Journal of Theoretical Biology ■ (■■■■) ■■■–■■■

Contents lists available at ScienceDirect

Journal of Theoretical Biology

journal homepage: www.elsevier.com/locate/yjtbi

Slow-wave oscillations in a corticothalamic model of sleep and wake

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HIGHLIGHTS

- We model cortical UP/DOWN states using a corticothalamic neural field model.
- We implement bursting dynamics in the reticular nucleus of the corticothalamic model.
- The neural field model is capable of reproducing deep amplitude cortical UP/DOWN oscillations in slow-wave sleep, while also reproducing EEG time series and power spectra characteristic of wake and spindle states.

ARTICLE INFO

Article history:
Received 2 May 2014
Received in revised form
21 January 2015
Accepted 24 January 2015

Keywords:
Slow wave sleep
Neural field theory
Thalamus
Cortex

ABSTRACT

A physiologically-based corticothalamic neural field model is used to study slow wave oscillations including cortical UP and DOWN states in deep sleep by extending it to incorporate bursting dynamics of neurons in the thalamic reticular nucleus. The interplay of local bursting dynamics and network interactions produces the cortical UP and DOWN states of slow wave sleep while preserving previously verified model predictions in the wake state. Results show that EEG spectral features in wake and sleep are reproduced. The bursting is subthreshold but acts to intensify the amplitude of oscillations in slow wave sleep with deep UP/DOWN oscillations on the cortex emerging naturally. Furthermore, there is a continuous cycle between the two regimes, rather than a flip–flop between discrete states.

1. Introduction

Clinically, the most studied range of electroencephalographic (EEG) frequencies is 0.1–100 Hz (Nunez and Srinivasan, 2006). There are numerous characteristic states discernible on the EEG and can allow for the identification of distinct sleep stages, eyes-open and eyes-closed states in wake, depth of anesthesia, seizures, and other neurological disorders. Each state is defined by key rhythms that dominate the EEG. Brain activation is associated with low-amplitude fluctuations at relatively high frequencies in the alpha rhythm which lies between 8 and 13 Hz and is most prominent when subjects are awake with eyes closed. Slow wave sleep (SWS) is dominated by high amplitude, low frequency components. Furthermore, SWS exhibits characteristic UP and DOWN states (≈ 1 Hz) observed in local field measures of the cortex (Sanchez-Vives and McCormick, 2000; Steriade et al., 1993a, 1993b). The UP state involves strong excitation of cortical neurons, whereas cortical neurons are hyperpolarized in the DOWN state. Alternation between cortical UP and DOWN states is observed in local field potential measurements as a slow wave oscillation at ≈ 1 Hz; however, understanding of cortical UP and DOWN states in SWS is still lacking. Numerous competing theories have been proposed that variously involve corticocortical and thalamocortical systems (Andersen and Andersson, 1968; Berger, 1933; Bishop, 1936; Steriade and Deschenes, 1984), but there is no consensus on the exact mechanisms generating the cortical UP and DOWN states.

The major cell populations involved in EEG generation are reticular thalamic neurons, cortical pyramidal cells, interneurons,

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http://dx.doi.org/10.1016/j.jtbi.2015.01.028
0022-5193/

and thalamocortical neurons (Steriade et al., 1993a, 1993b; Robinson et al., 1997). Excitation of the reticular thalamic nuclei causes inhibition of the thalamocortical cells in the relay nucleus. This in turn reduces excitation in the cortex, which leads to decreased afferent activity from the cortex back onto the reticular thalamus. This forms a negative feedback loop (Robinson et al., 2002).

Attempts at modeling the cortical UP and DOWN transition in deep sleep have primarily been made using neuronal networks (Bazhenov et al., 2002; Compte et al., 2003; Hill and Tononi, 2005) with most theories focusing on the bursting dynamics of thalamic neurons (Grenier et al., 1998; Steriade and Deschenes, 1984; Steriade et al., 1993a). This emphasizes the "pacemaker" qualities of thalamic neurons (i.e., their ability to fire or burst at a characteristic frequency), and has been extensively modeled in the context of single neurons and small networks (Destexhe et al., 1993, 1994). The approaches have varied from a purely cortical model to thalamocortical interactions. Invariably, the UP and DOWN states are generated from the interaction of single cells in the network, which represent slow wave activity through ion channel and synaptic dynamics. However, these network simulations of UP and DOWN transitions have only simulated on the order of 10^2–10^4 neurons, which is a severe limitation when studying global brain states such as SWS.

An alternative approach is to use neural field theory to average over the microstructure of neuronal connections to yield a neural field model (Deco et al., 2008). Such neural field theories have already accounted for many characteristic states observed on the EEG, such as several stages of sleep, eyes-open, and eyes-closed in wake (Robinson et al., 2004, 2005) plus non-linear dynamics of seizures and other phenomena (Breakspear et al., 2006; Deco et al., 2008; Robinson et al., 2002). Neural field theory based models allow tractable analysis of large-scale brain dynamics. Some efforts at modeling the sleep-wake transition have been previously made using neural field theory (Steyn-Ross et al., 2005). However, the analysis did not extend to the inclusion of bursting dynamics nor corticothalamic feedback. The current work builds upon a neural field model of corticothalamic dynamics (Robinson et al., 2002, 2004) that has previously been successfully used to explore wake and SWS based on physiological parameters (Rowe et al., 2004). These include reproducing characteristic features of the EEG such as alpha and beta spectral peaks and small amplitude, rapid oscillations in the wake state, slow wave oscillations (≈ 1 Hz) and $1/f$ spectrum in the sleep state (Robinson et al., 2002).

