Sensitivity to Interaural Temporal Disparities of Low- and High-Frequency Neurons in the Superior Olivary Complex. II. Coincidence Detection

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Batra, Ranjan, Shigeyuki Kuwada, and Douglas C. Fitzpatrick. Sensitivity to interaural temporal disparities of low- and high-frequency neurons in the superior olivary complex. II. Coincidence detection. J. Neurophysiol. 78: 1237–1247, 1997. In the companion paper we demonstrated that neurons in the superior olivary complex that were sensitive to interaural temporal disparities (ITDs) could be divided into two broad categories: peak type and trough type. Within these broad categories, many neurons exhibited various types of irregularities in their responses. In the present paper we devise three criteria to determine whether all types of neurons act as coincidence detectors. Each criterion relies on a comparison between the synchrony of the responses to the waveforms at either ear and the “interaural synchrony,” i.e., the response to a cyclically varying ITD. First, a neuron should exhibit synchrony to both the ipsilateral and contralateral waveforms over the entire range to which it is sensitive to ITDs. Second, the ITD that elicits maximal discharge should be equal to the delay required to bring the ipsilateral and contralateral waveforms into coincidence. Third, the strength of interaural synchrony should be predicted by the strengths of synchrony to the waveforms at either ear. We found that most neurons of all types in the superior olivary complex met these criteria. Thus coincidence detection is a basic operating principle for all forms of ITD sensitivity.

INTRODUCTION

In the companion paper (Batra et al. 1997) we demonstrated that there were neurons in the superior olivary complex (SOC) that were sensitive to interaural temporal disparities (ITDs) in the fine structure of low-frequency sounds and other neurons sensitive to ITDs in the envelopes of high-frequency sounds. Both kinds of neurons fell into two broad categories: peak type and trough type. Peak-type neurons discharged maximally at a particular ITD at all frequencies. Trough-type neurons, on the other hand, discharged minimally at a particular ITD. Within these broad categories, many neurons exhibited irregularities in their responses in that they showed variability in their ITD tuning across frequencies.

The ITD sensitivity of peak-type neurons is believed to be the result of excitatory inputs that are synchronized to the waveforms of the sounds at each ear (Goldberg and Brown 1969; Jeffress 1948; Yin and Chan 1990). Arrival of the signals from the two ears within a narrow time interval of one another produces maximal excitation. In this way, peak-type neurons act as “coincidence detectors.” The mechanism for trough-type neurons differs from that for peak-type neurons, because trough-type neurons most likely receive predominantly excitatory inputs from one ear and inhibitory inputs from the other (Batra et al. 1997; Joris 1996; Yin and Kuwada 1983). It is possible that these neurons are also coincidence detectors but that maximal suppression is produced by arrival of inputs from the two sides within a narrow time interval. Neurons with irregular responses may receive multiple types of phase-locked inputs from each side. Are these neurons coincidence detectors in that they detect inputs from either side arriving within a narrow time interval? Alternatively, is it possible these neurons are higher-order binaural neurons, i.e., neurons that inherit their ITD sensitivity from other ITD-sensitive neurons?

Previous studies have examined whether or not neurons in the SOC are coincidence detectors (Goldberg and Brown 1969; Joris 1996; Spitzer and Semple 1995; Yin and Chan 1990). The tests for coincidence included examining the presence of synchrony to the stimuli at either ear and comparing the phase of synchrony to the stimuli at the two ears with the ITD that evoked maximal discharge. The results indicated that although many of the neurons in the SOC are coincidence detectors, there are some that are higher-order binaural neurons. However, no studies have specifically examined the coincidence mechanism in low-frequency trough-type neurons or neurons with irregular responses.

In the present paper we define three criteria to be met before a neuron can be considered a coincidence detector and demonstrate that most neurons in the SOC meet these criteria.

METHODS

The methods for surgery, recording, and acoustic stimulation have already been described in the companion paper (Batra et al. 1997). Here we describe only the procedures used for analysis of the data.

