

Responses of Neurons in the Inferior Colliculus to Dynamic Interaural Phase Cues: Evidence for a Mechanism of Binaural Adaptation

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McAlpine, David, Dan Jiang, Trevor M. Shackleton, and Alan R. Palmer. Responses of neurons in the inferior colliculus to dynamic interaural phase cues: evidence for a mechanism of binaural adaptation. *J. Neurophysiol.* 83: 1356–1365, 2000. Responses to sound stimuli that humans perceive as moving were obtained for 89 neurons in the inferior colliculus (IC) of urethan-anesthetized guinea pigs. Triangular and sinusoidal interaural phase modulation (IPM), which produced dynamically varying interaural phase disparities (IPDs), was used to present stimuli with different depths, directions, centers, and rates of apparent motion. Many neurons *appeared* sensitive to dynamic IPDs, with responses at any given IPD depending strongly on the IPDs the stimulus had just passed through. However, it was the temporal pattern of the response, rather than the motion cues in the IPM, that determined sensitivity to features such as motion depth, direction, and center locus. IPM restricted only to the center of the IPD responsive area, evoked lower discharge rates than when the stimulus either moved through the IPD responsive area from outside, or up and down its flanks. When the stimulus was moved through the response area first in one direction and then back in the other, and the same IPDs evoked different responses, the response to the motion away from the center of the IPD responsive area was *always* lower than the response to the motion toward the center. When the IPD was closer at which the direction of motion reversed was to the center, the response to the following motion was lower. In no case did we find any evidence for neurons that under all conditions preferred one direction of motion to the other. We conclude that responses of IC neurons to IPM stimuli depend not on the history of *stimulation*, per se, but on the history of their *response* to stimulation, irrespective of the specific motion cues that evoke those responses. These data are consistent with the involvement of an adaptation mechanism that resides at or above the level of binaural integration. We conclude that our data provide no evidence for *specialized* motion detection involving dynamic IPD cues in the auditory midbrain of the mammal.

INTRODUCTION

It is well established that the azimuthal position of low-frequency (<1,500 Hz) sounds is determined by humans using microsecond differences in the timing of the signals at the two ears (Rayleigh 1907; Stevens and Newman 1936). A widely accepted model to account for this remarkable binaural sensitivity is the coincidence detection model (Jeffress 1948). In this model, an array of neurons receives inputs from the two ears such that a neuron fires maximally when the difference in arrival time at the two ears, due to the location of a sound

source, offsets the difference in neural conduction time to that neuron. A central tenet of this model is that the coincidence detectors signal the *instantaneous* value of the interaural delay. In other words, a neuron's probability of discharge is related solely to the relative time of arrival of the inputs from each ear, providing the auditory system with a representation of static azimuthal position. Recordings from single neurons in the medial superior olive (MSO) (Goldberg and Brown 1969; Spitzer and Semple 1995; Yin and Chan 1990) indicate that many neurons do act as coincidence detectors, firing maximally at a particular interaural delay of the stimulus, and at delays equivalent to multiple periods of the stimulating waveform. No evidence of sensitivity to motion was obtained in studies of the MSO.

More detailed analyses of the processing of interaural time delays comes from the inferior colliculus (IC), the major target of the MSO. Yin and his colleagues demonstrated that IC neurons responded to the dynamic interaural phase disparities (IPDs) of binaural beats like they responded to the static interaural delay of tonal stimuli (Yin and Kuwada 1983a). The vast majority of IC neurons were insensitive to the rate or direction of the apparent motion generated by binaural beats (Yin and Kuwada 1983b). These findings suggested that processing of interaural delay in the IC reflects the simple coincidence detection observed in the MSO. However, Spitzer and Semple (1993), using interaural phase modulation (IPM), which they described as a more "physiologically realistic" apparent-motion stimulus than binaural beats, found that the vast majority of IC neurons in gerbil and cat were responsive to IPD cues in a manner more reflective of the *change* of IPD than of the absolute IPDs over which the changes occurred. In particular, they observed that the neuronal discharge rates at any particular IPD were dependent on the direction in which the interaural phase was changed, the depth of the change, and the IPD around which the phase changes were centered. They concluded that the instantaneous probability of discharge of IC neurons reflects not only current stimulus conditions but also the recent history of stimulation. More recently, these same authors (Spitzer and Semple 1998) demonstrated that neurons in the MSO, the primary site of binaural interaction, respond only to the instantaneous IPD. This suggests a hierarchy of binaural responses, with the sensitivity to motion cues increasing from the level of the brain stem to the midbrain.

In the present study, we examined the possible mechanism/s that might be contributing to the apparent sensitivity of IC neurons to virtual-motion cues. We recorded responses of IC

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neurons to a wide range of IPM stimuli that produced apparent motion with different angular extents, directions, centers, and rates. Our data suggest that the responses of IC neurons to the apparent-motion cues of IPM are consistent with adaptation-of-excitation occurring subsequent to coincidence detection. Thus, whereas our results are consistent with those of Spitzer and Semple (1993) in that the instantaneous probability of discharge of IC neurons reflects the recent history, the effects may be nonspecific in that they are related to the history of the *response*, and not the history of the dynamic IPD cues per se.

METHODS

Many of the detailed methods have been described previously (McAlpine et al. 1996; Palmer et al. 1990) and are recounted only briefly here, but methods specific to the present study are described in detail.

Preparation and recording

Recordings were made from the central nucleus of the right IC of 300–400 g guinea pigs anesthetized with urethan (1.5 g/kg in 20% solution) with additional analgesia obtained using phenoperidine (1 mg/kg). A premedication of atropine sulfate (0.06 mg/kg) was administered to reduce bronchial secretions. Supplementary doses of urethan ($\frac{1}{2}$ to $\frac{1}{3}$ of the induction dose) or phenoperidine were administered when required. All animals were tracheotomized, and core temperature was maintained at 37°C with a heating blanket and rectal probe. Most animals respired spontaneously, but a few were artificially respired with 95% O₂-5% CO₂ and end-tidal CO₂ was monitored.

The animals were placed in a stereotaxic frame with hollow earbars into which fitted 12.7 mm Brüel and Kjær condenser earphones and 1-mm probe tubes fitted to 12.7-mm Brüel and Kjær microphones. In every experiment the probe tube microphone was used to calibrate the sound system in dB re 20 μ Pa a few millimeters from the tympanic membrane. The sound systems for each ear were flat ± 5 dB from 100 to 10,000 Hz and were matched to within ± 2 dB.

A silver wire electrode was placed on the round window of one side via a hole in the posterior aspect of the bulla, and the threshold of the cochlear action potential (CAP) evoked by short tone pips was examined as a function of frequency (from 500 to 30,000 Hz) throughout the experiment to monitor the condition of the cochlea. A thin (0.5-mm diam) polythene tube was sealed into the bulla of both sides, to provide pressure equalization while maintaining closed-field recording conditions.

Single-unit action potentials were measured using tungsten-in-glass microelectrodes (Bullock et al. 1988; Merrill and Ainsworth 1972).

Stimulus production and presentation

Stimuli were delivered to separate left and right signal mixers and presented to each ear via attenuators to the separate closed-field sound systems. Search stimuli consisted of 50-ms bursts of white noise presented binaurally. When a single unit was isolated, its best frequency (BF) and threshold to binaural tones at zero interaural delay were determined audiovisually.

