

Depth of Anaesthesia Assessment Based on Spectral Entropy

Jee Sook Ra (✉ nickira1228@gmail.com)

University of Southern Queensland Faculty of Engineering and Surveying: University of Southern Queensland Faculty of Health Engineering and Sciences <https://orcid.org/0000-0002-6069-2243>

Tianning Li

University of Southern Queensland

Yan Li

University of Southern Queensland

Research

Keywords: spectral entropy, EEG, depth of anaesthesia, machine learning, linear regression

Posted Date: December 9th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-118634/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Depth of Anaesthesia Assessment Based on Spectral Entropy

Jee Sook Ra¹, Tianning Li², Yan Li³

Jee Sook Ra

U1102792@uqmail.usq.edu.au

+61 433 530 573

Tianning Li

Tjanning.Li@usq.edu.au

+61 7 4631 2130

Yan Li

Yan.Li@usq.edu.au

+61 7 4631 5533

¹ PhD candidate, School of Sciences, University of Southern Queensland, West St, Darling Heights QLD 4350 Australia

² Lecturer, School of Sciences, University of Southern Queensland, West St, Darling Heights QLD 4350 Australia

³ Professor, School of Sciences, University of Southern Queensland, West St, Darling Heights QLD 4350 Australia

The total number of words: 5977

The number of words of the abstract: 200

The number of figures: 10

The number of tables: 7

Keyword: spectral entropy; EEG; depth of anaesthesia; machine learning; linear regression

Abstract

Anaesthesia is a state of temporary controlled loss of awareness induced for medical purposes. An accurate assessment of the depth of anaesthesia (DoA) has always been required. However, the current DoA algorithms have limitations such as inaccuracy or inflexibility. In this study, for more reliable DoA assessment, pre-denoised electroencephalograph (EEG) signals are divided into ten frequency bands (α , β_1 , β_2 , β_3 , β_4 , β , $\beta\gamma$, γ , δ and θ), and the basic complexity measure is done by using spectral entropy (SE). SE from beta-gamma frequency band (21.5 - 38.5 Hz) and SE from beta frequency band show the highest R squared value (0.8458 and 0.7312, respectively) with currently the most popular DoA index, bispectral index (BIS). A new DoA index is developed based on these two SE values for monitoring the DoA and evaluated by comparing with the BIS index. The highest Pearson correlation coefficient is 0.918, and the average is 0.80. In addition, the proposed index shows an earlier reaction

than BIS index when the patient from deep anaesthesia to moderate anaesthesia, and the consistency in the case of poor signal quality (SQ) while the BIS Index exhibits inflexibility with cases of poor SQ.

1. Introduction

Monitoring the patients' depth of anaesthesia (DoA) is one of the current challenges in medicine. An accurate assessment of the DoA is crucial as the patient under-dosage may lead to intraoperative awareness with recall, while the over-dosage may lead to prolonged recovery and an increased risk of postoperative complications for the patient. Various human and animal researchers confirmed that electrical brain activities significantly correlated with the DoA during surgery. Most of brain electrical activities can be represented by the electroencephalograph (EEG) signals. EEG monitoring methods are typically non-invasive, with small metal discs with thin wires (electrodes) placed on the scalp, and then send signals (voltage fluctuations resulting from ionic current within the neurons of the brain) to a computer to record the results. EEG patterns change during stages of anaesthesia, and, as the level of anaesthesia becomes deeper, EEG signals gradually shift toward higher-amplitude and lower-frequency activity. The DoA monitoring using EEG improves patient treatment outcomes by reducing the incidences of intra-operative awareness, minimizing anaesthetic drug consumption and resulting in faster wake-up and recovery [22, 6]. Consequently, most of the recent research has been turned their attention to developing and finding non-invasive ways to monitor the DoA based on electrical brain activities.

When using EEG signals to measure the DoA, the bispectral index (BIS) monitor is commonly the primary indicator for anesthesiologists. The BIS index is a statistically based, empirically derived complex parameter, which is a weighted sum of several EEG sub-parameters, including a time domain, frequency domain, and high order spectral sub-parameters [1]. The BIS takes an EEG complex signal and provides the result into a single dimensionless number, which ranges from 0 (almost flat EEG activity) to 100 (awake). An appropriate level for general anaesthesia takes place in a BIS value between 40 and 60 [8].

However, the BIS has limitations, such as being delayed, not robust with different anesthesia medications, and not accurate across patients [6]. There are some possible improvements in the algorithms. Different attempts have been made to construct a new index using EEG signals to provide a more reliable reference to the DoA for clinical practitioners. Various methods have been developed to decompose and extract features of a frequency segment of the raw EEG over recent years. While several algorithms have been used in clinical studies and applied to EEG analysis, an algorithm based on spectral entropy (SE) is proposed in this study and its performance is compared with a method applying permutation entropy (PE). A window segmentation technique [28] is also employed with decomposing its frequency bands of an EEG signal, and then each EEG segment is divided into a

number of small blocks. The parameters (SE and PE) are calculated from the blocks and averaged over each segment. Then, the selected parameters are trained, tested, and evaluated by the Pearson correlation coefficient to build a new DoA index model.

2. Methods

In this research, the original EEG signals were de-noised using a nonlocal means method [3]. EEG signals are hard to be processed due to the great complexity and non-stationarity. Decomposing an EEG signal into a set of signals with different frequency bands is one efficient strategy to analyse it. Then, one EEG signal is partitioned into small segments using a window segmentation technique [28]. The window size in this paper was 56 second (s) with overlapping of 55s. EEG segment was divided into a number of blocks. The parameters (SE and PE) are calculated from the above blocks and averaged over each segment. These values can be used in time-domain methods to calculate their correlations with their changing anaesthetic states. The methods for a new DoA index design are demonstrated in Fig. 1.

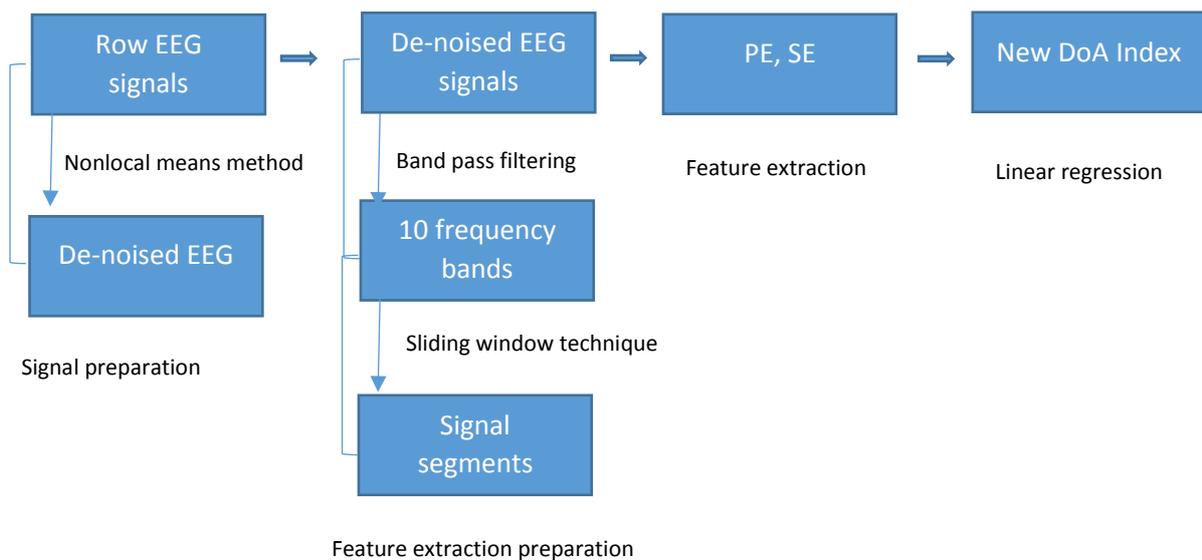


Fig. 1. The process of the new DoA index design and evaluation based on EEG

2.1 Experimental Data

The EEG data were collected at Toowoomba St Vincent’s Hospital from 24 adult patients. The demographics information of all the participants who involved in this study is explained in Table 1. Their typical drug administration included earlier pharmaceuticals intravenous midazolam 0.05 mg/kg, fentanyl 1.5-3 µg/kg or alfentanil 15-30 µg/kg. The research was approved by the University of Southern Queensland Human Research Ethics Committee (No: H09REA029) and the Toowoomba and

Darling Downs Health Service District Human Research Ethics Committee (No: TDDHSD HREC 2009/016).

Table 1 Patient demographics and intraoperative drug usage

Age (year)	Weight (kg)	Height (cm)	Gender (F/M)	Midazolam (mg)	Alfentanil (μg)	Propofol (mg)	Parecoxib (mg)	Fentanyl (μg)
22-83	55-130	154-194	15/22	2-5	500, 750, 1000	90-200	40	100, 150

2.1.1 EEG Data Processing

Research shows that EEGs collected from the scalp can reflect patients' anaesthetic states. Various methods have been used to extract useful segments for the raw type EEG analysis in recent articles. Bayesian learning of frequency bands [29, 35] is proposed to simultaneously optimize spectral filters and spatial filters along with a modified factored-sampling method. Wavelet transformation (WT) is one of the popular segment decomposing methods, which usually includes orthonormal WT and integral Wavelet [7, 13]. WT enables segment detection in both time and frequency responses of finite duration signal components. Fast Fourier transform (FFT) is also one of the analysis methods for processing EEG data. FFT decomposes linear differential equations with non-sinusoidal source terms and breaks them down into component equations (with sinusoidal source terms) that transform data into frequency domain variables. For example, Murugappan and Murugappan (2013) framed EEG signals into a short time duration of 5 seconds, and two statistical features (spectral centroid and SE) in four frequency bands, namely alpha (8 Hz-16 Hz), beta (16 Hz-32 Hz), gamma (32 Hz-60 Hz) and alpha to gamma (8 Hz-60 Hz) are extracted using FFT [19]. Applying a simple classifier such as K -nearest neighbor (KNN) with that frequency domain offered a maximum mean classification accuracy of 91.33 % on the beta band [19]. In this study, WT was not necessary for frequency discrimination because time-series filtering by Fourier transform was applied to obtain different frequency components of denoised EEG datasets.

2.1.2 Frequency bands of EEG signals

The EEG signals are normally classified into five basic frequency bands (α , β , γ , δ and θ) [20]. The EEG characteristics analysis is mostly based on the different frequency bands, and DoA algorithms are usually designed upon the frequency bands dynamics [31]. For the BIS index, the phase coupling between high frequency (40 to 47 Hz) and a broader frequency range (0.5 to 47 Hz) of EEG waves is quantified, and the ratio of higher frequency waves (30 to 47 Hz) to other waves of lower frequency (11 to 20 Hz) is measured to compute the bispectrum [10]. In this study, the frequency bands are divided

and filtered into ten frequency bands group (α , β_1 , β_2 , β_3 , β_4 , β , $\beta\gamma$, γ , δ , and θ) by FFT methods to find parameters which have a higher correlation with anaesthetic states.

