

Logic Programming and Artificial Neural Networks in Breast Cancer Detection

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Abstract. About 90% of breast cancers do not cause or are capable of producing death if detected at an early stage and treated properly. Indeed, it is still not known a specific cause for the illness. It may be not only a beginning, but also a set of associations that will determine the onset of the disease. Undeniably, there are some factors that seem to be associated with the boosted risk of the malady. Pondering the present study, different breast cancer risk assessment models were considered. It is our intention to develop a hybrid decision support system under a formal framework based on Logic Programming for knowledge representation and reasoning, complemented with an approach to computing centered on Artificial Neural Networks, to evaluate the risk of developing breast cancer and the respective Degree-of-Confidence that one has on such a happening.

Keywords: Breast cancer · Tyrer-cuzick model · Knowledge representation and reasoning · Logic programming · Artificial Neural Networks

1 Introduction

Breast cancer is the most frequent malignancy in female [1], affecting one million women worldwide and 4500 in Portugal, every year. In Portugal, even though the occurrence rate is high, i.e., 75/100000 in 2005 [2], the mortality rate was reduced, exposing the role of screening at an early stage of the illness [3]. This type of tumor has a large impact in our society, not only because of its frequency and severity, but also due to its social and domestic standing.

Mammography is the most common screening tool since it uses low dose X-rays to create an image of the breast to find breast cancer. Screening mammograms are used to look for breast disease in women who are asymptomatic. The American Cancer Society recommends that all women aged over 40 should undergo screening mammography once in a year.

Masses and microcalcification are an important early signs of breast cancer. However, it is often difficult to distinguish abnormalities from normal breast tissues because of their subtle appearance and ambiguous margins. Younger women, who tend to have denser breasts, can make mammograms harder to interpret and can provoke false positive results. According Kolb et al. [4], depending on the density of the breasts radiologists may miss up to 30% of breast cancers. Moreover, mass lesions vary in appearance from patient to patient and similar attributes are shared by some benign and malignant masses, as it is the mammography classification of mass lesions is a difficult task. Indeed, even experienced radiologists have difficulty to interpret screening mammograms in large numbers. Hence, computer-aided diagnostics is a promising tool for radiologists to produce an accurate and faster diagnosis result for breast cancer patients. Some general computer-aided diagnostics systems have been presented based on Kohonen's self-organizing map [5], neuro-fuzzy approach [6, 7], support vector machines [8], Artificial Neural Networks (ANNs) [9] ANNs combined with techniques for reducing the dimension of initial database like association rules [10], sequential forward selection, sequential backward selection, and principal component analysis [11], or clustering [12]. Other authors have developed computer-aided diagnostics systems combining different methodologies like genetic algorithms and ANNs [13] or swarm intelligence and wavelet neural networks [14, 15].

The computer-aided diagnostics systems presented above are related with the problem of distinguishing between abnormalities and normal breast tissues. However, the development of an all-inclusive risk assessment models should include other characteristics of patient like genetic risk factors (about 5% to 10% of breast cancer cases can be hereditary) or hormonal factors (women who have had more menstrual cycles have a slightly higher risk of breast cancer, due to a longer lifetime exposure to the hormones estrogen and progesterone) [16, 17, 18].

Breast cancer is typically asymptomatic until the development of clinical complications. Unfortunately, these complications appear at a relatively late stage of the progression of the disease. Thus, it is difficult to make an early diagnosis of the disease, since it needs to consider different conditions with intricate relations among them, where the available data may be incomplete, contradictory and even unknown, i.e., where the most common limitations are related with the poor quality of the available information. Those drawbacks are mainly due to their reliance on known risk factors like oral contraceptive pill use, ethnic group, breast density, and higher than second-degree relatives with breast cancer, which are yet to be studied.

In order to overcome the problems related with incomplete, contradictory and/or unknown information, the present work reports the founding of a computational framework that uses knowledge representation and reasoning techniques to set the structure of the information and the associate inference mechanisms. We will centre on a Logic Programming (LP) approach to knowledge representation and reasoning [19, 20], and look at a soft computing approach to data processing based on ANNs [21].

