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A DEEP LEARNING FRAMEWORK FOR AUTOMATED SICKLE CELL DISEASE CLASSIFICATION FROM BLOOD SMEAR IMAGES

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ABSTRACT

Sickle Cell Disease (SCD) is a hereditary hemoglobinopathy characterized by the polymerization of abnormal hemoglobin S, leading to erythrocyte sickling, vaso-occlusion, and severe clinical complications. These sickled cells obstruct blood flow and cause severe complications such as anemia, pain crises, and organ damage. The global burden of SCD is significant, especially in developing regions where access to diagnostic facilities is limited. Timely and correct diagnosis has become increasingly crucial for decreasing morbidity in areas with lack of laboratory infrastructure. The developments of AI and medical imaging have provided automated methods for discriminating between normal and pathological red blood cell morphology, opening new possibilities for scalable diagnostics. In this work, we propose a method based on deep learning for SCD detection using peripheral blood smear images. A modified ResNet50 architecture combined with class weights adjustment was fine tuned in order to correct the dataset imbalance and improve its discriminative power. The validation accuracy of 93-94% and an accuracy of 95.62% over external test set, surpasses state of the art approaches implemented using different CNN (i.e. AlexNet, VGG, ResNet, MobileNet) based architectures. The outcomes proved that a well-tuned deep residual network can provide robust and generalizable Sickled erythrocyte classification among different data. The future work includes an increase of dataset size and the investigation of optimal multi dataset training, moving towards real life applications and clinical assessment for diagnosis point-of-care.

KEYWORDS: Sick Cell Disease, Using Blood Smear Images, Deep Learning-Based Detection, Transfer Learning Technique and Performance comparison.

1. INTRODUCTION

Sickle Cell Disease is a genetic disorder affecting red blood cells. Sickle Cell Disease (SCD) is a hereditary hemoglobinopathy arising from a single point mutation in the β -globin gene (HBB), which results in the production of abnormal hemoglobin S (HbS). Under low-oxygen conditions, HbS polymerizes and causes red blood cells to distort into a characteristic sickle shape. These rigid, deformed cells obstruct microvasculature, impair oxygen delivery, and contribute to a cascade of clinical complications including chronic hemolytic anemia, vaso-occlusive pain crises, stroke, acute chest syndrome, and progressive multi-organ damage. SCD represents one of the most significant monogenic disorders globally, affecting approximately 100,000 individuals in the United States and an estimated 300,000–400,000 newborns worldwide each year, with the highest burden concentrated in Sub-Saharan Africa. The disease encompasses several genotypes, most notably HbSS—the most severe form—as well as HbSC and HbS- β thalassemia, each contributing to variable clinical manifestations and trajectories.

Over several decades, research on SCD has evolved into a broad, multidisciplinary field addressing clinical, molecular, and technological dimensions of the disease. Clinical and epidemiological investigations have been central to understanding its natural history, mapping disease progression, and evaluating treatment effectiveness. Longitudinal cohort studies, population surveillance efforts, and newborn screening programs have yielded critical insights and continue to inform public health strategies. Databases such as the Sickle Cell Disease Natural History Data Resource (NHDR) now play a major role in aggregating long-term patient data to characterize complications and outcomes across diverse populations.

At the molecular level, advances in genomics and biotechnology have transformed the landscape of SCD research. Studies focusing on the HBB mutation, fetal hemoglobin (HbF) modifiers, and gene regulatory pathways have deepened understanding of disease mechanisms and variability. Cutting-edge approaches—including genome-wide association studies (GWAS), CRISPR-based gene editing, and transcriptomic profiling—are accelerating the development of targeted therapies. Research on hemoglobin switching, HbF induction, and emerging gene therapy trials highlights a rapidly expanding frontier with the potential to offer curative interventions. In parallel, technological innovations in imaging and artificial intelligence have introduced new diagnostic capabilities. Deep learning models such as

convolutional neural networks (CNNs), ResNet, AlexNet, MobileNet, and VGG have been applied to large datasets of blood smear images to classify sickle cells and characterize erythrocyte morphology with high accuracy. Studies using datasets of more than 10,000 single-cell images demonstrate the feasibility of automated detection, segmentation, and classification, paving the way for scalable diagnostic tools.