2.2 Spectral entropy

Extracting features simplifies the amount of data needed to describe a huge set of data accurately. In addition, features extraction is important to minimize the loss of essential information embedded in a signal. Various methods have been used to extract the features from EEG signals. Among those methods are entropy [16], detrended moving average (DMA) [21], isomap-based estimation [11], Bayesian [35], and so on [4]. In the past decade, entropy algorithms have been widely used for features extraction in EEG signals during anaesthesia. EEG patterns during the course of anaesthesia are time series and nonlinear, and entropy algorithm is a measure of complexity that can be easily applied to any type of time series nonlinear data of complexity, including physiological data such as heart rate variability and EEG data. One of the entropy methods, SE quantifies the amount of potential information conveyed in the power spectrum of a given signal. Zhang et al. (2015) evaluated the inter-session prediction performance of the sensorimotor rhythm-based brain-computer interface using a SE predictor, and their results showed that the average classification accuracy of the inter-session prediction is up to 89 % [34]. Das and Bhuiyan (2016) also investigated the efficiency of several SE-based features in a comprehensive analysis of focal and non-focal EEGs [5]. When the log energy entropy values were utilised as features in a KNN classifier to classify the signals, it provided 89.4% accuracy and with 90.7% sensitivity, which was higher than those by some state-of-the-art methods [5]. Xu et al. (2006) studied the SE from rats' EEG to investigate and measure brain activity variations under different DoA. They found that the SE of EEG would decrease quickly while the DoA was from light to deep and vice versa [32]. However, despite numerous researches engaged with entropy-based algorithms, few articles among them were related to SE in human-related DoA assessment. Hence, this research examines the SE of each frequency band from an EEG signal and also investigates a PE to compare their performances from features extraction.

The SE of a signal is a measure of its power spectrum distribution [30]. The SE takes the signal's normalised power spectrum distribution in the frequency domain as a probability distribution and calculates its Shannon entropy. The equations for SE are derived from the equations for the power spectrum and probability distribution for a signal. For a signal $x(n)$, the power spectrum is $S(m) = |X(m)|^2$, where $X(m)$ is the discrete Fourier transform of $x(n)$. According to Ulrych [30], the probability distribution $P(m)$ is then:

$$P(m) = \frac{S(m)}{\sum_i S(i)} \quad (1)$$

The SE (H) follows as:

$$H = -\sum_{m=1}^N P(m) \log_2 P(m) \quad (2)$$

Normalizing

$$H_n = -\frac{\sum_{m=1}^N P(m) \log_2 P(m)}{\log_2 N} \quad (3)$$

where N is the total frequency points. The denominator, $\log_2 N$, represents the maximal SE of white noise, uniformly distributed in the frequency domain. If a time-frequency power spectrogram $S(t, f)$ is known, then the probability distribution $P(m)$ becomes:

$$P(m) = \frac{\sum_t S(t, m)}{\sum_f \sum_t S(t, f)} \quad (4)$$

Then the SE at time t ($H(t)$) is:

$$H(t) = -\sum_{m=1}^N P(t, m) \log_2 P(t, m) \quad (5)$$

2.2.1 Features extraction based on SE and PE

The parameters (SE and PE) are calculated from blocks in a segmented EEG and averaged over each segment. The SE or PE values in time domain analysis methods should be highly correlated with changing anaesthetic states. These correlations should also be robust for different patients. The degree of their correlation is measured by the coefficient of determination (R^2) in this research. The R^2 indicates the degree of the variance in the dependent variable that the independent variables explain collectively. The SE and PE values are calculated from 10 frequency bands (α , $\beta 1$, $\beta 2$, $\beta 3$, $\beta 4$, β , $\beta\gamma$, γ , δ , and θ) of each EEG episode and the R^2 is used to evaluate the correlation between parameters and anaesthetic states (referring to the BIS in this study). The definition of the R^2 [14] is:

$$R^2 = 1 - \frac{\sum_i (y_i - f_i)^2}{\sum_i (y_i - \bar{y})^2} \quad (6)$$

Where y_i is a data set, \bar{y} is the mean of a data set, and f_i is a set of predicted values. The greater the R^2 is, the higher correlation between the parameter and BIS value is.

2.3 Regression Models and Evaluation

The machine learning algorithms have been widely used in signal classification area. The calculated EEG signals from features extraction are utilized for training a machine learning model to find out how single feature or different combinations of them can discriminate between distinct stages of anaesthesia. A combination of the irregularity of EEG waveforms in time-domain or band powers in the frequency domain can describe the difference among anaesthetic states. To characterize these states, a set of optimum EEG parameters are extracted using frequency discrimination methods, and these parameters establish a relationship between input and output variables by fitting the best linear or nonlinear analysis. For example, Yildirim et al. (2018) combined the application of four fundamental ensemble learning methods of bagging, boosting, stacking, and voting with five different machine learning algorithms of a neural network, a support vector machines (SVM), a KNN, Naive Bayes, and C4.5 with the most optimal parameter values on EEG signal data sets for the assessment [33]. Some research employed a single model and still achieved high accuracy. Das and Bhuiyan (2016) utilised the log-energy entropy values as features in a KNN classifier to classify the signals. It provides 89.4% accuracy with 90.7% sensitivity [5]. Aydemir et al. (2014) proposed a fast and accurate decision tree structure-based classification method for analysing EEG data. The proposed decision tree structure achieved an 82.24% classification accuracy rate [2]. Liang et al. (2018) used a genetic algorithm and SVM to identify the emergence of EEG patterns. The accuracy obtained by the GA-SVM was between 90.64 - 72.86 % [15]. Linear regression analysis for EEG assessment has also been widely used in the DoA research area [12,17].

Linear regression, SVM, deep learning and a neural network are tested for a new DoA index in this study. Regression analysis consists of a set of *machine learning* methods that allow us to predict a continuous outcome variable (y) based on the value of one or multiple predictor variables (x). Once features are extracted, the regression technique is employed to evaluate the correlation between the predicted outcome by the model and the anaesthetic states, which is referred to as the BIS value. The Pearson correlation coefficient (r) and the root mean squared error ($RMSE$) are used to evaluate the correlation between the new index and the BIS index. The definition of r [25] is given below :

$$r = \frac{\sum(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum(x_i - \bar{x})^2 \sum(y_i - \bar{y})^2}} \quad (7)$$

where x is the new index value, \bar{x} is the mean of new index, y is the corresponding BIS value, and \bar{y} is the mean of BIS. The value of r is between [-1 1]. If r is closed to 1 or -1, it means that the two indexes are highly correlated. If r equals 0, it means that there is no correlation at all between the indexes.

The $RMSE$ is a square root of MSE [18]. The definition of the MSE is as follows :

$$MSE = \frac{1}{n} \sum_{i=1}^n (Y_i - \hat{Y}_i)^2 \quad (8)$$

Where n is the number of data points, Y_i is a set of observed values, and \hat{Y}_i is a set of predicted values.

3. Results

3.1 Features selection

Before parameters are calculated from different frequency bands, SE and PE values are calculated from EEG signals of channel 2 (Ch2) and the sum of EEG signals of channel 1 and channel 2 (Ch1+Ch2) to select the channel so that the experimental design can be simplified but more efficient. As shown in Fig. 2, the R^2 of SE and PE from Ch2 and Ch1+Ch2 (the reference is the BIS index) have very close to each other. Therefore, the EEG signals from Ch1 or Ch1+Ch2 are not necessary to be analyzed when the EEG signals from Ch2 are analyzed.

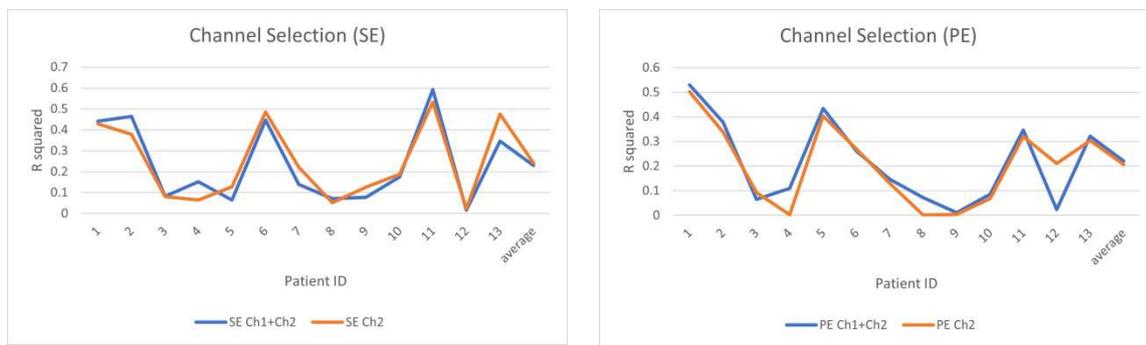


Fig. 2 The R^2 value of SE and PE from Ch1+Ch2 EEG and Ch2 EEG (the reference is the BIS index)

For further exploration of the relationship between the parameters and frequency bands, the EEG signals are decomposed into basic frequency bands (α , β , γ , δ and θ) and small frequency bands. As a result, ten sets of frequency bands from each episode of EEG signals are obtained. The SE and PE values are calculated based on both the amplitude and power of each basic frequency band. The scatter plot graphs for the SE and PE parameters and BIS (Fig. 3) shows that SE and PE parameters are linearly correlated with the BIS index.

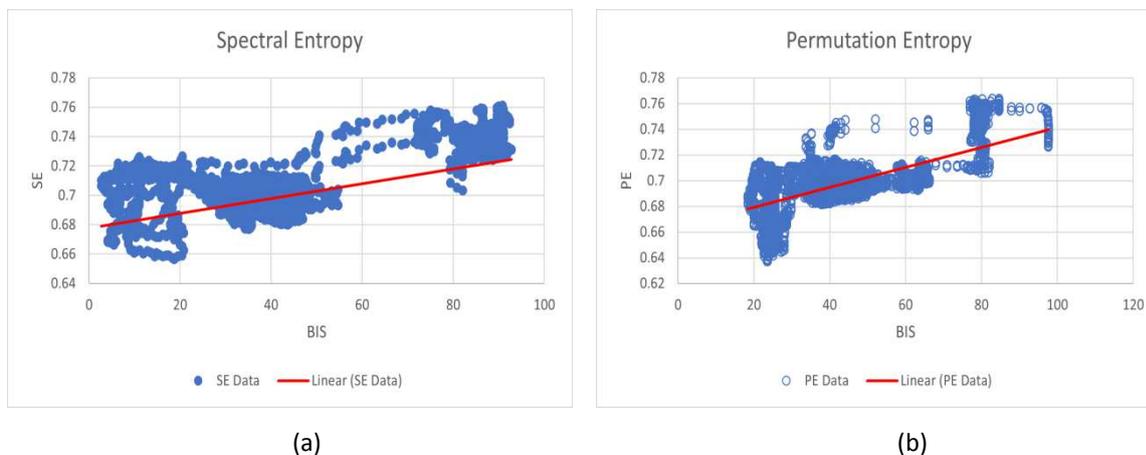


Fig. 3 The linear relationship between parameters with BIS value, (a) SE (b) PE. The best-fit line is red. fitted linear relation indicates that the two methods are correlated (SE and PE values from patient ID 10)

The average R^2 value of SE and PE in each frequency band from 13 patients (randomly chosen) of EEG signals are shown in Fig. 4.