2 Knowledge Representations and Reasoning

Many approaches to knowledge representation and reasoning have been proposed using the Logic Programming (LP) archetype, namely in the area of Model Theory [22, 23], and Proof Theory [19, 20]. In this work it is followed the proof theoretical approach in terms of an extension to the LP language to knowledge representations and reasoning. An Extended Logic Program is a finite set of clauses in the form:

$$\begin{aligned}
 &\{ \\
 &\quad p \leftarrow p_1, \dots, p_n, \text{not } q_1, \dots, \text{not } q_m \\
 &\quad ?(p_1, \dots, p_n, \text{not } q_1, \dots, \text{not } q_m) \quad (n, m \geq 0) \\
 &\quad \text{exception}_{p_1} \\
 &\quad \dots \\
 &\quad \text{exception}_{p_j} \quad (j \leq m, n) \\
 &\} :: \text{scoring}_{value}
 \end{aligned}$$

where “?” is a domain atom denoting falsity, the p_i , q_j , and p are classical ground literals, i.e., either positive atoms or atoms preceded by the classical negation sign \neg [19]. Under this formalism, every program is associated with a set of abducibles [22, 23], given here in the form of exceptions to the extensions of the predicates that make the program. The term *scoring_{value}* stands for the relative weight of the extension of a specific *predicate* with respect to the extensions of the peers ones that make the overall program.

In order to evaluate the knowledge that stems from a logic program an evaluation of the *Quality-of-Information (QoI)* was set in dynamic environments aiming at decision-making purposes [24, 25]. The objective is to build a quantification process of *QoI* and an assessment of the argument values of a given predicate with relation to their domains (here understood as *Degree-of-Confidence (DoC)*, which stands for one’s belief that its unknown values fits into the arguments ranges, taking into account their domains).

The *QoI* with respect to the extension of a predicate i will be given by a truth-value in the interval $[0, 1]$, i.e., if the information is *known (positive)* or *false (negative)* the *QoI* for the extension of *predicate_i* is 1. For situations where the information is unknown, the *QoI* is given by:

$$QoI_{\text{predicate}_i} = \lim_{N \rightarrow \infty} \frac{1}{N} = 0 \quad (N \gg 0) \quad (1)$$

where N denotes the cardinality of the set of terms or clauses of the extension of *predicate_i* that stand for the incompleteness under consideration. For situations where the extension of *predicate_i* is unknown but can be taken from a set of values, the *QoI* is given by:

$$Qol_{predicate_i} = 1/Card \quad (2)$$

where $Card$ denotes the cardinality of the *abducible* set for i , if the *abducible* set is disjoint. If the *abducible* set is not disjoint, the Qol is given by:

$$Qol_{predicate_i} = \frac{1}{C_1^{Card} + \dots + C_{Card}^{Card}} \quad (3)$$

where C_{Card}^{Card} is a card-combination subset, with $Card$ elements. The next element of the model to be considered is the relative importance that a predicate assigns to each of its attributes under observation, i.e., w_i^k , which stands for the relevance of attribute k in the extension of $predicate_i$. It is also assumed that the weights of all the attribute predicates are normalized, i.e.:

$$\sum_{1 \leq k \leq n} w_i^k = 1, \forall_i \quad (4)$$

where \forall denotes the universal quantifier. It is now possible to define a predicate's scoring function $V_i(x)$ so that, for a value $x = (x_1, \dots, x_n)$, defined in terms of the attributes of $predicate_i$, one may have:

$$V_i(x) = \sum_{1 \leq k \leq n} w_i^k * Qol_i(x)/n \quad (5)$$

allowing one to set:

$$predicate_i(x_1, \dots, x_n) :: V_i(x) \quad (6)$$

that denotes the inclusive quality of $predicate_i$ with respect to all the predicates that make the program. It is now possible to set a logic program (here understood as the predicates' extensions that make the program) scoring function, in the form:

$$LP_{Scoring\ Function} = \sum_{i=1}^n V_i(x) * p_i \quad (7)$$

where p_i stands for the relevance of the $predicate_i$ in relation to the other predicates whose extensions denote the logic program. It is also assumed that the weights of all the predicates' extensions are normalized, i.e.:

$$\sum_{i=1}^n p_i = 1, \forall_i \quad (8)$$

where \forall denotes the universal quantifier.

