AN EXTENSIVE REVIEW OF WHITE BLOOD CELLS DETECTION AND CLASSIFICATION FROM BLOOD SMEAR IMAGES

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Abstract

White blood cells (WBC) are immune system-protecting cells that can be utilized for monitoring a person's health. Images from WBC microscopy help hematologists diagnose abnormalities in the blood. It is challenging to examine microscopic images and categorize different cell types because of dissimilarities in the stage of maturation as well as intra-class differences within cell form in images brought on by using various acquisition and staining procedures. The purpose of the article is to present a comparison table of several papers that went through extensive research to derive conclusions based on the automated methodology applied with the final findings to obtain a replacement method for manual or existing methods. This document can be used as a resource in the future to learn about all the technologies and techniques currently available to provide the best results and accuracy. Researchers can obtain insights into WBC classifications using this review of the literature.

Keywords: Immune System, Monitoring, Microscopy, Hematologist, Staining procedures, Classifications.

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Introduction

An extremely specialized tissue, blood comprises various cell types and plasma constituents. This vital liquid nourishes and distributes oxygen across the physical tissues and organs. The removal of waste materials such as carbon dioxide and ammonia occurs in the blood. Additionally, it supports many other biological processes, such as the circulation of oxygen, regeneration of cells, blood clotting, internal temperature regulation, and immunity. Red blood cells(erythrocytes), white blood cells(leukocytes), platelets, and plasma constitute four of the main biological components of blood. Most of them, the RBCs, transport lung oxygen to all other critical tissues, making up 40–50% of the amount of blood in the body [1]. WBCs, on one hand, are present within lymphatic tissues in addition to blood. They only account for a small amount of the total blood volume, approximately 1% or less in a healthy person, yet they are the body's primary line of the fight against invaders from outside. To eradicate foreign proteins found in bacteria, viruses, and fungi, WBCs seek out, recognize, and connect to them. Additionally, there are various varieties of WBCs, and each one contributes to immunity differently [2].

WBC Structure

Inside the blood circulatory and lymphatic system, WBCs are created inside the bone marrow. A WBC contains a nucleus, which is used to identify it with normal cells in the systemic body. It is frequently big and lobed. The nucleus, the cytoplasm, and the membrane (cell wall) make up every WBC form, as exposed in Figure. 1. The WBC features are listed in Table 1.

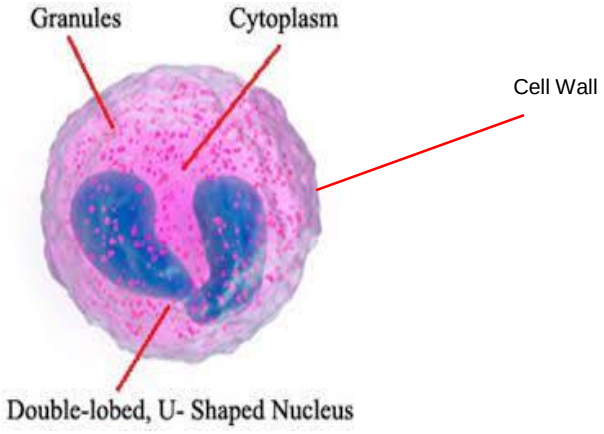


Figure 1. WBC structure

Categories of WBC

The nuclei of WBC have different shapes, textures, and sizes and might present one or more lobes based on the reaction of their specific granules with a staining process as shown in Table 1. The most useful shape, size, and texture information for cell segmentation and classification comes from the nuclei of the WBCs [3]. To provide a brief review and perspective, the features and functions of types and sub-types of WBCs and information about WBC nuclei shape are explained as follows. Granulocytes and agranulocytes are the two types of cells that are distinguished first based on granules.

Neutrophils

Granular leukocytes known as neutrophils are formed throughout bone marrow by the hematopoietic cell stem. With 40–70% of leukocytes in the peripheral bloodstream, they are the most prevalent kind. The immunological response to infections caused by bacteria is predominantly mediated by neutrophils, and an abundance of neutrophils in tissues is linked to severe inflammation. Neutropenia, or low neutrophil counts, can be brought on by specific medical treatments and underlying medical conditions. Neutropenia may raise susceptibility to infections. Their multilobed nucleus is 9 to 16 µm in diameter. Degradative enzyme-containing granules are present inside the cytoplasm and are released after phagocytosis. They are typically the first to react to invasive bacteria and possess a brief lifespan of two to three days.

