeps/s), the majority of the selective units responded preferentially to down-sweeps relative to up-sweeps. At high repetition rates (12 and 18 sweeps/s), however, this pattern was reversed, with a higher percentage of selective units responding preferentially to up-sweeps. Units showing direction selectivity outnumbered non-directional ones only at medium repetition rates, indicating that direction selectivity was most prominent at these rates.

Figure 6 shows response patterns of representative units to down-sweep and up-sweep stimuli as a function of repetition rate. Response patterns could be classified into four categories according to how the direction selectivity of the unit was influenced by repetition rate. For some units (33%) direction selectivity remained constant across all repetition rates (Fig. 6A). The direction selectivity of other units varied as a function of repetition rate: 40.5% of the recorded units were directionally selective at low and/or medium repetition rates, but became non-directional at the highest repetition rates (Fig. 6B). Other units (13.5%) did not show direction selectivity at low and/or medium repetition rates, but became directionally selective at the highest repetition rates (Fig. 6C). Finally, 13% of the units switched their direction selectivity (i.e., from up-sweep-selective

to down-sweep-selective or vice-versa) as a function of repetition rate (Fig. 6D). Note that whether these units were designated as directional when responses to all FM stimuli were considered (as in Fig. 3) depended on which stimuli evoked the strongest response.

3.4. Relationship between direction selectivity and frequency tuning

A total of 106 units were included in this analysis. The remaining five units were excluded because they did not exhibit frequency tuning. Figure 7 shows the distribution of best frequencies among directionally selective units. Most of the cells tuned to low frequencies (lower than 5 kHz) were selective for up-sweeps; down-sweep selectivity was absent among units tuned to low frequencies. Conversely, most of the units tuned to higher frequencies (above 15 kHz) were selective for down-sweeps. The majority of non-selective units were tuned to middle frequencies.

4. Discussion

In all of the neurons we recorded in rat auditory cortex, responses were dependent on the repetition rates of moving auditory gratings. Most responses (57%) were also dependent on the direction of frequency modulation. These results further demonstrate that sounds with highly similar spectra can evoke very different cortical responses based on their spectrotemporal features.

Our results show that for most of the recorded units, maximal responses were evoked by stimuli of low and medium repetition rates (in particular four and six sweeps/s), indicating that units were selective for those repetition rates. Few units responded preferentially to stimuli of repetition rates higher than 10 sweeps/s. These results are consistent with previous descriptions of maximal rates at which auditory cortical neurons can respond to periodic stimuli. For example, the highest rate at which rat cortical neurons can respond to repeated tone pips is around 15 Hz, with most neurons responding best at repetition rates up to about 10 Hz (Kilgard and Merzenich, 1999). Similarly, responses of auditory cortical neurons to amplitude- or frequency-modulated periodic stimuli exhibit best modulation frequencies between 4 and 15 Hz (guinea pigs: Creutzfeldt et al., 1980; rats: Gaese and Ostwald, 1995; ferrets: Depireux et al., 2001; cats: Whitfield and Evans, 1965; Schreiner and Urbas, 1988; Eggermont, 1992). Overall, these results indicate that the majority of units in the auditory cortex represent relatively slow temporal modulations. This is consistent with the progressive reduction in the maximum following rate of periodic modulations from the auditory nerve to more central