In the following, we use “waveform” to refer to either the cyclic pressure variations of a pure low-frequency tone or to the sinusoidally modulated envelope of a high-frequency tone. We assessed the degree to which a unit in the SOC acted as a coincidence detector by examining the relationship between the way in which it encoded temporal information about the waveform at either ear and the way in which it encoded ITDs. Directly assessing the encoding of monaural information proved difficult in many neurons because of their weak responses to monaural stimulation. For this reason we assessed the preferred phase and strength of synchrony of the response to monaural stimulation from the response to a binaural-beat stimulus. A binaural-beat stimulus con-
sists of tones to the two ears that differ slightly in frequency (1 Hz in our experiments), or, for testing high-frequency neurons, sinusoidally amplitude-modulated (SAM) tones to the two ears that have the same carrier frequency but modulation frequencies that differ slightly (1 Hz) (Batra et al. 1993; Kuwada et al. 1979; Yin et al. 1984). Neurons sensitive to ITDs respond to this stimulus with a discharge pattern that is synchronized to the beat or difference frequency. Moreover, the responses can be synchronized not only to the difference frequency (1 Hz) but to the frequencies (or modulation frequencies) of the tones at either ear. Such synchrony can be observed by calculating period histograms of the response to the binaural-beat stimulus on the basis of the period (or modulation aural stimulation (can be observed by calculating period histograms of the response to synchronization coefficients based on the responses to monaural stimulation) in four neurons. The neurons of Fig. 1, that have the same carrier frequency but modulation frequencies of units is shown in Fig. 2 for low-frequency peak- and trough-type units (● and ○, respectively) and for high-frequency peak- and trough-type units (▲ and △, respectively). In general, the agreement for both measures was good. On average, the mean phases extracted from both kinds of stimuli differed from analysis to avoid transient effects. A brief period was also a slight overall tendency for synchrony to be somewhat worse during the binaural-beat stimulus than during monaural stimulation.

**RESULTS**

The results presented here are based on the responses of the same peak-type and trough-type units as the companion paper (Batra et al. 1997).

**Comparison of synchrony with the use of monaural and binaural stimulation**

We first examined whether synchrony to the ipsilateral and contralateral waveforms measured in response to the binaural-beat stimulus was similar to that measured in response to monaural stimulation alone. This comparison was possible when responses to monaural stimulation were available (ipsilateral n = 57 units, contralateral n = 50 units). Figure 1 compares period histograms of synchrony to the ipsilateral (left) and contralateral (middle) waveforms during binaural-beat stimuli (curves) and during monaural stimulation (histograms) in four neurons. The neurons of Fig. 1, A and B, were low-frequency peak- and trough-type neurons, respectively, and the neurons of Fig. 1, C and D, were high-frequency peak- and trough-type neurons. In each case, the form of the period histogram based on the response to the binaural-beat stimulus was similar to that based on the response to monaural stimulation alone. The mean phases and synchronization coefficients based on the responses to monaural stimulation (left, number of pairs) and to the binaural-beat stimulus (right, number of pairs) were also similar. All four neurons were sensitive to ITDs, as demonstrated by significant synchrony to the beat frequency as shown in their interaural period histograms (right).

A comparison between the mean phases and synchronization coefficients extracted from both kinds of stimuli for our sample of units is shown in Fig. 2 for low-frequency peak- and trough-type units (● and ○, respectively) and for high-frequency peak- and trough-type units (▲ and △, respectively). Agreement between the synchronization coefficients was slightly poorer, especially for contralateral stimulation of trough-type units (Fig. 2D). There was also a slight overall tendency for synchrony to be somewhat worse during the binaural-beat stimulus than during monaural stimulation.

Note that synchrony to contralateral stimulation could be measured for several trough-type units in response to monaural stimulation, even though most of these were inhibited by contralateral stimulation or showed no change in firing rate at all (Fig. 7 of Batra et al. 1997). It appears that this was because stimulation modulated the spontaneous activity that was often present.
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P < 0.001) (Mardia 1972). Synchrony to the tones at either ear (middle and right) was present over a wider range (A–G, ipsilateral; B–F, contralateral).

