

Decision Support System for Multiuser Remote Microscopy in Telepathology

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Abstract

Recent advances in networking, robotics, and computer technology allow today real-time diagnosis, consultation, and education by using images obtained through remote microscopy. This paper presents a new approach in telepathology, the Image Guided Decision Support (IGDS) system, which integrates components for both remote microscope control and decision support. Using the Micro-Controller component the physician can command a robotic microscope from the distance, obtain high-quality images to be used in the diagnosis, and authorize other users to visualize the same images. The image understanding-based Decision Support component of the system locates, retrieves and displays cases which exhibit morphological profiles consistent to the case in question and suggests the most likely diagnosis based on majority logic. The IGDS system has a natural man-machine interface containing engines for speech recognition and voice feedback.

1. Introduction

The subtle visual differences exhibited by some malignant lymphomas and chronic lymphocytic leukemia give rise in practice to a significant number of false negatives (malignant cells classified as normal). If suspicious cells are detected, subsequent morphological evaluation of specimens by even experienced pathologists is often inconclusive. In these cases differential diagnosis can only be made after expensive supporting tests such as immunophenotyping by flow cytometry.

This paper describes a new approach in telepathology, the *Image Guided Decision Support* (IGDS) system, designed to assist pathologists to discriminate among malignant lymphomas and chronic lymphocytic leukemia directly from microscopic specimens. Since some parts of the system have been presented in [4], we will concentrate here on recent results. Currently, the system integrates components for remote microscope control, multiuser visualization, and decision support, all having a platform-independent implementation in Java.

The paper is organized as follows. Section 2 presents the Multiuser Micro-Controller component of the system. In Section 3 the Decision Support component is discussed. Experimental results and comparison to human expert performance on the same database are shown in Section 4.

2. Multiuser Micro-Controller

This component of the system allows one primary user and multiple secondary users to connect to the image server located at the microscope site. The primary user can control the remote microscope (AX70 Olympus equipped with motorized stage), receive and visualize diagnostic-quality images of tissue samples. In the same time, the transferred images are seen by the secondary users. Thus, the IGDS system provides support for consultation, when a fellow pathologist is logged in as secondary user, or teaching, when a group of students is connected to the image server.

A display capture of the Micro-Controller is shown in Figure 1. The bottom-left image is obtained during the initialization and represents the low resolution panoramic view of the specimen on the robotic stage. The center-right image is the current view using a lens of 100X and corresponds to the small rectangular region marked on the panoramic image.

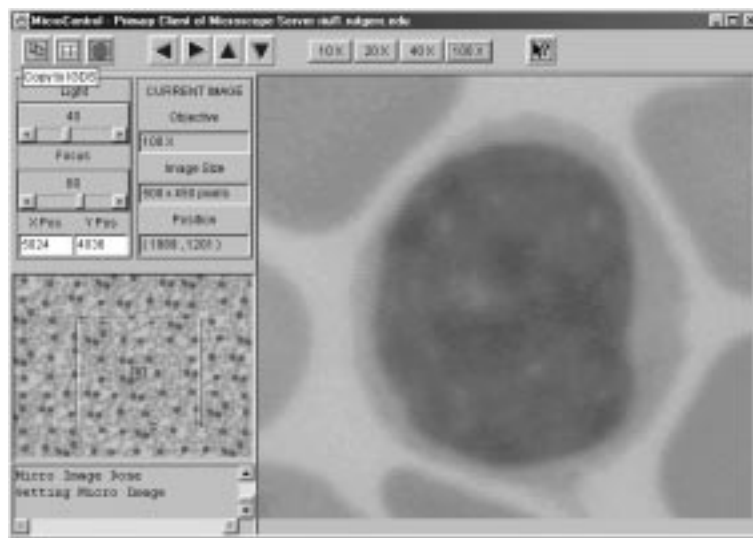


Figure 1. The Micro-Controller component.

The primary user can adjust the light path or focus of the microscope, change the objective lens, move the specimen on the robotic stage, or copy the current image to the Decision Support part for further analysis. These actions are possible by graphical input or by speech. A fusion agent capable of multimodal inputs interprets the commands, calls the appropriate method, and gives voice feedback. Examples of voice commands are: Set Light ##, Set Focus ##, Change #, Transfer, Move Right (Left, Up, Down), Update the System.

