A COMPUTER-BASED INTERACTIVE IMAGE PROCESSING SYSTEM FOR HIGH-SPEED IMAGE ANALYSIS

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ABSTRACT

This paper describes a computer-based interactive image processing system developed for biomedical image processing research.

In its present form, this software system is implemented under the RSX-11D executive on a PDP-11/50 computer which utilizes a Zeiss Axiomat microscope, a high quality plumbicon camera, and CRT display for image acquisition and display purposes. A custom built scanner controller facilitates computer selection of the scanner's x, y and z resolution, and in addition, provides for point by point shading correction.

An extensive interactive software system has been developed for this system to put the power of the hardware into the hands of biological researchers.

This software system not only provides a convenient means for scanning, storing and retrieving image data, it also contains numerous image processing and pattern recognition functions. The paper concentrates on the image processing aspects of this software package, and results obtained using it in biological cell analysis research will be presented.

SYSTÈME INTERACTIF POUR LE TRAITEMENT D'IMAGES PAR ORDINATEUR DANS L'ANALYSE D'IMAGES À HAUTE VITESSE

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ABRÉGÉ

Cet article décrit un système interactif, pour le traitement des images par ordinateur, utilisé en recherche dans le domaine biomédicale.

L'exécutif RSX-11D sur un ordinateur PDP 11/50 exécute présentement l'ensemble de programmes. Un microscope Zeiss axiomat, une caméra plumbicon de haute qualité et un système d'affichage CRT sont reliés à l'ordinateur et permettent l'acquisition et la projection des images. Un appareil de control a été construit sur la caméra pour faciliter la sélection par l'ordinateur de la résolution de la caméra en x, y et z et pour fournir une correction de l'ombrage point par point.

Un ensemble élaboré de programmes a été développé pour ce système interactif afin de permettre aux chercheurs en biologie d'utiliser la pleine capacité de l'équipement. Cet ensemble de programmes non seulement fournit les moyens d'analyser, entreposer et recouvrer les informations sur les images mais aussi possède de nombreux procédés pour le traitement et l'identification de ces images.

Cet article traite plus particulièrement de l'analyse des images par cette collection de programmes. Les résultats obtenus dans l'analyse biologique de cellules avec ce système y seront presentés.

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I. INTRODUCTION

The rapidly decreasing cost of computer hardware has made the digital computer a viable alternative to custom-built hardware to perform computational and control functions in complex systems. In fact, many complex systems could not economically be produced without the inclusion of some form of programmable digital computer.

In many instances, computer hardware costs have fallen to the extent that the economic feasibility of developing a complex computer-based system is almost entirely determined by the software development costs. Thus, if the full potential of the digital computer is to be realized, development costs of customized computer software must be sharply reduced.

In a research environment such as image processing and pattern recognition, software costs are particularly high. Large software systems are developed for use in but a few experimental runs, only to be discarded when the results (successful or otherwise) are obtained. In other instances, extensive software modification is required after each experimental run.

In an attempt to amortize software costs in an image processive environment, an interactive image processing system has been developed. Modular in structure, the interactive system is built upon functional modules common to many image processing applications. Hardware and software development has been tailored to needs of the interactive system design, so that the user may fully utilize all system resources. Particular attention has been paid to simplifying the system-user interface and to providing a convenient means for adding user-written modules with a minimum of software development overhead.

II Hardware

As shown in Fig. 1, the heart of the system is a DEC PDP 11/5Ø digital computer system. It includes a hardware floating point unit, 16K words of high speed MOS memory, 32K words of core memory, a programmable real time clock, an industry compatible magnetic tape unit, and a 20 million word disc drive. At present, two user terminals are provided for communication with the system. One is a 30 character per second hard copy device, while the second is an alpha-numeric CRT terminal operating at 2400 BAUD. Both terminals can be used for program development or to communicate with user programs.

