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# Component analysis reveals sharp tuning of the local field potential in the guinea pig auditory cortex

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de Cheveigné A, Edeline JM, Gaucher Q, Gourévitch B. Component analysis reveals sharp tuning of the local field potential in the guinea pig auditory cortex. J Neurophysiol 109: 261-272, 2013. First published October 10, 2012; doi:10.1152/jn.00040.2012.-Local field potentials (LFPs) recorded in the auditory cortex of mammals are known to reveal weakly selective and often multimodal spectrotemporal receptive fields in contrast to spiking activity. This may in part reflect the wider "listening sphere" of LFPs relative to spikes due to the greater current spread at low than high frequencies. We recorded LFPs and spikes from auditory cortex of guinea pigs using 16-channel electrode arrays. LFPs were processed by a component analysis technique that produces optimally tuned linear combinations of electrode signals. Linear combinations of LFPs were found to have sharply tuned responses, closer to spike-related tuning. The existence of a sharply tuned component implies that a cortical neuron (or group of neurons) capable of forming a linear combination of its inputs has access to that information. Linear combinations of signals from electrode arrays reveal information latent in the subspace spanned by multichannel LFP recordings and are justified by the fact that the observations themselves are linear combinations of neural sources.

multielectrode recording; electrode array; denoising source separation; independent component analysis; spectrotemporal receptive field; frequency selectivity

TONOTOPY IS AN IMPORTANT ORGANIZATIONAL principle in the auditory system (Escabi and Read 2005; Schreiner and Winer 2007): the gradient of frequency selectivity established in the cochlea (tonotopy) is systematically observed at all levels of the auditory system up to primary auditory cortex. The pioneering descriptions of cochleotopy/tonotopy were performed using evoked potentials or local field potentials (LFPs; Woolsey and Walzl 1942; Tunturi 1944), culminating with the description of maps of several auditory cortical fields (Woolsey 1961). The vast majority of subsequent single unit/multiunit (SU/MU) studies confirmed this tonotopic organization and led to parcellations of the cortical areas delineated by LFP studies (Davies et al. 1956; Merzenich et al. 1975; Reale and Imig 1980; Schreiner and Cynader 1984). Although most of the mapping studies have used SU/MU recordings, an increasing number of studies recently recorded LFPs to assess functional properties of neuronal groups (Eggermont 1996; Kayser et al. 2007; Katzner et al. 2009).

Due to the greater current spread at low frequencies, LFPs reflect the activity of a larger number of neurons than single/

multiunits (SU/MU) and thereby offer a more comprehensive but less detailed view of neural activity. LFPs complement spikes to the extent that they reflect the input to dendritic fields of cortical neurons rather than their output. This is useful if a large proportion of cortical cells are silent, or thrifty of their spikes (Hromádka et al. 2008; Barlow 1972), inasmuch that the computations performed on the input are of interest whether or not they lead to a spike. LFPs are a useful stepping stone between animal electrophysiology and human brain imaging that also reflects large ensembles of cells (Kayser et al. 2007; Berens et al. 2010).

In auditory cortex, studies that have measured the tuning of LFP recordings systematically reported bandwidths wider than those obtained for SU/MU recordings (Eggermont 1996; Noreña and Eggermont 2002; Noreña et al. 2008; Eggermont et al. 2011; Gaucher et al. 2012; Kajikawa and Schroeder 2011). Pharmacological manipulations revealed that shortrange or long-range intracortical connections considerably increase the spectral tuning provided by thalamocortical afferences (Kaur et al. 2004; Moeller et al. 2010; Happel et al. 2010). In fact, long-range horizontal pathways can provide subthreshold spectral inputs to adjacent cortical regions not receiving any corresponding thalamic input (Kaur et al. 2005; Liu et al. 2007). Thus the better tuning of SU/MU activity relative to LFPs could be explained by cortical processing. However, an alternative explanation is the greater current spread for LFPs compared with SU/MU (Lindén et al. 2010, 2011).

The LFP signal recorded by an electrode represents the weighted sum of multiple neural sources, each of which may contribute to several electrodes. Ideally, we would like to reverse the effects of this mixing by applying an "unmixing" matrix to the LFP signals, so as to retrieve the underlying neural sources. Unfortunately, the problem is ill posed as the number of unknowns greatly exceeds the number of observations. It is, however, possible to enhance the data by forming linear combinations of the measured signals, using a family of methods known as component analysis. Prominent among them, principal component analysis (PCA) yields orthogonal components ordered in terms of decreasing variance, and independent component analysis (ICA) maximizes some measure of "statistical independence." Current source density analysis (CSD; Mitzdorf 1985) and beamforming (Hillebrand et al. 2005) also fit this definition as they involve weighted sums of electrode signals. In this study, we use a form of component analysis known as denoising source separation (DSS; Särelä

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and Valpola 2005) that produces components that maximize a particular criterion. Whereas PCA produces orthogonal components in order of decreasing power, DSS produces orthogonal components in order of decreasing criterion score. In this study, the criterion is the ratio of power of the response to one stimulus frequency to the average power of the response to other frequencies. We retain only the first component of the analysis, which is the linear combination of electrode signals that is most selective to that frequency.

Repeating the process for each frequency within our stimulus set, we scan the multidimensional space spanned by the LFPs for hints of frequency selectivity. Applied to LFPs, this technique finds components with tuning curves, or spectrotemporal receptive fields (STRFs), that are considerably narrower than the LFP recorded by a single electrode. Although this outcome is consistent with the existence of narrowly tuned neural sources, a more conservative interpretation is that such selectivity is "latent" within the neural activity sampled by the LFPs, for example, available to any neuron (or group of neurons) that can linearly sum activity over the same neural substrate. In other terms, the unit of observation sampled by the electrode array is a subspace of the electrical activity within the brain that we interrogate, using component analysis, for evidence of sensitivity to stimulus frequency.

