

A Fuzzy Surface of the Relationship between Hormones in Autoimmune Thyroiditis

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Abstract: Thyroid disorders are common disorders of the thyroid gland. Thyroid disorders include such diseases and conditions as graves disease, thyroid nodules, Hashimoto's thyroiditis, trauma to the thyroid, thyroid cancer and birth defects. These include being born with a defective thyroid gland or without a thyroid gland. Thyroid disorder can be caused by hyperthyroidism, thyroid cancer, goiter, hyperparathyroidism and postpartum thyroiditis. Thyroid disorder are usually characterized by life threatening symptoms such as insomnia, irritability, nervousness, unexplained weight loss, heat sensitivity, increased perspiration, thinning of skin, warm skin, fine hair, brittle hair and thinning hair. Fuzzy Logic explores approximation techniques to finds the parameter of a fuzzy system. In this paper we have used Fuzzy-rule based systems to elaborate autoimmune thyroiditis diseases to study the relations between TSH, FT4 and patient's status. A surface is drawn to show the relationship between these parameters. We categories both inputs TSH, FT4 and one output in three categories. Finally we obtain a 3-D surface which shows a most practical relationship.

Keywords: fuzzy sets, fuzzy rule based systems, antibodies, autoimmune thyroiditis

I. Introduction

Autoimmune (Hashimoto's) thyroiditis is a complex disorder in which the immune system attacks the thyroid gland with both proteins and immune cells such as T cells, and cytokines for long periods. More precisely, as one aspect of autoimmune thyroiditis, the immune system produces proteins (thyroid peroxidase antibodies, TPOAb and thyroglobulin antibodies, TGAb) against the thyroid follicle cell membrane proteins (thyroid peroxidase, TPO and thyroglobulin, TG) in the blood. These proteins (TPOAb and TGAb) induce thyroid follicle cell lysis by binding with TPO and TG respectively. Thus, autoimmune thyroiditis interrupts the normal thyroid operation and eventually disrupts feedback control. Consequently, one develops symptoms (like, goiter), signs (like, hyperactivity), and some clinical conditions, like, euthyroidism (normal FT4 and TSH levels in the blood), subclinical hypothyroidism (normal FT4, but TSH above normal levels), overt (clinical) hypothyroidism (underactive thyroid gland- low FT4 levels and TSH above normal levels) or hashitoxicosis (transient hyper to hypothyroidism). Hashitoxicosis is a life-threatening abnormal clinical condition. It is one of the rare presentations of autoimmune thyroiditis, approximately 5% of all autoimmune thyroiditis patients. From the clinical viewpoint, the presence of anti-thyroid antibodies in blood serum is the hallmark of this disease and has been considered as a diagnostic tool of autoimmune thyroiditis in healthy and asymptomatic individuals. Their presence in normal individuals is the risk factor for overt hypothyroidism and also believed that, antibodies induce thyroid damage for long periods until hypothyroidism is clinically become evident. As a result, the set point of the HPT axis changes for long periods along with damaging thyroid gland. On the other hand, the absence of anti-thyroid antibodies is strong evidence against autoimmune thyroiditis [1]. Therefore, individuals with anti-thyroid antibodies (TPOAb and TGAb) considered being autoimmune (Hashimoto's) patients in the clinical setting. Cases of the disorders are more common in women than in men. Hashimoto's thyroiditis occurs most often in females between the ages of 30 and 50 years and appears to have a genetic component because it can run in families. People over the age of fifty who have hypertension or atherosclerosis are at risk for hyperthyroidism [2, 3 and 4]

In clinical practice, in general, physicians see three different kinds of patients with autoimmune (Hashimoto's) thyroiditis with or without goiter.

- a) Patients with euthyroidism (normal FT4 and TSH levels).
- b) Patients with subclinical hypothyroidism (normal FT4 but TSH above normal levels).
- c) Patients with overt (clinical) hypothyroidism (low FT4 and TSH above normal levels).

