AN APPLICATION OF A DESCRIPTIVE IMAGE ALGEBRA FOR DIAGNOSTIC ANALYSIS OF CYTOLOGICAL SPECIMENS

An Algebraic Model and Experimental Study

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Abstract: The paper is devoted to representation of a model of an information technology for automation of diagnostic analysis of cytological specimens of patient with lymphatic system tumors. The main contribution is implementation of the model by algebraic means. The theoretical base of the model is the Descriptive Approach to Image Analysis. The paper demonstrates a practical application of its algebraic tools – it is shown how to construct a model of a technology for automation of diagnostic analysis of cytological specimens using Descriptive Image Algebras.

1 INTRODUCTION

The paper is devoted to the development and formal representation of the descriptive model of the information technology for automating morphologic analysis of cytological specimens of patients with lymphatic system tumors (Gurevich et al., 2003). The main tasks of the paper are to structure the information technology and to describe it using algebraic means provided by the Descriptive Approach to Image Analysis (Gurevich, 1989). The developed mathematical model should ensure a uniform representation of an algorithm for task solution; this is essential for programming and useful for comparing different information technologies designed for solving the same task.

The theoretical base of the model is Descriptive Approach to Image Analysis (Gurevich, 1989) and its main tools – Descriptive Image Algebras (DIA) (Gurevich and Yashina, 2006), Descriptive Image Modes (DIM) and Generating Descriptive Trees (GDT) (Gurevich and Yashina, 2005).

DIA is a mathematical language developed for description, comparison and standardization of algorithms for image analysis, processing and recognition. Using image analysis operations as elements of algebra has made it possible to vary easily methods for subtask solution, keeping overall scheme of the technology the same.

Classes of image representation – DIM – are used for standardization of the data for recognition algorithms. GDT is an instrument for classification and representation of all information connected with image models. GDT is employed to make more convenient selection and construction of image models.

The main distinctive feature of the proposed paper is that the Descriptive Approach tools are applied for describing algorithms used for applied task solution. Algebraization of pattern recognition and image analysis has a long history: Unger, Sternberg, Serra (Serra, 1982), Zhuravlev (Zhuravlev, 1998), Grenander (Grenander, 1993), Ritter (Ritter and Wilson, 2001), but to our

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knowledge algebraic methods in general and Descriptive Approach methods in particular have never been employed for solving the task of medical image analysis and recognition.

In Sections 3, 4 the formal representation of the descriptive model of the information technology is presented. In order to make the theoretical basis clearer Section 2 provides brief introduction into the essential notions (DIA, DIM, GDT). Section 3 illustrates a simplified model of the image recognition task based on multi-model image representation. Section 4 presents a descriptive model of the information technology developed for automating morphologic analysis of cytological specimens of patients with lymphatic system tumors. The technology has been tested on the specimens from patients with aggressive lymphoid tumors (de novo large and mixed cell lymphomas (CL), and transformed chronic lymphatic leukemia (TCLL)), as well as innocent tumors (indolent chronic lymphatic leukemia (CLL)), the results are also presented in Section 4.

2 ALGEBRAIC TOOLS OF THE DESCRIPTIVE APPROACH

The main purpose of theoretical apparatus of the Descriptive Approach to Image Analysis is structuring of the variety of methods, operations and representations. The final goal of the Descriptive Approach is automated image mining: a) automated selection of techniques and algorithms for image recognition, estimation, and understanding; b) automated testing of the raw data quality and suitability for solving the image recognition problem.

2.1 Descriptive Image Models

DIM are mathematical objects – classes of image formal description – providing representation of information carried by an image in a form acceptable for a recognition algorithm. There are 4 classes of DIM: P-models (Parametric Models), G-models (Generating Models), T-models (Transformation or Procedure Models) and I-models (initial images as they are). Now we introduce two of them.

Definition 1: **P-model** is a description of an image by numerical features.

