



Esophageal cancer prediction based on qualitative features using adaptive fuzzy reasoning method



Raed I. Hamed

Department of Computer Science, Faculty of Computer, University of Anbar, Al-Anbar, Iraq

Received 21 December 2013; revised 11 April 2014; accepted 4 June 2014

Available online 4 April 2015

KEYWORDS

Esophageal cancer;
Fuzzy Petri nets;
Adaptive method;
Qualitative features;
Risk degrees

Abstract Esophageal cancer is one of the most common cancers world-wide and also the most common cause of cancer death. In this paper, we present an adaptive fuzzy reasoning algorithm for rule-based systems using fuzzy Petri nets (FPNs), where the fuzzy production rules are represented by FPN. We developed an adaptive fuzzy Petri net (AFPN) reasoning algorithm as a prognostic system to predict the outcome for esophageal cancer based on the serum concentrations of C-reactive protein and albumin as a set of input variables. The system can perform fuzzy reasoning automatically to evaluate the degree of truth of the proposition representing the risk degree value with a weight value to be optimally tuned based on the observed data. In addition, the implementation process for esophageal cancer prediction is fuzzily deducted by the AFPN algorithm. Performance of the composite model is evaluated through a set of experiments. Simulations and experimental results demonstrate the effectiveness and performance of the proposed algorithms. A comparison of the predictive performance of AFPN models with other methods and the analysis of the curve showed the same results with an intuitive behavior of AFPN models.

© 2015 The Author. Production and hosting by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Expert systems can be represented as a system with knowledge base of rules, and inference engine. The main concept of an expert system is the rule based systems, where the facts and rules represent the main referencing part of domain experts (Yang et al., 2003; Kuo and Chen, 2013).

The graphics as a model is easy for scientists to represent in their application domain. Most current scientists related to studying under the concept of FPNs (Li et al., 2000; Shen, 2003; Wai and Chu, 2007) are focusing on applying fuzzy reasoning mechanism over the adaptive FPN structure rather than utilizing fuzzy Petri net formalism to improve reasoning. Accurate algorithm AFPNs were thus proposed to estimate a risk degree of esophageal cancer problems with high performance. In this paper, our technique employed to model esophageal cancer problem is based on an AFPN. The technique uses 9 fuzzy rules which include the C-reactive protein (CRP) and albumin as two fuzzy input variables, and the risk degree as the output from the defuzzification stage.

Esophageal cancer is one of the most killer malignancies, and all survival rates are still unclear. All signs of the disease

E-mail address: raed.inf@gmail.com

Peer review under responsibility of King Saud University.



of esophageal cancer which are often insidious at the onset, exclude early diagnosis (Schneider and Urba, 2007). It is known that the patients, after undergoing surgery for esophageal cancer, suffer from several problems that affect most aspects of quality of life for a long time (Djävrv et al., 2008). Most of the patients present with cancer related problems and very few with early stage disease. The only real prospect of cure for early stage disease of cancer lies in surgical resection (Wang et al., 2009). With the high tumor-free survival rates, esophagectomy has been the standard treatment for patients with early esophageal cancer, with which all other therapies are considered (Chang et al., 2012).

More researches in the field of the esophageal cancer are presented. A Chang et al. Chang et al. (2012) proposed a process model for a fuzzy logic to improve the predictive performance of a risk score based on the C-reactive protein and albumin. Bhaskar et al. Bhaskar et al. (2012) presented and studied the fluorescence of the essential amino acid tryptophan in dissociated cells of the esophagus as well as in the esophageal tissue. Naoto et al. Naoto et al. (2009) introduced a weight tuning method for constructing multiclass classifier problems including a synthesized data set and some cancer diagnosis data sets from gene expression profiling. Mathe et al. Mathé et al. (2009) discovered that the low miR-375 expression was associated with poor prognosis in esophageal cancer, and then looked at the inflammatory risk score of adenocarcinoma. Yue et al. Yue et al. (2013) presented a HSCORE method to evaluate the predictive value of SIRT3 expression levels on esophageal cancer outcome. Some studies have focused on this problem in the diagnosis of esophageal cancer (Deans et al., 2007; Hamdan et al., 2010; Ramsey et al., 2007; McMillan et al., 2007). In this study, we determined the predictive value of risk degree for esophageal cancer prognosis.

We examined the values between the serum concentrations of C-reactive protein (CRP) and albumin as a set of input data of esophageal cancer. Our algorithm of the AFPN model can obtain a better or the same set of grades of risk degree than the conventional fuzzy logic as in Chang et al. (2012) by using the weight values specified for each place to be optimally tuned based on the observed data. The results demonstrate that, in most situations, our method can improve risk degree accuracy over CRP and albumin as input values. This illustrates that the AFPN model is able to perform as well as (Chang et al., 2012). Noting that the AFPNs approach could be a very good alternative to other methods of biological processes.

The rest of the paper is organized as follows: Section 2 presents brief introductions of esophageal cancer. Section 3 presents our FPN approach to creating the AFPN model of the esophageal cancer with the reasoning Algorithm. Section 4 presents the modeling and description of reasoning process and a five-layer fuzzy model of petri net. Section 5 presents fuzzy rules denoted as certainty factors, fuzzy sets, and rule verification. An execution of the AFPN model of the esophageal cancer and utilizing the algorithm is given in Section 6. In Section 7 we conclude the paper.

2. Brief introductions of esophageal cancer

Esophageal cancer is one of the most killer malignancies, and all survival rates are still unclear. All signs of the disease of esophageal cancer which are often insidious at the onset,

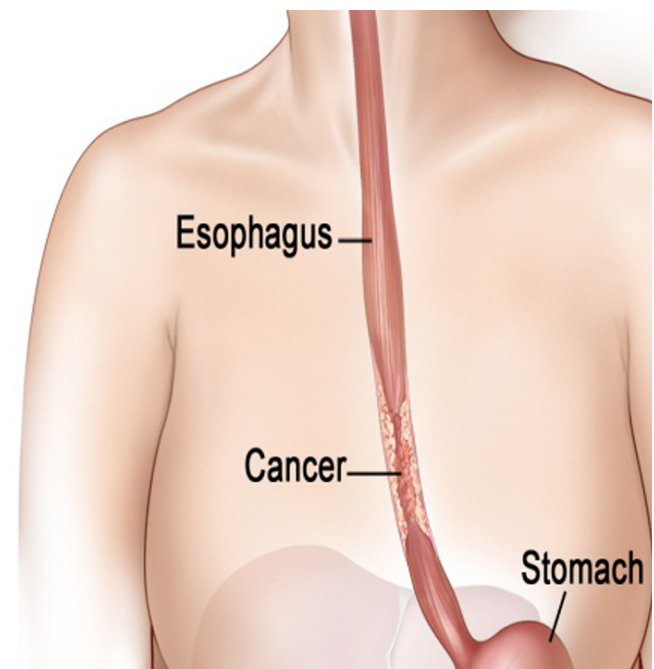


Figure 1 Illustration of the esophageal cancer (Brown et al., 2008).

exclude early diagnosis (Schneider and Urba, 2007). It is known that the patients, after undergoing surgery for esophageal cancer, suffer from several problems that affect most aspects of quality of life for a long time (Djävrv et al., 2008). Despite technological advances of improved diagnosis and therapeutics the prognosis for esophageal cancer remains inadequate.

The risk is real and we can describe the risk factors of esophageal cancer as a set of factors such as, exposure of esophageal tissue to acid, alcohol consumption, possibly hot liquids, tobacco smoke, and, unhealthy diet (Jagannath et al., 2013). The diagnosis of esophageal cancer at an advanced stage, making by surgical excision feasible for only 30–40% of patients (Schneider and Urba, 2007; Brown et al., 2008). Fig. 1 illustrates the well-known esophageal cancer with the organ that connects the mouth to the stomach.

