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Neural Mechanisms Underlying Selectivity for the Rate and Direction of Frequency-Modulated Sweeps in the Auditory Cortex of the Pallid Bat

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Razak, Khaleel A. and Zoltan M. Fuzessery. Neural mechanisms underlying selectivity for the rate and direction of frequency-modulated sweeps in the auditory cortex of the pallid bat. *J Neurophysiol* 96: 1303–1319, 2006. First published June 14, 2006; doi:10.1152/jn.00020.2006. Frequency-modulated (FM) sweeps are common in vocalizations, including human speech. Selectivity for FM sweep rate and direction is present in the auditory cortex of many species. The present study sought to determine the mechanisms underlying FM sweep selectivity in the auditory cortex of pallid bats. In the pallid bat inferior colliculus (IC), two mechanisms underlie selectivity for FM sweep rate. The first mechanism depends on duration tuning for tones that arises as a consequence of early inhibition generated by an excitatory tone. The second mechanism depends on a narrow band of delayed high-frequency inhibition. Direction selectivity depends on a broad band of early low-frequency inhibition. Here, the contributions of these mechanisms to cortical FM sweep selectivity were determined in pentobarbital-anesthetized pallid bats. We show that the majority of cortical neurons tuned to echolocation frequencies are selective for the downward direction and rate of FM sweeps. Unlike in IC neurons tuned in the echolocation range, duration tuning is rare in cortical neurons with similar tuning. As in the IC, consistent spectrotimbral differences exist between low- and high-frequency sidebands. A narrow band of delayed high-frequency inhibition is necessary for FM rate selectivity. Low-frequency inhibition has a broad bandwidth, early arrival time, and creates direction selectivity. Cortical neurons respond better to slower FM rates and exhibit broader rate tuning than IC neurons. Relative arrival time of high-frequency inhibition is slower in the cortex than in the IC. Thus whereas similar mechanisms shape direction selectivity of neurons tuned in the echolocation range in the IC and the cortex, only one of the two mechanisms underlying rate selectivity in the IC is present in the cortex.

INTRODUCTION

Selectivity for the rate and direction of stimulus movement across the receptor surface is a common feature of sensory systems. Although neural selectivity for these attributes plays an important role in representing motion in vision (Newsome et al. 1985) and frequency modulations in audition (Suga 1965a), the mechanisms underlying selectivity are topics of debate. In visual and somatosensory cortices, facilitation within the receptive field and inhibition from the receptive field surround are two mechanisms proposed to underlie direction selectivity (Gardner and Costanzo 1980; Movshon et al. 1978; Murthy and Humphrey 1999). In the visual cortex, rate (velocity) selectivity may arise either through sideband inhibition (Goodwin and Henry 1978), facilitation within the receptive field

(RF; Duysens et al. 1985a), or through temporal properties such as duration tuning (Duysens et al. 1985b). These similarities suggest that rate and direction selectivity arise through common mechanisms across sensory cortices processing different modalities. Similar mechanisms were previously proposed to underlie selectivity for rate and direction of frequency-modulated (FM) sweeps in the auditory system (Gordon and O'Neill 1998; Suga 1965a; Zhang et al. 2003), but the relative contributions of these mechanisms in the auditory cortex remain unclear. This report focuses on the mechanisms underlying rate and direction selectivity in the auditory cortex of the pallid bat, a species that uses FM sweeps for echolocation.

FM sweeps are common components of species-specific vocalizations. In human speech, for instance, the rate and direction of frequency transitions are used for phonemic discriminations and speech recognition (Lindblom and Studdert-Kennedy 1967; Zeng et al. 2005). The importance of FM sweep processing is also highlighted by the fact that neural selectivity for direction and rate of FM sweeps is found in the auditory cortex of many species (Hart et al. 2002; Heil and Irvine 1998; Heil et al. 1992b; Kowalski et al. 1995; Mendelson et al. 1993; Nelken and Versnel 2000; Razak and Fuzessery 2002; Suga 1965a; Taniguchi et al. 1986; Tian and Rauschecker 1994, 2004). Echolocating bats are useful model systems in the study of mechanisms underlying FM selectivity because of the stereotypic nature and the relative simplicity of the behaviorally relevant FM sweeps. The pallid bat is particularly suited for studies of FM rate and direction selectivity because the majority (>60%) of neurons in its inferior colliculus (IC) and auditory cortex tuned to the echolocation range (30–60 kHz) are selective for the rate and downward direction of FM sweeps (Fuzessery 1994; Razak and Fuzessery 2002).

Three models have been proposed to explain FM direction selectivity. The first model suggests that direction selectivity arises through asymmetric inhibitory sidebands (Suga 1965a,b). A sweep that traverses the inhibitory sideband before reaching excitatory frequencies will not produce a response because inhibition is evoked first, whereas a sweep in the opposite direction evokes excitation first. This model has found considerable experimental support (Fuzessery and Hall 1996; Gordon and O'Neill 1998; Heil et al. 1992a,b; Suga 1965a,b; Zhang et al. 2003). A limitation of the asymmetrical inhibition model is that it does not explain FM rate-dependent direction selectivity observed in several studies (Gordon and O'Neill 1998; Heil and Irvine 1998; Nelken and Versnel 2000; Suga 1968). FM sweeps traverse a neuron's excitatory and/or inhib-

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itory frequency response areas with a specific time sequence. Characterization of interactions between excitatory and inhibitory inputs at multiple delays is required to explain direction selectivity at all FM rates (Covey et al. 1996; Gordon and O'Neill 1998; Heil et al. 1992b). The other two models depend on either facilitation within the excitatory tuning curve or coincidence of rebound from inhibition with excitation for one direction and not the other (Covey and Casseday 1999). The predictions of these two models of direction selectivity remain to be tested in the cortex.

FM rate selectivity arises either through timing of sideband inhibition (Gordon and O'Neill 1998) or through duration tuning that arises as the result of an early inhibition generated by excitatory tones (Fuzessery et al. 2006). Gordon and O'Neill (1998) predicted FM rate selectivity in the mustached bat IC based on the timing of interactions between inhibitory and excitatory frequencies. A similar mechanism is observed in the pallid bat IC (Fuzessery et al. 2006). Fuzessery et al. (2006) also showed that FM rate selectivity depends on duration tuning to excitatory frequencies. Neurons that are selective for short-duration tones respond well to fast FM rates and poorly to slow rates, attributed to the nonoptimal duration of excitatory frequencies in a long-duration FM sweep. The relative contributions of duration tuning and inhibitory sidebands to FM rate selectivity in the auditory cortex are not known in any species.

In this study, we recorded from single neurons tuned in the echolocation range in the pallid bat auditory cortex to determine the mechanisms underlying FM rate and direction selectivity. The echolocation pulse of the pallid bat is a 1- to 6-ms-duration, 60- to 30-kHz downward FM sweep (Brown 1976; Fuzessery et al. 1993). The pallid bat listens passively to prey-generated noise to localize prey. Two adjacent regions of the cortex are known to exhibit specializations suited to processing downward FM sweeps and prey-generated noise (Razak and Fuzessery 2002). A low-frequency region contains a high percentage of neurons that respond maximally or exclusively to noise bursts. A high-frequency region contains a large percentage of neurons that respond selectively or exclusively to the spectrum, duration, and direction of the downward FM sweep of the echolocation pulse. We focused on the high-frequency region and quantified the bandwidth, arrival time, and duration of low- and high-frequency inhibitions to determine their role in shaping FM direction and rate selectivity. The contribution of duration tuning to cortical FM rate selectivity was also studied. In addition, the mechanisms that underlie cortical FM rate and direction selectivity were compared with those in the IC (Fuzessery et al. 2006) to gain insight into hierarchical processing of FM sweeps.

We present evidence that consistent differences in the timing and bandwidth of high- and low-frequency sideband inhibition explain rate and direction selectivity, and rate-dependent direction selectivity in cortex. Surprisingly, in contrast to the IC, duration tuning is not common in cortical neurons with similar best frequencies (BFs) and sweep selectivity as in the IC. In addition, duration tuning that results from an early-on BF inhibition does not contribute to FM rate selectivity, suggesting that a mechanism is lost in the ascending pathway. The applicability of these data from the pallid bat auditory cortex to the various models proposed to underlie FM rate and direction selectivity is discussed.

METHODS

Recordings were obtained from the auditory cortex of both cortical hemispheres in seven pallid bats. These bats were captured in New Mexico and housed within a 16 × 11-ft² room, where they were free to fly and obtain mealworms raised on vitamin-enriched ground Purina rat chow. The room was maintained on a reversed 12:12 light:dark cycle. A few days before surgery, the bats were moved to a cage and fed mealworms to increase body weight. All procedures followed the animal welfare guidelines required by the American Physiological Society, National Institutes of Health, and the Institutional Animal Care and Use Committee.

Surgical procedures

Recordings were obtained from bats that were lightly anesthetized with Metofane (methoxyflurane) inhalation, followed by an intraperitoneal injection of pentobarbital sodium (30 μg/g body wt) and acepromazine (2 μg/g body wt). To expose the auditory cortex, the head was held in a bite bar, a midline incision was made in the scalp, and the muscles over the dorsal surface of the skull were reflected to the sides. The front of the skull was scraped clean and a layer of glass microbeads applied, followed by a layer of dental cement. The bat was then placed in a Plexiglas restraining device. A cylindrical aluminum head pin was inserted through a cross bar over the bat's head and cemented to the previously prepared region of the skull. This pin served to secure and immobilize the bat's head during the recording session. Location of the auditory cortex was determined relative to the rostrocaudal extent of the midsagittal sinus, the distance laterally from the midsagittal sinus, and the location of a prominent lateral blood vessel that travels parallel to the midsagittal sinus. The size of the exposure was usually about 2 × 2 mm². Exposed muscle was covered with petroleum jelly (Vaseline) and exposed brain surface was covered with paraffin oil to prevent desiccation.

Recording procedures

Experiments were conducted in a heated (85–90°F), soundproof chamber lined with anechoic foam. Bats were kept lightly anesthetized throughout the course of the experiments, with sedation maintained by inhalation of Metofane and additional pentobarbital sodium (one third of presurgical dose) injections. Stimuli were generated using Modular Instruments and Tucker Davis Technologies digital hardware and custom-written software (Fuzessery et al. 1991). The waveforms were amplified with a stereo amplifier and presented as closed-field stimuli through Infinity emit-K ribbon tweeters fitted with funnels that were inserted into the bat's pinnae and sealed there with petroleum jelly. This procedure attenuated speaker intensity level at the opposite ear by ≥30 dB (Fuzessery 1996). The speaker–funnel frequency–response curve showed a gradual increase of 20 dB from 6 to 70 kHz, as measured with a Brüel & Kjær 1/8-in. microphone placed at the tip of the funnel.

Using glass microelectrodes (1 M NaCl, 2–7 MΩ impedance), recordings were obtained at depths between 200 and 500 μm. Penetrations were made orthogonal to the surface of the cortex. Action potentials were acquired and stored with a Modular Instruments high-speed clock controlled by custom software. Poststimulus time histograms were constructed from the timing of these action potentials relative to stimulus onset. Responses were quantified as the total number of spikes elicited over 20 stimulus presentations. All results are based on single-unit recordings, identified by the constancy of amplitude and waveform displayed on an oscilloscope.

Data acquisition

Because the objective of this study was to determine the mechanisms underlying FM rate and direction selectivity, we focused

exclusively on the high-frequency FM sweep-selective region. Once a neuron with BF >30 kHz and with strong response to FM sweeps, but not to noise, was isolated, the following response properties were determined.

EXCITATORY FREQUENCY TUNING CURVE. Pure tones (5–75 kHz, 3- to 5-ms duration, 1-ms rise/fall times, 1-Hz repetition rate) were used to determine BF and frequency tuning. BF was defined as the frequency that elicited action potentials to at least five successive stimulus repetitions at the lowest intensity. The intensity was then increased in 10-dB steps to record the frequency–intensity combinations that produced excitatory responses.

DURATION TUNING FOR TONES. A pure tone at the neuron's BF and at an intensity of ≥ 10 dB above threshold was used to test duration tuning. In 20 neurons, duration tuning was tested at multiple intensities. The range of tone durations tested was 0.5–70 ms. For tones <2 ms, the rise/fall time was half the tone duration. Neurons were classified as short-pass if their response to short-duration tones was at least twice that of the response to the longest-duration tone. Band-pass neurons were those that responded best to a narrow range of tone durations and responses decreased to <50% of maximum response at the shortest and longest durations tested. The responses of long-pass neurons to short-duration tones were <50% of responses elicited at the longest duration tested. All-pass neurons responded within 50% of maximum at all durations tested.

