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Modern Trends in Biomedical Image Analysis System Design

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1. Introduction

1.1 Automated microscopy systems

Nowadays the combination of progressive information technologies, modern methods and algorithms of processing, analysis and synthesis of images together with medicine has resulted in the emergence of a new branch or field, called telemedicine. Telemedicine is distant diagnostics based on image analysis and processing of human organs cells. There are the following directions in this field: medical-biological research automation (that is computer systems design, which provides input, processing and analysis of images); development and application of algorithms of biomedical images pre-processing, which improves quality of images; image analysis (feature extraction, classifiers development, etc.) and data transfer network technologies. This problem has been studied by many scientists.

Today the analysis of medical-biological specimens (cytological and histological smears) in diagnostic laboratories is conducted by visual inspection. This process is routine and labour intensive. That's why the automated microscopy systems (AMSs) – software-hardware complexes appeared for the digital processing of microscopic images. AMS includes motorized controlled microscope, video camera, optical adapters, computer, and specialized software modules. In general the medical complexes for automated microscopy are made to provide higher productivity of medical work; improve analysis accuracy, availability of intensive labour-consuming and rare analyses, quality control, telemedicine; to collect and archive specimen image; and better learning, service and certification. AMS provides the following levels of microscopic analyses automations:

1. Visual analysis, documenting and telemedicine;
2. Analysis of images in order to determine the specimen characteristics;
3. Automation of movements and inspection of specimen.

Morphometry of cells is only the one of the automated methods in AMS. Basic steps of cytological and histological analysis are the following: selection of an object of investigation, preparation for microscope inspection, microscopy techniques application, qualitative and quantitative analysis of images. Type, structure and functions of the system are dictated by actual task, objects class of research and financial ability of user.

Problem definition. The actual tasks are projecting of AMS hardware and software structures based on the hardware components existing in the market and development of the own software for histological and cytological image analysis.

1.2 Components of automated microscopy systems

In general, AMSs are divided into research-based and specialized (Egorova 2005, Egorova 2006). Research AMS is used for development of new methods of diagnostics. Specialized AMS provides implementation of a standardized clinical research. The key feature of research-based AMS is the use of multifunctional microscopes and cameras with increased sensitiveness and resolution. The research method is not preset, but formed by a user.

For microbiology investigations the world market offers AMSs or their components from different manufacturers, such as Carl Zeiss, Leica, Olympus, Nikon, Micromed (Russia), Motic (China), Konus (Italy).

Let's shortly describe the process of research with the help of AMS (Egorova, 2005). At the beginning, specimen is set on the microscope stage. The selected image area is displayed on the screen. All the necessary adjustment and image acquisition is derived in real-time. The image can be processed with filters, and it can be followed with text comments and calibrating marker. AMS allows selecting micro-objects on image in the automatic, semi-automatic or manual modes. The selected micro-objects are measured automatically and the results of measuring are displayed in a tabular form (Medovyi, 2006). Micro-objects can be classified according to any of the measured parameters. The results of analysis can be printed and saved in a database.

1.2.1 Software overview

The basic advantage of the use of software tools is a transition from subjective and qualitative analysis to objective and quantitative analysis. The basic disadvantage here is complication of adjustment and occurrence of errors of measurement.

AMS allows acquiring image by a photo camera, video camera, and scanner or from a file. The results of researches are displayed on a screen in a table form, or charts. Measuring accuracy is provided by calibration of camera with calibrating slide. Software complexes give a user a wide spectrum of tools for processing and analysis of biomedical images (BMI) and video stream (Richardson, 2005), in particular, in genetic, cytological, histological researches etc. The characteristic features of the modern systems are a high level of automation, possibility of remote work and decreasing of dependence on specialised video recording devices.

For the construction of the generalized structure of AMS, design and functions of existent software tools were investigated (table 1). In particular, comparison was based on the followings parameters:

- method of information acquisition: an image is acquired from real-time source (support of technology of MCI/TWAIN) or loading from a disk;
- modes of segmentation algorithms operation: manual (the operator in the manual mode selects micro-objects), automated (the operator learns the algorithm) or automatic (the parameters of algorithm are set automatically);
- previous processing of image: noise reduction, correction of brightness, contrast, filtration, selection to the area of interest, etc;
- calculation of numerical features of micro-objects: perimeter, area, nucleocytoplasmic relationship, diameter, corner between two segments, etc;
- calculation of statistical features: mathematical expectation, standard deviation, maximal (minimum) value, etc;
- presentation of results in a form of diagrams, histograms, or charts;

