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Estimating the depth of anesthesia using fuzzy soft computation applied to EEG features

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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 methods. A clinical study was conducted on 22 patients to construct subsets of reference data corresponding to four well-defined anesthetic states: awake, moderate anesthesia, surgical anesthesia and isoelectric.

Statistical analysis of features was used to design input membership functions (MFs). The input space was partitioned with respect to the derived MFs and the training data was used to label the partitions and extract efficient fuzzy if-then rules. Consequently, the fuzzy rule-base index (FRI) is derived between 0 (isoelectric) to 100 (fully awake) using fuzzy inference engine and designed output MFs.

We also applied the same features to an adaptive network-based fuzzy inference system (ANFIS) derived without any prior knowledge. The results show that FRI correlates more with the clinically accepted DOA index, CSI^{TM} (CSM, Danmeter, Denmark). In addition to this achievement the main idea behind this study is to simplify the mutual knowledge exchange between the human expert and the machine, leading to enhance both interpretability of the results and performance of the system.

Keywords: Electroencephalogram (EEG), fuzzy logic, depth of anesthesia, spectral analysis, linguistic rules

1. 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 movement during surgery. Neither plasma nor the effect site concentrations of the drugs are direct measures of clinical effect. 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 (SEF), median frequency and the relative

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and total power in the classical frequency bands [1–3]. Using parameters based on bispectrum made a progress in EEG-based anesthesia monitoring [4–6]. 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 [7–10]. 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 [11].

Although these parameters can distinguish well between awake and anesthetized states, they don't behave monotonically during transition between wakefulness and deep isoelectric states [2]. So we can't utilize them individually to continuously monitor anesthetic state changes during different phases of anesthesia and it is essential to utilize an efficient system to integrate these features.

Computational intelligence methods comprising fuzzy logic, neural networks and evolutionary computing have shown a promising prospective to make a suitable decision according to combination of features. In depth of anesthesia studies some efforts have been made to combine EEG features using neural networks and neuro-fuzzy inference systems [8,12,13], however the lack of interpretability in these systems led us to use a fuzzy knowledge based model.

Fuzzy logic, which is known as the oldest and most reported soft computing area, provides an effective tool for describing the characteristics of a system that is too complex or ill-defined to admit precise mathematical analysis. This theory is based on approximate reasoning which plays a major role in human thought process. Roughly, the aim of fuzzy logic is to build a flexible information processing system which provides soft decision strategy resembling human decision making [14].

The concept of fuzzy sets can be used at both the feature and classification levels. At feature level, it can be applied to represent input data as an array of membership values signifying the degree of possession of certain properties and also to represent linguistically phrased input features. At the classification level, it can be used for representing multiclass membership of objects, and for providing an estimate (or representation) of missing information in terms of membership values. In other words, fuzzy set theory provides a concept of embedding; we find a better solution to a crisp problem by looking in a large space at first, which has different (usually less) constraints and therefore allows the algorithm more freedom to avoid errors forced by commission to hard answers in intermediate stages [14,15].

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 [16,17]. 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 are 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 in conjunction with a FIS. To design input memberships of the fuzzy system, histogram analysis of these features have been done over 4 defined anesthetic states. Also we have used genetic algorithm to tune the MFs and to reduce the number of rules. Eventually we compared our proposed index naming FRI with CSI recorded from the CSM monitor and an ANFIS derived index using the same features.

2. Protocol design and data collection

22 patients, having ASA (American Society of Anesthesiologists) grade I or 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 5 mg/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 75 μg/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 values including it's depth of anesthesia index, CSI, Signal Quality Index (SQI), "EMG" percent and Burst Suppression (BS) percent were stored for later analysis.

