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Designing a Fuzzy Rule Based System to Estimate Depth of Anesthesia

V. Esmaeili [a] , A. Assareh [b] , M. B. Shamsollahi [a] , M. H. Moradi [b] and N. M. Arefian [c]

[a] Biomedical Signal and Image Processing Laboratory (BiSIPL), School of Electrical Engineering, Sharif University of Technology
[b] Faculty of Biomedical Engineering, Amirkabir University of Technology
[c] Department of Anesthesia, Shahid Beheshti University

Abstract- **Estimating the depth of anesthesia (DOA) is still a challenging area in anesthesia research. The objective of this study was to design a fuzzy rule based system which integrates electroencephalogram (EEG) features to quantitatively estimate the DOA.**

The proposed method is based on the analysis of single-channel EEG using frequency and time domain features as well as Shannon entropy measure. The fuzzy classifier is trained with features obtained from four subsets of data comprising well-defined anesthesia states: awake, moderate, general anesthesia, and isoelectric. The classifier extracts efficient fuzzy if-then rules and the DOA index is derived between 100 (full awake) to 0 (isoelectric) using fuzzy inference engine.

To validate the proposed method, a clinical study has conducted on 22 patients to construct 4 subsets of reference states and also to compare the results with CSM monitor (Danmeter, Denmark), which has revealed satisfactory correlation with clinical assessments.

I. Introduction

Depth of anesthesia assessment has remained a challenging problem for several decades. It is because none of the parameters used to this aim has satisfactorily described the complexity of the system. Patient hemodynamics like blood pressure, heart rate, tearing and sweating can not avoid awareness and movements during surgery. Neither plasma nor the effect site concentration of the drug can measure clinical effects directly. Solving this problem the Central Nervous System, the main target for anesthetic agents, has received a great deal of attention and EEG-based methods have been widely used for estimating the anesthetic depth.

Various types of features have been extracted from the electroencephalogram to predict depth of anesthesia. Early studies have used spectral edge frequency, median frequency and the relative and total power in the classical frequency bands [1]-[3]. Using parameters based on bispectrum made a progress in EEG-based anesthesia monitoring. The bispectrum power is said to indicate the presence of quadratic phase-coupling between different frequencies within the signal. Recently some researchers have used EEG entropy measures as an indicator of depth of anesthesia [4]-[7]. The concept behind this is that EEG becomes more regular as the anesthetic depth increases. Also Lempel-Ziv complexity of EEG has shown good correlation with increasing the anesthetic depth [8].

Although these parameters can distinguish well between awake and anesthetized states, they don't behave monotonically during transition from wakefulness to deep isoelectric states [2]. So we can't utilize them individually to continuously monitor anesthetic state changes during different phases of anesthesia. Concerning this, some efforts have been made to combine these features using computational intelligence techniques such as neural networks and neuro-fuzzy inference systems [5], [9-10].

In the present study we have proposed a rule-based fuzzy logic system merging different EEG derived measures to obtain an index for the depth of anesthesia. Several studies have introduced adaptive neuro-fuzzy inference system (ANFIS) as a powerful tool for classifying DOA. Although it led to good compatibility with clinical assessments, but the black box nature of neural learning makes these systems rigid to importing knowledge from human expert that may improve the performance of the system. Moreover, it is difficult to drive knowledge from artificially made rules of these systems. Considering the above mentioned problem we decided to use a fuzzy inference system (FIS) that was initially established by human expert and then optimized by machine learning procedures.

Two trends can be observed in development of anesthesia monitors. Some algorithms put more emphasis on some advanced parameters like bispectrum or entropy, while the others (like CSM, Cerebral State Monitor) combine some well-known spectral ratios and time domain characteristic of EEG applying them to a classification algorithm. CSM (Danmeter, Denmark) is a recently developed depth of anesthesia monitor having good correlation with clinical assessments. It uses 3 later defined spectral ratios: alpha-ratio, beta-ratio and difference between them, which is called theta ratio in this paper, accompany with burst-suppression, a time domain feature relating to deep iso-electric states. Each of these components is affecting in a specific range of anesthetic level where they perform best. Adaptive Neural Fuzzy Inference System (ANFIS) is used to calculate the CSI which is a scalar index changing between 0 and 100. In this study we utilized features used in calculating CSI and also SEF and Shannon entropy in conjunction with a FIS. We applied different combinations of features and also different methods of defining membership functions and eventually compared the results. We compared our index resulting from a FIS with CSI, ANFIS derived index, in steady state and transient phases of anesthesia.

