Iraqi Journal for Computer Science and Mathematics

Journal Homepage: http://journal.esj.edu.iq/index.php/IJCM

e-ISSN: 2788-7421 p-ISSN: 2958-0544

Blood Cell Microscopic Image Classification in Computer Aided Diagnosis Using Machine Learning: A Review

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DOI:https://doi.org/10.52866/ijcsm.2023.02.02.002

Received November 2023; Accepted January 2023; Available online February 2023

ABSTRACT: Blood cell detection can be considered as a gold standard key in diagnosing blood disease and can produce an automatic report to hematologists and doctors. Blood cell detection can consider a challenging task due to high number of overlapped cells per image, non-illumination level, the variety of staining process, and variations in cell densities among platelets, white blood cells and red blood cells. Traditional procedure of blood cell detection requires pathologist effort and time. In computer aided diagnosis system, machine learning and deep learning techniques become the practical way to automate the procedure of diagnosing, classify microscopic blood cells, and increase the accuracy and speed of the procedure. This paper provides a review of the blood cell detection and classification process, including white blood cells, red blood cells, and platelets and their characteristics using machine learning techniques. We also have detailed the dataset of microscope blood cell. The previous works have been divided into four categories based on the models, output, including pre-processing, segmentation, feature extraction and classification. Then, we discuss the challenges that face these methods and suggest the potential future techniques.

Keywords: Blood cell, detection, review, computer aided diagnosis, and machine learning.

1. INTRODUCTION

Classification of blood cell microscope image is an important step in Computer Aided Diagnosis (CAD) system and this process helps pathologists in diagnosing various types of diseases such as anemia, thalassemia, cancer, and other diseases. In clinical diagnosis, blood cell consists of bone marrow then develop as stem cells and mature into one of the types of blood cells. Blood cells consist of three types: Red Blood Cell (RBC), White

Blood Cell (WBC) and Platelets, as shown in Fig.1. Recently, researchers have attracted in development and designing different procedure for automated medical images analysis by combining advanced image processing, computer graphics techniques and artificial intelligent [1]. As a result, there are many automatic medical diagnosis systems that used to help the pathologist to prepare the report to doctor in order to diagnose disease of blood, particularly in term of WBC and RBC human that provides important information to pathologists. RBC is also known an erythrocyte and the function of RBC is carrying oxygen and transports it to all cells of the body. Blood cell contains 48% from RBC. WBC is also known leukocytes and it contains one nucleus or more segmented nuclei.

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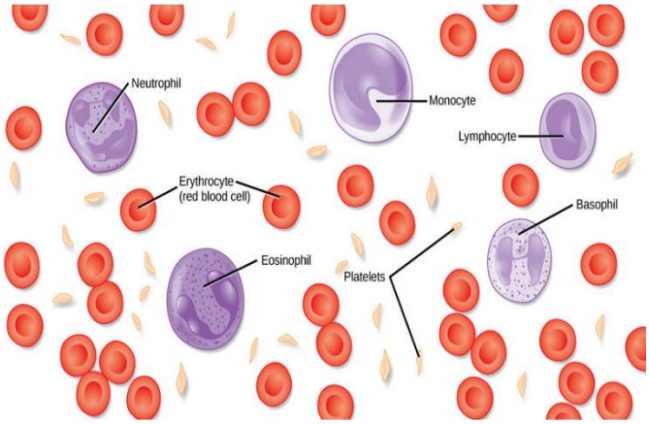

FIGURE 1. Blood Cell Structure. [2]

