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Sickle Cell Disease Identification by Using Region with Convolutional Neural Networks (R-CNN) and Digital Image Processing

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Abstract

In Sri Lanka, medical laboratory technicians manually diagnose sickle cell disease by examining microscopic images of strained blood samples on glass slides and calculating the infected blood cells. However, due to the several processes required in manual assessment, the method of analysis much time consuming and required skilled medical laboratory technicians because there is a possibility of human error. This research was conducted to provide an Artificial Intelligence integrated computerized solution to prevent the above difficulties in the identification process. Deep Learning is the most powerful approach for object detection and classification in many areas, and many researchers proved the deep learning approach is better than the other learning approaches. Deep learning concepts such as Convolutional Neural Networks (CNN) plays a major role in medical image processing diagnostics. In this research, we develop a region classification Convolutional Neural Network (R-CNN) algorithm for the sickle blood cell identification process, which is one of the most demanding processes in blood classification. The proposed identification algorithm was developed and trained by using a dataset of 150 blood smear sample images and validate by using 20 sample images. According to the algorithm validation results, the prosed method achieved an accuracy of more than 90%.

Keywords: Artificial Intelligence, Blood Cell Detection, Deep Learning, R-CNN, Sickle Cells, Support Vector Machine

1. Introduction

The human blood consists of mainly three categories of cells, which were identified as erythrocytes (red blood cells), leukocytes (white blood cells) and thrombocytes (platelets). Amount wise blood contains 40-45% of red blood cells (RBCs), 1% of white blood cells (WBCs) and huge amount of Platelets [1]. The red blood cells deliver oxygen molecules to the organ tissues therefore the amount of oxygen delivers to the tissues depend on the red blood cells. White blood cells are immune cells that defends the body from infectious diseases as well as invading immigrants. Platelets working on blood coagulation and another important fact is that terminates excessive bleeding when a blood artery becomes damaged. Many different types of blood disorders and cancers affected human blood cells. We can identify the most common blood disorders include anemia, blood cancers such as Leukemia, lymphoma, myeloma and bleeding disorders such as Hemophilia, blood clots. In this research, we mainly focused on identification of anemia disorder (Sickle Cell Anemia Disorder) by using Deep Learning approach. Most of the people affected by Sickle cell anemia disease whose families originate from Saudi Arabia, Mediterranean countries, Caribbean islands, South or Central America and India. In the present situation, approximately 250 million people of the entire world have lived with gene reason for sick-le cell disease [2]. Sickle cell anemia is a blood disorder often called as sickle cell disease, which is, an abnormality of the red blood cells that is passed down through the generations. Due to this disorder, the required amount of healthy blood cells decrease. Therefore, there are not enough RBCs to fulfil the oxygen requirements for internal metabolisms of the human body.

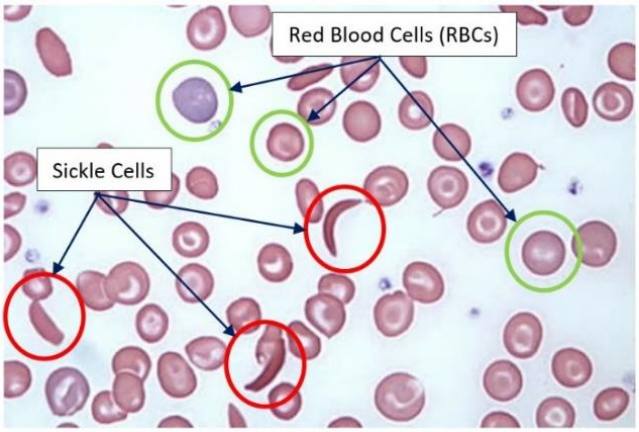

Fig. 1. Microscopic image of blood smear

Berjaoui, Zeina & Youness, Mohamad & Matar, Jad & Ariss, Abdel. (2016). PREVALENCE OF SICKLE CELL TRAIT IN THE SUBURBS OF BEIRUT, LEBANON. Mediterranean Journal of Hematology and Infectious Diseases. 8. e2016015. 10.4084/mjhid.2016.015.

The normal red blood cells take a circular shape as shown in Fig.1, which provides the ability of easy movement through blood vessels. Due to the sickle cell anemia disease, the red blood cells turned in to like sickles or crescent moon shape as shown in Figure 1. These sickle-shaped cells will be stuck in the small blood vessels, which tend to block the blood flow [3]. In the medical field, several laboratory tests have been developed for sickle cell disease identification.