## METHODS

#### Stimuli and Data Collection

Subjects. Pigmented guinea pigs free of middle ear infection were used as subjects. The animals were housed in a humidity (50-55%)and temperature (22-24°C)-controlled facility on a 12:12-h light-dark cycle (light on at 7:30 AM) with free access to food and water. Guinea pigs were young adults (age 3-4 mo, 490-590 g) from our own breeding colony. All procedures conformed to the European (86/609/ EEC) and French (JO 887-848) legislations on animal experimentation (which are similar to those described in the Guidelines for the Use of Animals in Neuroscience Research of the Society of Neuroscience). The study was performed under national authorization to work on live animals (no. A 91-557 delivered to J.-M. Edeline). Two days before the experiment, hearing thresholds were evaluated from auditory brainstem responses (ABRs) while the animals were under isoflurane anesthesia (2.5%). The protocol for ABR recording was previously detailed (Gourévitch et al. 2009). The ABR thresholds obtained for the animals included here were comparable to those obtained from normal-hearing guinea pigs (Gourévitch et al. 2009).

Animal preparation and recording procedures. Guinea pigs were anesthetized by an initial injection of diazepam (4 mg/kg ip) followed by urethane (1.5 g/kg ip). Additional doses of urethane (0.5 g/kg ip) were systematically delivered when reflex movements were observed after pinching the hindpaw (usually once or twice during a 8-h recording session). The body temperature was maintained at  $\sim$ 37°C by a heating pad throughout the experiment. The stereotaxic frame supporting the animal was placed in a sound-attenuating chamber (IAC, model AC1). A large opening was made in the temporal bone, and the dura mater was removed under microscopic control. The location of the primary auditory field (AI) was estimated based on the pattern of vasculature and previous studies in guinea pig (Edeline et al. 1993; Manunta and Edeline 1999; Wallace et al. 2000; Gourévitch and Edeline 2011). LFPs were recorded with an array of 16 tungsten electrodes [33  $\mu$ m in diameter, impedance <1 M $\Omega$ ; Tucker-Davis Technologies (TDT)] arranged in a  $8 \times 2$  configuration with 0.25-mm electrode separation within a row and 0.5-mm separation between rows. The array was oriented such that all electrodes were simultaneously touching the cortical surface. Recordings were obtained at a depth of 500–1,000  $\mu$ m below pia, which corresponds to layer III and the upper part of layer IV (Wallace and Palmer 2008). The signals were amplified 10,000 times (TDT LP16CH, 100-G $\Omega$ input impedance) and then processed by an RX5 multichannel data acquisition system (TDT). Signals were initially sampled at 24,400 Hz and subsequently band-pass filtered between 5 and 305 Hz and downsampled to 610 Hz for LFP analysis. Two or three positions of the electrode array were used to map the entire field AI on each animal. At the end of the recording session, a lethal dose of pentobarbital (200 mg/kg) was administered to the animal.

Acoustical stimulation. Acoustic stimuli were generated in Matlab and transferred to a RP2.1-based sound delivery system (TDT) and then to a speaker system (Fostex FE87E). The speaker was placed at 2 cm from the guinea pig's right ear, a distance at which the speaker produced a flat spectrum (±3 dB) between 140 and 36 kHz. Calibration of the speaker was made by recording noise and pure tones from the speaker with a Bruel & Kjaer microphone 4133 coupled to a preamplifier B&K 2169 and a digital recorder Marantz PMD671. The tuning properties of neurons were determined using 97 or 129 pure tone pip frequencies spaced logarithmically at intervals of 1/16th octave (4.4%), covering 6 (0.28-18 or 0.56-36 kHz) or 8 (0.14-36 kHz) octaves, respectively. Tones were presented at peak intensities of 35, 55 and 75 dB SPL. At a given intensity, each frequency was repeated eight times at a rate of 2.35 Hz in pseudorandom order. Tone pips had  $\gamma$ -envelopes given by  $\gamma(t) = (t/4)^2 \exp(-t/4)$ , where t is time in milliseconds. The duration of these tones over half-peak amplitude was  $\sim 15$  ms, while the total duration of the tone was 50 ms.

Data were gathered from 11 guinea pigs, with one to four recording positions of the array per animal. Forty-seven recording sessions were carried out, one session being a set of 16 electrodes implanted in a given position in an animal's auditory cortex, yielding a total of 752 recordings. Nineteen sessions were recorded at 75 dB SPL, 14 at 55 dB SPL, and 14 at 35 dB SPL. Data are reported for all sessions and electrodes, including those for which little selectivity was found in either LFPs or spikes.

#### Data Analysis

On the basis of a peristimulus epoch of 100 ms starting at stimulus onset, the data sampled at 610 Hz were arranged into a four-dimensional matrix with dimensions time (T = 61 samples), channel (K = 16), repeat (8), and stimulus frequency (J = 97 or 129). Data were averaged over repeats (8) and analyzed using the DSS component analysis method.

*DSS analysis.* Figure 1*A* summarizes the principle of the analysis. Neural sources (*left*) summate to produce electrode signals (*middle*). Due to current spread the electrodes are less well tuned than the sources, and there may also be contributions from untuned sources. DSS forms a linear combination of electrode signals that is optimally selective to a particular frequency (*right*).

The main steps of the DSS method are illustrated in Fig. 1*B*. The set of *K* electrode signals (*left*) is spatially whitened by PCA and normalized to obtain a data set with spherical symmetry, i.e., with no privileged direction of variance in *K*-dimensional space (*middle*). The whitened data are then submitted to a bias function [which Särelä and Valpola (2005) call "denoising function"] that breaks the spatial symmetry and causes the variance to be greater along certain orientations in the data space. A second PCA produces components collinear with these orientations, and the result is a set of *K* orthogonal components ordered in terms of decreasing bias score.