II. Materials and Methods

A. Protocol Design and Data Collection

22 patients, having ASA grade I and II and undergoing elective urologic surgery entered the study. Patient ranged in age from 15 to 75 years (mean=44.36, SD=19.93), and in weight from 50 to 96 kg (mean=68.64, SD=12.99). Written informed consent was obtained from all the study patients.

All the patients were premedicated with 0.03 mg/kg midazolam and 2 µg/kg fentanyl. The Anesthesia was induced with 5mg/kg (4 mg/kg at the first and 1 mg/kg before intubation) tiopanthal. The muscle relaxant used in this study was cisatracurium (0.1 mg/kg in the induction phase). After orotracheal intubation, patients were ventilated using a mixture of N_20 and O_2. Anesthesia was maintained with 75µg/kg/h propofol by means of an infusion pump.

One channel EEG recording was made using CSM with the sampling rate of 100 Hz. The EEG electrodes were placed at F_z (positive at middle forehead), T_5 (negative at left mastoid) and reference electrode at F_{p1} (left forehead). Data was transferred to a portable computer by RF interface using CSM link and software (CSM link software v.3.01). All the EEG data and the CSM calculated indices were stored for later analysis. Hemodynamic parameters i.e. blood pressure, heart rate, blood O_2 saturation and also the time occurrence of movement or gagging of the patient were manually recorded. The exact time of all drug infusions were also noted.

For later described comparison of discriminating power of each EEG feature, 4 EEG observation sets each containing 15 minutes have been recorded:

- Awake reference: recorded from 3 healthy adult subjects.
- Moderate reference: extracted from 14 patients during induction or recovery from anesthesia.
- Anesthetized reference: extracted from 10 patients during steady state anesthesia.
- Isoelectric reference: recorded from a brain death subject in ICU.

B. Spectral features

As mentioned above, in this study we have used 4 spectral features including: spectral edge frequency (SEF), alpha-ratio, beta-ratio and theta-ratio. SEF is the frequency below which a defined percent of total power is located. SEF 95, 90 and median frequency (SEF 50) are the most common definition of this measure. D. Schwender et al have shown that SEF decreases during general anesthesia with isoflurane or propofol compared with the awake state.

We performed power spectral analysis using fast Fourier transformation (FFT). Epoch length of EEG acquisition was 4s and the window shifting was 1 s. Spectral Edge frequency 90 (SEF 90) was calculated. The SEF value was determined by averaging the data from 10 consecutive epochs.

Alpha, beta and theta ratios show logarithmic relative power of two distinct frequency bands. Alpha-ratio decreases as anesthesia deepens

$$Alpha\_ratio = \log \frac{E(30-42.5Hz)}{E(6-12Hz)} \qquad (1)$$

It is the part that identifies surgical anesthesia in CSI algorithm. Beta-ratio which relates to identifying awake state is defined as follows

$$Beta\_ratio = \log \frac{E(30-42.5Hz)}{E(11-21Hz)} \qquad (2)$$

We named the difference between alpha and beta ratios as theta ratio. It can well distinguish between moderate anesthesia and other states

$$Theta\_ratio = \log \frac{E(6-12Hz)}{E(11-21Hz)} \qquad (3)$$

C. Burst suppression ratio

During deep anesthesia, the EEG may develop a peculiar pattern of activity, which is evident in the time domain trend of signal. This pattern, known as burst suppression, is characterized by alternating periods of normal to high voltage activity changing to low voltage or even isoelectricity rendering the EEG inactive in appearance. The burst suppression ratio (BSR) is a time domain EEG parameter developed to quantify this phenomenon. To calculate this parameter, suppression is recognized as those periods longer than 0.50 s, during which the EEG voltage does not exceed approximately +/- 3.5 µV. The time in a suppressed state is measured, and the BSR is reported as the fraction of the epoch length where the EEG is suppressed [11].