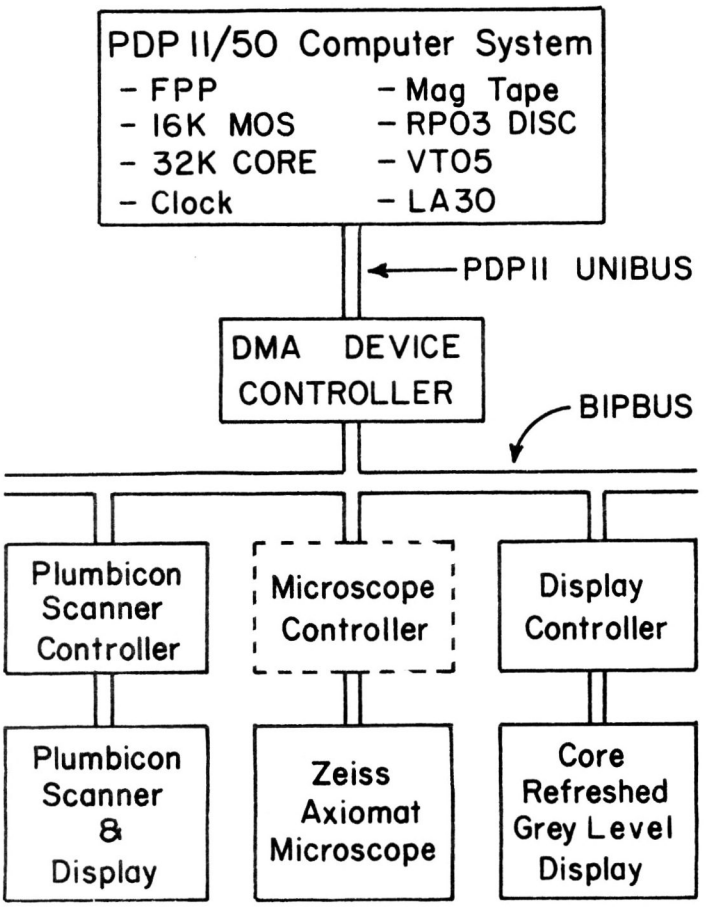

Fig. 1. Hardware Configuration at the Macdonald-Stewart Biomedical Image Processing Laboratory.

In addition to the computer hardware described above, the system includes a Quantimet 720D plumbicon scanner connected to a Zeiss Axiomat microscope and a custom-built core-refreshed grey-level display. These non-standard computer peripherals are interfaced to the PDP 11/5Ø via a custom device interfacing system developed in our laboratory. This interfacing system is capable of supporting up to 16 DMA peripheral devices using a single DMA type interface to the PDP 11 UNIBUS. Each custom device controller is connected to an intermediate bussing system (labelled the BIPBUS in Fig. 1) in a uniform fashion and may operate either in the programmed data transfer mode or using the DMA facility. This interfacing architecture provides a convenient method of adding non-standard computer peripherals to the system at a minimum cost. At present, device controllers have been developed for the Quantimet 720D plumbicon scanner, the core-refreshed grey level display and a third is under development for the Zeiss Axiomat microscope.

The Quantimet 720D scanner controller was developed to provide high speed data transfers from the scanner directly to the computer's memory. In addition, it contains a facility for point by point shading correction to compensate for shading in the optical system or in the scanner itself. A third important feature of the scanner controller is that it provides for frame to frame integration of image data directly in hardware to improve the signal to noise ratio of the scanned image data when required. Shading corrected fields as large as 180 x 220 picture points can be acquired with 4 frame integration in typically less than a second.

The core-refreshed visual display operates in a continuous DMA mode and outputs multiple grey level images on a Tektronix x, y, z monitor. The display controller provides a basic display raster of 1024 x 1024 picture points; however, for flicker free displays image size is limited to approximately 160 x 200 points. Images with up to 255 levels of grey (8 bits) can be displayed and a point flagging mechanism is also provided so that selected image points can be brightened to a constant value.

A device controller for the Zeiss Axiomat microscope is now under development. It will provide computer control over stage positioning and focussing. This will provide an accurate means of positioning the microscope stage to within plus or minus 5 microns over a range of 120 mm in the x direction and 60 mm in the y direction. The stage translation rate will be up to 240 steps per second with a 10 micron step size.

III The Interactive Software System

The interactive software provides the system user with image scanning, storage, retrieval and display functions on a highly interactive basis. In addition, it supports interactive design and evaluation ofimage processing procedures for pattern recognition applications. Image processing procedures are executed by the system Real-Time Scan Processor module. The complete system is highly overlayed and runs under the PDP 11's RSX-11D multiprogramming executive. It is written in a mix of FORTRAN and MACRO-11 assembler language. FORTRAN has been emphasized in the system for documentation purposes wherever possible. Assembler written modules have been written to be compatible with the standard PDP11 FORTRAN calling sequence in all cases.