An example of P-model is an image representation by numerical feature vector. An image feature is a result of calculation of some function f on an image during or as a result of its processing. Let I be an initial image, vector $F=(f_1,f_2,\ldots,f_n)$ be a feature vector (the values of features are calculated on an image). Thus, a model $M_P(I)=(f_1(I),f_2(I),\ldots,f_n(I))$ is a parametrical models of an image I.

Definition 2: **T-model** is an image representation as a sequence of transforms converting one or several initial images into a given one.

Let $\{I_i\}_1^n$ be a set of initial images (fragments of an image *I)* used for creating a T-model. Solution of an image recognition problem often requires enhancing quality of an image before calculating feature values. For instance, it can be contrast enhancement, denoising, histogram equalization, etc. Let $\{t_j\}_1^m$ be transforms which should be applied to an initial images in sequential or parallel modes to get some formal description allowable by a pattern recognition algorithm for further processing. The transforms could be the predetermined one (to turn an initial image 90 degrees) or the transforms with some stopping criterion (to increase an image contrast till the maximum in brightness histogram would become equal to some value *N*). Then $M_T=\{t_i\}_1^m(\{I_j\}_1^n)$ is a T-model of an initial image.

2.2 Descriptive Image Algebras

DIA is a new type of image algebra. Its main purpose is to provide a new mathematical language for representation, comparison, testing and standardization of algorithms for image analysis, recognition, and processing.

Definition 3: An Algebra is called **DIA** if its basic operands are image models or operations on images, or both the models and operations.

Let us introduce DIA with one ring, which will be used further for describing an algorithmic scheme of a recognition task. For each DIA both the operands and operations are described.

DIA 1 is a set of color images. *The operands*: The set U of $\{I\}$ is the set of images I={{(r(x,y), g(x,y), b(x,y)), r(x,y), g(x,y), b(x,y) $\in$ [0..M-1]}, (x,y) $\in$X}, M=256 is the value of maximum intensity of a color component, n is the number of initial images, X is the set of pixels. *The operations*: The set U of {I} is the DIA with the ring of color images over the field of real numbers with standard algebraic operations of addition, multiplication and multiplication by an element from the field of real numbers.

DIA 2 is a set of gray scale images. *The operands:* Elements of DIA2 are images J= $\{\{gray(x,y)\}_{(x,y) \in X}, (x,y)\in[0,...,M-1]\}$. *The operations:* a set V of {J} is the DIA with ring of color images over the field of real numbers with standard algebraic operations of addition, multiplication and multiplication by an element from the field of real numbers.

DIA 3 is a set F of operations $f(U\rightarrow V)$ converting elements from the set of color images into elements of the set of gray scale images. *The operands:* Elements of DIA2 are operations $f(U\rightarrow V)\in F$. Such transforms can be used for elimination luminance and color differences of images. *The operations:* Operations of addition, multiplication and multiplication by an element from the field of real numbers are introduced on the set of functions *f* as sequential operations of obtaining gray scale images and their addition, multiplication and multiplication by an element from the field of real numbers correspondingly.

DIA 4 is a set G of operations $g(V\rightarrow P_1)$ of calculation of a gray scale image features. *The operands:* DIA4 is a ring of functions $g(V\rightarrow P_1)\in G$, P_1 is a set of P-models. *The operations:* Operations of addition, multiplication and multiplication by a field element are introduced on the set of functions *g* as operations of sequential calculation of corresponding P-models and their addition, multiplication and multiplication by a field element.

DIA 5 is a set P_1 of P-models. *The operands:* a set P_1 of P-models. *The operations:* a) addition – an operation of unification of numerical image descriptions; b) multiplication of 2 P-models – an operation of obtaining a complement of numerical image descriptions; c) multiplication by a field element - operation of multiplication of a number, a vector, or a matrix by an element of the field. The addition is applied for constructing joint parametric image representation. The multiplication is applied for reducing a set of image features to a set of significant features. The multiplication by an element from the field of real numbers is applied for feature vector normalization.