The intuition behind DSS is illustrated in cartoon format in Fig. 1*C* for two dimensions (e.g., 2 electrodes). Data are selective to some feature of interest, coded as color, but its gradient does not align with either of the observation dimensions (*left*). The selectivity gradient is also not colinear with the direction of maximum (or minimum) variance, so that PCA cannot isolate it (second to *left*). Normalization removes the influence of variance so that the data are "spherical" and



Fig. 1. Principle of the analysis. A: neural sources (left), some of which are well tuned (top), others not (bottom), combine to produce poorly tuned local field potentials (LFPs) recorded by an electrode array (mid*dle*). These are combined optimally using the denoising source separation (DSS) method to produce a well-tuned component (right). Plots depict schematized spectrotemporal receptive fields (STRF) that represent the response over time (abscissa) for each stimulus frequency (ordinate). B: stages of the DSS analysis. Matrix of observations (left) is submitted to a principal component analysis (PCA) and the principal components (PCs) are normalized (middle). A bias function is applied (see text), and a second PCA is performed. First PC yields the optimally tuned component (right). C: schematic illustration of how DSS works: raw data (left, e1 and e2) are selective to a feature (represented here as color), but this selectivity is obscured by other nonselective features. PCA (second to *left*) by itself cannot help because the selective dimension does not correspond to a dimension of maximal (or minimal) variance. Normalization (middle) removes all influence of variance, so the data are now spherically symmetrical. Bias (next to right) then breaks the symmetry, emphasizing the selective direction, and a final PCA (right, c1 and c2) aligns it with the coordinate axes in such a way that the first component (vertical) is the direction of maximal selectivity in the data. In the present study, the "selective direction" that we are searching for is the linear combination of LFPs that maximizes selectivity to a particular stimulus frequency.

free to rotate (*middle*). The bias then emphasizes variance along the direction of interest, and the second PCA rotates the data so that that direction is aligned with the axes (*right*). In our case, the feature of interest is stimulus frequency, accordingly the bias function is implemented by multiplying the LFP signals in response to one particular stimulus frequency  $f_i$  by 1, and those to all other frequencies by 0.

In mathematical terms, supposing that the responses to all the *J* frequencies are concatenated along the time axis, t = 1, ..., JT, let  $\mathbf{X} = [x_{kt}]$ , dimensions  $K \times JT$ , be the matrix of LFP signals recorded by the *K* electrodes. The PCA matrix **P**, dimensions  $K \times K$ , is obtained by eigendecomposition of the covariance matrix  $\mathbf{XX}^T$ . The spatially whitened signals are obtained as  $\hat{\mathbf{X}} = \mathbf{NPX}$ , dimensions  $K \times JT$ , where **N** is the normalization matrix, so that  $\hat{\mathbf{XX}}^T = \mathbf{I}$ , identity matrix. The bias is implemented by multiplying  $\hat{\mathbf{X}} = [\hat{x}_{kt}]$  by zero for values of *t* outside the  $f_j$  trial and by one for values of *t* within that trial. Denoting the result of this biasing as  $\hat{\mathbf{X}}'$ , dimensions  $K \times JT$ , the second PCA matrix is obtained by eigendecomposition of  $\hat{\mathbf{X}}'\hat{\mathbf{X}}'^T$ . We are interested only in the first row of this matrix, that we denote by  $\mathbf{Q}'$ .

The component  $y_t^j$  optimally tuned to  $f_i$  is thus related to **X** by:

$$y_t^j = \mathbf{W}^j \mathbf{X}.\tag{1}$$

where  $\mathbf{W}^{j} = \mathbf{Q}^{j}\mathbf{NP}$ . The matrix  $\mathbf{W}^{j}$ , dimensions  $1 \times K$ , defines the *K* weights to apply to the electrode signals to obtain a signal optimally tuned to  $f_{i}$ . Repeating the operation for each of the *J* stimulus

frequencies results in a matrix of optimally-tuned component signals  $\mathbf{Y} = [y_i^j]$ , dimensions  $J \times JT$ , each tuned to a particular stimulus frequency. Computationally, each matrix  $\mathbf{W}^j$  is calculated from two covariance matrices:  $\mathbf{C}_0 = \mathbf{X}\mathbf{X}^T$ , covariance of the entire data set, and  $\mathbf{C}_1 = \mathbf{X}^j \mathbf{X}^{jT}$ , covariance of data restricted to one stimulus frequency  $f_i$ .

The DSS method (Valpola and Pajunen 2001; Sarela 2004; Särelä and Valpola 2005) is related to the filtering by optimal projection (FOP) and common spatial pattern (CSP) algorithms (Koles et al. 1990; Boudet et al. 2007; Blankertz et al. 2008), which have been widely used for classification in the brain computer interface (BCI) literature (see also Fukunaga 1990; Parra et al. 2005). In previous studies, we used this technique to remove noise components so as to maximize a trial-averaged response (de Cheveigné and Simon 2008; de Cheveigné 2010, 2012). Processing was performed using the NoiseTools toolbox (http://audition.ens.fr/adc/NoiseTools).

*Optimally tuned LFP components.* DSS analysis was applied as described above, once for each stimulus frequency, each time keeping only the first component (the linear combination best tuned to that frequency). This yielded a set of optimally tuned components, one for each stimulus frequency. Each component is associated with a set of weights to be applied to the electrode signals and a time series (weighted sum of electrode signals). To test for overfitting, we also performed the calculation according to a jackknife "leave one out"

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procedure. The DSS solution was calculated based on a subset of seven trials and applied to the eighth, and this was repeated eight times, permuting the roles of the trials. The outcome of these eight calculations were averaged to obtain the "optimal component."

