Suppression in auditory-nerve fibers of cats using low-side suppressors.
I. Temporal aspects

Yidao Cai 1, C. Daniel Geisler *

Departments of Neurophysiology and Electrical and Computer Engineering, University of Wisconsin-Madison, 275 Medical Sciences Building, 1300 University Avenue, Madison, WI 53706, USA

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Abstract

Two-tone suppression was studied in the auditory nerve fibers of anesthetized cats, using low-frequency suppressors (50–2000 Hz). The response to the characteristic-frequency (CF) tone was suppressed in a phase-specific manner, attaining one or two minimums in 1 cycle of the suppressor (SUP) tone. The suppression phase-lead (i.e., the phase of maximum suppression leading the phase of response to the SUP tone) was about 1/4 cycle for lower-frequency suppressors (50, 100 and 200 Hz), and was close to 1/2 cycle for higher-frequency suppressors (500, 1000 and 2000 Hz). Both the phase of suppression and the suppression phase-lead are independent of fiber spontaneous rate (SR). Some fibers also show a secondary (minor) suppression at higher SUP intensities, which is always about 1/2 cycle away from the first (major) one. Fibers with higher CFs (> 2 kHz) are more likely to show a secondary suppression than those with lower CFs. The threshold difference between the major and minor suppressions is CF-dependent: lower CF fibers usually show differences of 10 dB or greater, while higher CF fibers show smaller differences. The secondary suppression is suppressor-frequency-dependent, usually restricted to lower-frequency suppressors (≤ 200 Hz). No fibers showed a secondary suppression with a SUP frequency 1000 Hz or greater. The phases of suppressions (both the major and minor suppressions) are not affected by the intensity of the CF tone. Non-excitatory, low-frequency suppressors can also give rise to significant suppression. The threshold of synchronization to the SUP tone in the two-tone part was usually the lowest, while the SUP-alone rate threshold was highest. The threshold of synchronization in the SUP-alone segment and threshold of suppression were in between. In some low-SR fibers, complete suppression can be seen.

Keywords: Two-tone suppression; Auditory nerve; Suppression phase-lead

1. Introduction

Two-tone suppression (2TS) is the phenomenon by which the responses to a tone at or near the characteristic frequency (CF) are suppressed by a second tone, the suppressor (SUP) tone. This phenomenon has been shown to exist at different stages of the auditory periphery: the basilar membrane (BM), the inner hair cell (IHC), and the auditory nerve (AN) fiber (i.e., mechanical, electrical and neural). It has been related to the cochlea’s ‘active’ process, also referred to as the ‘cochlear amplifier’ (Dallos, 1992). On the AN fibers, there have been many studies of 2TS since the first study by Galambos and Davis (1944) more than 5 decades ago. But most studies of 2TS (both experimental and model studies) seem to be restricted mainly to exploring reductions of discharge rate. Only a few studies concentrated on the temporal aspects of this suppression. However, since extensive knowledge of the rate aspects of 2TS has not been sufficient to resolve outstanding problems in our understanding of the 2TS phenomenon and the cochlear amplifier in general, the temporal aspects become increasingly more important to our thinking.

Among the limited number of temporal studies, different techniques have been used. For example, Javel et al. (1983) used AN discharge synchrony (i.e., the synchronization to the CF tone) as a measure of the suppression strength, and Deng and Geisler (1985) looked at the
changes in the phase of the AN-fiber responses to the CF tone induced by the suppressor. One particular approach, used in several studies, involves harmonically related CF tones and low-frequency SUP tones, which allows one to see how the responses to the CF tone are suppressed in a cycle by cycle manner by the SUP tone (e.g., Sachs and Hubbard, 1981, Sellick et al., 1982; Patuzzi et al., 1984a on AN; Patuzzi and Sellick, 1984 on IHC; Patuzzi et al., 1984b; Ruggero et al., 1992; Rhode and Cooper, 1993 on BM). Patuzzi et al. (1984b) measured the responses of the basal region of the guinea pig BM, using a 33-Hz SUP tone. They found that, at low SUP intensities, the suppression occurs at the phase of maximum displacement of the BM towards the scala tympani (ST), while at high SUP intensities a second (and less pronounced) suppression phase appears, corresponding to the maximum displacement towards the scala vestibuli (SV). However, the relatively insensitive and non-linear Mössbauer method prevented them from obtaining further details of the BM responses. Recently, with the advance of technology, several groups have begun to use a laser interferometer to study the BM responses. Using a displacement-sensitive laser interferometer, Rhode and Cooper (1993) recorded from the hook region of the cat's BM. They found a 2TS pattern which generally agrees with that of the Patuzzi et al. (1984b), but also noticed a 0.1-ms lag when a 1000-Hz suppressor was used. In both studies, the time between the two phases of suppression was about 1/2 cycle. Ruggero et al. (1992) used a velocity-sensitive laser device to study the two-tone responses of the basal region of chinchilla BM, using 300–500-Hz suppressors. Although they found basically the same suppression patterns as the other investigators did (i.e., one phase of suppression at lower intensities, also a second one at higher intensities), they observed, however, that the maximum suppression occurred at the phase when the BM was moving with maximum velocity toward ST. The differences in these various studies have not yet been resolved.

At the IHC level, Patuzzi and Sellick (1984) found that both the AC and DC components of the CF-tone elicited receptor potentials of IHCs from basal region of the guinea pig were modulated in synchrony with a simultaneously applied low-frequency SUP tone (40 Hz). The suppression pattern was similar to those observed on the BM by Patuzzi et al. (1984b).

Sachs and Hubbard (1981) were the first who studied 2TS on the AN fibers of cats using harmonically related stimuli. They found that, with 500- and 100-Hz suppressors, there was usually one phase of suppression in the cycle of the SUP tone at lower intensities, but a second one appeared when higher intensities were used. This basic pattern, which is the same as that revealed at the BM and IHC stages, was also confirmed by Sellick et al. (1982) and Patuzzi et al. (1984a) in the ganglion cells from the basal region of guinea-pig cochleae, using 40-Hz SUP tones. In addition, Sellick et al. (1982), using the cochlear microphonic (CM) recorded from ST as reference, found that the major AN suppression (which appears at lower intensities) was in phase with maximum BM displacement towards ST while the minor one (which appeared at higher intensities) was in phase with maximum BM displacement towards SV. In their study, Sachs and Hubbard (1981) noticed that the major suppression was in phase with the phase of excitation to the SUP-alone tone. However, a close examination of the figures in their publication revealed some examples that depart from this general conclusion, especially in their limited number of low-CF units.

Because of the discrepancies existing in the different studies and the fact that so far there has been no temporal study of 2TS from the apical region of the cochlea at any level using harmonically related stimuli, we believe that more systematic studies in the basal as well as apical regions are needed at all levels of the system. It is the goal of this paper to provide a more systematic and thorough study at the AN level, using harmonically related CF and SUP tones. Some of the data in this report have been presented previously (Cai and Geisler, 1994).

2. Methods

The animal preparation, sound delivery and recording system have been described in detail elsewhere (Cai and Geisler, 1996a; Cai, 1995). Briefly, the pinna of the anesthetized cat was removed. The skull was opened in the posterior fossa area and the auditory nerve was exposed. A Trent–Wells hydraulic microdrive was mounted and fixed onto the skull, and a glass electrode (30–70 mΩ) was inserted into the nerve under visual guidance.

