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Review Article

Propagating waves in thalamus, cortex and the thalamocortical system: Experiments and models

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ABSTRACT

Propagating waves of activity have been recorded in many species, in various brain states, brain areas, and under various stimulation conditions. Here, we review the experimental literature on propagating activity in thalamus and neocortex across various levels of anesthesia and stimulation conditions. We also review computational models of propagating waves in networks of thalamic cells, cortical cells and of the thalamocortical system. Some discrepancies between experiments can be explained by the "network state", which differs vastly between anesthetized and awake conditions. We introduce a network model displaying different states and investigate their effect on the spatial structure of self-sustained and externally driven activity. This approach is a step towards understanding how the intrinsically-generated ongoing activity of the network affects its ability to process and propagate extrinsic input.

Contents

1. Introduction

Recent years have seen an increase in measurements of large-scale spatiotemporal dynamics of neocortical networks, due to improvements in voltage-sensitive dye (VSD) (Shoham et al., 1999) and in multielectrode array (MEA) (Maynard et al., 1997) technologies. With these technological advancements, it is now generally possible to use single-trial imaging to observe the detailed dynamics of cortical circuits, whose trial-to-trial variability may preclude measurement by averaging techniques. Following preliminary evidence from electrophysiological and optical imaging studies *in vitro* (Chagnac-Amitai and Connors, 1989; Langdon and Sur, 1990; Hirsch and Gilbert, 1991; Metherate and Cruikshank, 1999; Sanchez-Vives and McCormick, 2000; Wu et al., 2001; Huang et al., 2004; Pinto et al., 2005), VSD and MEA

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experiments have provided direct observations of spatiotemporally coherent population activity in many cortical areas, anesthetic states, and stimulation conditions. For example, propagating waves have been observed *in vivo* in the visual (Grinvald et al., 1994; Kitano et al., 1994; Slovin et al., 2002; Jancke et al., 2004; Xu et al., 2007; Ahmed et al., 2008; Han et al., 2008; Nauhaus et al., 2009), somatosensory (Derdikman et al., 2003; Petersen et al., 2003; Civillico and Contreras, 2006), auditory (Reimer et al., 2010); and motor (Rubino et al., 2006) cortices under both spontaneous and evoked conditions. These diverse observations suggest that propagating waves could potentially be a general phenomenon in the large-scale dynamics of neocortex. These results, however, have been obtained under a myriad of anesthetic conditions and brain states, and a unified account of the dependence of propagating waves on network state has not yet emerged. It is therefore necessary to first determine the relationship of propagating waves to awake, activated brain states.

In the present paper, we first review the experimental literature from multichannel recording techniques, focusing specifically on propagating activity in thalamic, cortical and thalamocortical networks. In cortical networks, we also emphasize the brain state involved in each study, to assess the functional relevance of propagating waves to the awake brain. The critical factor in determining a network's responsiveness to perturbations is its conductance state (Destexhe and Paré, 1999; Destexhe et al., 2003), as the conductance state determines the average membrane potential throughout the network and the driving force on a single input, given a fixed conductance change at the synapse. Changes in global brain state, such as anesthesia or arousal (from sleep to wake), affect the spatiotemporal dynamics of cortical networks via changes in conductance state. Thus, we will analyze changes in brain state within the framework of conductance-based effects at the network level. We will focus mainly on experimental results from primary visual cortex and refer to the results from other brain areas (auditory, somatosensory, motor) for purposes of comparison. We also review both experiments and models of propagating waves in thalamic, cortical and thalamocortical networks. Finally, we present preliminary results from a computational study using network models of nonlinear adaptive exponential integrate and fire (AdEx) neurons (Brette and Gerstner, 2005). Neuronal adaptation has previously been shown to be critical for modeling the transition between UP/DOWN and AI states (Destexhe, 2009); here, we study the contributions of neuronal adaptation to low-frequency activity (1–4 Hz) and excitatory/inhibitory (E/I) interactions to high-frequency activity (20–80 Hz) as parallel factors determining the network state. Moreover, because the adaptation variable in the AdEx model has a straightforward interpretation in terms of specific membrane conductances (K^+), which are also those affected by many anesthetic drugs (Sanchez-Vives and McCormick, 2000; Franks, 2008; Destexhe, 2009), a connection among basic pharmacology, brain state, and spatiotemporal network dynamics becomes possible.

