Cross-Recurrence Rate for Discriminating ‘Conscious’ and ‘Unconscious’ State in Propofol General Anesthesia

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Abstract—This paper introduces the use of cross recurrence rate (CRR) for discriminating between ‘conscious’ and ‘unconscious’ state from the electrical brain activity (EEG) of patients under general anesthesia. CRR measures the bivariate dependencies between two time series by looking at recurrences of the phase space from one system to the other. Here, the feasibility of pairwise electrode CRR to discriminate ‘conscious’ and ‘unconscious’ state is investigated using the EEG of 10 subjects during recovery of consciousness from general anesthesia with propofol. Performance is investigated with a Support Vector Machine. An average accuracy of 98% is obtained.

I. INTRODUCTION

General anesthesia is a chemically-induced reversible state of unconsciousness and depression of reflexes to afferent stimuli. Modern anesthesia involves the administration of different drugs to achieve the desired components of unconsciousness, amnesia, analgesia and immobility. Awareness during general anesthesia, even though considered a rare event, has severe psychological consequences for those who experience it. The incidence of awareness ranges from 0.1-0.8% [1] and is affected by a number of factors, such as patient characteristics and the type of surgery [2]. Devices that monitor the depth of anesthesia are now commercially available; such devices could provide a valuable means of identifying awareness during surgery, particularly since the patient himself cannot communicate this to the anesthetist due to the induced immobility. These devices function by monitoring specific changes in the electrical brain activity (EEG), as obtained through 2 electrodes placed on the patient’s forehead, and usually converting them to a number corresponding to the level of hypnosis (0-100; no activity – fully awake respectively). Available monitors are based largely on changes in the spectral content of the EEG, which are non-unique to anaesthesia.

Recently, the use of recurrence methods has been introduced to study how the EEG activity is affected by the administration of anesthetic agents during general anesthesia. Recurrence methods are advanced nonlinear techniques which study the recurrence of the phase space trajectories of a dynamical system [3]. Recurrence methods revealed an increase in the determinism of the EEG with increasing concentrations of sevoflurane [4]. It was also found that recurrence quantification analysis displayed an increased ability, as measured with prediction probability, to separate consciousness from unconsciousness under different anesthetic regimes [5, 6].

In this paper we utilize a Support Vector Machine (SVM) to classify EEG segments, obtained from 10 patients recovering from surgery under general anaesthesia, into one of the two states ‘Conscious’ and ‘Unconscious’ using the Cross-Recurrence Rate.

II. METHODOLOGY

A. Dataset

The data used in this study were collected from 10 male patients of age 42.1±21.1 undergoing general and urological surgery at Nicosia General Hospital, Cyprus. The 24-channel configuration of the TruScan32 (Deymed Diagnostic) was used and electrodes placed at positions Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1 and O2, according to the International 10/20 system, with an FCz reference. No filtering was performed during or after data collection and data was sampled at 256Hz. Data recording usually commenced while patients were still awake prior to administration of the anesthetic agents (induction), continued throughout the entire surgery, and until patients regained consciousness (ROC) at the end of surgery some time after the intravenous administration of anesthetics was switched off. ROC was defined as the point at which the patient regained consciousness started responding to verbal commands or tactile stimuli by the anesthetist at the end of surgery. GA was induced by the on duty anesthetist using the regular procedures of the hospital. Standard patient monitoring was used and all patients were preoxygenated via a face mask prior to anesthesia induction with a propofol bolus. During induction some patients also received boluses of neuromuscular blocking agents and analgesic drugs. Maintenance of GA was achieved with an intravenous administration of propofol at concentrations ranging between

This work falls under the Cyprus Research Promotion Foundation’s Program for Research, Technological Development and Innovation 2008 (DESMI 2008), co-funded by the Republic of Cyprus and the European Regional Development Fund (Grant: DIDAKTOR/DISEK/0308/20).
20-50 ml/h (200-500 mg/h) depending on patient characteristics and surgery requirements. In most patients remifentanil hydrochloride (Ultiva®, 2 mg, dissolved in 40ml) was also administered intravenously throughout surgery at a rate ranging between 2-15 ml/h (0.1-0.75 mg/h).