The stimuli were two harmonically related pure tones: CF and SUP tones. The frequency of the SUP tone was always lower than fiber CF (with a frequency ratio no greater than 1/3), and it usually took one of the following values: 50, 100, 200, 500, 1000 and 2000 Hz. The frequency of the CF tone was adjusted slightly to ensure a harmonic relationship between it and the SUP tone. The CF intensity was usually fixed at 10–30 dB above fiber threshold at CF. The SUP intensity was varied over a range (e.g., from 70 to 95 dB SPL), usually in 5 dB steps. When a fiber was located by a frequency-modulated stimulus, a short paradigm in which two tones are presented simultaneously was used to determine whether or not 2TS existed. If so, the paradigm of overlapping tones shown in Fig. 1 was used. Each tone lasted 500 ms. The repetition interval was 1000 ms. The suppressor was delayed by 200 ms so that there were three time windows corresponding to stimulation by CF tone alone, two-tone (CF + SUP), and SUP tone alone. Each SUP frequency and intensity combination was repeated 75 times. The responses were added together to form histograms.

The data were obtained from eight cats, labeled for convenience as A,B,D,E,F,H,I and J, respectively (see Cai
two-tones (250–500 ms) and SUP-alone (575–700 ms), using the period of the SUP tone as base. The initial portions in each segment were excluded from analysis. The rate versus SUP-intensity curves were also plotted for the three time windows.

In determining the phase of maximum response to the SUP-alone tone, the vector phase was used (cf., Cai and Geisler, 1996a). The phase of maximum suppression was visually determined from the period histogram due to the often asymmetrical nature of the period histograms of the two-tone segments. In most cases it was quite obvious where the point of maximum suppression lay. When it was not obvious, the mid-point of a horizontal line connecting both sides of the suppression valley was considered to be the point of maximum suppression. In some cases, a secondary suppression phase was also found, often at a higher SUP intensity, resulting in two envelope minima occurring during the SUP period (cf., Fig. 7). In this case, the phase of the major suppression was used. In an extremely small number of cases, the two suppressions were about equally strong, and those units were excluded from the general pool of phase data. The amount by which the maximum suppression led the maximum response to the SUP tone was then termed the suppression phase-lead (cf., Fig. 3). Each period histogram was statistically compared against the uniform distribution, and only those period histograms that have a Rayleigh coefficient less than or equal to 0.001 were included in the phase analysis (cf., Cai and Geisler, 1996a).

Analysis of the data included the determination of the synchronization thresholds, rate-suppression thresholds and rate-excitation thresholds. The lowest SUP intensity which produced histograms with a Rayleigh coefficient less than or equal to 0.001 was considered to be the synchronization threshold. To determine the excitation threshold (the responses to SUP-alone tone), either one of two criteria had to be satisfied. The first criterion was if the SUP-alone rate exceeded by 15% the rate of the spontaneous activity which occurred in the last 200-ms window that ended the 1-s repetition period (and thus immediately preceded the next stimulus presentation). Although this criterion was sufficient in most cases, it may overestimate the excitation thresholds in some cases, since the fiber was in different states of adaptation during the two analysis windows (575–700 ms for SUP-alone and 800–1000 ms for spontaneous firing; cf., Fig. 1). Thus, we also used a second criterion, which was if the SUP-alone rate exceeded by 15% the rate at the lowest SUP intensity used. The rate threshold to the SUP-alone was then taken as the lowest intensity at which either condition was satisfied.

In determining the threshold of rate suppression, we compared the response rates in the two-tone segment and the CF-alone segment. Due to the complication of adaptation in the initial portions of the CF-alone segment, we must consider the time course of adaptation in fibers with different spontaneous rates (SR) in order to find a realistic
criteria. ‘Lower’-SR (< 20/s) fibers are known to have longer time courses of adaptation than ‘high’-SR (≥ 20/s) fibers (e.g., Relkin and Doucet, 1991). In the middle and bottom panels of Fig. 1, the PST histograms of two fibers are shown to illustrate the different time courses of adaptation in ‘low’-(≤ 1/s) and high-SR fibers. The responses corresponding to the three stimulus conditions are clear: the first segments (0–200 ms) are the responses to CF tone alone, followed by the two-tone responses (200–500 ms, which are suppressed) and the responses to the SUP-alone tone (500–700 ms). For the low-SR fiber (bottom panel), there was basically no response to the SUP-alone tone.

We will concentrate on the CF-alone responses. The bars over the PST represent the time windows (75–200 ms) from which the CF-alone rates were estimated. The solid lines below the bars represent the average numbers of spikes in the CF-alone analysis windows. For the high-SR fiber (middle panel), the adaptation process is practically completed before the start of the CF-alone analysis window at 75 ms. But for the low-SR fiber (bottom panel), the adaptation process is obviously not complete at the start of the analysis window. Thus the use of this time window overestimated the steady-state response rate of this fiber for CF-alone stimulation. As a result, our program might occasionally report suppression when there was in fact no suppression at all. To minimize this problem, we used a rather strict criterion, requiring the steady-state two-tone rate to be at least 18% lower than the steady-state CF-alone rate. We understand that this overestimates the suppression threshold for high-SR fibers. The exact percentages used to estimate the suppression threshold (18%) and the rate threshold in the SUP-alone segment (15%) were determined from a sample of about 30 cases by checking the computer-reported results against visual analysis of the actual rate curves and PST histograms. Agreement in all 30 cases was satisfactory.

The care and use of animals reported in this study were approved by the Animal Care and Use Committee of the University of Wisconsin-Madison.

3. Results

3.1. Phase of suppression and suppression phase-lead

Fig. 2 shows typical rate-intensity curves from an AN fiber (fiber D16). The frequencies of the CF and SUP tones were 1400 and 100 Hz, respectively. As the SUP intensity was increased, the discharge rate in the two-tone segment gradually decreased. At the same time, the SUP-alone rate increased. Somewhere between 85 and 90 dB SPL, the two-tone rate reached its minimum (arrows) and then increased. This non-monotonic two-tone rate-intensity curve is a general characteristic of AN fibers exhibiting ‘low-side’ suppression (Sachs, 1969; Hill and Palmer, 1991; Hill and Geisler, 1992). Notice that there are also

![Fig. 2. Rate vs. suppressor-intensity curves of a medium-SR fiber (D16, CF = 1300 Hz, SR = 8.0/s, TH = 12 dB SPL) obtained with paradigm shown in Fig. 1. The frequencies of the CF and SUP tones were 1400 Hz and 100 Hz, respectively. The CF tone was presented at 25 dB SPL.](image)

![Fig. 3. Period histograms of fiber D16. The corresponding rate vs. suppressor-intensity curves are shown in Fig. 2. The period histograms in all three columns were binned to the SUP-tone period, so that each abscissa covers the period of the SUP tone. The phase is always referred to in terms of period (T) of SUP tone (e.g., 0.45T) in the text. Unless otherwise noted, this convention applies to all figures. The arrows in the two-tone column indicate estimated phase of maximum suppression, while the arrow in the SUP-alone column indicates the ‘vector phase’ of excitation due to the SUP tone alone. In this and all similar plots, the period histograms in the three (unequally long) time windows were scaled to the two-tone (CF+SUP) case, so that equal discharge rates produced equal bin heights.](image)
decreases in the responses to the CF-alone tone (top line) as the intensity of the suppressor was increased. This phenomenon, which we have termed long-term suppression, is the subject of a companion paper (Cai and Geisler, 1996d). By always obtaining the then-current CF-alone response and two-tone response nearly simultaneously (cf., Fig. 1), we have always been able to determine the additional suppression caused by the presence of the SUP tone. This long-term suppression does not affect the phases of suppression and excitation (Cai and Geisler, 1996d).

