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Application of CNN in blood smeared images: A Review

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Abstract-Disorders such as malaria, leukemia, thrombocytopenia, sickle cell anemia, and many others cause morphological and physiological changes in the blood cells which can be used as an indicator in the diagnosis process of such diseases. Blood smear analysis is a routine work carried out in laboratories to diagnose a disease. Microscopic evaluation is one of the widely used techniques for blood smear analysis. However, the diagnostic result may vary depending on the skill and experience of the technician, instruments and methods used to analyze the blood sample. Manual microscopic examination is time consuming and is less repeatability. The advent of digital imaging taken using Light microscopy has enhanced diagnostic role. In recent years several technological innovations in the field of image processing and Convolutional Neural Networks (CNN) are employed in automated medical diagnosis. This paper focuses on the recent works reported in the field of automated disease diagnosis from blood-smeared images.

I. Introduction

Digital Image Processing deals with transforming a visual signal of the real world to a digital image that can be interpretable. It spans from the study of image formation, as a result of the acquisition of light signals by specifically designed sensors, to the interpretation of the image as an array of connected values. Digital image processing involves the conception, design, development, and enhancement of digital imaging algorithms and programs [1]. With the advancement of Digital image processing it is applied in various fields especially in the field of medical. Malaria is a life-threatening disease caused by Plasmodium parasites. Human expertise is required to diagnose malaria in laboratories. There can be many disadvantages like extensive training is required for a microscopist to become a proficient malaria slide reader, the high cost of training and employing, maintaining skills, and the large component of manual work involved[2]. If there is any fault in diagnosis it can be life threatening. To overcome such faults there is a need to automatically detect malaria pathogens from the microscopic images with high accuracy results. Convolutional Neural Network (CNN) based model for the diagnosis of malaria from the microscopic blood smear images is proposed by many authors.The process involves acquiring the images, pre-processing and image analysis.

Acquiring the blood smeared image from microscope

In any image processing task the first step is acquisition of digital images of blood smears, which largely depends on the equipment and materials being used. The results may depend on the quality of the image. This has been a challenging task at the beginning but with the advancement of new technology new tools are available for acquiring images.

Sample images are shared with technologically-advanced hospitals for further consultations and evaluations, through a medical communication standard (DICOM [3]) for handling of digital images. The advent of digital imaging taken using Light microscopy has enhanced diagnostic role. The availability of this technology is limited to rural and developing areas. There was a need to develop some cheaper and readily available technology. Mobile phones are now a days are mounted with a good quality inbuilt camera. A camera-enabled mobile phone can be used to capture images from the eyepiece of a standard microscope [4]. Leishman stained peripheral blood smear images of malaria patients' slides were optically grabbed by Leica Observer (Leica DM750)[5]. Sinha et al. acquired captured color images of the blood smear on the slide using a digital camera mounted on the Microscope[6]. A mobile phone mounted light microscope was developed for clinical use by imaging P. falciparum-infected and sickle red blood cells in brightfield and M. tuberculosis-infected sputum samples in fluorescence with LED excitation [7]. Images are acquired using a charge-coupled device camera connected to a light microscope[8]. Poostchi et al. listed (Table 1) all published systems according to the type of microscopy used[2]. The images were acquired using the Optical Magnification Prototype (Fig.1) coupled to a smartphone[9]. Kaewkamnerd et al designed a motorized unit (Fig.2) controlling the precise movements of objective lens and microscope stage to collect images[10].

Fig. 1[9]

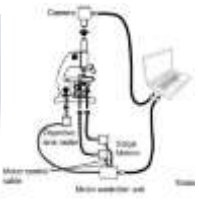

Fig. 2[10]

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Table 1: Imaging Techniques

Sl No	Imaging Techniques
1	Light Microscopy
2	Binocolor Microscopy
3	Fluorescent Microscopy
4	Polarized Microscopy
5	Image-based Cytometer
6	Sub-pixel Resolving Optofluidic Microscopy (SROFM)
7	Quantitative phase imaging (QPI)
8	Quantitative Cartridge-scanner System
9	Scanning electron microscopy (SEM)
10	Fiber array-based Raman imaging
11	Serial block-face scanning electron microscopy (SBFSEM)
12	SightDx Digital Imaging Scanning

II. Pre-processing

Image preprocessing are the steps taken to convert an image in its raw form into a form that is ready to use for training and inference. Images collected might be of various sizes, they might be of different contrast levels, and they might be oriented wrongly in different ways. Image preprocessing are rule based largely deterministic steps that are taken to make sure that the images are formatted correctly. Three key objectives can be identified: noise removal, contrast improvement, illumination and staining correction.