Usually patients with euthyroidism progress to subclinical hypothyroidism and then progress to overt hypothyroidism. This is a sequential event in most patients. But, euthyroidism in some patients may persist for many years even lifelong. This means to say that overt hypothyroidism is not an obligated evolution of the autoimmune thyroiditis. Similarly subclinical hypothyroidism in some patients may persist for many years even

lifelong. It means to say that again overt hypothyroidism is not an obligated evolution of the autoimmune thyroiditis. Overt hypothyroidism is the end stage of the course of autoimmune thyroiditis where patients need thyroid hormone replacement treatment. Levothyroxine (synthetic free thyroxine) is commonly used drug as thyroid hormone replacement. In this paper we are developing a Fuzzy Expert system by which we can gain more knowledge about the relation of TSH ,FT4 and status of patients.

II. Fuzzy Expert System (FES)

Fuzzy logic[5], [6] is a superset of conventional Boolean logic and extends it to deal with new aspects such as partial truth and uncertainty. Fuzzy inference is the process of formulating the mapping from a given input set to an output using fuzzy logic. The basic elements of fuzzy logic are linguistic variables, fuzzy sets, and fuzzy rules [7]. The linguistic variables' values are words, specifically adjectives like "small," "little," "medium," "high," and so on. A fuzzy set is a collection of couples of elements. It generalizes the concept of a classical set, allowing its elements to have a partial membership. The degree to which the generic element "x" belongs to the fuzzy set A (expressed by the linguistic statement x is A) is characterized by a membership function (MF), $f_A(x)$. The membership function of a fuzzy set corresponds to the indicator function of the classical sets. It can be expressed in the form of a curve that defines how each point in the input space is mapped to a membership value or a degree of truth between 0 and 1. The most common shape of a membership function is triangular, although trapezoidal and bell curves are also used. This operation normalizes all inputs to the same range and has a direct effect on system performance and accuracy.

A fuzzy set "A" defined within a finite interval called universe of discourse U as follows:

$$A = \{(x, f_A(x)), f_A(x): U \rightarrow [0,1]\}$$

U is the completely input range allowed for a given fuzzy linguistic variable. All fuzzy sets related to a given variable make up the term set, the set of labels within the linguistic variable described or, more properly, granulated. Fuzzy rules form the basis of fuzzy reasoning. They describe relationships among imprecise, qualitative, linguistic expressions of the system's input and output. Generally, these rules are natural language representations of human or expert knowledge and provide an easily understood knowledge representation scheme. Interpreting an if-then rule involves two distinct parts: first evaluating the antecedent and then applying results to the consequent (known as implication) [8]. In the case of two-valued or binary logic, if-then rules do not present much difficulty. If the premise is true, then the conclusion is true, whereas with fuzzy approach, if the antecedent is true to some degree of membership, then the consequent is also true to that same degree.

There are two types of fuzzy inference models:

- 1. Mamdani [9],**
- 2. Tsk Or Sugeno [10].**

Mamdani-type [8] inference expects the output membership functions to be fuzzy sets. After the aggregation process, there is a fuzzy set for each output variable that needs defuzzification. It is possible, and in many cases much more efficient, to use a single spike as the output's membership function rather than a distributed fuzzy set. This is sometimes known as a singleton output membership function, and it can be thought of as a pre-defuzzified fuzzy set. It enhances the efficiency of the defuzzification process because it greatly simplifies the computation required by the more general Mamdani method, which finds the centroid of a two-dimensional function. Rather than integrating across the two-dimensional function to find the centroid, Sugeno-type systems use weighted sum of a few data points. In general, Sugeno-type systems can be used to model any inference system in which the output membership functions are either linear or constant. Fuzzy Logic is presented in Figure 1.

