Computational Intelligence for Medical Knowledge Acquisition with Application to Glaucoma

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Abstract

This paper presents an approach that integrates computational intelligence/soft computing paradigms with clinical investigation methods and knowledge. Computational intelligence methods (including fuzzy logic, neural networks and genetic algorithms) deal in a suitable way with imprecision, uncertainty and partial truth. These aspects can be found quite often in practical medical activities and in medical knowledge. The proposed approach uses a knowledge discovery process in order to develop an intelligent system for diagnosis and prediction of glaucoma. The knowledge acquired is embedded in a fuzzy logic inference system. The resulting Neuro-fuzzy Glaucoma Diagnosis and Prediction System is expected to lower the effort, difficulties and risk cost related to this disease (the leading cause of blindness in North America.)

Key words: Computational intelligence, fuzzy logic, knowledge discovery, glaucoma, risk evaluation, prediction

1. Introduction

In 1982 Marr established two principles [1]:
I. Principle of Least Commitment
Don't do something that may later have to be undone
II. Principle of Graceful Degradation
Degrading the data will not prevent the delivery of at least some of the answer

Both are very important in classification and decision-making processes for expert systems: the first principle is consistent with the continuous degree of belonging to fuzzy sets (equivalent with continuous degree of truth in fuzzy logic), and ensures the conservation of uncertainty until a crisp (binary) decision is necessary. The second principle asks for robust methods/algorithms to be used. The implementation of these two principles can be expressed in a natural way by using the fuzzy paradigm and classifications approaches [2].

The diagnosis as a medical activity will state if a patient suffers of a specific disease, and if the answer is yes, the specialist will provide a specific treatment.

Despite the difficulties, the diagnosis of glaucoma is solved for the majority of cases. An important challenge for an ophthalmologist remains on the evaluation of the risk of occurrence and the prediction of progression to establish the suitable follow up and treatment accordingly.

A major concern is the reliability of the diagnostic tools used by the physician. There is usually low confidence in these rules mainly due to their negative prediction rate[1]. One of the glaucoma characteristics is that it can be "triggered" in very short periods of time (one hour for example) and without notice – which makes evident the challenge facing any attempt to predict it. Our goal is to face this challenge in developing a machine that can evaluate more precisely the risk factors.

According to the Mars' "Principle of Least Commitment" we need to preserve as much as possible the natural embedded uncertainty in medical approaches (due of the natural complexity of the human); and according to his "Principle of Graceful Degradation" we need to build a robust system. And a natural way to fulfill these natural medical requirements is to use fuzzy sets and fuzzy "if-then" rules.

As software tool we use Fuzzy Control Manager (FCM) from Transfertech GmbH, Germany, a fuzzy development system. [9]

[1] A clear example of a negative prediction could be this: the machine determines that the patient has a low risk of glaucoma and the patient is not treated; after 6 months the patient comes back for follow-up, and he or she has a great damage

2. Glaucoma, basics and challenges

Glaucoma is a progressive eye disease that damages the optic nerve, usually associated with increased intraocular pressure (IOP). If left untreated, it can lead to blindness.

Glaucoma is affecting round 67 million people all over the world. In Canada there are about 200,000 glaucoma cases [3].

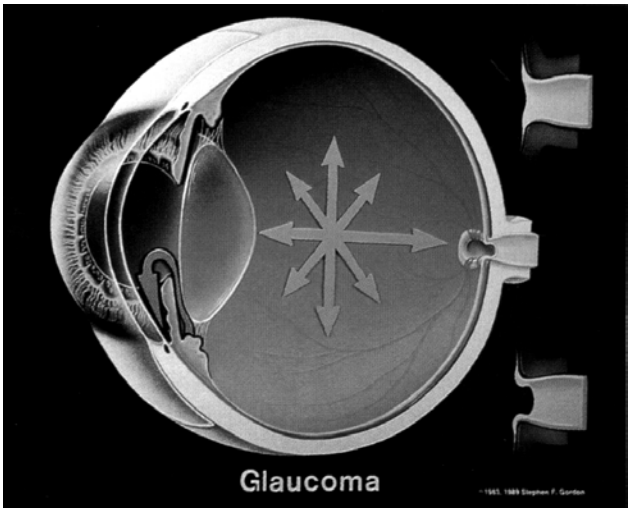

Fig. 2.1: Flow of fluid through eye (from [3])

