Interareal Neocortical Actions By Neuronal Populations

Steven L. Bressler
Center for Complex Systems and Brain Sciences
Florida Atlantic University

Manuscript submitted as chapter for book on Collective Brain Dynamics:
Extending Beyond the Neuron Doctrine
Springer Series on Studies in Systems, Decision, and Control

Submitted: 3/22/2015
Introduction

The purpose of this short chapter is to advance our understanding of the functional actions that occur between different areas of the mammalian neocortex. This topic is of immense importance to the question of the neural basis of cognition, both in animals and humans. For example, one conceptual framework that has emerged over many years describes cognitive function in terms of actions between areas in large-scale networks of the neocortex, or neurocognitive networks (Mesulam 1990, 1998; Bressler 2008; Meehan & Bressler 2012). It posits the neocortical area as a computational processing entity in the brain, and the large-scale structure of anatomical pathways connecting those areas as the connectivity matrix that determines the interareal actions underlying the cortical computations of a species. The inhomogeneity of the large-scale cortical connectivity suggests that the neocortex is not a homogeneous computational medium and that interareal cortical connectivity is important for cortical function. The neurocognitive network framework is directly linked to the idea that cognition is a collective phenomena that emerges from the actions exerted between cortical areas. In short, the nature of cognition in the human brain is intimately tied to an understanding of how cortical areas act upon one another, and how those actions lead to emergent neurocognitive phenomena.

The actions brought to bear between neocortical areas are no doubt synaptic and excitatory, and the excitatory synapses are found at the terminals of fiber pathways that project from a sending area to a receiving area. These interareal pathways consist of axons from the large projection neurons in the sending area. These are the excitatory pyramidal cells, which are the cellular generators of many of the observable macroscopic neural fields of the brain, such as the electroencephalogram (EEG), magnetoencephalogram (MEG), electrocorticogram (ECoG), and local field potential (LFP) (Lopes da Silva 2013). The cell types in the receiving area that receive the pyramidal cell axonal terminals are multiple and variable (Barbas 1993, 2000; Rempel-Clower & Barbas 2000). Interareal feedforward excitation occurs when projection neurons excite recipient excitatory neurons (either other projection neurons or excitatory interneurons), and interareal feedforward inhibition occurs when the projection neurons excite recipient inhibitory interneurons. For projections between hierarchically arranged areas such as in visual cortex, the termination layer pattern depends on whether the projection is bottom-up, top-down, or lateral (Felleman & Van Essen 1991). Since the pathways between cortical areas are predominantly bi-directional, the actions are usually exerted concurrently in both directions. Hence, each area is typically both sending and receiving, and bi-directional cortical interactions are much more prevalent than uni-directional actions.

In this chapter, I will contrast evidence for two radically different models of the actions exerted by neurons in a sending cortical area on those in a receiving area. The first (neuron-neuron) model considers that actions (or interactions) occur between individual cortical neurons, whereas the second considers that they occur
between neuronal populations. From the well established neuron doctrine (Barlow 1972; Shepherd 1991), it often seems intuitive to suppose that single neurons are the basis for interareal actions in the neocortex, and hence that the neuron-neuron model is the correct one. However, although the individual cortical neuron has repeatedly been shown to signal specific sensory features, it does not necessarily follow that the transmission of sensory information from one cortical area to another transpires, point-to-point, from one cortical neuron to another. Hence, the second (population-population) model, although counterintuitive, may be the correct one.

The distinction between the neuron-neuron and the population-population models may appear at first glance to rest on the difference between single-neuron and population coding of perceptual and cognitive features. However, interaction models are independent of coding models, and it be that single neurons perform coding within cortical areas whereas the transmission of cognition-relevant activity between areas is by neuronal populations. Similarly, local, within-area processing may be performed by the neuronal assembly, whereas the action exerted between areas may be by way of single neurons. In any case, the question under consideration is not whether neurons carry influences between neocortical areas. Both the neuron-neuron and the population-population models hold that they do. Rather, the question is whether interareal interactions are organized at the level of the single neuron or the neuronal population.

The prevalence of interareal functional effects observed in the cortex (Hupé et al. 1998, 2001; Young 2000) suggests that interareal interactions are important for cortical computation. However, it is not known whether the interactions are organized at the single neuron or neuronal population levels. One way to approach this question is by comparison of the evidence for interareal neuron-neuron and population-population interactions. If there is ample evidence for interareal neuron-neuron but not population-population interactions, then the neuron-neuron model is to be preferred. If there is ample evidence for interareal population-population but not neuron-neuron interactions, or there is ample evidence for both, then the population-population model is favored.