For comparison of results with CSI we used these values that are the same with burst suppression calculation in CSI.

D. Shannon Entropy

The concept of entropy in the literature of information theory was first introduced by Shannon, and it can be interpreted as a measure of order in the signal. In other words entropy rates are measures designed to quantify the regularity of a time series or the predictability of new values based on previous observations.

Shannon entropy, ShEn, quantifies the probability density function of the signal and it can be calculated as:

$$ShEn = \sum_i p_i \log p_i \qquad (4)$$

where i goes over all amplitude values of the signal and p_i is the probability that amplitude value a_i occurs anywhere in the signal.

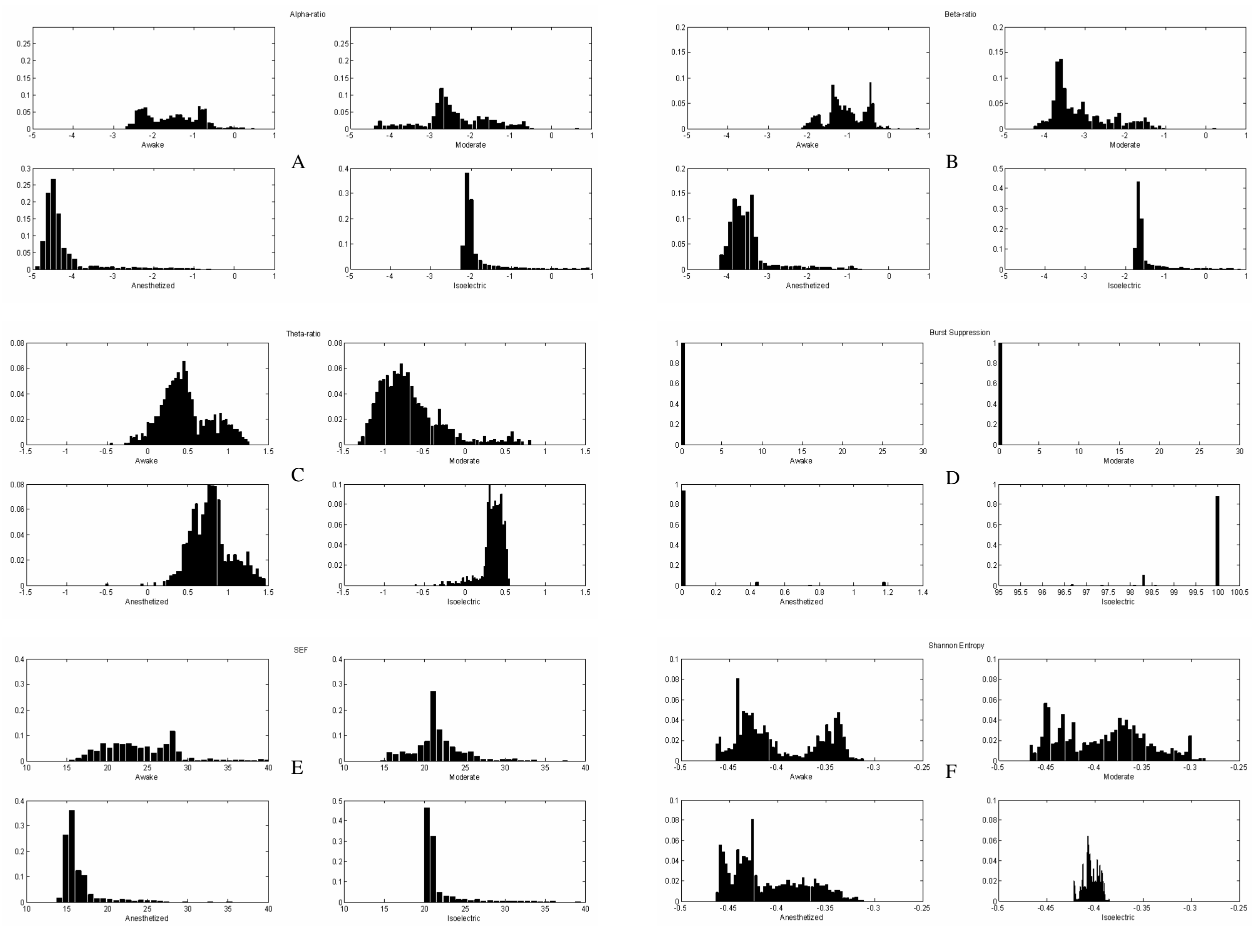

Figure l. Histogram analysis of alpha ratio, beta ratio, theta ratio, burst suppression, SEF and Shannon Entropy.

However, in the case of measured signals the PDF is not known and should be estimated. Also, it is generally not reasonable to take into account all amplitude values a_i . The easiest way to estimate the PDF is to use the histogram method where the amplitude range of the signal is linearly divided into k bins so that the ratio k/N is constant (N is the number of signal samples). The ratio k/N characterizes the average filling of the histogram. In order to get normalized values, ShEn should be divided by log k

$$ShEn = \frac{ShEn}{\log k} \qquad (5)$$

E. Statistical analysis of features

All of the six mentioned features which have shown good results in previous studies were calculated for each epoch of 4 data sets.

In order to see distribution of features over different classes (awake, moderate, general anesthesia, isoelectric), we compared PDF of the features over each subset. In this way we performed histogram analysis as a powerful tool that can help us to shape membership functions used in our fuzzy system (Fig. 1).

In alpha ratio histogram (fig. 1-A) general anesthesia state values are well apart from other states. Fig. 1.B shows that although moderate and anesthetized states result in nearly similar beta values but awake values of beta is well distinguishable. Theta histogram (fig. 1-C) indicates acceptable discrimination of moderate state. Although it has a biphasic fashion in changing from awake to isoelectricity but we can extract periods of moderate anesthesia with the use of this feature. It is not so important what are isoelectric subset