They are larger than RBCs, and the diameter between 6 to 20 µ, and 4000–10000 /ul from blood may contain WBC. It plays an important role in defending the body against diseases, which part of the immune system. The final type is platelets which contribute to the process of blood clotting in case of bleeding [3]. Experts can segment and classify the blood cells based on the morphological features, including shape, size and nucleus position whether or not they contain a nucleus, color of nucleus and cytoplasm [4]. Previously, the pathologists used the traditional procedure of blood cell analysis-based microscope properties. The traditional procedure requires an expertise to manually segment and classify the cells which is daunting, time-consuming and qualitative process [5]. In addition, the existing methods suffers from inconsistency, poor reliability diagnosis, and inaccuracy that cause of a wrong diagnosis diseases. In order to overcome the issue, artificial intelligent and image processing techniques are, increasingly recognized as a very useful techniques for the automated blood cell analysis. The technique of blood microscopic smear image analysis in CAD system requires six main steps: 1) Image acquisition, 2) Image enhancement, 3) Segmentation, 4) Features Extraction, 5) Classification and 6) Evaluation of class type, as shown in Fig.2.

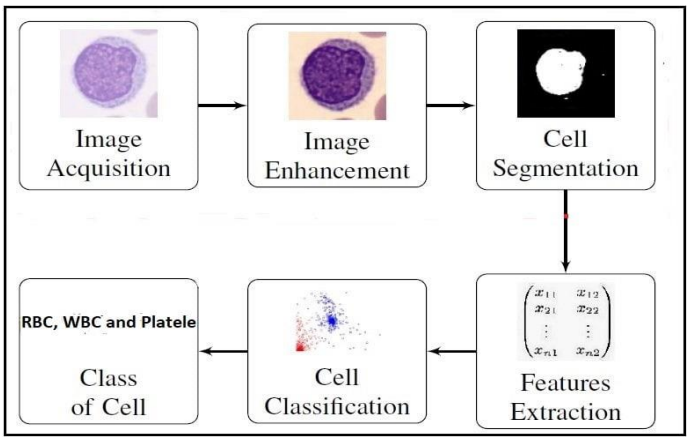

FIGURE 2. An Automatic Analysis of Blood Cell Process [6].

The earliest works in classification and recognition of blood field date had returned back to the early 1990's, including [7] [8]. Few works have done in this field due to finite using of digital microscopes in pathology and producing a small number of databases. Recently, advances research hava done in the classification and detection blood cell and its types, for example, blood cell and types of cancer analysis [9], and leukemia blood cell image detection [10] [11].

Recent studies have been applied a variety of classification and detection approaches used to automated classifying blood cell, especially RBCs, WBCs[12] [13] [14]. However, Recent studies have shown [15] [16] [17] [18], that machine learning algorithms make more efficient and accurate alternatives method, when dealing with complicated blood cell images. Among these machine learning algorithms, Support Vector Machines (SVMs) have been common used for blood cell classification [19], [20], [21].

This paper aims to discuss problems that face blood cell detection using machine learning techniques in CAD system. The contributions of this paper are:

1. Study the effects the structure of microscopic blood cell and the characteristics for detecting the WBCs, RBCs and palates in CAD.

2. Check the machine learning methods that were employed to handle microscopic blood cell under different conditions.

3. Discuss the exciting techniques that employed to handle with features as well as the effectives performance on machine learning and deep learning.

4. Describe recent investigations regarding publicly available datasets and discuss of the architectures that are used for data augmentation.

5. Present potential techniques that can help the pathologists' researchers in a digital laboratory to design and develop CAD software.

This paper is organized as follows: a structure of blood cell types and characteristics is presented in Section-2 Section-3 describes challenges of blood cell detection , describes the dataset of microscopic blood cell images in Section-4, related work of blood cell application is explained and future work are presented in Section-5 and Section-6, respectively.

2. STRUCTURE OF BLOOD CELT TYPES AND CHARACTERISTICS

2.1. Red Blood Cell (RBC)

RBC is also known erythrocytes and it works for transferring an oxygen from human lungs to human body's tissues. Human tissues can production an energy with the oxygen and release a waste, it is known carbon dioxide. It has the shape of a "flat disk or ball-shaped", as shown in Fig.3(a), which is round with an indentation in the center, but it is not hollow. RBC does not have a nucleus which allowing to change shape, and can move throughout human body easier unlike WBC [22]. The life of RBC is about 120 days. However, Iron that found hemoglobin, can be extracted from RBC by the liver and spleen, and the remaining heme can be excreted as bile pigments by the liver. The cells are about 7 µ in diameter. Fig.3 shows an image of RBCs at higher magnification that the shape of cells is clear at this magnification [23].