Obstruction to flow in the front of the eye (left curved arrow in fig. 2.1) increases pressure in the eye – IOP - (central arrows) leading to damage to the optic nerve at the back of the eye. The depressed area in the middle of the optic nerve is the result of an abnormal process called cupping. It can be observed in the figure 2.2:

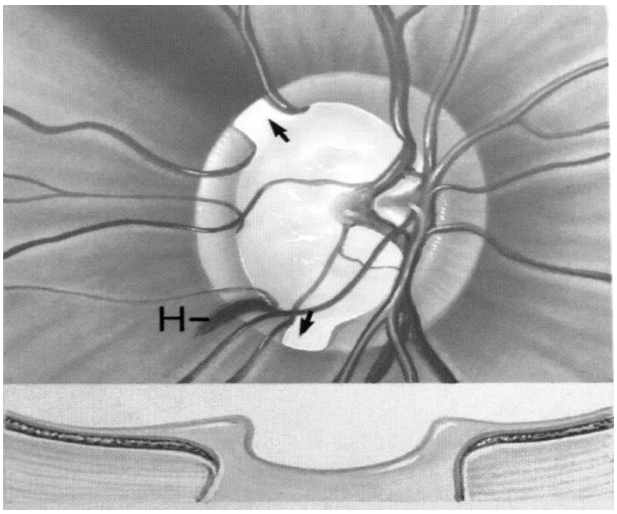

Fig. 2.2: Nerve damage in glaucoma (from [3])

The central white area is known as the cup. The arrows show areas of damage (notches) on the rim of the nerve. "H" is a haemorrhage on the rim of the nerve. Haemorrhages, notches, and cuppings occur if the pressure in the eye (IOP) is at unacceptable level. The bottom of the picture shows a severely cupped nerve.

We can consider glaucoma as a group of conditions characterized by [4]:

-elevation of intraocular pressure (IOP)

-cupping of the optic nerve head

-visual field loss,

This definition is not entirely satisfactory because, for example, visual field loss does not always correlate with high intraocular pressure (IOP).

Regardless this lack of consensus in the *definition* of glaucoma most of the cases of diagnosis of glaucoma (approximately 70%) are pretty evident for ophthalmologists. This is because the characteristics of the disease are well defined, just as mentioned in the previous paragraph. However in about 5% of all cases where the specialist doesn't know if the patient has glaucoma. For these special cases and also further about 25% of the cases the diagnosis function of our machine will be of much help.

The problems of diagnosis of glaucoma by applying soft computing/computational intelligence methods where tackled by Ulieru et al. in [5], based on an experimental basis and on a relevant bibliography ([6], [7], [8] and others).

In parallel with diagnosis, one important output of the system is the potential to evaluate the risk of occurrence as well as the progression of the disease.

3. Knowledge representation

Our design of the Neuro-Fuzzy Glaucoma Diagnosis and Prediction System is based on a fuzzy inference system that matches some input values with a fuzzy diagnostic model (designed as a collection of fuzzy IF-THEN rules) to assign a risk factor and/or progression estimation. It uses a process like the one described in figure 3.1.

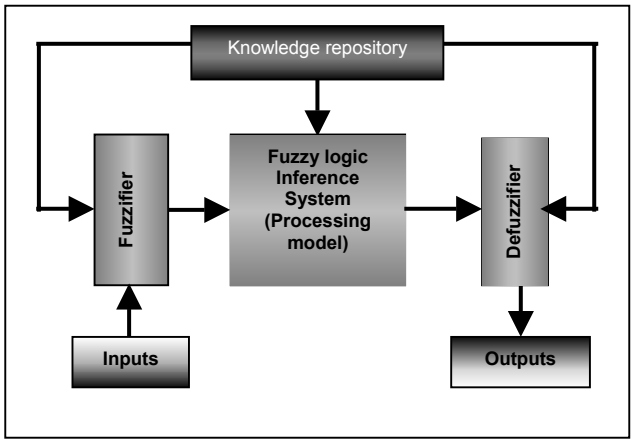

Fig. 3.1: Fuzzy logic decision infrastructure.