Eosinophils

Granular leukocytes that originate from the hematopoietic lineage of cells in the bone marrow are referred to as eosinophils given that they by histology stain by using eosin stain. They represent 1-3% of all leukocytes in circulation. Eosinophils are mostly found in tissues and typically spend an hour throughout the peripheral circulation. They feature a bilobed, integration-shaped nucleus with an outer diameter between 12–17µm. Granular cells contain chemicals like peroxidase, cationic

protein, and major basic protein (MBP). Toxic to parasites are these compounds. Complexes of antigens-antibodies are also phagocytosed by neutrophils. Patients who suffer from parasite infections, allergic responses, or certain autoimmune illnesses might exhibit excessive eosinophil counts.

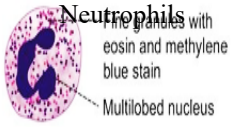
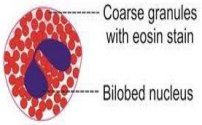
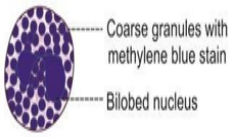
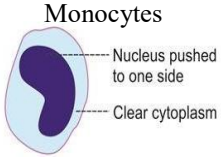
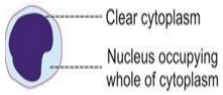
WBC Type	WBC Size	% of WBCs in Blood	WBC Nuclei Shape	Cytoplasm	WBC Lifespan in blood	Primary Functions
Granulocytes						
Neutrophils 	10-12 µm	55-70%	Segmented, Multi-lobed (2-5), Densely Stained	Neutral pale, finely granular, evenly dispersed specific granules	Hours to a few days	-Immune defenses
Eosinophils 	12-17 µm	1-4%	Bi-lobed, Clumped, chromatin pattern, densely Stained	Large homogeneous red granules that are coarse and highly refractile	Hours to days	-Defence against parasites
Basophils 	12-15 µm	0.5-1%	Bi-lobed or segmented	Large blue specific granules that stain with basic dyes and often obscure nucleus	Hours to days	- Inflammatory response
Agranulocytes						
Monocytes 	12-20 µm	2-8%	Indented, Kidney-shaped, lightly stained	Agranular, pale blue cytoplasm with lysosomes	Days to months	-Immune surveillance
Lymphocytes 	7-18 µm (varies)	20-40%	Small, Round and slightly indented, darkly stained	Agranular, faintly basophilic, blue to Gray	Days to years	-Antibody production -cellular immune response

Table 1. WBC Features

Basophils

Granular leukocytes belonging to the myeloid stem are basophils. These feature a regional S-shaped nucleus with a diameter of approximately 14 and 16 µm. They exist for around two weeks & flow in the peripheral circulation. They perform a similar role as mast cells, which are found inside tissues, and look extremely similar to them. Although their function in the immune system is unclear, they may work in tandem with mast cells in an attempt to regulate type I allergic reactions. The allergic reaction, as well as asthma, are two examples. High basophil levels are typical in patients who experience allergic responses.

Lymphocytes

Agranular leukocytes known as lymphocytes develop through the lymphoid cells found inside the bone's marrow. The tiniest leukocytes, measuring 6 to 15 µm overall diameter, typically exhibit responses to infections caused by viruses. Round, heavily stained lymphocyte nuclei in little cytoplasm. They move through the lymphatic system, which includes blood from the peripheral organs and tissues. The subtype in which they differentiate affects their lifespan as well. Natural killer cells, T cells, and B cells are the three main subtypes of lymphocytes.

Monocytes

The hematopoietic cell line found in the bone's marrow includes monocytes. Monocytes make up around 5–10% of all leukocytes that circulate and are predominantly involved in the immunological response to bacterial infection. Their nucleus is formed like the kidney bean. Leukocytes that circulate called monocytes normally stay in circulation for 8 hours prior to moving into the tissue, so they undergo differentiation to become macrophages. The majority of phagocytic cells found in tissues are then macrophages, which have a much greater lifespan than neutrophils, which endure months or even years. Localized macrophages are known by unique names in some organs, such as Kupffer cells within the liver or osteoclasts in bones. With an outer diameter of 25 to 50 µm, these cells are substantially bigger than monocytes and contain a spherical, single-lobed nucleus.

