



Multistability in the corticothalamic system



Paula Sanz-Leon^{a,b,*}, P.A. Robinson^{a,b}

^aSchool of Physics, University of Sydney, NSW 2006, Australia

^bCenter for Integrative Brain Function, University of Sydney, NSW 2006, Australia

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ABSTRACT

Neural field theory of the corticothalamic system is used to analyze the properties of its steady-state solutions, including their linear stability, in the parameter space of synaptic couplings for physiological parameter ranges representing normal arousal waking states in adult humans. The independent connections of the corticothalamic model define an eight-dimensional parameter space, while specific combinations of these connections parameterize intracortical, corticothalamic, and intrathalamic loops. Multistable regions are systematically identified and the existence of up to five steady-state solutions is confirmed, up to three of which are linearly stable. A key determinant for the existence of five steady states is found to be the number of nonzero connections. This finding had not been previously proposed as the determining factor of high multiplicities of multistability in mesoscopic models of the brain. In the corticothalamic model presented here, multistability occurs when the intrathalamic loop is present (i.e., the reticular nucleus inhibits the relay nuclei), and when the net synaptic effect of the intracortical loop is inhibitory. The signature of these additional waking states is an overall increased level of thalamic activity. It is argued that the additional steady states found may represent hyperarousal states which occur when the corticothalamic projections do not attenuate the activity of the cortex.

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1. Introduction

To understand how the brain operates, how it transitions between different states, and how experimental recordings reflect these mechanisms, it is not only crucial to understand the dynamical properties of key brain structures but also how interactions between those structures produce large-scale brain activity. The study of large-scale brain dynamics can be used to concisely describe distinct states, such as normal arousal (Abey Suriya et al., 2015; O'Connor and Robinson, 2004; Robinson et al., 2001a; 2001b), sleep (Abey Suriya et al., 2014; Robinson et al., 2011), and anesthetic-induced coma (Steyn-Ross et al., 2001a; 2001b; 1999). Furthermore, understanding how and when qualitative changes in large-scale activity occur enables the identification of transitions between states, like those observed between sleep and wake (Abey Suriya et al., 2014), and potentially coma and wake (Steyn-Ross et al., 2001b; Wang et al., 2014), and normal arousal and seizure states (Breakspear et al., 2006; Robinson et al., 2002).

In many cases we can use neural field theory (NFT) (Deco et al., 2008; Robinson et al., 1997; 2001b) to approximate the brain's

large-scale activity as small perturbations relative to a spatially uniform steady state. This enables predictions of global brain dynamics to be obtained analytically (Robinson et al., 1997) from a system's steady-state equation (Robinson et al., 1998; Rowe et al., 2004). The presence of multiple solutions to the steady-state equation for a system implies that the system has enough degrees of freedom to capture multiple operating points (i.e., global brain states). A previous investigation of the steady-state equation for a purely cortical system showed that there are stable solutions corresponding to both low and very high mean firing rates (Robinson et al., 1998). The low firing rate steady-states have been identified with normal states of brain activity (Robinson et al., 1997), while high firing rate steady-states were associated with seizure-like activity. In this purely cortical system regions of the parameter space with five or more solutions were predicted. However, using the random connectivity approach (RCA) of cortical synaptic densities, in which the number of connections and the connectivity strengths are proportional to the numbers of neurons (Braitenberg and Schüz, 1998; Wright et al., 1994), Robinson et al. (1998) found that no zones with five or more steady states could exist. If the RCA is relaxed, these possible additional steady states could potentially include less explored arousal states such as meditative states (Bajjal and Srinivasan, 2010; Cahn et al., 2010; Cahn and Polich, 2006; Hauswald et al., 2015; Lutz et al., 2004; Sagar et al., 2015); states such as hyperarousal states

* Corresponding author at: School of Physics, University of Sydney, NSW 2006, Australia.

E-mail address: paula.sanz-leon@sydney.edu.au (P. Sanz-Leon).

related to insomnia (Bastien et al., 2003; Grønli et al., 2016); attention deficit hyperactivity disorder (ADHD) states (Zylowska et al., 2008); or low vigilance states (Roth, 1961).

A way to move beyond the limitations of a purely cortical model is to introduce additional brain structures, such as the thalamus. Such a model of the corticothalamic system (Robinson et al., 2002) has successfully reproduced many features of linear and nonlinear brain dynamics (Abey Suriya et al., 2015; Breakspear et al., 2006; Robinson et al., 2004a; 2001b). Furthermore, Robinson et al. (2002) used a reduced three-dimensional space where each axis parametrizes the stability of a loop in the system: x (cortical loop), y (corticothalamic loop), and z (intrathalamic loop). This reduced model has been used to have a compact representation and visualization of stable global brain states of the corticothalamic system. Studying the stability of the lowest firing rate solution in this xyz space permits the identification of a boundary separating the stable and unstable zones (Roberts and Robinson, 2012; Robinson et al., 2002). Normal arousal states have been identified as lying close to this boundary (Robinson et al., 2002) where they are near-critical and usually display strong spectral peaks. Moving far from this boundary in the direction of increasing linear stability most likely corresponds to coma-like states, while moving in an unstable direction results in seizure activity (Breakspear et al., 2006; Robinson et al., 2002).

