Depth of anaesthesia assessment based on adult electroencephalograph Beta frequency band

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ABSTRACT This paper presents a new method to apply timing characteristics of electroencephalograph (EEG) Beta frequency bands to assess the depth of anaesthesia (DoA). Firstly, the measured EEG signals are denoised and decomposed into 20 different frequency bands. The Mobility (M), permutation entropy (PE) and Lempel-Ziv complexity (LCZ) of each frequency band are calculated. The M, PE and LCZ values of Beta frequency bands (21.5-30Hz) are selected to derive a new index. The new index is evaluated and compared with measured Bispectral (BIS). The results show that there is a very close correlation between the proposed index and the BIS during different anaesthetic states. The new index also shows a 25-264 seconds earlier time response than BIS during the transient period of anaesthetic states. In addition, the proposed index is able to continuously assess the DoA when the quality of signal is poor and the BIS does not have any valid outputs.

Keywords Depth of anaesthesia • Mobility • permutation entropy • Lempel-Ziv complexity

1. Introduction

Evidence shows that the depth of anaesthesia monitoring using electroencephalograph (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 [1, 2]. For an accurate and reliable depth of anaesthesia (DoA) assessment, intensive research has been conducted, and various algorithms were developed. The latest methods includes Entropy [3], Detrended moving-average (DMA) [4], Isomap-based estimation [5], Empirical-mode decomposition (EMD) [2], and Bayesian [6]. Olofsen et al. developed a composite permutation entropy index (CPEI) which tracked the anaesthetic-related EEG changes and showed a promising measurement of g-amino-butyric acid (GABA)-ergic anaesthetic drug effect [7]. Other studies also consistently showed that permutation entropy could be used to efficiently discriminate different levels of consciousness during anesthesia [8, 9]. Rain et al. [10] presented that approximate entropy, Lempel-Ziv complexity (LZC), and Higuchi fractal dimension were highly sensitive to the presence of high-frequency components in electroencephalograph signals.

Most DoA algorithms are designed based on the characteristics of different frequency bands of EEG. The Bispectral (BIS) index is a statistically based, empirically derived complex parameter. The Bispectral analysis includes the calculation of bicoherence, bispectrum and real triple product as its sub parameters. For the Bispectral monitor, the β-ratio is calculated based on the power spectrums of the frequency bands 30-47Hz and 11-20 Hz [11]. Another important parameter, Synch-fast-slow from Bispectral analysis, is based on the frequency bands of 0.5-47Hz and 40-47Hz. The frequency domain analysis of Narcotrend monitor is related to the α, β, δ and θ frequency bands. The frequency interval for the Narcotrend monitor is calculated based on the signals of 0.5Hz to 47Hz frequency band. As for the AEP-monitor/2 monitor, the signals of 25-65Hz frequency band are used to autoregressive the model with exogenous input (ARX). Its undisclosed algorithm is applied to frequency band (3-47Hz). Burst suppression is also analyzed using the signals of 1-35Hz frequency band. The total frequency band from 0.5 to 50Hz is used for the PSA 4000 monitor. The frequency domain analysis method of Cerebral state monitors includes α-ratio, β-ratio and (β-α)-ratio which are more relevant to low frequency bands than high frequency bands. For the Entropy-Module, the signals of frequency bands 0.8 to 32 Hz and 0.8 to 47Hz are filtered out using the FFT method [11].

In this study, the Mobility, permutation entropy and Lempel-Ziv complexity of different frequency bands in the EEG signal are calculated. A regression technology-based parameter evaluation method is used to evaluate the correlation between these parameters with the anaesthetic states. Then, these parameters are used to develop a new DoA index. The performance of the new index is evaluated in comparison with the popular BIS index.

The rest of the paper is organized as follows. We first describe the Mobility, permutation entropy and Lempel-Ziv complexity methods in Section 2. Their applications in DoA assessment is introduced in Section 3. The results are presented and evaluated in Section 4. The limitations of this study are presented in discussion section. Finally, the concluding remarks are drawn in Section 6.

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2. Method

The Mobility is defined as below:

$$M=\sqrt{\frac{\sigma_1}{\sigma_0}} \quad (1)$$

where σ_0 is the variance and σ_1 is the variance of the first derivative [12]. In this research, we select 56s as the window size and 55s as the overlap for the Mobility calculation.

