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Estimation the Depth of Anesthesia by the Use of Artificial Neural Network

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1. Introduction

Anesthesia is used in surgery to minimize pain, shock, and discomfort for surgical patients. There are several types of anesthesia which can be used depending on the needs of the surgery: general, local, regional, and conscious sedation (Jones, 1994). When anesthesia works as expected, the patient feels no pain during a procedure, and often does not remember the proceedings either. Anesthesia increases patient comfort, which can in turn decrease recovery times. With the knowledge that they are not inflicting pain, it also makes it easier for a medical staff to work. When anesthesia comes to mind, most people think of general anesthesia. General anesthesia is a complete loss of consciousness in the patient accomplished through a combination of injected and inhaled drugs (Rampil, 1998). This type of anesthesia is often used for highly invasive surgeries or cases when total relaxation of the patient is required. General anesthesia carries the most surgical risk because of the state of complete unconsciousness. As a result, the anesthesiologist is essential in providing optimal working conditions for surgeons, and in ensuring patient safety and comfort. To achieve these endpoints, anesthesiologists employ a variety of drugs to alter cognitive processing, regulate cardiorespiratory functions, and block muscle movement. One major aspect of the practice is to use these drugs in quantities that warrant unconsciousness and the absence of response to surgical stress, while avoiding pharmacological toxicity (e.g., cardiac morbidity).

1.1 Depth Of Anesthesia (DOA)

One of the objectives of modern anesthesia is to ensure adequate depth of anesthesia (DOA) to prevent awareness without inadvertently overloading the patients with potent drugs (Welling, 1997). For this reason, the specialist must be able to monitor DOA. Various methods have been described to measure the DOA from time to time. The traditional monitoring of the DOA are based on automatic responses of patient body such as respiration pattern, blood pressure, body temperature, tearing, sweating and heart rate (Viertiö-Oja et al., 2004; Miller, 2005). However, considering the following major clinical problems at anesthesia discussion, i.e., sudden conscious during the surgery at the rate of 2-3% (in all under surgery patients) and the rate more than 4% for the patients with brain tumor and the patients under the heart surgery (Jameson & Sloan, 2006), and applying overdose anesthetic agents for the patients relying on the hemodynamic parameters as a criterion for the anesthesia conditions, encouraged the researchers to make an essential effort to introduce more reliable methods (Haddad et al., 2007). In this base, during the present two decades, some novel methods based on

electroencephalogram (EEG) signal processing instead of the traditional methods based on hemodynamic parameters have been used by medical engineers to estimate DOA. Since the central neural system (CNS) is the main aim of the anesthetic agents, the EEG signals have been significantly considered by the anesthesia experts (Sebel et al., 1997). There is not an exact and comprehensive theory, but it is generally accepted that making any change on the synaptic function of the neural cells results in change at the brain functions (Kreuer et al., 1997). Although, the electrical potential resulted from neural cell activities can be observed and registered by EEG signals, but the necessary information about DOA should be extracted from EEG signals using the special techniques. These techniques help experts to have accurate information about DOA and assist doctors during surgical practical in the operation room.

1.2 A short survey on EEG-based methods for measuring the DOA

Estimating the patient's anesthesia depth during the surgery has an important role to prescribe suitable doses of anesthetic agents; because there is the possibility of sudden awareness if the prescribed dose is not sufficient and the overdose agents can also increase the patient's DOA and result in irretrievable consequences. Therefore, it is necessary to have accurate information about DOA to balance the injected dose of anesthetic agents. It is shown that anesthetic agents have direct effects on synaptic activity of brain neurons (Welling, 1997). So, it is preferred to use an EEG analysis as a DOA estimator. Automatic and computer based signal processing methods are taken to evaluate DOA because of the difficulties in visual explanation of EEG. Therefore, EEG can be used as an objective quantitative measure of consciousness which could be taken as a performance variable for closed-loop control of anesthesia (Glass et al., 1997). However, EEG is considered as a complex of multiple time series that its analysis is a difficult task. One of the earliest methods proposed in (Traast & Kalkman, 1995) is based on the Fourier transform that determines the power of EEG in different frequency bands. Zikov et al. proposed a wavelet based anesthetic value for central nervous system monitoring (WAVCNS) that quantifies the depth of consciousness between awake and isoelectric state (Zikov et al., 2006). Ferenets et al. analyzed the performance of several new measures based on the regularity of the EEG signal. These measures consist of spectral entropy, approximate entropy, fractal dimension and Lempel-Ziv complexity. Their results show highly sensitive behavior of the mentioned measures on frequency content of signal and the dose of anesthetic agent (Ferenets et al., 2007). It has been shown in (Hagihira et al., 2001) that there is phase coupling between different frequency bands of EEG. This is known as quadratic phase coupling (QPC) and the amount of QPC changes in different DOA levels. Bispectral analysis (also referred to as the bispectrum) is a technique that incorporates the phase relationship between waves by determining the phase coupling between different frequencies.

1.2 Artificial Neural Network

In fact, there is a potential of artificial neural networks (ANNs) for various units of medicine, such as anesthesia and care unit. Neural networks (NNs) propose a proper framework for identifying on-line systems and the dynamical behaviours for them. Application of artificial neural networks (ANNs) and selecting proper parameters as neural network (NN) inputs in estimating DOA is reviewed in (Robert et al., 2002). In this work, various strategies of choosing the NN model were presented and discussed. In (Haddad et al., 2007), a neural adaptive output feedback control framework which is used to control the infusion of the anesthetic drug is developed. Knorr et al. proposed a NN classifier used to identify airway obstructions (Knorr

et al., 2006). Bailey et al. used neuro-adaptive feedback control algorithms for clinical pharmacology, and showed excellent regulation of unconsciousness allowing for a safe and effective administration of the anesthetic agent propofol (Bailey et al., 2006).