B. Cross-Recurrence Rate

Recurrence plots provide a tool for studying the coupling properties of a dynamical system at different points in time [3]. They are representations of the recurrence of the phase space trajectory of a system to the same state. In order to estimate a recurrence plot, the phase space of each time series is, first, reconstructed. For a time series, \( u_k \), each phase space trajectory at time \( t \) is reconstructed following Taken’s embedding theorem using an appropriate embedding dimension, \( m \), and a time delay, \( \tau \):

\[
x(t) = x_i = (u_i, u_{i+\tau}, \ldots, u_{i+(m-1)\tau})
\]

(1)

The amplitude values of the reconstructed trajectories are then ranked and converted to a symbolic sequence, \( \pi_k(i) \), e.g. the trajectory \( x(t) = x_i = (2,3,1) \) corresponds to the amplitude-ranked symbol \( \pi_k(i) = (1,2,0) \). The resulting symbols are then compared with respect to a fixed time lag, \( \tau' \):

\[
R_{i,i+\tau'} = \delta(\pi_k(i) - \pi_k(i+\tau'))
\]

(2)

where \( \delta(x) \) is the delta function. The recurrence rate is then estimated as:

\[
\frac{1}{N-m-\tau'} \sum_{i=1}^{N-m-\tau'} R_{i,i+\tau'}.
\]

Cross-recurrence plots allow one to estimate the times at which a state in one dynamical system, \( x_i \), \( i = 1, \ldots, N \), occurs simultaneously with the state \( y_j \), \( j = 1, \ldots, M \) in a second dynamical system [7]. The cross-recurrence rate (CRR) is an estimate of the probability of the occurrence of similar states in two systems with a certain delay, \( \tau' \). It can be considered as the bivariate equivalent to the recurrence rate and is estimated in an analogous manner for the reconstructed phase spaces of the two systems, with:

\[
R_{i,i+\tau'} = \delta(x_i - y_{i+\tau'})
\]

(3)

The choice of the parameters \( m \) and \( \tau \) is important and methods for estimating them should be used, such as the method of false nearest neighbours (for \( m \)) and mutual information (for \( \tau \)) [8]. CRR is non-symmetric, thus it also allows investigations of the direction of coupling.

C. Support Vector Machine

SVMs belong to the family of kernel-based classifiers [9]. The main idea behind SVMs is to use kernel functions to perform operations in the “data” space, corresponding to an implicit mapping of the data in a higher dimensional “feature” space where a hyperplane (decision boundary) that can separate the classes can be found. The simplest case is a linear SVM trained to classify linearly separable data. The constructed constraints define two parallel hyperplanes whose distance from the estimated decision boundary is maximal. The points lying on the two hyperplanes are called the support vectors. Estimating the decision boundary subject to the set of given constraints is a constrained optimization problem that can be solved in the Lagrange optimization framework.

D. Analysis

The main function of a DOA monitor is to alert the anesthetist when a subject becomes aware during surgery. Therefore, a minimal requirement for a DOA monitor is the ability to distinguish between the two states ‘Conscious’ and ‘Unconscious’ (class ‘A’ and ‘B’ respectively). This was assessed through the following analysis:

1. Segments corresponding to the two classes were extracted from the continuous EEG recordings of 10 subjects around the ROC marker.

2. Electrodes with no signal due to bad contact were manually excluded from further analysis. The EEG segments were windowed using a 2-s non-overlapping window, and the CRR was then estimated pairwise over each window for all available electrodes, resulting in a maximum of 342 electrode pairs if all 19 electrodes were available. The CRR was estimated for \( m = 3 \) and \( \tau = 1 \) (see Results for discussion). The estimated CRR values were smoothed using a moving average filter of length 10 samples. No artefact removal was performed, as the CRR is robust to artefacts [7].

3. The dimensions of the resulting CRRs were reduced using Principal Component Analysis. The features consisted of the CRR time series projected onto the principal components which cumulatively contributed 90% of the total component variance. As a result, the dimensions of the resulting feature vectors varied between subjects (see table I).

4. The subject-wise performance was evaluated over \( B=100 \) bootstrap repetitions. In each repetition 70% of the available data were used for training, with the remaining 30% of the data used for testing. Classification with a linear SVM was investigated. Performance was assessed as the sensitivity (4), specificity (5) and average accuracy (6):

\[
SE = \frac{TN}{TN_p} \quad (4), \quad SP = \frac{TP}{TN_p} \quad (5)
\]

\[
AC = \frac{1}{2} \left( \frac{1}{B} \sum_{h=1}^{B} \frac{TP}{TN_p} + \frac{1}{B} \sum_{h=1}^{B} \frac{TN}{TN_n} \right) \quad (6)
\]

where \( TP \) (\( TN \)) is the number of true positives (negatives), and \( TN_p \) (\( TN_n \)) is the total number of positive (negative) examples. Here, ‘conscious’ were considered as positive, and ‘unconscious’ as negative examples.