The PE is calculated using the following algorithm [13]. Firstly, define the EEG signal [*x*(*i*),*i*=1,2,...] into a *m*-dimension space *X*[*x(i),x(i+L),...,x(i+(m-1)L)*], *m* is the number of dimension，*L* is the time delay. Then sort the EEG series in the *m* dimension space in increasing sequence:

$$[x(i+(j_1\text{-}1)L)\le x(i+(j_2\text{-}1)L)\le ...\le x(i+(j_m\text{-}1)L)] \quad (2)$$

j_1 , $j_2, \dots,$ and j_m show the new order of the series. For a *m*-dimension space, there are total *m!* orders. Each *X*[*x(i),x(i+L),...,x(i+(m-1)L)*] reflects one of these ‘*m!*’orders. Assume the probabilities of each order are P_1, P_2,..., P_K respectively. According to the Shannon Entropy, the permutation entropy *PE(m)* is calculated as follows:

$$PE(m)= -\sum_{j=1}^{K} P_j \, lnP_j \quad (3)$$

The smaller the *PE(m) is,* the more regular the time series are.

The LZC is calculated in the following steps. Firstly, the original signal (numerical sequence) need be transformed into a 1/0 symbolic sequence *S* by comparing the signal to a threshold value. In this research, the median value of the signal is used as the threshold value. Whenever the signal is larger than the median value, one maps the signal to 1, otherwise, to 0 [14].

After converting the whole signal into its symbolic 1/0 sequence, distinct “words” can be obtained by parsing this sequence and they can be encoded. The sequence $S = S1S2...Sn$ is rewritten as a concatenation $W = W1-W2...Wm$ of *m* “words” chosen such that $W1= S1= 0$ or 1 and *Wj* (*j*=2, 3…*m*) is the shortest “word” that has not appeared previously. Therefore, the number of the encoded distinct “words” (*m*) is decided by timing characteristics of the symbolic 1/0 sequence. The value of Lempel-Ziv complexity is relevant to the number of the encoded distinct “words” (*m*) and the length of the signal *n*. It is defined mathematically as

$$LZC \;=\frac{m(log_2^m+1)}{n} \quad (4)$$

Based on methods presented in [14], the complexity features were computed using five-second small windows with 50% overlap. The LZC value for a 56s window size signal is the mean of LZCs of 21 small window size signal.

3. Applications in DoA assessment

3.1. Parameter selection

The EEG data were collected at the Toowoomba St Vincent’s Hospital from 28 adult patients (age 22-83 yr, weight 60-130kg, gender 12F/16M). This work only focuses on adults does not includes paediatrics. The raw EEG signals were sampled at the frequency of 128Hz for each channel (two channels) and each EEG sample was a 16-bit signed integer in units of 0.05 μV. In addition, the BIS values, EMG and signal quantity index (SQI) were also obtained at the same time. Because the raw EEG data were presented as binary files and they were unfiltered signals, they were converted into decimal numbers firstly and then denoised using nonlocal mean (NLM) methods [15].

To evaluate the correlation between parameters and anaesthetic states, the parameters for each patient’s two channel EEG signals are calculated for different frequency bands separately. Then these parameters from different patients are put together. Finally, the regression result for each frequency band is obtained. The coefficient of determination (R squared) is used to calculate the correlation between the parameters and the anaesthetic states (referred to the BIS values).

Generally, the anaesthesia states include awake, light anaesthetic, moderate anaesthetic and deep anaesthetic states. The awake states are corresponding to the BIS range from 80 to 100, the light anaesthetic states are corresponding to the BIS range from 60 to 80, the moderate anaesthetic states are corresponding to the BIS range from 40 to 60, and the deep anaesthetic states are corresponding to the BIS range from 10 to 40 [6]. To accurately measure the correlation between parameters and different anaesthetic states for developing reliable DoA algorithms, the sample selected for parameters evaluation should be representative and diverse. The data selected for the sample should balance both the anaesthetic states and awake states. As a result, the data of Patient 2, Patient 3, Patient 4, Patient 5 and Patient 7 are selected to make up the sample (16693 seconds EEG data totally). The lengths of their anaesthetic states are similar to each other.

