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A Probabilistic Framework for Time-Frequency Detection of Burst Suppression *

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Abstract— **General anesthesia is a drug-induced, reversible condition comprised of hypnosis, amnesia, analgesia, akinesia, and autonomic stability. During the deepest levels of anesthesia, *burst suppression* is observed in the EEG, which consists of alternating periods of bursting and isoelectric activity. By accurately tracking anesthesia-induced burst suppression, it may be possible to provide a higher level of care for patients receiving general anesthesia. We develop a probabilistic framework for detecting burst suppression events. The algorithm uses multinomial regression to estimate the probability of burst, suppression, and artifact states at each time given EEG frequency-domain data. We test the efficacy of this method on clinical EEG acquired during operating room surgery with GA under propofol.**

I. Introduction

General anesthesia (GA) is a drug-induced, reversible condition comprised of hypnosis (loss of consciousness), amnesia (loss of memory), analgesia (loss of pain sensation), akinesia (immobility), and autonomic stability. Every day, in United States alone, over 100,000 patients depend on general anesthesia for the ability to undergo vital clinical procedures. During GA, patients must be adequately anesthetized to prevent awareness or post-operative recall. However, patients should not be over-anesthetized, which can delay emergence and could contribute to post-operative delirium or cognitive dysfunction. It is therefore important to be able to characterize and monitor clinically observable biomarkers of depth of anesthesia so that complications from over- or under-anesthetizing patients may be mitigated.

One such biomarker is the phenomenon of *burst suppression,* which is a state occurring at the deepest levels of GA, consisting of alternating epochs of electrical bursting and isoelectric activity in the EEG. As the level of anesthetic drug is increased, the period between the burst epochs increases. Thus, tracking burst suppression provides an important tool in monitoring depth of anesthesia. Burst suppression is also observed in coma patients, and can be induced using anesthetic drugs or cooling as a neuroprotective therapy. Consequently, accurate characterization of burst suppression has broad applicability in neuro-critical care as well. The current clinical standard for evaluating burst suppression is through visual inspection of filtered EEG time-domain traces by a trained clinician or technician. There is currently no single, universally-accepted clinical definition of burst activity. Consequently, visual scoring of burst suppression data is highly subjective, and can result in great variability in output between scorers.

Several methods for automated tracking of burst suppression have been proposed. The majority of these methods involve computing an index that is a function of the EEG time series related to signal amplitude or energy [1–5]. When the index crosses a specified threshold, the EEG is said to have transitioned into a burst or suppression state, depending of the direction of crossing. These methods are limited by the fact that they reduce the data to a single dimension, and rely on subjectively-defined thresholds that have no statistical interpretation. Consequently, these methods are unable to distinguish between bursts and high-amplitude motion artifacts, which occur frequently in clinical scenarios. Furthermore, these methods do not address the interdependence and temporal evolution of burst and suppression states, and could therefore produce physiologically implausible results.

Alternatively, machine-learning unsupervised classification techniques using support vector machine and hidden Markov model algorithms have been proposed for measuring pathological burst suppression detection in neonatal asphyxia [6], [7]. These methods use feature vectors derived from the EEG. While these methods address multi-dimensionality, the features used are predominantly statistical measures of time-domain distribution properties rather than physiologically motivated metrics. These methods also require manual removal of motion artifacts.

More importantly, all of these these methods have two major potential drawbacks. First, they all pose the problem of burst suppression characterization in terms of binary classification in a feature-space, rather than in a statistical framework, which computes the likelihood of competing models given observed data. Thus, results from these methods currently do not produce any degree of confidence in their classification, which is important in settings involving clinical decision-making.

Second, these methods address burst suppression detection in the time domain. Demarcating burst onset and offset time in the time domain can be extremely difficult and variable between graders, especially during periods of transitions into unconsciousness when the burst period is small. When the data is transformed into frequency domain, the resulting spectral structure makes it significantly easier to visually differentiate between burst, suppression and artifact states [Fig. 1]. By leveraging the observation that the spectral content between artifacts and bursts differ, we can more effectively discriminate between the two states.