Hemoglobin extraction [4], isoelectric focusing [5] and high-performance liquid chromatography (HPLC) [6] are some of the laboratory based methods for SCD identification. In addition to the above complex laboratory based methods, there are point of care (POC) tests available. The results of POC tests mainly extract by human readings and these readings mainly effect by human errors. Furthermore, these POC tests require special controllable environment conditions to preserve chemical reactions. These requirements degrade the effectiveness of test results in resource limited conditions [7]. The microscopic inspection of the blood smear is another alternative method used to SCD identification by skilled laboratory per-son. This blood smears show variations of red blood cells such as size, color and shape, furthermore provides diagnostic information about blood diseases including SDC [8]. Blood smears are also used to assess medical treatments and monitor patients health condition [9]. The blood smear preparing and analyzing negatively affected by the condition of an analyzer, slide propagation errors, analytical measurement errors, documentation errors and labour intensive procedures involving highly qualified laboratory technicians [10-11].

The problem is the availability of such trained medical examiners limited in the medical field. Furthermore, manual testing is a time-consuming operation. As a result, in order to eliminate this bottleneck, we propose an automated sickle cell identification model, which based on deep learning and image processing. The new trend of deep learning with convolutional neural networks (CNN) was incredibly successful in natural image classification or analysis. In the medical field, deep learning models provide a great contribution to medical image processing. The core of deep learning is to train large neural networks with a large amount of input data and high performance computers. Deep learning is a branch of machine learning algorithms, which consists of constitutional, pooling and neural networks. It provides more advantages and accurate results than machine learning algorithms [12]. Therefore, CNN based deep learning approaches to blood cell identification have been increasingly evolving. In this research we focused on development of region with convolutional neural network model (R-CNN) to detection of the sickle cells.

2 Related Works

Most of the researchers use deep learning and machine learning approaches for image classification and object recognition in many fields. Among deep learning and machine learning models, the researchers conclude that deep learning models provide better performance. The previous researchers conclude the deep learning models provide a considerable contribution to many areas (cancer detection, blood cell classification, brain image analyzing, and COVID 19 detection by using lung image analyzing) in the medical field. Qiwei et al. [13] have developed deep learning model to identify the peripheral leukocyte. They used CNN based approaches, SSD (Single Shot Multibox Detector) and YOLOv3 (An Incremental Improvement Version of You Only Look Once), as the detection method. According to their experimental results, CNN base methods provide better performance in peripheral leukocyte recognition.

Mu Chun Su et al. [14] have proposed a technique for classifying white blood cells based on artificial neural networks. According to their research, they extract three kinds of characteristics of segmented individual blood cells and feed that into the ANN model. The developed MLP with the architecture $20 \times 12 \times 10 \times 5$ layers. Tran et al. [15] have proposed a Convolutional Neural Network (CNN) based method to identify Leukemia blood cells. The developed network consists of seven layers, five layers for feature extraction and two layers to classify the extract features. They pre-processed (rotation, shearing, reflection, translation) the training images to increase the amount of training images, by that they improved the efficiency of the CCN model. According to their results, the deep learning model has good accuracy.

Prayag et al. [16] have proposed an algorithm to classify the images of blood cells into sub categories. The developed network algorithm included of two convolutional layers, one pooling layer and fully connected layer. Finally, the results compared with NaiveBayer (NB) and Support Vector Machine (SVM) classification models. Furthermore, they analyze results for the pooling layer: MaxPooling and Average-Pooling. Moutaz et al. [17] have devised a method for retrieving data from X-ray images scans by using deep learning to detect and predict COVID-19. They used a collection of 1000 X-ray images to developed a deep learning model. They use 128 sample images to conduct the research. The number of sample images in-creased to 1000 by using image augmentations. The finalized model achieved the accuracy of more than 90 per cent.

