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Research paper

Analysis of responses to noise in the ventral cochlear nucleus
using Wiener kernelsAlberto Recio-Spinoso^{a,b,*}, Pim van Dijk^{c,d}^a *University of Wisconsin-Madison, Department of Physiology, 1300 University Avenue, Madison, WI 53706, USA*^b *Leiden University Medical Centre, ENT Department, P.O. Box 9600, 2300 RC Leiden, The Netherlands*^c *Department of Otorhinolaryngology, University Medical Centre Groningen, The Netherlands*^d *School of Behavioural and Cognitive Neurosciences, University of Groningen, P.O. Box 30001, 9700 RB Groningen, The Netherlands*

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Abstract

Responses to noise were recorded in ventral cochlear nucleus (VCN) neurons of anesthetized chinchillas and cats, then analyzed using Wiener-kernel theory. First-order kernels, which are proportional to reverse-correlation functions, of primary-like (PL) and primary-like with notch (PLN) neurons having low characteristic frequency (CF) are similar to those obtained in auditory nerve fibers (ANFs). Such kernels consist of lightly damped transient oscillations with frequency equal to the neuron's CF. The first-order kernel of high-CF PL and PLN neurons displays no evidence of tuning to CF. Second-order kernels of the aforementioned VCN neuron types also resemble those in the nerve, irrespective of CF. In general, first- and second-order Wiener kernels of chopper neurons are similar to those obtained in high-CF ANFs. This is likely the consequence of the poor phase-locking capabilities to near-CF tones exhibited by chopper neurons. By analyzing second-order kernels using singular-value decomposition, it was possible to estimate group delays for the entire neuronal population, regardless of the neuron's type or CF. This was done by analyzing the highest-ranking singular vector (FSV). Amplitude values of FSVs in chopper neurons in the cat are substantially larger than in high-spontaneous ANFs.

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Keywords: Wiener kernels; Cochlear nucleus; Nonlinear analysis**1. Introduction**

Following the introduction of the reverse correlation (revcor) technique to the field of auditory physiology by de Boer (1967), several studies have applied this technique to the responses of auditory nerve fibers (ANFs) to noise in both mammals (de Boer and de Jongh, 1978; Carney and Yin, 1988; Carney et al., 1999; Evans, 1977; Møller, 1977) and non-mammals (Van Dijk et al., 1994). A revcor function represents the average noise-stimulus waveform preceding an action potential, or spike. Revcor functions, computed from the responses of ANFs with low character-

istic frequency (CF), reveal tuning characteristics similar to those obtained using tuning curves. By contrast, revcor functions of high-CF ANFs fail to reveal any significant tuning. This results from the poor phase-locking of ANFs to responses to high-frequency tones (Johnson, 1980b).

Tuning properties of high-CF ANFs can be calculated using Wiener-kernel analysis (Van Dijk et al., 1994). The first-order Wiener kernel, which is proportional to the revcor function (Van Dijk et al., 1994), is identical to the impulse response of a linear system (Marmarelis and Marmarelis, 1978). Second-order Wiener kernels are non-existent for linear systems, but have significant values for nonlinear systems with even nonlinearities. Because of those even-order nonlinearities, which are a fundamental component of envelope detection, Fourier analysis of such kernels has revealed tuning characteristics of high-CF ANFs in both frogs (Van Dijk et al., 1994; Yamada and

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Lewis, 1999) and mammals (Lewis et al., 2002; Recio-Spinoso et al., 2005).

As a complement to our previous study of Wiener kernels in ANFs of the chinchilla, we decided to analyze the responses to noise of neurons in the ventral part of the CN (VCN) in both chinchilla and cat. ANFs project to the cochlear nucleus, whose anatomy and physiology are well understood. The CN is divided into a dorsal and a ventral part (DCN and VCN, respectively). Whereas ANF responses are relatively similar to each other, each type of CN neuron displays a particular pattern as seen in post-stimulus time histograms (PSTHs) computed from their responses to CF tones (Rhode and Smith, 1986). Three of the most common PSTHs obtained in the CN are the primary-like (PL), primary-like with notch (PLN) and chopper neurons. In general, PL and PLN responses originate from spherical and globular bushy cells, respectively. Chopper responses are associated with stellate cells. Most of our recordings in the VCN likely originated from bushy and stellate cells.

