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A Quantitative Representation of Continuous Brain State During Sleep*

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***Abstract*— Electroencephalography (EEG) recording during sleep is a powerful tool for studying neural oscillatory dynamics. Current practice, however, limits our ability to observe the potentially-important features of the sleeping brain because it focuses on discrete stage-based averaging of manually labeled metrics. This study proposes a high-resolution objective framework that can comprehensively represent individualized continuous brain states during sleep. We develop a computational framework around a novel visualization called the slow-oscillation power spectrogram (*SOPS*), which describes EEG spectral activity as a function of a continuum of sleep depth rather than over discrete stages. Continuous sleep depth is represented by the instantaneous ratio of slow-oscillation (0.5 - 2 Hz) power to the total power (SO-power ratio). We analyzed sleep EEG of two consecutive nights of polysomnography obtained from 10 healthy subjects (mean age of 25.8 ± 5.09 years, 50% female). Through visualization and quantitative analysis, our results suggest that the *SOPS* can offer a concise high-resolution summary of an individual's unique depth-of-sleep profile. Our framework provides a basis for exploring the critical biomarker of neurocognitive functions for which sleep EEG properties are significantly relevant.**

***Keywords*— sleep depth, slow oscillation, polysomnography (PSG), electroencephalography (EEG), spectral analysis, multitaper, phenotype, precision medicine**

I. INTRODUCTION

Sleep quality and structure have received much attention in recent years with emerging evidence of their various effects on physical and mental health. In particular, linkages between sleep and aging, as well as with psychiatric, developmental, and neurodegenerative disorders have driven a recent effort towards a better understanding of sleep neurophysiology [1]. As cognitive processing during sleep has been revealed to rely on the precisely synchronized interactions of rhythmic neural activity, numerous studies have investigated specific frequency components of EEG and their dynamics in correlation with various neuropsychological outcomes [2].

Unfortunately, the current practice of sleep staging still relies on the traditional subjective visual categorization of brain state during sleep into five discrete categories—Wake, rapid eye movement (REM), and non-REM (NREM) stages 1 through 3 (N1-N3), which are defined over fixed 30s epochs. Not surprisingly, sleep staging is highly inconsistent, with an inter-scorer variability greater than 20%, even in healthy subjects [3]. Moreover, spectral analysis of the sleep EEG aggregates power into discrete frequency bands. This discretization across the state, time, and frequency imposes significant limitations on our ability to observe and quantify the complex neurophysiological activity underlying healthy and pathological sleep.

Beyond these methodological considerations, sleep dynamics can be highly variable across nights, as sleep is an active and adaptive process reflecting homeostatic sleep pressure and the circadian rhythm of daily life [4]. Moreover, within laboratories or with device use, there is the concept of a first-night effect, in which several aspects of sleep are disrupted (e.g., reduced total sleep time, increased arousal number and duration) due to physical discomfort from the recording device and the psychological pressure of being monitored [5]. The difficulty of having vast night-to-night variability is further compounded by limited data, as the cost of performing a sleep study may limit observation to a single night recording or even the use of split-night evaluation [6].

We thus are left with the question: How do we accurately characterize a highly variable dynamic process with limited observations and a discrete framework of analysis? Although various sophisticated signal analysis techniques have been introduced for automatic sleep staging or quantifying the component of sleep EEG waveforms, most of them are still limited to mimic the current semantic-rule based practice as they compare and validate their results through human scoring/labeling data [7].

To investigate the dynamics of the sleeping brain activity more precisely, an objective and quantitative framework with high-resolution is needed to overcome the intrinsic intra-individual variability of sleep EEG data and the implications of the current subjective and discrete analysis framework. Previously, we demonstrated how multitaper spectral analysis of sleep EEG could depict the nonstationary oscillatory structure of sleeping brain states instantaneously, which closely paralleled the traditional hypnogram and revealed the richness of objective neurophysiological information [8]. In this study, we replace discrete sleep stages with the slow-oscillation (SO) power ratio extracted from the multitaper spectrogram, which acts as an objective, continuous-valued quantitative metric of the temporal evolution of sleep depth during the night. Rather than spectral bands, we use the full frequency range of the multitaper spectrogram. Together, these form the slow-oscillation power spectrogram, which provides a clear representation of personal intrinsic brain activity during sleep. This framework reveals that despite differences in sleep architecture between nights, subjects show strong intra-individual stability in brain state during sleep.