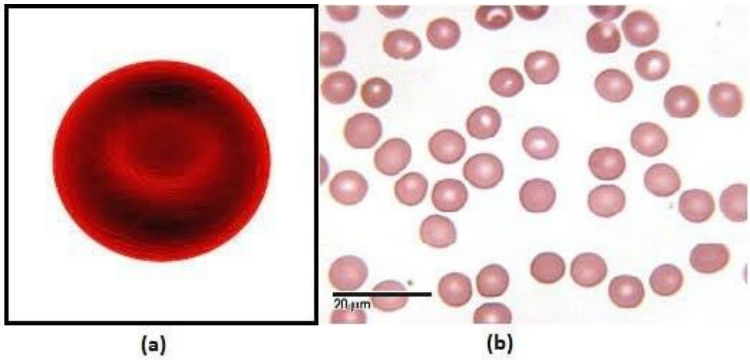

FIGURE 3. (a) Represents RBC Shape and (b) RBCs at Higher Magnification. [23]

2.2. White Blood Cell (WBC)

WBC is less common than RBC. It also known leukocytes. There are three types and seven sub-types of WBCs, as shown in Fig4. WBC is divided into three main types: "Granulocytes", "Monocytes", and

"Lymphocytes". Each main type can be divided into sub-types. "Granulocytes" classified into Band "neutrophils", "Basophils" or "Eosinophils". "Monocytes" classified into "Macrophages" or "Dendritic" cells, and "Lymphocytes" classified into "B- lymphocytes" or "T-lymphocytes". The WBC classification is based on using light microscopy and common staining process whether it can help distinguishing granules in their cytoplasm. It can be difficult to differentiate leucocytes types in blood smears. Pathologists can identify between types of WBCs types using morphological features, such as the shape of the nucleus, and compare their size unlike other blood cell, such as RBCs and platelets [6, 24].

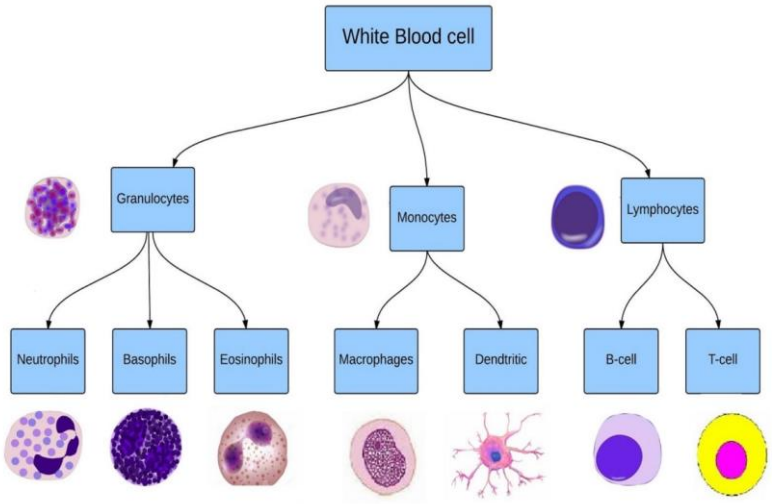

FIGURE 4. Structure of WBC [24].

2.3. Platelets

Platelets are the smallest component of blood cells, due of its small size, can be only seen it with a microscope. Platelets are shaped as small in their passive form. The blood vessel, when it is damaged, will send a signal. A normal platelet count ranges from "150,000 - 450,000" platelets per microliter of blood. If person has platelets count more than "450,000" platelets, the condition is called "thrombocytosis"; otherwise has less than "150,000" platelets, it is called "thrombocytopenia". Platelets have a round or oval shape in blood, a pale blue cytoplasm and measure 1.5–3 µ in diameter, as shown in Figure-5. They contain both dense granules and alpha granules. Alpha granules can appear on routine blood smears and the dying of them is fine purple granules [25].