Here we extend this neural field theory to explain cortical UP and DOWN transitions in SWS. Our previous work explained some aspects of the SWS oscillation (Robinson et al., 2002), but did not fully generate cortical UP and DOWN states with the prominent depths at low frequencies observed in the current work.

To extend the previously studied neural field model (Robinson et al., 2002, 2004) we incorporate a well-known bursting neuron model (Wilson, 1999a) whose dynamics has previously been expressed in terms of rate-based equations that are compatible with neural field theory (Robinson et al., 2008). We proceed to examine the effects of bursting dynamics in the thalamus on the neural field model and show that our new model is capable of producing cortical UP and DOWN states in SWS while preserving previous results in wake and sleep (Robinson et al., 2002).

This contrasts with previous modeling work that implemented intrinsic rebound bursting in thalamic neurons because we contend that the ≈ 1 Hz oscillation arises from network resonances that couple to the intrinsic bursting dynamics of neurons in the thalamic reticular nucleus, rather than solely arising from the pacemaker properties of rebound bursts. We implement bursting dynamics only in the reticular nucleus because it has been shown to be crucial for the generation of oscillations in the thalamus (Steriade et al., 1985) and is the most parsimonious ansatz. It is possible to add bursting dynamics in other populations such as the thalamic relay nuclei; however, the present work shows that this additional complication is not required to generate cortical UP and DOWN states in SWS. We emphasize that in the current study UP and DOWN states specifically refer to oscillations on the cortex, unless otherwise noted.

Beginning from Section 2 we incorporate bursting dynamics into an existing neural field model. Then we recapitulate the salient features of the neural field model and the parameter states we use for the current work. Following this, in Section 3 we demonstrate the presence of spontaneous UP and DOWN states during SWS dynamics. Subsequently we show the abolition of this behavior as the system shifts to the wake state and reproduces characteristic spectral features of the wake EEG. Thus, in the current work we extend the domain of the neural field model's physiological activity to include UP and DOWN states in SWS while replicating all previous results. We conclude in Section 4 with our main findings and discuss future directions for our neural field model with the incorporation of bursting dynamics.

2. Methods

We begin with a single compartment bursting neuron (Wilson, 1999a) and using previously published results, show how its behavior can be expressed in terms of rate dynamics and incorporated into the reticular thalamus of our neural field model. The bursting dynamics in the reticular thalamus then interacts with the cortex and thalamic relay nucleus through a damped wave equation and dendritic filtering. The current work explores the role of simple bursting dynamics in place of rebound bursting in the reticular nucleus although the difference is not critical in the present context because we only explore parameters that are subthreshold for the bursting dynamics.

2.1. Single neuron model

We briefly introduce the single compartment neuron (Wilson, 1999a), described by

$$C\frac{dV}{dt} = -g(V)(V-V_{Na}) - g_R R(V-V_K) - g_X X(V-V_X) - g_H H(V-V_K) + I_{ext}, \quad (1)$$

where C is membrane capacitance per unit area, V is the membrane potential, and R is a recovery variable. The variables V and R together constitute the fast variables that control the spike shape, while X and H are slow variables, discussed below. Eq. (1) describes changes in the membrane potential V, that arise from interactions of ionic currents, the capacitance C and the externally applied current per unit area I_{ext}. Here, $V_{\rm Na}$ is the Na^+ reversal potential, $V_{\rm K}$ is the K^+ reversal potential, and g_R is the membrane conductance for R, while $g(V)$ represents the Na^+ activation function. The reversal potentials for the slow variables are V_X and V_K, while the conductances for the slow variables are g_X and g_H. The dynamics of the fast variables are described by (1) and

$$\frac{dR}{dt} = -\frac{1}{\tau_R}[R - R_\infty(V)], \quad (2)$$

$$g(V) = \nu_0 + \nu_1 V + \nu_2 V^2, \quad (3)$$

$$R_\infty(V) = 0.79 + r_1 V + r_2 (V - V_3)^2, \quad (4)$$

$$R_\infty(V) = 0.17 + r_2 (V - V_4)^2. \quad (5)$$

Eq. (5) describes activation of K^+ channels, $R_\infty(V)$ is the equilibrium state, and τ_R is the time constant for relaxation of R. The values of the parameters are given in Table 1. Note that we had assigned V_1 and V_2 to $V_{\rm Na}$ and $V_{\rm K}$, respectively, in previous work (Robinson et al., 2008).

Please cite this article as: Zhao, X., et al., Slow-wave oscillations in a corticothalamic model of sleep and wake. J. Theor. Biol. (2015), http://dx.doi.org/10.1016/j.jtbi.2015.01.028