values for the first 5 features, because the last feature named burst suppression can detect periods of isoelectricity clearly. Fig. 1-D illustrates this fact well. Fig. 1-E shows that SEF decreases from awake to general anesthesia, and then increases till deep isoelectric EEG. It is equivalent to previous results which have used SEF for discriminating between awake and anesthetized state. We can see that all of 4 subsets overlap in SEF in some regions. But it seems that it is capable to distinguish between general anesthesia and other states.

Histogram analysis of ShEn did not show good discrimination ability between different classes (fig. 1-F). Statistical analyzing of features declared our first hypothesis that none of the features can individually estimate the depth of anesthesia in all states.

F. Designing Membership Functions for Fuzzy Classifier

Designing membership functions (MFs) is the fundamental stage in constructing a fuzzy classifier. MFs should partition the input space efficiently such that the different subsets of training patterns can be well learned by the classifier. If this stage is not well done the classification will be corrupted despite the kind of classifier. Here, we designed input membership functions with respect to data distribution pattern over each dimension (histogram analysis of data in fig. 1). Fig. 2 illustrates the designed membership functions of four features that have led to the best performance in later mentioned results. The putative features are alpha ratio, beta ratio, theta ratio and burst suppression which have 2, 2, 3, and 2 MFs respectively.

For training purpose, we utilized combinations of features derived from 4 sets of 15 minutes EEG signal belonged to the predefined reference states.

In order to have concise and interpretable rules we based our method on combination of four features for designing membership functions and constructing rules. Considering 4 features as inputs, we have 4 dimensions in input space.

G. Constructing Fuzzy If-Then Rules

Ishibuchi et al. [12] proposed an intuitive method for constructing fuzzy if-then rules in fuzzy classification problems. We also developed our fuzzy rule base according to their approach. Here is the summary of the rule building procedure:

As we mentioned before, our input space has 4 dimensions corresponding to 4 selected features. As a result, we have 2×3×2×2=24 fuzzy subspaces. Our goal is to derive a suitable rule for each of these subspaces.

