Automated Cell Counting System For Chronic Leukemia

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***Abstract*— Leukemia is a group of cancers which create a large amount of immature white blood cells. Abnormal numbers of white blood cells may suggest a screening of leukemia, and the blood sample is examined under the microscope to observe if the cells appear abnormal. The manual screening of chronic leukemia is time consuming and tedious while the Automated Hematology Analyzer is too expensive, particularly for the third world countries. This has been made exacerbated by the gold standard of biopsy inspiration which is painful and invasive for the patient. An automated cell counting (ACC) system for chronic leukemia has been developed to support and ease the routine of hematologist and technologist in the screening process and to give a quick and accurate result. The fusion of image processing technique has been proposed, which include four main stages, i.e. image acquisition, image segmentation, noise removal and counting process. Based on the sensitivity test over 100 images of chronic cells, an overall result shows 98.94% sensitivity of the system performance and the processing time recorded is less than 6 second per image. This proved an excellent level of ACC system performance. It is concluded that the system is suitable to be used as an automated counting system for chronic leukemia disease due to its sensitivity and ability to reduce the time taken for screening process.**

Keywords—Automated Cell Counting System (ACC), Segmentation, Morphological Operation, Blood Cell.

I. Introduction

Leukemia is a group of cancers which create a large amount of immature blood cells. These immature blood cells take up space in the bone marrow, preventing the bone marrow from making healthy blood cells such as platelets, red blood cells, and white blood cells. Leukemia can be classified into two, which are chronic leukemia and acute leukemia [1]. Acute leukemia grows rapidly and will spread over the body within a short period. Whereas, chronic leukemia grows slower than acute leukemia and become more serious over years [2].

According to [3], screening process based on microscopic blood images appeared to have an error rate between 30 to 40% depending on the haematologists' experience and also the difficulties to distinguish between the normal and abnormal cells [4].

The utilization of image processing technique as an automated counting system for diagnosis of leukemia disease has been studied in [5] and [6] in which the image segmentation technique such as K-mean clustering is employed in several leukemia cases. In [7], K-mean clustering is used for automated acute lymphocytic leukemia detection. While in [8], K-mean clustering is integrated with histogram equalization and Zack algorithm to determine leukemia. Recent study also used K-mean clustering to identify the leukemia cells and features extraction, and image refinement [9]. Another study presented the integration of K-mean clustering and machine learning technique to differentiate among Acute lymphoblastic leukemia (ALL), Acute myeloid leukemia (AML), Chronic lymphocytic leukemia (CLL) and Chronic myeloid leukemia (CML) [10].

What is learnt from the above is the effectiveness of image processing technique in automating leukemia diagnosis. However, most of the studies in the field of image processing only focused on cases outside Malaysia. Hence, this study serves as a replication study which focuses on leukemia cases in Malaysia. The key contribution of this study is the development of an ACC for Chronic Leukemia to improve the reliability of the counting blood cell and decrease the dependency on human experts.

ACC is introduced to automatically count chronic leukemia cell and at the same time promised an acceptable result for screening process based on blood sample. Details of the development of the system is discussed in Section II and III. Section IV of this paper concludes the work that is presented in the earlier sections.

II. Development of ACC System

ACC was developed using MATLAB environment which utilized image processing technique for chronic cell counting based on the blood samples. There are four stages including image acquisition, image segmentation, noise removal and counting process. Fig. 1 indicates the combination of image

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processing techniques which were used to determine the chronic cell count.

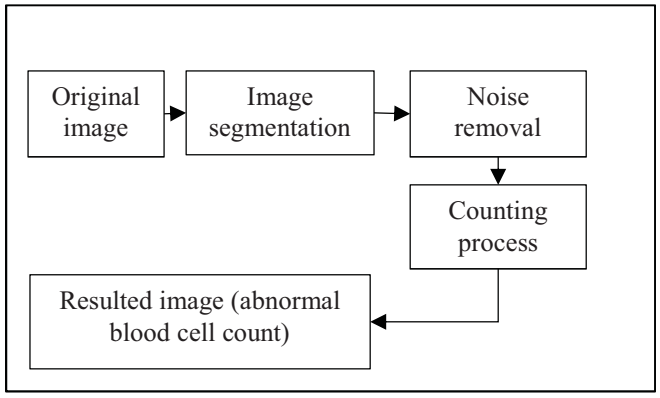
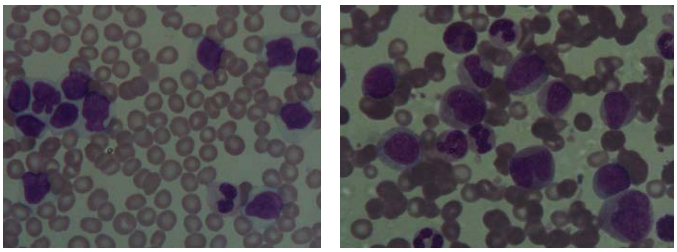


