Multicriteria Fuzzy Assignment Method: A useful tool to assist medical diagnosis

by

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Abstract

The aim of this paper is to provide a concise portrayal of medical applications of a new fuzzy classification method called *PROAFTN*, which uses a multicriteria decision aid approach. The method is presented after a brief description of classification methods and the formulation of the problematic. Subsequently, the review summarizes and discusses medical applications of the proposed method in acute leukaemia, astrocytic and bladder tumours. Although still an investigative method, the preliminary results are very encouraging and demonstrate the potential performances of this procedure for solving medical classification problems.

Key words: Multicriteria decision aid, Classification, Fuzzy sets, *PROAFTN*, Medical applications.

Résumé

Le but de cet article est de fournir une représentation concise des applications médicales d'une nouvelle méthode de classification baptisée *PROAFTN*. Cette dernière utilise l'approche de l'aide multicritère à la décision. Après une brève description des méthodes de classification et la formulation de la problématique, la méthode *PROAFTN* est présentée. Ensuite l'article récapitule et discute les applications médicales de la méthode proposée dans le domaine de l'aide au diagnostic des leucémie aiguës et des tumeurs astrocytaires et de la vessie. Bien que la méthode est toujours sous investigation, les résultats préliminaires sont très encourageants et montrent les performances potentielles de cette procédure pour résoudre certains problèmes de classification médicale.

Mots Clés: Aide multicritère à la décision, Classification, Sous-ensemble flou, *PROAFTN*, Applications médicales.

1. Introduction

Classification methods are characterized by a learning phase, which consists in elaborating the classification rules from the available knowledge. This phase usually uses either inductive or deductive learning. In inductive learning algorithms, the classification rules are acquired from examples with each example belonging to a well-known class. The aim of this algorithm is to produce classification rules for assigning new examples to classes. There are numerous methods which use inductive learning, including the k nearest neighbor, Bayesian techniques, discriminant analysis, neural network, decision tree and others [15,19,23]. In deductive learning algorithms, the classification rules are given a priori by the interaction with the decision-maker, or the expert. From these rules we determine the assignment classes of the objects. The expert system [2] and the rough set approaches [14] belong to this kind of learning. In general, the methods mentioned above can only use either inductive or deductive learning, but not both at the same time. In practice, some problems are such that we need a method that can employ both types of learning in order to resolve them. This is one of the reasons why the fuzzy assignment procedure "*PROAFTN*" presented here was developed. This method uses the multicriteria decision aid (MCDA) approach, which based on the preference relational system described by Roy [20] and Vincke [22]. In the MCDA approach, the decision problems require the comparison between the alternatives through the scores of different criteria using the relative or the absolute evaluations. The relative evaluation compares the alternatives in order to select the best one or to rank them in decreasing order of preference, while the absolute evaluation compares the alternatives with the different reference actions of classes in order to assign the alternatives to specific classes. Moreover, the MCDA approach avoids resorting to distance and allows to use qualitative and/or quantitative criteria, and, furthermore, it helps to overcome some difficulties encountered when data are expressed in different units. These advantages offered by the MCDA approach constitute the another reason for developing our procedure. On the other hand, only a few methods using the MCDA approach have been applied to medical diagnosis, and this fact constitutes another reason for developing our method. The purpose here is to review briefly the results of medical applications of the *PROAFTN* procedure in acute leukaemia, astrocytic and bladder tumours. The paper is organized as follows. The next section briefly presents the *PROAFTN* method. The third section presents the medical applications and the fourth section concludes and identifies future developments.