The response of a component (or electrode signal) was characterized by plotting its time course for each stimulus frequency to obtain a STRF as in Fig. 2A. Tuning along the frequency axis was summarized by calculating the root mean square (RMS) of the LFP averaged over the initial 100 ms postonset interval, and plotting this value as a function of stimulus frequency as in Fig. 2B. Tuning curves were smoothed by convolution with a three-point square window, and the best frequency (BF) of the electrode or component was defined as the frequency that produced the largest RMS. The bandwidth of tuning was quantified as follows. A criterion RMS value was set half way between the peak and mean values of the RMS over frequency. Starting from the peak, the right edge was defined as the first frequency for which the response I) fell below criterion and 2) remained below criterion for at least one octave. The left edge was defined in an analogous fashion, and the bandwidth was defined to be the ratio (in octaves) between right and left edges (Valentine and Eggermont 2004; Shechter and Depireux 2007). If the criterion was exceeded for some frequency outside the left-right interval, the tuning curve was classified as multimodal (multiple peaks); otherwise it was unimodal (single peak).

To compare tuning between raw LFPs and DSS components, for each electrode we selected the DSS component with the most similar tuning curve (quantified by the Pearson product-moment coefficient between electrode and component tuning curves). This gave us a selection of 16 components with characteristics most similar to each of the 16 electrode signals. For comparison purposes, we also quantified the Multi-Unit response collected from each electrode [see Gaucher et al. (2012) for details]. The spectrotemporal characteristics of the spike response of an electrode were characterized by plotting the firing rate as a function of time for each stimulus frequency (spike-based STRF). Tuning and bandwidths were calculated as for the LFPs. Thus for each of the 16 electrodes we had bandwidth estimates for the LFP, the closest DSS component, and the spikes.

#### RESULTS

Figure 2A shows data obtained at 75 dB SPL from a typical session. For each electrode, the initial 100 ms of the LFP signal is represented according to a color scale (red = positive, blue = negative) as a function of time (abscissa) for each stimulus frequency (ordinate). The response generally includes an initial short deflection that peaks at a latency of  $\sim$ 15–20 ms, followed by a later, slower deflection of opposite polarity. Some electrodes respond over much of the frequency range (e.g., electrodes 1-3 or 14-16 in Fig. 2A), for others the response is greatest for a restricted range of stimulus frequencies. Frequency responses are summarized in Fig. 2B, each row representing in color the "tuning curve" of one electrode, defined as the RMS of the LFP over the first 100 ms as a function of frequency. For most electrodes, the response is tuned to a particular frequency, and furthermore the BFs appear to be distributed following a tonotopic gradient, evident in Fig. 2C. For comparison, Fig. 2D shows tuning curves for spikes on the same electrodes. BFs seem to be similar for



Fig. 2. Data collected at 75 dB in the auditory cortex of a guinea pig. A: time course of LFP for each stimulus frequency (ordinate) for each electrode (also called spectrotemporal receptive field, STRF). For visual convenience, data for 37 each electrode are normalized by dividing by the maximum absolute value. Time is counted from stimulus onset, and values are coded as color. B: normalized LFP tuning curves for each electrode [root mean square (RMS) of signal over the first 100 ms of the response as a function of frequency coded as color]. C: spatial distribution of LFP-based best frequencies (BFs) coded as color. D: normalized spike tuning curves for each electrode (number of spikes over the first 22 ms as a function of frequency coded as color). Note the wider tuning of LFPs compared with spikes.



spikes and LFPs, but tuning is somewhat narrower for spikes (compare Fig. 2, *B* and *D*).

These trends hold over the population of electrodes and sessions (16 electrodes  $\times$  47 sessions). For the subpopulation for which both LFP and spike tuning curves were unimodal, BFs were roughly matched (Fig. 3, *left*; red points are clustered around the diagonal). Spike tuning curves were generally narrower than LFP tuning curves (Fig. 3, *right*; most red dots are below the diagonal). Median bandwidths for LFPs and spikes were 1.5 and 1.1 octaves, respectively (Wilcoxon rank sum test P = 0.0002). The 10th percentiles were 1 and 0.6 octaves, respectively. This is consistent with previous studies that found LFP responses to be less well tuned than spikes (Eggermont 1996; Noreña and Eggermont 2002; Noreña et al. 2008; Eggermont et al. 2011; Gaucher et al. 2012; Kajikawa and Schroeder 2011).

DSS was applied repeatedly to the 16-channel data of each LFP session, each repetition favoring a different stimulus frequency (see METHODS). This resulted in a set of 97 or 129 components, depending on the number of frequencies in the stimulus set. Figure 4B shows the STRF of one particular component, chosen for the similarity of its BF (10.7 kHz) to that of one electrode (electrode 11 in Fig. 2A). The STRF of this component appears narrower than that of the electrode, as evident in Fig. 4C where their tuning curves are compared. Tuning curves of all 97 components are plotted in Fig. 4B as a raster plot. Stimulus frequency is indicated on the abscissa, and the RMS amplitude at each stimulus frequency is coded as color. Over the range for which electrodes were well tuned (5-20 kHz), the components were quite narrow and their BFs formed a continuum covering that range. Figure 4D shows the same result obtained with a jackknife procedure designed to test for overfitting (see METHODS). The similarity with Fig. 4B suggests that overfitting does not play a major role in these results (see DISCUSSION). Figure 4E shows the weights applied to each electrode signal to obtain the optimally tuned component in Fig. 4C. Figure 4F shows weights for all components (see DISCUSSION).

