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Brain tumor characterization using the soft computing technique of fuzzy cognitive maps

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Abstract

The characterization and accurate determination of brain tumor grade is very important because it influences and specifies patient's treatment planning and eventually his life. A new method for characterizing brain tumors is presented in this research work, which models the human thinking approach and the classification results are compared with other computational intelligent techniques proving the efficiency of the proposed methodology. The novelty of the method is based on the use of the soft computing method of fuzzy cognitive maps (FCMs) to represent and model experts' knowledge (experience, expertise, heuristic). The FCM grading model classification ability was enhanced introducing a computational intelligent training technique, the Activation Hebbian Algorithm. The proposed method was validated for clinical material, comprising of 100 cases. FCM grading model achieved a diagnostic output of accuracy of 90.26% (37/41) and 93.22% (55/59) for brain tumors of low-grade and high-grade, respectively. The results of the proposed grading model present reasonably high accuracy, and are comparable with existing algorithms, such as decision trees and fuzzy decision trees which were tested at the same type of initial data. The main advantage of the proposed FCM grading model is the sufficient interpretability and transparency in decision process, which make it a convenient consulting tool in characterizing tumor aggressiveness for every day clinical practice.

Keywords: Soft computing; Computational intelligence; Fuzzy logic; Fuzzy cognitive maps; Classification; Brain tumors

1. Introduction

Brain tumors are considered as one of the most lethal and difficult to identify and be treated forms of cancer [1,2]. Pathologists evaluate the aggressiveness of brain tumors by visually examining tissue section (biopsies) based on guidelines determined by the World Health Organization (WHO) [3]. According to the WHO grading system, the appearance of certain histopathological features, such as cellularity, pleomorphism, mitosis, necrosis, vascular proliferation, and apoptosis, classify tumors on the basis of their aggressiveness as low or high-grade tumors. Low-grade tumors are less insistent and are associated generally with good prognosis. High-grade tumors are more aggressive, and are characterized by rapid growth and tendency to invade to nearby tissues [4]. The characterization of the degree of tumor grade is the most critical step when diagnosing brain tumors because it specifies treatment planning and patient management [5].

Although the WHO grading scheme provides accurate definitions for tumor grade determination, every pathologist gives different relative importance to each of the grading criteria. Thus, there is significantly promoting inter and intra observer variability that has been shown to significantly influence the quality of diagnosis [6].

Computer based techniques, have been extensively examined for improving grade diagnosis [7–11] and until today remains an

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active research area [12–14]. Significant efforts on assisting tumor characterization have been focused on the application of pattern recognition techniques incorporating a variety of quantified nuclear characteristics, mainly by means of image analysis [15]. Although the reported accuracy on tumor characterization of the proposed computerized methods is quite promising, still these approaches have not gained wide acceptance among the pathologists, for every day clinical practice. The main reason might be the lack of standardized procedures, because these computerized grading systems are designed following different and most of the times specific staining protocols to imprint nuclei morphological characteristics, and they have employed modifications of the WHO grading system. Another possible reason might be the deficiency of the existed methods to assist medical decision with a transparent and interpretable way. The latter is very important for computer aided medical diagnosis where the demand for reasoning and explanation is of main priority.

In this work, we propose an advanced system based on fuzzy cognitive maps (FCMs) for the classification of the astrocytomas as low or high-grade, following the widely accepted WHO classification system. The proposed system determines the degree of tumor abnormality based solely on qualitative information, in a similar way that the experts–histopathologists visualize regularly stained Hematoxylin–Eosin tissue biopsies.

The FCMs constitute an attractive knowledge-based method, combining the robust properties of fuzzy logic and neural networks [16]. More specifically, FCMs is a workable soft computing methodology that has been successfully applied in a number of discipline scientific areas. FCMs have been employed to model the causal inference [17], to make decision analysis in geographic information systems [18], to develop decision support systems [19,20], to perform failure modes and effects analysis in the process industry [21], and to model supervisory control systems [22].

In the medical application area, FCMs used to model and analyze the radiotherapy process and they successfully used for decision-making in radiation therapy planning systems [23]. FCMs were used to analyze the problem of specific language impairment diagnosis in a critical way using several experts' opinions [24]. In the tumor grading area, an FCM Grading Tool proposed to characterize bladder tumors, working exclusively on the qualitative assessments of histopathological variables [25–27].

Here the soft computing technique of FCMs is proposed to model the process of grading brain tumors and develop an FCM grading model. This approach not only automates the diagnostic process of tumor grading, but also builds a human-friendly assisting tool, compatible with clinical routine, exhibiting interpretability, and providing some insight on how it derives its outputs. The latter might be beneficial for the pathologists for better evaluation and understanding, of the diagnostic criteria for brain tumors characterization.