It is now possible to engender the universe of discourse, according to the information given in the logic programs that endorse the information about the problem under consideration, according to productions of the type:

$$predicate_i - \bigcup_{1 \leq j \leq m} clause_j(x_1, \dots, x_n) :: Qol_i :: DoC_i \quad (9)$$

where U and m stand, respectively, for *set union* and the *cardinality* of the extension of *predicate_i*. DoC_i denotes one's confidence on the attribute's values of a particular term of the extension of *predicate_i*, whose evaluation is given in [26]. In order to advance with a broad-spectrum, let us suppose that the *Universe of Discourse* is described by the extension of the predicates:

$$f_1(\dots), f_2(\dots), \dots, f_n(\dots) \text{ where } (n \geq 0) \quad (10)$$

Assuming that a clause denotes a happening, a clause has as argument all the attributes that make the event. The argument values may be of the type unknown or members of a set, or may be in the scope of a given interval, or may qualify a particular observation.

3 A Case Study

In order to exemplify the applicability of our method, we will look at the relational database model, since it provides a basic framework that fits into our prospects, and is understood as the genesis of the *LP* approach to Knowledge Representation and Reasoning [19].

As a case study, consider the scenario where a relational database is given in terms of the extensions of the relations (or tables) depicted in Fig. 1, which stands for a situation where one has to manage information about breast cancer. Under this scenario some incomplete and/or default data is also available. For instance, in the *Hormonal Factors* table, the age of menarche in case 2 is unknown, while in the last case the age of menopause ranges in the interval [1, 2].

In Fig. 1 one may find four large groups of variables, i.e., *Personal Information*, *Hormonal Factors*, *Family History* and *Personal Breast Disease*. The *Personal Information* can be affected by the *Age* (whose value is either 0 (zero) if the age is below 50 (fifty) or 1 (one) if it is above 50 (fifty); and by the *Body Mass Index* (whose value is 0 (zero) if it is below 25 (twenty five), 1 (one) if it is above 25 (twenty five) but below 35 (thirty five), and 2 (two) if it is above 35 (thirty five)).

The *Hormonal Factors* are affected by the age when menarche happened (0 (zero) if it occurred below 12 (twelve) or 1 (one) if it is above); by the age when an individual had her first born child (0 (zero) if it is nulliparous or with an age below 30 (thirty), or 1 (one) if it is above); and by the age when menopause happened (0 (zero) if the individual is not yet in the menopause, 1 (one) if it happened before the age of 50 (fifty), and 2 (two) if the age is above 50 (fifty)).

The *Family History* and *Personal Breast Disease* columns can be affected by five and three parameters, respectively. Each one can be either 0 (zero) or 1 (one), where 0 (zero) means the absence and 1 (one) the presence of the disease on the first and second degree relatives, an early onset of cancer in any relative, bilateral breast cancer and ovarian cancer for the first column and breast biopsies, atypical hyperplasia and Lobular Carcinoma In Situ (LCIS) for the second [16, 17].