1.3 EEG-based monitors

According to the various methods proposed for analysis of acquered EEG signal (e.g., such as above techniques), different EEG monitors have been introduced. An essential effort has been done in the development of EEG-based monitors which analyze the raw EEG data to extract a single measure of the DOA. Fig. 1 shows the flow diagram procedure of these monitors. The best identified case of these monitors is the bispectral-based or BIS monitor, which calculates a single composite EEG measure with high correlation with the DOA (Bailey et al., 2006). Based on other different proposed methods, other EEG monitors are suggested such as Narcotrend™ monitor (Monitor Technik, Bad Bramsted, Germany) (Kreuer et al., 1997) that is based on pattern recognition of the raw EEG and classification of EEG into different stages, SEDLine™ EEG monitor that is able to calculate the PSI™ index using the shift in power between the frontal and occipital areas (Droveret al., 2002), Datex-Ohmeda™ s/5 Entropy Module (Viertiö-Oja et al., 2004) that uses the entropy of EEG waves to predict DOA.
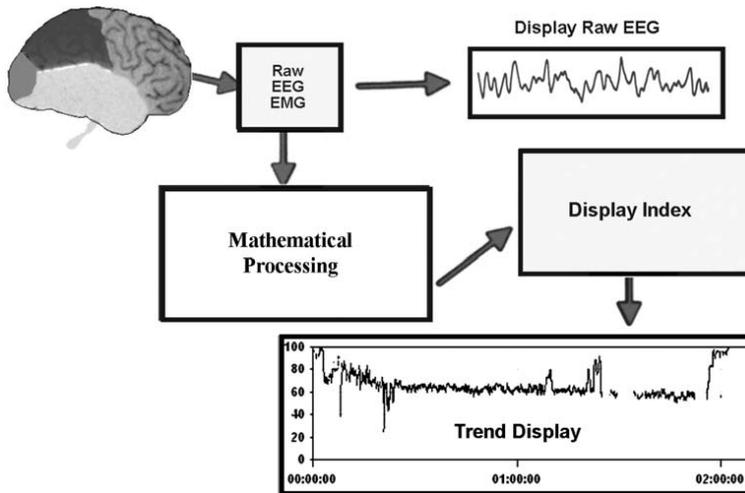

Fig. 1. Flow diagram Procedure of DOA monitors

1.3.1 BIS monitor

One of the most important equipments that is able to monitor the DOA based on analysis of EEG is BIS monitor (Fig. 2) confirmed by FDA (Bailey et al., 2006). The BIS™ index is a unit-less number between 100 (awake state) and 0 (isoelectric state) and as the manufacturer claim, the BIS index ranging between 40 and 60 is considered as proper safe range for the operative objectives. Bispectral index is a complex parameter, including a combination of time domain, frequency domain and higher order spectral (HOS) sub-parameters respectively named Burst Suppression Ratio (BSR as defined in subsection 3.4), Relative Beta Ratio ($RBR = \log(P_{30-47Hz} / P_{11-20Hz})$), where $P_{30-47Hz}$ and $P_{11-20Hz}$ are the power spectrum

of frequency bands of 30Hz to 47 Hz and 11Hz to 20 Hz respectively) and Sych Fast Slow ($SFS = \log(B_{0.5-47Hz} / B_{40-47Hz})$ where $B_{0.5-47Hz}$ an $B_{40-47Hz}$ are Bi-Spectrum value of the windowed signal in the ranges 0.5 to 47 Hz and 40 to 47 Hz respectively). This monitor integrates these three sub-parameters to produce BIS index, however, a detailed algorithm of this monitor is not published yet (Jameson & Sloan, 2006). Between 1990 and 2006, approximately 450 peer-reviewed publications have been examined the clinical effectiveness and accuracy of the BIS™ monitor (Jameson & Sloan, 2006). Thus, besides the clinical usages, the BIS index can be as a proper criterion for comparing the achieved results with the new methods of the estimating anesthesia.
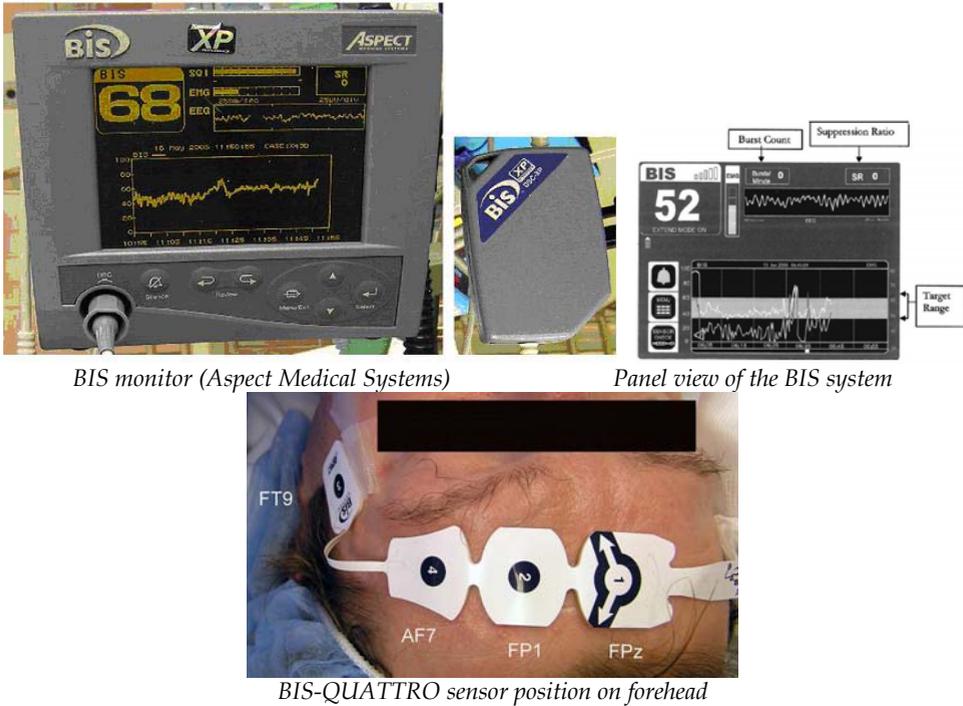

BIS monitor (Aspect Medical Systems)   *Panel view of the BIS system*

BIS-QUATTRO sensor position on forehead

Fig. 2. BIS monitor

1.4 This chapter

In the data classification trials which the feature dimensionality of the data are big compared to the number of data samples, the conventional classifiers are not applicable, therefore the use of nonlinear classifiers such as NN maybe helpful in discrimination of different classes. Medical data such as EEG, Microarray extracts of gene expression or 1H NMR spectra of the normal and cancerous tissue are the data with high dimension. Classification of these type data to different categories is limited to the number of acquirable samples. The limitations on acquisition of these types of data depend on different causes such as cost, limited number of candidates, or limited technical resources. The solution is the reduction of the dimensionality of features to an optimum value. There would be some

dimensionality reduction methods for removing dependent features before applying the classifiers on the data. In the case of important independent features, the dimensionality reduction is limited to the categorization based on the most significant features such as PCA. In this study several features are extracted from EEG signal to obtain the awareness level of patients. These features are used as inputs of NNs to estimate the DOA by reducing the dimensionality of features.