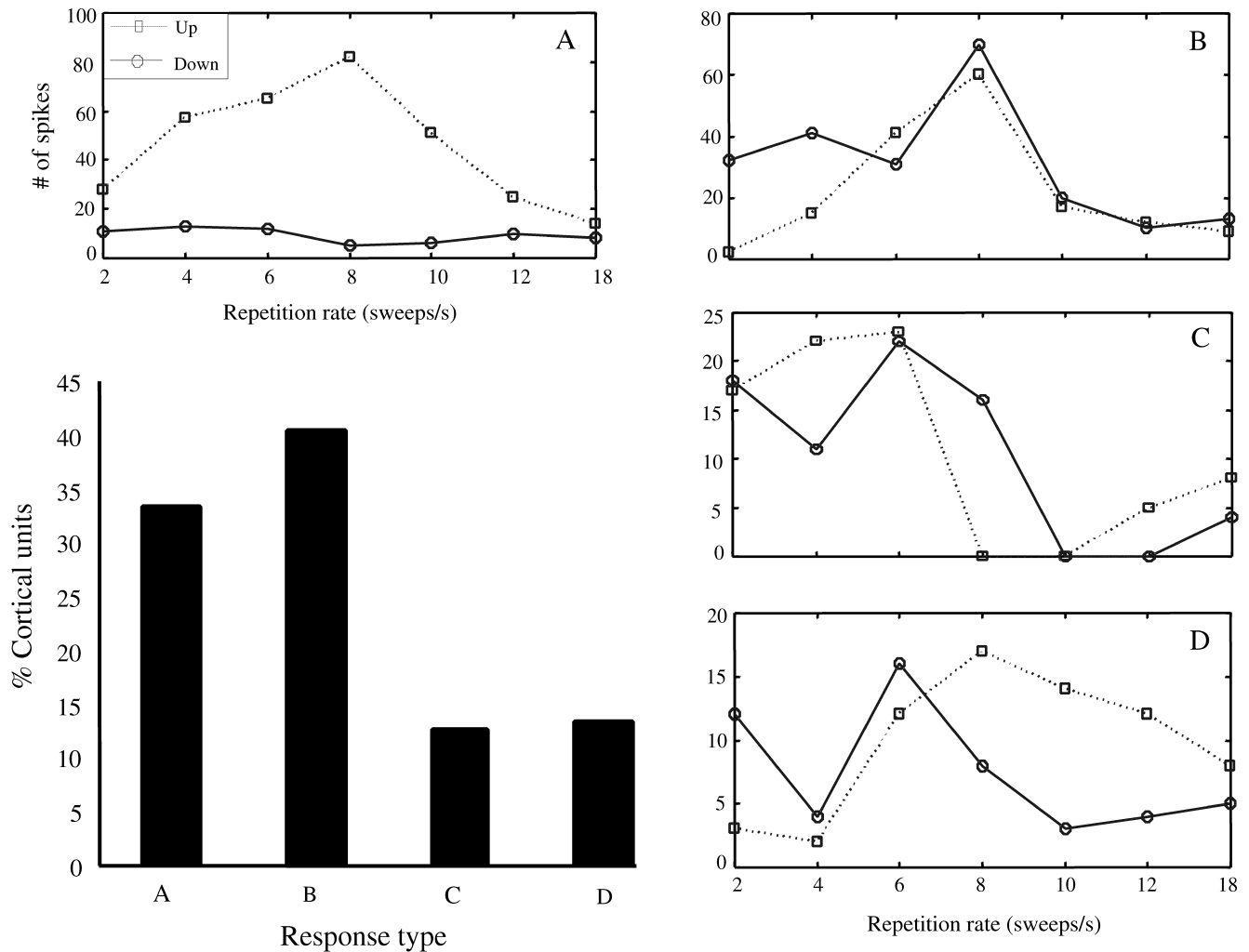


Fig. 6. Examples of the observed response patterns of individual units to down-sweep and up-sweep stimuli as a function of repetition rate. (A) Direction selectivity remained constant across all repetition rates for this unit (see also Fig. 4b). (B) Direction selectivity was present at low repetition rates, but the unit became non-selective at higher repetition rates (see also Fig. 4a). (C) No direction selectivity is exhibited at low and medium repetition rates, but the unit became directionally selective at the highest repetition rates. (D) Direction selectivity reverses (in this example from down-sweep-selective to up-sweep-selective) as a function of repetition rate. The bar graph shows the percentage of recorded units belonging to each of the above categories.

structures in the auditory system (for a review, see Langner, 1992).

In the present study, periodic responses were restricted to stimuli of low and medium repetition rates (at and below 10 sweeps/s). At these rates, the period of the responses was the same as the period of the stimulus, and each response occurred shortly after the onset of each sweep within the train. For our stimuli, each individual sweep within a train overlapped to some extent with the previous one, resulting in the temporary simultaneity of two frequencies during the overlap. These simultaneously presented frequencies were at all times 2 octaves apart from each other and were identical for all of the stimuli. Consequently, this overlap cannot account for the differential neural responses

we observed to stimuli of different repetition rates. The onset of each individual sweep within a train was also correlated with an increase in stimulus intensity. Thus, neurons could potentially have been responding to increments in stimulus intensity rather than to sweep onsets. In rat auditory cortical cells, oscillatory responses evoked by amplitude-modulated stimuli do not substantially differ from the oscillations observed in response to FM stimuli (Gaese and Ostwald, 1995). It is unlikely, however, that neurons in our study were responding primarily to increments in amplitude. If intensity changes alone were driving these cells, no selectivity for direction would have been observed because changes in intensity were identical for both directions of frequency modulation.