Ensaf et al. [18] have developed a pre trained deep learning model to white blood cells classification. Their proposed model includes four stages, image pre-processing, feature extraction, classification and performance evaluation. In the image processing step, they separate individual white blood cells by using thresholding techniques and resize images into the fixed resolution for feature extraction. Then the features feed into the fully connected network to classification. They reached more than 95 per cent of overall performance on model validation. Abdullah et al. [19] have used machine learning techniques to explore white blood cell categorization. In their study, they processed 350-blood smear with six kinds of machine learning algorithms (Decision Tree Classifier, Random Forest, k-Nearest Neighbors (k-NN), Multinomial Logistic Regression (MLR), Naïve Bayes and Support Vector Machine (SVM)). According to the results, the best

performance occurred in Multinomial Logistic Regression (MLR) algorithm with more than 90 per cent. They extracted 35 blood cell features for training the machine learning algorithms.

Clara et al. [20] have used 15 characteristics to train machine learning algorithm. The results obtained to five types of machine learning algorithms (AdaBoost, Bagging, Boosting Tree Ranking, Ogistic Regression, Performance measurement: ROC curve). According to the results, the AdaBoost and Rank-tree achieved more than 90 per cent accuracy compared to other methods.

Mo Zhang et al. [21] have developed deformable U-Net for sickle cell segmentation and classification. The deformable convolution layer allows the function learning process to deform freely, making the entire network more resilient to different cell geometries and image conditions. In this research, they used 128 images (256×256 square pixels) samples to train the model. The proposed model has three layers for both the encoder and decoder paths. According to their results, the deformable U-Net achieved an accuracy of more than 80 per cent for Sickle cell segmentation and classification. Some of the researchers used color and morphological operations for bool cell segmentation. Huey Nee Lim et al. [22] have developed a methodology for white blood cell (WBC) segmentation by using morphological operations. In their research, they eliminate back ground, red blood cells (RBC) and platelets by using K-means clustering and partitioning algorithm. There were five clusters to object segmentation. According to their results, they conclude the accuracy of segmentation can improve by applying K-means clustering before the watershed segmentation.

3 Proposed Methodology

The proposed methodology incudes two phases, which are deep learning model training and model verification process. In this research, we used Regions with Convolutional Neural Network (R-CNN) model under the topic of deep learning and all the development steps explain below. The proposed deep learning algorithm developed in MATLAB development environment.

The paragraph provides a summary of various studies that have used deep learning and machine learning approaches for image classification and object recognition in the medical field. These studies have found that deep learning models provide better performance for tasks such as cancer detection, blood cell classification, and COVID-19 detection. Different researchers have used different methods and models, including Convolutional Neural Networks (CNN), Single Shot Multibox Detector (SSD), YOLOv3, artificial neural networks, MaxPooling, and Average-Pooling, among others. The results of these studies have shown good accuracy for deep learning models and good performance for machine learning algorithms such as Multinomial Logistic Regression (MLR) and AdaBoost. The studies have also used techniques such as image pre-processing, feature extraction, and image augmentations to improve the performance of their models.

Recently, deep learning techniques, particularly convolutional neural networks (CNNs), have been applied to the task of identifying sickle cells in blood samples. R-CNNs, a type of CNN, have been proposed as a promising approach for the automated classification of blood cells. Studies have shown that R-CNNs can accurately identify sickle cells in blood samples, with high levels of accuracy and efficiency.

For example, a study by Al-Hakim et al. [23] used an R-CNN to classify blood cells in images, achieving an accuracy of 96.4% on a test dataset. Another study by Raza et al. [24] proposed an R-CNN-based framework for the classification of blood cells, achieving high levels of accuracy and efficiency in comparison to traditional machine learning methods. In general, the use of R-CNNs for sickle cell disease identification has the potential to improve the accuracy, efficiency, and cost-effectiveness of the diagnostic process. However, further research is needed to fully validate the potential of this approach and to optimize the performance of R-CNNs for this specific task.

In conclusion, the use of R-CNNs for sickle cell disease identification is an area of active research, with several studies showing promising results. Further research is needed to fully validate the potential of this approach and to optimize its performance for the classification of Sickle cells.

3.1 Regions with Convolutional Neural Network (R-CNN) Development

R-CNN is an improved Deep Learning concept beyond the Artificial Neural Networks (ANN), which mostly used in object recognition and classification by using images. R-CNN is an object identification deep learning approach, which classify image regions within an image by using convolutional neural network (CNN) and support vector machines (SVM). In this method, convolutional neural network (CNN) is used to feature extraction and support vector machines (SVM) is used to classify the extracted features. The R-CNN detector only interested in areas that are similar to contain an object, these regions classify by using a sliding filter on sample image. Initially R-CNN detector makes the region predictions by using an algorithm similar to Edge Boxes. Then the predicted regions cropped out from the image and resized. After that these cropped regions feed into CNN classifier and classify image regions. Finally a support vector machine (SVM) trained with CNN features, extract the region proposal bounding boxes. The figure 2 shows architecture of R-CNN algorithm used foe classify sickle cells.