A test of our full sample of units is shown in Fig. 4. In Fig. 4, A and B, we compare the lowest frequency (or modulation frequency) at which a unit was sensitive to ITDs with the lowest frequency (or modulation frequency) at which it synchronized to the ipsilateral (A) and contralateral (B) waveforms. For nearly all units, synchrony to the waveform extended to frequencies at least as low as those at which ITD sensitivity was present (ipsilateral, 66 of 72; contralateral, 65 of 73).

Synchrony to the waveforms also extended to the highest frequencies at which ITD sensitivity was present (ipsilateral, Fig. 4C; contralateral, Fig. 4D). Synchrony to the ipsilateral

**Relationship between sensitivity to ITDs and synchrony to the waveform**

We established three criteria for a unit to be considered a coincidence detector. All three criteria relied on comparisons between the interaural synchrony of the response and synchrony to the waveforms at either ear during a binaural-beat stimulus. When applied to trough-type units, some of the procedures actually tested for anticoincidence, or the point in time at which the inputs to the unit are 180° out of phase. However, coincidence and anticoincidence are two facets of the same phenomenon, so the procedures are still valid.

**CRITERION 1.** The first criterion was that the neuron synchronize to both the ipsilateral and contralateral waveforms at all frequencies at which it was sensitive to ITDs, because such synchrony is necessary for the generation of ITD sensitivity. Responses of a low-frequency neuron that met this criterion are shown in Fig. 3. The interaural period histograms (left) demonstrate that this unit was sensitive to ITDs from 250 to 550 Hz (B–E; Rayleigh test of uniformity, 60/63 dB SPL.)
were excluded for this reason. All those included were sensitive to ITDs (Fig. 6, highest frequency at which synchrony to the waveform was observed with (as extracted from the response to the binaural-beat stimu-

that sensitivity to ITDs arises from the coincident arrival of coincidence occurred. This prediction was based on the notion and contralateral sides should predict the ITD at which coin-

in the times required for signals to travel from the ipsilateral and contralateral waveforms usually occurred to the same and contralateral waveforms into coincidence. Examples that illustrate this relationship are shown in Fig. 1. For the low-frequency peak-type neuron in Fig. 1A, the difference between the ipsilateral and contralateral phase estimates was ~0.1 cycles, which matched the interaural phase difference that evoked the maximal response. The relationship also held for the high-frequency peak-type neuron (Fig. 1C), as well as for the low- and high-frequency trough-type neurons (Fig. 1, B and D).

Figure 5 examines this relationship for our sample of neu-

rons. The actual interaural phase difference is the mean inter-

aural phase of the response to the binaural-beat stimulus. The predicted interaural phase difference is the difference between the phases of synchronization to the ipsilateral and contralateral components of the binaural-beat stimulus. Agreement between the actual and predicted interaural phase differences is excellent for all types of units (r > 0.98 for all 4 types), with the data points lying close to the line of equality (- - -).

For trough-type units, the above procedure really tested anticoincidence. This is because trough-type units respond minimally at coincidence and the procedure evaluates the relationship at the ITD at which the response is maximal. A mathematically equivalent approach is to measure the times required for signals to arrive at a unit from the two ears with the use of the slopes of the phase-versus-frequency plots and to use these times to predict the unit’s characteristic delay (CD). The CD is a measure of the ITD at which coincidence occurs (Kuwada et al. 1987; Rose et al. 1966; Yin and Kuwada 1983). Figure 6 illustrates the monaural phase plots (as extracted from the response to the binaural-beat stimu-

lus) for four neurons: a low-frequency peak- and a low-frequency trough-type neuron (Fig. 6, A and B) and a high-

frequency peak- and a high-frequency trough-type neuron (Fig. 6, C and D) (for interaural phase plots of these units,
These delays were similar for each unit, i.e., they fell near the line of equality, the delays of different units varied widely, ranging from \( \sim 3.5 - 8 \) ms. This suggests that units in the SOC receive a wide range of delays from either side but that for a given neuron the two delays are closely matched.

**Criterion III.** The third criterion involved the relationship between the width of ITD tuning of a unit and how tightly it synchronized to the ipsilateral and contralateral stimuli. The idea behind this criterion is diagrammed for a peak-type neuron in Fig. 8. In this schematic, the ITD and time are measured in stimulus cycles. Figure 8A schematizes two trains of action potentials arriving at the neuron, one from each side. Each train represents two cycles of input, with three action potentials per cycle for each input. To simplify the argument, the action potentials have been evenly spaced.

