

## Extracting fuzzy rules for the diagnosis of breast cancer

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**Abstract:** About one million women are diagnosed with breast cancer every year. Breast cancer makes up one-third of all cancer diagnoses in women. Diagnosing breast cancer early is vital for successful treatment. Among the breast cancer screening methods available today, mammography is the most effective, although the low precision rate of breast biopsy caused by mammogram interpretation results in approximately 70% unnecessary biopsies with benign outcomes.

The aim of this study was to extract strong diagnostic fuzzy rules for the inference engine of an expert system to be used for the diagnosis of breast cancer. These rules have been extracted through the use of artificial intelligence technologies. For this, a neuro-fuzzy classification tool called NEFCLASS was used. The learning algorithm of this tool is heuristic and it has efficient performance diagnosis and classification tasks. The rule base to be used for diagnosis consists of 9 rules using the Breast Imaging Reporting and Data System (BI-RADS), mass shape, and mass margin attributes. The positive predictive value of this rule base is 75% and the negative predictive value is 93%. When the approximately 70% rate of unnecessary biopsy in the diagnosis process is taken into consideration, an expert system that has this strong rule base with a high predictive value can be used by doctors in deciding whether to conduct biopsies.

**Key words:** Neuro-fuzzy system, extracting rule, medical diagnosis, breast cancer, mammography

### 1. Introduction

Researchers are encouraged by the improvements in computer technology to develop software for helping doctors to make decisions without consulting specialists. The potential of human intelligence, such as in reasoning, decision making, learning by experience, and many other areas, is used when developing software. Artificial intelligence (AI) is not a new notion, yet it has been accepted as a new technology in computer science. It has been used in many areas such as education, business, medicine, and manufacturing.

Medicine has been the most appropriate area for the application of AI and its subbranches for approximately 2 decades. The greatest reason for this is that some definitions such as indefiniteness, subjectivity, and sensitivity are the most important properties that characterize medical diagnoses.

According to Clancey and Shortliffe [1], medical AI is mainly involved with the construction of AI programs that perform diagnosis and make treatment suggestions. Unlike medical applications based on other programming methods, such as entirely statistical and probabilistic methods, medical AI programs are based on symbolic representations of disease entities and their connections to patient factors and clinical signs [1].

Classifiers can be used to help with the decision-making process in many medical diagnosis problems. It is better not to use black-box approaches in some domains, particularly in medicine. The user should be able

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to understand the classifier and evaluate its results. That is why fuzzy rule-based classifiers are quite suitable, as they are made of simple, linguistically interpretable rules and they do not have some of the disadvantages of symbolic or crisp rule-based classifiers. Classifiers are usually created from data by a learning process, because available expert knowledge is not sufficient to determine their parameters entirely. Neuro-fuzzy approaches provide an easy and convenient way to learn fuzzy classifiers from data. According to the American Cancer Society, breast cancer is the most common type of cancer among women, responsible for nearly 1 in 3 cancer cases diagnosed in US women. With more than 40,000 women dying from breast cancer in the United States each year, only lung cancer surpasses breast cancer as the leading cause of deaths among women [2].

In initial stages, breast cancer does not show any symptoms, while the tumor is small and treatment is easier. Thus, detecting breast cancer early is difficult but quite important. In screening mammography, both randomized studies and population-based evaluations show that recognizing breast cancer early through mammography significantly increases the survival rate [3,4].

Mammography can detect the cancer several years before the appearance of physical symptoms; consequently, it is the best screening test at present. However, before more detailed screenings are performed, such as ultrasound imaging or breast biopsy, approximately 5%–10% of the mammography readings are interpreted as irregular or inconclusive, until final interpretations confirm normal or benign breast tissue. In fact, reports say that malignant pathology is only found in 10%–30% of biopsies [5]. The large number of avoidable breast biopsies is a source of serious emotional and physical distress for the patients, in addition to financial costs. Recently, computer-aided diagnosis (CAD) systems are used that employ lesion descriptions based on the Breast Imaging Reporting and Data System (BI-RADS) [6] standard lexicon as input attributes. This helps the physician to decide whether a breast biopsy is needed or just a short follow-up procedure is enough for a suspected area that appears in a mammogram.