№	Software	Support of additional formats of files	Converting of file to other format	Editing of image	Converting to other colour space	A selection of micro-objects in manual / automated / automatic modes	Calculation of characteristic features	Determination of co-ordinates of convex rectangle	Use of plugging	Use of scenarios	Forming of reports	Communication with third-party software	Printing	Tuning of parameters	Calibration of camera	Presence of the help system
1	Image Tool v.2.00	+	+	+	+	+/-/-	+	-	-	+	+	-	+	+	-	+
2	Image Warp	-	+	+	-	+/-/-	+	-	+	+	+	-	+	+	-	+
3	"Imager-CG"	-	+	+	-	+/-/-	+	-	-	-	+	-	+	+	-	+
4	VideoTest-Morpho 3.2	+	+	+	+	+/+/-	+	-	+	+	+	-	+	+	-	+
5	Vido-Test Morphology 5.0	+	+	+	+	+/+/+	+	-	+	+	+	+	+	+	+	+
6	Micromed Images	+	+	+	-	+/-/-	+	-	-	+	+	-	+	+	-	+
7	Screen Meter	-	-	-	-	+/-/-	+	-	-	-	+	-	-	+	-	+
8	Image Expert Pro 3	-	+	+	+	+/+/-	+	-	+	+	+	-	+	+	-	+
9	Image Expert™ Gauge	-	+	+	+	+/+/-	+	-	+	+	+	-	+	+	-	+
10	AnalySIS Five	-	+	+	+	+/+/-	+	-	+	+	+	-	+	+	-	+
11	Bio Vision	-	+	+	+	+/+/-	+	-	+	+	+	-	+	+	-	+
12	QCapture PRO 6.0	-	+	+	+	+/+/-	+	-	+	+	+	-	+	+	-	+
13	Motic Images Advanced 3.2	+	+	+	+	+/+/+	+	+	+	+	+	+	+	+	-	+
14	MCID™ Core	-	+	+	+	+/+/-	+	-	+	+	+	-	+	+	-	+
15	Image-Pro Plus 6.2	+	+	+	+	+/+/-	+	-	+	+	+	-	+	+	-	+
16	MetaMorph 7.5	-	+	+	+	+/+/-	+	-	+	+	+	-	+	+	-	+
17	ImageJ (NIH, USA)	-	+	+	+	+/-/-	+	-	+	+	+	-	+	+	-	+
18	Pixels	-	-	+	-	+/-/-	+	-	-	-	+	-	+	+	-	+
19	NIH Image	-	+	+	+	+/+/+	+	+	+	+	+	+	+	+	-	+
20	Xite v3.45	-	-	+	-	+/-/-	+	-	-	-	+	-	+	+	-	+
21	DiaMorph	-	+	+	+	+/+/+	+	+	+	+	+	+	+	+	-	+

Table 1. Comparison of software

- co-operating with third-party software: MS Word, MS Excel, MS Access, FoxPro, etc;
- the use of scripts and presence of built-in language for the batch processing;
- presence of the detailed technical documentation.

1.2.2 Hardware components overview

The typical structure of hardware consists of microscope, video camera or photo camera, computer, printer and monitor (Egorova, 2005). The subsystem of image acquisition (Berezsky, 2008, b) consists of light microscope, camera, photo adapter, objective changing device, focusing device, stage moving device, specimen supplying device and illumination device (figure 1).

Minimum requirements for the computer is processor with 1 GHz frequency, amount of main memory is not less than 1 GB and USB or IEEE interfaces for incorporation with a digital camera (Egorova, 2005).

The transmitted light microscope consists of a stand, to which all units are fastened: illumination device, specimen stage, systems of imaging and visualization. The basic characteristics of microscope is its class, magnification ratio, optical resolution, size of the linear field view on object and degree of optical aberration correction (Egorova 2005). For cytology and histology AMSs use the biological direct microscopes of work, laboratory and research classes.

Biological microscopes have the following methods of research: light field, phase contrast, polarization and luminescence. Microscope includes three basic functional parts (Egorova, 2006): illumination system, imaging system, and visualization system.

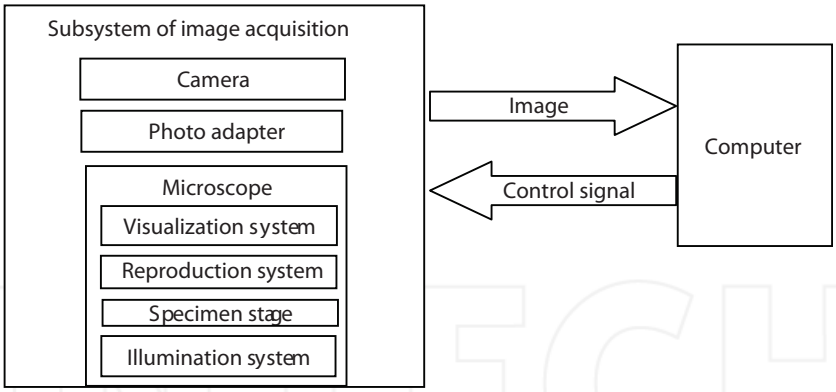

Fig. 1. Structure of AMS hardware

The illumination system of light microscope is intended for creation of uniform luminous flux and consists of light source and optical-mechanical system (field stop, collector, and condenser). The imaging system provides the first degree of magnification and includes objective fastening unit, objective, optical filters changing device and focusing device. The visualization system is intended to acquire the real image of micro-object on the retina of eye, film, and screen monitor with an additional magnification. Visualizing part is located between the image plane of objective and eyes of observer (or camera).

To capture image with a microscope the following cameras are used: digital single-lens reflex camera, digital non reflex photo camera, and digital video camera (Wu, 2008). The

general device of input in microscopy is digital video camera. Firms, engaged in development and trade of the special video cameras for a microscopy are: Carl Zeiss (Germany), Axiovision, Motic (China), Tucsen (China), Lumenera Corp. (Canada), SPOT Imaging Solutions (USA). For digital photo- and video cameras basic characteristics are the following: a dynamic range of sensor, signal-noise ratio, resolution, and fastening compatibility with a microscope. For mechanical connection of camera and video port of microscope the special photo adapter is used. It provides an image transfer without distortions with the certain coefficient of magnification on the photosensitive matrix of camera. Let's summarize the basic parameters of devices, on which AMS are synthesized, in a table 2.

For planning of the system it is necessary to define the area of its application, magnification degree for specific medical research, sizes of micro-objects and level of automation. The choice of specific components of the system is based on heuristic rules. The basic tasks of AMS designing are: selection of optical elements of microscope, choice of digital camera and proper photo adapter, optical connection of system devices, and electric connection of devices.

The minimal requirements to the microscope during the histological researches with the use of AMS are the following: class not lower than laboratory, objectives magnification 10, 40; eyepieces with field of 20 mm or 18 mm, and mounted powerful illumination device. For histology application the use of differential- interference contrast allows to attain better results.

One of the basic parameters of microscope is resolution, which determines quality of the obtained image (Egorova, 2006). Resolution depends on the numerical aperture of objective and condenser, and also on the wave-length of light.