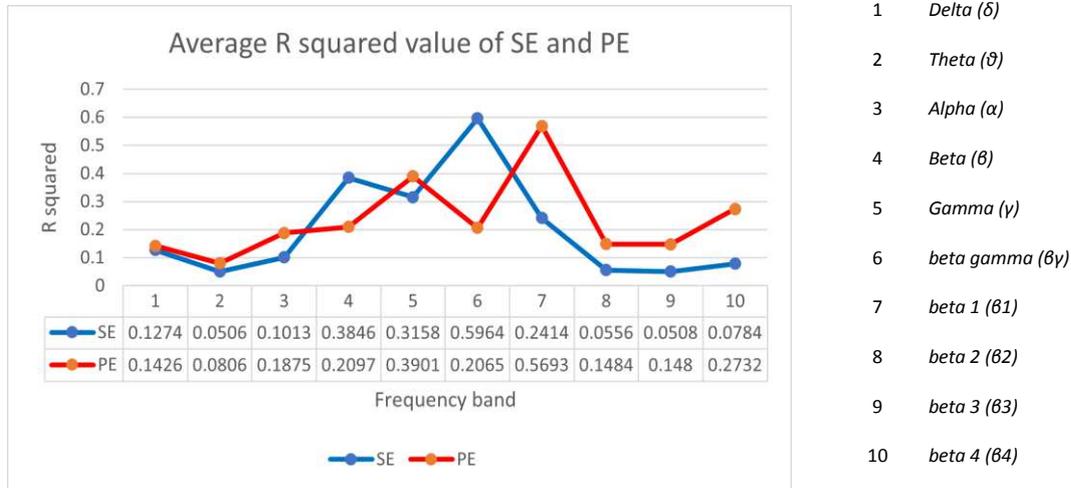
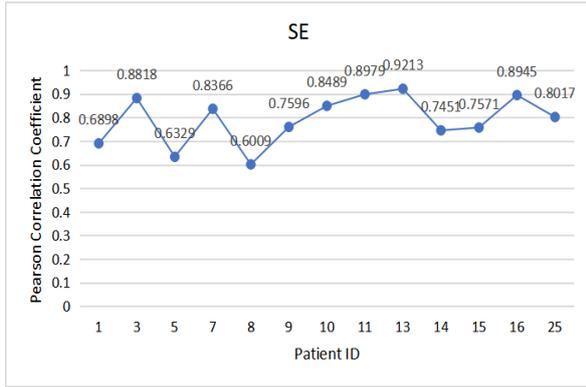


Fig. 4 Comparison of SE and PE from different frequency bands (the reference is the BIS index)

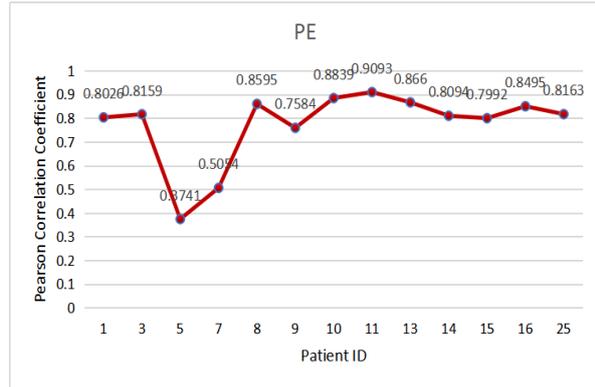
From Fig. 4, SE-based features outperform PE-based features in two frequency bands (β and $\beta\gamma$) distinctively. For example, the highest R^2 calculated from SE of $\beta\gamma$ is 0.8459, whereas the highest R^2 for PE is 0.7927. Therefore, the most suitable parameters from different frequency bands for the DoA assessment using time-domain methods in this study are:

- the SE parameters which are calculated from the amplitude of β frequency band,
- the SE parameters which are calculated from the amplitude of $\beta\gamma$ frequency band.

The proposed new DoA index based on the time characteristics is designed using these two parameters. Simple linear regression analysis can determine if these two numeric variables are significantly linearly related to the BIS. Correlation analysis provides information on the strength and direction of the linear relationship between two variables, while a simple linear regression analysis estimates parameters in a linear equation that can be used to predict values of one variable based on the other.

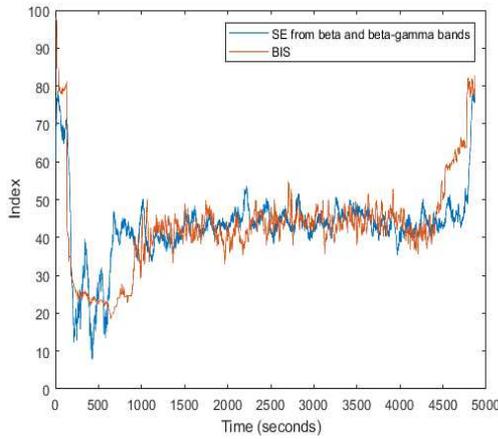


(a)

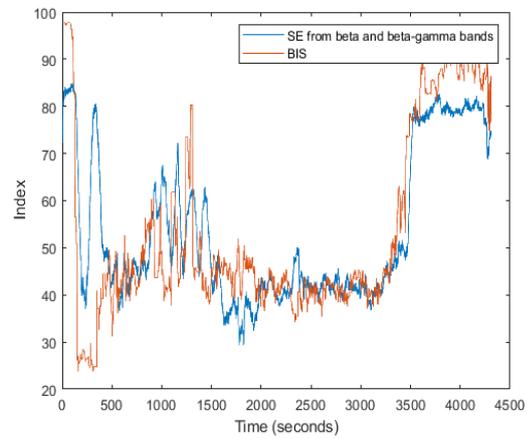


(b)

Fig. 4 r values: (a) SE calculated from β and $\beta\gamma$ frequency bands vs. BIS Index (b) PE calculated from β and $\beta\gamma$ frequency bands vs. BIS Index



(a)



(b)

Fig. 5 Index from the linear regression equation of SE calculated from β and $\beta\gamma$ frequency bands vs. BIS Index (a). Patient ID 9; (b). Patient ID 25

3.2 Models based on Regression analysis

Four methods of a linear regression, SVM, deep learning and neural network were employed to select the most suitable model for the DoA measurement, and the linear regression analysis was proved to be the best analytical model for the DoA assessment based on the Pearson correlation coefficient (r), the root mean squared error ($RMSE$) and execution time in this study. To determine the method of analysis, ten sets of subjects of the selected parameters (SE calculated from β and $\beta\gamma$) are trained by four candidates of regression models, and randomly chosen seven sets of those were tested. The predicted values by the models are evaluated by comparing with the BIS indexes. r and $RMSE$ are used to examine the correlation of the predicted value and the BIS index. The results are shown in Fig. 6

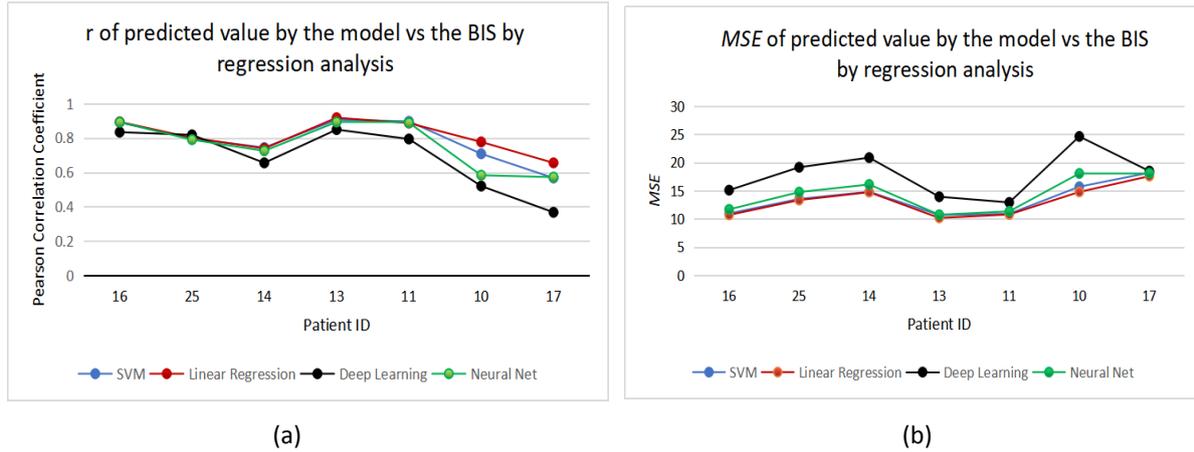


Fig 6 (a) r of predicted value by the model vs the BIS by regression analysis (b) $RMSE$ of predicted value by the model vs the BIS by regression analysis

From Fig. 6, r values from linear regression analysis are higher (more correlated with the BIS) than those from other methods, SVM (kernel type: polynomial, Kernel degree: 2.0, kernel cache: 200, max iterations: 100000), deep learning (activation: rectifier, hidden layer sizes: 50, epochs: 10), and neural network (training cycles: 200, learning rate: 0.01, momentum: 0.9). The highest r from linear regression analysis is 0.914 (Fig. 6 (a)). In addition, the **$RMSE$ from the linear regression analysis is lower than any other analytical methods in this study. The lowest $RMSE$ from the linear regression of these samples is 10.16** (Fig. 6 (b)). The execution time is also an important factor of selecting analytical methods because the execution time for analysis is crucial in the real-time measurements of the DoA. The average execution time for each regression analysis is measured and shown in Table 2. The linear regression analysis records the shortest execution duration (0.5 seconds), and SVM takes the longest time for the analysis (186 seconds).

Table 2 The average **execution time** of regression analysis (simulated by RapidMiner version 9.4)

	SVM	Linear Regression	Deep Learning	Neural Net
Average Execution Time	186 seconds	0.5 seconds	4 seconds	6 seconds

3.3 New DoA design and evaluation by linear regression

The selected parameters (SE calculated from β and $\beta\gamma$) of the EEG data from ten subjects (patient ID: 1, 2, 4, 5, 6, 8, 15, 20, 22 and 23. 18,448 seconds which contain 2,361,344 data points) are used to obtain the coefficients for the new DoA index, which employs the linear regression model. The new index is evaluated by comparing with the BIS index. r values are used to examine the correlation between the new index and the BIS index. The new DoA index is proposed as follows:

$$\text{New DoA Index} = 0.209 * SE_{\beta} + 0.510 * SE_{\beta\gamma} \quad (8)$$

Where SE_{β} is the SE values calculated from β frequency band (13-30 Hz) and $SE_{\beta\gamma}$ is the SE values calculated from $\beta\gamma$ frequency band (21.5-38.5 Hz).