FM DURATION, RATE, AND DIRECTION SELECTIVITY. The first step in determining FM rate selectivity was recording responses to FM sweeps of various durations (1–70 ms) and bandwidths centered near the BF of the neuron. The second step was plotting the selectivity of a neuron as a function of FM rate [kilohertz per millisecond (kHz/ms)] by dividing the spectral bandwidth by the duration of the sweep. This procedure allowed us to determine whether the neuron was tuned for the rate of change of frequency. A neuron was defined as *rate selective* if the response declined to 50% of maximum as the sweep rate was decreased and if the rate at which response declines to 50% of maximum for multiple sweep bandwidths were within 1 kHz/ms of each other. In addition to sweeps centered near the BF, we also used a downward FM sweep that started inside the excitatory frequency tuning curve. This sweep was used to test the hypothesis that high-frequency inhibition was necessary for rate selectivity. Because the exclusion of high-frequency inhibition from the sweep was predicted to alter rate selectivity of the neuron, this sweep was not used in determining whether a neuron was rate selective according to the 50% criterion defined above. The sweep that started inside the tuning curve was used only to test the notion that high-frequency inhibition was necessary for rate selectivity.

To test for direction selectivity, responses to upward FM sweeps with the same range of duration and bandwidth as the downward sweeps were recorded. A direction selectivity index (DSI) was calculated to quantify direction selectivity in the pallid bat auditory cortex (O'Neill and Brimijoin 2002). The formula used was

$$DSI = (D - U)/(D + U)$$

where D and U are the maximum response magnitudes for downward and upward sweeps, respectively. The DSI was not necessarily calculated at the same sweep rate for the two directions because the maximum responses could occur at different durations for the two sweep directions. The DSI of each neuron was calculated using upward and downward sweeps of the same bandwidth. Values of DSI can range between -1 and +1, with more positive values indicating higher selectivity for the downward direction. DSI values >0.6 show that the maximum response to the upward sweep was $\geq 75\%$ lower than the maximum response to the downward sweep. To determine whether inhibitory sidebands contributed to FM rate and direction selectivity, upward and downward sweeps were started from within the excitatory tuning curve.

Delay-frequency tuning curve

One hypothesis tested in this study was that the bandwidth and the arrival time of inhibition relative to excitation shape rate and direction selectivity. To determine both relative arrival time and bandwidth of inhibition, a "two-tone inhibition over time" (TTI over time) paradigm was used (Brosch and Schreiner 1997; Calford and Semple 1995; Gordon and O'Neill 1998; Fuzessery et al., unpublished observations). In this method, the delay between an excitatory and inhibitory frequency tone was varied, whereas the intensity of the two tones was kept constant. The frequency of the excitatory tone was set at the BF of the neuron and was presented at an intensity of 10–20 dB above threshold and with a duration of either 3 or 5 ms. A second tone (10-ms duration) with frequencies ranging from 5 to 70 kHz was presented before, beginning with, or after the onset of the excitatory tone. The delay between the onset of the two tones was varied to determine the delay-frequency combinations that resulted in inhibition of response to the excitatory tone for at least four of five (80% inhibition) consecutive presentations. A delay-inhibitory frequency tuning curve was constructed based on the delay-frequency combinations that caused 80% inhibition. The two-tone procedure was repeated with the best inhibitory frequency (center frequency of the inhibitory tuning curve) and the BF tone to determine the delay at which response magnitude decreased to 50% of excitatory tone-alone (control) response. The delay at which the response recovered to 50% of control response was also determined. In all the graphs, negative delays denote that the onset of the excitatory tone was before the onset of the inhibitory tone. Positive delays denote a temporal advantage to the inhibitory tone.

RESULTS

The majority of cortical neurons is tuned for the rate and downward direction of FM sweeps

Rate selectivity was determined in 61 neurons with BF between 30 and 60 kHz. To determine rate selectivity, FM sweeps of different bandwidths were presented at various durations, typically ranging between 1 and 70 ms. The FM sweep duration functions were converted to rate selectivity functions by dividing the bandwidth by duration (kHz/ms). In 46/61 (75.4%) neurons, the response was dependent on the sweep duration. Nearly 35% (16/46) of these neurons responded best to short-duration FM sweeps and showed a decrease in response magnitude of $\geq 50\%$ of maximum response as sweep duration was increased. These neurons were classified as fast-pass neurons (e.g., Fig. 1A). The neuron in Fig. 1A responded best to downward FM sweeps with durations between 1 and 5 ms when presented with a 50- to 30-kHz downward FM sweep. For durations >5 ms, the responses began to decline. When presented with a 60- to 20-kHz sweep, the neuron responded best to durations between 1 and 10 ms. As the bandwidth of the FM sweep increased, the range of sweep durations that elicited maximum responses also increased, showing that the neuron was selective for the rate of change of frequencies. The sweep rate-selectivity functions for the same neuron are shown in Fig. 1B. The neuron responded best to sweeps with rates >4 kHz/ms. Importantly, the sweep rate-selectivity functions were similar, regardless of the sweep bandwidth.

Of 46 neurons 26 (57%) were classified as band-pass neurons because they responded best to a narrow range of sweep rates, with response declining for faster and slower rates (e.g., Fig. 1D). When presented with a 50- to 40-kHz sweep, the

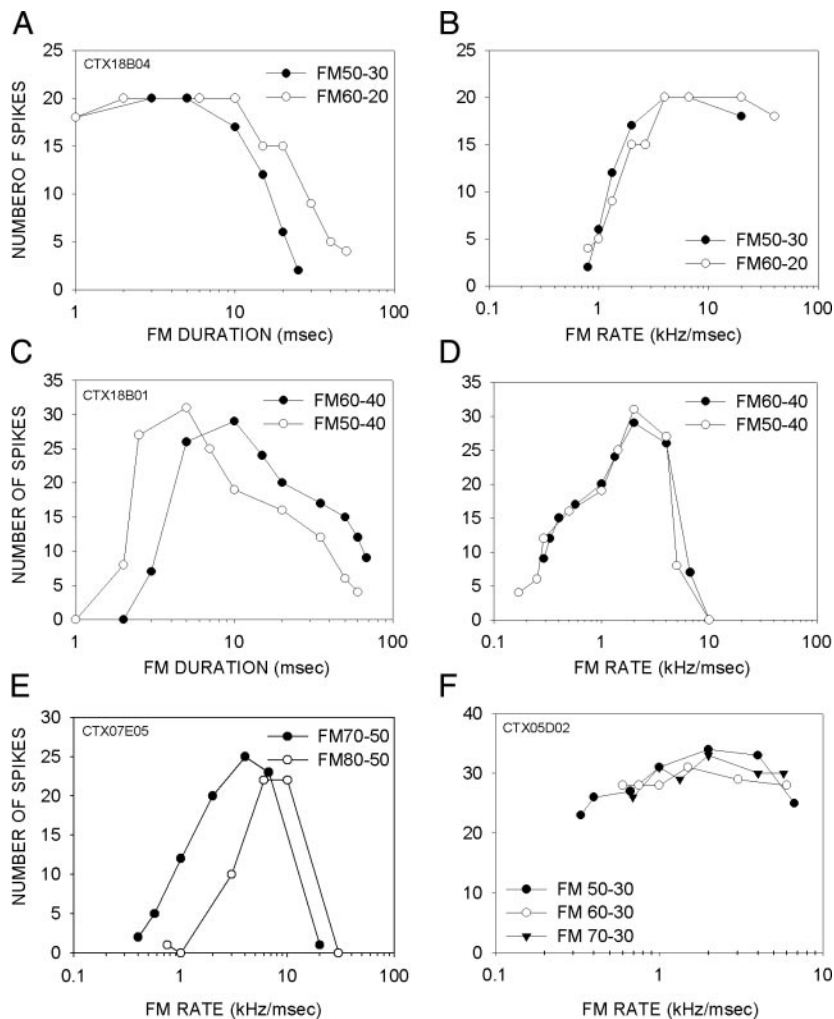


FIG. 1. Selectivity for downward frequency-modulated (FM) sweep rate in auditory cortex. *Left and right columns:* selectivity for duration of a sweep at various bandwidths and rate selectivity functions, respectively. Rate selectivity functions were estimated from the duration functions by dividing bandwidth of sweep by duration; y-axis shows the number of spikes to 20 stimulus repetitions; different sweep bandwidths tested are represented by the different symbols in each panel. *A and B:* a neuron that responded best to rates faster than 4 kHz/ms. *C and D:* a neuron that responded best to a narrow range of FM rates centered at 2 kHz/ms. *E:* a neuron in which response was modulated by sweep rate but did not satisfy the criterion (see text) to be selective for FM rate. *F:* response of this neuron, classified as nonselective, was not modulated >50% of maximum by FM sweep rate.

neuron in Fig. 1C responded best to a duration of 5 ms. When the bandwidth of the sweep was doubled to 60–40 kHz, the best duration was 10 ms. The sweep rate-selectivity functions show that the neuron responded best to the 2-kHz/ms sweep rate, with responses declining for faster and slower sweeps. It must be noted that the fast-pass/band-pass distinction is applicable only for the range of durations tested here and fast-pass neurons may show reduced response at shorter durations than those tested.

The criterion used to classify a neuron as sweep rate selective was that the rates at which the response decreased to <50% of maximum were within 1 kHz/ms of each other. Most neurons of this study (42/46) satisfied this criterion (e.g., Fig. 1, *B* and *D*). For the fast-pass neuron shown in Fig. 1*B* the rate at which response declined to <50% of maximum (around 1.5 kHz/ms) did not vary by more than 1 kHz/ms across the two bandwidths tested. The band-pass neuron shown in Fig. 1*D* responded best to 2 kHz/ms and the rate at which response declined to 50% of maximum for decreasing rates did not vary by more than 1 kHz/ms. The remaining four neurons did not show a consistent preference for sweep rate across different bandwidths (e.g., Fig. 1*E*). Nearly 25% (15/61) of cortical neurons exhibited weak or no selectivity for the rate of downward FM sweeps (Fig. 1*F*). This was true at all FM bandwidths

tested. These neurons were classified as being nonselective for FM rate.

The best FM rate was determined in neurons with band-pass-type selectivity (Fig. 1*D*) as the center of the range of FM rates that produced >80% of maximal response. Of 26 band-pass neurons 24 (92%) responded best to an FM sweep rate between 2 and 5 kHz/ms (Fig. 2*A*). Best FM rates >7 kHz/ms were not observed. In neurons with fast-pass-type selectivity (Fig. 1*B*), the FM rate at which response declined to <50% of maximum was determined. In 81% (13/16) of fast-pass neurons, the rate at which response decreased to <50% of maximum was <2 kHz/ms (Fig. 2*B*).