IPM stimuli were produced by fixing the phase at the left (contralateral) ear and sinusoidally or triangularly modulating the phase at the right (ipsilateral) ear. Thus the stimulus at the left ear was a simple sine wave

$$A(t) = \sin(2\pi f_c t)$$

When the interaural phase was modulated sinusoidally, the instantaneous amplitude of the sine wave at the right ear was

$$A(t) = \sin[\theta + 2\pi f_c t + m * \sin(2\pi f_m t)]$$

where f_c is the carrier frequency, f_m is the IPM rate, m is IPM depth in radians, and θ is center IPD (i.e., center “locus”) in radians.

When the interaural phase was modulated triangularly, the instantaneous amplitude of the sine wave at the right ear was

$$A(t) = \sin[\theta + 2\pi f_c t + m * \text{tri}(f_m t)]$$

where

$$\begin{aligned} \text{tri}(f_m t) &= 4t f_m & t < 1/4f_m \\ &= 2 - 4t f_m & 1/4f_m < t < 3/4f_m \\ &= 4t f_m - 4 & 3/4f_m < t < 1/f_m \end{aligned}$$

The range of IPDs traversed was controlled by adjusting the depth of the phase modulation at the right ear. The largest excursion of IPD was $\pm 180^\circ$, which modulated the IPD through 360° in each direction. The center IPD is defined as the IPD midway through the excursion in each direction. Figure 1 shows several examples of stimuli with different center IPDs and modulation depths. The stimulus in Fig. 1A, for example, had a center IPD of zero and a modulation depth of $\pm 180^\circ$. Its IPD moved from 0° at *time 0*, through a half cycle (i.e., 180°) in the clockwise direction (gray; because we are recording from the right IC this means toward ipsilateral, or negative, IPDs), before changing direction and moving through one complete cycle of IPD (100% modulation, or 360°) in the counterclockwise direction (black, toward more contralateral, or positive, IPDs). At this point, it then reversed direction and moved through a complete cycle in the clockwise direction. This process was repeated, and the process ended with the stimulus moving through a half cycle from its furthest extent to finish at 0° . Figure 1B shows other examples of IPM, in which the interaural phase was modulated sinusoidally over a depth of $\pm 90^\circ$ around three different center IPDs. Figure 1, C and D, shows representations of triangular IPM centered at 0° , with IPM depths of $\pm 180^\circ$ (thick lines), $\pm 90^\circ$ (medium lines), and $\pm 45^\circ$ (thin lines). In Fig. 1C, the rate of IPM has been maintained at 1 Hz for all IPM depths. The consequence of this is that the velocity of motion was reduced with reducing depth. In Fig. 1D, the rate of IPM has been adjusted to maintain the same velocity for all IPM depths (720° s^{-1}). Finally, Fig. 1E illustrates the change in IPD over time for a 1-Hz binaural beat. Here the interaural phase shifts in a constant direction, determined by whichever ear receives the higher-frequency tone, and with constant velocity at a rate determined by the frequency difference, in this case 360° s^{-1} (see Yin and Kuwada 1983a, for a fuller description of binaural beats).

RESULTS

A total of 89 IC neurons was examined with IPM stimuli. For 39 the interaural phase was sinusoidally modulated, and for 50 the interaural phase was triangularly modulated. BFs ranged from 98 Hz to 1.16 kHz. Of the 89 neurons, 85 were examined at BF, and only 4 below BF. In these four cases, IPM using BF signals only poorly modulated the response, and a lower signal frequency was used.

Responses to partially overlapping IPMs

Figures 2 and 3 illustrate the range of responses that we observed in this study. Figure 2 shows responses of an IC neuron that was insensitive to the apparent-motion cues of IPM. Responses to the partially overlapping IPMs modulated around various center IPDs ($-60, 0, +60, +120, 180$ and -90°) at a rate of 2 Hz and at $\pm 45^\circ$ depth, in both the counterclockwise (Fig. 2A) and clockwise (Fig. 2B) directions, evoked similar responses at each IPD. Responses to the two directions of motion were virtually identical. Neurons insensi-

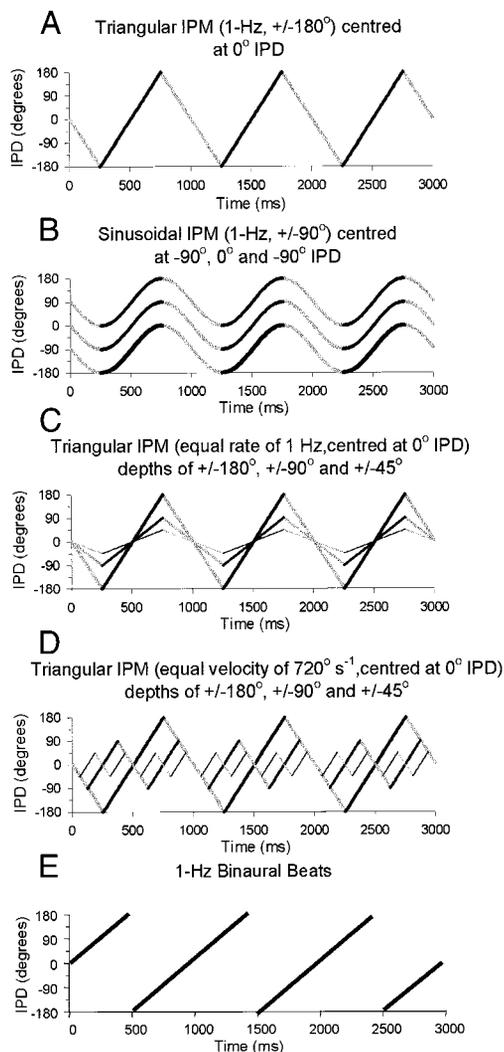


FIG. 1. Graphic representation of a range of different phase-modulated stimuli used in this study. *A*: triangular interaural phase modulation (IPM), in which the interaural phase is modulated linearly. The stimulus always started with a half-cycle in the clockwise direction (gray), before moving through 5 complete cycles of motion: 3 in the counterclockwise direction (black) and 2 in the clockwise direction, ending with a half cycle in the clockwise direction. The motion velocity was identical across all interaural phase disparities (IPDs). *B*: sinusoidal IPM for 3 different IPM centers ($+90^\circ$, 0° , and -90°). The IPM was modulated over $\pm 90^\circ$ at each center. Note that the slope of each function was not the same across all IPDs, but was reduced at IPDs close to the point at which the motion direction was reversed. *C*: triangular IPM for 3 different IPM depths ($\pm 180^\circ$, $\pm 90^\circ$, and $\pm 45^\circ$) at a rate of 1 Hz, and centered at 0° . As the depth of motion was reduced, the velocity of motion was also reduced. *D*: triangular IPM for 3 different IPM depths ($\pm 180^\circ$, $\pm 90^\circ$, and $\pm 45^\circ$) for which the IPM rate was 1, 2, and 4 Hz, respectively. The increase in IPM rate with decreasing IPM depth has the effect of maintaining a constant velocity across all IPM depths. *E*: binaural beats presented at a rate of 1 Hz.

tive to the motion cues were relatively rare in our study, as also reported by Spitzer and Semple (1993).