The level of AMS automation depends on its setting and desired speed of specimen analysis. For automation the device of focusing motorization, moving of specimen stage, changes of current objective and changes of filter are set on a microscope.

Camera is chosen according to the problem specifications: type of the investigated specimen, system of illumination, size of necessary increase, geometrical sizes of the least micro-object. Therefore, the main characteristics of camera are the following: type of sensor (monochrome, colour), resolution of sensor, and type of fastening of camera objective (Rietdorf, 2005). For histological specimen research, the coloured camera with a resolution not less than 1280x1024 points, the interface of USB connecting, mounting of objective of C-mount, CCD by sensor and relation of signal/noise not less than 65 dB are recommended (Egorova, 2005).

Optical connection of camera and microscope. It is possible to select three methods to acquire microscopic image by means of a digital camera (Murphy, 2001). Usually light rays quit the eyepiece of microscope in form parallel rays, but with the help of focusing it is possible to get a consilient bunch. The first method consists in that the objective of camera is placed as near as possible to the eyepiece of microscope. The system is used for editing of digital video camera or digital camera. However, such system requires setting up the special adapter that would firmly fasten the lens of camera on the ocular tube of microscope.

The second method consists in the direct projecting of image from objective on sensor of camera. For this purpose, when fastening to the ocular tube, eyepiece and lens of camera are removed, and the proper adapter is set (without optical elements). When fastening to the special video port on a microscope, the proper adapter, which is included in the complete set of microscope, is set.

Device	Basic parameters
Microscope	Type: light microscope System: monocular, binocular Manufacturer: Carl Zeiss, Nikon, Olympus, Leica, Motic Class: educational, laboratory (mechanical), work (motorized), research (digital) Photo adaptation: without video port, with video port Amount of objectives: 4 pieces, ×4, ×10, ×40, ×100 Type of objectives: dry, immersion Class of objectives: without correction of aberration, semi plan, achromatic, achromatic – aplanatic Numerical aperture of objective. Research methods: light field, dark field, phase contrast, polarized light, fluorescence Condenser: regular, achromatic, achromatic – aplanatic Illumination: halogen lamp, light-emitting diode Specimen stage: mechanical, motorized Accessories: photo adapter, digital camera
Video camera	Manufacturer: CarlZeiss, Nikon, Webbers, Olympus, Qimaging, MicroCam, CARTON, ScopeTek, KONUS, Motic Type of sensor: monochrome, colour Type of sensor: CCD, CMOS Resolution: 1, 2, 3, 5, 8 MPixel Sensor sensitivity: 0,8v/lux.sec with 550 nm (colour CMOS) Signal-noise ratio: larger than 45 dB Dynamic range larger than 60 dB (colour CMOS) Matrix size: 1/3", 1/2", 2/3" Frame rate during video capturing in maximal resolution Interface: IEEE 1394, video composite, USB Type of objective mounting: C-mount, T-mount
Computer	Processor with 2 GHz clock frequency Memory: not less then 1 GB Video card with 256 NB video RAM Hard drive with capacity not less than 250 GB
Monitor	Size: minimum 17", advisable 19"
Printer	For the reports – laser printer For the pictures of specimens – colour inkjet printer

Table 2. Basic parameters of AMS hardware devices

The third method consists in adapter, set up between a camera and video port, which has the own optical system, so-called reverse objective. Its purpose is to reproduce correctly an image on-the-spot of sensor, namely to decrease the size of image from objective, so that it covers a sensor area fully. Relation of linear sizes of sensors toward eyepiece field of view is described in fig. 3.

Some reverse lenses are in a position to change an image, that is, they work as a transfocator. Digital cameras, developed specially for a microscopy, are assembled by means of the first and third methods.

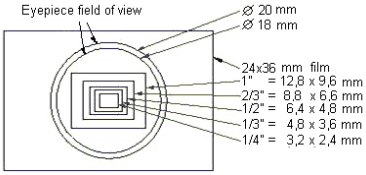

Fig. 3. Correlation of sizes of digital camera matrix and main image of microscope

The digital scale is calculated according to the expression:

$$m = d_{YFO}{}^{*} k_M / w$$

in which m is a linear digital scale, micrometer/pixel;
d_{YFO} – a diameter of field of view on the object, micrometer;
k_M – a coefficient of the overlap of field of view by the matrix (Fig. 3); and
w – number of pixels on the horizontal row of sensor.

2. Automated microscopy system design

2.1 Design of AND-OR tree for AMS hardware

The tasks of systems structures synthesis are hard to formalize on the whole (Berezsky, 2009, a). Input information for structural synthesis consists of description of designed object demands, its operating condition and limited elements composition. Output is the information about composition of the system and methods of elements connection. Formally, decision support task for structural synthesis is possible to present in such way:

$$DSS = \langle \mathbf{A}, \mathbf{K}, M, RS \rangle$$

where $\mathbf{A} = \langle A_1, A_2, ..., A_n \rangle$ is a set of alternatives, $\mathbf{K} = \langle K_1, K_2, ..., K_n \rangle$ is a set of criteria, M:$\mathbf{A} \rightarrow \mathbf{K}$ is a model, which allows to find the criteria vector for every alternative, RS – a decision rule, which provides the choice of optimum alternative. For every alternative there is an ordered set of attributes $\mathbf{X} = \langle X_1, X_2, ..., X_p \rangle$. If mathematical model $\mathbf{X} \rightarrow \mathbf{K}$ is unknown, an approach of expert system is used. In most cases the tasks of structural synthesis are solved with the help of heuristic methods. The set of alternatives **A** can be presented as $\mathbf{A} = \langle \mathbf{P}, \mathbf{E} \rangle$, where **P** is a set of rules, **E** is a set of system elements. Morphological tables and AND-OR tree for **P** and **E** are used for description.