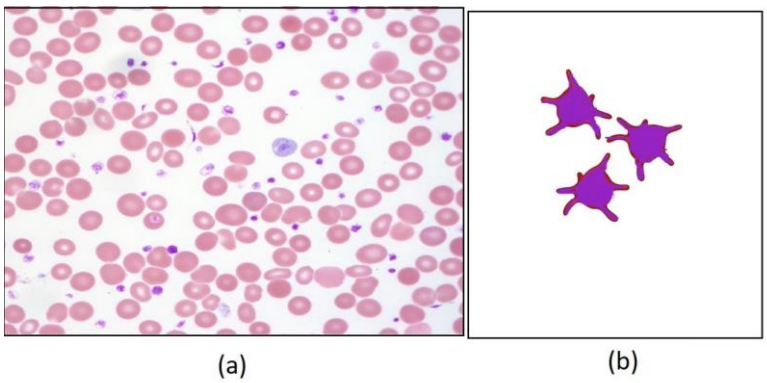

FIGURE 5. (a) Blood Cell Microscopic Image has Platelets and (b) Platelets have Pale Blue Cytoplasm. [25]

3. CHALLENGES OF BLOOD CELL DETECTION

To overcome the challenges of blood cell detection from previous work, we detail them as below points, including different staining techniques, difference in illumination, variation stages of maturation, cell morphology and poor image quality.

1. Different staining techniques: difficulty distinguishing between blood cells components due to different staining processes especially segmentation method based on colour, because some different staining processes lead to cell deformation.

2. Non-illumination: the intensity of the microscope light can affect the appearance of the image. Different types of lighting leads to differences in the distribution of illumination and color of the image and causes difficulty in uniformity of illumination and distinguishing between blood cells.

3. Variation in maturity stage: peripheral blood smears can be divided and matured to form new blood cells, which are RBCs, WBCs, or platelets. These stages of maturity can be complicated and difficult in the status of defining separate criteria for ever blood cell components, specifically platelets because they are small.

4. Cell morphology: the shape and size of the blood cell components differ from each other. It is difficult to trace the morphological changes of the blood cell components due to the deformation of the cells, difficulty in identifying cells arises when they merge, divide, or when borders are formed concave, convex, or have acute angles. In addition, some cells contain cytoplasm and nucleus and others are not.

5. Techniques are applied to a small or limited database in CAD and they could not be as active when applied to a larger, more popular, or available the public database. Researchers have used hospital or research centre databases to deal with specific problems in terms of segmentation or classification process under specific conditions. Public databases, such as [36], [41], [26], [27] are more public and consists examples of most conditions, thus , they can be used to comparison various techniques.

6. Image quality: using poor and different cameras can lead to image noise and contrast changes.

4. DATASET OF MICROSCOPIC BLOOD CELL IMAGES

Dataset of microscope images refers digital image possessing through a microscope or such device to display zoomed image of a cell. An image which is also taken on a microscope, but is only a little enlarged, usually little than 10 times. It is also captured under various conditions of various illumination, overlapping, staining process, diseases, noises, changes in the cell topology and maturity stage. These conditions have a significant impact on blood cell segmentation and classification. Blood disorders and immune system-related diseases, such as leukemia, anemia, autoimmune anemias and allergy, can affect the segmentation and classification accuracy [28]. There are private datasets and public datasets. The private dataset is always collected from a hospital, medical center, research-center related to university or pathology. It is not free access and the evaluation measurement is difficult. This dataset may be related-to a specific problem need to be solved. Some researchers use only private dataset or combining it with public datasets as done [29]. Most researches prefer using public datasets, which are free access, such as ALL-IDB2, BloodSeg, Leukocytes, Kaggle, JTSC Database, Raabin-WBC and CellaVision DM96 [30]. Those datasets specifically designed to evaluate and the compare among segmentation and classification techniques. They contain challenging images under different conditions.

