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Fuzzy Logics and Medical Diagnosis of Neonatal Assessment at Birth

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ABSTRACT

This paper argues that fuzzy representations are appropriate in applications where there are major sources of imprecision and / or uncertainty. Case studies of fuzzy approaches to specific problems of medical diagnosis and classification are described in support of this argument. The solutions use a variety of fuzzy methods including clustering, fuzzy set aggregation and type- 2 fuzzy set modeling of linguistic approximations. It is concluded that the fuzzy approach to the development of artificial intelligence in application systems is beneficial in these contexts because of the need to focus on uncertainty as a main issue.

Keywords: Resuscitation, retrospective, umbilical, metabolism, plausible, linguistic, spearman, severe.

1. Introduction

The development of artificial intelligence methodology has been recognised as an important requirement in complex problem solving situations. Medical diagnosis is a particularly good example because of the complexity of the human mind and body and our limited and vague knowledge of how these function. This knowledge also varies with the expertise of the user. In a systematic approach to the acquisition of domain knowledge, the analysis of human physiology/psychology quickly produces large numbers of cause-effect relations at many interacting levels of both description and function. Necessarily, the relations are poor approximations of complex dynamic systems and some account has to be made for uncertainty at this level of description. Furthermore, the information available for searching this domain knowledge for a specific diagnosis is also usually vague (at least initially) in that evidence is indirect (reported symptoms or lack of them) and observations are incomplete and inaccurate due to the stochastic nature of mind/body psychology/physiology. The level of expertise of the clinician cannot be discounted in this process. Given that speed is also important on the diagnostic procedure, we should develop techniques in artificial intelligence that can support fast, reliable and accurate diagnosis with limited and vague information.

2. Preliminaries

Definition 1. For any fuzzy set A, the function μ_A represents the membership function for which $\mu_A(x)$ indicates the degree of membership that x, of the universal set X, belongs to set A and is, usually, expressed as a number between 0 and 1:

$$\mu_A(x): X \to [0,1].$$

For a discrete fuzzy set A, with members $x_{1,}......, x_N$ the usual notation is to write $A = \mu_1 / x_1 + \mu_2 / x_2 + ... + \mu_N / x_{N.}$ In this case the + means union.

Definition 2. A type-2 fuzzy set is characterised by a fuzzy membership function. i.e. the membership value (or membership grade) for each element of this set is a fuzzy set in [0,1], unlike type-1 fuzzy set where the membership grade is number in [0,1].

3. Neonatal assessment at birth

An assessment of neonatal outcome may be obtained from analysis of blood in the umbilical cord of an infant immediately after delivery, and has been recommended in the United Kingdom by the Royal College of obstetricians and Gynaecologists [1]. The umbilical cord vein carries blood from the placenta to the fetus and the two smaller cord arteries return blood from the fetus. The blood from the placenta has been freshly oxygenated, and has a relatively high partial pressure of oxygen (pO_2) and low partial pressure of carbon dioxide (pCO_2). Oxygen in the fuels aerobic cell metabolism, with carbon dioxide produced as 'waste'. Thus the blood returning from the fetus has relatively low oxygen and high carbon dioxide content. Some carbon dioxide dissociates to form carbonic acid in the blood, which increases the acidity (lowers the pH). If oxygen supplies are too low, anaerobic (without oxygen) metabolism can supplement aerobic metabolism to maintain essential cell function, but this produces lactic acid as 'waste'. This further acidifies the blood, and can indicate serious problems for the fetus.

A sample of blood taken from each of the blood vessels in the clamped umbilical cord and a blood gas analysis machine measures pH, pO_2 and $pCO_{2.}$ A parameter termed base deficit of extra cellular fluid (BD_{ecf}) can be derived from the pH and pCO_2 parameters [2]. This can distinguish the cause of a low pH between the distinct physiological conditions of respiratory acidosis, due to a short- term accumulation of $CO_{2,}$ and a metabolic acidosis, due to lactic acid from a longer-term oxygen deficiency. An interpretation is then made based on the pH and BD_{ecf} parameters ('the acid-base status') of both arterial and venous blood.