The majority of cortical neurons with BF in the echolocation range (31/51, 61%) was also selective for the downward direction of the FM sweep. Direction-selective neurons were defined as those in which upward sweeps elicited a response that was <25% of response to a downward sweep with the same bandwidth (e.g., Fig. 3*A*). The DSI was used as a measure to determine the degree of selectivity. A DSI value of 0.6 corresponds to the 25% criterion used for direction selectivity. Most cortical neurons exhibited DSI values between 0.6 and 1, demonstrating strong selectivity for the downward sweep direction (Fig. 3*B*). No significant differences in DSI were found across different BF ranges (*t*-test, $P > 0.05$ for all pairs), suggesting that most neurons with tuning in the echolocation

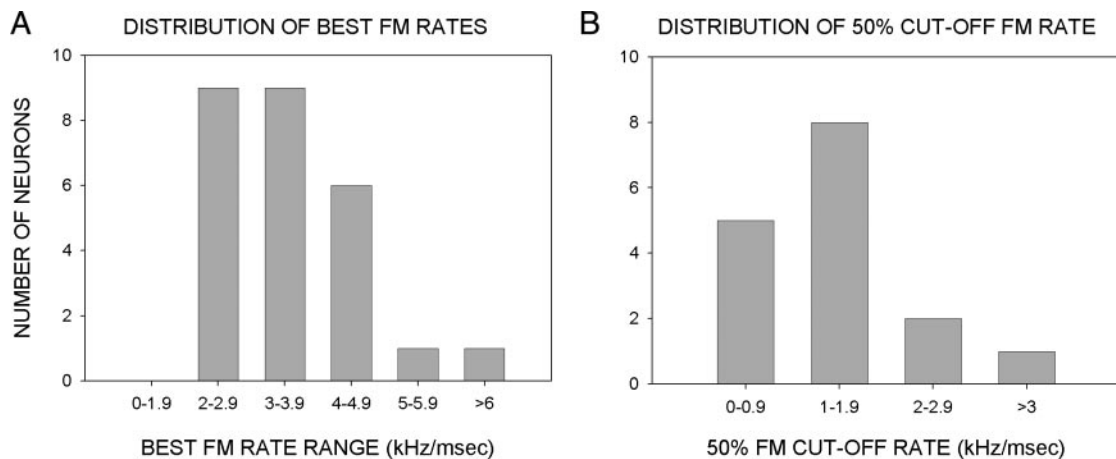


FIG. 2. Range of downward FM rate selectivity in cortex. *A*: most FM rate-selective neurons with band-pass type selectivity respond best to rates <5 kHz/ms. *B*: for decreasing rates, most FM rate-selective neurons with fast-pass type selectivity show a 50% decline in response from maximum at rates <2 kHz/ms.

frequency range prefer the downward sweep direction, regardless of BF.

Taken together, these data show that most cortical neurons with BFs in the echolocation range respond best to downward

FM sweeps. In addition, most neurons respond poorly to sweep rates <2 kHz/ms. The rest of this report addresses mechanisms that underlie such selectivity.

Mechanisms of FM rate selectivity

In the IC of the pallid bat, two mechanisms contribute to rate selectivity. The first mechanism relies on duration tuning for tones present in the sweep, whereas the second mechanism requires delayed high-frequency inhibition, relative to the arrival time of the excitatory BF input, to suppress responses to slow FM sweeps. To test whether similar mechanisms create rate selectivity in the cortex, duration tuning for the BF tone and the presence and contribution of high-frequency inhibition to FM rate selectivity were examined.

Duration tuning for tones was rare in cortical neurons with BFs in the echolocation range (6/58, 10.3%). Two of the six neurons that were duration tuned are shown in Fig. 4, *A* and *B*. Durations between 2 and 5 ms elicited maximal response with longer durations causing a decrease in response by $\geq 50\%$ (Fig. 4*A*). Cortical duration-tuned neurons typically showed a slow decline in response with increasing tone duration (e.g., Fig. 4*B*). The majority of cortical neurons with BFs between 30 and 60 kHz (52/58, 89.7%) were not duration tuned. The examples shown in Fig. 5, *A* and *B* are typical of the duration-tuning functions in the FM region of the pallid bat cortex, with responses within 20% of the maximum response at all durations tested.

Duration tuning in the auditory cortex of the little brown bat is known to be intensity dependent (Galazyuk and Feng 1997). To test for this possibility in the pallid bat cortex, duration tuning was determined at multiple intensities in 20 neurons. Most neurons with BF >30 kHz have nonmonotonic rate-level functions (Razak and Fuzessery 2002). Therefore an examination of the effects of intensity on duration tuning could be carried out only over a narrow range of intensities. In 40% (8/20) of neurons, intensities ranging from 5 to 10 dB above threshold had no effect on duration tuning (Fig. 5*A*). In neurons with monotonic rate-level functions, no duration tuning was observed ≤ 30 dB above threshold (Fig. 5*B*). In the remaining 60% (12/20) of the neurons tested, a consistent effect of intensity on duration tuning was observed. Close to threshold, neurons responded poorly to short-duration tones, resulting in

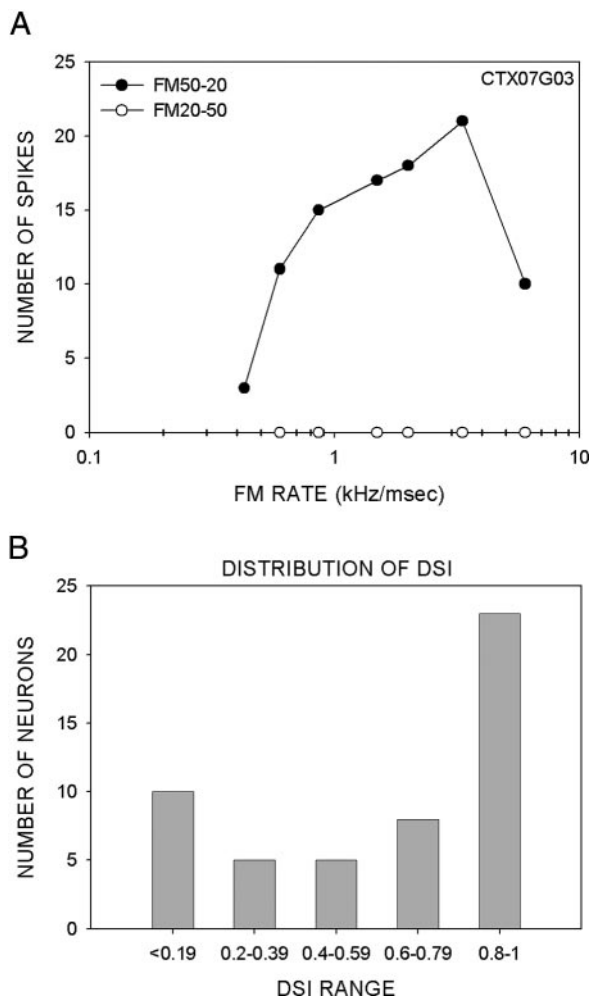


FIG. 3. Most cortical neurons are selective for the downward direction of FM sweep. *A*: a neuron that was strongly selective for FM sweep direction. An upward sweep with the same bandwidth and frequencies as a downward sweep produced no response. *B*: majority of the neurons tested had a direction selectivity index (DSI) >0.6 .

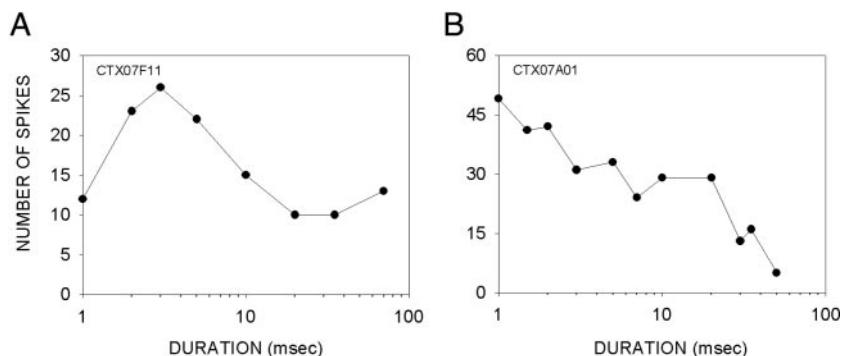


FIG. 4. Duration tuning in the auditory cortex. *A* and *B*: neurons selective for short-duration tones.

a long-pass response profile (Fig. 5C). Increasing the intensity to ≥ 10 dB above threshold caused the neuron to respond well at all durations tested, resulting in the typical all-pass profile. In the cortex, none of the neurons tested at multiple intensities exhibited selectivity for short-duration tones at any intensity. This suggests that the rare occurrence of duration tuning in the studied area of the pallid bat auditory cortex is not a result of the intensity of tones used.

Late-arriving high-frequency inhibition underlies FM rate tuning in the cortex

If high-frequency inhibition is important for constructing FM rate selectivity, FM rate-selective neurons should exhibit high-frequency inhibition. Moreover, if the FM sweep did not include high-frequency inhibition, neurons were predicted to lose rate selectivity. Finally, neurons without the high-frequency inhibition were expected to be nonselective for FM rate. All three predictions were satisfied by cortical neurons, suggesting that cortical neurons depend on delayed high-frequency inhibition for FM rate selectivity.

In almost all FM rate-selective neurons for which delay-frequency tuning curves were obtained (29/30, 96.7%), a high-frequency band of inhibition was present (e.g., Figs. 6A, 7, A and C, and 9A). In all 29 neurons, high-frequency inhibition arrived late (e.g., Figs. 6A, 7, A and C, and 9A; population histogram in Fig. 12A). For the neuron shown in Fig. 6, A–C, frequencies between 49.5 and 50.5 kHz inhibited the response to the BF tone when the onset of the inhibitory tone was advanced ≥ 2 ms relative to the excitatory tone onset. The fact that the high-frequency inhibitory tone had to be advanced to observe inhibition suggests that the inhibition arrived late. On the other hand, low-frequency inhibition (centered at 40 kHz) was apparent at 0 delay. This shows that low-frequency inhibition arrived at the same time as or earlier than the excitatory input. Figure 6B shows response magnitudes at various delays between inhibitory and excitatory tones. The low-frequency inhibitory tone (42 kHz) caused $\geq 80\%$ inhibition of the response to the BF tone at a delay of 0 ms. Starting the BF tone simultaneously with the high-frequency inhibitory tone (49.8 kHz), however, produced a response close to control (response to the excitatory tone alone). Onset of the high-frequency inhibitory tone had to be advanced 2 ms to cause maximal inhibition. For the examples shown in Fig. 7, A and C, the high-frequency inhibition arrived 5 and 2 ms late, respectively.

The effect of starting the downward FM sweep from inside the excitatory tuning curve was studied in 36/46 rate-selective

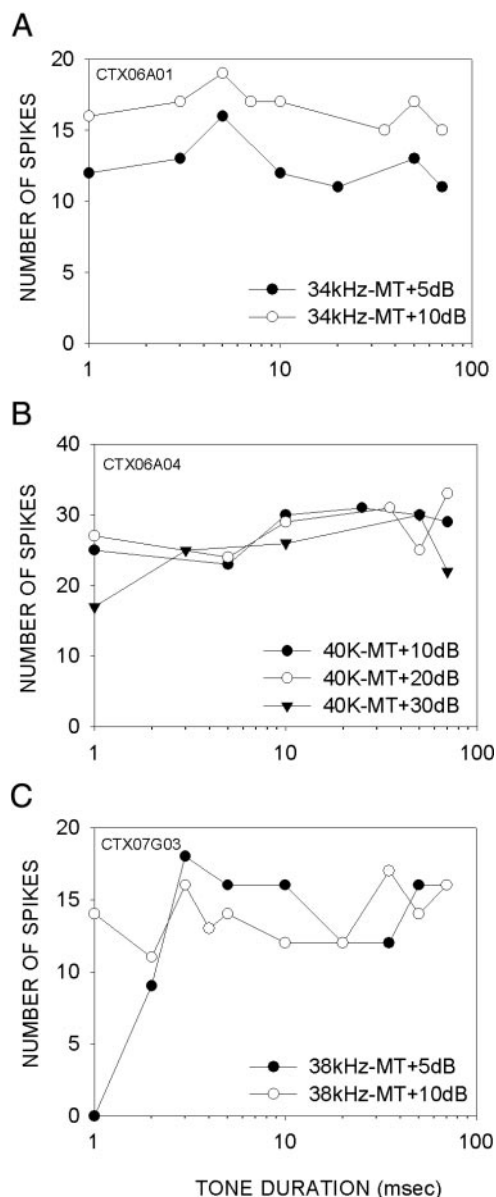


FIG. 5. Effects of intensity on duration tuning. *A*: this neuron was not duration selective at the intensities tested. Additional intensities were not tested in this neuron because it was sharply tuned for intensity. MT, minimum threshold. *B*: this neuron was not duration tuned at intensities between 10 and 30 dB above MT. *C*: a neuron that responded poorly to short-duration tones near threshold. At 10 dB above threshold, the response of the neuron was similar at all intensities.