The system-user interface is provided via the command decoder module. When theinteractive system is called from the keyboard, the command decoder module is activated and issues the identifying prompt sequence (RSP>) indicating it is ready to accept a user command. Such commands are in the form of keywords followed by a parameterlist. For example, the sequence:

RSP> SCN 4; 4; Ø, Ø; 144, 144; CR (carriage return)

would cause the command decoder to activate the scanner module "SCN" and pass it the parameters specified in the remainder of the command. Upon completion of this command, control is returned to the command decoder and the prompt is re-issued.

The command decoder is so constructed to allow the user to add additional FORTRAN or MACRO-11 program modules in straight forward and uniform manner. Such modules can be added simply by entering the command keywords and the command sequence number in the command definition module plus a FORTRAN subroutine call to the new module in the main program module.

Currently, the interactive software system contains well over 60 program modules which are accessed by some 35 commands. These modules are grouped into three basic packages which are described below.

1) The Scanner/Display Package

The scanner/display package is a set of program modules used to control the Quartimet 720 plumbicon scanner and the core-refreshed visual display. At present, the scanner modules support scanning resolutions of 1 times, $\frac{1}{2}$ times and $\frac{1}{4}$ times the basic scanner resolution over a rectangular frame selected within the basic 700 x 900 point raster of the Quartimet 720. Full point by point shading correction of the optical density information and frame to frame integration of up to 4 frames is supported. Commands issued to the scanner package cause data to be transferred from the

plumbicon scanner to the computer's memory. The maximum image size that can be accommodated by the system is 20,736 picture points (144 x 144). A sample scan command is given below.

RSP> SCN 4; 4; Ø, Ø; 144, 144; (CR)

The above parameters indicate from left to right: scan at $\frac{1}{4}$ resolution with 4 frame integration an image centered in the plumbicon's field (Ø,Ø) and with 144 image points in both vertical and horizontal directions. A second scan with the same parameters could be effected by simply issuing a short form of the scan command as follows and the previous parameters would be assumed.

RSP>SCN (CR)

A scan with the same size and resolution which is centered 100 basic scanner resolution units to the right and above the center of the plumbicon's field would be done as follows:

RSP> SCN 4;4;100,100; (CR)

The core-refreshed display has a basic display raster of 1024 by 1024 image points and is interactively controlled by software similar to the scanner software except that the frame integration parameter will be interpreted as a repeat count for photography and if it has the value Ø, a continuous display is created. The current software uses the computer's CRT terminal for output of binary visual data. In the future binary visual information (normally points in an image flagged by an image processing procedure) will be superimposed as bright points on the 256 level core-refreshed grey level display.

2) The Data Management Package

The data management package provides a capability for high-speed storage and retrieval of images, image descriptions and image processing procedures. It is centered about an assembler-written disc I/O package (DPX) that replaces the conventional disc I/O supported under RSX-11D. The DPX package enables transfers of up to 32 K words of data to or from disc (RPØ3) to be made in a single disc access as opposed to 1 access for every 256 words. In addition, the DPX package permits simultaneous I/O and processing to be carried out from within a single RSX-11D task thus maximizing CPU utility. DPX is capable of transferring 20,000 byte data records to or from the RPØ3 disc in 1/8 of a second.

The power of the DPX package is brought to the interactive user via a high level data management package (DBM) that utilizes the DPX functions in performing disc I/O. Although the DBM package has not reached its final form, at this time it provides for interactive allocation of disc space for images, image descriptions and image processing procedures. In addition, these three types of data can be stored and retrieved interactively and a facility exists whereby objects located in images by image processing procedures can be labelled or described interactively by the user. Such information is

stored for later use by learning or self-optimising pattern recognition programs.

The DBM package supports two forms of storage allocation for images and image processing procedures. The first is in the form of a standard RSX-11D file on a file per image (or procedure) basis. Using this method, storage allocation is implied in the command as follows:

```
RSP>WRITE DATA = FILENAME.EXT; version number
```

The above command will allocate disc space for the core resident image and write out a file with the name as indicated in the command to the right of the equals sign. The second method of allocating disc space for images and image processing procedures is the creation of a VIRTUAL VOLUME on an interactive basis prior to any storage or retrieval commands. A virtual volume is a contiguous disc space that is used to store VIRTUAL FILES with file management under control of the DBM module and not RSX-11D. This preallocation is done using the DBM 'OPEN' function which interacts with the user at the keyboard. Using this method of space allocation, an image processing procedure for example would be written out by specifying its sequence number (as opposed to file name) as shown below:

```
RSP>WRITE PROC 1Ø
```

The advantage of the second method is primarily that of speed, since any transfer is completed in a single disc access. Beyond the advantages of the DPX type access, the fact that the virtual volume is allocated as physically contiguous disc space can greatly reduce seek times.

