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Rapid acquisition of auditory subcortical steady state responses using multichannel recordings ☆

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HIGHLIGHTS

- Multi-electrode measurement of auditory subcortical steady-state responses reduces noise by 3–4-fold compared to traditional approaches.
- This improvement makes acquisition of responses for many conditions within a single, one-hour experimental session feasible.
- Simulations and human results both reveal the benefits of the multi-channel technique.

ABSTRACT

Objective: Auditory subcortical steady state responses (SSSRs), also known as frequency following responses (FFRs), provide a non-invasive measure of phase-locked neural responses to acoustic and cochlear-induced periodicities. SSSRs have been used both clinically and in basic neurophysiological investigation of auditory function. SSSR data acquisition typically involves thousands of presentations of each stimulus type, sometimes in two polarities, with acquisition times often exceeding an hour per subject. Here, we present a novel approach to reduce the data acquisition times significantly.
Methods: Because the sources of the SSSR are deep compared to the primary noise sources, namely background spontaneous cortical activity, the SSSR varies more smoothly over the scalp than the noise. We exploit this property and extract SSSRs efficiently, using multichannel recordings and an eigendecomposition of the complex cross-channel spectral density matrix.
Results: Our proposed method yields SNR improvement exceeding a factor of 3 compared to traditional single-channel methods.
Conclusions: It is possible to reduce data acquisition times for SSSRs significantly with our approach.
Significance: The proposed method allows SSSRs to be recorded for several stimulus conditions within a single session and also makes it possible to acquire both SSSRs and cortical EEG responses without increasing the session length.

1. Introduction

Subcortical steady state responses (SSSRs), frequently referred to as frequency following responses (FFRs), are the scalp-recorded responses originating from sub-cortical portions of the auditory nervous system. These responses phase lock to periodicities in the acoustic waveform and to periodicities induced by cochlear processing (Glaser et al., 1976). The responses specifically phase locked to the envelopes of amplitude modulated sounds are sometimes called amplitude modulation following responses (AMFRs) or envelope following responses (EFRs) (Dolphin and Mountain, 1992; Kuwada et al., 2002). Responses to amplitude-modulated sounds originating from both the sub-cortical and cortical portions of the auditory pathway are also collectively referred to as auditory steady-state responses (ASSR) (Rees et al., 1986). In contrast to

☆ Software for procedures outlined in this manuscript is publicly available at http://nmr.mgh.harvard.edu/~hari/ANLffr/.

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auditory brainstem responses (ABRs; the stereotypical responses to sound onsets and offsets; Jewett et al., 1970), SSSRs are the sustained responses to ongoing sounds and include responses phase-locked to both the fine structure and the cochlear induced envelopes of broadband sounds. Since the term FFR, originally used to denote phase locked responses to pure tones, is suggestive of responses phase-locked to the fine-structure of narrowband or locally narrowband sounds, here we will use the term SSSR to describe the sustained responses originating from subcortical portions of the auditory pathway. This name distinguishes them from transient onset-offset related responses and responses generated at the cortical level. SSSRs have been used extensively in basic neurophysiologic investigation of auditory function and sound encoding (e.g. Aiken and Picton, 2008; Kuwada et al., 1986; Gockel et al., 2011 also see Chandrasekaran and Kraus, 2010; Krishnan et al., 2006; Picton et al., 2003, for reviews). Given the frequency specificity possible with SSSRs, they have also been recommended for objective clinical audiometry (Lins et al., 1996).

SSSRs are traditionally recorded with a single electrode pair placed in either a vertical or a horizontal montage (which differ in which underlying generators are emphasized; see Krishnan et al., 2006, 2010). To achieve an adequate signal-to-noise ratio (SNR) when measuring the SSSR, the stimulus is typically repeated thousands of times. Often, stimuli are presented in opposite polarities to separate the response components phase locked to the envelope from those phase locked to the fine structure of the acoustic waveform (Aiken and Picton, 2008; Ruggles et al., 2012). Since many studies require SSSR data acquisition for multiple conditions or with multiple stimuli, this often results in recording sessions exceeding an hour per subject.

Multichannel electroencephalography (EEG), which is widely used for the investigation of cortical processing, uses the same basic sensors as SSSR measurements, but requires many fewer trials because the cortical response generators are closer to the scalp and produce stronger electric fields. EEG systems with high-density arrays include as many as 64, 128, or sometimes even 256 scalp electrodes. Although the frequency response characteristics of some cortical EEG systems are not always optimized for picking up subcortical signals (which typically are at 80 Hz and above), these multi-electrode setups can nonetheless be used to record SSSR data from multiple scalp locations.