3. Adaptive of fuzzy reasoning algorithm

3.1. Formal basis of adaptive fuzzy Petri net

In this section, we present an adaptive fuzzy Petri net model to solve the problem of esophageal cancer. Following are a few definitions of FPN that are needed to comprehend the modeling capability of AFPN. Fig. 2 shows an example of the AFPN model. We can use AFPN to represent the fuzzy production rules. For example, the following fuzzy production rule can be modeled by a FPN as shown in Fig. 2.

$$R_i : \text{IF } d_i \text{ THEN } d_k(\lambda_1, \text{CF} = \mu_1, w_1)$$

where μ_i is the value of the certainty factor (CF) which indicates the degree of belief of the rule R_i , and $\mu_i \in [0,1]$. If the antecedent portion or consequence portion of a fuzzy production rule contains “and” or “or” connectors, then it is called a

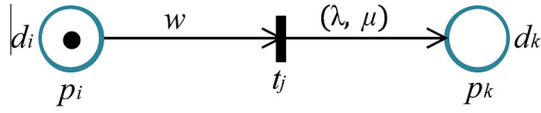


Figure 2 Knowledge representation with a marked AFPN model.

composite fuzzy production rule (Yoo et al., 2013; Liu et al., 2013), as shown in Fig. 3.

The markings of the tokens at its input and output places are modified by firing of a transition, as follows:

$$M^{(k)}(p_i) = \begin{cases} 0 & \text{if } p_i \in (\cdot t_j) \\ 1 & \text{if } p_i \in (t_j \cdot) \\ M^{(k-1)}(p_i) & \text{others} \end{cases}$$

We follow the common firing principle as in Liu et al. (2013), Yuan et al. (1488), Raed and Syed (2011), Liu et al. (2013). The firing fuzzy production rules can be considered as firing transitions. Once transition t_j meets its firing principles, the degrees of truth under the state marking $M^{(k)}$ are computed by:

$$M^{(k)}(p_i) = \begin{cases} \text{Min}\{M^{(k)}(t_j)\} \times u_j & p_i \in t_j^* \text{ and } p_i \notin (t_j) \\ M^{(k-1)}(p_i) & \text{others} \end{cases}$$

where

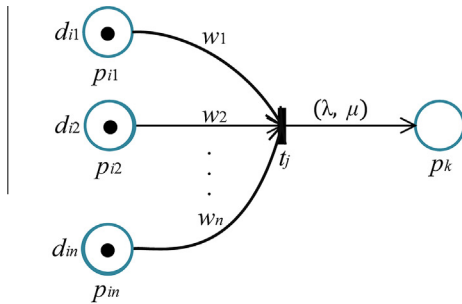
$$t_j \in T, j = 1, 2, \dots, n;$$

$$p_i \in P, i = 1, 2, \dots, m;$$

$M^{(k)}(p_i)$ denoted the degree of truth of the p_i under the state marking $M^{(k)}$;

The transition $t_j \in T$ with marking $M : P \rightarrow [0, 1]$ is enabled from the moment at which the degree of satisfying the condition $\alpha(p_i) \geq \lambda$, which is assigned for the transition. A transition t_j is enabled if $\alpha(p_i)$ possesses fuzzy beliefs for $\forall (p_i) \in i(t_j)$, the concept of enabled t_j fires by generating a new token at its output place. The output value is given by:

$$t_j(t+1) = \begin{cases} \left[\bigwedge_{v_i} \{n_i | p_i \in i(t_j)\} - \lambda \right] & \text{if } \bigwedge_{v_i} \{n_i | p_i \in i(t_j)\} > \lambda \\ 0 & \text{otherwise} \end{cases}$$



An AFPN shares the same notations with the FPN, where the model that can predict the output for esophageal cancer according to the ability of adaptive feature is constructed with respect to relations, rules, certainty factors and weights.

3.2. Reasoning algorithm for cancer diagnosis

The algorithm of AFPNs for esophageal cancer can be explained as follows:

Let k denote the k th reasoning step, then the fuzzy reasoning algorithm of the FRPN is as follows:

Step 1: Initialize an AFPN: I, O, F, λ, W and M^0 .

Step 2: Let $k = 0$.

Step 3: Compute the vector of equivalent fuzzy truth values of the places $\alpha(p_i)$ depending on the value of weight, $\rho^k = W^t \alpha^k$.

Step 4: Compute the output enabled matrix V_k which indicates the enabled output arcs of the transitions. Let f_{ij}^k be the comparison result between the equivalent fuzzy truth value and the output threshold of transition t_i during the k th iteration, then

1. $N^k = [\rho^k(\text{vector})]^{T \circ} O$.
2. $F^k = (f_{ij}^k)_{m \times n} = N^k - \lambda, i = 1, 2, \dots, m; j = 1, 2, \dots, n$,
3. $V^k = (v_{ij}^k)_{m \times n}$; where $v_{ij} = \begin{cases} 1 & f_{ij}^k \geq 0 \\ 0 & f_{ij}^k < 0, i = 1, 2, \dots, m; j = 1, 2, \dots, n. \end{cases}$

Step 5: If $V^k = (v_{ij}^k)_{m \times n}$ is a non-zero matrix, the matrix, then the values of β^k is computed the following function otherwise the process with completed and the last value of marking reached.

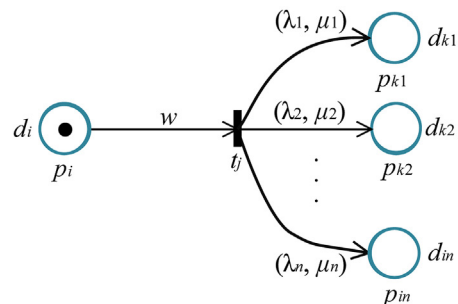
1. $\beta^k = V^k \circ U$

Step 6: To check the fuzzy model status a new marking will be determined M_{k+1} from M_k based on the following function:

1. $M_{k+1} = M_k \oplus (\beta^k \otimes \rho^k)$

Step 7: If there is no marking (i.e. $\alpha^{k+1} = \alpha^k$), then the process is completed, otherwise go to step 4.

Step 8: For every output $\alpha(p_i)$, determine



(b) AFPN net representation of type-1 rules (c) AFPN representation of type-2 rules

Figure 3 A marked adaptive fuzzy Petri net representation of weighted fuzzy production rules.

$$\begin{aligned} \text{AFP}N_{p_{12}}^3 &= \sum_j (w_{jp_{12}}^3 \alpha(p_{ij}^3) \text{CF}_{x,y}, \quad y_j^3 = f_{p_{12}}^3(\text{AFP}N_{p_{12}}^3) \\ &= \text{AFP}N_j^3, \end{aligned}$$

where $\alpha(p_{ij}^4)$ represents the j th input to the node of layer 4; w_{jp}^4 , the weights of each inputs of p_i as shown in Table 1, and $\text{CF}_{x,y}$ represents the value of transitions t_j .

Step 9: For the next layer compute the *max* operation and the center of gravity function applied to get the value of p_{12}

$$\text{AFP}N(p_{12}) = \frac{\sum_{i=1}^5 \mu[i] \times y_i}{\sum_{i=1}^5 \mu[i]}$$

Step 10: Decide the final position of the t_j value according to fuzzy membership functions.

Step 11: According to step 7, the t_j value becomes an actual output, so the reasoning is over.

These modules can be used to create AFPN simulation of the risk degree to predict the outcome for esophageal cancer.

4. AFPN model of the esophageal cancer

4.1. Formulation of fuzzy truth value and linguistic variables

For adaptive and represented fuzzy rules for modeling of all CRP and albumin and the output of esophageal cancer into representing fuzzy sets see Fig. 4. Our model implemented in this paper has two inputs and one output. In this way, for any given value of the CRP and albumin, the degree of

membership μ , to which it belongs to each of these sets, can be determined, and the risk degree based on this information can be obtained. Thus, 9 fuzzy rules were required for the reasoning process as a prognostic model of esophageal cancer. The AFPN model is created and trained with input data on weight s $w(p_i)$, certainty factor s $\text{CF}(t_j)$, and threshold value s λ . However, sometimes it is necessary to depend on experts to determine the parameters of the adaptive model.

4.2. Description of the AFPN model of the esophageal cancer

Five layers of the AFPN model are shown in Fig. 5. Nodes at layer 1 are input nodes, which represent input linguistic variables. Layer 5 is the output layer. Nodes at layer 2 and layer 4 are term nodes, which act as membership functions to represent the terms of the respective linguistic variable. Each node at layer 3 is a rule node, which represents a fuzzy rule. All nodes at layer 3 form a fuzzy rule base. All these layers and the basic function in each layer are introduced below.

