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AN IMAGE ANALYSIS BASED SYSTEM FOR ISOLATION OF LEUKEMIA INFECTED CELLS

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Abstract

A novel method is proposed for the accurate isolation of the erythrocytes infected with plasmodium parasites in images acquired from Giemsa-stained blood samples using conventional light microscopes for diagnosis of Leukemia . As Leukemia is an infectious disease so rapid diagnosis is necessary for accurate medication. The automated system is designed to positively isolate Leukemia parasites in microscopic images. We applied image processing techniques namely morphological operations, edge detection, image normalization and image segmentation. The robustness and effectiveness of our method have been assessed through the comparison with more than thirty microscopic blood images. The experimental results show that the proposed method is more robust, highly accurate in true isolation of infected cells, extremely fast and simple to execute. This work is useful in medical applications and can help to identify Leukemia disease and construct a computer- aided diagnosis system in rural areas where health care manpower is limited. Future work is outlined.

Keywords: Leukemia, Diagnosis, Segmentation, Edge detection, Erythrocytes, Normalization, Morphological operations, isolation.

1. INTRODUCTION

Leukemia is a type of cancer that affects the blood and bone marrow, which are the organs responsible for producing blood cells. It is a complex disease that can affect people of all ages and can be difficult to diagnose and treat. Leukemia is one of the most common types of cancer. According to the World Health Organization (WHO), there were an estimated 437,033 new cases of leukemia worldwide in 2020 [1]. Here are some facts and figures about leukemia as of 2022: Leukemia accounts for around 3.3% of all new cancer cases and 2.8% of all cancer deaths worldwide, There are four main types of leukemia: acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and chronic myeloid leukemia (CML), The incidence of leukemia increases with age, with the highest rates occurring in people over 65 years old, The exact causes of leukemia are unknown, but risk factors include exposure to radiation or certain chemicals, genetic factors, and certain medical conditions such as Down syndrome, Symptoms of leukemia can include fatigue, fever, weight loss, night sweats, and easy bruising or bleeding, Diagnosis of leukemia involves blood tests, bone marrow biopsy, and other imaging tests,

Treatment options for leukemia include chemotherapy, radiation therapy, bone marrow transplants, and targeted therapy, The survival rates for leukemia vary depending on the type and stage of the disease, with five-year survival rates ranging from 95% for CLL to 28% for AML, Research is ongoing to develop new treatments for leukemia, including immunotherapy and gene therapy, Leukemia is a serious disease that can have a significant impact on quality of life and overall health, but early detection and treatment can improve outcomes for many patients.

Survival rates for leukemia vary depending on various factors, including the type and stage of the disease, age, overall health, and access to treatment [2-5]. It's important to note that survival rates are general statistics and may not reflect an individual's prognosis. According to the American Cancer Society's estimates for 2021:

For ALL in children, the 5-year survival rate is about 92%.

For AML in adults, the 5-year survival rate is about 29%.

For CLL, the 5-year survival rate is about 84%.

For CML, the 5-year survival rate is about 70%.

Treatment options for leukemia depend on the type and stage of the disease. They may include chemotherapy, targeted therapy, immunotherapy, radiation therapy, stem cell transplantation, and in some cases, surgery.It's important to consult with healthcare professionals or medical experts for accurate and up-to-date information on leukemia, as research and understanding of the disease continue to evolve. Diagnosing Leukemia is the first step to control the spread of the disease. Currently, there are several methods employed to pronounce Leukemia. Among these techniques, visual evaluation of Giemsa stained blood film by means of light microscopy is by far the most widely used in developing countries. Beside numerous advantages, the use of light microscope in diagnosing Leukemia also has some drawbacks [6-9]. It relies heavily on the expertise of medical practitioner in the field. In addition, confirming negative status of a Leukemia slide take considerable time and efforts. Therefore, an automated image analysis system would improve the performance of microscopy by circumventing its main limitation in term of dependency on the ability of medical practitioner to diagnose blood image accurately, thus providing a milestone for fast and accurate diagnosis of Leukemia.

2. RELATED WORK

In the article, "Automatic Segmentation and Classification of Leukocytes Using Convolutional Neural Networks" by Esteva et al. (2017) proposes a deep learning approach using convolutional neural networks (CNNs) for the segmentation and classification of leukocytes in peripheral blood smears. It demonstrates accurate and efficient analysis of different types of leukemia cells. "Automated Detection and Classification of Acute Lymphoblastic Leukemia Cells in Microscopic Images" by Saini et al. (2018) proposed an automated approach for the detection and classification of acute lymphoblastic leukemia (ALL) cells in microscopic images. It utilizes image processing techniques for segmentation and features extraction, followed by machine learning algorithms for classification.