2. Presentation of the *PROAFTN* method

In this section we briefly describe the fuzzy assignment procedure *PROAFTN* (for a detailed account, see references [3]). This procedure forms part of a supervised learning algorithm. It starts with a set of cases designated as the training set. These cases are partitioned into mutually exclusive classes (e.g. grades of tumour aggressiveness) and are described by their values for a set of criteria or attributes (e.g. cyto-histological parameters). The rule for assigning actions (i.e., cases) to

classes is formulated as follows: "A*ction 'a' is assigned to a class if and only if 'a' is indifferent or (roughly) equivalent to at least one of the prototypes of this class"*. Let $\{g_1,..., g_n\}$be a set of attributes. Let us denote by $\Omega = \{C^1, C^2, ..., C^k\}$ the set of classes. Based on the assignment rule and the data mentioned above, the procedure proceeds as follows:

0). *Initialization*:

For each class C^h, $h=1,...,k$, we determine a set of L_h prototypes $B^h = \{b_1^h, b_2^h, ..., b_{L_h}^h\}$ by combining the available knowledge (e.g., classification rules) with the data (e.g., clinical cases). The prototypes are considered as good representatives of their class and are described by the score upon each of the n attributes. More precisely, to each prototype b_i^h and each attribute g_j, $j=1,...,n,$ an interval $[S_j^1(b_i^h), S_j^2(b_i^h)]$ is defined, with $S_j^2(b_i^h) \geq S_j^1(b_i^h)$, $j=1,...,n$, $h = 1,...,k$ and $i = 1,...,L_h$. In addition, we assign values to the parameters (weights, thresholds,...), which are used to calculate the membership degree (MSD) of the object to the classes.

1)- *Computing the indifference indices*:

Let $I(a, b_i^h)$ be a degree of validation of the statement "a and b_i^h are indifferent or roughly equivalent". The *PROAFTN* method calculates the indifference indices $I(a,b_i^h)$, $h=1,...,k$ and $i=1,...,L_h$, on the so-called *concordance* and *non-discordance principles* [8, 19]. More precisely, the indifference index is calculated by

$$I(a, b_i^h) = \left(\sum_{j=1}^{n} (W_j^h \times C_j(a, b_i^h)) \times \prod_{j=1}^{n} (1 - D_j(a, b_i^h))^{w_j^h}\right) \tag{1}$$

where

- W_j^h is the positive coefficient reflecting the relative importance attached by a decision-maker to an attribute g_j of the class C^h. It is not restrictive to normalize these coefficients for each class:

$$\sum_{j=1}^{n} W_j^h = 1, \ \forall h \in \{1,...,k\}.$$

- $C_j(a, b_i^h)$, $j=1,...,n,$ is the degree with which attribute g_j is in favour of the indifference relationship between a and b_i^h. Figure 1 illustrates how it is calculated. In this figure, two positive discrimination thresholds $d^+_j(b_i^h)$ and $d^-_j(b^h_i)$, are used to take into account the imprecision of the data.

- $D_j(a, b_i^h)$, $j = 1,...,n,$ is the degree with which attribute g_j is against the indifference relationship between a and b^h_i. Figure 2 illustrates how it is calculated. In this figure, veto thresholds $v^-_j(b^h_i)$ and $v^+_j(b^h_i)$, $j= 1,...,n,$ are used to define the values for which a is considered as very different from b^h_i for attribute g_j. In general, the veto threshold values are obtained from the available knowledge. For example, in the acute leukaemia application, the veto threshold values, for each attribute, are obtained from the F.A.B. classification criteria [1].

Expression (1) defining I(a, b^h_i) shows that this index increases with the quantities $C_j(a, b^h_i)$ and decreases with the $D_j(a, b^h_i)$, $j=1,...,n$. For a more detailed analysis of concordance and discordance indices, see references [7-8,18].