Medical image analysis (MIA) has improved dramatically as a result of advances in deep learning (DL) and conventional machine learning (ML) approaches in computer vision. These advancements have increased prediction accuracy, allowing for more effective planning and diagnosis. These techniques can help hematologists and physicians by offering a second view, and they have significantly improved the diagnosis of automatic brain tumors and leukemia/blood cancer detection. This paper thoroughly examines the TML and DL methods currently available for MIA, with a particular emphasis on the classification of leukocytes in blood smear pictures and other medical imaging domains, such as MRI, CT, X-ray, and ultrasound images. Finding the best TML and DL approaches in MIA, particularly for WBC categorization in blood smear pictures, is the primary impact of the suggested review.

Figure 2 illustrates the various cell detection processes. Finding the best TML and DL approaches in MIA, particularly for WBC categorization in blood smear pictures, is the primary impact of the suggested review. This review article thoroughly examines the advanced DL techniques, especially the developing models in the MIA area that are built on convolutional neural networks. According to a review of related literature, white blood cell analysis using microscopic blood smear pictures is an established use of traditional TML approaches. They aid in the recognition of numerous hematic illnesses, including AIDS and blood cancer (leukemia), and they supply vital information to medical professionals. For scientists and practitioners working in the MIA domain, we derive future research directions based on the detailed analysis of the WBC-related literature study offered in this paper.

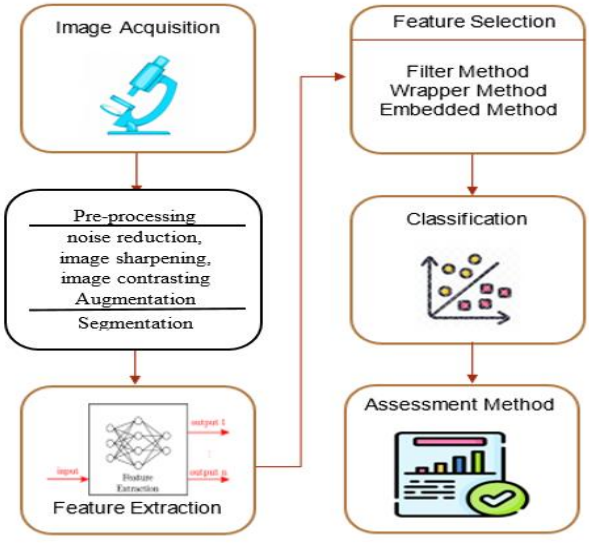


Figure 2. Steps of WBC classification.

Materials and Methods

Image acquisition

In automatic classification, acquiring images is the initial step. Recognizing the process used to capture the initial images of WBCs using peripheral blood smear data on microscope slides is crucial. Using a digital camera and high magnification, these images are captured by putting slides of material under a microscope with an optical zoom and taking pictures. Analysis in microscopes starts at 10x magnification and then continues to a maximum of 1000x. High-quality

digital cameras take pictures for evaluation, augmenting, and display of blood cells. There are digital cameras that can be handled independently from the microscope. A computer can download the photographs as a 24-bitmap (bmp), Joint Photographic Experts Group (jpeg), or video clip from the internal memory cards (USB) that are used for archiving. The majority of microscopes have SLR adapters that can be used to connect SLR cameras optically, and the images are then automatically downloaded onto the computer [4].

Following a staining technique causing the cells of cytoplasm and nuclei to differ in colour from the background of the blood image (plasma), microscopic images of the cells are produced. Cell structures can be seen more clearly by using the WBC staining technique, which increases contrast by changing the colour of some cell structure components. The term "Romanowsky stains" refers to a range of tiny stains which can be applied. To identify malarial parasites in blood, the Romanowsky stain applies a methylene blue dye [5]. Leishman, Wright, Giemsa, and Wright-Giemsa staining techniques are utilized to stain WBC.