To allow a quantitative comparison among the tuning of LFPs, DSS components, and spikes, for each electrode we chose a single component with tuning curve most similar to that of the electrode (quantified by the Pearson product moment coefficient, see METHODS). The 16 components obtained in this way, one for each electrode, can be seen as "cleaned" or "sharpened" versions of the 16 LFP signals. Bandwidths of electrodes and closest components for the entire data set are plotted as a scatterplot in Fig. 5, *left*. Most points are well below the diagonal, indicating that tuning of components is

Fig. 3. LFP vs. spike tuning. Left: scatterplot of BFs of spikes and LFPs. Red symbols are recordings for which tuning curves of both spike and LFP responses were unimodal (see text), and small black dots are all others. Diagonal represents equal BF. Right: scatterplot of bandwidths (BW) of spikes and LFPs. Red symbols are recordings for which both tuning curves were unimodal. Green circles are those for which the spike tuning was unimodal but the LFP tuning was multimodal, black stars those for which the opposite was true, and small black dots are all other data. Diagonal represents equal bandwidth. For visual clarity, in this and other plots, the coordinates of each point were randomly jittered within  $\pm 0.05$  octave.

sharper than that of LFPs (Wilcoxon rank sum test P < 0.0001). The numerous green circles indicate that in many cases the LFP was multimodal whereas the corresponding component was unimodal. Components were more often unimodal than either raw LFPs or spikes (471 vs. 122 and 315, respectively, out of a total of 752 recordings, Wilcoxon rank sum test P < 0.0001). Spike and component bandwidths are plotted as a scatterplot in Fig. 5, *left*. The lower limit of component bandwidths, as quantified by their 10th percentile, is similar to that of spikes (0.5 octave for components and 0.6 octave for spikes, vs. 1.1 for LFPs).

In several instances (14 sessions), data were collected at three stimulus intensities (35, 55, and 75 dB SPL) for the same electrode position in the same animal. Figure 6A shows DSS tuning curves for one such instance. Plots on a row represent DSS solutions calculated at a particular stimulus intensity, and plots within a column represent the result of applying DSS solutions to data for a particular stimulus intensity. For plots on the diagonal, the DSS solutions were calculated based on, and applied to, data for the same stimulus intensity. Results were similar at all three intensities (plots on the diagonal). Plots off the diagonal represent solutions calculated at one intensity and applied to another. The similarity of diagonal and off-diagonal plots suggests that solutions generalized, to some extent, to data measured at another intensity. For this particular position of the electrode array, tuned components were found for frequencies >8 kHz. Below that frequency, tuning curves are more erratic, presumably because the electrode array did not span regions responsive to low frequencies. For a different penetration in the same animal, the range of well-tuned components was shifted to lower frequencies (not shown).

Figure 6*B* shows component bandwidth as a function of BF for each intensity (restricted to recordings for which the tuning curve was unimodal at all 3 intensities). Relative bandwidths tend to be smaller for high than low BF, as expected from well-known properties of cochlear selectivity. They are also smaller at lower intensities (medians: 0.9, 1.2, and 1.5 octaves at 35, 55, and 75 dB, respectively; Wilcoxon rank sum test for 35 vs. 55 dB, P < 0.0001; 55 vs. 75 dB, P = 0.0034). The same trend was observed for raw LFPs (medians: 1.5, 2, and 2.9 octaves at 35, 55, and 75 dB, P < 0.0001; 55 vs. 75 dB, P < 0.0001; and provide the same test for 35 vs. 55 dB, P < 0.0001; 55 vs. 75 dB,



Fig. 4. Tuning of DSS components. A: STRF for a DSS component with a bias near 11 kHz, chosen because its BF is close to that of *electrode 11* (STRF in Fig 2A). B: tuning curves of all DSS components. Each line represents the RMS of 1 component (bias in ordinate) as a function of stimulus frequency (abscissa). C: tuning curves of *electrode 11* and most similar component. D: tuning curves for components calculated with jacknife cross-validation (see METHODS). The similarity of this plot to B suggests that overfitting plays a minimal role in our results. E: weights applied to electrode signals to obtain the optimally tuned components. Each row represents the weights for a component optimally tuned to a particular frequency (in ordinate). Positive weights are red, negative are blue, and green is zero. AU, arbitrary units.

than high intensities, at least for spectrally sparse stimuli (Galván et al. 2001; Pienkowski and Eggermont 2011).

## Simulations

To better understand the nature of the DSS components, and assign them a physiological meaning, we ran a simulation involving a set of 40 simulated "neural sources" observed from a set of 16 simulated "electrodes." Each source responded to stimulation with a stereotyped time course consisting of one cycle of a sinusoid (to mimic the time course of an LFP response), with an amplitude that depended on stimulus frequency (to mimic frequency tuning). Source BFs ranged from 0.25 to 32 kHz (Fig. 7A). These 40 source signals were mixed

Fig. 5. *Left*: scatterplot of bandwidths of components (ordinate) and LFPs (abscissa). Red symbols are electrodes/sessions for which both component and LFP tuning curves were unimodal. Green circles represent those for which the component was unimodal but the LFP was not, black stars are those for which the opposite was true. Dots are all other data. *Right*: scatterplot of bandwidths of components vs. spikes. Meaning of symbols as at *left*.



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Fig. 6. A: component tuning at several intensities. Each row represents a DSS solution calculated at a particular stimulus intensity, each column represents the result of applying that solution to data for a particular intensity. *B*: bandwidths of recordings for which the tuning curve was unimodal, plotted as a function of BF for each intensity.



relatively well-tuned components over much of the fre-

quency range (Fig. 7B, right). Note that the aim here is not

to accurately model LFP recordings but to clarify the mechanisms of source-to-electrode mixing and electrode-to-component analysis.