2) *Evaluating the membership degree* $d(a, C^h)$

The *membership degree (MSD)* of an object a to a class C^h, $h=1,...,k$, is defined by a set of prototypes B^h, $h=1,...,k$, and it is measured by the indifference degrees between a and its nearest neighbour in B^h according to the fuzzy indifference relation I:

$$d(a,C^h) = \max\{I(a,b_1^h), I(a,b_2^h),..., I(a,b_{L_h}^h)\},\ h=1,...,k. \qquad (2)$$

3) *Assigning the object 'a' to a specific class*

Once the MSD $d(a, C^h)$, $h= 1,...,k$, has been computed for an object a and for all classes C^h, $h=1,..., k$, the assignment decision (a crisp assignment) of object a is made:

$$a \in C^h \quad \Leftrightarrow \quad d(a, C^h) = max\{d(a, C^l) \,/\, l \in \{1,..., k\}\} \qquad (3)$$

Note that the method assigns the object to a set of classes, which have the highest value of the MSD.

3. Medical applications

3.1 Procurement of data and results

The *PROAFTN* procedure was implemented and applied in three clinical entities namely acute leukaemia, astrocytic and bladder tumours. In the following subsections, we describe the data set, cyto-histopathological characteristics and the classification results of each entity.

3.1.1 Acute leukaemia

The clinical data were supplied by courtesy of Professor J.M. Scheiff (Laboratory of Haematology, Saint-Luc Hospital, Brussels, Belgium). The data set contains 191 cases of acute leukaemia (AL), which were divided into two groups: 129 cases of acute myeloblastic leukaemia (AML) and 62 cases of acute lymphoblastic leukaemia (ALL), and each group is subdivided into several subtypes (see Table 1). According to the French-American-British classification (FAB) rules, a haematologist classified each case. The clinical characteristics related to this data set can be found in [6]. Each case is characterized by forty-seven parameters obtained by examining the patient's bone-morrow smears with an optical microscope. The performances of the method were evaluated on an experimental test of 83 new cases of AL, independently of the training set. After submitting the parameter values to the *PROAFTN* procedure, the values of the MSD of each case in each subtype were determined. Note that the highest value of MSD given by the procedure corresponds to the favourite subtype of AL. Table 1 summarizes the results of correct and misclassification cases obtained on the test set. As indicated in this table, 96.4 % of the cases were correctly classified while only 3.6 % were incorrectly classified. The latter were observed only with AML M3 variant subtype, which constitutes a

subgroup of AML M3 subtype. In fact, the misclassification of the cases can be partially explained by the heterogeneity of this subtype.

3.1.2 Astrocytic and bladder tumours

The data were supplied by courtesy of Dr. Decaestecker (Laboratory of Histology, Faculty of Medicine, University Free of Brussels, Belgium). The data set consists of 250 cases of astrocytic tumours (AT) and 292 cases of bladder tumours (BT). The cases of AT were divided into three histopathological groups namely astrocytomas (AST), anaplastic astrocytomas (ANA) and glioblastomas (GBM). AST is considered to be low-grade (benign) while ANA and GBM are considered as high-grade (malignant) [9,16]. In the same way, the BT are divided into three levels of malignancy namely low (I), intermediate (II) and high (III) grades. Each case was labelled according to its histopathological group as established previously by a clinician. The clinical characteristics related to this data set as well as the determination of the parameters can be found in [10-11]. The parameter values were generated by computer-assisted microscope analysis of cell image. For each case, 26 parameters for AT and 24 parameters for BT were submitted to the *PROAFTN* procedure, which determines the MSD values of each case in each grade. The performances of the method were evaluated using the 10-fold cross validation technique described by Weiss and Kulikowski [23]. Tables 2 and 3 show the performances of the *PROAFTN* procedure applied to astrocytic and bladder tumours respectively. Each grade of AT and BT was tested separately. For each clinical entity, the details were previously described elsewhere [4-5].

