Multi-level Fuzzy Inference using Hair Tissue Mineral Analysis for Estimating Diagnoses

Young Im Cho[1†] and Sanggil Kang[2††],

[1†] University of Suwon, Hwaseong, Gyeonggi-do, Korea
[2††]INHA University, 254 Younghyun-dong, Nam-gu, Inchon, Korea

Summary
In this paper we introduce a multi-level fuzzy inference system using hair tissue mineral analysis (HTMA) for estimating diagnoses. In HTMA, the characteristics of mineral ratios can be represented in linguistic terms of the metabolic characteristics and nutritional requirements. Thus the mechanism can be expressed in fuzzy sets, i.e., 'high', 'low', and 'acceptable.' Based on the fuzzy sets of mineral ratios, we can build fuzzy rules between the mineral ratios and doctors' diagnosis reports. Conventional fuzzy inference system can not be suitable for the hair tissue mineral analysis because a lot of mineral examination is needed to make various diagnoses for a patient. It causes fuzzy inference to be complicated because of increasing the combination of rules. To solve the problem, we introduce a multi-level fuzzy inference system which breaks down the fuzzy rules used for estimating a diagnosis into basic units of fuzzy rules which are connected in a chain form according to the premise and conclusion in the basic units. By using the multi-level fuzzy rules, we can infer a diagnosis without whole mineral ratios required for estimating diagnoses. In the experimental section, we showed the efficiency of our method by comparing with the conventional method using 500 patients' hair tissue mineral analysis information.

Key words:
Diagnosis, fuzzy set, multi-level fuzzy inference system, TMA.

1. Introduction

Tissue mineral analysis (TMA) plays an important role for understanding human body's mineral state. From the analysis, doctors can make diagnoses and begin appropriate treatments. As a traditional test of TMA, blood test has been done. It is subject to variations on a daily and sometimes hourly basis. Hair [2, 3] is used as a feature for TMA because it is stable and provides an average reading of past two to three months. From hair tissue mineral test, we can figure out the deficiencies, unbalances, or toxicities of minerals in body [1]. In general hair tissue mineral analysis (HTMA) represents the TMA. From this point, both terms can be exchangeable for convenience in this paper.

TMA proposes a cell level activation (adrenal and thyroid gland) and describes the possibility of diseases by the unbalance of nutrition and hormone. From TMA, we can obtain 30 nutritional minerals information and 8 toxic minerals information [4-6]. The ratios of the minerals, i.e., Ca/P, Ca/K, Ca/Mg, Na/K, Na/Mg, etc, are important for estimating diagnoses rather than numerical value itself of each mineral. It is because the ratios of minerals to each other are in many respects equally as important as the individual level of any single mineral. Thus, the ratios between minerals can be an indicator of metabolic balance.

In TMA, the characteristics of mineral ratios can be represented in linguistic terms of the metabolic characteristics and nutritional requirements. Thus the mechanism can be expressed in fuzzy sets [5], i.e., 'high', 'low', and 'acceptable.' Based on the fuzzy sets of mineral ratios, we can build fuzzy rules between the mineral ratios and doctors' diagnosis reports. Using the fuzzy rules, a fuzzy inference system can be established for estimating diagnoses.

Conventional fuzzy inference system [7, 8] can not be suitable for the hair tissue mineral analysis because a lot of mineral examination is necessary to make various diagnoses for a patient. It causes fuzzy inference to be complicated because of increasing the combination of rules.

To solve the problem, we introduce a multi-level fuzzy inference system which breaks down the fuzzy rules into basic units of fuzzy rules which are connected in a chain form according to the premise and conclusion in the basic units. In the system, a conclusion of fuzzy rule can be a statement of the premise in its related unit fuzzy rule. By using the multi-level fuzzy rules, we can infer a diagnosis without whole mineral ratios required for pathologic examination.

The remainder of this paper is organized as follows. Section 2 introduces the fundamentals of HTMA and the basic concept of fuzzy inference system. In Section 3, the core part of this paper, we demonstrate the multi-level fuzzy inference diagnosis system. In Section 4, we compare our system with the conventional fuzzy inference system in terms of efficiency for estimating diagnoses

Manuscript received September 5, 2008.
Manuscript revised September 20, 2008.

using TMA information. In Section 5, we conclude our paper.