Data Set

White blood cell microscopic image datasets from many sources were used by different authors, producing a large series of dataset sizes for training, testing, and validation. Table 2 provides the list of standard datasets and their corresponding number of images. A large-scale dataset called Raabin-WBC was made available in 2021. For classification, there are actually three distinct sets of cropped sub-images: Train, Test-A, and Test-B. Two experts have independently labeled the different kinds of each image for every WBC in the Train and Test-A sets. However, the images in Test-B lack thorough labeling.

There are 257 WBCs compared to peripheral blood in LISC that have only been categorized through one expert. Consuming a light microscope (Model: Microscope-Axioskope 40) along with a capturing device typically an electronic camera (Model: Sony-SSCDC50AP), the imageries in this dataset were obtained from a smear of peripheral blood and stained using the Gismo-right technique. The images were taken at an amplification of 100.

BCCD was extracted from peripheral blood, and one expert labeled a total of 349 WBCs. The blood smears have been stained using the Gismo-right technique. Additionally, every image in this set of images has been captured with a CCD color camera and a standard light microscope at a resolution of 100. Furthermore, in keeping with this, we rectify the incorrect label of a single image.

One of the most widely used, freely available databases for diagnosing, dividing, and categorizing acute leukemia is ALL-IDB. There are two distinct kinds of ALL-IDB: ALLIDB1 and ALL-IDB2. This dataset was developed in September 2005 and contains approximately 39,000 blood cells. WBC segmentation and detection involves using 108 images (59 healthy and 49 cancerous) each of which contains multiple cores. These images are part of the ALL-IDB1 dataset. The ALL-IDB2 dataset, which comprises 260 images with one lymphoblast per image, is designed to assess the performance of various classification algorithms. The publicly available datasets are listed in Table 2.

Table 2. Sample WBC datasets

S.No.	Dataset	Total Images & Size	Image File Format & Memory	Access & Staining	Camera & Microscope
1	LISC	266 720X576	Bmp / 179 MB	Public Gismo-right	Sony-SSCDC50AP Axioskope40 Zoom : 100×
2	BCCD	367 640X480	JPG / 143MB	Public Gismo-right	CCD color camera Regular light microscope Zoom : 100x
3	CellaVision	100 120X120	BMP / 14 MB	Public hematology reagent	Motic Moticam Pro 252A N800-D motorized auto-focus microscope
4	MISP	148 775X519	BMP	Public	Canon V1
5	ALL-IDB	108	JPG / 182 MB	Public	Canon PowerShot G5
6	Raabin cropped double-labelled	17975 575X575	JPG / 546 MB	Public Giemsa	Camera Phone Galaxy S5 1. Olympus CX18 2. Zeiss microscope Zoom: 100×

7	BloodSeg	367 640 × 480	JPG	Public	CCD Color Camera
8	JTSC	300 120X120	BMP	Public hematology reagent	Motic Moticam Pro 252A / N800-D motorized auto-focus microscope

Data pre-processing

Pre-processing, also known as image enhancement, is a step in the process of improving an image by suppressing unwanted distortion, eliminating noise, or enhancing certain image features that are crucial for further investigation into the segmentation and classification processes. Additionally, geometric image transformations like rotation, scaling, and translation are part of the pre-processing stage.

For better results, images undergo operations like noise reduction, grey level conversion, image sharpening, image contrasting, and image enhancement. Operations such as median and max/min filtering, image subtraction, histogram equalization, image smoothing, neighbor-hood averaging, and image sharpening are part of the image enhancement process. Histogram equalization can enhance an image's contrast and visual appeal. Reducing the effects of camera noise, spurious pixels, and missing pixel values is the goal of image smoothing. The purpose of image sharpening is to improve certain details in the bloodstain image and to remove any blurring.

