Fuzzy-Evolutionary Synergism in an Intelligent Medical Diagnosis System

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Abstract. In this paper, we present the design, implementation and evaluation of HIGAS, a hybrid intelligent system that deals with diagnosis and treatment consultation of acid-base disturbances based on blood gas analysis data. The system mainly consists of a fuzzy expert system that incorporates an evolutionary algorithm in an off-line mode. The diagnosis process, the input variables and their values were modeled based on expert's knowledge and existing literature. The fuzzy rules are organized in groups to be able to simulate the diagnosis process. Differential evolution algorithm is used to fine-tune the membership functions of the fuzzy variables. Medium scale experimental results show that HIGAS does better than its non-hybrid version, non-experts and other previous computer-based approaches.

Keywords: *acid-base disturbances, hybrid expert systems, fuzzy-evolutionary synergism, computer diagnosis*

1. Introduction

Accurate diagnosis and treatment of electrolyte disturbances is an ability that only experienced doctors that have faced many patients for many years can perform. Unfortunately, even undergraduate studies on human physiology do not pay attention to this topic, so that many difficulties are faced during every-day clinical practice by general doctors, intensive care personnel, etc. Understanding a disturbance occurred after a cardiovascular shock or after an operation is crucial for a clinician who has to treat this serious situation for patients' life. There are two main acid-base balance disturbances, acidosis and alkalosis, further distinguished into metabolic acidosis, metabolic alkalosis, respiratory acidosis, respiratory alkalosis and their combinations (mixed disorders).

A number of attempts to tackle disturbances have already been proved successful, but not for all the types of them. Simple calculations [1, 2], diagrams [3, 4, 5] and other computer-based methods [6] are used to help doctors to evaluate and treat the mixed or plain disturbances. In [5], in order to examine the diagnostic validity of the proposed diagrammatic methods, arterial blood gas samples drawn from 114 Intensive Care Unit (ICU) patients were used. The samples were interpreted using the Grogono diagram [4] and the following approaches, as comparators: (a) The Siggaard-Andersen (S-A) chart [3], (b) the Oxygen Status Algorithm (OSA) [2] and (c) two physicians with more than 10 years of experience in ICUs, considered as experts in acid-base balance disturbances. There, has been proved that the Grogono diagram gives better results than OSA, and both better than the S-A chart. However, the authors conclude that Grogono diagram cannot be safely used for the diagnosis of acid-base balance disturbances in everyday clinical practice, because it has been shown to provide inaccurate diagnoses in at least 25% of the cases. So, they suggest that the creation of a better computer-based system to assist at least non-expert doctors in making an initial diagnosis is still very desirable.

There have been some efforts to use intelligent systems to deal with aspects of the above problem [7, 8, 9, 10]. From them, [8] and [10] refer to infants related aspects. The rest deal with what we call 'disturbances' and not with all aspects of what we call 'disorders' (the causes of disturbances). They also don't deal with treatment proposals.

Hybrid intelligent systems are systems that mix different intelligent methods and make them "work together" to achieve a better solution to a problem, compared to using a single method for the same problem. During last decade hybrid intelligent systems have been used to tackle medical problems [11]. From the above efforts, [7] and [10] use hybrid intelligent systems. In [6] a combination of frames and rules is used, whereas in [10] a combination of a back-propagation neural net and decision algorithms. Neither uses fuzzy sets to represent the inherent vagueness in some of the parameters.

In this paper, we present HIGAS, a **H**ybrid **I**ntelligent system for the diagnosis and treatment of acid-base disturbances based on blood **GAS** analysis data. Diagnosis is achieved in two stages. In the first stage, diagnosis of the disturbance is made, whereas in the second, diagnosis of the possible disorder and corresponding treatment is made.

The paper is organized as follows: in Section 2 we introduce the medical knowledge involved and the diagnosis process model we designed. In Section 3, development issues of our intelligent system are presented. Section 4 presents evaluation results for the system and finally Section 5 concludes the paper.

2. Medical Knowledge Modelling

Acid-base state in a body fluid is physically determined by several independent variables. In blood plasma *in vivo*, the independent variables are: (1) PCO_2; (2) the 'strong ion difference' (SID), i.e. the difference between the sums of all the strong (fully dissociated, chemically non-reacting) cations (Na^+, K^+, Ca^{2+}, Mg^{2+}) and all the strong anions (Cl^- and other strong anions) and (3) concentrations of nonvolatile weak acids (i.e., for each of them, the sum of its dissociated and undissociated forms, Stewart's symbol A_{tot}). Normal acid-base status is obtained when the independent variables have normal (empirically established) values. Abnormality of one or more of the independent variables underlies all acid-base disturbances. Adjustment of the independent variables is the essence of all therapeutic interventions, because none of the "dependent variables" (e.g., pH, $[HCO_3^-]$) can be changed primarily or individually: all dependent variables change simultaneously, if and only if one or more of the independent variables changes.

