Discovering Differences in Patients with Uveitis through Typical Testors by Class

José Fco. Martínez-Trinidad¹, Miriam Velasco-Sánchez², E. E. Contreras-Arevalo²

¹Centro de Investigación en Computación, IPN
Juan de Dios Batiz s/n esq. Othón de Mendizabal, UPALM; C.P. 07738, México D.F.
e. mail: fmartine@cic.ipn.mx

²Fundación Hospital Nuestra Señora de la Luz (FHNSL)
Ezequiel Montes No. 135, Col. Tabacalera, CP 06030, México D.F.

Abstract. An analysis of clinical features on patients with uveitis attending to their localization through typical testors is presented. The main goal for the physician was to discover feature sets such that distinguish four groups of patients with uveitis. In order to solve the problem was used the Testor Theory in the Logical Combinatorial Pattern Recognition context.

1. Introduction to Clinical Problem

Uveitis is a group of diseases that affect typically the intermediate layer of the eye. This pathology represents between 3% and 5% of ophthalmological consultation. Uveitis had been subject of different classifications the most frequently is based in the location of the lesion in anterior uveitis, intermediate uveitis and posterior uveitis [1].

Uveitis can affect corneal endothelium by inflammation or retrokeratic deposits. Endothelial damage depends upon the intensity and location of the inflammation [2,3]. We studied a group of patients with active uveitis by using specular microscopy. The specular microscopy is a procedure that was initially used by David Maurice in 1968 [4]. In our study we included patients with anterior uveitis, pars planitis and toxoplasmosis.

The goal of our research was to discover feature sets that allow us distinguishing patients in the following four groups of uveitis: pars planitis, toxoplasmosis, anterior uveitis (in patients before 40 years old) and anterior uveitis (after 40 years old).

2. Typical Testors by Class

The Logical Combinatorial Pattern Recognition (LCPR) has as main characteristic that allow us handle information of the objects (their descriptions) under study in terms of a set of features or attributes [5]. These features may be of any nature, that is to say, numeric or not numeric. It allows us to model the problem according to the specialist do it in the practice, instead of force the mathematical tools to adapt to the practical problem.

Let $\Omega=\{O_1,...,O_m\}$ a finite set of objects. Let $R=\{x_1,...,x_n\}$ a set of features, each feature x_i has associated a set of admissible values denoted as M_i $i=1,...,n$. A description $I(O_p)$ is defined for each object O_p $p=1,...,m$, as a finite sequence of values of features $(x_1(O_p),...,x_n(O_p))$. Also for every variable is defined a comparison criterion for the admissible values $C_i:M_i\times M_i\rightarrow L_i$ $i=1,...,n$. It is known that the set Ω is divided in a finite number of subsets $K_1,...,K_l$ called classes. Each class K_j $j=1,...,l$ is defined by a number of objects. This information about objects and classes is in a learning matrix (LM) as the one shown in the Table 1.

The LCPR allows computing feature sets that distinguish objects in a class against the other classes through *Testors Theory* [6].

If the problem is related with Medicine and the number of the objects in each class is greater than one, it means that characterization is done on patients by means of their symptoms and signs associated with a particular disease. In this way the objects O_p in LM are the patients, features x_i $i=1,...,n$ are the symptoms and classes K_j $j=1,...,l$ are the different diseases a patient can suffer.

Table 1. Learning Matrix with m objects, n features and l classes

LM	Objects	Features		
		x_1	...	x_n
K_1	O_1	$x_1(O_1)$	...	$x_n(O_1)$
	...	...	...	...
	O_p	$x_1(O_p)$	...	$x_n(O_p)$
...	...	...	...	...
K_l	O_q	$x_1(O_q)$	...	$x_n(O_q)$
	...	...	...	...
	O_m	$x_1(O_m)$	...	$x_n(O_m)$

In this context, a set of features $\{x_{i1},...,x_{il}\}$ of LM is called a *testor by class (TC)* for the class K_i from LM if after deleting from LM all columns except $\{x_{i1},...,x_{il}\}$, all rows of LM corresponding to K_i are different to rows corresponding to K_j $j\neq i$. A *TC* is called *typical testor by class (TTC)* if none of its proper subsets is a *TC* [7]. *TTC* will be used too instead of *typical testors by class* indistinctly.

In general, we can say that finding all typical testors of a matrix is equivalent to doing an exhaustive search on all feature subsets, which are $2^{|R|}$, where $|R|$ is R 's cardinal number. When the number of rows, columns or classes increases, the time necessary for this procedure could grow until it becomes impossible to be computed. As a consequence of this, many studies have been developed; in fact, this problem alone is a research line within Testor Theory framework [6].

Through computation of *TTC*, it is possible to discover feature sets that allow distinguishing patients in different classes.