In this paper, a model was created by using a neuro-fuzzy classification tool called NEFCLASS to extract strong diagnostic rules. To create this model, the “Mammographic Mass” dataset taken from the University of California - Irvine (UCI) Machine Learning Repository was used. Strong fuzzy rules were found for this model, in which negative and positive predictive values are respectively 93% and 75%. This study also served the aim of creating an inference engine of an expert system (Ex-DBC) to diagnosis breast cancer.

This study is arranged as follows: Section 2 includes the basic background information about the dataset and the neuro-fuzzy system. Section 3 deals with an explanation of the model, which provides strong diagnostic rules for breast cancer diagnosis. Section 4 provides the discussion, while the final section is the conclusion.

## 2. Background

### 2.1. Mammographic mass dataset

For this study, a mammography mass dataset [7] was provided by UCI. This dataset estimates the severity (benign or malignant) of a mammographic mass lesion based on BI-RADS attributes and the patient’s age. It includes a BI-RADS evaluation, the patient’s age, and 3 BI-RADS attributes together with the ground truth (the severity field) for 516 benign and 445 malignant masses that have been identified on full-field digital mammograms gathered at the Institute of Radiology of the University of Erlangen-Nuremberg between 2003 and 2006. Each case has an associated BI-RADS assessment ranging from 1 (certainly benign) to 5 (highly indicative of malignancy) assigned in a double-review method by physicians. Supposing that all cases with BI-RADS assessments greater than or equal to a given value (varying from 1 to 5) are malignant and the other cases are benign, sensitivities and associated specificities can be calculated. This indicates that a CAD system

performs better than a radiologist. Names and codes of attributes of this dataset are presented in Table 1.

**Table 1.** Attributes of mammographic mass data.

Attribute information	
BI-RADS	BI-RADS assessment: 1 to 5 (ordinal)
Age	Age: patient's age in years (integer)
Shape	Shape: mass shape: round = 1, oval = 2, lobular = 3, irregular = 4 (nominal)
Margin	Margin: mass margin: circumscribed = 1, microlobulated = 2, obscured = 3, ill-defined = 4, spiculated = 5 (nominal)
Density	Density: mass density: high = 1, iso = 2, low = 3, fat-containing = 4 (ordinal)
Class	Severity: benign = 0 or malignant = 1 (binominal)

## 2.2. Neuro-fuzzy system for classification

Through learning techniques acquired from neural networks, the neuro-fuzzy system aims to find the necessary parameters of a fuzzy system. Structure learning should be a part of learning in fuzzy systems, such as creation of a rule base, parameter learning, and optimization of fuzzy sets. Parameter learning is usually done by algorithms that are based on neural network learning, but structure learning is not generally taken from neural networks. The term “neuro-fuzzy”, though, is used for almost all methods of learning in fuzzy systems recently; for example, the learning of fuzzy rules is also incorporated under this notion [8,9]. There are only distinctions when fuzzy rules are generated by fuzzy decision tree learning [10] or by genetic algorithms [11,12].

## 2.3. NEFCLASS algorithm

One of the tuning methods of the fuzzy systems is the neuro-fuzzy classification (NEFCLASS) algorithm, which is based on adding and deleting the rules. The NEFCLASS algorithm was introduced by Nauck and his colleagues [13,14]. The algorithm is established on a general multilayer perception structure. The weights are computed by using fuzzy sets and the all functions (activation–output–propagation) are adjusted accordingly. Although this method carries on the general NN architecture, it allows the interpretation of the resulting system by the related fuzzy system. Throughout the learning process, the shape and position of the membership functions are modified iteratively. Detailed knowledge on NEFCLASS can be found in the work of Nauck and Kruse [13].

The NEFCLASS system has a 3-layer feed-forward architecture that originates from a generic fuzzy perception [9]. The units in this network use t-norms or t-conorms as activation functions. The hidden layer represents fuzzy rules (Figure 1). Fuzzy sets are encoded as (fuzzy) connection weights. This approach of a fuzzy system demonstrates the data flow in the system (data and error signals) and its similar nature.