A classification of acid-base disturbances based on this view is shown in Table 1a. Metabolic acid-base disturbances can be caused by two types of abnormalities: mixed and unmixed abnormal concentrations of nonvolatile weak acids.

Table 1a: Examples of acid-base disturbances

Disturbance	pH	Primary Disturbance	Expected response
Unmixed Disturbances			
A. Metabolic acidosis	< 7.38	HCO3 < 22 meq/l	DPCO2 (↓) = (1.0-1.3) DHCO3
B. Metabolic alkalosis	> 7.42	HCO3 > 25 meq/l	DPCO2 (↑) = (0.4-0.9) DHCO3
C. Respiratory acidosis	< 7.38	PCO2 > 43 mmHg	
C1. Acute C			DHCO3 (↑) = (0.08-0.12)DPCO2
C2. Chronic C			DHCO3 (↑) = (0.25-0.55)DPCO2
C3. C1 and A or B			DHCO3 (↑) = (0.12-0.19)DPCO2
C4. C1 → C2			DHCO3 (↑) = (0.16-0.25)DPCO2
…			
Mixed disturbances (primary and secondary)			
1) A and C	< 7.38	HCO3 < 22 meq/l	DPCO2 (↓) < 1.0 DHCO3 or PCO2 > 40 mmHg
2) A and D	<7.38	HCO3 < 22 meq/l	DPCO2 (↓) > 1.3 DHCO3
…			
9) A and B	7.38-7.42 and AG > 14		

Table 1b: Examples of disorders that cause acid-base disturbances

Metabolic Alkalosis with AG = normal (10-14)				
	Na + K < Cl in urine samples	**K > 5.5**	**HCO3 in dose of 0.5-2 meq/Kg**	**Urine PCO2 if alkalic**
RTA II	No	No	Urine pH > 7.4 and HCO3 < 24 meq/l (FE) HCO3 > 15%	
RTA III	No	No	Urine pH > 7.4 and HCO3 = 24 meq/l (FE) HCO3 =1-3 %	PCO2 > 70 mmHg
RTA I …	No	No	Urine pH > 7.4 and HCO3 = 24 meq/l (FE) HCO3 = 1-3 %	Urine PCO2 = plasma PCO2

The initial knowledge on the field of acid-base disturbances has been acquired from experts as well as from the existing literature. Based on that, we constructed the model of Fig. 1 for the diagnosis and treatment process. According to that, initially, an expert clinician requires the following information from the blood gas analyser: (a) the pH value, (b) the HCO_3 concentration , (c) the partial pressure value of CO_2 (PCO_2) and (d) the Anion Gap value, to make an initial diagnosis, concerning the type of disturbance.

To confirm the disturbance diagnosis, it goes a step further by diagnosing the underlying disorder, which causes the disturbance. In this second stage, further information related to specific diagnostic laboratory tests is required. Variable dependences and diagnostic rules can be seen in Table 1b.

In blood-gas interpretation there is a complete interdependence of laboratory and clinical data and, although the former is often quite precise, the latter may not be, yet both must be accounted for and reconciled for a successful diagnostic solution. Dependencies also exist in that, whenever a major system is affected, the effect on the body may be global and other systems may follow into the destabilisation spiral, if the situation is not quickly rectified. Thus, measurement trends are closely observed.

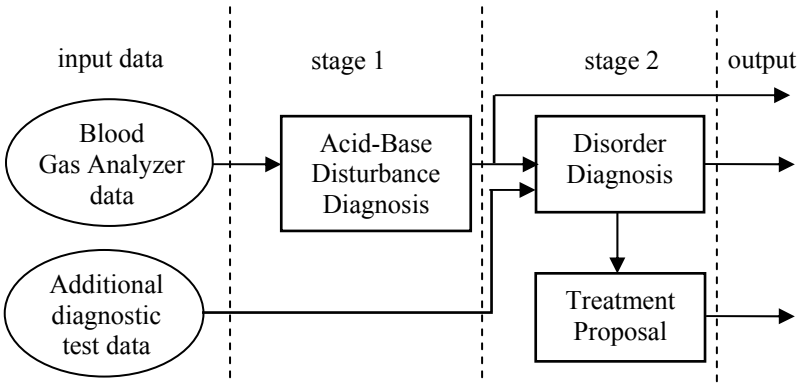

Figure 1: General Model for Blood Gas Disturbance Diagnosis and Treatment Process