This paper is structured in the following way: Section 2 briefly describes the construction methodology of FCMs and presents the applicability of learning algorithms. In Section 3, the specific developing methodology of the FCM model for brain tumor grading is given. Section 4 provides the material used for the specific medical problem. Section 5 evaluates the FCM grading process and presents comparison results with existing techniques, such as decision trees and fuzzy decision trees. Finally, Section 6 discusses the results of the tumor classification and concludes the advantages of the proposed methodology.

2. A brief description of fuzzy cognitive maps

Fuzzy Cognitive Map is a soft computing technique that follows a reasoning approach similar to the human reasoning and human decision-making process. Soft computing methodologies have been investigated and proposed for the description and modelling of complex systems [22]. The FCM model incorporates the available knowledge and expertise in the kind of concepts and in the type and value of the interconnections between concepts. Generally, concepts reflect attributes, characteristics, qualities, variables and states of the system. Each concept represents one of the key-factors of the modeled system and having a value A_i. The interconnections between concepts of FCM signify the cause and effect relationships that a concept has on the others. These causal relationships between concepts are illustrated by weighted links connecting the nodes of the FCM [28].

The weighted interconnections show the direction and the degree with which a concept influences the interconnected concepts [23]. Each interconnection e_{ji} between two concepts C_i and C_j, has a weight, belonging to the interval $[-1, 1]$. The sign of weight indicates whether the relation between the two concepts is direct or inverse. Fig. 1 illustrates the graphical representation of a simple FCM.

The methodology for developing FCMs is described analytically in [23] and it is based on a group of experts who are asked to define concepts and describe relationships among concepts. Every expert describes each interconnection with a fuzzy rule; the inference of the rule is a linguistic variable, which determines the grade of causality between the two concepts. For each interconnection the inferred fuzzy variables are all aggregated and through the defuzzification method of Center of Gravity [24], an overall linguistic weight is produced, which is transformed to a numerical weight e_{ji}, belonging to the interval $[-1, 1]$ which represents the overall suggestion of experts.

The value A_i of each concept C_i is calculated by collecting–aggregating the influence of the interconnected concepts to the

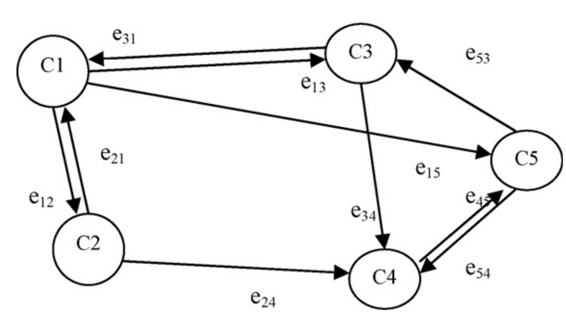


Fig. 1. A simple fuzzy cognitive map.

specific one, by applying the following rule:

$$A_i^{(k+1)} = f\left(A_i^{(k)} + \sum_{j \neq i; j=1}^{N} A_j^{(k)} \cdot e_{ji}\right) \quad (1)$$

where $A_i^{(k+1)}$ is the value of concept C_i at time $k+1$, $A_j^{(k)}$ the value of concept C_j at time k, and f is a sigmoid threshold function.

The FCM takes different types of initial values for its concepts: real values derived from measurements, are normalized in [0, 1], and fuzzy values qualitatively described by experts or other sources. When the FCM is initialized is free to interact.

This interaction of the concepts continues until the FCM model:

- Reaches an equilibrium at a fixed point, where the output values are stabilized at fixed numerical values.
- Exhibits limit cycle behavior, where the output concept values are falling in a loop under a specific-time period.
- Exhibits a chaotic behavior, where each concept value is reaching a variety of numerical values in a non-deterministic, random way.

Simplest FCMs act as asymmetrical networks of threshold or continuous concepts and converge to an equilibrium point or limit cycles. FCMs differ from neural networks in the way they are developed as they are based on extracting knowledge from experts. FCMs have non-linear structure of their concepts and represent global feedback dynamics [30].

2.1. Constructing fuzzy cognitive map

The development and construction method of FCM has great importance for its potential to sufficiently model a system. Proposed methods are dependent on the group of experts who operate, monitor, supervise the system and they know its behaviour. This methodology extracts the knowledge from the experts and exploits their experience of the system's model and behaviour [16].

The group of experts determines the number and kind of concepts that comprise the FCM model. An expert from his/her experience knows the main factors that describe the behaviour of the system; each of these factors is represented by one concept of the FCM. Experts know which elements of the systems influence other elements; for the corresponding concepts they determine the negative or positive effect of one concept on the others, with a fuzzy degree of causation. In this way, an expert transforms his/her knowledge in a dynamic weighted graph, the FCM. Following the developing methodology experts are forced to think about and they describe the existing relationship between the concepts and thus justify their suggestions. Each expert, indeed, determines the influence of one concept on another as "negative" or "positive" and then evaluates the degree of influence using a linguistic variable, such as "strong influence", "medium influence", "weak influence", etc.