Fig. 1. *Combination of image processing techniques*

A. Images Acquisition

This study used 100 images of blood cells which were acquired from Haematology Department, University of Science Malaysia Hospital. Images were captured at the resolution of 800×600 pixels and saved in the bitmap (.bmp) file format. A resolution of 800×600 pixels was used in this study, to ensure that morphological features of chronic cell were sharp, good quality and provided relevant information. The Fig. 2(a) and Fig. 2(b) show examples of original image captured for chronic lymphoid leukemia (CLL) and chronic myeloid Leukemia (CML) respectively.



(a) (b)

Fig. 2. *Sample Chronic Leukemia Images. (a) CLL (b) CML*

B. Images Segmentation

K-means clustering algorithm is selected to segment the region of interest (ROI) of chronic leukemia cells in original image. The algorithm of K-Means works iteratively to assign each data point to one of K groups based on the features that are provided. Data points are clustered based on feature similarity using the following clustering code:

```
ab=double(lab_i(:,:,2:3));
nrows = size(ab,1);
ncols= size(ab,2);
ab=reshape(ab,nrows*ncols,2);
nColors=3;
[cluster_idx cluster_center] =
kmeans(ab,nColors,'distance','sqEuclidean', 'Repli-cates',3);
```

C. Noise Removal

The unwanted noises in an input image need to be filtered in order to improve the image quality. At this stage, the blood cell images which have been clustered were filtered using median filter algorithm, as shown below:

```
I = rgb2gray(RGB);
J = imnoise(I,'salt & pepper',0.02);
K = filter2(fspecial('average',3),J)/255;
L = medfilt2(J,[3 3]);
```

This process determined the region of interest such as the nucleus in the images. Median filter algorithm removed the unwanted noises, mainly salt and pepper noises, from segmented images.

Another filter used at this stage is unsharp filter. This is a simple sharpening operator which sharpens edges of the elements without increasing noise or blemish. It will sharpen the chronic cell by subtracts an unsharp, or smoothed version of an image from the original image. The unsharp masking code is as shown below:

```
h = fspecial('unsharp');
I2 = imfilter(I,h);
```

Watershed algorithm has been applied on unsharped image to separates adjacent drainage basins. The watershed transformation treats the chronic cell image it operates upon with the brightness of each point representing its height, and finds the lines that run along the tops of ridges. The watershed algorithm code is shown as below:

```
Ld = watershed(D);
```

D. Morphological Operation

When the blood cell images completely undergo unsharp masking process, the resultant image of it will apply morphological operation for the purpose of split the overlapped cells. Morphological operators referred as a tool for extracting image components that are useful in the representation and description of region shape. Most of the operations used here are combination of two processes, dilation and erosion. In this study, we proposed dilate and erosion method for removing holes and splitting the overlapped cell.

Morphological Closing

Morphological closing of an image involved dilates (probing and expanding the shapes contained in the input image) an image and then erodes (erode away the boundaries of regions of foreground pixels) the dilated image using the same structuring element for both operations. This technique removes small holes and split the overlapped cell to ease of counting process. The imclose code is as shown below:

```
bw4=imclose(bw3 strel('disk'2));
se = strel('disk',1,0);
bw5 = imerode(bw4,se);
se = strel('disk',1,0);
app.erodedBW = imerode(bw5,se);
```

E. Total Cell Count

The resulted image will then be used to get the total cell count by using the following algorithm.

```
image2 = app.erodedBW;
bw=im2bw(image2);
ax=app.UIAxes_7;
background = imclose(bw, strel('disk', 200));
diffr = imsubtract(background, bw);
filled = imfill(diffr,'holes');
removedImg = bwareaopen(filled, 500);
bw = imclearborder(removedImg);
A=~bw;
[row, column]=size(A);
imshow(A,'Parent',ax);
B = bwboundaries(bw);
pause(2);
hold(ax,'on');
hold(ax,'on');
for k = 1:length(B)
boundary = B{k};
plot(ax,boundary(:,2), boundary(:,1), 'g', 'LineWidth', 0.2);
app.EditField_2.Value=k;
pause(0.05);
End
```

The total number of chronic cell counted in this stage will depend on the previous process. If the previous process (refer Figure 1) well performed and yielded promising morphological features, indeed the system developed will be reliable, convenient and trusted support tools to clinician.