Layer 1: Input layer. Every node i correspond to the *CRP* and *albumin*, in this input layer can be represented with the fuzzy model input and the fuzzy model output as follows:

$$\text{AFP}N_i^1 = \text{CRP}, \text{albumin}, O_i^1 = f_i^1(\text{AFP}N_i^1) = \text{AFP}N_i^1, i = 1, 2,$$

Layer 2: In this layer each node performs a membership function. A triangular membership function is employed and represented as follows:

$$\text{AFP}N_i^2 = \begin{cases} 0, & x \leq a. \\ \frac{x-a}{b-a}, & a \leq x \leq b. \\ \frac{c-x}{c-b}, & b \leq x \leq c. \\ 0, & c \leq x. \end{cases}, y_j^2 = f_j^2(\text{AFP}N_i^2) = \exp(\text{AFP}N_i^2), j = 1, \dots, n,$$

Table 1 Rules, propositions, truth degree, initial marking and ISR of adaptive fuzzy model.

Rules	Condition propositions	Places p_i	Initial truth degree $\alpha(p_i)$	Initial marking M_0	Place $\text{ISR}(p_i)$
R1	CRP	CRP	66.5	1	$\{p_1, p_2, p_3\}$
R2	Albumin	Albumin	3.44	1	$\{p_4, p_5, p_6\}$
R3	$\alpha(p_1)$ -Low $\alpha(p_4)$ -Low	p_1	0.0	1	$\{p_7, p_8, p_9\}$
R4	$\alpha(p_1)$ -Low $\alpha(p_5)$ -Medium	p_2	0.058	1	$\{p_8, p_9, p_{10}\}$
R5	$\alpha(p_1)$ -Low $\alpha(p_6)$ -High	p_3	0.942	1	$\{p_9, p_{10}, p_{11}\}$
R6	$\alpha(p_2)$ -Medium $\alpha(p_4)$ -Low	p_4	0.12	1	$\{p_7, p_8, p_9\}$
R7	$\alpha(p_2)$ -Medium $\alpha(p_5)$ -Medium	p_5	0.88	1	$\{p_8, p_9, p_{10}\}$
R8	$\alpha(p_2)$ -Medium $\alpha(p_6)$ -High	p_6	0.0	1	$\{p_9, p_{10}, p_{11}\}$
R9	$\alpha(p_3)$ -High $\alpha(p_4)$ -Low	p_7	0.0	0	$\{p_{12}\}$
R10	$\alpha(p_3)$ -High $\alpha(p_5)$ -Medium	p_8	0.0	0	$\{p_{12}\}$
R11	$\alpha(p_3)$ -High $\alpha(p_6)$ -High	p_9	0.0	0	$\{p_{12}\}$
R12	$\alpha(p_7)$ -Vlow $\alpha(p_8)$ -Low $\alpha(p_9)$ -Medium $\alpha(p_{10})$ -High $\alpha(p_{11})$ -Vhigh	p_{10} p_{11} p_{12}	0.0 0.0 0.0	0 0 0	$\{p_{12}\}$ $\{p_{12}\}$ $\{-\}$

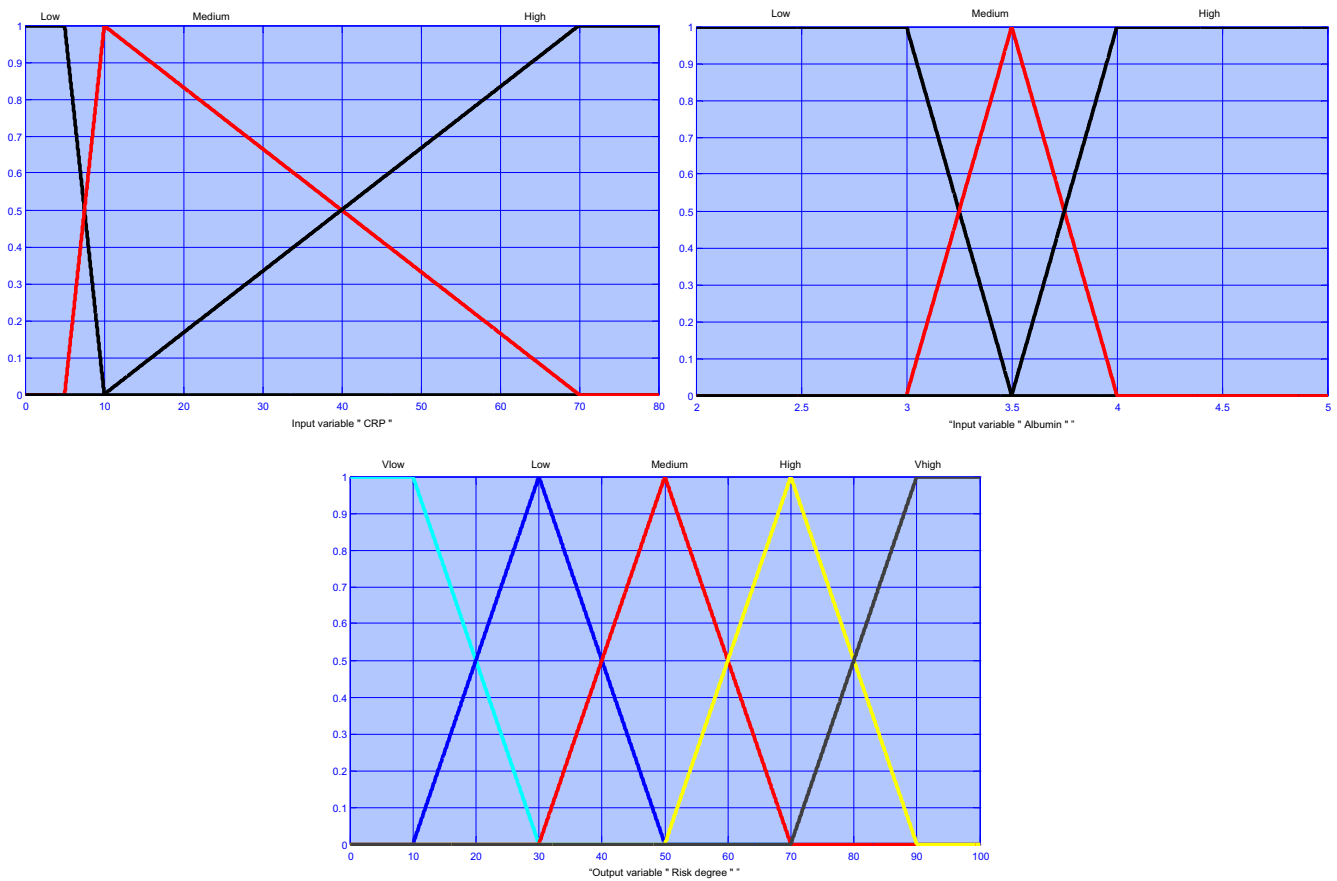


Figure 4 Membership functions for input variables “CRP and albumin” and output variable “risk degree”.