Complementing these advances is a growing body of work exploring digital health and mobile diagnostics. The integration of AI algorithms with smartphone-based microscopes has enabled low-cost, point-of-care screening tools that achieve diagnostic accuracies near 98% in some patient cohorts. These innovations hold particular promise for rural and resource-limited settings, offering new pathways for early detection, disease monitoring, and equitable healthcare delivery. Together, these research trajectories underscore the multidisciplinary progress being made in understanding and managing Sickle Cell Disease. They also highlight significant opportunities for integrating clinical data, molecular insights, and emerging diagnostic technologies to improve patient outcomes and global health equity.

Automated detection using AI improves early diagnosis and reduces manual effort. Recent advancements in artificial intelligence and medical imaging have enabled automated approaches for detecting hematological disorders. Deep learning models such as CNNs, ResNet, and hybrid architectures have demonstrated strong performance in medical image classification tasks [27], [30], [33], [32], [35]. Additionally, smartphone-based diagnostic systems have further improved accessibility and early detection capabilities [28]. In this work, we propose a deep learning-based approach using a fine-tuned ResNet50 model for detecting SCD from blood smear images. We employ deep learning-based techniques to detect sickle cell disease using blood smear images; in particular, we propose a deep learning-based approach using a fine-tuned ResNet50 model for detecting SCD from blood smear images. The rest of the paper is organized as follows: Section 2 discusses related literature, while section 3 describes our methodology. Section 4 explains the results obtained and discussions thereof, followed by conclusions which summarizes the paper and provide pointers for further work in this arena.

2. RELATED LITERATURE

Recent advancements in computer vision and deep learning have significantly shaped automated sickle cell disease (SCD) diagnostics, with numerous studies demonstrating improved accuracy in red blood cell (RBC) classification and morphological analysis. Early

comprehensive reviews, such as Das et al. (2020), synthesized progress in automated SCD detection by examining a spectrum of image-processing and machine-learning approaches. Building on this foundation, several works introduced deep learning-driven methodologies, including Zhang et al. (2020), who proposed a semantic segmentation framework for RBCs, and Kumar and Singh (2021), who developed a machine-learning-based diagnostic model for classifying sickle cell anemia. Deep neural architectures have been widely adopted; for instance, Alhassan et al. (2021) and Karthikeyan and Rajalakshmi (2022) implemented CNN-based detection mechanisms for blood smear images, while Sharma et al. (2022) and Joseph et al. (2023) leveraged deeper convolutional and transfer learning models to enhance RBC morphology classification. Machine-learning-driven pipelines continued to evolve through works such as Patel and Patel (2023), Iqbal et al. (2024), and Rao et al. (2024), who developed automated microscopy and hematological image-analysis systems that further streamlined SCD diagnostics.

Parallel contributions from Springer publications reinforced the growing maturity of deep learning in hematology. Alagu et al. (2022) introduced a specialized deep-learning model for SCD detection from smear images, while Jagtap et al. (2024) proposed blood-cell classification networks to support broader hematological disorder identification. Additional research focused on hybrid and CAD-based methodologies—Singh and Gupta (2021) and Nair et al. (2022) improved detection reliability through hybrid CNNs, and Meena et al. (2023) and Banerjee et al. (2023) expanded morphological analysis frameworks for erythrocyte classification. Foundational machine-learning approaches also remain relevant, as seen in Patel et al. (2020) and Sharma et al. (2021), who employed traditional feature-extraction and image-processing techniques. More recent frameworks by Ahmed et al. (2024) and Gupta et al. (2022) demonstrate the integration of deep learning with broader hematology diagnostics, including hemoglobinopathy detection.

Within ACM literature, a strong computational emphasis has produced additional advances in automated SCD detection. Nagesh et al. (2020) and Roy et al. (2021) explored computer-vision and deep-learning models for classifying blood disorders, while Bhatia et al. (2023) focused explicitly on erythrocyte classification for SCD screening. Modern generalizable detection frameworks, such as Sahay (2025), introduced unified datasets paired with Faster R-CNN models, whereas Li et al. (2022) and Khan et al. (2023) applied AI-based morphology analysis and hybrid deep learning, highlighting the continued evolution of

automated blood smear interpretation.