The architecture of the system consists of 3 units. These are input (x), rule (R), and output (C) units. The learning task is  $\tilde{L} = \{(p_1, t_1), \dots, (p_s, t_s)\}$  for s patterns. The target pattern is represented as  $t \in \{0, 1\}^m$ . The learning algorithm generates k rule units by using the following cycles.

**Cycle 1:** Choose the next pattern from the pattern set.

**Cycle 2:** Find the membership function for all input units.

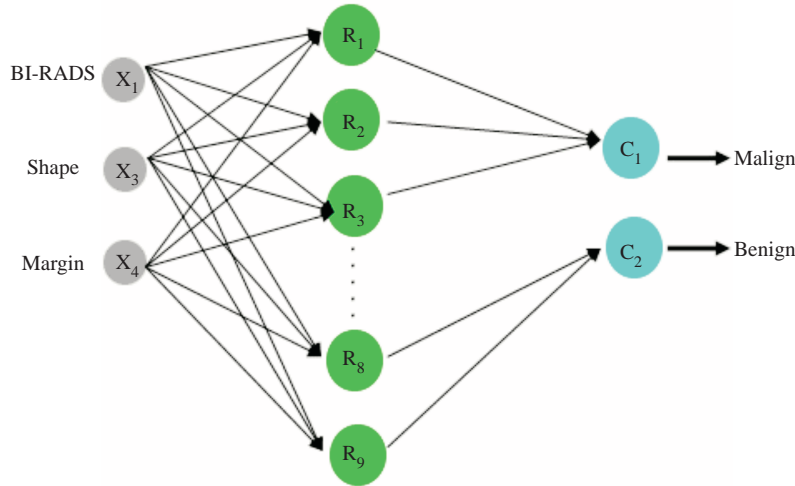
$$\mu_{j_i}^{(i)}(p_i) = \max_{j \in \{1, \dots, q_i\}} \left\{ \mu_j^{(i)}(x_i) \right\} \quad x_i \in U_1$$

**Cycle 3:** Create a rule node with the following equation as long as the rule node is smaller than maximum

rule nodes ( $k < k_{max}$ ) or there is any rule.

$$W(x_1, R) = \mu_{j_1}^{(1)}, \dots, W(x_n, R) = \mu_{j_n}^{(n)}$$

**Cycle 4:** Go to Cycle 1 until there is unprocessed pattern and, if not, stop [13].



**Figure 1.** The architecture of the model with 9 rules created for diagnosis of breast cancer.

### 3. Application and result

There are many studies on medical data analysis with AI methods. Nauck and Kruse [15] applied NEFCLASS and other methods (discriminant analysis (SPSS), multilayer perceptron, decision tree (C4.5), and C4.5 rules) to the well-known Wisconsin Breast Cancer Study data. Keleş and Keleş [16] also used the NEFCLASS tool for the diagnosis of thyroid diseases. A thyroid dataset was used to compare the performance of many AI methods [17]. These studies show that NEFCLASS can be a valuable tool for medical data analysis.

NEFCLASS intends to find a small group of rules that is available for linguistic interpretation. If the classifier is used for the diagnosis of some patients, the physician and the patient can be informed about the chosen diagnosis and how precise the results are. This information is acquired from the degrees of fulfillment of the fuzzy classification rules. The rules also give information about the degrees of fulfillment of the linguistic terms in their antecedents, i.e. about the influence of individual variables [15].

The patient and physician can easily access the diagnosis. The diagnosis can be explained to the patient by using the rules of the classifier. The probability of the outcome as additional information can be calculated by classifiers that are not rule-based, but they cannot offer an intuitive explanation of the diagnosis. The information acquired from a fuzzy classifier is richer and the language is simple. A probability is not given by the classifier, but it identifies the patient among hundreds of other patients that are clearly described by a few active fuzzy rules. This benefit compensates for a small loss of accuracy [15].

Keles et al. investigated the benefits of NEFCLASS-J for medical data analysis and the effects of selected parameters on classifier performances. Creating a classifier with high performance depends on determining the membership type initially, the number of fuzzy sets, and the validation procedure, and after the selection of the proper topology, other parameters should be studied to improve this classifier [17].