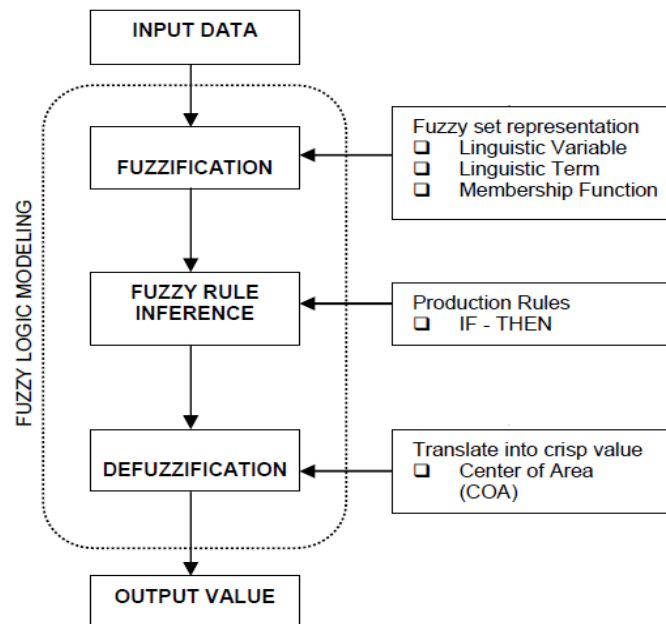


Figure 1: Conceptual modelling

The detail discussion about the modelling steps is presented in the following sections. In [11] varying conditions of ET and ITCT parameters, the maximum value of OBT likely to be changes accordingly that depends on the inference engine mechanism. A detailed exposition of the application combining linguistic approach to optimize OBT considering heterogeneous environment is presented in this study. [12] In this paper authors conclude that centroid bisector and MOM methods of defuzzification are better as compared to the LOM, SOM on the basis of more consistency in results. In [13] they proposed a model, the input stage consists of three input variables i.e. CPU Time, Failure Rate and Reliability. CPU Time is the actual amount of time a task requires on CPU to get executed, failure rate is the frequency with which a system fails; and reliability is the probability that the system would execute all the tasks assigned to it. In [14] they vitalized the uncertainty and fuzzy rule consideration in the estimation of phosphorus loading and eutrophication status of hydrologic system namely detention pond using fuzzy logic. [15] in this paper reveals mathematical models of the simplest mamdani PI/PD controllers which employ two fuzzy set on the universe of discourse of each of two variables and three fuzzy sets on the UOD of output variable. [16] In this paper the authors tell how a fuzzy modelling offers a unique advantage—the relationship between the linguistic description and the mathematical model can be used to verify the validity of the verbal explanation suggested by the observer. Knowledge-based expert systems (KBES), or simply expert systems, use human knowledge to solve problems that normally would require human intelligence. Most expert systems are developed via specialized software tools called shells. These shells come equipped with an inference mechanism (backward chaining, forward chaining, or both), and require knowledge to be entered according to a specified format [17 and 18]

The close relation between the linguistic information and the fuzzy model offers many important advantages. A fuzzy model represents the real system in the form that corresponds closely to the way humans perceive it. Thus, the model is easily understandable, even by a non-professional audience and each parameter has a readily perceivable meaning. The model can be easily altered to incorporate new phenomena and if its behaviour is different than expected. It is usually easy to find which rule/ term should be modified and how. We propose to utilize fuzzy modelling as a tool for assisting human observation in the difficult task of transforming their observation into mathematical model.

III. Proposed Model

As shown in figure, the major factor in the autoimmune (Hosimoto's) thyroiditis are TSH and FT4. In the proposed fuzzy expert system we are taking two input variables as TSH and FT4 in three categories and one output as status of patients (SOP) also in three categories. The both inputs membership function TSH and FT4 are categories in three categories as— below normal level, normal level and above normal level. The output variable are categories in three categories as follows—

- i. euthyroidism which is represented as ET.
- ii. subclinical hypothyroidism which is represented as SCLT.
- iii. clinical hypothyroidism which is represented as CLT.

