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Automatic Segmentation of Leukocytes for the Detection of Leukemia Using a New Computing Algorithm

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Abstract

Hematological disorders refer to the diseases caused with the changes in blood cells or blood system such as Leukemia, Anemia, Malaria and Azotemia. Leukocytes are the cells of immune system derived in the bone marrow as hematopoietic stem cell. The presence of immature cells changes the granularity and geometry of leukocytes. Detection of white blood cells plays an important role in the diagnosis of diseases like leukemia. Features such as nucleus and cytoplasm area, average color co-ordinates and number of pixels in the nuclear perimeter are used. Accurate classification of human blood cells plays a decisive role in the diagnosis and treatment of diseases. Hematological disorders refer to the diseases caused with the changes in blood cells or blood system such as Leukemia, Anemia, Malaria and Azotemia. This paper explores the techniques used in the automatic segmentation of leukocytes using a new computing technique.

Keywords: Acquisition; Segmentation; Thresholding; Morphology; Soft computing; Threshold segmentation mathematical morphology; Fuzzy and cellular neural networks

Introduction

Soft Computing is a well-established paradigm where the theories with sound understanding of biological and various natural phenomena have been used for various computations. Blood is composed of blood cells suspended in blood plasma. Cells present in blood are white blood cells (Leukocytes), red blood cells (Erythrocytes) and platelets (Thrombocytes). The blood also acts as the main agent that circulates the hormones, enzymes and vitamins.

The basic immunity to the body is offered by the white blood cells, which is done by fighting against any foreign entrant. Thrombocytes (blood platelets) are fragment cells that do not have nuclei and facilitate blood clotting. Platelets have many granules and round in shape.

The presence of immature cells changes the granularity and geometry of leukocytes. The composition of WBC gives valuable information and plays an important role in the diagnosis of different diseases like Leukemia. The general steps involved in the detection of leukemia are given in Figure 1.

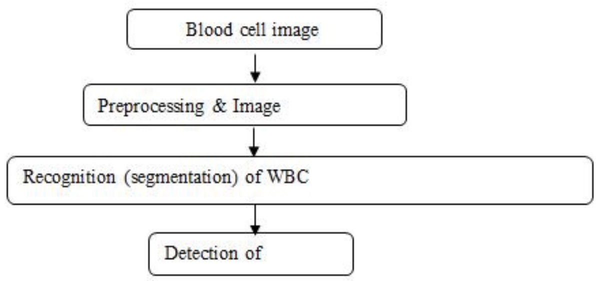

Figure 1: General steps involved in detection of leukemia.

Binary image is subject to number of erosions and dilutions. The number is set by experience. Interpretations of blood cell images with visual subjective method and image analysis mediated objective methods have their own limitations.

The development of image processing and soft computing tools makes it feasible to automate the task manually performed by the experts [1]. Hence medical image processing techniques such as image enhancement and edge detection are done prior to segmentation of white blood cells from blood smear.

Blood cell image acquisition requires 100x magnifications on the blood smear and preprocessing requires the application of frequency domain filters and edge operators. In this paper, fuzzy cellular neural networks are employed for the detection of leukemia. This proposed method combines the advantages of threshold segmentation mathematical morphology and fuzzy logic.

Threshold Segmentation Based on Mathematical Morphology (TSMM)

Automatic recognition of white cells is very challenging because there exists red blood cells and platelets besides white blood cells. To discriminate one object from the other becomes exigent due to the inconsistency of occlusion, staining reagent and illumination. Moreover, cells overlap frequently and there is a wide variation of size and shape of the nuclei and cytoplasm within the classes of cell. In order to decouple the effect of segmentation errors and to maintain redundancy still manual detection is needed in many cases.

Threshold segmentation by mathematical morphology was proposed by Xiao-Min [2]. A method based on fuzzy logic was introduced by Sobrevilla [3]. Binary threshold segmentation is done as a first step as the gray value of leukocytes is the smallest in the image.