DIA 6 is a set P_2 of P-models (P_2 includes feature vectors of the same length). *The operands:* a set P_2 of P-models. *The operations:* Operations of addition, multiplication and multiplication by a field element are introduced on the set P_2 as operations of a vector addition, multiplication and multiplication by a field element.

Table 1 shows all DIA with one ring presented above, which are used for describing the algorithmic scheme for solving the task of cytological image recognition.

Table 1: DIAs with one ring used for describing algorithmic scheme for solving the task of cytological image recognition.

	Ring elements	Ring operations	Purpose
1	color images	standard algebraic operations	description of initial images
2	gray scale images	standard algebraic operations	description of separated nucleus on images
3	operations reducing color images to gray scale images	standard algebraic operations	elimination luminance and color differences of images
4	operations of image feature calculation	standard algebraic operations	feature calculation
5	P-models	image algebra operations (union, complement, multiplication by real number)	selection of informative features
6	P-models	standard algebraic operations	image reduction to a recognizable form

2.3 Generating Descriptive Trees

GDT (Gurevich and Yashina, 2005) is a mathematical object for generation multitude of image models, i.e. it is a tool for creating and combining image models.

Definition 4: **GDT** is a tree-like structure intended for classification and automation of generating formal image descriptions with the following properties:

1) each element of the tree (descriptor) reflects some image property;

2) each GDT combines descriptors of the same type, i.e. GDT represents single-type properties of an image (parametric, generic, procedural GDT and I- GDT);

3) each element of a GDT can be combined with another one to generate a new partial multi-aspect model of an image.

Every type of GDT represents the properties of the image model class that constitutes its basis. P-models are based on image features; hence parametrical GDT is a tree of feature descriptions

(Figure 1). T-models are based on image transformations; so procedural GDT is a tree of operations over images (Figure 2).

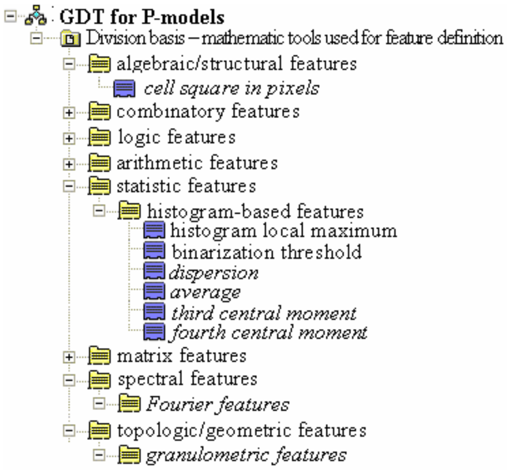

Figure 1: GDT for P-models.

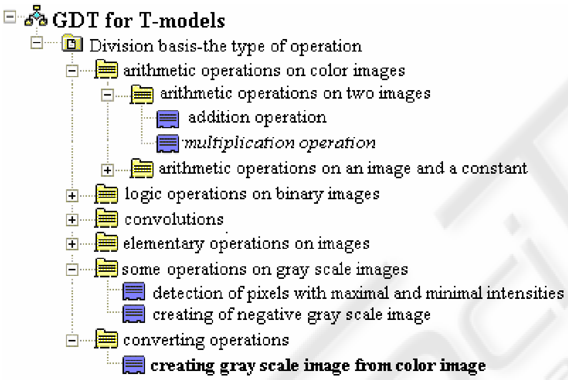

Figure 2: GDT for T-models.

