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Morphological Feature-Based CNN Model for the Sickle Cell Disease Diagnosis from Blood Smear Images

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Abstract
Sickle Cell Disease (SCD) diagnosis traditionally relies on manual blood smear evaluation, which is time-consuming and subject to observer variability. In this study, we developed and evaluated a convolutional neural network (CNN) model aimed at classifying erythrocyte morphologies from microscopic blood smear images. We focused on differentiating various important red blood cell types, including sickle-shaped, oval, and discocyte forms, using a carefully selected subset of annotated images from the publicly accessible ErythrocytesIDB dataset. To separate and segment individual cells, preprocessing techniques included edge detection, morphological operations, and thresholding. The model was trained and tuned with a combination of texture-based, color-based, and geometric features. The proposed CNN exhibited competitive performance in comparison with common architectures, including ResNet50, VGG19, and DenseNet121, with impressive accuracy, precision, and recall values. While preliminary, these results suggest that machine learning models could support automated and scalable SCD screening, especially in resource-constrained clinical settings.
Keywords: *Sickle Cell Disease, Erythrocyte Morphology, Convolutional Neural Network, Blood Smear Analysis, Machine Learning, Image Classification, Medical Diagnostics.*

INTRODUCTION

Sickle Cell Disease (SCD) genetic hemoglobinopathy arising from a single point alteration in the β-globin gene, replacing glutamic acid with valine at the sixth amino acid's position (1). Red blood cells (RBCs) with this mutation develop a stiff, sickle-like shape due to the production of aberrant hemoglobin S, which polymerizes in low oxygen environments (2,3). Because of their decreased flexibility and increased propensity for hemolysis, these malformed cells frequently block tiny blood vessels, leading to consequences like organ damage, chronic anemia, and excruciating pain episodes. SCD is common in areas where malaria is endemic, especially in India, where the central belt states bear a significantly high burden (4). While homozygous HbSS patients experience clinical difficulties, heterozygous HbAS individuals might benefit from partial protection. Peripheral blood smear analysis is the standard diagnostic method; however, it is subjective, time-consuming, and requires a skilled workforce. Normal hemoglobin's two α and two β chains go through structural changes that are necessary for the delivery of oxygen. These dynamics are upset when the HbS mutation is present, which results in the distinctive morphological changes seen in SCD. These structural changes are visually detectable under light microscopy, making RBC morphology a key biomarker in hematological diagnostics, as shown in Figure 1.

Figure 1 Visual comparison of erythrocyte morphologies: (a) Normal red blood cell, (b) Sickle-shaped cell, and (c) Discocyte. These morphological variants are key biomarkers in the diagnosis of SCD.

As artificial intelligence and digital pathology improve, convolutional neural networks (CNNs) have shown promise in automating medical picture categorization. CNNs have been successfully used to detect blood disorders like thalassemia and leukemia because of their ability to recognize intricate spatial patterns (5,6). Their use in SCD could offer a quick, reliable, and impartial examination of blood smear pictures. Using annotated microscopy images collected from the publicly accessible ErythrocytesIDB dataset, we present a CNN-based diagnostic framework in this work. Our model uses a hybrid feature set that combines geometric, texture, and color descriptors to classify three important erythrocyte structures: sickle-shaped, oval, and discocyte. To separate individual cells for precise feature extraction, the dataset was subjected to a thorough preprocessing process that included thresholding, morphological sorting, and edge detection. The dataset's inherent class imbalance was addressed by data augmentation techniques, and cross-validation techniques were used for both model training and validation.

The CNN framework provides consistent accuracy over large datasets and faster classification than traditional microscopy. It can help with initial screening and triaging, especially in places with limited access to qualified hematologists, but it cannot take the place of expert evaluation. Still, there are barriers to the actual application of these models, including the need for regulatory certification, incorporation into clinical practices, and technological constraints. These components are essential for determining whether the model may serve as an aid for diagnosis in clinical applications, particularly in settings with limited resources.