The detailed steps are as follows:

1. Compression of the original image by pyramidal method.

2. Binary segmentation using the average gray value of the cytoplasm as threshold.

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3. Binary image is subjected to n erosions/dilations where n is set by experience.

4. Segmentation of nuclei by using shape features such as area and round degree.

5. Restoration of original image by setting the proper size of window and recover the original image.

The idea of threshold segmentation mathematical morphology (TSMM) is to subtract the background first and then eliminate red blood cells and other small disturbing objects. Moreover it only applies to gray images, especially to those images in which gray value of the nuclei is smallest. However, inconsistent illumination and a different staining reagent can result in diverse microscopic images for the same microscopic field.

Devoid of a proper transformation method, the color image may also suffer loss of information when transformed into corresponding gray image. The threshold value used in step 2 is the statistical result of all pixels in cytoplasm regions. The parameter in step 3 is also determined by human experience. Such drawbacks make this method very complicated for practical applications.

Fuzzy Logic Method

The fuzzy logic method proposed assumes that the blood cell image consists of two regions. First one is the interest region. Second one is the on interest region which contains the back ground, contour of leukocytes as well as the red blood cells [3]. Regions having a very light gray level correspond to background which also has homogenous texture. Regions with light medium gray level and having homogenous texture correspond to red blood cells. Contours of white blood cell have no homogenous textures. By this method fuzzy rule base was determined. Unlike TSMM, fuzzy logic method takes gray and homogeneity information into account. But it involves the determination of more parameters and functions by statistics. This method also faces difficulties in color conversion and illumination/staining inconsistence. More over fuzzy logic method is better suited only for grey images with clear differences among white blood cells, red blood cells and background.

Segmentation Based on Fuzzy Cellular Neural Networks (FCNN)

In this paper, a successful attempt has been made to combine the advantages of threshold segmentation based on mathematical morphology as well as fuzzy logic. Fuzzy cellular neural networks have inherent connections with mathematical morphology [4]. Fuzzy logic has been introduced into the cellular neural networks without destroying its local interconnection features.

The structure of Fuzzy cellular neural networks is shown in Figure 2. The output of a neuron is connected to the input of every neuron in its r × r neighbourhood. Similarly inputs of a neuron are connected to the outputs of every neuron in its r × r neighbourhood. Each neuron in the Fuzzy cellular neural networks performs as follows.

The expression for the state of cell C_{ij} is given by:

$$C\frac{dx}{dt} = -\frac{1}{R_x}x_{ij}$$
$$+\sum_{ckl\in Nr(i,j)} A(i,j;k,l)$$
$$+\sum_{ckl\in Nr(i,j)} B(i,j;k,l)$$

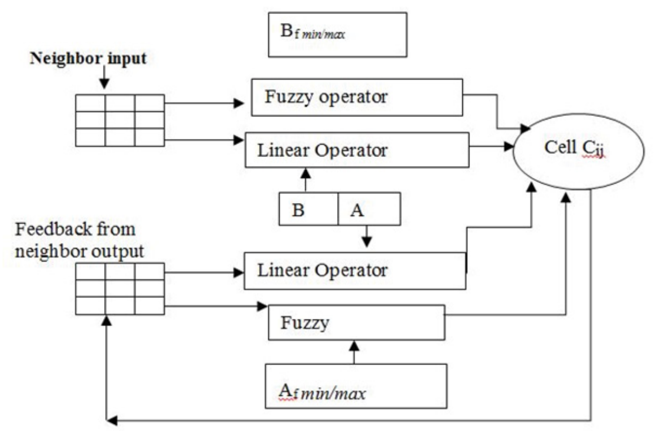

Figure 2: Fuzzy cellular neural networks.

$$+\wedge_{(ckl\in Nr(i,j)} \left(Af_{\min}(i,j;k,l)+y_{kl}\right)$$
$$+\vee_{\wedge(ckl\in Nr(i,j)} \left(Af_{\max}(i,j;k,l)+y_{kl}\right)$$
$$+\wedge_{(ckl\in Nr(i,j)} \left(Bf_{\min}(i,j;k,l)+u_{kl}\right)$$
$$+\vee_{\wedge(ckl\in Nr(i,j)} \left(Bf_{\max}(i,j;k,l)+u_{kl}\right)$$