There are, however, a number of difficulties with such umbilical acid-base analysis machines require regular calibration and quality control checks to ensure continuing performance to the manufacture's specifications. Careful retrospective analysis of the acid-base results obtained during a trail on electronic fetal monitoring highlighted a 25% failure rate to obtain arterial and venous paired samples with all parameters [3]. This sampling error rate is broadly in line with other studies in which the importance of paired samples was recognised. The study also highlighted the fact that considerable expertise was required to reliably recognise these errors and accurately interpret results.

3.1. A fuzzy expert system for the analysis of umbilical acid-base status

A fuzzy expert system was developed for the analysis of umbilical cord acid-base status, encapsulating the knowledge of leading obstetricians, neonatologists and physiologists gained over years of acid-base interpretation. The expert system combines knowledge of the errors likely to occur in acid-base measurement, physiological knowledge of plausible results, statistical analysis of a large database of results and clinical experience of acid-base interpretation. It automatically cheeks for errors in input parameters, identifies the vessel origin (artery or vein) of the results and provides an interpretation in an objective, consistent and intelligent manner.

This process is carried out in two distinct phases; validation of parameters and interpretation of parameters. The expert system comprises two separate fuzzy rule bases, one for each phase.

3.2. Validation of parameters

The three measured parameters (pH, pO_2, and pCO_2) for each sample are introduced to the expert system without labeling- the detection of parameter errors and identification of vessel origin for each sample is an entirely automatic data- driven process carried out by the expert system.

There are two main classes of parameter error:

- sample source—for some reason the blood drawn into the two syringes does not constitute the intended samples of arterial and venous blood (for example, it is relatively easy to inadvertently stick the needle right through a cord artery and mistakenly draw blood from the vein, due to either inadequate umbilical cord segment or poor sampling technique);
- parameter inaccuracy – the measurements reported by the blood gas analysis machine do not accurately represent the true parameter values of the blood sample.

This can be caused by either :

- machine error – the blood gas analysis machine has drifted somewhat from true calibration;
- sample error – the sample contains air bubbles or other miscellaneous contaminants.
- time delays – the umbilical cord was not clamped immediately, or there is some time delay between taking the samples and then in introducing samples into the blood gas machine for measurement (note that it has been experimentally verified that parameter values remain stable in a clamped cord segment for around one hour).

As a first step, the expert system examines the relationship between the pH and pCO_2 parameters for each sample independently. Briefly, there is a biochemical relationship between these parameters such that, for neonatal blood, bounds can be established on a physiologically possible pCO_2 for any given pH. The expert system checks that the parameters fall within these bounds to exclude, for example, samples where non-blood fluid has accidentally sampled. Once it has been established that the parameters are compatible with neonatal blood, the parameters can be compared across sample to detect further errors and identify vessel origin. A number of experiments were carried out in order to establish the maximum likely error in each parameter (given a known sample source) as summarised in Table 1. The consequent likely error in the derived base deficit parameter was determined mathematically from the component uncertainties.

	δpH	δpCO_2	δpO_2
Arterial	0.025 kPa	0.61 kPa	0.31 kPa
Venous	0.010 kPa	0.24 kPa	0.15 kPa

Table 3.2 (1): The combined maximum likely uncertainty (two standard deviations from the mean) in each umbilical cord acid-base parameter

Physiologically, it can be expected that the arterial $pH(pH^A)$ is lower than the venous $pH(pH^v)$, the arterial $pCO_2(pCO_2{}^A)$ is higher than the venous $pCO_2(pCO_2{}^v)$, the arterial $pO_2(pO_2{}^A)$ is lower than the venous $pO_2(pO_2{}^v)$, and the arterial $BD_{ecf}(BD^A)$ is higher than the venous $BD_{ecf}(BD^v)$. These facts are expressed in the definitions of parameter differences as show in Table 2 such that the Δ's are all expected to be positive.

If two good venous samples were obtained, then each parameter should differ by amounts close to, or less than, the venous values shown in Table 1. As two samples may both be accidentally obtained from the vein, both from the arteries, one may be mixed arterial-venous, or both may be mixed, a 'safe' vessel identification rule may be that if all parameters differ by more than the largest uncertainties in Table 1, then the samples can definitely be taken as a true arterial- venous pair.