The new DoA index (patient ID 16, $r = 0.893$) and the BIS index are shown in Fig. 7. The trend of the new DoA index line shows a close similarity with the BIS index, with less fluctuations.

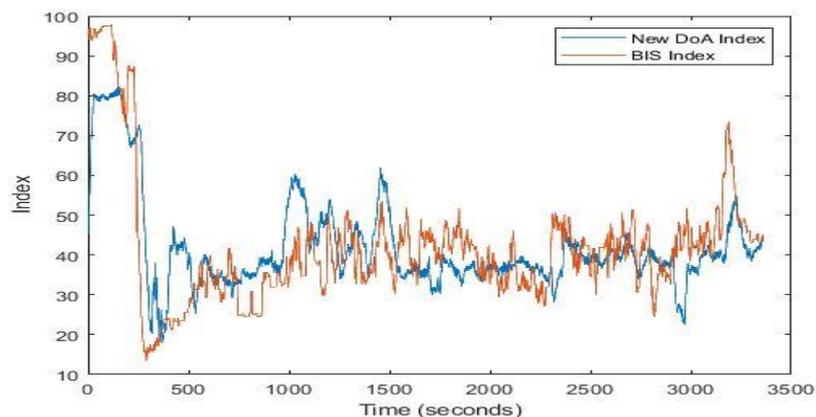


Fig. 7 The new DoA index (patient ID 16, $r = 0.893$) and the BIS index

The performances of the new DoA index for randomly selected fourteen patients (23,288 seconds which contain 2,980,864 data) are evaluated. r values for the fourteen cases are shown in Fig. 8.

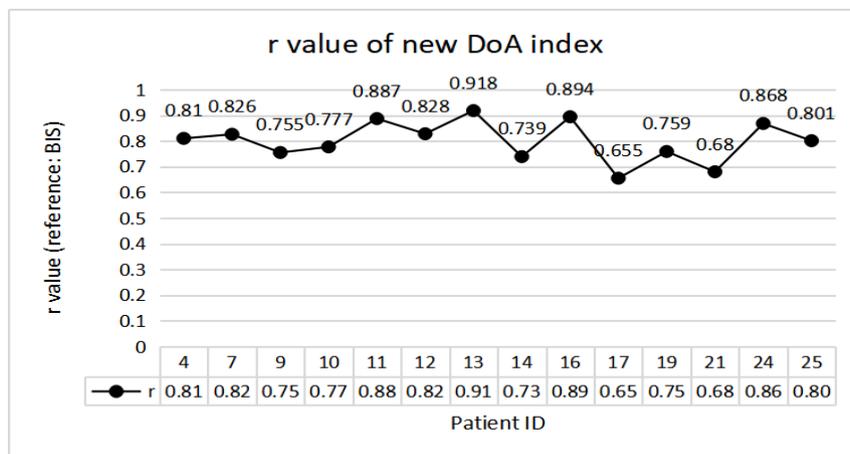


Fig. 8 The performances of the new DoA index for randomly selected fourteen patients (r values)

The average r values for the fourteen patients is 0.8079, and the highest score is 0.914. The lowest $RMSE$ is 8.62. The high r values show that there is a very close correlation between the proposed index and the BIS index. However, the performance of two cases (patient IDs 17 and 21) were not good enough (r values are 0.65 and 0.68). The poor performance can be explained by the poor signal quality of the EEG from that patient.

3.4 Patient's state in the case of poor signal quality

The signal quality indicator (SQI) is an index for signal quality which is calculated based on impedance data, artefacts, and other variables. The BIS index is not capable of calculating the valid values on the screen when SQI is lower than 15. In these cases, the value -3276.8 was labeled as a notice "excessive artefact detected in signal" [23]. The performance of the new index in poor signal quality cases (according to SQI) is also evaluated. The new index produces the DoA values when SQI is lower than 15, where the BIS index could not calculate the index. In Fig. 8 and Fig. 9, for patient ID 3, the BIS index is -3276.8 from 611 to 629 seconds and from 1294 to 1301 seconds. In Fig. 10, for patient ID 14, the BIS index is -3276.8 from 956 to 971 seconds, from 1040 to 1045 seconds, from 1153 to 1185 seconds, from 1299 to 1310 seconds and from 2396 to 2433 seconds. However, the new index shows the measured DoA value clearly during those periods. Along with the anaesthetists' records, there was no alteration of patients' anaesthetic states during this period. Consequently, the new index is more consistent to show the changes from one state of anaesthesia to another state of anaesthesia.

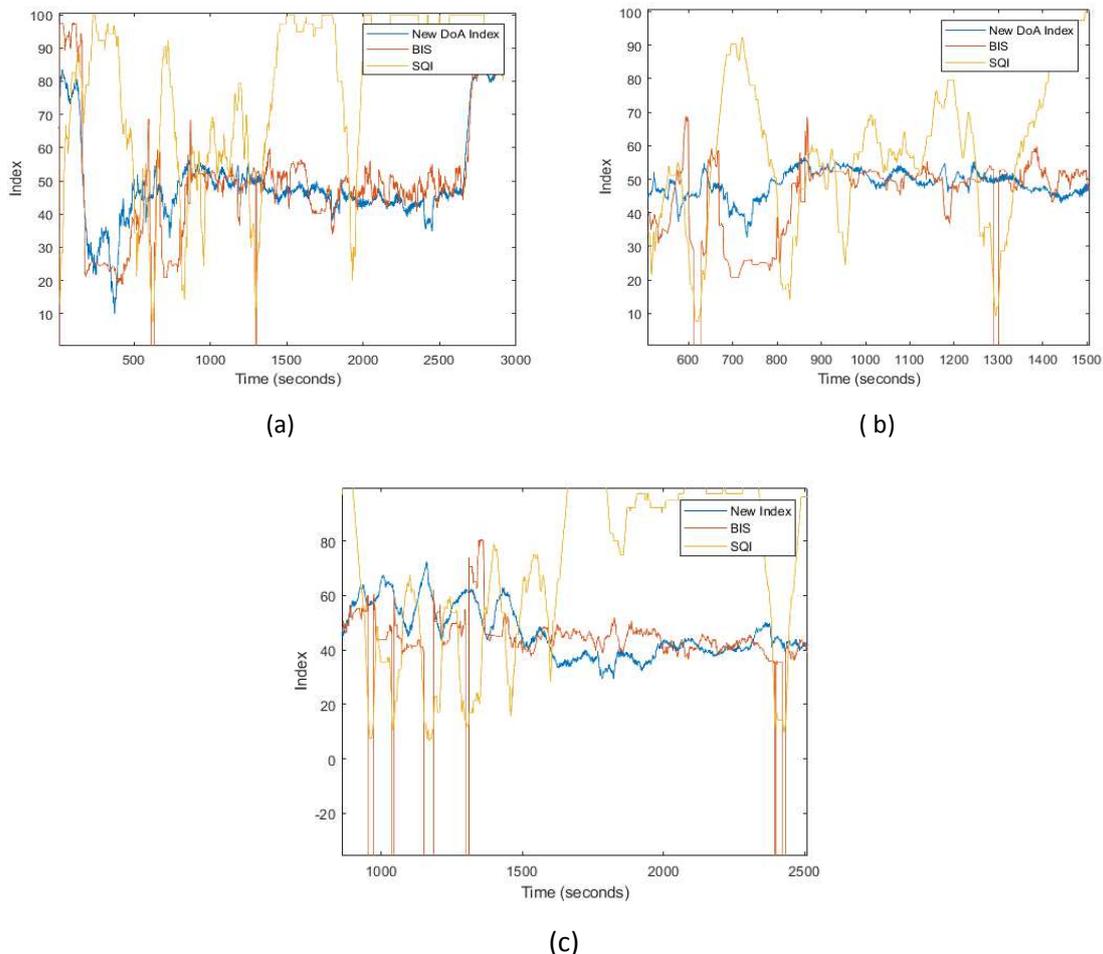


Fig. 9 Comparison of New Index and BIS index with SQI; **(a)**. patient ID: 18, range: 0 - 3000 seconds; **(b)**. patient ID: 18, range: 500 - 1500 seconds; **(c)**. patient ID: 25, range: 800 - 2300 seconds

3.4 Time delay from deep anaesthesia to moderate anaesthesia

The new index shows a high correlation with the BIS throughout the states of conscious, light anaesthesia and deep anaesthesia. Nonetheless, the new index shows an earlier reaction than the BIS index when the patient from deep anaesthesia to moderate anaesthesia. This type of earlier reaction exists in all the cases of the 14 patients. The new index for patient IDs 9 and 12 are selected as examples to show the time deference between the BIS index graphically in Fig. 10. The index value 35 is assumed to be the point at which the anaesthetic states transfers from deep anaesthesia to moderate anaesthesia. We can observe that the upward transit of the BIS from 20 to 50 is lethargic and delayed than the new index in the graph below (Fig 10). The time difference for 14 patients are provided in Table 3.