Although a user may create and use many VIRTUAL VOLUMES, only one may be open at a time. The VIRTUAL VOLUME that is currently open serves to define the environment within which the interactive system is operating, and thus each such environment can be associated with a specific user, experiment, or project.

3) The Real-Time Scan Processor Package

The Real-Time Scan Processor Simulator (RSPS) is a set of programs used to interactively develop, execute and evaluate image processing procedures. This module simulates on the PDP-11/5Ø a high-speed special purpose parallel computer architecture. Thus, a pattern recognition algorithm specified in terms of an RSPS procedure is applied to each point in an image. The evaluation of a procedure at a particular point is independent of its evaluation at any other point.

At present, the simulator package is being used to study the processor's effectiveness in image processing applications such as prescreening cervical smears for cancer. Such applications are typified by extremely high data processing rates. In the ensuing

discussion, the cervical cancer screening problem will be used as an example to illustrate both the form of image processing procedures that can be executed by the RSPS package and also, how one would go about developing an image processing procedure interactively.

A typical image processing procedure is shown in Table 1. The procedure is specified in terms of two sets of parameters namely, primary feature generation parameters and pattern modelling parameters. The feature generation parameters specify the form of the primary feature extractors in terms of which patterns or objects to be detected will subsequently be modelled. The modelling parameters specify how the values obtained by applying the primary feature extractors at each image point should be combined and logically tested to determine whether the pattern to be detected is in fact present at an image point. Let us consider the feature generation parameters first.

The system's feature generation parameters consist of a set of up to eight feature generation functions denoted M1 to M8 in the Table. Each of these functions specify a two-dimensional circularly symmetric primary feature extractor as a function of distance from its central point. Figure 2 shows the primary feature extractor generated by the third feature generation function given in Table 1.

3	9	10	9	3
9	4		4	9
10				10
9	4		4	9
3	9	10	9	3

Fig. 2 The Third Primary Feature Extractor.

The values shown in Fig. 2 are the relative weight values used to calculate the value of the third primary feature when the feature extractor is applied at a point in the image. It should be emphasized that these are relative values since the feature extraction algorithm normalizes the resulting primary feature value by dividing by the sum of the primary feature extractor weights (140 in this case). The remainder of the feature generation functions in the example shown in Table 1 are of approximately the same form as the third described above except for a difference in scale. Thus, the primary feature extractors defined in the example consist of the first which extracts the value of the image point at which the masks are applied and the remainder which extract the average value of image points in annular rings of increasing radius about that same point. This set of primary feature extractors has been found to be very useful in our research in cell analysis; however, in other applications where spatial frequency information is of prime importance, one could consider other forms such as spherical bessel functions.

FEATURE EXTRACTOR GENERATION PARAMETERS

M1:	1	0	0	0	0	0	0	0	0	0	0	0
M2:	0	10	0	0	0	0	0	0	0	0	0	0
M3:	0	0	10	0	0	0	0	0	0	0	0	0
M4:	0	0	0	10	0	0	0	0	0	0	0	0
M5:	0	0	0	0	10	0	0	0	0	0	0	0
M6:	0	0	0	0	0	10	0	0	0	0	0	0
M7:	0	0	0	0	0	0	10	0	0	0	0	0
M8:	0	0	0	0	0	0	0	10	0	0	0	0

PATTERN MODELLING PARAMETERS

L11A	T:	20	100	W:	1							
L21A	T:	12	100	W:	-1	2						
L22	T:	0	0	W:	0	0						
L23	T:	0	0	W:	0	0						
L31	T:	0	0	W:	0	0	0					
L32	T:	0	0	W:	0	0	0					
L33	T:	0	0	W:	0	0	0					
L41A	T:	90	1000	W:	1	2	0	-1				
L42A	T:	165	1000	W:	1	2	3	0				
L43A	T:	300	1000	W:	1	2	3	4				
L51A	T:	5	20	W:	0	0	1	0	0			
L52A	T:	5	20	W:	0	0	0	1	0			
L53A	T:	5	20	W:	0	0	0	0	1			
L61A	T:	0	100	W:	0	1	0	-2	0	0		
L62A	T:	0	100	W:	0	1	1	0	-4	0		
L63A	T:	0	100	W:	0	0	1	1	0	-3		
L71A	T:	-10	100	W:	0	0	2	0	-3	0	0	
L72A	T:	0	100	W:	0	0	0	2	0	-3	0	
L73A	T:	0	100	W:	0	0	0	0	2	0	-3	
L81A	T:	0	15	W:	0	0	0	1	0	0	0	0
L82A	T:	0	10	W:	0	0	0	0	1	0	0	0
L83A	T:	0	7	W:	0	0	0	0	0	1	0	0