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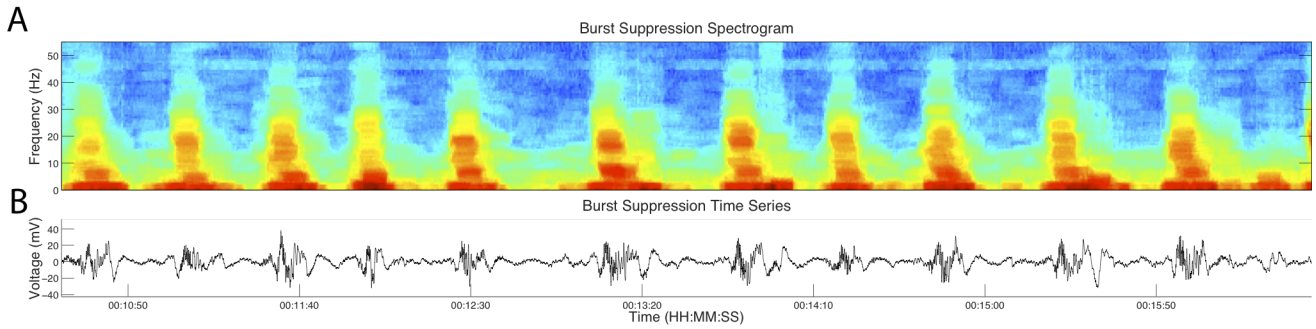

Figure 1: Spectral (A) and time domain (B) representations of burst suppression under propofol. Bursts show a clear and consistent spectral structure.

In anesthesia-induced burst suppression, burst and suppression intervals can be much narrower, and in general more variable, than those encountered in other settings (coma patients, for example). In addition, and artifacts are prevalent in the operating room due to the ongoing surgical procedure. Therefore, characterization of anesthesia-induced burst suppression can be far more challenging than burst suppression encountered in other settings.

In this paper, we develop a probabilistic framework for detecting burst suppression events. This algorithm uses multinomial regression to estimate the probability of burst, suppression, and artifact states at each time given frequency-domain EEG data. This method estimates the probability of each state, which may then be used for classification. Moreover, the method provides a temporal continuity constraint on the state estimates, which ensures that the output remains physiologically plausible. We test the efficacy of this method on clinical EEG acquired during operating room surgery with GA under propofol.

II. Methods

A. Clinical Data

To develop and evaluate the algorithm, clinical data records were gathered from 6 patients (5 female, 1 male) between the ages of 36 and 59 years old, who were undergoing surgery at Massachusetts General Hospital. A 4-channel frontal EEG recording was extracted the records. For each channel, a multi-taper spectrogram [8] was computed, and the median spectrogram across all channels was used as input for the algorithm.

For model evaluation, bursts and artifact periods were visually scored in the time domain by a trained expert with over 15 years of experience in reading clinical and experimental EEG (P.L.P.).

B. Spectral Estimation of the Burst State

To estimate the burst, suppression, and artifact states, we developed a probabilistic framework for the discrete state estimation from temporally evolving frequency-domain data.

The analysis is in discrete time, which we define as

$$t_k = k\Delta t\,, \tag{1}$$

where Δt is the time interval between each of the T observations, and $k = \{1,...,T\}$.

We also define a set of F fixed-interval frequency bins centered at

$$f_j = j\Delta f\,, \tag{2}$$

where Δf is the frequency interval between each bins, and $j = \{1,...,F\}$.

Given EEG observations from times t_1 to t_T and frequency bins centered at f_1 to f_F, we can construct a FxT matrix of the frequency domain observations

$$M = \begin{pmatrix} m_{1,1} & \cdots & m_{1,T} \\ \vdots & \ddots & \vdots \\ m_{F,1} & \cdots & m_{F,T} \end{pmatrix}, \tag{3}$$

such that $m_{i,j}$ is the magnitude of the multitaper power spectrum within frequency bin f_i, at time t_j.

