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Kalman smoother based time-varying spectrum estimation of EEG during single agent propofol anesthesia

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Abstract— **A time-varying parametric spectrum estimation method for analyzing EEG dynamics is presented. EEG signals are first modeled as a time-varying auto-regressive stochastic process and the model parameters are estimated recursively with a Kalman smoother algorithm. Time-varying spectrum estimates are then obtained from the estimated parameters. The proposed method was applied to measurements collected during low dose propofol anesthesia. The method was able to detect changes of event related (de)synchronization type elicited by verbal command.**

I. INTRODUCTION

Anesthetic medications have substantial effects on neuronal activity and this change appears to produce the characteristic central nervous system (CNS) effects defined as anesthesia, i.e. alter brain's ability to process information from the environment impacting on consciousness and memory. Electroencephalogram (EEG) provides a high-temporal resolution imaging modality for relating brain activity to cognitive function [1]. Because it is believed that general anesthetics block consciousness by depressing the CNS, and electrical activity of the cerebral cortex can be measured with EEG, it is expected that some component of the EEG should relate to depth of anesthesia [2]. In fact, the use of processed EEG as a supplement to other monitoring techniques is based on the observation that anesthetic medications all alter the synaptic function which produces the EEG.

Measuring brain electrical activity in an attempt to prevent inadequate anesthesia states, such as responsiveness to surgical stimuli and awareness, is still a difficult task. This is evident when considering the wide variety of electrophysiological variables described in the literature. Frequency and time domain derivations of spontaneous EEG have been involved in anesthesia research and monitoring, e.g. [3], [4], [5], [6]. Processed auditory evoked potentials (AEP) have been proposed as a potential method for the detection of intra-operative awareness [7]. Furthermore, it has been suggested that the assessment of deep states of anesthesia may be improved by the use of components of somatosensory evoked potentials (SSEP), rather than just burst suppression patterns of EEG [8].

An event related deshynchronization (ERD) type of EEG response is, for instance, the disappearance of the occipital alpha rhythm in the awake state when the eyes are opened [1]. During anesthesia, sensory stimulation can elicit an arousal reaction of the ERD type, a behavior also observed during emergence from anesthesia [9], [10]. Alternatively, stimulation may evoke an event related synchronization (ERS) type of reaction, that is a shift towards lower-frequency, high amplitude activity [11]. This kind of phenomenon is typically related to deeper anesthesia states.

In this paper, we present a method for estimating time-varying spectral characteristics of EEG signals. The measured signals are first modeled with a non-stationary auto-regressive (AR) process. Estimates for the model parameters are obtained with a Kalman smoother algorithm. The time-varying spectrum is finally obtained from the estimated parameters. The presented algorithmic work is a continuation of the previous work of some of the authors [12], [13]. The proposed method was applied to measurements collected during low dose propofol anesthesia. The method was able to detect ERS/ERD type of responses elicited by verbal command.

II. METHODS

For dynamic spectral estimation of EEG we use a state-space mathematical formalism. Then, Kalman filter and fixed interval smoother algorithms can be applied for estimating the model parameters [12]. In the following, a short description of the Kalman smoother spectrum estimation approach is given, for details see also [13].

An EEG signal is here modeled with a time-varying AR model of order p defined as

$$x_t = -\sum_{j=1}^{p} a_t^{(j)} x_{t-j} + e_t, \qquad (1)$$

where x_t is the measured signal, $a_t^{(j)}$ is the value of j'th AR parameter at time t and e_t is the observation error. By using

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the notation

$$H_t = (x_{t-1}, \ldots, x_{t-p}) \quad (2)$$

$$\theta_t = (-a_t^{(1)}, \ldots, -a_t^{(p)})^T \quad (3)$$

the time-varying AR model can be written in the form

$$x_t = H_t \theta_t + e_t, \quad (4)$$

which is a linear observation model. For the time evolution of the states a random walk model is here used

$$\theta_{t+1} = \theta_t + w_t, \quad (5)$$

where w_t is the state noise vector process. Equations (4) and (5) form a state-space signal model for the time-varying AR process x_t, and the model parameters can be estimated by using the Kalman smoother algorithm.