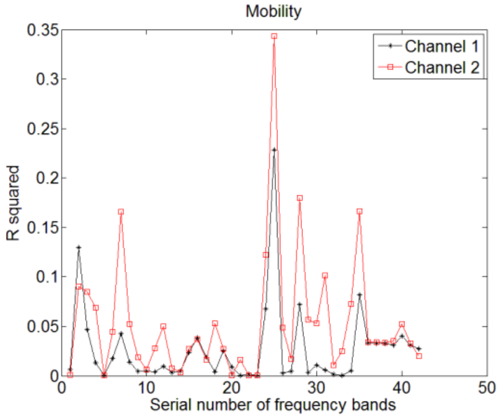
The EEG signals are divided into five basic frequency bands (α, β, γ, δ and θ) [16] and 15 small frequency bands using fast Fourier transform method. These bands are listed in Table 1:

Table 1 15 small frequency bands

Basic frequency band	*Small frequency band*	*Frequency (Hz)*
α (Alfa)	*αa*	7-10
	αb	10-13
β (Beta)	*β1*	13-17
	β2	17-21.5
	β3	21.5-26
	β4	26-30
	βa	13-21.5
	βb	21.5-30
	βγ	21.5-38.5
γ (Gama)	*γ1*	30-38.5
	γ2	38.6-47
	γ3	47-55.5
	γ4	55.5-64
	*γ*a	30-47
	*γ*b	47-64
δ (Delta)		0.5 - 3.5
θ (Theta)		3.5 - 7

The original signal bands are also added as a reference. As a result, we obtained 5+15+1=21 sets of frequency bands from each episode of EEG signal. The Mobility, Lempel-Ziv complexity and PE values are calculated based on both amplitude and power of each basic frequency band. The power sequence of frequency band was calculated from the square of its amplitude. The regression results of channel 1 and channel 2 are shown in Fig. 1.

It can be seen from Fig 1, the results from Channel 2 are much better than those of Channel 1. For example, the highest R squared calculated from the power of *β* (13-30 Hz) is 0.3436 for Channel 2, and the highest R squared for Channel 1 is only 0.2281. The difference is more apparent for permutation entropy parameters as the highest R squared for Channel 2 (0.6050) is 0.2376 higher than that for Channel 1 (0.3674). For the parameters of Lempel-Ziv complexity, the highest R squared calculated from the power of *β* (13-30 Hz) is 0.3702 for Channel 2 which is also higher than that for Channel 1 (0.3008). To sum up, based on the timing characteristics analysis methods and samples in this research, the parameters calculated from Channel 2 are much more helpful for DoA assessment. Therefore, we only use the parameters calculated from Channel 2 to design the new DoA index.



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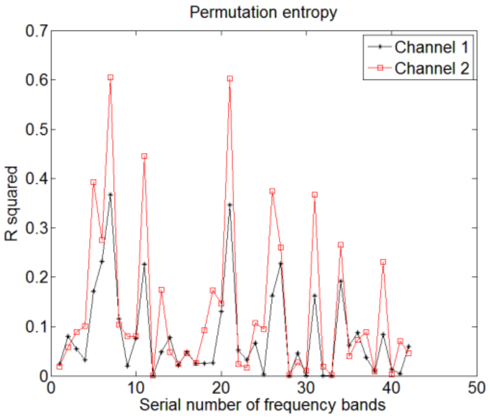

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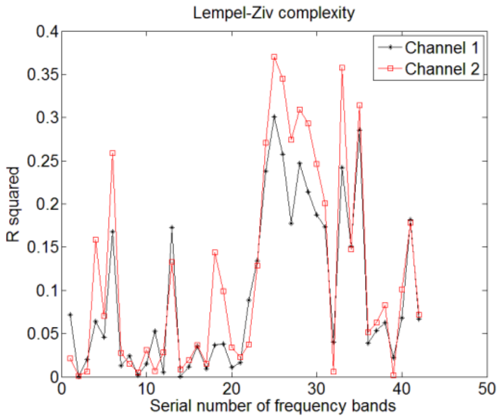


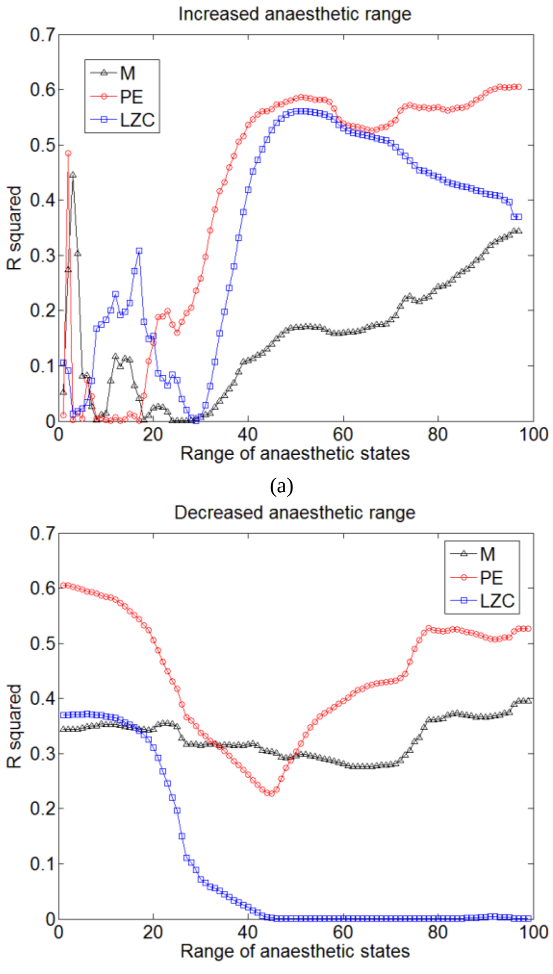
(c)