In Fig. 3, the period histograms of these responses are shown in three columns corresponding to the three analysis windows. At 75 dB SPL, there is a clear suppression phase in the two-tone histogram (arrow). At 80 dB SPL, the fiber began to show a response to the SUP-alone tone (tilted arrow), with a response peak at a phase of about 0.1T (T is the period of the SUP tone), which leads the phase of (maximum) suppression at the same intensity (arrow) by about 3/4 cycle (or lags by 1/4 cycle). At 85 dB SPL, there is also a minor suppression phase at about 0.35T. Further increases of SUP intensity produced more suppression and also larger responses to the SUP-alone tone. At 90 and 95 dB SPL, the two-tone responses reflect mainly the SUP tone, synchronization to the CF tone being lost.

The suppression-phase data for four SUP frequencies (50, 100, 200 and 500 Hz) which we obtained from all of our fibers are plotted in Fig. 4. For each of the three lowest frequencies, the phase lag of suppression (increasing lag plotted downwards) increased slightly with decreasing CF. Comparing suppression phase to the BM phase estimated from the CM responses recorded near the round window (horizontal bars on the left-hand ordinate; cf., Cai and Geisler, 1996a), it is clear that near the basal region, the suppression phase roughly corresponds to the BM displacement towards SV at 50 Hz, and is between SV displacement and SV velocity at 100 and 200 Hz. Similar figures are not shown for the two highest SUP frequencies (1000 and 2000 Hz), as the large phase shifts with distance (CF) which are superimposed by the traveling-wave propagation delays of those tones (cf., Kim et al., 1980) make interpretation difficult (cf., 500-Hz data in Fig. 4D).

Fig. 5 shows, for all fibers, the phase by which the major suppression phase leads the (SUP-alone) excitation phase (described in Cai and Geisler, 1996a). For lower SUP frequencies, (Fig. 5A–C), the average suppression phase-lead is close to 1/4 cycle. For higher SUP frequencies (Fig. 5D–F), the average suppression phase-lead values are closer to 0.5T. Although there is a lot of scatter in both the phases of suppression (Fig. 4D) and of excitation to the SUP-alone (cf., Cai and Geisler, 1996a; also Cai,

**Fig. 4.** Phase of maximum suppression as a function of fiber CF, for different suppressor frequencies. Different symbols encode suppressor intensities as indicated in the figure. More than one point might be entered for one fiber if the phase values at different suppressor intensities are available for the same fiber. The solid lines are the running averages over 1 octave, in steps of half-octave (outlier points omitted). The small bars on the left hand ordinates indicate estimated phases of BM motion based on CM recorded near the RW (cf., Cai and Geisler, 1996a).
the suppression phase-lead data for these higher frequencies are distributed within a much narrower range. This is particularly true for the 1000- and 2000-Hz cases.

3.1.1. Outlying points

Although the averages in the lower SUP frequency data (both the phase of suppression and suppression phase-lead) seem to reflect the behaviors of most neurons, there are some points that are outside the main groupings (Figs. 4 and 5). Some of these outlying points are about 1/2 cycle away from the usual range. Similar 1/2-cycle scattering also exists in the phase of response to the SUP-alone tone (cf., Ruggero, 1995; Cai and Geisler, 1996a; also see Cai, 1995 for listing of all the fibers in our experiments that showed phase values about 1/2 cycle away from the usual ranges, for each of the three lower frequencies).

There are several observations to be made about these outlying points. First, fibers showing unusual phase values (either phase of suppression, phase of excitation to SUP-alone tone, or suppression phase-lead) usually had CFs either below about 2–3 kHz or above about 9 kHz. Fibers from the mid-CF region rarely showed unusual phase values. Most of the high-CF fibers that showed unusual phase values were from experiment H, which had a slight ‘damage’ history but recovered at the time the data were collected. But all eight experiments contributed to such outlying points. The involved fibers (35 total) constitute about 18% of the total number of fibers studied. Second,
an unusual suppression phase-lead value is mostly caused by an unusual phase of response to the SUP-alone tone, only occasionally due to an unusual phase of suppression. Sometimes both the phase of response to the SUP-alone tone and the phase of suppression were about 1/2 cycle away from their usual ranges, but the corresponding suppression phase-lead values are within the usual ranges. Third, this unusual phase behavior is dependent upon SUP frequency. That is, a particular fiber may show a phase within the usual range at one frequency and a phase outside the usual range at another frequency, either for the phase of suppression or the phase of responses to the SUP-alone tone. Finally, some of the fibers showed a second phase of suppression (see Section 3.1.2). For all the cases that showed both an unusual suppression phase-lead value and a second phase of suppression, the suppression phase-lead value falls in the usual range if the second phase is used to calculate the suppression phase-lead.

In general, the suppression phase-lead data for higher SUP frequencies (≥ 500 Hz) showed much less variation. But for 500 Hz, there are some points with suppression phase-lead values around zero, which is about 1/2 cycle from the usual range (cf., Fig. 5D). In those cases (see Cai, 1995 for an individual example), suppression occurred at the same phase as the response to the SUP tone when presented alone. Such a phase relationship between suppression and excitation was described as a general feature in Sachs and Hubbard (1981, with 500- and 100-Hz suppressors) and Sellick et al. (1982, with a 40-Hz suppressor), but it is obviously not the case in most of our data (Fig. 5).

3.1.2. Effects of suppressor intensity

Fig. 6 shows the pooled data of the changes of phase of suppression which occurred with increasing SUP intensity, for several frequencies. Each line represents the phase values obtained from the same fiber at one frequency, relative to the phase value occurring at the lowest intensity that showed suppression. For the 50-Hz suppressor, a slight lag is exhibited for most fibers with CFs less than 1 kHz, but not for fibers with CFs equal to or greater than 1 kHz (Fig. 6A,B). The change of phase of suppression did not show any obvious trend at 100 Hz (Fig. 6C,D) or at other SUP frequencies. This dearth of trends in suppression phase-lead plots is in contrast to the trends seen in the phases of the excitatory responses to those SUP tones alone (Cai and Geisler, 1996a). For higher SUP frequencies, there were sometimes larger changes in suppression phases with intensity (not shown).

3.1.3. SR effect

Patuzzi et al. (1984a) observed no difference in the phases of suppression in a pair of high- and low-SR ganglion cells from the basal region of a guinea pig. We have plotted our suppression-phase data as a function of fiber SR, for each of the six SUP frequencies (cf., Cai, 1995). We saw no obvious trends in the data (not shown). The suppression phase-lead data (cf., Cai, 1995) also did not show any sign of SR dependence.

3.2. Secondary suppression

It is well documented that in addition to a major suppression which appears at lower SUP intensities, a second (minor) suppression often occurs when the intensity of the SUP tone is increased (see Section 1). We also saw such secondary suppressions in our data. For example, fiber D16 demonstrated a very small secondary suppression phase at SUP intensity of 85 dB SPL (Fig. 3). In Fig.