III. Results and Discussions

A. System Interface and Main Functional Requirements

This standalone application is portable application that can be easily copied to any hardware and strictly secured with login system. Fig. 3 show the interface of the ACC system development for cell counting of chronic leukemia.

Fig. 3. *Login page*

Login page

Users can login after enter the correct user ID and password in the login page as shown in Fig. 3. If users enter the wrong user ID or password, an error message will pop up to prompt users to enter the correct user ID or password.

Fig. 4. *Home page*

Home page

Home page display the introduction of the ACC system. User can click OPERATION tab to enter to OPERATION page as shown in Fig. 4.

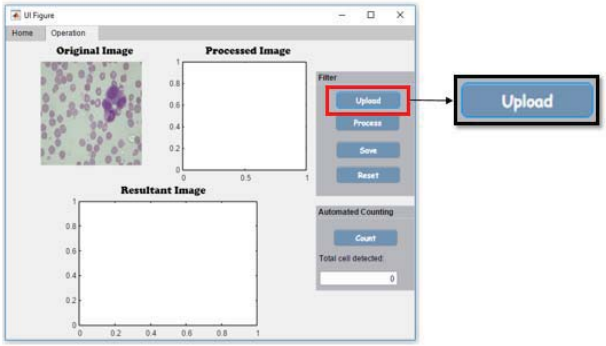


Fig. 5. *Upload raw image*

Upload raw image

Users can upload image from the selected file by clicking the UPLOAD button in operation page as shown in Fig. 5. The bitmap (.bmp) is set as default format.

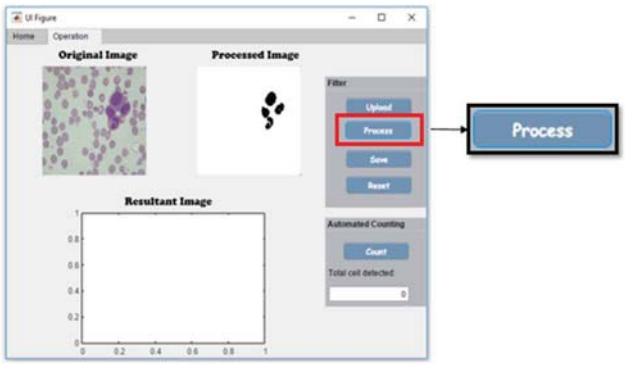


Fig. 6. *Processed image after segmentation and morphological operation applied*

Process

K-means clustering algorithm is selected to segment the ROI of chronic leukaemia cells from WBC (white blood cells), platelet, background, and others in RGB image. The K-means clustering algorithm is also combined with median filter and unsharp masking in the PROCESS button as shown in Fig. 6. Salt and pepper noise in the image is removed by using median filter. Median filtering is good in removing the outliers without reducing the sharpness of the image. While the unsharp masking is used to sharpen cell edge in the image. Morphological Operation has been applied to split the overlapped cells. Watershed algorithm and imclose (dilation followed by an erosion, using the same structuring element for both operations) have been applied.

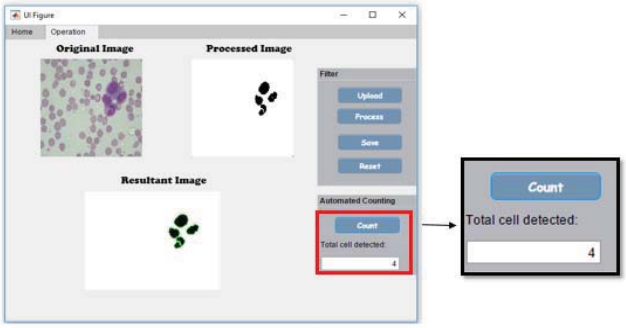


Fig. 7. *Total blood cell count based on processed image*

Count

The COUNT button as shown in Fig. 7 shows the total cell count based on the processed image in the text field box.