Fig. 1. Comparisons of different frequency bands from Channel 1 and Channel 2, (a) Mobility, (b) Permutation entropy and (c) Lempel-Ziv complexity. The No.1 to No.21 of frequency bands represent the amplitude of *δ* (0.5- 3.5Hz), *θ* (3.5-7Hz), *α* (7-13Hz), *β* (13-30 Hz), *γ* (30-64 Hz), original signal (0.01-64Hz), *βb* (21.5-30Hz), *γ1* (30-38.5Hz), *γ2* (38.6-47Hz), *γ3* (47-55.5Hz), *γ4* (55.5-64Hz), *γa* (30-47Hz), *γb* (47-64Hz), *βa* (13-21.5Hz), *αa*(7-10Hz), *αb*(10-13Hz), *β1*(13-17Hz), *β2*(17-21.5Hz), *β3*(21.5-26Hz), *β4*(26-30Hz), and *βγ*(21.5-38.5Hz) respectively. The No.22 to No.42 of frequency bands represent the power of the frequency bands mentioned above.

As shown in Fig. 1, the parameters with the highest R squared are the Mobility values which are calculated from the power of *β* (13-30 Hz) frequency band, the PE values which are calculated from the amplitude of *βb* (21.5-30Hz) frequency band and the Lempel-Ziv complexity values which are calculated from the power of *β* (13-30 Hz) frequency band. They are selected to form the best parameters pool for new DoA design.

3.2 New DoA design

In this research, we also analysed the relationship between the performances and the best parameters in different anaesthetic states. The original three best parameters are separated into different groups according to different anaesthetic ranges (referred to BIS value, for example, BIS value 70-99), and then the R squareds for three parameters are calculated for different anaesthetic ranges respectively. The results are shown in Fig. 2.



(a)

(b)

Fig. 2. Performance of the three best parameters for different anaesthetic ranges, (a) Increased anaesthetic range, (b) Decreased anaesthetic range. Increased anaesthetic range: the anaesthetic range from BIS range (2-3), BIS range (2-4) to BIS range (2-99); Decreased anaesthetic range: from BIS range (1-99), BIS range (2-99) to BIS range (98-99).

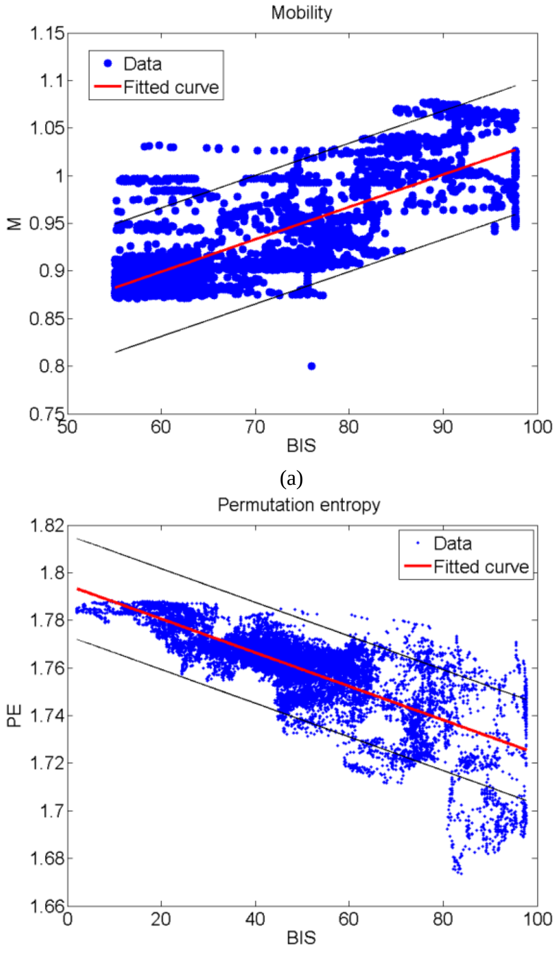
Table 2 The highest R squared based on different anaesthetic range