![Figure 6](image)

Fig. 6. Normalized phase-intensity plot for several stimulus frequencies. The data were obtained from the same fibers that contributed to Fig. 4(Fig. 5). The phase at the lowest intensity that showed a significant phase-locked response was set to zero. The phase values at subsequent intensities are relative to the phase at that first intensity. A positive value indicates a phase lag, while a negative value indicates a suppression phase-lead.
7, we show an example (fiber A4) that demonstrated a much clearer secondary suppression with a 200-Hz suppressor (second column from left). At 75 dB SPL, the lowest SUP intensity used, suppression is quite obvious; the minimum in the two-tone period histogram is at a phase of about 0.88T. When the SUP intensity was increased to 80 dB SPL, there is some sign of a minor suppression occurring about 1/2 cycle away from the major suppression. This minor suppression becomes obvious at SUP intensities of 85 and 90 dB SPL (arrows).

Unlike those reported before (e.g., Sachs and Hubbard, 1981; Sellick et al., 1982; Patuzzi et al., 1984a), not all fibers in our study showed a secondary suppression at higher intensities. In fact, only about one-third of the fibers we studied showed secondary suppressions, although examples of secondary suppression were observed in all of our experiments (see Cai, 1995 for complete list). This might be due to our use of lower SUP intensities (see Section 4).

When they did occur, the secondary suppressions did not necessarily appear at all SUP frequencies studied. For example, examination of fiber A4’s two-tone period histograms for eight different suppressors (100–4500 Hz, Fig. 7) shows that this fiber only exhibited clear secondary suppressions at 200 Hz (arrows), but not at any other frequencies, although one might be developing at 100 Hz. The general tendency in our data is for minor suppressions to appear only at lower SUP frequencies (50, 100 and 200 Hz), with 200 Hz being the frequency which produced the largest percentage of secondary suppressions. Fibers that showed secondary suppressions at 200 Hz often (but not always) showed secondary suppressions at 50 and 100 Hz. We saw only five cases of secondary suppression at a SUP frequency of 500 Hz, and we never saw secondary suppressions at 1000 Hz or above.

3.2.1. Occurrence of secondary suppression with respect to CF

Analysis of our secondary-suppression data seemed to suggest that fibers with higher CFs are more likely to demonstrate secondary suppressions. In Table 1, we have listed the number of cases in which we saw secondary suppressions for the three lowest-frequency suppressors (50, 100 and 200 Hz), arranged according to fiber CFs. The data from this table confirm our impression. For all three SUP frequencies, a larger percentage of fibers with higher CFs showed secondary suppressions than those with lower CFs. The CF division seems to be dependent upon the frequency of the suppressor that was used: it was about 1 kHz for a 50-Hz suppressor, 2 kHz for a 100-Hz suppressor and 4 kHz for a 200-Hz suppressor. Moreover, all of the five fibers that showed secondary suppressions at 500 Hz (not listed) had CFs at or above 10 kHz.

3.2.2. Threshold differences between major and minor suppressions

As will be shown in Cai and Geisler (1996c), the shape of the envelope suppression induced by low-side suppressors can be accounted for by the hypothesis that the suppression is caused by saturation of OHC receptor currents. Due to the near symmetry of OHC transfer (input/output) curves in the base of the cochlea (c.f., Russell et al., 1986), it would be expected that the major and minor phases of suppression would occur at about the same intensities for high-CF fibers. By contrast, apical OHCs have asymmetrical transfer curves, and so the major suppression would be expected to appear at lower SUP intensities than the minor phase. To test these inferences, we have quantified the difference between the threshold intensities of these two phases of suppression. The results (Fig. 8) are consistent with expectations. Most of the high-CF fibers had threshold differences between 0 and 5 dB (lower panel), while most low-CF fibers had threshold differences greater than 5 dB (top panel).

3.2.3. Phase distance between two suppressions

In an attempt to characterize further the two suppressions, we measured the phase distance between them (i.e., the phase differences between the two minima), using the convention that the minor suppression led the major one. Fig. 9 shows the pooled population data for four SUP frequencies (50, 100, 200 and 500 Hz). All points are distributed within 0.1 cycle of the line of 0.5T, suggesting that the two suppressions are always about 1/2 cycle.

Table 1

<table>
<thead>
<tr>
<th>CF (kHz)</th>
<th>50</th>
<th>100</th>
<th>200</th>
<th>All a</th>
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<tr>
<td>≤ 1</td>
<td>17.1% (6/35)</td>
<td>8.8% (3/34)</td>
<td>0.0% (0/6)</td>
<td>13.2% (7/53)</td>
</tr>
<tr>
<td>1–2</td>
<td>33.3% (4/12)</td>
<td>13.6% (3/22)</td>
<td>0.0% (0/10)</td>
<td>24.0% (6/25)</td>
</tr>
<tr>
<td>2–4</td>
<td>36.4% (4/11)</td>
<td>48.0% (12/25)</td>
<td>22.2% (2/9)</td>
<td>45.2% (14/31)</td>
</tr>
<tr>
<td>4–8</td>
<td>80.0% (4/5)</td>
<td>78.6% (11/14)</td>
<td>88.8% (8/9)</td>
<td>63.2% (12/19)</td>
</tr>
<tr>
<td>8–12</td>
<td>75.0% (6/8)</td>
<td>100.0% (13/13)</td>
<td>57.1% (4/7)</td>
<td>53.6% (15/28)</td>
</tr>
<tr>
<td>12–16</td>
<td>33.3% (1/3)</td>
<td>57.1% (4/7)</td>
<td>0.0% (0/1)</td>
<td>26.3% (5/19)</td>
</tr>
<tr>
<td>&gt; 16</td>
<td>0.0% (0/1)</td>
<td>22.2% (4/18)</td>
<td></td>
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a Fibers showing secondary suppressions for at least one suppressor frequency, including 500 Hz. The fractions inside the brackets give, for each class, the number of those fibers compared to the total number of fibers studied.
Fig. 7. Two-tone period histograms of a fiber (A4, CF = 9400 Hz, SR = 7.0/s, TH = −5 dB SPL) for stimulation at various intensities at eight different suppressor frequencies (100–4500 Hz). The CF tone was presented at 10 dB SPL. With a 200-Hz suppressor (second column from left), there is a clear second (minor) suppression (arrows) occurring about 1/2 cycle away from the major suppression at 85 and 90 dB SPL. This fiber showed clear secondary suppressions only at 200 Hz, but not at other frequencies.
Fig. 8. Number of fibers showing the indicated differences between major and minor suppression thresholds (see text). Fibers with lower CFs (≤ 2 kHz) mostly had threshold differences of 10 dB. For fibers with CFs between 2 and 4 kHz, the peak in the histogram is shifted to 5 dB. Fibers with higher CFs (> 4 kHz) mostly had threshold differences of zero or 5 dB.

Another observation from this figure is that there is a gap near CF of 2 kHz. Since this gap has no counterpart in the phase-of-suppression vs. CF plot (Fig. 4), it suggests that fibers with CFs near 2 kHz tend not to show secondary suppressions. The thresholds of primary suppressions for fibers near 2 kHz were no higher than those for their neighbors.

3.2.4. Degree and phase of secondary suppression

It is common to find fibers showing different degrees of secondary suppressions in all experiments. Occasionally, a fiber’s major suppression happened at the phase where minor suppression usually appeared in other fibers. In experiment H, we were able to find several fibers with similar CFs that showed different degrees and patterns of secondary suppressions. Fig. 10 shows the period histograms produced by these fibers with a 200-Hz suppressor presented at 85 and 90 dB SPL. Their responses to the 200 Hz SUP tone alone (not shown) were all very small, and showed vector phases between 0.7 and 0.9T. The two-tone histograms of these fibers are arranged, from top to bottom, with increasing degrees of suppression in the first half cycle. It is interesting to note that the major suppression happened in the second half cycle for the top two fibers (H62 and H47), while the minor suppression happened in the first half cycle. The suppression in the first half cycle becomes equal in magnitude to the suppressors.