5. RELATED WORK OF BLOOD CELL APPLICATION

Many automated techniques have been proposed to segment, classify and detect blood cell microscope images in CAD system, and addressed the challenges that face microscope image analysis. These techniques include image processing, signal processing, machine learning and deep learning techniques.

5.1. Preprocessing Phase

The pre-processing step is used in blood cell image analysis to enhance the quality of microscope images and increase the accuracy of the segmentation and classification processes. This step eliminates the background noise and increase the visibility of cell (foreground). The background noise can be occurred due to different factors,

such as poor quality images, non-illumination, and inaccurate camera sensor [31]. There are different factors affect illumination of images, including microscopic images taken under a various lighting source of different microscopes types. Different steps have an effect on the image pre-processing such as different illumination, color distributions, maturity stage of the cells, staining process, and overlapped cells. Despite using different techniques of capturing images for blood cell identification, the contrast process is one of the complicated task in CAD system that requires an enhancement due to non-illumination condition that cause noise [6]. In [32], they used several methods for preprocessing, such as the median filtering method, conversion color (RGB to HSV) to initialize the cells and thresholding method to get the pattern of blood cells. These used to enhance the foreground and remove the background information. The reference of [33] using morphological image processing to remove dots and noise by accounting for the form and structure of the blood cell image. Then, they used edge detection, such as Sobel and Canny filters to detect, or identify boundary of cell of a similar size and color.

5.2. Segmentation Phase

Segmentation of blood cells is one of the most significant steps in diagnose diseases such as anemia, cancer malaria, etc. Many automated techniques have been proposed to segment blood cell and addressed the challenges of segmentation process, specifically RBC and WBC segmentation. These techniques include: Fuzzy C Means (FCM) algorithm was proposed for the segmentation of WBCs in [34]. The method was applied to 1000 images stained with May-Grunwald-Giesma. Dataset were obtained from "Southern Illinonois University School of Medicine's online blood cell sample images", which considered private data set. This method has less computational experience and is more reliable. It produced good results of 98% in identifying WBCs. However, due to the complicated structure of blood cell components, they faced a problem in segmentation RBCs that were damaged or distorted due to staining process. The research of [35] proposed an intelligent system for segmenting blood cell by using Neural Network method by using private dataset consisted of 360 cells from 90 patients. The proposed method produced good results regardless of cell size and shape using data augmentation by changing size of original image to 70 × 70. In [36], they used K-mean clustering and thresholding technique for segmentation of blood cell. The proposed method applied on 78 blood cell images and achieved an accuracy of 95.5% with Giemsa stained. Edge detection and watershed also employed for separating overlapped cells. Recently, deep learning techniques have been used in segmentation of blood cell components to yield more accurate results. Convolutional encoder-decoder and VGG-16 was proposed in [37] to solve segmentation problem of whole-slide blood cell. The results showed with accuracy 97.45%, 93.34%, and 85.11% for RBCs, WBCs, and platelets, respectively. In this method, they used ALL-IDB1 dataset composed of 108 images contains 39000 blood elements. These images were taken with various zooming of the microscope ranging from 300-500. However, there were some cells that did not segment properly due to non-illumination in images. Deep learning semantic segmentation - cutting-edge technology was employed in [38] for segmentation RBCs and WBCs in blood smear images. The model yielded accuracy of 89.45%. Deep learning semantic segmentation cutting-edge technique was employed for segmentation RBCs and WBCs in blood smear images in [38]. The overall accuracy of the model yielded 89.45%. Some cells did not segment due to overlapped cells. Many techniques have been proposed to segment blood cell component. In [39], FCM was also used for segmentation of blood cells with an optimization strategy based on Slap Swarm. Initially, graph equation was used to process images and remove disturbing contents. Then, features had been extracted by using a Gray Level Co-occurrence Matrix (GLCM), which helps increase the proposed detection algorithm performance. Most research focus on segmentation of WBCs based on nucleus and cytoplasm due to different morphological properties of WBC, that help to identify WBC types among other components of blood cell. Other research tends to segment only RBCs [36], [40] while few methods have proposed to segment platelets due to complicated shape and morphology features, such as circularity, perimeter, spread and area[41], [42].