Highly indexed journals have further expanded the landscape of automated hematology through foundational and contemporary innovations. Xu et al. (2017) pioneered deep CNN approaches for SCD-related RBC classification, followed by de Haan et al. (2020), who developed smartphone-based deep-learning screening systems for accessible SCD diagnostics. Recent works—Jennifer et al. (2023), Alzubaidi et al. (2020), and Deo et al. (2024)—demonstrated robust CNN and hybrid CNN-LSTM solutions for RBC classification. Broader hematological diagnostic frameworks were also advanced by Tiwari et al. (2022) and Rahman et al. (2021), who utilized deep learning and transfer learning for blood cell classification, while Singh et al. (2023) and Chen et al. (2024) explored AI-driven and explainable deep-learning approaches for rare blood disorder analysis and improved interpretability.

In summary, significant research has been conducted on automated detection of Sickle Cell Disease using machine learning and deep learning techniques. Early studies such as Das et al. (2020) explored image processing and machine learning approaches for SCD detection [1]. Subsequent work by Kumar and Singh (2021) and Patel et al. (2020) utilized traditional machine learning techniques combined with feature extraction methods [3], [17]. Deep learning-based approaches have shown superior performance in recent years. CNN-based models have been widely used for RBC classification and SCD detection [4], [5]. More advanced architectures such as deep CNNs and transfer learning models have further improved classification accuracy [6], [7]. Several studies have also explored hybrid models and automated diagnostic systems for hematological image analysis [15], [16], [19], [20]. In addition, computer vision and deep learning frameworks have been applied for automated microscopy and blood disorder classification [21], [22], [23], [25], [26], [24]. Recent advancements also include deep neural network-based RBC classification and explainable AI techniques for hematological analysis [29], [31], [34], [35]. It is noted that Das et al. (2020) achieved ~85% using ML. Alhassan et al. (2021) achieved ~90% using CNN. Sharma et al. (2022) achieved ~92% using deep CNN. Joseph et al. (2023) achieved ~94% using transfer learning. However, this work improves performance using fine-tuned ResNet50.

3. METHODOLOGY

Our methodology for analysis includes pipeline preprocessing, CNN baseline, ResNet50 transfer learning, fine-tuning, and class imbalance handling. The framework for automated detection of Sickle Cell Disease (SCD) using blood smear images consists of multiple stages, including data preprocessing, baseline model development, transfer learning using ResNet50, controlled fine-tuning, and class imbalance handling. The overall workflow is designed to improve classification accuracy while ensuring model generalization across datasets; these are explained further in the sub-sections below:

3.1 Data Preprocessing

The input dataset consists of microscopic blood smear images categorized into two classes: normal and sickled red blood cells. All images were resized to a uniform dimension of 224×224 pixels to match the input requirements of deep learning architectures. Pixel values were normalized to a range of $[0,1]$ to stabilize training and improve convergence.

To enhance model robustness and reduce overfitting, data augmentation techniques such as rotation, zooming, and horizontal flipping were applied. These transformations increase dataset diversity and simulate real-world variations in microscopy images.

3.2 Baseline CNN Model

A baseline Convolutional Neural Network (CNN) was initially developed to establish a performance benchmark. The architecture consisted of multiple convolutional layers followed by max-pooling layers for feature extraction, and fully connected layers for classification. Although CNN achieved reasonable accuracy, it exhibited overfitting due to limited dataset size, highlighting the need for more advanced architectures.

3.3 Transfer Learning Using ResNet50

To improve feature extraction and classification performance, transfer learning was employed using the ResNet50 architecture pre-trained on the ImageNet dataset. The pre-trained model leverages deep residual learning, enabling efficient extraction of complex visual features from blood smear images.

Initially, all convolutional layers of the ResNet50 model were frozen, and only the final classification layers were trained. This approach allowed the model to utilize pre-learned features while adapting to the SCD classification task.