More especially, in this study, we gathered EEG of the patients who were undergoing surgery, and then we used wavelet transform to extract an index indicate level of consciousness (WAI index). For this reason, wavelet coefficients calculated from the EEG signal are compared to three well-defined states, i.e., completely awake state, moderate state, and isoelectric state, and finally WAI quantifies the depth of consciousness between these three states. In addition, besides WAI obtained using wavelet transform, we extract 15 sub-parameters from the recorded EEG data. By applying these sub-parameters into neural and neuro-fuzzy networks, we obtain a new index to estimate the DOA. Finally, a comparison is done between the obtained results from the suggested methods and the obtained results from BIS monitor.

Work presentation is organized as follows: In Section 2, data acquisition procedure is presented. In Section 3, we explain about WAI index. The extracted features for estimation of DOA such as BSR, spectral edge frequency (SEF), signal quality index (SQI), and alpha, beta and theta ratio are used as inputs of NNs and an appropriate index for DOA are obtained in Section 4. The results are presented in Section 5, and finally this chapter is concluded in Section 6.

2. Data acquisition procedure

This study is performed on 33 under surgery coroner vessel patients. To limit the conditions of this research, the patients with equal kind of surgery and anesthesia diets are chosen. Having no records of diseases related to CNS is a criterion in this study (21 males, 12 females, with average age of 54 and the average weight of 67 kg). Anesthesia diets for all patients were the same. The anesthesia stage was obtained by the use of intravenous agents, Tupental sodium (5mg/kg), Pancronim Burmid (0/1 mg/kg), Fontanel (5mg/kg), and Lidokain (1/5 mg/kg). The next stage is following the anesthesia process by inhalation and using Isofloran agents (MAC). After finishing the surgery, the patients were taken to ICU. To relax them in ICU, morphine (2mg/kg) was injected if needed. BIS monitor was used for obtaining and registering EEG besides the related DOA evaluation by BIS software (these signals are transferred to computer). Two other series of data also related to awareness, including EEG signals of 10 persons (15 minutes for each one) and isoelectric states, including 40 minutes recorded EEG signals from one patient recorded from a brain death are recorded. Fig. 3 shows sample recorded EEG signals.

The EEG signal was collected by using a BISQUATTRO Sensor™ that bands holding four electrodes, applied to the forehead of the patients. The used EEG lead was Fpz-At1, and the reference lead was placed at FP1. A Sensor was connected to a BIS-VISTA Monitor and all binary data packets containing raw EEG data wave signals and BIS index were recorded via an RS232 interface on a laptop using a bispectrum analyzer developed by Hagihira (Hagihira et al., 2001). A sensor was attached to patient forehead at ICU and data were collected continuously until he/she awaked.
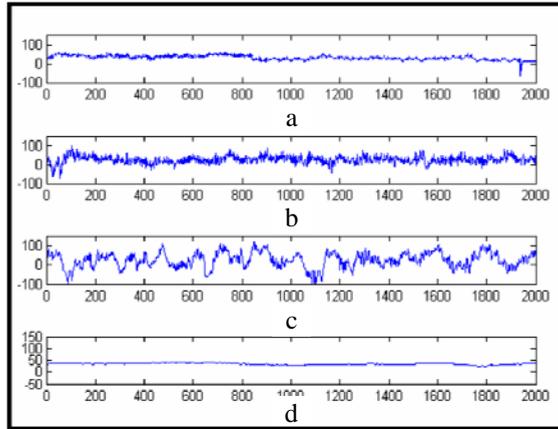
Fig. 3. Sample recorded EEG signals (15 sec. epochs). a) awake person, b) moderate anesthesia (recorded at ICU after surgery), c) deep anesthesia, d) isoelectric case

3. Anesthesia index based on wavelet (WAI)

The effect of anesthetic agents on EEG is studied by considering non aggressive state of this type of measurement. Besides increasing the blood pressure, most of the agents cause changes on EEG signal with low range and big frequency band-width with big range signal and quiet behaviour. Increasing the dose of anesthetic agents resulted to destruction of the recordable EEG activity at brain cortex and finally making isoelectric state (Smith et al., 1996). Therefore, it is supposed that EEG can be used for estimating the conscious level of the patient which shows the amount of this agents influence for saving time and complex interpretations of using EEG row signal to derive an index which shows the awareness state of the person. One of the processing instruments for obtaining information from EEG is as a result of giving an index to estimate the DOA through using wavelet transform. To show a method of computing the DOA, Zikov et al. supposed the patient as a system variant between the two states of *a* (completely awake) and *b* (totally isoelectric) and they identified an index by wavelet transform to show the state and features of this system (Zikov et al., 2006). To increase the precision, we suppose the patient as a system variant between three specified states of *a* (completely awake), *b* (moderate state or general anesthesia) and *c* (isoelectric state) as shown in Fig. 4. At complete awareness state, the patient has all his/her senses and he/she can give proper answers to all stimulations around him/her. Moderate state is a state when the patient has received anesthetic agents and is senseless to pain and other stimulations. In this state, he/she is in the best condition for going under surgery operation, meaning that he/she has received a suitable dose of anesthetic agent (neither too much nor too less). This state is determined by the anesthesia expert. Isoelectric state is related to brain death state or the least EEG signal activity state. According to Fig. 4, *f* is a function respect to x, where x is between *a* and *c*, and also the range of this function is between zero to one. In other words, x is a part of the signal with length *n*, that is mapping to *m* dimensional feature space extracted from x. *h* is scaled versions of *f* which indicates a number between zero and 100 representing the DOA.

$$x \in R^n \rightarrow f \in R^m \rightarrow h : z \in [a,c] \rightarrow i \in [0,100] \tag{1}$$

To define f , it is important to identify a, b, and c points. To analyze EEG, we choose these points as we defined them in above, we can obtain 3 series of reference data which are related to our observations of this system at a, b, and c states.
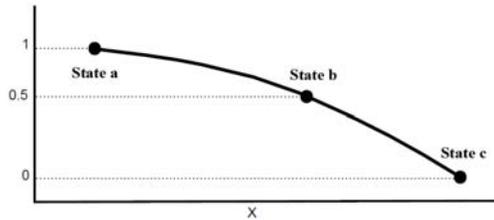