Table 1. Summary of Segmentation Methods

References	Data Set	Method	Accuracy	issues
(P. K. Mondal, U. K. Prodhan ,at al)[34]	1000 images of blood cell stained with May-Grunwald-Giesma	fuzzy C means segmentation algorithm	98%	hey faced a problem in segmentation RBCs that were damaged or distorted due to staining process
(A. Khashman) [35]	Dataset consisted of 360 cells from 90 patients.	Neural Network	99.17%	Use small data set
(S. Savkare and S. Narote,et al) [36]	Applied on 78 blood cell images	K-mean clustering and thresholding technique	95.5%	separation of overlapping cell suffers from over-segmentation
(M. Shahzad, A. I. Umar, et al) [37]	ALL-IDB1 dataset composed of 108 images contains 39000 blood elements.	Convolutional encoder-decoder and VGG-16	97.45%, 93.34%, and 85.11% for RBCs, WBCs, and platelets, respectively	some cells that did not segment properly due to non-illumination in images
(T. Tran, O.-H. Kwon, et al) [38]	Not mention this paper for data set	Semantic segmentation cutting-edge technology	89.45%	Some cells did not segment due to overlapped cells.

Table-1 has shown that the method and accuracy results of the segmentation of blood cell types. The research of using Neural Network in [35] achieved the highest accuracy, but they used small data while Convolutional encoder-decoder and VGG-16 [37] has achieved high accuracy segmentation of the three types of blood cells with the using large data. The FCM was used for WBCs segmentation properly but faced a problem in segmentation RBCs due to being damaged by the staining process. K-mean clustering[36] , and Semantic segmentation cutting-edge technology [38] obtained good results and solved the problem of overlapping of some cells. However, all previous methods had not employed to segment platelets due to small size.

5.3. Feature Extraction and Classification Phase

In CAD system, blood cells and their components may have five biological morphological forms that can play a key role for human experts in distinguishing the blood cells types and using image processing analysis to detect these forms. Biological morphological features are shape, complex structure, size, pattern and color. For example, in [43], morphology feature such as shape and boundary has been used with deep learning to classify RBC. The results have shown highly classification of RBCs rate and less processing time. However, the performance of this method needs to be improved because not all RBCs could be trained and learned due to the variety and irregularity of RBCs morphology due to staining process. A method was proposed in [26] using the K-means algorithm to classify WBCs into four types “neutrophil”, “lymphocyte”, “monocyte”, and “eosinophil”. Features were extracted area, circularity, eccentricity, normalized parameter, and solidity. They used K-means clustering to classify WBCs. The results carried out depending on the choice of type of features and the accuracy value by circular feature was 67% while accuracy value by eccentricity feature was 43% it was less valuable than the features. A classification method was proposed in [44] to classify red blood cells using the K-Nearest Neighbor technique (KNN) and Naïve Bayes algorithm. The proposed method firstly segmented RBCs by using two method fuzzy C-means and adaptive (local) thresholding. Then, the morphological factors were used to remove distortions and unwanted things. The features were extracted, including minor axis, aspect ratio, area, perimeter, form factor (metric value), eccentricity and solidity of each cell. The extracted features were used for classification cells by using both Naïve Bayes classifier and KNN, the accuracy result achieved by KNN was 98.87%. In research of [45], they used Convolution Neural Network (CNN) algorithm for classifying WBCs, 21 images are entered and classified using three CNN models AlexNet, GoogLeNet and ResNet-101. The result had shown that AlexNet