CSI grades the anesthetic depth between 0 and 100. CSI close to 100 indicates awake and CSI around zero belongs to patients with deep anesthesia or close to coma. Adequate anesthesia for surgical processes is related to CSI between 40 and 60 and CSI 60–80 reveals moderate or light anesthesia. During the maintenance of anesthesia if CSI was greater than 60 or anesthesiologist assessments were showing lightness of anesthesia, thiopental was induced.

We used a Nerve Stimulator (Xavant technology, South Africa) to quantify the muscle tone. It stimulates the ulnar nerve through two superficial electrodes and records the thumb reflex using a ceramic accelerometer. We applied the routinely used stimulation patterns: train of four (per min) and post titanic count (per 6 mins) and the results were documented. Neuromuscular blocking agent was repeated due to these measurements.

Hemodynamic parameters i.e. blood pressure, heart rate, blood O_2 saturation and also the time occurrence of movements, intubation, extubation or gagging of the patient were manually recorded. The exact time and dose of all drug infusions were also noted.

In this study we have defined four anesthetic states due to all the measured parameters including time schedule of drugs (specially hypnotics), muscle relaxation and of course the anesthesiologists assessments. These states contain awake, moderate anesthesia, surgical anesthesia and isoelectric state. Four reference EEG database containing 15 minutes (900 epochs) have been recorded as follows:

– Awake reference: recorded from 3 healthy adult subjects. They were asked to keep their eyes closed and minimize the muscle activity while concentrating on a mental task.
– Moderate reference: extracted from 14 patients during transient phases of anesthesia (induction or recovery). After induction, due to time of drug injection and knowing the maximum influence time of it, we extracted periods of moderate anesthesia. In the recovery phase, periods of EEG a few minutes after closing all the drugs were used as moderate reference data.
– Anesthetized reference: extracted from 10 patients during steady state anesthesia. These data were determined as periods more than 5 minutes away from last changes in the drug pattern and also including no symptoms of awareness or noticeable hemodynamic changes.
– Isoelectric reference: recorded from a subject close to coma in ICU.

We divided our data sets 2:1 for training and testing respectively. So, we had four 1×900 vectors as training sets and four 1×300 vectors as testing sets corresponding to the four classes.

3. Feature extraction

A variety of features have been used in DOA studies, but only some have made good correlation with clinical experiments. Our previous study demonstrated that a vector of features containing alpha ratio, beta ratio, theta ratio and BS can distinguish better between different states of anesthesia compared with combinations of SEF or Shannon entropy [18]. Therefore we used these features in the present study.

3.1. Spectral features

As mentioned above, 3 spectral features including: alpha-ratio, beta-ratio and theta-ratio have been used here. Different methods can be used in estimating the power spectrum. We performed power spectral analysis using periodogram. Epoch length of EEG acquisition was 4s and the window shifting was 1 s.

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

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

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

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

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

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

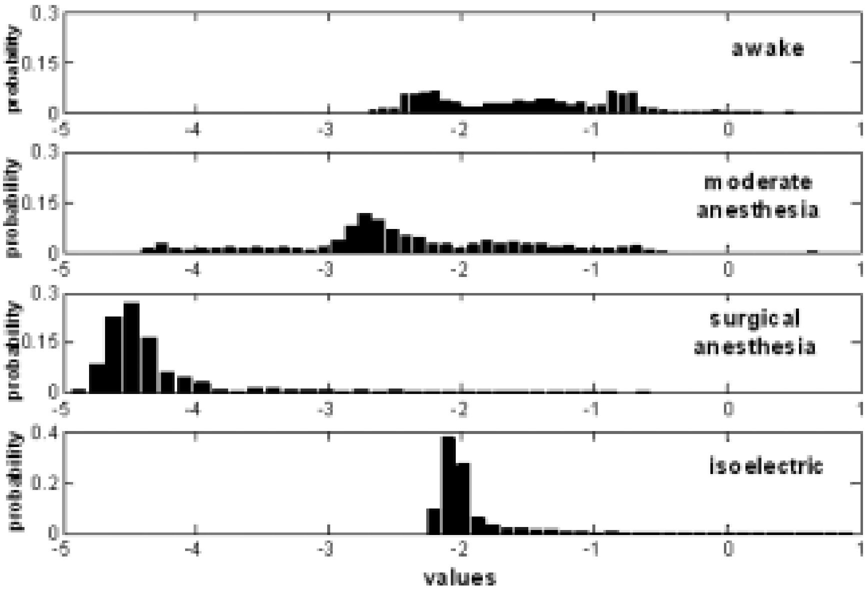
3.2. Burst suppression ratio

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 [19].