Morphological tables represent alternatives as $\mathbf{M} = \langle \mathbf{X}, \mathbf{R} \rangle$, where **X** is a set of object characteristics (functions), **R** is a set of methods of functions implementation. The disadvantage of morphological tables is ignoring forbidden elements combination in structures and mutual independence of realizations set R_i. These disadvantages are absent in AND-OR tree, which is an aggregate of morphological tables. In AND-OR tree the "AND" node corresponds to a partial morphological table M_j, each "OR" node that is incidental to M_j table, corresponds to the set of variants of realization of i- function.

AND-OR tree based synthesis anticipates the existence of decision rules in every "OR" node. These rules are based on and related to the demands of requirement specification. During their creation it is necessary to use such production rules as:

IF condition 1, condition 2, condition n, THEN action 1, action 2, action m.

On the basis of AMS classification and analysis of its structure we can build the AND-OR tree for system structure according to the set of its functions and characteristics (Fig. 4) (ribs which are connected to "And" nodes are marked with arcs). For system design it is necessary to define the application field, magnification degree of actual medical research, micro-objects sizes and level of automation. IIS can be built on the basis of digital or Photo Adapted Microscopes and camera. Selecting of actual system components is based on their characteristics using heuristic rules. The level of AMS automation depends on its purpose and desired speed of specimen analysis. For automation purpose microscopes can include devices of focusing motorization, moving of specimen table, objective and filter changing.

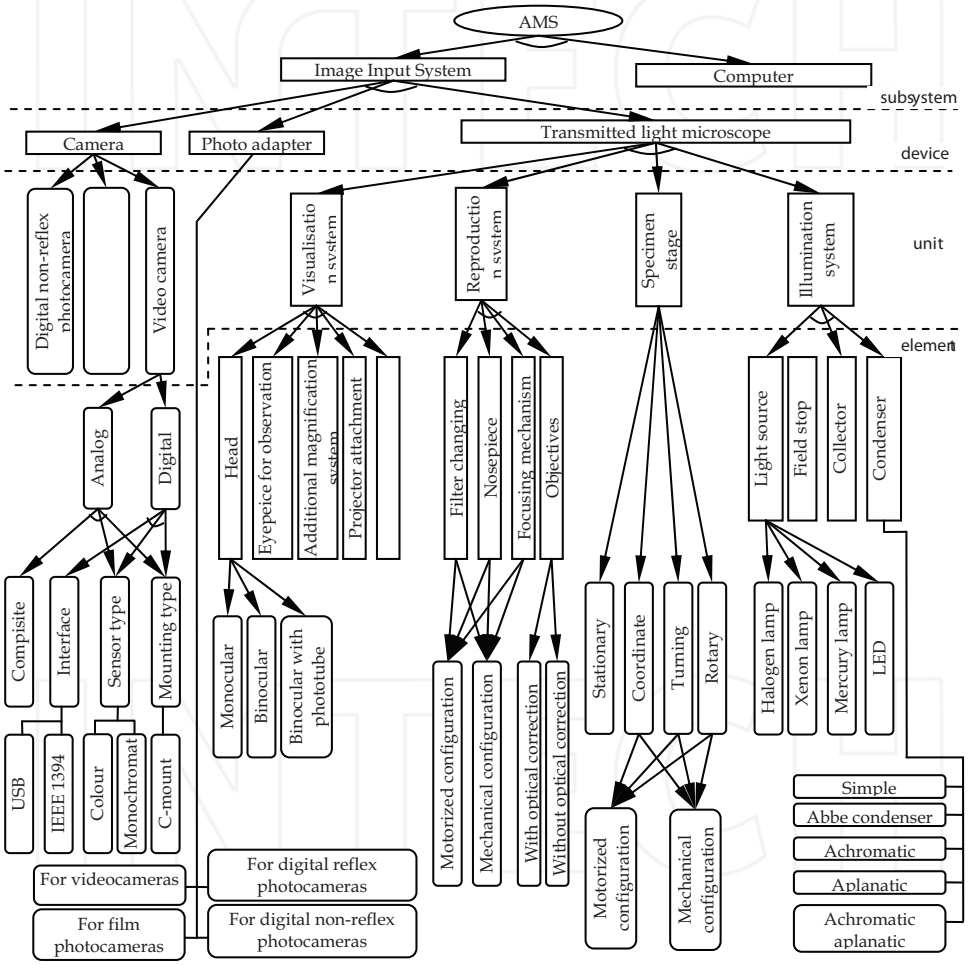

Fig. 4. AND-OR tree of hardware part of AMS

AMS consists of the image input system (IIS) and computer. Typical IIS consists of camera, photo adapter and light microscope. The IIS components are based on optical compatibility properties and connected with the special photo adapter, which can be put in the phototube

of trinocular head, in the eyepiece tube of binocular head or in the special adapter on the microscope stage.

Let us define parameters, which can help to choose alternative variants of system arrangement:

1. Medical field: cytology, histology, haematology, chromosome analysis, and telemedicine;
2. Research types: morphometry, cytophotometry, and densitometry;
3. Research methods: bright field microscopy: phase contrast, differential interference contrast, dark field;
4. Magnification ratio: 80 - 1000;
5. Micro-object size: micrometer;
6. Digital scale: micrometer/pixel;
7. Level of automation.

On the basis of AND-OR tree for the choice of separate components of the system we will bring fragment of product rules, which form the alternative variants of configuration of the system.

If medical field is histology,
then AMS consists of IIS and computer.

If medical field is histology **and** research method is light microscopy,
then IIS consists of a camera, photo adapter and transmitted light microscope.

The product rules allow us to generate the set of variants of structural arrangement of the system, which satisfies a requirement specification. Parametric optimization is conducted on the set of possible solutions.