A. Kalman smoother algorithm

The Kalman filtering problem is related to the determination of the mean square estimator $\hat{\theta}_t$ for the state θ_t based on the observations $x_1, x_2, \ldots, x_t$. The optimal mean square estimator can be obtained recursively by restricting to a linear form, or by assuming the noise processes to be Gaussian. Then the filter algorithm can be written as

$$C_{\tilde{\theta}_{t|t-1}} = C_{\tilde{\theta}_{t-1}} + C_{w_{t-1}} \quad (6)$$

$$K_t = C_{\tilde{\theta}_{t|t-1}} H_t^T (H_t C_{\tilde{\theta}_{t|t-1}} H_t^T + C_{e_t})^{-1} \quad (7)$$

$$\hat{\theta}_t = \hat{\theta}_{t-1} + K_t(x_t - H_t \hat{\theta}_{t-1}) \quad (8)$$

$$C_{\tilde{\theta}_t} = (I - K_t H_t) C_{\tilde{\theta}_{t|t-1}} \quad (9)$$

where $\tilde{\theta}_t$ is the state estimation error $\tilde{\theta}_t = \theta_t - \hat{\theta}_t$, and $\tilde{\theta}_{t|t-1}$ is the state prediction error $\tilde{\theta}_{t|t-1} = \theta_t - \hat{\theta}_{t-1}$, K_t is the Kalman gain vector, and C_{e_t} and C_{w_t} are the observation and state noise covariances, respectively.

If all the measurements $x_1, x_2, \ldots, x_N$ are available, then the fixed interval smoothing problem can be considered, that is the determination of estimates $\hat{\theta}_t^{\mathrm{S}}$ (S denotes smoothed estimates) for each state θ_t given all the observations $x_1, x_2, \ldots, x_N$. The complementary fixed-interval smoothing equations (forward-backward smoother algorithm) can be written as

$$\hat{\theta}_t^{\mathrm{S}} = \hat{\theta}_t + A_t(\hat{\theta}_{t+1}^{\mathrm{S}} - \hat{\theta}_t) \quad (10)$$

$$C_{\tilde{\theta}_t^{\mathrm{S}}} = C_{\tilde{\theta}_t} + A_t(C_{\tilde{\theta}_{t+1}^{\mathrm{S}}} - C_{\tilde{\theta}_{t+1|t}}) A_t^T \quad (11)$$

where $A_t = C_{\tilde{\theta}_t} C_{\tilde{\theta}_{t+1|t}}^{-1}$ and the filter estimates are used for the initialization, i.e. $\hat{\theta}_N^{\mathrm{S}} = \hat{\theta}_N$ and $C_{\tilde{\theta}_N^{\mathrm{S}}} = C_{\tilde{\theta}_N}$.

B. Adaptation of the algorithm

The adaptation of Kalman smoother algorithm can be controlled through the determination of the state and observation noise covariances C_{w_t} and $C_{e_t} = \sigma_e^2$. The observation noise variance can be estimated iteratively at every step of the Kalman filter equations as

$$\hat{\sigma}_{e_t}^2 = 0.95\, \hat{\sigma}_{e_{t-1}}^2 + 0.05\, \epsilon_t^2, \quad (12)$$

where ϵ_t is the one step prediction error $\epsilon_t = x_t - H_t \hat{\theta}_{t-1}$. Furthermore, the state noise covariance is selected to be diagonal $C_{w_t} = \sigma_w^2 I$, and σ_w^2 is adjusted at every step of the Kalman filter equations as

$$\hat{\sigma}_{w_t}^2 = \mathrm{UC}\, \hat{\sigma}_{e_t}^2 / \hat{\sigma}_{x_t}^2, \quad (13)$$

where $\hat{\sigma}_{x_t}^2$ is the estimated variance of the observed signal at time t and UC is an update coefficient through which the adaptation of the algorithm can be adjusted.