In the beginning, models that have different membership functions (triangular, bell-shaped, and trapezoidal) and a number of fuzzy sets were created by using all attributes. As a result, the proposed model was obtained by using a triangular membership function and 5 fuzzy sets for 3 attributes. The model was evaluated in terms of classification performance, accuracy of diagnosis, sensitivity, negative predictive value, and fewer rules. The model includes 3 inputs, 9 rules, and 2 outputs with average accuracy of classification of 80.78 (Table 1) for each class. From the point of view of diagnosis accuracy, the negative and positive predictive value of the 9 fuzzy rules extracted from the proposed model is respectively 0.93% and 0.75%.

The architecture of the planned model in this study is shown in Figure 1. The first layer has 3 input units, representing the pattern features. The hidden layer holds rule units representing the fuzzy rules, and the third layer consists of 2 output units. In this study, the hidden layer contains 9 fuzzy rules using BI-RADS, Shape, and Margin attributes, respectively:

1. If *BI-RADS* is very large (vlg) and *Shape* is vlg and *Margin* is vlg then **Malign**
2. If *BI-RADS* is vlg and *Shape* is vlg and *Margin* is medium (md) then **Malign**
3. If *BI-RADS* is vlg and *Shape* is large (lg) and *Margin* is small (sm) then **Malign**
4. If *BI-RADS* is vlg and *Shape* is lg and *Margin* is md then **Malign**
5. If *BI-RADS* is vlg and *Shape* is lg and *Margin* is vlg then **Malign**
6. If BI-RADS is vlg and *Shape* is sm then **Malign**
7. If *BI-RADS* is md then **Benign**
8. If *BI-RADS* is sm then **Benign**
9. If *BI-RADS* is lg then **Benign**

To create the fuzzy rules of the model, all attribute were divided into 5 fuzzy sets (very small, small, medium, large, and very large). All rules acquired during classification were tested according to accuracy classification and power diagnosis. In particular, the large and medium parts of the BI-RADS attribute were seen to have clashed in the fuzzy set. This will only decrease the number of correct diagnoses that are conducted by BI-RAD. Therefore, classification accuracy is enhanced through the rules by including the attributes of shape and margin.

To create this model, 377 malign and 393 benign cases were used. All cases were diagnosed by conducting a biopsy, the gold standard of diagnosis. This study is a retrospective study in terms of reliability. When the model was created, 2 validation methods were followed. The first method was a single test. In this method, the dataset was separated arbitrarily into 2 parts in accordance with the given percentage value. In this study, 384 cases (51.0% of total cases) were used for training, and classification performance was 80.73%. Meanwhile, 386 cases (49%) were used for testing, and classification performance was 80.83%. The classification performance of the model for the whole dataset was 80.78%. The confusion matrix of the fuzzy model is given in Table 2.

In the cross-validation, the dataset was randomly divided into a number of parts that one can set. In this study, we chose 10 parts for the procedure of cross-validation (10-fold cross-validation). We have 770 patterns and 10 parts are chosen. Therefore, each part consists of 77 patterns. The first part was taken to test the classifier, and the rest of the dataset, consisting of 693 patterns, was used to train the classifier. An error value

was calculated for the test process for each part. That was also applied to the remaining 9 parts. Thus, in each run of training and testing the whole dataset was used, but the mixture of the training and the test set changed all the time. In the end, a mean of errors was calculated using 10 obtained error values.

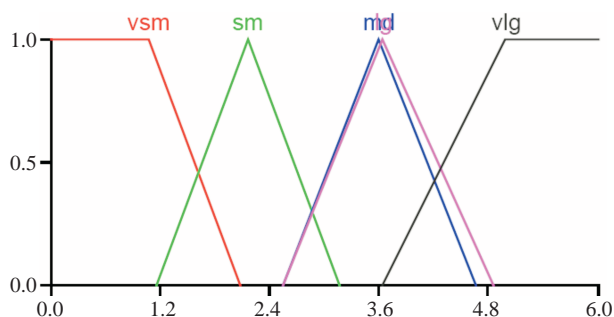
**Table 2.** The confusion matrix of the model created for the mammographic mass dataset.