3.2 Discussion

Many studies have been undertaken to identify and to classify tumour aggressiveness according to parameters measured by image analyzing systems such as size, cell, shape, density of staining, etc. However, only a few of these studies have used the MCDA approach to assist medical classification problems. In this paper, we evaluated the performances of a new classification method, which belongs to MCDA domain. This evaluation was carried out on three clinical entities namely AL, AT and BT. From the parameter values, the *PROAFTN* procedure calculates the MSD value of the case, i.e., a number indicating the degree of the assignment of the considered case to its grade (or subtype). We have compared the classification results obtained by this procedure with those given previously by an experienced specialist in order to determine whether the case was correctly classified or not. In this study, we focused our analysis on the most important indicator of performance, namely the accuracy of classification. The main reason for doing so is the structure of the available data. On the training set (n = 83) of AL, we only had three classification errors (3.6 %). Except for these, all the cases of this set were correctly classified. This result suggests that the *PROAFTN* procedure yields very good results in terms of discrimination between different AL subtypes.

The average percentages of the whole testing sets were 66 % for correct classification, 27 % for misclassification and 7 % for not discriminatory cases in the AT group. It is true that the average percentage of the correctly classified cases is unsatisfactory, nevertheless it is similar to those reported by the other classifiers (see

Figure 3). This result means that the method based on the MCDA approach yields comparable results in terms of separation of different AT groups. Note that the performances of the classifiers illustrated in Figure 3 were obtained on the same data set used in this study. About one in fifteen of the AT cases were designated not discriminatory by our procedure. This is because their MSD values were equal in at least two histopathological groups. As a consequence, an additional group may be defined by the method without any corresponding clinical significance. These cases may, in part, be assimilated to borderline cases. It is interesting to point out that no cases of the ANA set was classified in the AST group. This result shows that is possible to distinguish high grade, i.e., ANA, from the low grade malignancy, i.e., AST, only on the basis of the parameters generated by computer-assisted microscope analysis of cell image. However, the fact that some cases of the AST group were classified as ANA and/or GBM does not allow such a conclusion.

Despite the low average percentage (59 %) of correctly classified cases in the BT group, the *PROAFTN* procedure was able to distinguish between low and high grades. This is very encouraging since we only had one case (3 %), belonging to grade III (high grade) which was classified as grade I (low grade). This result further indicates that the set of features computed by means of image analysis is reasonably discriminated for grades III and I. About one half of BT grade II, under study was incorrectly classified indicating that the procedure is unable to provide a satisfying discrimination within this intermediate grade. However, this result seems to be in concordance with what is described in the literature concerning the clinical heterogeneity of grade II. Several studies agree that grades I and III are two distinct histopathological entities while grade II seems to be a continuum between grades I and III [13-22]. In the two clinical entities, namely AT and BT, we think that it is essential to combine the features generated by computer-assisted microscope analysis of cell images with the clinical data in order to improve the accuracy of classification. Recent studies have shown that the addition of clinical data to image features significantly improves the accuracy of classification of neuroepithelial tumours [13]. This appears very encouraging and suggests the usefulness of clinical data.

Otherwise, by opposition to the other classifiers, our method offers several advantages. First the value of the MSD provides an indication of the degree of membership of the case to the class. This value provides some interesting information to the decision-maker by indicating whether the case is "*strongly*" or "*weakly*" assigned to a class. Moreover, the MSD value, in some cases, may lead the decision-maker to eliminate one or more classes while the other classifiers are unable to do this. The second advantage resulting from the fact that our method can combine both deductive (decision rules) and inductive (microscope parameters) learning, is that it is quite easy to add new attributes (clinical data) to the method in order to improve the accuracy of classification. It is important to remember that the results presented here were obtained only on the basis of the parameters measured by image analyzing systems. The third advantage is the possibility offered by the method to modify easily the parameters of the prototypes (discrimination thresholds, veto thresholds, etc.). This possibility may contribute to increase the percentage of correct classification and to determine the most important criteria for each grade.