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II. METHODS

A. Polysomnography data description

We used polysomnography (PSG) data recorded for two consecutive nights from 10 healthy subjects (mean age of 25.8 ± 5.09 years, range 19-32 years old, 50% female) as part of unrelated research, which was approved by the Human Research Committee Institutional Review Board at Massachusetts General Hospital, Boston, MA. Experimental details for these studies have been described previously [9].

EEG data were collected from a 64-channel BrainVision system, which was re-referenced to a standard 6-channel clinical montage sampled at 200Hz. Artifact periods were removed using an automated outlier detection procedure. We analyzed each night's EEG signal from the left central electrode derivation (n = 7), using the right central electrode's signal (n =3) given signal corruption. The data were limited to the period from "lights-off" to "lights-on" in the clinical study.

B. Multitaper spectral analysis

The EEG spectrogram was computed using the multitaper method, a spectral estimator designed to have improved bias & variance properties compared to standard techniques [8]. The spectral estimator parameters were set based on previous studies of optimal sleep EEG analysis [9]. We used a temporal window of the 60s with a 5s step size. We set the spectral resolution (Δf) at 1 Hz, the time half-bandwidth product (TW) to 15, and the number of tapers (L) to 29. Spectrograms were normalized with individual spectra integrating to 1.0.

We define the multitaper spectrogram (S) as

$$S = [\boldsymbol{s_1} \dots \boldsymbol{s_T}],\ \boldsymbol{s_t} = [m_{t,1} \quad \dots \quad m_{t,F}]^T \qquad (1)$$

where the spectra $\boldsymbol{s_t}$ are represented as column vectors containing spectral power $m_{t,f}$ defined over a range of $f \in \{1, \dots, F\}$ frequency bins and $t \in \{1, \dots, T\}$ time bins.

C. SO-power ratio as an objective metric of sleep depth

The SO of sleep EEG is typically defined as an activity between 0 and ~2Hz. The relative increase of the SO over the night chiefly defines the progression from NREM Stage 1 (N1, light sleep) to NREM Stage 3 slow-wave sleep (N3, deep sleep) [10]. Thus, the time-course of the SO has been regarded as an indicator of sleep depth, as well as an established marker representing the homeostatic process [4].

To account for inter-subject variability and intra-subject differences in recording impedance across nights, we use the SO-power ratio (0.5~2 Hz) to the total power (0.5~30 Hz). We refer to this objective, continuous-valued metric of sleep depth as, SOp_t, the SO-power ratio at time t.

D. SO-power spectrogram

We aim to create a comprehensive summary of personal intrinsic brain activity during sleep, which is robust to night-to-night variability and does not rely on pre-defined subjective sleep stages. The slow-oscillation power spectrum (*SOPS*) is a non-parametric model that predicts EEG spectral activity across all frequencies as a function of increasing sleep depth, as measured by the SOp_t.

We define the *SOPS* as

$$SOPS = [\tilde{\boldsymbol{s}}_1 \dots \tilde{\boldsymbol{s}}_P],\ \tilde{\boldsymbol{s}}_P = [\tilde{m}_{t,1} \quad \dots \quad \tilde{m}_{t,F}]^T \qquad (2)$$

where the $\tilde{\boldsymbol{s}}_P$ column vectors containing the median spectral power across the set of original spectral estimates in S for the times at which the SO-power falls in a given range of values specified by power bin $p \in \{1, \dots, P\}$. Bins with fewer than ten observations are omitted from the *SOPS*.

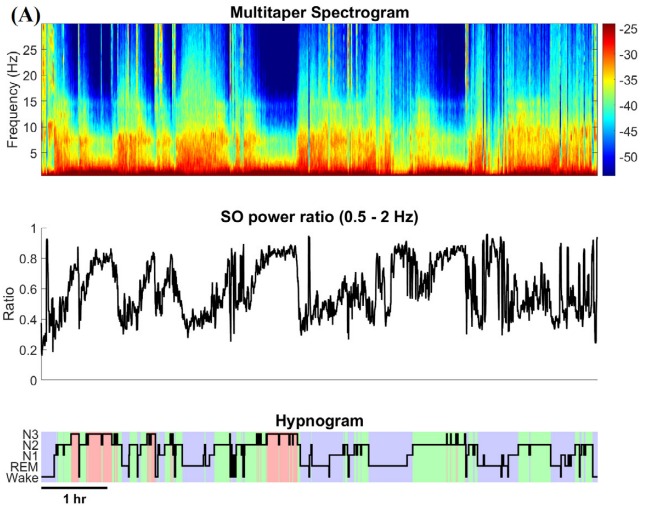
Practically, this is computed by looping over all power bins, selecting the times in the spectrogram at which the SOp_t falls within that bin, and taking the median spectrum for those time points. The power bins were defined for each subject by taking the range between the 1 and 99 percentiles of SOp across both nights, and dividing that range into 30 equally sized bins.