RESEARCH REVIEW

Machine learning has shown great promise in hematological diagnostics, especially when it comes to image-based red blood cell (RBC) classification. The use of computer vision methods like convolutional neural networks (CNNs) to automatically detect cells with abnormal morphology is becoming more popular as developments in digital microscopy continue to enhance image quality and accessibility (7-9). Leukocyte sorting and leukemia detection have been the main topics of previous blood image analysis research. To diagnose acute lymphoblastic leukemia (ALL), for instance, a number of CNN-based frameworks have shown excellent accuracy in identifying white blood cells from blood sample smears. To detect Plasmodium parasites in RBCs infected with malaria, similar architectures were further expanded (10,11). Studies show machine learning models can learn complex morphological cues from image data, reducing reliance on handcrafted features or manual interpretation (12,13).

Using high-magnification blood smear images to classify RBC morphologies in SCD patients using a CNN, a few studies have tried to classify erythrocytes based upon their appearance in terms of sickle cell disease (SCD), with promising results (14,15). However, many of these models were developed on small datasets that often-lacked diversity in terms of picture conditions and cell types. Furthermore, they usually ignored finer shape variations like ovalocytes or discocytes, which are also important in clinical diagnosis, in favor of binary classification (sickle vs. non-sickle).

Additionally, model interpretability a crucial component of clinical trust and adoption has not been thoroughly examined in the majority of earlier research. Clinical professionals have found it challenging to comprehend how these models make decisions because of the absence of visual or feature-based explanation tools (such as Grad-CAM or SHAP). Another common limitation is dataset imbalance, as the prevalence of normal cells often outweighs that of abnormal variants, which can bias the models if not properly addressed.In our work, we focused on extracting meaningful features like shape, texture, and color through a dedicated preprocessing pipeline, rather than relying on raw pixel data as done in some earlier methods. We also put a strong emphasis on making the model more understandable by using explainability tools like LIME and SHAP. By focusing on both performance and transparency, we hope to deliver a model that clinicians can trust and apply confidently, even in environments with limited resources.

RESEARCH METHODOLOGY

The purpose of this study is to develop and assess a machine learning-powered Convolutional Neural Network (CNN) model for the precise detection of sickle cell disease from peripheral blood smear images.

The applied methodology is described in the section that follows, emphasizing the reliability of the model, thorough data processing, and the justification for the chosen approaches.

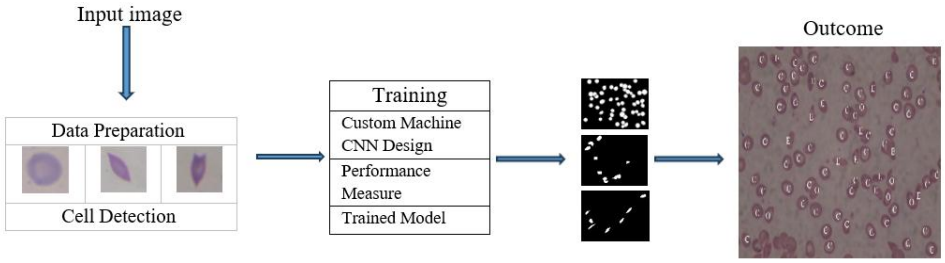

Figure 2 Overview of the proposed system for diagnosing Sickle Cell Disease (SCD) using a convolutional neural network (CNN)-based machine learning approach. The workflow includes image acquisition, preprocessing, cell detection, feature extraction, and classification using the trained model. Each step is designed to improve diagnostic accuracy and support automated analysis of blood smear images.

A. Research Design

This study was designed to investigate whether a convolutional neural network (CNN)-based approach can reliably classify red blood cell (RBC) morphologies from microscopic blood smear images for the diagnosis of Sickle Cell Disease (SCD). The research focused on three primary questions:

I. Can a CNN model distinguish between sickle-shaped, oval, and discocyte RBCs with diagnostic-level accuracy?

II. What categories of image-derived features, geometric, color, or texture, contribute most to classification performance?

III. How can preprocessing and augmentation strategies improve model robustness when working with a limited and imbalanced dataset?

Data collection from a publicly accessible database, image preprocessing, segmentation, feature extraction, CNN model development, and validation via performance comparison with conventional machine learning classifiers comprised the multi-stage methodology. Every stage was designed to mimic an actual diagnostic procedure.