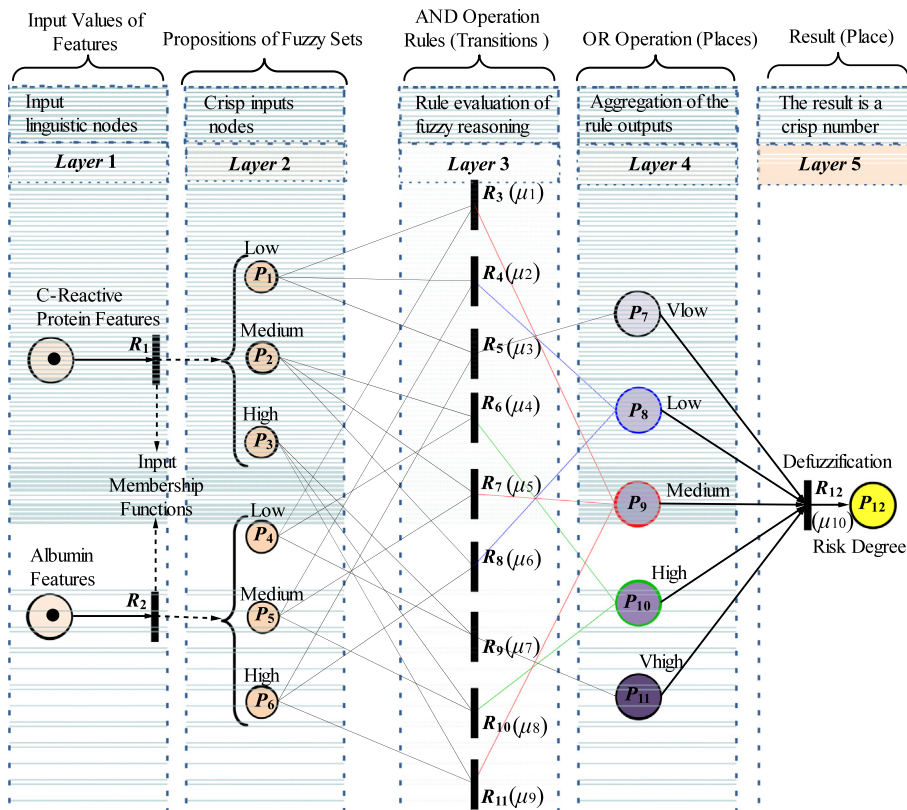


Figure 5 Block diagram of fuzzy inference reasoning of the overall proposed structure.

Layer 3: Each node t_j (transitions) of AFPN in this layer is denoted by a set of fuzzy rules. For the i th rule node, the output of each node represents the firing strength of the corresponding fuzzy rule.

$$\begin{aligned} \text{AFPN}_{p_i}^3 &= \prod_j (w_{jp_i}^3 \alpha(p_i)_j^3) \text{CF}_{x,y}, y_{p_i}^3 = f_j^3(\text{AFPN}_{p_i}^3) = \text{AFPN}_{p_i}^3 p_i \\ &= 1, \dots, n, \end{aligned}$$

$\alpha(p_i)_j^3$ where represents the j th input to the node of layer 3; $w_{jp_i}^3$, the weights of each inputs of p_i as shown in Table 1, and $\text{CF}_{x,y}$ represent the value of transitions t_j .

Layer 4: In layer 4 carry out *max* processing, with respect to weights and certainty factors.

$$\begin{aligned} \text{AFPN}_{p_i}^4 &= \max(R_j), \quad y_j^4 = f_{p_i}^4(\text{AFPN}_{p_i}^4) = \text{AFPN}_{p_i}^4, \\ R_j &= 3, \dots, 11. \end{aligned}$$

Layer 5: The single node represents the output of the fuzzy model (i.e. p_{12}) in this layer we used center of gravity function.

$$\text{AFPN}_{p_{12}}^5 = \frac{\sum_{i=1}^5 \mu[i] \times y_i}{\sum_{i=1}^5 \mu[i]}$$

AFPN module to predict the output for esophageal cancer is constructed according to the structure as shown in Fig. 5.

5. Formulation of fuzzy inference reasoning

The process of getting the output of an actual value for esophageal cancer is referred to as shown in algorithm Section 3.2. Fig. 6 represents the modules of all types of rules created and defined for each fuzzy set of Fig. 5 as follows: p_7 -vlow; p_8 -low; p_9 -medium; p_{10} -high; p_{11} -vhigh. Each rule is modeled as a transition, while each linguist variables of CRP, albumin and risk degree are modeled as knowledge place of each rule, a model of inference reasoning system is built, based on fuzzy rules. In this model the rule is denoted as: $R_j = \{R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, R11, R12\}$, where R_j is R_i : IF d_i THEN d_k ($\lambda_1, \text{CF} = \mu_1, w_1$) for example consider the rule 4 of Fig. 5 will be as follows R_4 : IF $d_1(p_1)$ and $d_5(p_5)$ THEN $d_8(p_8)$ ($\lambda_2 = 0.24, \text{CF}_2 = 0.94, w_2 = 0.44, w_{13} = 0.39$) where d_i and d_k are condition proposition and conclusion proposition respectively. $\mu_i \in [0, 1]$ is deterministic factor to characterize the confidence degree of each fuzzy rule, $\lambda \in [0, 1]$ is the threshold of generating fuzzy rule, and $\omega_i \in [0, 1]$ is weight value of proposition d_i . Depending on the value of places $\alpha(p_i)$ then the rules R_i can be activated and the conclusion proposition of d_k can be computed and a new value marking m_2 is obtained as follows $\forall p_i \in O(t_j) : m_{k+1}(p_i) = (m_k(p_i) \cdot \omega_i) \cdot u_i$,

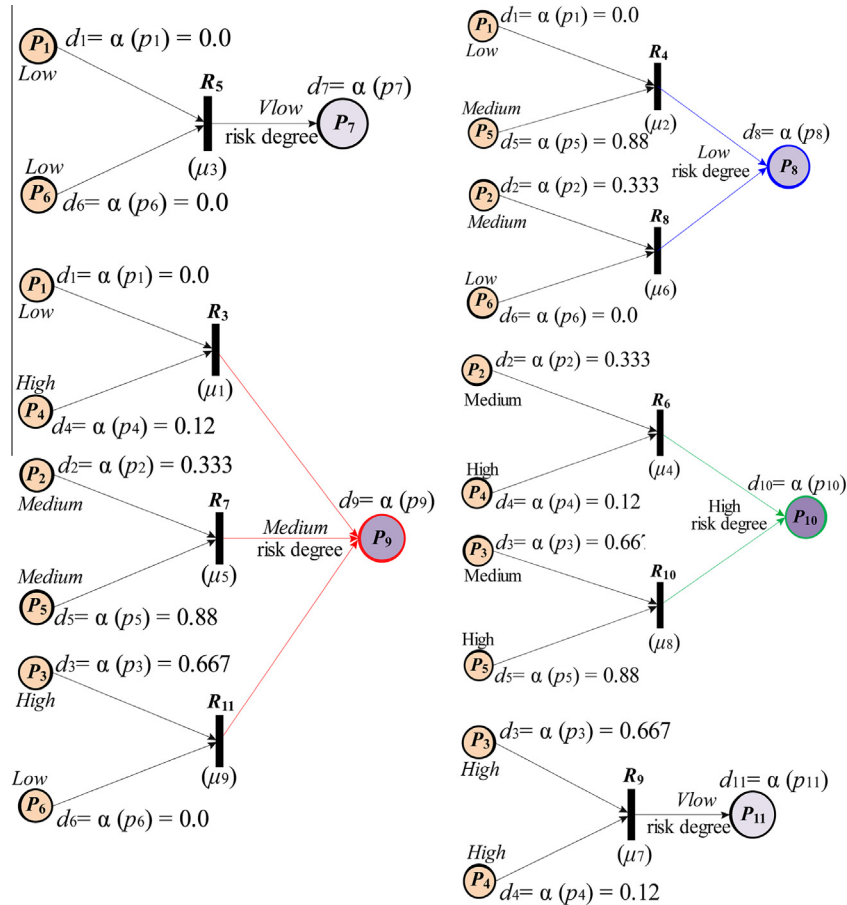


Figure 6 Fuzzy reasoning of AFPN of change risk degree level as p_7 -vlow, p_8 -low, p_9 -medium, p_{10} -high p_{11} -vhigh.

Table 2 The results inferred using the membership function for CRP and Albumin.