2. Related Work

2.1 TMA

Hair tissue mineral analysis is a screening test, which measures the mineral content of hair. Mineral content of hair reflects the mineral content of the body's tissues [1, 9-11]. If a mineral deficiency exists in the hair, it usually indicates a mineral deficiency or excess within the body. Since the structure of hair remains unchanged, the minerals are fixed in the hair. The levels in hair are not subject to change and the analysis accurately provides concentrations of minerals that have accumulated in the hair tissue over the hair growth period, approximately the last three months.

Hair TMA shows individual deficiencies or excesses as well as the presence of toxic minerals. The TMA focuses the interrelationships of the various nutrients. There is a biological antagonism that exists between certain nutrients. It is important for the mineral ratios to be in the expected ranges so that one mineral excess or deficiency does not affect the metabolism of another. Vitamins cannot function and cannot be assimilated without the aid of minerals and though the body can synthesize some vitamins, it cannot manufacture a single mineral. Minerals affect on the activity of internal glands. Fig.1 shows the biological antagonism among internal glands. As seen in the figure, an increase in an internal gland will cause a decrease in the other one.

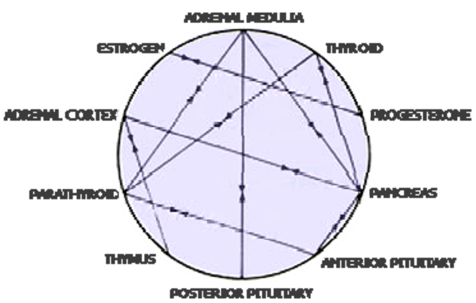

Fig. 1. Antagonism among internal glands

An excess of sodium relative to potassium can increase the need for potassium. Excess sodium relative to potassium may result in weight gain and water retention. A potassium deficiency of this type can be a result of inadequate intake and decreased retention. Calcium and potassium will antagonize each other's absorption and utilization by the body; excess in, calcium intake, or the increased retention of calcium will increase the need for additional potassium. High calcium relative to potassium will usually indicate a trend toward hypothyroidism. The mineral calcium antagonizes the retention of potassium within the cell. Since potassium is necessary in sufficient quantity to suggest reduced thyroid function or cellular response to thyroxin. If this imbalance has been present for an extended period of time, the following symptoms may occur - Fatigue, Depression, Dry skin, Constipation. The zinc level is high relative to tissue copper status. A zinc-copper imbalance in conjunction with low copper levels is a strong indicator of a decrease in the role of copper in many functions of metabolism. One of the main functions of copper is its necessity in collagen synthesis. If this profile becomes both severe and chronic, a decrease in collagen synthesis can occur. This can then be an indication to capillary fragility, osteoporosis and premature graying of the hair. The adrenal glands play an essential role in regulating sodium retention and excretion. Studies have shown that magnesium will affect adrenal cortical activity and response, and increased adrenal activity results in decreased magnesium retention. The sodium-magnesium profile is indicative of increased adrenal cortical function. These are the following symptoms. Anxiety, muscle cramps, palpitations, increased perspiration. Calcium and magnesium should always be in proper balance to one another. If the equilibrium is upset, one mineral will become dominant. Toxic metal accumulations in the body such as aluminum, arsenic, cadmium and lead may interfere with proper mineral and vitamin utilization and can induce un-favorable metabolic consequences. Hair treatment such as dyes, color treatment and perms may contribute to high levels of some nutrients. Hair coloring agents may contain manganese, lead, copper and iron. Bleaching agents can elevate levels of calcium and magnesium.

Approximately, 17 minerals out of 30 are essential in human nutrition. Although only 4 or 5 percent of the human body weight is mineral matter, minerals are vital to overall mental and physical well being. Like vitamins, minerals function as co-enzymes, enabling the body to perform its functions, including energy production, growth, and healing. Because all enzyme activities involve minerals, minerals are essential for the proper utilization of vitamins and other nutrients.