Whereas the noise techniques mentioned above have had success in the auditory periphery, their application to the CN has had mixed results (For a theoretical discussion of the applicability of Wiener kernels to the auditory system see Johnson, 1980a). Van Gisbergen et al. (1975) obtained revcor functions from the responses to noise of low-CF cochlear nucleus (CN) neurons in the cat. Their findings indicate that frequency selectivity measured using revcor functions is similar to that gathered from single tones, which implies that frequency selectivity results from of a linear process. The study by Wickesberg et al. (1984) is the first and only published application of the first- and second-order Wiener kernels to the mammalian CN. That study included only one chopper and six primary-like neurons of the anteroventral part of the VCN (AVCN), all the neurons having CFs < 1400 Hz. Although second-order Wiener kernels obtained from the responses to noise of those neurons failed to show any visible temporal structure, Fourier analysis of those kernels showed a significant amount of tuning to the neuron's CF. Because second-order Wiener kernels did not predict very well the responses of low-CF neurons, Wickesberg et al. (1984) concluded that the Wiener kernels were of limited usefulness. Furthermore, they did not study the responses of high-CF CN neurons.

To retrieve amplitude and phase information from the responses of high-CF cochlear nucleus neurons, second-order Wiener kernels were further analyzed using single-value decomposition, as pioneered by Lewis and colleagues (Yamada et al., 1997; Yamada and Lewis, 1999). Because of the phase-locking capabilities of VCN neurons (e.g., Rhode and Smith, 1986; Blackburn and Sachs, 1989), we expect fewer stimulus-related components in first-order Wiener kernels of VCN neurons, at least for CFs > 1 kHz, than in ANFs. Second-order Wiener kernels of VCN neurons should be at least as prominent as those computed from ANFs. This is because second-order kernels of ANFs depend on their envelope detection capabilities, and the

enhancement of those capabilities in the VCN is well documented (Møller, 1974; Frisina et al., 1990; Rhode and Greenberg, 1994a).

2. Methods

Results from this paper come from two cats and four chinchillas. Cats were anesthetized with an initial injection of sodium pentobarbital (75 mg/kg, i.p.), supplemented with additional smaller intravenous doses of pentobarbital to maintain a complete absence of limb-withdrawal reflexes. The latter doses were applied through a catheter inserted into the femoral vein. In the chinchillas, anesthesia was induced with an injection of sodium pentobarbital (50 mg/kg, i.p.), supplemented with smaller intraperitoneal injections of pentobarbital. The procedures to access and record from the CN are similar for both species as described below.

Rectal temperature of the animals was maintained around 37 °C with a servo-controlled electrical heating pad. Tracheal intubation allowed for forced respiration, which was usually not performed. In cats, resection of the pinna allowed visualization of the tympanic membrane and insertion of the earpiece; in chinchillas, part of the bony external ear canal was also removed to visualize the tympanic membrane. After insertion of a tracheal cannula, the left pinna was removed and the bulla was vented with 20 cm of a 1-mm plastic tube. Following removal of the overlying cerebellum, the left cochlear nucleus was covered with agar. To further reduce brain pulsations, a chamber was mounted over the skull, filled with mineral oil and then sealed with a cover glass. Recordings were done with KCl-filled micropipettes whose impedances were 10–20 M Ω . The location of the AVCN was verified histologically in one animal, in which a current (6 μ A, 6 s) was passed via the recording metal electrode. Recordings from the posteroventral cochlear nucleus (PVCN) were obtained after advancing the electrode through the dorsal cochlear nucleus (DCN), which is easily identified. In both the DCN and PVCN, the best frequency decreases as the electrode moves ventrally. Therefore, a transition from low to high CF served as an indication that the recording electrode had entered the PVCN.

In two chinchillas, recordings were also taken from the ventral acoustic stria (VAS), or trapezoid body. Axons in the VAS are thought to originate from neurons in the AVCN (Smith et al., 1991). The VAS was accessed dorsally by inserting an electrode at least 4 mm through the floor of the IV ventricle.

The protocol for these experiments was approved by the Animal Care and Use Committee of the University of Wisconsin-Madison and meets NIH guidelines.

2.1. Unit classification

Following the determination of the neuron's CF using a response-area paradigm, a 60-dB SPL short tone (60 ms) at

CF was presented to the neuron. VCN units were classified according to criteria provided by two groups (Blackburn and Sachs, 1989; Rhode and Smith, 1986). These criteria are based on the shapes of post-stimulus time histograms (PSTHs), obtained from responses to 60 dB SPL short tones at CF, and on regularity analysis (Blackburn and Sachs, 1989). Most of the VCN neurons collected in this study fall in one these four categories: primary-like (PL), primary-like with a notch (PLN), choppers, and onset choppers (OC). The PSTH of PL neurons resembles that of ANFs, hence their name. The histogram of PLN neurons contains a notch that results from the coincidence of the initial refractory period of the neuron and could last several milliseconds (Blackburn and Sachs, 1989). Labeling studies (e.g., Rhode and Smith, 1986) have identified PL and PLN neurons as spherical and globular bushy cells, respectively. Chopper neurons have PSTHs with multiples modes following the stimulus onset; such modes are not a function of stimulus frequency (Rhode and Smith, 1986). Chopper neurons have been classified as stellate cells (Rhode and Smith, 1986). OC neurons have a large dynamic range and also display a multi-peaked (2–4) response pattern at the onset (Rhode and Smith, 1986). OC are stellate cells.