3. Decision Support

The task of this component is to locate, retrieve and display cases with morphological profiles consistent to the case in question, and to suggest during each retrieval the most likely diagnosis based on majority logic. It has a client-server architecture (Figure 2). The Client part is intended to be used in small hospitals and laboratories to access through the Internet the database at the Server site.

Two versions of the Client were implemented: a Java application and an applet. The application allows natural communication with the system based on speech recognition and voice feedback, while the applet runs in a Web browser.

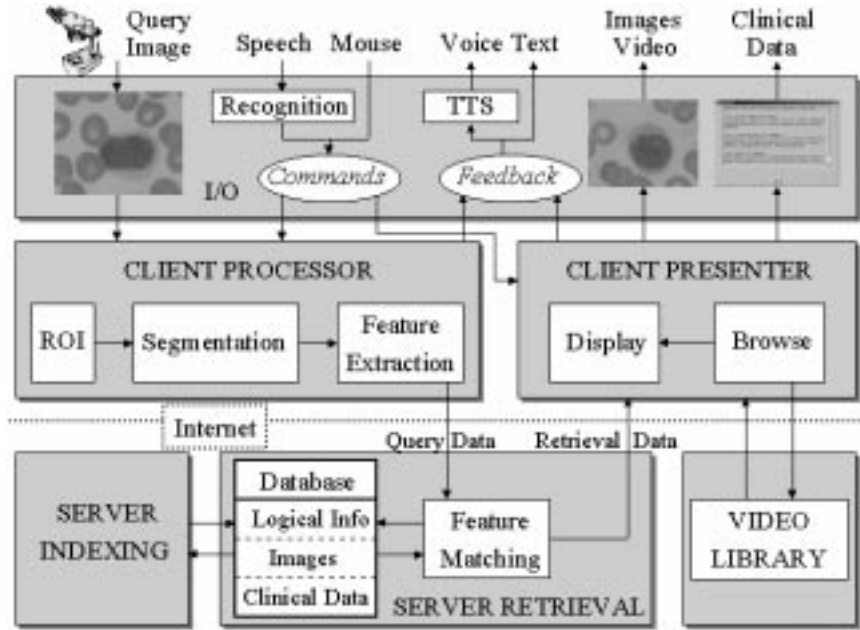


Figure 2. Architecture of the Decision Support component.

3.1. Query analysis

A typical IGDS retrieval session starts by loading the query image and selecting a rectangular region which contains the cell of interest. The reliability of the color segmenter [5] integrated into the system makes possible unsupervised on-line analysis of the selection and extraction of the nucleus features: shape, area, texture, and color. Medical literature uses frequently the first three of the above attributes to morphologically describe the appearance of malignant cells [1].

We characterize the nuclear shape through similarity invariant Fourier descriptors [8]. Fourier invariants were recently proved to be superior to methods based on autoregressive models [7]. The uncertainty introduced by the segmentation process is taken into account to determine the number of harmonics which reliably represent the shape. Since all the digitized specimens in the database have the same magnification, the nuclear area is computed from the chain-coded contour.

The texture analysis is based on a multiresolution simultaneous autoregressive model (MRSAR) [9]. This is a second-order noncausal model characterized by five parameters at each resolution level (5×5 , 7×7 , and 9×9 neighborhoods). To estimate the model parameters 21×21 overlapping windows moving every two pixels in both horizontal and vertical directions are used and for each window a multiresolution feature vector is obtained. The mean vector and the covariance matrix over all windows inside a given cell nucleus are the MRSAR features associated with that nucleus. Thus, the texture dissimilarity has to be measured by the distance between two multivariate distributions with known mean vectors and covariance matrices. We use the Mahalanobis distance between the MRSAR feature vectors to express this dissimilarity.

However, our own research [6] showed that the retrieval performance can be improved by using the Bhattacharyya distance as a dissimilarity measure. In addition, efficient computation of this distance is possible by taking into account that most of the energy in the feature space is often restricted to a low dimensional subspace. The improved representation will be incorporated into the IGDS system.

3.2. Retrieval

The retrieval process is multithreaded, simultaneous accesses to the database being authorized. During feature matching the query data and the logical information in the database are compared to derive a ranking of the retrievals.

The overall dissimilarity metric between two nuclei is defined as a linear combination of the normalized distances corresponding to each visual attribute. The weights are obtained off-line by optimizing the probability of correct classification over the entire database. We found this metric to provide better results than the joint rank criterion expressed as the weighted sum of individual ranks.