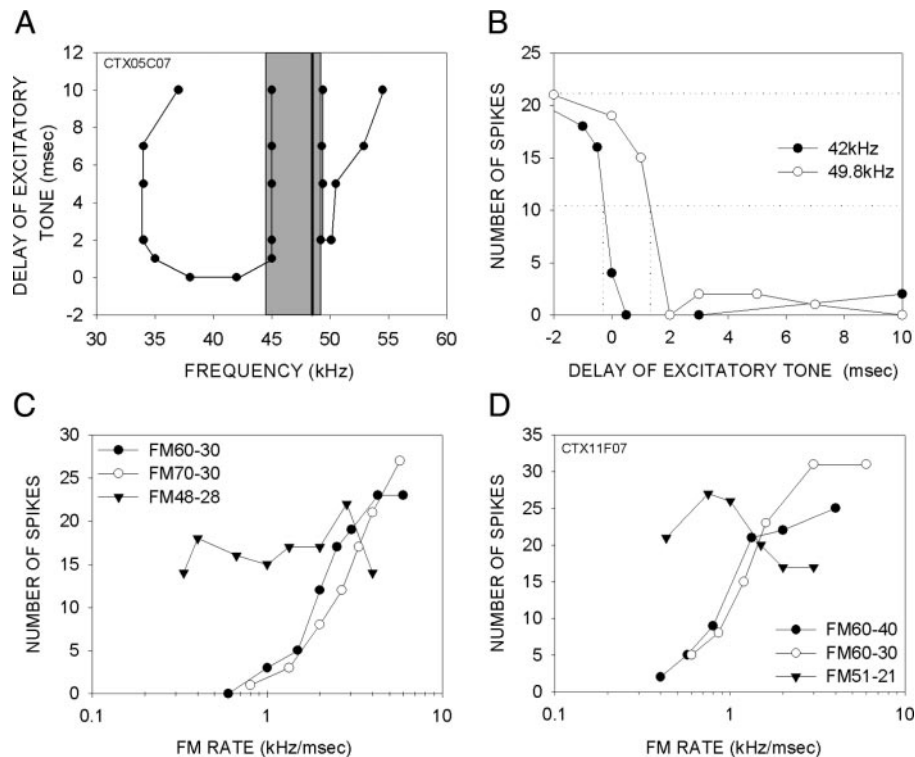


FIG. 6. Mechanisms of FM rate selectivity. *A*: delay-frequency tuning curve shows the frequency-delay combinations that suppress the response to the best-frequency (BF) tone by $\geq 80\%$. Frequency-delay combinations producing inhibition were determined using the 2-tone-over-time method (see METHODS). On the y-axis, positive delays denote the onset of inhibitory tone before the onset of excitatory tone. Negative delays denote the onset of inhibitory tone after the excitatory tone. Both inhibitory and excitatory frequencies are presented at the same intensity. Shaded area is the range of excitatory frequencies at the intensity used for the 2-tone paradigm. Dark line is the BF of the neuron. In this neuron, low-frequency inhibition (centered at 40 kHz) arrived faster than high-frequency inhibition (centered at 50 kHz) and had a broader bandwidth. *B*: details of 2-tone inhibition. Dashed line on the top shows response to the BF tone presented alone (control). Dashed line in the middle shows 50% of control. Dotted lines show the 2-tone delays at which response declined to 50% of control levels. Neural response produced by presenting 2 tones with variable delays shows that low-frequency inhibition (42 kHz) arrived faster than high-frequency inhibition (49.8 kHz). *C*: rate selectivity is shaped by delayed high-frequency inhibition. This neuron was selective for the rate of downward FM sweeps when the band of high-frequency inhibition was included in the sweep (dark and open circles), with rates < 2 kHz/ms producing poor response. However, for a sweep starting inside the excitatory tuning curve (triangle), rate selectivity was decreased. *D*: rate-selectivity functions of the duration-tuned neuron shown in Fig. 4A. Even though this neuron was duration tuned, delayed high-frequency inhibition shaped rate selectivity, which is evidenced by the fact that the neuron was not rate selective for a sweep that excluded high-frequency inhibition (FM 51–21).

neurons. All (36/36) of these neurons lost rate tuning if the FM sweep started inside the tuning curve, suggesting that the delayed high-frequency inhibition was necessary for rate selectivity (Figs. 6C and 7, B and D). For the neuron shown in Fig. 6, A–C, a narrow range of frequencies centered at 50 kHz formed the delayed high-frequency inhibitory band. In this neuron, if downward sweeps included this band of inhibitory frequencies (e.g., 60- to 30- and 70- to 30-kHz sweeps), rates < 2 kHz/ms produced a response that was $< 50\%$ of maximum. When the FM sweep was started at 48 kHz (the 48- to 28-kHz sweep), leaving out the high-frequency inhibition, no rate selectivity was observed. The neuron responded $> 50\%$ of maximum for all rates tested. Even in neurons that were duration tuned for tones, rate selectivity was eliminated by the removal of high-frequency inhibition from the sweep. For example, Fig. 6D shows rate-selectivity functions of the duration-tuned neuron shown in Fig. 4A. This neuron exhibited a narrow band (2-kHz bandwidth) of high-frequency inhibition centered at 52 kHz and arrived 1 ms late (not shown). The neuron exhibited strong rate selectivity for sweeps (60–30 and 60–40 kHz) that included the high-frequency inhibition. However, the neuron was not rate selective for the downward sweep

(51–21 kHz) that excluded this inhibition. Thus duration selectivity does not shape rate selectivity in this neuron. Figure 7 shows additional examples of the loss of rate tuning when the downward FM sweep does not include high-frequency inhibition.

All neurons ($n = 9$) without high-frequency inhibition at any delay (Fig. 8, A and D) were also not selective for the rate of downward FM sweeps (Fig. 8, B and C). This was true at all FM bandwidths tested. Taken together, these data suggest that high-frequency inhibition underlies FM rate selectivity in the FM sweep-selective region of the pallid bat auditory cortex.

Predicting FM rate selectivity

In addition to the arrival time, another feature of inhibition that will influence rate selectivity is the bandwidth of inhibitory frequencies. The broader the bandwidth of inhibition, the earlier an inhibitory frequency will be reached in an FM sweep, resulting in a relatively earlier triggering of inhibition. Therefore if high-frequency inhibition has a broad bandwidth, the early triggering of high-frequency inhibition relative to exci-

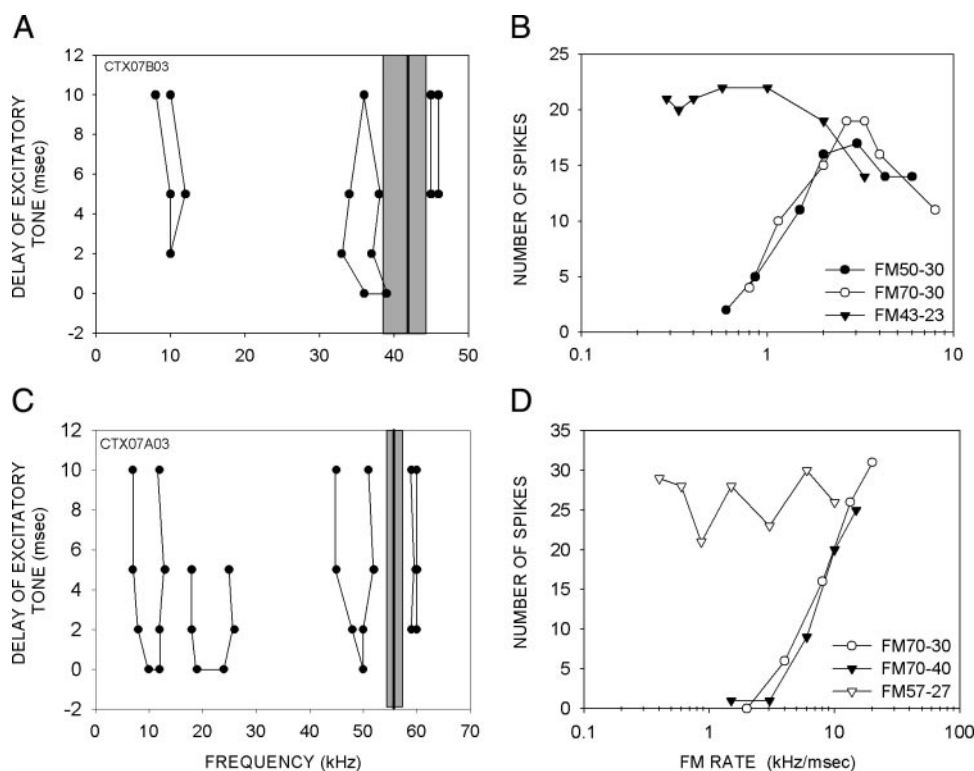


FIG. 7. Contribution of delayed high-frequency inhibition to FM rate selectivity. *Left and right columns:* delay-frequency curve and FM rate selectivity functions, respectively. *A:* a neuron in which high-frequency inhibition was delayed by 5 ms relative to excitation. In addition to the high-frequency inhibition, 2 other distinct bands of inhibition were centered at 38 and 10 kHz. Each band of frequency had a different arrival time. *B:* inclusion of the high-frequency inhibition caused rate selectivity, whereas excluding it by starting the sweep within the excitatory frequency range caused a loss of rate selectivity. *C:* delay of high-frequency inhibition in this neuron was 2 ms. This neuron had 3 bands of low-frequency inhibition, each of which arrived at the same time as excitation. *D:* once again, rate selectivity was lost if the downward sweep excluded high-frequency inhibition.

tation by a downward sweep can offset the delay in arrival time of inhibition and prevent a response at any FM rate. In most rate-selective neurons, however, high-frequency inhibition had a bandwidth < 2 kHz (see examples in Figs. 7 and 9 and histogram in Fig. 12B). The broadest high-frequency band observed was < 8 kHz wide (Fig. 12B, gray bars). The narrow bandwidth of high-frequency inhibition would ensure that the

delay in arrival time was not offset by an early triggering of high-frequency inhibition.

Arrival time and bandwidth of high-frequency inhibition predict the rate selectivity of cortical neurons. The prediction method is explained using an example shown in Fig. 9, A–C. The equation used to predict the rate at which the response decreased to 50% of maximum for slower FM rates was

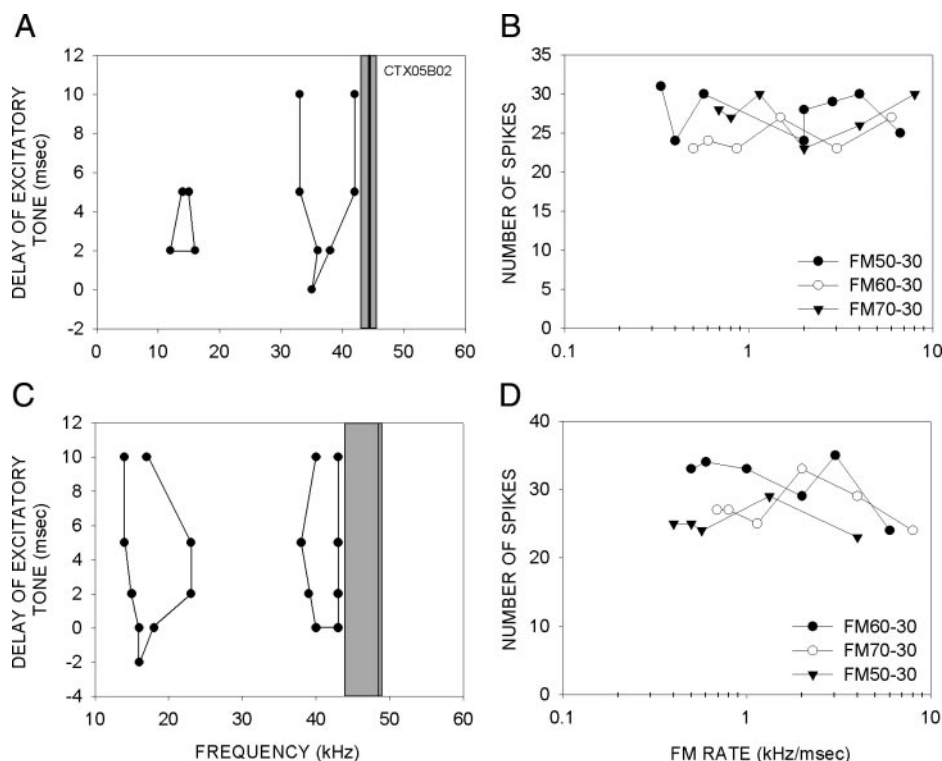


FIG. 8. Neurons without high-frequency inhibition were not FM rate selective. *Left and right columns:* delay-frequency tuning curve and the FM rate selectivity functions, respectively. Both neurons exhibited 2 bands of low-frequency inhibition (A, C), but no high-frequency inhibition at any delay tested. Both neurons were nonselective for downward FM rate (B, D).