We then define S, a set of Q mutually exclusive states. In this case, $Q = 3$ to represent the *burst*, *suppression*, and *artifact* neural states

$$S = \left\{ s_{\text{Burst}}, s_{\text{Suppresion}}, s_{\text{Artifact}} \right\}, \tag{4}$$

where s_q references the q^{th} element of S, and S_k represents the neural state at time t_k.

As the only possible states are those in S,

$$\sum_{q=1}^{Q} \Pr\left(S_k = s_q\right) = 1 \tag{5}$$

for any time point t_k.

It follows that $\hat{S}_k$, the predicted state at each time, will be

$$\hat{S}_k = \arg\max_{s_c \in S} \left[\Pr\left(S_k = s_c\right) \right]. \tag{6}$$

Given a set of EEG spectral observations during a period of burst suppression, our goal is to estimate Y, the QxT matrix of temporally evolving state probabilities

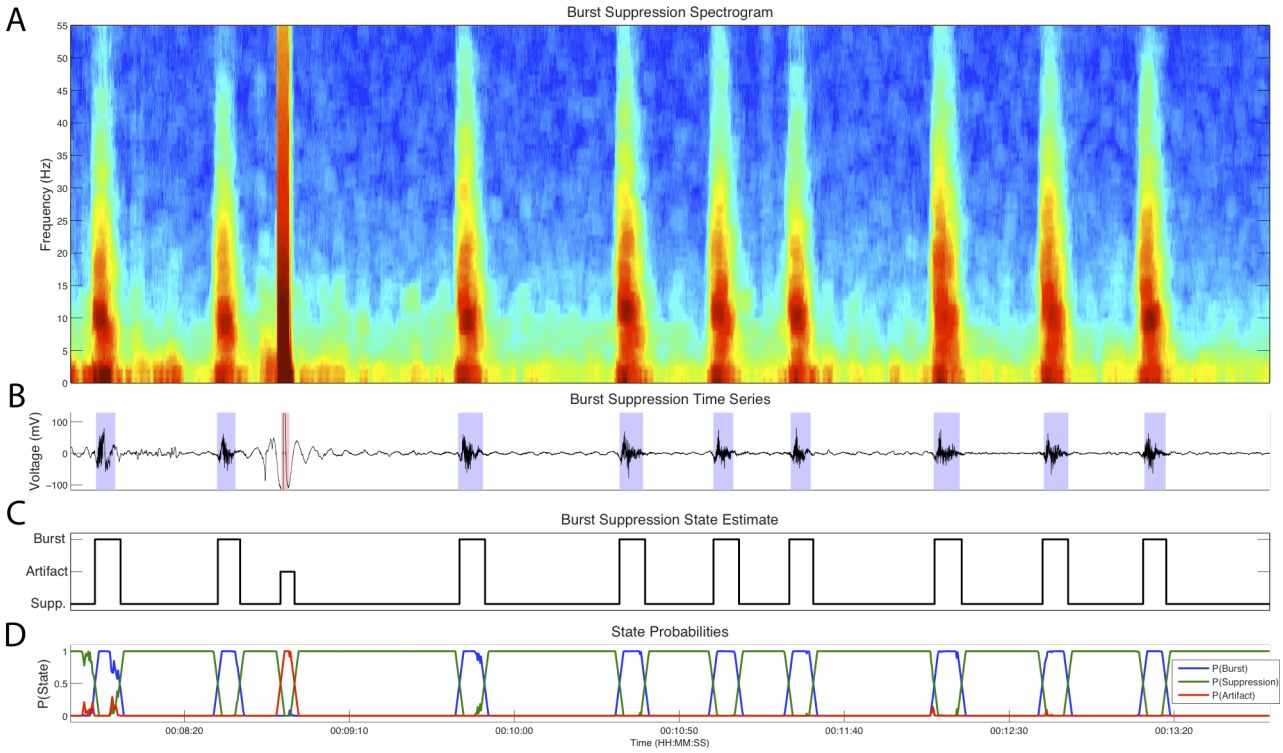

Figure 2: Algorithm output. The spectrogram (A) and the time series (B) representation of EEG burst suppression under propofol are computed from human data from the OR. The algorithm estimates whether the EEG is in the burst, suppression, or artifact states (C) using the state probabilities computed using multinomial regression, and compared to the visually scored burst (B, blue regions) and artifact (B, red regions).

$$Y = \begin{pmatrix} \Pr(S_1 = s_{\text{Burst}}) & \cdots & \Pr(S_T = s_{\text{Burst}}) \\ \Pr(S_1 = s_{\text{Suppresion}}) & \cdots & \Pr(S_T = s_{\text{Suppresion}}) \\ \Pr(S_1 = s_{\text{Artifact}}) & \cdots & \Pr(S_T = s_{\text{Artifact}}) \end{pmatrix}. \quad (7)$$

We characterize the state probabilities using a multinomial logistic model of neural state probability with the form