Membership function value of CRP and Albumin							
CRP value	Low CRP	Med. CRP	High CRP	Albumin value	Low Albumin	Med. Albumin	High Albumin
15	0.0833	0.9167	0.0	2.7	1.0	0.0	0.0
9.5	0.1	0.9	0.0	2.69	1.0	0.0	0.0
30	0.0	0.333	0.667	3.44	0.12	0.88	0.0
66.5	0.0	0.058	0.942	3.82	0.0	0.36	0.64
5.7	0.86	0.14	0.0	3.1	0.0	0.2	0.8
9.3	0.14	0.86	0.0	4.9	0.0	0.0	1.0

The concept of reachability is defined as follows: suppose there exists two places p_i and p_k when $p_i \in I(t_i)$ and $p_k \in O(t_i)$ exist, then we call p_k is the immediate reachability place to p_i . So the immediate reachability place can be denoted as $IRS(p_i)$ see Table 1. Depending on the model of AFPN in Fig. 5 there exist:

$$p_i = (CRP, Albumin, p_1, p_2, p_4, p_5, p_6, p_7, p_8, p_9, p_{10}, p_{11}, p_{12})$$

$$r_j = (r_1, r_2, r_3, r_4, r_5, r_6, r_7, r_8, r_9, r_{10}, r_{11}, r_{12}),$$

$$d_i = (d_1, d_2, d_3, d_4, d_5, d_6, d_7, d_8, d_9, d_{10}, d_{11}, d_{12}, d_{13}, d_{14})$$

$$f(t_j) = (\mu_1 = 0.99, \mu_2 = 0.94, \mu_3 = 0.91, \mu_4 = 0.89, \mu_5 = 0.87, \mu_6 = 0.92, \mu_7 = 0.83, \mu_8 = 0.89, \mu_9 = 0.95, \mu_{10} = 0.87),$$

$$\begin{aligned} \omega_i &= (\omega_1 = 0.38, \omega_2 = 0.44, \omega_3 = 0.29, \omega_4 = 0.43, \omega_5 = 0.49, \omega_6 = 0.47, \omega_7 = 0.31, \omega_8 = 0.51, \omega_9 = 0.46, \omega_{10} = 0.51, \omega_{11} = 0.47, \omega_{12} = 0.28, \omega_{13} = 0.39, \omega_{14} = 0.19, \omega_{15} = 0.42, \omega_{16} = 0.47, \omega_{17} = 0.35, \omega_{18} = 0.36, \omega_{19} = 0.52, \omega_{20} = 0.46, \omega_{21} = 0.37, \omega_{22} = 0.36, \omega_{23} = 0.27), \end{aligned}$$

$$\lambda_j = (\lambda_1 = 0.19, \lambda_2 = 0.24, \lambda_3 = 0.21, \lambda_4 = 0.18, \lambda_5 = 0.17, \lambda_6 = 0.22, \lambda_7 = 0.23, \lambda_8 = 0.19, \lambda_9 = 0.95, \lambda_{10} = 0.17)$$

Table 2 shows some of the results inferred using the membership function. Hence our AFPN model will be able to handle large datasets of CRP and Albumin values at a lower computation time.

We input assumed crisp data into those corresponding membership functions, and get the membership function value for all CRP and Albumin values as listed in Table 2. Then we compute the final outputs, of p_{12} see Fig. 5 for this we can make the final decision of risk degree.

As in our model Fig. 5 we depended on a set of functions together with fuzzy input membership function (FIMF) of degree of truth, as follows:

fimf for CRP and albumin with low, medium and high variables exist

$$d_{1_low} = \text{fimf of CRP_low value} = \mu_{low}CRP = \alpha(p_1)$$

$$d_{2_medium} = \text{fimf of CRP_medium value} = \mu_{medium}CRP = \alpha(p_2)$$

$$d_{3_high} = \text{fimf of CRP_high value} = \mu_{high}CRP = \alpha(p_3)$$

$$d_{4_low} = \text{fimf of albumin_low value} = \mu_{low}albumin = \alpha(p_4)$$

$$d_{5_medium} = \text{fimf of albumin_medium value} = \mu_{medium}albumin = \alpha(p_5)$$

$$d_{6_high} = \text{fimf of albumin_high value} = \mu_{high}albumin = \alpha(p_6)$$

Suppose that the value of CRP = 30 and albumin = 3.44 then the condition proposition of $\alpha(p_i)$ will be

$$d_{1_low} = \mu_{low}CRP = \alpha(p_1) = 0.0$$

$$d_{2_medium} = \mu_{medium}CRP = \alpha(p_2) = 0.333$$

$$d_{3_high} = \mu_{high}CRP = \alpha(p_3) = 0.667$$

$$d_{4_low} = \mu_{low}albumin = \alpha(p_4) = 0.12$$

$$d_{5_medium} = \mu_{medium}albumin = \alpha(p_5) = 0.88$$

$$d_{6_high} = \mu_{high}albumin = \alpha(p_6) = 0.0$$

The AFPN model in Fig. 5 can be adapted to reason the production fuzzy rules comprising five consequent propositions.

The first production rule derives the possibility that the change risk degree level is *low*; the second production rule derives the possibility that the change risk degree level is *low*, the third production rule derives the possibility that the change risk degree level is *medium*, the fourth production rule derives the possibility that the change risk degree level is *high*, the fifth production rule derives the possibility that the change risk degree level is *high*.

A result of each model in Fig. 6 reveals different probability for risk degree level as shown in Fig. 7. Furthermore, the certainty factors (CF) of the transitions (rules) in the AFPN model may be associated with the significance of the corresponding terms in the production rules.

A result of the model in Fig. 7 reveals different probability of each fuzzy set variable (a) the places with weights $w_1 = 0.38$; $w_2 = 0.24$; $w_3 = 0.29$; $w_4 = 0.43$; $w_5 = 0.49$; (b) the places with weights $w_1 = 0.82$; $w_2 = 0.74$; $w_3 = 0.79$; $w_4 = 0.33$; $w_5 = 0.95$. In the Fig. 7 we set the different degree weights of each place, the best one depending on the behavior of the results.

The values of linguistic variables are fuzzified to obtain the truth degree by membership function (Mohamed et al., 2014). That is, a 3-d membership vector for the fuzzy sets low, medium and high corresponding to fuzzy position OCR, albumin and risk degree estimation of (p_{12}) is given by:

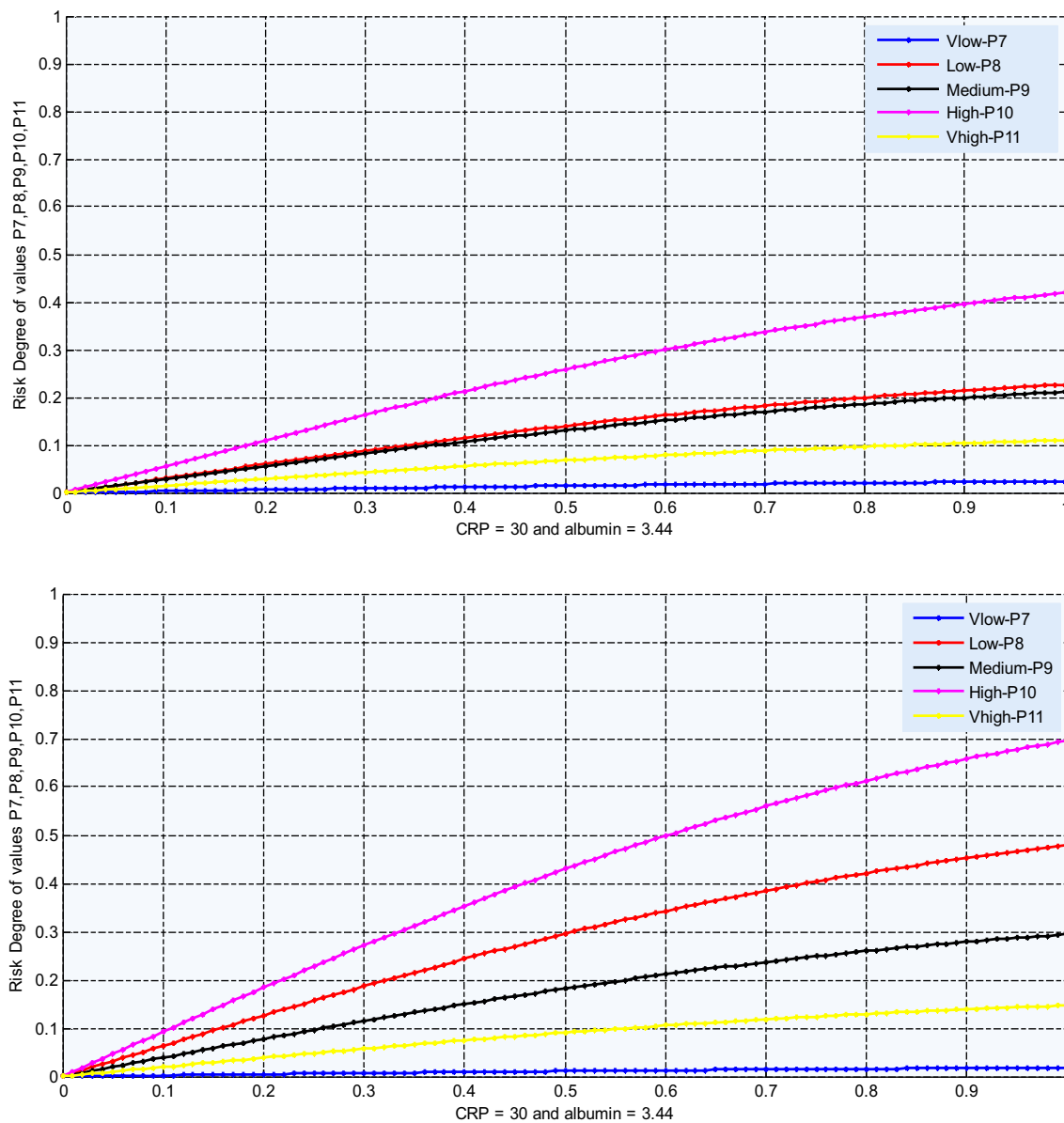


Figure 7 The risk degree of values P7, P8, P9, P10, P11, show the behavior of fuzzy sets with different places weights.

$$VOCR = [\mu_{Low-OCR}, \mu_{Medium-OCR}, \mu_{High-OCR}]^T$$

$$VAlbumin = [\mu_{Low-Albumin}, \mu_{Medium-Albumin}, \mu_{High-Albumin}]^T$$

$$VRiskDegree = [\mu_{Low-RiskDegree}, \mu_{Medium-RiskDegree}, \mu_{High-RiskDegree}]^T$$

6. Experimental results of algorithm’s performance evaluation

In this section the prognostic AFPN model to predict the esophageal cancer outcome is known. The marking and truth degree vectors can be derived from the membership functions to obtain the esophageal cancer outcome. To get the conclusion on the risk degree with a specific truth degree value of $\alpha(p_{12})$. As we have shown in Fig. 5 it is possible to compute the firing composition. Here we describe existing variables CRP and albumin following the Method (Chang et al., Nov. 2012) which has been used for comparative analysis.

These values can be used as the truth degree of each antecedent proposition in our AFPN models. For example to determine risk degree, supposed we have the following values for each of these variables CRP = 30 and albumin = 3.44 the execution of our algorithm to compute the result of truth

$$I = \begin{bmatrix} 11100000 \\ 00011100 \\ 00000011 \\ 10010010 \\ 01001001 \\ 001001001 \\ 00000000 \\ 00000000 \\ 00000000 \\ 00000000 \\ 00000000 \\ 00000000 \\ 00000000 \end{bmatrix} \quad O = \begin{bmatrix} 00000000 \\ 00000000 \\ 00000000 \\ 00000000 \\ 00000000 \\ 00000000 \\ 00100000 \\ 01000100 \\ 100010001 \\ 000100010 \\ 000000100 \end{bmatrix}$$

degree $\alpha(p_i)$ of the proposition listed as follows:

- R3: If $P1 = 0.0$ and $P4 = 0.12$ then $P9$ is “Medium” ($CF(\mu_j) = 0.85$).
- R4: If $P1 = 0.0$ and $P5 = 0.88$ then $P8$ is “Low” ($CF(\mu_j) = 0.84$).
- R5: If $P1 = 0.0$ and $P6 = 0.0$ then $P7$ is “Vlow” ($CF(\mu_j) = 0.54$).
- R6: If $P2 = 0.333$ and $P4 = 0.12$ then $P10$ is “High” ($CF(\mu_j) = 0.97$).
- R7: If $P2 = 0.333$ and $P5 = 0.88$ then $P9$ is “Medium” ($CF(\mu_j) = 0.87$).
- R8: If $P2 = 0.0333$ and $P6 = 0.0$ then $P8$ is “Low” ($CF(\mu_j) = 0.65$).
- R9: If $P3 = 0.667$ and $P4 = 0.12$ then $P11$ is “Vhigh” ($CF(\mu_j) = 0.94$).
- R10: If $P3 = 0.667$ and $P5 = 0.88$ then $P10$ is “High” ($CF(\mu_j) = 0.93$).
- R11: If $P3 = 0.667$ and $P6 = 0.0$ then $P9$ is “Medium” ($CF(\mu_j) = 0.87$).

According to our proposed algorithm we have the following reasoning steps:

- (1) For the first iteration, $k = 1$
 $M^1 = (1, 1, 1, 1, 1, 1, 0, 0, 0, 0, 0, 0)^T$,
 $\alpha^1 = (0, 0.333, 0.667, 0.12, 0.88, 0, 0, 0, 0, 0, 0, 0)^T$.
- (2) For the second iteration, $k = 2$
 Depending on the values of places, weights, and certainty factors the result is a list containing the result of each rule:
 $R3 = 0.0520, R4 = 0.4361, R5 = 0, R6 = 0.3659,$
 $R7 = 0.7782, R8 = 0.0289, R9 = 0.4179, R10 = 0.6554, R11 = 0.0918;$
 $\mu_{Vlow_Risk\ Degree} = \alpha(P_7)_Rules (5) = 0.0$
 $\mu_{Low_Risk\ Degree} = \alpha(P_8)_Rules (4, 8) = 0.4361$
 $\mu_{Medium_Risk\ Degree} = \alpha(P_9)_Rules (3, 7, 11) = 0.7782$
 $\mu_{High_Risk\ Degree} = \alpha(P_{10})_Rules (6, 10) = 0.6554$

$$\mu_{Vhigh_Risk\ Degree} = \alpha(P_{11})_Rules (9) = 0.4179M^2 = (1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 0)^T,$$

$$\alpha^2 = (0, 0.333, 0.667, 0.12, 0.88, 0, 0, 0.4361, 0.7782, 0.6554, 0.4179, 0)^T.$$

- (3) For the third iteration, $k = 3$

$$M^3 = (1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1)^T,$$

$$P_{12} = \frac{\sum_{i=1}^5 \mu^{[i] \times y_i}}{\sum_{i=1}^5 \mu^{[i]}} = \frac{0 \times Vlow + 0.4361 \times low + 0.7782 \times medium + 0.6554 \times high + 0.4179 \times Vhigh}{0 + 0.4361 + 0.7782 + 0.6554 + 0.4179} = 59.2242$$

$$\alpha^3 = (0, 0.333, 0.667, 0.12, 0.88, 0, 0, 0.4361, 0.7782, 0.6554, 0.4179, 59.2242)^T.$$

- (4) For the fourth iteration, $k = 4$

$$\alpha^4 = (0, 0.333, 0.667, 0.12, 0.88, 0, 0, 0.4361, 0.7782, 0.6554, 0.4179, 59.2242)^T.$$

As $\alpha^3 = \alpha^4$ the final state of places truth p_{12} degree vector is $(0, 0.333, 0.667, 0.12, 0.88, 0, 0, 0.4361, 0.7782, 0.6554, 0.4179, 59.2242)^T$ and the marking vector is $M^3 = (1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1)^T$, then the final value of $\alpha(p_{12})$ Risk Degree = 59.2242 see Fig. 8.

Another example from Chang et al. (2012) will be implemented with values of CRP = 15 and albumin = 2.7.