Suppose that we have 900 training epochs $\mathbf{x}_1$, $\mathbf{x}_2$, …, $\mathbf{x}_{900}$, each of which is described by 4 features as $\mathbf{x_p} = (x_{p1}, x_{p2}, x_{p3}, x_{p4})$, p = 1, 2, …, 900, are given as training pattern. We assume that all 900 epochs already have one of the labels of the 4 classes (m>>4): class 1 (awake), class 2 (moderate), class 3 (anesthesia) and class 4 (isoelectric). Our rule template is as follows:

Rule R_{ijkl}: If x_{p1} is A^1_i and x_{p2} is A^2_j and x_{p3} is A^3_k and x_{p4} is A^4_l, then x_p belong to class C_{ijkl} with $CF=CF_{ijkl}$.

i=1,2; j=1,2; k=1,2,3; l=1,2 (6)

where R_{ijkl} is the label of the fuzzy if-then rule, A^1_i , A^2_j, A^3_k and A^4_l are fuzzy subsets on the first, second, third and forth dimensions respectively. The subscripted indices i, j, k and l corresponds to the membership functions. C_{ijkl} is the consequent of the rule which is one of the 4 classes, and CF_{ijkl} is the grade of certainty of the fuzzy if-then rule.

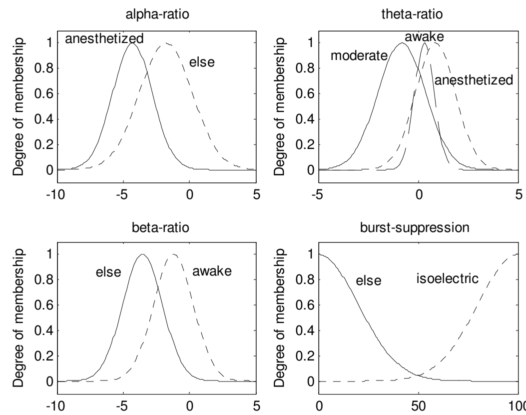

Figure 2. Initial membership functions of four selected features.

The consequent C_{ijkl} and certainty factor CF_{ijkl} of the if-then rules are determined in following steps:

Step 1: Calculate β_{CT} for each of four classes (T=1, 2, 3, 4) as:

$$\beta_{CT} = \sum_{x_p \in CT} \mu_i(x_{p_1}).\mu_j(x_{p_2}).\mu_k(x_{p_3}).\mu_l(x_{p_4}) \qquad (7)$$

where β_{CT} is the sum of the compatibility of $\mathbf{x}_p$'s in class T to the fuzzy if-then rule R_{ijkl} in (6).

Step 2: Find Class X(CX) such that

$$\beta_{CX} = \max\{\beta_{C1}, \beta_{C2}, \beta_{C3}, \beta_{C4}\} \qquad (8)$$

If two or more classes take the maximum value or all the β_{CT}'s are zero, the consequent C_{ijkl} of the fuzzy if-then rule corresponding to the fuzzy subspace $A^1_i \times A^2_j \times A^3_k \times A^4_l$ can not be determined uniquely. In this case, let C_{ijkl} be null**.** If a single class takes the maximum value**,** C_{ijkl} is determined as CX in (8).

Step 3: If a single class takes the maximum value in step 2, Then CF_{ijkl} is determined as:

$$CF_{ijkl} = \frac{(\beta_{CX} - \beta)}{\sum_{T=1}^{M} \beta_{CT}} \qquad (9)$$

Where

$$\beta = \sum_{\substack{T=1 \\ T \neq X}}^{M} \frac{\beta_{CT}}{M-1} \qquad (10)$$

where M is the number of classes which is 4 in this case. In this procedure, the consequent C_{ijkl} is determined as class X that has the largest sum of $\mu_i(x_{p1}).\mu j(x_{p2}).\mu_k(x_{p3}).\mu_l(x_{p4})$ over the all classes.