Fig. 4. f function for presenting the system features

$$\begin{cases} R_a = \{X_{a,k} \quad k = 1,2,3,...,M\} \\ R_b = \{X_{b,k} \quad k = 1,2,3,...,M\} \\ R_c = \{X_{c,k} \quad k = 1,2,3,...,M\} \end{cases} \quad (2)$$

$X_{a,k}$, $X_{b,k}$ and $X_{c,k}$ contain a finite number of samples (10 seconds of EEG to make it comparable with BIS index) and represent the kth epoch of R_a, R_b and R_c data sets. In order to obtain reference data set, feature selection function f is applied to each data set. For one dimensional case, this feature function is defined as follows:

$$f : x \rightarrow f(x) = f \quad (3)$$

The ability of the index depends on f at [a, c] to identify the states of the patients. As shown in Fig. 4, f function can be either linear, or non-linear. At any general state, the first order derivative of f should not have any sign change.
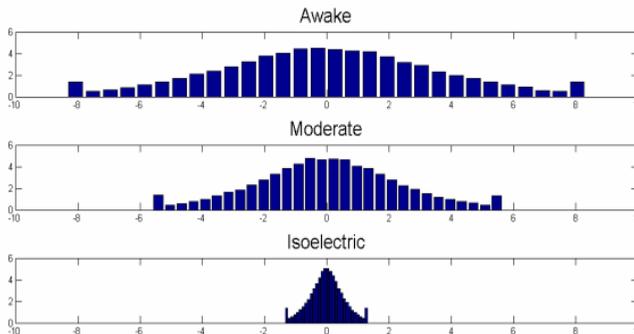

Fig. 5. PDF of awareness (awake), general anesthesia and isoelectric anesthesia

One choice for selecting f , is using probability density function (PDF) of d1 coefficients (details subbund at first scale of Daubichies wavelet (Zikov et al., 2006)). In Fig. 5, the PDF of d1 coefficients are presented where histogram is used for estimating PDF. It is shown that

this histogram has more concentration around zero in isoelectric state while it is more scattered at awareness state. So, the variance of this histogram can be used as an appropriate feature:

$$f_{t,k} = \text{var}(hist(d1)), \quad t = a,b,c \quad k = 1,2,...M \tag{4}$$

By using three series of reference signals, the awareness reference feature vector, general anesthesia, and isoelectric states are measured through the following equation:

$$\overline{ft} = \frac{1}{M} \Sigma_{k=1}^{M} ft,k \quad t = a,b,c \tag{5}$$

where $f_{a,k}$, $k = 1,2,...,M$ are obtained by applying 10-second awake reference data sets to f function, and $f_{b,k}$ and $f_{c,k}$ are characterized respectively by the same manner for b and c states. $\overline{f_a}$, $\overline{f_b}$ and $\overline{f_c}$ are average of this feature in the corresponding states and are the reference features. Now, this feature on every 10-second period for unidentified EEG signal (e.g., state d) can be measured by comparing this feature with $\overline{f_a}$, $\overline{f_b}$ and $\overline{f_c}$, and obtaining the similarity between the patient's condition with these amounts. As a result, we define the following quantities as below:

$$j_t = \left\| f_d - \overline{f_t} \right\| \quad ,t = a,b,c \tag{6}$$

The norm vector V, $\|.\|_1$ is defined as:

$$\|.\|_1 = \Sigma_{n=1}^{N} |v(n)| \tag{7}$$

j_a, j_b and j_c indexes measure the distance of the system from a, b, and c states. High norms can be applied for this analysis but in this case j_a, j_b and j_c may increase and this increase might cause noisy state of the output index.

Since we have three points of reference, it's possible to use either a second order function or a partial-linear function to show properties of function f. First, using the concept of interpolation a second order function was designed in MATLAB. The data were fitted to the reference, but in all cases first order derivative of this curve changed, which shows the intermediate stats are not diagnosed clearly with this function. Instead, we can define this function linearly between a and b, also linearly between b and c (partially-linear function). To maximize signal to noise ratio, we can combine j_a, j_b and j_c, to define two descriptors $j_1 = j_b - j_a$ and $j_2 = j_c - j_b$. For this reason, we define functions g₁(x), g₂(x) as follows:

$$g_1 : x \rightarrow g_1(x) = j_1 = \left\| f(x) - \overline{f_b} \right\| - \left\| f(x) - \overline{f_a} \right\| \tag{8}$$

$$g_2 : x \rightarrow g_2(x) = j_2 = \left\| f(x) - \overline{f_c} \right\| - \left\| f(x) - \overline{f_b} \right\| \tag{9}$$

In order to scale the final index namely wavelet anesthetized index (WAI) such that h=WAI=1 for state a, WAI=0.5 for state b, and WAI=0 for state c, the function g_1 is applied to the entire reference data sets a & b, and the function g_2 is applied to the entire reference data sets b & c. This yields four sets J_a, J_{b1}, J_{b2} and J_c:

$$\begin{cases} h=1:\rightarrow J_a = \{j_{a,k}, & k=1,2,3,...,N\} \\ h=0.5:\rightarrow J_{b1} = \{j_{b1,k}, & k=1,2,3,...,T\} \end{cases} \tag{10}$$

$$\begin{cases} h=0.5:\rightarrow J_{b2} = \{j_{b,k}, & k=1,2,3,...,N\} \\ h=0:\rightarrow J_c = \{j_{c,k}, & k=1,2,3,...,T\} \end{cases} \tag{11}$$

Now, assume that d is a state between a and c, WAI is defined as follows (the scaled version of g_1 and g_2):

$$WAI : x \rightarrow WAI(x) = i$$

$$= \begin{cases} g_1(x).\dfrac{1}{\overline{J_a}-\overline{J_{b1}}} - \dfrac{\overline{J_{b1}}}{\overline{J_a}-\overline{J_{b1}}} & if \quad b<d<a \\ g_2(x).\dfrac{1}{\overline{J_{b2}}-\overline{J_c}} - \dfrac{\overline{J_c}}{\overline{J_{b2}}-\overline{J_c}} & if \quad c<d<b \end{cases} \tag{12}$$

where

$$\overline{J_t} = \frac{1}{M}\Sigma_{k=1}^{M} J_{t,k} \quad ,t=a,b1,b2,c \tag{13}$$