	Predicted class							
	Benign		Malign		n.c.		Sum	
Benign	358	46.49%	29	3.77%	6	0.78%	393	51.04%
Malign (cancer)	89	11.56%	264	34.29%	24	3.12%	377	48.96%
Sum	447	58.05%	293	38.05%	30	3.90%	770	100.00%

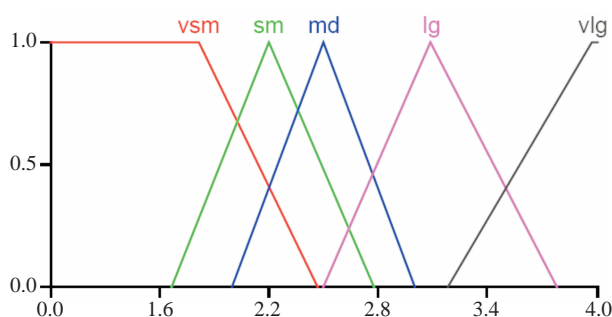
Correct: 622 (80.78%), misclassified: 148 (19.22%), n.c.: not classified.

When the cross-validation method was used for the parameters of the model, classification performance of the model was 86.75%. However, the rule number of the model increased to 92 rules. These rules will decrease the interpretability of the model. Thus, the 9 rules found with the first method were selected for this model.

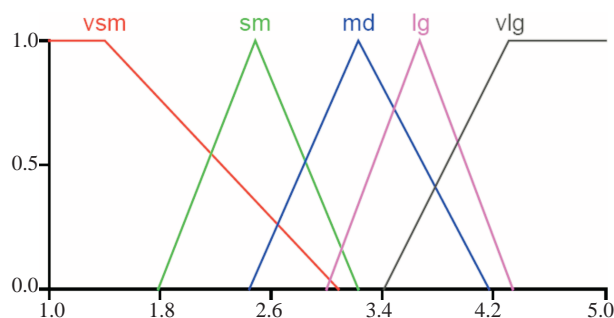
The varied membership functions were tested for the attributes when creating the model. The best results for this model were obtained with the triangular membership function. The triangular membership functions after the training are shown in Figures 2–4.



**Figure 2.** Fuzzy set of BI-RADS attribute (vsm: very small, sm: small, md: medium, lg: large, vlg: very large).



**Figure 3.** Fuzzy set of shape attribute (vsm: very small, sm: small, md: medium, lg: large, vlg: very large).



**Figure 4.** Fuzzy set of margin attribute (vsm: very small, sm: small, md: medium, lg: large, vlg: very large).

In medical care, diagnosis is a vital step. This usually includes diagnostic tests of some description. A health check is also a group of diagnostic tests. Medical treatment decisions are made on the basis of test results. These tests calculate sensitivity, specificity, and positive and negative predictive values.

One of the most intuitive methods for the analysis of diagnostic examinations is the simple 2-by-2 table. [14]. This method has the ability to display strength and power in illuminating and understanding the performance and analysis of diagnostic examinations. Diagnostic test interpretation calculates the likelihood of a patient having the disease under consideration in case of a certain test result. Therefore, a 2-by-2 table is used as a mnemonic device [18]. Table 3 is labeled with the test results on the left side and the disease status across the top.

**Table 3.** The 2-by-2 table.

Test, T (neuro-fuzzy rules)	Disease present (D+)	Disease absent (D-)	Total
Test positive (T+)	True positives (TP = 264)	False positives (FP = 89)	353
Test negative (T-)	False negatives (FN = 29)	True negatives (TN = 358)	387
Total	293	447	740

There are 2 measures to separately evaluate a classifier's performance on different classes, sensitivity and specificity (used often in biomedical and medical applications).

$$\text{Sensitivity} = \frac{TP}{TP + FN} = \frac{264}{264 + 29} = 0.90$$

$$\text{Specificity} = \frac{TN}{FP + TN} = \frac{358}{89 + 358} = 0.80$$

Here, TP = true positive, TN = true negative, FP = false positive, and FN = false negative.