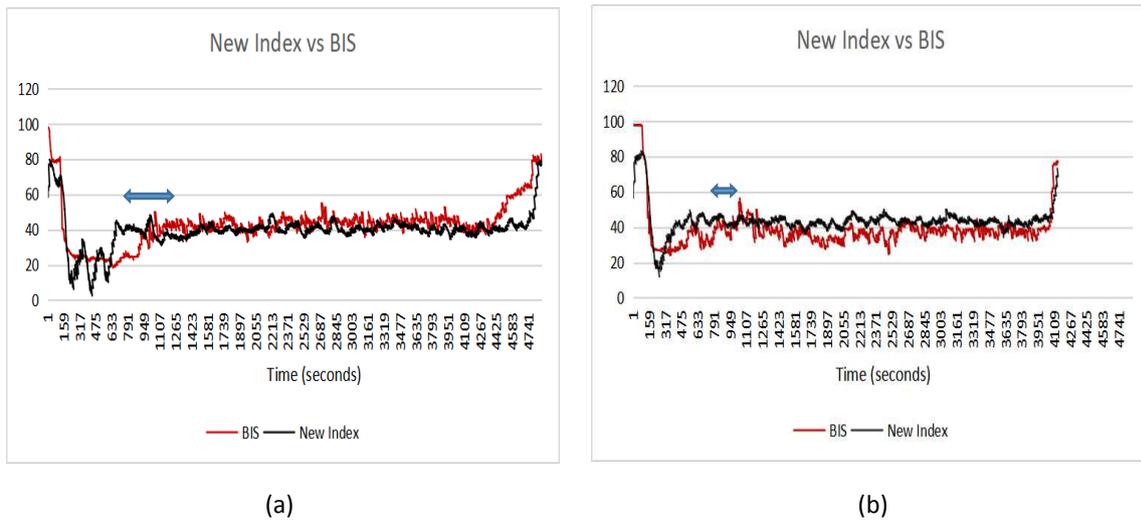


Fig 10 The comparison of the new index and the BIS index; (a) patient ID 9, (b) patient ID 12. The blue markers show the earlier reaction by the new index

Table 3 The time response comparison between the new index and the BIS

Patient ID	4	7	9	10	11	12	13	14	16	17	19	21	24	25
Time difference	200	75	258	231	41	116	331	100	6	157	288	266	132	14

4. Discussion

Extracted features reduce the number of data points needed to describe a huge set of data accurately as well as minimize the loss of essential information embedded in signals. The features extraction based on SE in this study successfully leads to develop a reliable DoA algorithm for accurate DoA assessment. The denoised EEG signals were, firstly, divided into ten sub-frequency bands (α , β_1 , β_2 , β_3 , β_4 , β , $\beta\gamma$, γ , δ , and θ), and then the basic complexity measure was done by using SE and PE. The SE from $\beta\gamma$ frequency band and the SE from the β frequency band yield the highest R^2 value (0.8458 and 0.7312, respectively) with the BIS in this study. Frequency bands decomposition from EEGs were enabled by the FFT, and SE values were obtained from ten sub-frequency bands. WT was not necessary for time-

domain frequency bands decomposition in this study because software MATLAB offers an FFT filter, which performs time-series filtering by using an FFT to analyse the frequency components in the input data sets. There are six types of filters available in the FFT filter function, and the band-pass filter function was used to separate the frequency bands in this study.

This study proves that the results of the experiment by Xu et al. [32], which showed that SE was sensitive to the states of rats' light and deep sleeps. Some studies [9, 24] [27] proposed that the PE is the promising parameter selecting algorithm discriminating different levels of consciousness during anaesthesia. The PE showed a high correlation (the highest $R^2 = 0.793$) with the BIS index, but the SE presented an improved correlation (the highest $R^2 = 0.846$) than PE in this study. Along with other studies that were related to the analyses of the human brain activity [26, 34], the SE was proved to be a useful algorithm to monitor the stages of human anaesthesia during surgery.

5. Conclusions

The new DoA index was developed based on two SE values (from β and $\beta\gamma$) for monitoring the DoA. It was evaluated by comparing with the BIS index. The highest r value is 0.918, and its average value is 0.80. The lowest $RMSE$ is 8.62. The high r values indicate the new DoA index highly correlates with the BIS index. Furthermore, the proposed index shows an earlier reaction than the BIS index when a patient from deep anaesthesia to moderate anaesthesia, and the proposed DoA index demonstrates the consistency in the case of poor signal quality ($SQI < 15$) while the BIS Index exhibits inflexibility with cases of poor SQ. Some cases of simulation exhibit poor correlations with the BIS, which may be due to the BIS index is inflexible with cases of poor signal quality. The new DoA index by linear regression provides some benefits regarding the real-time assessment. Four machine learning methods of SVM, neural network, deep learning and linear regression were employed to evaluate the accuracy of their DoA assessments. Linear regression outperformed other methods not only in accuracy (average $r = 0.80$) but also in shorter execution time. Linear regression took only 0.5 seconds to simulate more than 35000 data (run by RapidMiner version 9.4).

In conclusion, SE of the EEG is highly sensitive to the levels of anaesthesia. Therefore, an improvement can be expected with SE application in the accuracy of DoA assessment in the future.

REFERENCES

1. Ahmadi B, Negahbani E, Amirfattahi R, Zaghari B, Mansouri M Extraction of BISTM index sub-parameters in different anesthetic and sedative levels. In: 2008 9th International Conference on Signal Processing, 2008. IEEE, pp 2665-2668
2. Aydemir O, Kayikcioglu T (2014) Decision tree structure based classification of EEG signals recorded during two dimensional cursor movement imagery. Journal of Neuroscience Methods 229:68-75

3. Bernier MI, Chamberland M, Houde J-C, Descoteaux M, Whittingstall K (2014) Using fMRI non-local means denoising to uncover activation in sub-cortical structures at 1.5 T for guided HARDI tractography. *Frontiers in Human Neuroscience* 8
4. Burke DP, Kelly SP, deChazal P, Reilly RB, Finucane C (2005) A Parametric Feature Extraction and Classification Strategy for Brain-Computer Interfacing. *IEEE Transactions on Neural Systems and Rehabilitation Engineering* 13:12-17
5. Das AB, Bhuiyan MIH (2016) Discrimination and classification of focal and non-focal EEG signals using entropy-based features in the EMD-DWT domain. *Biomedical Signal Processing and Control* 29:11-21
6. Diykh M, Li Y, Wen P, Li T (2018) Complex networks approach for depth of anesthesia assessment. *Measurement* 119:178-189
7. Faust O, Acharya UR, Adeli H, Adeli A (2015) Wavelet-based EEG processing for computer-aided seizure detection and epilepsy diagnosis. *Seizure* 26:56-64
8. Iselin-Chaves IA, Willems SJ, Jermann FC, Forster A, Adam SR, Van der Linden M (2005) Investigation of implicit memory during isoflurane anesthesia for elective surgery using the process dissociation procedure. *Anesthesiology: The Journal of the American Society of Anesthesiologists* 103:925-933
9. Jordan D, Stockmanns G, Kochs E F, Pilge S, & Schneider G (2008) Electroencephalographic order pattern analysis for the separation of consciousness and unconsciousness: an analysis of approximate entropy, permutation entropy, recurrence rate, and phase coupling of order recurrence plots. *Anesthesiology* 109:1014-1022
10. Kertai MD, Whitlock EL, Avidan MS (2012) Brain Monitoring with Electroencephalography and the Electroencephalogram-Derived Bispectral Index During Cardiac Surgery. *Anesthesia & Analgesia* 114:533-546
11. Kortelainen J, Väyrynen E, Seppänen T (2011) Isomap Approach to EEG-Based Assessment of Neurophysiological Changes During Anesthesia. *IEEE Transactions on Neural Systems and Rehabilitation Engineering* 19:113-120
12. Kumar A, Anand S (2006) A Depth of Anaesthesia Index from Linear Regression of Eeg Parameters. *Journal of Clinical Monitoring and Computing* 20:67-73
13. Lee S-H, Lim JS, Kim J-K, Yang J, Lee Y (2014) Classification of normal and epileptic seizure EEG signals using wavelet transform, phase-space reconstruction, and Euclidean distance. *Computer Methods and Programs in Biomedicine* 116:10-25
14. Lewis-Beck MS, Skalaban A (1990) The R-squared: Some straight talk. *Political Analysis* 2:153-171
15. Liang Z, Huang C, Li Y, Hight DF, Voss LJ, Sleight JW, Li X, Bai Y (2018) Emergence EEG pattern classification in sevoflurane anesthesia. *Physiological measurement* 39:045006
16. Liang Z, Wang Y, Sun X, Li D, Voss LJ, Sleight JW, Hagihira S, Li X (2015) EEG entropy measures in anesthesia. *Frontiers in Computational Neuroscience* 9
17. Liu Q, Ma L, Fan S-Z, Abbod MF, Shieh J-S (2018) Sample entropy analysis for the estimating depth of anaesthesia through human EEG signal at different levels of unconsciousness during surgeries. *PeerJ* 6:e4817
18. Marmolin H (1986) Subjective MSE measures. *IEEE transactions on systems, man, and cybernetics* 16:486-489
19. Murugappan M, Murugappan S (2013) Human emotion recognition through short time Electroencephalogram (EEG) signals using Fast Fourier Transform (FFT). 2013 IEEE 9th International Colloquium on Signal Processing and its Applications. IEEE, Kuala Lumpur
20. Musizza B, Ribaric S (2010) Monitoring the Depth of Anaesthesia. *Sensors* 10:10896-10935
21. Nguyen-Ky T, Peng W, Yan L (2010) An Improved Detrended Moving-Average Method for Monitoring the Depth of Anesthesia. *IEEE Transactions on Biomedical Engineering* 57:2369-2378
22. Nguyen-Ky T, Wen P, Li Y (2009) Theoretical basis for identification of different anesthetic states based on routinely recorded EEG during operation. *Computers in Biology and Medicine* 39:40-45

23. Nguyen-Ky T, Wen P, Li Y (2013) Consciousness and Depth of Anesthesia Assessment Based on Bayesian Analysis of EEG Signals. *IEEE Transactions on Biomedical Engineering* 60:1488-1498
24. Olofsen E, Sleigh, J., & Dahan, A. (2008) Permutation entropy of the electroencephalogram: a measure of anaesthetic drug effect. *British journal of anaesthesia* 101:810-821
25. Pearson K (1930) *The Life, Letters and Labors of Francis Galton*, Cambridge Univ. Press,
26. Raghu S, Sriraam N (2017) Optimal configuration of multilayer perceptron neural network classifier for recognition of intracranial epileptic seizures. *Expert Systems With Applications* 89:205-221
27. Silva A, Campos, S., Monteiro, J., Venâncio, C., Costa, B., de Pinho, P. G., & Antunes, L. (2011) Performance of anaesthetic depth indexes in rabbits under propofol anaesthesia: prediction probabilities and concentration-effect relations. *Anaesthesiology* 115:303-314
28. Siuly NA, Li Y, Wen P (2013) Identification of motor imagery tasks through CC-LR algorithm in brain computer interface. *International Journal of Bioinformatics Research and Applications* 9:156
29. Suk H-I, Lee S-W (2013) A Novel Bayesian Framework for Discriminative Feature Extraction in Brain-Computer Interfaces. *IEEE Transactions on Pattern Analysis and Machine Intelligence* 35:286-299
30. Ulrych TJ (1972) Maximum entropy power spectrum of truncated sinusoids. *Journal of Geophysical Research* 77:1396-1400
31. Vakkuri A, Yli- Hankala A, Talja P, Mustola S, Tolvanen- Laakso H, Sampson T, Viertiö- Oja H (2004) Time- frequency balanced spectral entropy as a measure of anesthetic drug effect in central nervous system during sevoflurane, propofol, and thiopental anesthesia. *Acta Anaesthesiologica Scandinavica* 48:145-153
32. Xu J, Zheng, C., Liu, X., Pei, X. and Jing, G. (2006) Detecting brain activity variation of rat during anaesthesia by spectral entropy. Paper presented at the In 2005 IEEE Engineering in Medicine and Biology 27th Annual Conference,
33. Yildirim P, Birant KU, Radevski V, Kut A, Birant D (2018) Comparative analysis of ensemble learning methods for signal classification. 2018 26th Signal Processing and Communications Applications Conference (SIU). IEEE, Izmir
34. Zhang R, Xu P, Chen R, Li F, Guo L, Li P, Zhang T, Yao D (2015) Predicting Inter-session Performance of SMR-Based Brain-Computer Interface Using the Spectral Entropy of Resting-State EEG. *Brain Topography* 28:680-690
35. Zhang Y, Wang Y, Jin J, Wang X (2017) Sparse Bayesian Learning for Obtaining Sparsity of EEG Frequency Bands Based Feature Vectors in Motor Imagery Classification. *International Journal of Neural Systems* 27:1650032

Author's biography

Jee S Ra received M.Sc. degree in the School of Sciences from University of Southern Queensland (USQ), Australia, in 2019. Currently, she is a Ph.D. candidate of USQ. Her research area is in biomedical signal processing, especially, in depth of anaesthetic state detection and epileptic seizure prediction based on EEG analysis.