2.2 Fuzzy Inference System

The conventional CRI is the fuzzy inference method with multiple rules using 'max' and 'min' operators and is represented by possibility distribution values [7, 8]. Let '*X is A'* and '*Y is B'* be a fuzzy statement of premise and its conclusion, respectively. For a rule, the possibility distribution values of a specific premise fuzzy set *A* and its corresponding conclusion fuzzy set *B* can be denoted as $\Pi_X = \mu_A$ and $\Pi_Y = \mu_B$ as seen in eq. (1). Here, μ_A and μ_B is a membership function of fuzzy set *A* and *B*, respectively.

$$IF\ X\ is\ A\ THEN\ Y\ is\ B \rightarrow IF\ \Pi_x = \mu_A\ THEN\ \Pi_Y = \mu_B \tag{1}$$

If a test premise, denoted as *A′*, is given then its conclusion, denoted as *B′*, can be expressed as Eq. (2). Here, *R* is a fuzzy relation between them.

$$B' = A' \circ (X \rightarrow Y) = A' \circ R \tag{2}$$

Eq. (2) can be expressed in a membership function as following:

$$\begin{aligned}\mu_{B'}(v) &= \underset{u\in U, v\in V}{Max}\ \underset{i=1,n}{Max}(\mu_{A'}(u), \mu_{A_i}(u) \rightarrow \mu_{B_i}(v)) \\ &= \underset{u\in U, v\in V}{Max}\ \underset{i=1,n}{Min}(MaxMin(\mu_{A'}(u), \mu_{A_i}(u)), \mu_{B_i}(v))\end{aligned} \tag{3}$$

where $u \in U$ and $v \in V$ (*U* and *V* are universe of discourses). Also, A_i and B_i are the premise and its conclusion of rule *i*, here *i* = 1, 2, . . ., *n*.

Eq. (3) produces a big error for a premise which is very similar or identical to one of premises in rules due to no consideration of importance of rules. The more similar is the test premise to the premise, the more error we can have.