Let Ψ be the set of all *TTC* for K_i $i=1,...,l$, of a given problem and $\Psi(x)$ the subset of all *TTC* that contain feature x . To each feature x we assign the value obtained by the equation 1.

$$F(x)=|\Psi(x)|/|\Psi|$$

(1)

The value $F(x)$ is called informational weight based in the apparition frequency of the feature in the *TTC* and we identify it as a measure of its importance [6]. In

addition, we assign to each *TTC* a weight based in the informational weight of the features as follows:

$$\sigma(t)=\frac{1}{|t|}\sum_{x_i\in t}F(x_i) \tag{2}$$

It is clear according to this approach that between more frequent is a feature in the set of *TTC* (*the feature is more useful than other to distinguish objects belonging to different classes*) most important will be it. Consequently the *TTC* with the highest weight will be those containing features with the highest weight. Therefore, we consider that a typical testor with highest weight is more important to distinguish objects belonging to different classes than a typical testor with low weight.

3. Methodology

In our study, we include patients treated in the FHNSL from March to August in 1999. These patients satisfied the following clinical criteria: active uveitis, first inflammatory manifestation, specular microscopy, fulfillment of treatment, complete clinical file. We exclude those patients with: diabetes mellitus of any type, contact lens user, associated or previous ocular or corneal pathology, previous ocular trauma or ocular surgery, other systemic pathologies (neurological disease).

In the specular microscopy, the features shown in the table 2 were analyzed.

Table 2. Clinical features used to describe patients with uveitis

Feature	Admissible values	Type
Age (<i>A</i>)	10-80	Quantitative
Gender (<i>G</i>)	M= Male, F= Female	Qualitative Boolean
Cellular Density (<i>CD</i>)	500-2500	Quantitative
Pleomorphism (<i>Pl</i>)	absent light moderate severe	Qualitative Ordinal
Polimegathism (<i>Po</i>)	absent light moderate severe	Qualitative Ordinal
Tyndall (<i>T</i>)	- + ++ +++	Qualitative Ordinal
Flare (<i>F</i>)	- + ++ +++	Qualitative Ordinal
Guttatas (<i>Gu</i>)	0 I II III	Qualitative Ordinal

From the 38 studied patients, 5 were eliminated (because they did not satisfy clinical criteria) and 33 were considered. The patients were separated in four classes taking account the localization of the uveitis as is shown in the table 3.

Note that the classes toxoplasmosis and pars planitis have only three and four patients respectively, nevertheless the physicians consider that these descriptions of patients are representatives of these groups of patients.

As first step, we modeled jointly with the specialists, the comparison criteria for the values of the features. For qualitative features was used a comparison criterion based in the matching, see equation (3).

$$C_{x_i}(x_i(I(O_i)),x_i(I(O_j)))=\begin{cases}1 & \text{if } x_i(I(O_i))\neq x_i(I(O_j)) \\ 0 & \text{otherwise}\end{cases} \tag{3}$$

In the case of quantitative features was used a comparison criterion with threshold, that is to say, two values are different if the absolute difference between them is greater than a threshold, see equation (4).

C_{x_i}(x_i(I(O_i)), x_i(I(O_j))) = \begin{cases} 1 & \text{if } |x_i(I(O_i)) - x_i(I(O_j))| > \epsilon \\ 0 & \text{otherwise} \end{cases} \tag{4}

The specialists according to their expertise proposed the threshold for this criterion. So the threshold used for age feature was $\epsilon = 5$ and $\epsilon = 100$ for cellular density feature.

Table 3. Sample of patients with uveitis

	Num	A	G	CD	Pl	Po	T	F	Gu
Pars Planitis	P1	12	F	1500	light	moderate	-	-	I
	p2	12	M	1500	absent	absent	++	-	0
	P3	35	M	2200	absent	absent	++	-	0
	P4	13	F	2000	light	light	++	-	0
Toxoplasmosis	P5	20	M	1400	absent	absent	+	-	0
	P6	16	F	1000	severe	severe	+	-	0
	P7	30	F	1200	absent	light	+	-	0
Anterior Uveitis <=40	P8	38	M	1200	light	light	+	-	I
	P9	21	F	1400	light	light	+	++	I
	P10	22	M	1200	absent	light	-	-	0
	P11	30	M	1200	light	light	+++	-	I
	P12	38	F	1200	moderate	light	++	+++	II
	P13	24	M	800	severe	severe	++	++	I
	P14	30	F	1000	severe	severe	++	+	II
	P15	19	F	1200	severe	severe	+	-	I
	P16	40	F	1200	light	light	++	-	I
Anterior Uveitis >40	P17	52	F	600	severe	severe	+	-	III
	P18	70	F	600	light	severe	+++	++	III
	P19	49	M	600	moderate	severe	+++	++	III
	P20	66	F	700	moderate	severe	+	-	II
	P21	44	M	1200	light	light	++	-	0
	P22	53	F	900	light	moderate	+++	+++	II
	P23	49	F	1200	light	light	++	+	II
	P24	80	F	600	severe	severe	+	-	II
	P25	45	F	1200	absent	absent	++	-	0
	P26	47	F	800	severe	severe	++	-	II
	P27	41	M	1200	light	light	+++	+++	I
	P28	43	M	1400	moderate	absent	++	+++	0
	P29	42	M	1000	moderate	light	++	+	II
	P30	70	M	600	moderate	severe	+	-	II
	P31	44	F	800	moderate	moderate	++	++	I
	P32	55	F	900	severe	moderate	++	++	II
	P33	42	M	700	moderate	severe	+	++	III

It exists several algorithms to compute the typical testors [8], in this particular problem was applied the CC algorithm. The *TTC* for the four classes of patients are shown in the table 4.