2. Propagating waves in different networks and network states

2.1. In vitro

The possibility of coherent propagating activity was first raised by VSD, MEA, and intracellular studies *in vitro*. Though some studies have used disinhibited slices to study the spatial component of epileptiform activity (Chagnac-Amitai and Connors, 1989; Huang et al., 2004; Pinto et al., 2005), many studies have observed propagating activity in pharmacologically normal slices (Langdon and Sur, 1990; Hirsch and Gilbert, 1991; Metherate and Cruikshank, 1999, Wu et al., 2001). It is well known that neurons *in vitro*, which lack a large fraction of synaptic input, have low membrane potentials and high input resistances (Cruikshank et al., 2007) compared to those measured *in vivo* (Steriade et al., 2001), similar to a neocortical DOWN state (Steriade et al., 1993; Destexhe et al., 2003). Propagating activity *in vitro* is typically initiated by means of electrical stimulation, either directly to cortical areas (Wu et al., 1999, 2001; Buonomano, 2003; Pinto et al., 2005) or to thalamocortical afferents (Metherate and Cruikshank, 1999), although in at least one study activity was stimulated using local application of glutamate (Sanchez-Vives and McCormick, 2000). While these stimuli certainly have different statistics from those induced by the sensory stimulation delivered *in vivo*, these artifically induced depolarizations may serve as a basic pulse perturbation. Because of the quiescent state of these neuronal networks, the driving force on the EPSPs evoked by these stimuli will be strong and synchronously drive many neurons close to spiking threshold. Interestingly, recent evidence *in vitro* also suggests a critical role for the infragranular layers (and interlayer interactions) in supporting the horizontal spread of activity across the cortex (Wester and Contreras, 2012).

The pharmacological dependence of propagating activity has been well-characterized by *in vitro* studies and has been localized to individual receptor classes. Several studies have shown that the non-NMDA glutamatergic ionotropic receptor antagonists CNQX[1] and DNQX[2] block horizontal propagation (Fukuda et al., 1998; Metherate and Cruikshank, 1999; Sanchez-Vives and McCormick, 2000; Wu et al., 2001; Pinto et al., 2005), specifically implicating polysynaptic fast glutamatergic transmission in sustaining propagating activity. NMDA-mediated conductances have also been shown to play a role in horizontal propagation, albeit to a lesser extent, with some studies showing a clear dependence of the generation of propagating activity on these receptors (Metherate and Cruikshank, 1999; Wu et al., 2001) and others showing only a modulatory effect (Fig. 1A) (Fukuda et al., 1998; Sanchez-Vives and McCormick, 2000). Blockage of $GABA_A$ receptors has a dramatic affect on neuronal activity, transforming normal horizontal propagation into epileptiform activity (Wu et al., 2001; Pinto et al., 2005), speeding up the propagation (from 11 ± 6 mm/s to 125 ± 24 mm/s – Fig. 1B), and focusing activity around the wavefront.

Combined with intracellular studies of horizontal axonal conduction, which falls in the range of 100–500 mm/s for unmyelinated intracortical fibers across species and cortical areas (Bringuier et al., 1999; Hirsch and Gilbert, 1991; González-Burgos et al., 2000; Murakoshi et al., 1993; Telfeian and Connors, 2003), VSD and MEA studies *in vitro* captured the first estimates of the speed of horizontal propagation of population events across the surface of the cortex (Fukuda et al., 1998). This estimation of propagation speed is in general agreement for the speeds observed *in vivo* (Grinvald et al., 1994; Jancke et al., 2004; Nauhaus et al., 2009), though some studies have reported values one order of magnitude lower in the anesthetized rat (Xu et al., 2007; Han et al., 2008) and slice preparations (Sanchez-Vives and McCormick, 2000; Wester and Contreras, 2012). While the cause for this discrepancy is unclear, possible sources include the vast differences in brain state for individual experiments, species-specific differences between rodents and other mammals, or differing techniques for measuring propagation speed (e.g. center of mass methods (Xu et al., 2007; Han et al., 2008), latency analysis (Tanifuji et al., 1994), and the offset of maximum correlation (Sanchez-Vives and McCormick, 2000)).

[1] 6-Cyano-7-nitroquinoxaline.
[2] 6,7-Dinitroquinoxaline-2,3-diome.