3. HIGAS Architecture and Development

3.1 Fuzzy variables and values

As it is known, real world medical knowledge is often characterized by inaccuracy. Medical terms do not usually have a clear-cut interpretation. Fuzzy logic makes possible to define inexact medical entities via fuzzy sets. During last decade, a number of hybrid techniques based on fuzzy sets and rules have appeared which have been applied to medical systems [12, 13]. One of the reasons is that fuzzy logic provides capabilities for

approximate reasoning, which is reasoning with inaccurate (or fuzzy) values, expressed as linguistic terms.

Based on our expert, we specified a set of parameters that play a role in diagnosis for each of the entities in the process model (Fig. 1). Finally, we resulted in a number of parameters, which are distinguished in:.

Input parameters: pH, HCO_3 concentration, partial pressure of CO_2 (PCO_2) and anion gap (which represent gas analyzer data). They are used in the form of some ratios (see Table 1a), which are represented as fuzzy variables (see Fig. 2).

Intermediate output parameters: disturbance_diagnosis (which represents the possible disturbance, i.e. one of: metabolic acidosis, metabolic alkalosis, respiratory acidosis, respiratory alkalosis and their combinations).

Intermediate input parameters: urine pH, plasma pH, Standard Base Excess, etc (which represent laboratory test data). They are also represented as fuzzy variables.

Output parameters: disorder_diagnosis (which represents the diagnosed disorder, which can be one of RTA II, gastric fluid loss, etc) and proposed_treatment (with as possible values: intravenous dilute hydrochloric acid, ammonium chloride, etc.).

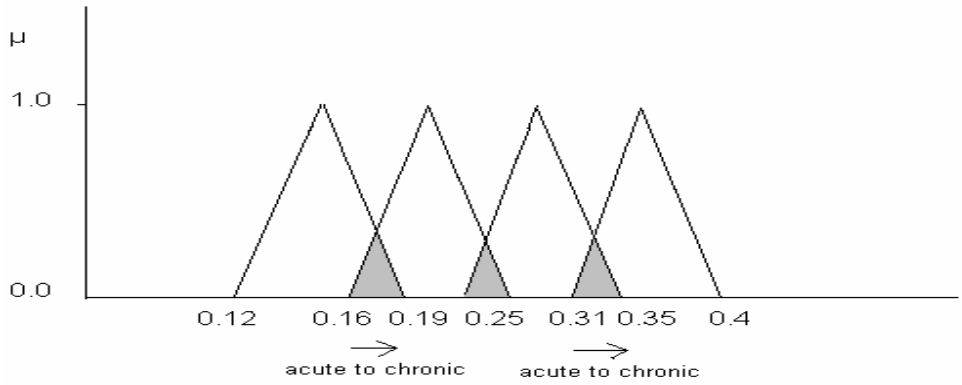

Figure 2. Fuzzy values and membership function for 'DHCO3/DPCO2'.

Fuzzy values and corresponding membership functions have been determined by the aid of the expert and the literature. Examples of values and corresponding membership functions are shown in Fig. 2. Due to the nature of the values and for better performance of the evolution algorithm, used to fine-tune them, we use only triangles to represent membership functions.

3.2 The fuzzy expert system

The developed fuzzy expert system has the typical structure of such systems [12, 13]. The *rule base* of the expert system includes (actually) *crisp* and *fuzzy rules*. A fuzzy rule includes one or more fuzzy variables. Definition of each fuzzy variable consists of definitions of its values. Each fuzzy value is represented by a *fuzzy set*, a range of crisp (i.e. non-linguistic) values with different degrees of membership to the set. The degrees are specified via a *membership function*.

Reasoning in such a system includes three stages: fuzzification, inference, defuzzification. In *fuzzification*, the crisp input values (from the fact database) are converted to membership degrees (fuzzy values). In the *inference* stage, the MIN method is used for the combination of a rule's conditions, to produce the membership value of the conclusion, and the MAX method is used to combine the conclusions of the rules. In *defuzzification*, the centroid method is used to convert a fuzzy output to a crisp value, where applicable.