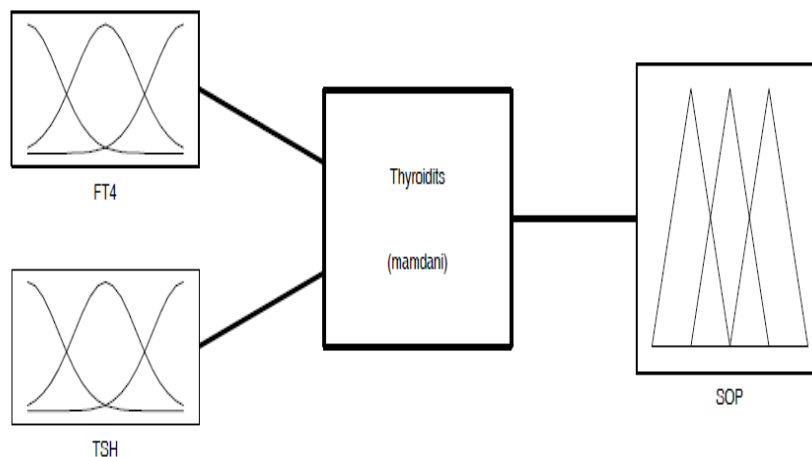


Fig. 2 Inference system Block Diagram

Fuzzification

For fuzzification of input variable FT4, and TSH three linguistic variables, namely, ‘Below Normal (BN)’, ‘Normal (N)’, ‘Above Normal (AN)’ have been used. Similarly for Output variable Patients Status, another Three linguistic variables i.e. ‘euthyroidism (ET)’, ‘subclinical hypothyroidism (SCHT)’, and ‘clinical hypothyroidism (VHT)’ have been considered.

$$FT4(i_1) = \begin{cases} i_1; 0 \leq i_1 \leq 1 \\ 0; otherwise \end{cases}$$

$$TSH(i_1) = \begin{cases} i_1; 0 \leq i_1 \leq 1 \\ 0; otherwise \end{cases}$$

$$PC(PC_i) = \begin{cases} PC_i; 0 \leq PC_i \leq 1 \\ 0; otherwise \end{cases}$$

Membership Function

Using MATLAB FUZZY Toolbox, prototype triangular fuzzy sets for the fuzzy variables, ET, TSH and pi-shaped fuzzy set for variable SOP are set up [19]. The membership values used for the FIS were obtained from above the above the functions 1, 2 and 3 are shown in the Figures 3a–3c.