4. Conclusion

We have applied a new multicriteria classification method to assist diagnosis of three clinical entities namely acute leukaemia, astrocytic and bladder tumours. For the classification, the determination by the *PROAFTN* procedure of the maximum value of the MSD of each case indicates the degree of assignment of the case to the presumed grade (or subtype). The preliminary results show a good efficacy of the *PROAFTN* procedure. This gives further reason to explore fully its efficacy when combined with the clinical data. In the future, *PROAFTN* may be extended to more complex situations where the objects are only partially understood and are described by fuzzy subsets of the criteria. Further developments of the procedure include the following research directions: (*i*) the implementation of this procedure; and (*ii*) the generalization of this application to other problems such as diagnosis of machines breakdowns, pattern recognition and data mining.

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Figure 1. Illustrates the graphical representation of the partial indifference index between the object a and the prototype b_i^h. This graph assumes continuity and linear interpolation.

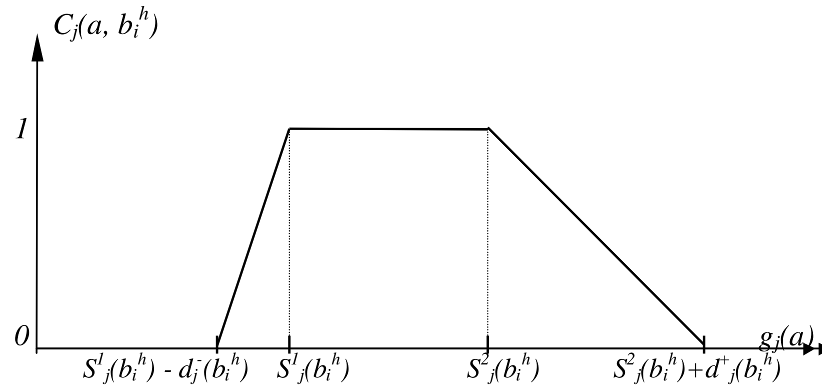

Figure 2. Illustrates the graphical representation of the partial discordance index with regard to the indifference relation between the object *a* and the prototype b^h_i. This graph assumes continuity and linear interpolation.

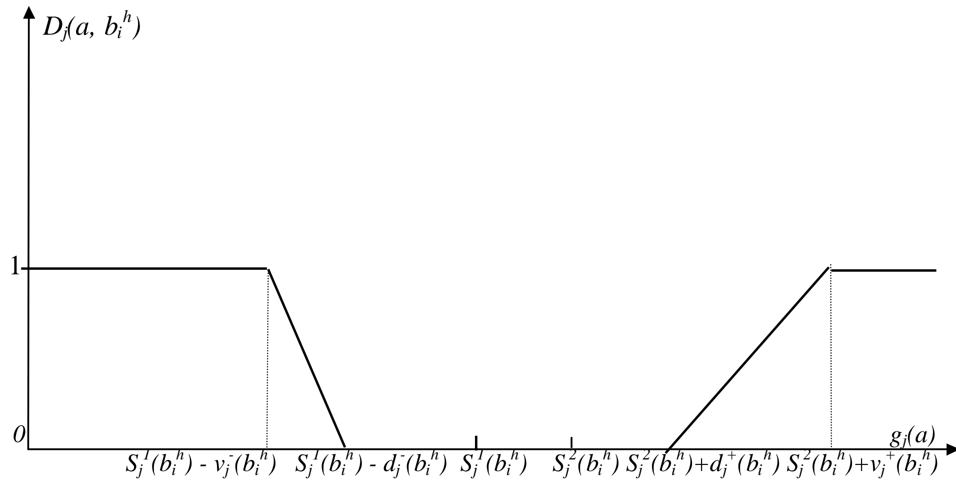

Figure 3. Illustrates the performances of the different classifiers obtained from the three histopathological groups. On the horizontal axes the different classifiers are labelled: 1 = decision tree; 2 = production rules; 3 = 1-nearest neighbor; 4 = 3-nearest neighbors; 5 = logistic regression; 6 = multilayer perceptron; 7 = *PROAFTN*. For each classifier the figure gives the accuracy estimated by the 10-fold cross-validation technique.