![Figure 6](image1.png)  
*Fig. 6.* Phases of synchronization to the waveform for 4 neurons. A and B: low-frequency peak- and trough-type neurons. C and D: high-frequency peak- and trough-type neurons. All phases were measured during stimulation with binaural-beat stimuli, \( \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot 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at intervals of 0.1 cycles. For this neuron, the path lengths from the two sides differ, so that when tones are delivered simultaneously to the two ears (ITD = 0 cycles) the action potentials do not arrive simultaneously (Fig. 8A, top). As the ITD is varied, the times at which the action potentials from the two sides arrive begin to overlap (ITD = 0.1 cycles). The binaural neuron detects the simultaneous arrival of action potentials from the two sides and in turn fires an action potential. As the overlap increases (ITD = 0.2 and 0.3 cycles), the binaural neuron fires more action potentials. Further change in the ITD decreases the overlap, reducing the number of action potentials produced by the binaural neuron (ITD = 0.4–0.6 cycles). Note that the response of the binaural neuron is spread over a wider range of ITDs (0.4 cycles) than synchrony of the inputs to the monaural stimuli is spread over time (0.2 cycles).

This relationship means that the synchronization coefficient (r) to the monaural stimuli must be stronger than the interaural synchronization coefficient, as shown in the period histograms of Fig. 8B. Assuming the period histograms roughly follow a wrapped normal distribution, the synchronization coefficient for the interaural phase histogram should equal the product of those for the monaural phase histograms (Mardia 1972), because coincidence detection is essentially a process of convolution. This is analogous to the result that convolving two normal distributions produces another normal distribution with a width that is equal to the root mean square of the widths of the constituent distributions. For the hypothetical neuron illustrated here, the synchronization coefficients do indeed obey this relationship (0.87 × 0.87 = 0.76).

Note that, for simplicity, the above arguments have been made with the use of the inputs and outputs of a peak-type neuron. However, the binaural integration really occurs across the postsynaptic potentials produced by the inputs, and therefore the relationship applies to trough-type neurons as well.

Examples of tests of this quantitative relationship are shown for four neurons in Fig. 9. This figure compares the synchronization coefficient to the ipsilateral and contralateral stimuli with the interaural synchronization coefficient as a function of frequency for a low-frequency peak- and a low-frequency trough-type neuron (A and B) or as a function of modulation frequency for a high-frequency peak- and a high-frequency trough-type neuron (C and D). Open symbols mark where synchrony was statistically significant (P < 0.001, Rayleigh test of uniformity) (Mardia 1972). For all four neurons, synchrony to the beat (C) was less than that to the ipsilateral (Δ) and contralateral (▽) waveforms. The solid line connects the product of the ipsilateral and contralateral synchronization coefficients. Thus for these neurons the quantitative relationship appears to hold.

An evaluation of our full sample of neurons is shown in Fig. 10. Each point represents one unit at the frequency at which it synchronized best to the beat frequency. The synchrony of most units to the monaural waveforms was stronger than to the beat (Fig. 10, A and B).

Figure 10C shows the relationship between the measured interaural synchronization coefficient and that predicted from the product of the synchronization coefficients to the ipsilateral and contralateral waveforms. The measured synchronizing coefficient and the product were nearly equal for most units (peak type, 39 of 58; trough type, 44 of 58) in that they lay within 20% of one another. Units that had irregularities in their interaural phase plots did not show greater deviation from equality than other units.

Units that deviated by >20% tended to have weak interaural synchrony. Despite this, the interaural synchronization coefficients of most deviant units was greater than predicted (i.e., lay below the line of equality). Most units that deviated from the relationship in this direction were low frequency (23 of 24) and of the peak type (low frequency, 15 of 23; high frequency, 1 of 1). In contrast, all units that deviated in the other direction (i.e., lay above the line) were high frequency (peak type, 3; trough type, 6). The deviations in this direction were smaller.