Additionally, to simulate the potential effect of incomplete sampling of the tonotopic axis by the electrode array, or the effect of nontuned sources, the values of the mixing matrix for low-frequency sources were set to zero, and those for high-frequency sources were given the same value for all electrodes (Fig. 7D, *left*). Tuning of DSS components in this case is shown in Fig. 7D, *right*. The outcome is similar except that components for bias frequencies within the missing ranges were poorly tuned (Fig. 7D, *right*), not

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Fig. 7. Simulations. A: tuning curves of an array of 40 simulated neural sources. Source signals are mixed via a mixing matrix (B) to produce 16 simulated electrode signals. Values along a column of the mixing matrix represent the coefficients applied to sources contributing to one electrode. C: simulated STRFs for a subset of electrodes. D: tuning curves of optimally tuned components obtained by DSS. Each row represents the tuning curve of the component that maximizes the response to a bias frequency (ordinate). In (B, *right*), the first 5 rows of the mixing matrix were set to zero and the last 10 rows to a nonzero constant (see text). The result of the DSS analysis in this case is plotted in D, *right*.

unlike patterns observed for real data in some frequency ranges (e.g., Fig. 4D or Fig. 6A).

Looking at the narrow and regularly distributed tuning curves of Fig. 7B, right, it is tempting to conclude that the method discovered a "demixing matrix" that recovered the welltuned sources that underlie the data. Two additional simulations show that this is not necessarily the case. In Fig. 8A, the tuning of the sources was three times wider than in Fig. 7, and in Fig. 8C, it consisted of a high-pass transition rather than a peak. For these simulations we used the same "incomplete" mixing matrix as in Fig. 7D, left. Despite the wider and/or high-pass tuning of the sources, the recovered components (Fig. 8B, left) and (Fig. 8D, left) appear to be at least as narrow as for the previous simulation. Interestingly, with a wider tuning (Fig. 8A) the component array is well tuned over a wider range of frequencies than with narrow tuning (compare Fig. 8B with Fig. 7D, right). We also investigated the effect of adding noise to the electrode signals. In the presence of Gaussian white noise at 0 dB signal-to-noise ratio (equal power for noise and signal), component tuning is wider (more similar to that observed in real data) and more strongly dependent on the tuning of the underlying sources (Fig. 8B, right) and (Fig. 8D, right). This suggests that the degree of component tuning that we see for real data is determined by multiple factors including noise. The main message to retain from these simulations is that we cannot assume that the components recovered by DSS correspond one-to-one to neural sources that produced the LFPs. The issue of how to interpret the components is addressed further in the DISCUS-SION.

# DISCUSSION

Our analysis found linear combinations of LFPs with tuning characteristics that were often simpler (unimodal instead of multimodal) and narrower than those of the raw signals collected by the electrodes.

#### How Does the Analysis Work?

The DSS algorithm is conceptually easy to understand (see cartoon in Fig. 1C). Each of the LFP signals measured by the electrode array reflects neural sources to varying degrees, because of the different amplitudes, gains, and degrees of spread across electrodes. The measured signals are usually strongly correlated between electrodes. The first step of the DSS algorithm, PCA followed by normalization, factors out these "nuisance parameters" by decorrelating the data and giving equal variance to all dimensions, so that the data are "spherical" and free to rotate in multidimensional space (Fig. 1C, middle). The second step, bias, has the effect of emphasizing certain directions in this space, so that the data cloud is no longer spherical but rather extends more along certain directions, like a rugby ball. The last step of DSS, PCA, finds a new coordinate system aligned with the principal axes of the biased data (Fig. 1C, right). The transform that takes the initial data (electrode signals) to this new basis (DSS components) is linear, and in particular the first component is the most selective linear combination of electrode signals. The selectivity of a component benefits both from an emphasis to the appropriately tuned sources (via large weights to those electrodes with a good signal-to-noise ratio) and from suppression of spurious sources (via a combination of positive

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Fig. 8. Simulations (continued). A: tuning curves of an array of 40 simulated neural sources with bandwidths 3 times wider than those of Fig. 7A. B: tuning curves of optimally tuned DSS components in the absence of noise (*left*) or in the presence of gaussian noise at a signal-to-noise ratio of 0 dB (*right*). C: tuning curves of an array of 40 simulated neural sources with high-pass tuning characteristics. D: tuning curves of optimally tuned DSS components in the absence of noise (*left*) or in the presence of gaussian noise at a signal-to-noise ratio of 0 dB (*right*). Reserves of noise (*left*) or in the presence of gaussian noise at a signal-to-noise ratio of 0 dB (*right*). Mixing matrix was in all cases the same as in Fig. 7B, *right*.

and negative weights that cancels them). This is obvious in Fig. 4, E and F, which shows nonzero weights over much of the electrode array.

# Risk of Overfitting

The optimal linear combinations are guaranteed to be better tuned than any of the electrodes, as evident in Fig. 5, left: almost all points are below the diagonal (the rare exceptions are explained by the fact that maximizing the power ratio between one frequency and all others does not precisely minimize bandwidth according to our definition). Sixteen free parameters are involved in each component, and therefore some degree of tuning might emerge due to a chance combination of parameters. Several features suggest that this is not a major factor in our results. First, solutions calculated from one data set generalized to other data sets (see, for example, the off-diagonal plots in Fig. 6A, for which the solution was derived at one intensity and applied to another). Second, the method readily failed over frequency regions not sampled by the electrodes (e.g., Fig. 4B or Fig. 7D, right). Third, we explicitly tested for overfitting with a jackknife "leave one out" procedure, in which the solution was calculated based on a subset of seven trials and applied to the eighth. This calculation was repeated, leaving out each of the trials in turn, and the results were averaged. The outcome of the standard and jackknife procedures is very similar. Comparing Fig. 4, B and D, the only obvious difference is a faint ridge along the diagonal present in the former and absent in the latter, reflecting the better fit for frequencies matching the bias (average correlation coefficient between rows >0.99). The tuning revealed by DSS thus appears to reflect a genuine property of the neural activity sampled by the LFPs rather than the effect of overfitting.