Previous work on the corticothalamic system has primarily studied the properties of the first stable solution at low firing rate (Abey Suriya et al., 2015; Robinson et al., 2002; 2004a). This focus was based on the fact that these low firing rate solutions have properties constrained by normal adult physiology and are consistent with normal brain states.

The purpose of the present work is to generalize the study of steady states in a model of the corticothalamic system and determine the parameters that allow for multistability to exist. In this work, multistability refers to the coexistence of multiple steady-state solutions for a particular combination of model parameters and should not be confused with multiple types of equilibria (e.g., a fixed point and a limit cycle). Furthermore, the linear stability of all steady-state solutions is investigated. We are particularly interested in identifying those stable solutions that lie between high firing-rate solutions (unsustainable states in practice) and previously studied low firing-rate solutions (associated with normal states). The aims are to (i) find conditions the steady-state equation must meet for multistable behavior to exist; (ii) characterize the activity levels of these additional stable steady states; (iii) determine the zone of the parameter space where they lie and how close they are to known arousal states; and (iv) propose links between these additional states and less common brain states.

We introduce the NFT equations of the corticothalamic system and the reduced xyz parameter space in Section 2. Section 3 details the derivation of the fixed-point equation whose solutions determine the steady-states of the system. Section 4 provides an analysis of the conditions required for the existence of single and multiple steady-states in special cases. In Section 5, numerical results are presented showing the regions with different numbers of steady-state solutions found in subspaces of the overall eight dimensional parameter space. The corticothalamic model is found to possess at most five steady states, for the specific nonlinear relationship between soma voltage and firing rate that we adopt. In Section 6 we quantify the firing rate levels of the multistable solutions. Finally, Section 7 summarizes the main findings and discusses their implications.

2. Theory

In this section we outline the equations of the corticothalamic system and a reduced NFT model derived from it. A complete descrip-

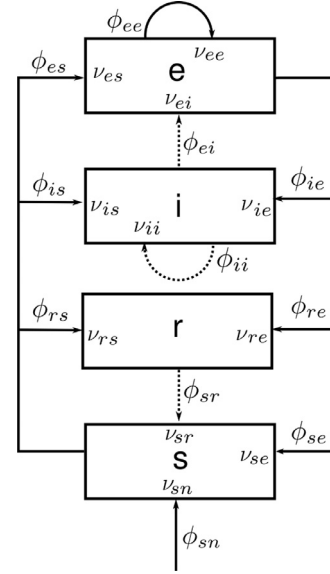


Fig. 1. Diagram of the corticothalamic system with four internal neural populations. The overall connection strengths, v_{ab} , quantifies the effect on population a from population b . Inhibitory connections are shown as dashed lines, while excitatory connections are shown in solid lines. Excitatory (e) and inhibitory (i) are cortical populations, and the specific relay (s) and reticular (r) are thalamic populations. The system is driven by an external input, ϕ_{sn} , from the brain stem and sensory systems to the specific nucleus.

tion of these models can be found in earlier work (Robinson et al., 2001a; 2002; 2004a).

2.1. Corticothalamic model formulation

There are four neural populations modeled as shown in Fig. 1: two cortical populations, excitatory (e) and inhibitory (i), and two thalamic populations representing the specific relay (s) and reticular (r) nuclei. There is an external input from other subcortical structures and sensory systems (n) driving the system through s .

Each neural population $a = e, i, r, s$ is characterized by a mean soma potential V_a relative to resting and a mean firing rate Q_a , which are related via a nonlinear activation function $Q_a = S[V_a]$, well approximated by the sigmoid function (Freeman, 1975; Wilson and Cowan, 1973).

$$S[V_a(\mathbf{r}, t)] = \frac{Q_{\max}}{1 + \exp[-(V_a(\mathbf{r}, t) - \theta)/\sigma]}, \quad (1)$$

where θ is the mean threshold voltage, $\sigma = \sigma'\pi/\sqrt{3}$ is the standard deviation of the threshold distribution, and Q_{\max} is the maximum possible firing rate for population a . Here the cell body potential,

$$V_a(\mathbf{r}, t) = \sum_b V_{ab}(\mathbf{r}, t), \quad (2)$$

is the sum of all the postsynaptic potentials, with

$$D_{ab}V_{ab} = v_{ab}\phi_{ab}(\mathbf{r}, t - \tau_{ab}), \quad (3)$$

$$D_{ab}(\mathbf{r}, t) = \frac{1}{\alpha_{ab}\beta_{ab}} \frac{d^2}{dt^2} + \left(\frac{1}{\alpha_{ab}} + \frac{1}{\beta_{ab}} \right) \frac{d}{dt} + 1, \quad (4)$$

where V_{ab} is the contribution due to input ϕ_{ab} at postsynaptic population a from presynaptic population b after a mean axonal delay τ_{ab} ; the operator D_{ab} encapsulates the synaptodendritic dynamics and soma capacitance and α_{ab} and β_{ab} are the inverse decay and rise times, respectively, of the soma response at a to input from b . The overall connection strength between two neural populations is

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