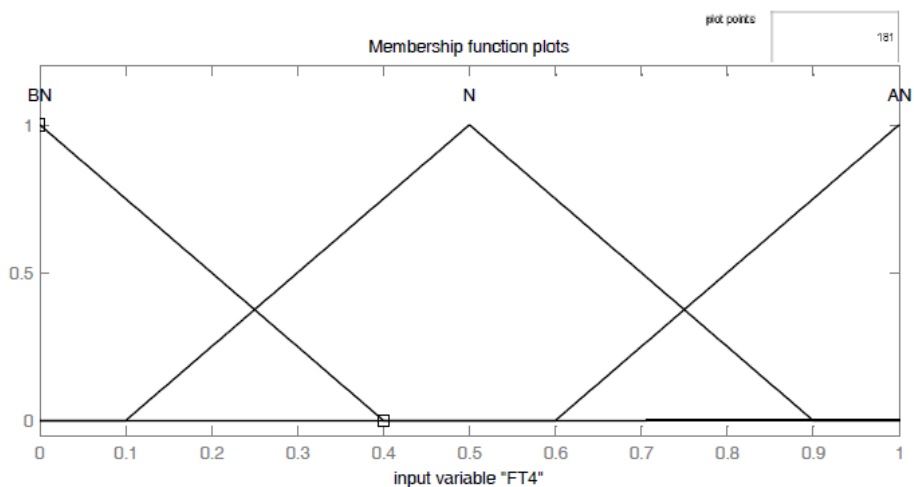


Figure 3(a): Membership Functions Plots of FT4

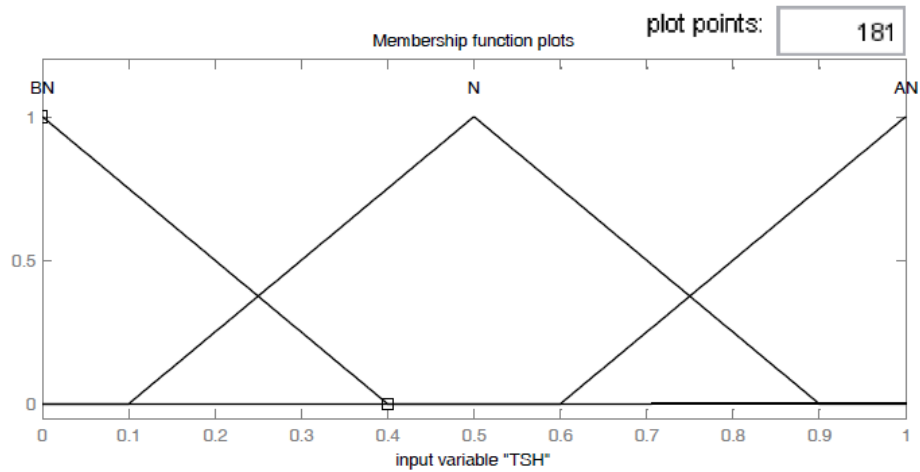


Figure 3(b): Membership Functions Plots of TSH

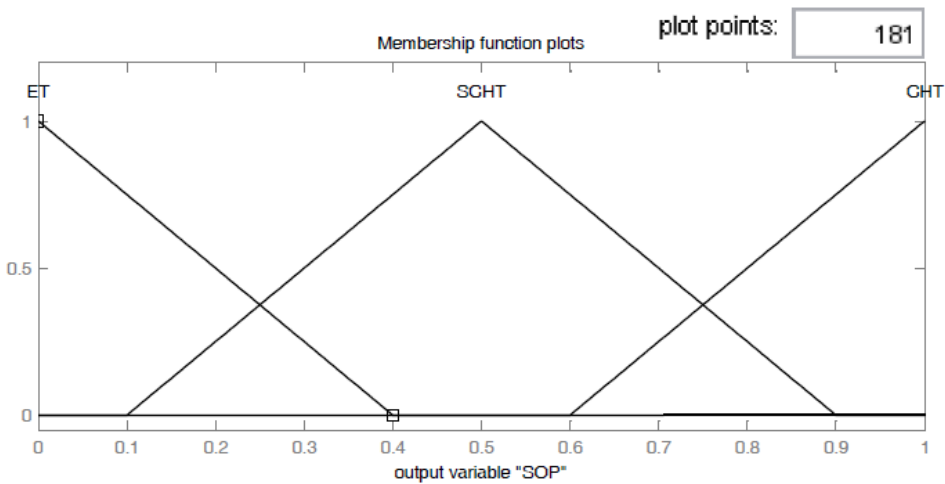


Figure 3(c): Membership Functions Plots of SOP

These membership functions helped in converting numeric variables into linguistic terms. For example, the linguistic expressions and membership functions for FT4 obtained from the developed rules and above the formula are given as following.

$$\mu_{BN}(i_1) = \left\{ \begin{array}{l} 0; i_1 \leq 0 \\ \frac{0.4 - i_1}{0.4}; 0.0 \leq i_1 < 0.4 \\ 0; i_1 > 0.4 \end{array} \right\}$$

$$\mu_{BN}(i_1) = \{1/0 + 0.5/0.2 + 0/0.4\}$$

$$\mu_N(i_1) = \left\{ \begin{array}{l} \frac{i_1 - 0.1}{0.4}; 0.1 \leq i_1 < 0.5 \\ \frac{0.9 - i_1}{0.4}; 0.5 \leq i_1 < 0.9 \\ 0; i_1 > 0.9 \text{ or } i_1 \leq 0.1 \end{array} \right\}$$

$$\mu_N(i_1) = \{0.0/.1 + 0.5/0.3 + 1/0.5 + 0.50/.7 + 0/0.9\}$$

$$\mu_{AN}(i_1) = \left\{ \begin{array}{l} 0; i_1 < 0.6 \\ \frac{i_1 - 0.6}{0.4}; 0.6 \leq i_1 < 1 \\ 0; i_1 > 1 \end{array} \right\}$$

$$\mu_{AN}(i_1) = \{0.0/.6 + 0.5/0.8 + 1/1\}$$

Fuzzy rules try to combine these parameters as they are connected in real worlds. Some of these rules are mentioned here:

If (TSH is below normal) and (FT4 is above normal), then (status of patients is CHT).

If (TSH is normal) and (FT4 is normal), then (status of patients is ET).

If (TSH is normal) and (FT4 is above normal), then (status of patients is SCHT).

IV. Results & Discussions

The methodology applied in the presented research gives the output as follows.