E. Spectrogram reconstruction visualization

If the *SOPS* is a faithful representation of the underlying activity, we can accurately reconstruct a spectrogram given a *SOPS* and the observed SOp_t. We do this by using the observed SO power at a given time to reference the *SOPS* as a look-up table, which gives the reconstructed spectral estimate at each time. Given an $SOPS$ and an observed SOp_t, we compute the reconstructed spectrogram $\hat{S}$

$$\hat{S} = [\hat{\boldsymbol{s}}_{\boldsymbol{p_1}} \dots \hat{\boldsymbol{s}}_{\boldsymbol{p_T}}] \qquad (3)$$

where $\hat{\boldsymbol{s}}_{\boldsymbol{p_t}}$ is the $SOPS$ column $\tilde{\boldsymbol{s}}_{\boldsymbol{P}}$ that corresponds with SOp_t at time t.



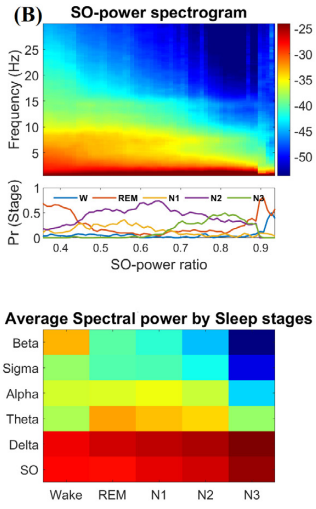


Figure 1. The slow-oscillation power spectrogram (*SOPS*) representation of sleep brain state.

(A) The spectral dynamics of the sleep EEG observed in the multitaper spectrogram (top) are tracked by SOp_t, the slow oscillation power ratio (middle), which serves as an objective, continuous-valued alternative to the subjective and discretized clinical hypnogram (bottom).

(B) We develop the *SOPS* (top), which shows average EEG spectral activity as a function of *SOp*. Compared to the low-resolution and subjective description represented by the traditional staging and frequency bands (bottom), the *SOPS* provides a high resolution and objective descriptor of brain state during sleep, which tracks with traditional staging (middle).

Algorithm 1: Spectrogram Reconstruction

Input: $\boldsymbol{SOp_{1\ to\ T}}$, $SOPS = [\tilde{\boldsymbol{s}}_1 \ldots \tilde{\boldsymbol{s}}_P]$, power bins

Output: $\hat{S}$

1: **For** $t = 1\ to\ T$ **do**

2: $\quad p \leftarrow$ power bin index containing SOp_t

3: $\quad \hat{\boldsymbol{s}}_{p_t} \leftarrow \tilde{\boldsymbol{s}}_P$

4: $\hat{S} = [\hat{\boldsymbol{s}}_{p_1} \ldots \hat{\boldsymbol{s}}_{p_T}]$

F. Power reconstruction and prediction evaluation

Likewise, we can use a given *SOPS* and spectrogram to reconstruct the SOp_t at each time. We define $\widehat{SOp}_t$, the reconstructed SO-power ratio at time t as

$$\widehat{SOp}_t = \underset{p}{\operatorname{argmin}}\ \mathrm{MSE}(\boldsymbol{s}_t, \tilde{\boldsymbol{s}}_P) \quad (4)$$

which selects the power bin associated with the SOPS column with the minimum mean-squared error (MSE) at each time point.

Algorithm 2: Power Reconstruction

Input: $S = [\boldsymbol{s}_1 \ldots \boldsymbol{s}_T]$, $SOPS = [\tilde{\boldsymbol{s}}_1 \ldots \tilde{\boldsymbol{s}}_P]$, power bins

Output: $\boldsymbol{\widehat{SOp}_{1\ to\ T}}$

1: **For** $t = 1\ to\ T$ **do**

2: $\quad p \leftarrow \underset{p}{\operatorname{argmin}}\ \mathrm{MSE}(\boldsymbol{s}_t, \tilde{\boldsymbol{s}}_P)$

3: $\quad \widehat{SOp}_t \leftarrow$ power in bin p

4: $\boldsymbol{\widehat{SOp}_{1\ to\ T}} = [\widehat{SOp}_1 \quad \ldots \quad \widehat{SOp}_T]^T$

In this procedure, we omit the SO range (0.5~2.0 Hz) component from both the $\boldsymbol{s}_t$ and *SOPS*. This provides a form of cross-validation, as well as a means of highlighting the degree to which the SOp_t is determined by the spectral structure at all other frequencies. We use a quadratic weighted Cohen's kappa and Pearson's correlation coefficient to describe the predictive and correlative qualities of the reconstruction for the observed SOp_t.