Figure 3.1 (see [11]) illustrates the basic flow of information of a fuzzy logic decision mechanism.

The knowledge repository contains a set of linguistic variables defined as a quintuple of the following form <*X, T(X), U, G, M*>, where *X* is the name of the variable (inputs or outputs), *T(X)* is the set of linguistic terms for *X*, each of these terms has associated a fuzzy set in *U,* the Universe of discourse. U is the range of all possible values for this linguistic variable. The syntactic rule *G* is the grammar for generating the terms in the term set *T(X)*. *M* is a semantic rule used for associating each linguistic term from *T(X)* with its meaning (membership function). The linguistic variables are the "vocabulary" that the fuzzy rules use to express the mapping from inputs into outputs.

For example, we can define "X", the *Intraocular Pressure (IOP),* as a linguistic variable where the set term could be defined as *T(IOP)* = {**Low**, **Normal**, **High**}

Each term in *T (IOP)* can be associated to a fuzzy set of values in the Universe of discourse *U = [0, 45]* (measured in mm of Hg).

It is possible to define rules represented in the following way:

IF *(X is A)* AND *(Y is B)* THEN *(Z is C)*

Where *X, Y* and *Z* are linguistic variables, like *IOP* in the example; and *A, B* and *C* are linguistic terms, like any from the term set defined for this example.

Data and facts of glaucoma diagnosis and prediction (modeling environment) are transformed from a numerical level to the conceptual framework of fuzzy sets.

Low might be interpreted as "*a pressure above 0 mm Hg and around 11mm Hg*"; **Normal** as "*a pressure around 16.5 mm Hg*" and **High** as "*a pressure around 21 mm Hg and bellow 45 mm Hg*". Every term can be described as fuzzy sets whose membership functions are like the ones drawn in figure 3.2.

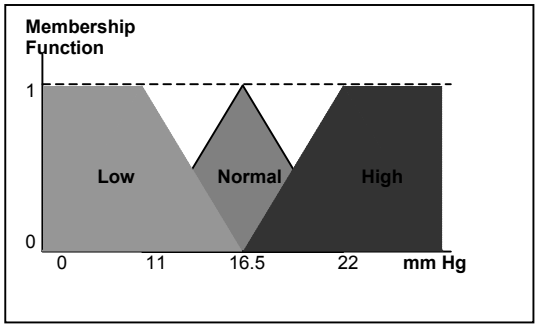

Fig. 3.2: Fuzzy sets (linguistic terms: **Low**, **Normal**, **High**) to characterize the linguistic variable *Intraocular Pressure - IOP*

The processing module is the algorithmic part of the schema, and its results are converted by the output interface (using some defuzzification technique) and returned to the modeling environment.

4. Knowledge acquisition

Knowledge acquisition (KA) is usually an iterative process that consists of various steps and needs the interaction of domain expert(s)[2], knowledge engineers and the computer. These steps include: developing an understanding of the application domain; determination of knowledge representation; selection, preparation and transformation of data and prior knowledge; knowledge extraction (machine learning); and model evaluation and refinement [10].

Fuzzy IF-THEN Rules (the knowledge representation selected for this project) are "extracted" from an expert's knowledge and experience in a particular field. In some specific cases it is possible to "obtain automatically" such rules from data. This is not the case for our Neuro–Fuzzy Glaucoma Diagnosis and Prediction System, due to the complexity of the diagnosis risk evaluation and prediction processes. In our case, it is essential to work close with medical specialists in order to obtain the knowledge necessary to build a complete set of IF-THEN rules; and to "confront" these rules with "mathematical tools" for verification and validation where appropriate.