4. Discussion and Conclusions

In the first column of tables 4a to 4d, we can see the sets of features that allow us to distinguish the patients of the respective class against the rest patients (*TTC*). In the fourth column appears the weight associated to the feature in the column third.

Remind that the weight associated to the features is computed using (1). On basis of this weight is computed the weight associated to the typical testor through (2), it appears in the second column. Note that if we observe the subdescriptions in a particular class, attending only to the features in the typical testor for this class, all those are different to the subdescriptions in the other classes. Therefore, through *TTC* computation it is possible discover the sets of features that allow us detect the differences between the patients under study.

Table 4. Typical testors by class for 4a) Pars Planitis; 4b) Toxoplasmosis; 4c)Anterior uveitis <=40 and 4d) Anterior uveitis > 40 classes.

Typical Testor	Weight	Feature	Weight	Typical Testor	Weight	Feature	Weight
{CD, T, F}	0.4583	A	0.75	{T,G}	0.49995	A	0.5714
{CD, Pl, Tl}	0.4167	G	0	{CD, PO,T}	0.52376	G	0
{A,T,Gu}	0.5416	CD	0.625	{CD, Pl, T}	0.52376	CD	0.7142
{A, Po}	0.4375	Pl	0.375	{A, Po, Gu}	0.42853	Pl	0.2857
{A, Pl,T}	0.5833	Po	0.125	<i>{A, CD, Gu}</i>	<i>0.5713</i>	Po	0.2857
{A, CD, Gu}	0.5416	T	0.625	{A, CD, T, F}	0.49995	T	0.5714
<i>{A,CD,T}</i>	<i>0.6666</i>	F	0.125	{A, CD, Pl}	0.5237	F	0.1428
{A, CD, Pl}	0.5833	Gu	0.25			Gu	0.4285
4a				4b			
Typical Testor	Weight	Feature	Weight	Typical Testor	Weight	Feature	Weight
{Po,T,F,Gu}	0.7083	A	0.6666	{CD, Po,T,F,Gu}	0.72	A	0.4
{Pl,T,F,Gu}	0.6666	G	0	{CD, Pl,T,F,Gu}	0.72	G	0
<i>{A, T,F,Gu}</i>	<i>0.7916</i>	CD	0.3333	{CD,Pl,Po,F,Gu}	0.68	CD	0.8
{A,Po,F,Gu}	0.7083	Pl	0.1666	<i>{A, F, Gu}</i>	<i>0.73</i>	Pl	0.4
{A,CD,F,Gu}	0.7083	Po	0.3333	{A, CD, T, Gu}	0.70	Po	0.4
{A,CD,T,Gu}	0.6666	T	0.6666			T	0.6
		F	0.8333			F	0.8
		Gu	1			G	1
4c				4d			

After compute the *TTC*, it is possible to evaluate the informational weight for features based in its importance to distinguish patients of a class against the rest. Remind that we consider that between more frequent is a feature in the set of *TTC*, then the feature is more useful than other to distinguish objects belonging to different classes. Consequently, it is possible to use the weight of features to associate a weight to the typical testors as is expressed in (2). This weight can be interpreted as the importance that the typical testor has to distinguish patients of a particular class against the rest. In some cases may be useful only consider the *TTC* with highest weight (See the rows in cursive in the tables 4a-4d).

The typical testors by class are important to select those sets of features that are most efficient to preserve class separability. So, these sets of features can be used to classify new patients.

As future work, in a second phase, we pretend to construct a computer system to realize differential diagnosis of intraocular inflammatory diseases. We will use the algorithms based in partial precedence as *voting algorithms*, *Kora-Ω* and

representative sets [9]. These algorithms allow us in natural way consider both *TTC* and their weights, in order to classify new patients. The idea of these algorithms is to classify objects according to their description and their similitude with the objects already classified in the K_i classes. The similarity is evaluated analyzing subdescriptions of objects instead of whole descriptions. The *TTC* define the set of features that should be compared through a convenient similarity function and the weight of the testors weigh this similarity. Therefore, It would be possible to apply any of these algorithms to LM in order to classify a new object, obtaining the decision criteria for the class it belongs to.

In this paper, a methodology to discover differences between patients with uveitis was presented. In order to solve this problem *TTC* were used.

The analysis here presented constitute a first step for solve the differential diagnosis of intraocular inflammatory diseases. Besides, based on this work the construction of a computer system in order to realize differential diagnosis of intraocular inflammatory diseases was proposed as future work.

Of course, we will add feedback to the process enriching jointly with the physicians the sample of patients in LM.

Finally, the methodology proposed in this paper is of extremely useful, not only to discover differences between patients with uveitis, but also, to discover differences between patients of any diseases.

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