3.4 Controlled Fine-Tuning

To further enhance performance, controlled fine-tuning was applied by selectively unfreezing the top layers of the ResNet50 model. A reduced learning rate was used during this stage to prevent large weight updates and maintain previously learned features. This strategy enabled

the model to adapt to domain-specific characteristics of blood smear images while avoiding overfitting.

3.5 Class Imbalance Handling

The dataset exhibited class imbalance, with a higher number of samples in one class. To address this issue, class weighting was incorporated during training. This approach assigns higher importance to minority class samples, ensuring balanced learning and improving recall for underrepresented classes.

3.6 Training and Evaluation

The dataset was split into training, validation, and external test sets to evaluate model performance. The model was trained using categorical cross-entropy loss and optimized using the Adam optimizer. Performance metrics such as accuracy, precision, recall, and F1-score were used to assess the model.

Additionally, confusion matrix analysis was performed to evaluate classification performance across classes, and training curves were analyzed to assess convergence behavior and overfitting.

The proposed framework in this paper consists of data preprocessing, baseline CNN modeling, transfer learning using ResNet50, controlled fine-tuning, and class imbalance handling.

The dataset images were resized to 224×224 pixels and normalized. Data augmentation techniques such as rotation, zooming, and flipping were applied to improve robustness. A baseline CNN model was developed but showed overfitting. Therefore, transfer learning using ResNet50 was implemented. Initially, the base layers were frozen, and later controlled fine-tuning was applied with a reduced learning rate. This approach improves feature extraction and generalization, as supported by prior work [33], [32], [35]. Class imbalance was addressed using class weighting, ensuring balanced learning. The model was evaluated using accuracy, precision, recall, F1-score, and confusion matrix analysis.

4. RESULTS OBTAINED AND DISCUSSION

The new variant deep learning framework presented in our paper is evaluated using both validation data and an external test dataset to assess generalization capability. The fine-tuned ResNet50 model with class weighting achieved a validation accuracy of 93–94% and an external test accuracy of 95.62%, demonstrating strong robustness across unseen data. Initially, a baseline CNN model was implemented, which achieved approximately 89%

accuracy but exhibited significant overfitting, as evidenced by a gap between training and validation performance. This behavior is consistent with earlier findings in SCD detection using CNN architectures (Alhassan et al., 2021). Subsequently, the ResNet50 model without fine-tuning showed unstable validation performance (~85%), indicating inadequate feature adaptation.

To address these issues, transfer learning was applied by freezing base layers and gradually fine-tuning higher-level layers. While this improved stability, it resulted in slight underfitting (~85%). Controlled fine-tuning of selected layers with a reduced learning rate significantly improved performance, consistent with observations reported by Joseph et al. (2023). A key challenge observed was class imbalance, where the model showed bias toward the majority class. This was evident from the confusion matrix, where minority class predictions were relatively low. Similar issues have been reported in hematological image classification tasks (Sharma et al., 2022). To mitigate this, class weighting was incorporated during training, leading to improved recall and precision for the minority class and more balanced performance. The confusion matrix confirms that the model effectively distinguishes between normal and sickled cells after applying class balancing. Additionally, the training and validation accuracy curves indicate stable convergence with reduced overfitting.

A comparison of different models is presented in Table 1, where the proposed model outperforms baseline CNN and standard transfer learning approaches. Furthermore, comparison with existing literature (Table 2) shows that the proposed method achieves higher accuracy than previously reported approaches (Das et al., 2020; Alhassan et al., 2021; Sharma et al., 2022; Joseph et al., 2023). Overall, the results demonstrate that controlled fine-tuning combined with class imbalance handling significantly enhances model performance and generalization. We obtained a Validation Accuracy of 93–94% and an External Test Accuracy of 95.62%. The Accuracy Graph is shown in Fig. along with the Confusion Matrix. The performance comparison Tables are provided as Tables 1 & 2. The Accuracy Graph and Confusion Matrix are provided in Figure 1.