In the article "Automated Leukocyte Segmentation and Recognition Using Deep Convolutional Neural Networks" by Coudray et al. (2018) focuses on the automated segmentation and recognition of leukocytes using deep convolutional neural networks. The

proposed method achieves high accuracy in distinguishing between normal and abnormal cells, aiding in the diagnosis of leukemia. In "Automated Classification of Acute Lymphoblastic Leukemia Subtypes from Microscopic Images Using Deep Learning" by Khan et al. (2019) presents a deep learning-based approach for the automated classification of acute lymphoblastic leukemia (ALL) subtypes from microscopic images. It demonstrates the potential of deep learning models in accurate and efficient leukemia diagnosis. In "Detection and Classification of Leukemia Cells Using Convolutional Neural Network" by Chakraborty et al. (2020) proposes a convolutional neural network (CNN) based method for the detection and classification of leukemia cells. It introduces an efficient approach for feature extraction and demonstrates promising results in differentiating between normal and abnormal cells. In this article, we have proposed a isolation of leukaemia infected cells for accurate diagnosis.

3. PROPOSED SCHEME

We segment the erythrocytes and then check it a parasites has infected them. We develop a color based method to isolate the parasites infected RBCs. The input images are obtained in RGB color space [10]. The sample Leukemia color microscopic image infected with parasites as shown in figure 1. The sequence of procedures for isolation of parasites infected RBCs is given in Figure 2.

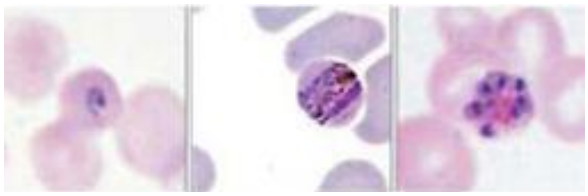


Figure1. Typical digital images of Leukemia infected blood smears, which present different coloration and illumination conditions

3.1 IMAGE PRE-PROCESSING

Pre-processing step includes gray scale conversion, noise reduction, smoothening of image. Here the Laplacian filter is used for smoothening the color image. The median filter is a non-linear digital filtering technique, often used to remove noise from images or other signals. It is usually necessary to perform high degree of noise reduction in an image before performing higher-level processing steps, such as edge detection[11-14].

The median filter is a nonlinear filter, which can reduce impulsive distortions in an image and without too much distortion to the edges of such an image. It is a effective method that of suppressing isolated noise without blurring sharp edges. Median filtering operation replaces a pixel by the median of all pixels in the neighbourhood of small sliding window. It gives better results than the neighbourhood averaging in the case where noise is of impulsive nature. We find the threshold value using histogram.

Histogram equalisation is nothing but a finding of cumulative distribution function for a given probability density function. Modelling of the histogram is usually done by the use of continuous process functions rather than discrete process functions[15].

The histogram of original image and its equalization as shown in Figure 3. Suppose for a given image the intensity levels are continuous quantities and is normalized to the range [0 1]. According to Gonzalez and Woods [2002] transformation can be performed on the probability density function of the intensity levels input image Pr(r) is to obtain S as shown below:

$$S=T(r)=\int P_r(w)\,dw$$

Where w is the variable of integration and $0<w<r$.