III. Results

A. SOPS visualizes personal intrinsic brain states

Fig. 1 demonstrates the construction of the *SOPS* in a single subject. In Fig. 1A, we show the multitaper spectrogram for a subject (top) with the SOp_t (middle). The hypnogram (bottom)—the trace of stages visually scored by a sleep technician—is the clinical gold standard for sleep state identification. The SOp_t temporal structure agrees strongly with that of the clinical hypnogram. Thus, the SOp_t can objectively represent the continuous dynamics of the brain during sleep at a higher state and temporal resolution than current approaches.

In Fig. 1B, we show the *SOPS* computed from the spectrogram and SOp_t. Compared with the frequency band and stage averaged spectral power (bottom), the *SOPS* (top) encapsulates the continuous spectral dynamics of the neural activity at a much higher resolution. The power of SOp_t is further demonstrated by examining the distribution of scored sleep stages for each power bin (middle). Although blind to the human staging, SOp_t separates the scored stages, progressing appropriately through deepening sleep from Wake through N3 slow-wave sleep as SOp_t increases.

We can then compare the *SOPS* from different nights to compare intra-subject stability. Fig. 2A shows the *SOPS* from night 1 (left) and night 2 (middle), as well as the difference magnitude (right) for the subject from Fig 1. Overall, the structures are highly similar, with difference magnitude largest in the high frequencies often associated with muscle artifact. Fig. 2B shows the night 1 and 2 *SOPS* from 4 additional subjects, highlighting the considerable inter-subject variability but strong night-to-night intra-subject stability.

B. Intra-subject stability of SOPS

To assess the degree to which the *SOPS* encapsulates information from observed EEG, we can use the *SOPS* to reconstruct either the SO power or the spectrogram of neural activity from the other.

Given that we have two nights of data, we can reconstruct the original data from the same night (self-reconstruction) or the other night (cross-reconstruction). In doing so, we are able to examine the stability of the *SOPS* across nights.

Fig. 3A shows the observed spectrogram from the same subject for night 1 (left) and night 2 (right), as well as the self- and cross-reconstructed spectrograms. Fig. 3B shows the original (black), self (cyan), and cross (red) reconstructions of SOp_t. Visually, the reconstructions appear to be very close to

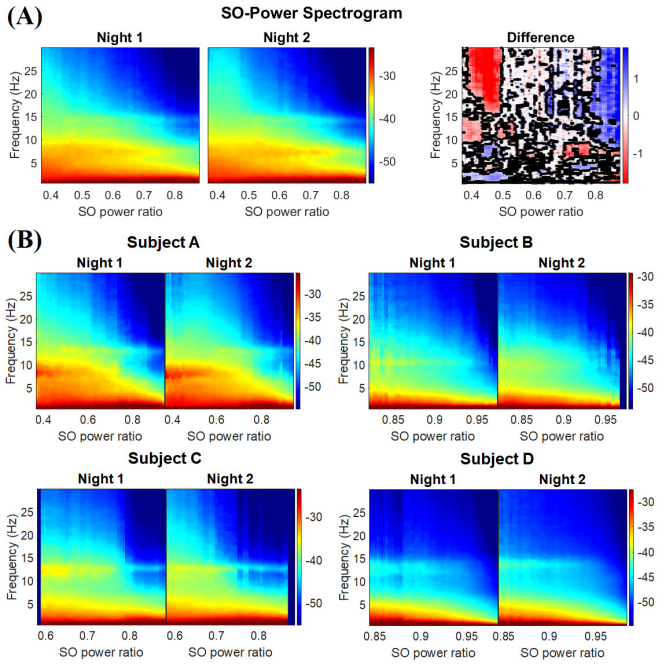


Figure 2. The slow-oscillation power spectrogram (*SOPS*) has strong night-to-night stability.

(A) The *SOPS* from night 1 (left) and night 2 (middle), as well as the difference magnitude (right) for the subject from Fig. 1. Significant regions by permutation test are shown as black outlines. **(B)** The night 1 and 2 *SOPS* from 4 additional subjects from the population. This illustrates the large inter-subject variability but strong night-to-night stability.