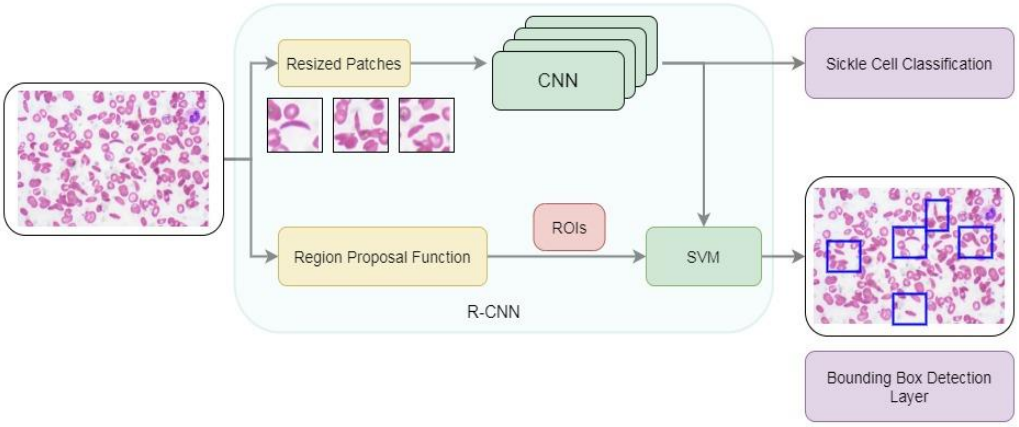

Fig. 2. R-CNN architecture for sickle cell classification

3.2 Regions with Convolutional Neural Network (R-CNN) Development

The CNN use individual pixels as input and generates the probabilities then classify according to the input image. Instead of developing fully connected neural network, the CNN used extra layers which are convolution and pooling layers. These layers reduce the magnitude of input raw data and reduce the processing time. The features of the input image, extract during the convolutional operation in the convolution layer. After the convolution operation, the result features passed into pooling layer, which used to reduce convolved features. There are several types of pooing algorithms. In this research, the maximum pooling technique used to pooling process. After that, the results of the pooling are fed into a fully connected layer. The fully connected layer consists of interconnected neural network layers. Finally, the output of the fully connected network feed into classifying layer. The fig. 3 shows the proposed architecture of CNN model. The proposed model require 50×50×3 pixel image as an input image.