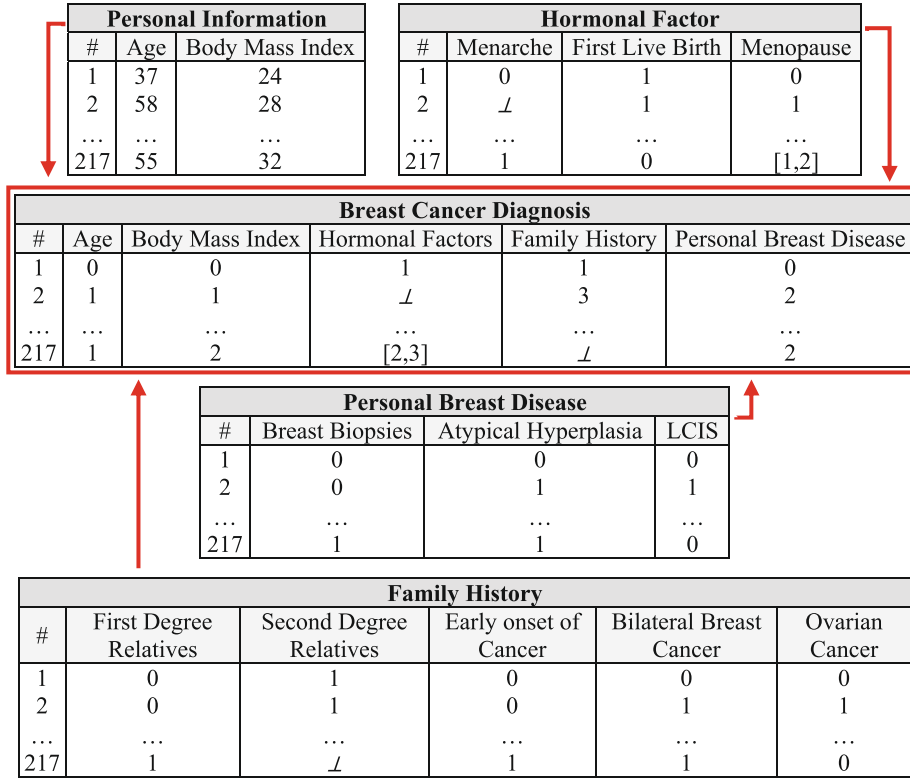


Fig. 1. An extension of the relational database model

Now, applying the rewritten algorithm presented in [26], to all the tables that make the Extension of the Relational Database model for Liver Diseases Diagnosis (Fig. 1), excluding of such a process the *Breast Cancer Diagnosis* one, and looking to the DoC_s values obtained in this manner, it is possible to set the arguments of the predicate referred to below, that also denotes the objective function with respect to the problem under analyze.

$breast_cancer: Age, B_{ody}M_{ass}I_{ndex}, H_{ormonal}F_{actors},$

$$F_{amily}H_{istory}, P_{ersonal}B_{reast}D_{isease} \rightarrow \{0,1\}$$

where 0 (zero) and 1 (one) denote, respectively, the truth values *false* and *true*. Indeed, the arguments of this predicate where set by a process of sensibility analysis, where the arguments chosen where those that present the higher DoC_s values, i.e., the ones that have a greater influence on the output of the objective function referred to above. Their terms also make the training and test sets of the Artificial Neural Network (ANN) given in Fig. 2.

Now, let us consider a patient that presents the symptoms $Age = 1$, $BMI = 2$, $HF = [3, 4]$, $FH = \perp$, $PBD = 1$, to which it is applied the rewritten algorithm presented in [23]. One may get:

Begin,

The predicate's extensions that make the Universe-of-Discourse for the patient under observation are set \leftarrow

$$\{$$

$$\neg\text{breast_cancer}(Age, BMI, HF, FH, PBD)$$

$$\leftarrow \text{not breast_cancer}(Age, BMI, HF, FH, PBD)$$

$$\text{breast_cancer}\left(\underbrace{1, 2, [3, 4], \perp, 1}_{\text{attribute's values}}\right) :: 1 :: DoC$$

$$\underbrace{[0, 1][0, 2][0, 4] [0, 5][0, 3]}_{\text{attribute's domains}}$$

$$\} :: 1$$

The attribute's values ranges are rewritten \leftarrow

$$\{$$

$$\neg\text{breast_cancer}(Age, BMI, HF, FH, PBD)$$

$$\leftarrow \text{not breast_cancer}(Age, BMI, HF, FH, PBD)$$

$$\text{breast_cancer}\left(\underbrace{[1, 1], [2, 2], [3, 4], [0, 5], [1, 1]}_{\text{attribute's values ranges}}\right) :: 1 :: DoC$$

$$\underbrace{[0, 1] [0, 2] [0, 4] [0, 5] [0, 3]}_{\text{attribute's domains}}$$

$$\} :: 1$$

The attribute's boundaries are set to the interval $[0,1]$ \leftarrow

$$\{$$

$$\neg\text{breast_cancer}(Age, BMI, HF, FH, PBD)$$

$$\leftarrow \text{not breast_cancer}(Age, BMI, HF, FH, PBD)$$

$$\text{breast_cancer}\left(\underbrace{[1, 1], [1, 1], [0.75, 1], [0, 1], [0.33, 0.33]}_{\text{attribute's values ranges once normalized}}\right) :: 1 :: DoC$$

$$\underbrace{[0, 1] [0, 1] [0, 1] [0, 1] [0, 1]}_{\text{attribute's domains once normalized}}$$

$$\} :: 1$$

The DoC's values are evaluated ←

{

\neg breast_cancer(Age, BMI, HF, FH, PBD)

← not breast_cancer(Age, BMI, HF, FH, PBD)

breast_cancer $\left(\underbrace{1, 1, 0.97, 0, 1}_{\text{attribute's confidence values}} \right) :: 1 :: 0.79$

$\underbrace{[1, 1][1, 1][0.75, 1][0, 1][0.33, 0.33]}_{\text{attribute's values ranges once normalized}}$

$\underbrace{[0, 1][0, 1] [0, 1] [0, 1] [0, 1]}_{\text{attribute's domains once normalized}}$

} :: 1

End.

where its argument values, i.e., (1, 1, 0.97, 0, 1) make the input to the Artificial Neural Network (ANN) given in Fig. 2. The output of ANN stands for the patient diagnosis.