Since most of our recordings were obtained using micropipettes, several heuristic rules were employed to differentiate between ANFs and VCN neurons (Rhode, 1998). Occurrences of bipolar waveforms and/or of single-tone suppression, above or below CF, are properties of CN neurons and were used to distinguish ANFs from PL or PLN neurons. The shapes of the interspike interval and PST histograms were also used to classify the type of neuron.

2.2. Acoustic stimuli and experimental protocol

A modified RadioShack supertweeter speaker presented the stimuli. After in situ calibration of the acoustic system (50–20,000 in 50 Hz steps) using a Brüel & Kjær 0.5" condenser microphone, stimuli were digitally compensated by the transfer function of the acoustic system being presented. A routine (randn) in Matlab™ was used to generate 50,000 independent samples of white Gaussian noise. The samples were stored in the experimental computer (VAX station) and played at a rate of 50,000 samples/s. The original Matlab™ array was the same for all the experiments in this paper. Each neuron was stimulated with a 1-s sample of this noise, presented 300 times every 2.5 s. Each stimulus presentation was different from the others; this was achieved by shifting by a fixed amount, after each presentation, the starting point of the array to be played. Some neurons were stimulated at more than one stimulus level.

2.3. Computation and processing of the Wiener kernels

Only the zeroth-, first- and second-order Wiener kernels were computed in this work. These were calculated from the spike times and the noise sample stored in the com-

puter. Let $x(t)$ represent the Gaussian white noise waveform and $y(t)$ be the spike train measured in a cochlear nucleus neuron. It is usually considered that all of the information carried by the spike train is in the time of occurrence of each individual spike. Hence, $y(t)$ can be expressed as follows:

$$y(t) = \sum_{i=1}^N \delta(t - t_i) \quad (1)$$

where $\delta(t)$, the Dirac-delta function, equals one if a spike has occurred at time t and zero otherwise, and N is the total number of spikes evoked by the noise stimulus.

The zeroth-order Wiener kernel represents the average output of the system (Schetzen, 1989):

$$h_0 = \langle y(t) \rangle \quad (2)$$

$$h_0 \cong \frac{1}{T} \int_0^T y(t) dt \quad (3)$$

where T is the stimulus duration

$$h_0 = \frac{1}{T} \sum_{i=1}^N \int_0^T \delta(t - t_i) dt \quad (4)$$

$$h_0 \cong N_0 \quad (5)$$

i.e., h_0 represents the average firing rate $N_0 = \frac{N}{T}$.

The first-order Wiener kernel was obtained by cross-correlating (Schetzen, 1989) the input, $x(t)$, to the output, $y(t)$:

$$h_1(\tau_1) = \frac{1}{A} \langle y(t)x(t - \tau_1) \rangle \quad (6)$$

$$h_1(\tau_1) \cong \frac{1}{AT} \sum_{i=1}^N \int_0^T \delta(t - t_i)x(t - \tau_1) dt \quad (7)$$

$$h_1(\tau_1) = \frac{N_0}{A} R_1(\tau_1) \quad (8)$$

where A is the power spectral density of the noise stimulus and

$$R_1(\tau_1) = \frac{1}{N} \sum_{i=1}^N x(t_i - \tau_1) \quad (9)$$

is the reverse correlation function (de Boer, 1967; Van Dijk et al., 1994).

Using the previous equations, one can interpret the first-order Wiener kernel as the average value of the stimulus, $x(t)$, at a time τ_1 before the occurrence of a spike, normalized to the stimulus power spectral density.