3. Modeling Multi-Level TMA Diagnosis System

A.Overall Architecture of the Proposed System

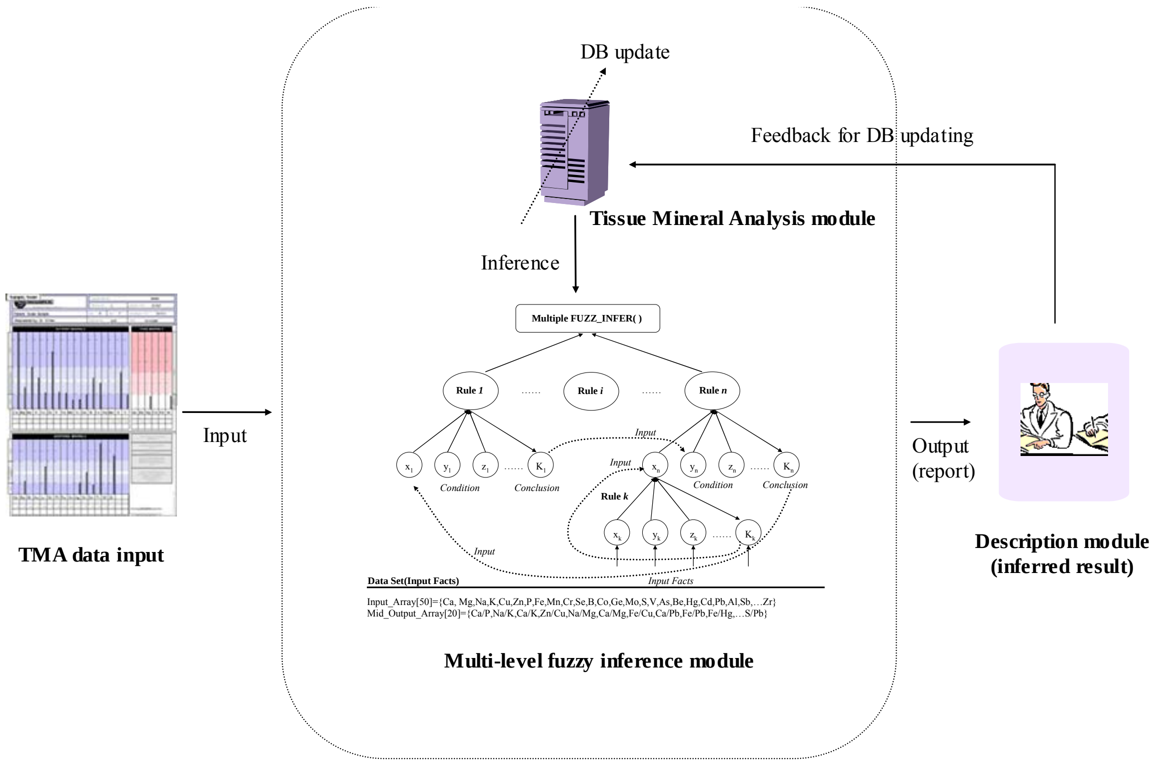

Fig. 2. Overall architecture of multi-level TMA diagnosis system

Fig. 2 is the overall architecture of our proposed system for modeling multi-level TMA diagnosis system. As seen in the figure, the system is consisted of three parts such as Tissue Mineral Analysis Module (TMAM), and Multi-level Fuzzy Inference Module (MFIM), and Description Module (DM). The TMAM collects patient hair analysis data such as mineral ratios, metabolic types, and internal glands and stores them into data base (DB). The mineral ratios include Ca/P, Ca/K, Ca/Mg, Na/K, Na/Mg, Zn/Cu, and Fe/Cu. The metabolic types include 8 types of metabolic in human biology system, 4 for the slow metabolic type and 4 for the fast metabolic type. The internal glands include Progesterone, Thyroid, Adrenal Cortex, etc. Also, TMAM update the DB whenever new patient's hair analysis data is collected.

In general the metabolic types play an important role on making a diagnosis from patients' symptoms. It is because each metabolic type has distinctive metabolic characteristics and nutritional requirements with respect to the mechanism of the internal glands. Table 1 shows an example of the linguistic mechanism of the metabolic characteristics and nutritional requirements. The mechanism can be expressed in fuzzy sets, i.e., 'high', 'low', and 'acceptable', which are represented by fuzzy membership functions as shown in Fig. 3 where *X* axis and Y axis represents mineral ratios and fuzzy membership function values, respectively.

Table 1. An example of the linguistic mechanism of the metabolic characteristics and nutritional requirements

Class Criterion	Adrenal Function			Thyroid Function		Metabolic Types
Ca/P>2.63	Parasympathetic nerve development	Na/Mg=4.0	Low value→ low function	Ca/K=4.2	High Value→ Low function	Slow type #1
	Parasympathetic nerve development	Na/Mg=4.0	High value → high function	Ca/K=4.2	High value → Low function	Slow type #2
	Parasympathetic nerve development	Na/Mg=4.0	Low value→ low function	Ca/K=4.2	Low value → High function	Slow type #3
	Parasympathetic nerve development	Na/Mg=4.0	High value → high function	Ca/K=4.2	Low value → High function	Slow type #4
Ca/P=2.63	Acceptable (Reference value)					
Ca/P<2.63	Sympathetic nerve development	Na/Mg=4.0	High value → high function	Ca/K=4.2	Low value → High function	Fast type #1
	Sympathetic nerve development	Na/Mg=4.0	High value → high function	Ca/K=4.2	High value → Low function	Fast type #2
	Sympathetic nerve development	Na/Mg=4.0	Low value→ low function	Ca/K=4.2	Low value → High function	Fast type #3
	Sympathetic nerve development	Na/Mg=4.0	Low value→ low function	Ca/K=4.2	High value → Low function	Fast type #4