The process of modifying images to make them suited and of higher quality for the next steps is called image preprocessing. There are a number of reasons why the quality of microscopic photographs can change. Many methods to identify and prepare the blood pictures for segmenting the Region of Interest (ROI) have been suggested by researchers. In order to effectively detect ROI, they have upgraded the image by switching to a different domain, such as converting RGB color (R-Red, G-Green, B-Blue) to HSV color (H-Hue, S- Saturation, V-Value) or CMYK color (Cyan, Magenta, Yellow, and Key (black)). Several methods are used to improve image quality, including normalization, minimum filter, unsharp masking, median filter, linear contrast stretching, histogram equalization, and Gaussian filter [6][7].
In the majority of the jobs, we looked at, the network received images in RGB picture color space as input. In some preprocessing steps, the RGB image was converted to L*a*b color space and used as the network's input image [8] [9] [10]. Lightness (L*) is used to represent L*a*b*, and the other (a*) and (b*) are used to represent two color components. converted RGB to HSV color space as an input image format in [11] [12]. For their model's input, Abdeldaim et al. transformed RGB color space to CMYK [13].

Segmentation

One of the primary tasks in the analysis of microscopic images is segmentation. The goal of segmentation in a microscopic cell image is to divide the image into four distinct regions: the background, Red Blood Cells (RBCs), cytoplasm, and white blood cell nucleus. [14] proposed a three-part algorithm, which includes first, the cell segmentation, next, the nucleus segmentation, and also splitting of contacting cells and nuclei as well, which allows for the segmentation of WBCs and their nuclei.

Segmentation is a means of fragmenting an image into distinct portions for different uses. WBC segmentation is challenging due to the complex nature of blood cells and the ambiguity found in a microscopic bloodstream image. Current WBC segmentation methods range from traditional image processing techniques to cutting-edge machine learning and deep learning techniques.

More conventional algorithms for machine learning have been used for leukocyte segmentation. ML techniques were employed in several investigations to segment along with extract the leukocyte and its nucleus among other blood cells in an attempt to recognize and distinguish between leukocytes. The majority of segmentation approaches integrate boundaries with region criteria. The main categories of segmentation techniques are threshold methods, boundaries-based segmentation, region-based segmentation, and hybrid methods incorporating boundary and region standards [15-17]. Researchers have focused more on two blood smear image segmentation algorithms that are more widely used.

Cell segmentation serves to define the boundary between the cytoplasm and the nucleus so that additional characterization can be performed, including nuclear and cytoplasmic property characterization and the nuclear-to-cytoplasmic ratio that occurs which is helpful for destructive identification [18,19]. Numerous segmentation techniques have been published in the literature;

however, among the most popular and extensively used algorithms were the basic machine learning algorithms which relied on specific attributes. The computational foundation of two distinct kinds of segmentation uses machine learning methods. They are region-based segmentation and pixel-based segmentation of images. The various ML and DL basic segmentation methods and their corresponding result accuracy for WBC classifications are shown in Table 3.

Table 3. Segmentation Technique – Overview

Author	Segmentation	No. of images	Result
Narjes Ghane et al., 2017[16]	K-Means Clustering with Modified Watershed Algorithm	431 images	three stages algorithm used which includes WBCs segmentation and extraction of nuclei from the cell's image, and also the separation of overlapping cells and nuclei. Nucleus segmentation: Similarity measure=92.07, Precision=96.07, & Sensitivity =94.30%. Cell segmentation: Similarity measure=92.93, Precision=97.41, & Sensitivity = 93.78%
Cao *et al*., 2018[20]	HSG transformed images segmented using SWAM method	Set 1 -70853 Set 2 -6331	Minimizing fuzzy divergence was used for cytoplasm segmentation, and performed better than interval-valued intuitionistic fuzzy sets. Acc:93.75%
Al-Hafiz *et al*., 2018 [21]	Canny edge detection method, boundary-based methods, and morphological operators	5 image sin DIC format	This method provides a higher average accuracy and average similarity. Acc: 87.5%
Puttamade Gowda ert al., 2019[22]	Improved Spectral Angle Mapper, Orthogonalization using Gram Schmidt k-Means clustering for WBC cell extraction	All 5 types	Accurately extracts cytoplasm and nucleus of white blood cells. Acc:98.38%
Hegde *et al*., 2019[23]	Colour segmentation	ALL-IDB2 - 260	Manages brightness variations. Acc: 97%
Hegde *et al*., 2019[24]	Colour transformation with tissue quant and brightness variation method	ALL-IDB2 – 160 Dataset 2 – 160	Large number of labelled data is required with good infrastructure. Acc: Dataset 1 - 97% Dataset 2 – 96%
Kutlu *et al*., 2020[25]	R-CNN	LISC - 250 BCCD - 364	Multiple CNN architectures are tested using full learning and transfer learning for best results. Acc:97%
Sapna *et al*., 2020[26]	Fuzzy C-means clustering	LISC - 242 MISP - 150	Neural network better classified the nucleus characteristics, count of WBC's. Acc: 92.8%
Sajad Tavakoli et al., 2021[27]	Otsu's thresholding for nucleus segmentation	Raabin-WBC-14,514, LISC-257, and BCCD- 349	This method has two contributions. The first contribution: formulating an algorithm for segmenting the nucleus with fast and accurate. The second contribution: for obtaining four colour features from the cytoplasm and nucleus. Acc: 94.65%, 92.21%, and 94.20%
Roy et al., 2021 [28]	semantic segmentation using DeepLabv3+network	Dataset 1, 2, 3	Mean Accuracy of 96.15%, Mean IoU of 92.1%
Amal et al., 2022[29]	ResNet + UNet networks to extract features and segment leukocytes	ISBI C-NMC - 10600	The proposed method achieved robustness in segmenting peripheral blood, WBC, and bone marrow images with a mean accuracy of 96%.
SivaRao et al., 2023[30]	SegNet Deep Neural model	BCCD - 367	Deep learning and machine learning-based hybrid method for the automatic detection of WBC subsets. Acc: 99.02%