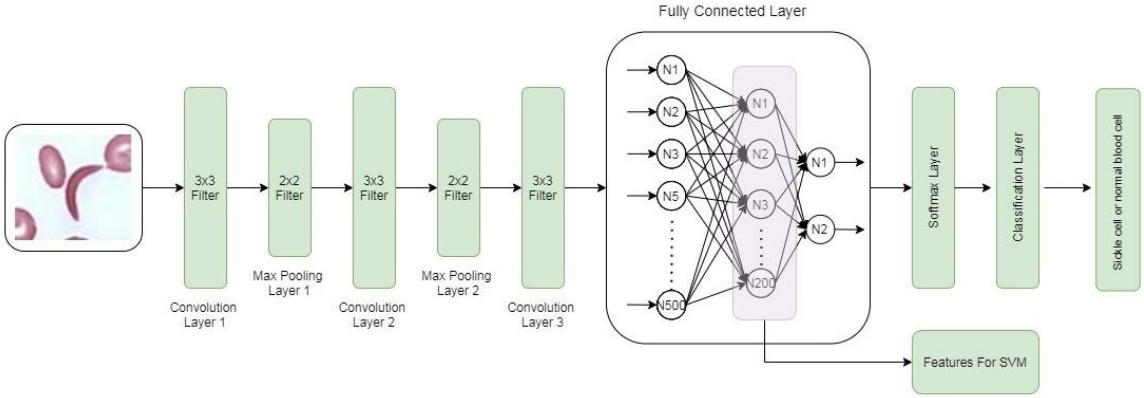

Fig. 3. CNN architecture for sickle cell classification

There are two stages to the suggested CNN architecture, feature learning and classification. The feature-learning step includes two sets of convolution, ReLU and pooling layers. After the image convolution, there are batch normalizations and Rectified Linear Unit (ReLU) to reduce the processing time and increase the speed of the training process. The first convolution layer consists 3×3 convolutional filter with the stride of two for the feature extraction. Then ReLU activation function is applied and result moves to maximum pooling layer, which consists 2×2 filter. Again, the second convolution layer consists 3×3 convolutional filter with the stride of two for next feature extraction. Then ReLU activation function is applied and result moves to maximum pooling layer, which consists 2×2 filter. The definition of the convolution process of multichannel images defines by (1) and definition of the maximum pooling define by (2) [25].

$$U_{ijm} = \sum_{k=0}^{K-1} \sum_{p=0}^{H-1} \sum_{q=0}^{H-1} Z_{i+p,j+q,k}^{l-1} {}^{h_{pqkm}+b_{ijm}} \quad (1)$$

$$U_{ijm} = max_{p,q \epsilon P_{ij}}^{Zpqk} \quad (2)$$

The resultant feature matrix then moves to classification stage. The classification stage consists fully connected neural network developed by using three neural network layers. First layer consists of five hundred artificial neurons, second layer consists of two hundred artificial neurons and final layer includes two artificial neurons. Following the fully connected layer, the softmax function (3) and cross-entropy function (4) put into place to generate final probability and predicted labels.

$$Q' = \delta(q_i) = {e^{q_i}}\Big/{\sum_{j=1}^{N} e^{q_i}} \quad (3)$$

$$D(Q', Q) = -\sum_{i=1}^{N} Q_i \log\left(Q_i'\right) \quad (4)$$

The softmax function able to convert fully connected layer output vector Q = {qi|i = 1, 2 … n} to a n-dimension probability vector δ(qi) to classify input image regions. This proposed CNN architecture trained by using following hyper parameters shows in Table. 1.

Table 1: Selected hyper parameters.

Hyper Parameter	Value
MiniBatchSize	32
Solver	sgdm
InitialLearnRate	0.01
MaxEpochs	5

The hyper parameters of the model are properties that control the entire training phase. This includes the variables that determine the network's structure and the factors that influence how the network is learned. To reduce the GPU memory usage, we used mini-batch size as 32. The stochastic gradient descent with momentum (SGDM) optimizer [26] is used as system solver with 0.01 initial learning rate. Finally, the ReLU activation function was used to activate the nodes. After the CNN training process, the fully connected layer retrieved 200 feature vectors from proposed region suggestions and utilized them to train an individual linear SVM classifier for each class. This determines whether or not an object belongs to a specific class. During the SVM training, all region proposals with an Intersection over Union (IoU) overlap of less than 0.25 with the corresponding ground truth box are regarded as negatives for that class. The properties of the ground truth bounding boxes themselves are the positives for that category. The classification stage applies the Binary Cross-Entropy loss function. The measure of randomness in the features being processed is called entropy and the difference in unpredictability between two random variables is measured by cross entropy [27]. Finally, the proposed CNN and SVM was trained in high performance central processing unit (CPU) which integrated Intel Core i5-7200U processor, 4GB Random Access Memory (RAM) and NVIDIA GeForce 940MX graphics processing unit (GPU).

3.3 Training Data Set

The training dataset was prepared by the help of clinical lab microscope under 400x magnification and glass slides. These blood smear slide tested under oil immersion technique. Then the blood smear images captured by using 2 megapixel camera and converted to 640×480 pixel resolution size for reduce the computational processing time. We prepared 150 sample images by using blood smear on glass slides. There are certain drawbacks typically found in deep learning. The absences of training data, which was one major drawback that directly affected the accuracy of the model. Deep Learning requires a large amount of data to train a more accurate model.