The expression for the output state of C_{ij} is given by |

$$y_{ij} = f\left(x_{ij}\right) = \left(\left|x\_ij+1\right|-\left|x_{ij}-1\right|\right)/2$$

The constraint conditions are

$$|x_{ij}-(0)|\le 1;\ |u_{ij}|\le 1;$$
$$\mathrm{A}(i,j,k,l) = A(k,l;i,j)$$
$$Af_{min}(i,j;k,l) = Af_{\min}(k,l;i,j)$$
$$Af_{max}(i,j;k,l) = Af_{\max}(k,l;i,j)$$
$$1\le i\le m,\quad 1\le j\le n$$

Where u denotes the input variable and x denotes the state variable and y denotes the output variable; $Af_{min}(i,j;k,l)$ denotes fuzzy feedback MIN template; $Af_{max}(i,j;k,l)$ denotes fuzzy feedback MAX template; $Bf_{min}(i,j;k,l)$ denotes fuzzy feed-forward MIN template; $Bf_{max}(i,j;k,l)$ denotes fuzzy feed-forward MAX template.

Λ represents fuzzy and **Λ** represents fuzzy OR. The output range of FCNN is **[-11]** representing binary image and **[01]** representing a gray image.

The Proposed Computing Algorithm

Fuzzy cellular neural networks are implemented using various morphological operators such as erosion dilation, opening and closing [4]. Suppose M, X and Y represent the mask, the input mage and the output image respectively. The parameter for erosion is:

Y=X θ M; A=0, B=0,

A_{fmin} = undefined; B_{fmin} = – M

A_{fmax} = undefined; *Bfmax* = undefined

Similarly the parameter for dilation is

$$Y = X \underset{\oplus}{M}; A = 0, B = 0,$$

A_{fmin} = undefined; B_{fmin} = M

A_{fmax} = undefined; $B_{fmax =}$ undefined

The step by step procedure for the algorithm is as follows:

S (1) The images were compressed using pyramidal method to compress the R- image, G-image, and the B-image respectively.

S (2) The color image was transformed from (R, G, B) to the hue element. Let *(r,g,b)* represents a pixel in a RGB image (Figure 3).

$$(r, g, b) \in [0, 1, ...255],$$

$$\mathrm{v} = \min(r, g, b); u = \max(r, \mathrm{g}, \mathrm{b});$$

$$\mathrm{r}' = \frac{g-b}{v-u}, \mathrm{g}' = \frac{b-r}{v-u}, b' = \frac{r-g}{v-u}$$

$$h' = \begin{cases} r', r = \max(r, g, b) \\ 2 + g', g = \max(r, gb) \\ 4 + b', b = \max(r, gb) \end{cases}$$

h=60h'

S (3) The hue image was normalized with the formula:

$$H = \begin{cases} H - h, H - h > 0 \\ H - h + 240, H - h \leq 0 \end{cases}$$

Where h is the peak value in the histogram of the hue image.

S (4) The hue image was linearly contrasted with the formula:

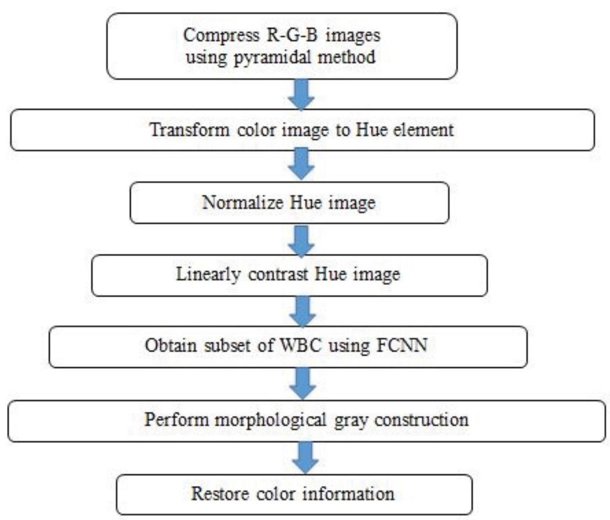

Figure 3: Steps involved in the proposed algorithm for the detection of leucocytes.

$$g(i, j) = \left(\frac{y2 - y1}{x2 - x1}\right)\left[f(i, j) - x1\right] + y1$$

Where x_1 and x_2 are the minimum and maximum values in the image, and y_1 and y_2 are the minimum and maximum values in the contrasted image.