$$\begin{aligned} \ln\left(\frac{\Pr(S_k = s_1)}{\Pr(S_k = s_Q)}\right) &= \bar{\beta}_1^T \bar{M}_k \\ &\vdots \\ \ln\left(\frac{\Pr(S_k = s_{Q-1})}{\Pr(S_k = s_Q)}\right) &= \bar{\beta}_{Q-1}^T \bar{M}_k \end{aligned}, \quad (8)$$

where β is a F x (Q-1) matrix of model parameters, and $\bar{\beta}_i$ and $\bar{M}_i$ represent the i^{th} columns of the corresponding matrices.

It follows from (5) that the probability of each state at time t_k is

$$\Pr(S_k = s_q) = \exp\left(\bar{\beta}_q^T \bar{M}_k\right)\left[1 + \sum_{j=1}^{Q-1} \exp\left(\bar{\beta}_j^T \bar{M}_k\right)\right]^{-1} \quad (9)$$

for $q < Q$, and

$$\Pr(S_k = s_Q) = \left[1 + \sum_{j=1}^{Q-1} \exp\left(\bar{\beta}_j^T \bar{M}_k\right)\right]^{-1} \quad (10)$$

for $q = Q$.

Thus, in this 3-state model, the state probabilities are

$$\begin{aligned} \Pr(S_k = s_{\text{Burst}}) &= \exp\left(\bar{\beta}_1^T \bar{M}_k\right)\left[1 + \sum_{j=1}^{2} \exp\left(\bar{\beta}_j^T \bar{M}_k\right)\right]^{-1} \\ \Pr(S_k = s_{\text{Suppression}}) &= \exp\left(\bar{\beta}_2^T \bar{M}_k\right)\left[1 + \sum_{j=1}^{2} \exp\left(\bar{\beta}_j^T \bar{M}_k\right)\right]^{-1} \\ \Pr(S_k = s_{\text{Artifact}}) &= \left[1 + \sum_{j=1}^{2} \exp\left(\bar{\beta}_j^T \bar{M}_k\right)\right]^{-1} \end{aligned}. \quad (11)$$

To set up the regression, we generated multitaper spectrograms from each of the experimental time series. Using the frequency-domain data only, a small subset of clear burst, suppression, and artifact periods were selected across all of the subjects. For each identified segment, the median power spectrum was computed and stored in the corresponding column in M. Since the neural state corresponding to each segment is known, we could then construct a Y matrix such that the row corresponding to the scored state at each time has probability of 1 with the remaining elements 0.

