Multi-scale analysis of neural activity in humans: Implications for micro-scale electrocorticography

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HIGHLIGHTS

- We recorded neural activity using standard clinical ECoG grids, micro-ECoG grids, and intracortical micro-electrodes from human patients.
- We found that non-penetrating micro-ECoG grid recorded neural activity at scales closer to penetrating intracortical micro-electrodes than clinical ECoG grids.
- These novel micro-electrode technologies are enabling examination of cortical activity at the scale of cortical columns and could lead to improved diagnostics and neural prosthetic applications.

ABSTRACT

Objective: Electrocorticography grids have been used to study and diagnose neural pathophysiology for over 50 years, and recently have been used for various neural prosthetic applications. Here we provide evidence that micro-scale electrodes are better suited for studying cortical pathology and function, and for implementing neural prostheses.
Methods: This work compares dynamics in space, time, and frequency of cortical field potentials recorded by three types of electrodes: electrocorticographic (ECoG) electrodes, non-penetrating micro-ECoG (μECoG) electrodes that use microelectrodes and have tighter interelectrode spacing; and penetrating microelectrodes (MEA) that penetrate the cortex to record single- or multiunit activity (SUA or MUA) and local field potentials (LFP).
Results: While the finest spatial scales are found in LFPs recorded intracortically, we found that LFP recorded from μECoG electrodes demonstrate scales of linear similarity (i.e., correlation, coherence, and phase) closer to the intracortical electrodes than the clinical ECoG electrodes.
Conclusions: We conclude that LFPs can be recorded intracortically and epicortically at finer scales than clinical ECoG electrodes are capable of capturing.
Significance: Recorded with appropriately scaled electrodes and grids, field potentials expose a more detailed representation of cortical network activity, enabling advanced analyses of cortical pathology and demanding applications such as brain–computer interfaces.

1. Introduction

The activity of the cerebral cortex may be recorded at a variety of scales and depths—from microelectrodes within the

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cortex to magnetic resonance imaging. Selecting an appropriate technology requires balancing a number of trade-offs including clinical responsibility to mitigate risk, signal integrity, cortical coverage, and specificity in time, space, or frequency. For example, electroencephalography may record brain potentials without any invasive procedure, but with less detail at a given cortical site than a penetrating microelectrode. Some applications, such as localization of epileptogenic zones, need coverage over large areas of cortex while others, like brain–computer interfaces, depend more on signal integrity and specificity. Understanding the properties of neural activity at various spatial and temporal scales and levels of invasiveness is important input for optimizing electrode array design for acquiring specific neural data.

1.1. Signals and dynamics

Low-frequency (i.e., <500 Hz) intracortical, extracellular potentials are generated primarily by the sum of excitatory postsynaptic dendritic current sinks and sources near the recording electrode (Mitzdorf, 1985, 1987; Engel et al., 1990; Bullock, 1997; Buzsaki et al., 2012). Likewise, electrical potentials at the cortical surface consist principally of a summation of nearby synaptic dendritic activity (Freeman and Barrie, 2000), and are typically analyzed in the same or similar frequency range as LFPs (e.g., <500 Hz). Neuronal firing activity may bleed into the upper portion of the frequency range of either LFP or surface potentials, though likely with less power and specificity at the surface than within the cortex since the intracortical electrodes are closer to those small-amplitude sources. Because field potentials constitute a summation, synchronized oscillations will sum to larger contributions than asynchronous oscillations (Freeman and Barrie, 2000; Mehring et al., 2004; Ray et al., 2008). Also, since gray matter is a resistive medium within the frequency range of interest (Logothetis et al., 2007), there will be little or no capacitive filtering of these signals, and the frequency content of field potentials recorded intracortically should be similar to that recorded epicortically. Thus, for example, modulation of power in the gamma band (i.e., 30–80 Hz) coincident with motor activity is evident in both LFPs and surface potentials. However, the properties of electric fields would suggest that with increasing distance between the source and electrode, electric potentials will be smaller in magnitude and more diffuse in space.