Table 1: A Typical Image Processing Procedure

The second set of image processing procedure parameters shown in Table 1 are the pattern modelling parameters. These parameters specify the manner in which the primary feature values derived at a point in the image are to be combined and tested in order to detect the presence of a particular pattern in the image. These parameters are grouped in up to eight levels with up to three sub-levels per level. These are labelled in the left hand column of Table 1. (i.e. level 6, sub-level 1 is labelled L61). Note that the label L61 is followed immediately by the letter A indicating that the sub-level is "active" and would participate in any image processing action carried out.

Each sub-level is composed of two distinct sets of parameters; a set of weights W, and a set of thresholds T. The weights specify the manner in which primary feature values are combined in a decision function while the thresholds specify the lower and upper bounds on the value of the decision function consistent with the presence of a particular sub-pattern to be tested for in the sub-level. Thus, in L61, if at a particular point in the image 1 times the second primary feature value plus -2 times the fourth primary feature value falls in the range zero to one hundred then, the sub-pattern modelled in L61 is determined to be present at the point in question.

It is important to note that the thresholded values obtained for each active sub-level in a processing level are logically ORed, so that only one of the sub-patterns modelled in a level need be present for the pattern modelled in the level to be considered present. This feature of the system allows the user to specify pattern recognition algorithms that are relatively insensitive to scale (size) since different size ranges of the same pattern can be tested for in successive sub-levels. The reader will note that several levels of the image processing procedure shown in Table 1 have that form.

Combination of processing results obtained in successive levels (as opposed to sub-levels) is of a different form. In this case, the results obtained in each level are logically ANDed, so that at any particular point in an image, all sub-patterns or pattern features modelled in the individual levels of an image processing procedure must be present for the overall pattern modelled in the procedure to be detected at that image point.

The interactive user is provided with several system commands to aid him in the development of an image processing procedure. These include a set of procedure editing and listing commands, a set of procedure execution commands and another set of commands used to obtain statistical information about internal decisions made during the processing of an image.

The procedure editing commands enable the user to quickly make changes to image processing procedures at the feature extraction function orpattern modelling weight or threshold level. This set of commands also includes commands to activate or deactivate complete

processing levels or sub-levels and to obtain a partial or full listing of the image processing procedure.

The procedure execution commands permit the user to apply an image processing procedure to an image in either a single step or in a level by level fashion to produce displays showing objects detected by the procedure or at any stage of processing respectively. Commands also exist to enable one to run a procedure stored on disc in a named disc-resident image file. Subsequent to the complete or partial application of procedure to an image, visual displays of the processing results are generated. In addition, the user may request a partial or full statistical summary of the processing results by issuing the appropriate system command. An example of a partial statistical summary of a processing action is shown below. Both the command used to obtain this display and the results are shown.

```
RSP  L   A4

      L41A  A41:  754  S11:  0  S12:    4  S13:    0  S: 84
      L42A  A42:  754  S21:  4  S22:   97  S23:  183  S: 84
      L43A  A43:  754  S31:  0  S32:  183  S33:    0  S: 84
```

In the above example 754 image points were flagged at level 3 of processing (as this is level 4). Within level 4, no points were flagged by level 41 alone (S11: = 0), 97 were flagged by level 42 alone (S22: = 97) and none were flagged by level 43 alone. Also, 4 were flagged by levels 1 and 2 together (S21: = 4), 183 were flagged by levels 2 and 3 together and 84 were flagged by levels 1, 2 and 3.