The highest R squared (Frequency band)	*BIS (1-55)*	*BIS (55-100)*	*BIS (1-100)*
M	0.4758 (power of α)	0.5957 (amplitude of β)	0.3436 (power of β)
PE	0.6548 (power of βa)	0.6878 (amplitude of β)	0.6050 (amplitude of βb)
LZC	0.5595 (power of β)	0.4425 (amplitude of $\gamma 4$)	0.3702 (power of β)

It can be seen from Fig. 2. The R squared of three parameters reaches the peak for the BIS range (2-53) and the R squared of three parameters is the smallest for the BIS range (45-99). In this research, the whole parameters pool is divided into two parts: the parameters refer to the BIS range (1-55) and the parameters refer to the BIS range (55-100). The linear regression analysis is done between the parameters and two different BIS ranges. The best R squared is shown in Table 2.

As shown in the Table 2, the performance of PE parameters is always better (R squared is higher than 60), however, only the M parameters calculated from the amplitude of β Frequency band show a high R squared (0.5957) for the BIS range (55-100). As for LZC parameters, the best R squared calculated from the power of β Frequency band is 0.5595 for the BIS range (1-55). The relationship between these three parameters with the BIS value is shown in Fig. 3.

The scatter plot graphs for the parameters and BIS are shown in Fig. 3 for the samples (five patients, 16973 data points). The black line shows 95% confidence boundaries around the linear pink bold line. Few data points go beyond the 95% confidence boundaries. As for the Mobility, linear equation is fitted to all data points during the BIS range (55-100) with the relation as BIS = -93.3097 + 175.3189 * M. As for the permutation entropy, linear equation is fitted to all data points with the relation as BIS = 1553.2 - 854.9 * PE. As for the Lempel-Ziv complexity, linear equation is fitted to all data points BIS range (1-55) with the relation as BIS = 289.0848 - 635.2348 * LZC.



(a)

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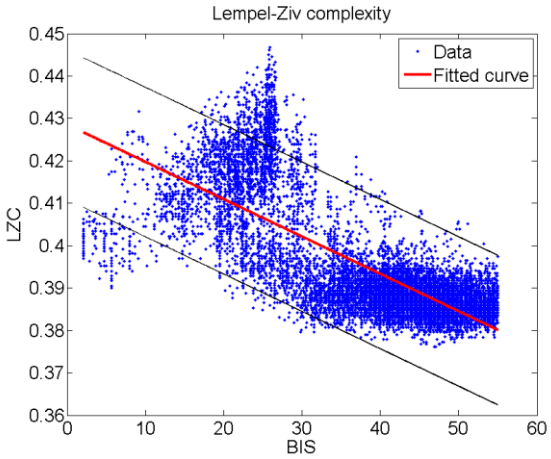


(c)

Fig. 3. The linear relationship between parameters with BIS value, (a) Mobility, (b) Permutation entropy and (c) Lempel-Ziv complexity.The best-fit line is bold and black lines correspond to the 95% confidence boundaries. This fitted linear relation indicates that the two methods are extremely correlated.

It can be seen from Fig. 3(b), the linear relationship between PE parameters with BIS values is weak during the BIS range (80-100), therefore, when we design the new DoA index, the Mobility parameters are used to adjust the DoA assessment result of PE parameters during the awake and light anaesthetic states. In addition, the Lempel-Ziv complexity parameters are used to adjust the DoA assessment result of PE parameters during the deep anaesthetic states. The new Tindex is designed as follows:

$$\text{Tindex}=\frac{1553.2-854.9*PE+t_1*(-93.31+175.32*M)+t_2*(289.08-635.23*LZC)}{1+t_1+t_2} \quad (5)$$

According to BIS = 1553.2 - 854.9 * PE, when PE is equal to 1.7596, BIS is equal to 50. The 1.7596 is used as the PE threshold. According to BIS = -93.3097 + 175.3189 * M, when M is equal to 0.8459, BIS is equal to 55. When M is equal to 1.1026, BIS is equal to 100. If PE <= 1.7596 and 0.8459 < M < 1.1026, t_1=1, otherwise, t_1=0. According to BIS = 289.0848 - 635.2348 * LZC, When LZC is equal to 0.4535, BIS is equal to 1. When LZC is equal to 0.3685, BIS is equal to 55. If PE > 1.7596 and 0.3685 < LZC < 0.4535, t_2=1, otherwise, t_2=0.