Figure 3 shows responses of an IC neuron to IPM, with many similarities to those reported by Spitzer and Semple (1993). Responses to partially overlapping IPMs for motion in both the counterclockwise (Fig. 3A) and clockwise directions (Fig. 3B) around center IPDs of IPDs of 0° , $+90^\circ$, 180° , and -90° (1 Hz IPM rate and $\pm 90^\circ$ depth) are clearly discontinuous, with very different discharges evoked by the same IPD. The discharge rate depends on the center IPD

around which the phase was modulated, and not simply the absolute IPD.

Responses to IPMs with different centers

The effect of altering center IPD on the responses to IPM is illustrated in Fig. 2, C–F, and Fig. 3, C–F. Changing the IPD around which the interaural phase is modulated changes the position or “locus” of the apparent motion. In both cases the IPM was modulated over $\pm 180^\circ$. In each case, the center IPDs were 0° (Figs. 2C and 3C), $+90^\circ$ (Fig. 2D), 180° (Fig. 2E) and -90° (Fig. 2F). In Fig. 2, C–F, altering the center IPD had no effect on the neuron’s response, and responses to counterclockwise (black lines) and clockwise motion (gray lines) were identical. In Fig. 3, C–F, the responses to the two directions of motion differed greatly at each center IPD. The neuron appears to be sensitive to the motion direction, with greatly differing response profiles depending on the center IPD. Of particular note is that this neuron was more responsive to clockwise motion when centered at 180° (Fig. 3E), whereas it was more responsive to counterclockwise motion for the other three centers (Fig. 3, C, D, and F).

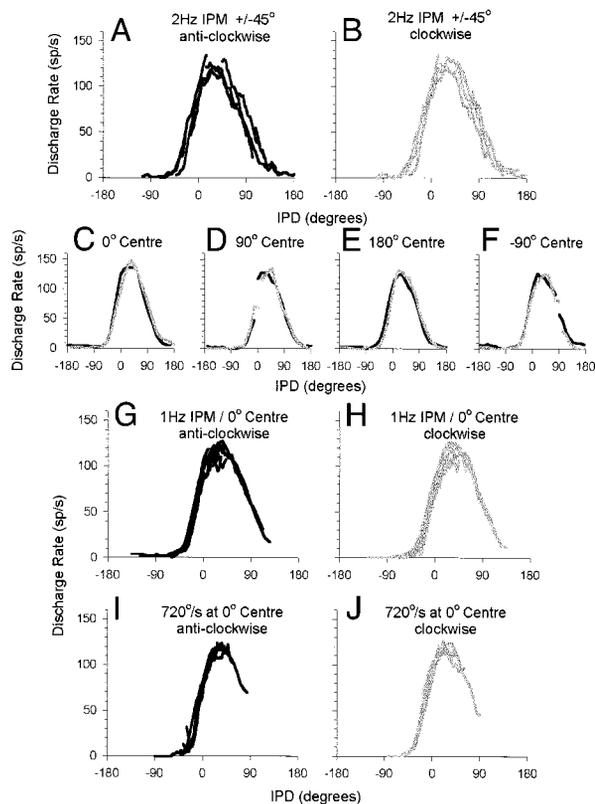


FIG. 2. Responses of an inferior colliculus (IC) neuron with a best frequency (BF) of 345 Hz that was insensitive to the motion cues of IPM. Overlapping responses to triangular 2-Hz IPMs over $\pm 45^\circ$ for counterclockwise (A) and clockwise motion (B). C and D: responses to counterclockwise (black) and clockwise (gray) motion for 1-Hz IPMs over $\pm 180^\circ$ and centered at 0° (C), $+90^\circ$ (D), 180° (E), and -90° (F). Responses to equal rate (1 Hz, centered at 0°) IPM at depths of $\pm 135^\circ$, $\pm 120^\circ$, $\pm 90^\circ$, $\pm 60^\circ$, $\pm 45^\circ$, $\pm 36^\circ$, and $\pm 30^\circ$ for counterclockwise (G) and clockwise (H). Responses to equal velocity IPMs ($720^\circ/\text{s}$ centered at 0°) at depths of $\pm 90^\circ$, $\pm 60^\circ$, $\pm 45^\circ$, $\pm 36^\circ$, and $\pm 30^\circ$ for counterclockwise (I) and clockwise (J) motion. See METHODS for further details of equal rate and equal velocity IPM stimuli.

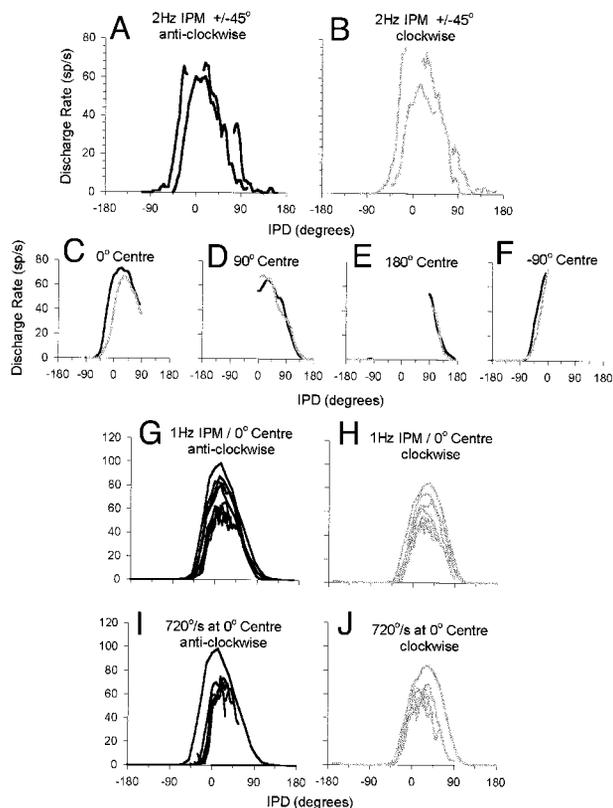


FIG. 3. Response of an IC neuron that was highly sensitive to the motion cues of IPM. The BF was 355 Hz, close to that of the neuron in Fig. 2. Overlapping responses to triangular 1-Hz IPMs over $\pm 135^\circ$ for counterclockwise (A) and clockwise (B) motion. C–F: responses to counterclockwise (black) and clockwise (gray) motion for 1-Hz IPMs over $\pm 180^\circ$ and centered at 0° (C), $+90^\circ$ (D), 180° (E), and -90° (F). Responses to equal rate (1-Hz, centered at 0°) IPM at depths of $\pm 180^\circ$, $\pm 135^\circ$, $\pm 120^\circ$, $\pm 90^\circ$, $\pm 60^\circ$, $\pm 45^\circ$, and $\pm 30^\circ$ for counterclockwise (G) and clockwise (H). Responses to equal velocity IPMs (720°/s centered at 0°) at depths of $\pm 180^\circ$, $\pm 90^\circ$, and $\pm 45^\circ$ for counterclockwise (I) and clockwise motion (J).

Responses to different depths of IPM

The effect of reducing the depth of IPM was examined for 52 neurons: 28 neurons using triangular IPM and 24 neurons using sinusoidal IPM. For triangular IPM, the two paradigms of Fig. 1, C and D, were used. First, IPM rate was kept constant as depth was reduced, so that the velocity was also reduced. Second, as depth was reduced, the IPM rate was increased to maintain equal velocity of motion. Generally, the effects observed were similar for equal rate and equal velocity stimuli, and this is illustrated in Fig. 2, G–J, and Fig. 3, G–J.