3 DESCRIPTIVE MODEL OF AN IMAGE RECOGNITION PROBLEM

The Descriptive Approach provides the following model for an image recognition process (Gurevich, 1989; Gurevich and Yashina, 2005):

$$\{I_1^n\} \rightarrow \{M_1^s\} \rightarrow \{A_1^l\} \rightarrow \{P_1^r(I_j)\}_1^n \qquad (1)$$

$\{I_1^n\}$ is a set of initial images. $\{I_1^n\} \subset \bigcup_1^r K_i$, where $\{K_1^r\}$ is a set of classes determined by image recognition task. $\{M_1^s\}$ is multi-model representation of an image I_j. An algorithm combination $\{A_1^l\}$ solves an image recognition problem, if it puts a set of predicates $\{P_1^r(I_j)\}_1^n$ into correspondence to the set of initial images, where predicate $P_j(I_i)=\alpha_{ij}$ has the values: $\alpha_{ij}=1$, if an image I_i belongs to a class K_j; $\alpha_{ij}=0$, if an image I_i does not belong to a class K_j; $\alpha_{ij}=\Delta$, if an algorithm combination does not establish membership of an image I_i to a class K_j.

Multi-model representation is generated by the set of GDT. Different ways for constructing multi-aspect image representations are used different GDT types. Image representation becomes multi-model if it is generated by different types of GDT.

Multi-model image representation M_1^s is created as follows: 1) a set of GDT $\{T_j\}_1^n$ is generated; 2) each GDT T_j generates one or several formal representations $\{M_k\}_1^{n_j}$ of an image, they precisely reflect image properties essential for solving the problem at hand; 3) these representations are united into one multi-model representation Ψ = $\{\{M_k\}_1^{n_j}\}_1^n$ or several multi-model representations M_1^s, which may be used for all, or for some initial images presented for recognition.

This scheme takes no account of training sample recognition. To correct this fact the scheme should be modified as follows:

$$\begin{array}{l} \{I_1^m\} \xrightarrow{1} \{M_1^s\} \xrightarrow{Training(2)} \{A_1^l\} \rightarrow parameters \\ \{I_{m+1}^\infty\} \xrightarrow{1} \{M_1^S\} \xrightarrow{Recognition(3)} \{A_1^l\} \rightarrow \{P_1^r(I_j)\}_{m+1}^\infty \end{array} \qquad (2)$$

The step of image model (models) construction is a step of "image reduction to a recognizable form" (Step 1). Construction of the multi-model representation is conceptually the same for both training set and recognition set; however, as it will be shown below, training and recognition process can ramify inside Step 1. Step 2 is a training step and Step 3 is a recognition step.

4 THE MORPHOLOGICAL ANALYSIS OF THE LYMPHOID CELL NUCLEUSES

The developed information technology will be described below and represented by the algorithmic scheme (2) which is interpreted by means of DIA, DIM and GDT.

4.1 Initial Data

A database (DB) of specimens of lymphatic tissue imprints was created to select and describe diagnostically important features of lymphocyte nuclei images. DB contains 1830 specimens of 43 patients. DB contains both specimen images and the contours of diagnostically important lymphocyte cell nucleus indicated by experts.

Table 2: Database filling.

Diagnosis	Patient number	Image number	Nuclei number
CL	18	986	1639
TCLL	12	536	1025
CLL	13	308	2497
Total:	43	1830	5161

Footprints of lymphoid tissues were Romanovski-Giemsa stained and photographed with digital camera mounted on Leica DMRB microscope using PlanApo 100/1.3 objective. The equivalent size of a pixel was 0,0036 mcm^2. 24-bit color images were stored in TIFF format.

Initial images $\{I_1^n\}$ are described by DIA1 (n=1830). Figure 1 gives specimen nucleus of patients with CL, TCLL and CLL diagnosis.

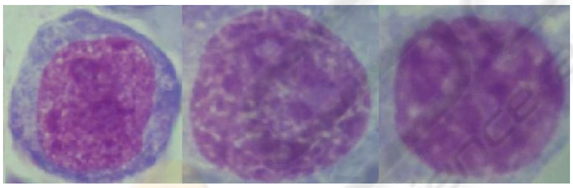

Figure 3: Specimen nucleus of patients with CL, TCLL and CLL diagnosis accordingly (from left to right).