Fig. 9. Distance between the estimated phases of major and minor suppressions for the twin-suppression responses at four suppressor frequencies (50, 100, 200 and 500 Hz). All points are shown. The phase distance, measured in terms of period of the respective SUP tone is that by which the minor suppression led the major suppression.
suppression at a SUP intensity of 75 dB SPL (arrow). As the SUP intensity was increased, suppression became more obvious. At 95 dB SPL, there was also a strong secondary suppression at a phase of about 0.05T (arrow).

The two-tone responses of this fiber with a higher CF intensity (50 dB SPL) are shown in Fig. 11B. As expected, the overall responses were increased, as compared to the responses when the CF tone was presented at 35 dB SPL (Fig. 11A). Several additional observations can be made. First, there was no obvious suppression when the suppressor was presented at 75 dB SPL, the intensity at which suppression was first seen when CF tone was presented at 35 dB SPL (Fig. 11A). It required a SUP intensity of 80 dB SPL to produce a small phase-specific suppression (arrow). At a SUP intensity of 95 dB SPL, there is also a secondary suppression (arrow), but it is much shallower than the one in Fig. 11A. Notice that the phases of suppressions did not change with increasing CF intensity; the major suppression was still at a phase of about 0.5T and the minor suppression at a phase of about 0.05T. Comparing the responses shown in Fig. 11A, B, we see that although there was a 15-dB increase in CF intensity, the suppression in the second half in fiber H44. In the next fibers, the major and minor suppressions reversed their positions. In fiber H37, the suppression in the first half cycle became the major suppression, while fiber H41 showed only one phase of suppression, and that occurred in the first half cycle. It should be emphasized that such examples of fibers of similar CFs showing different degrees and patterns of secondary suppressions are not limited to experiment H, although in no other experiments did we obtain enough data to form a continuous spectrum like that of Fig. 10.

### 3.3. Effect of CF-tone intensity

In addition to varying the intensity of the SUP tone, we also varied the intensity of the CF tone in some fibers. In Fig. 11, we show the responses of one fiber (16) for which the CF intensity was varied. The frequency of the SUP tone was 50 Hz. This fiber displayed very little response to the SUP-alone tone regardless of the SUP intensities which we used (Fig. 11C). When the CF tone was presented at 35 dB SPL (Fig. 11A), the fiber began to show a phase-specific

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**Fig. 11.** The two-tone responses of one fiber at different CF and SUP intensities (fiber 16, CF = 758 Hz, SR = 21.5, TH = 21 dB SPL). The frequency of the SUP tone was 50 Hz. When the CF tone (800 Hz) was presented at 35 dB SPL (A), the fiber began to show a phase-specific suppression at a SUP intensity of 75 dB SPL (arrow). At 95 dB SPL, there is also a strong secondary suppression at phase of about 0.05T (arrow), the depth of which decreased with increasing CF intensity. The threshold of suppression increased with CF intensity (B) but the suppression phases stayed approximately constant. See text for details.

**Fig. 12.** Two-tone responses from the same fiber as in Fig. 11, at different CF and SUP intensities. The SUP frequency was 100 Hz. Of particular interest are the responses at higher SUP intensities. A: (CF intensity of 30 dB SPL). There are responses between the peaks at SUP intensity of 85 dB SPL (bar), which must be due to excitation by the SUP tone (see responses to the SUP tone alone in C, bar). B; (CF intensity of 50 dB SPL) There are no similar responses between the small peaks (bar). Similar phenomenon also existed in the responses when SUP intensity was 90 dB SPL.
Peak and frequency of the synchronization threshold only increased by about 5 dB. This relative insensitivity to CF intensity is a common feature in our data.

Fig. 12 shows the responses from the same fiber with a SUP frequency of 100 Hz. The responses in this figure bear some common features to those shown for 50-Hz suppressor: the phases of suppressions did not change with CF intensity, and the suppression threshold increased only slightly as CF intensity was increased. Of particular interest are the responses at higher SUP intensities. In Fig. 12A (CF intensity of $30 \text{ dB SPL}$), the response components between the CF peaks at a SUP intensity of $85 \text{ dB SPL}$ (bar) must be due to drive from the SUP tone (cf., Fig. 12C, bar). But in Fig. 12B (CF intensity of $50 \text{ dB SPL}$), there are no comparable SUP-response components (bar). Even more striking differences existed in the responses obtained at different CF intensities with a SUP intensity of $90 \text{ dB SPL}$ (bottom row). These data show clearly that complex interactions can occur between the CF and SUP tones; in addition to the suppressive effect of the SUP upon the CF tone, the CF tone also can affect the fiber’s responses to the SUP tone.

3.4. Synchronization threshold vs. suppression threshold

Javel et al. (1983) studied low-side suppression in AN fibers of cats and found that the ‘synchrony suppression’ threshold was always higher than the synchronization threshold for SUP-alone. For comparison purposes, we show rate-suppression threshold data only from fibers with SRs of $10/\text{s}$ or greater (since only they have synchronization thresholds different from rate thresholds). Fig. 13 shows the rate-suppression threshold as a function of the synchronization threshold in the SUP-alone segment. The diagonal lines indicate equal rate-suppression thresholds and synchronization thresholds. With lower-frequency suppressors (50, 100 and 200 Hz; Fig. 13A), both thresholds were generally higher than those with higher-frequency suppressors (500, 1000 and 2000 Hz; Fig. 13B). But for all SUP frequencies, the data seem to be scattered on both sides of the diagonal line, with a slight majority of the points falling above the line (cf., figure caption).

Fig. 14 shows the rate-suppression threshold as a function of the rate threshold in the SUP-alone segment. In this figure, almost all of the data points lie below the equality line, indicating that the rate threshold was almost always higher (more intense) than the suppression threshold. Similar results were obtained by Javel et al. (1983). Of particular significance is that this relationship holds not only for higher-frequency suppressors (Fig. 14B), but for lower-frequency suppressors as well (Fig. 14A), since it has been suggested that very-low-frequency, non-excitatory suppressors could not cause appreciable rate suppression (cf., Cheatham and Dallos, 1992; Cheatham and Dallos, 1995). Our data clearly indicate otherwise. The data shown in Fig. 11 are a clear example of such suppression.

In Fig. 15, the threshold data shown in Figs. 13 and 14 are plotted for groups of fibers having different CFs. We also added an additional measure to these graphs, the threshold of synchronization to the SUP tone in the two-tone segment. Two major observations can be made. First, regardless of fiber CF and the frequency of the suppressor, the synchronization threshold in the two-tone segment is always the lowest among the four measures, and the SUP-alone rate threshold is always the highest. Second, the threshold of synchronization (in the SUP-alone segment) and the threshold of rate suppression are generally very close to each other, but for lower-frequency suppressors and in fibers with lower CFs ($< 4 \text{ kHz}$), the synchronization threshold is usually below suppression threshold, a trend which is statistically significant ($P < 0.01$ and 0.001, $F$ test).
3.5. Tonic suppression

In some low-SR fibers, the response due to the CF tone can be greatly (even completely) suppressed, as previously described by others (e.g., Fahey and Allen, 1985). Similar suppressions were also observed in our study. The term complete suppression implies that there was no response at any phase in the period histogram, either due to the CF or SUP tones. In practice, this condition is difficult to meet, so instead, we adopted the criterion that if the remaining
two-tone period histogram, with a minimum at a phase of 0.5–0.67T (arrow). Although the two-tone period histogram resembles its counterpart in the SUP-alone column at the same intensity, the phases of the minimums in the two histograms do not match exactly. Further increasing the SUP intensity to 85 dB SPL produced period histograms in the two-tone and SUP-alone segments almost exactly alike in phase and shape.