3.3. User interface

A display capture of the Decision Support applet running in a Web browser is shown in Figure 3. The query image *mcl40-19* with the region of interest is top-left, the delineated nucleus of the cell and the normalized shape of the nucleus recovered from 40 Fourier invariants are top-middle, and the first four retrieved images are at the bottom. Actions such as selecting different query attributes, browsing the retrievals, selecting a different scale for visualization, and displaying specific clinical data and video clips are possible.

For the Java application, typical voice commands are: Show Microscope, Open Image ##, Segment the Image, Search the Database, Show Video, Clinical Data #. Examples of voice feedback are: Image ## Opened, Segmentation Completed, Analyzing Texture, Database Search Completed, Suggested Class: CLL (FCC, MCL, NORMAL).

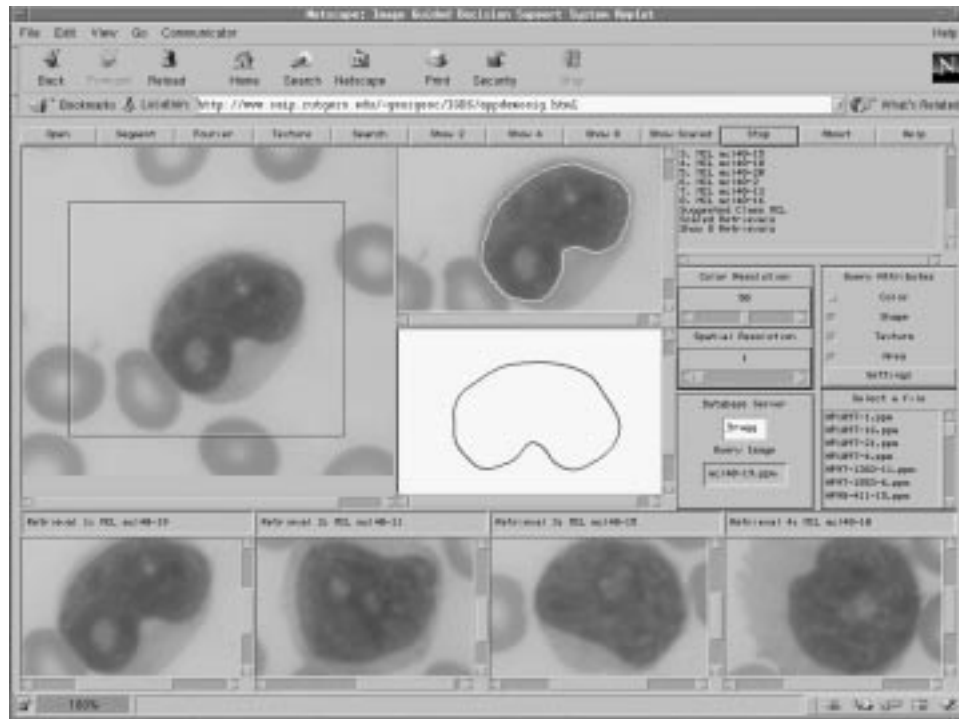


Figure 3. The Decision Support applet of the IGDS system.

4. Performance Evaluation

The system performance was quantitatively evaluated and compared to the human expert results. The reason of this comparison however is only to assess the usefulness of the

Table 1. Confusion Matrix: IGDS System

	CLL	FCC	MCL	NRML	NO DEC
CLL	.8389	.0200	.0711	.0700	.0000
FCC	.0250	.9000	.0000	.0500	.0250
MCL	.1357	.0143	.8333	.0000	.0167
NRML	.1333	.1200	.0000	.7300	.0167

system. In a real analysis scenario, a lot of context information difficult to quantize is taken into account for the diagnosis and no technique can ever replace the pathologist and light microscopy. Our system is designed as a tool to help the physician during its own analysis and not as an automatic cell classifier.

4.1. Database

The ground truth of the cases recorded in the database is obtained a priori through immunophenotyping. Currently, the image server uses a database of 261 color 640 x 480 images, containing cells which belong to 3 classes of lymphoproliferative disorders (98 Chronic Lymphocytic Leukemia - CLL, 38 Follicular Center Cell Lymphoma - FCC, 66 Mantle Cell Lymphoma - MCL) and a class of healthy leukocytes (59 NORMAL). The database indexing is performed off-line, the incoming cases being first analyzed and registered. Then, the weights of the dissimilarity measure are re-learned to account for the new entries in the database.