4.2 Reducing an Image to a Recognizable Form

All initial images are divided into two groups: training image set $\{I_1^{[n/2]}\}$ and recognition image set $\{I_{[n/2]+1}^n\}$. Below the steps 1.1-1.5 (that form together step 1 “Reducing an image to a recognizable form”) are described as follows: description, model construction, step operands, step operations. It will be highlighted where processing of training and recognition sets differs.

Step 1.1 (equation 3): segmentation of diagnostically important nucleus on images. The contours of indicated by experts lymphocyte cell nucleus were defined on images of cytological specimens. The applied algorithm of threshold segmentation was supplemented by morphological processing of derivable nuclei images in order to obtain a corresponding mask. The mask multiplication by initial image gives indicated nuclei image (m is the number of segmented nucleus on all images).

$$\underset{DIA1}{\{I_i\}_1^n, \{B_j\}_1^m} \xrightarrow{Step1.1-DIA1} \underset{DIA1}{\{M_1^T(I_{i(j)}, B_j)\}_1^m} \quad (3)$$

Model construction: The image T-models $\{I_j^1\}_1^m \equiv \{M_1^T(I_{i(j)}, B_j)\}_1^m$ are constructed for both the initial images $\{I_i\}_1^n$ and binary masks $\{B_j\}_1^m$ (n=1830, m=5161, index i(j) corresponds to the mask number j). The number of binary masks equals to the number of separated nucleus on initial images. At Fig. 2 operation of this type is marked by italics - *multiplication operation.*

Step operands: initial images and binary masks represented as color images

$$I = \begin{cases} (0,0,0), (x,y) \in X, value(x,y) = 0, \\ (1,1,1), (x,y) \in X, value(x,y) = 1 \end{cases}.$$

Step operation: Operation of segmenting cell nucleuses on the initial image is *operation of multiplication of 2 elements of DIA1* (an initial image is multiplied by corresponding binary mask).

Step 1.2 (equation 4): reducing color images to gray scale images. To compensate different illumination conditions and different colors of stain specimen images were processed before feature calculation.

$$\underset{DIA1}{\{I_j^1\}_1^m} \xrightarrow{Step1.2-DIA2} \underset{DIA3}{\{M_2^T(I_j^1)\}_1^m} \quad (4)$$

Model construction: The image T-models $\{I_j^2\}_1^m \equiv \{M_2^T(I_j^1)\}_1^m$ are constructed from image models $\{I_j^1\}_1^m$. At Fig. 2 operation of this type is marked by bold - **creating gray scale image from color image.**

Step operands: image models $\{I_j^1\}_1^m$.

Step operations are described by the elements of the DIA2. Such representation gives flexibility for using different kinds of processing operations. Here the function f(U→V)∈F (DIA 2 element) has a form

(I={{(r(x,y),g(x,y),b(x,y)),r(x,y),g(x,y),b(x,y) $\in$[0..M-1]}$_{(x,y)}$ $_{\in X}$}): f(I)=J={{gray(x,y)}$_{(x,y)\in X}$, (x,y)$\in$[0..M-1]}, where gray(x,y)=g(*x,y*) $\frac{2R}{M}$, *R* is an average brightness of a red component of an initial RGB-image. The green tone in this case is the most informative.

Step 1.3 (equation 5): feature calculation on constructed image models of *the training set*. To describe each image 47 features were selected: the size of nucleus in pixels, 4 statistical features calculated on the histogram of nucleus intensity, 16 granulometric and 26 Fourier features of nucleus. (m_1 equals to the number of segmented nucleus on training set).

$$\underset{DIA2}{\{I_j^2\}_1^{m_1}} \xrightarrow{Step1.3-DIA4} \underset{DIA5}{\{M_1^P(I_j^2)\}_1^{m_1}} \qquad (5)$$

Model construction: P-model is generated by features from P-GDT. 47 selected features are marked in italics on P-GDT (Fig. 1). P-model $M_1^P(j) \equiv M_1^P(I_j^2)$ is the vector with dimension 47, j=1,...,m_1.

Step operands: image models $\{I_j^2\}_1^m$.