Tianning Li received a Ph.D. degree from University of Southern Queensland (USQ). Currently, he is a computing lecturer in School of Sciences , USQ. His research interests include Machine Learning Algorithms, Signal Processing, EEG Research.



Yan Li received her PhD degree from the Flinders University of South Australia, Australia. She is currently a full Professor in Computer Science and the Associate Head (Research) in the School of Sciences at the University of Southern Queensland, Australia. Her research interests lie in the areas of Artificial Intelligence, Machine Learning, Big Data and Internet Technologies, Signal/Image Processing and EEG Research.

Figures

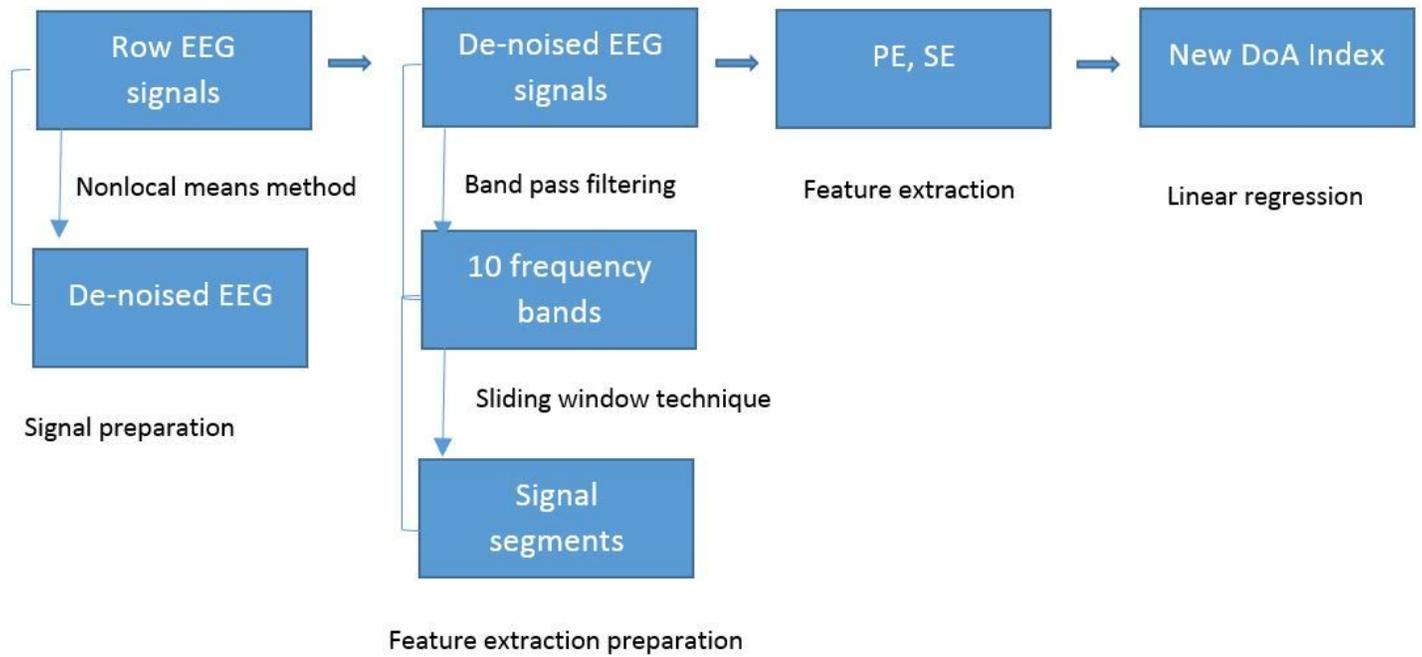


Figure 1

The process of the new DoA index design and evaluation based on EEG

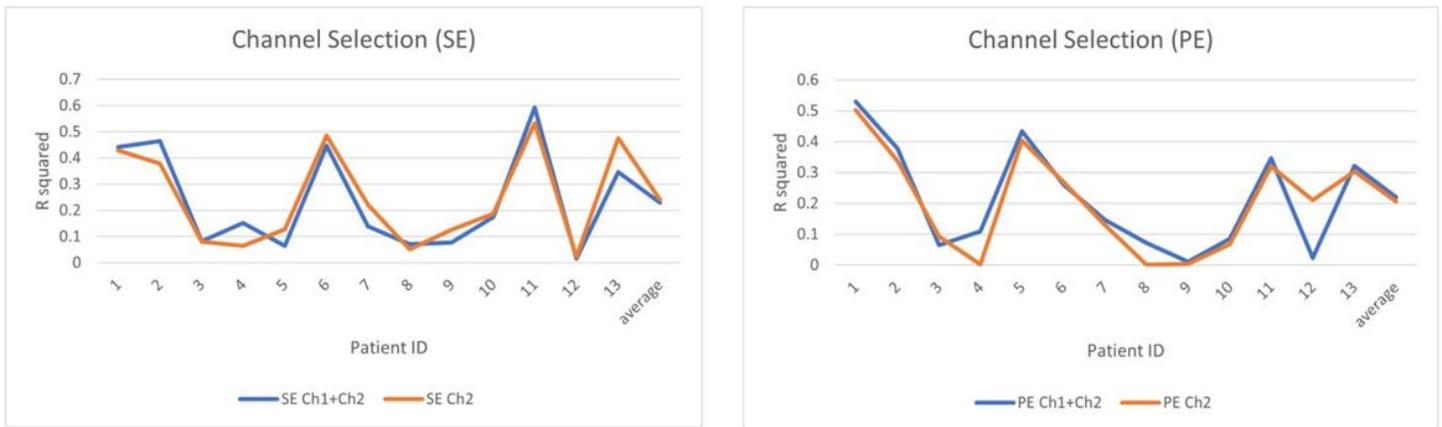
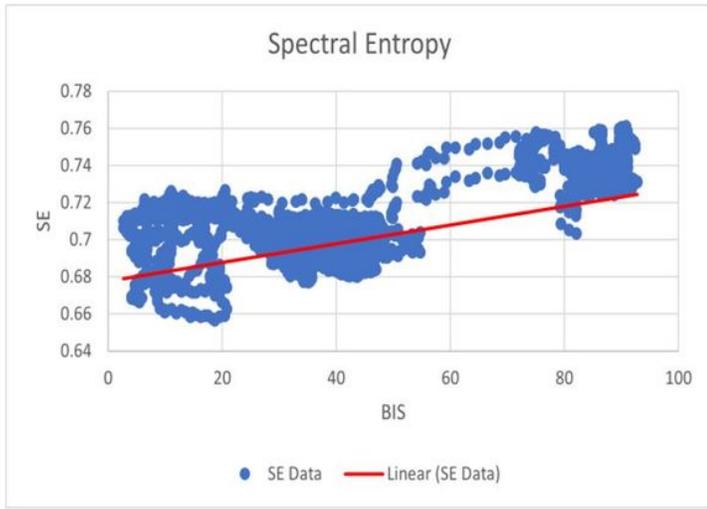
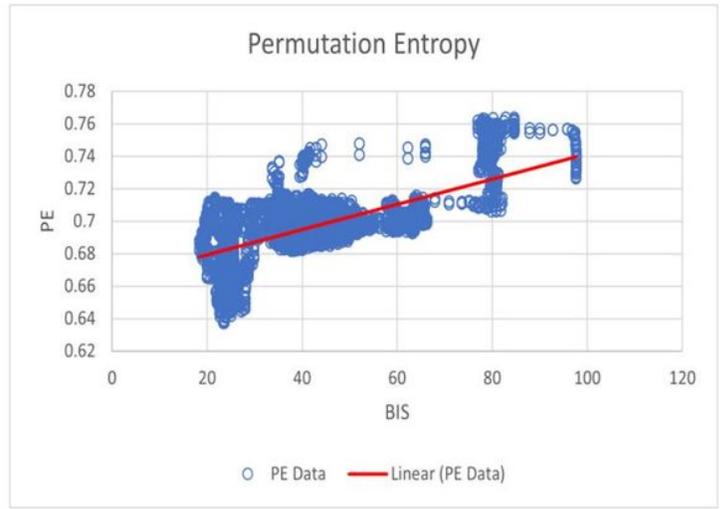


Figure 2

The R2 value of SE and PE from Ch1+Ch2 EEG and Ch2 EEG (the reference is the BIS index)



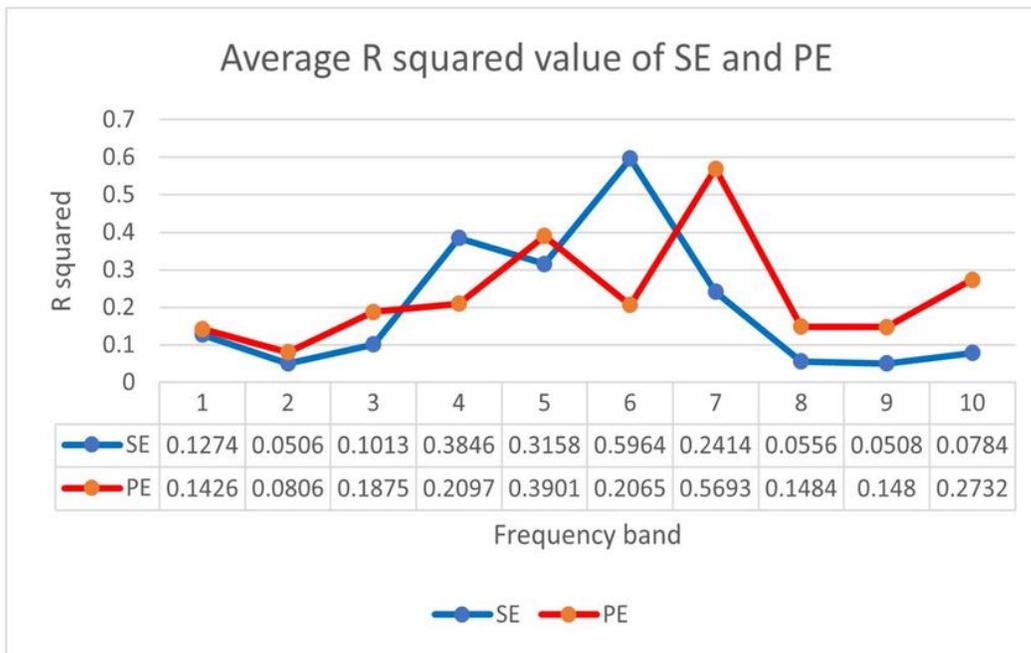
(a)