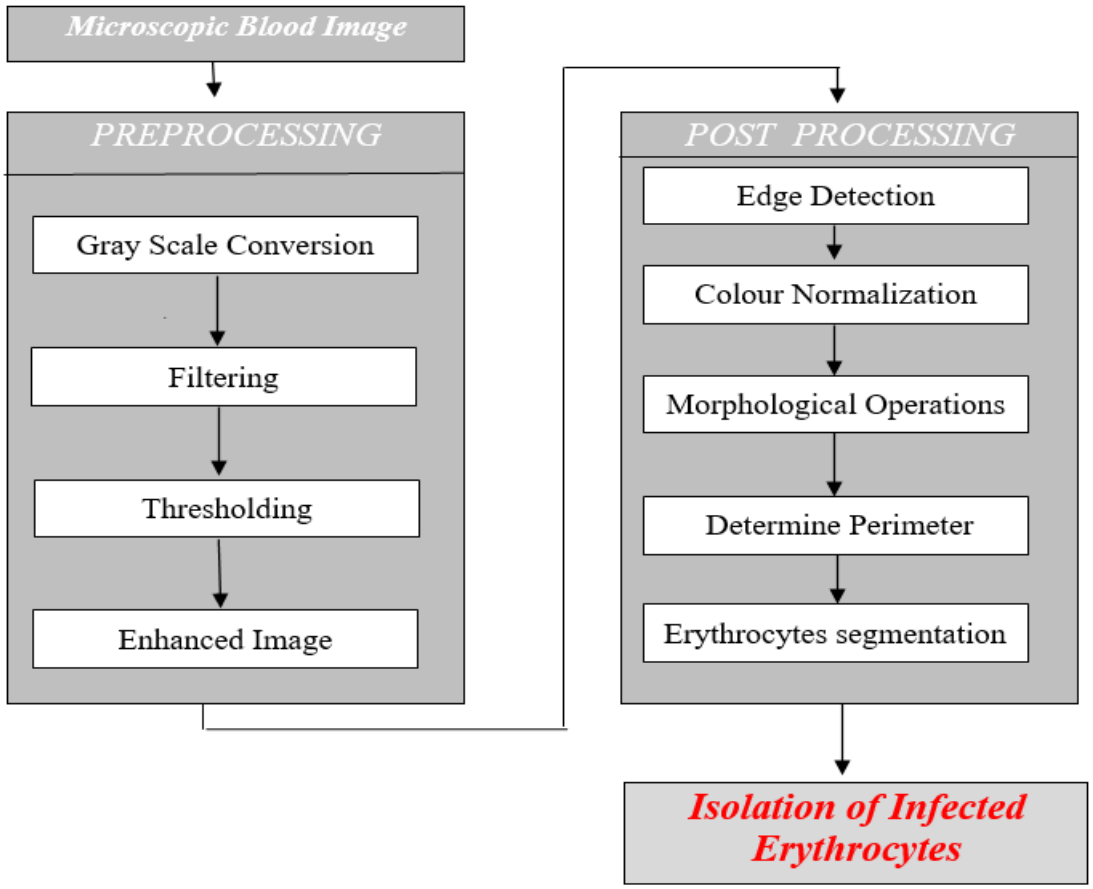
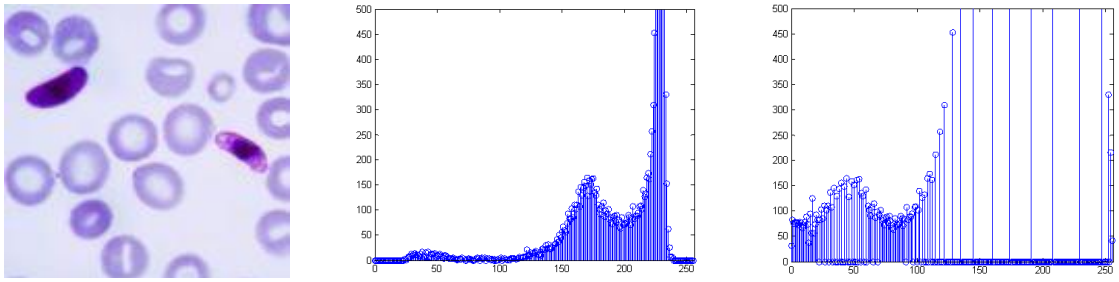


Figure 2: The flowchart of the proposed method

3.2 IMAGE POST PROCESSING

After pre-processing of an image, we have to send image to post processing for isolation of RBCs infected with parasite. This phase comprises edge detection, color normalization, morphological operations, and segmentation. Edges are boundaries between different textures [16-18]. Edge also can be defined as discontinuities in image intensity from one pixel to another. The edges for an image are always the important characteristics that offer an indication for a higher frequency. Detection of edges for an image may help for image segmentation. The Roberts method finds edges using the Roberts approximation to the derivative. It returns edges at those points where the gradient of the image is maximum.



(a) (b) (c)

Figure 3 :(a)parasite infected blood image(b) its histogram(c) histogram equalization

Color nomalization is concerned with artificial color vision and object recognition. In general, the distribution of color values in an image depends on the illumination which may vary i.e. depending on different lighting conditions or different cameras [19]. Colour normalisation allows for object recognition techniques based on colour, to compensate for these variations Since the segmentation utilise colour information, it is essential to apply colour normalisation to the images to decrease the effect of different light sources. The procedure is demonstrated with an example image in Figure 4.