More specifically, the causal interrelationships among concepts are declared using the variable *Influence* which is interpreted as a linguistic variable taking values in the universe $U = [-1, 1]$. Its term set T(influence) is suggested to comprise seven variables. Using seven linguistic variables, an expert can describe in detail the influence of one concept on another and can discern between different degrees of influence. The seven variables used here are: T(influence) = {very very low, very low, low, medium, high, very high, and very very high}. The corresponding memberships functions for these terms are shown in Fig. 2 and they are: $\mu_{\text{vvl}}, \mu_{\text{vl}}, \mu_{\text{l}}, \mu_{\text{m}}, \mu_{\text{h}}, \mu_{\text{vh}}$ and μ_{vvh}.

Thus, each interconnection is described by an expert with a fuzzy linguistic variable from the determined set, which associates the relationship between the two concepts and determines the grade of causality between the two concepts. Then, all the proposed linguistic variables suggested by experts, are aggregated using the SUM method and an overall linguistic weight is produced, which with the defuzzification method of Center Of Gravity [29], is transformed to a numerical weight w_{ji}, belonging to the interval $[-1, 1]$. A detailed description of the development of FCM model is given in [22].

2.2. Learning algorithms for fuzzy cognitive maps

Utilization of appropriate learning algorithms can overcome the most significant weaknesses of the FCMs, namely the potential convergence to undesired regions. Thus, learning algorithms recalculate the weights when new strategies are adopted. The learning procedures increase the efficiency and robustness of FCMs, contributing to advanced FCMs by modifying the FCM weight matrix. Moreover, the learning rules supply FCMs with useful characteristics such as the ability to learn arbitrary non-linear mappings, and the capability to generalize situations, adaptively.

FCMs are constructed by experts who determine concepts and causality among them. This approach may yield to a distorted model, since sometimes experts may not consider appropriate factors and they may assign inappropriate causality weights among FCM concepts. The best conductance of FCMs can be updated by combining them with neural network characteristics and integrating their advantages.

The learning algorithms, proposed for FCMs are mostly based on ideas coming from the field of artificial neural networks training. Recently, there have been proposed two approaches for FCM training, the Active Hebbian Learning

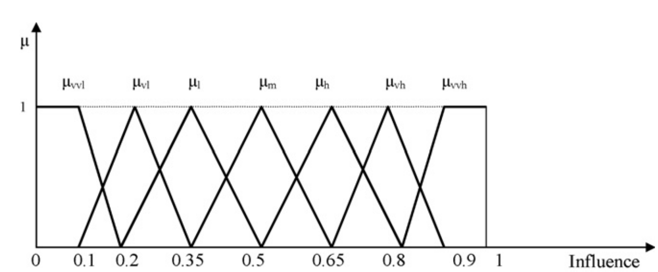


Fig. 2. The seven membership functions corresponding to each one of the seven linguistic variables.

(AHL) and the Non-linear Hebbian Learning (NHL) algorithms [31–33]. The AHL algorithm has been introduced and implemented successfully for process control problems and for characterizing bladder tumors [31,25]. This algorithm takes into consideration the initial experts' knowledge and experience, starting from the initial values of elements of the weight matrix which are derived from the summation of experts' opinions.

The AHL algorithm adapts all the weights of the FCM model based on an acyclic fragment approach for concepts (asynchronous activation and interaction among concepts exploiting the experts' knowledge). Moreover, it is based on an asynchronous decision-making process exactly the same as human does and it takes into consideration the input values of concepts so that to strengthen or weaken the FCM causal links between concepts increasing the classification capabilities of the FCM.

The novelty of the algorithm is based on introducing the sequence of influence from one concept to others, in this way a cycle is dividing in steps. When the experts develop the FCM, they are asked to determine the sequence of activation concepts, the activation steps and thus the activation cycle. At every activation step, one (or more) concept(s) becomes activated concept(s), triggered by the other interconnecting concepts, which in turn, at the next simulation step, may become activation concept(s). When all the concepts have become activated concepts, the simulation cycle is closed and a new one starts till the system converges into an equilibrium region.

According to AHL algorithm the experts determine the sequence of activation concepts and they select a limited number of concepts as outputs for each specific problem which defined as the Activation Decision Concepts. These concepts stand for the main factors and characteristics of the system and their values represent the final state of the system. The expert's intervention is the only way to address the definition of input and output concepts. The AHL algorithm extracts the most valuable knowledge and experience of experts and increases the applicability of FCMs.

The AHL algorithm uses the active weight adaptation rule which has the following mathematical form:

$$e_{ji}(k) = (1-\gamma)\cdot e_{ji}(k-1) + \eta \cdot A_j^{\mathrm{act}}(k-1) \cdot [A_i(k-1) - e_{ji}(k-1)\cdot(A_j^{\mathrm{act}}(k-1))] \quad (2)$$

where the parameters η, γ are the learning rate parameters, taking small values [31].