(b)

Figure 3

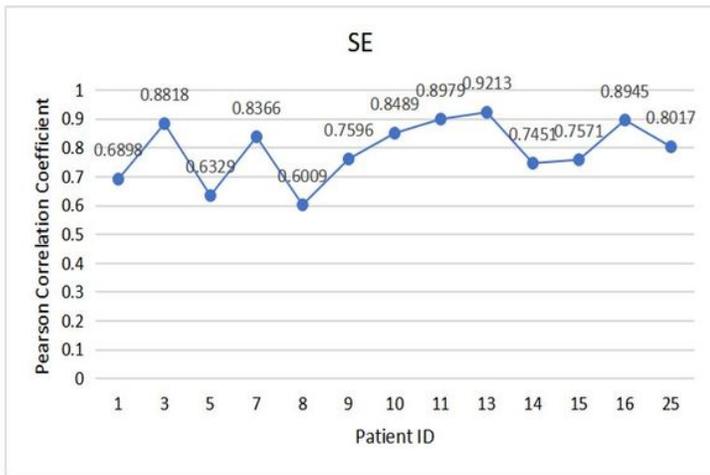
The linear relationship between parameters with BIS value, (a) SE (b) PE. The best-fit line is red. fitted linear relation indicates that the two methods are correlated (SE and PE values from patient ID 10) The average R2 value of SE and PE in each frequency band from 13 patients (randomly chosen) of EEG signals are shown in Fig. 4.



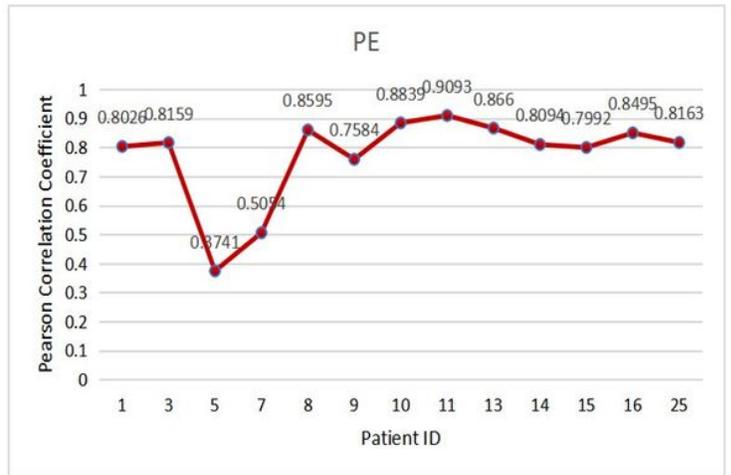
- 1 *Delta (δ)*
- 2 *Theta (ϑ)*
- 3 *Alpha (α)*
- 4 *Beta (β)*
- 5 *Gamma (γ)*
- 6 *beta gamma ($\beta\gamma$)*
- 7 *beta 1 (β_1)*
- 8 *beta 2 (β_2)*
- 9 *beta 3 (β_3)*
- 10 *beta 4 (β_4)*

Figure 4

Comparison of SE and PE from different frequency bands (the reference is the BIS index)



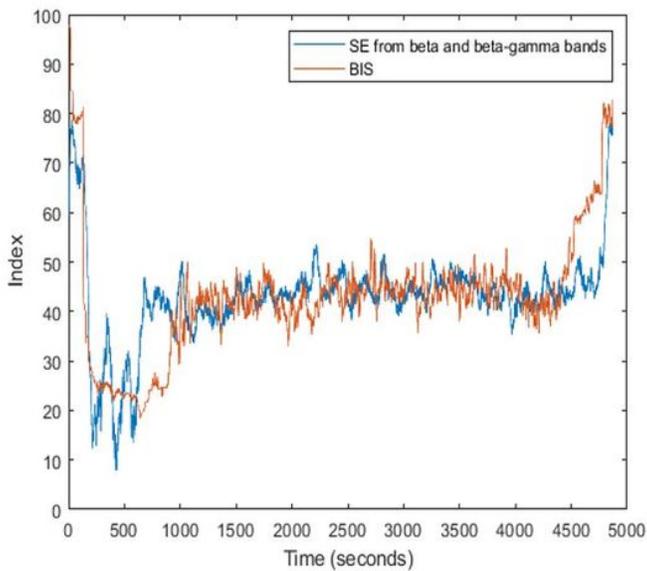
(a)



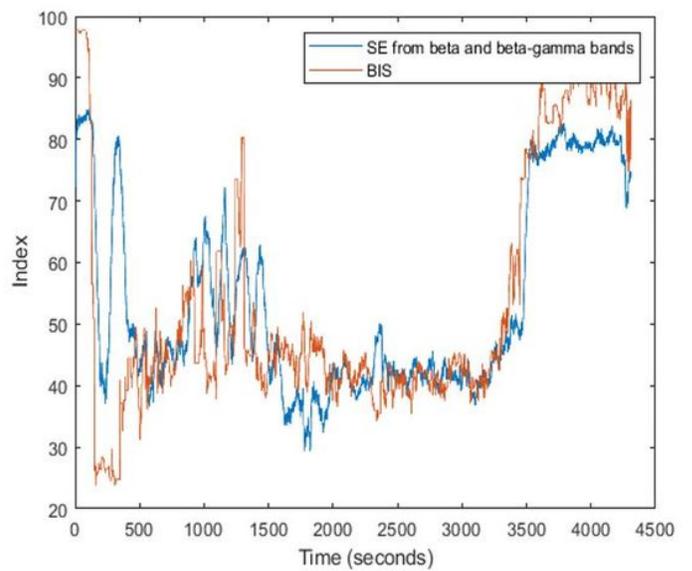
(b)

Figure 5

r values: (a) SE calculated from β and $\beta\gamma$ frequency bands vs. BIS Index (b) PE calculated from β and $\beta\gamma$ frequency bands vs. BIS Index



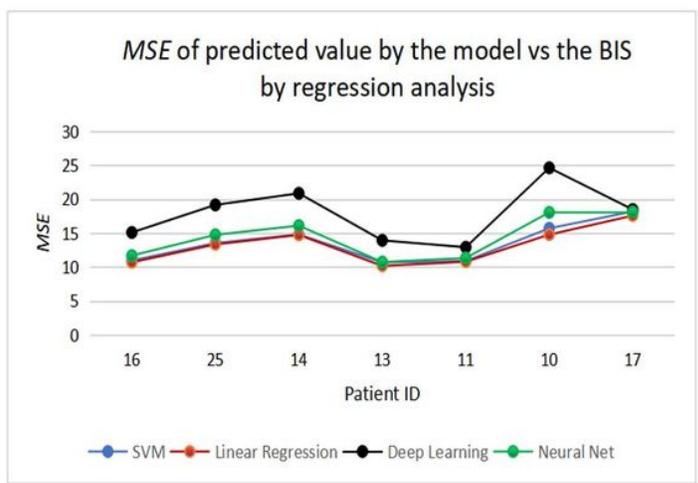
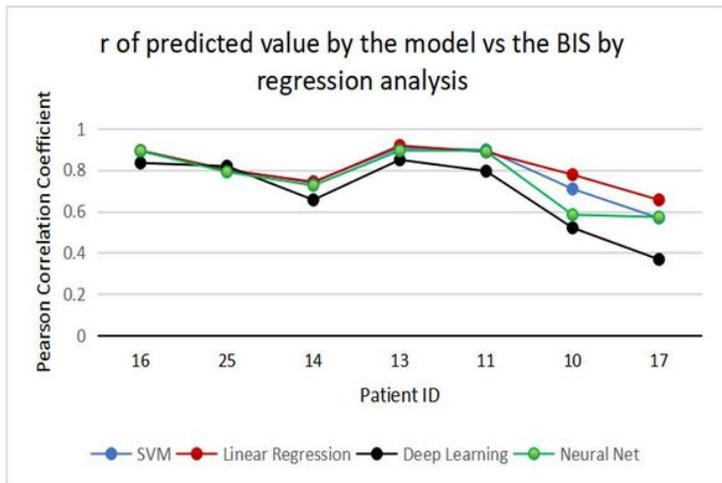
(a)



(b)

Figure 6

Index from the linear regression equation of SE calculated from β and $\beta\gamma$ frequency bands vs. BIS Index (a). Patient ID 9; (b). Patient ID 25



(a)

(b)

Figure 7

(a) r of predicted value by the model vs the BIS by regression analysis (b) RMSE of predicted value by the model vs the BIS by regression analysis