In addition to passive propagation through the extracellular space, active processing by cortical circuits will play a role in defining spatiotemporal properties of field potentials. Synchronous oscillations are a fundamental property of the brain's processing mechanisms (Engel et al., 1990; Singer and Gray, 1995; von der Malsburg, 1995; Buzsaki and Draguhn, 2004; Fries, 2009). Temporally and spatially transient binding between and within populations of neurons will be reflected in dynamic and distributed correlations across cortex, if the signals are recorded with enough resolution in space and time. In some areas of the brain, such as in striate cortex, neurons with similar processing preferences have been shown to organize in cortical columns with diameters in the range of several hundred microns (Mountcastle, 1957; Singer and Gray, 1995). Interactions both within and between columns in visual cortex have demonstrated dynamic spatiotemporal patterns which are thought to represent the binding of features for cortical processing (Engel et al., 1990; Singer and Gray, 1995; von der Malsburg, 1995; Buzsaki and Draguhn, 2004; Fries, 2009; Ayzenshtat et al., 2010; Jia et al., 2011). Similar types of neuronal assemblies have been demonstrated in other areas of cortex (Georgopoulos et al., 1993; Amirikian and Georgopoulos, 2003), and subcentimeter organization has been observed in still other areas (Flinker et al., 2011). These assemblies comprise mesoscopic

building blocks of cortical information processing and establish a lower limit on the actively-induced component of the field potentials' spatial extent on the order of a few hundred microns. It is of historical interest that the basic design of ECoG electrode grids instantiated in the 1950s has changed little since that time, while the evidence supporting mesoscopic information processing in the cerebral cortex has accumulated (Penfield and Jasper, 1954; Mountcastle, 1997).

The spatial extent of LFP has been characterized in a number of studies reporting a wide range of values, from a few hundred microns (Liu and Newsome, 2006; Katzner et al., 2009; Xing et al., 2009; Leski et al., 2013) to a millimeter or more (Engel et al., 1990; Kreiman et al., 2006; Berens et al., 2008; Jia et al., 2011; Leski et al., 2013; Seyedhosseini et al., 2014). These disparate results reflect the complexity inherent in continuous fields produced by the massive, intricate network of electrical sources and pathways in the cortex, and the complex way in which these elements interact to produce coherent outputs from myriad sensory and cognitive inputs (Linden et al., 2011). Indeed, the spatial properties of cortical field potentials have been shown to depend on frequency (Destexhe et al., 1999; Buzsaki and Draguhn, 2004; Liu and Newsome, 2006; Berens et al., 2008; Canolty and Knight, 2010; Leski et al., 2013), brain state (Destexhe et al., 1999), the nature of stimuli (Jia et al., 2011) and behavior (Fetz et al., 2000), across cortical layers (Xing et al., 2009; Linden et al., 2011; Leski et al., 2013), with anatomical location and between subjects (Aoki et al., 1999), and on neuron morphology, synapse distribution, and correlation in the synaptic activity (Linden et al., 2011; Leski et al., 2013).

The dynamic properties of recorded field potentials will also be influenced by the electrodes and electronics used to record them. When the voltages of two sensors are differentially amplified with respect to the same reference, active signals on the common reference could spuriously increase correlations between the amplified signals (Fein et al., 1988; Guevara et al., 2005). If two sensors record electric signals that originate from one or more common sources by volume conduction, those common signals will also increase the correlation between the two recorded signals. Finally, increased oscillatory synchronicity among neuronal populations recorded separately by the two sensors could also lead to higher correlations (Salinas and Sejnowski, 2001). Higher correlations are common to each of these scenarios; however, in the first case, the increase is an artifact of the recording setup, whereas in the latter two scenarios, the correlations reflect the underlying neural dynamics and the ability of the electrodes to capture those dynamics at a given spatiotemporal resolution. Recording artifact may be mitigated to a large extent by using a proper reference with high input-impedance amplifiers employing common-mode rejection as near the sensors as possible (Stacey et al., 2012, 2013). Phase relationships between signals may be used to distinguish volume conduction (in which the phase is necessarily 0 mod π) from other more physiologically-based correlations (Stam et al., 2007).

Although the true relationship between LFPs and ECoG may not be entirely understood, their similar underpinnings suggest that some information content may be shared and that some aspects of dynamic spatial and temporal scales may be similar. The principal advantage of intracortical LFP versus subdural ECoG has been better specificity of the intracortical field potentials; however, that comparison has typically been made between LFPs recorded on microelectrodes and ECoG recorded on relatively large disc electrodes. The discrepancy in electrode size is an important distinction, since broader synchronization would be required to effect change in the summed potential of larger neuronal populations integrated by the larger electrodes (Mehring et al., 2004; Ray et al., 2008; Slutzky et al., 2008, 2010).