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Interval Type-2 Fuzzy System in Prostate Cancer

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Abstract. Establishing the stage of prostate cancer is important to help the physicians define the therapy to be used. The purpose of this paper is to verify if an interval type-2 fuzzy rule-based system can present better results to identify patients with organ-confined prostate cancer than the traditional approach. We constructed a system and we classified patients in a database according their cancer stage. The area under Receiver Operating Characteristic used to evaluate the system is equal to 0.837 while the area for traditional fuzzy rule-based system is 0.824.

Keywords. Fuzzy rule-based system, prognosis, Sugeno' inference method.

1 Introduction

According to the World Health Organization (WHO), prostate cancer is the second most common cancer among men, claiming half a million lives each year worldwide. When man is diagnosed with localized prostate cancer, the probability of cure after surgery is approximately 80%. In case there is extension beyond the prostate, it is important to discuss not only cure, but also quality of life.

There are many studies to help the physicians establish the prognosis. Kattan et al [5] developed nomograms to predict the probability that a man with prostate cancer has an indolent tumor based on clinical variables (serum prostatic specific antigen (PSA), clinical stage, prostate biopsy Gleason grade and ultrasound volume) and variables derived from the analysis of systematic biopsies. Steyerberg et al [11] validated and updated a

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prognostic nomogram that predict indolent prostate cancer. Indolent cancer is so small, low grade and noninvasive that offer little risk to the patient.

Soft computing techniques have been used to this purpose. Ren-Jieh et al [10] developed a two-stage Fuzzy Neural Network using Particle Swarm Optimization algorithm) and concluded that if the clinical data are known, the prognosis of prostate cancer patient can be forecast. Castanho et al [2] used Fuzzy Set Theory and Genetic Algorithms to construct a fuzzy expert system to identify patients with confined or non-confined prostate cancer. Ozkan et al [8] utilized a type-2 fuzzy expert system to determine prostate cancer diagnosis.

Type-2 fuzzy rule-based systems have presented better results than traditional fuzzy rule-based systems. Among the research result we cited the follows: control architecture for autonomous mobile robots [3]; development and extension of a new supplier selection decision-making method, which directly impact on the manufactures' performance [9] and in the problem of forecasting the Mackey-Glass chaotic time-series [4].

The aim of this paper is to verify if an interval type-2 fuzzy rule-based system (IT2FRBS) can give better results to identify patients with organ-confined prostate cancer than the traditional approach.

2 Preliminaries

This section reviews some basic concepts of interval type-2 fuzzy sets, to be directly used in the next sections.

Definition 2.1. *A traditional fuzzy set A defined in the universal set X is the function*

$$\begin{array}{rccc} \mu_A & : & X & \rightarrow & [0,1] \\ & & x & \rightarrow & \mu_A(x). \end{array}$$

In others words, a fuzzy set A is given by:

$$A = \left\{ (x, \mu_A(x)) : x \in X, \mu_A(x) \in [0,1] \right\}.$$

Definition 2.2. *A type-2 fuzzy set $\tilde{A}$ defined in the universal set X is the function*

$$\begin{array}{rcccc} \mu_{\tilde{A}} & : & X \times [0,1] & \rightarrow & [0,1] \\ & & (x,u) & \rightarrow & \mu_{\tilde{A}}(x,u). \end{array}$$

That is,

$$\tilde{A} = \left\{ ((x,u), \mu_{\tilde{A}}(x,u)) | (x,u) \in X \times [0,1], \mu_{\tilde{A}}(x,u) \in [0,1] \right\}.$$

In particular, when $\mu_{\tilde{A}}(x,u(x)) = 1$ for all $u(x) \in J_x$ and $x \in X$, the fuzzy set is called interval type-2 fuzzy set.

The upper and lower primary membership function of the traditional fuzzy set are denoted by $\overline{\mu}_{\tilde{A}}(x)$, $\underline{\mu}_{\tilde{A}}(x)$, $x \in X$, respectively, and defined by [7]:

$$\overline{\mu}_{\tilde{A}}(x) = \sup\{u | u \in [0,1], \mu_{\tilde{A}}(x,u) > 0\},$$

$$\underline{\mu}_{\widetilde{A}}(x) = \inf\{u | u \in [0,1], \mu_{\widetilde{A}}(x,u) > 0\}.$$

The primary membership is defined as $I_x = \{u | u \in [0,1], \mu_{\widetilde{A}}(x,u) > 0\}$. Another important component of $\widetilde{A}$ is,

$$J_x = \{(x,u) | u \in [0,1], \mu_{\widetilde{A}}(x,u) > 0\},$$

so that, if J_x is connected, then,

$$J_x = \{(x,u) | u \in [\underline{\mu}_{\widetilde{A}}(x), \overline{\mu}_{\widetilde{A}}(x)]\}.$$

