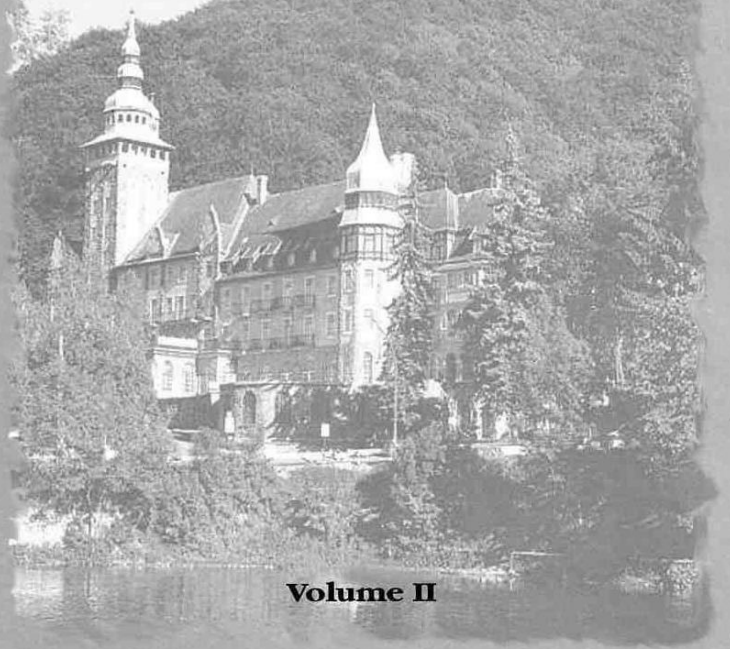
ICCC'2005

Proceedings of

6th INTERNATIONAL CARPATHIAN CONTROL CONFERENCE



Volume II

Miskolc-Lillafüred, HUNGARY

May 24 - 27, 2005

The authors are responsible for the contents and English language of each paper in the proceedings. As some delivered papers had not met the given format requirements, the editors performed them according to the necessary editing in order to unify the proceedings.

Editors	Tihamér **ÁDÁM**	Péter **SERFŐZŐ**
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Preparation for printing	Attila K. **VARGA**	Péter **SERFŐZŐ**
Cover designed by	Attila K. **VARGA**	
Publisher	**Department of Automation** *Institute of Electrical Engineering* UNIVERSITY OF MISKOLC	
Printed	**Budai Nyomdaipari** **Kereskedelmi és Szolgáltató Kft.** H-3530 Miskolc, Meggyesalja u. 38.	

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Department of Automation
UNIVERSITY OF MISKOLC
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Printing has been supported by the GMK project, No. GVOP-3.1.1-2004-05-0333/3.0

ISBN 963 661 645 0
ISBN 963 661 643 4 ö

International
Carpathian Control
Conference ICCC'2005
Miskolc-Lillafüred, Hungary
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PROPOSAL FOR A COMPUTERIZED CYTOLOGICAL SCREENING SYSTEM

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Abstract: The traditional process for detecting the cervical cancer is called Pap smear testing and it is the most widely used screening technique. The pathologists diagnose the smear according to its normality or abnormality. The huge number of slides to be analyzed requires an automated computer-aided system which can help in diagnosis process. This paper proposes architecture appropriate for a system that automatically scans the slides and extracts the regions of interests looking for signs of precancerous and cancerous changes.

Key words: intelligent environment for medical assistance, medical imaging, intelligent measurement systems, robots and intelligent positioning systems.

1 Introduction

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The number of slides that must be examined is huge. There are some fundamental characteristics that influence the investigation process: the huge number of slides with no cancerous signs that are being analyzed; the huge number of cells examined on each slide; the big number of images (slide's zones) that must be explored.

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Statistics prove that over 90% of the slides examined by a pathologist are normal, and each slide may contain up to several tens of thousands of cells. Beside the fact that the slides having tumor are very rare, they have approximately only 100-200 suspect cells on the whole surface of the slide. That is the reason why it is very difficult, even impossible for the human eye to detect all cases of early cancer. Due to large volume and fast turnover of the test slides in a typical histology laboratory, when relying only on manual inspection, it becomes inevitable that some abnormal Pap smears will be missed, meaning that some positive test results are sometimes overlooked. Even the best laboratories can miss from 10% up to 30% abnormal cases. When this occurs, a potentially curable carcinoma-in-situ can progress to an invasive cancer.

The above mentioned facts are clearly demonstrating that is worth to investigate the architectures appropriate for the design and implementation of a system able to automatically handle the problem of recognizing abnormal nuclei in a series of slides.