An incremental development, a close relation to the ophthalmologists and a well-documented progressive work were the foundation for the design of a process to create the Fuzzy IF-THEN Rules that will be used in the Neuro-fuzzy Glaucoma Diagnosis and Prediction System.

The Fuzzy IF-THEN Rules Creation Process (FRCP) is an incremental development process in which a set of Fuzzy IF-THEN Rules will be developed as a succession of cumulative subsets of Fuzzy IF-THEN Rules.

[2] ophthalmologist(s) in this case

The first step within this incremental process is to understand the existing data, the requirements and the goals of the system. After analyzing all this information, top-level specifications are defined and an incremental development plan is designed.
The FRCP incremental development definition is represented in figure 4.1.

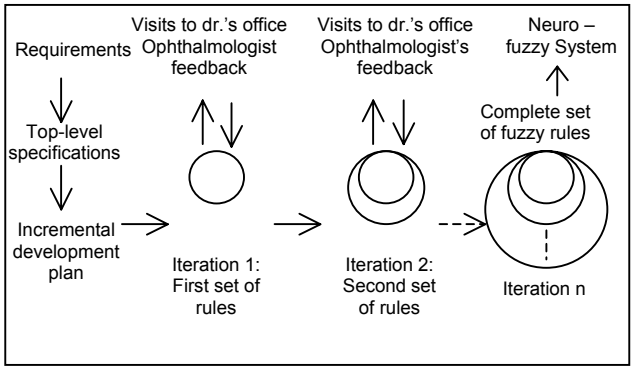

Fig 4.1: Incremental development process.

The process iterates through four main steps:

1. *Gather and select relevant information* to create or modify the set of rules. The gathering of information can be done in different ways. One way is to use the help of the ophthalmologist; he can add useful information by explaining new concepts or just letting the knowledge engineer watch him (and ask him questions) while he is examining his patients. Another way, for example, is going through patients' charts looking for specific information.
2. *Create, add or modify linguistic variables and/or fuzzy rules.* With the new data, during the first iteration, it is possible to create a set of linguistic variables and infer a preliminary set of fuzzy rules; and during the following iterations, it is possible to add or modify linguistic variables and/or rules.
3. *Ophthalmologist's feedback.* When the ophthalmologists review the set of rules, they use their knowledge and experience in order to validate it.
4. *Rule set evaluation and refinement.* After the ophthalmologists' validation, the set is refined and the first step starts once again until the final set of rules has been developed.

This cycle will be repeated as many times as needed to create a set of rules that fully defines how an ophthalmologist can determine whether or not a patient has glaucoma, and how to determine the suitable treatment and to predict the disease progression.

5. Implementation of the FRCP

During the first iteration after several visits to the ophthalmologist office to watch him examining patients and studying about glaucoma, we found 12 glaucoma risk factors as variable inputs for the FCM software tool.

For each variable we built one or more terms (fuzzy sets) characterizing it; every term was designated according to some medical meaning.

For example, for the variable *Age* we use the term **Old** defined as a fuzzy set (figure 5.1); for the variable *IOP* we use the terms **High**, **Normal** and **Low** defined as fuzzy sets like in figure 3.2.

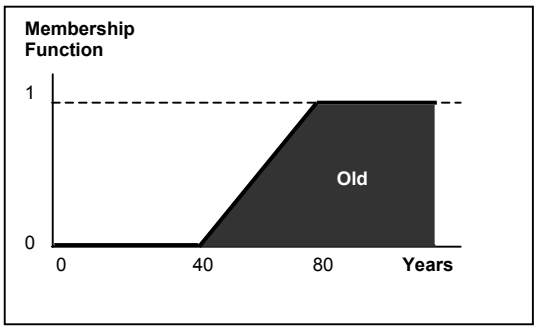

Fig. 5.1: Fuzzy set (linguistic term **Old**) to characterize the linguistic variable **Age**.

We choose as output of the system the risk of progress of the disease, therefore the variable for output is *Risk* with three terms: **Low**, **Moderate** and **High** defined in the respect of the medical experience.