Step operations are described by the elements of the DIA4. Such representation gives flexibility for calculation of different features.

The step 1.4 is additional step of image model reduction. As it will be shown below the recognizing algorithm was applied to both full model $M_1^P(j)$ (j=m_1+1,...,m), and reduced model $M_2^P(j)$. (j=m_1+1,...,m).

Step 1.4 (equation 6): selection of informative features. At this step the constructed image descriptions are investigated for selecting most informative features. Applying factor analysis to training image set detects 14 important features (Vorobjev et al., 2004).

$$\underset{DIA5}{\{M_1^P(j)\}_1^{m_1}} \xrightarrow{Step1.4-DIA5} \underset{DIA6}{\{M_2^P(M_1^P(j))\}_1^{m_1}} \qquad (6)$$

Model construction: Image representation $\{M_1^P(j)\}$ is reduced to image representation $M_2^P(j) \equiv M_2^P(M_1^P(j))$ (j=1,...,m_1). In our case it is a vector with dimension 14.

Step operands: Image models $\{M_1^P(j)\}_1^{m_1}$ are feature vectors with dimension 47. Step operands are any P-models, represented as feature vectors that form a part of vector $\{M_1^P(j)\}_1^{m_1}$.

Step operations are described by the operations of the DIA5.

Step 1.5: feature calculation (calculation of features of full model $\{M_1^P(j)\}$ or reduced model $M_2^P(j)$ for recognition set (j=m_1+1,…,n)). Note that multi-model representation of images $\Psi(j) \equiv M_2^P(j) \vee M_1^P(j)$ was constructed.

4.3 Training and Recognition

Algorithms based on estimate calculations (AEC) were chosen as recognition algorithms since they can be conveniently represented by algebraic tools (Zhuravlev, 1998).

The set of predicate values {0, 1, Δ} derived by algorithm combination $\{A_1^I\}$ (equations 1, 2) does not allow to construct intentional algebraic operations. To realize algebra of algorithms the algebraic approach of Yu.I.Zhuravlev goes from the set of predicate values to more general set of values - the field of real numbers. Each AEC is defined as *A = B·C*, where *B* is recognition operator (it calculates real estimates), and *C* is decision rule (for example, threshold rule).

Recognition algorithm B requires the feature vectors as the initial data. DIA 6 describes these initial data.

AEC was applied to both full image models $M_1^P(j)$ (j=1,...,m, 47 features) and reduced image models $M_2^P(j)$ (j=1,...,m, 14 features). Figures 2 and 3 present the descriptive and the structural scheme of information technology.

The software system «Recognition 1.0» (Zhuravlev et al., 2005), used for experimental investigation, includes effective realization of AEC methods and allows to apply them for practical task solution. It was experimentally verified that the best results are achieved by voting using all possible support sets, while automatic definition of support set capacity and definition of fixed support set capacity give lower precision.

Recognition rate for full feature set amounts to 86,75%, while the rates differ for different recognition classes (see Table 3). High recognition rates for CLL diagnosis are likely to be connected with innocent nature of CLL as opposed to LC and TCLL, which are malignant. Thus cells of CLL diagnosis have pronounced distinctions from cells of other diagnosis, and cells of LC and TCLL diagnosis are more similar to each other.