3.1 WAI vs. BIS
This algorithm is applied for the data obtained from a sample patient and the obtained amounts of WAI along with BIS index amount are figured in Fig. 6.
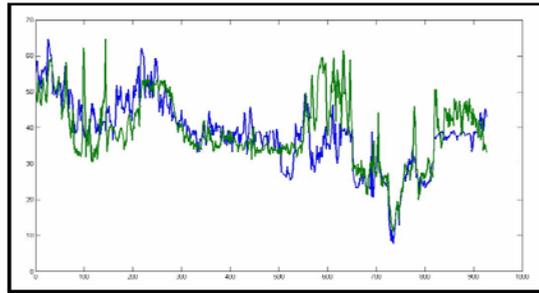

Fig. 6. WAI index vs. BIS index

Number of reference states	Correlation With BIS	Time Complexity (second)
2	45%	5
3	77%	7
4	73%	15

Table 1. Correlation and time complexity compared using two, three and four reference state to obtain WAI

To extract WAI, we also tested two, three and four reference states and compared the results. First, by using awake and isoelectric stats, only 45% correlation with BIS were achieved (Table 1), total time needed to calculate the reference vectors and extracting the desired index from samples was almost five seconds. Using three reference states (as explained in section 3), correlation increased to 77 percent and total operation time increased to seven seconds. The main reason of this improvement is using 3 states instead of two states. So, we examined using 4 references, but the correlation decreased to 73 percent and the time increased to 15 seconds. Considering the time complexity and amount of correlations we can conclude that choosing 3 references is the best choice.

3.2 Further discussions in time-frequency domain

The mentioned results are obtaind using Daubechies wavelet. We also used other wavelet transforms such as complex wavelet transform (Selesnick et al., 2005), however considerable improvement didn't obtain in results. In addition, we employed other joint time-frequency tools such as spectogram, scalogram, Wigner-Ville transform, and Choi-Villiams transform (Mallat, 2009). The results for isoelectric, awake and moderate states are illustrated in Fig. 7. Our simulations show that wavelet transform is superior for estimation of the DOA.

4. Index of the DOA using ANN

ANN is basically a wide processer with parallel structure which is able to save experimental data and use them in the next processer. There is a potential of ANN for various units of medicine, such as anesthesia and care unit. We divide the collected signals to 10-second periods, and extract 15 features for each epoch. The calculated parameters are classified as follows.

4.1 Spectral edge frequency of 95 and 90

The spectral edge frequency 95 (SEF95) is the frequency that 95% of the power in the spectrum exists within. It's clear that in the case of anesthesia SEF95 becomes small. A similar definition can be also used for SEF90.

4.2 Alpha, beta and theta ratio

Alpha, beta and theta ratios indicate logarithmic relative power of two distinct frequency bands. Alpha-ratio decreases as anesthesia becomes deeper as follows:

$$\alpha_{ratio} = \log \frac{E(30-42.5Hz)}{E(6-12Hz)} \tag{14}$$

Beta-ratio is defined as follows:

$$\beta_{ratio} = \log \frac{E(30-42.5Hz)}{E(11-21Hz)} \tag{15}$$

The difference between alpha and beta ratios is considered as theta ratio:

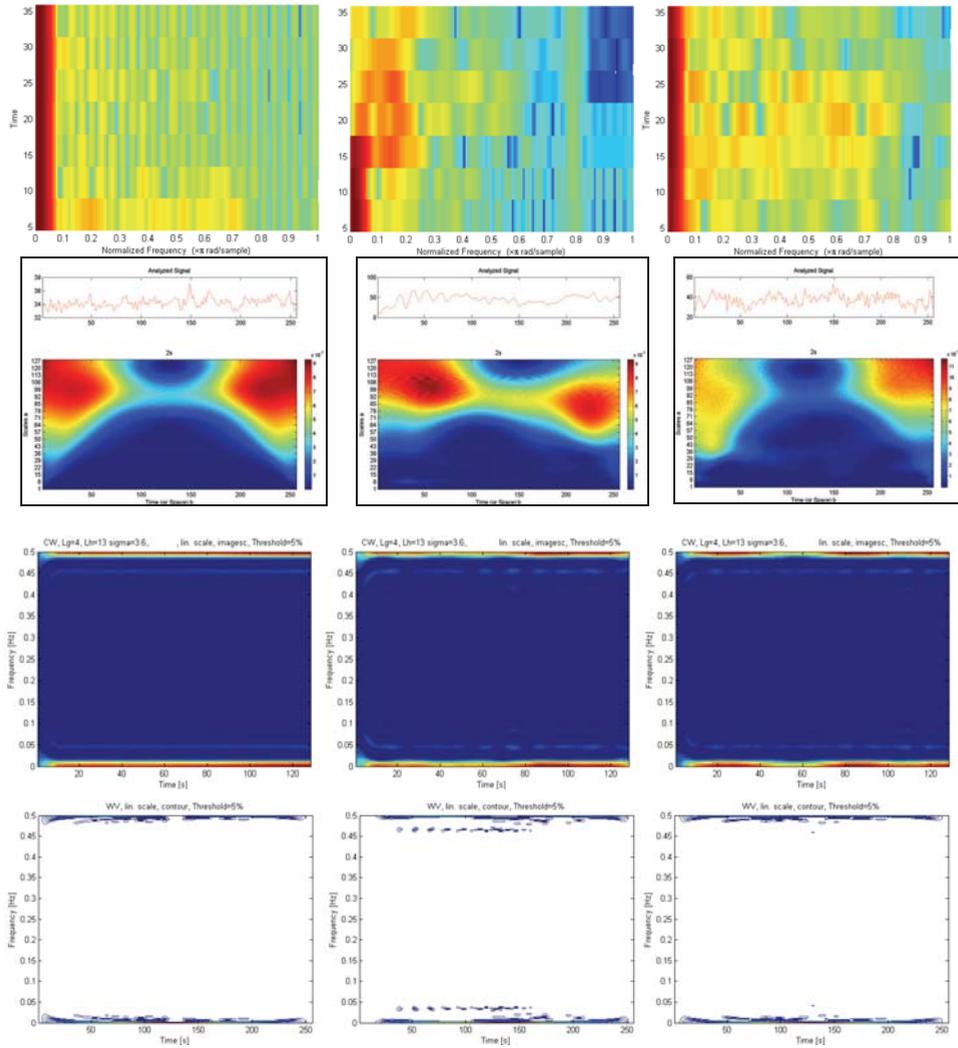$$\theta_{ratio} = \beta_{ratio} - \alpha_{ratio} = \log \frac{E(6-12Hz)}{E(11-21Hz)} \tag{16}$$

Fig. 7. First, second, third and fourth rows respectively show the spectogram (2 sec. window), scalogram (2 sec. window), Choi-Villiams transform (1024 samples), and Wigner-Ville transform (256 samples). First, second and third column respectively illustrate isoelectric, awake states, and general anesthesia.