For the AHL algorithm termination, two criteria have been used. The first criterion is referred to the minimization of an objective function and the second one is referred to the minimization of the subsequent values of activation decision concepts for simulation cycle c. The training process implementing the AHL into an n-concept FCM is described analytically in [31]. The AHL algorithm has been proved that enhances the FCMs' effectiveness, flexibility and robustness [33].

3. Fuzzy cognitive map model for grading brain tumors

For this specific medical application our experts were histopathologists with deep knowledge and great clinical experience, affiliated with the department of Pathology, University Hospital of Patras, Greece. The three experts–histopathologists were asked to describe the conceptual methodology that they use in every day clinical practice to assign the grade of a tumor. Experts stated that they usually utilize eight concepts to judge for the tumor grading (see Table 1). These eight concepts are the main histopathological features and key characteristics, which encode the degree of tumor malignancy and are well documented in bibliography. Thus, the FCM model is consisted of these 8 concepts: C_1, the cellularity; C_2, the mitoses; C_3, the apoptosis; C_4, the multinucleated cells; C_5, the giant cells; C_6, the vascular proliferation; C_7, the necrosis; C_8, the pleomorphism. And there is a ninth concept on the FCM model representing the tumor grade [34].

Then, histopathologists were asked to describe the degree of influence between the concepts and they determine their interrelationship using the following IF–THEN rule to infer a linguistic weight representing the cause and effect relationship between every pair of concepts:

*IF value of concept C_i is **A** THEN value of concept C_j is **B** and thus the linguistic weight e_{ij} is **C***

where $\boldsymbol{A}$, $\boldsymbol{B}$, $\boldsymbol{C}$ are linguistic variables taking values in the range [0, 1].

The three linguistic variables, proposed by the three experts for each interconnection, are aggregated using the SUM method and so an overall linguistic weight is produced which is defuzzified with the Centre of Gravity method and finally a numerical weight for e_{ij} is calculated. Using this method all the weights of the FCM model are inferred. The developed FCM is shown in Fig. 3.

The three histopathologists–experts suggested that the degree of influence between concepts was described by a linguistic variable taking value in [0, 1] and its fuzzy set defined in Section 2.1, corresponds to a membership function shown in Fig. 2. It is noticeable that these membership functions have a finer distinction between grades in the lowest and highest end of the influence scale.

Two examples for the specific problem of astrocytomas are given:

IF a **small** change occurs in the value of concept C_4 (multinucleated cells) **THEN** a **small** change in the value of concept C_8 (pleomorpism) is caused.

Table 1
Main histopathological features of tumor grading

ID	Features (concepts)	Qualitative description
C1	Cellularity	Mildly, moderate, intense
C2	Mitoses	Present, absent
C3	Apoptosis	Present, absent
C4	Multinucleated cells	Present, absent, numerous
C5	Giant cells	Present, absent, numerous
C6	Vascular proliferation	Present, absent, intense
C7	Necrosis	Present, absent, intense
C8	Pleomorphism	Mildly, moderate, intense
C9	Tumor grade	Low, high

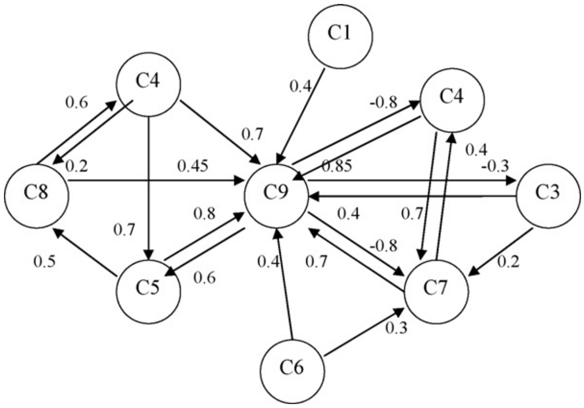


Fig. 3. The FCM model for grading brain tumors.

This means that: the influence from concept C_4 to C_8 is **low**.
IF a **high** change occurs in the value of concept C_2 (mitoses) **THEN** a **very high** change in the value of concept C_9 (tumor grade) is caused.
This means that: the influence from concept C_2 to C_9 is **very high**.

The advantage of this methodology is that experts do not have to describe the causality relationships using numerical values, but rather to describe qualitatively the degree of causality between concepts. The fuzzy rule for each interconnection is evaluated using fuzzy reasoning and the inferred fuzzy weight is defuzzified using the Center of Gravity defuzzification method. Thus, the initial weight matrix of the FCM is assigned.