The threshold is not 1.7561 (Corresponding BIS=55) because the DoA assessment for BIS=55 range will be inaccurate if the threshold is set as 1.7561. According to the tests on the sample, the Pearson correlation coefficients [17] between the Tindex and the BIS index changes as the corresponding BIS values of the threshold increase. The relationship is shown in Fig. 4. When the 1.7596 of PE value is used as the threshold, the Tindex show the highest corelation with BIS index.

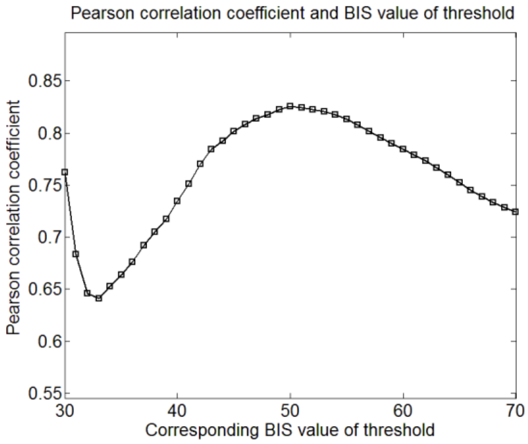


Fig. 4. The Pearson correlation coefficient and the BIS value of threshold

4. Results and evaluation

According to DoA monitors industry reports, 90% of the famous brands have BIS modules and more than 3400 papers published are related to the BIS. The BIS monitors were and are still the most popular monitor in the market. Although the BIS monitor has received some critical press, it is still an important reference or benchmark for a newly developed DoA index. Therefore, the new Tindex is evaluated by comparing with the recorded BIS. The Tindex and BIS index for the samples (Patient 2-5, 7) are showed in Fig. 5.

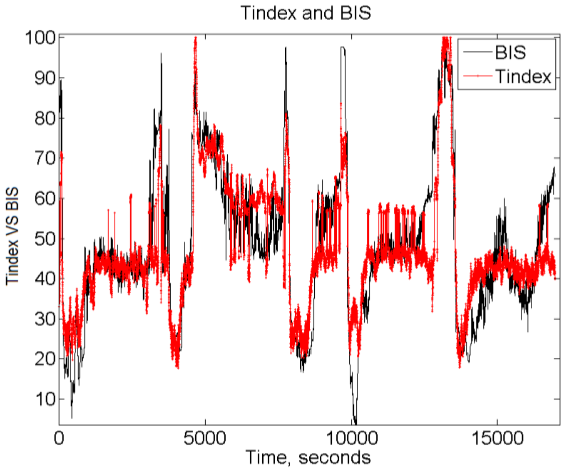


Fig. 5. Tindex and BIS index.

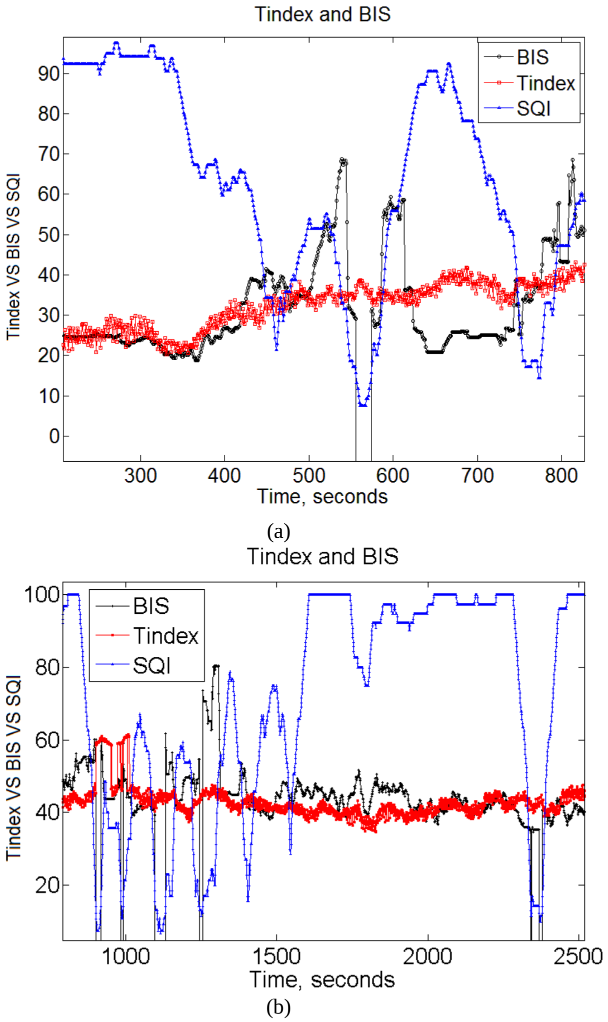
The high Pearson correlation coefficient ($corr_{\text{Patient } 2-5,7}$ = 0.8227) show that there is a very close correlation between the proposed index and the BIS during different anaesthetic states. In addition to the sample, the performances of the new index for another random selected 20 patients (Patient 9 to Patient 28) are evaluated. The Pearson correlation coefficients for 20 cases are shown in Table 3.