4. Discussion

4.1. Summary of results

The responses of AN fibers to a CF tone and a low-side SUP tone were studied in cats. The main findings can be summarized as follows.

Not all fibers showed suppression with the stimulus parameters which we used. For those that did show suppression, it almost always had a phase-specific waveshape. For any one SUP frequency, the average phase of maximum suppression within the SUP tone period is a monotonic function of fiber CF. On average, the phase of suppression led the phase of response to the SUP-alone tone (so-called ‘suppression phase-lead’) by about 1/4 cycle for lower-frequency suppressors (50, 100 and 200 Hz), and was close to 1/2 cycle for higher-frequency suppressors (500, 1000 and 2000 Hz). For lower-frequency suppressors, the suppression phase-lead is also CF-dependent, with a bigger average value at both very low and very high CFs. Both the phase of suppression and the phase of response to the SUP-alone tone are independent of fiber SR.

Some fibers also show a secondary (minor) suppression at higher SUP intensities, which is always about 1/2 cycle away from the first (major) one. Fibers with higher CFs (> 2 kHz) are more likely to show a secondary suppression than those with lower CFs. The differences between threshold intensities for the major and minor suppressions are CF-dependent: lower CF fibers usually show differences of 10 dB or greater, while higher CF fibers show smaller differences. The occurrence of secondary suppression is dependent upon SUP frequency: that is, a fiber may show a secondary suppression at one SUP frequency but not at another. The secondary suppressions are usually restricted to lower-frequency suppressors (≤ 200 Hz). We did not see a secondary suppression with a SUP frequency of 1000 Hz or greater.

The phases of maximum suppressions (both the major and minor ones) are not affected by the intensity of the CF tone, but the threshold of suppression is increased slightly when the CF intensity is increased. At higher CF intensities, the CF tone can suppress the response to the SUP tone at some specific phases.

Non-excitative low-frequency suppressors can also give

suppressed response rate was quite small (e.g., average rate < 2% of the response in CF-alone segment), we considered it to be 'complete suppression'. With this criterion, we found that a total of 18 fibers (out of ~ 190) which showed complete suppression at one or more SUP frequencies, usually at 500 or 1000 Hz.

Fig. 16 shows the responses of a low-SR fiber (J12), which showed no response to the SUP-alone tones, even at 95 dB SPL (Fig. 16B,D, with suppressors of 50 and 100 Hz, respectively). With a 50-Hz suppressor, there was a strong suppression at phase 0.55T (Fig. 16A) at a SUP intensity of 80 dB SPL. As the SUP intensity was increased, more and more responsiveness was suppressed. At 90 dB SPL, there was a secondary suppression at phase of about 0.05T. At 95 dB SPL, there was basically no response in the two-tone histogram, except for the two small peaks at phases of about 0.2T and 0.85T, respectively (arrows). The same fiber showed complete suppression at 90 dB SPL with a 100-Hz suppressor (Fig. 16C, arrow).

Fig. 17 shows examples of both tonic and phase-specific suppression exhibited by a high-CF fiber (I12) when a 1000-Hz SUP tone was used. At 75 dB SPL, this fiber showed only tonic suppression (cf., dashed lines and arrow). To emphasize that this is not due to our choice of analysis windows, the PST at this intensity is shown in the inset, where there is obvious rate suppression between 200 and 500 ms, the two-tone segment. At a SUP intensity of 80 dB SPL, a phase-specific suppression occurred in the
rise to significant suppression. For any one fiber (with SR > 10/s), the threshold of synchronization to the SUP tone in the two-tone segment was usually the lowest (most sensitive), while the SUP-alone rate threshold was highest. The threshold of suppressor synchronization in the SUP-alone segment and the threshold of rate suppression fell somewhere in between.

5. In some low-SR fibers, complete suppression can be seen. In general, it is more difficult to achieve complete suppression with either very low- (≤ 100 Hz) or high-frequency (≥ 2000 Hz) suppressors.

4.2. Comparisons with previous AN two-tone suppression studies

4.2.1. Phase of suppression

There are very few studies of the temporal aspects of 2TS in the AN-fiber literature (Romahn and Boerger, 1978; Sachs and Hubbard, 1981; Sellick et al., 1982; Patuzzi et al., 1984a). In the Romahn–Boerger study, a 50-Hz tone was used to provide biasing for a short train of tone bursts at CF placed at different phases of the 50-Hz tone. They found that in only 7% of the fibers were the discharges due to the CF tone burst affected by the biasing tone. This result is obviously at variance with other studies and also with this study. Sachs and Hubbard (1981) studied the two-tone responses of AN fibers of cats, using low-frequency suppressors (≤ 1 kHz). Most of the fibers they studied had CFs above 5 kHz. For 500- and 100-Hz suppressors, there are usually two phases of suppression: a major one at lower intensities, and also a minor one at higher intensities. They concluded that at low SUP intensities the phase of the SUP tone which causes the instantaneous rate to increase when presented alone causes a rate decrease when added to a CF tone. This corresponds to a zero suppression phase-lead in our case. Such zero suppression phase-lead cases also exist in our data, but only in small numbers (Fig. 5B,D). Since Sachs and Hubbard (1981) did not show population data, it is difficult to compare the phases from their study directly with ours, particularly since the data which they published display considerable scatter. For example, in one of their low-CF examples (1500 Hz), the fiber showed a suppression phase-lead of 1/4 cycle with a 50-Hz suppressor (their Fig. 9), which agrees with the major trend in our comparable data (e.g., Fig. 5A).

Sellick et al. (1982) and Patuzzi et al. (1984a) recorded from the ganglion cells of guinea pigs, in the high-CF region (> 10 kHz), while using a 40-Hz SUP tone. They observed suppression patterns similar to those of Sachs and Hubbard (1981), a major suppression which appeared at lower intensities and a minor one at higher intensities. At lower intensities, the two-tone response was enhanced at one phase and suppressed at another. There was no example in their papers in which the SUP-alone excitation phase and the 2TS phase were collected at the same intensities. If the SUP-alone excitation phases at higher intensities are used, the two examples they showed (Figs. 4 and 5 of Sellick et al., 1982) would give suppression phase-lead values of about +1/4 and −1/4 cycles, respectively. Although we have a few examples of −1/4 cycle suppression phase-lead in our 50-Hz data for low-frequencies fibers (Fig. 5A), their +1/4 cycle suppression phase-lead example is much more in keeping with what we observed. Again, lack of population data in their work prevents further comparison.

Although different SUP frequencies were used, there is a common feature in the studies of both Sachs and Hubbard (1981) and Sellick et al. (1982). Both groups concluded that zero suppression phase-lead was a general finding and presented an example to support their conclusion. However, both groups also presented data with quite different phase relationships. Based on our more extensive sample, we believe our data to be more general.