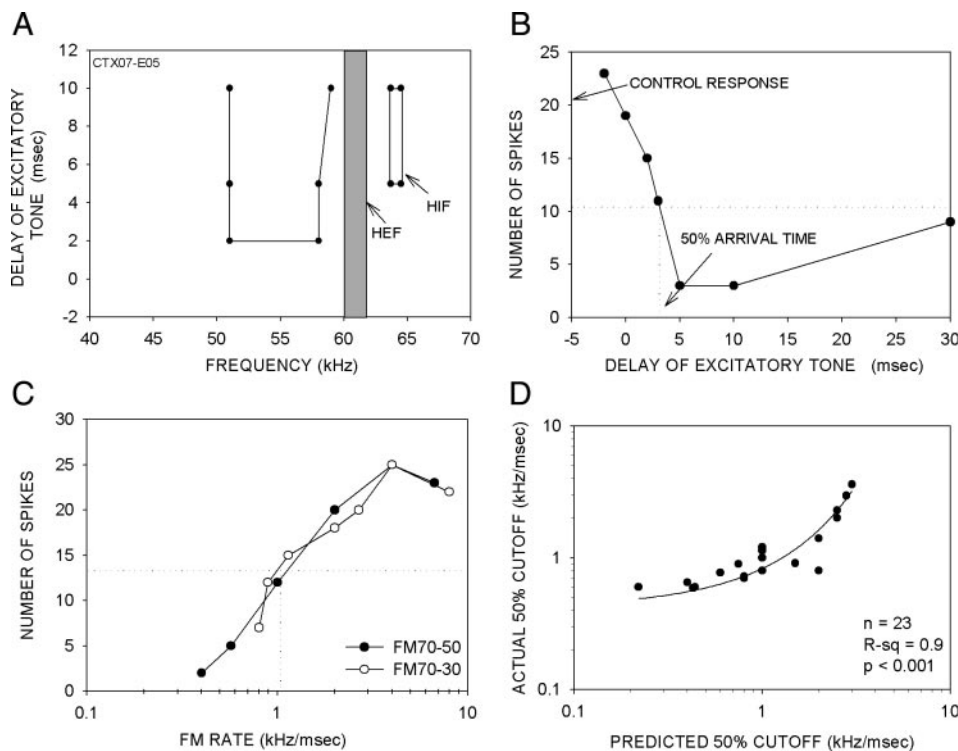


FIG. 9. Arrival time and bandwidth of high-frequency inhibition predict rate selectivity. A–C: example used to illustrate the method used to predict rate selectivity. From the delay-frequency tuning curve of each neuron (A), the spectral distance between the high inhibitory frequency (HIF) and the high excitatory frequency (HEF) was estimated. In this example, HIF – HEF is 3 kHz. From the 2-tone inhibition curve (B), the arrival time of inhibition that caused 50% suppression from control response (horizontal dotted line) was estimated. In this example, 50% arrival time is 3 ms. Predicted 50% cutoff rate for this neuron is 3 kHz/3 ms = 1 kHz/ms (vertical dotted line). Measured rate selectivity functions (C) show that the 50% cutoff for this neuron was near 1 kHz/ms, supporting the prediction. Horizontal dotted line is the 50% response, whereas the vertical dotted line shows the time at which response decreased to 50% of control. D: summary plot based on data from 23 neurons shows a good correlation (exponential fit, $R^2 = 0.9$, $P < 0.001$) between the predicted and actual 50% cutoff rates.

$$50\% \text{ cutoff rate (kHz/ms)} = (\text{HIF} - \text{HEF}) / (50\% \text{ arrival time of inhibition})$$

where HIF is the highest inhibitory frequency and HEF is the highest excitatory frequency. The 50% arrival time of inhibition was the delay between the excitatory and inhibitory frequencies that caused a 50% suppression of response from maximum. The actual 50% cutoff was determined from the FM rate-selectivity curves. In the example neuron (Fig. 9A), the difference between the HIF (65 kHz) and the HEF (62 kHz) was 3 kHz. The delay of inhibition that caused a 50% reduction in response to the excitatory tone was 3 ms (Fig. 9B). For downward FM sweeps $>3 \text{ kHz/3 ms}$ ($=1 \text{ kHz/ms}$), excitation would occur before inhibition. In sweeps with rates $<1 \text{ kHz/ms}$, inhibition would occur before or together with excitation and reduce responses.

This prediction was met by the neuron (Fig. 9C). FM rates $<1 \text{ kHz/ms}$ elicited $<50\%$ of maximum response. A similar prediction was made in 25 neurons in which high-frequency inhibitory bandwidth, 50% arrival time, and rate-selectivity data were available. A strong correlation (exponential fit, $r^2 = 0.9$, $P < 0.001$) exists between the predicted and the actual 50% cutoff rates, adding support to the view that the delayed high-frequency inhibition contributes to rate selectivity in the pallid bat auditory cortex (Fig. 9D).

Cortical mechanisms of FM direction selectivity

In the IC of the pallid bat, direction selectivity is created by early low-frequency inhibition. In addition, the bandwidth of low-frequency inhibition is broad. To test whether the cortex creates direction selectivity similarly, the presence and contribution of early low-frequency inhibition to direction selectivity was tested in 45 neurons. All 45 neurons exhibited a band of low-frequency inhibition adjacent to the excitatory tuning curve (e.g., Fig. 10, A and D; also see Figs. 6–9). In 86.7%

(39/45) of these neurons, low-frequency inhibition arrived either at the same time as or earlier than excitation (Figs. 6–9, 10A, and population histogram in Fig. 12A). For instance, in the neuron shown in Fig. 10A, frequencies between 40 and 50 kHz suppressed the response to the 52-kHz excitatory tone when they started simultaneously. Figure 10B shows that the best inhibitory tone almost completely inhibited the response to the BF tone at 0-ms delay. This neuron was direction selective (Fig. 10C, DSI = 1), with no response to upward sweeps that included the low-frequency inhibition.

If low-frequency inhibition suppressed responses to an upward sweep, starting an upward sweep from inside the excitatory tuning curve should reduce direction selectivity. This prediction was tested in 33 direction-selective neurons. In all (100%) of these neurons, the response to the upward sweep was increased if the sweep started inside the excitatory tuning curve. In the example shown in Fig. 10, a 40- to 60-kHz upward sweep that included the low-frequency inhibition produced no response (Fig. 10C). A 53- to 73-kHz sweep that excluded low-frequency inhibition produced a response similar in magnitude to the downward sweep. These data suggest that, as in the IC, early low-frequency inhibition contributes to FM direction selectivity.

In three of five neurons in which low-frequency inhibition arrived late, direction selectivity was poor. For the neuron shown in Fig. 10, D and E, frequencies between 36 and 38 kHz were inhibitory when they were advanced by 2 ms relative to the excitatory tone onset. The delayed arrival of low-frequency inhibition predicts that fast upward sweeps should produce a strong response and slower sweeps should cause weaker responses. As predicted, this neuron was rate selective for upward FM sweeps, but not direction selective (Fig. 10F, DSI = 0). Exclusion of low-frequency inhibition from the upward sweep (47- to 67-kHz sweep) eliminated rate selectivity. This

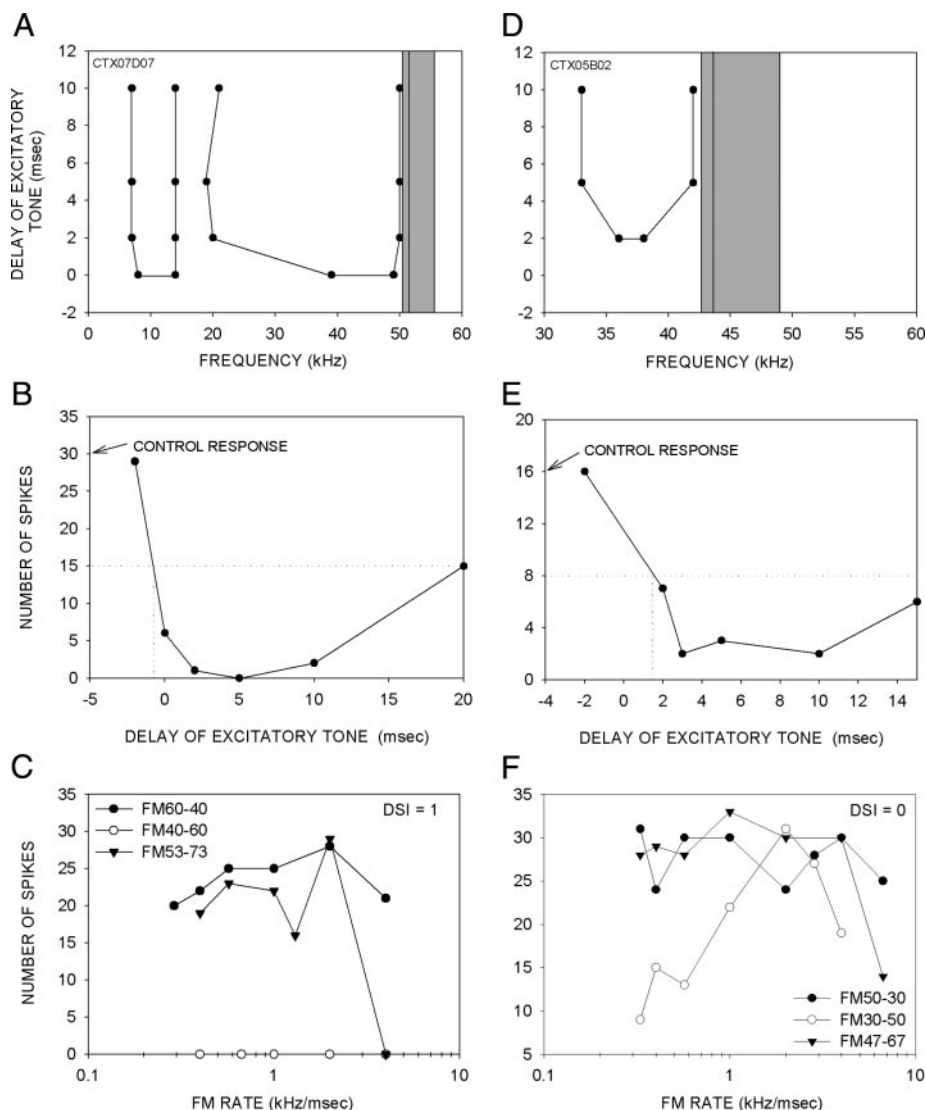


FIG. 10. Mechanisms of direction selectivity. *Left column:* neuron with strong direction selectivity. *Right column:* example with poor direction selectivity. *A:* this neuron had a broad band of low-frequency inhibition centered at 35 kHz. Inhibition triggered by frequencies between 38 and 48 kHz arrived simultaneously with excitation. *B:* 2-tone graph shows that when the onset of the inhibitory tone was delayed by 1 ms, it was still able to suppress the response to the excitatory tone by 50%, suggesting the early arrival of inhibition. *C:* although responding strongly to downward FM sweeps, this neuron responded poorly to upward sweeps with the same spectrum ($DSI = 1$). When the low band of inhibitory frequencies was excluded by starting an upward sweep inside the tuning curve, direction selectivity was lost. *D:* an example neuron that had broad low-frequency inhibition. *E:* low-frequency inhibition arrived late in this neuron relative to excitation. *F:* neuron was not direction selective because a strong response was obtained for both upward and downward FM sweeps at certain rates. Rate-dependent response to the upward FM sweep arose because of the delayed low-frequency inhibition. Neuron was nonselective for FM rate if the inhibitory frequencies were excluded from the sweep. Horizontal dotted lines in *B* and *E* represent the 50% response, whereas the vertical dotted lines represent the delay at which 50% response occurs.

is similar to delayed high-frequency inhibition creating downward FM rate selectivity.