The average Pearson correlation coefficient for 19 patients (No.9-14, No 16-28) is 0.8049. However, the performances of the new Tindex are not good enough for Patient 15. According to the SQI index of Patient 15, the signal quality of Patient 15 is poor and the BIS did not have any valid outputs at the beginning of awake states. The unreliable BIS may cause the low Pearson correlation coefficient for Patient 15.

4.1. *Patient's state in the case of poor signal quality*

We also evaluated the performance of the new Tindex in poor signal quality cases (according to Signal Quality Index), where the SQI is lower than 15, the BIS index could not output any valid values.

In the results, the Tindex shows the DoA values in most cases where the BIS index could not. In Fig. 6(a), for patient 1, the BIS index is always -3276.8 from 556 to 574 seconds, but the Tindex outputs valid DoA value during this period. In addition, while the BIS index shows significant upward trends from 532 to 538 seconds and from 582 to 588 seconds, the Tindex is flat in general during this period. The same situation also happened during 1156 to 1311 seconds of patient 8 in Fig. 6(b). According to the anaesthetists' records, there was no recovery of consciousness (RoC) during this period, and there are low SQI values about one minute before these significant upward trends of the BIS, the BIS index might be influenced by noise such as EMG. Therefore, the new Tindex is more reliable in this noise cases.



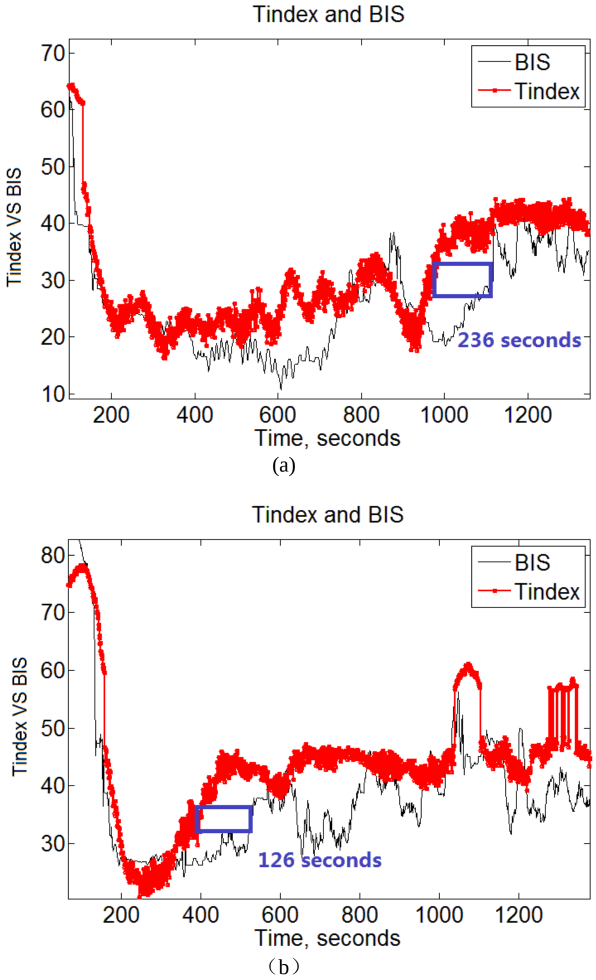
(a)

(b)

Fig. 6. Comparison of the Tindex and BIS index, (a) patient 1, (b) patient 8.

4.2. *Time delay from deep anaesthesia to moderate anaesthesia*

To evaluate the performance of the new Tindex, the time delay (deep anaesthesia to moderate anaesthesia) of both Tindex and BIS index are measured. The new index shows a very high correlation with BIS during the states of awake, light anaesthesia, moderate anaesthesia and deep anaesthesia. However, the new Tindex shows an earlier reaction than the BIS index when the patient moved from deep anaesthesia to moderate anaesthesia. Take Patients 6 and 16 as examples, the comparison of the Tindex and BIS index is shown in Fig. 7.



(a)

（b）

Fig. 7. Comparison of the Tindex and BIS index, (a) patient 6, (b) patient 16. The blue square frames show the earlier reaction of Tindex compared with the BIS.