The Domain of Uncertainty (DOU) for a type-2 fuzzy set is a union of the sets (J_x), given by [7]:

$$DOU(\widetilde{A}) = \bigcup_{x \in X} J_x$$

The Footprint of Uncertainty (FOU) is the DOU for connected domains, defined by [7]:

$$FOU(\tilde{A}) = \{(x,u) | \quad x \in X \quad and \quad u \in [\underline{\mu}_{\widetilde{A}}(x), \overline{\mu}_{\widetilde{A}}(x)]\},$$

Definition 2.3. *The set, A_e, a traditional fuzzy set, is said to be embedded in $\widetilde{A}$ if,*

$$\underline{\mu}_{\widetilde{A}}(x) \leq \mu_{A_e}(x) \leq \overline{\mu}_{\widetilde{A}}(x), \qquad x \in X.$$

An IT2FRBS is a fuzzy system that has at least one type-2 fuzzy set in the antecedent or consequent of a rule [4]. The IT2FRBS with Takagi-Sugeno-Kang as an inference method is structured as follows [1]:

1. **Fuzzifier:** the fuzzifier transforms the input vector $x' = (x'_1, x'_2, \cdots, x'_I)$ into a traditional or type-2 fuzzy sets.

2. **Rule Base:** the rule base of type-2 FRBS has a similar structure as the traditional FRBS. Usually first-order type-2 Takagi-Sugeno-Kang inference method is a rule base of m rules, each having l antecedents. The ith rule can be expressed as:
   R^i**:** If x'_1 is $\widetilde{A}^i_1$ and ... and x'_l is $\widetilde{A}^i_l$ then $Y^i = D^i_0 + D^i_1 x'_1 + \ldots + D^i_r x'_r$;
   where $i = 1, \ldots, m$. The consequents D^i_j $(j = 1, \ldots, r)$ are traditional fuzzy sets; Y^i, the output of ith rule is also a traditional fuzzy set (because it is a linear combination of traditional fuzzy sets); and $\widetilde{A}^i_k$ $(k = 1 \ldots l)$ are type-2 antecedent fuzzy sets.

3. **Inference Method:** This research utilizes zero-order type-2 Takagi-Sugeno-Kang inference method, thus, the consequents $Y^i = D^i_0$ are traditional fuzzy sets. Let $D^i_0 = [d^i_0 - s^i_0, d^i_0 + s^i_0]$ where d^i_0 and s^i_0 are center and spread of D^i_0, respectively. For a IT2FRBS with three inputs and with the product t-norm we obtain,

$$\alpha^i = [\underline{\alpha}^i, \overline{\alpha}^i] = [\underline{\mu}_{\widetilde{A}^i_1}(x'_1).\underline{\mu}_{\widetilde{A}^i_2}(x'_2).\underline{\mu}_{\widetilde{A}^i_3}(x'_3), \overline{\mu}_{\widetilde{A}^i_1}(x'_1).\overline{\mu}_{\widetilde{A}^i_2}(x'_2).\overline{\mu}_{\widetilde{A}^i_3}(x'_3)].$$

4. **Defuzzifier:** the defuzzified value is given by $C = \frac{C_L + C_R}{2}$,
   where $C_L = \dfrac{\sum_{i=1}^{m} \underline{\alpha}^i (d^i_0 - s^i_0)}{\sum_{i=1}^{m} \underline{\alpha}^i}$ and $C_R = \dfrac{\sum_{i=1}^{m} \overline{\alpha}^i (d^i_0 + s^i_0)}{\sum_{i=1}^{m} \overline{\alpha}^i}$.

3 Methods

According to Mendel [6], when a traditional fuzzy set is used, it is necessary to have some measure of dispersion to capture more linguistic uncertainties. This measure is provided by type-2 fuzzy set.

Castanho et al [2] constructed a genetic-fuzzy system that is a fuzzy rule-based system where a genetic algorithm was used to optimize the parameters. The genetic algorithm utilized a database with 331 patients treated with radical prostatectomy. Information about PSA level, Gleason score, clinical stage and pathologic stage (organ-confined or non-confined cancer) were in database. If we adapt the resultant system to a interval type-2 fuzzy rule-based system, we include a measure of dispersion, which allows flexibility.

The IT2FRBS developed maintains the same input and output linguistic variables and rule-base of the traditional system [2]. The input variables are PSA level, Gleason score and the clinical stage of cancer. The serum PSA level is classified, for this study, as Normal (N), Slightly Elevated (SE), Moderately Elevated (ME), Very Elevated (VE), Highly Elevated (HE) or Extremely Elevated (EE). The linguistic variable Gleason score is classified with the following linguistic labels: Well-Differentiated (WD), tumor with less aggressive behavior; Moderately Differentiated (MD) and Poorly Differentiated (PD), with more aggressive behavior. Regarding the linguistic variable clinical stage, labels are given according to the Tumor, Node and Metastasis (TNM) staging system. The four membership functions clinical stage were cT1 (which includes the sub-classes cT1a, cT1b, cT1c), cT2a, cT2b and cT2c.

The output variable, cancer stage, has the following labels: confined, if all cancer is confined within the prostate, and non-confined, if cancer is outside the prostate. The membership functions of input and output variables of IT2FRBS are represented in Figure 1.