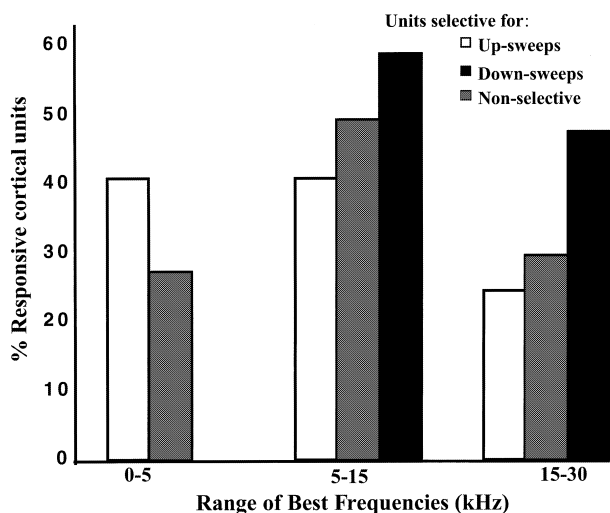


Fig. 7. Distribution of best frequencies as related to direction selectivity. Up-sweep selectivity predominates in cells tuned to low frequencies, whereas cells tuned to high frequencies were mostly selective for down-sweeps. Low frequencies include the initial frequency for up-sweeps (i.e., 2 kHz), and high frequencies include the initial frequency for down-sweeps (i.e., 16 kHz). Notice the absence of down-sweep selectivity among units tuned to low frequencies.

Repetition rate selectivity may be the result of the strong inhibition that follows excitatory input, which creates a refractory period. Recovery from inhibition can facilitate responses to periodic stimuli at certain rates, resulting in oscillatory responses that are facilitated when the inputs are coincidental with the periods of neuronal excitability (Eggermont, 1992). In agreement with this idea, auditory cortical neurons in the cat are more likely to effectively follow a periodic stimulus when the repetition rate matches the duration of the post-activation suppression (Eggermont, 1992). Similarly, best repetition rates are well correlated with the period of intrinsic oscillations, so that fast (i.e., high frequency), spontaneous oscillations are predictive of selectivity for fast repetition rates, and vice-versa (Kanomochi and Eggermont, 1997; Gaese and Ostwald, 1995). Selectivity for repetition rate may thus emerge as a result of intrinsic properties of the cortical circuitry that impose physiological constraints on the processing of periodic stimuli.

Over half of the units recorded in our experiments (57%) exhibited selectivity for the direction of frequency modulation. Most of these directional units were selective for downward-directed stimuli. Increased cortical sensitivity to sounds that decrease in frequency over time has previously been described in cats (Mendelson and Cynader, 1985; Mendelson et al., 1993; Heil et al., 1992a). Similarly, studies of inhibition evoked by two-tone sequences in guinea pigs (Horikawa et al., 1997) have shown that second tones are inhibited more strongly when preceded by a lower frequency tone, con-

sistent with enhanced cortical sensitivity to down-sweeps relative to up-sweeps.

Other studies describing responses to FM stimuli in rat auditory cortex, however, have reported a majority of units responding preferentially to up-sweeps (Gaese and Ostwald, 1995; Ricketts et al., 1998). It is possible that differences in procedure may account for these apparently conflicting results. Gaese and Ostwald used sinusoidal FM stimuli, and Ricketts et al. used individual, short duration sweeps that began and ended at frequencies outside the hearing range of the rat. Sounds used in both of these studies were substantially different from the periodic sweep trains used in the current study. Changes in even more subtle features of FM stimuli, such as the shape of the modulation function, are known to influence the directional selectivity of cortical neurons (Nelken and Versnel, 2000), suggesting that directional sensitivities may be highly stimulus-dependent.

Differences in directional sensitivity may also arise from differences in the cortical hemisphere from which responses are recorded. Gerbils with total ablation of the right auditory cortex cannot discriminate the direction of frequency modulation; this capacity is spared, however, when the lesions are located in the left auditory cortex (Wetsel et al., 1998). These results suggest that there might be important differences in the way the left and right auditory cortices in mammals represent time-varying stimuli. Such encoding differences might preclude direct comparisons of studies in which responses are recorded from different cortical hemispheres. In this study, we report responses from neurons in the right auditory cortex, whereas Gaese and Ostwald (1995) reported responses from the left auditory cortex; Ricketts et al. (1998) did not report from which hemisphere they recorded responses.