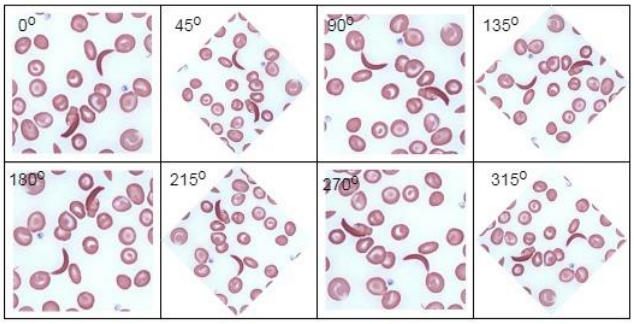

Fig. 4. Augmentation angles of sample images

The available data is adequate to achieve a good output model under most cases, but there is often a shortage of data for direct use of deep learning [28]. In this research, the data augmentation process used to deal with the problem of an absence of training data. The data augmentation process used to increase the number of training samples to enhance CNN performance. By applying several transformations, the augmentation process is achieved. In this research work, several rotational transformations apply to the sample images. The rotational angles are (45, 90, 135, 180, 215, 270, and 315) as shown in Fig 3. Due to this process, the sample image regenerates eight times with different angles. In order to avoid the overfitting issue, data augmentation provides a large volume of data. If the CNN model has more capacity for learning than the dataset has information, the over-fitting problem will occur. However, this training model able to avoid the overfitting issue by data augmentation.

Then possible positive regions of augmented images extract manually by using MATLAB Image Labeller application for the training of CNN model. In this process we manually marked the areas where the sickle cells located in the sample image as shown in figure 5 and also these are the regions of interests (ROIs) for the training of SVM. The goal of SVM is to find the optimal boundary between different classes in the data that maximizes the margin between these classes. This boundary is known as a hyperplane. The points closest to the hyperplane, known as support vectors, have the greatest impact on the position of the hyperplane and the classification of new data points. SVM is particularly useful when the data is not linearly separable, and it can be used

with various kernel functions to handle non-linear relationships in the data.

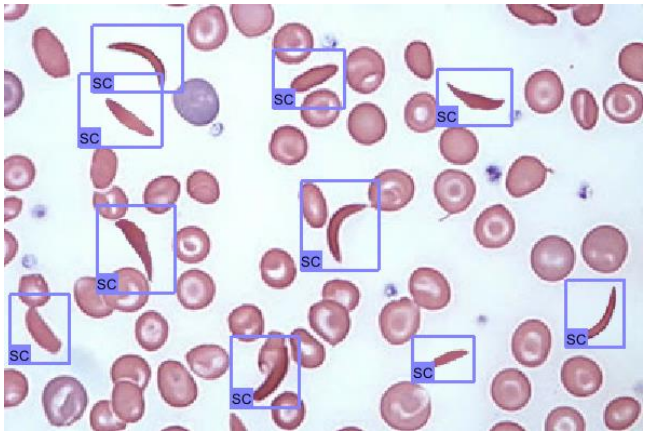

Fig. 5. Manually marked positive ROIs of sickle sells for training process

In the upcoming topic, we will delve into and clarify the performance of the model during the training and validation phases after the training process has been completed.

4 Results & Discussion

In order to enhance the accuracy of the system, 158×8 augmented image samples were utilized in the training process. The training took place over 5 epochs, with 55 iterations to achieve optimal model parameters. Figure 6 displays the training accuracy curve of the proposed algorithm. The statistical data presented in figure 6 indicates that the average classification accuracy for each mini-batch reached 98.20% at the conclusion of the 5 epochs.