The knowledge of ophthalmologist was embedded in a first set of 29 fuzzy "if-then" rules.

With the list of risk factors and their respective membership functions and this set of rules we asked for the ophthalmologists' feedback to create a stable list of rules.

The complete set of linguistic variables is shown in table 5.1.

Tab. 5.1: Linguistic variables (Glaucoma Risk factors)

N.	Variable	TERMS	Membership in FCM format	Measure-ment unit
1	*Age*	OLD	(0/0) (40/0) (80/1) (100/1)	Year
2	*Myopia*	HIGH	(0/0) (4/0) (7/1) (20/1)	No.
3	*Last eye examination*	LONG TIME AGO	(0/0) (2/0) (5/1) (10/1)	Year
4	*Steroids using*	FOR LONG TIME	(0/0) (0.5/0) (6/1) (12/1)	Month
5	*Diabetes*	FOR LONG TIME	(0/0) (5/0) (20/1) (100/1)	Year
6	*Family history (parents or brothers and sisters with glaucoma)*	BAD	(None/0) (Brother(s)-sister(s)/0.3) (One parent/0.4) (Both parents/0.7) (Parent(s) and brother-sister/1)	-
7.	*IOP*	HIGH NORMAL	(0/0) (16.5/0) (22/1) (45/1) (11/0) (16.5/1) (22/0)	mmHg

		LOW	(0/1) (11/1) (16.5/0) (45/0)	
8.	*Diurnal Fluctuations of IOP*	LOW HIGH	(0/1) (5/0) (10/0) (0/0) (3/1) (10/1)	MmHg
9.	*Race*	NAME	(White/0) (Assian/0.5) (African-American/1)	-
10.	*Abnormal visual field tests**	LOW MODERATE HIGH	(0/1) (33/1) (50/0) (100/0) (0/0) (33/0) (50/1) (66/0) (100/0) (0/0) (50/0) (66/1) (100/1)	Conventional scale: 0 -100
11.	*Hypertension*	PRESENT	(80/0) (140/0) (200/1) (300/1)	MmHg
12.	*Weight*	OBESE		BMI factor Number
13.	*Caffeine intake*	LARGE	(0/0) (3/0) (6/1) (12/1)	Cup/day
14.	*Smoking*	LARGE	(0/0) (10/0) (20/1) (60/1)	Cigarettes (or equiv.) / day
15.	*Cold Hands/Feet*	PRESENT	(No/0) (Yes/1)	-
16.	*History of migraine/Reynaud's*	PRESENT	(No/0) (Yes/1)	-
17.	*History of eye injury*	PRESENT	(No/0) (Yes/1)	-
18.	*History of uveitis*	PRESENT	(No/0) (Yes/1)	-
19.	*History of retinal detachments*	PRESENT	(No/0) (Yes/1)	-
20.	*History of pigment dispersion*	PRESENT	(No/0) (Yes/1)	-
21.	*History of pseudoexfoliation*	PRESENT	(No/0) (Yes/1)	-
22.	*Risk*	LOW MODERATE HIGH	Output	

* Different machines provide different measurements (due to different standards used)-we will provide a unified pondered conventional scale.

The fuzzy terms included in table 5.1 and the following Fuzzy IF-THEN Rules for evaluating the Glaucoma Risk where validated by ophthalmologists. Having a medical meaning too, they already differentiate a person with normal vision from one with glaucoma or more precisely, with different degrees of risk for glaucoma.