In addition to the spatial scale of interaction (neuron-neuron or population-population), the temporal scale is also relevant. The temporal scale refers to the length of time over which the interaction is in effect. To be relevant for neocortical function, significant interactions must transpire on a time scale commensurate with that of functional events. Since these events may be brief (i.e. on a sub-second time scale), evidence must exist that interareal interactions are also brief.

**Neuron-Neuron Interactions**

Neuron-neuron interactions in the neocortex are typically studied by cross-correlation analysis of simultaneously recorded multiple neuron spike trains (Aertsen & Arndt 1993). Similar analyses focus on detecting repeated firing patterns
in multiple-neuron spike-train data that repeat with above-chance likelihood (Abeles et al. 1993). Cross-correlation analysis reveals neuron-neuron spike synchrony that is brief and significantly above the background level. Often, neuron-neuron synchronous firing is observed to occur briefly in sensory cortex in response to a sensory stimulus or briefly in motor cortex in relation to a movement: sensory and motor event-related neuron-neuron synchrony is well established and has important functional relations (Aertsen & Gerstein 1985; Aertsen & Arndt 1993; Riehle et al. 1997). For example, the task-related synchronous firing of auditory cortical neurons reflects the strengthening of functional synaptic connections between them (Ahissar et al. 1992), and neuron pairs in prefrontal cortex show briefly correlated activity in relation to working memory processes (Funahashi & Inoue 2000).

There have been numerous reports of stimulus-evoked briefly synchronous firing between neurons in different visual cortical areas of the cat (Eckhorn et al, 1988, 1992; Engel et al. 1991a,b; Nelson et al. 1992) and monkey (Bullier et al. 1992; Roe & Ts’o 1992; Nowak et al. 1994). Inter-neuron coupling is most often observed between cells having overlapping receptive fields during co-activation by visual stimuli (Singer & Gray 1995; Smith et al. 2013). Although neurons with the same orientation selectivity in different visual areas are not preferentially linked (Nelson et al. 1992), the incidence of synchronous firing is greater for cells having overlapping receptive fields and similar orientation preference (Singer & Gray 1995).

Synchronous interareal firing is usually weak except when neuronal activity is oscillatory, implying that interareal synchrony depends on population activity. This is because oscillations are thought to arise in neuronal activity due to the interactions of intra-areal neuronal populations, not individual neurons. Thus, although individual cortical neurons display oscillatory activity, it is because they are imbedded in intra-areal neuronal populations that oscillate; the synaptic connectivity that is responsible for the oscillation is a population property that is shared by the neurons in the population (Freeman 2005). This explanation can account for the finding that stimulus-induced coupling of V1-V2 spiking activity depends on the presence of a strong and coherent gamma rhythm in these visual cortical areas (Jia et al. 2013). The implication for interareal interaction is that interareal neuron-neuron interaction depends on intra-areal population activity, supporting the idea that interareal interactions are organized at the population level.

**Population-Population Interactions**

That interareal cortical interactions are organized at the level of neuronal populations is suggested by the high degree of divergence and convergence, and the high level of density, in the anatomical connectivity between cortical areas. Because the axons of single projection neurons branch profusely in receiving areas, each projection neuron provides excitatory drive to multiple recipient neurons and each
recipient neuron receives excitatory drive from multiple projection neurons. Furthermore, because of the high density of connectivity, the divergence and convergence ratios are extremely high. Therefore, based solely on anatomical projection patterns, interareal cortical interactions are most likely to be organized at the level of neuronal populations.

Interactions between neuronal populations in different areas of the neocortex are typically measured by the cross-correlation or spectral coherence between LFPs simultaneously recorded from the areas. The LFP arises in the neocortex as dendritic potentials from neuronal populations (Lopes da Silva 2013). It is generally agreed that the LFP is not transmitted between areas (although see Alle & Geiger 2006; Shu et al. 2006; Kruger & Otis 2007). However, the LFP at a cortical recording site may serve as an index of the joint neuronal activity of the population located at that site that is more readily recorded with cortical microelectrodes than unit activity. Also, since the LFP is more highly correlated with the fMRI BOLD signal than unit activity (Logothetis et al. 2001), the LFP more closely reflects the neurovascular response of a neuronal population in the neocortex.