Difference	Definition	
△pH	venous pH	– arterial pH
△$p$$CO_2$	arterial $p$$CO_2$	– venous $p$$CO_2$
△$p$$O_2$	venous $p$$O_2$	– arterial $p$$O_2$
△BD_{ecf}	arterial BD_{ecf}	– venous BD_{ecf}

Table 3.2 (2): The definition of △ for acid-base parameters

Given that lowest pH is initially as the (or the pH's are the same the highest pCO_2 is labelled as artery, or if the pH's and pCO_2 are the same, the lowest pO_2 is labelled as the artery), then the list possible sample differences and their associated vessel identification are shown in Table 3, a '0' indicates that parameter is zero, a '–' indicates that parameter is negative, and a '+' indicates that parameter is positive.

A fuzzy rule -base was designed to produce the target behavior shown in Table 3, with smoth transitions between each of the categories. The rule-base consisted of a set of five rules relating the differences in fuzzy input parameters (the pH, pCO_2 and pO_2 in both samples) to a single fuzzy output variable, the origin of samples. Each input parameter was first fuzzified to process a width equal to the largest (arterial) uncertainties in Table 1, as shown for example in Figure 1. The fuzzified input variable was then passed through the vessel identification rule-set with rules of the form:

IF pH^A IS-EQUAL-TO pH^V
AND $pCO_2{}^A$ IS-ABOUT-EQUAL-TO $pCO_2{}^V$
AND $pO_2{}^A$ IS-ABOUT-EQUAL-TO $pO_2{}^V$

THEN origin IS paired

△pH	△pCO$_2$	△pO$_2$	Origin
0	0	0	definitely same
0	0	+	probably same
0	+	0	probably same
0	+	–	probably mixed
0	+	+	probably different
+	0	0	probably same
+	0	–	probably mixed
+	0	+	probably different
+	–	0	probably mixed
+	–	–	definitely mixed
+	–	+	definitely mixed
+	+	0	probably different
+	+	–	definitely mixed
+	+	+	definitely different

Table 3.2 (3): List of possible sample differences and the associated vessel identification

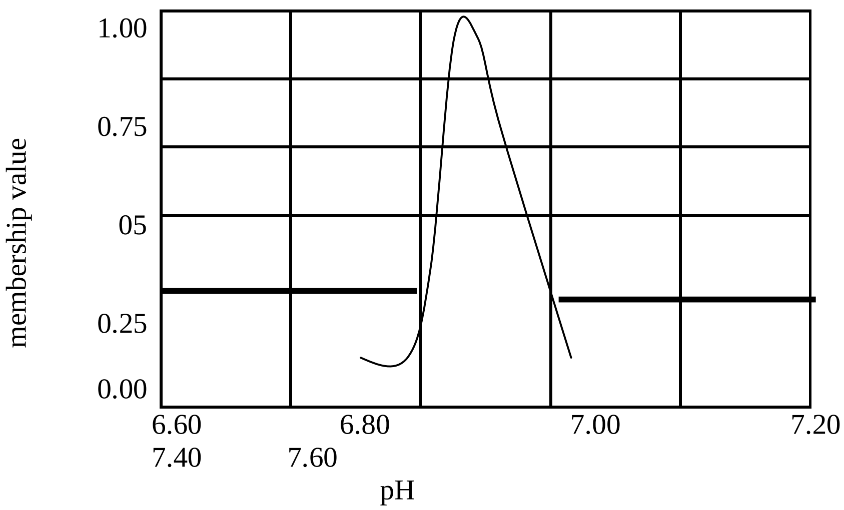

Figure 3.2 (1): An example of a pH input parameter with a fuzzy width (note that the width has been exaggerated for clarity)

Linguistic approximation of the origin output variable was used to determine the appropriate vessel labeling. A linguistic output corresponding to different, mixed/different or not same causes the vessel to be labelled as an arterial-venous pair. Any other linguistic output, or the presences of only one input sample, caused the sample to be labelled as a single venous vessel. An arterial-venous pair would then have its input variables re-initialised with the crisp values of the input parameters, fuzzified to have a width equal to those in Table 1. The BD_{ecf} for each vessel is then calcucalated from the pH and pCO_2 parameters, and then fuzzified to the derived width.

