LFP phase in motor cortex reveals precise spiking

A Review of: Reimer J, Hatsopoulos NG (2010) Periodicity and evoked responses in motor cortex. J Neurosci 30(34):11506-11515.

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Despite the classical view of the primary motor cortex as an encoder of motor commands, neurons in this area have also been shown to respond to sensory information relevant to impending action. Determining how these two functions are coordinated, such that the appropriate information is shared between neural ensembles with different jobs (while minimizing interference) addresses a fundamental question about brain function: How do ensembles with different inputs, variable processing latencies, and complex connectivity patterns organize their outputs in order to process incoming information in a parallel manner? Brain rhythms have been implicated in the synchronization of neural firing, both within a local area and across anatomically distant areas (Singer 2009; Canolty et al., 2010). Significant power in the beta frequency band (10-45Hz) of local field potential (LFP) oscillations in M1 appears during movement preparation but drops off during movement (Sanes et al., 1993). Beta oscillations have been observed in pyramidal tract neuron discharge, EMG recordings of muscle contractions, and single spinal motoneuron firing (Conway et al., 1995; Kilner et al., 2002). Strong beta power also appears in M1 and S1 during tactile exploration, as in retrieving raisins from a Kluver board, but not in "automatic" overtrained motor actions (Murthy et al., 1992). Thus it would appear that beta oscillations are a component of motor system functions that require complex or coupled sensorimotor processing, rather than simple feedforward motor command generation.

Figure 1. Each row represents a hypothetical brain area, with specific examples from the sensorimotor system indicated. The light-colored spikes are unrelated to the LFP oscillations, which are indicated for each area by a sine wave. Instead they are driven by roughly linear feed-forward connections with ascending sensory information, and have relatively low temporal specificity (i.e. they are using a rate-coding scheme, where the downstream decoder must average over an interval to gain reliable information). The dark colored spikes are still sensitive to the rate-based afferent input (note that the mean firing rate is constant throughout the duration of the stimulus), but also show local LFP phase-specific increases in the precision of the timing of their spiking (note repeatability of spiking patterns in dark regions during the descending phase). This enables more complex multi-region computations to take place during periods of coordination, while each area maintains its own continuous rate correspondence with the rough estimation of stimulus intensity.

In their recent Journal of Neuroscience paper, Reimer and Hatsopoulos (2010) investigate the organizational principles underlying the sensory function of M1 by looking at the interaction between the phase of LFP beta oscillations and the precise timing of individual spikes . The primary finding in their work is that when monkeys perform a self-paced reaching task to serially presented visual targets, the spikes evoked by the appearance of new targets become most informative about target location at times that are dictated not only by a mean latency period but also by the phase of the local beta oscillation in the LFP. The authors show that LFP is partially phase-locked to the appearance of the target, beginning immediately and increasing in strength of locking (i.e. decreasing in entropy of the phase distribution) up to peak strength at a latency of ~100ms. They hypothesize that the immediate increase may reflect anticipation of the target presentation based on the time of approach of the prior target; new targets appeared immediately after successful movements to previous targets. This anticipation may reflect internal timing, other sensory input, or a combination of both. The exact mechanisms that drive the immediate phase-locking of cortical oscillations to external events remain obscure. Nonetheless,
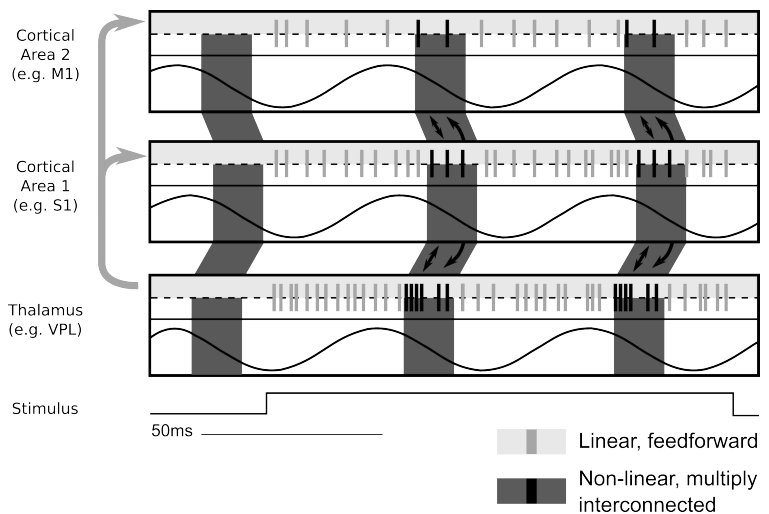
the authors claim that phase-locked beta oscillations provide a significant modulator of firing, defining periods of increased precision in the exact timing of spikes. As evidence for this the authors use a spike-resampling scheme in which the number of spikes in a narrow window (5 ms) centered on a particular latency is compared to the number of spikes expected in that window based on randomly shuffling the spike times occurring in a larger surrounding time period (25ms). This is done to control for the effect of the underlying rate increase evoked by the appearance of the target stimulus. The level of significance (p-value) of the increase in the narrow window is taken as a measure of spiking precision at the given latency (Reimer et al,. Fig. 3f,g). The authors show that the maximum precision of spiking is much greater when calibrating spike times to the peak of beta oscillation closest to 100ms post-event rather than when using absolute post-event time of spikes (Reimer et al., Fig. 6f,g).

