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Real-time automated EEG tracking of brain states using neural field theory

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HIGHLIGHTS

- A real-time automated fitting system is developed to fit a neural field model to EEG.
- Inferred physiological parameters are objectively tracked over the sleep–wake cycle.
- Continuous trajectories supersede discrete Rechtschaffen–Kales sleep stages.

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ABSTRACT

A real-time fitting system is developed and used to fit the predictions of an established physiologically-based neural field model to electroencephalographic spectra, yielding a trajectory in a physiological parameter space that parametrizes intracortical, intrathalamic, and corticothalamic feedbacks as the arousal state evolves continuously over time. This avoids traditional sleep/wake staging (e.g., using Rechtschaffen–Kales stages), which is fundamentally limited because it forces classification of continuous dynamics into a few discrete categories that are neither physiologically informative nor individualized. The classification is also subject to substantial interobserver disagreement because traditional staging relies in part on subjective evaluations. The fitting routine objectively and robustly tracks arousal parameters over the course of a full night of sleep, and runs in real-time on a desktop computer. The system developed here supersedes discrete staging systems by representing arousal states in terms of physiology, and provides an objective measure of arousal state which solves the problem of interobserver disagreement. Discrete stages from traditional schemes can be expressed in terms of model parameters for backward compatibility with prior studies.

1. Introduction

Neural physiology and arousal state change significantly and continuously over the course of the sleep–wake cycle, but arousal state is typically analyzed using the Rechtschaffen and Kales (R&K) or American Academy of Sleep Medicine (AASM) classification schemes (Rechtschaffen and Kales, 1968; Iber et al., 2007). These schemes artificially force classification of continuous dynamics into a small selection of discrete population-averaged stages: wake (W); stage 1 sleep (called S1 in R&K, N1 in AASM), which corresponds to light sleep; stage 2 sleep (called S2 in R&K, N2 in AASM), which is a deeper stage of sleep marked by K-complexes (transient waveforms typically marked by a large negative peak in the EEG, followed by a positive peak, similar to an evoked response) and sleep spindles (short bursts of activity at around 12–14 Hz); slow wave sleep (called S3 and S4 in R&K, N3 in AASM), which corresponds to deep sleep in which K-complexes and sleep spindles are sometimes present; and rapid eye movement (REM) sleep, which occurs during dreaming.

Although sleep stages can a provide a useful qualitative summary, they have serious deficiencies when used to analyze brain states, dynamics, and physiology for several reasons (Abeysuriya et al., 2015). Real brain states vary continuously and cannot be accurately captured by a few discrete stages, and the small number of traditional sleep stages results in a wide range of different brain substates being grouped together into the same sleep stage. Traditional stages are also based on group averages of EEG and other

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polysomnographic features, and do not account for the significant individual variation seen in experimental data. In some cases, subjective decisions contribute to determining the sleep stage, which adversely affects the objectivity and validity of the assigned sleep stage. This is reflected in the low interobserver agreement for the classified sleep stages; for AASM staging agreement is only 83% (Rosenberg and Van Hout, 2013), and Norman et al. (2000) reported interobserver agreement of just 73% for R&K staging. Finally, traditional stages are typically assigned to 30-s epochs based on the EEG features present within that epoch (e.g., sleep spindles), so the classification can be quite sensitive to the arbitrary timing of the epoch boundaries because this affects which epoch an EEG feature is assigned to.

Note that throughout this study we use the term 'state' to refer to the physiological state of the brain at an instant in time, and the term 'stage' to refer to R&K or AASM classifications. We relate each state to a single set of underlying physiological parameters in our model. Brain states evolve continuously (notwithstanding transitions between sleep and wake, which are rapid but still continuous) and are linked by trajectories in the parameter space, whereas assigned sleep stages change discontinuously and instantaneously.

The issues with sleep staging are illustrated in Fig. 1 (Abeysuriya et al., 2015). In Fig. 1(a), evolving brain states are represented schematically in terms of physiology, and continuous trajectories. In Fig. 1(b), traditional sleep stages are superimposed on the trajectories. In this frame, the stages are represented in terms of physiology because there are quantitative parameters associated with the trajectories, although the definitions of the stages from AASM or R&K are not based on physiology. The significant overlap between the stages reflects the fact that a single combination of parameters can be consistent with more than one assigned arousal stage. In Fig. 1(c), the arousal stages have been decoupled from the underlying physiology, and the degree of overlap between the stages can only be inferred via interobserver disagreement. Finally, Fig. 1(d) shows the current common usage of sleep staging, where each epoch of EEG is forced to be classified into a single sleep stage. Thus the true continuous trajectories in Fig. 1(a) have been replaced by discrete jumps between artificially defined stages, losing information about the physical processes underlying the change in brain state and resulting in inconsistency in assignment of stages (Abeysuriya et al., 2015).

