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BOLD and spiking activity

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Viswanathan and Freeman[1] claim that oxygen concentration and, by inference, blood oxygen level–dependent (BOLD) functional magnetic resonance imaging (fMRI) reflect synaptic activity more than spiking activity. As this is a fundamental and controversial issue in fMRI research, this claim, if incorrect, may erroneously bias the interpretation of a large body of data.

The authors simultaneously recorded multi-unit activity (MUA), local field potentials (LFP) and tissue oxygen concentration in primary visual cortex of anesthetized cats stimulated with moving gratings. During high temporal-frequency stimulation, when thalamic inputs were active, but few cortical neurons responded, oxygen signals were observed without MUA. Therefore, the authors concluded that oxygen responses reflect synaptic inputs more than spiking. However, careful inspection of their results leads to the opposite conclusion and supports a tight coupling between oxygen signals and local cortical spiking.

Tissue oxygen responses show an initial decrease that is attributed to local oxygen consumption (negative peak) and a delayed increase that is attributed to more global changes in blood flow (positive peak). The authors showed that the initial negative peak was greater than zero during high-frequency stimulation (when spiking activity was absent), but it was in fact 80–90% smaller to high-frequency stimulation than to low-frequency stimulation (calculated from ref. 1, see red arrow in Fig. 1). Given that roughly the same thalamic input is expected on stimulation of either temporal frequency[2], we conclude that the initial negative oxygen response depended only slightly (10–20%) on thalamocortical synaptic activity and mostly (80–90%) on cortical spiking.

What about the more widespread delayed positive oxygen response? This component was evident during stimulation at high frequencies, but only in one of their two experiments that used large stimuli. A previous study demonstrated that delayed positive oxygen responses were associated with spiking outside the field of view of the electrode when using such large stimuli[3]. There is, therefore, a mismatch between the spatial extents of MUA (which

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involves the neurons closest to the electrode tip) and positive oxygen responses (which reflect a much larger neuronal population), making the comparison between the two measurements difficult to interpret. MUA measurements may also suffer from a sampling bias by failing to record spiking activity in particular types of neurons (small neurons or specific cortical layers). For example, neurons in layer 4 and adjacent area 18 that respond to higher frequencies[4,5] may have contributed to the residual LFP and delayed oxygen responses while being invisible to the MUA electrode.

The problem of deducing the population's state from a few recording sites is a general methodological concern in any attempt to compare spiking activity with LFP and vascular responses[6]. Spiking not detected by the electrode may be reflected in LFP and vascular responses, which sum activity over a larger population. An ostensible mismatch between the measured spiking activity and LFP or vascular responses may be a result of these biases even when the spiking, LFP and BOLD are well correlated[7].

We do not mean to suggest that vascular responses are driven directly by spiking, as if blood vessels are voltage sensitive. Indeed vascular responses are likely to be of synaptic origin[8]. In contrast to subcortical structures, however, cortical circuits are dominated by massive local connectivity in which most synaptic inputs originate from nearby neurons[9] and only a small minority of inputs originate from distant sites such as the thalamus. Thus, synaptic 'inputs' in cerebral cortex are mostly produced by local spiking of neighboring neurons, leading invariably to a tight coupling between synaptic and spiking activity, as well as oxygen responses[10].

The difficulty of Viswanathan and Freeman[1] in decoupling synaptic from spiking activity in the cortex is not surprising. The authors implicitly assumed a feedforward model of cortical processing, which is inaccurate. Whatever the mechanisms of neurovascular coupling are, the extent of decoupling between synaptic and spiking activity ultimately depends on the nature of cortical processing; that is, whether the cortical dynamics can be switched from a local recurrent mode to a strictly feedforward mode in which synaptic inputs to a cortical area and the targets of its spiking outputs are segregated. The Viswanathan and Freeman[1] study was designed to reveal such decoupling, but the results of their experiments argue against such segregation by showing that 80-90% of the local vascular response is coupled to local spiking activity.

References

1. Viswanathan A, Freeman RD. Nat. Neurosci. 2007; 10:1308–1312. [PubMed: 17828254]
2. Bonin V, Mante V, Carandini M. J. Neurosci. 2005; 25:10844–10856. [PubMed: 16306397]
3. Thompson JK, Peterson MR, Freeman RD. J. Neurosci. 2005; 25:9046–9058. [PubMed: 16192396]
4. Hawken MJ, Shapley RM, Grosof DH. Vis. Neurosci. 1996; 13:477–492. [PubMed: 8782375]
5. Li B, Peterson MR, Thompson JK, Duong T, Freeman RD. J. Neurophysiol. 2005; 94:1645–1650. [PubMed: 15843483]
6. Logothetis NK, Pauls J, Augath M, Trinath T, Oeltermann A. Nature. 2001; 412:150–157. [PubMed: 11449264]
7. Nir Y, et al. Curr. Biol. 2007; 17:1275–1285. [PubMed: 17686438]
8. Iadecola C, Nedergaard M. Nat. Neurosci. 2007; 10:1369–1376. [PubMed: 17965657]

9. Amir Y, Harel M, Malach R. J. Comp. Neurol. 1993; 334:19–46. [PubMed: 8408757]
10. Heeger DJ, Ress D. Nat. Rev. Neurosci. 2002; 3:142–151. [PubMed: 11836522]

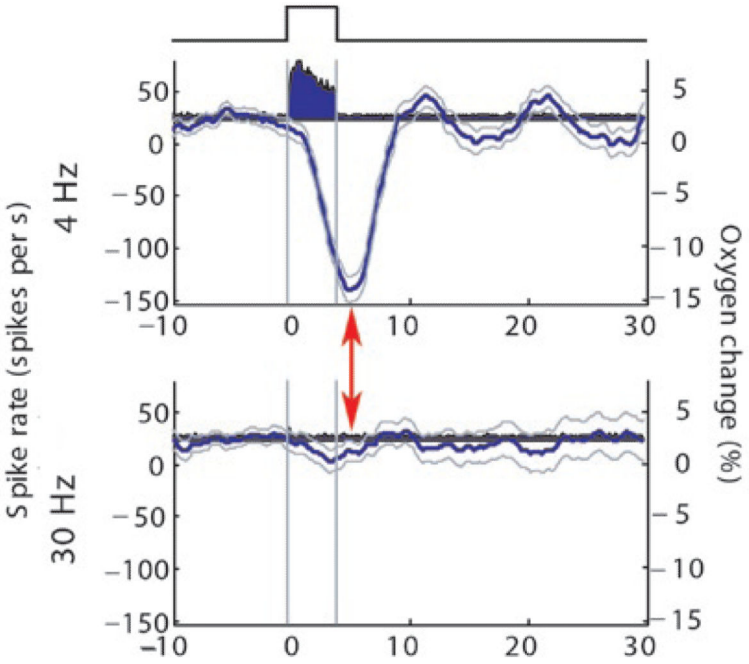

Figure 1.

MUA and oxygen responses for low (top) and high (bottom) temporal frequencies (reprinted from Viswanathan and Freeman[1]).