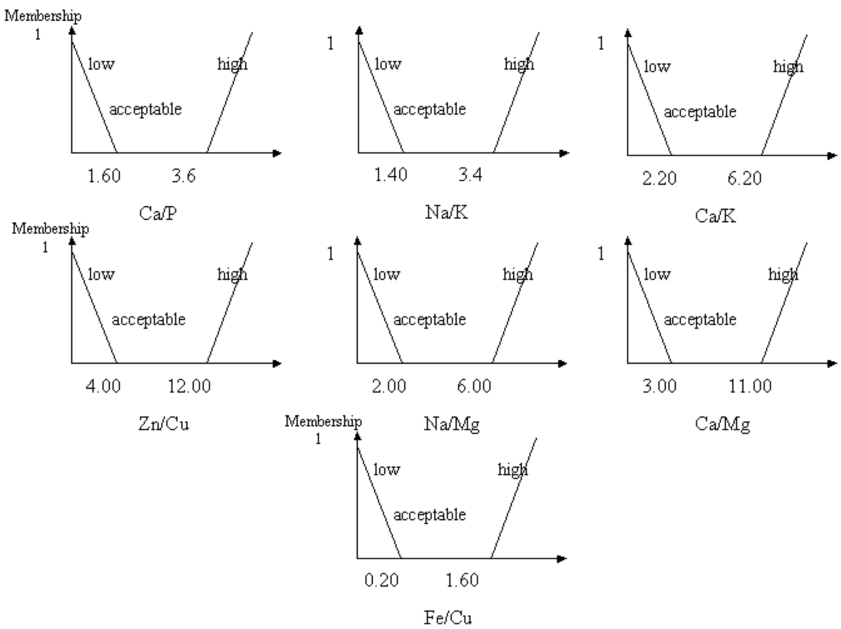

Fig. 3. Examples of fuzzy membership function of mineral ratios

To make various diagnoses for a patient, a lot of mineral examination is necessary, which causes fuzzy inference to be complicated because of increasing the combination of rules when the conventional fuzzy inference is used. To solve the problem, we developed the multi-level fuzzy inference in MFIM, which will be explained in detail at the following section. A diagnosis is estimated by MFIM and it is showed through a user interface in diagnosis paragraph form stored in the DB with its ID number as seen in Fig. 4.

ID	Diagnosis
…	…
13002311	*Low magnesium intake has been found in groups of people experiencing lung problems such as wheezing and asthma. Histamine can trigger lung problems and are also known to increase the requirement for magnesium*
13002312	*Magnesium deficiency has been shown to be associated with decreased antibody production. Published studies have revealed that the lymphocytes, which are the body's defense against foreign invaders, are inhibited when there is a deficiency of Magnesium*
13002313	*Low tissue calcium is associated with increased central nervous system sensitivity and increased serum lactic acid levels, both of which may contribute to increased anxiety states. Anxiety may be contributed to be any factor that interfaces with normal calcium metabolism such as stress or accumulation of toxic metals such as lead and mercury*
…	…

Fig. 4. An example of a diagnosis report stored in the DB

B. Multi-Level Fuzzy Inference

Fig. 5 is an example of the conventional fuzzy inference for making the diagnosis ID# 13002312. As seen in the figure, we need to know all mineral ratios premises, such as Ca/P is high and Ca/K is high and Na/K is low and Zn/Cu is high and Fe/Cu is high and Progesterone is high and Thyroid is high and Adrenal Cortex is high and Adrenal Cortex is high and Na/Mg is high, to make the diagnosis ID# 13002312. Thus, we have to analyze whole mineral ratios required for pathologic examination.

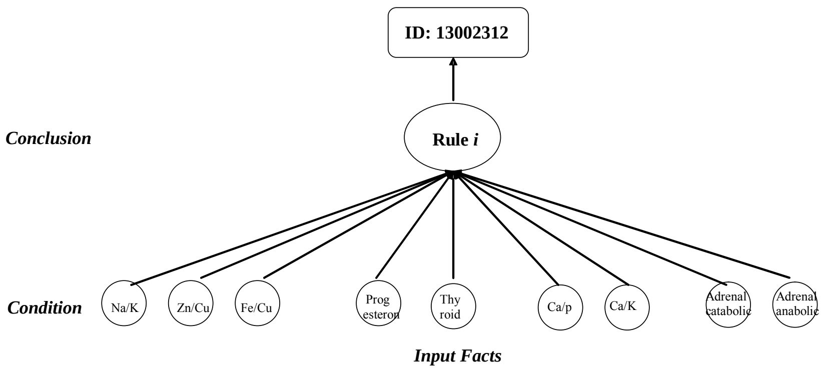

Fig. 5. Conventional fuzzy inference for making the diagnosis ID 13002312

However, our method breaks down the fuzzy rules into 5 rules named Rule#1, Rule#2, Rule#3, Rule#4, and Rule#5. As seen in Fig. 6, the conclusion in Rule#1 is fed into as a statement of the premise in Rule#2. Also, the conclusion of Rule#2 is fed into Rule#5 with that of Rule#3 and Rule#4 as the statements of the premise in Rule#5. The rules are defined as following:

- Rule#1: IF Na/K is low and Zn/Cu is high and Fe/Cu is high THEN Progesterone is high
- Rule#2: IF Progesterone is high and Thyroid is high THEN Ca/K is low
- Rule#3: IF Ca/P is high and Ca/K is high THEN S1
- Rule#4: IF Adrenal Cortex in Catabolic is high and Adrenal Cortex in Anabolic is high
- THEN Na/Mg is high
- Rule#5: IF S1 and Ca/K is low and Na/Mg is high THEN ID# 13002312