The second-order Wiener kernel is obtained by second-order cross-correlation between $x(t)$ and $y(t) - h_0$ (Schetzen, 1989; Van Dijk et al., 1994):

$$h_2(\tau_1, \tau_2) = \frac{1}{2A^2} \langle [y(t) - h_0]x(t - \tau_1)x(t - \tau_2) \rangle \quad (10)$$

$$h_2(\tau_1, \tau_2) \cong \frac{1}{2A^2 T} \int_0^T \left(\sum_{i=1}^N \delta(t - t_i) - N_0 \right) x(t - \tau_1)x(t - \tau_2) dt \quad (11)$$

$$h_2(\tau_1, \tau_2) = \frac{N_0}{2A^2} [R_2(\tau_1, \tau_2) - \phi_{xx}(\tau_2 - \tau_1)] \quad (12)$$

where $\phi_{xx}(\tau)$ is the autocorrelation function of the input signal $x(t)$ and

$$R_2(\tau_1, \tau_2) = \frac{1}{N} \sum_{i=1}^N x(t_i - \tau_1)x(t_i - \tau_2) \quad (13)$$

is the second-order reverse correlation function. At $\tau_1 \neq \tau_2$, the value of the second-order kernel is proportional to the firing rate. The second-order reverse correlation is the mean of the product of the value of the stimulus $x(t)$ at two times, τ_1 and τ_2 , before the occurrence of a spike.

For linear systems, the first-order Wiener kernel $h_1(t)$ is identical to the impulse response. For nonlinear systems, the first-order kernel is only a component of the impulse response, which contains contributions from higher kernels. In general, the first-order Wiener kernel of a nonlinear system differs from the linear part of the system and might contain some of the system's nonlinearities (Marmarelis and Marmarelis, 1978). Second-order Wiener kernels give a measure of the nonlinear interaction, or “cross-talk,” between the responses to two impulses (Marmarelis and Marmarelis, 1978). In other words, the second-order kernels give a measure of the deviation from superposition due to the nonlinearity of the system. The properties of second-order Wiener kernel have also been shown to be related to the envelope detection properties of auditory nerve fibers (Yamada and Lewis, 1999).

First- and second-order Wiener kernels were obtained by cross-correlation in the time domain, using ad-hoc computer programs coded in Matlab functions. First-order kernels were computed using 256, 512 or 1024 bins. Second-order kernels were computed using $N \times N$ square matrices, where N is the size of the first-order kernel. Both first- and second-order kernels were zero-phase low-pass filtered. This was done using the Matlab function `filtfilt` for first-order kernels and a Matlab implementation of a two-dimensional Butterworth filter for the second-order kernel. The (filtered) second-order kernels were subjected to eigenvector decomposition (Yamada et al., 1997; Yamada and Lewis, 1999; Lewis et al., 2002) using the Matlab function `eig`:

$$h_2 = USU^T \quad (14)$$

where U and S square matrices of the same size as h_2 , and T indicates the transpose operator. The columns of U are called the eigenvectors, respectively. S is a positive diagonal matrix. Hence, h_2 can be decomposed as follows:

$$h_2 = \sum_{i=1}^N d_i u_i u_i^T \quad (15)$$

where the eigenvector u_i is a column element of U (i.e., $U = [u_1, u_2, \dots, u_N]$), and d_i represents the corresponding eigenvalue. The eigenvector u_i associated with the largest eigenvalue (i.e., the first singular vector) will be of great use in this paper. The first singular vector (FSV) accounts for the largest percentage of the total energy of the second-order kernel. For the sake of continuity with our previous

work (Recio-Spinoso et al., 2005), we refer to the eigenvectors as singular vectors since for real symmetric matrices – such as second-order Wiener kernels – they are the same. Eq. (15) makes clear that the contribution of the eigenvector u_i to h_2 is the same regardless of its sign or polarity.

3. Results

Forty four neurons, 24 recorded from cats and 20 from chinchillas, were used for the results in this paper. At least one level of noise stimulus was presented to all of these neurons.

3.1. General characteristics of first- and second-order Wiener kernels

Fig. 1 displays first- and second-order Wiener kernels for two low-CF neurons in the CN of the chinchilla. The time domain waveform h_1 for the PL neuron (Fig. 1A) is a transient but relatively undamped oscillation, characteristic of a bandpass system. The period of this oscillation (1.11 ms, thin line in Fig. 1A) is approximately the inverse of the neuron's CF, which was obtained from responses to single tones. This waveform is very similar in shape to the first-order Wiener kernel of an auditory nerve fiber (Recio-Spinoso et al., 2005). By contrast, h_1 of a chopper neuron of similar CF does not contain any visible oscillation. The lack of oscillations is probably a consequence of the phase-locking capabilities of chopper neurons, which are inferior to those exhibited by PL neurons and ANFs (Rhode and Smith, 1986).