1. **IF** *IOP* is High and *Diurnal Fluctuations of IOP* is High and *Abnormal visual field tests* is High **THEN** *Risk* is High
2. **IF** *IOP* is High and *Diurnal Fluctuations of IOP* is Low and *Abnormal visual field tests* is Low **THEN** *Risk* is Moderate
3. **IF** *Family history* is Bad and *Age* is Old and *Abnormal visual field tests* is High **THEN** *Risk* is High
4. **IF** *Family history* is Bad and *Diabetes* is High and *Abnormal visual field tests* is High **THEN** *Risk* is High
5. **IF** *Family history* is Bad and *Cold hands/Feet* is Present **THEN** *Risk* is High
6. **IF** *Myopia* is High and *IOP* is High **THEN** *Risk* is High
7. **IF** *Cold hands/Feet* is Present and *Hypertension* is Present **THEN** *Risk* is Moderate
8. **IF** *Myopia* is High and *Race* is Afro-American and *Last eye examination* is Long time ago **THEN** *Risk* is Moderate
9. **IF** *Myopia* is High and *Steroids using* is For long time **THEN** *Risk* is Moderate
10. **IF** *Myopia* is High and *Age* is Old **THEN** *Risk* is High
11. **IF** *Cold hands/Feet* is Present and *Age* is Old **THEN** *Risk* is High
12. **IF** *Cold hands/Feet* is Present and *Myopia* is High **THEN** *Risk* is Moderate
13. **IF** *Cold hands/Feet* is Present and *IOP* is High **THEN** *Risk* is High
14. **IF** *Cold hands/Feet* is Present and *Steroids using* is For long time **THEN** *Risk* is Moderate
15. **IF** *Hypertension* is Present and *Myopia* is High **THEN** *Risk* is Moderate
16. **IF** *Hypertension* is Present and *Family history* is Bad **THEN** *Risk* is High
17. **IF** *Hypertension* is Present and *Diurnal Fluctuations of IOP* is Low **THEN** *Risk* is Low
18. **IF** *Hypertension* is Present and *Race* is Afro-American **THEN** *Risk* is Moderate
19. **IF** *Hypertension* is Present and *Diurnal Fluctuations of IOP* is High **THEN** *Risk* is High
20. **IF** *Hypertension* is Present and *Steroids using* is For long time **THEN** *Risk* is Moderate
21. **IF** *Hypertension* is Present and *Diabetes* is High **THEN** *Risk* is Moderate
22. **IF** *Race* is Afro-American and *Abnormal visual field tests* **THEN** *Risk* is High
23. **IF** *Race* is Afro-American and *Cold hands/Feet* is Present **THEN** *Risk* is Moderate
24. **IF** *Race* is Afro-American and *Diabetes* is High **THEN** *Risk* is Moderate
25. **IF** *Steroids using* is For long time and *Diurnal Fluctuations of IOP* is Low THEN *Risk* is Moderate
26. **IF** *Steroids using* is For long time and *Age* is Old **THEN** *Risk* is Moderate
27. **IF** *Steroids using* is For long time and *Race* is Afro-American **THEN** *Risk* is Moderate
28. **IF** *Steroids using* is For long time **THEN** *Risk* is Low
29. **IF** *Weight* is Obese and *Caffeine intake* is Large and *Smoking* is Large and *History of retinal detachments* is Present **THEN** *Risk* is Moderate

30. **IF** *History of migraine/Reynaud's* is Present and *History of eye injury* is Present and *History of uveitis* is Present and *History of pigment dispersion* is Present and *History of pseudoexfoliation* is Present **THEN** *Risk* is High

The next step that we are following is to go through patients' charts and gathering data to run the proposed rules system with FCM. Afterwards, we will use the Neuro Control Manager – NeuroCoM Application v. 1.3 – and the Evolutionary Optimizer v. 1.3 (a Evolutionary Algorithms based machine), both programs from TransferTech, in order to adjust the input fuzzy sets and the fuzzy 'IF-THEN" rules [12].

All the results obtained by these methods will be presented to the ophthalmologist so that we can get his feedback once again.

This procedure will be repeated in each successive increment until the set is complete. Each increment will contain all previously developed rules, plus some new ones, though there may be iterations where we will decide to modify or even drop some rules.

6. Conclusion

As presented, the computational intelligence methods increase the accuracy and consistency of diagnosing, risk evaluation and prognostic of glaucoma.

Different from classical methods, computational intelligence can embed in a natural way the uncertainty surrounding the complex medical processes, and in our specific situation can increase the accuracy and consistency of diagnosing, risk evaluation and prognostic of glaucoma.

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