4.3 Burst Suppression Ratio (BSR)

We define burst suppression (BS) as amplitude less than 5mV lasts more than 0.5 sec in the processed wave. Fig. 8 illustrates EEG signal with burst and without burst suppression. Note that the small amplitude waves that have fast frequency also appear in the light anesthetic state causes a false BS detection. The BSR is the summation of the times with burst suppression divided to whole windowed time range which includes burst events (Fig. 9).

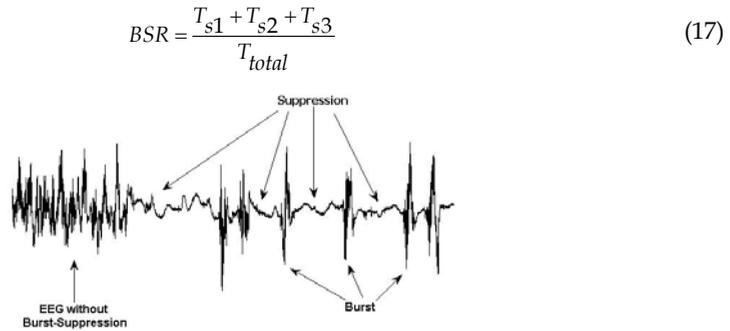$$BSR = \frac{T_{s1} + T_{s2} + T_{s3}}{T_{total}} \qquad (17)$$

Fig. 8. EEG signal with burst and without burst suppression

It shows that BSR alone is not an appropriate feature for DOA in all cases.
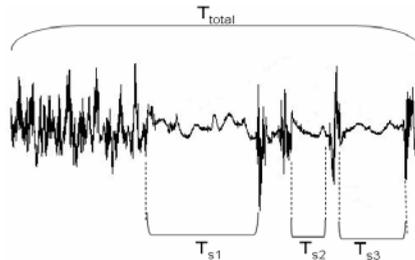

Fig. 9. The EEG windows with burst suppression

4.4 Signal Quality Index (SQI)

The ratio of the number of epochs that are without artifact to the number of total epochs is known as SQI.

4.5 Wavelet coefficients

For the γ-band, an optimal result for classifying different anesthetics state can be obtained by using Daubechies wavelet coefficients $(w[Db_6])$. We extract the amplitude of PDF of wavelet coefficients, mean and variance of these coefficients in each epoch as features for estimation of DOA (since the mean of wavelet coefficients tends to zero we can exclude this feature).

4.6 Applying Back Propagation (BP) algorithm

In addition to the mentioned features in this section, other features like mean-amplitude, mean and variance of each epoch, are also extracted and all of the obtained fifteen features (see caption of Fig. 11 for a list of these features) set in a 15×7440 matrix to train the ANN using BP algorithm with sigmoid function (Fig. 10). To train the ANN, the 20 hours collected data taken from 25 patients were used (data from 8 patients were held to use for testing the ANN). In this way, we divided the 20 hours collected data into 10-second epochs and extracted 15 features mentioned in previous part for every 10-second epochs. The all 15 features were applied to an ANN. At first, we designed a structure with 15 input neurons,

20 neurons at hidden layer and one neuron in output layer (which we prepared besides a bias for hidden and output layers). We applied all 7440 data in the proposed structure, and set BIS index as the desired output in the output of this network. After training step, we used the data taken from patient number 7 (who hadn't taken part in network training process) for testing our network and comparing the output of network with the output of

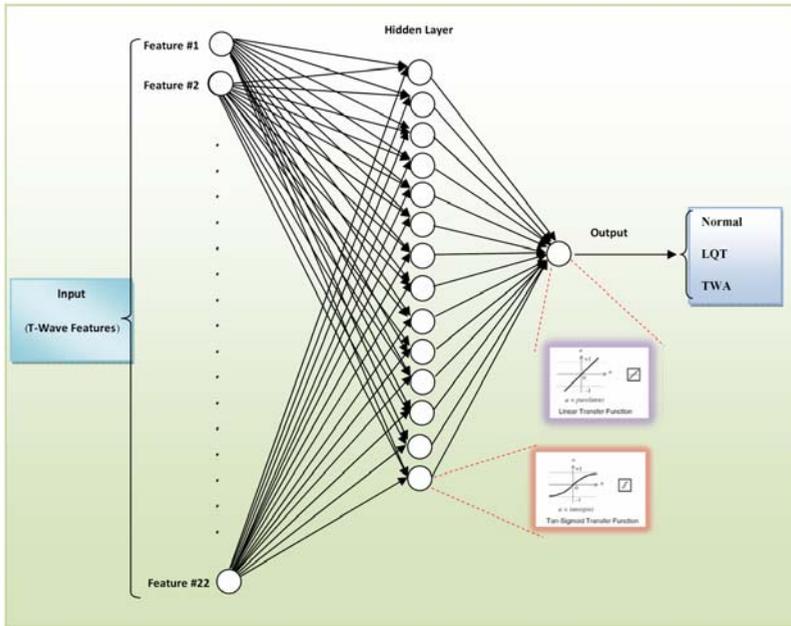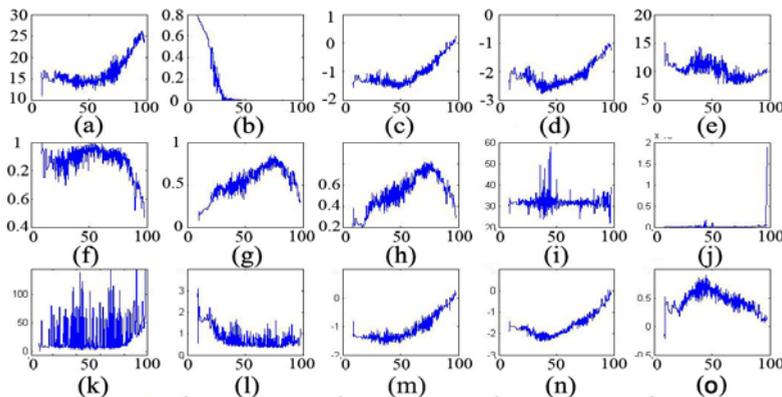Fig. 10. Multi-layer perceptron (MLP) NN architecture.

