Electrical Signals Propagate Unbiased in Cortex

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The greater spatial coherence of local field potentials (LFPs) compared with that of spiking activity has been attributed to frequency-dependent propagation of signals through the cortical medium. However, in this issue of *Neuron*, Logothetis and colleagues show that signal propagation within cortex is largely unbiased across different frequencies, thus suggesting a more functional and interpretable basis of LFP coherence.

In recent years, the search for neural signatures of perception, motor preparation, and cognition within the cerebral cortex has prompted a growing number of investigators to extend their measurement of neural activity to include the low-frequency signals present in local field potentials (LFPs). LFPs are made up of summed excitatory and inhibitory postsynaptic potentials, as well as a number of integrative processes, including somatic and dendritic spikes with their ensuing afterpotentials and voltage-dependent membrane oscillations (Mitzdorf, 1985; Llinas, 1988). Thus, they may well be ideal indicators of microcircuit function (Logothetis and Wandell, 2004). This fact has motivated comparisons of properties of LFPs, such as the stimulus selectivity and spatial coherence of certain frequency components, with that of spiking activity (e.g., Kreiman et al., 2006; Liu and Newsome, 2006), as well as tests of the extent to which the coherence of LFP components with spiking activity provides a unique signature of brain states (e.g., Buschman and Miller, 2007; Saalmann et al., 2007). However, crucial for the interpretation of LFP signals, and particularly for comparisons across its frequency components and with spiking activity, are some basic facts about how electrical signals are propagated through the cortical medium. For example, the observation that low-frequency signals can be recorded at much larger distances from an electrode than higher frequencies (e.g., Destexhe et al., 1999) has been interpreted as reflecting a frequency dependence of signal propagation within cortex (Bedard et al., 2004). If true, such a frequency dependence would complicate the use of LFPs in neurophysiological studies, as it would severely limit the interpretation of observed amplitude and phase differences across varying frequency components of the LFP. Fortunately, this problem does not appear to exist. As Logothetis et al. (2007) demonstrate in this issue of *Neuron*, the propagation of electrical signals within cortex occurs almost entirely without bias.

Through the development and use of a principled measurement method, Logothetis and colleagues have directly quantified the signal transfer properties of macaque visual cortex. Their findings provide solid evidence that the recording environment of cortex is reassuringly uninteresting! By injecting and measuring current in cortex they found almost no phase distortion and a flat frequency response. Further, they show that the cortical gray matter is isotropic, while the white matter has anisotropic properties. In short, the cortex transmits essentially unadulterated electrical signals, and in gray matter, measurements are independent of direction.

The "uninteresting" electrical properties of cortical gray matter have some fortunate implications for electrophysiologists, which we highlight by analogy in Figure 1. We examine three major points from the findings of Logothetis and colleagues: flat frequency response, linear phase, and isotropy. In this analogy, we replace neural signals with a trio of instruments being played in a room and replace the electrodes with two listeners. The listeners are far enough from the trio that each instrument is essentially equidistant. We examine a brief instant in time in which each instrument plays an idealized sound: the bass plays a single low-pitch note, the piano plays a higher-pitch note, and the drum is hit once (with constant pressure). The musicians and listeners are all placed in a medium with specific sound transfer characteristics. We will alter these characteristics and examine the outcome. With linear phase and a flat frequency response, each instrument's sound reaches the listener with the intended relative volume and timing.

If linear phase is maintained but the frequency response is shaped (for example, the medium does not transmit higher frequencies well), the listener's experience is quite different from what is played. Notice that the volume of the piano is highly attenuated, and so the bass line drowns out the melody. Although the timing of the drum is preserved, it is less crisp, giving it a muffled quality. For electrophysiologists, such a shaped frequency response could selectively filter out different signal generators, thus obscuring their contribution to functional architecture. For example, the observation that speed and direction tuning of LFPs measured in visual area MT is degraded below 40 Hz could be the result of greater spread of low frequencies beyond the limits of cortical columns (Liu and Newsome, 2006). However, the evidence that the cortical impedance spectrum is flat means that selectivity beyond 40 Hz is more