**Comparison of ipsilateral and contralateral synchrony**

Peak-type and trough-type units differed in their relative synchrony to the ipsilateral and contralateral waveforms. Trough-type units (Fig. 11B) synchronized more strongly to the ipsilateral waveform. In contrast, peak-type units were equally likely to synchronize more strongly to the ipsilateral or to the contralateral waveform (Fig. 11A).

To further compare the synchrony of peak-type and trough-type units, we constructed average functions describing synchrony to the ipsilateral and contralateral waveforms as a function of frequency for low-frequency peak-type and trough-type units (Fig. 11C). The strongest synchrony at all frequencies was seen in trough-type units to ipsilateral tones.
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FIG. 10. Comparison between strength of interaural synchrony and strengths of synchrony to the waveforms at either ear for all units. A and B: strength of interaural synchrony compared with strengths of ipsilateral and contralateral synchrony. C: product of ipsilateral and contralateral synchrony compared with interaural synchrony. Selection of responses and number of units as for Fig. 5. Dashed lines: equality.

(△). The average synchrony of peak-type units to ipsilateral (▲) and to contralateral (●) tones was similar. Average synchrony of trough-type units to contralateral tones (○) was similar to that of peak-type units at intermediate frequencies, but weaker at low and high frequencies.

If ipsilateral synchrony is stronger in trough-type units, then interaural synchrony should also be stronger at the intermediate frequencies where contralateral synchrony is not weak. Figure 11D compares average functions for synchronization to the beat for peak-type and trough-type units. At intermediate frequencies, interaural synchrony was indeed stronger for trough-type units.

**DISCUSSION**

Our recordings show that most peak-type and trough-type units in the SOC met three criteria for acting as coincidence detectors in generating a sensitivity to ITDs. First, they were synchronized to the monaural waveforms at essentially all frequencies at which they were sensitive to ITDs. Second, the ITD that elicited maximal discharge was equal to the difference in time of arrival of the input signals. Third, the interval of ITDs over which a unit responded was predicted by convolution of the inputs, i.e., the interaural synchronization coefficient was equal to the product of the synchronization coefficients for the ipsilateral and contralateral waveforms.

In the following, we first discuss the validity of the synchronization measurements derived from binaural stimuli. We then consider each of the criteria in turn.

**Validity of synchronization measurements obtained with the use of the binaural-beat stimulus**

Assessing synchrony with the use of a binaural-beat stimulus had advantages over using monaural stimuli. A binaural-beat stimulus often elicited a stronger response than did monaural stimuli, allowing more robust measurement of the synchronization. In addition, many neurons did not respond to monaural stimulation of one or both ears or were inhibited, so without the binaural-beat stimulus the analyses would have been impossible.

We have demonstrated that measurements of the phase and strength of synchronization were similar when a sound was presented monaurally and when it was part of a binaural-beat stimulus. There was, however, a slight tendency for synchrony to be weaker during the binaural-beat stimulus than during monaural stimulation (Fig. 2). This may have been due to a sustained level of activity driven by stimulation of the opposite ear, which could have added action potentials that were unsynchronized to the waveform at the ear under consideration. Alternatively, it may have been an effect of adaptation during binaural stimulation, because the monaural stimuli were usually of shorter duration.

The synchrony to tones and envelopes measured with the use of binaural-beat stimuli is not a mathematical artifact as Yin and Chan (1990) have intimated. First, in the inferior colliculus, as in the SOC, the strength and phase of synchronization to the waveform is, in general, similar whether the sound is delivered alone or as part of a binaural-beat stimulus (Batra et al. 1989). Second, in the inferior colliculus and
The second criterion was that the difference in the times required for signals to travel from the ipsilateral and contralateral sides should predict the ITD at which coincidence occurred. This was tested by comparing the phases at which each unit synchronized to the waveform at each ear with the ITD that evoked maximal response, a technique that has been used by others to indicate coincidence detection by low-frequency neurons in the vicinity of the medial superior olive (MSO) (Goldberg and Brown 1969; Spitzer and Semple 1995; Yin and Chan 1990) and by neurons sensitive to high frequencies (Joris 1996; Yin and Chan 1990). Here we show that the same relationship applies to all varieties of ITD-sensitive neurons in the SOC.