In the literature are found more attempts to realize such a system, more or less finalized. A working one, used in USA is PAPNET [2] system, which is an artificial neural networks-based screening method. The PAPNET is a supplementary screening method that eliminates the searching process, reduces human fatigue and improves accuracy of diagnosis leaving in the responsibility of a qualified pathologist to make the final diagnosis.

Another approach based on fractal geometry was used to characterize irregularly shaped and complex figures, and as a result, to identify the abnormal cells [3]. Another attempt was done at the University of Colorado at Boulder, using optics [4]. Slides containing abnormal cells (enlarged nuclei) are detected, using an optical implementation of the hit-miss algorithm [5]. A more complex, digitally implemented, and time-consuming second stage analysis is then performed on the remaining suspicious slides to characterize the degree of CIN. Another method in development, called direct visual inspection (DVI), uses light to detect cellular changes in cervical tissues [6]. In this case, no sample is taken. Instead, light is shined into a woman's cervix. The way in which light reflects back gives physicians a full image of the cervix, allowing them to mark exactly the location of precancerous and cancerous conditions. The main drawbacks of this method are the facts that its specificity is very low and there is a very high level of user variability in results due to the technique and experience in using the instrument.

In the present paper we propose a system which could perform the automated screening of the cytological slides and the first phase would be the automatic detection of the slide regions containing abnormal cells. The main dyskariotic features of the cells which can be used for this preprocessing phase is the disproportionate nuclear enlargement, which leads to high nuclear-to-cytoplasm ratio. The slide regions containing such cells will be retained for further automated analysis or final diagnosis by qualified pathologists.

2 Overview of the proposed architecture

The functionality of the proposed architecture is based on the use of algorithms for automated image analysis applied to series of images of the cytological slides, obtained using a slide positioning system and an image acquisition system. The purpose of these algorithms is the selection of the image regions which are contained in tissue regions, cells or other cellular constituents with modified properties, which are suggesting abnormality. The result of their applying is image series containing the suspect regions of the slide and the associated qualitative and quantitative indicators. These image series will be examined by a specialist for final diagnostic, either on a local workstation or from a remote

workstation through the telemedicine application. The automated scanning process is done using two systems, based on intelligent modules with DSP and microcontrollers: a manipulating robot for supplying the microscope with slides and a positioning system for planar movement of the slides under the microscope. A database will be developed for storing the relevant images along with the associated diagnostics.

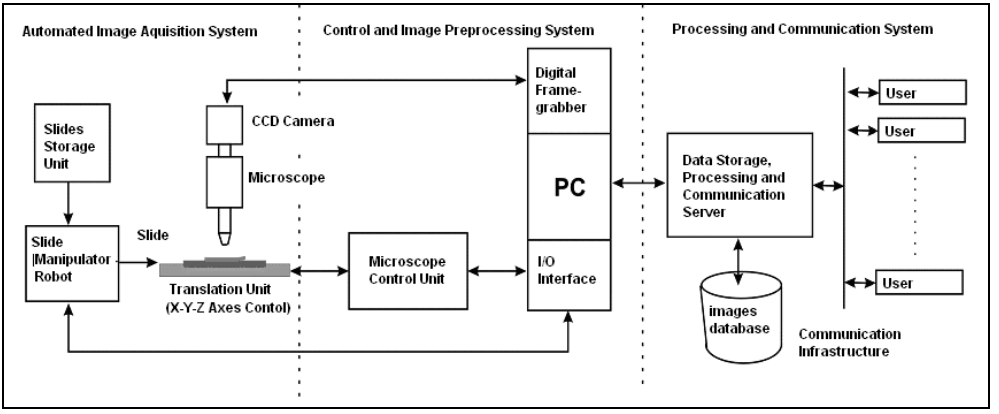


Fig. 1. Schematic view of the proposed architecture

3 The slide positioning module

The components of the slide positioning module (fig. 2) are: PC, command module, translation unit in XY horizontal plane for the slide manipulation robot and translation unit in Z direction for the microscope focusing unit. The communication between PC and command module is realized through the USB interface. The microcontroller based command module features an interpreter which translates the set of instructions given by the PC and sends them forward to the microcontrollers responsible with the driving of the poisoning motors, manipulating motor and USB camera.