The cross-correlation or spectral coherence between LFPs simultaneously recorded from two cortical areas thus represents a measure of the interaction between those areas, even though the population spiking activity that carries the influences between areas is not directly recorded. Since the LFP is thought to reflect the input to, and intracortical processing of, an area, and spiking activity the output, the spike-field coherence, with simultaneous recording of spiking in one area and the field (LFP) in the other, is also used to measure interareal cortical interactions (Pesaran et al. 2008; Salazar et al. 2012).

One of the first reports on the functional relevance of interareal cortical interaction was in the paleocortex, where synchrony between simultaneously recorded LFPs from the olfactory bulb and cortex was found to relate to respiratory inhalation (Bressler 1987). Subsequently, a number of studies have used the cross-correlation or spectral coherence of simultaneously recorded LFPs to demonstrate the functional relevance of interareal neocortical interactions: interareal synchrony between visual and motor cortical areas indexes visuomotor behavior (Bressler et al. 1993); interareal visual cortical synchrony reflects stimulus expectancy (von Stein et al. 2000); interareal cortical synchrony in the dorsal visual pathway reflects spatial attention (Saalmann et al. 2007); interareal synchrony between pre- and postcentral cortical areas reveals a distributed large-scale sensorimotor network related to the maintenance of steady arm and hand muscle contractions (Brovelli et al. 2004); the magnitude and frequency of synchrony between prefrontal and posterior parietal cortical areas distinguish bottom-up from top-down forms of attention (Buschman & Miller 2007); the synchrony between prefrontal and posterior parietal cortical areas distinguishes the content of visual working memory (Salazar et al. 2012); the synchrony between visual areas V1 and V2 reflects contrast stimulation (Roberts et al. 2013); and interareal visual synchrony reflects attentional stimulus selection (Bosman et al. 2012). Likewise, spike-field coherence
demonstrates interareal interaction between posterior parietal and premotor cortices in relation to free choice (Pesaran et al. 2008), and between posterior parietal and prefrontal cortices in relation to visual working memory (Salazar et al. 2012).

Another line of evidence that relates to interareal interaction comes from studies of cryogenic blockade. Generally, the reversible cooling of one cortical area affects the function of neurons in another area. Cells in visual cortical area 17 of the squirrel monkey become less responsive to visual stimulation when area 19 is cooled (Sandell & Schiller 1982); cooling of either the dorsolateral prefrontal cortex or the inferotemporal cortex lowers spontaneous neuronal firing, and that related to a visual short-term memory task, in the other area (Fuster et al. 1985); cooling of posterior parietal cortex lowers firing rates of prefrontal neurons (Quintana et al. 1989); cooling of either posterior parietal or dorsolateral prefrontal cortex impairs neuronal firing related to an oculomotor delayed response task in the other area (Chafee & Goldman-Rakic 2000); and cooling of either primary or secondary auditory cortex suppresses neuronal responses to tonal stimulation in the other area (Carrasco & Lomber 2010). Since the cooling in these studies is applied to an entire cortical area, the results appear to support the population-population model of interaction between cortical areas. However, the neuron-neuron interaction model cannot be ruled out because cooling of an entire area affects the individual neurons within it.

Discussion

The question of how neocortical areas act upon one another is of immense importance for understanding the neural basis of cognition. It is well established that the neocortex is critically important for cognitive functions. To realize the veracity of this point, one need only consider the devastating cognitive impairments that result from cortical lesions. Many brain theories of cognition rely on coherent interactions between different cortical areas (Singer 1994; Dehaene & Naccache 2000; Fan & Posner 2004; Horwitz & Braun 2004; Fries 2005).

The bulk of currently available evidence, both from neuroanatomy and neurophysiology, suggests that the interactions between cortical areas are organized at the level of the neuronal population. Studies of correlated spiking from neurons in different areas of the neocortex show that synchronous interareal firing is only robust when neuronal population activity is oscillatory. This finding suggests that interareal neuron-neuron cortical interactions are embedded in oscillatory population-population interactions, and that interareal neuron-neuron correlations result from population-population correlations. In contrast to the evidence for interareal neuron-neuron interactions, the evidence for interareal population-population interactions, suggested by ample studies of interareal field-field and spike-field correlations, and by interareal cortical cooling effects, is robust.
References


Funahashi S, Inoue M. Neuronal interactions related to working memory processes in the primate prefrontal cortex revealed by cross-correlation analysis. Cerebral Cortex, 2000, 10:535-551.


Rempel-Clower NL, Barbas H. The laminar pattern of connections between prefrontal and anterior temporal cortices in the Rhesus monkey is related to cortical structure and function. Cerebral Cortex, 2000, 10:851-865.