In Fig. 2, G and H, reducing the depth of IPM from $\pm 135^\circ$ to $\pm 30^\circ$ for a fixed IPM rate of 1 Hz had little effect on the discharge rate evoked at favorable IPDs by either counterclockwise (Fig. 2G) or clockwise (Fig. 2H) excursions. Similarly, when the IPM rate was increased to maintain equal velocity (Fig. 2, I and J), peak discharge rates were unaltered when the depth of IPM was reduced. For the other example in Fig. 3, G and H, reducing the depth of IPM for a fixed IPM rate of 1 Hz reduced maximum discharge rates at favorable IPDs. Similarly, reducing the depth of IPM while increasing the IPM rate to maintain a constant velocity (Fig. 3, I and J) also had the effect of reducing maximum discharge rates at favorable IPDs.

The only differences that were observed between equal IPM rate and equal velocity responses arose because as the IPM rate

was increased, the neuronal latencies constituted an increasing proportion of each cycle of IPM. As IPM rate increases, responses are plotted further into the IPM cycle. This was manifested as a slight shift in the response in the direction of the motion. This was commonly observed for all neurons for which responses to equal IPM rate and equal velocity stimuli were obtained and has been well described previously (e.g., Spitzer and Semple 1998).

Temporal order of the response underlies apparent sensitivity to IPM direction

We suggest that it is *response history* that determines sensitivity to IPM. Evidence for this hypothesis is provided in Fig. 4. Figure 4, A–D, shows peristimulus time histograms (PSTHs) of the response to 1-Hz IPM centered at 0° (Fig. 4A), 90° (Fig. 4B), 180° (Fig. 4C), and -90° (Fig. 4D). In each case, the PSTH shows the response to the complete 3 s of the IPM stimulus, modulated over $\pm 180^\circ$. There were 5 complete excursions of motion (i.e., a full 360° in one direction or the

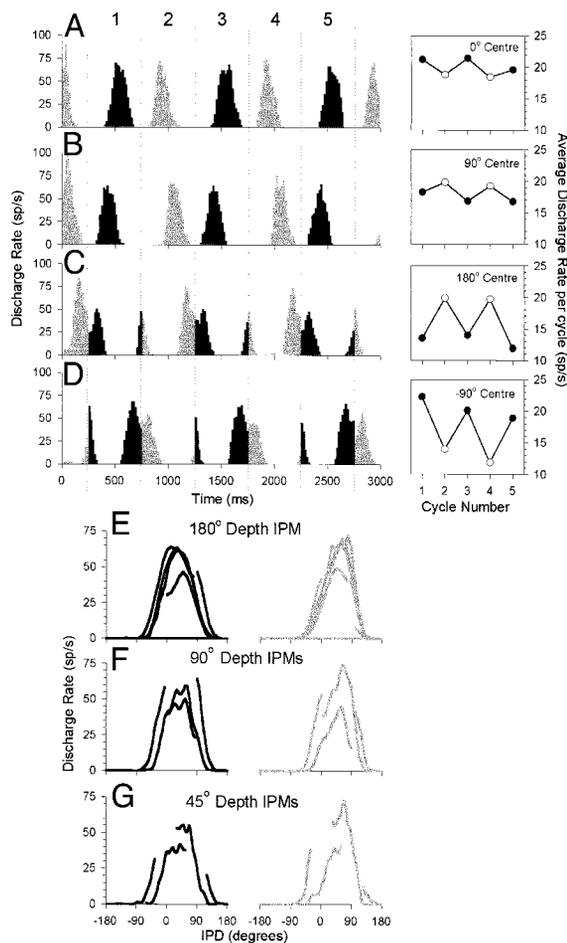


FIG. 4. A–D: peristimulus time histograms (PSTHs) of the response of an IC neuron with a BF of 250 Hz to $\pm 180^\circ$ IPMs at center IPDs of 0° (A), $+90^\circ$ (B), 180° (C), and -90° (D). Responses to counterclockwise motion are indicated in black, and responses to clockwise motion are indicated in gray. Right panels: average discharge rates over each of the motion excursions labeled 1 to 5 in the PSTHs. E–G: responses to IPM depicted as overlapping IPD functions of the responses to counterclockwise motion (left panels) and clockwise motion (right panels) for IPM depths of $\pm 180^\circ$ (E), $\pm 90^\circ$ (F), and $\pm 45^\circ$ (G).

other) over the 3 s of the stimulus as in Fig. 1A. The complete unidirectional motion excursions are labeled 1–5 in Fig. 4, A–D. Odd numbers (black) indicate counterclockwise excursions, whereas even numbers (gray) indicate clockwise excursions. The dotted vertical lines indicate the point at which the direction of motion reversed. It is evident from Fig. 4A that, for IPM centered at 0° , the response evoked by the clockwise excursion was preceded by a slightly shorter period during which no response was elicited than was the response evoked by the counterclockwise excursion. This is an inevitable consequence of the fact that IPD functions are asymmetrically placed around zero IPD, the center IPD used in Fig. 4A. The panel to the right of the PSTH in Fig. 4A plots the average discharge rate over each of the five complete cycles of motion. The average discharge rate varied systematically from cycle to cycle, interleaving relatively higher and relatively lower average discharge rates, with counterclockwise excursions always evoking higher discharge rates than clockwise excursions. The situation was reversed when the stimulus was centered at $+90^\circ$ (Fig. 4B). Here, the period of time preceding the response to each cycle of clockwise excursions (gray) was greater than that preceding the response to counterclockwise excursions (black). Accordingly, the interleaving of relatively higher and lower discharge rates from counterclockwise to clockwise excursions was opposite to that when the IPM stimulus was centered at 0° IPD. For IPM centered at 180° (Fig. 4C) and -90° (Fig. 4D), the asymmetry was greater than observed for centers of 0° and $+90^\circ$. For IPM centered at 180° (Figs. 4C), there was no time at all between the response to counterclockwise excursions and the response to clockwise excursions; the motion reversed direction immediately after passing through the neuron's most favorable range of IPDs. Here, the cycle-by-cycle variation in discharge rate was considerable. The situation was reversed again for IPM centered at -90° (Fig. 4D). Now, counterclockwise excursions were preceded by a longer period of time during which the neuron was not responding, whereas clockwise excursions were followed immediately after the response to counterclockwise excursions. The cycle-by-cycle variation in discharge rate was therefore opposite to that when IPM was centered at 180° . When the PSTHs are "folded" and displayed as IPD functions at different center IPDs (Fig. 4E, and Figs. 2 and 3), the effect is to produce discontinuous responses to partially overlapping IPMs: i.e., very different discharge rates for the same IPD values. However, we would argue that this folded display can be misleading because it obscures the response history evident in the full PSTH.