The link between the command module and the XY translation unit and the microscope focusing control unit respectively is implemented through the RS485 interface. At the level of each translation axis the control is provided by a microcontroller able to recognize the messages sent by the command unit and using its own command algorithm is able to transmit to the drivers the corresponding stepping sequence. The sequence is transmitted on 5 pairs of wires, a pair for each phase, to the driver which commands the stepper. The commands which can be transmitted to the microcontrollers are: *forward*, *backward*, *start*, *stop* and *home*. From the PC, the command is transmitted to the control unit through the USB interface. The command is coded in character strings and contains the axis identifier, the direction and the number of steps. This command will be decoded in the control unit, which will forward the command through the RS485 interface through the X, Y, Z translation units' microcontrollers. The destination microcontroller identifies its own command upon the encoded identifier and executes the command. To detect the origin position a travel limiting device will be used. This will allow the positioning of the slide at fixed coordinates at the beginning of its exploring process. The slide is moved to the origin position by the *home* command.

The control of slides the manipulating robot is done using its second RS485 interface available at the command module. The Command module is able to activate by request the

snapping trigger of the USB camera through a hardware interrupt. This way the image capturing is only after the slide was placed in the new location. This mechanism is used also for the microscope focusing control unit which controls the microscope lens system on Z direction. The focusing control unit is activated only during the optical system calibration unit, using similar commands with the XY translation unit.

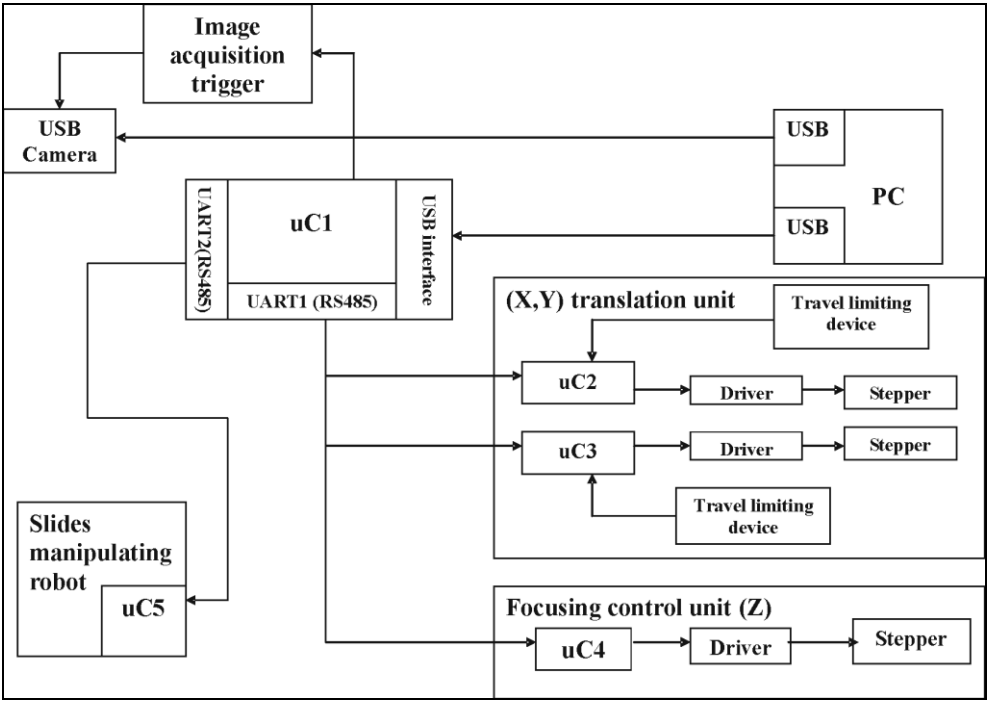


Fig. 2. Architecture of the slide positioning module

4 Microscopic image acquisition module

For the image acquisition a high resolution (3 Megapixel) USB 2.0 camera was chosen, able to work in live acquisition mode or snap mode (software or hardware triggered). The architecture of the image acquisition module is presented in figure 3. The optical system calibration sub-module is activated only at the system initialization or when the magnifying lens of the microscope is changed and has as purpose the optimal settings of the acquisition parameters (image focus and intensity). In this case the camera will work in live modus [7, 8]. If the image is not properly in focus, a refocusing command is sent to the microscope focusing module to move the microscope lens system on Z axis. If the image intensity is not in the required range, the acquisition parameters (camera exposure and gain) are adjusted.

The image acquisition sub-module captures the current view of the slide and stores the images of interest (exhibiting abnormal nuclei). For that purpose, the current view is acquired in Snap modus, hardware triggered by the slide positioning module (as mentioned above). Then the current view is preprocessed in order to identify automatically the existence of abnormal nuclei. For the positive cases, the images are stored for further detailed examination/classification.

The image acquisition module was implemented using the acquisition functions available in the camera API [7] in the conformity with the manufacturer's technical documentations and the specifications regarding the USB camera's image acquisition design [8].