To illustrate how numerical values of weights are produced the following example is given. The three experts described the interconnection between concept C_2 (nuclei) and concept C_9 (tumor grade) using the following rules:

1st Expert:
IF a *medium* change occurs in the value of concept C_2 **THEN** a *high* change at value of concept C_9 is caused.
Infer: The influence from C_2 to C_9 is ***very high***.
2nd Expert:
IF a *small* change occurs in the value of concept C_2 **THEN** a very *high* change in value of concept C_9 is caused.
Infer: The influence from C_2 to C_9 is ***very high***.
3rd Expert:
IF a *medium* change occurs in the value of concept C_2 **THEN** a very *high* change in value of concept C_9 is caused.
Infer: The influence from C_2 to C_9 is ***very very high***.

Fig. 4 illustrates the three suggested linguistic variables, for this particular example.

These linguistic variables (very high, very high and very very high) are summed and an overall linguistic weight is produced (also in Fig. 4), with which the defuzzification method of Center of Gravity is transformed into the numerical value of $e_{29} = 0.85$.

The same approach was used to determine all the weights of the FCM. A weight matrix $\mathbf{E}^{\text{initial}}$ gathering the initially suggested weights of all the interconnections among the concepts of the FCM model was produced.

$$\boldsymbol{E}^{\text{initial}} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0.4 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0.7 & 0 & 0.85 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0.2 & 0 & 0.4 \\ 0 & 0 & 0 & 0 & 0.7 & 0 & 0 & 0.2 & 0.7 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0.5 & 0.8 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0.3 & 0 & 0.4 \\ 0 & 0.4 & 0 & 0 & 0 & 0 & 0 & 0 & 0.7 \\ 0 & 0 & 0 & 0.6 & 0 & 0 & 0 & 0 & 0.45 \\ 0 & -0.8 & -0.3 & 0 & 0.6 & 0 & -0.8 & 0 & 0 \end{bmatrix}$$

The concept values correspond to the feature values that histopathologists assign in every day practice when they examine brain tumor astrocytomas on the microscope. They usually use fuzzy values (low, medium, high) to describe the qualitative characteristics of each concept that are shown in Table 1. The corresponding fuzzy sets for each one characteristic–attribute are summarized in Table 2.

To increase the classification ability of the FCM model, the Active Hebbian Learning (AHL) algorithm is utilized to adjust the weights of the FCM [31]. The main aspects of this algorithm