These data show that neurons with early low-frequency inhibition are direction selective, whereas neurons with delayed low-frequency inhibition are not direction selective because they respond to upward sweeps at fast rates. Figure 11 shows the relationship ($r^2 = 0.34$, $P < 0.001$) between the 50% arrival time of low-frequency inhibition and the DSI in the recorded population. Most neurons with early-arriving low-frequency inhibition had a $DSI > 0.6$, indicating strong direction selectivity. Most (four of five) neurons with delayed low-frequency inhibition exhibited poor direction selectivity. The arrival time alone, however, does not completely predict direction selectivity. For instance, two of six neurons in which low-frequency inhibition was delayed showed $DSI > 0.6$, indicating strong direction selectivity (Fig. 11). In addition, a considerable spread is seen in DSI values at any given arrival time. Another factor that will have an effect on direction selectivity is the bandwidth of low-frequency inhibition. For two neurons with the same arrival time of low-frequency inhibition, the neuron with the broader bandwidth of inhibition will have the inhibition start earlier when presented with an

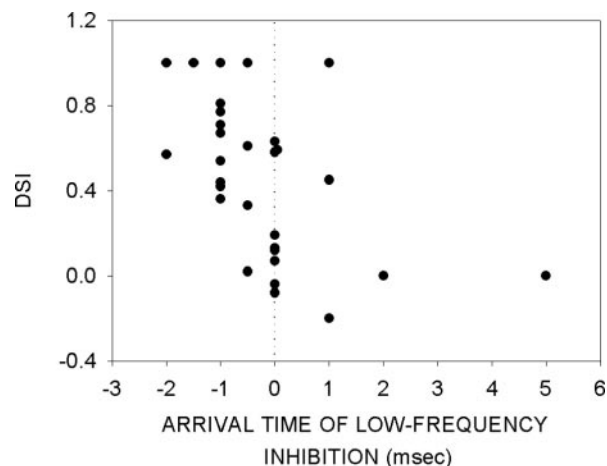


FIG. 11. Arrival time of low-frequency inhibition predicts direction selectivity in most cortical neurons. Vertical dotted line separates neurons with early and delayed arrivals of low-frequency inhibition. Arrival times are those that caused a 50% suppression of response from control. Most neurons with early arrival time were selective for direction, whereas most neurons with delayed arrival times were nonselective.

upward sweep. The bandwidth of low-frequency inhibition in most FM sweep-selective neurons was >8 kHz and always significantly broader than the bandwidth of high-frequency inhibition (e.g., Figs. 6, 7, 8, 10, and histogram in Fig. 12). High-frequency inhibition, in all the neurons recorded, was <8 kHz. Thus both the broad bandwidth and early arrival time of low-frequency inhibition are likely to initiate inhibition earlier than the excitation and prevent responses to upward FM sweeps.

Complexity of inhibitory bands in cortical neurons

In addition to the low- and high-frequency inhibitory sidebands discussed above, additional low-frequency bands of inhibition were observed in nine of 30 neurons (e.g., Figs. 7, A and C, 8, A and C, and 10A). In the example shown in Fig. 7A, the three bands of inhibition arrived with different latencies. The 37-kHz low-frequency inhibition arrived at the same time as excitation, whereas the 10-kHz inhibition was delayed by 2 ms. The high-frequency inhibition (45 kHz) arrived 5 ms late. The neuron shown in Fig. 7C exhibited four bands of inhibition. As with all FM rate-selective neurons, high-frequency inhibition in this neuron arrived late compared with the three bands of low-frequency inhibition.

Despite the variability in the number of inhibitory bands, two consistent features were observed. First, all neurons exhibited one band of low-frequency inhibition adjacent to the excitatory tuning curve (e.g., Figs. 6A, 7, A and C, 8, A and C, 9A, and 10, A and D). This was true even for neurons that were not direction selective (Fig. 10, D–F) because the delay of inhibition and bandwidth, but not the presence of low-frequency inhibition, constituted the key factors in determining direction selectivity. Second, whenever a band of inhibition was present below 30 kHz, it was consistently centered at 10–15 kHz (e.g., Figs. 7, A and C, 8, and 10A).

Duration of inhibition in the cortex

The duration of inhibition is another property that is likely to affect rate and direction selectivity. For instance, if the duration of low-frequency inhibition was short, neurons could respond to upward sweeps because the early inhibition might be over

before the sweep-triggered excitation. The duration of inhibition was measured in 38 FM sweep-selective neurons. To measure duration of inhibition, a tone at the neuron's BF was presented with a duration of either 3 or 5 ms and the duration of the inhibitory tone was set at 10 ms. Various delays were interposed between the onsets of the inhibitory and the excitatory tones to determine the delay at which response returned to the control level (BF alone response). In 23/38 neurons inhibition lasted longer than the duration of the inhibitory tone. The neuron shown in Fig. 13A, for example, exhibited the longest durations of inhibition observed in this study. The 10-kHz tone inhibited response to BF tone for 300 ms, whereas inhibition from the 45- and 61-kHz tones lasted nearly 200 ms. Across the population, however, the average duration of inhibition generated by a 10-ms inhibitory tone was around 150 ms with no significant difference between different inhibitory frequencies (Fig. 13B, *t*-test, $P > 0.05$).

In 11/38 neurons inhibition did not persist longer than the duration of the inhibitory tone. For instance, the neuron in Fig. 13C was inhibited for nearly 10 ms when a 10-ms inhibitory tone was used. In such neurons, additional inhibitory tone durations were used to determine whether the inhibition was brief or whether it depended on the duration of the inhibitory tone. For longer-duration inhibitory tones, the response recovered to control levels near the offset of the inhibitory tone, suggesting that the duration of inhibition in this neuron increased with the duration of the inhibitory tone. In the remaining four of 38 neurons, inhibition was reduced near the offset of the inhibitory tone, but increased again at longer delays before the response returned to control level (Fig. 13D).

Comparison of FM rate selectivity in the IC and auditory cortex

Arrival time and bandwidth of inhibition and FM rate selectivity were compared between cortex and IC. Data for IC neurons were obtained using identical methods as in cortex and were summarized from Fuzessery et al. (2006). The arrival time of inhibition relative to excitation in the auditory cortex was delayed compared with that in the IC (Fig. 14A). The average arrival time of high-frequency inhibition was signifi-

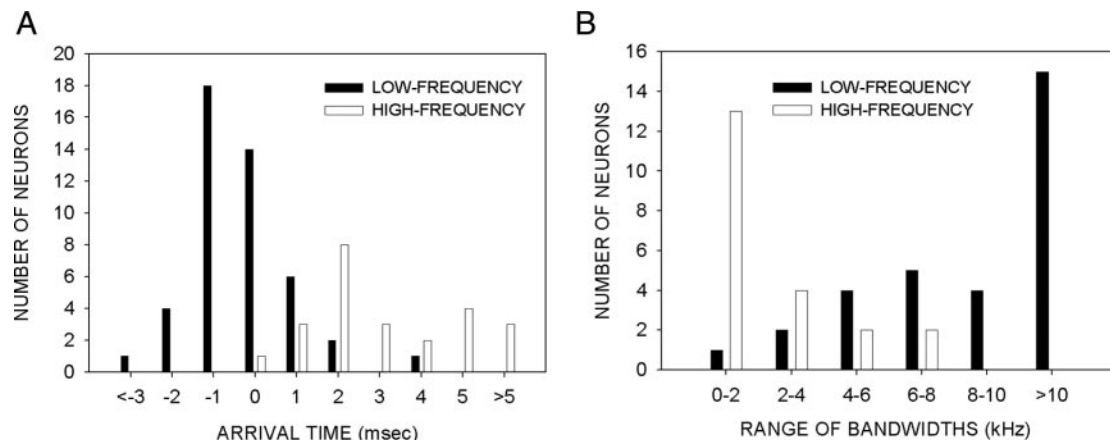


FIG. 12. Differences in arrival time and bandwidth of low- and high-frequency inhibition. A: in most neurons, low-frequency inhibition arrives early, whereas high-frequency inhibition is delayed. Mean (\pm SE) arrival time of low-frequency inhibition was -0.39 ± 0.2 ms and high-frequency inhibition was 3.35 ± 0.51 ms. These values were significantly different ($P < 0.001$, paired *t*-test). B: bandwidth of low-frequency inhibition in most cortical neurons was wider than 8 kHz, whereas the bandwidth of high-frequency inhibition was narrower than 4 kHz.

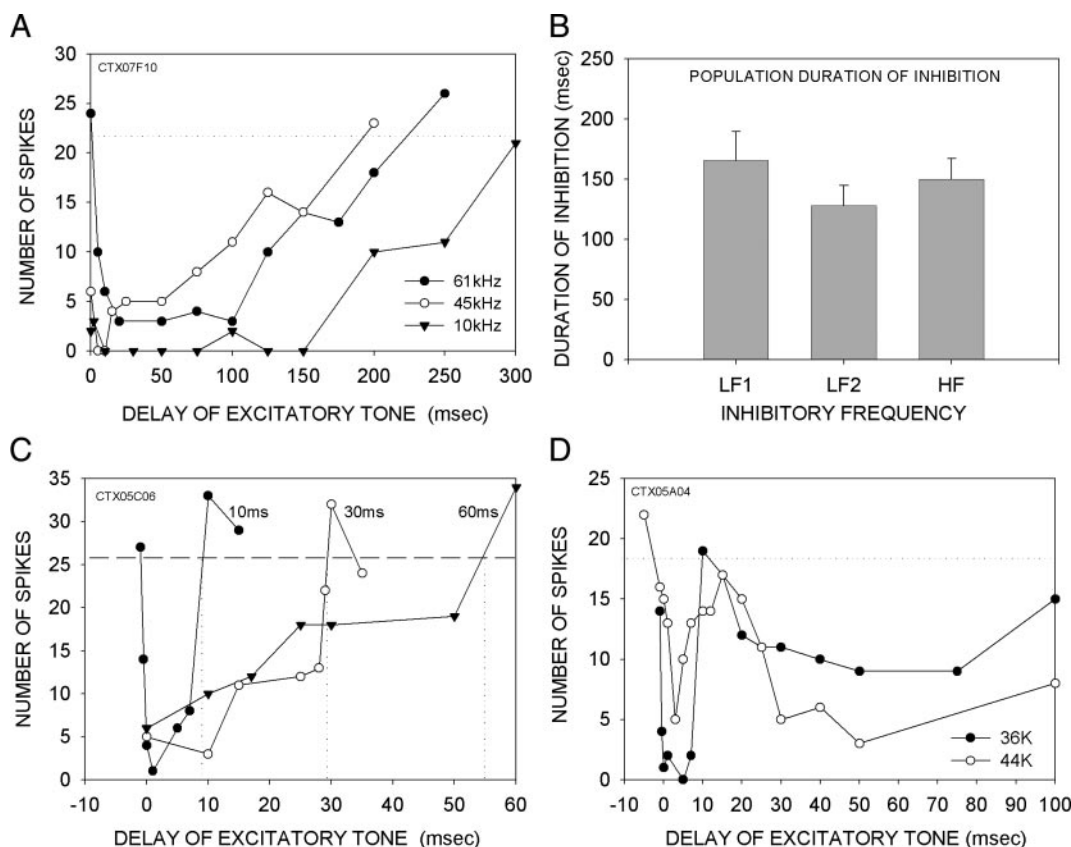


FIG. 13. Duration of inhibition in cortical neurons. *A*: in most cortical neurons the duration of inhibition lasts much longer than the duration of the inhibitory tone. This neuron showed 3 bands of inhibition and the duration of inhibition generated by each frequency lasted ≥ 200 ms. Duration of the inhibitory tone was 10 ms in each case. *B*: population summary shows that a 10-ms-duration inhibitory tone produced inhibition that lasted >100 ms on average, regardless of the frequency of the inhibitory tone. LF1 is the inhibition centered at 10 kHz found in nearly 50% of the recorded neurons, whereas LF2 and HF represent the low- and high-frequency inhibitions contributing to direction and rate selectivity, respectively. *C*: in this neuron, the duration of inhibition depended on the duration of the inhibitory tone. Recovery from inhibition occurred when the delay between the 2 tones was equal to the duration of the inhibitory tone. Duration of the inhibitory tone is shown next to corresponding 2-tone plots. Vertical dotted lines indicate the delays at which response recovers to control level for the 3 different durations of the inhibitory tone. *D*: in this neuron, long-lasting inhibition followed recovery from inhibition at the offset of the tone. Strong inhibition at 2 distinct delays separated by a recovery to control was observed for both low- and high-frequency inhibitory tones. Horizontal dotted lines in *A*, *C*, and *D* show control response.

cantly ($*P < 0.05$, *t*-test) faster in the IC (0.49 ± 0.5 ms) than in the cortex (3.35 ± 0.51 ms). A significant ($*P < 0.05$, *t*-test) difference in arrival time was also found for low-frequency inhibition that contributed to direction selectivity. In the IC, low-frequency inhibition arrived 1.3 ± 0.28 ms before excitation, whereas in the cortex it arrived 0.39 ± 0.2 ms before excitation. No significant differences were seen in the bandwidths of low- and high-frequency inhibitions between the two regions (Fig. 14*B*, $P > 0.05$, *t*-test).