model produced better result than GoogLeNet and ResNet-101 results and the overall sensitivity, specificity and accuracy were 89.18%, 97.85%, and 96.63% respectively. However, the images were not sufficient to give wide perspective about the result. Also, the algorithm only worked under illumination condition. In [27], a CNN method was proposed to classify WBC into four groups: lymphocytes, monocytes, neutrophils and eosinophils. Regions with Convolutional Neural Networks (R-CNN) network was applied identification of the region of interest of WBCs to separate binuclear cells from mononuclear cells, then used two parallel convolutional neural networks with MobileNet model to identify subcategories. This method achieved accurate results. In [46], the CNN method-based Double Convolution Layer Neural Network (DCLNN) was used to classify white blood cell types. The proposed method was applied to a data set containing 13,000 images of all types of WBCs. It achieved results with an accuracy of 93% for the classification of two classes mononuclear and polynuclear , and accuracy of 83% for the classification of four classes neutrophil, lymphocyte, monocyte, and eosinophil. This method produced better results than SVM and Naive Bayes methods. In [47], CNN was used to classify only WBCs, using ResNet and Inception model, where ResNet achieved results with an accuracy of 97% higher than Inception. They applied on 11200 images and they were poor quality. The authors enhanced the images using saturation and contrast adjustment. In [48] was use BCNet, a framework based on deep learning, artificial intelligence, was used Classification of WBC using a transfer learning strategy and tested with three optimizers for ADAM, RMSprop, and (SGD). It achieved the highest accuracy with the RMSprop optimizer at 98.51%. The BCNet model achieved higher accuracy when compared with DenseNet, ResNet, Inception, and MobileNet in terms of time and results. It was applied to a set of general data obtained from the "Barcelona Medical Clinic" containing 17092 images of healthy people. Deep neural network “via discriminative region detection assisted feature aggregation” (DRFA-Net) has been proposed in [49] for WBC classification. DRFA-Net used an adaptive feature enhancement module to refine multi-level deep features. They used Rabin-WBC database. This work did not focus on accurate WBC segmentation, it only used the WBC detection module to locate the discriminative region for final classification. Thus, it did not require any other post-processing technique for refining the detection results. The overlapped cells are the issues that could not be solved in this work.

Table 2. Summary of Features Extraction and Classification Methods

References	Method	features	Accuracy	Issues
(M. Jiang *et al*.,) [43]	quantitative phase imaging (QPI) technology was combined with deep learning	Including shape and boundary	97.3%	RBCs morphology due to staining this issue could not be trained and learned all RBCs
(T. Rosyadi, and B. Achmad et al)[26]	K- means algorithm	Including area, circularity, eccentricity, normalized parameter, and solidity.	by circular feature was 67% while accuracy value by eccentricity feature was 43%	Use only for classification Type WBCs
(C. Patgiri and A. Ganguly) [44]	K-Nearest Neighbor technique (KNN) and Naïve Bayes algorithm.	Including minor axis, aspect ratio, area, perimeter, form factor (metric value), eccentricity and solidity of each cell.	the accuracy result achieved by KNN was 98.87%	_____
(M. J. Macawile, V. V. Quiñones et al) [45]	CNN algorithm with three models AlexNet, GoogLeNet and ResNet-101	_____	89.18%, 97.85%, and 96.63% respectively.	due to illumination this issue could not be trained and learned all cells
(C. Cheuque, M. Querales, et al) [27]	R-CNN	_____	98.4٪	Used small data set

(M. Habibzadeh, M. Jannesari et al) [47]	CNN algorithm with two models ResNet and Inception model	_____	97% with ResNet	Poor quality for image data Set
(C. Chola et al) [48]	BCNet	_____	accuracy with the RMSprop optimizer at 98.51%	_____
(P. Tiwari et al) [46]	CNN method-based (DCLNN)	_____	It achieved results with an accuracy of 93% for the classification of two classes and accuracy of 83% four classes	_____

The Table-2 has shown that the methods and accuracy obtained results of the features extraction and Classification using KNN [44] achieved the high accuracy with the use of extracted features to classify only RBCs. R-CCN in [27] has also achieved high accuracy for classifying only WBCs types. CNN in [45] has achieved results for classifying blood cell types with less accuracy with the use of three models AlexNet, GoogLeNet and ResNet-101, quantitative phase imaging with deep learning with features extraction, shape and boundary to classify blood cell achieved good accuracy despite exposure RBCs on the staining process. Also, using CNN with ResNet in [47] achieved the highest and solve problems of poor quality of image.