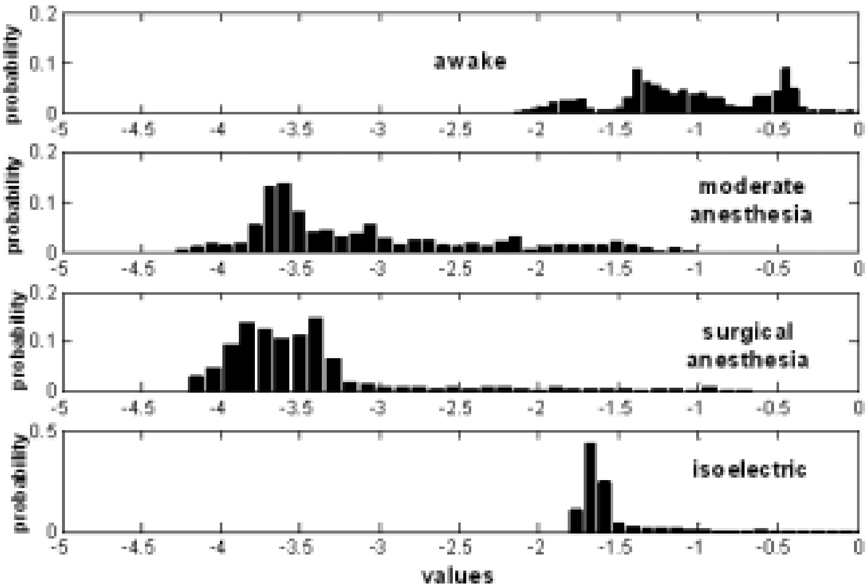
For comparison of results with CSI we used these values that are the same with burst suppression calculation in CSI.

4. Statistical analysis of features

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



(A)

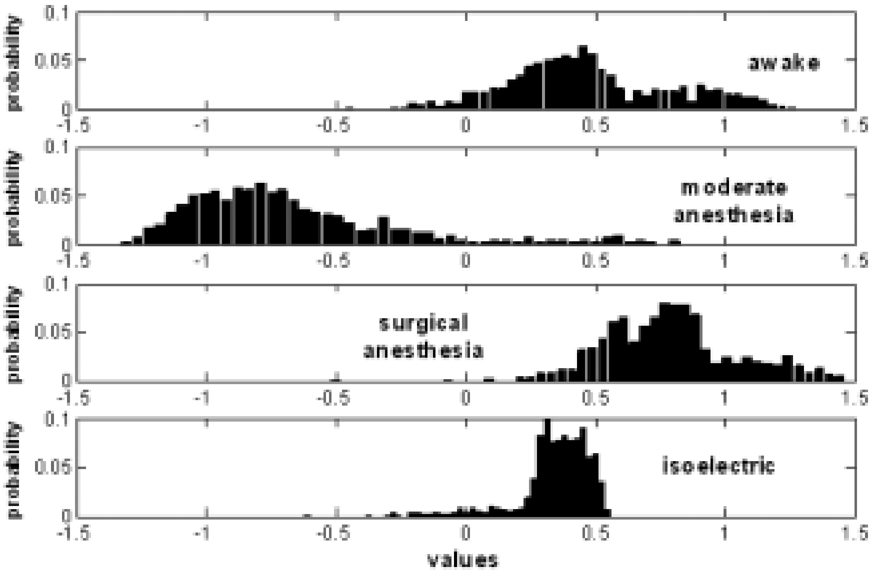


(B)