The rule base is composed of 47 rules like the following:

"If PSA Level is Moderately Elevated (ME) and Gleason score is Poorly Differentiated (PD) and clinical stage is cT2b, then cancer stage is non-confined".

We utilize Interval Type-2 Fuzzy Logic Toolbox of MatLab® [1].

Between July 2008 and November 2011, 48 patients with average age of 63 were treated with radical prostatectomy for clinically localized prostate cancer at the hospital of the Universidade Estadual de Campinas, Brazil. The surgical specimens (prostate and adjacent structures) from each patient were examined by the same pathologist and the pathologic stage established: 34 patients had organ-confined cancer (TNM, pT2) and 14 patients had extraprostatic cancer (TNM, >pT2). It is the same database utilized to validate the traditional fuzzy rule-based system [2].

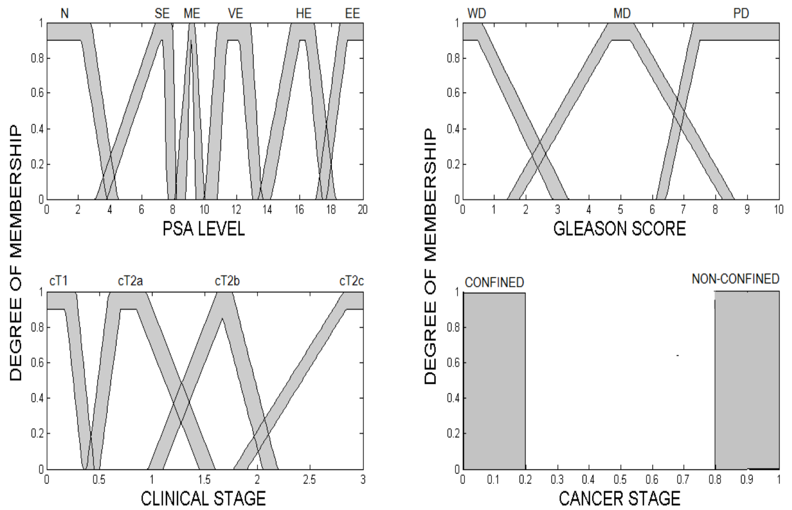

Figure 1: Input and output variables of the IT2FRBS.

4 Results and Discussion

We utilized the Receiver Operating Characteristic (ROC) curve to evaluate the IT2FRBS. This curve depends of two performance measures: sensitivity (probability that the test correctly classifies a patient with non-confined cancer) and specificity (probability of correctly classifying a patient with organ-confined cancer). It is also used to identify a decision threshold (cut-off point) that corresponds to the best combination of sensitivity and specificity. A test with perfect discrimination has an area under the curve (AUC) equal to 1 and when there is no discrimination the area is 0.5.

The output of a IT2FRBS is given by C_L, C and C_R in which $C = \frac{C_L + C_R}{2}$ is the defuzzified value. Thus, we have three possible results for each patient, which means we can calculate three ROC curves (see Table 1).

Table 1: Area under ROC curve.

RESULTS	AUC	95% CI
C_L	0.837	0.702 to 0.928
C	0.831	0.695 to 0.923
C_R	0.816	0.678 to 0.913

The AUC shown in Figure 2 is 0.837 (95% CI: 0.702 to 0.928). The cut-off point is 0.5458 for sensitivity equal 78.57 and specificity equal to 88.24.

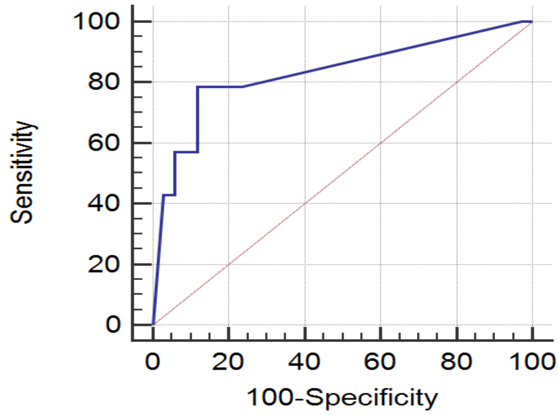

Figure 2: ROC curve.

For the traditional FRBS, the area under the ROC curve is 0.824 (95% CI: 0.686 to 0.918). The difference between the ROC curves is only 0.013. Comparing them, the p-value is equal to 0.7146, that is, there is no significant difference between the two systems.

5 Conclusion

The use of interval type-2 fuzzy rule-based system to predict the prostate cancer stage (organ-confined or non-confined) was investigated. The results show us that there is no significant difference between traditional FRBS and IT2FRBS. We believe that this has occurred because the traditional FRBS had better performance than that found in the literature ($0.58 \leq AUC \leq 0.73$) [2]. Although they do not differ statistically, the fact that the area under ROC curve has given a larger value means that the modification to a type-2 fuzzy sets can improve the result.

Future research will focus on the difference between traditional FBRS and IT2FRBS in systems constructed based on opinion of specialists. In these cases, there are some divergence of opinion that can be modeled by several membership functions embedded in the interval type-2 fuzzy set.

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