4.2.2. Two-phased suppression pattern

In studies by Sachs and Hubbard (1981) and by Sellick, Patuzzi and colleagues, the two-phase suppression pattern was a general characteristic. In our study, we did not see this pattern in all fibers. Instead, we found a CF dependence of the occurrence of the secondary suppression: a large percentage of high-CF fibers (> 2 kHz) showed secondary suppressions while only a small number of low-CF fibers did. Considering the fact that in previous studies data were collected only or mainly from high-CF regions, and that higher SUP intensities were used (which probably would cause more secondary suppressions), our results are probably not significantly different from previous studies in this regard. For the fibers with higher CFs, we did not find any secondary suppressions with suppressors of 1000 Hz or above, which basically agrees with Sachs and Hubbard (1981) who ‘rarely’ saw secondary suppressions with a 1000-Hz suppressor. We found only a few cases of secondary suppressions when using 500-Hz suppressors; while for Sachs and Hubbard (1981) the secondary suppression seems to be a general characteristic at that SUP frequency. However, in their 500-Hz examples, the fibers were responding strongly to the SUP-alone tone (their Fig. 2). Thus, the patterns they saw might be due to a combination of CF suppression and the response to the SUP-alone tone, rather than being a pure suppression pattern.

One question concerning the two-phased suppression pattern is its relationship with ‘peak-splitting’ in single-tone responses (Cai and Geisler, 1996a), since both types display more than one peak (valley) in a period histogram. Our paradigm (Fig. 1) enabled us to study the single-tone response (to the SUP-alone tone) and two-tone response of a fiber quasi-simultaneously. In our data, there are total of 63 fibers showed secondary suppressions at one or more SUP frequencies, and total of 45 fibers showed peak-splitting in response to one or more SUP tones (cf., Cai and
Geisler, 1996a). Only 17 fibers showed both. The secondary suppressions mainly happen in fibers with CF greater than 2 kHz (Table 1), while peak-splitting mainly happens in fibers with CF less than 2 kHz (Cai and Geisler, 1996a). Besides, the distances between two suppression phases are always about 1/2 cycle away (Fig. 9) and we never saw 3-phased suppression patterns. In single-tone peak-splitting, the two peaks are not necessarily 1/2 cycle away, and more than two peaks are often seen in 1 cycle of the SUP tone. These differences suggest that the two phenomena are not closely related. A similar conclusion was also reached by Sachs and Hubbard (1981).

4.2.3. Effect of CF intensity

Our observation that the threshold of low-side suppression is only a weak function of CF intensity (cf., Figs. 11 and 12) is consistent with the reports of others. Although they used somewhat different paradigms, Abbas and Sachs (1976) also showed low-side suppression thresholds which were only a weak function of CF intensity. For example, in their Fig. 3, the suppression threshold (for a 500-Hz suppressor) increased by only about 10 dB when the CF tone (at 6.2 kHz) was increased by 30 dB. Also consistent with our observation is the demonstration by Schmidt (1982) that the threshold for low-side suppression is relatively independent of both fiber CF and its threshold.

We also observed that the phase of maximum suppression generated with a low-side suppressor seems to be independent of CF intensity (cf., Figs. 11 and 12). A similar independence of suppression phase from CF level is seen in the data of Patuzzi et al. (1984a) and Sachs and Hubbard (1981). The latter paper also shows data similar to our Fig. 12, wherein the CF tone turns the tables and does some suppressing of its own, reducing certain components in the responses that are excited by the SUP-alone tone.

4.2.4. Relationships among synchrony, excitation and suppression

Javel et al. (1983) studied the two-tone synchrony suppression in the AN fibers of cats, using synchrony as an indicator. Although we used a different measure of suppression (reductions in discharge rate), much of the data in the two studies should be comparable, for the suppression thresholds determined by those two measures should be virtually identical (the main component in a response cannot be reduced without reducing the discharge rate also). As expected, our data which show suppression threshold as a function of SUP-tone rate threshold (Fig. 14) are very similar to theirs (their Fig. 7a). Both data sets show that, for low-frequency suppressors (the high-frequency points in their data), the suppression threshold is almost always lower (less intense) than the rate threshold to the SUP-alone tone.

What comes as a surprise are the differences observed when synchronization threshold (for the SUP-alone tone) is used as the independent variable. In their data (Fig. 8a) the suppression threshold is almost always greater (more intense) than the synchronization threshold. By contrast, only a minority of cases followed that pattern in our data (Fig. 13). We feel that this discrepancy is at least partially due to the fact that their SUP tones were often placed in the tip region (where thresholds were low) while ours were always placed at frequencies far below CF (where thresholds were high). Such differences can be important. In their Fig. 9a, for example, much smaller differences are seen between the synchronization and suppression thresholds of a 700-Hz fiber at low SUP frequencies (50 and 100 Hz) than at those near CF. What is new in our data is the finding that the threshold for low-frequency modulation of AN-fiber responses to CF tones is almost always the lowest (most sensitive) of all thresholds. In other words, in order for low-side suppression to occur, the intensity of the SUP tone had to be greater than the minimum needed to modulate the neuron’s responses to the CF tone. Moreover, the suppressor at this minimum intensity might also modulate spontaneous activity when presented alone, but need not do so. Such relationships provide stringent tests for models of low-side suppression (see Cai and Geisler, 1996c).

4.3. Comparisons with BM two-tone suppression studies

4.3.1. Suppression patterns on the BM

There have been several studies of 2TS in the basal region of the BM (Patuzzi et al., 1984b; Ruggero et al., 1992; Rhode and Cooper, 1993; Nuttall and Dolan, 1993). All except that of Nuttall and Dolan (1993), which used suppressors with frequencies close to CF, provide suppression patterns comparable with those observed on AN. Patuzzi et al. (1984b) studied the two-tone responses of the guinea pig’s BM with a low-frequency SUP tone (33 Hz). Although their relatively insensitive Mössbauer method prevented them from obtaining the fine temporal details of the waveforms, they were able to show two phases of suppression in 1 cycle of the SUP tone: a major one which corresponded to maximum displacement of the BM towards ST and a minor one corresponding to maximum SV displacement. Using a velocity-sensitive laser interferometer, Ruggero et al. (1992) studied chinchilla BM responses, with higher SUP frequencies (300–500 Hz). They also found a similar two-phased suppression pattern in their preparation, but the two suppression phases corresponded to maximum BM velocity towards ST and SV, respectively. Recently, Rhode and Cooper (1993) used a displacement-sensitive laser interferometer to study the BM response of the hook region of the cat. In one of their examples, they used a 1000-Hz SUP and 34-kHz CF tone. The basic response pattern was similar to that of the previous two studies, i.e., a major suppression at lower SUP intensities and also a minor one at higher SUP intensities. The major suppression roughly corresponded in
phase to BM displacement towards ST. In all three studies, and particularly the latter two which used the much more sensitive laser interferometer, the temporal distance between the two suppression phases was about 1/2 cycle.

In many respects, the suppression patterns which characterize BM vibrations are qualitatively very similar to those exhibited by our AN data. In all three sets of comparable BM data, as well as in our AN data, two phases of suppression occur: first a major suppression, and then at higher intensities, a minor one appears about a half-period away. These patterns of suppression can be readily reproduced with models of the cochlea which utilize feedback processes from OHCs which have nearly symmetrical input–output (transfer) functions (cf., Geisler, 1992; Cai and Geisler, 1996c).

Also similar are the phases of major suppression seen in our study and in the BM study of Ruggiero et al. (1992). Their maximum suppression, obtained with 300- and 500-Hz suppressors, occurred at approximately the instants of maximum velocity towards SV. With a 200-Hz suppressor (our closest comparison), the major suppressions exhibited by high-CF fibers lagged that velocity by about 45° (Fig. 4C). Given the uncertainties involved in our estimates of BM phases (cf., Cai and Geisler, 1996a), this agreement seems satisfactory.