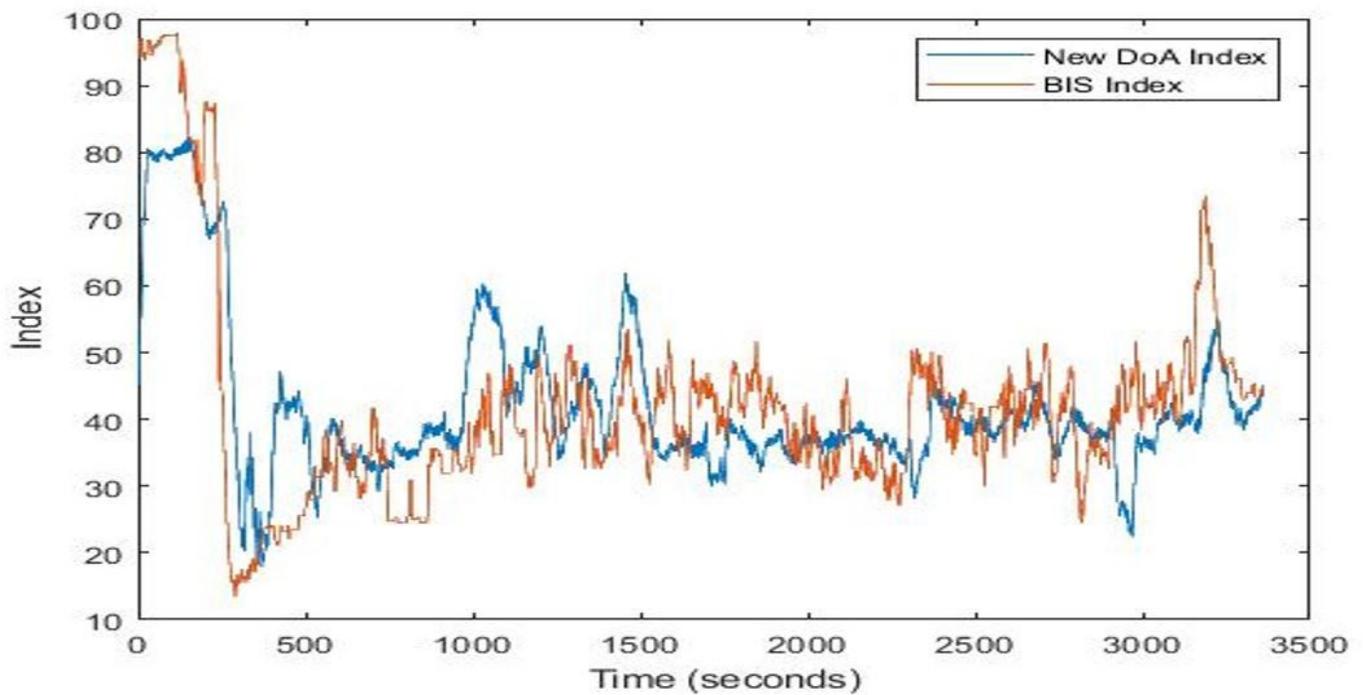


Figure 8

The new DoA index (patient ID 16, $r = 0.893$) and the BIS index

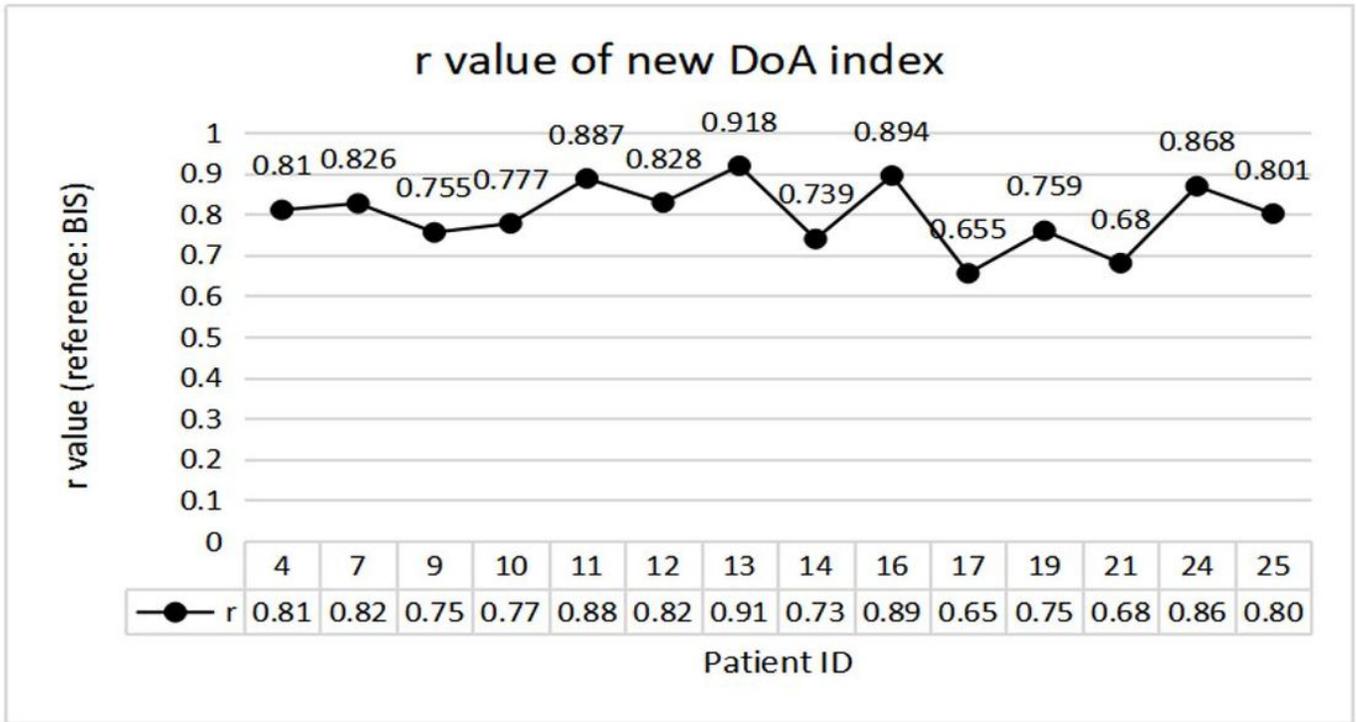
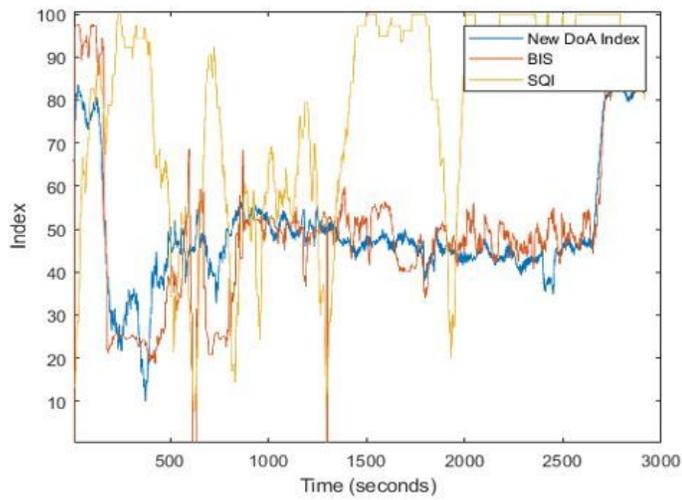
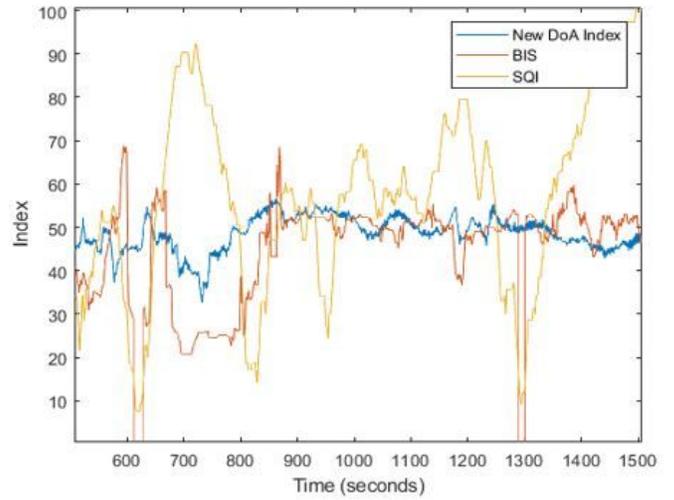


Figure 9

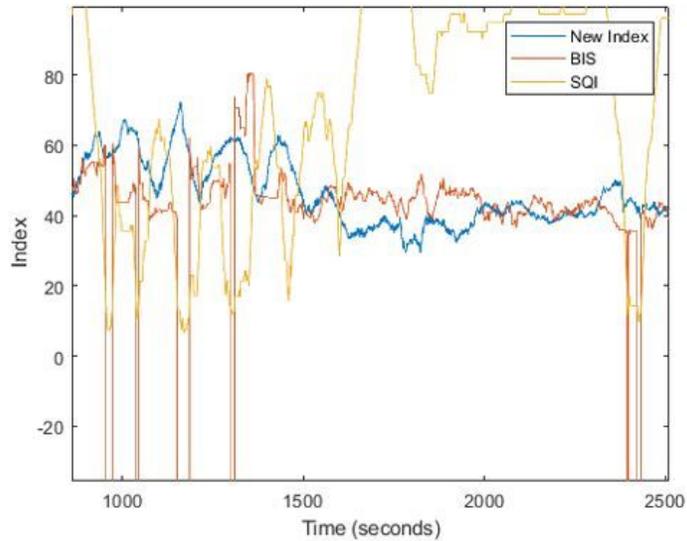
The performances of the new DoA index for randomly selected fourteen patients (r values)



(a)



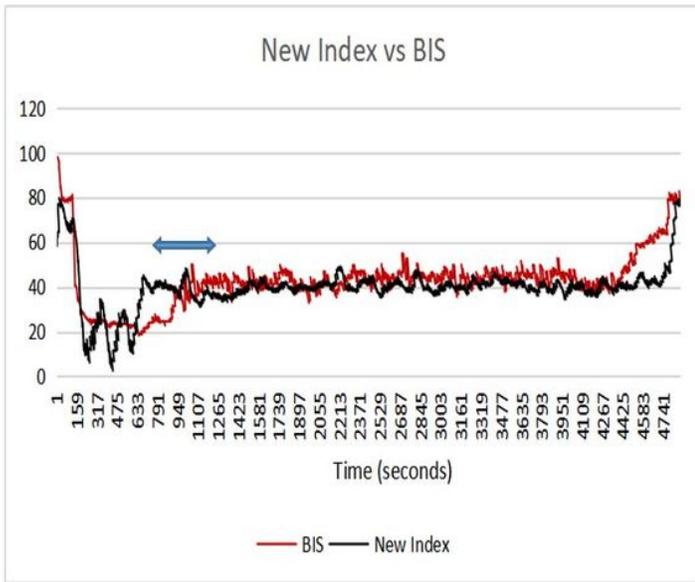
(b)



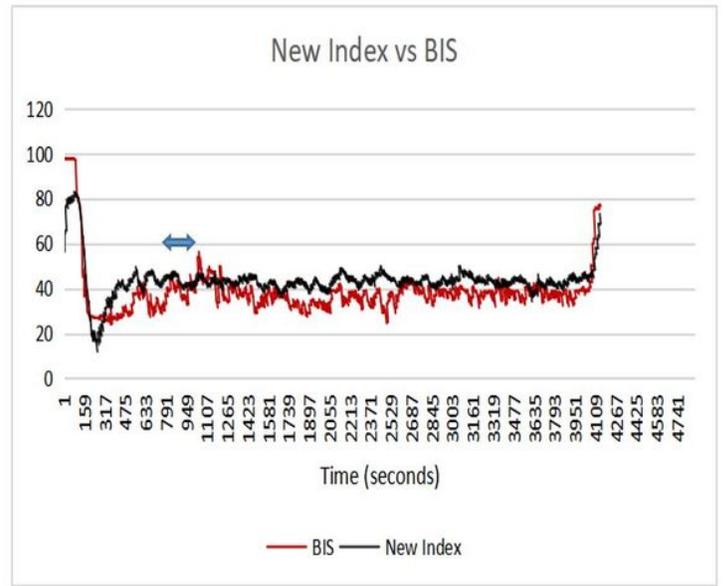
(c)

Figure 10

Comparison of New Index and BIS index with SQI; (a). patient ID: 18, range: 0 - 3000 seconds; (b). patient ID: 18, range: 500 - 1500 seconds; (c). patient ID: 25, range: 800 - 2300 seconds



(a)



(b)

Figure 11

The comparison of the new index and the BIS index; (a) patient ID 9, (b) patient ID 12. The blue markers show the earlier reaction by the new index