Figs. 1C and D show $h_2(\tau_1, \tau_2)$ for the PL and chopper neurons, respectively. In both cases, the kernels were computed from the same response to noise represented in Figs. 1A and B. Figs. 1C and D represent the projection of a 3D function onto a 2D plane. As is the case of second-order Wiener kernels for low-CF ANFs, the $h_2(\tau_1, \tau_2)$ function for the PL neuron (Fig. 1C) consists of the intersection of two waves moving in a direction parallel and perpendicular to the diagonal, creating a “checkerboard” pattern (Van Dijk et al., 1994). This type of pattern represents the existence of nonlinearities in the phase-locked responses (Lewis et al., 2002). By contrast, $h_2(\tau_1, \tau_2)$ obtained from the responses of a chopper neuron (Fig. 1D) consists mostly of waves in the direction parallel to the diagonal. The pattern of $h_2(\tau_1, \tau_2)$ for the PL neuron resembles that of a linear system followed by a square-law device (Marmarelis and Marmarelis, 1978). Adding a low-pass filter to the output of the nonlinear device just described creates a “sandwich model” (Van Dijk et al., 1994), which can be shown to have first- and second-order Wiener kernels similar to those displayed by the chopper neuron in Fig. 1 (Recio-Spinoso et al., 2005). In the Van Dijk et al. model (1994), the square-law device followed by the low-pass filter components constitute an envelope detector. Second-order kernels of high-CF neurons have

Fig. 1. First and second-order Wiener kernels of two cochlear nucleus neurons in the chinchilla. (A) Primary-like neuron (PLN) recorded from the ventral acoustic stria (VAS). Thin line under the waveform representing the first-order kernel, $h_1(\tau)$, indicates its period ($1/CF$). (B) $h_1(\tau)$ computed from the responses to noise of a low-CF chopper neuron. (C and D) The second-order kernel, $h_2(\tau_1, \tau_2)$, obtained from the responses of the PL and chopper neurons, respectively.

meaningful values because of the envelope detection properties of ANFs.

Figs. 2A and B feature $h_2(\tau_1, \tau_2)$ for two high-CF neurons in the chinchilla. Although the kernel in Fig. 2A was obtained from the responses of a PLN neuron, it shares many similarities with the kernels in Figs. 1D and 2B, which came from chopper neurons. In other words, both kernels consist mostly of waves in the direction parallel to the diagonal. However, the beginning of the oscillation of $h_2(\tau_1, \tau_2)$ for the chopper neuron occurs later than that measured in the PLN neuron. There are also differences in the duration of their oscillations, as $h_2(\tau_1, \tau_2)$ for the PLN neuron appears to last longer than the oscillations in the kernel of the chopper neuron. Note also that the $h_2(\tau_1, \tau_2)$ function shown in Fig. 2A displays a “two-lobe” pattern, with one lobe centered around $\tau_1 = \tau_2 = 3$ ms, and the other between 4 and 5.5 ms. This pattern was shown by several chopper, PL and PLN neurons in both cats and chinchillas.

Whereas the first-order Wiener kernels (not shown) for the neurons in Fig. 2 lack any indication of the neuron’s CF, the “slices” through $h_2(\tau_1, \tau_2)$ shown in Fig. 2C (PLN neuron) and D (chopper neuron) display undamped

oscillations. Fig. 2C displays the values of the kernel at $\tau_1 = 3$ ms, and Fig. 2D at $\tau_1 = 3.8$ ms. Periodicities in both waveforms (Figs. 2C and D) are approximately equal to the inverse of the neuron’s CF.

3.2. Singular-value decomposition of Wiener kernels

Fig. 3 displays the results of the SVD analysis of the second-order Wiener kernels of two neurons. For the low-CF neuron (Figs. 3A and C), a good match exists between the FSV (thick line) and h_1 (thin line). The first- and second-order Wiener kernels for this neuron are shown in Figs. 1A and C, respectively. In general, for low-CF neurons the magnitude of the Fourier transform of h_1 is similar to that of the FSV. The phase characteristics of h_1 and FSV (not shown) are, however, either very similar to each other or 180° apart. The difference in sign is due to the uncertainty in the polarity of the FSV (see Section 2). The FSV waveform for the high-CF neuron (Fig. 3B) resembles the waveforms of high-CF auditory nerve fibers (Recio-Spinoso et al., 2005). The second-ranked singular value is also displayed in the same figure (thin line). The waveforms of the FSV and second-ranked singular value are almost

Fig. 2. Projection of second-order Wiener kernels of high-CF PLN (A) and chopper (B) neurons onto a two-dimensional space. (C) Plot $h_2(\tau_1, 3 \text{ ms})$ obtained from the kernel of the PLN neuron. (D) Waveform representing $h_2(\tau_1, 3.8 \text{ ms})$ for the chopper neuron. Note that the time axes in this plot start at 2 ms.

identical, except for a phase difference of around 90° . This property of the singular values was originally found in auditory nerve recordings in the bullfrog (Yamada and Lewis, 1999). The magnitudes of the Fourier transform of FSV for both neurons have maximum peaks whose frequency match the location of the peaks obtained using single tones, as indicated by arrows in Figs. 3C and D.