Table 2: Pre-processing techniques

Objectives	Techniques
Noise removal	Mean and median filters, or Gaussian low pass filtering[11],
Contrast improvement	Contrast Stretching techniques, and histogram equalization
Illumination and staining variations	Color normalization techniques including the popular use of gray-scale colors

III.Image Segmentation

Segmentation is the process of partitioning a digital image into multiple regions and extracting the meaningful region which is known as Region of Interest. Image segmentation locates objects and boundaries in images. The traditional image segmentation algorithm mainly includes the segmentation method based on the threshold value [12], edge [13]and region [14]. Toha et al used histogram thresholding for image segmentation. The thresholding value is ranged within 1 to 255. All the intensity value which lies below the threshold value will be set as 0 while for the intensity value above the input value will be set as 255. This will result to a segmented image where black color will represent the background of the digitized red blood specimens while the white color will characterize the Malaria parasites existed in the image[15]. Adaptive thresholding is applied in [9]. Zheng et al. proposed an image segmentation algorithm which used the adaptive K-means method. It has a lot of advantages over other traditional methods such as elbow methods, This method saves a lot of code, time and improves efficiency. It has another advantage of transforming into 1 determined LAB color space. The background is influenced by the parameter provided to the filter which improves the accuracy of the final segmented image[16]. Ali et al. presented a object based segmentation using fuzzy clustering (OSF) that overcomes the previous shape based algorithms. Their analysis showed it has superiority over fuzzy k-rings, fuzzy k-ellipse, Gustafson-Kessel, fuzzy c-circular shell, fuzzy c-elliptical shell and FISG shape based algorithms[17]. Ruberto et al. introduced a morphological approach to cell image segmentation that improves the accuracy of the classical watershed-based algorithm. The detection of the parasites is done using microscopic color images of stained malarial blood in order to evaluate the parasitaemia(the number of parasites per number of red blood cells). The knowledge RBC structure is used along with the flat disk shaped structuring element that were not used in the existing watershed based algorithms[18]. WBC segmentation a two-step process carried out on the HSV-equivalent of the image, using K-Means clustering and EM-algorithm[6]. Using active contour models (snakes and ballons), that were initialized using morphological operators, cells is segmented.[19] . In blood smear images detection and classification of leukocytes is a daily task in medical diagnosis. Ramoser et al. presented automated approach to leukocyte segmentation that is robust with respect to cell appearance and image quality. To discriminate between cell types Pairwise SVM classification is used. In a set of 1166 images (13 classes) resulted in 95% correct segmentations and 75% to 99% correct classification[20].A automatic seeded region growing algorithm is presented for image segmentation by G´omez et al. The algorithm automatically generates

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seeds via histogram analysis. The algorithm was tested on several leukemia medical images[21]. A fuzzy based two stage color segmentation viz. Gustafson
Kessel clustering [22], followed by nearest neighbor classification in L*a*b* space for segregating leukocytes or white blood cells (WBC) from other blood components[23]. Mazalan et al. proposed a method to count a total number of RBC in peripheral blood smear image by using circular Hough transform (CHT) method. The operation was per formed on a sigle cell of RBC. Then it was pre-processed and segmented. Otsu method[9], [24] is applied to set the threshold level and convert the gray level image into a segmented binary image. Using the CHT method 91.87% accuracy was gained.[25]

IV. CNN Based automation of peripheral blood smears for diagnostic purpose

CNN is a mathematical construct that is typically composed of three types of layers (or building blocks): convolution, pooling, and fully connected layers. The first two, convolution and pooling layers, perform feature extraction, whereas the third, a fully connected layer, maps the extracted features into final output, such as classification. A convolution layer plays a key role in CNN, which is composed of a stack of mathematical operations, such as convolution, a specialized type of linear operation. In digital images, pixel values are stored in a two-dimensional (2D) grid, i.e., an array of numbers, and a small grid of parameters called kernel, an optimizable feature extractor, is applied at each image position, which makes CNNs highly efficient for image processing, since a feature may occur anywhere in the image. As one layer feeds its output into the next layer, extracted features can hierarchically and progressively become more complex. The process of optimizing parameters such as kernels is called training, which is performed so as to minimize the difference between outputs and ground truth labels through an optimization algorithm called backpropagation and gradient descent, among others.