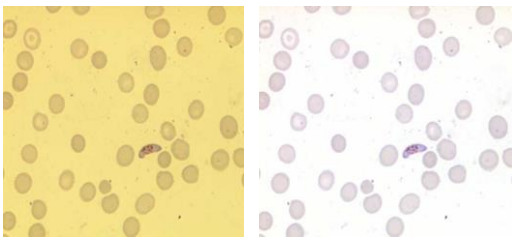


Figure 4. Colour normalisation: (a) An input image (b) after normalisation

We have chosen to use an adapted grey world normalisation method based on the diagonal model of illumination change which utilises certain characteristics of microscopic peripheral blood images [20]. Grey world normalisation assumes that there is a constant grey value of the image which does not change among different conditions. In the diagonal model an image of unknown illumination I^u can be simply transformed to known illuminant space I^k by multiplying pixel values with a diagonal matrix ($I^k_{rgb}=MI^u_{rgb}(x)$) . Based on the grey world assumption, if there is an image with known illuminate I^k, the entries of the M can be calculated.

$$M=\begin{bmatrix} m_{11} & & \\ & m_{22} & \\ & & m_{33} \end{bmatrix}$$

Where, m_{11}, m_{22}, m_{33} are moments for channels R,G,B.

Morphological operations play a key role in digital image processing with special application in the field of machine vision and automatic object detection [21]. The morphological operations include dilation, erosion, opening, closing and skeletonization etc. Erosion shrinks or thins the objects in a binary image by the use of structuring element. The mathematical representation of erosion is as shown below.

$$A \copyright As = \{z|\ (As)\ z \cap Ac \neq \Phi\}$$

For calculation of perimeter (P), the number of pixels along the contour was counted and this number was multiplied by length of the pixel. One of the most common tasks in image analysis system is segmentation. Segmentation aims to partition the image plane into meaningful regions. The definition of the meaningful regions and partitioning method is usually application specific. We segmented infected cells from input image with binary mask.

4. EXPERIMENTAL RESULTS AND DISCUSSIONS

The entire novel method outlined in Figure 2 was carried out by employing the GUI using MATLAB software supported with windows 2000/XP operating system. The performance of the proposed method was assessed in the two main sub-tasks: extraction of cells infected with parasite and isolate infected cells from non-infected RBCs.

The proposed novel method is applied to several microscopic blood images and the sample isolation result and the complete image pre and post processing steps are shown in Figure 5. The final isolation result is given in Figure 5(K) in which red contours indicating Leukemia parasite infected cells. In order to evaluate the performance of our method we apply it to some uninfected microscopic blood images and the result is

satisfactory where the system indicated that the cell is not infected [22].

In order to analyze isolation performance, we have to measure the true isolation versus false isolation percentages. Independent of the test result (isolation) a test sample blood image can be *positive* (infected) or *negative* (not infected), as determined by another reliable method.