The arrival time and bandwidth of high-frequency inhibition predict the FM rate at which response declines to 50% of maximum. The delayed arrival time of inhibition in the cortex suggests that cortical neurons will respond to slower FM sweep rates than IC neurons. Bandwidth of inhibition is similar in both regions and is unlikely to create the differences in rate selectivity between IC and cortex. Responses declined to 50% of maximum in the cortex at slower FM rates than in the IC (Fig. 15*A*, mean \pm SE, IC 2.91 ± 0.33 kHz/ms, cortex 1.5 ± 0.21 , $*P < 0.05$, *t*-test), indicating that cortical neurons respond better than IC neurons to slower rates.

In neurons with band-pass selectivity for rate (Fig. 1*D*, for example), the bandwidth of rate selectivity and the best rate were measured. The bandwidth of selectivity was the range of

FM rates that elicited $>50\%$ of maximum response. The center of the range of FM rates that produced $>80\%$ of maximum response was taken as the best rate. A comparison of the bandwidth of selectivity between the IC and the cortex shows that cortical neurons respond to a broader range of FM rates than IC neurons (Fig. 15*B*, IC: 4.19 ± 0.33 kHz/ms; cortex: 6.1 ± 0.31 kHz/ms, $*P < 0.05$, *t*-test). Best rate was not significantly different between the two regions (Fig. 15*C*, $P > 0.05$, *t*-test). These data suggest that there is a decrease in selectivity for FM rate from the IC to the cortex.

DISCUSSION

Different characteristics of low- and high-frequency inhibitions and mechanisms of FM direction and rate selectivity

In the pallid bat auditory cortex, consistent bandwidth and arrival time differences exist between high- and low-frequency inhibitions. In most neurons that are selective for the downward sweep direction and rate, inhibition generated by low frequencies arrives at least as fast as excitation, whereas high-frequency inhibition is delayed. The bandwidth of low-

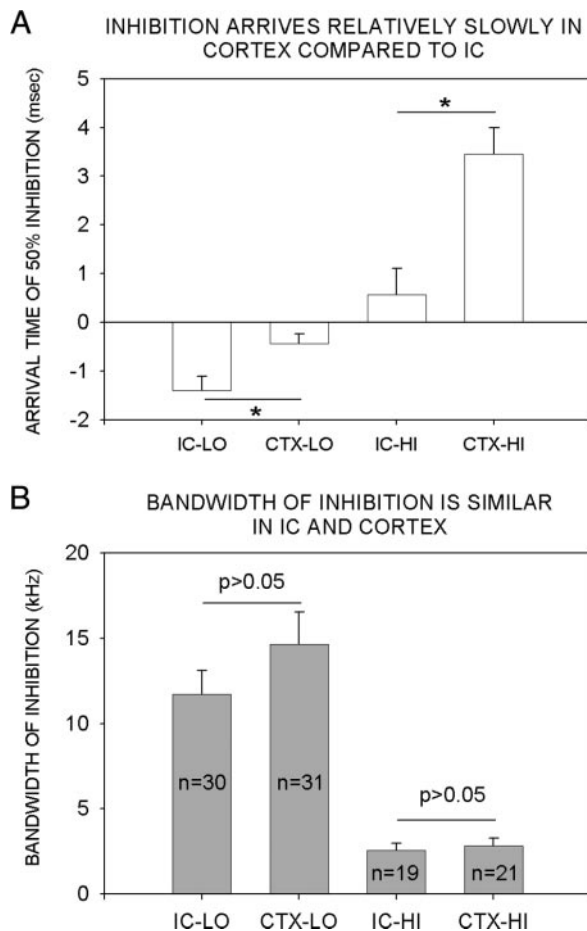


FIG. 14. Comparison of properties of inhibition in the inferior colliculus (IC) and cortex. *A*: high-frequency inhibition in both regions arrives slower than excitation, whereas low-frequency inhibition arrives faster. In the IC, the relative arrival times of both low- and high-frequency inhibitions were earlier than in the cortex ($*P < 0.05$, *t*-test). *B*: in both IC and cortex, bandwidth of low-frequency inhibition was broader than high-frequency inhibition. No differences in bandwidth of inhibition were found between IC and cortex.

frequency inhibition is broad compared with that of high-frequency inhibition. The broader the bandwidth, the earlier the inhibitory input will be triggered before excitation in response to FM sweeps. Because of the broad bandwidth and early arrival of low-frequency inhibition, upward sweeps will generate inhibition first and elicit a poor response. Downward sweeps elicit strong responses for fast sweep rates because the late arrival of high-frequency inhibition allows excitation to occur first. For slow sweep rates, high-frequency inhibition arrives at the same time as or earlier than excitation and reduces response magnitude. This mechanism is similar to that observed in the IC of the pallid bat (Fuzessery et al. 2006).

Rate and direction selectivity are purported to be shaped by either inhibition from the sidebands or through facilitation (Covey and Casseday 1999; Fuzessery and Hall 1996; Gordon and O'Neill 1998; Heil et al. 1992a; Phillips et al. 1985; Suga 1965a). The facilitation model predicts that sweeps confined to the excitatory tuning curve should elicit directionally selective responses. Direction selectivity for sweeps confined within the excitatory tuning curve has been reported in cat AI (Phillips et al. 1985). FM sweeps toward the BF evoked strong responses, whereas those away from the BF evoked weak responses. Heil

et al. (1992a) also reported that the difference in latencies of excitatory responses to the instantaneous frequencies that triggered a response to the sweep was correlated with the best FM rate, suggesting excitatory summation as a mechanism. In the pallid bat auditory cortex, the timing and bandwidth of inhibitory sidebands explain FM direction and rate selectivity in most neurons. Direction selectivity was lost if the upward FM sweep was started within the excitatory tuning curve, suggesting that low-frequency inhibition was necessary for direction selectivity. The second facilitation model depends on interac-

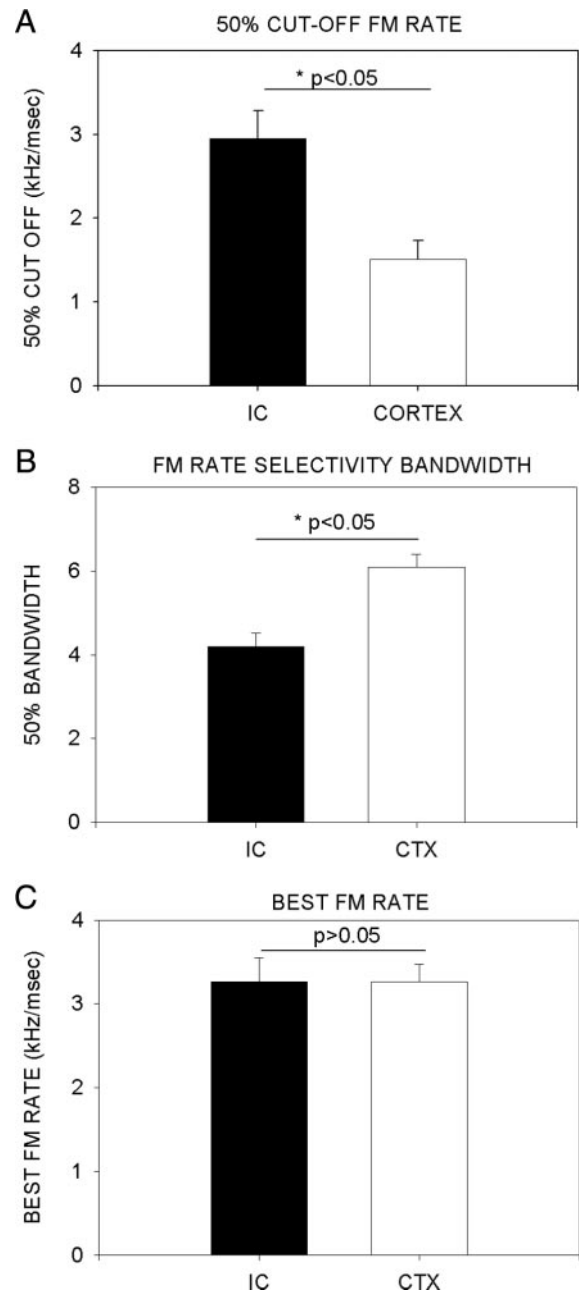


FIG. 15. Comparison of FM rate selectivity in the IC and cortex. *A*: for decreasing rates, the rate at which response decreased to 50% of maximum was compared between cortex and IC. On average, cortical neurons were suppressed at slower rates than IC neurons ($*P < 0.05$, *t*-test). *B*: in neurons with a band-pass type FM rate selectivity, the 50% bandwidth of selectivity was narrower in the IC than in the cortex ($*P < 0.05$, *t*-test). *C*: best rate in the band-pass type neurons was not different between IC and cortex.

tions between excitation and rebound from inhibition (Covey and Casseday 1999). If high-frequency inhibition arrives early and the rebound from this inhibition coincides with a delayed, subthreshold excitation, responses should occur only for downward sweeps and not for upward sweeps. However, in the pallid bat cortex, the arrival time of high-frequency inhibition was delayed relative to excitation. Moreover, starting a downward FM sweep inside the excitatory tuning curve produced responses that were as strong as the maximum response obtained when the sweep included high-frequency inhibition. However, because our data are based on extracellular recordings, we cannot preclude the presence of subthreshold events that may show nonlinear interactions. Such mechanisms may play a role in shaping selectivity of FM specialists that respond only to downward FM sweeps (Razak and Fuzessery 2002).

The data presented here also explain FM rate-dependent direction selectivity (Gordon and O'Neill 1998). In neurons with early low-frequency inhibition, upward FM sweeps produced no response. In neurons with delayed low-frequency inhibition, however, fast upward FM sweeps were able to elicit responses, whereas slow upward sweeps produced weak responses. If inhibitory frequencies had been determined using the two-tone paradigm only at 0-ms delay, delayed low-frequency inhibition would have been missed and direction selectivity at slow FM rates could not be explained. Besides suggesting that a complete picture of direction selectivity will emerge only if measured at multiple sweep rates, these data show that even if inhibition is present on both sides of the tuning curve, the relative timing and bandwidth of inhibition dictate directional selectivity measured at various sweep rates.

Two different mechanisms have been proposed to explain FM rate selectivity in the auditory system of mustached and pallid bats (Gordon and O'Neill 1998; Fuzessery et al. 2006). The first mechanism depends on high-frequency inhibition that arrives later than excitation. The second mechanism depends on duration tuning for component tones. Our data show that the pallid bat auditory cortex uses the former mechanism for rate selectivity. Both correlative and causative results support the contention that delayed high-frequency inhibition shapes FM rate selectivity. It was possible to predict the 50% cutoff point for FM rate selectivity based on arrival time and bandwidth of high-frequency inhibition. Neurons without high-frequency inhibition were not FM rate selective. In all cortical neurons with delayed high-frequency inhibition, the exclusion of the inhibitory frequencies from the downward FM sweep resulted in a loss of rate selectivity. In the duration-tuned neurons in the IC, starting a downward FM sweep inside the tuning curve did not eliminate FM rate selectivity (Fuzessery et al. 2006). In the few cortical neurons that were duration tuned for BF tones, starting a downward sweep inside the tuning curve eliminated rate selectivity (e.g., Figs. 4A and 6D). This suggests that duration tuning does not play a role in FM rate selectivity in the studied area of the cortex. One explanation for why duration tuning does not contribute to rate selectivity in these neurons is that the duration selectivity of cortical neurons is not as sharp as that seen in the IC. In most duration-tuned neurons (e.g., Fig. 4B), the decrease in response for increasing durations is gradual. In

addition, these neurons may have been nonselective for the duration of other tones within the excitatory tuning curve. Excitation produced by long-duration tones may override the inhibition generated by the BF tone at nonoptimal durations. Additional studies are required to test this possibility.