Applications of CNN started in early 1990s for Time-Delay Neural Network (TDNN) approach to speech recognition [26] followed by Gradient-Based Learning Applied to Document Recognition[27]. Its use is then extended to handwriting recognition on MNIST [28] and later to natural image recognition [29].
There are currently three major techniques that successfully employ CNNs to medical image classification: 1) training the "CNN from scratch" [30], [31], [32], [33] , [34] 2) using "off-the-shelf CNN" features (without retraining the CNN) as complementary information channels to existing hand-crafted image features, for Chest X-rays [35] and CT lung nodule identification [36], [37]; and 3) performing unsupervised pre-training on natural or medical images and fine-tuning on medical target images using CNN or other types of deep learning models [38], [39], [40], [41].

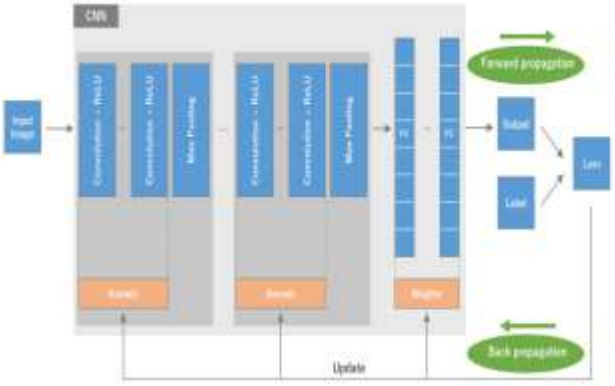

Fig. 3 :An overview of a convolutional neural network (CNN)[8].

A. RBC Analysis

Red blood cells (RBCs) are one of the major components of blood. By classifying RBC allows us to diagnose different diseases. RBC can be manually visualized under a microscope but it may cause human error while interpreting it. The various health conditions can change the shape, texture, and size of normal RBCs. Parab et al. developed an image processing and CNN based system that can detect normal and abnormal RBC and also classify different types of abnormal RBCs into 9 different classes[42]. Using CNN, classification of RBCs into normal and sickle cell is done previously. Xu et al. proposed in an automated classification of sickle shape RBCs with high accuracy, they provided the corresponding shape factor analysis, which can be used synergistically with the CNN analysis for more robust predictions[43]. Zhang et al. proposed a learning-based, simultaneous cell segmentation and classification for sickle cell disease based on the deep U-Net structure with deformable convolution layers[44]. Classification of RBCs based on its shape deformation was also addressed using deep learning method. Durant et al. implemented a deep CNN consisting of more than 150 layers for classification of RBCs[45]. Michal et al. proposed a method for automatic counting classification of RBCs. They applied image processing methods for RBCs separation and counting. For RBCs classification of normal and abnormal cells, eigenfaces methods were coupled with the neural networks. [46].

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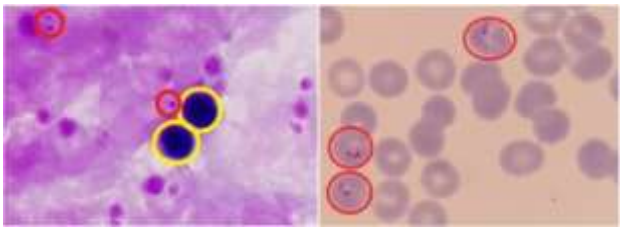
B. WBC Analysis

Zhao et al. proposed an automated method for detection of WBCs using R and B components of RGB images, and morphological operations. They detected eosinophils and basophils using handcrafted features to train SVM. They used features extracted from CNN approach to train random forest classifier for classification of lymphocytes, monocytes and neutrophils.[47]. Shahin et al. used deep CNN for classification of WBCs. They proposed a WBCsNet architecture which is the first trained CNNs for WBCs identification. They designed CNN from scratch and also used a pre-trained network for the classification [48].



a)Thick blood Smear b)Thin blood smear

Fig. 4. Examples of thick and thin blood smears. Red circles are parasites and yellow circles are white blood cells.[49]

Table 3: Summarized RBC and WBC Analysis

	Objectives	**Results**
Parab et al.[42]	Detection of normal and abnormal RBC	**Accuracy** 98 %
Xu et al. [43]	Classification of deoxygenated RBCs for the elongated and sickle (DeOxy) category	**Accuracy** 93.8%
Zhang et al. [44]	Classification Red Blood Cells for the sickle cell disease.	Cell-level segmentation accuracy (97.8% for deformable U-Net, 94.7% for U-Net) and reasonable classification accuracy (82.7% for deformable U-Net, 73.1% for U-Net)
Durant et al. [45]	Morphologic Classification of Erythrocytes	In 288th, 295th, and 292nd epochs for each training replicate, with validation accuracies of 97.5%, 96.6% and 97.19 %
Wąsowicz et al. [46]	Detecting abnormal erythrocytes for analysis of the in vitro interactions of nanodiamonds with human blood	**Accuracy** 95%
Zhao et al. [47]	Automatic detection and classification of leukocytes	The accuracy of monocyte and neutrophil is 85.3 and 97.1%. Classification for lymphocyte is 74.7%
Shahin et al. [48]	White Blood Cells Identification	Accuracy score with 96.1% for Dataset3 and 92.9% for Dataset_All