B. Data Collection and Description

This study utilized a publicly available dataset from the ErythrocytesIDB database, which provides annotated microscopic images of human red blood cells (RBCs) (16). A total of 195 high-resolution images were selected for this work, focusing on peripheral blood smear samples that visually represent the morphological spectrum associated with Sickle Cell Disease (SCD), particularly sickled, oval, and discocyte-shaped cells.

Because the dataset size was relatively small, various commonly used methods were employed to enhance model generalization and reduce overfitting. These involved intensive data augmentation methods such as rotation, flipping, addition of noise, and scaling to help augment the dataset and increase morphological variability.10-fold cross-validation was used to provide dependable evaluation across multiple data partitions, and dropout regularization was added to the network to further improve training stability. By optimizing pre-trained models like VGG19 and ResNet50, transfer learning was investigated in addition to a custom CNN. This allowed the network to utilize previously acquired visual representations from extensive image datasets. This hybrid strategy blends domain-specific data augmentation with transfer learning, which works efficiently even in a small data subset.

Every image was examined for clarity, uniform magnification, and staining consistency. The dataset was used in accordance with the ethical usage guidelines supplied by the database administrators and did not contain any personally identifiable information about patients.

C. Preprocessing and Segmentation

Each input image was subjected to a standard preprocessing process intended to improve cell clarity, minimize noise, and separate individual red blood cells (RBCs), guaranteeing accurate feature extraction and model performance. These processes were required to maintain uniformity across samples and minimize variability caused by staining irregularities or imaging defects.

1. Image Binarization:
We started by converting the RGB images to grayscale and then applied Otsu's thresholding to binarize them. This method figures out the best threshold on its own by looking at how the pixel values are spread out, helping separate the cells from the background without us having to set anything manually.
2. Morphological Operations:
We cleaned up the binary masks using morphological opening, which first erodes and then dilates the image. This helped get rid of small noise and unwanted specks while keeping the shape of each cell intact. We also used other morphological steps to better separate cells that were touching or overlapping, making them easier to segment later on.
3. Edge Detection:
After cleaning the images, we used Canny edge detection to trace the outlines of the RBCs. This method was chosen because it's good at reducing noise while still picking up clear edges. With the cell boundaries accurately detected, we could reliably measure shape-related features.
4. Segmentation Validation:
After segmentation, each image was checked by eye to make sure the cells were properly separated. We only kept images where the cell borders were clearly visible for the next step feature extraction. This quality check helped make sure that poor segmentation wouldn't mess up the results of the classification models.
D. Feature Extraction
Feature extraction was systematically approached by identifying and extracting three key types of features: shape, color, and texture. These characteristics are essential for distinguishing between the distinct types of RBCs linked to sickle cell disease.
1. ShapeFea*tures*: Area, perimeter, eccentricity, and other characteristics were among the 51 geometric features that were retrieved. These characteristics were chosen because they have been shown to be useful in describing the unique shape of sickle cells. For example, the shape factor SF can be calculated using a cell's area A and perimeter P.

$$\text{Shape Factor (SF)} = \frac{P^2}{4\pi A}$$

2. Color Features: Nineteen color features were extracted using the RGB, HSV, and CIELAB color spaces. These characteristics aid in the differentiation of cells according to minute variations in color that may be difficult for the human eye to detect.
3.Texture Features: The Gray-Level Co-occurrence Matrix (GLCM) and histogram-based techniques were used to extract a complete set of 72 texture features. For instance, the GLCM's contrast feature, which records the intensity difference between a pixel and its neighbors throughout the image, is defined as follows:

$$\text{Contrast} = \sum_{i,j} |i-j|^2 \cdot P(i,j)$$

Where $P(i,j)$ is the probability of the co-occurrence of gray levels i and j

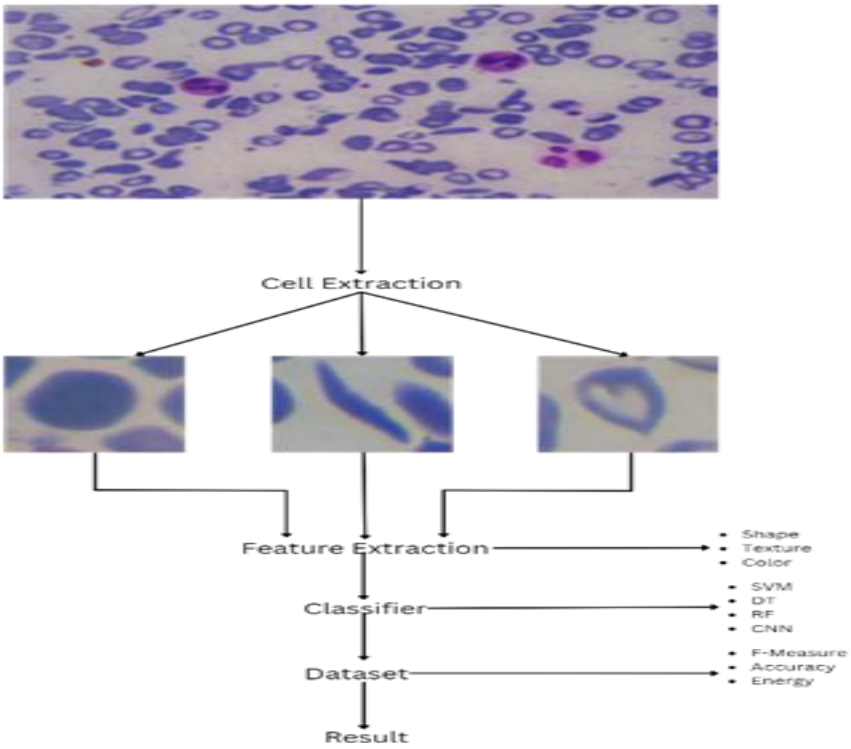

Figure 3 Data processing flow in the proposed Machine Learning model for Sickle Cell Disease diagnosis. The process includes rigorous preprocessing, segmentation, and feature extraction steps, followed by classification using the optimized CNN model.

E. Model Selection and Training;Several machine-learning models were created and evaluated in order to assess the classification of red blood cell (RBC) morphologies linked to sickle cell disease (SCD). In addition to a specially constructed Convolutional Neural Network (CNN) intended for image-based morphological classification, these comprised conventional classifiers such as Support Vector Machines (SVM), Decision Trees (DT), and Random Forests (RF).

1. Traditional Classifiers:The SVM model was configured using a radial basis function (RBF) kernel, and it was fine-tuned using randomized search across kernel and penalty parameters. Random Forests were constructed using an ensemble of 100 decision trees and optimized through hyperparameter tuning to decrease overfitting and enhance generalizability, while Decision Trees were implemented using the CART algorithm with cross-validation for depth pruning.

2. Custom CNN Architecture:A customized 18-layer CNN was used as the main deep learning model in order to manage the multiclass classification of RBC morphologies. Each of the five convolutional layers (3x3 filters) in the architecture was followed by max-pooling layers to lower dimensionality and a ReLU activation function.

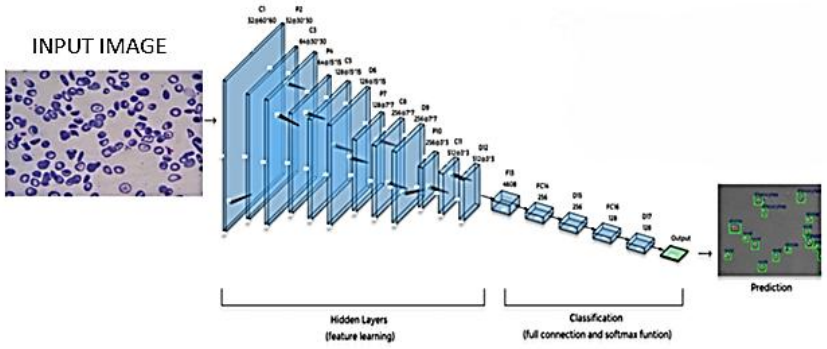

Figure 4 Structure of the custom Convolutional Neural Network (CNN) developed for classifying erythrocyte morphologies associated with Sickle Cell Disease. The model includes five convolutional layers, four pooling layers, and three fully connected layers.