2.2 Design of software ASM part AND-OR tree

We will build the AND-OR tree for the synthesis of alternative variants of creation of programming constituent, which is based on the conducted analysis systems of morphometric analysis (Berezsky, 2009, b). The basic criteria, which influence on the choice of the systems, are (Berezsky, 2009, c): quality of input images, type of micro-objects, types of numerical descriptions of micro-objects, and their statistical descriptions (Fig. 5).

We will build alternative decision AND-OR tree, using the parameters:

1. medical area: cytology, histology, haematology, analysis of chromosomes, telemedicine;
2. source data type: local, global;
3. quality of entrance images: with noise, without noise;
4. level of automation;
5. type selection of objects;
6. necessary characteristics;
7. types of research objects : separate objects, groups of objects;
8. the way of results delivery: internal or external software.

We will show fragment rules of how to choose the product structures of the programming system for morphometric analysis.

If medical area is histology **and** class of the system is specialized
then system is automated.

If medical area is histology
then the system consists of the module of input information, module of previous processing, module of selection of objects and module of determination of informative descriptions.

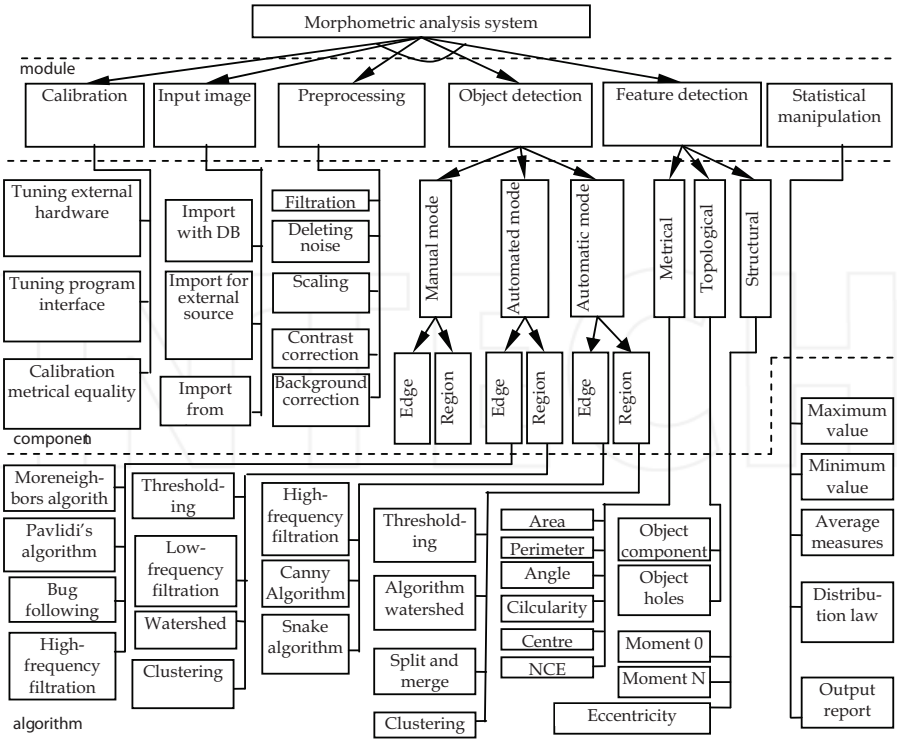

Fig. 5. AND-OR tree for software part of AMS

2.3 Examples of logical production rules for specialized AMS

Karyotyping

The basic method of chromosomal violation diagnostics in reproductive medicine is a cytogenetic research - karyotyping. Rules for AMS constructions are the following:

Hardware

If karyotyping, **then** microscope (class (work), objective (10x, 100x).

If karyotyping with Q-painting, **then** microscope (method (fluorescence)).

If karyotyping, **then** camera (type (digital), sensor (monochrome, CCD), resolution (1280x1024).

If karyotyping, **then** computer (processor (2,4 GHz), RAM (1 GB), HDD (250 GB), video adapter (256 MB)).

Software

If karyotyping, **then** software includes such modules: image pre-processing, editing, storage is to DB, print of results.

DNA Research

CGH Method. The kernel of every cell has chromosomes, in which there are genes that consist of segments of desoxyribonucleic acid (DNA), where genetic information is accumulated and saved. In order to expose quantitative violations in a genome it is possible

to apply the method of comparative hybridization (Comparative Genome Hybridization - CGH). Investigated and normal donor DNA is marked by means of fluorophors of different colour. After leading through FISH, metaphases are analysed on a fluorescent microscope, and with the help of the specialized program of computer analysis of images, intensity of fluorescence of two fluorophors on all length of every chromosome is determined. AMS construction rules are the following:

If method CGH, **then** microscope (class (work), method (fluorescence), block for colour filters mounting, objective (magnification (10x, 100x)).

If method CGH, **then** camera (digital) and camera (black and white) and sensor (type CCD, resolution (1280x1024), charge accumulation mode).

Computer

If method CGH, **then** computer (processor (Pentium IV 2,4 GHz)), computer (RAM (512MB)), computer (HDD (250GB)), computer (video card (256MB RAM)).

Software

If method CGH, **then** software includes such modules: image pre-processing, editing, storage is in DB, print of results, specialized functions.

Spermatology is medical-biological branch, which is engaged in research of sperm of man and animal.

Interest to the analysis of human sperm is closely related to the needs of genesial medicine, which solves the problems of birth of children, birth control and planning of family.

The systems of computer analysis, based on technologies of digital processing of video images, allow with the less waste of time estimate the parameters of sperm more objectively and avoid subjectivity of interpretation of results, which happens in standard spermogram. Moreover, determination of additional indexes of mobility appeared, such as, curvilinear speed and linearness of motion. The use of the similar systems for automation of analysis of sperm underlay direction in andrology – CASA. AMS construction rules are the following:

If CASA, **then** microscope (class (work), objective (magnification 20x)).

If CASA, **then** video camera (digital, coloured, sensor (type (CCD), resolution (above 640x480), frame rate(50 fps))).