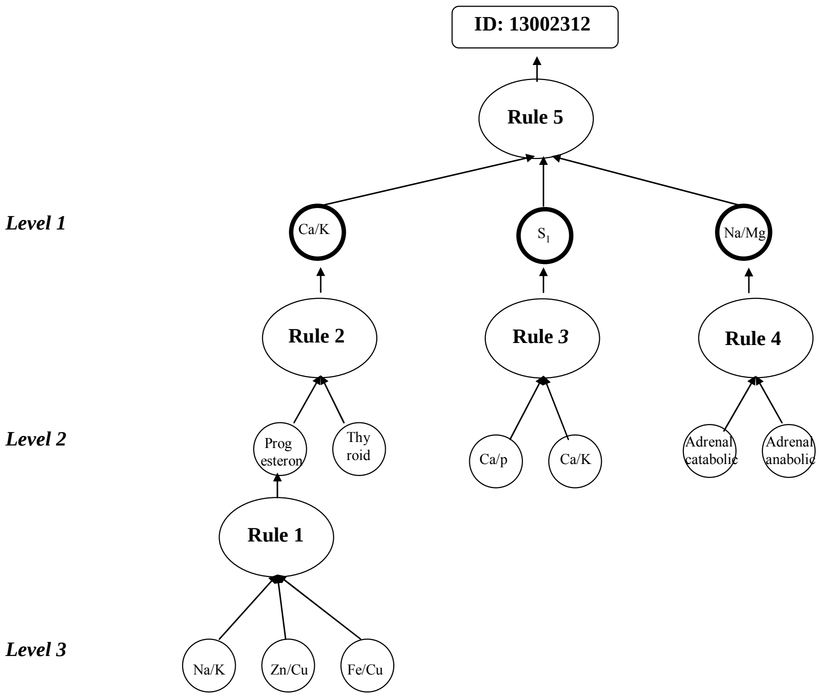

Fig. 6. Multi-level fuzzy inference for making the diagnosis ID 13002312

By using the multi level fuzzy rules, we can infer a diagnosis without whole mineral ratios required for pathologic examination. For example, if the mineral ratio Ca/K is low and Na/Mg is high and a metabolic type is S_1 can be obtained at the first stage, the diagnosis ID# 13002312 can be made by only Rule # 5. In this case, we do not need further analysis of the other mineral ratios such as Na/K, Zn/Cu Fe/Cu, and Ca/P and the internal secretions such as Progesterone, Thyroid, and Adrenal Cortex. In addition, just in case that a mineral ratio or an internal glands are needed for inferring a statement of premise of upper level, we go further analysis process. For example, if the metabolic type is not to be obtained at the current stage, then we analyze Ca/P and Ca/K and obtain S_1 by Rule#3. As explained, our method is more efficient than the conventional method.

Fig. 7 represents an algorithm in the multi-level fuzzy inference module. A fuzzy rule base and its corresponding fuzzy inference algorithm in the function named as *FUZZY_INFER( )* algorithm with two sub-functions named *FUZZY_INFER_I( )* and *FUZZY_INFER_II( )*, respectively as followed. Here, dataset (input facts) means the mineral ratios entering into the condition part of a rule in the fuzzy rule base.

```
FUZZY _INFER( ) ALGORITHM:

Enter of input facts to Rule i (initial input) ;
Production of rule set having some relations with Rule i;
Transformation to Input types capable of fuzzy inference;
If input fact == conditional part of Rule m (relative rules)
  then FUZZ_INFER_I(Rule base, input facts);
  // Fuzzy inference process in case of coinciding between inputs and condition part of a rule and the
     conclusion part of a rule is simple set, namely multi relationship among rules are absent.
If input fact == some conditional part of Rule n (relative rules)
  then FUZZ_INFERI_II(Rule base, input facts);
   {
     for( i=0; i<=n; i++)    // m, n are the number of fuzzy rules
       for(j=0; j<=m; j++)
         { x[i] of Rule[i] = K[j] of Rule[j];
           y[i] of Rule[i] = K[k] of Rule[k];
           x[i] of Rule[i] = K[m] of Rule[m];
         }
   }
  // Fuzzy inference process in case of a little coinciding between inputs and condition part of a rule and
     the conclusion part of a rule is derived another rules, namely multi relationship among rules are important.
```