The parameter matrix β was then estimated using an iteratively reweighted least squares algorithm, which finds the maximum *a posteriori* solution given the data in M and the known states in Y. We can now use β to estimate the probability of the neural states given any newly observed neural data, which in turn can be used with (6) to form the state prediction, $\hat{S}_k$.

C. State Dynamics Constraints

To impose a continuity constraint in the temporal dynamics of the states, the maximum change in each state's probability was limited a fixed quantity Δp at each time point. For each state s_q at each time t_k, the state probability is restricted such that

$$\left|\Pr\left(S_k = s_q\right) - \Pr\left(S_{k-1} = s_q\right)\right| \le \Delta p \quad . \tag{12}$$

State probabilities are then renormalized so that the distribution sums to one.

We can further refine our state prediction $\hat{S}_k$, such that state transitions only occur when there is a high degree of certainty in $\Pr\left(S_k = s_q\right)$. Starting with the equation for the multinomial prediction of state (6), we now set

$$\begin{cases} \hat{S}_k = \arg\max_{s_c \in S}\left[\Pr\left(S_k = s_c\right)\right] \text{ if } \hat{S}_k \ge \alpha \\ \hat{S}_k = \hat{S}_{k-1} \text{ otherwise} \end{cases}, \tag{13}$$

where α is the desired confidence level. This provides a statistically principled interpretation of the threshold used to detect states.

Moreover, bursts lasting less than a specified duration $B_{\min}$ may be filtered out to make sure only physiologically plausible activity is extracted.

Together, equations (12) and (13) provide a computationally efficient means of implementing a model of state temporal dynamics with a fixed continuity constraint as well as a state transition probability that is robust to noise.

In this implementation, we set $\Delta p = 0.06$, $\alpha = 2/3$, and $B_{\min} = 0.5s$.

III. Results

An example of the algorithm output using EEG data from one of the propofol subjects is shown in Figure 2. The spectrogram (A) is computed from the EEG time series (B), which has been visually scored (B, blue, red regions). In the spectral domain, bursts show a broadband frequency structure, with modes in the slow/delta and alpha bands. This structure is distinct from artifacts, which have a structure with high power at all frequencies. Using the frequency-domain EEG data, the algorithm estimates the burst suppression state $\hat{S}_k = \left\{s_{\text{Burst}}, s_{\text{Suppresion}}, s_{\text{Artifact}}\right\}$ at each time (C), given the state probabilities estimated with the multinomial logistic regression (D). As shown in Figure 2, this algorithm is able to distinguish clearly between bursts, suppression periods, and artifacts.

Since this validation of this method is based on comparing a visually scored, time-domain definition of burst suppression with the output of an algorithm trained on a spectral domain definition of burst suppression, we discuss the results in terms of agreement rather than accuracy. Across all subjects, visual scoring identified 210 burst epochs and the algorithm identified 205 burst epochs. Overall, the algorithm agreed well with the visual scoring across all subjects, with 92.9% (195/210) of the total scored burst epochs intersecting with those selected by the algorithm. We found that 95.9% (187/195) of the intersecting burst epochs had a 1-to-1 correspondence with the visually scored bursts. In addition, 3.90% (8/205) of the burst epochs by the algorithm, contained multiple visually scored bursts, and 4.29% (9/210) of the visually scored burst epochs contained multiple algorithm-identified epochs. We also found that 2.04% (15/210) of the visually scored burst epochs were unmatched by the algorithm, and 2.04% (4/205) of the algorithm burst epochs were unmatched by visual scoring. These data show that the present method is able to use frequency-domain information to automatically detect burst and suppression events in a manner that agrees closely with time-domain visual scoring.

IV. Discussion and Conclusions

In this paper, we have developed a statistically-principled method to characterize burst suppression that is automated and more objective than visual scoring. Our use of frequency-domain information takes advantage of the physiological insight that bursts have an underlying oscillatory structure [9], which could be difficult to capture consistently with methods relying on time-domain representations of the data. In future studies we will apply this method to study burst suppression phenomena encountered in other clinical settings.

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