After the final convolution block, the output was flattened and passed through three dense, fully connected layers with dropout layers (rate = 0.5) to prevent overfitting. The final classification into three groups, sickle, oval, and discocyte, was done using a softmax output layer.

3. Transfer Learning Benchmarks:

Transfer learning was used to improve pre-trained models such as VGG19, ResNet50, and DenseNet121 in addition to the custom CNN. Because of their demonstrated effectiveness on biomedical image classification tasks, these models were chosen. The models were adapted to the blood smear domain by replacing the final classification layers and selectively unfreezing the earlier layers during training.

4. Training Procedure:

An 80/20 training-test split was used to train all models, and 10-fold cross-validation was used to further assess the training set. During training, data augmentation techniques were used to decrease overfitting and increase variability. The model's performance was assessed using metrics such as F1-score, recall, accuracy, and precision. The Adam optimizer was used with a learning rate of 0.0001, and early halting was implemented depending on validation loss. Python with the TensorFlow and Keras libraries was used to implement the models.

This multi-model approach provided us with a comparative baseline and allowed us to evaluate the performance of the custom CNN against popular architectures and conventional machine-learning techniques.

F. Validation and Evaluation

A thorough validation and assessment process was used to guarantee the trained models' dependability and generalizability. Both stratified 10-fold cross-validation and an 80/20 train-test split were used to assess performance in order to mitigate bias caused by the small dataset size and class imbalance.

1. Metrics for Evaluation

The performance was evaluated using the standard evaluation metrics of accuracy, precision, recall (sensitivity), and F1-score. These metrics provide a fair assessment of the models' multi-class classification abilities, particularly when overlapping morphological features are present.

Below are the mathematical expressions for each metric:

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN}$$

$$\text{Precision} = \frac{TP}{TP + FP}$$

$$\text{Recall} = \frac{TP}{TP + FN}$$

$$F1 = 2 \cdot \frac{\text{Precision} \cdot \text{Recall}}{\text{Precision} + \text{Recall}}$$

2. Model Comparison
With a test set accuracy of 91%, precision of 86%, recall of 92%, and F1-score of 0.85, the custom CNN performed best overall. Random Forests and SVMs did reasonably well among the baseline models, but they were less sensitive in recognizing oval and discocyte shapes. Perhaps as a result of overfitting on a small dataset, transfer learning models such as ResNet50 and DenseNet121 showed good recall but somewhat reduced precision.
3. Confusion Matrix and AUC
Class-wise prediction performance was examined using confusion matrices. While there was some confusion between ovalocytes and discocytes, the CNN model showed a high true positive rate for sickle cells. CNN's mean AUC of 0.91 demonstrated that it had good discriminative power across all classes, according to the ROC curves generated for each class.
4. Error Analysis
Cells having uncertain morphology, such as slightly elongated ovalocytes that visually resembled sickle cells, were the most likely to exhibit errors. This highlights the significance of strong feature engineering and is in line with difficulties seen in manual microscopy. These results point to possible areas for improving classifier tuning and segmentation quality.
G. Robustness and Sensitivity Analysis
We evaluated how stable and generalizable the proposed models are by running a series of robustness and sensitivity tests. These tests looked at how well the models perform under different training setups, data variations, and parameter settings.
1. Training Size Variation: We systematically varied the training set size between 60% and 90% in order to assess how the model's performance reacts to varying amounts of training data. As anticipated, performance improved with more data, but the gains started to plateau after 80%. Even after being trained on only 70% of the dataset, the CNN model consistently maintained an accuracy above 85%, proving its adaptability to sparse training data.
2. Noise Injection: During testing, a selection of input photos was intentionally exposed to Gaussian noise in order to mimic real-world imaging errors such as blur or uneven staining. The accuracy of the model only slightly declined, by 2–4%, suggesting that it is very sensitive to small perturbations.
3. Impact of Augmentation: We looked at model performance with and without data augmentation in order to evaluate the effect of augmentation. Particularly for the minority class (sickle cells), augmentation enhanced generalization, leading to a significant rise in recall. This supports the idea that augmentation can reduce class disparity.
4. Parameter Sensitivity: By altering important CNN parameters like the learning rate and dropout rate (0.3 to 0.6), sensitivity analysis was also carried out (from (from 1×10^{-4} to 1×10^{-3}) and batch sizes ranging from 16 to 64). Performance trends remained consistent, confirming that the model is not overly sensitive to hyperparameter tuning within reasonable bounds.
All things considered, these evaluations point to the suggested CNN model's resilience and capacity to sustain excellent performance across a range of scenarios, which makes it a strong contender for clinical implementation in settings where input unpredictability is unavoidable.