Given this, it is possible to simultaneously record subcortical and cortical processing of sounds with the high-frequency portions analyzed to yield SSSRs and the low-frequency portions representing cortical activity (Krishnan et al., 2012). The primary source of noise for the high-frequency SSSR portion of the recordings is background cortical activity (i.e., neural noise). Since the SSSR sources are deep compared to the dominant sources of noise (in the cortex), the SSSR varies more smoothly over the scalp than the noise (for a discussion of the physics of the measurement process and how scalp fields relate to neural activity, see Hämäläinen et al., 1993). Scalp fields arising from cortical sources can cancel each other out if they are out of phase (Irimia et al., 2012). This can be exploited to help separate cortical and subcortical responses from the same EEG recordings by combining information obtained from a dense sensor array. Here, we propose and evaluate one method for combining measurements from multiple scalp channels to improve the SNR of SSSRs measured using cortical EEG arrays.

Although SSSRs can provide insight into auditory function and subcortical encoding, interpreting them can be a challenge. Multichannel recordings of brainstem responses have been used primarily in the analysis of the sources of the onset ABR, in which the activity from different generators can be temporally separated, into stereotypical responses known as waves I, III, and V (Grandori, 1986; Parkkonen et al., 2009; Scherg and Von Cramon, 1986). In contrast, since the SSSRs represent sustained activity, temporal separation of the activity from different generators is not possible. Moreover, in any narrow frequency band, particularly at high frequencies, multiple SSSR sources likely contribute to the aggregate measured response, each of which is a phase-locked response at a different phase. This notion is consistent with the observation that there are spectral notches and occasional phase discontinuities in the SSSR as a function of modulation frequency for amplitude modulated stimuli (Dolphin and Mountain, 1992; Kuwada et al., 2002; Purcell et al., 2004). This is also consistent with the observation that responses are attenuated but not eliminated in studies inducing isolated lesions of single auditory nuclei (Smith et al., 1975; Kiren et al., 1994). This multisource population activity produces scalp potentials that are different mixtures of the source activity at different scalp locations, depending on the geometry of the generators, the recording electrodes, and the volume conductor in between (Hubbard et al., 1971; Okada et al., 1997; Irimia et al., 2013). Consistent with this notion, the steady-state phase of the summed, observed response at a given frequency varies across different channels, as illustrated in Fig. 1.

Unfortunately, time-domain methods to combine multichannel recordings, such as simple across electrode averaging or principal component analysis (PCA), assume that the signal is at the same phase across sensors. For instance, time-domain PCA involves recombination of multiple measurements with real-valued weights based on the covariance matrix. As a result, these methods lead to signal attenuation when the signal components in each sensor are not at the same phase. In other fields of analysis, complex principal component analysis (cPCA) in the frequency domain has been used to effectively combine multiple measurements when the signal components are correlated, but have phase differences (Brillinger, 1981; Horel, 1984). In contrast to traditional time-domain PCA, frequency domain cPCA recombines measurement channels using the complex-valued weights obtained by decomposing the complex cross-channel spectral density matrix. The weights thus include channel-specific magnitudes and phases in each frequency bin; the phases of each complex weight specifically adjust for phase differences between responses measured at different sites to optimally combine responses across multiple sensors. Here we apply cPCA to multichannel EEG recordings, thereby accounting for phase discrepancies across the scalp and extract SSSRs efficiently. We show that compared to single-channel recording, this approach reduces the data acquisition required to achieve the same SNR, both when applied to simulations and when analyzing real multichannel SSSR recordings.

2. Methods

First, we describe the steps involved in the cPCA method. Then, we describe our procedure to validate the method using simulated data. Finally, using EEG-data acquired from normal-hearing human listeners, we demonstrate how to apply the approach to extract SSSRs from multi-electrode recordings.

2.1. Complex principal component analysis (cPCA)

Frequency-domain PCA can be used to effectively reduce the dimensionality of vector-valued time-series in the presence of between-component dependencies at delayed time intervals (Brillinger, 1981). As illustrated in Fig. 1, for any frequency component, responses at different scalp locations occur with different effective phases. This is unlikely to be due to conduction delays between the recording site and the sources since the brain tissue and head together can be treated as a pure conductor (no capacitive effects) for frequencies below about 20 kHz. That is, the forward model that relates the measured potentials to the source currents can be treated