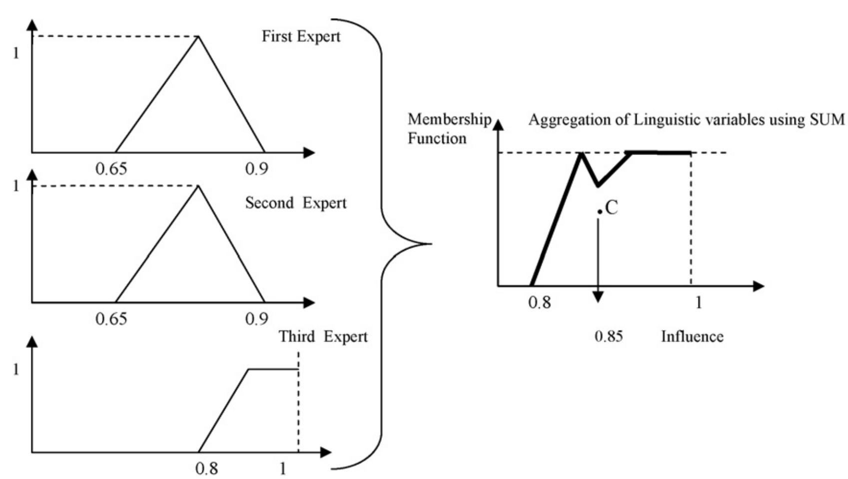
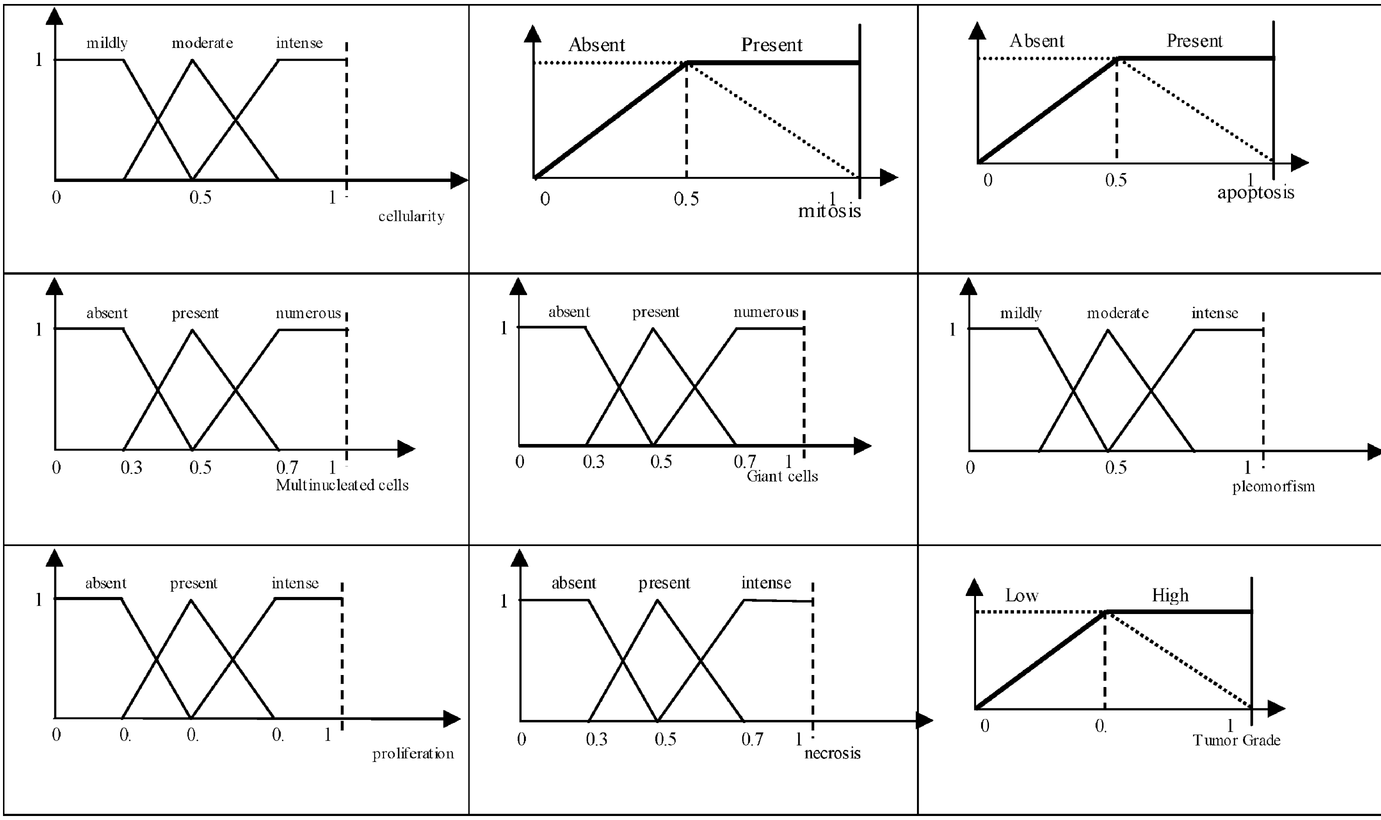


Fig. 4. Aggregation of three linguistic variables using the SUM technique. Point C is the numerical weight after defuzzification using the Center of Gravity method.

Table 2
Fuzzy sets for nine histopathological attributes



are the sequence of activation concepts, the activation steps and the activation cycle. The AHL algorithm follows an asynchronous decision-making process where experts select the number of attributes–concepts and their sequence with which are examined. In clinical practice, histopathologists first examine the cellularity and assign a qualitative value on it. This is the first activation step ($k = 1$). Then they examine mitosis and apoptosis which are the second activation step ($k = 2$). Next they examine the multinucleated cells and this is the third activation step ($k = 3$). Then they are looking for giant cells; this corresponds to the forth activation step ($k = 4$). Following, the examination of vascular proliferation and necrosis constitute the fifth activation step ($k = 5$). Finally, experts evaluate the pleomorphism which is the sixth activation step ($k = 6$) and the cycle is completed.

Fig. 5 depicts the sequence of activation of FCM concepts for each activation cycle.

After the FCM model development and the determination of the necessary specifications for the implementation of the AHL algorithm, the proposed FCM model for tumor grading was used to evaluate 100 cases (tissue biopsies) of brain cancer. For every case, the qualitative linguistic values for each concept was transformed in the interval [0, 1].

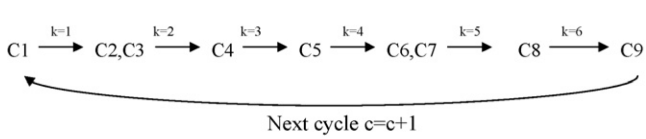


Fig. 5. Sequence of activation concepts for the cycle c.

For every case, FCM starts to interact through Eq. (1), where the weights e_{ji} are updated to $e_{ji}(k)$ at each iteration step k and they are recalculated through the AHL algorithm (Eq. (2)). The values of the learning parameters η, γ have been defined as $\eta = 0.02\exp(-0.2c)$ and $\gamma = 0.01\exp(-0.6c)$ [31].

After 4 cycles, FCM values converge in an equilibrium point (where no more changes occurred between subsequent values of concepts) and the value of C9 ‘‘Grade’’ is outlined. This value gives the decision about the degree of tumor malignancy.