We also tested the second criterion by measuring the travel times (delays) from the two ears for each unit with the use of the slopes of the phase-frequency plots and comparing these times with the CD. Again, most neurons of all types showed good agreement between the predicted CD and the actual CD. This test has the conceptual advantage that it tests for coincidence, rather than for maximal discharge, although the two tests are mathematically equivalent.

The good match between the ipsilateral and contralateral delays was somewhat surprising for the trough-type neurons of the lateral superior olive (LSO), because an inhibitory synapse is interposed on the contralateral side in the chain of input neurons but not on the ipsilateral side. To compensate for the synaptic delay, as well as for the longer distance to be traversed, the conduction velocity on the contralateral side and thus the axon diameter must be greater.

The first criterion for a neuron to be a coincidence detector was that it synchronize to both the ipsilateral and contralateral waveforms. The necessity of such synchrony for the generation of ITD sensitivity has been posited previously (Batra et al. 1989; Brugge et al. 1970; Goldberg and Brown 1969; Stanford et al. 1992; Yin and Chan 1990) and has been observed in neurons of the SOC sensitive to ITDs of low-frequency tones and envelopes of high-frequency tones (Crow et al. 1978; Finlayson and Caspary 1991; Goldberg and Brown 1969; Joris and Yin 1995; Moushegian et al. 1975; Spitzer and Semple 1995; Yin and Chan 1990). The present paper demonstrates that at any frequency where there is ITD sensitivity, most neurons in the SOC synchronize to the waveforms at either ear. This is true for both peak-type and trough-type neurons, even those that are irregular to varying degrees (Batra et al. 1997).

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This is indeed the case in the cat, where the axons of the globular bushy cells of the anteroventral cochlear nucleus (AVCN; typical diameter ~10 μm) (Spangler et al. 1985) and those of principal cells of the medial nucleus of the trapezoid body (MNTB; ~5 μm), which comprise the contralateral relay, are larger than the axons of spherical bushy cells of the AVCN (typically ~5 μm) (Smith et al. 1993), which provide the ipsilateral input.

The variation in the delay from the ipsilateral or the contralateral side was quite wide for low-frequency units, despite the narrow range in the difference in delays from the two sides. The range of delays we measured in the SOC is, in fact, similar to that observed in auditory nerve fibers as a function of characteristic frequency (Anderson et al. 1971). This variation is due to the time required for the acoustic wave to travel to differently tuned regions of the basilar membrane. There was, in fact, a weak correlation between the best frequency of low-frequency units (as determined from the response to the binaural-beat stimulus) and the delay (r ≈ −0.5). Thus, in the SOC, the matching of the delays from the two sides may be partially due to matching of the frequencies of the inputs from either side. However, the weakness of the correlation leaves open the possibility that there may be other mechanisms as well.

The third and final criterion was the relationship between the interaural synchrony and the strength of synchrony to the waveforms at either ear. The expectation was that the interaural synchronization coefficient would be less than the monaural synchronization coefficients and equal to the product of the monaural coefficients. This was indeed the case. The interaural synchronization coefficient was less than the monaural coefficients for nearly all units and for about three-
fourths of them was equal to the product of the monaural coefficients. Both peak- and trough-type units, including those that had irregularities, met this criterion, indicating that a coincidence mechanism is responsible for generating all types of ITD sensitivity in the SOC.

The low-frequency units that did not meet the third criterion had stronger interaural synchrony than expected. One possible explanation is that these units were not the primary coincidence detectors, but were instead higher-order neurons that inherited their ITD sensitivity from other ITD-sensitive neurons, in the process losing synchrony to the acoustic waveforms. Another possibility in some cases is that the weak monaural synchrony was a result of our method of measurement. As we have observed, measurement of synchrony during the binaural-beat stimulus could sometimes yield smaller synchronization coefficients than measurement during monaural stimulation.