Fig. 11. BIS Index versus : a) SEF95, b) BSR, c) SEF90, d)SEF50 , e) Mean Amplitude, f) SQI of time domain, g) SQI of frequency domain, h) SQI of bispetral domain, i) Mean of each epoch, j) Variance of each epoch, k) Amplitude of pdf of wavelet coefficient, l) Variance of pdf of wavelet coefficient , m) Alpha ratio, n) Beta ratio, p) Theta ratio

BIS monitor. We can also see how these 15 features change during the changes of BIS index in Fig. 11. As represented in this figure, most of these features are changing corresponding to the changes of BIS index.

In second proposed structure for ANN, based on results of Fig. 11, we omitted 5 features which didn't have regular changes with the changes in BIS and had poor correlation with BIS index (features *e, g, i, j, k* in Fig. 11). As a result, we designed a new network (named second structure) with 10 input neurons, 20 neurons in first hidden layer, 10 neurons in the second hidden layer and one neuron in output. Using BP algorithm, we trained our proposed structure. After 30000 iteration, our network was trained properly and the data from patient number 23 and 7 were applied to the network, and achieved a correlation more than 89% (95%, corr=[88.9%,93.44%]) with BIS index. The result is represented in Fig. 12.
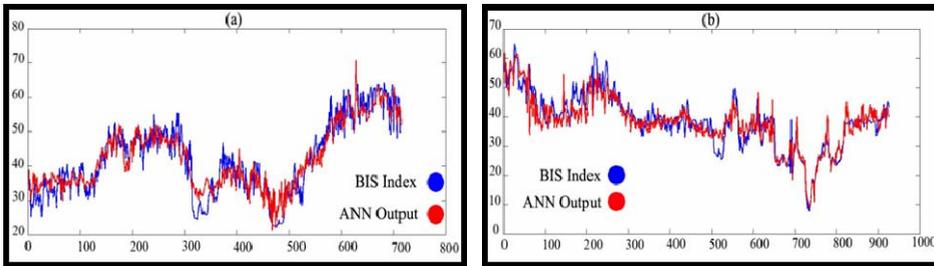

Fig. 12. a) BIS versus ANN output with correlation 93% for patient no 7, b) BIS versus Ann output with correlation 90% for patient no 23

4.7 Additional works

We use complex wavelet transform (Selesnick et al., 2005) to estimate the DOA by using second, third, fourth central moments (μ_2, μ_3, μ_4), skewness (S), kurtosis (K), and the difference between maximum and minimum values of PDF (Δ) (Papoulis & Pillai, 2001). These features extracted from the real part of first scale (high frequency subband d_1), and our simulations show that similar results can be obtained from imaginary part. We use a BP-based NN with 6 input neurons, 6 neurons (with Gaussian function) at hidden layer and one neuron (with linear function) in output layer. For training we classified the data into 10 classes according to Table 2. For each class we have 15 minutes recorded data that after 10-second windowing we would have 90 training data. We used 35 test data for each class and finally the correlation between the output of this NN and BIS index was calculated 65.7%. We can see how these 6 features change during the changes of BIS index in Fig. 13. From this figure we can conclude that third and fourth central moments don't differ as good as other features.

Regarding to ANN-based method, other networks such as ANFIS (Jang, 1993) was also tested. For this reason, at first complex wavelet transform with four stages was applied on data. Then, maximum, minimun, mean, standard deviation and the VP=var(hist(w)) were extracted where w shows the wavelet coefficients for real and imaginary parts. We use this features for all subbands d_1, d_2, d_3, d_4, and low-pass subband a_4. So, we would have 50 features for each class. Table 3 illustrates the values of these features for various BIS ranges.

The range of data is [BIS-5, BIS+5]	Extracted features					
	Δ	K	S	μ_4	μ_3	μ_2
BIS=95	80	3.94	0.057	31.45	0.27	2.82
BIS=85	60	2.81	-0.092	14.7	-0.32	2.29
BIS=75	76	3.92	0.095	4.68	0.1092	1.092
BIS=65	62	2.01	0.16	0.85	0.063	0.53
BIS=55	122	23.05	-1.8	1.44	-0.23	0.25
BIS=45	244	49.17	-2.95	5.09	-0.53	0.31
BIS=35	365	83.98	-1.98	55.9	-1.46	0.81
BIS=25	359	95.7	51.0	44.5	0.29	0.68
BIS=15	400	305.3	-14.2	27.3	-2.33	0.29
BIS=5	230	125.8	7.49	0.34	0.089	0.052

Table 2. Extracted features from 10 classes of anesthesia for the real part of first scale (high frequency subband d_1) of complex wavelet coefficients

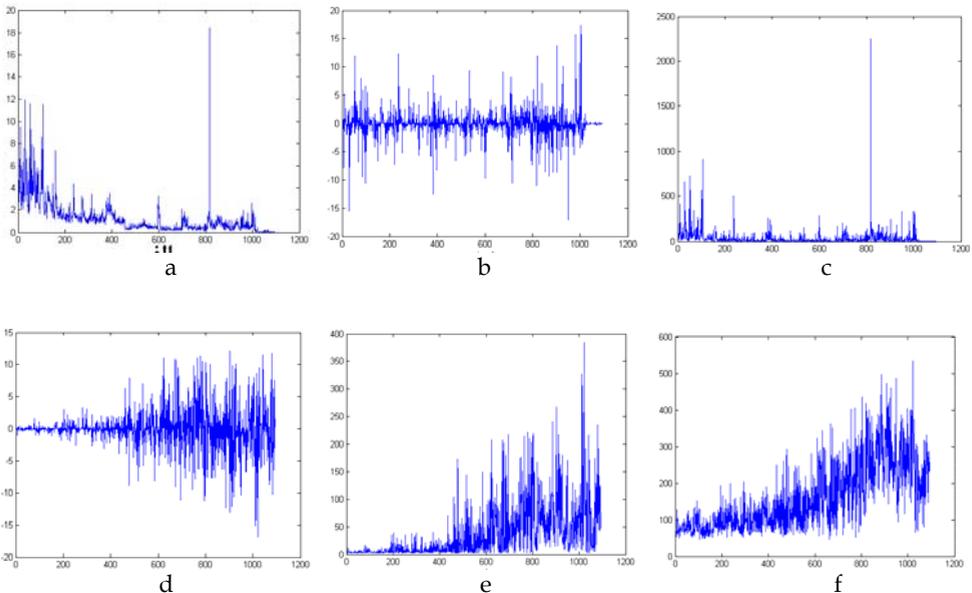Fig. 13. BIS index versus : a) second central moment (μ_2), b) third central moment (μ_3), c) fourth central moment (μ_4), d), skewness (S), e) kurtosis (K), and f) the difference between maximum and minimum values of PDF (Δ)