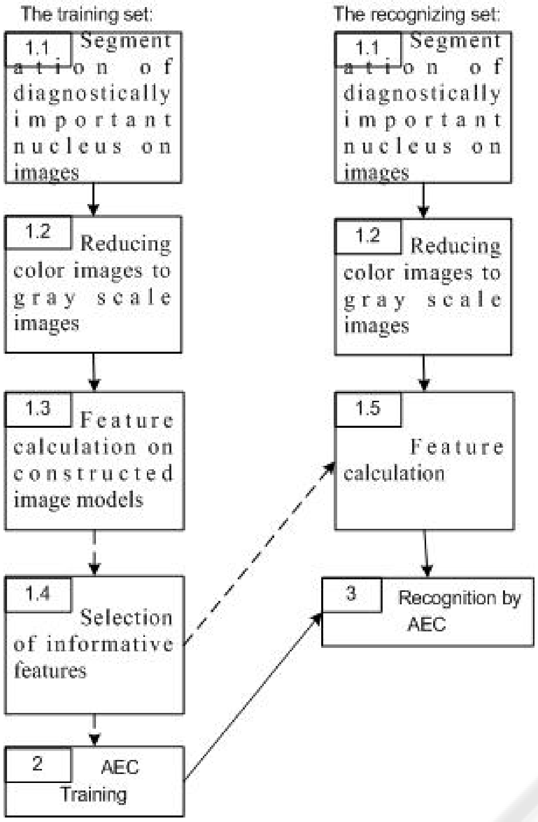

Figure 4: The descriptive scheme of recognition.

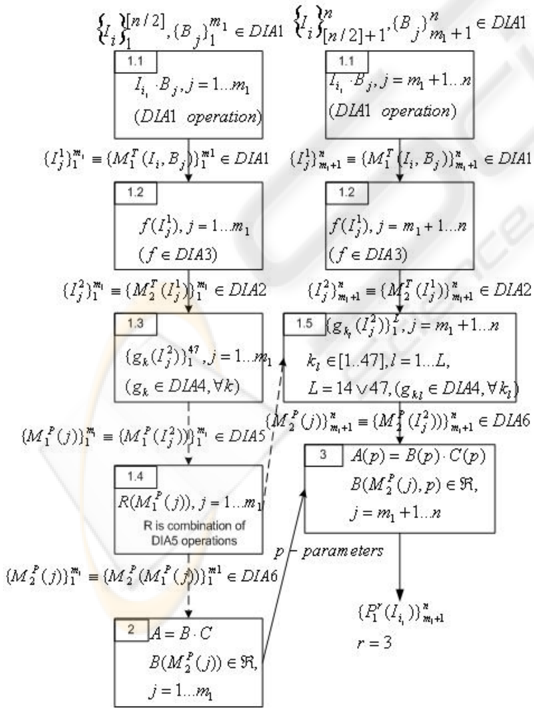

Figure 5: The structural scheme of recognition.

Table 3: The recognition rates for feature description consisted of 47 features.

Diagnosis	The number of correctly recognized cells	Total number of cells	The recognition rate
LC	693	820	84,51%
TCLL	325	513	63,35%
CLL	1221	1248	97,84%
Total cell set	2239	2581	86,75%

Reducing feature set to 14 features obtained by factor analysis the recognition rate decrease to 83,18% (see Table 4). This feature set includes following features: the size of nucleus in pixels, average by intensity histogram (statistic feature), the number of elements with typical size in nuclear (granulometric feature), the number of elements with minimal size (granulometric feature) and 9 Fourier features of nucleus.

Table 4: The recognition rates using reduced feature description consisted of 14 features.

Diagnosis	The number of correctly recognized cells	Total number of cells	The recognition rate
LC	626	820	76,34%
TCLL	300	513	58,48%
CLL	1221	1248	97,84%
Full cell set	2147	2581	83,18%

5 CONCLUSION

The paper demonstrates practical application of algebraic tools of the Descriptive Approach to Image Analysis - it is shown how to construct a model of a technology for automation of diagnostic analysis of cytological slides of patient with tumors of the lymphatic system using Descriptive Image Algebras. The presented model of the information technology for automation of diagnostic analysis of medical images will be used for creating software implementation of the technology, its testing and performance evaluation.

While the method for solving medical task has been developed previously, the contribution of this paper is construction of the model of the information technology, providing uniform representation for the technology. So the paper solves dual task: firstly it presents technology by well structured mathematic model, and secondly it shows how DIA can be used in image analysis task.

In the future research the Descriptive Approach to Image Analysis and its main tools (DIA, DIM, and GDT) will be applied for constructing models of information technologies for automation of diagnostic analysis in other fields of medicine.

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