S (5) Subset of white blood cell was obtained the fuzzy cellular neural networks with the given parameters:

$$A = \begin{bmatrix} \frac{1}{9} & \frac{1}{9} & \frac{1}{9} \\ \frac{1}{9} & \frac{1}{9} & \frac{1}{9} \\ \frac{1}{9} & \frac{1}{9} & \frac{1}{9} \end{bmatrix}, B = 0,$$

A_{fmin} = undefined; B_{fmin} = undefined

A_{fmax} = undefined; $B_{fmax =}$ 0; R_x = 0.

S (6) Using subset of white blood cell as the mark image and hue image as original image, morphological gray construction was done based on fuzzy cellular neural networks regarding the.

S (7) Color information inside the white blood cell regions was restored.

It has been observed that the fuzzy cellular neural networks are applicable to color images as well apart from gray images. Three FCNNs were constructed for R-image. G-image and B-image. A gray image needs less processing time and storage capacity than color image of the same size. Some useful information should not be lost during color conversion.

For this reason, we use HLS (hue-light-saturation) model rather than traditional color conversion with the function D = 0.3R + 0.59G + 0.11B.

After observing images from step 4, it is found that leukocytes show smaller gray value than erythrocytes and the leukocytes are in round shape because of the nuclei inside, whereas the erythrocytes are in ring form because of no nuclei inside.

The subset of white blood cell regions in constructed to make use of the gray information and the structural knowledge for the fuzzy cellular neural networks. With threshold segmentation mathematical morphology, the contour of white blood cells is disturbed; whereas in FCNN yields the white blood cells with complete contour. Sometimes an image can contain two white blood cells where one is much larger than the other. So there is a possibility of smaller one getting omitted in case of TSMM. With adaptive FCNN these disturbers are eliminated. The contour of the white blood cells has to be perfectly preserved for further feature extraction for the detection of hematological disorders like leukemia. Finally, the original image inside white cell regions is restored [5-13].

Experimental Results and Comparison

From the analysis of results shown in Figures 4 and 5 the proposed detection algorithm is found show three advantages.

1. All the white blood cells are detected since it has made use both the structure knowledge and color information.

2. Each detected cell is nearly complete with perfect contour

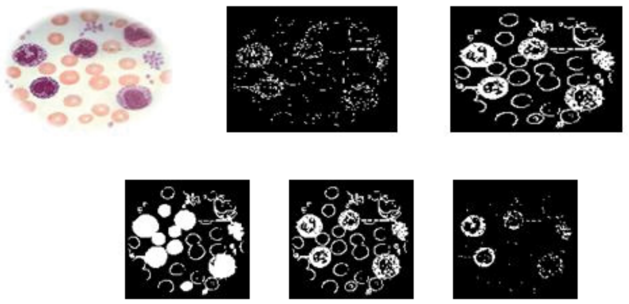

Figure 4: Results of TSMM.

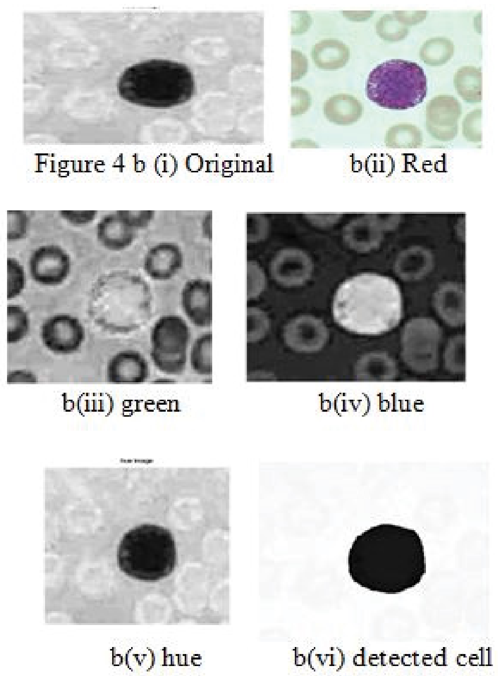

Figure 5: Results of FCNN.