4 Artificial Neural Networks

It was set a soft computing approach to model the universe of discourse of any patient suffering from breast cancer, based on Artificial Neural Networks (ANNs), which are used to structure data and capture complex relationships between inputs and outputs [27, 28, 29]. ANNs simulate the structure of the human brain, being populated by multiple layers of neurons, with a valuable set of activation functions. As an example, let us consider the case listed above, where one may have a situation in which the diagnosis of breast cancer is needed. In Fig. 2 it is shown how the normalized values of the interval boundaries and their DoC_s and QoI_s values work as inputs to the ANN. The output depicts a breast cancer diagnostic, plus the confidence that one has on such a happening.

In this study were considered 217 patients with an age average of 58.2 years, ranging from 28 to 87 years old. Breast cancer was diagnosed in 41 patients, i.e., 18.9% of the analysed population. The data came from a main health care center in the north of Portugal. The dataset holds information about risk factors considered critical in the prediction of breast cancer. Thirteen variables were selected allowing one to have a multivariable dataset with 217 records (Fig. 1). Table 1 shows a brief description of each variable and the data type, i.e., numeric or nominal.

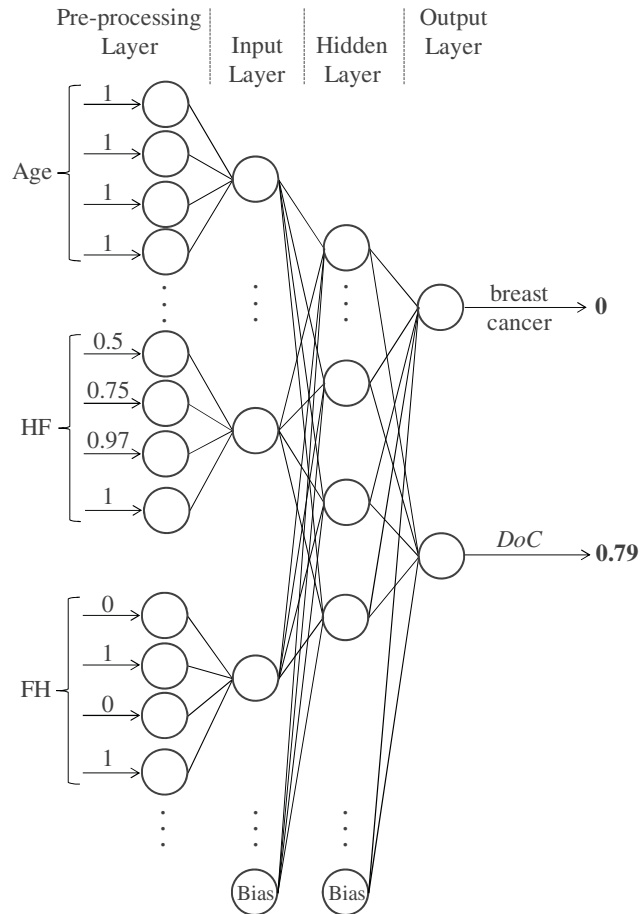


Fig. 2. The Artificial Neural Network topology

To ensure statistical significance of the attained results, 25 (twenty five) experiments were applied in all tests. In each simulation, the available data was randomly divided into two mutually exclusive partitions, i.e., the training set with 70% of the available data and, the test set with the remaining 30% of the cases. The back propagation algorithm was used in the learning process of the ANN. As the output function in the pre-processing layer it was used the identity one. In the other layers we used the sigmoid function.

A common tool to evaluate the results presented by the classification models is the coincidence matrix, a matrix of size $L \times L$, where L denotes the number of possible classes. This matrix is created by matching the predicted and target values. L was set to 2 (two) in the present case. Table 2 present the coincidence matrix (the values denote the average of the 25 experiments). Table 2 shows that the model accuracy was 96.1% for the training set (146 correctly classified in 152) and 95.4% for test set (62 correctly classified in 65).