Fig. 7. An algorithm in the multi-level fuzzy inference module

4. Experiment

In this section, we compare the performance of multi-level fuzzy inference with that of conventional fuzzy inference in terms of the number of mineral ratios, internal glands, and metabolic types to be measured, for making diagnoses. We stored the 1,073 diagnosis paragraphs, provided by Trace Elements Inc, which is the Korean government approval company, to the DB in Tissue Mineral Analysis Module (TMAM) explained in the previous section. Each diagnosis has its own identification number such as ID# 13002312 explained the previous section. In addition, the company provided 500 patients' TMA information data. Based on the TMA information and 1,073 diagnosis paragraphs, we built the conventional fuzzy inference system and the multi-level fuzzy inference system.

In order to demonstrate the efficiency of our method, we show the saving percentage of our method for estimating the diagnosis ID# 13002312 in terms of the needed number of TMA information, compared to the conventional method. It was done by each case of level needed for estimating the diagnosis as seen in Table 2. As seen in the table, if the TMA information of Ca/K, S_1, and Na/Ma is known at level 1, the 3 TMA information are enough for estimating the diagnosis in our method while 9 TMA information is needed for the conventional method. Thus, we can save 66.6% of the TMA information by using our method.

If we need to go further down to level 2, we can save 66.6% (4 cases as seen in the table) or 56.6% (2 cases as seen in the table). If the TMA information of Ca/K is unknown, it is needed to go further down to level 3. For S_1 and Na/Mg are known, it is saved by 33.3%. For only S_1 isknown or only Na/Mg is known, it is saved by 22.2%. When no TMA at level 1 is available, we need 8 TMA information. In this case, it can be saved by 11.1% only.

Table 2 The number of TMA information for estimating diagnosis

Needed level for estimating diagnosis	Known TMA information (mineral ratios, internal glands, metabolic types)	Needed number of TMA information		Saving (%)
		Our method	Conventional	
Level 1	(Ca/K, S_1, Na/Ma)	3	9	66.6%
Level 2	(Ca/K, S_1, Adrenal Catabolic) or (Ca/K, S_1, Adrenal Anabolic)	3	9	66.6%
	(Ca/P, Nam/Mg , Ca/P) or (Ca/P, Na/Mg ,Ca/K, Adrenal)	3	9	66.6%
	(Ca/P, S_1) or (Ca/P, Na/Mg)	4	9	56.6%
Level 3	(S_1, Na/Mg)	6	9	33.3%
	(S1)	7	9	22.2%
	(Na/Mg)	7	9	22.2%
	None	8	9	11.1%

Therefore, if our method is used, the TMA information is saved from minimum 11.1% to maximum 66.6%

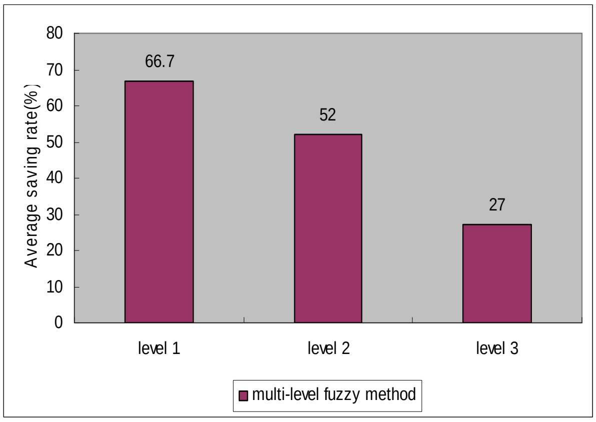

Fig. 8. The average saving percentage of our method

Fig. 8 shows the average saving percentage of our method for estimating the 1,073 diagnosis paragraphs. The figure shows that our method can save 66.7%, 52%, and 27% if the estimation can be made at level 1, level 2, and level 3, respectively.

5. Conclusion

In this paper, we have introduced a multi-level fuzzy inference using hair tissue mineral analysis information for estimating diagnoses. The experimental results in the previous section showed that our system is more efficient than the conventional fuzzy inference system if TMA information at lower level is available. However, our system needs more fuzzy rules than the conventional method. From our empirical experience, our system needs 5 fuzzy rules on average. In general the diagnosis can be estimated at level 1 or 2 so our system can successfully be executed with one or two rules. Therefore our method can save TMA information by about 59% on average for estimating diagnoses, compared to the conventional method.