This kind of earlier reaction appears in all the cases of the 12 patients. For the index value change (from 20 to 50), we assume that an index value of 35 corresponds to the inflection point where the patient's anaesthetic states changed from deep anaesthesia to moderate anaesthesia. In some cases, there is no significant upward trend near 35, so we compare the significant upward trends between BIS and Tindex. The time difference and Pearson correlation coefficients for 20 patients are indicated in Table 3.

The time difference from deep anaesthesia to moderate anaesthesia is about 25 to 264 seconds.

Table 3 Pearson correlation and time response comparison between Tindex and BIS

Patients	*9*	*10*	*11*	*12*	*13*
Time difference (s)	128	122	33	264	223
Pearson correlation	0.80	0.83	0.79	0.77	0.87

Patients	*14*	*15*	*16*	*17*	*18*
Time difference (s)	103	168	126	169	41
Pearson correlation	0.89	0.53	0.67	0.89	0.80

Patients	*19*	*20*	*21*	*22*	*23*
Time difference (s)	74	125	102	143	175
Pearson correlation	0.71	0.84	0.70	0.79	0.73

Patients	*24*	*25*	*26*	*27*	*28*
Time difference (s)	84	91	161	26	25
Pearson correlation	0.87	0.89	0.80	0.90	0.77

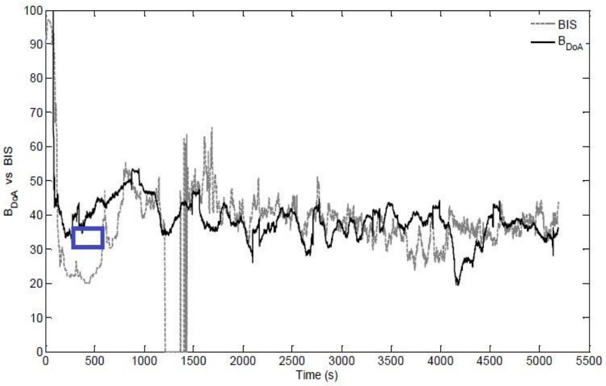


Fig. 8. Comparison of the B_{DoA} and BIS index [6].The blue square frame shows the later reaction of BIS index compared with the B_{DoA}.

It is hard to detect when the patients moved from deep anaesthesia to moderate anaesthesia based on clinical notes. However, the time delay for BIS index is indeed existed which can be proved by the results from [6, 18]. It can be seen from Fig. 8 which is from Nguyen-Ky et al.'s paper [6], the BIS index also shows a later reaction when patients' anaesthetic states change from deep anaesthesia to moderate anaesthesia compared with B_{DoA} (DoA assessmnent function based on Maximum a Posterior). These types of later reactions for BIS index also appear in Fig. 13 and Fig.15 of Nguyen-Ky et al.'s paper.

5. Discussion

Comparing with BIS, the new Tindex does not perform well at the beginning in some cases. One important reason is that when designing the new indexes, the regression technique is used to find the best coefficients which make the new index highly correlate to the BIS index. It is observed that the BIS values at the beginning of awake states are not reliable as it is always at 97.7 without any change. Another reason is that all of the data are collected from the anaesthetic patients, thus the period of anaesthetic state is much longer than the awake state. As a result, the regression results from the sample can only obtain the higher R squared in anaesthetic state. Although the optimization of samples has already been tried in this study, more work can be done in the future research. The larger sample size and higher quality samples are helpful to increase the robustness of the new indexes.

Although R squared and Pearson correlation coefficients are widely used for assess the correlation, their performances are not good enough to reflect the real correlation in some cases from our study, especially, in the period of dramatic anaesthetic states changes. In future research, separating different anaesthetic states for correlation evaluation or applying improved correlation evaluation method may lead to a more accurate correlation evaluation.

6. Conclusion

In this study, the Mobility, Lempel-Ziv complexity and permutation entropy methods are applied to obtain the parameters for DoA assessment. After the parameters are calculated from different frequency bands, the proposed new DoA index is designed based on: the M parameters which are calculated from the amplitude of β Frequency band, the LZC parameters which are calculated from the power of β Frequency band and the PE parameters which are calculated from the amplitude of βb frequency band. Then the new DoA index is evaluated using the measured EEG data and recorded BIS readings.

The results show that the average Pearson correlation coefficient for 19 patients is 0.8049. The results also show a 25-264 seconds earlier response than BIS during anesthetic states changes. Furthermore, compared with BIS, the proposed new index can assess the DoA while the EEG is corrupted with noise. For example, even when the SQI value is below 15 and the BIS failed to output any valid value, the new DoA index works well. This means the proposed index can estimate the patient's anaesthetic states in poor signal quality.

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