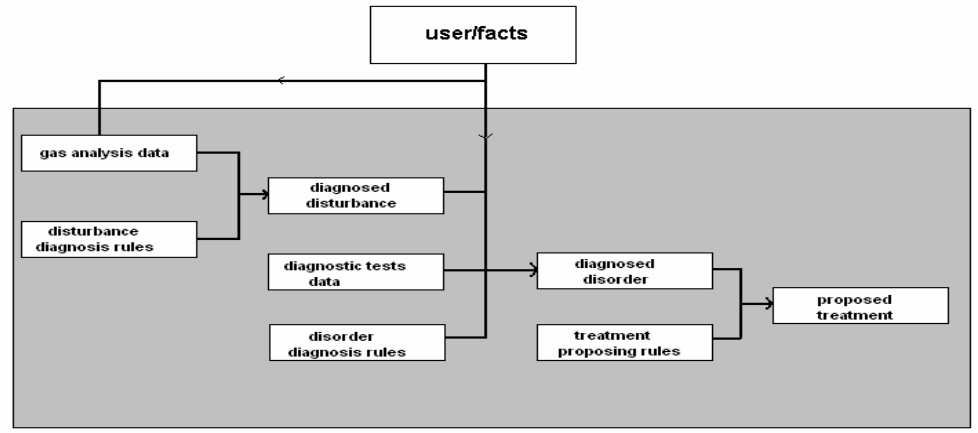

Figure 3. Inference flow in HIGAS

The system gives its outputs in a semi-fuzzy form. E.g. the values of the diagnosed disorder with their corresponding membership values are presented to the user alongside system's decision. This gives the user the opportunity to decide by himself/herself something different from the system in some special cases and also acts as some kind of explanation for the final decision of the system, given that membership values are presented as degrees of certainty.

To represent the diagnosis process model of Fig. 1, we organized rules in the rule base into three groups: *disturbance diagnosis rules*, *disorder diagnosis rules* and *treatment proposing rules*. The current patient data are stored as *facts*. Each time the reasoning process requires a value, it gets it from the facts list. In an interactive mode, it could be given by the user. Figure 3 presents how the rule groups and the facts/user are used/participates during the reasoning process to simulate the diagnosis process, whereas Figure 4 presents the architecture of HIGAS, where apart from the expert systems modules an evolutionary algorithm module is used off-line to fine-tune membership functions, as explained in the next section.

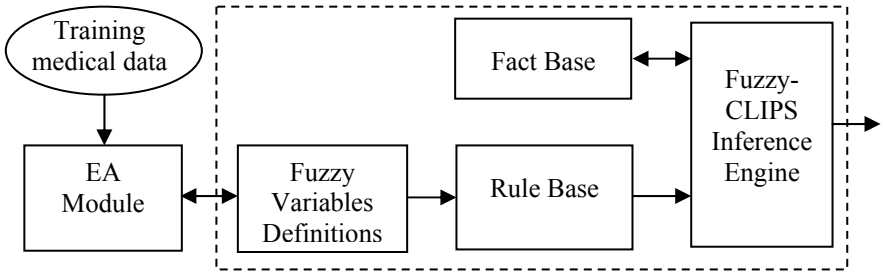

Figure 4. The architecture of HIGAS

3.3 The EA Module

An evolutionary algorithm (EA) is used for membership functions optimization, which are initially intuitively chosen. Given that the optimization of fuzzy membership functions may involve many changes to many different functions, and that a change to one function may effect others, the large possible solution space for this problem is a natural candidate

for an EA based approach despite many neuro-fuzzy approaches that use a gradient descent-learning algorithm to fine-tune the parameters of the fuzzy systems. The evolutionary algorithm optimises the antecedent and consequent membership functions of a number of fuzzy rules.

We use the 'differential evolution' (DE) algorithm [14, 15] to achieve that. As other evolutionary algorithms, DE maintains a population (a set) of solutions to the optimization problem at hand. The main idea in DE is to use vector differences in the creation of new candidate solutions, whereas traditional EAs rely on random perturbation (mutation) of a solution and mixing of two or more solutions (recombination). Another major difference is that the three phases of a standard EA (selection, recombination, and mutation) are combined to one operation, which is carried out for each individual. In the standard EA, each phase is performed on the entire population. In contrast, the DE algorithm iterates through the population and creates, for each population index i, a potential candidate C[i] by vector addition (mutation) and a variant of uniform crossover (recombination). Selection is straightforward and very simple; the candidate solution C[i] replaces P[i] if it is better.