Feature Extraction

A crucial stage in the WBC classification process is feature extraction representation. Textural features including momentum, contrast, entropy, and skewness; geometrical features like area, radius, perimeter, convex area, major axis length, compactness, and orientation; and color features like color distribution and histogram are among the features that were extracted. Numerous previous studies have been conducted on the classification

of WBCs in the form of feature extraction representations. Table 4 lists the conventional and deep learning-based feature extraction methodologies.

Feature Selection

During the feature selection stage, the vector dimensions obtained in the previous step are decreased and relevant and crucial characteristics are identified. To find appropriate models, this phase reduces irrelevant features and lowers computational complexity and expense. Standard machine learning methods for choosing features include Principal Component Analysis, Random Forest, Gabor Wavelets, and LBP. The categorization results were influenced by the intersecting attributes of the feature subsets obtained using a combination of MIC and Ridge approaches.

Table 4. WBC Feature Extraction and Classification Methods

Author	Feature Extraction Method and Types	Classifier	Accuracy (%)	Remarks
Duan et al. [31]	texture, shape, and spectrum features	SVM	98.3%	Certain leukocyte types clearly perform better than NN, with segmentation accuracy of both the nucleus and the entire leukocyte reaching 93%. With the integration of spectral along with spatial data, cross-validation can lead to a final classification accuracy of 98.3%.
Sharma et al. [32]	bio-inspired optimized grey wolf algorithm to find the optimal features,	SVM, decision tree, RF, and k-nearest neighbor classifiers	97.8%	The best way to detect white blood cells is to utilize the Quantum Grey Wolf method to determine the smallest number of features that are optimal from the available features. While the lowest number of optimal features is also found using the standard Grey Wolf Optimisation approach, the computational time efficiency of the features chosen by qGWO is superior.
Meenakshi et al. [33]	CNN features	RNN-LSTM	97.5%	Three phases:Feature extraction: AlexNet + GoogleNet + ResNet-50, Feature Selection:MA-PSO, Classification:RNN-LSTM
Mohamed et al. [34]	MobileNet-224 model.	fully connected network with logical regression classifier	97.03%	Six distinct machine learning models with ten distinct pre-trained models are used. The greatest rank 1 classification accuracy was achieved by the Logistic Regression classifier.
Habibzadeh et al.[35]	Inception and ResNet models	DL classifier	ResNet V1152:99.84% ResNet 101:99.46%	various Inception and ResNet deep learning classifications are presented and the use of these theories is outlined.
Dong et al. [36]	Geometry + Color + Texture features	particle swarm optimization +SVM	LISC: 97.96% BCCD:88.44% Raabin:98.71%	By merging the benefits of ResNet and DenseNet, the suggested approach is able to learn improved feature representation.
Liang et al.[37]	CNN-RNN (recurrent neural network)	DNN+RNN-dense softmax	90.79%	this model preserves the temporal and spatial information of image features and can learn structured information of image features
Togacar et al.[38]	GoogleNet-DenseNet	Quadratic Discriminant Analysis	97.95%	Convolutional neural network models with feature selection methods contributed to improve the classification success of white blood cell types.
Özyurt et al.[39]	AlexNet + VGG-16 + GoogleNet + ResNet	Extreme Learning Machines (ELM)	96.03%.	Using ELM Classification, effective CNN features produced acceptable results in a reduced execution time.
Patil et al. [40]	extraction of overlapping and multiple nuclei patches CCA+RNN	Dense softmax	CCA-(CNN_Xception +RNN_LSTM): 95.89%	Deep learning architecture for blood cell image categorization based on canonical correlation analysis and merging CNN and LSTM
Baghel et al. [41]	CNN features	a two-stage classification	Binary classification:9	The suggested system uses data augmentation techniques to boost robustness