The concepts of FCM have been described qualitatively by experts and have been converted into fuzzy sets with corresponding membership functions, given in Table 2. Then, the initial values of concepts are transformed into the range [0, 1] with quantification based on fuzzy sets theory [29,30].

FCM model interact and new values for concepts are calculated till the FCM tool reaches an equilibrium point where the values of concepts do not change any more. After this limited number of interactions for the FCM convergence, the value of concept C_9 represents the classification grade for the examining case.

4. Material

The clinical material is comprised of 100 Hematoxylin–Eosin stained biopsies of brain tumors collected from the Department of Pathology of the University Hospital of Patras, Greece. Tumors were classified by experienced staff (histopathologists) as low or high according to the WHO grading system. All cases were reviewed independently by the experts to safeguard reproducibility. Cases were classified following the WHO grading system [3] as follows: 41 cases as low-grade, and 59 as high-grade.

Following grade diagnosis, each case was evaluated retrospectively, using a set of eight, well documented in the bibliography histopathological criteria, which are essential for tumor grading (Table 1). Each criterion was accompanied by two, three or four possible values [25,34].

To design the FCM model for astrocytomas tumor grading, three experienced histopathologists played the role of experts who designed the FCM model following the developing methodology described previously [25,26].

5. Evaluation of fuzzy cognitive map grading model

The proposed FCM grading tool was evaluated for 100 cases. The value of the output-concept grade is essential and it categorizes the tumor as low and high-grade using a simple discrimination method.

Fig. 6 illustrates the final values of concept C_9 in the convergence region (we refer to this value as ‘‘Grade’’) for each one of the 100 brain tumor cases. The horizontal axis (X) gives the calculated values of ‘‘Grade’’ and the vertical axis (Y) represents the number of cases used. For low-grade cases the estimated ‘‘Grade’’ values are represented by ‘+’, and for high-grade cases the estimated ‘‘Grade’’ values are represented by ‘*’.

The classification task requires the determination of a decision or a threshold line. The minimum distance method was employed to determine the decision line defining each grade category. More specifically, using this method the mean values $m1$ and $m2$, for low-grade and high-grade categories, were estimated. The decision line is determined as the perpendicular bisector of the line joining $m1$ and $m2$. In Fig. 6, the decision line is illustrated, which separates the calculated ‘‘Grade’’ into two categories, low-grade and high-grade, respectively. ‘‘Grade’’ values greater than 0.9085 represent high-grade cases, whereas values lower than 0.9085 represent low-grade cases. The estimated threshold value resulted in a classification accuracy of 90.26% (37/41) for low-grade and 93.22% (55/59) for high-grade brain tumors.

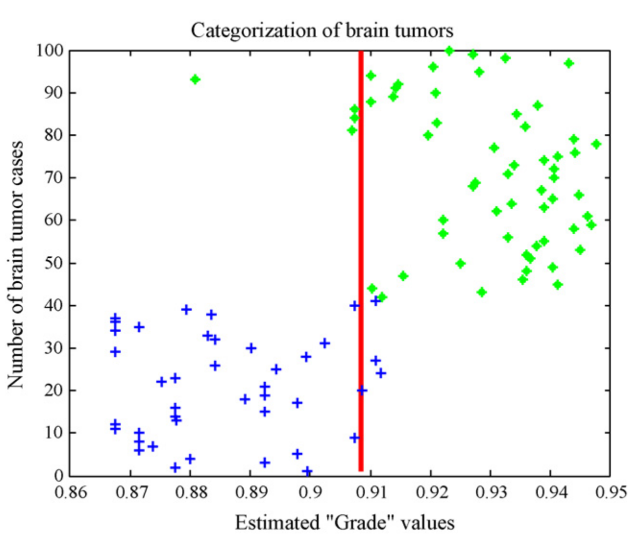


Fig. 6. Categorization of brain tumors.

Table 3
Comparative results

Technique/ accuracy	FCM grading tool (%)	ID3 (%)	J48 (%)	Fuzzy decision trees (%)
Low	90.3	72.2	81.3	90.3
High	93.2	88.2	89.5	94.9
Overall	92	80	85.71	93

For comparison purposes we employed decision trees and fuzzy decision trees at the same data set [35–38]. Both methods are machine learning techniques that accommodate efficiently numeric data as well as categorical or symbolic data. Other approaches that are used in data mining [35,39], such as, neural networks, statistical classifiers, and support vector machines rely on numerical variables and are not suitable techniques for nominal data type.

Decision trees took great awareness by Quinlan [36] with the ID3 algorithm and fuzzy decision trees were introduced by Janikow [37]. The fuzzy decision trees (FID) enhance the representative power of decision trees with the knowledge component inherent in fuzzy logic, leading to better robustness and applicability in uncertain/imprecise contexts. They assume that all domain attributes or linguistic variables have pre-defined fuzzy terms, determined in a data-driven manner using fuzzy restrictions [37].