#### Sources, Electrodes, and Components

What do we mean by "neural source"? At the microscopic level, each synaptic event (excitatory postsynaptic current or inhibitory postsynaptic current) is reflected by multiple current sources and sinks distributed along the dendrites, soma, and axon of the postsynaptic neuron, with waveforms that vary with position due to membrane filtering properties (Lindén et al. 2010). Assuming linearity between currents and potential (Ohm's law), each synaptic event induces a potential at the electrode that is the weighted sum of these elementary sources and sinks. The measured LFP integrates these potentials over events and neurons (Nunez and Srinivasan 2006; Lindén et al. 2010), thus collapsing a very high-dimensional space of activity into a single signal (for a single electrode) or set of signals (for an electrode array). In mathematical terms, the neural activity is projected on the subspace spanned by the electrodes, so that many distinct patterns of neural activity map to exactly the same measured response. The contribution of any given neural source to this projection depends on multiple factors, including distance to the electrode, geometry of the neuron's dendritic field, e.g., "open" vs. "closed," and parallel orientation of neighboring neurons (Nunez and Srinivasan 2006; Lindén et al. 2010).

LFPs therefore offer an impoverished view of the neural activity because of the small dimensionality of the subspace

that they span. Component analysis addresses a different problem, which is to find points within that subspace (i.e., linear combinations of electrode signals) that are the most meaningful. Raw electrode signals span the observation subspace by definition, but they are not necessarily its most interesting points. Component analysis searches for more interesting signals that might correspond to groups of neurons that are functionally related (for example similarly tuned) or that reflect information that a downstream neuron might usefully extract.

To recapitulate: the interpretation of LFPs recorded by electrode arrays is limited in two fundamental ways: *1*) the observed signals sample a low-dimensional subspace of the high-dimensional neural activity, and 2) they are not the most informative elements of this subspace. Component analysis addresses the second limitation by offering a better view of the available information, but there is no way to alleviate the first except by using more electrodes or positioning them better.

It is tempting to assign each component to the activity of an individual neural source within the brain and to infer neural tuning from the component tuning. Such a lucky outcome cannot be ruled out, but our simulation warned us that sharp and unimodal component tuning curves can also arise from underlying sources with a variety of tuning patterns. Thus it is not necessarily the case that components map to neural sources. Rather, the existence of a sharply tuned component implies that the tuning is "latent" in the LFP signals sampled by the electrodes, in the sense that it could be read out by a downstream neuron capable of forming a linear combination of its inputs. This weaker interpretation is probably the best we can hope for, given that the measured LFPs themselves are linear combinations of multiple neural sources with unknown weights.

From an epistemological point of view, we may feel uncomfortable with the idea of reporting "components" in lieu of, or in addition to, directly observed data such as raw LFPs. However, the power of multichannel recording (beyond the efficiency gain provided by parallel observations) resides precisely in the possibility of performing such linear analyses. In this sense, the unit of observation is the subspace spanned by electrode signals, and component analysis is required to make the most of this observation. Here we used component analysis to reveal frequency tuning, but it is potentially useful as a general tool to find evidence of neural activity that reflects task or stimulus conditions, reveal oscillatory activity, etc. (see *A General Tool for LFP Analysis*). We argue that this is a paradigm shift that is rendered inevitable by multichannel techniques if we are to reap their full benefit.

As an aside, it is interesting to note that the components obtained for the widely tuned or high-pass sources of Fig. 8A were similarly tuned as those for the narrowly tuned sources of Fig. 7A. This illustrates the point made by Pouget et al. (1999) that narrow tuning is not an essential quality for a population code, as various tuning functions can be "resynthesized" by combining adjacent channels, subject to noise constraints. Mach and Helmholtz had earlier put forward the idea that the resolution of a coarsely sampled sensory continuum can be increased by interpolation between its elements, and various schemes based on lateral inhibition have been proposed to increase selectivity within the auditory system (e.g., Huggins and Licklider 1951; Shamma 1985). Interpolation and lateral inhibition are special cases of the wider class of linear combi-

nations that are subsumed by component analysis algorithms such as DSS.

# Frequency Tuning in Auditory Cortex of Guinea Pigs

LFP recordings were frequency selective but with tuning curves that were often multimodal (black dots and green circles in Fig. 3, *right*), as observed in other studies (Noreña and Eggermont 2002; Eggermont et al. 2011; Gaucher et al. 2012). Those tuning curves that were unimodal were wide (median 1.5 octave) relative to tuning curves of spikes recorded on the same electrode (median 1.1 octave), as found in other studies (Noreña and Eggermont 2002; Eggermont et al. 2011; Gaucher et al. 2012; Gourévitch and Edeline 2011; Kajikawa and Schroeder 2011).

LFPs are assumed to mainly reflect the input, and spikes the output of cortical neurons, and thus narrower tuning for spikes has been interpreted as the result of cortical processing (Noreña and Eggermont 2002), for example based on the balance of inhibitory and excitatory inputs to individual neurons (Wehr and Zador 2003; Wu et al. 2008). Our results offer a new perspective on this issue. Components were more often unimodal than raw LFPs, a major effect of component analysis being to suppress secondary modes, presumably by reducing the contamination from more distant sources that are either broadly tuned or tuned to other frequencies. They were also narrower (Fig. 5, left) with bandwidths more in line with spikes. This is consistent with two possible interpretations: 1) neural sources underlying the LFP are well tuned, the mismatch between LFPs and spikes being due to the low-pass filtering of more distant sources (Bedard et al. 2010; Lindén et al. 2010). 2) Neural sources underlying the LFP are no better tuned than the LFP, but narrow tuning can be "read out" by a downstream neuron capable of forming a linear combination of activity similar to that sampled by the LFP. We cannot distinguish between these two hypotheses, but we can rule out a third: 3) tuning is not present within the LFP activity.