The highest-ranking eigenvalues associated with chopper neurons in cats are usually larger than the eigenvalues of ANFs (Fig. 4A). The eigenvalues of high-spontaneous ANFs (filled inverted triangles in Fig. 4A) tend to be smaller than those obtained from the responses to noise of low-spontaneous ANFs (inverted open triangles in Fig. 4A). Similar analysis in the chinchilla (Fig. 4B), however, shows that the eigenvalues of chopper, PL and PLN neurons are very similar to each other and smaller than those computed in cats. We did not collect responses to noise of chinchilla ANFs for this work. Because second-order Wiener kernels are due to the existence of even-order nonlinearities, the strength of these kernels can be seen as a measure of envelope detection. The results in the cat, therefore, indicate that the envelope encoding capabilities of chopper neurons are stronger than those displayed by ANFs.

3.3. Wiener kernels across CF

Fig. 5A shows FSVs for several chopper neurons in the same cat, with the CF printed next to each waveform. Each FSV consists of a damped oscillation with an onset that increases as the CF of the neuron decreases. Fig. 5B displays the amplitude of the Fourier transforms of each of the FSVs in Fig. 5A. Neurons CFs, which were obtained using single tones, are also indicated with arrows. For these neurons, there is a good match between CF and the frequency at which the peak amplitude occurs. Similar results were found for our entire sample (Figs. 6A and B) in chinchillas and cats.

Fig. 5C presents a phase vs. frequency plot for each of the neurons in Fig. 5A. Near-CF group delays (i.e., the negative of the first derivative of the phase function) were gathered and show a tendency to increase as CF decreases (4.63, 3.15, 3.04, 2.43 and 2.74 ms, in ascending order of CF). Fig. 6C shows the near-CF group delays for our neuronal population, with squares ($\square$), triangles ($\triangle$) and inverted triangles (∇) representing choppers, PLs and PLNs, and ANFs, respectively. Filled symbols represent recordings from the VAS. The solid thin line represents the best fit to the near-CF group delays of ANFs from

Fig. 3. Singular-value decomposition of h_2 of a low-CF PL (A and C) and a high-CF PLN (B and D) neuron. Continuous thick lines in (A) and (C) represent the first-singular vectors (FSVs). Thin lines in (A) and (B) display the revcor function h_1 and the second-ranked singular vector, respectively. (C) Fourier transform magnitude of the FSV (thick line) and of h_1 (thin line) for the PL neuron. (D) Fourier transform magnitude of the FSV (thick line) and of the second-ranked singular vector (thin line). The PL neuron is the same shown in Figs. 1A and C. Note that the time axis of panel B starts at 2 ms.

our previous study in the chinchilla (Recio-Spinoso et al., 2005). Note also that the same function matches the group delays measured in the ANFs in the cat. The dashed line shows the same function plus a constant value of 1 ms. Such a line provides a good fit for the group delays in chopper neurons in cats (Fig. 6D) and to a lesser extent in the chinchilla (Fig. 6D).

When phase functions are computed from second-order Wiener kernels, their absolute value is arbitrary (e.g., Eq. (28) in Van Dijk et al., 1994). This also applies to the phase of singular vectors. First-order derivatives, such as group delay computations, however, are well defined.

3.4. Stimulus level effects on Wiener kernels

Effects of stimulus levels were studied mostly on chopper neurons since, in our experience, extracellular recordings from those neurons tend to be the most stable among all the VCN neuron types. We used the quality factor

($Q_{10\text{dB}} = \text{CF}/\text{bandwidth}$) and the group delay to quantify changes in the FSV due to changes in stimulus level.

Figs. 7A and B show the effects of increasing the stimulus level on FSVs of two chopper neurons. The stimulus level is printed next to each waveform. The FSV obtained from responses to the lower stimulus level (upper trace in each figure) has a “center of gravity” that is delayed relative to the one obtained using the louder stimulus (lower trace in Figs. 7A and B). Changes in near-CF group delays were also observed: 800 and 50 μs for the neurons in Figs. 7A and B, respectively.

The magnitude Fourier spectrum of the FSV also shows changes in tuning. Changes in $Q_{10\text{dB}}$ were observed in the results shown in Fig. 7C (3.2 and 3.1, for 12 and 52 dB, respectively) and in Fig. 7D (4.16 and 3.35, for 10 and 50 dB, respectively). There are also changes in the frequency at which the maximum occurs, this being more obvious in Fig. 7D than in Fig. 7C. Such frequency shifts are toward lower frequencies as the stimulus level increases.