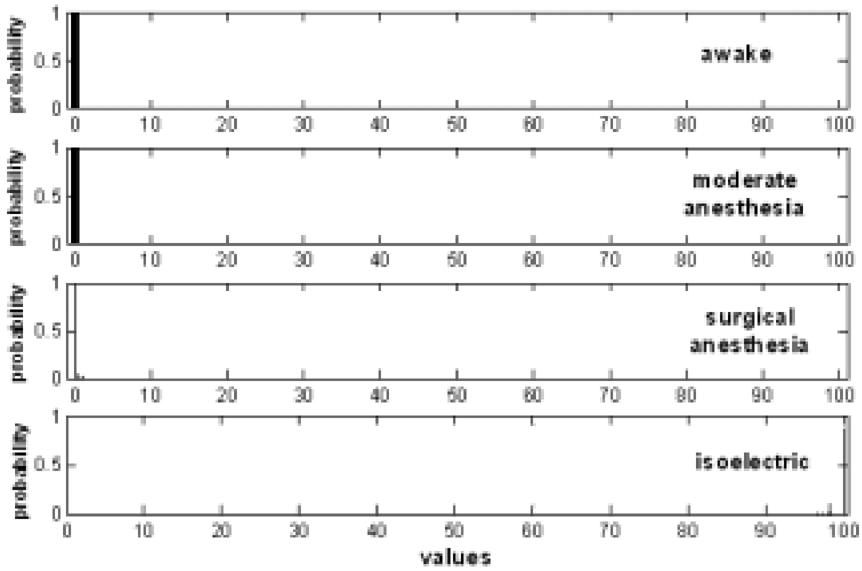
Fig. 1. Histogram analysis of (A) alpha ratio, (B) beta ratio, (C) theta ratio and (D) burst suppression.

In order to see distribution of features over different classes (awake, moderate, general anesthesia, isoelectric), we compared PDF of the features over training epochs of 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. 1A) general anesthesia state values are well apart from other states.



(C)



(D)

Fig. 1, continued.

Figure 1B shows that although moderate and anesthetized states result in nearly similar beta values but awake values of beta is well distinguishable. Theta histogram (Fig. 1C) 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 3 features, because the last feature named burst suppression can detect periods of isoelectricity clearly. Figure 1D illustrates this fact well. Statistical analyzing of features declared our first hypothesis that none of the features can individually estimate the depth of anesthesia in all states.

5. Constructing fuzzy system

As we mentioned former, here we utilized soft computing characteristic of fuzzy logic in order to combine the extracted features efficiently. Consequently, the designing process was conducted in following steps:

– Assigning suitable MFs for input and output space.
– Deriving fuzzy if-then rules from training patterns.
– Determining fuzzification and defuzzification methods and the properties of fuzzy inference system.

Note that in this part we pursued two roughly distinct aims. First we intended to allocate one of four anesthetic labels to each new pattern and then, as our major goal, to derive a continuous index in [0 100] describing the patient state with more precision.

5.1. 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 of training set (histogram analysis of data in Fig. 1). Figure 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.

5.2. Constructing fuzzy if-then rules

There are several ways for rule induction from labeled data. A rule classifier can be built by recursive partitioning, that is, by building a decision tree, which is then reexpressed as a rule set in a straightforward fashion. A rule is simply a path from the root to a terminal node, and the tree itself is a disjunction over all these rules (paths). In fuzzy decision trees, the comprehensibility of rules generated based on decision tree and the expressive power of fuzzy sets are combined to enhance the classification performance. An alternative way of inducing decision rules is by set covering. In this approach, rules are created one at a time, and the examples covered by the new rules are removed from the training set. Another approach is to construct rules with respect to distribution pattern of the data. In this way, first the input space is partitioned to several sub-space and then each sub-space is assigned to one class based on the comparison of different class labels of train set located in that partition. Here, the difference between crisp rule induction and fuzzy one is the crisp and soft natures of the partitions' boundaries. In this study, we chose third approach for rule induction (i.e. partitioning the input space), since this approach is both intuitive and straightforward and inherently eliminates redundancy that the former approaches may be suffered from. Ishibuchi et al. [20] proposed a mathematical framework for this aim which we applied in our study. Here is the summary of the rule building procedure:

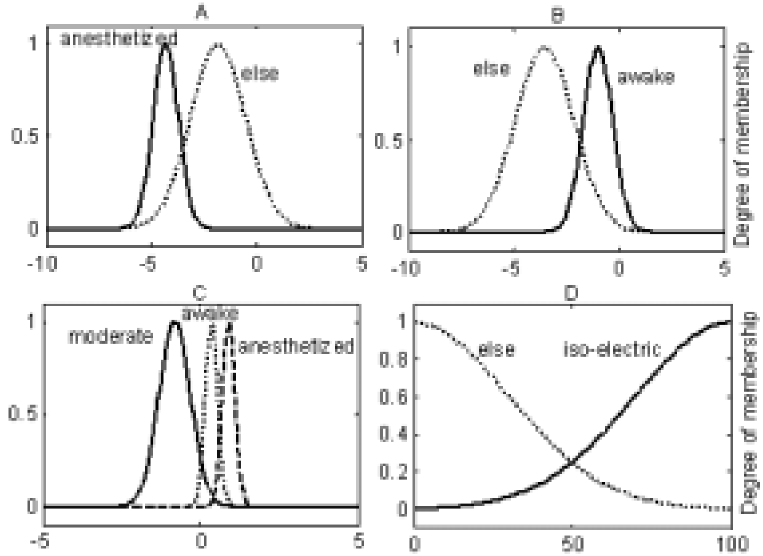


Fig. 2. Initial membership functions of the selected features: alpha ratio (A), beta ratio (B), theta ratio (C), and burst suppression (D).

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

Suppose that we have m training epochs (m is 2400 in this study) $\mathbf{x}_1$, $\mathbf{x}_2$, ..., $\mathbf{x}_m$, each of which is described by 4 features as $\mathbf{x}_p = (x_{p1}, x_{p2}, x_{p3}, x_{p4})$, $p = 1, 2, \ldots, m$, are given as training pattern. We assume that all m epochs already have one of the labels of the 4 classes ($m \gg 4$): 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_i^1 *and* x_{p2} *is* A_j^2 *and* x_{p3} *is* A_k^3
and x_{p4} *is* A_l^4, *then* x_p *belong to class* C_{ijkl}
with $CF = CF_{ijkl}$.
$i = 1, 2;\ j = 1, 2;\ k = 1, 2, 3;\ l = 1, 2$ (4)

where R_{ijkl} is the label of the fuzzy if-then rule, A_i^1, A_j^2, A_k^3 and A_l^4 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.

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:

$$\beta_{CT} = \sum_{x_p \in CT} \mu_i(x_{p1}).\mu_j(x_{p2}).\mu_k(x_{p3}).\mu_l(x_{p4}) \tag{5}$$

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 Eq. (4).

Step 2: Find Class X(CX) such that

$$\beta_{CX} = \max\{\beta_{C1},\ \beta_{C2},\ \beta_{C3},\ \beta_{C4}\} \tag{6}$$

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 $A_i^1\times A_j^2\times A_k^3\times A_l^4$ 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 Eq. (6).

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

$$CF_{ijkl} = \frac{(\beta_{CX} - \beta)}{\sum_{T=1}^{M} \beta_{CT}} \tag{7}$$

Where

$$\beta = \sum_{\substack{T=1 \\ T \neq X}}^{M} \frac{\beta_{CT}}{M-1} \tag{8}$$

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 all classes.