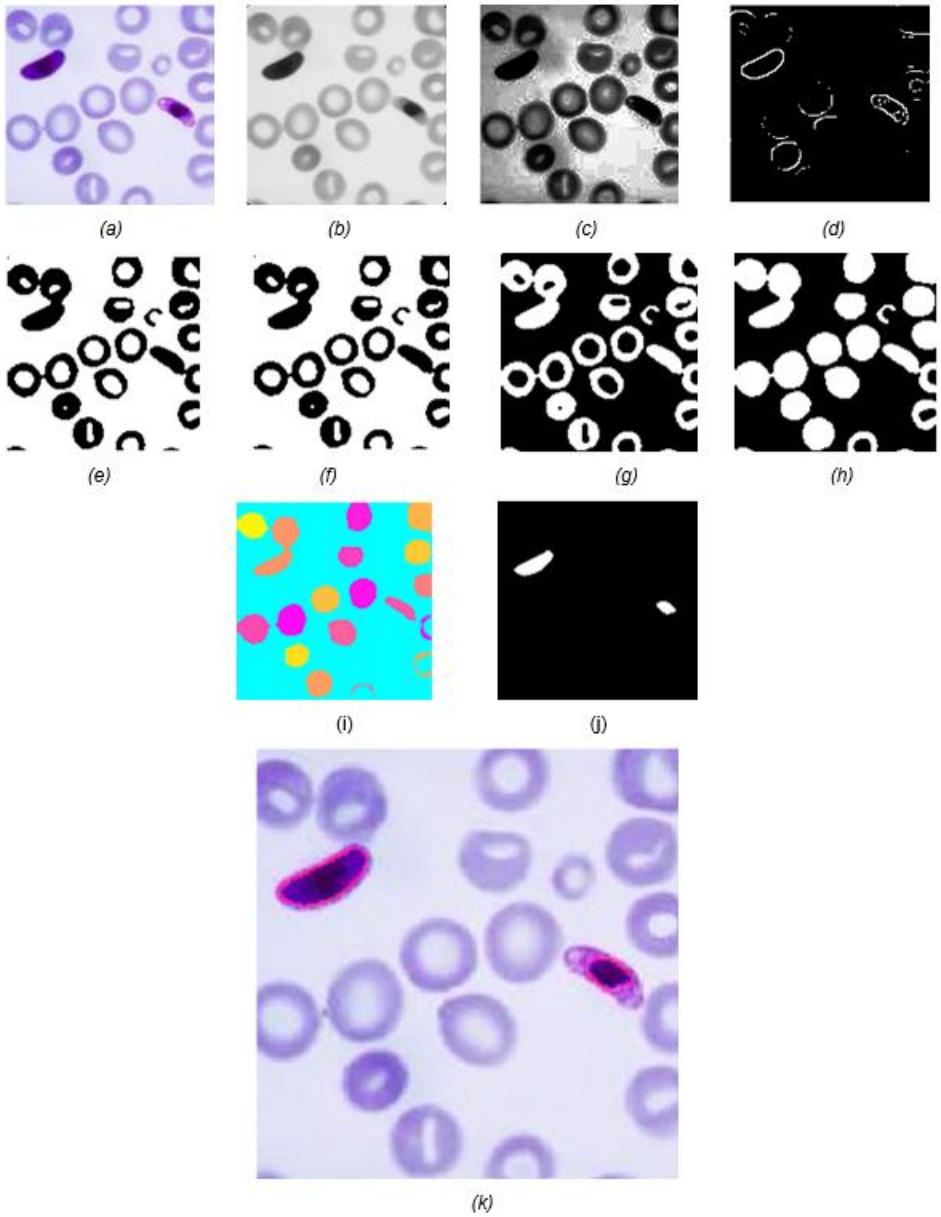


Figure 5: The various stages of processing of microscopic blood images are graphically illustrated in the following sequence: (a) Original color microscopic blood image, (b) Gray level image after median filtering, (c) Histogram equalization (d) Roberts edge detection (e)The binary image after thresholding (f)Removing back ground noise (g)Image complement Filling holes in an image (h)Erosion using imerode (i)Color to assign each of object of input image based on the number of objects in label matrix (j)Binary mask of infected RBCs (k) Isolation in which red color contours indicating Leukemia infected cells.

There can be four different outcomes after the isolation of infected erythrocytes: (TP) True Positive (the isolation result is positive for a positive sample); (TN) True Negative (the isolation result is negative for a negative sample); (*FP*) False Positive (the isolation result is positive for a negative sample); (*FN*) False Negative (the isolation result is negative for a positive sample).Sensitivity is the proportion of the samples that are isolated as positive among all the positive samples. For our task, it is the probability of a positive result among infected RBCs.

$$SE = TP / (TP + FN)$$

which is usually called the true detection rate . The higher the sensitivity, the less likely that an infected RBC will be missed. Consequently, an infected person is more likely to be diagnosed as sick.

Specificity is the proportion of the samples that are isolated as negative among all the negative samples. It is the probability of a negative result for a negative object.

$$SP = TN / (TN + FP)$$

The higher the specificity, the less likely that a healthy blood component will be isolated as a parasite. Consequently, a healthy person is more likely to be diagnosed as healthy. Sensitivity and specificity values of a diagnosis test should be interpreted together. Positive Prediction Value is the proportion of the positive samples of all that are isolated as positive.

$$PPV = TP/(TP + FP)$$

Positive prediction value indicates the reliability of a positive result. Negative Prediction Value is the proportion of the negative samples of all that are isolated as negative.

$$NPV = TN/(TN + FN)$$

Negative prediction value is the opposite of *PPV*. The average accuracy can be expressed as follows:

$$ACC = (TP + TN)/(TP + FP + TN + FN)$$

From the result, the method has sensitivity = 0.94, specificity = 0.98 and accuracy = 0.92. The proposed novel method offers high accuracy for true isolation of infected RBCs.

5. CONCLUSION

An approach was proposed to isolate red blood cells with consecutive classification into Leukemia parasite infected and uninfected cells for diagnosis of Leukemia. First the infected cells are separated with binary mask from uninfected erythrocytes after pre and post processing of an image. In a dependent step, we isolated the cells infected with Leukemia. Experimental results show that the proposed method yields significantly better results. The work is useful in telepathology applications and can automate the screening of Leukemia in rural areas where healthcare manpower is limited. The proposed work can be further enhanced and expanded for the automatic isolation and classification of severity of parasitemia for appropriate treatment and identify the species of parasites and all available techniques will be compared for the optimum accuracy.

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