The certainty CF_{ijkl} has the following intuitively acceptable two properties:

1) if all the patterns in the fuzzy subspace $A^1_i \times A^2_j \times A^3_k \times A^4_l$ belong to the same class, then CF_{ijkl} = 1 (the maximum

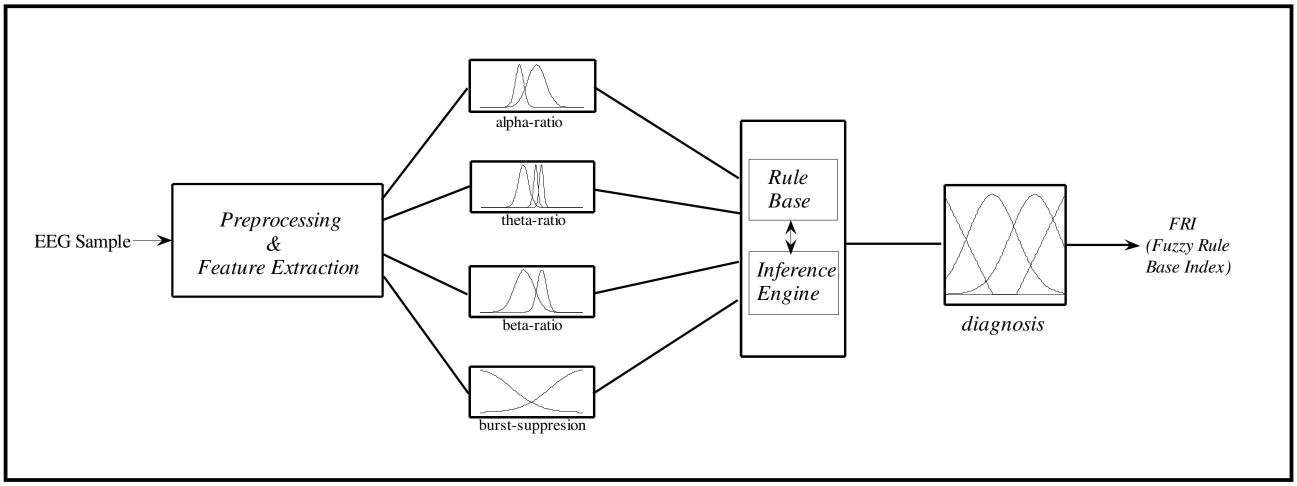

Figure 3. The Block diagram of the fuzzy system

certainty). In this case, it is certain that any patterns in $A^1_i \times A^2_j \times A^3_k \times A^4_l$ belongs to the consequent class of the generated fuzzy if-then rule.

2) If all the values of β_{CX}'s are not so different from each other, then $CF_{ijkl} \approx 0$ (the minimum certainty) .In this case, it is uncertain that any pattern in $A^1_i \times A^2_j \times A^3_k \times A^4_l$ belongs to the consequent class of the generated fuzzy if-then rule.

H. Classifying a new pattern

Let us assume that we have 2×2×3×2=24 fuzzy if-then rules generated for all input partitions. An input vector $\mathbf{x}_p=(x_{p1}, x_{p2}, x_{p3}, x_{p4})$ is classified by the single winner rule R_w that has the maximum product of the compatibility and the certainty grade among the whole rules:

$$\alpha_{CT} = \mu_w(\mathbf{x}_p).CF_w = \max\{\mu_r(\mathbf{x}_p).CF_r \mid r = 1,2,...,24\} \qquad (11)$$

Where $\mu_w(\mathbf{x}_p)$ is the compatibility of the input vector $\mathbf{x}_p=(x_{p1}, x_{p2}, x_{p3}, x_{p4})$ with the fuzzy if-then rule R_w, which is defined as follows:

$$\mu_w(\mathbf{x}_p) = \mu_{wi}(x_{p1}).\mu_{wj}(x_{p2}).\mu_{wk}(x_{p3}).\mu_{wl}(x_{p4}) \qquad (12)$$

We refer to the fuzzy if-then rule R_w as the single winner rule in our fuzzy reasoning procedure. The input pattern $\mathbf{x}_p$ is classified as the class label C_w of the single winner rule, R_w, [13].