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

1) if all the patterns in the fuzzy subspace $A_i^1\times A_j^2\times A_k^3\times A_l^4$ belong to the same class, then $CF_{ijkl} =$ 1 (the maximum certainty). In this case, it is certain that any patterns in $A_i^1\times A_j^2\times A_k^3\times A_l^4$ 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 $A_i^1\times A_j^2\times A_k^3\times A_l^4$ belongs to the consequent class of the generated fuzzy if-then rule.

5.3. Classifying a new pattern

Let us assume that we have $2\times 2\times 3\times 2 = 24$ 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:

$$\alpha_{CT} = \mu_w(\mathbf{x}_p).CF_w = \max\{\mu_r(\mathbf{x}_p).CF_r \mid r = 1,\, 2,\, \ldots\, ,\, 24\} \tag{9}$$

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:

$$\mu_w(\mathbf{x}_p) = \mu_{wi}(x_{p1}).\mu_{wj}(x_{p2}).\mu_{wk}(x_{p3}).\mu_{wl}(x_{p4}) \tag{10}$$

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 [21]'

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.

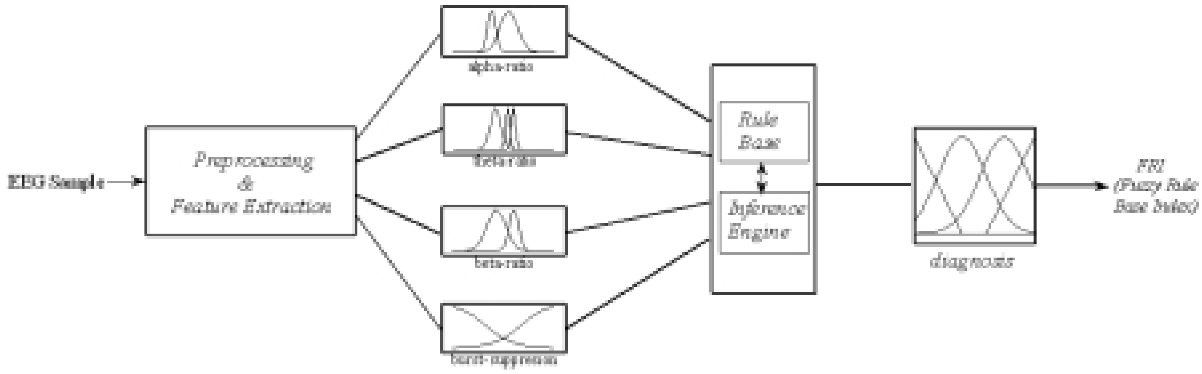


Fig. 3. The block diagram of the fuzzy system.

5.4. 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 [22]: 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 level based on the intuitive insight to different stages of anesthesia. Hence we assigned 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. The output value represents the fuzzy rule base index so called FRI.

6. Implementing an ANFIS model

In order to compare our results, we fed the same features used in the FIS system to a black box ANFIS structure, i.e. no prior knowledge is injected to the system in designing initial MFs and the whole knowledge acquisition process is performed by a neural learning strategy. In this way we utilized ANFIS system embedded in Matlab toolbox which uses a hybrid learning algorithm to identify parameters of Sugeno-type fuzzy inference system. It applies a combination of least squares method and the back propagation gradient descent algorithm for training FIS MFs parameters.

The training data is a 2400×5 matrix with all but the last column containing input data, while the last column containing single vector of output data. The output of the system is a unitless index between 0 to 100.

Table 1
The average classification performance of different methods over 4 classes

Method	Accuracy
FRI	96.75%
ANFIS	94.33%
LDA	91.42%

7. Results

We pursued two different goals in this study. Firstly to find out how can single features 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.