Computer

If CASA, **then** computer (processor (Pentium IV 2,4 GHz)), computer (RAM (512MB)), computer (HDD (250GB)), computer (video card (256MB RAM)).

Software

If CASA, **then** software includes such modules: image pre-processing, editing, storage is in DB, printing of results, specialized functions.

Hematology

Hematology is the section of medicine that investigates structure and functions of blood system (blood, organs of blood formation), reasons and mechanisms of development of blood illnesses, and develops the methods of their recognition, treatment and prophylaxis.

AMS construction rules are:

Microscope

If hematology, **then** microscope (class work), objective (magnification 10x, 100x), specimen table (motorized)).

Camera

If hematology, **then** camera (digital, coloured, sensor (type (CCD), resolution (1280*1024), adjustability on colours)).

Computer

If hematology, **then** computer (processor (Pentium IV 2,4 GHz), RAM (512MB), HDD (160GB), video adapter (512MB RAM)).

Software

If hematology, **then** software includes such modules: image pre-processing, editing, storage in DB, printing of results, blood cells atlas, specialized functions.

2.4 Functions of microscopic image processing and their realization

Let us consider the components of the typical AMS(s) software and algorithms of their realization.

3.1 Micro-objects segmentation task

We will make the table of the use of the proper methods of segmentation according to the type of investigated micro-objects (Table 3).

All the process of analysis can be divided into such stages: image acquisition (loading, sight selection, etc.) (Pratt, 2007), pre-processing (noise reduction, recoding, etc.) (Duda, 2000), (Shapiro, 2001), analysis (segmentation) of image (*Gonzalez, 2008)* (Duda, 2000) (Wismullera, 2004) and description (extraction of characteristic features) (Avtandilov, 1990) (Jahne, 2005) of micro-objects.

Amount of types micro-objects	Type of objects	Clearness of border	Algorithm
Single objects	Objects one to the type	clear border	threshold segmentation, high-frequency filtration
		not clear border	watershed, clusterization
	Objects of different types	clear border	threshold segmentation, clusterization, region growing
		not clear border	watershed, clusterization
Groups of objects	Objects one to the type	clear border	clusterization, high-frequency filtration
		not clear border	threshold segmentation, clusterization
	Objects of different types	clear border	clusterization, region growing, watershed
		not clear border	watershed, clusterization

Table 3. Criteria of choice of algorithms of image segmentation

One of the important stages of automation of analysis process of biomedical preparations is a selection of micro-objects (Avtandilov, 1990). This task is solved by means of images digital analysis (Pratt, 2007). Principal reason of complication of histology research automation is high variability and low contrast of the most histological structures.

One of the most widely used segmentation BMI approaches is the selection of micro-objects borders. It is predefined by clear borders of micro-objects. This group includes the following algorithms: threshold segmentation, active contours algorithm, high-frequency filtration,

etc. As a rule, algorithms of this group are used in the morphological operations (Al-Jarrahb, 2008) of dilatation and erosion (Batko, 2009). The choice of segmentation thresholds is based on a priori information about micro-objects and analysis of histograms of brightness distribution (Furman, 2003).

Advantages of these algorithms are high speed action and realization simplicity. And disadvantages are low efficiency of work with poorly contrasting images, work with imposition of micro-objects, and work with uneven backgrounds.

Another approach for solving micro-objects detection problems is a selection micro-object form on the template. The main task is to find that part of image (the micro-object contour) that better coincides with the form of standard micro-object. Advantage of this approach is possibility of work with images with well-known set of templates. Among the disadvantages of this approach we determine the result dependence on template accuracy and exactness, high complication and, as a result, low speed action.

The third approach is based on determination of areas, which are identical to micro-objects. Among the algorithms of this group there are: clusterization of image (Forsyth, 2004), sectional segmentation, increase of areas, images marking and others. The selection of areas has found its wide application in morphometric researches, because often a structure of fabric is a background, and it does not give it possible to select a cell, because its elements have brightness and different levels of brightness, which coincide with the brightness of background. Difficulties at the choice of starting points of segmentation (by chance, or on the basis of a priori information) are the main disadvantages of algorithms of this group.

4. AMS design and testing example in the area of histology and cytology

We describe the examples of AMS design for histology and cytology purpose and determine the rules for AMS design (Berezsky, 2009, a).

Rules for hardware are the following:

If medical field is histology **and** medical field is cytology, **then** AMSs consist of IIS and computer.

If medical field is histology, **and** medical field is cytology, **and** research method is light microscopy, **then** IIS consists of camera, photo adapter and transmitted light microscope.

If medical field is histology, **or** cytology, **and** research method is light microscopy, **then** IIS consists of camera, photo adapter and transmitted light microscope.

Rules for software are the following:

If class of the system is research, **then** system is manual.

If medical area is histology **and** medical field is cytology, **then** the system consists of: module of manual selection of objects, module of input information, module of pre-processing, and module of determination of informing descriptions.

Structure of AMS software

The structure of the projected AMS software is presented in fig. 6. For the acquisition images the module of information input was implemented. The module information input allows working with loaded and captured in real-time images. The module of pre-processing is provided for improvement of images quality, emphasis of characteristic features of micro-objects and choice of areas of interest. For the selection of micro-objects there is a module of segmentation. It provides three algorithms of selection: pixel-wise (manual), block and automated (based on key points). To acquire the characteristic features of objects, the

contour and texture analyses are used. By means of the algorithms of contour analysis the followings characteristic features are calculated: perimeter, length, angle of slope of micro-object, and others. For the statistical analysis of data the module of statistical processing, which provides the calculation of maximum, minimum and medium values of elements selection, is implemented. The important stage of work of the system is presenting of findings both in electronic and printing variants. The module of reports formation is implemented for this purpose.