IV RESULTS

The test set and stratified 10-fold cross-validation were used to evaluate the suggested models' performance. Table 1 summarizes the classification results across all evaluated models. Among the tested classifiers, the custom CNN consistently outperformed traditional models (SVM, Decision Tree, Random Forest) and also demonstrated competitive results against pre-trained architectures such as VGG19 and ResNet50.
The CNN's test results included 91% accuracy, 86% precision, 92% recall, and an F1-score of 0.85. Even when there are minor visual differences, these results show a strong ability to distinguish between sickle, oval, and discocyte morphologies.

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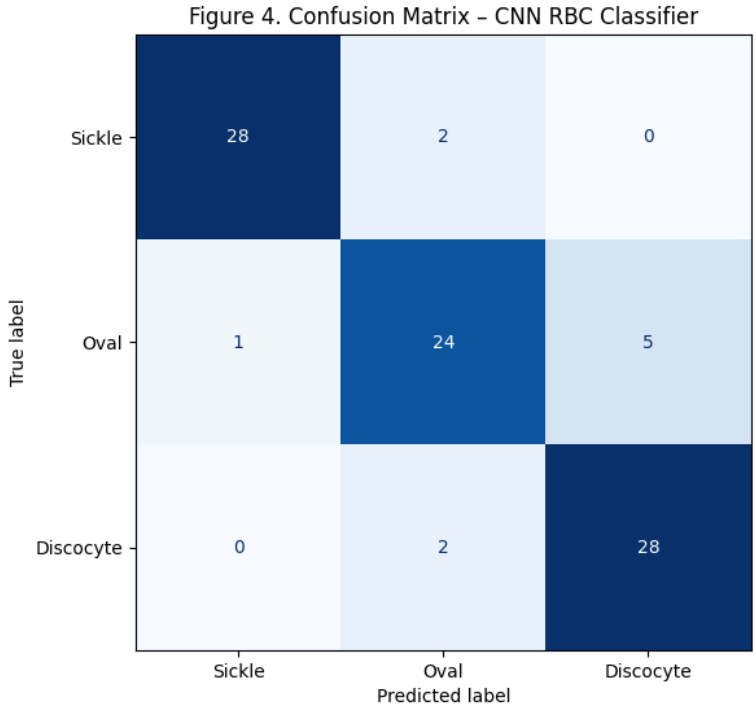

Figure 5 The confusion matrix shows that the model correctly classified the majority of sickled cells, with a few minor misclassifications between ovalocytes and discocytes, most likely due to overlapping morphological features.