We calculated a "recovery time" as the time between the peak response evoked by counterclockwise motion to the peak response evoked by the clockwise excursion (i.e., from peak response in *cycle 2* to peak response in *cycle 3*, and from peak response in *cycle 4* to peak response in *cycle 5*, in each panel of Fig. 4A). We then plotted the ratio of the clockwise average discharge rate to the counterclockwise average discharge rate as a function of the recovery time. The dependence of the average discharge rate on recovery time is illustrated in Fig. 5. Figure 5A plots the relationship between the recovery time and the ratio of average discharge rates for four representative neurons. Figure 5A, *top left*, shows data from the neuron in Fig. 4. When the recovery time preceding the main response peak of clockwise responses was relatively long (Fig. 4, B and C), the ratio of the discharge rates was relatively high; i.e., more

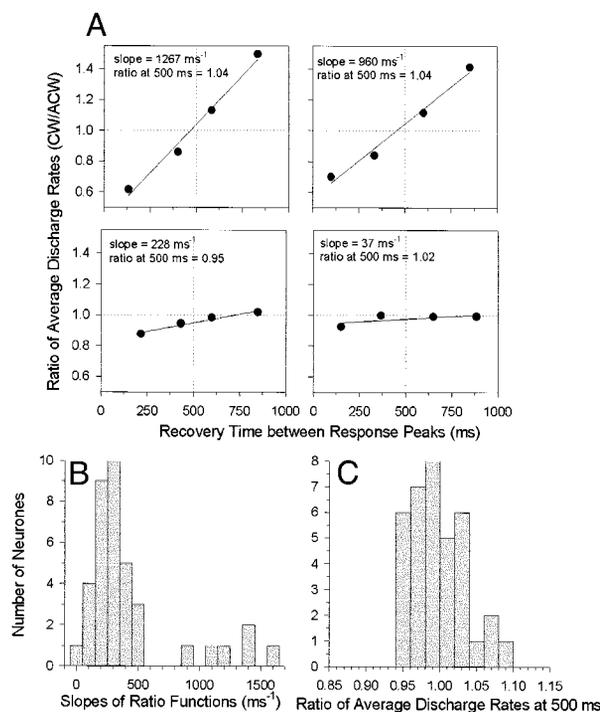


FIG. 5. A: plots of discharge rate ratios (clockwise vs. counterclockwise) as a function of recovery time for 4 IC neurons with BFs of 132, 155, 162, and 780 Hz, respectively. The data in the *top left panel* is from the neuron in Fig. 4. The intercept of the horizontal and vertical dotted lines indicates a ratio of 1.0 at 500 ms recovery time. B: distribution of slopes of functions ($n = 37$) relating discharge ratio to recovery time. The mean slope is 328 ms^{-1} . C: distribution of ratio of average discharge rates at 500 ms. The mean ratio at 500 ms was 0.98 ± 0.05 . See RESULTS for further details.

activity was evoked during clockwise excursions. However, when the recovery time preceding clockwise motion was relatively short (Fig. 4, A and D), the ratio of discharge rates was relatively low; i.e., more activity was evoked during counterclockwise excursions. The dependence of this neuron's response on the preceding recovery time is indicated by the steepness of the regression line fitted to the data points in Fig. 5A, *top left*, which is a measure of the magnitude of the adaptation in the neuron. Figure 5A, *bottom right*, comes from the neuron in Fig. 2, which appeared insensitive to the motion cues of IPM. Other neurons showed different slopes of their discharge ratio versus recovery time functions (e.g., remaining panels in Fig. 5A). Figure 5B plots the distribution of slopes of discharge ratio versus recovery times for the 37 neurons for which this analysis was performed. Apart from the few cells that show slopes $>1,000 \text{ ms}^{-1}$, the slopes are centered around a peak of $200\text{--}300 \text{ ms}^{-1}$.

If response adaptation is causing the asymmetry of responses, then equal recovery time between the responses to the two directions should give equal average discharge rates. In each of the panels in Fig. 5A, the intercept of the vertical and horizontal dotted lines indicates a ratio of 1.0 and an equal recovery time of 500 ms. In each case, the regression line fitted to the data points crossed the horizontal dotted line at a ratio very close to 1.0. The distribution of ratios of discharge rates at equal recovery time is plotted in Fig. 5C. For the 37 neurons for which this analysis was performed, the mean ratio at 500 ms was 0.98 ± 0.05 (mean \pm SE), indicating that equal recovery times between counterclockwise and clockwise ex-

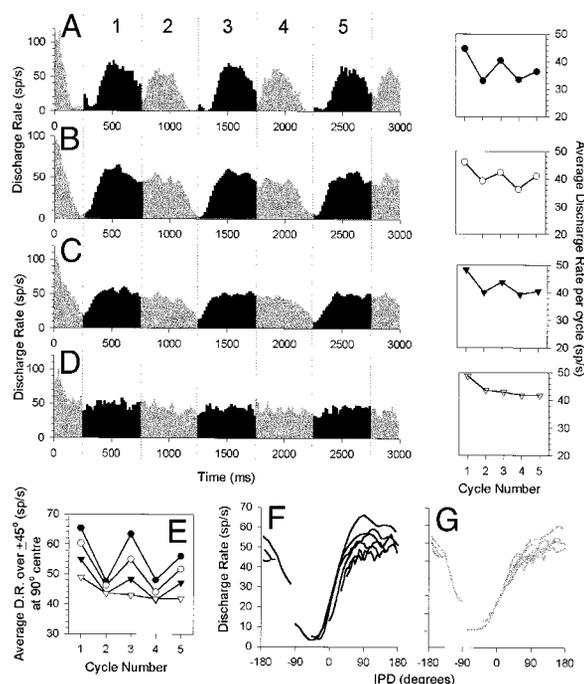


FIG. 6. *A–D*: PSTHs of the response of an IC neuron with a BF of 260 Hz to 1-Hz IPMs at a center IPD of $+90^\circ$ and depths of $\pm 180^\circ$ (*A*), $\pm 135^\circ$ (*B*), $\pm 90^\circ$ (*C*), and $\pm 45^\circ$ (*D*). Responses to counterclockwise motion are indicated in black, and responses to clockwise motion are indicated in gray. *Right panels*: average discharge rates over each of the motion excursions labeled 1 to 5 in the PSTHs. *E*: average discharge over the middle $\pm 45^\circ$ for each of the responses shown in *A–D*. *F* and *G*: response to different depths of IPM centered at $\pm 90^\circ$ for counterclockwise (*F*) and clockwise (*G*) motion.

cursions produces equal average discharge rates for the two directions of motion. This argues for a nonspecific adaptation rather than a direction-related motion mechanism. There was no difference between neurons examined using trapezoidal IPM (0.99 ± 0.06 , $n = 15$) and sinusoidal IPM (0.97 ± 0.03 , $n = 22$).

The effect of recovery time suggests that a process of adaptation is occurring when favorable IPDs are presented and the neuron is strongly activated. One would therefore predict that the longer the neuron spends within the range of favorable IPDs, the greater will be the reduction in peak discharge rates at those favorable IPDs, as the recovery time afforded between periods of strong activation evoked by IPM in either direction is reduced. This is indeed what was observed. Figure 6 shows the response of an IC neuron to counterclockwise and clockwise motion for different depth IPMs. The motion reversed direction from counterclockwise to clockwise in the middle of the range of favorable IPDs. As the IPM depth was reduced (Fig. 6, *A–D*), the stimulus was increasingly confined to the range of favorable IPDs. This reduced the recovery time, and the cycle-by-cycle variation in discharge rate (*panels to right of Fig. 6, A–D*) gradually diminished, so that for the $\pm 45^\circ$ IPM (Fig. 6*D*) it had disappeared completely. In Fig. 6*E*, the average discharge rate over IPDs in the range $\pm 45^\circ$ (centered at $+90^\circ$) is plotted for the four modulation depths examined in Fig. 6, *A–D*. Similar to the panel to the right of Fig. 6*A*, the average discharge rate over the range $\pm 45^\circ$ clearly alternated between higher and lower values when the IPM depth was $\pm 180^\circ$ (●). As the IPM depth was reduced to $+135^\circ$ (○) and $+90^\circ$ (▼), however, the difference between the average dis-

charge rate for the two directions was reduced until, for the $\pm 45^\circ$ IPM (▼), the cyclic pattern was no longer evident. Notice that the effect of reducing IPM depth was mainly to reduce the discharge rates of the counterclockwise excursions, clockwise excursions remained low at all depths (cf. Fig. 6, *F* and *G*). The likely reason for this is that clockwise motion always starts at a favorable IPD. Therefore the response is already adapted from the counterclockwise response ending at that favorable IPD.