Perhaps most interestingly, the authors also show that spikes occurring during the descending phase of the oscillation are more informative about the target location. Using mutual information, a Shannon-entropy based measure of the reduction in uncertainty about a stimulus attributable to the occurrence of spikes, they show that information about target location varies widely on an external time scale (Reimer et al., Fig. 5). They then apply the same measure to spike times recalibrated to local beta oscillation phase, and find phase-locked oscillations in informativeness (Reimer et al., Fig. 7 g,h). So overall, spikes occurring approximately 100 to 400 ms after the event onset in external time are more informative than those occurring before this (naturally, based on sensory afferent and processing latency), but within that period the informativeness varies on a finer scale with the phase of the underlying local beta oscillation. The authors looked at the above effects in three different cell types, differentiated by spike waveform and presence or absence of bursting. The exact correspondence between the classes they observed and perviously known functional classes is unclear, but the authors show the highest precision and most informativeness for narrow-waveform non-bursting cells, compared to wide- or narrow-waveform bursting cells. The functional significance of this remains to be seen, but may involve the differences between cell types that generate the beta oscillations and synchronize them across brain regions (hypothesized to be interneurons), and those that leverage this underlying oscillation to selectively communicate with downstream targets (Uhlhaas et al., 2009).

Sensory input informs motor plans, and motor output likewise gates or modulates afferent sensory signals. Such calculations can occur at the level of a single neuron. Indeed, single cells in M1 have shown activity simultaneously related to sensory input, impending motor output, and a learned conjunction rule mapping between the two (Zhang et al., 1997). Nonetheless, a great deal of information is only revealed when looking at activity of whole ensembles (e.g. Georgopoulos et al., 1986), and M1 activity is clearly influenced by activity in other areas. Thus the computations performed by multiple brain networks must communicate in order to act as an adaptable controller with feedback, as required for sensorimotor adaptation to changing environmental conditions as well as sensory perception based on motor commands. Understanding integrated sensorimotor function requires knowledge of the neural mechanisms used to share sensory information across disparate neural ensembles both within M1, and between it and other sensorimotor areas (e.g. S1, PMd, PPC, VL thalamus, VPL thalamus). General insight into the mechanisms by which spatial sensory information (such as visual, or proprioceptive) is represented in M1, such as that provided by Reimer et al., gives clues as to the means by which information of a much broader class of modalities may be represented and integrated to perform specific tasks in various neural circuits. Which neural areas direct these interactions under given circumstances is still very much an open question. For example, the above results may reflect phase-locking and spike timing modulated primarily by thalamic activity, or by an intracortical process. Application of the authors' methods to a wider set of brain areas including the thalamus, posterior parietal and association cortex, and basal ganglia will likely be valuable in establishing a more general theory for brain function.

A general hypothesis for the organization of sensorimotor processing in primates consistent with the findings of Reimer et al. is illustrated by Figure 1. Sensory information from thalamus (which may be modulated by remote cortical activity) is relayed to motor and sensory cortex roughly linearly, such that a rate-based encoding scheme with a temporal resolution of 25ms or more can be used to differentiate sensory states (e.g. loci of cutaneous stimulation, or joint angles based on proprioception) with fidelity good enough to provide a continuous 'background' estimate of their values. During particular phases of LFP beta oscillation, however, these same cells express a lowered threshold for activation by much more widely distributed networks, whose combined activity comprises a (very) non-linear calculation wherein particular spike times become essential, but offers greatly improved resolution across more dimensions of a stimulus (or action). By 'riding' on their respective local linear input, all participating members of the non-linear ensemble are assured at all times of being at least roughly accurate about the state of the local calculation, which they may thereby render up to the larger network.

The findings by Reimer et al. offer tantalizing clues into the means by which motor cortex is able to flexibly incorporate plans from frontal areas with sensory input from multiple brain systems in order to compute appropriate motor outputs. Furthermore, they provide evidence for a framework with which to understand how local and distributed neural processes interact, and to search for the principles of operation used by brain networks subserving such functions as sensorimotor control and perception, procedural memory, and attention.

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