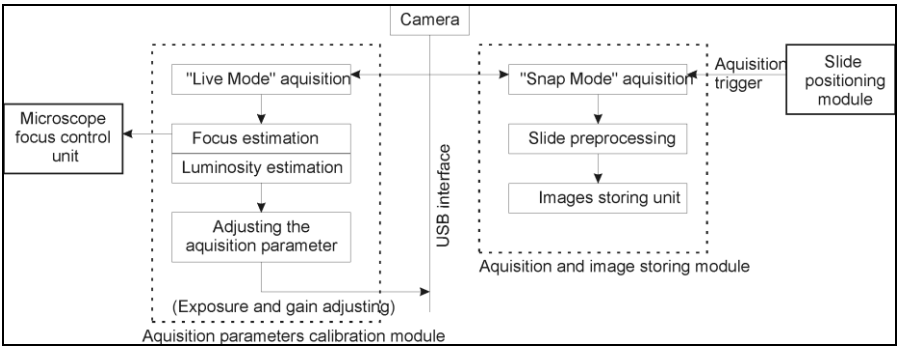


Fig. 3. Image acquisition and storing module

5 Automated detection of abnormal nuclei

The preprocessing step for abnormal nuclei detection [9] follows two steps: nuclei segmentation and atypical nuclei detection. The purpose of this step is to obtain from the initial image (which contains multiple cells each cell containing one or more nuclei in the case of mutinucleation) a binarized image which contains only the nuclei outlined. This phase is one of the most important and difficult one because incorrect segmentation can lead to false detection and incorrect diagnosis.

For the nuclei segmentation an edge detection based approach was considered which has been proved the most suited. This method has the advantage that is totally unsupervised and can be integrated into a completely automated system. The segmentation algorithm can be resumed in the following steps: color to grayscale image conversion, edge detection, dilation and image reconstruction (interior gap filling).

For the atypical nuclei detection (which exhibit enlarged demotions) the hit&miss transform was used, which detects objects having diameters in specific range [9]. The results of the preprocessing phase are presented in figure 4 and 5:

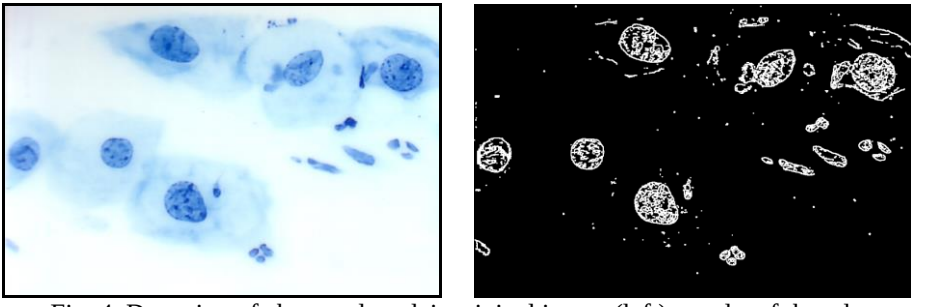
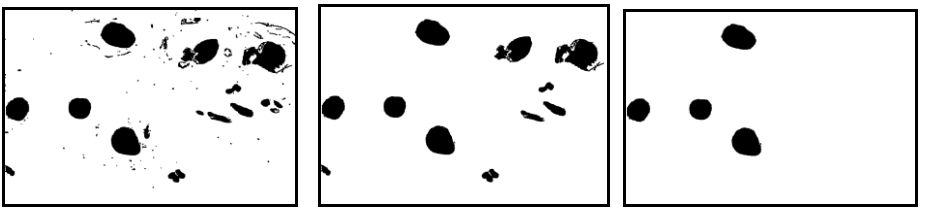


Fig. 4. Detection of abnormal nuclei: original image (left), results of the edge detection and succesive dilations (right)



a. b. c.

Fig. 5. Detection of abnormal nuclei: a. Results of image reconstruction applied on the edge image from figure 4 – right; b. Results after noise removal; c. Final result: only abnormal (enlarged) nuclei are outlined

6 Conclusions

The system architecture proposed in this paper is able to cover most of the functionality expected from an integrated automatic system intended to support diagnosis based on smear screening. While the speed of such system is of primary importance, its smartness, in terms of successfully recognizing and categorizing abnormal areas is even more important. That "smartness" relies entirely on the effectiveness of the processing algorithms. That is the main motivation for which finding appropriate models, able to translate the knowledge of the pathologists into patterns suitable for algorithmic approaches, is in our view, the one who should dictate the roadmap of future research in these topics.

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