6. DISCUSSION AND FUTURE WORK

Recently, numbers of research paper have been published in the area of hematology microscope images using machine learning and deep learning techniques focusing on segmentation and classification field. Few studies have been done in blood cell segmentation and classification area while other open research areas have characteristic challenges, which can be addressed in future work. One of the most important issues is the lack of benchmark and standard evaluation assessment. Some proposed methods from research literature review [37],[36], [41],[45] have been used public datasets because the researchers can access to these datasets and can evaluate to get benchmark while few studies have used their own private datasets [34]. Some databases have been illustrated using various applications by different people who do not work in field of pathology. As a result, it is a challenging task to evaluate and compare different studies based on different annotation. To the best of authors' knowledge, there is no benchmarking dataset, the researchers used public datasets, various evaluation and performance metrics, different programming environment, and various CPU time performance. For benchmarking dataset, it is necessary to prepare programmable environment and build benchmarking datasets as done in research [50, 51] which used benchmark dataset. Most works have been tended to segment and classify WBCs and RBCs separately or together due to different structure between them. WBCs have different shapes and size, and also have cytoplasm and one or more nucleus. Also, different types of WBCs can be found in the blood while one type of RBC exists. Consequence, CAD system can be easily differentiated between WBCs and RBCs as done in [14], [19], [21], [24], [32], [32]. For segmentation and classification platelets, few studies have done in this filed due to small size of platelets. To the best of authors' knowledge, there is no works in CAD system focus on classifying blood cell into three types: RBCs, WBCs and platelets. The previous works focus on detection and classification one type.

Many machine learning techniques have been proposed for segmentation and classification of blood cell components. One of these methods (FCM) used an automatic model to generate segment WBCs. It was achieved high accuracy. However, this method was designed to work specific dataset and segment only WBCs without segment other components of blood. A CNN method was proposed in [27] to classify WBC into four groups. In spite of the high-performance accuracy of this approach, it was still not implemented under real-time applications due to its complication in terms of quickness and memory space. It was not considered the illumination and overlapped condition. For example, supervised classification of WBCs in [47] has been proposed to classify the cell into their four primary types including "Neutrophils"," Eosinophils", "Lymphocytes", and "Monocytes" using pre-trained deep learning models: ResNet and Inception. The results have display that DL methods achieved high-accurate performance, rapid processing time and improved CAD results. However, at this point in time, DL

techniques to segmentation and classification of blood cell components problem are still in the early stages. Examples are in [38] which used deep learning semantic segmentation-cutting-edge technology is employed to blood cell segmentation in blood smear images. In [52], they used Canonical Correlation Analysis (CCA) employed using CNN-LSTM network architecture to segment a WBC and its nucleus. Various techniques have been proposed for segmentation and classification of blood cell and its components while also considering overlapped cells problem with level of success mentioned in the literature. These methods have focused on WBCs rather than RBCs and platelets.

Building an accurate CAD system to detect and classify blood cell into three components that can process the whole slide of blood smear, including millions of RBCs, WBCs and platelets components remains an open challenge in CAD. Hyperspectral imaging and DL techniques can be used as a potential solution to address the detection of blood cell problems, including color distribution, shape and location variation and cell density. To the best of authors' knowledge, the techniques are still an open research in term of exploration and investigation as in [53].

Parallel computing with DL techniques can be used as another potential solution to improve the cost of large-scale microscope image analysis and running time [54]. In future, healthcare services perspective shows that robust CAD system will play a vital role in the smart devices.

Funding

None

ACKNOLEDGEMENT

The author we would like to thank the reviewers for their valuable contribution in the publication of this paper.

CONFLICTS OF INTEREST

The author declares no conflict of interest.

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