Even though about one-fourth of the low-frequency units were potentially of higher order, they appeared distinct from the higher-order units encountered by Spitzer and Semple (1995) in the gerbil. The units in the gerbil did not synchronize to tones at all, whereas nearly all units in the rabbit synchronized to tones over the entire range of frequencies at which they were ITD sensitive. Spitzer and Semple did not employ our third criterion, so some of the units they classified as primary binaural units may have been considered higher order with the use of this more stringent criterion. Furthermore, most units in the gerbil that were considered to be of higher order were of a particular class, ‘monaurally unresponsive,’ which did not respond to monaural stimulation of at least one ear. In the rabbit, even monaurally unresponsive units (the E0, 0E, and 00 units of Batra et al. 1997) synchronized well to both the ipsilateral and contralateral tones. It is unclear whether these differences are a result of sampling different regions of the SOC, a result of the use of anesthesia, or a result of the difference in species.

Units with irregular responses

The units with irregular responses that we encountered in the companion paper (Batra et al. 1997) did not differ from the general population in that most synchronized to the waveform at either ear at all frequencies at which they were ITD sensitive, and the strength of synchrony to the waveforms was commensurate with that required to account for the strength of interaural synchrony. Thus there was no indication that a greater proportion of these units were of higher order than in our sample as a whole. The inference is that most units with irregular responses were located in the main binaural nuclei of the SOC, namely the MSO and LSO.

In the companion paper we suggest that irregular responses might arise from additional phase-locked inputs to the primary binaural neuron. If this is so, then it is surprising that units with irregular responses still behave as coincidence detectors, because more than two inputs are interacting. Perhaps the reason that the criteria were met is that they are based on responses of the postsynaptic cell, where all inputs from one side are summed. Thus adherence to the criteria indicates that the unit acts as a coincidence detector insofar as comparing the summed inputs from each side but gives no indication as to interactions between multiple inputs from the same side.

Synchrony to the waveforms

A surprising observation was the tight ipsilateral synchrony of some trough-type units, which was stronger than the ipsilateral or contralateral synchrony of peak-type units. Unusually strong ipsilateral synchrony has been noted by others for low-frequency neurons of the LSO (Finlayson and Caspary 1991; Joris and Yin 1995). However, these studies did not compare the strength of this synchrony with that of neurons in the MSO. The stronger ipsilateral synchrony of trough-type units is at first surprising, because ipsilateral inputs to the LSO come from the same type of cells as input to the MSO, namely the spherical bushy cells of the AVCN (Cant and Casseday 1986; Smith et al. 1993). However, the LSO receives an additional projection from a more posterior region of AVCN that does not contain spherical bushy cells (Cant and Casseday 1986). Some other cell type may therefore be responsible for the high synchrony of neurons in the LSO. Alternatively, the degree of convergence of the inputs onto neurons in the LSO may be greater than in the MSO, resulting in higher synchrony. Such convergence has been invoked to explain the higher synchrony to the acoustic waveform of some axons in the trapezoid body relative to the auditory nerve (Joris et al. 1994).

Another surprising observation was the similarity in the strength of synchrony between neurons that synchronized to the fine structure of low-frequency tones and those that synchronized to the SAM envelope of high-frequency tones. The synchrony of low-frequency neurons should follow a half-wave rectified sine wave because of the rectification in the peripheral transduction process. In contrast, the synchrony of high-frequency neurons should approximately follow a full sine wave because of the shape of the modulation envelope. The differing patterns of synchronization should theoretically yield a synchronization coefficient of 0.79 for low-frequency neurons and one of 0.40 for high-frequency neurons (assuming our usual modulation depth of 80%). In the auditory nerve, there does appear to be a difference between synchrony of low-frequency fibers to pure tones and that of high-frequency fibers to SAM tones, although both have synchronization coefficients higher than the theoretical values (Fig. 19 of Joris and Yin 1992). In contrast, both low- and high-frequency neurons of the SOC exhibited similar strengths of synchrony, and the synchronization coefficients of both frequently exceeded the theoretical values.