C. Time-varying spectrum estimation

The time-varying spectrum estimate is obtained from the time-varying AR parameter estimates $\hat{a}_t^{(j)}$ as

$$P_t(f) = \frac{\hat{\sigma}_{e_t}^2 / f_s}{|1 + \sum_{j=1}^{p} \hat{a}_t^{(j)} e^{-i2\pi j f / f_s}|^2}, \quad (14)$$

where f_s is the sampling frequency, $\hat{a}_t^{(j)}$ is the j'th AR parameter estimate at time t, and $\hat{\sigma}_{e_t}^2$ is the variance of the estimated observation error process that can be estimated as

$$\hat{\sigma}_{e_t}^2 = 0.99\, \hat{\sigma}_{e_{t-1}}^2 + 0.01\, \hat{e}_t^2, \quad (15)$$

based on the smoother estimates, i.e. $\hat{e}_t = x_t - H_t \hat{\theta}_t^S$. Here, a non-causal operation for (15) is used.

III. Results

Data from ten healthy male subjects (age 19-28 years) undergoing propofol anesthesia were analyzed. Propofol was administered intravenously using target control infusion (TCI) aiming at pseudo steady-state plasma concentrations at 10 min intervals starting from 1.0 μg/ml and followed by 0.25-0.5 μg/ml increases until loss of consciousness (LOC) was reached. After LOC, propofol infusion was terminated. At each concentration level and after terminating the infusion, consciousness was assessed by asking the subject to open his eyes. LOC was defined as no response to the "open your eyes" request and return of consciousness (ROC) as a meaningful response to the same request. A semantic presentation of the study setup is given in Fig. 1. However, subjects reached LOC at different concentration levels. Additionally, the time interval needed for reaching ROC varied.

EEG channels were recorded using a Galileo (Medtronic, Italy) EEG acquisition system (reference: linked mastoids). The sampling rate of the EEG signal was 256 Hz. For analysis, we present here only estimates obtained from channel Fz. This is a reasonable location to observe the strong synchronization and amplitude increase of frontal alpha to beta bands close to loss of consciousness induced by propofol medication (e.g. [6], [5]). Multichannel analysis showed a consistent behavior for all the subjects participating in the experiment, that is a gradual increase in frontal activity towards LOC as it was expected from previous studies.

The signals were first high pass filtered (Butterworth filter, order 6, cutoff frequency 1 Hz). The power line noise was also removed. Finally, in order to facilitate the model order selection, the signals were decimated at half the sampling

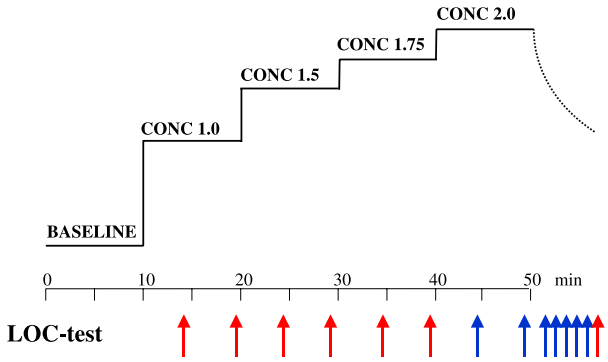

Fig. 1. Semantic presentation of the study setup. Consciousness was tested twice at each drug level and at 1 min intervals after the infusion was terminated. The color of arrows on the bottom indicate the result of LOC-testing (red=response, blue=no response).