		method based on a CNN model to identify mononuclear and polymorphonuclear entities.	8.51 Multi-class classification:97.70%	and improve the accuracy of numerous cells overlapping.
Balasubramanian et al.[42]	CNN features	RBF-SVM	Raabin-WBC:99.45% LISC:98.62% and BCCD:98.81%	Experiments indicated that the modified U Net segmentation can detect the WBC nucleus with a dice similarity coefficient of 0.972.
R. Ahmad et al.[43]	DenseNet201 and Darknet53	multiple baseline classifiers	99.9%	This work proposes a complete WBCs classification pipeline that performs transfer learning using deep neural networks followed by an efficient feature reduction algorithm.
Bhuiyan et al.[44]	CNN features	ML classifiers	97.92%	Minimizes the dispersion of predictions and improves model performance
Elhassan et al.[45]	Context-free WBC attributes	Deep Convolutional Autoencoder (DCAE-CNN)	97%	The DCAE and a CNN extract more discriminant WBC features and present a new model for classifying atypical WBCs

Classification

There are five different types of leukocytes. These include basophils, lymphocytes, monocytes, eosinophils, and neutrophils. Different qualities and characteristics exist in each form of WBC. It is crucial for identifying the type of WBC. Accurately identifying and quantifying the various WBCs are essential steps. Various automatic classification techniques have been employed to attain rapid and precise classification. White Blood Cells in microscopic blood smear pictures have been classified using a range of conventional supervised learning techniques, including Support Vector Machine, or SVM, [46]–[48], Naive Bayes (NB) [49]–[51], K-Nearest Neighbour (KNN) [52]–[54], and Artificial Neural Network (ANN) [55]–[57]. Studies that used supervised techniques to detect the WBCs almost worked in the classification step. Three components comprised the classification process as a result: classic, DNN, and combination approaches. The category's supervised classification type served as the division's foundation. After reviewing numerous papers, some of the classification methods and their classifiers with accuracy are listed in Table 4.

Apart from the use of ANNs and support vector machines (SVMs), which are highly significant in MIA, other models such as mixtures, Bayesian, ensemble models, K-NN, and tree models were also utilized to address issues in various medical imaging sub-domains, including leukocyte classification, brain tumor identification, and lung cancer detection. Inspired by the organic nerve system found in the human brain, ANN is a method of learning that is supervised. It has hidden layers, input, and output that are connected by weighted connections. These weights are values that indicate the way an ANN approach performs. Based on the inputs and the weights, error function, and neurons in the hidden layer, the output layer produces results. Because ANN has a variety of uses, including the classification of leucocytes, brain tumors, breast cancer, and lung cancer, it has been used in the framework of MIA in numerous research papers.

Many people now choose to analyze medical data using DL methods, especially convolutional networks. These methods operate particularly well in fields where analyzing vast amounts of data requires intelligence equal to that of a person. To extract rich features from a huge quantity of raw data, one must also possess a solid understanding. However, when a significant quantity of data needs to be managed effectively, this work becomes difficult and time-consuming. End-to-end learning is offered by DL, which also removes all additional overhead associated with feature selection and feature descriptor selection. The key benefit of DL methods is their ability to automatically identify and extract semantically rich features from unprocessed input.