Sensitivity to motion direction

The responses to counterclockwise (black) and clockwise (gray) motion for four representative IC neurons are compared in Fig. 7. In Fig. 7, *A–D*, responses are shown for IPM centered at two different IPDs, with the extent of the motion indicated by the arrows above each plot. For the example in Fig. 7*A*, clockwise motion centered at 0° evoked lower discharge rates than did counterclockwise motion, because counterclockwise motion was preceded by a period of recovery. Conversely, for motion centered at $+90^\circ$, counterclockwise motion centered at 0° evoked lower discharge rates than did clockwise motion; as for this IPM paradigm clockwise motion was preceded by a period of recovery. For all neurons we recorded, responses to motion *into* the range of favorable IPDs, reversing near the best IPD, evoked higher peak discharge rates than did the subsequent motion out of the neuron's range of favorable IPDs, which show the effects of adaptation. If the reversal, however, occurs at unfavorable IPDs, adaptation will be equivalent for the two directions, and no effects of motion direction are observed. This occurred irrespective of the direction in which the stimulus approached the favorable IPD range and is consistent with the response history effects that we have described thus far, and described by Spitzer and Semple (1993).

Sensitivity to the direction of motion was also manifest in the mean best interaural time differences (ITDs), calculated as the ITD equivalent of the mean best interaural phase at the IPM

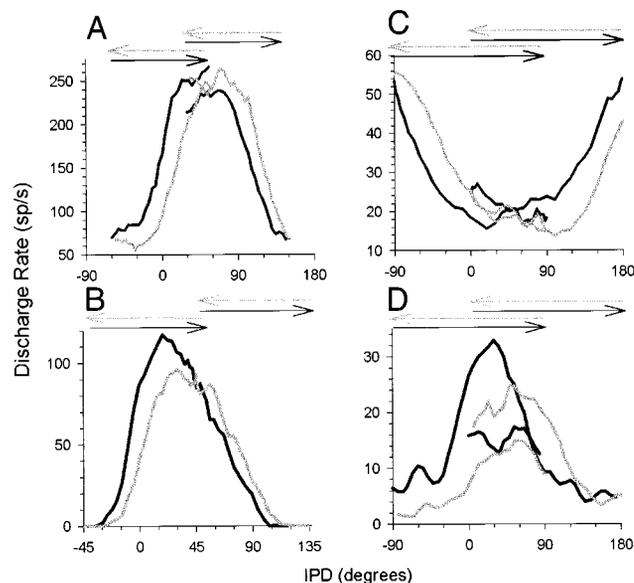


FIG. 7. *A–D*: responses of 4 IC neurons to counterclockwise (black lines) and clockwise (gray lines) motion produced by 1-Hz IPM and centered at either 0 or $+90^\circ$. IPM depths were $\pm 60^\circ$ in *A*, $\pm 45^\circ$ in *B*, and $\pm 90^\circ$ in *C* and *D*. BFs were 345, 243, 582, and 355 Hz, respectively.

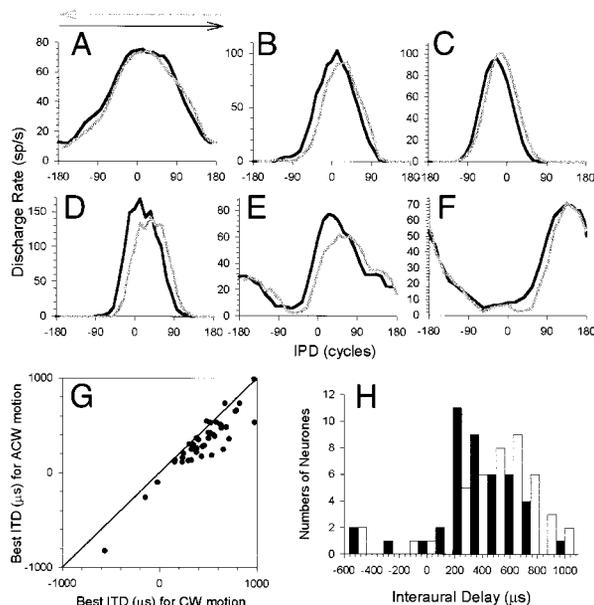


FIG. 8. *A–F*: responses to counterclockwise and clockwise motion modulated over $\pm 180^\circ$, and centered at 0° IPD. BF of the 6 neurons in *A–F* were 159, 98, 263, 144, 341, and 185 Hz, respectively. *G*: mean best interaural time difference (ITD) for clockwise motion plotted as a function of mean best ITD for 55 IC neurons computed from the response to counterclockwise and clockwise motion for $\pm 180^\circ$ IPMs centered at 0° IPD. The solid line has a slope of 1.0. *H*: distribution of mean best ITDs for the 55 neurons for counterclockwise (\blacksquare) and clockwise (\square) motion indicating that mean best ITDs are, relative to each other, skewed toward the direction from which the stimulus moves. The mean best ITD for counterclockwise motion was $+319 \pm 293 \mu$ s and $+448 \pm 284 \mu$ s for clockwise motion.

stimulus frequency, obtained in response to counterclockwise and clockwise motion. Figure 8, *A–F*, compares responses to counterclockwise and clockwise motion for six IC neurons, all for IPM modulated over $\pm 180^\circ$ and centered at 0° IPD. As we have shown above, for many neurons, responses to the two motion directions did not overlap completely. This was similarly the case for neurons with peak-type (Fig. 8, *A–E*) and trough-type (Fig. 8*F*) neurons. Figure 8*G* plots mean best ITDs for clockwise motion against those for counterclockwise motion for 55 IC neurons computed from the response to counterclockwise and clockwise motion for $\pm 180^\circ$ IPMs centered at 0° IPD. Relatively few neurons showed identical mean best ITDs to the two directions of motion, as evidenced from their departure from the line of equality in Fig. 8*G*. The distribution of mean best ITDs for these 55 neurons is shown in Fig. 8*H* and are skewed toward the direction from which the stimulus moves. For the counterclockwise motion, the mean of the best ITDs calculated for the 55 neurons was $+319 \mu$ s, whereas for the clockwise motion, the mean of the best ITDs calculated for the 55 neurons was $+448 \mu$ s. This cannot be attributed to the effects of latency described earlier, which would tend to shift the functions slightly in the same direction as the motion, i.e., in the opposite direction to that observed. Adaptation effects exceed any latency effects and may be underestimated.