If both vessels were missing, both the arterial and venous parameters would be initialiased with $\mu_A(x) = 1$ across the universe of discourse. In such situation all rules fire with maximum strength and the output of all variables tends to $\mu_A(x) = 1$. In practice such a situation is very rare (1 case out of > 10000), and the much more common occurrence is the single vessel. In this case, a single vessel is always labeled as venous for the reasons that firstly, the vein is much easier to sample than the artery and hence an arterial sample without a venous sample is unlikely in the extreme and, secondly, as the artery is effectively 'worse' than the form a health point of view, assuming a single vessel is a vein is the safest option. It might be thought that the subsequent arterial parameters would simply be initialized with $\mu_A(x) = 1$ across the entire the fuzzy set. However, this ignores the fact that, physiologically, the arterial parameters would be such as to maintain positive Δ's- i.e if the arterial pH was not known, it could still be assumed to be lower than the venous pH. Thus, the actual produce was to initialize a missing arterial pH parameter with a fuzzy set consisting of the inverted left-hand edge of the venous fuzzy set, and to initialise a missing BD_{ecf} parameter with a fuzzy set consisting of the inverted right –hand edge of the venous fuzzy set. This is demonstrated in Figure 2, in which missing arterial values have been set to $\mu_A(x) = 1$ relative to venous values of pH = 7.10 and BD_{ecf} = 9.7 mmol.l^{-1}

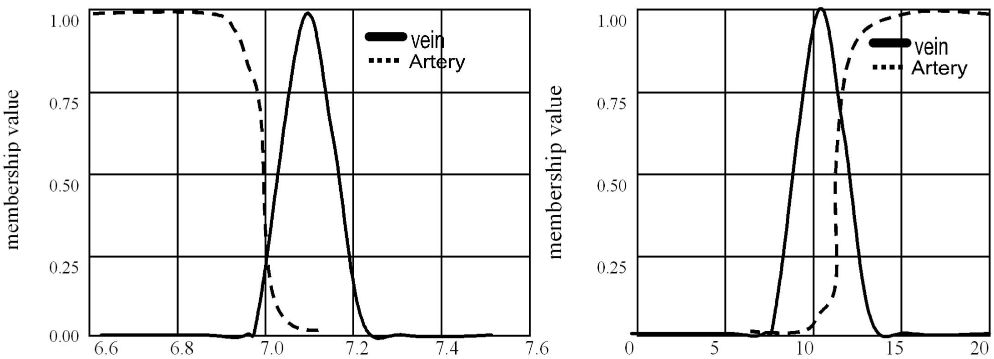

Figure 3.2 (2) : Illustration of missing arterial values given known venous values of pH = 7.10 and BD_{ecf} = 9.7 mmol.l^{-1} (note that parameter widths have been exaggerated for clarity)

3.3. Interpretation of parameters

Once vessel identification has been carried out, the sample(s) are passed through the interpretation rules. The basic principles of acid-base analysis elicited from the experts were that:

(i) acidemia is based on the absolute value of arterial pH (lower arterial pH implies worse acidemia), refined by the value of the venous pH;

(ii) component is based on arterial BD_{ecf} (high BD_{ecf} implies metabolic component, low BD_{ecf} implies respiratory component), refined by venous BD_{ecf} ; and

(iii) duration is based on pH and BD_{ecf} differences (smaller differences imply chronic duration, larger differences imply acute duration), refines by absolute arterial values.

These basic principles were encapsulated in a set of fuzzy rules developed over series of elicitation and comparison sessions with acknowledged umbilical acid-base experts. The fuzzy output variables (acidemia component, and duration) were utilized in rule consequences, with the availability of graphical output of the consequence fuzzy sets. The consequent fuzzy sets were defuzzified by both the centroid method and linguistic approximation, and results were validated against international expert opinion.

3.4. Validation of the fuzzy interpretation

The centroids of the fuzzy output variables were combined into single index by:

$$condition = acidemia + \frac{component}{20} + \frac{duration}{10}$$

The experts were given the two sets of pH and BD_{ecf} parameters from each of fifty cases, and were asked to indicate there opinion of the closest linguistic interpretation for three linguistic variables; acidemia, component, and duration. For each variable they were instructed to mark zero, one or two terms to indicate the closest match. This was specifically designed to allow the expert to make two adjacent labels if they felt a result fell in- between two labels, or to make no label was appropriate. To measure the agreement between two expert's linguistic categorization a measure of (nominal) categorical agreement was required. The kappa statistic [4] was used to measure exact agreement between experts and the expert system linguistic outputs and weighted kappa [5] was used for partial agreement.