Range of FM rate selectivity in the pallid bat auditory cortex

The pallid bat echolocation call is a 60- to 30-kHz downward FM sweep with durations between 1 and 6 ms. This corresponds to rates between 5 and 30 kHz/ms. Most of the fast-pass neurons have a 50% cutoff <3 kHz/ms for slower sweeps, suggesting that they will respond to the entire range of rates in the echolocation call. However, most of the band-pass neurons in the auditory cortex exhibited best FM rates <5 kHz/ms. This suggests that these neurons will respond only to the slowest rates present in the bat's call. It is not entirely clear why the band-pass neurons have their best rate at the lower end of the range of rates in the echolocation call. The pallid bat call is exponential in nature, whereas we used a linear sweep in this study. The exponential sweep does contain sweeps <5 kHz/ms (Razak and Fuzessery, unpublished observations). It is possible that the range of optimal rates is different for different types of sweeps (Nelken and Versnel 2000).

Strong selectivity for behaviorally relevant sounds in the pallid bat auditory system

A striking feature of the pallid bat auditory system is the high degree of selectivity for FM sweep direction and a narrow range of FM sweep rates. Compared with other species of FM bats, which have <15% of neurons that are selective for the echolocation pulse (O'Neill 1985; Suga 1965b), nearly 70% of neurons tuned between 30 and 60 kHz in the pallid bat IC and cortex (Fuzessery 1994; Razak and Fuzessery 2002; this study; Fuzessery et al., unpublished observation) show such selectivity. As suggested before, one reason the pallid bat FM selective region is so specialized may be the gleaning lifestyle of the pallid bat (Fuzessery 1994). The pallid bat uses echolocation for obstacle avoidance, but listens passively to prey-generated noise (Bell 1982; Fuzessery et al. 1993). It is likely to receive prey-generated noise and echoes at the same time, and one way to separate these two streams of information is by using parallel pathways with strong filters for each sound (Bregman 1990). If a neuron with BF in the echolocation range responds, it is most likely to a downward FM sweep with rates >2 kHz/ms. Similarly, an area of neurons with BF <30 kHz exhibits a high degree of selectivity for broadband noise over tones and may represent prey-generated noise (Razak and Fuzessery 2002).

Another feature of the pallid bat auditory cortex that may be related to enhancing segregation between the two pathways is the presence of inhibitory bands at frequencies involved with passive-prey localization. Many FM sweep-selective neurons showed a band of inhibition centered near 10–15 kHz (examples in Figs. 7, 8, and 10). Noise-selective neurons that may represent prey-generated noise are tuned in this low-frequency range (Razak and Fuzessery 2002). Although the pathways that process echolocation and noise are mostly segregated at the

cortical level, there are inhibitory interactions between them (Razak and Fuzessery, *ARO Abstracts* 2000). The inhibitory band centered near 10–15 kHz may underlie inhibition of FM sweep-selective neurons if prey-generated noise precedes echoes, a situation likely to occur in nature. Modeling and psychophysical studies suggest that inhibitory interactions between different frequency channels enhance segregation of sources with different spectral content (Beauvois and Meddis 1996; McCabe and Denham 1997). Such a mechanism suggests differential functional roles for each of the inhibitory bands, with the sidebands creating response properties such as FM rate and direction selectivity, and the 10- to 15-kHz band underlying noise–echo context-dependent interactions.

Comparison of rate and direction selectivity in auditory cortex across species

Selectivity for FM rate and direction is observed in the auditory cortex of several species (Hart et al. 2002; Heil and Irvine 1998; Heil et al. 1992b; Mendelson et al. 1993; Nelken and Versnel 2000; Suga 1965a,b; Taniguchi et al. 1986; Tian and Rauschecker 1994, 2004). In some species, systematic changes in FM sweep selectivity with BF have been reported. For instance, in the domestic chick forebrain (field L), most neurons with BFs <2 kHz preferred upward sweeps, whereas those with BF >2 kHz preferred downward sweeps (Heil et al. 1992a). A similar finding was reported in the rat auditory cortex (Zhang et al. 2003). The finding that the DSIs are similar across the FM sweep-selective region suggests that a frequency-dependent organization of direction selectivity is not present in the pallid bat, at least for neurons with BF between 30 and 60 kHz. Another form of topography is found in the cat cortex, where the central part of each isofrequency contour is biased toward selectivity for downward FM sweeps and slow sweep rates (Heil et al. 1992b; Mendelson et al. 1993). Although a systematic spatial survey of selectivity for direction and rate was not conducted in this study, it is unlikely that the pallid bat cortex shows such topographies for several reasons. Even though the entire FM sweep-selective region was sampled in two different studies (Razak and Fuzessery 2002; this study), the vast majority of neurons are selective for the downward direction. Neurons that were nonselective were present among neurons that were selective for direction. None of the neurons was selective for upward FM sweeps. Similarly, most neurons were selective for a narrow range of rates. Neurons with no FM rate selectivity were present among neurons with sharp rate selectivity. The auditory cortex of the rat and cat may be organized to represent FM sweeps with a wide range of rates and both sweep directions, with the topographies potentially underlying a place code for discriminating different sweeps according to rate and direction. The pallid bat, on the other hand, appears to have developed a specialized area with BF >30 kHz for representing sweeps with a narrow range of rates and the downward direction.

Comparison of rate and direction selectivity mechanisms in visual and auditory cortex

Selectivity for the rate and direction of stimuli moving across the receptor surface is a property common to both visual

and auditory cortex. Whereas similar mechanisms are used to shape selectivity, the predominant mechanism appears to be different in the two cortical areas. In the visual cortex, facilitatory interactions for optimal directions underlie selectivity. In visual cortical layer 4 simple cells, response timing is known to change across the receptive field, a property termed *spatiotemporal orientation*. A stimulus moving in the optimal direction causes responses of progressively shorter latencies from different receptive field (RF) locations, causing summation (Movshon et al. 1978; Reid et al. 1991). Stimuli moving in the opposite direction do not cause summation, resulting in direction selectivity. Neurons exhibit directionally selective responses even if the stimulus is confined to a small portion of the excitatory receptive field. Inhibition is known to play a role in direction selectivity by enhancing the summation (Murthy and Humphrey 1999). In the auditory cortex, the emphasis has been on inhibitory sidebands (Heil 1992a,b; Suga 1965a,b; Zhang et al. 2003; this study). Starting FM sweeps inside the receptive field and thus excluding the inhibitory frequencies results in a decline in the direction selectivity, a result not predicted if the direction of sweep elicited differences in excitatory summation.

Similar to the auditory cortex, visual cortical neurons display selectivity for stimulus movement rates (also called velocity or speed). Facilitatory mechanisms are also involved in rate selectivity (Duysens et al. 1985a). Summation of excitatory inputs caused facilitation for fast but not slow rates, giving rise to selectivity for fast moving stimuli. If a similar mechanism were present in the pallid bat auditory cortex, removal of inhibitory frequencies from the sweep should not affect selectivity. However, the ability to predict FM rate and direction selectivity, based on temporal interactions between excitatory and inhibitory frequencies in most neurons, suggests that facilitatory interactions are not common in the pallid bat auditory cortex, at least in neurons tuned in the echolocation range. In almost all the recorded neurons in the pallid bat cortex, removal of low-frequency inhibition eliminated or reduced direction selectivity and removal of high-frequency inhibition eliminated or reduced rate selectivity.

Spatiotemporal interactions between inhibitory and excitatory regions and duration tuning are primarily involved in shaping selectivity for slow moving stimuli (Duysens et al. 1985a,b). It is not clear how these mechanisms can explain selectivity for fast velocities. However, in the visual layers of the superior colliculus, it has been suggested that a delayed inhibition from the RF surround may suppress responses to slow moving stimuli, but allow responses to fast moving stimuli (Razak and Pallas 2005). This is similar to observations in the pallid bat IC and cortex. These comparisons suggest that similar mechanisms shape selectivity in the visual and auditory systems, but different mechanisms predominate in different areas. A fundamental difference between the auditory and visual systems, however, must be pointed out. It is unlikely that duration tuning underlies selectivity for fast rates in the visual cortex because selectivity for short-duration stimuli does not seem to be present. If a neuron responds to short-duration stimuli, it will also respond to long-duration stimuli because the visual system appears to depend on response duration to create duration tuning (Duysens et al. 1996).

Duration tuning in cortical neurons tuned in the echolocation range

In the IC of the pallid bat, >50% of FM rate-selective neurons are selective for short-duration tones (Fuzessery et al. 2006). In the auditory cortex, among neurons with similar BF and selectivity for FM sweep rate and direction as in the IC, only 10% of rate-selective neurons are duration tuned. Duration tuning in the cortex may be either inherited from subcortical sites or/and refined in the cortex. If inputs from duration-selective and nonselective neurons converge on cortical neurons, the inherited duration tuning is likely to be obscured, and this may underlie the observed rarity of duration tuning in the auditory cortex of the pallid bat. An alternate hypothesis for the lack of duration tuning in the cortex is that the FM sweep-selective cortical neurons receive their inputs from pathways that bypass the IC. A pathway through the supragenulate nucleus of the thalamus constitutes an extralemniscal system that does not receive input from the IC in the mustached bat (Casseday et al. 1989; Gordon and O'Neill 2000). Preliminary tracing studies in the pallid bat have shown that the FM sweep-selective cortical neurons receive input predominantly from the supragenulate nucleus (Razak et al., *SFN Abstracts* 2004). It remains to be seen whether the FM sweep-selective IC neurons project to the supragenulate or have separate projections to other parts of the medial geniculate body (MGB). It should be noted, however, that this study focused on a region of cortex selective for FM sweeps used by the bat in echolocation. The conclusion that duration tuning is rare in the cortex is based on a comparison of neurons with similar BF and FM rate/direction selectivity between the IC and cortex. It is possible that other regions of the cortex exhibit duration selectivity.

FM rate selectivity in the ascending auditory system of the pallid bat

The loss of a mechanism underlying rate selectivity from the IC to the cortex does not result in a decrease in the number of cortical neurons selective for FM rate. The percentage of cortical FM rate-selective neurons (75%) is comparable to that found in the IC (82%), suggesting that high-frequency inhibition compensates for the lack of duration tuning in creating rate-selective cortical neurons. The arrival time of high-frequency inhibition was slower in the cortex than in the IC. Because the arrival time of high-frequency inhibition is correlated with the FM rate at which the neuron shuts down, one prediction was that cortical neurons would respond to slower FM rates than would IC neurons. This prediction was supported, suggesting that many cortical neurons respond to slow FM rates that suppress IC neurons. In addition, the bandwidth of selectivity was broader in the cortex, suggesting that a reduction in selectivity occurs in the ascending pathway. The significance of maintaining activity in the cortex for slower FM rates that suppress most IC neurons remains unclear. A similar finding regarding reduced selectivity for FM sweeps in the ascending auditory pathway was previously reported in the mustached bat (O'Neill and Brimijoin 2002). In this study, direction selectivity was lower in the supragenulate nucleus of the MGB in the thalamus, compared with the IC. The authors suggested that a possible reason for this is that selec-

tivity is created de novo at each hierarchical stage. Initial tests of this idea using iontophoresis of γ -aminobutyric acid antagonists in the cortex suggest that the auditory cortex indeed re-creates properties found in the IC, providing a substrate for different selectivity in the ascending pathway (Razak and Fuzessery, *ARO Abstracts* 2006).

In conclusion, hierarchical processing in sensory systems is typically thought to involve increased complexity of mechanisms. In the pallid bat auditory pathway representing echolocation frequencies, however, a subcortical mechanism underlying FM rate selectivity is not present in the cortex. This suggests that hierarchical processing may also involve a reduction in the number of mechanisms. The rarity of duration tuning in cortical neurons with BF between 30 and 60 kHz may be a result of convergence of duration-selective and nonselective neurons. Although one mechanism of FM rate selectivity is lost from the IC to the cortex, the percentage of FM rate-selective neurons is not reduced. Counter to the notion that auditory cortex inherits basic response properties from subcortical structures (Nelken et al. 2002), this raises the possibility that intracortical inhibition shapes some FM rate selectivity in the cortex. This possibility is being currently tested using pharmacological blockade of receptors of inhibitory neurotransmitters (Razak and Fuzessery, *ARO Abstracts* 2006).

Although it is known that different inhibitory sidebands exhibit different properties in auditory cortex (Loftus and Sutter 2001), we show that these differences give rise to functionally relevant properties such as FM direction and rate selectivity. Whether different mechanisms create low- and high-frequency inhibitions, and whether these differences are present early in ontogeny or require experience to develop, are currently being explored.

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