7.1. Classification performance of fuzzy classifier

For classifying anesthesia states to 4 classes we trained the proposed fuzzy classifier with 4 training 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 IV-C. 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 also implemented linear discriminant analysis (LDA) and ANFIS on our data sets to compare their performance with our proposed method. The classification accuracies are demonstrated in Table 1.

Apparently, the results show excellence of our proposed approach compared with others.

7.2. 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 applied the features as inputs to the fuzzy system. The shape of input membership functions was designed with respect to histograms of features over reference data sets. Figure 2 shows the input membership functions. We constructed fuzzy if-then rules and fuzzy inference system to drive DOA index (FRI). In order to test the performance of system we calculated FRI for all the patients in their complete session of data under anesthesia. We calculated 4 mentioned features for each epoch (1 s) of data and used them to calculate the DOA index for that epoch. Figure 4 shows FRI and the ANFIS derived index in comparison with CSI (device calculated index) for a typical patient (no. 19).

In order to increase interpretability it was essential to eliminate the redundant rules. We used genetic algorithm for this purpose [20]. We defined the fitness function as the difference between the derived index (FRI) and CSI values of a typical patient (19th patient). Remaining only 5 rules, the correlation improved up to 95.97%. Table 2 illustrates the resulting rules.

Considering that genetic algorithm made optimizations based on minimizing the defined error for patient 19, we examined the resulted parameters on the other patients. To compare the result of this strategy with prior results (FRI using 24 rules and ANFIS derived index) we calculated the Pearson correlation coefficient between each of the indices and CSI. Table 3 demonstrates the results according to which we can infer that the rule elimination strategy not only enhances the interpretability but also in general sense promotes the performance of the system.

Table 2
The final fuzzy if-then rules

Rule	If Alpha ratio is	And Beta ratio is	And Theta ratio is	And BS is	Then the diagnosis is	weight
1	Anesthetized	Awake	Awake	Else	Awake	0.595
2	Anesthetized	Awake	Anesthetized	Else	Awake	0.545
3	Else	Else	Moderate	Else	Moderate	0.712
4	Anesthetized	Else	Anesthetized	Else	Anesthetized	0.776
5	Else	Else	Moderate	Isoelectric	Isoelectric	1

Table 3
Pearson correlation of DOA indices with CSI for all patients

Patient No.	FRI (using 24 rules)	FRI (using only5 rules)	ANFIS derived index
1	81.73	85.02	70.31
2	91.62	94.12	70.08
3	83.42	82.42	79.17
4	90.12	90.06	84.99
5	87.25	87.11	86.34
6	90.10	92.45	84.84
7	86.47	86.96	85.38
8	87.92	90.75	78.58
9	97.51	96.88	92.76
10	81.46	72.84	84.04
11	94.25	93.83	88
12	91.33	94.25	90.58
13	89.12	89.68	81.88
14	83.41	79.88	90.47
15	70.40	76.67	73.04
16	97.26	97.18	97.15
17	81.02	78.17	82.22
18	89.72	87.49	80.58
19	94.06	95.97	91.15
20	85.97	85.02	88.54
21	71.97	74.17	55.57
22	81.86	84.84	74.13
Mean (**SD**)	**86.73** (**7.03**)	**87.08** (**7.32**)	**82.26** (**9.37**)

Another point that should be argued here is that both of the original and modified fuzzy systems have higher similarity with CSI index than the ANFIS index. This highlights the fact that the initial adjustment of MFs according to class-conditional distributions of training data is a significant factor that neural learning (in ANFIS structure) can not replace it.

In Fig. 5 fuzzy rule base index (FRI), ANFIS derived index and CSI are plotted for the same patient. It can be inferred from this figure that FRI admits more acceptable values in the recovery phase of the anesthesia.

8. Discussion

In this study four database of distinct anesthetic states, comprising awake, moderate anesthesia, surgical anesthesia and isoelectric, were constructed. Spectral and time domain features from the raw EEG were extracted. In contrast with prior studies in which distributions of features in just two states of anesthesia (awake and anesthetized) is taken into account, here we investigated them over four defined states that led us to well tune initial fuzzy MFs.