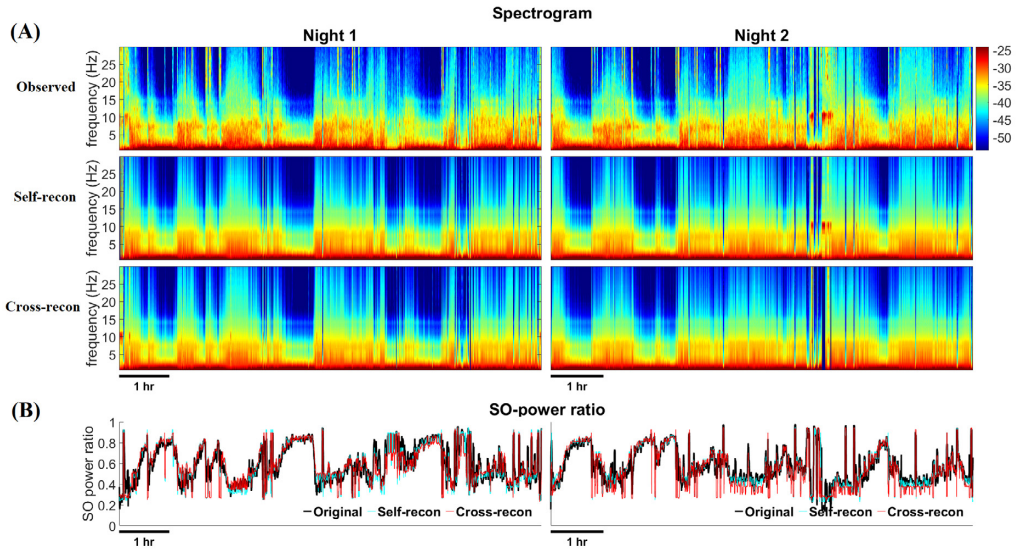


Figure 3. Visualizing the way in which slow-oscillation power spectrogram (*SOPS*) strongly encapsulates stable brain states from a full night of sleep.

(A) The *SOPS* and SOp_t can be used to reconstruct the spectrogram from a given night. The observed (top), self-reconstructed (middle), and cross-reconstructed (bottom) spectrograms are shown for nights 1 (left) and 2 (right) for the same subject from Fig 1. The reconstructed spectrograms closely resemble the observed spectrogram.

(B) The *SOPS* and spectrogram can be used to reconstruct the SOp_t, The true (black), self (cyan), and cross (red) reconstructions of SOp_t are shown for both nights.

the actual data. Given the evident similarity of all reconstructions, this visualization suggests that the *SOPS* may comprehensively represent an intrinsic set of stable brain states for this subject.

C. *Quantifying SOPS stability across subjects*

In order to quantify the degree to which the *SOPS* predicted neural activity, we computed self- and cross-reconstructed SOp_t for all ten subjects across both nights of sleep. The reconstructed $\widehat{SOp_t}$ exhibited high correlation coefficients regardless of which *SOPS* was template (self: mean $\rho = 0.918 \pm 0.050$, cross: mean $\rho = 0.894 \pm 0.056$, $p<0.001$). The reconstructions were also highly predictive, with high quadratic weighted Cohen's kappa values (self: mean $\kappa = 0.921 \pm 0.041$, cross: mean $\kappa = 0.870 \pm 0.065$, $p<0.001$).

IV. Discussion

These results provide proof-of-concept for this novel framework as well as strong initial evidence that the *SOPS* is a good encapsulation of the brain state, with high stability across nights. We also demonstrate that SOp_t is a good surrogate marker not only for sleep depth but is also highly linked to the spectral dynamics of the brain during sleep. The SO is known to be relatively free from the daily changing homeostatic sleep pressure and reflect the thalamocortical system's intrinsic rhythmic activities [11]. The *SOPS* shows promise as a quantitative phenotype of neural activity and potential as a method for EEG biomarker exploration.

Overall, this approach serves as a comprehensive objective summary of continuous brain state dynamics during sleep, which contrasts to traditional sleep staging, which provides a subjective, discretized description of the temporal evolution of sleep dynamics over the night. As such, our method provides substantial information not currently captured in standard sleep analyses and is thus a powerful tool for characterizing the vast heterogeneity seen in both healthy and pathological sleep.

Future computational work will focus on creating a parametric version of the *SOPS* as well as exploring whether any modification to the SOp_t or use of other signals provides more robust night-to-night stability. Additionally, improved measures of *SOPS* variability and a framework for model selection are required. In particular, bootstrap methods that sample from the observed spectral estimates can be developed to express variability and conduct hypothesis tests.

Further experimental studies are needed to assess whether the SOPS provides enhanced prognostic information by identifying subtypes of different sleep disorders and their underlying pathophysiological mechanisms.

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