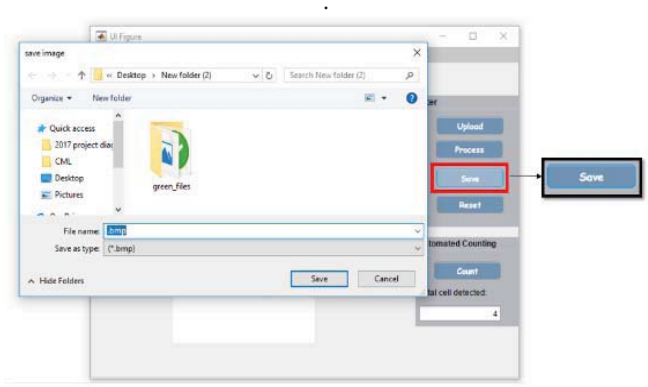


Fig. 8. *Save the processed image*

Save image

Users can save the final processed image in the selected location with a new file name as shown in Fig. 8. The image can either be saved in bitmap (.bmp) format or any other file formats.

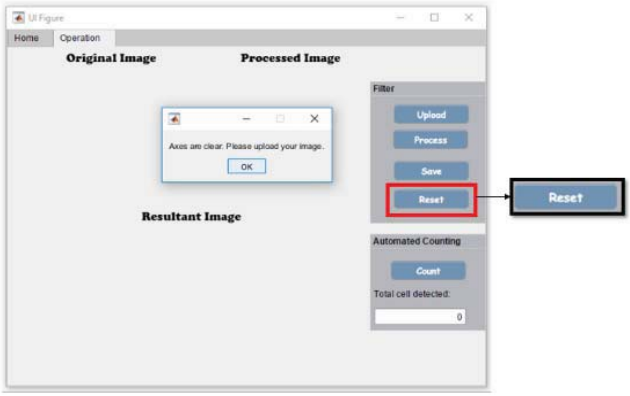


Fig. 9. *Reset the axes to proceed with next image*

Reset

Users can click RESET button to reset or clear all the axes and text field to proceed to the next image as shown in Fig. 9.

B. System performance

Table I shows the result of overall system performance based on the sensitivity test for 100 images of WBC. Out of 100 images, 40 images is a normal white blood cell, 30 images for acute leukemia CML type and 30 images represented abnormal image of acute leukemia CLL. Sensitivity of the system performance is calculated based on the true positive rate. True positive indicates the outcome where the image correctly counted the real normal, CML and CLL image. While false positive means the image counted incorrectly predicts the true normal, CML and CLL image and false negative predict incorrectly on the false normal, CML and CLL image.

TABLE I. RESULT OF OVERALL SYSTEM PERFORMANCE BASED ON 100 IMAGE

Type	No. of image	Manual counting	System counting	True positive (TP)	False positive (FP)	False negative (FN)	Sensitivity (%)
Normal image	40	18	21	17	3	1	94.44
CML image	30	150	170	147	14	3	98.00
CLL image	30	400	425	398	10	2	99.55
Total	100	568	616	562	27	6	98.94

$$\text{Sensitivity}\ (\%) = \frac{\text{TP}_\text{S}}{\text{TP}_\text{S} + \text{TP}_\text{S}} \times 100\% \quad (1)$$

Percentage of system performance sensitivity is presented using equation 1. From Table I, the average percentage of system sensitivity in detecting and calculating the total number of white blood cells from 40 normal blood images is 94.44%. For CML data sets type, the average for system sensitivity is 98.00% and followed by data set of CLL type images in which the sensitivity is 99.55%. Overall, the amount of WBC detected and calculated from 100 images tested, 568 cells were found through manually counted by trained staff and 616 white blood cells detected by the system.

The system found a WBC (TP) of 562 out of 616 WBC detected by the system. In addition, there are 27 non-WBC (FPs) that have been detected by the system and a total of 6 undetectable WBC (FNs) by this system. Hence, overall system performance sensitivity is 98.94%.

The time taken for the process of calculating cells by ACC for each image is not more than 6 seconds. During the system testing, all programs have been turned off with the aim to ensure that there were no interruption in system processing time. This means that for every 100 images tested, the time used by the system is less than 10 minutes. Thus, the computerized screening system for chronic leukemia has also helped reduce the time spent on the process of calculating cells manually performed by trained staff.

IV. CONCLUSION

Overall, it can be concluded that ACC System for Chronic Leukemia is a very simple and convenience system which can used as decision support system due to its performance. The need to speed up the screening process, reduce the differences in manual calculation among clinician, improve sensitivity performance and reduce the reliance on haematologists and lab technologists, ACC System are able to comply with the requirement. A total of 100 images of WBC tested to evaluate the sensitivity and processing time of the ACC System. The result shows 98.94% of system sensitivity with processing time less than 6 second per image proved an excellent level of ACC System performance. Hence, this achievement may help to reduce the complexity during screening by using image processing based on blood sample.

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