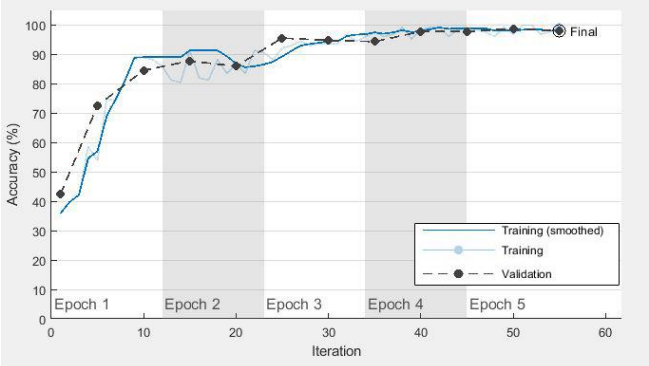

Fig. 6. Accuracy of the model training for 5 epochs

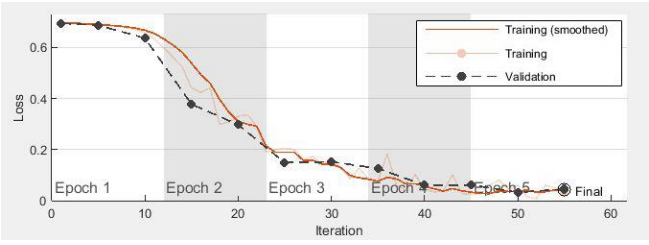

Fig. 7. Mini-batch loss of the model training for 5 epochs

The mini-batch loss curve in figure 7 demonstrates that the training loss decreases from 0.69 to 0.05 at the conclusion of the training process. Both the accuracy and loss curves show that the training and validation curves converge, indicating that the system was effectively trained. After the training was completed, the developed model was validated using 20 sample images from 20 blood smear slides. These sample images were captured using the same procedure as the one previously described for the training data preparation. Each blood smear slide image contains both sickle cells and other blood cells. To validate the results, we first manually counted the number of sickle cells in the images and then processed the images using the developed model to identify and count the positive regions. Figure 8 shows the result comparison of the results analysis and the yellow bar indicates the system count and the blue bar represents the manually counted cells.

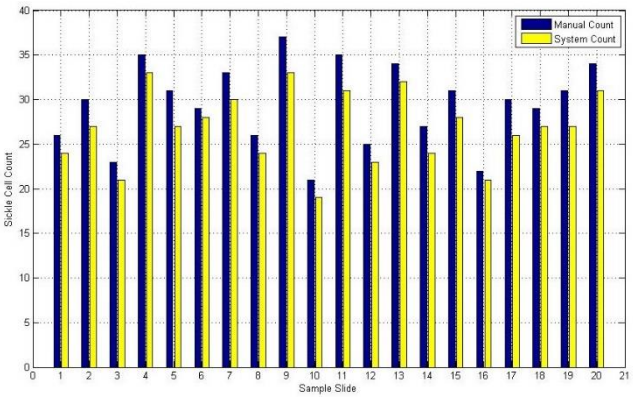

Fig. 8. Result comparison of manually counted values and system counted values for 20 samples

The slight discrepancy between the actual count and the system-detected count in the proposed sickle cell detection algorithm raises concerns about the accuracy of the results. . The average detection value of 91% for the tested samples is a good result, but the slight difference between the actual count and the detected value by the algorithm indicates that there is room for improvement. One possible explanation for the difference is the presence of highly overlapped blood cell regions in the sample images, which can cause difficulties in accurately detecting the number of sickle cells. The challenge of detecting and separating highly overlapped regions in microscopic images is a common issue in image analysis, and various techniques have been proposed to address this problem. It is important to consider the impact of these difficulties on the results and to develop strategies to overcome them in future studies. For example, techniques such as image enhancement, segmentation, and morphological operations can be applied to improve the accuracy of the results. In conclusion, while the results of the proposed algorithm are promising, the slight difference between the actual counted value and the system-detected count highlights the importance of continuing to refine and improve the accuracy of the algorithm. Further research and development are needed to address the challenges of detecting highly overlapped regions in microscopic images and to achieve higher accuracy in the detection of sickle cells.

5 Conclusion

The use of deep learning algorithms, particularly the R-CNN algorithm, for the detection of sickle cells in blood sample images is a promising approach for improving the accuracy and efficiency of the diagnostic process for sickle cell disease in Sri Lanka. The results of this research indicate that the proposed algorithm can accurately detect sickle cells in microscopic blood smear images with a high accuracy rate of more than 90%. The ability of the R-CNN algorithm to detect multiple positive regions in a multi-object image is a significant advantage over traditional convolutional neural networks, which can only classify single objects. However, the study identified some challenges, such as the difficulty in identifying highly overlapped regions in sample images. To address these challenges, future developments should consider combining several AI algorithms to improve the accuracy and efficiency of sickle cell detection in these overlap regions. R-CNN is a complex algorithm and requires significant computational resources to train and run. This can be a challenge for resource-constrained settings, such as remote or rural areas with limited access to high-performance computing resources. The performance of the R-CNN algorithm is highly dependent on the quality of the training data. If the training data is not representative of the target population, the algorithm may not generalize well and may not perform well on new, unseen data. In conclusion, while R-CNN has the potential to be a valuable tool for sickle cell detection, there are several challenges that need to be overcome in order to achieve accurate and reliable results. Addressing these challenges will require ongoing research and development efforts. Additionally, we can optimize the algorithm's efficiency by experimenting with modifications to the CNN architecture and hyperparameters during testing.

Acknowledgments

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