The interactive image processing system has been used primarily for biological cell analysis research and particularly to develop low resolution image processing methods for high-speed location of suspect cells (those that could indicate the presence of cancer) in routine cervical (PAP) smears [1]. The image processing algorithm shown in Table 1 is in fact one developed for detection of certain types of cancer or precancerous cells in cervical smears and has been developed for use in the specimen enrichment stage of a dual resolution prescreening device [2]. The image processing procedure shown models several cell parameters including nuclear size and density, integrated nuclear density, cytoplasm density, nuclear border, cytoplasmic border and average background density. Although space does not permit a full description of the modelling of these various cell parameters, let us examine just one of these, the presence of a distinct nuclear border which is modelled in level 6 of the procedure shown in Table 1. The parameters of level 6 are reproduced below.

```
L61A   T:   0   100   W:   0   1   0   -2    0   0
L62A   T:   0   100   W:   0   1   1    0   -4   0
L63A   T:   0   100   W:   0   0   1    1    0  -3
```

In Figure 3, a cancer cell (one with a relatively large nucleus and a reduced cytoplasm) is outlined with a set of circularly symmetric rings (dotted lines) superimposed on it. These rings indicate the areas where the first five primary feature extractors defined in Table 1 would measure the average optical density.

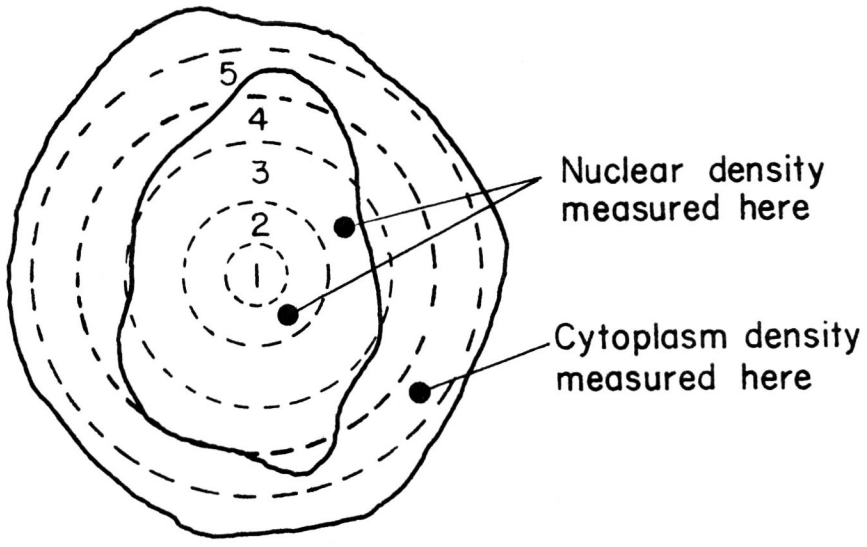

Fig. 3 Detection of the nuclear border

Referring to level 6, sub-level 2 (L62) in the parameter list above, we see that the weighting function defined would subtract four times the average optical density in ring 5 from the sum of the values for rings 2 and 3. The value thus calculated would then indicate the presence of a distinct nuclear border (a sharp drop in average optical density between nucleus and cytoplasm) if it was in the range 0 to 100. That is, the average nuclear density would be required to be at least double the average cytoplasmic density. Note that the circular symmetry of the detection mechanism is quite insensitive to the elongation of the nucleus because optical density is averaged in the whole ring in each case. Further, note that cells, or in this case cells with nuclei smaller or larger than the one shown, would be accommodated by sub-levels 1 or 3 respectively. Using the image processing procedure shown in Table 1, a large number of cells of various categories have been measured in low resolution (4 micron sample spacing) scans. The results obtained are shown in Table 2. These results indicate that approximately 80% of the cancer cells in a smear can be detected with this algorithm while considerably less than one percent ofnormal cells were picked up. The four normal squamous cells shown to be detected were actually metaplastic cells which should be detected in cervical smears even though they are not considered to be cancer cells. Further discussions of this research can be found elsewhere. [1,3,4]

Cell Type	Number	Number Detected	Percent
Isolated Normal Squamous	165	4	2.4%
Overlapped Normal Squamous	290	4	1.4%
Clumped Normal Squamous	475	0	0%
Polymorphonuclear Leukocytes	12,500	50	0.4%
Well Preserved Isolated or Slightly Overlapped Abnormal Cells	49	39	78%

Table 2. Performance of low resolution image processing method on various cell types.

Conclusion

This paper has presented some aspects of an interactive image processing system developed for biomedical image processing research. Although, several man-years of development have been required to bring it to its present state, we feel that the effort has been more than justified in terms of its usefulness as a research tool. Experiments can be conducted over a large spectrum of image processing applications without any reprogramming effort and we feel the fast turn around time achieved with the interactive approach has allowed us to carry out experiments that would not have been possible otherwise.

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