Accuracy index	TSMM	Fuzzy Logic	FCNN
D1	0.92	0.94	0.97
D2	0.94	0.93	0.98
D3	0.727	1.12	0.946

Table 1: Comparison of TSMM, FLM and FCNN- detection of leukocytes.

because of the morphological gray construction.

3. The proposed algorithm has stronger adaptability to staining and illumination because of the proper color transformation.

In this work, these three methods TSMM, Fuzzy logic and FCNN were applied to twenty microscopic images under various conditions of illumination and staining. TSMM and Fuzzy logic methods are only applicable to gray images. It was necessary to transform the color images into gray ones using conversion.

D = 0.3R + 0.59G0.11B.

Results are shown in Table 1. In this Table D_1 denotes the ratio of number of detected white blood cells to the existing number of white blood cells. D_2 denotes the ratio of the number of white blood cells to the number of detected white blood cells. D_3 denotes the ratio of pixels in the detected white cells and to the existing pixels in the same white blood cells.

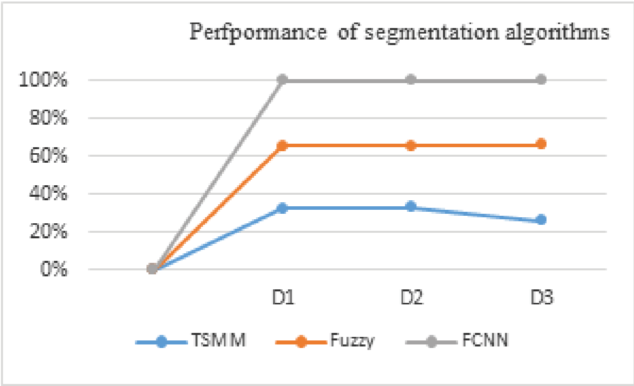

Figure 6: Comparison of performance of various segmentation algorithms.

When D_1 is equal to one, it demonstrates that we can detect all white blood cells completely. If D_2 is equal to one, it demonstrates that there is no false detection. When D_3 is equal to one, it demonstrates the classification accuracy is good. From the table we can infer that D_1 value of TSMM and Fuzzy logic is acceptable.

However, these methods could not ensure that the contour of the detected cell is complete [2]. Moreover, these methods suffer from inconsistency in staining and illumination. These disadvantages were overcome by employing proposed algorithm based on fuzzy cellular neural networks because it combines the advantages of other two methods while avoiding their disadvantages (Figure 6).

This can be easily implemented in hardware. It is also obvious that the algorithm has stronger adaptability and superior performance in real time image processing with high running speed comparatively with other methods employed for the recognition of leukocytes for the detection of leukemia.

Conclusion

After carefully analyzing the disadvantages of existing two methods a new detection algorithm based on fuzzy cellular neural networks was applied for the recognition of leukocytes for the detection of leukemia. With this new algorithm, it was to detect all most all the white blood cells, and each detected cell was complete. Its adaptability was strong and execution speed was high. However, the analysis of results presented here was only the first step in the exploration of automatic recognition systems. The challenges ahead are distinguishing nucleus from cytoplasm and improving the FCNN to have better performance. So it gives a scope for future work in exploring other soft computing algorithms for the automatic recognition of leukocytes, classification of the leukocytes as neutrophils, basophil, eosinophil, lymphocyte and monocyte, and the identification of leukemia using new developed feature extraction classifiers integrating the features of other evolutionary and intelligent computing techniques.

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