- (1) For the first iteration, $k = 1$
 $M^1 = (1, 1, 1, 1, 1, 1, 0, 0, 0, 0, 0, 0)^T, \alpha^1 = (0.0833, 0.9167, 0, 0.1, 0, 0, 0, 0, 0, 0, 0, 0)^T$.
- (2) For the second iteration, $k = 2$
 $M^2 = (1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 0)^T,$
 $\alpha^2 = (0.0833, 0.9167, 0, 0.1, 0, 0, 0.0092, 0.0796, 0.4746, 1.5528, 0.8178, 0)^T$.
- (3) For the third iteration, $k = 3$
 $M^3 = (1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1)^T,$
 $P_{12} = \frac{\sum_{i=1}^5 \mu^{[i] \times y_i}}{\sum_{i=1}^5 \mu^{[i]}} = \frac{0.0092 \times Vlow + 0.0796 \times low + 0.4746 \times medium + 1.5528 \times high + 0.8178 \times Vhigh}{0.0092 + 0.0796 + 0.4746 + 1.5528 + 0.8178} = 71.0663$

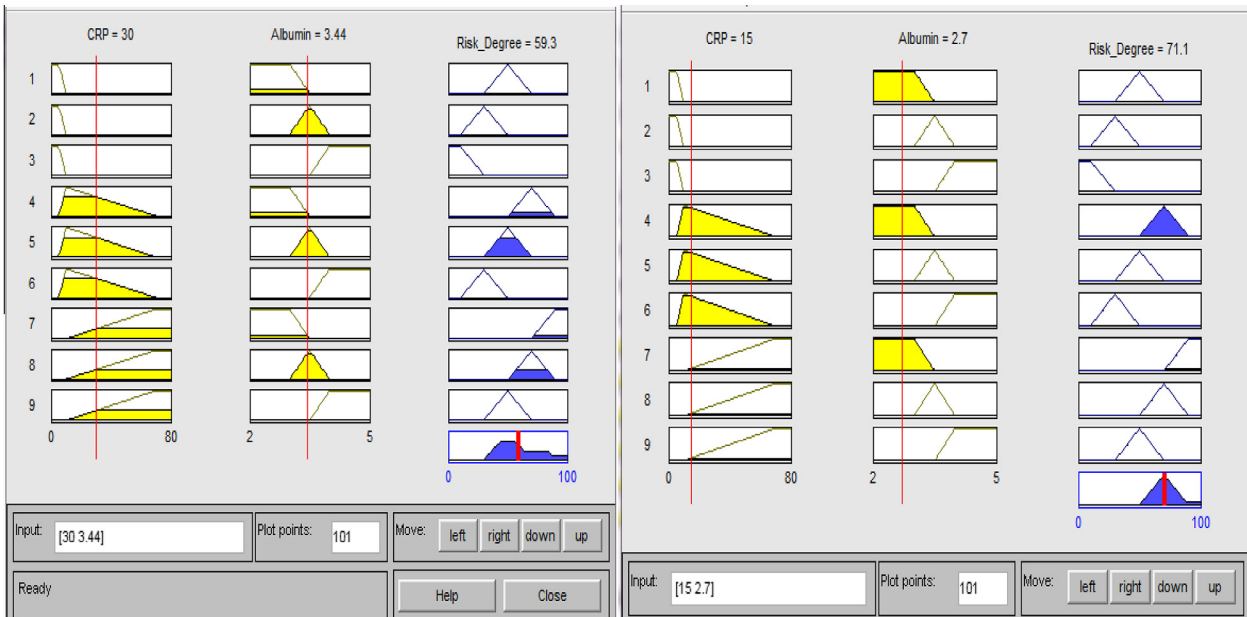


Figure 8 A Final decision of the with (a) CRP = 30 and albumin = 3.44, (b) values of CRP = 15 and albumin = 2.7.

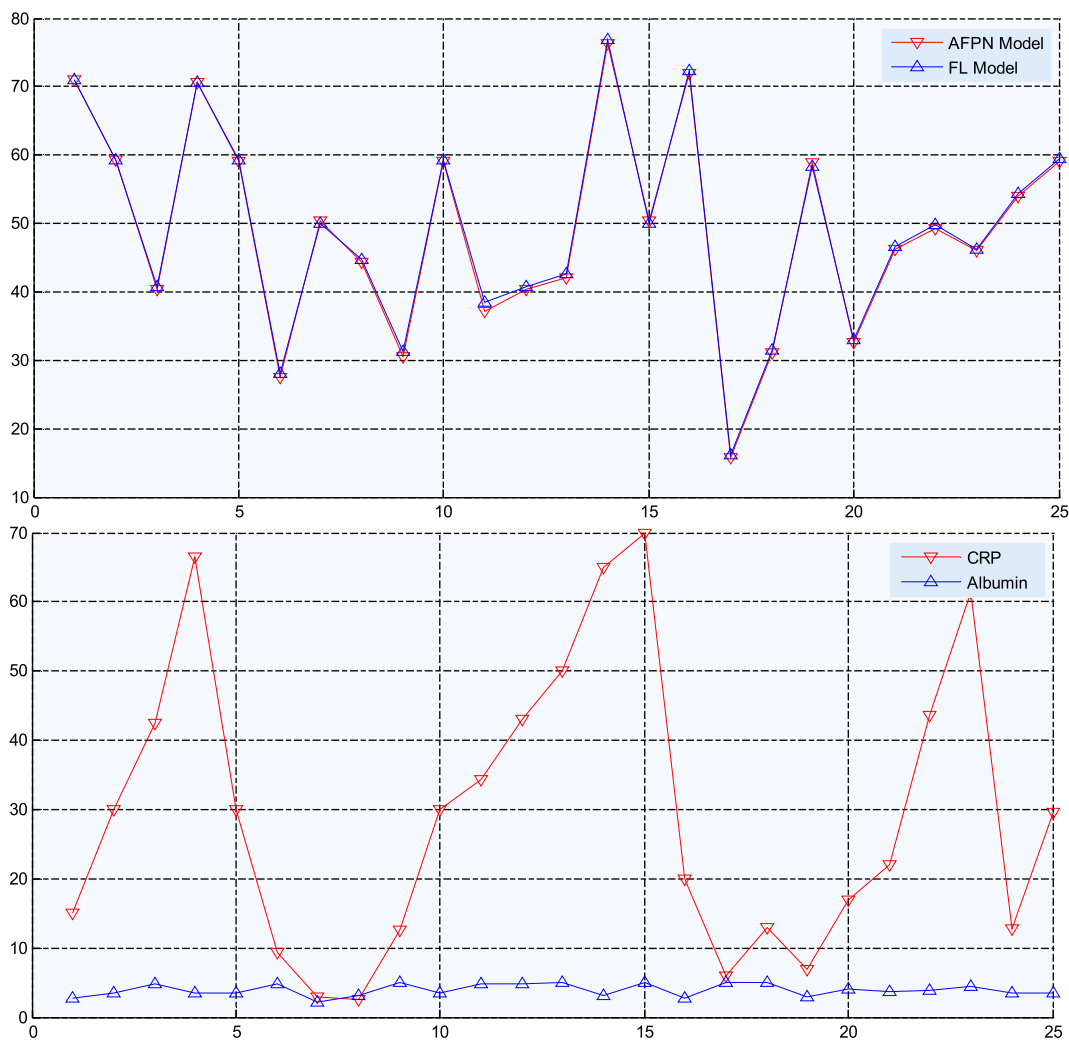


Figure 9 Risk degree estimation of (p_{12}) for both AFPNs Model and FL model with CRP and albumin.

$$\alpha^3 = (0.0833, 0.9167, 0, 0.1, 0, 0, 0.0092, 0.0796, 0.4746, 1.5528, 0.8178, 71.0663)^T.$$

(4) For the fourth iteration, $k = 4$

$$\alpha^4 = (0.0833, 0.9167, 0, 0.1, 0, 0, 0.0092, 0.0796, 0.4746, 1.5528, 0.8178, 71.0663)^T.$$

As $\alpha^3 = \alpha^4$ the final state of places p_{12} truth degree vector is $(0.0833, 0.9167, 0, 0.1, 0, 0, 0.0092, 0.0796, 0.4746, 1.5528, 0.8178, 71.0663)^T$ and the marking vector is $M^3 = (1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1)^T$, then the final value of $\alpha(p_{12})\text{RiskDegree} = 71.0663$ see Fig. 8.

We can see that the proposed algorithm has adaptive capacity with the change of weights and certainty factor values to get best values. A set of experiments were performed to test the performance of the AFPN model.