Although it seems that all features have a reasonable changes for various BIS ranges, but using all of them results in an ANFIS network with high computational complexity. Computing the correlation of these features with BIS index we extract 16 features with highest correlation as shown in Table 4. Applying 4 features with highest positive correlation to ANFIS network achives 88.7% correlation with BIS index. For this method (that is a combination of complex wavelet transform and neuro-fuzzy network) the specificity, sensitivity, and the total classification accuracy were calculted. The results have been concluded in Table 5. It's clear from this table that for 20<BIS<30 we have highest sensitivity and for 40<BIS<60 we have the least. For all levels of anesthesia the specificity is higher than 90% and except 50<BIS<60, in all cases the total classification accuracy is higher than 90%.

The range of data is [BIS-5, BIS+5]	features	subband				
		a_4	d_4	d_3	d_2	d_1
BIS=95	Max.	123.7	13.72	10.59	8.68	5.85
	Min.	33.78	-9.72	-12.22	-9.44	-6.68
	mean	93.76	0.442	0.328	0.097	-0.036
	std.	18	4.72	3.77	2.61	1.9
	VP	1.15	1.05	3.69	11.07	41.95
BIS=65	Max.	150.63	34.18	19.14	11.49	7.8
	Min.	51.09	-32.51	-21.34	-8.1	-7.33
	mean	85.66	-0.39	-0.15	-0.12	0.007
	std.	18.74	12.006	7.35	2.59	1.07
	VP	1.33	1.09	3.21	16.8	52.18
BIS=45	Max.	153.2	21.74	18.9	6.99	71.01
	Min.	10.97	-25.52	-14.26	-8.1	-11.47
	mean	95.87	-0.29	0.14	-0.012	0.005
	std.	8.07	8.24	6.35	1.57	0.7
	VP	0.96	1.27	3.23	23.93	486
BIS=5	Max.	118.5	4.3	3.3	1.58	2.13
	Min.	80.98	-5.59	-2.8	-1.8	-0.4
	mean	95.8	0.13	0.005	0.007	0.009
	std.	6.07	1.4	0.8	0.33	0.17
	VP	1.37	1.75	5.91	27.19	156.15

Table 3. Extracted features from 4 classes of anesthesia for complex wavelet coefficients

Features	Correlation with BIS (-)	Features	Correlation with BIS (+)
VP of real part of d_1	-67.74	-std of imaginary part of d_1	73.22
VP of imaginary part of d_1	-65.09	std of real part of d_1	68.3
VP of real part of d_2	-64.4	Max. of imaginary part of d_1	62.22
VP of real part of d_3	-62.3	std of imaginary part of d_2	62.09
VP of imaginary part of d_2	-57.4	std of real part of d_2	48.2
VP of real part of d_4	-56.8	Max. of real part of d_2	40.08
VP of imaginary part of d_3	-55.9	std of real part of d_3	39
VP of imaginary part of d_4	-55.13	Max. of imaginary part of d_2	36.8

Table 4. Features with highest correlation with BIS

5. Results

Our aim is to maximize the correlation between BIS index and output of our proposed methods. For this reason several methos based on wavelet transform and ANN have been proposed and we can conclude from the correlation between BIS and the obtained index from methods that second structure of BP-based NN (section 4.6) is the best in most cases. For this network, the correlation between BIS index and the extracted sub-parameters was investigated with the model-independent prediction probability (PK) (Smith et al., 1996). These results represented that among the extracted feature, BSR, Beta Ratio and SEF90 features respectively had the highest weight for calculating the outputs of ANN. In this way, BSR had individually proper results for 44% cases for the depth below 40, and for the cases above 40, Beta ratio and SEF95 had individually proper results for 35% of cases.

The obvious outcome of the algorithms is that, Alpha and Beta ratio decreases and BSR increases with the increasing DOA (decreasing BIS index). As Fig. 12 shows, there is a high correlation 90% between BIS index and output values of proposed ANN in the moderate anesthetized range.

The results indicate that the SEF95, Alpha and Beta ratio decreases and BSR increases as BIS decreases. Other parameters are weak and somehow unrelated to BIS index. This confirms the results of (Haddad et al., 2007), which indicate that "bispectral analysis adds nothing but complexity". Due to equations (14, 15), Alpha and Beta ratio quantifies the activity of β waves, and this confirms the fact that anesthetic drugs affect these waves. The burst-suppression pattern usually occurs in deep anesthesia (Fig. 12-b). Our results demonstrate a high correlation between BSR and BIS index. Our findings show that in deep anesthesia (below 40), BSR could predict BIS index lonely.

The level of anesthesia	sensitivity	specificity	total classification accuracy
90<BIS<100	99.22	75.4	97.89
80<BIS<90	97.98	60	94.5
70<BIS<80	96.5	58.2	91.0
60<BIS<70	92.08	68.2	91.2
50<BIS<60	93.6	49.47	89.7
40<BIS<50	93.85	49.54	90.6
30<BIS<40	96.71	58.93	94.63
20<BIS<30	98.84	93	96.8
10<BIS<20	97.85	70.8	97.07
0<BIS<10	99.51	64.6	97.4

Table 5. The specificity, sensitivity, and total classification accuracy of complex-wavelet-neuro-fuzzy system for estimation of DOA

6. Conclusion

In this work, we used wavelet transform (WAI index) for extracting DOA index, and also employed several sub-parameters for assessing DOA based on ANN with the back propagation (BP) learning algorithm and ANFIS algorithm. The output of second structure of proposed BP-based NN has a high correlation with the output of the BIS index in compared with the WAI. However, using wavelet transform to extract WAI has less complexity (computational time) than ANN method. The combination between complex wavelet transform and neuro-fuzzy network also achieves a new method with high sensitivity and total classification accuracy between various level of anesthesia.
We can also test this algorithm by adding other features extracted from other clinical devices or combined features (as inputs of ANN). In addition, since the extracted EEG may be corrupted with noise and interferences, we can use some pre-processing steps in wavelet domain to improve the results of wavelet-based method without considerable increscent in computational complexity.

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