Table 1. Variables characterization

Variable	Description	Data type
Age	Patient's age	Numeric
Body Mass Index	Patient's body mass index	Numeric
Menarche	Age when menarche happened	Nominal
First Live Birth	Age when patient had her first born child	Nominal
Menopause	Age when menarche happened	Nominal
Breast Biopsies	Had breast biopsies	Nominal
Atypical Hyperplasia	Has atypical hyperplasia	Nominal
LCIS	Has lobular carcinoma in situ	Nominal
First Degree Relatives	Presence of disease on first degree relatives	Nominal
Second Degree Relatives	Presence of disease on second degree relatives	Nominal
Early onset of Cancer	Early onset of cancer in any relative	Nominal
Bilateral Breast Cancer	Presence of disease in any relative	Nominal
Ovarian Cancer	Presence of disease in any relative	Nominal

Based on coincidence matrix it is possible to compute sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of the classifier. Briefly, sensitivity and specificity are statistical measures of the performance of a binary classifier, while sensitivity measures the proportion of true positives that are correctly identified as such. Specificity measures the proportion of true negatives that are correctly identified. Moreover, it is necessary to know the probability of the classifier that give the correct diagnosis. Thus, it is also calculated both PPV and NPV, while PPV stands for the proportion of cases with positive results which are correctly diagnosed, NPV is the proportion of cases with negative results which are successfully labeled. The corresponding sensitivity, specificity, PPV and NPV values are displayed in Table 3 for training and test sets.

Table 2. The coincidence matrix for the ANN model

Target	Predictive			
	Training set		Test set	
	True (1)	False (0)	True (1)	False (0)
True (1)	28	1	12	0
False (0)	5	118	3	50

Table 3. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for for the ANN model

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Training set	96.6	95.9	84.8	99.2
Test set	100.0	94.3	80.0	100.0

A perusal of Table 3 shows that the sensitivity ranges from 96.6% to 100%, while the specificity ranges from 94.3% to 95.9%. The sensitivity of the proposed model is higher than the reported in literature for medical imaging diagnosis, ranging from 70.21% to 94.17% [13, 14, 15]. PPV ranges from 80.0% to 84.8%, while NPV ranges from 99.2% to 100%. For comparison, the reported PPV for medical imaging diagnosis ranges between 64.03% and 87.09%, while the corresponding NPV ranges between 90.96% and 94.71% [13]. Thus, it is our claim that the proposed model is able to predict breast cancer predisposition properly. The inclusion of other patient's characteristics, like genetic risk and hormonal factors may be responsible for the good performance exhibited by the presented model.

5 Conclusions and Future Work

This risk assessment system is able to give an adequate response to the need for a good method of breast cancer prediction. To go around the problem, more effectively, much more variables must be studied and considered, thus fulfilling important gaps in the existent risk assessment methods.

Being an area filled with incomplete and unknown data it may be tackled by Artificial Intelligence based methodologies and techniques for problem solving. This work presents the founding of a computational framework that uses powerful knowledge representation and reasoning techniques to set the structure of the information and the associate inference mechanisms.

The knowledge representation and reasoning techniques presented above are very versatile and capable of covering almost every possible instance, namely by considering incomplete, contradictory, and even unknown data, a marker that is not present in existing systems. Indeed, this method brings a new approach that can revolutionize prediction tools in all its variants, making it more complete than the existing methodologies and tools available. The new paradigm of knowledge representation and reasoning enables the use of the normalized values of the interval boundaries and their *DoC* values, as inputs to the ANN. The output translates a diagnosis of liver disease and the confidence that one has on such a happening.

Our main contribution relies on the fact that at the end, the extensions of the predicates that make the universe of discourse are given in terms of *DoCs* that stand for one's confidence that the predicates arguments values fit into their respective domains. It also encapsulates, in itself, a new vision of Multi-value Logics, once a proof of a theorem in a conventional way, is evaluated to the interval $[0, 1]$. Indeed, some interesting results have been obtained, namely in the fields of Coronary Risk Evaluation [30], Hyperactivity Disorder [31] and Length of Hospital Stay [32] among others. Furthermore, this approach potentiates the use of diverse computational paradigms, in particular the *Logic Programming* one. Future work may recommend that the same problem must be approached using others computational frameworks like Genetic Programming [20], Case Based Reasoning [33] or Particle Swarm [34], just to name a few.

Acknowledgments. This work has been supported by FCT – Fundação para a Ciência e Tecnologia within the Project Scope UID/CEC/00319/2013.

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