The strength of synchrony of neurons to tones in the SOC of the rabbit appears similar to that observed in gerbils (Spitzer and Semple 1995) but weaker than that observed in cats (Yin and Chan 1990). One possible reason for this difference is the difference in species. Another possible reason is the use of pentobarbital sodium anesthesia in the study of the cat MSO. Although pentobarbital was also used for initial anesthesia in the study of the gerbil SOC, anesthesia during recording was maintained with ketamine. Pentobarbital can raise the threshold for action potentials of neurons in the cochlear nucleus (Wu and Oertel 1986), necessitating greater coincidence of the inputs for activation of these neurons. Greater coincidence could result in increased synchronization in the cochlear nucleus, which would then be mirrored in the SOC. It is unlikely that the differences in the strength of synchrony are a consequence of extracting this
measure from the responses to binaural-beat stimuli, because our measurements with the use of monaural stimuli (Fig. 2) also indicate that synchronization coefficients are lower in the rabbit than in the cat.

Coincidence detection in the SOC: one membrane property or two?

We have demonstrated that most ITD-sensitive neurons of all types act as coincidence detectors. We and others have shown that peak-type neurons lie in the vicinity of the MSO (Batra et al. 1997; Joris 1996; Spitzer and Semple 1995; Yin and Chan 1990) and trough-type neurons lie in the vicinity of the LSO (Batra et al. 1997; Joris 1996). The neurons of the LSO and MSO appear to be part of a system that is designed to preserve and process timing information. The neurons that supply input to the LSO and MSO receive their inputs via large, secure synapses, i.e., the end bulbs of Held in the case of the bushy cells (Held 1893; Ramón y Cajal 1909) and the calyces of Held in the case of the MNTB principal cells (Banks and Smith 1992; Held 1893; Kuwabara et al. 1991; Ramón y Cajal 1909). These neurons also share common membrane properties. The bushy cells of the AVCN, as well as the principal cells of the MNTB, respond transiently to steps of current and repolarize rapidly (Banks and Smith 1992; Oertel 1983; Wu and Kelly 1991), permitting them to accurately follow input patterns. In the MNTB, these characteristics are produced by specialized voltage-gated channels (Brew and Forsythe 1995; Forsythe and Barnes-Davies 1993). The principal cells of the MSO have similar membrane properties (Smith 1995), which presumably aids them in detecting the coincident arrival of excitation from the two sides.

The neurons of the LSO appear to have different membrane properties. These neurons respond to intracellularly injected steps of current with a sustained discharge (Sanes 1990; Wu and Kelly 1991). Also, direct intracellular measurement of the inhibitory postsynaptic potential evoked by contralateral stimulation indicates that it is long (Sanes 1990). Both of these factors would hinder interaural timing. However, extracellular measurements appear to contradict those made intracellularly. We have found that ipsilateral synchrony in trough-type units is as good as or better than those made intracellularly. In the MSO, the neurons that supply input to the LSO and MSO receive their inputs via large, secure synapses, i.e., the end bulbs of Held in the case of the bushy cells (Held 1893; Ramón y Cajal 1909) and the calyces of Held in the case of the MNTB principal cells (Banks and Smith 1992; Held 1893; Kuwabara et al. 1991; Ramón y Cajal 1909). These neurons also share common membrane properties. The bushy cells of the AVCN, as well as the principal cells of the MNTB, respond transiently to steps of current and repolarize rapidly (Banks and Smith 1992; Oertel 1983; Wu and Kelly 1991), permitting them to accurately follow input patterns. In the MNTB, these characteristics are produced by specialized voltage-gated channels (Brew and Forsythe 1995; Forsythe and Barnes-Davies 1993). The principal cells of the MSO have similar membrane properties (Smith 1995), which presumably aids them in detecting the coincident arrival of excitation from the two sides.

SOC as the site for generation of ITD sensitivity

We have shown here that neurons of the SOC meet three criteria for being coincidence detectors: they synchronize to the waveform at either ear over the full range over which they exhibit sensitivity to ITDs; the ITD at which coincidence occurs is predicted by the difference in travel times from either ear; and the strength of interaural synchrony can be predicted from the strength of synchrony to the waveforms at either ear. In contrast, most neurons at the next major stage of the auditory pathway, the inferior colliculus, synchronize to the waveform at either ear only over a restricted range (Batra et al. 1989; Stanford et al. 1992), and the strength of interaural synchrony is always stronger than predicted by the strength of synchrony to the waveforms (personal observations). Thus ITD sensitivity in the inferior colliculus is likely inherited from the MSO and LSO.

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