However, there are also some quantitative differences between the BM and our AN data. For instance, Patuzzi et al. (1984b), using a 33-Hz suppressor, found the major suppression to occur at a phase which corresponded to the maximal deflection of the BM towards ST. By contrast, the major suppressions in our data caused by a suppressor of comparable frequency (50 Hz) were estimated to have occurred about half a period later, when the BM was maximally deflected towards SV (Fig. 4A). Intensity differences may play a role here, as their BM data were taken with high-intensity suppressors (e.g., >110 dB SPL), while our intensities were limited to 95 dB SPL. Perhaps the approximately 180° phase shifts which have been observed in the single-tone responses of AN fibers at higher intensities (e.g., Ruggiero and Rich, 1988) have a counterpart in suppression phases as well.

Another quantitative difference between BM and AN suppression data concerns the SUP frequencies at which two phases of suppression occur. In our AN data, we never saw secondary suppressions with SUP frequencies greater than 500 Hz, and rarely did Sachs and Hubbard (1981) with a 1000-Hz suppressor. Yet Rhode and Cooper (1993) commonly measured two phases of suppression in BM vibrations using a 1000-Hz suppressor. One possible explanation for this difference is that in those high-CF cases suppression and excitation can be easily confused: the high-frequency CF (>3 kHz) components in the IHC potentials (which carry the information of CF suppression produced at the BM stage) are attenuated by the basolateral membrane filter of IHC, and there are strong SUP components in the IHC potentials (cf., Cai and Geisler, 1996c). Nevertheless, this difference must be treated as tentative, since our sample of fibers innervating the hook region of the cochlea (CF > 30 kHz) is very small.

The largest quantitative differences between the BM and AN suppressed responses, however, concern the overall levels of response. For their part, AN fibers can be strongly suppressed over long periods of time by a low-side suppressor, even totally shut off (cf., Fig. 16). By contrast, the instantaneous amplitudes of BM vibrations achieved using such suppressors apparently always exceed, at some phase, a level greater than that produced by the CF tone alone (for documentation, see Cai and Geisler, 1996b). That is, at least sometime during each cycle of any particular low-side SUP tone, regardless of its intensity or frequency, the amplitude of the BM vibrations becomes greater than that produced by the unsuppressed CF tone. Crudely put, the final filter in the classical two-filter model of AN suppression (Pfiffner, 1970) appears to be missing on the BM. The implications of this absence for our understanding of the cochlea's suppressive mechanisms are addressed in the third paper of this series (Cai and Geisler, 1996b).

4.4. Characteristics of the suppressed responses

4.4.1. Difference between basal and apical responses

There have been many indications that the apical and basal regions of the cochlea may be working differently (e.g., Sewell, 1984; Ohlemiller and Siegel, 1994; Cooper and Rhode, 1995). In this study, we also found some differences between the two-tone responses of fibers located in different cochlear regions. In particular, fibers with higher CFs tend to show more secondary suppressions (Table 1) and the threshold differences between the major and minor suppressions are usually smaller. These differences suggest that the transfer characteristics of the OHCs are more symmetrical in the basal region (for explanation, see Cai and Geisler, 1996c). This in fact agrees with the differences observed in the in-vivo recordings from single OHCs in different cochlear regions (e.g., Dallos, 1986; Russell et al., 1986). The fact that no fibers with CFs near 2 kHz showed secondary suppressions in our data (Fig. 9) suggests a division around 2 kHz. The differential rates of growth of suppression for both low- and high-side suppressions which is observed between basal and apical fibers also seems to have a division line near 2 kHz (Delgutte, 1990). Differences in the slopes of AN-fiber spatial tuning curves also suggest a division in character near this same CF (Geisler and Cai, 1996). Thus, there is growing evidence that the basal and the apical cochlea are working in different ways, at least quantitatively.

4.4.2. Variation in the phase data

Although both the phase of suppression and suppression phase-lead data showed clear trends, there is some scatter-
ing in the data points (Figs. 4 and 5). The scatter in the suppression-phase data becomes more obvious at higher SUP frequencies (500 Hz in Fig. 4D; also see Cai, 1995 for 1000- and 2000-Hz data), as it does in the phase of excitation to the SUP-alone tone (Cai, 1995; Cai and Geisler, 1996a). Such wide variation in the phases of neural excitation to low-frequency tones is not uncommon, as Ruggero (1995) has clearly shown similar variability for chinchilla primary fibers. These variations are caused, at least in part, by the variations in synaptic delay and neural travel time, as reflected in the variations of click latency of those fibers (cf., Fig. 1–3 of Cai, 1995). Although such variations are small in time, they convert to large variations in phase at higher frequencies (> 200 Hz). Apparently the same variations affected both the phases of suppression and excitation to the SUP-alone tone, as the phase-lead measure, which is the difference of the two, showed much less variation at those higher SUP frequencies (Fig. 5D–F).

One particular type of variation in the phase data are the points which are about 1/2 cycle away from the bulk. Such unusual phase values existed in the plots of phase-lead, phase of suppression and phase of excitation to the SUP-alone tone (Figs. 4 and 5; also see Cai, 1995; Cai and Geisler, 1996a). The unusual suppression phase-lead values are mostly caused by unusual phases of responses to the SUP-alone tone (cf., Table 2-1 of Cai, 1995). In only a small number of our cases was the variability caused by unusual phases of suppression. In a few other cases, both the phase of suppression and the phase of response to SUP tone are outside their usual ranges, but their effects canceled each other, giving a suppression phase-lead value in the usual range. Thus it seems that the determinants of the phases of suppression and excitation evoked by the SUP tone are somewhat independent. This view is supported by our examples of neighboring fibers (with similar CFs) which responded with similar phases to the 200-Hz SUP-alone tone, but showed different suppression patterns (Fig. 10). Discussion of possible mechanisms is given in the third paper in this series (Cai and Geisler, 1996c).

4.4.2.1. Dependence on suppressor frequency. There are several aspects of suppression that are dependent upon the SUP frequency. One of them is the phase of suppression and suppression phase-lead. For some fibers, the phase of suppression or the suppression phase-lead is outside the normal range at one frequency but not at others. For suppressors of 200 Hz or less, the suppression phase-lead is also CF dependent: at both high- and low-CF ends, the suppression phase-lead tends to be bigger. Another phenomenon dependent upon SUP frequency is secondary suppression, which does not appear to happen at all SUP frequencies. In particular, it never occurred in our 1000- and 2000-Hz data.

Another effect of SUP frequency concerns the values of the ‘suppression phase-lead’ which are produced. The data in Fig. 5 show that the average value of this suppression phase-lead is about 90° for suppressors less than 200 Hz, but nearly 180° for higher-frequency suppressors. There are, no doubt, many possible explanations for this progression. One of them relates to the observation that IHCs (and hence AN fibers) appear to respond to the velocity of BM displacements at low frequencies (e.g., < 500 Hz), but to the amplitude of BM displacements at higher frequencies (Sellick and Russell, 1980; Nuttall et al., 1981). Since velocity is the derivative of displacement, and hence has a 90° phase-lead relative to displacement phase, the loss of this phase-lead at higher frequencies should produce a 90° phase lag in the phase of excitation produced by the suppressor. This increased phase lag of the excitation in turn produces very neatly the desired 90° increase in the ‘suppression phase-lead’ of the maximum suppression (which is, remember, measured relative to excitation phase).

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References