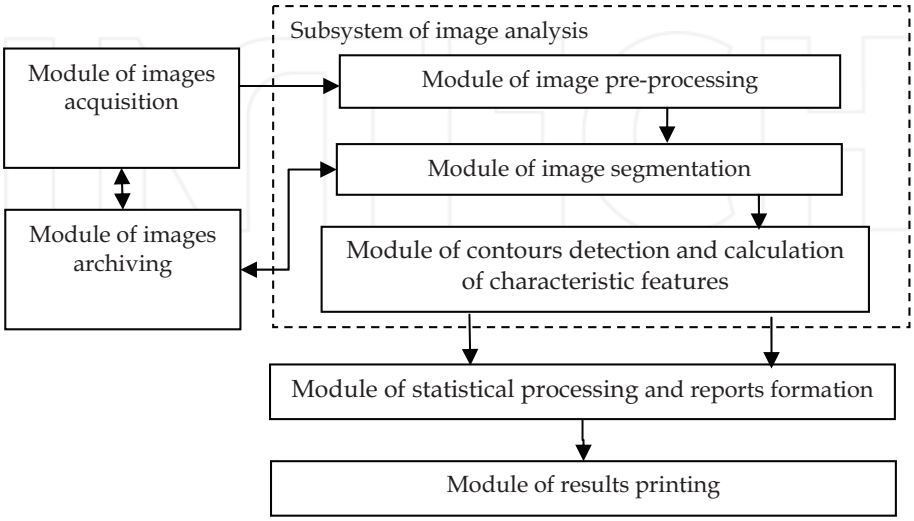

Fig. 6. Flow diagram of AMS software

Software is developed in Delphi IDE for Windows of the based work stations. The use of technology of TWAIN allowed organizing co-operation with majority of modern hardware tools, including video cameras. TWAIN is the industrial standard of interface of software tool for the transmission of images from different hardware tools in OS Windows and Macintosh (scanner, web-camera, video camera etc). Important advantage of the developed system is possibility of large size images processing. We will consider the algorithms of realization of the modules of software consistently.

Module of images acquisition. Input images can be loaded from a disk or captured from a video recording hardware. The system allows capturing an image from a video recording hardware in real-time mode. Video information, which is captured from a video recording hardware, is displayed in the working window of the system. To transfer an image into the working area of the program, double click of the left button mouse is used. After that the program stops displaying of video stream and transfers captured image to module of pre-processing.

Module of image pre-processing. In order to remove artefacts, improve quality and perform additional processing, functions of image pre-processing are used. Among accessible functions there are:

- selection of image part;
- down-scaling of image;
- transformation from one colour base to another;

- correction of image brightness;
- correction of colour gamut.

Module of image segmentation. According to the tasks and necessary selection of objects a user is able to choose three variants of selection (Berezsky, 2010):

- pixel-wise selection of objects;
- block selection of objects;
- selection of objects on the basis of characteristic points.

These algorithms can be compared according to the followings criteria: exactness, speed of selection and level of process automation. Exactness is defined as relationship of the correctly selected points (that belong to the object and amount of the ignored points that do not belong to the object) and the points selected by mistake (points that were selected, but do not belong to the object and the ignored points that belong to the object). Speed of selection is determined as time necessary for the selection of micro-objects in the selected area. Level of automation is a relationship of amount of the selected points, necessary for the selection of all objects in the selected area that the system selects to the amount of points selected by the operator.

During the implementation of manual pixel-wise selection exactness is maximum, however, process automation is not present. As result, there is more investigation time (Hea, 2008). During the implementation of block processing exactness of selection is sufficient. The result of such selection sometimes needs partial correction. The level of automation and speed is high.

During the implementation of processing on the basis of characteristic points exactness of selection is sufficient. The result of such selection sometimes needs partial correction. The level of automation is the greatest among the algorithms offered in the system. The results of comparison of algorithms of selection of micro-objects are presented in a table 4.

№	Algorithm	Exactness	Speed of selection	Level of automation
1	Pixel wise selection	>99%	>30c	0
2	Block selection	97%	10-15c	92%
3	Selection on the basis of characteristic points	95%	3-5c	99%

Table 4. Comparison of algorithms of selection of objects

Module of contours detection and calculation of characteristic features. For the calculation of contour features, the additional processing of received data is foreseen in the system (Berezsky, 2009, f). This additional analysis is provided by means of functions:

- passing a contour;
- selection of major axis;
- selection of characteristic points;
- contour approximation.

Except visual information, the program presents the results of its work in a tabular format. During statistical analysis the system calculates the following morphometric characteristics:

- area of nuclei;
- area of cytoplasm;
- area of cell;
- nucleocytoplasmic relationship (NCR);

- medium selective;
- minimum value of selection;
- maximum value of selection.

The calculation of additional informative characteristics is also foreseen in the program, in particular:

- measuring of distance between two points;
- relationship between lengths of two segments;
- corner between two unparallel segments.

The use of this module allows conducting the previous statistical processing of the received data. The received results allow the expert to conduct the preliminary estimation of findings.

Module of statistical processing and reports formation. In order to increase functional possibilities in the software system, the functions of co-operating with other external software tools are foreseen, in particular, with tabular editor MS Excel (Berezsky, 2009, e). An information transfer takes place with the help of OLE functions, which realize the interface of co-operation between a software tool and tabular editor. The use of MS Excel allowed decreasing of loading on the system and substantial increasing of statistical processing possibilities, and presenting the findings in a diagram format.

Module of results printing. The standard dialog box of information output is implemented on a print. An information transfer is carried out by built-in to MACAW functions, which realize the interface of co-operation between a software tool and printing unit. A user is able to choose a necessary device for a print, amount of copies, amount of pages on a sheet etc.

Module of images archiving. There is a set of procedures and functions for work with the base of information (Berezsky, 2008, a). Basic functions are: search of image in the base of information and formation of reports.