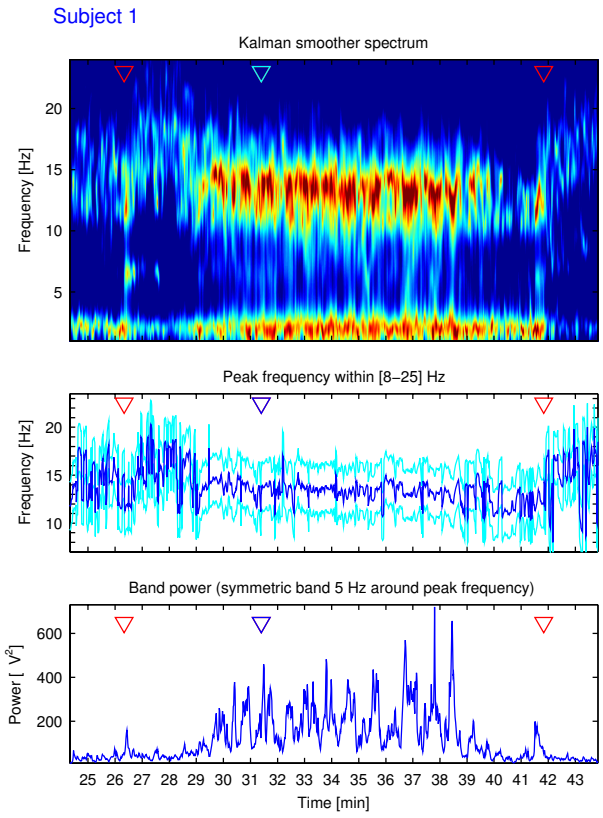

Fig. 2. Representative subject (Subject 1) under propofol anesthesia (drug concentration at LOC 1.75 μg/ml). Kalman smoother time-varying spectrum (top) for the EEG band [0.5-25] Hz. Peak frequency within the band [8-25] Hz (middle) as a function of time and an adaptive band selection (symmetric around the peak frequency, 5 Hz wide). At the bottom, the power of the selected band is presented. Red markers denote response to verbal command and the blue marker represent the moment of no response (LOC). The time is presented in minutes from the beginning of the experiment. Kalman smoother algorithm was able to track meaningful brain reactions in multiple signal components.

rate. For analysis, the time interval from 2 minutes before PLOC (moment of the last response prior to LOC) to 2 minutes after ROC was selected. In order to avoid any concerns related to the initialization of the algorithm, 2 minutes longer data segments were used, i.e. an extra minute at the beginning and an extra minute at the end of the above mentioned time interval. Then Kalman smoother spectrum estimates were calculated (AR model order $p = 30$, update coefficient UC=$9 \cdot 10^{-6}$). The same selections were applied for all the subjects.

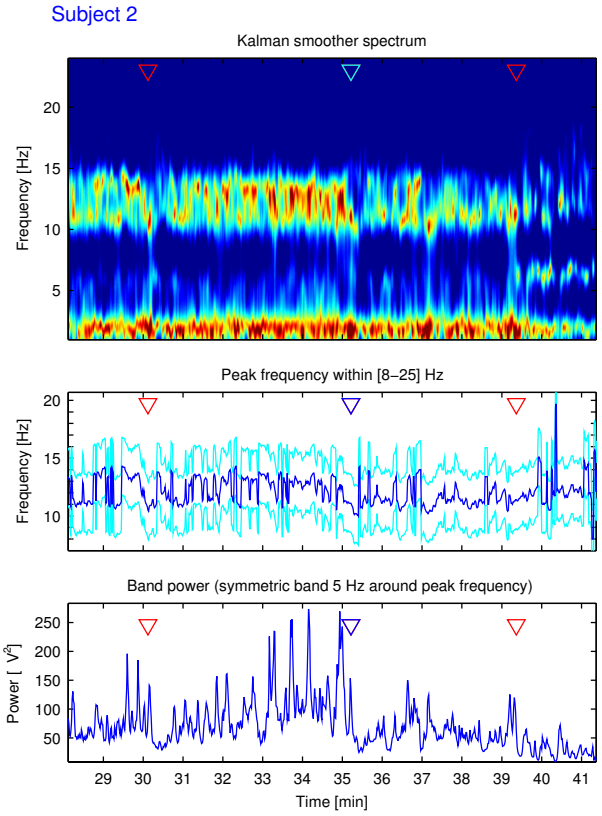

Fig. 3. Representative subject (Subject 2) under propofol anesthesia (drug concentration at LOC 1.75 μg/ml). Figure description as in Fig. 2. A strong brain response during LOC is also observable.