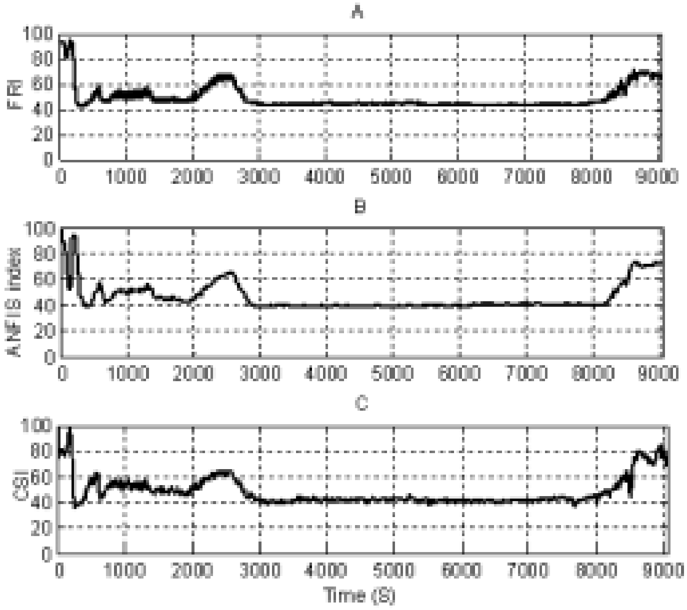


Fig. 4. Fuzzy rule base index (A) using 24 rules compared with ANFIS derived index (B) and CSI$^{\mathrm{TM}}$ (C) for patient no. 19.

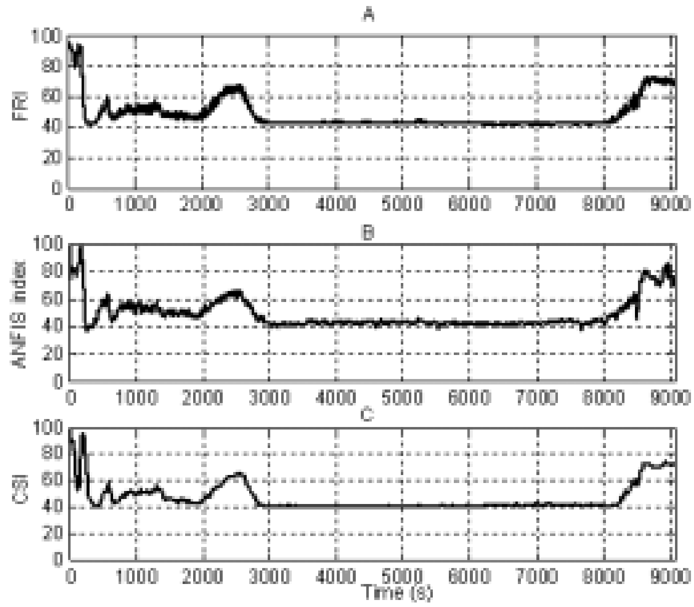


Fig. 5. Fuzzy rule base index using 5 rules (selected with genetic algorithm) (A) compared with ANFIS derived index (B) and CSI$^{\mathrm{TM}}$ (C) for patient no. 19.

The proposed fuzzy rule based system has following advantages: 1) Classification results are so improved in comparison with LDA and ANFIS classifiers; 2) Assigning appropriate output MFs based on intuitive insight of different anesthetic levels makes the transition between continuous levels gradually rather than abrupt. It is essential in the operation room to prevent patient awareness during surgery.

Needless to say, such an index can help the anesthesiologist to monitor the anesthetic depth continuously, thus preventing the patient from being conscious; 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 5 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. The most useful parameters which are derived from the EEG are dependent upon the signal processing technique used. 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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