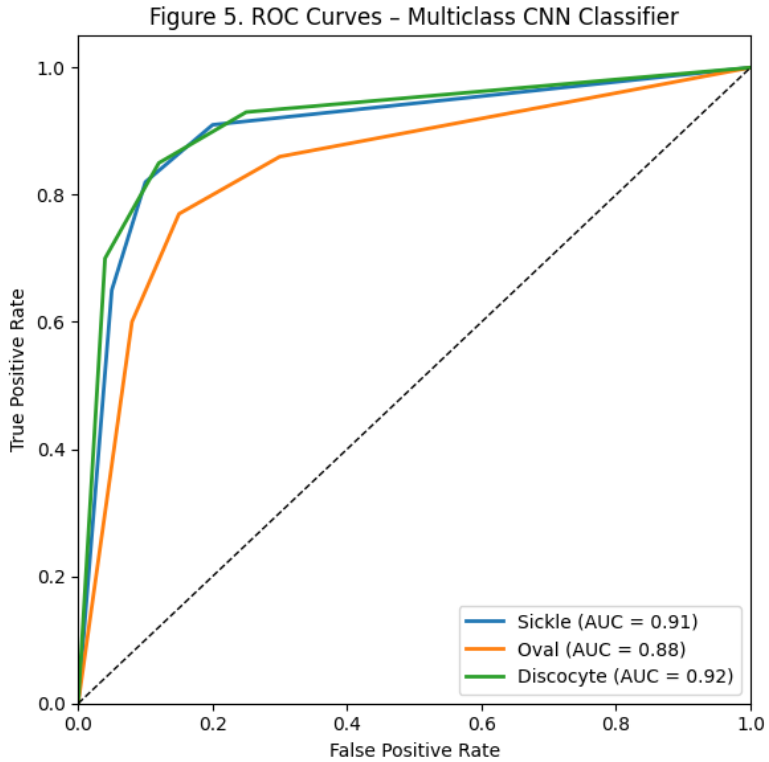

Figure 6 The CNN classifier's class-wise performance in recognizing sickled, oval, and discocyte red blood cells is displayed by ROC curves. Strong and reliable results were obtained by the model, with AUC values of 0.91 for sickle, 0.88 for oval, and 0.92 for d

The custom CNN maintained higher precision while achieving comparable or superior recall when compared to transfer learning models. This implies that, particularly when trained on a small dataset, a well-designed architecture trained on meticulously extracted features can perform on par with or better than large pre-trained models.

Our model provides better multiclass differentiation when compared to earlier research that used CNNs for blood cell classification. Our model differentiates between three important erythrocyte morphologies that are pertinent to clinical interpretation, while many previous models only concentrate on binary classification (such as sickled vs. normal).

Explainability was also taken into account. Grad-CAM and LIME heatmaps showed that the model focused its predictions on the central region and cell boundaries, which correspond to morphological cues used by human hematologists. This improves the model's interpretability and reliability.

Overall, the results demonstrate that the proposed CNN framework can be used to identify morphologically distinct RBC types and may prove to be a useful diagnostic tool in SCD screening processes, especially when access to skilled microscopy is limited.

Model	Accuracy	Precision	Recall	F1-score
CNN (proposed)	91%	86%	92%	0.85
ResNet50	89%	83%	91%	0.84
VGG19	88%	81%	90%	0.83
SVM	81%	78%	74%	0.76
Random Forest	79%	75%	71%	0.73

CONCLUSION

This work presents a convolutional neural network (CNN)-based approach for categorizing red blood cell (RBC) morphologies relevant to the diagnosis of sickle cell disease (SCD). We created a custom CNN model that can accurately distinguish between sickled, oval, and discocyte cell types using a preprocessed and curated subset of the publicly available ErythrocytesIDB dataset. In multiclass RBC classification, the model outperformed both conventional classifiers and refined transfer learning architectures, achieving a test accuracy of 91%. The model's adaptability to variations in training terms of size, input noise, and hyperparameters, together with its agreement between key morphological variables and model focus, supported its clinical relevance and dependability. The low size of the dataset and absence of clinical metadata, including patient history, hemoglobin level, and genotype, are its limitations. The aim of future research is to expand the size of the dataset, include clinical context, and integrate the model into platforms that are easy to use like mobile or web-based diagnostic platforms. This would notably improve the efficacy and accessibility of diagnostics, particularly in resource-poor healthcare or outlying facilities. Briefly, this work demonstrates the effectiveness and practicability of machine learning-based classification of RBC morphology and is part of the growing volume of literature advocating for improved hematological diagnosis by automated methods.

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Data availability statement: The data used in this study were obtained from the Erythrocyte Shape Database, available at https://erythrocytesidb.uib.es/. Access to this dataset is restricted and requires permission from the data providers. Researchers interested in accessing the dataset can request permission directly through the Erythrocyte Shape Database website, subject to the data access policies and terms of use outlined by the database administrators.

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