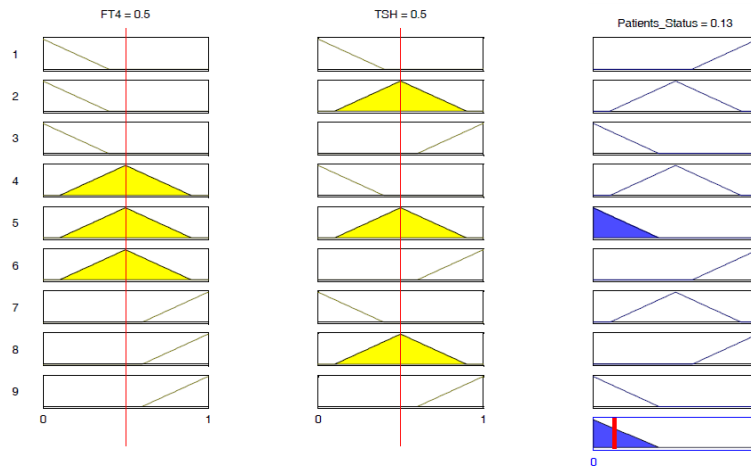


Fig. 5 Rules of the inference system

The proposed method is different from all the research methods presented in the past by various researchers as it is the very first time used in the autoimmune thyroiditis diseases and the relation between the TSH and FT4 and the status of patients are considered through fuzzy Experts system. The decision surface corresponding to rules and membership functions is illustrated in Fig. 5

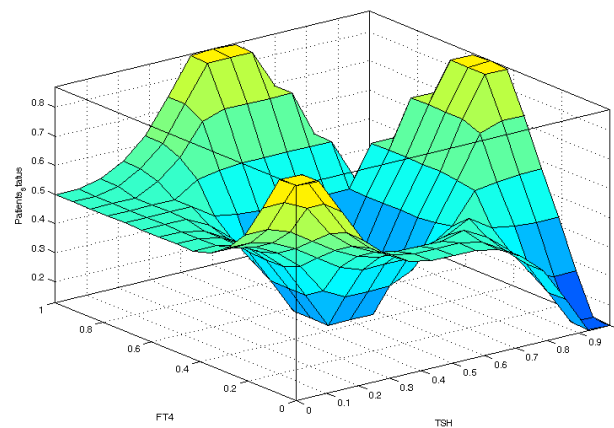


Fig. 6 Surface of The Hormonal Relations

V. Conclusion

The fuzzy experts system, which is proposed in this paper, has low complexity and more clarity due to the simplicity of fuzzy expert system. A detained exposition of the application combining linguistic approach to optimize the realistic relation with status of patients is presented in this study.

We would like to highlight the advantages of using fuzzy rule-based models as opposed to deterministic models:

- several differential equations parameters of the thyroid type systems are not available;
- in the fuzzy model, we have used a rule base, instead of systems given by equations, eliminating the difficulty of obtaining the parameters; these parameters can be obtained, if needed, through curve fitting

procedure from the solutions obtained by the fuzzy rule-based models;

- the input and output sets of fuzzy rule-based systems can be easily constructed with the help of specialists in the field, that is, a specialist will know when the level of TSH, FT4 are below normal, normal and above normal and so forth.

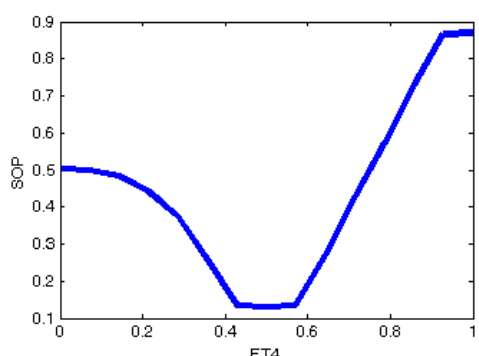


Fig. 7(a) graph between SOP and FT4

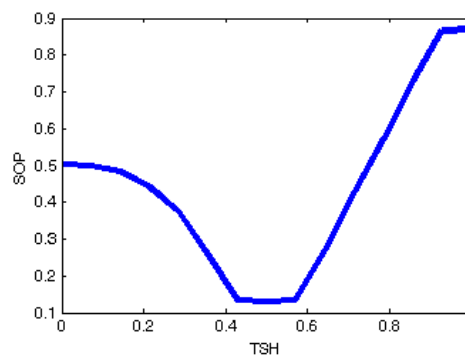


Fig. 7(b) graph between SOP and TSH

By the study of these two graphs of figure 7(a) and 7(b), we can conclude that there is symmetry between both the graphs. It means both the hormones are harmful for the patient's status in the above normal cases. In the above normal cases patients are very much prone to have thyroid.

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