The predictive value is an important measure of the performance of a diagnostic test. The positive predictive value (PPV) represents the really positive rate of all positive results. The negative predictive value (NPV) represents the really negative rate of all negative results.

$$PPV = TP/(TP + FP) = 264/(264 + 89) = 0.75$$

$$NPV = TN/(TN + FN) = 358/(381 + 91) = 0.93$$

#### 4. Discussion

AI models can be chosen to acquire a second viewpoint in medical settings. Gündoğan et al. [19] presented an effective genetic algorithm for a classification rule mining method that applies understandable (if ... then) rules using a generalized uniform population method and a uniform operator based on the uniform population method. The initial population was created by systematically removing the randomness by a generalized uniform population method in the study. In the following generations, genetic diversity was provided and premature convergence was prevented by the uniform operator. They used 2 datasets (breast cancer and dermatology) from UCI. These datasets have been widely used for classification.

Breast cancer is a very common cancer among women in the world. Today, in cancer treatment, survival rates have increased due to technological improvements. According to many theoretic and experimental studies, a multiple classifier system proves to be an effective technique for reducing prediction errors. This may improve the sensitivity and specificity of diagnoses, in addition to the cost effectiveness and physician's effort.

There are several computer-supported diagnosis studies on mammographic mass data to decrease the high number of unnecessary breast biopsies. Elter et al. [20] presented 2 novel CAD approaches (decision tree and case-based reasoning [CBR]) that both emphasize an understandable decision process to predict breast biopsy results from BI-RADS findings. As input attributes for the CBR system, the patient's age, BI-RADS descriptions, and mass density were used in particular. The performance of the proposed decision tree and CBR approaches with artificial neural networks (ANNs) were then compared. The CBR approach performed slightly better than the ANN approach; as a result, it has a slightly better performance than the decision tree approach.

Huang et al. applied 3 classification methods (particle swarm optimization [PSO], the adaptive neuro-fuzzy inference system [ANFIS], and CBR) to the mammographic mass dataset and detected its improvements in accuracy and classification errors. Obtained results indicated that the best accuracy of CBR-based classification was 83.60%, and the classification accuracies of the PSO-based ANN classifier and ANFIS were 91.10% and 92.80% [21].

In the current study, the NEFCLASS fuzzy classifier was used to create strong diagnostic fuzzy rules that could be used in the diagnosis of breast cancer from mammographic mass attributes. Reports say that only 10%–30% of all breast biopsies actually show a malignant pathology for breast cancer [5]. For breast cancer prediction, high sensitivity is generally thought to be more important than high specificity, i.e. it is better to falsely define a benign region as malignant rather than miss breast cancer by classifying a malignant region as benign.

The high number of avoidable breast biopsies is a source of serious psychological and physical distress for the patients, in addition to the unnecessary financial cost of examinations. The findings of this study show that strong diagnostic rules have high sensitivity and negative predictive value. Therefore, this study can significantly contribute to preventing avoidable biopsies in the diagnosis of breast cancer.

## 5. Conclusion

AI techniques have been used to adjust complex medical models. Particularly, many studies on cancers have shown that usage of these techniques improved the accuracy rate in diagnosing, staging, and estimating posttreatment outcomes when compared to conventional statistical analysis. Moreover, implementing AI techniques is easy by means of the powerful developed tools. They can use up-to-date data and have a flexible way of “learning”, which may provide better medical decision support.

This paper focused on developing a model to diagnose breast cancer because it is quite difficult to distinguish between benign and malignant mammographic findings. For this, the neuro-fuzzy method was used, which has given the best results in medical implementations. The proportion of the biopsies performed on nonpalpable lesions is only 15%–30%; however, mammographically suspicious lesions prove to be malignant.

In breast cancer, the golden standard for diagnosis is biopsy. However, biopsy can be uncomfortable for patients, it may cause bleeding and infection, and it is a financial burden to the health care system. Therefore, decreasing the unnecessary biopsy rate has become quite significant. Additionally, as early detection significantly increases the chance of a patient's recovery from breast cancer, the correct diagnosis of these 2 ailments, where the first is benign and the second is malignant, is vital.

Consequently, 9 short rules using 3 variables were obtained for diagnosis from this study. The diagnosis was made with a 93% negative predictive value. The negative predictive value of the proposed model being high is very important.

In light of this study, an expert system called Ex-DBC was developed. To design an inference engine,



this system was utilized from the current study. Ex-DBC is a strong diagnostic tool for the diagnosis of breast cancer. It could also be beneficial to use this system for the training of medical students [22].

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