Challenges of WBC Classification

The manual examination of blood cell counts can occasionally be inaccurate due to interoperability issues, fatigue, expert skill requirements, and time constraints. Specifically, the examination of white blood cells (WBC) becomes crucial in the diagnosis of diseases such as leukemia, leukopenia, and the like. WBCs are not regularly arranged because they circulate throughout the bloodstream, making it difficult to analyze WBC and its various types for shape and structure. The procedure of feature extraction and segmentation

has a significant impact on the accuracy of WBC classification systems. Algorithms for classification must also take account of factors such as cell rotation, varying maturation phases, nucleus size and position, and variations in location.

Recent Challenges and Requirements

Researchers discovered several essential features, applications, and benefits of the methods of Machine Learning (ML) and Deep Learning (DL) for Medical Image Analysis (MIA), especially for the categorization of WBC in blood smear pictures. Additionally, they found the main research problems and requirements associated with the two methods. Certain conventional and robust ML and DL models have been developed over the last few years for MIA, including the localization and classification of brain tumors from MRI, the detection and classification of leukocytes in blood smear pictures, and the detection of lung cancer in CT images [58].

Dedicated medical expertise, lightweight ML, as well as DL, approaches, and the lack of huge, high-quality datasets that are freely available are the issues. A number of the difficulties stem from the theoretical and mathematical foundations of numerous ML approaches [59]. Unsupervised or semi-supervised systems are needed to overcome these obstacles [60]. To prevent these problems, the effectiveness of unsupervised and semi-supervised techniques in MIA will be undermined. Transitioning from supervised to unsupervised learning methodologies presents a difficulty in maintaining system correctness and efficiency. There is still much room for development in MIA applications and systems that use ML and DL techniques. These systems and applications are still far from ideal.

Training a predictor is the main problem with MIA and leucocyte detection and classification. To solve this issue, an optimal learning method with a more balanced ability for over-generalization and a computationally effective heuristic model is needed. Training a model with impressive generalization abilities requires a learning paradigm that makes use of true or random labels, and offers useful tools to work with accessible datasets and efficient training algorithms. In the subject of MIA, deep neural network-based learning has seen tremendous empirical success in the past few years on a wide range of tasks, including leucocyte categorization, brain tumor detection, lung cancer, and breast cancer detection. Even though it's a challenging, non-convex optimization problem, straightforward techniques like stochastic gradient descent (SGD) can find workable solutions that reduce the training error. Even when the total amount of parameters is far greater than the quantity of training data [61], the networks that are learned in this manner exhibit excessive generalized abilities [62]. This is more surprising. Without medical experience, the current TML and DL approaches are not reliable enough to be used in real-world health diagnosing systems. Both technical and expert skills are necessary to develop a model of learning for the classification of leucocytes and MIA.

Conclusion

An overview of numerous works on the subject of blood sample analysis used in diagnostics is given in this publication. The computer-aided technology used to extract and categorize the WBCs decreases time and errors because traditional detection and categorization of WBCs is difficult. It is feasible to achieve robustness for managing changes in texture, color, and illumination in blood sample images by using an automated method. The paper provided an in-depth examination of the deep learning and traditional machine learning techniques utilized in the identification of WBCs in blood sample images. The pre-processing step of the framework for microscopic blood cell detection involves improving the obtained image quality and removing noise. This includes thresholding, filtering, stretching the histogram, morphological procedures, and gray-scale conversion. The portioned pre-processed image is used to identify the area of interest for additional processing. Due to various staining conditions, the complexity of microscopic blood pictures, and the morphological variety of WBCs, WBC segmentation presents many obstacles. The methods used in WBC segmentation today range from deep learning and sophisticated machine learning algorithms to traditional image processing techniques. Over the past three decades, the research community paid a lot of attention to blood smear images as an emerging topic in MIA. This work presents standard features and applications of DL and TML in MIA. The challenges exist in the large and intricate amount of data that needs to be analyzed for deep learning to be an effective solution. The research community will gain from the study's compilation of all this data since it will show where to begin for future TML and DL model research on MIA.

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