4.1 Testing of the module of image segmentation

The computer system is used for analysis and research of cytological images of multi-layered images of epithelium for the different types of dysplasia of epithelium of uterus neck of women of reproductive age (Berezsky, 2009, d). The results of work of segmentation algorithms are described on the example of images of cells of uterus neck. In Fig. 7.

Fig. 7. The example of selection of micro-objects during pixel segmentation

After completion of segmentation procedure, the program forms a report, which indicated descriptions of the selected objects. The example of report is presented in the table 5.

Number of cell	Area of nuclei	Area of cell	Area of cytoplasm	NCR
1	369	18475	18106	0,02038
2	365	19379	19014	0,0191964
3	628	18006	17378	0,0361376
4	467	20712	20245	0,0230674
5	360	16509	16149	0,0222924
6	324	15271	14947	0,0216766
7	463	18085	17622	0,026274
Medium values	425,1428571	18062,42857	17637,28571	0,0241463
Minimum values	324	15271	14947	0,0191964
Maximum values	628	20712	20245	0,0361376
Medium square deviation	104,5457293	1785,717023	1752,86924	0,0057403

Table 5. Descriptions of micro-objects are during a pixel selection

4.3 Approbation of the module of image archiving

Test DB of images contains about 500 full-colour cytological and histological images of tumour cells. Storage of the following information is foreseen in DB of BMI:

- Image of sample. This information is saved in a graphic file. The name of file is encoded on the basis of date, when the sample was received, and identification code of a patient in the medical establishment.
- Quantitative results of the sample, processed by the program. This information is saved in a tabular form. The name of file is identical to the name of file with digital sample image. In this file the saved information is about the kernel area, cell, cytoplasm area, and nucleocytoplasmic relationship of the selected cells. Besides, some statistical information is saved: areas of maximum, medium, and minimum of kernel, cell, cytoplasm and NCR.
- Annotation of sample image. This information is saved in a text format. The name of file is identical to the name of file with digital image. In this file the saved information is about the date of material reception, type of material, diagnosis, method of treatment and so on.

The developed system additionally checks process of treatment, analyses the results of inspections of group of people, etc. Two functions of work with data base are implemented for this purpose: search of image and forming of summarizing report about the group of images. General view of window of information search in a database is possible to see in fig. 8.

The result of search in DB is the description of image. In the case of absence of the proper files the system informs about an error message. If the file with a text representation is absent, the user is able to fill the proper fields. If the file with quantitative results is absent, the user must do additional testing of image.

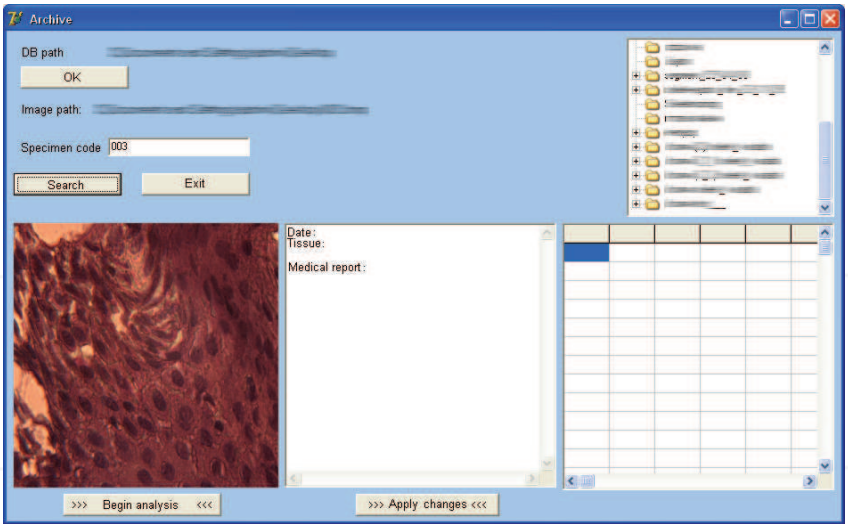

Fig. 8. The result of image search of image based on its description

5. Conclusion

The performed researches proved that at the present time in the modern market there is a wide spectrum of software and hardware tools for AMS design. Modern AMSs have different hardware and software specification, which is reflected on their cost. But even the universal AMS can not completely satisfy the demands of clinical practice and, moreover, scientific researches. Therefore, researches in the area of AMS design are important, especially those that are oriented on the specialized use. This article is devoted to this significant problem.

In this work the following results are achieved:

- Review and classification of AMS are provided: hardware and software. AND-OR tree for the generation of set of alternatives of structure and rules of products are developed. AND-OR tree allows to decrease power of set of alternative decisions restricted by requirement specification;
- The example of development of the software system, which is intended for acquisition, processing, analysis and storage of biomedical images, is shown;
- The use of modular design and object-oriented technique of programming resulted in easy modification and flexibility of the software system adjustment.

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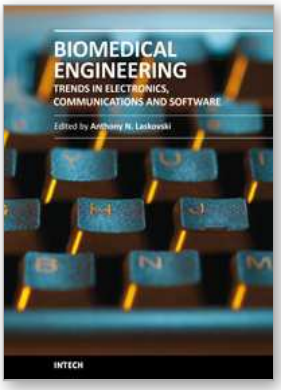

Biomedical Engineering, Trends in Electronics, Communications and Software

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Rapid technological developments in the last century have brought the field of biomedical engineering into a totally new realm. Breakthroughs in materials science, imaging, electronics and, more recently, the information age have improved our understanding of the human body. As a result, the field of biomedical engineering is thriving, with innovations that aim to improve the quality and reduce the cost of medical care. This book is the first in a series of three that will present recent trends in biomedical engineering, with a particular focus on applications in electronics and communications. More specifically: wireless monitoring, sensors, medical imaging and the management of medical information are covered, among other subjects.

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