4. Results

The individual inter- expert and expert- fuzzy spearman rank order correlation co-efficients obtained are shown in Table 4. The average inter- expert agreement is calculated by taking the average of each expert against the other three experts, and the average fuzzy agreement by taking the average of agreement with all *f*our experts. As can be seen, the fuzzy expert system performed exceptionally well against experts A, B, and C. These three experts had taken place in the previous study, and the average expert system agreement with these three is 0.94-slightly lower correlation was obtained against expert D, although the fuzzy expert system was no worse than the other experts. These results are illustrated in Figure 6, in which each of the expert's rankings are plotted against the fuzzy expert system rankings- perfect agreement would result in a diagonal line from (1,1) to (50,50).

The results of the linguistic interpretation agreement were generally found to be relatively low, even for weighted kappa, both for inter-expert agreement and expert-Fuzzy agreement. An attempt was made to investigate the effect of different pH and BD_{ecf} weights on these linguistic agreements, but in general it was found that performance was not significantly increased above the results achieved with default weights. It would seem that while the experts can agree on relative 'badness' of results, placing a linguistic label on the results is much more subjective.

5. Conclusion

The resultant fuzzy expert system explicitly represented uncertainty in both the input data and the knowledge base. Although presented as a single achievement, the eventual fuzzy system was only arrived after a long, iterative development process, beginning with the creation of a crisp expert system [6, 7], followed by an intermediate fuzzy expert system, which performed only interpretation of previously validated parameters [8]. The fuzzy expert system was tested in a validation study and was found to perform favourably compared to internationally acknowledged domain experts.

Expert	A	B	C	D
A	–	0.899	0.888	0.577
B	0.899	–	0.908	0.701
C	0.888	0.908	–	0.537
D	0.577	0.701	0.537	–
Average	0.788	0.836	0.777	0.605

Table 5 (4): Agreement for numeric interpretation by rank order correlation

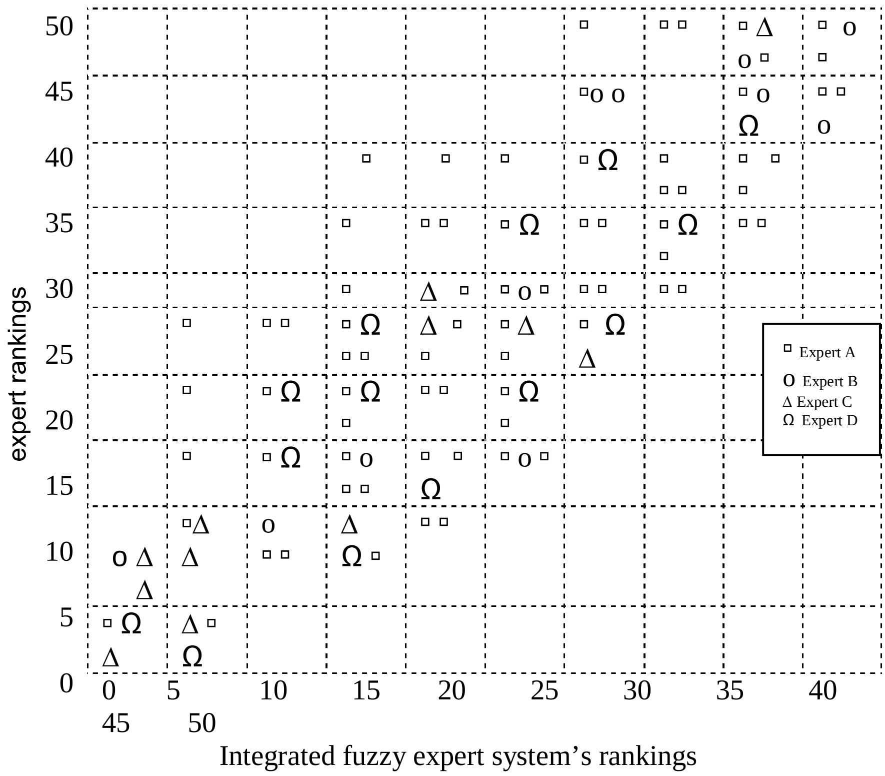

Figure 5 (3): Graph of four expert's rankings against the integrated fuzzy expert system

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