C. Automatic Malaria Parasite Detection from Blood Smear

Malaria is a serious global health problem, and there are various diagnoses available for detecting this disease. It is very much essential to diagnosis this disease accurately because fault in diagnosis may lead to serious problem to the patients even death. So there is a need in automating the process of diagnosis. Researchers have developed various models and applications to detect malaria automatically. Ross et al. have developed an automated image processing method for the diagnosis and classification of malaria on thin blood smears. They have used morphological and novel thresholding selection techniques for identification of erythrocytes[8]. Raviraja et al. used statistical approach to detect erythrocytes infected by malaria parasites[50]. Mohanty et al. developed deep-learning-based auto encoder technique for automatic detection of malaria parasite. [51]. Anggraini et al. designed an expert system to obtain possibly infected erythrocyte using multiple threshold from malaria thin blood smears. Otsu's[52] Method was used for automatically selecting threshold level [53]. Das et al. proposed a comprehensive image characterization cum classification frame work for malaria-infected stage detection using microscopic images of thin blood smears that is capable of evaluating erythrocytes malarial infection more efficiently with respect to its sensitivity, specificity and positive predictive value.[54]

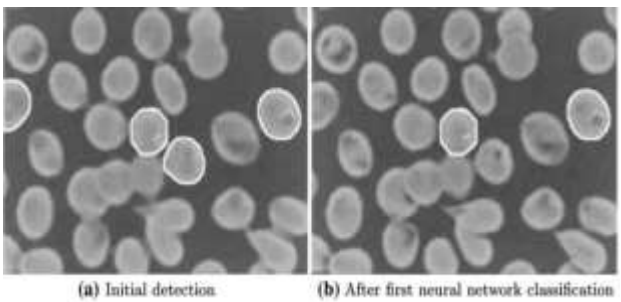


Fig 5 : Infected erythrocytes (circled)[8]

Quinn et al. proposed a parasite detection by training a four-layer CNN model on overlapping patches, which are extracted from the downsampled RGB images [55].
Liang et al. developed a 16 layer Convolutional Neural Network (CNN) model to automatically classify single cells in thin blood smears on standard microscope slides as either infected or uninfected. The trained CNN model showed much better representation of the training images than the transfer learning model, which relies on feature extraction from a pre-trained model trained on an entirely different image set [56]

D. Applications for smart phones

Fuhad et al. proposed an entirely automated Convolutional Neural Network (CNN) based model for diagnosis of malaria. Knowledge distillation, data augmentation, Autoencoder, feature extraction by a CNN model and classified by Support Vector Machine (SVM) or K-Nearest Neighbors (KNN) were performed under three training procedures named general training, distillation training and autoencoder training to optimize and improve the model accuracy and inference performance. They have deployed the miniaturized model in different mobile phones and a server-backed web application[57]. Yang et al. implemented a deep learning application for smartphones to detect malaria parasites in thick smear images [49]. Rosado et al. also explored the use of smartphones to detect malaria parasites and white blood cells [9].

V. Conclusion

This review highlights the growing impact of Convolutional Neural Networks (CNNs) in automating the diagnosis of various blood disorders through the analysis of blood smear images. Traditional methods of manual blood smear analysis can be slow, resource-intensive, and subject to human error, especially in rural or resource-limited settings. By leveraging CNNs for feature extraction, segmentation, and classification, researchers have achieved significant improvements in diagnostic accuracy, speed, and consistency across diseases such as malaria, leukemia, and sickle cell anemia. The integration of CNNs in medical imaging enables robust detection and classification of blood cell abnormalities, facilitating the early diagnosis and monitoring of these conditions. Smartphone-based applications further expand the accessibility of these diagnostic tools, making it feasible to deploy such technology in field or low-resource environments. Despite these advancements, challenges remain in standardizing and optimizing CNN models for diverse image qualities and variations. Future research should focus on improving model accuracy across different datasets, developing more adaptive preprocessing techniques, and refining mobile integration. Continued innovation in CNN applications for blood smear analysis holds the potential to improve global healthcare by providing rapid, affordable, and accurate diagnostic solutions.

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