For the decision trees algorithms, we used the standard approaches included in Waikato Environment for Knowledge Analysis (WEKA) system. WEKA system provides a comprehensive suite of facilities for applying data mining techniques to different type of data [35,40].

Two representative algorithms for decision trees, namely the simple ID3 induction algorithm (implementation of the first release of C4.5) and an advanced version of this algorithm, the J48, were used to test our data sets. The J48 algorithm, an implementation of C4.5 release 8 [36], is an efficient method of decision-making and classification of symbolic data and it is generally not suitable in cases where numerical values are to be operated upon.

Considering the fuzzy decision tree, the fuzzy inductive learning algorithm (FID version 3.4 free software [37]) was tested in our data set. The learning method of fuzzy decision trees is most suitable for stationary problems, with both numerical and symbolic variables, when the goal is both high knowledge comprehensibility and high accuracy.

The results from the implementation of FCM tool and comparison results obtained by FID, ID3 and J48 are given in Table 3.

6. Discussion and conclusions

Grading brain tumors is a very important procedure because it provides information not only regarding tumors' biologic behavior but also essential information that is used to guide treatment decisions. In tumor characterization, differential diagnosis poses a problem and misdiagnosis may have severe prognostic consequences for the patient.

Literature review on inter- and intra-observer variability highlights the lack of reproducibility in identifying the degree of tumor malignancy. This variability is partly due to the inherent difficulty of the speciality, to varying levels of expertise among pathologists and to differences in subjective interpretation of pathological images.

For the diagnostic process in pathology, we can discern two main steps. First pathologists observe tissue biopsies and recognize certain histological attributes related to the degree of tumor malignancy. In a second step, experts interpret their histological findings and come up with a decision related to tumor grade. In the most of the cases, pathologists are unaware of precisely how many attributes have considered in their decision but they are able to classify tumors almost instantly and unconscious of the complexity of the task performed. Pathologists are capable to verbalize their impression of particular features. For example, they can call mitosis and apoptosis as ‘‘present’’ or ‘‘absent’’ but they do not know how precisely these concepts have to be taken into account in the decision process. To this end, although the same set of features is recognized by different histopathologists, each one is likely to reach to a different diagnostic output.

To confine subjectivity, considerable efforts have been made based on computer-assisted methods with a considerable high level of accuracy. Other researchers proposed data-driven grading models [39,41–45] such as statistical classifiers, support vector machines, artificial neural networks, and decision trees coupled with image analysis techniques to incorporate quantitative histological features.

However, besides the retention and enhancement of achieved diagnostic accuracies in supporting medical decision, one of the main objectives, is to enlarge the interpretability and increase transparency in decision-making. The latter is of major importance in clinical practice, where a premium is placed on the reasoning and comprehensibility of consulting systems. In this paper, we extend the research line on computerized brain tumor characterization, utilizing traditional diagnostic concepts and exploiting human specialized knowledge. The novelty of the method was based on the use of FCMs to represent and model experts' knowledge and on the use of the efficient AHL algorithm for enhancing the classification ability of the FCM.

The proposed FCM grading model was able to give diagnostic output with reasonably high accuracy. More specifically, a classification accuracy of 92.68% (38/41) and 93.22% (55/59) was achieved for brain tumors of low and high-grade, respectively. This classification accuracy is interpreted as specificity (correct diagnosis of low-grade tumors) and sensitivity (correct diagnosis of high-grade tumors).

From the results in Table 3, we can safely conclude that FCMs provide diagnosis with the same degree of accuracy as well known state-of-the-art classification engines such us fuzzy decision trees. In addition, FCM possesses several other benefits which render FCM attractive engine to the clinical practice. FCM, unlike data-driven models, is built on human expertise. Moreover, its robustness is not depended on any training procedure which is biased to the size of the available data sets. It offers a degree of transparency and has the ability to explain decisions accurately when diagnosing new cases. The latter is of particular interest since provides means for better understanding of the diagnostic criteria for tumor grading, reducing the uncertainty level and improving the inter- and/or intra-observer agreement.

In addition, FCM is a flexible tool that exploits knowledge and experience, and elicits different representations. New features can easily be introduced or deleted, following histopathologists grading criteria that continuously evolve. Furthermore, the proposed approach is compatible with clinical practice since there is no any necessity for pathologist to adapt any specific staining protocol to highlight cell morphological properties, nor to follow modified classification protocols.

Concluding, a new alternative to computer-assisted brain tumor characterization based on the soft computing technique of FCMs has been introduced. The ability of the FCMs to model and structure accumulated knowledge and expertise might be an important contributor in enhancing the pathologists' consensus at the diagnostic level.

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