Sensitivity to motion center correlates with sensitivity to motion depth

Those neurons that were most sensitive to changes in IPM depth were also those neurons that were most sensitive to

changes in the center IPD around which the interaural phase was modulated. This is quantified in Fig. 9*A*, which plots the *modulation depth index* as a function of the *modulation center index* for 27 neurons. The modulation depth index is a measure of how sensitive IC neurons were to changing the depth of IPM (the extent of apparent motion). It was calculated as the ratio of the peak discharge rate for $\pm 45^\circ$ motion to the peak discharge rate for $\pm 180^\circ$ motion at the center IPD closest to the neuron's most favorable IPDs. Neurons were included in this analysis only if the $\pm 45^\circ$ IPM moved through the range of favorable IPDs. The modulation center index is a measure of how sensitive IC neurons were to changing the center IPD. It was calculated as the ratio of the lowest peak discharge to the highest peak discharge rate evoked $\pm 180^\circ$ IPM measured at each of the four center IPDs, 0, $+90$, 180 , and -90° .

The 27 neurons each contribute 2 data points to Fig. 9*A*, one for counterclockwise motion (\bullet) and one for clockwise motion (\circ). It is clear from Fig. 9*A* that those neurons most sensitive to motion depth were also those neurons that were most sensitive to motion center. The regressions fitted to the counterclockwise and clockwise data had coefficients of 0.80 and 0.73, respectively.

It is possible that adaptation below the level of binaural integration might have contributed to the effects observed. Such effects, residing in monaural neurons/fibers only, would not be related to the IPM cycle but, rather, would be manifest as a reduction in activity over the entire duration of the IPM

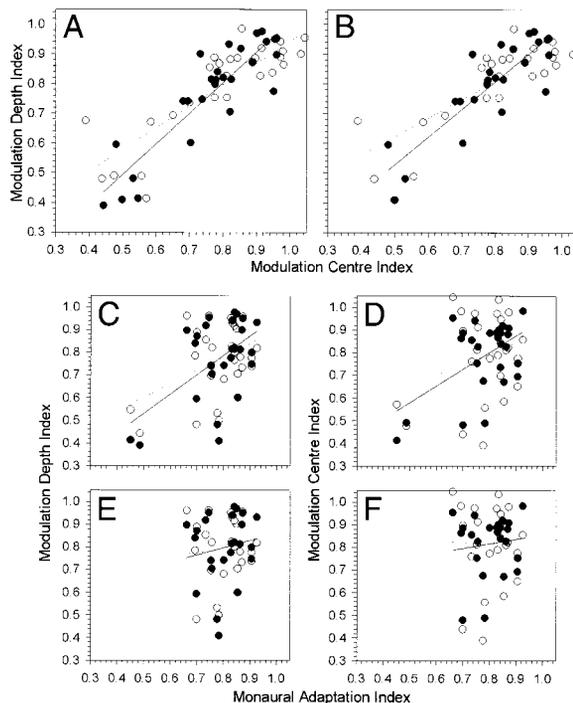


FIG. 9. *A*: plot of the *modulation depth index* as a function of the *modulation center index* for 27 neurons, for counterclockwise motion (\bullet) and clockwise motion (\circ). Regressions fitted to the counterclockwise and clockwise data had coefficients of 0.80 and 0.73, respectively. *B*: plot of the modulation depth index as a function of the modulation center index in which the neurons that showed greatest sensitivity to monaural adaptation effects have been removed from the analysis. *C* and *D*: comparison of the *monaural adaptation index* with the modulation depth index (*C*) and with the modulation center index (*D*). *E* and *F*: comparison of the monaural adaptation index with the modulation depth index in which the neurons that showed greatest sensitivity to monaural adaptation effects have been removed from the analysis.

stimulus. Spitzer and Semple (1993) discarded the first few seconds of the responses evoked by their 10-s long stimulus specifically to avoid the effects of such “monaural” adaptation. The effects that they observed, which are qualitatively similar to the effects reported in the present study, were unlikely to be contaminated with the effects of monaural adaptation. We only discarded the first and final 0.25 s of our 3-s stimulus, and it is possible that some responses may be subject also to monaural adaptation effects, but these should be equal for both motion directions.

However, to assess possible contributions of monaural adaptation, we compared the adaptation over the duration of the stimulus with the cycle-by-cycle variation in discharge rate. The discharge rate for the first full motion excursion was compared with the discharge rate over the final full motion excursion (i.e., a comparison of *cycles 1* and *5* of PSTHs, averaged across the 4 IPM centers of 0, +90, 180, and -90°, such as in Fig. 4). As all responses for which this analysis was performed were obtained using 1-Hz IPM; this involved comparing the discharge rate evoked from 250 to 750 ms of the 3,000-ms stimulus with the discharge rate evoked from 2,250 to 2,750 ms of the 3,000-ms stimulus. This ratio was termed the *monaural adaptation index*. The monaural adaptation index is compared with the modulation depth index in Fig. 9C, and with the modulation center index in Fig. 9D. Of the 27 neurons for which this analysis was performed, 2 showed large reductions (>50%) in discharge rate from *cycle 1* to *cycle 5* of motion. Both of these neurons also showed great sensitivity to the locus and depth of IPM (denoted by arrows in Fig. 9A). When these data points were removed from the analysis, there was insignificant correlation between the degree to which neurons showed adaptation over the duration of the IPM stimulus and the degree to which they were sensitive to changing the depth or the center of motion (Fig. 9, *E* and *F*, respectively). However, in the absence of these data points, correlation coefficients for the variation of modulation depth index with modulation center index were reduced only slightly to 0.73 and 0.70, respectively, for counterclockwise and clockwise motion (Fig. 9B). This suggests that there is no significant relationship between the cycle-by-cycle variation in the response observed, and any decline in activity over the 3,000-ms time course of the IPM stimulus that might be attributed to adaptation mechanisms below the level of binaural integration.

DISCUSSION

The major finding of this study is that the sensitivity of IC neurons to the apparent-motion cues contained in IPM can be explained in terms of adaptation-of-excitation. We have replicated, qualitatively at least, the effects reported by Spitzer and Semple (1993), both for triangular IPM and for sinusoidal IPM. Spitzer and Semple concluded that the responses they observed were a result of the stimulus history. However, it is clear from our analyses that presenting data in the form of partially overlapping IPD functions as Spitzer and Semple did, and as we do in Figs. 2–4, 6, and 7, obscures the response history at any particular IPD. Responses of IC neurons to IPM stimuli depend not on the history of stimulation, per se, but on the history of their response to stimulation, irrespective of the specific motion cues that evoke those responses. When PSTHs of IC neurons were examined for a range of different IPM

center loci, it was the temporal pattern of the response to IPM, and not the motion cues contained in the IPM, that determined sensitivity to features such as motion depth, direction, and center locus. When any cycle of IPM contained motion that was restricted to the most favorable IPDs only, discharge rates were lower than when the stimulus moved through the responsive area from outside, or moved up and down the flanks of IPD functions only. This occurred irrespective of the motion configuration produced by different IPMs. It was *always* the case that whenever motion in the two directions over the same IPDs evoked different responses, the response to the motion moving away from a peak of activity was lower than the response to the direction moving into the peak of activity. When the reversal point was closer to the most favorable IPDs, the response to the opposite direction of motion was lower. This occurred irrespective of whether the motion through the favorable IPDs was first counterclockwise or clockwise. Motion that was restricted to the flanks of IPD functions only, or motion that was restricted to the most favorable IPDs only, showed much less effect of motion direction and often showed responses that overlapped completely. In no case did we find any evidence for neurons that preferred one direction of motion to the other, or that showed differences in their response to a wide variety of IPM center loci, depths, rates, or directions that were not consistent with an adaptation-of-excitation mechanism.