In the present study, we found that the percentage of units responding preferentially to each direction of FM varies as a function of repetition rate. At low and medium repetition rates (10 sweeps/s and below), selectivity for down-sweeps predominated, whereas at faster rates selectivity for up-sweeps was most common. In addition, the proportion of directional responses decreased at the fastest repetition rates (12 and 18 sweeps/s). These differences may have resulted from the fact that the direction selectivity of units can change as a function of repetition rate, so that a unit that is selective for a particular direction at low or medium repetition rates may switch or lose its directional sensitivity when presented with stimuli of higher repetition rates (see Fig. 6). Such interactions indicate that the direction selectivity of a given neuron can be highly sensitive to stimulus parameters other than the direction of frequency modulation. We do not know of any previous study examining variations in direction selectivity

as a function of repetition rate, but studies using single FM sweeps have shown that direction selectivity varies as a function of the rate of frequency modulation (Heil et al., 1992b; Phillips et al., 1985; Schulze et al., 1997). For the stimuli used in our study, the rate of frequency modulation co-varies with repetition rate. It is therefore possible that the variations in directional selectivity we observed resulted from differences in the rate of frequency modulation across stimuli.

We also found that direction selectivity was roughly related to frequency tuning. The majority of the units tuned to low frequencies were selective for up-sweeps, whereas units tuned to high frequencies were mostly selective for down-sweeps. Previous studies investigating the relationship of frequency tuning to direction selectivity in the cat auditory cortex have found no systematic relationship between these two variables (Heil et al., 1992a; Mendelson and Cynader, 1985; Mendelson and Grasse, 1992; Mendelson et al., 1993). We do not know, however, of any previous study examining this matter in the rat auditory cortex. Direction selectivity in auditory cortical neurons has been related to other variables such as inhibitory side band asymmetry in the ferret (Kowalski et al., 1995; Nelken and Versnel, 2000), position along isofrequency bands in the cat (Mendelson et al., 1993, but see Heil et al., 1992b), and both of these variables in the ferret (Shamma et al., 1993). Systematic variations in direction selectivity along isofrequency bands indicate that units with similar frequency sensitivities can have differential preferences for the direction of FM. These additional variables, as well as their interrelationships were not examined in the present study, and have not been studied in the rat. As a result, we cannot exclude the possibility that response changes that appear to depend on frequency tuning reflect systematic variations of inhibitory side bands or the positions of units along isofrequency bands. Further studies relating these variables in the auditory cortex of the rat should be performed to clarify this issue.

Direction selectivity has previously been explained based on the arrangement of inhibitory side bands in the tuning curve, so that selective responses to down-sweeps are related to inhibition of the low frequency side, and responses to up-sweeps are related to inhibition of the high frequency side (e.g., Wang and Shamma, 1995). In support of this idea, a correlation between the direction selectivity and the arrangement of the inhibitory side bands in auditory cortical neurons has been found for several species (cats: Heil et al., 1992c; ferrets: Shamma et al., 1993; bats: Suga, 1965). This explanation, however, does not take into account interactions between the temporal course of inhibition and the frequency content of the sound, which together likely determine the directional selectiv-

ity of cortical neurons. Studies with two-tone sequences have demonstrated that whether or not a second tone in a sequence is inhibited depends on the duration of silence following the presentation of the first tone, as well as the frequency of the first tone (Calford and Semple, 1995; Horikawa et al., 1997). Responses to second tones in a sequence can also in some cases be facilitated; such facilitation is time- and frequency-dependent (Brosch and Schreiner, 2000; Brosch et al., 1999). Selectivity for direction in auditory cortical cells thus seems to be determined by the temporal dynamics of excitation and inhibition.

5. Conclusions

In the present study, we showed that the response patterns exhibited by rat auditory cortical neurons to FM sounds are similar to those observed in the auditory cortex of other mammalian species, providing additional evidence that the auditory cortex is critically involved in encoding complex stimulus parameters. Responses evoked by moving auditory gratings in rat cortical cells were similar to those described by deCharms et al. (1998) in the auditory cortices of awake primates. This similarity across species suggests that such response patterns might reflect general encoding properties of the mammalian auditory cortex.

Because all of the up-sweep trains used in our study were spectrally equivalent to the down-sweep trains, differential responses to these stimuli demonstrate that a pure spectral analysis is not sufficient to predict how auditory cortical cells will respond to complex acoustic events occurring in a rat's environment. Neuronal selectivity for repetition rate shows that the temporal structure of stimuli is an important factor in determining how cells will respond. Similarly, selectivity for direction in cortical neurons indicates that the relative order of the frequencies in a sequence (i.e., high followed by low or vice-versa) strongly influences the responses of these cells.

Our results, in combination with the results of similar studies, suggest that what determines the response properties of auditory cortical cells is a dynamic interaction between the temporal and spectral features of sound. Further studies should evaluate the particular mechanisms through which these responses are shaped, such as the time course of interactions between excitatory and inhibitory zones in the receptive fields of cortical neurons.

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