In Fig. 2 and Fig. 3, Kalman smoother spectral estimates for two representative subjects are presented. The subjects reached LOC at the same drug concentration level. Clearly, both subjects demonstrate strong reactions at PLOC time instances (drug concentration 1.5 μg/ml) resembling those at ROC. The responses are of both ERS and ERD type involving multiple frequency bands. By visual inspection, a similar behavior is observed at least for Subject 2 also during LOC. Based on the Kalman smoother spectral estimates, this kind of response during LOC was consistent and easily observable for several of the subjects in the study group. In Fig. 4 we also present results obtained from all the subjects in the study group. Brain reactivity during PLOC, LOC, as well as ROC is observable from these plots.

IV. Conclusions

A Kalman smoother based time-varying EEG spectrum estimation method was presented. Considering parametric spectrum estimation methods based on time-varying AR model, Kalman smoother algorithm is an optimal method for

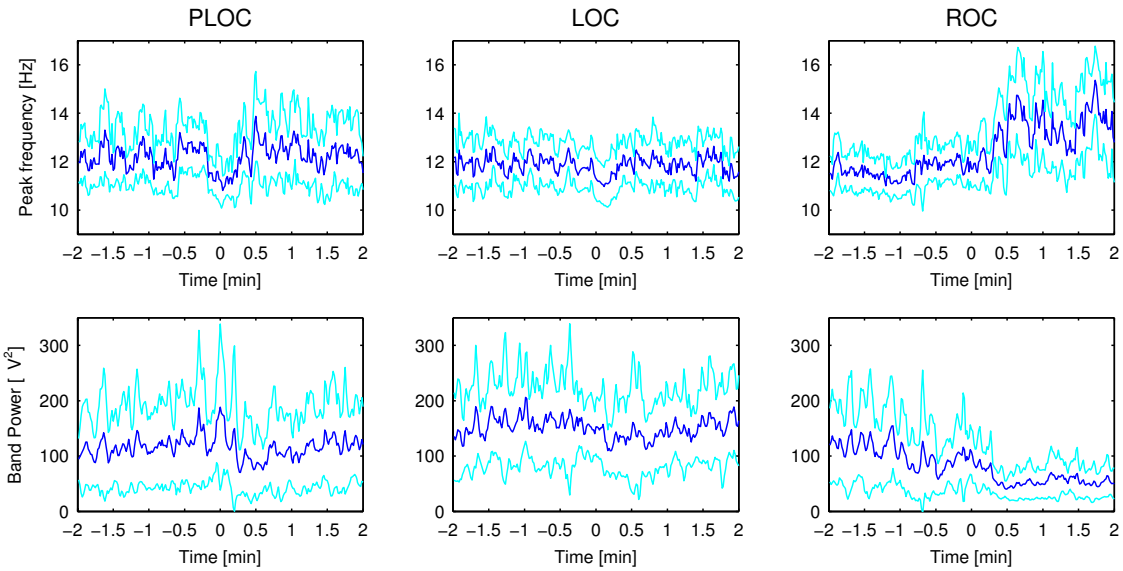

Fig. 4. Group results: average (blue), +-2 times the standard error (cyan) obtained for all the subjects (n=10) in the experiment. The results are presented close, i.e.-2 m to +2 m, to the moments of PLOC (last response prior to loss of consciousness), LOC (loss of consciousness), ROC (first meaningful response after LOC). In the first line (top) is the peak frequency within the band [8-25] Hz and at the second line (bottom) the band power based on an adaptive band selection (subject specific, symmetric around the individual peak frequencies, 5 Hz wide). Brain reaction at LOC can also be observed.

estimating the model parameters. Of importance is the selection of model order and update coefficient. Those were here selected based on visual inspection of the estimates.

The method was applied to measurements collected during low dose propofol anesthesia. The method was able to track ERS/ERD type of changes elicited by verbal command covering a wide frequency range and in different sedation levels. The results obtained so far seem important for anesthesia research and monitoring and require deeper physiological investigation. For example, brain reactivity during loss of consciousness was observed for several subjects in the study group. The approach will also be applied to subjects undergoing anesthesia induced by other anesthetic agents.

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