Narrow tuning has also been found in the CSD profile from electrode arrays inserted perpendicularly to the surface of auditory cortex of awake monkeys, compared with raw LFPs from individual electrodes (Kajikawa and Schroeder 2011). CSD is based on the second spatial derivative of the electrode array that involves a series of weights with alternating signs. If that pattern of weights were optimal for frequency tuning, it would necessarily be found by DSS, and indeed, there is some hint that nonzero weights of individual components may sometimes occur in pairs (e.g., +-) or triplets (e.g., +-+) with alternating signs, although in general the patterns are more complex (Fig. 4*E*). The advantage of our technique is that it is guaranteed to find the optimally tuned component whatever the underlying geometry.

Component analysis is a useful tool for data analysis, but it can also be taken as a model of linear processing within the dendritic field of a cortical neuron, excitatory and inhibitory inputs mapping to positive and negative weights, respectively. This model subsumes classic hypotheses of enhancement of sensory representations by interpolation or lateral inhibition, as well as recent proposals of linear summation of excitatory and inhibitory input (Wehr and Zador 2003; Wu et al. 2008; Eggermont et al. 2011). The optimal solution found by DSS provides an upper limit of the selectivity that such a neuron could potentially achieve, if its inputs were restricted to the subspace sampled by the electrode array. The two ingredients of DSS, PCA and normalization, can be performed by neural mechanisms such as Hebbian plasticity (Oja 1982; Swinehart and Abbott 2006; Carandini and Heeger 2011), suggesting that a cortical neuron might find these optimal weights adaptively according to the task at hand. This hypothesis is attractive as frequency discrimination is only one of many tasks that an organism needs to do with its ears. The model might explain the super-sharp tuning that has recently been observed in cortex of both humans (Bitterman et al. 2008) and monkeys (Bartlett and Wang 2011). Analysis techniques such as we propose give a more complete picture of the information carried by the LFPs sampled by multielectrode arrays.

# A General Tool for LFP Analysis

DSS offers a simple way to "interrogate" multichannel LFP data for sensitivity to a parameter of interest. Here we focused on selectivity to stimulus frequency, but stimulus-locked activity (de Cheveigné and Simon 2008), narrowband oscillatory activity, and activity specific to a class of stimuli (e.g., animal calls) or behavior (e.g., hit vs. miss) can likewise be isolated.

As an example, DSS may be used to isolate narrowband cortical activity within multichannel data, such as EEG or MEG. In this case, the bias applied is a bandpass filter, and the method produces a series of components ordered in terms of decreasing power in that band. The first component is the linear combination of channels with highest power at the output of the filter relative to the input. The second is optimal within the subspace orthogonal to the first and so-on. The subspace spanned by the first few components may be projected back into electrode or sensor space, or individual components may be singled out for analysis. In contrast to time-frequency analysis, where temporal smearing occurs due to the temporal extent of the analysis filters, DSS involves no loss of temporal resolution. Although a filter is used to derive the DSS matrix, no filter is involved when the matrix is applied. The time course of features such as "event-related synchronization or resynchronization" (ERS, ERD) may thus be followed accurately.

The method is effective to factor out irrelevant response components and noise, for example, common-mode components. Other techniques may have a similar effect (e.g., subtraction of the mean over electrodes, or CSD, or differential montages used in EEG), but DSS is at least as effective by construction and in many cases significantly more. In the future, as the density of electrode arrays increases, such linear processing will be needed to take full advantage of the data: given the redundancy between electrodes caused by current spread, increasing the density of an array does not produce radically new LFP waveforms, but it does increase the dimensionality of the data that the component analysis can exploit to tease apart weak components of the response.

The basic linear DSS can be extended in several ways, for example, by applying convolutional or nonlinear transforms to the data (de Cheveigné 2010, 2012). The authors of the DSS method (Särelä and Valpola 2005) also discuss nonlinear versions of the algorithm. From a practical point of view, the algorithm requires calculation of two covariance matrixes (see METHODS), one for each of the conditions to contrast (in our case: response to all frequencies, and response to one frequency). These undergo a generalized eigenvalue decomposition (Parra et al. 2005) from which the analysis matrix **W** is derived. Similar techniques have proved useful in brain computer interfaces (Blankertz et al. 2008).

#### Conclusion

In the auditory cortex, the wider and more complex tuning recorded from LFP compared with spiking activities can result from a greater overlap of responses from neural sources with different tuning due to current spread. Such mixing effects can potentially be reversed by forming linear combinations of electrode signals using component analysis techniques. We used DSS to calculate optimally tuned components based on LFPs recorded with a 16-channel array in auditory cortex of guinea pigs. Component receptive fields were in general simpler (unimodal rather than multimodal) and narrower than LFPs, with tuning characteristics similar to spikes. Component analysis gives a more complete picture of the electrical activity sampled by the multichannel LFP signals than the raw LFP signals and usefully complements descriptions of the raw data.

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#### DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

#### AUTHOR CONTRIBUTIONS

A.d.C., J.-M.E., and B.G. conception and design of research; A.d.C. analyzed data; A.d.C., J.-M.E., and B.G. interpreted results of experiments; A.d.C. prepared figures; A.d.C. drafted manuscript; A.d.C., J.-M.E., and B.G. edited and revised manuscript; A.d.C., J.-M.E., Q.G., and B.G. approved final version of manuscript; J.-M.E., Q.G., and B.G. performed experiments.

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