If two or more classes take the maximum value in, or all the α_{CT}'s are zero, then the classification of $\mathbf{x}_p$ is rejected (i.e., $\mathbf{x}_p$ is left as an unclassifiable pattern), else assign $\mathbf{x}_p$ to Class X determined by step 2.

I. Fuzzy Inference System

In addition to four-class classification, we intend to derive an index in [0 100] that reflects the level of anesthesia and furthermore can be compared with clinically accepted indices like CSI and BIS. Consequently, we decided to use the whole rule set instead of only considered one winner rule in this stage. In order to infer a result from a set of rules, we must add a fuzzy inference engine to our system. We chose the product inference engine with following properties [14]: individual-rule base inference, union combination of results, Mamdani's product implication, algebraic product for all T-norm operations, and maximum for all the S-norm operations.

In the other hand, to derive a crisp number representing the depth of anesthesia, it is essential to design an appropriate membership function for output space and choose a defuzzification method as well. In this way, we put 4 membership functions corresponding to 4 class of isoelectric, anesthesia, moderate and awake in output and assign values of 0, 40, 75 and 100 as their membership function centers respectively. We also used the defuzzifier with respect to average of centers. Block diagram of complete system is described in fig. 3.

III. Results

We pursued two different goals in this study. Firstly to find out how can a single feature or different combinations of features discriminate between distinct stages of anesthesia. Another purpose of this paper was to define a unitless index, witch can measure DOA continuously.

A. Classification performance of fuzzy classifier

For classifying anesthesia states to 4 classes we trained the proposed fuzzy classifier with 4 train sets (2400 epochs of whole 3600) each of which containing 600 epochs from reference data sets. The classifier performance was tested with 1200 remaining epochs of data. The classification was performed with finding the winner rule based on method mentioned in section II-H. The accuracy for each group was defined as the ratio of truly classified patterns of the class to the total number of epochs belonging to it (300).

We used different combinations of features to design fuzzy classifier. The best results were aimed using the same combination with CSI which is alpha ratio, beta ratio, theta ratio, and burst suppression as input features. In this case the accuracies of all groups were 100% except for moderate state group which was 87%. So, the total accuracy was 96.75 for whole data test (1200 epochs). The results show excellence of our proposed approach compared with other methods classifying just two classes of awake and anesthetized.

B. Deriving a continuous index for DOA

As described in fuzzy inference section we intended to derive an index that can continuously measure the anesthetic changes. We used 4 selected features which led to best results in classification and applied them to the fuzzy system. The shape of input membership functions was designed with respect to histograms of features over reference data sets. Fig. 4 shows the initial membership functions. We constructed fuzzy if-then rules and fuzzy inference system to drive DOA index. In order to test the performance of system we used a typical data obtaining from a complete session of one patient under anesthesia. We calculated 4 selected features for each epoch (1s) of data and used them to calculate the DOA index for that epoch. Fig. 5 shows CSI and DOA index and also the error between them every second.

We used the Pearson correlation coefficient (r) as a measure of association between CSI and the index derived from fuzzy system. The value r was 89.87% for initial membership function design. With optimizing some parameters of the system like standard deviation of input membership functions and also number of rules we succeed to enhance the correlation coefficient [12].

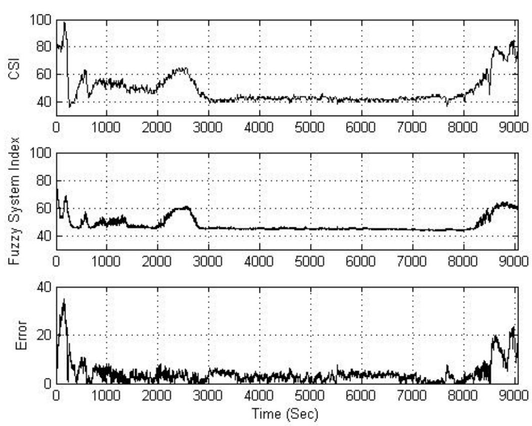

Figure 4. Derived fuzzy system index compared with CSI™ index (for 19th patient). Error is the absolute difference between CSI and proposed index.