Altered binaural code in the IC?

The degree to which the representation of binaural signals is altered at subsequent levels of the auditory system remains controversial. Early studies of responses to interaural time delays, both in the IC and in primary auditory cortex, generally indicated that responses were consistent with the output of the simple coincidence detectors at the superior olivary complex (SOC) (e.g., Kuwada et al. 1984; Reale and Brugge 1990; Rose et al. 1966; Yin and Kuwada 1983b; Yin et al. 1986, 1987). However, even in these studies there were indications of further complications in the way that the IC responded to interaural delays. The simple coincidence detector model predicts that plots of mean best phase as a function of stimulating frequency (phase plots) are linear and intersect the frequency origin at zero or ± 0.5 cycles of phase (corresponding to the peak or trough of the IPD function, respectively). Cells in the IC, however, often had phase plots that were nonlinear and intersected the ordinate at values between 0 and ± 0.5 . Evidence for one explanation for this behavior comes from a recent study by McAlpine et al. (1998), which demonstrated that neurons with intermediate-type and/or nonlinear phase plots were likely the consequence of convergent input from simple coincidence detectors in the brain stem.

Furthermore, Spitzer and Semple (1993), and the data in this paper, have convincingly demonstrated that the response to dynamically varying interaural phase differences in the IC may be quite different, depending on the context in which the stimulus is presented. These data are inconsistent with the simple Jeffress model of coincidence detection and appear to differ from principal cells in the MSO, which are insensitive to the motion cues of IPM (Spitzer and Semple 1998). Although they found a small number of neurons in the region of the superior olive that were sensitive to motion cues, they inferred

that they were responses from descending neurons and not MSO or lateral superior olive (LSO) principal neurons. The basis for this was that these neurons did not show monaural phase-locking, were clustered in regions where known descending inputs from the IC terminate in rodents, and had long latencies. This suggests that the mechanism responsible for such sensitivity is first encountered above the level of the brain stem.

Finally, there is the issue of the small number of IC neurons sensitive to the direction and/or velocity of binaural beats, as reported by Yin and Kuwada (1983b). Although such neurons showed a preferred direction and/or rate of binaural beats, they did so over velocities in the range 360° to $3,600^\circ \text{ s}^{-1}$, which are undoubtedly at the upper limits and outside that of physically encountered motion. Nevertheless, the fact that such neurons were found requires explanation, and Yin and Kuwada's inclusion into a coincidence detection model of a presynaptic inhibitory collateral from one side gating the input from the other side may account for this phenomenon. However, as we discuss below, it remains the case that for our data, and for our interpretation of Spitzer and Semple's (1993) data, a mechanism of adaptation-of-excitation appears sufficient.

Mechanism of adaptation-of-excitation in the IC?

Spitzer and Semple (1993, 1998) suggested that one possible explanation for the effects that they observed was the presence of binaural inhibitory inputs onto IC neurons, possibly from the dorsal nucleus of lateral lemniscus, or via local circuits in the IC itself. IC neurons receive many more binaural and monaural inputs than do SOC neurons, with a proportion of them characterized as binaural and inhibitory (Adams and Mugnaini 1984; Roberts and Ribak 1987). However, as we have demonstrated above, the incorporation of inhibitory inputs is not a necessary requirement for the data we observed, all of which may be explained by the adaptation-of-excitation hypothesis.

It is undoubtedly the case that monaural adaptation-of-excitation was present in the responses of the neurons reported here. The general reduction in discharge rate over the 3,000-ms duration of the IPM stimulus suggests that the responses of auditory nerve fibers and/or the bushy cell outputs to the binaural neurons in the lower brain stem adapted to the monaural stimulus presented to each ear. However, such adaptation cannot account for the cycle-by-cycle variation in discharge rate observed in the vast majority of IC neurons, because this cycle-by-cycle variation indicates a change in discharge rate that depends on binaural stimulation. If this variation is attributable to an adaptation mechanism, then it must occur at the level of the MSO or higher, where responses depend on IPD. We have termed this putative mechanism "binaural adaptation." Our use of this term, however, should not be confused with the use of the same term by Hafer (e.g., Hafer 1997). Hafer describes as binaural adaptation the reduction in the amount of binaural information derived from successive portions of a signal with increasing signal duration. In his studies, this appears to derive from processes occurring in monaural channels before binaural integration. Conversely, our data, and the circumstantial evidence of differences between the SOC and IC described by Spitzer and Semple (1993, 1998), suggest

that whatever contributes to sensitivity to the apparent-motion cues of IPM must occur subsequent to primary binaural integration in the SOC. As such, our use of the term binaural adaptation appears entirely appropriate.

A recent model of binaural processing in the IC (Cai et al. 1998a,b) adds weight to our proposal that the mechanism responsible for sensitivity to the motion cues of IPM is one of adaptation-of-excitation. In the first of these papers (Cai et al. 1998a), the authors were able to simulate many of the binaural phenomena reported in various physiological studies of the IC. This included sensitivity to static ITDs (Kuwada and Yin 1983; Kuwada et al. 1984; Yin and Kuwada 1983a,b), binaural beats (Yin and Kuwada 1983a), binaural clicks (Carney and Yin 1989), and pairs of binaural clicks (Fitzpatrick et al. 1995; Litovsky and Yin 1998a,b). However, the model was unable to simulate the responses to IPM stimulus reported by Spitzer and Semple (1993). Subsequently, in a second paper (Cai et al. 1998b), the authors demonstrated that the addition of an adaptation mechanism, specifically a calcium-activated, voltage-independent potassium channel responsible for afterhyperpolarization, enabled their model to simulate sensitivity to IPM stimuli. They suggested that such a mechanism, which they modeled with a 500-ms time constant, could account for the results of Spitzer and Semple (1993) in the IC. Interestingly, the presence of strong delay-sensitive inhibition resulted in the modeled neurons showing less sensitivity to the apparent motion cues of IPM. Cai et al.'s suggested reason for this was that the reduction in discharge rate brought about by the inhibition reduced the amount of adaptation-of-excitation experienced by the neuron and, hence, the extent to which its response was influenced by apparent-motion cues. Thus contrary to the conclusion reached by Spitzer and Semple (1993, 1998), the less inhibition, the greater the sensitivity to the apparent motion cues of IPM. Cai et al.'s (1998b) suggestion that the sensitivity to IPM may be explained by an afterhyperpolarization current residing at the level of the IC appears to be the simplest explanation for both our data and those of Spitzer and Semple (1993).

Nevertheless, our interpretation does not exclude other, possibly inhibitory, mechanisms that might contribute to the apparent sensitivity to IPM cues observed by Spitzer and Semple (1993) and in the present study. Sanes et al. (1998) have recently demonstrated, using dynamically varying interaural level differences, responses of IC neurons that appear to require long-lasting inhibitory mechanisms to provide an adequate explanation for their sensitivity to apparent motion stimuli. In addition, free-field motion studies in the barn owl IC (Wagner and Takahashi 1992) appear to indicate some form of sensitivity to apparent motion, and which may be dependent on binaural inhibition, although motion-sensitive cells appeared to be confined to external nucleus of the IC and the tectum. However, whether any of these observations indicate unequivocally the existence of specialized motion detectors is open to debate. Further studies are required to resolve the issue of how moving sound sources are encoded in the auditory system.

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