Fig. 4. Highest-ranking eigenvalues plotted as a function of CF for a population of chopper (□), PL and PLN (△) and ANFs (▽) in cats (A) and chinchillas (B). Filled symbols indicate high-spontaneous ANFs.

4. Discussion

4.1. First-order Wiener kernels of VCN neurons

First-order Wiener kernels of PL and PLN neurons resemble the kernels of ANFs. Kernels of low-CF PL and PLN neurons contain oscillations whose frequency is similar to their CF. Although the existence of “frequency glides” in h_1 was not demonstrated in Section 3, it is obvious from some of those waveforms (Fig. 1A) that the instantaneous frequency of the oscillation changes over time, until it reaches a value similar to CF. Frequency glides were first shown by Møller and his group (Møller, 1977; Møller and Nilsson, 1979) in the revcor functions obtained from low-CF ANFs in rats. Later ANF studies in other species have confirmed the existence of those glides (e.g., cat: Carney et al., 1999; chinchilla: Recio-Spinoso et al., 2005).

Several authors (e.g., Rhode and Smith, 1986; Blackburn and Sachs, 1989) have shown that chopper neurons in the cat have synchronization indices to CF tones that are lower than those yielded by PL, PLN and onset neu-

rons. Similar results have been obtained from the responses of CN neurons to vowel-like sounds in both cats (Blackburn and Sachs, 1990) and chinchillas (Recio and Rhode, 2002). Therefore, the lack of stimulus-related components found in the h_1 waveforms of low-CF chopper neurons was not unexpected. In the case of high-CF neurons, h_1 showed no oscillation regardless of the VCN neuron type.

In some of our previous work (Recio-Spinoso et al., 2005) we showed that first-order Wiener kernels of ANFs contain a time structure that is related to the CF of the fiber. We did not find this type of fine structure in first-order kernels of VCN neurons. This is not surprising, because the amount of phase-locking to around-CF stimuli decreases in the CN relative to the auditory nerve (e.g., Rhode and Smith, 1986). Although for this work we did not use the chinchilla to collect responses to noise of ANFs, we did collect this type of response in a few ANFs of the cat. We did not find, however, a time structure related to CF in the waveforms of the first-order kernels. One possible explanation for this discrepancy could be species differences.

4.2. Second-order Wiener kernels

Second-order Wiener kernels were introduced to cochlear nucleus physiology by Wickesberg et al. (1984) in a study of the responses to noise of low-CF VCN neurons. In the temporal domain, it is impractical to compare the results of this study to theirs, in part because of the difficulty in discerning any pattern in the plots of h_2 presented by Wickesberg et al. (1984). Some possible explanations for their results were given in Recio-Spinoso et al. (2005). In their frequency domain results, however, evidence of CF tuning was clear.

Results of the present study showed that second-order Wiener kernels h_2 obtained from the responses of PL and PLN neurons are very similar to those obtained in ANFs:

- (1) h_2 s of low-CF neurons display a “checkerboard” pattern, with periodicity equal to CF.
- (2) For low-CF neurons, the FSV is almost identical to the reverse correlation function or h_1 .
- (3) For high-CF neurons, h_2 consists of oscillations parallel to the diagonal. Fourier analysis of those kernels shows the existence of CF tuning.

Chopper neurons have second-order Wiener kernels that resemble ANF kernels of mid- and high-CFs. As mentioned before, in response to CF tones chopper neurons yield lower synchronization indices than ANFs, PL and PLN neurons, which might explain why low-CF chopper neurons have h_2 functions that are similar to ANFs’.

The effects of increasing stimulus level on h_2 in VCN neurons resemble to the effects observed in ANFs (Recio-Spinoso et al., 2005). That is, as a result of an increase of stimulus level, FSVs show a decrease in their frequency selectivity (lower $Q_{10\text{dB}}$ values). The Fourier transform

Fig. 5. (A) FSVs of five chopper neurons in the same cat. (B) Fourier transform magnitude of the FSV shown in (A). Arrows indicate the CF estimated using single tones. (C) Fourier transform phases for the FSVs shown in (A), with (●) indicating the phase at CF. Note that the time axis in panel A start at 2 ms.

magnitude of FSVs also shows a change, toward lower frequencies, in the frequency associated with the peak amplitude. Using revcor functions, Møller (1983) showed similar effects as a result of increasing stimulus level in the responses to noise of ANFs in the rat. Kim and Young (1994) found similar effects in the cat. Changes in near-CF group delays were also observed as a function of stimulus level.