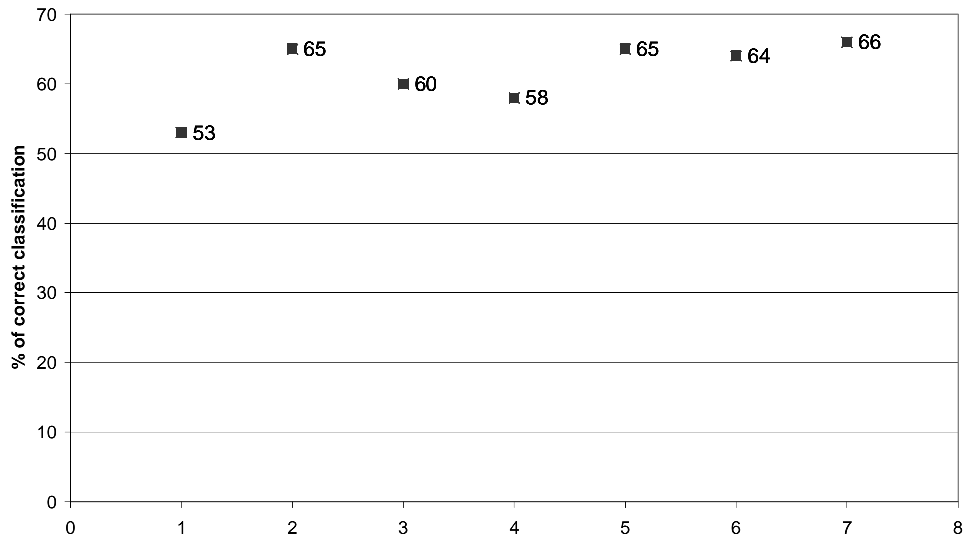

Table 1. Shows the number and the percentage of correct classification and misclassification cases of acute leukaemia subtypes.

Acute leukaemia subtypes	Correct classification Number (%)	Misclassification Number (%)
AML M1 (n=11)	11 (100)	0 (0)
AML M2 (n=11)	11 (100)	0 (0)
AML M3 (n=7)	4 (55.5)	3 (45.5)
AML M4 (n=11)	11 (100)	0 (0)
AML M5 (n=9)	9 (100)	0 (0)
AML M6 (n=7)	7 (100)	0 (0)
ALL L1 (n=13)	13 (100)	0 (0)
ALL L2 (n=10)	10 (100)	0 (0)
ALL L3 (n= 4)	4 (100)	0 (0)
Total (n=83)	80 (96.4)	3 (3.6)

Abbreviations:

AML: acute myeloblastic leukaemia

ALL: acute lymphoblastic leukaemia

Table 2. Indicates the average percentages of correct classification and misclassification and not-discriminatory cases of astrocytic tumours. For each group the table gives the accuracy estimated by the 10-fold cross-validation technique.

PROAFTN procedure → / Effective grades: ↓	AST	ANA	GBM	AST + ANA	AST+ GBM	ANA+ GBM	AST+ ANA +GBM
AST	67	8	20	5	0	0	0
ANA	0	68	28	0	2	0	2
GBM	15	11	62	1	2	3	6

Abreviation:
AST: Astrocytomas; ANA: Anaplastic astrocytomas; GBM: Glioblastomas.
From Belacel *et al.* [6] In Innovation and Technology in Biology and Medicine.

Table 3. Indicates the average percentages of correct classification and misclassification and not-discriminatory cases of bladder tumours. For each group the table gives the accuracy estimated by the 10-fold cross-validation technique.

PROAFTN procedure → / Effective grades ↓	Grade I	Grade II	Grade III	Grade I+II+III	Grade II+III
Grade I	69	28	0	0	3
Grade II	39	52	9	0	0
Grade III	3	38	56	3	0