4.2. Experiments

The confusion matrix of the system, shown in Table 1, was obtained through ten-fold cross-validated classification to provide a more realistic estimate. The confusion matrices representing the results of three human experts classifying 242 digitized specimens from the same database were also obtained. The experts were shown one digitized specimen at a time on a high resolution screen with no other distractor displayed. The different confusion matrices are shown in Table 2.

Examining Table 1 and Table 2 we observe that the human expert performance is similar to that of the system for the FCC and NORMAL cases, but it is worse for the CLL and MCL cases, both in terms of probabilities of correct decision (the marked diagonals) and probabilities of false negatives (the NRML column). The correlation between the human and machine results is also noteworthy. The classification of the FCC cells proved to be the easiest task while the CLL and MCL cells resulted in similar levels of difficulty.

In a real classification scenario however, the human expert uses a lot of context information including both patient data and additional data inferred from the digitized specimens. We therefore stress the *decision support* function of the IGDS system. The system is not intended to provide automatic identification of the disorder, but to assist the pathologist to improve its own analysis. The pathologist combines the objective classification suggested by the system with the context information to obtain a robust diagnostic decision.

At present, the system is being evaluated in real retrieval scenarios at the Department of Pathology, UMDNJ-RWJ Medical School. An important goal of this research is the establishment of new guidelines for visually characterizing lymphoproliferative disorders. Other query attributes are being investigated such as the ratio of the nuclear area over the cytoplasm area of the cell.

Table 2. Confusion Matrix: Human Experts

	CLL	FCC	MCL	NRML	NO DEC
CLL	.5647	.0352	.2117	.1764	.0117
FCC	.0285	.9428	.0000	.0285	.0000
MCL	.1538	.0769	.5538	.1692	.0461
NRML	.1228	.0000	.1053	.7543	.0175

	CLL	FCC	MCL	NRML	NO DEC
CLL	.4000	.0588	.1647	.3765	.0000
FCC	.0000	1.000	.0000	.0000	.0000
MCL	.0769	.0923	.5538	.1692	.0923
NRML	.0000	.0877	.1053	.7719	.0351

	CLL	FCC	MCL	NRML	NO DEC
CLL	.4941	.0235	.2118	.2000	.0471
FCC	.0000	.8857	.0857	.0286	.0000
MCL	.4308	.0154	.3077	.0308	.2154
NRML	.2000	.0364	.1455	.3455	.2727

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References

- [1] P.M. Banks et al., "Mantle Cell Lymphoma: A proposal for Unification of Morphologic, Immunologic, and Molecular Data", *Am. J. Surg. Pathology*, 16:637-640, 1992.
- [2] E. Campo, E. Jaffe, "Mantle Cell Lymphoma", *Arch. Pathol. Lab. Med.*, 120:12-14, 1996.
- [3] J. Chan et al., "A Revised European-American Classification of Lymphoid Neoplasms Proposed by the International Lymphoma Study Group", *Am. J. Clin. Pathol.*, 103:543-560, 1995.
- [4] D. Comaniciu, P. Meer, D. Foran, A. Medl, "Bimodal System for Interactive Indexing and Retrieval of Pathology Images", *IEEE Workshop on Applications of Comp. Vis.*, Princeton NJ, 76-81, 1998.
- [5] D. Comaniciu, P. Meer, "Distribution Free Decomposition of Multivariate Data", To appear, *Pattern Anal. and Applications*, 1999.
- [6] D. Comaniciu, P. Meer, K. Xu, D. Tyler, "Retrieval Performance Improvement through Low Rank Corrections", To appear, *IEEE Workshop on Content-Based Access of Image and Video Lib.*, Fort Collins CO, 1999.
- [7] H. Kauppinen, T. Seppanen, M. Pietikainen, "An Experimental Comparison of Autoregressive and Fourier-Based Descriptors in 2D Shape Classification", *IEEE Trans. Pattern Anal. Machine Intell.*, 17:201-207, 1995.
- [8] F.P. Kuhl, C.R. Giardina, "Elliptic Fourier Features of a Closed Contour", *Comp. Graphics Image Process.*, 18:236-258, 1982.
- [9] J. Mao, A.K. Jain, "Texture Classification and Segmentation using Multiresolution Simultaneous Autoregressive Models", *Pattern Recognition*, 25:173-188, 1992.
- [10] H.D. Tagare, C.C. Jaffe, J. Duncan, "Medical Image Databases: A Content-based Retrieval Approach", *J. of the American Medical Inform. Assoc.*, 4:184-198, 1997.