III. Results

A. Classification accuracy

The estimated CRR features are shown in fig. 1 for a randomly chosen subject (S9). For S9, the feature space was reduced from 342 pairwise CRR values to 3 dimensions. It can be seen that CRR displays distinct values for ‘consciousness’
Figure 1. CRR features for subject S9. For this subject all electrodes were available, thus a total of 342 pairwise-electrode CRR time series were estimated. This 342-dimensional feature vector was transformed using the first 3 PCs, resulting in a 3-dimensional feature vector of CRR values. (a) Thin line: Original CRR for electrode pair Fp1-O2. Thick line: reconstructed CRR using only the 1st PC (shown in (b)). Vertical dotted line: manual marker for ROC. X-axis in arbitrary samples (each sample corresponds to a 2-s EEG segment).

Figure 2. Effect of parameters $\tau$ (a) and $m$ (b) on the CRR estimations for electrode pair Fp2-O2 for patient S5. (a) The choice of the time delay, $\tau$, affects the shape of the CRR time series. Thin line: CRR for $\tau = 1$. Dash-dot line: mean CRR for $\tau = 2,\ldots,10$, plotted with $\pm$ standard deviation (shaded area). Thick line: CRR for $\tau = 12$. (b) CRR estimated for $\tau = 1$ and $m = 2,\ldots,5$. The choice of $m$ has a bigger effect on the actual CRR values than the CRR shape.

and ‘unconsciousness’ and discrimination between the two states is clear. The remaining patients display similar CRR patterns, but with some inter-subject variability in the actual estimated values. Table I shows the subject-wise performance obtained averaged over 100 bootstrap repetitions, as well as the overall average classification for all patients. The CRR shows the ability to discriminate between ‘conscious’ and ‘unconscious’ state, with average performances of
(mean±standard deviation) 99.7±0.005, 98.6±0.014, and 99.1±0.007 for SP, SE and Acc respectively. The high classification accuracy obtained with a linear SVM implies that CRR features are linearly separable and, thus, it is not necessary to utilize a more complex nonlinear classifier.

B. The effect of the parameters \( m \) and \( \tau \)

The parameters \( m \) and \( \tau \) play an important role in the ability to discriminate between ‘conscious’ and ‘unconscious’ state. Jordan et al. state that the ability to separate the two states decreases for values \( \tau > 4 \) [5]. Here, we have also found such an effect for the 10 subjects investigated. However, we found that discriminating ability between the two states was best for \( \tau = 1 \). Figure 2(a) shows the CRR estimated for a randomly chosen subject (S5) between electrodes Fp2 and O2 for \( m = 3 \) and \( \tau = 1, 2, \ldots, 10, 12 \) (the value \( \tau = 12 \) is the delay estimated from the minimum of the mutual information function). We can see that the best discrimination between ‘conscious’ and ‘unconscious’ state is obtained for \( \tau = 1 \), as the differences in the CRR values between the two states are more pronounced. Using other delays, including the ‘optimum’ delay as estimated from the delayed mutual information function, does not provide as good discrimination between the two states. Regarding the ‘optimum’ delay, this could be due to the fact that there is no theoretical reason why there should always be a minimum in the delayed mutual information function, and in many cases the first minimum found reflects statistical fluctuations [8]. The CRR is also estimated for \( \tau = 1 \) and \( m = 2, \ldots, 5 \) (fig. 2(b)), for the same time series. Larger values of \( m \) constitute the estimation very computationally complex and, thus, inappropriate for this particular application. It can be seen that the choice of \( m \) only affects the actual values of the CRR but not the observed CRR patterns.

<table>
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TABLE I. AVERAGE SINGLE-SUBJECT PERFORMANCE (%) USING CROSS-RECURRENCE RATES AND LINEAR SVM, SP: SPECIFICITY, SE: SENSITIVITY, ACC: ACCURACY, DIM: FEATURE DIMENSIONALITY

C. CRR patterns

The non-symmetric property of CRR allows us to investigate the direction of coupling between the two time series. Depending on which of the two time series is delayed, we can deduce information concerning the direction of influence from one time series to the other. If \( CRR(x(t), y(t + \tau)) > CRR(y(t), x(t + \tau)) \), then \( x \) leads \( y \), and vice versa for the opposite inequality. Here, there appears to be strong unidirectional CRR from some brain areas to others during anesthesia, which disappears when the patient recovers consciousness (fig. 2). Thus, it appears that some brain areas lead others during anesthesia. However, this is not within the scope of the current paper and remains the subject of future work.

IV. CONCLUSION

The use of cross-recurrence rate has been applied for discriminating ‘conscious’ and ‘unconscious’ state under propofol general anesthesia. An average classification accuracy of is obtained, which is encouraging for the application of cross-recurrence methods to track the depth of anesthesia. Further investigations will concentrate on studying the CRR pairwise electrode patterns in order to establish how the administration of anesthetics affects the coupling between various brain areas, and under different anesthetic regimes.

ACKNOWLEDGMENT

The authors would like to thank the hospital staff and the anonymous volunteers who participated in this study.

REFERENCES