Our central aim is to represent brain states using physiologically meaningful trajectories rather than sequences of arbitrary and unphysiologically discrete stages. In previous work, we showed that the physiologically meaningful parameters of an established neural field corticothalamic model (Rowe et al., 2004b; Robinson et al., 2001, 2002, 2004, 2005) are suitable quantities to reproduce Fig. 1(b) quantitatively (Abeysuriya et al., 2015). Moreover, the model reproduces a wide range of other phenomena such as the alpha rhythm (Robinson et al., 2003; O'Connor and Robinson, 2004), age-related changes to the physiology of the brain (van Albada et al., 2010), evoked response potentials (Rennie et al., 2002), sleep spindles (Abeysuriya et al., 2014a,b), and many other effects. Predictions from the model can be fitted to EEG spectra to estimate physiological parameters (van Albada et al., 2010, 2007; Rowe et al., 2004b; Robinson et al., 2003a, 2005), and these estimates are consistent with a range of EEG-related phenomena (Robinson et al., 2004; Rowe et al., 2004b). Overall, this represents a unified approach to brain dynamics, unlike traditional sleep staging which exists in isolation.

In a previous study (Abeysuriya et al., 2015) we investigated the relationship between sleep stages and the model's physiological parameter space for a population of subjects, corresponding to the colored regions in Fig. 1. Although it is important to be able to understand and interpret traditional sleep stages in terms of our new framework, ultimately it is the individual parameter

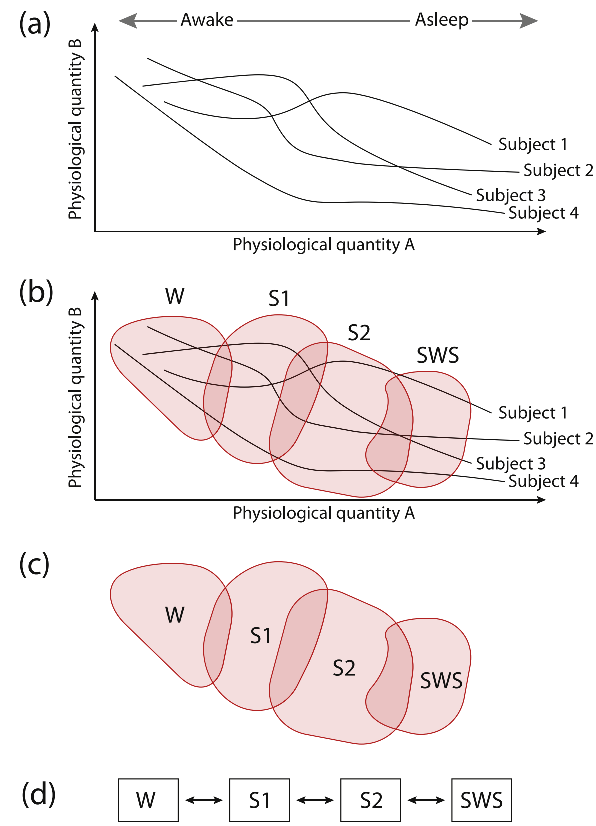

Fig. 1. Schematic illustration showing how physiological brain states are related to traditional sleep stages. (a) Brain states are differentiated by their physiology. Two quantities are shown here for clarity. Over time, brain states follow continuous trajectories. Both the states and the shape of the trajectories are individualized. (b) Traditional sleep stages are superimposed on the trajectories, showing their association with the underlying physiology. The overlap between stages can be quantified in terms of physiology. (c) Removing the physiological axes and trajectories shows only the sleep stages, without reference to the underlying physiology, but still acknowledging the overlap between stage assignments. (d) Common use of traditional sleep stages, with discrete classifications that permit no overlap. The arrows between the stages correspond to discrete jumps, that are the discrete analogs of the trajectories in (a). From Abeysuriya et al. (2015) with permission from Elsevier.

trajectories that are fundamental and take full advantage of our model-based approach, while discrete stages must be abandoned. In this study, we develop a real time, automated approach for fitting the model to an experimental EEG power spectrum and present a first analysis of full-night parameter trajectories. In other recent work, Dadok et al. (2014) examined fitting and tracking neural field parameters to sleep EEG data. Their work fitted two parameters (cortical excitatory feedback strength, and change in resting potential of cortical excitatory neurons) of a purely cortical model (Steyn-Ross et al., 2005) to features extracted from the EEG, and used a hidden Markov model to incorporate temporal continuity of brain states. Because their work did not provide a closed-form analytic expression for the EEG spectrum, their model is computationally expensive to simulate, and produces a stochastic output that has different EEG features each time it is run. In contrast, our approach fits an analytic power spectrum to the EEG spectrum directly, which removes the need to choose a set of extracted features for fitting, scales efficiently as the number of parameters is increased, and enables rapid comparison of different models. In Section 2 we present a brief overview of the model and its key elements. In Section 3 we develop our fitting approach, first for a single EEG power spectrum, and then for tracking the state over time. Finally, in Section 4 we analyze the fitted trajectories to