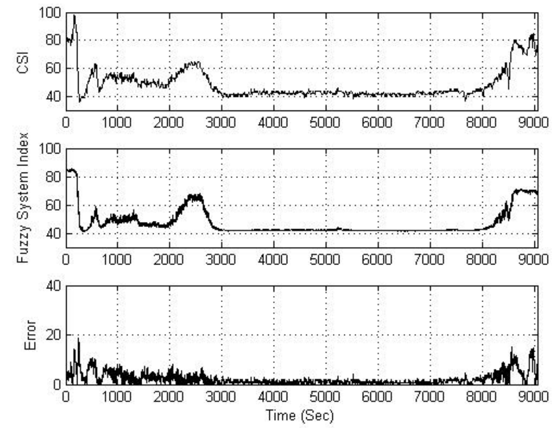

Figure 5. Derived fuzzy system index optimized with genetic algorithm, compared with CSI™ index (for 19th patient). Error is the absolute difference between CSI and proposed index.

We used genetic algorithm for this purpose. Fitness function was defined as the difference between the derived index and CSI values of a typical patient (19th patient). We used genetic algorithm in two steps, to tune input membership functions and also to eliminate the redundant rules. By optimizing sigma values and selecting only 7 rules the correlation improved up to 95.88%. In fig. 5 fuzzy derived index and CSI for the same patient are plotted.

Considering that genetic algorithm made optimizations based on minimizing the defined error for patient 19, we tested the resulted parameters with a randomly selected patient (4th patient) data to test the subject-independency of system performance (fig. 6). The correlation value was 94.67% which is so similar to the first result.

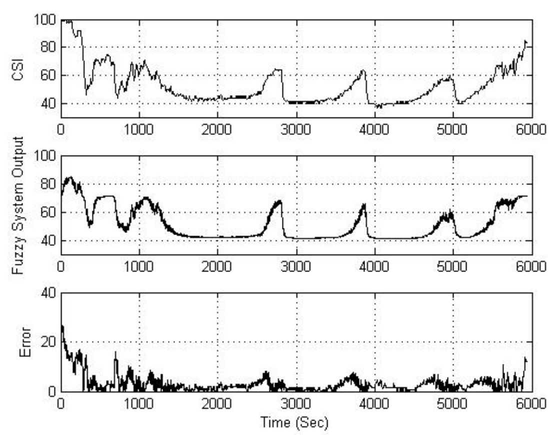

Figure 6. Derived fuzzy system index optimized with genetic algorithm, compared with CSI™ index (for 4th patient). Error is the absolute difference between CSI and proposed index.

IV. Discussion

The proposed fuzzy rule based system has following advantages: 1) Classification results are so improved in comparison with other methods using single features. We could completely discriminate between awake and general anesthesia (accuracy=100%), and also we could well classify the moderate state; 2) Continuous monitoring of anesthesia changes from full awake 100 to deep anesthesia 0 which is easy to understand for anesthesia providers; 3) It is easy to fuse and extract knowledge to and from the system. Because it was first initialized by the human expert and final rules are just 7 rules. 4) Independence from subject to test; 5) predictive for the appearance of clinical signs of inadequate anesthesia like movement.

The performance of proposed fuzzy rule based system for assessment of DOA varies with input features selection. As we demonstrated combination of three spectral features accompanied with BS will yield best results. The most useful parameters which are derived from the EEG are dependent upon the signal processing technique used. Although the results with Shannon entropy and SEF were not so desirable, they may result better in combination with other relevant features. Researchers have used combination of different entropy and complexity measures to estimate DOA [5]. To extract more robust features further works must be done on the signal artifact rejection and denoising of the raw EEG. For future we intend to add some other features and examine different combination of them as an input to the fuzzy system.

Although EEG has sufficient information of DOA but it can't monitor the whole complexity of the anesthesia. So combining EEG features with hemodynamics information and also measurements of muscle relaxation may result to more confident indices of depth of anesthesia.

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