In our system, the fuzzy rules for each diagnosis are critical to estimate accurate diagnosis. The 500 sample patients' reports used for modeling our system can not be enough for making the fuzzy rules. As a further work of this paper, we need to redo to model our system using more sample data.

Acknowledgments

This research was supported by the Ministry of Knowledge Economy, Korea, under the Information Technology Research Center support program supervised by the Institute of Information Technology Advancement. (grant number IITA-2008-C1090-0801-0031)

REFERENCES

[1] Karpas Z, Lorber A, Sela H, Paz-Tal O, Hagag Y, Kurttio P, Salonen L., Measurement of the 234U/238U ratio by MC-ICPMS in drinking water, hair, nails, and urine as an indicator of uranium exposure source. *Health Phys,* vol. 89, no.3, pp.315-321. *2005.*

[2] Watts, D.L., *Trace Elements and Other Essential Nutrients-Clinical Application of Tissue Mineral Analysis*, 2nd Writer's BLOCK edition, 1997.

[3] Baumgartner, W.A., and Hill,V.A., and Blahd, W.H., "Hair Analysis for Drugs of Abuse", *Journal of Forensic Science*, vol.34, no.6, 1989.

[4] Vir etal, "Serum and hair concentrations of Copper During Pregnancy", *American Journal of Clinical Nutrition*, vol.34, 1981.

[5] http://www.traceelements.com

[6] Jang, S.I. etal., "Research of hair tissue minerals in a diabetic", *Medical news,* .vol.45, no.5, 2002.

[7] Turksen, I.B., and Zhong, Z., "An approximate analogical reasoning schema based on similarity measures and interval valued fuzzy sets", *Fuzzy Sets and Systems*, North-Holland, vol.34, pp.323-346, 1990.

[8] Mamdani, E.: Application of Fuzzy Logic to Approximate Reasoning using Linguistic Systems. IEEE Transactions on Computers. vol. 26, no.12, pp.1182-1191, 1977

[9] Miekeley, N., et al., "Elemental Anomalies in Hair as Indicators of Endocrinologic Pathologies and Deficiencies in Calcium and Bone Metabolism.", *J. Trace Elem. Med. Biol.* 2005

[10] Kilic E, Saraymen R, Demiroglu A, Ok E. "Chromium and manganese levels in the scalp hair of normals and patients with breast cancer.", *Biol Trace Elem Res.* vol.102, no.1-3, pp.19-25, 2004.

[11] Spallholz JE, Boylan LM, Palace V, Chen J, Smith L, Rahman MM, Robertson JD., "Arsenic and Selenium in Human Hair; A comparison of Five Countries With and Without Arsenicosis.", *Biol Trace Elem Res.* vol.106, no.2, pp.133-144, 2005.

[12] Kozielec T, Salacka A, Karakiewicz B., "The influence of magnesium supplementation on concentrations of chosen bioelements and toxic metals in adult human hair.

Magnesium and chosen bioelements in hair.", *Magnes Res.* vol.17, no.3, pp.183-188, 2004.
[13] Sukumar A., "Factors influencing levels of trace elements in human hair.", *Rev Environ Contam Toxicol.* vol.175, pp.47-78, 2002.
[14] Black AP, Knight R, Batty J, Haswell SJ, Lindow SW., "An analysis of maternal and fetal hair lead levels.", *BJOG.* vol.109, no.11, pp.1295-1297, 2002.

Young Im Cho received the B.A. and M.S. and Ph.D. degrees in Computer Science from KOREA University at Korea in 1988, 1990 and 1994, respectively. Currently, she is a professor in Computer Science at Suwon University, Korea. Her research interests include Artificial Intelligence, Agent System, Information Retrieval, Inference Systems, Bioinformatics, etc

Sanggil Kang received the M.S. and Ph.D. degrees in Electrical Engineering from Columbia University and Syracuse University, USA in 1995 and 2002, respectively. He is currently a faculty in Computer Science and Information Engineering at Inha University, Korea. His research interests include Artificial Intelligence, Mobile Computing, Multimedia Systems, Inference Systems, Time Series, etc