Fig. 9 shows the responses of the AFPN model at twenty-five different values. As is seen from Fig. 9 the model shows the model responses robustly risk degree. In order to examine the behavior of the model to predict risk degree, the experimental results of the AFPN model to compare with (Chang et al., 2012) shown that our model is appropriate as a prognostic model for esophageal cancer. The weights value of the our model were chosen to be accurate, while those in Chang et al.

(2012) it seems to be less accurate, so the results obtained from our model are high accuracy. The results of the effects of 9 rules yielded satisfactory output risk degree. The result displayed in Fig. 9 reveals that the curve will be considerably the results of the AFPN model and fuzzy logic model (Chang et al., 2012), with CRP and albumin.

7. Conclusion

In this paper, we proposed an approach to estimate the outcome of esophageal cancer based on the adaptive fuzzy Petri net reasoning algorithm with a capability of using the weight, certainty factor and threshold values specified for each component (places and transitions) of the model to be optimally tuned based on the observed data.

Considering the tradeoff between estimation accuracy of the AFPN model and fuzzy logic model (Chang et al., 2012), simple method and good estimation accuracy has been revealed with our approach. The proposed prognostic approach uses AFPN reasoning algorithm to obtain accurate estimate of the esophageal cancer. This approach combines the capability of fuzzy Petri net reasoning and the capability

of adaptive mechanism in learning from reasoning. An experimental system has been tested and the algorithm is implemented to show the effectiveness of the algorithm. The proposed algorithm of AFPN implemented on the developed experimental system can estimate esophageal cancer based on the serum concentrations C-reactive protein (CRP) and albumin as input variables accurately. The model of AFPN reasoning algorithm exposes that the model was a powerful tool to combine medical experts' knowledge into a prognostic model based on input data.

To the best of my knowledge it is the first time that an adaptive fuzzy Petri net is used to make qualitative inferences of a biological system. As far as future work, other qualitative based analysis of an adaptive fuzzy Petri net model such as high-level fuzzy Petri net, and fuzzy colored Petri Nets (FCPNs), etc. can be performed which form the future scope in regard to the enhancement of this paper.

References

- Bhaskar, B., Logan, R.G., Urs, U., 2012. Tryptophan fluorescence of cells and tissue in esophageal carcinoma. *IEEE Sens. J.* 12 (11).
- L.M. Brown and S.S. Devesa. Esophageal Cancer. *Interna. Encyclopedia of Public Health*, 2008, pp. 459–468.
- Chang, Y.W., Tsair, F.L., Chun, H.F., Jyh, H.C., 2012. Fuzzy logic-based prognostic score for outcome prediction in esophageal cancer. *IEEE Trans. Inf Technol. Biomed.* 16 (6).
- Deans, D.A., Wigmore, S.J., de Beaux, A.C., Paterson-Brown, S., Garden, O.J., Fearon, K.C., Dec. 2007. Clinical prognostic scoring system to aid decision-making in gastro-oesophageal cancer. *Br. J. Surg.* 94, 1501–1508.
- Djäv, T., Lagergren, J., Blazebj, J., Lagergren, P., 2008. Long-term health-related quality of life following surgery for oesophageal cancer. *Br. J. Surg.* 95, 1121–1126.
- Hamdan, H., Garibaldi, J.M., 2010. Adaptive neuro-fuzzy inference system (ANFIS) in modelling breast cancer survival. *Proc. IEEE Int. Conf. Fuzzy Syst.*, 1–8.
- Jagannath, P., Jason, S.G., Nikhil, C.M., Masood, A.S., 2013. Biology of telomeres: importance in etiology of esophageal cancer and as therapeutic target. *Transl. Res.* 162 (6).
- Kuo, C., Chen, T., 2013. Controllable Petri net-based implementation approach for motor control systems. *IEEE Trans. Ind. Electron.* 60 (10), 4599–4612.
- Li, X., Yu, W., Lara-Rosano, F., 2000. Dynamic knowledge inference and learning under adaptive fuzzy Petri net framework. *IEEE Trans. Syst. Man Cybern. Part C Appl. Rev.* 30 (4), 442–450.
- Liu, H., Liu, L., Lin, Q., Liu, N., 2013. Knowledge acquisition and representation using fuzzy evidential reasoning and dynamic adaptive fuzzy Petri nets. *IEEE Trans. Cybern.* 43 (3).
- Liu, H., Lin, Q., Mao, L., Zhang, Z., 2013. Dynamic adaptive fuzzy Petri nets for knowledge representation and reasoning. *IEEE Trans. Syst. Man Cybern. B Cybern.* 43 (6).
- Mathé, E.A., Nguyen, G.H., Bowman, E.D., Zhao, Y., et al, 2009. MicroRNA expression in squamous cell carcinoma and adenocarcinoma of the esophagus: associations with survival. *Clin. Cancer Res.* 15 (19), 6192–6200.
- McMillan, D.C., Crozier, J.E., Canna, K., Angerson, W.J., McArdle, C.S., 2007. Evaluation of an inflammation-based prognostic score (GPS) in patients undergoing resection for colon and rectal cancer. *Int. J. Colorectal Dis.* 22, 881–886.
- Mohamed, S.H., Ramdane, M., Yacine, K., Maamar, S., 2014. Unexpected rules using a conceptual distance based on fuzzy ontology. *Science Direct-Elsevier, J. King Saud Univ. Comput. Inf. Sci.* 26, 99–109.
- Naoto, Y., Shigeyuki, O., Kikuya, K., Shin, I., 2009. Optimal Aggregation of Binary Classifiers for Multiclass Cancer Diagnosis Using Gene Expression Profiles. *IEEE/ACM Trans. Comput. Biol. Bioinf.* 6 (2).
- Raed, I.H., Syed, I.A., 2011. Confidence value prediction of DNA sequencing with Petri net model. *Science Direct-Elsevier, J. King Saud Univ. Comput. Inf. Sci., KSU-CIS J.* 23 (2), 79–89.
- Ramsey, S., Lamb, G.W., Aitchison, M., Graham, J., McMillan, D.C., 2007. Evaluation of an inflammation-based prognostic score in patients with metastatic renal cancer. *Cancer* 109, 205–212.
- Schneider, B.J., Urba, S.G., 2007. Preoperative chemoradiation for the treatment of locoregional esophageal cancer: the standard of care? *Semin. Radiat. Oncol.* 17 (1), 45–52.
- Schneider, B.J., Urba, S.G., 2007. Preoperative chemoradiation for the treatment of locoregional esophageal cancer: the standard of care? *Semin. Radiat. Oncol.* 17, 45–52.
- Shen, V.R.L., 2003. Reinforcement learning for high-level fuzzy Petri nets. *IEEE Trans. Syst. Man Cybern. B Cybern.* 33 (2), 351–362.
- Wai, R., Chu, C., 2007. Motion Control of Linear Induction Motor via Petri Fuzzy Neural Network. *IEEE Trans. Industr. Electron.* 54 (1).
- Wang, C.Y., Hsieh, M.J., Chiu, Y.C., Li, S.H., Huang, H.W., Fang, F.M., Huang, Y.J., 2009. Higher serum C-reactive protein concentration and hypoalbuminemia are poor prognostic indicators in patients with esophageal cancer undergoing radiotherapy. *Radiother. Oncol.* 92, 270–275.
- Yang, J.H., Tsai, J.P., Chen, C., 2003. Fuzzy Rule Base Systems Verification Using High-Level Petri Nets. *IEEE Trans. Knowl. Data Eng.* 15 (2).
- Yoo, J., Lee, J., Hong, S., 2013. Petri net-based FTL architecture for parametric WCET estimation via FTL operation sequence derivation. *IEEE Trans. Comput.* 62 (11), 2238–2251.
- Yuan, J., Shi, H., Liu, C., Shang, W. 2008. Improved basic inference models of fuzzy Petri nets. In: *Proc. 7th World Conference Intelligent Control and Automation*. pp. 1488–1493.
- Yue, Z., Huichai, Y., Xiaoling, W., et al, 2013. Sirtuin-3 (SIRT3) expression is associated with overall survival in esophageal cancer. *Ann. Diagn. Pathol.* 17, 483–485.