DE algorithm runs separately for each fuzzy variable. Let v be a fuzzy variable that has three fuzzy sets/values (A, B and C) and $\mu_A(v)$, $\mu_B(v)$, $\mu_C(v)$ be the three membership distributions over fuzzy sets A, B and C respectively. All membership curves are isosceles triangles (see e.g. Fig. 2). For optimization purposes, we code each triangle via six pairs of values (x_i, y_i), i.e. two pairs for each edge of the triangle or one pair for each node of an edge. Each pair consists of the two co-ordinates of the corresponding node of an edge. Thus, the genome in the corresponding population has 19 fields, 18 (=3x6) for the three fuzzy sets and one for the expected output. A number of training medical data is used to specify the "better" genome, the one that satisfies more training examples. The result of the DE algorithm application is changes to the co-ordinate pairs of the triangles of the membership functions of the values of a fuzzy variable.

3.4 Implementation issues

The system has been implemented in FuzzyCLIPS 6.1b expert system shell [16]. Finally, about 72 rules and 10 templates have been constructed. Patient data is organized by using CLIPS templates. To implement reasoning flow, different priorities have been used for different rule groups. The EA module has been implemented using the software provided in [17].

4. System Evaluation

To evaluate HIGAS, we used 200 patient cases, successfully diagnosed and treated by the experts in critical care, from the database of the University Hospital of Patras, Greece. We used two versions of HIGAS, one without the use of the EA module results (untuned) and the other after having tuned the membership functions of the fuzzy values of the fuzzy variables of the system via the EA module. We used 40% of the cases as the training data set for the DE algorithm needs and the rest 60% as the test data set. We also used a third participant in the experiment, a group of three non-expert clinical doctors in critical care.

4.1 HIGAS vs Clinical Doctors

The results are presented in Tables 2a and 2b. Table 2a refers to disorder diagnosis, whereas Table 2b to treatment proposal. We used 'accuracy' as the main metric accompanied by 'specificity' and 'sensitivity' for better interpretation of the results. The results show that the tuned version of HIGAS did better than any other participant (85%

and 87%) as far as accuracy is concerned with a good balance between specificity and sensitivity.

Table 2a. Comparison of HIGAS with clinicians (disorder diagnosis)

DISORDER DIAGNOSIS	CLINICIANS			HIGAS	
	1st	2nd	3rd	TUNED	UNTUNED
Specificity	0.62	0.74	0.67	**0.83**	**0.79**
Sensitivity	0.67	0.70	0.65	**0.88**	**0.83**
Accuracy	0.64	0.72	0.66	**0.85**	**0.81**

Table 2b. Comparison of HYGAS with clinicians (proposed treatment)

TREATMENT	CLINICIANS			HIGAS	
	1st	2nd	3rd	TUNED	UNTUNED
Specificity	0.69	0.75	0.66	**0.89**	**0.80**
Sensitivity	0.70	0.80	0.69	**0.83**	**0.84**
Accuracy	0.70	0.77	0.67	**0.87**	**0.82**

4.2 HIGAS vs Computer-based systems

We also compared the tuned version of HIGAS with other two classical computer-based methods, the Grogono diagram and the Oxygen Status Algorithm (OSA), whose implementations are available in the web [4, 18]. The results, presented in Table 3, show the superiority of HIGAS. Notice, that the results concern only disturbance diagnosis, because those systems do not support disorder diagnosis and treatment proposal.

Table 3. Comparison of the HIGAS and other systems (disturbance diagnosis)

POSSIBLE DIAGNOSIS	GROGONO DIAGRAM	HIGAS	OXYGEN STATUS ALGORITHM
Specificity	0.75	**0.85**	0.71
Sensitivity	0.77	**0.89**	0.69
Accuracy	0.76	**0.87**	0.70

5. Conclusions

In this paper, we present HIGAS, a hybrid intelligent system that deals with diagnosis and treatment of blood gas (acid-base) disturbances and disorders. The diagnosis process was modeled based on expert's knowledge and the existing literature. Fuzzy variables were specified based again on expert's knowledge. A characteristic of the system is the synergism between an EA module and a fuzzy rule base. The DE algorithm is used to tune the membership functions of the fuzzy values of the fuzzy variables. This improves the accuracy of the system. Medium scale experimental results showed that HIGAS did quite better than non-experts and other systems, but worse than the expert.

There are two directions that the system can be further improved. First, concerning its performance, a more drastic way of tuning could be applied. Instead of tuning the limits of the membership functions, we could also change the number of fuzzy values for some or all of the fuzzy variables, using e.g. a machine learning technique. Second, it could be enhanced with an explanation facility or/and other modules to be used as an educational system for non-experts.

Acknowledgements

We thank the European Social Fund (ESF), Operational Program for Educational and Vocational Training II (EPEAEK II), and particularly the Program PYTHAGORAS I, for funding the above work. We would also like to thank Mr. Apostolos Kandylis, an MSc student, who implemented a core of the fuzzy expert system.

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