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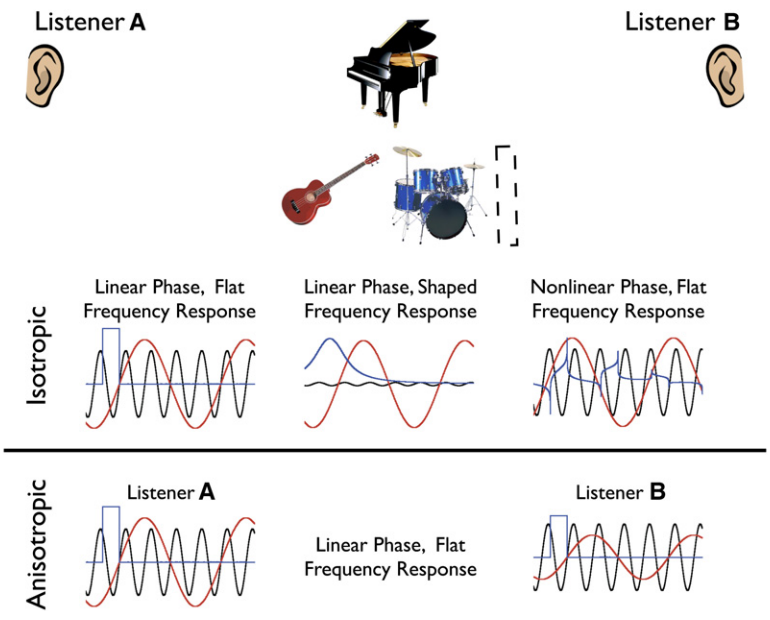

Figure 1. A Music Analogy to the Biased and Unbiased Propagation of Signals through the Cortical Medium

If we approximate the distance between three instruments as infinitesimal, then in an isotropic medium, two listeners (ears) share the same experience. For a linear phase/flat frequency response, the relative timing and volume of each instrument is correct, regardless of listener position. With a shaped (low-pass) frequency response, relative volumes are not preserved, and the drum is muffled. A nonlinear (quadratic) phase response preserves relative volume but not timing; also note that the drum is distorted and echoes. In anisotropic conditions (the dotted line is an attenuating wall, and the medium and wall are assumed to have linear phase and flat frequency response), listeners A and B have different experiences. The relative volume of each instrument is a function of the listener's position. For listener B, the bass and drum are attenuated because the wall blocks the line of sight.

likely due to correlations in the LFP source itself.

If frequency response is preserved but the phase is nonlinear, information about the relative timing of frequencies is lost. Note that the sinusoids are each shifted relative to one another. Of more dire consequence is the loss of precise timing from the drum; this signal becomes quite distorted in time, making it more difficult to estimate when the drum was hit. For the neurophysiologist, this analogy directly relates to the measurement of event-related potentials, where the timing of signals is of particular interest. Clearly, the phase nonlinearity would undermine the interpretation of differences in the response of varying frequency components to an external event (e.g., a stimulus, Gray and Singer, 1989; Siegel and Konig, 2003). But perhaps more seriously, a significant phase nonlinearity would distort temporal correlations of LFP components with spiking activity depending on the distances between the sources of the two signals and the electrode. This would presumably make it both harder to measure and to interpret changes in coherence between spikes and the LFP due to different behavioral states, such as attention (Fries et al., 2001; Womelsdorf et al., 2006; Buschman and Miller, 2007; Saalmann et al., 2007).

Finally, Logothetis et al. (2007) found that gray matter is isotropic, and thus signal transmission is unaffected by recording location. In our music example, we assume that the listeners are far away enough from the instruments that we can approximate the distances from each instrument as all being equal. Thus, in an isotropic medium, we expect the experience to be the same for listeners 1 and 2. However, in an anisotropic medium, it is possible for their experiences to differ. Imagine that listener 2 opted for a cheap seat with a partially obstructed view (dotted line). This obstruction creates an anisotropy: since the wall is between listener 2 and all instruments except the piano, the drum and bass are attenuated relative to the piano. For listener 1, who has an unobstructed view, the relative volume of each instrument is preserved. Thus, in gray matter we can assume that the relative strength of signals is based on the summing of distant sources attenuated by a factor proportional only to their distance from the recording electrode. This quality of gray matter thus allows neurophysiologists to pursue variations in LFP signals across the depths of cortical tissue (e.g., Chrobak and Buzsaki, 1998) with less concern that it is the medium itself that causes the variations.

Taken together, the observations of Logothetis and colleagues indicate that the cortex is a fairly safe place within which to measure and interpret LFPs in our increased attempt to understand what they reveal about the computations carried out by cortical circuits.

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