It is well known that PL and PLN neurons in the VCN share many of the properties of ANFs (e.g., Pfeiffer, 1966; Rhode and Smith, 1985). There are certain differences,

however, such as in the maximum amount of phase-locking, which can be larger for PL and PLN neurons than for ANFs (Joris et al., 1994). By contrast, the amount of phase-locking to CF tones displayed by chopper neurons is usually less than that yielded by ANFs (Rhode and Smith, 1986). Another difference in the processing of sounds between the CN and ANFs is in the encoding of amplitude-modulated sounds. Such encoding is enhanced in the CN relative to the auditory nerve (Møller, 1974; Frisina et al., 1990; Rhode and Greenberg, 1994a). Unlike ANFs, VCN neurons can also show single-tone rate sup-

Fig. 6. Plots of CFs obtained from Fourier analysis of the FSVs as a function of their CF computed from tones in chinchillas (A) and cats (B) for a population of chopper ($\square$), PL and PLN ($\triangle$), and ANFs (∇). Filled symbols indicate VAS recordings. Plots of near-CF group delays in chinchillas (C) and cats (D). Continuous lines in (C) and (D) correspond to the equation: $\tau_{CF} = 1.721 + 1.863 CF^{-0.771}$ (Recio-Spinoso et al., 2005), which represent the fit function to near-CF group delays in chinchilla's ANFs. Dashed lines in (C) and (D) show the values for $\tau_{CF} + 1$ ms in chinchillas and cats, respectively.

pression, at frequencies below and above CF (Rhode and Greenberg, 1994b). Because of the aforementioned differences between second-order neurons and ANFs, it was surprising that h_1 and h_2 functions of VCN neurons were quite similar to those produced by ANFs. The lack of significant differences in h_1 and h_2 among VCN neuron types was also unexpected.

The amplitude of the highest-ranking eigenvalues was shown to be larger, on average, for chopper neurons than for ANFs in the cat. As with second-order Wiener kernels, envelope detection depends on the existence of even-order nonlinearities; hence we consider the strength of the second-order kernels an indicator of the envelope detection properties of a neuron. Therefore, the results shown in Fig. 4A indicate that chopper neurons have better envelope detection capabilities than ANFs, particularly high-spontaneous ANFs. In a study of AM encoding in the cochlear nucleus, Rhode and Greenberg (1994a) found that synchronization to the envelope of AM sounds is better in the CN than in high-spontaneous ANFs. Our results are therefore consistent with Rhode and Greenberg's study.

Second-order Wiener kernels of certain VCN neurons show an extra amount of "ringing." For example, in

Fig. 2A, the kernel exhibits a "two-lobe" pattern, which is also seen in ANF kernels in the chinchilla and cat. Several other chopper, PL and PLN neurons displayed the same pattern in their second-order kernels. It is possible to decompose a second-order Wiener kernel into two sub-kernels (Lewis et al., 2002): an "excitatory" one, which reflects processes that produce increases in the instantaneous firing rate, and an "inhibitory" subkernel that yields decreases in the instantaneous spike rate. Preliminary analysis (not shown) of those kernels using SVD indicates that oscillations occurring during the second lobe are a result of "inhibitory" processes. These are due to the existence of singular vector(s) of rank > 2 that are tuned to CF and whose eigenvalue is negative. A final report on these properties will be published later.

4.3. Comparisons to previous works

Wiener kernel technique is not the only technique that allows the estimation of high-frequency tuning and timing information even in the absence of phase locking. Using click pairs as stimulus, Møller (1970) was able to find tuning information from the responses of high-CF (up to

Fig. 7. Effects of stimulus level on FSVs. A and B display the FSV at two levels for a chinchilla chopper neuron (A) and a cat chopper neuron (B). C and D display the Fourier transform amplitude of the corresponding waveform shown in (A) and (B), respectively. Stimulus levels are expressed in dB SPL/ $\sqrt{\text{Hz}}$.

30.5 kHz) ANFs in the rat. More recently, [Van der Heijden and Joris \(2003\)](#) used tone complexes, instead of white noise, to extract amplitude and phase information from the responses of high-CF ANFs in the cat. Both methods rely on the envelope detection properties of ANFs, which are a consequence of second-order nonlinearities.

Another type of second-order analysis, the spectro-temporal receptive field (STRF) has been proposed as an alternative to first-order Wiener kernels when there is an absence of phase locking in the neural responses ([Eggermont, 1993](#)). [Clopton and Backoff \(1991\)](#) computed STRFs from the responses to white noise of CN neurons in guinea pigs. Peaks in the STRFs were usually restricted to certain frequencies and times relative to spike occurrence. The frequencies of the maximum values on STRFs matched the CF obtained using tones. Phase functions, such as group delays, cannot be computed using this technique.

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