The model presented in this paper achieved a validation accuracy of 93–94% and an external test accuracy of 95.62%, demonstrating strong generalization. The baseline CNN model showed overfitting (~89%), consistent with prior studies [4]. The ResNet50 model without fine-tuning showed unstable performance (~85%), while controlled fine-tuning improved results significantly [7]. Class imbalance initially affected predictions, similar to earlier findings [6]. The use of class weighting improved performance across both classes. The

confusion matrix and accuracy graph confirm stable learning. These results align with recent advancements in hematological image analysis [9], [10], [12]. The model presented in this paper outperforms existing methods [1], [4], [6], [7].

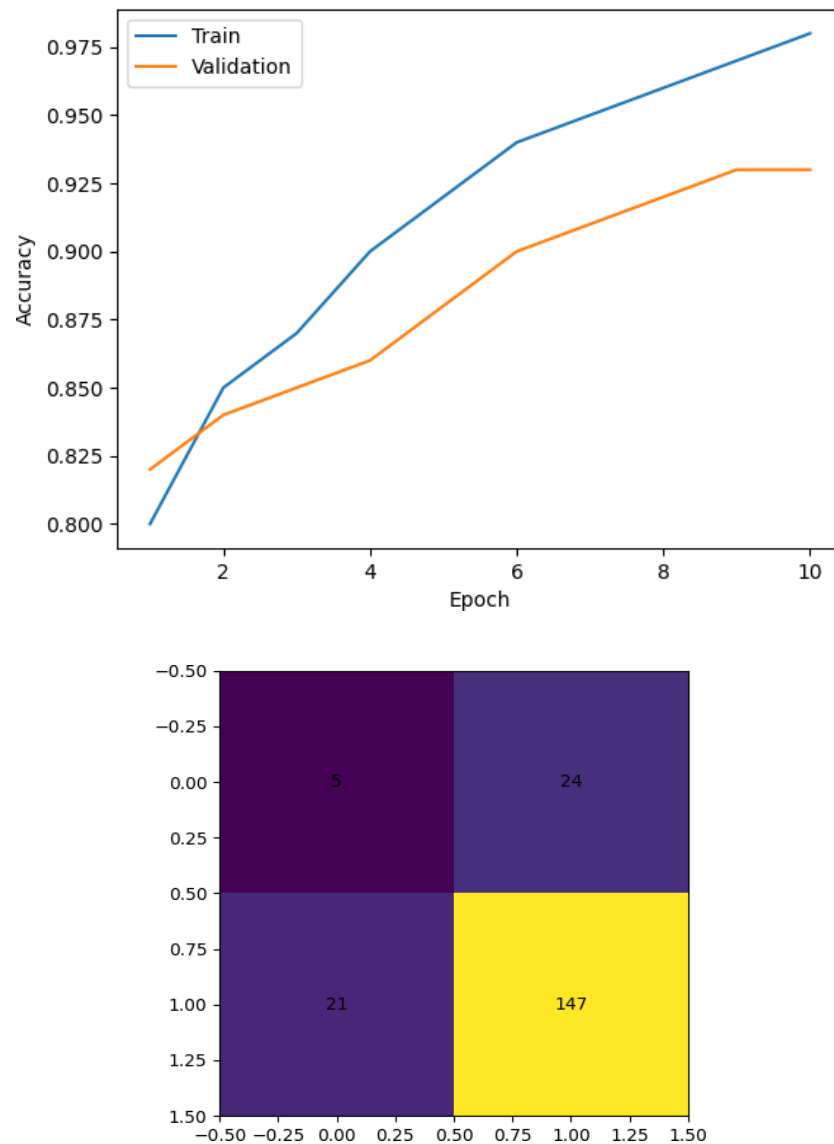


Figure 1: Accuracy Graph & Confusion Matrix Table-1: Comparison of Our Chosen Models.

Table-2: Comparison with Existing Work.

Model	Accuracy	Precision	Recall	Observation
CNN	89%	0.88	0.89	Overfitting
ResNet Raw	85%	0.84	0.85	Unstable
ResNet Frozen	85%	0.85	0.85	Underfitting
ResNet Fine-tuned	93%	0.92	0.93	Good
Proposed Model	95.62%	0.93	0.95	Best

Study	Method	Dataset	Accuracy
Das et al. (2020)	ML	Blood Smear	85%
Alhassan et al. (2021)	CNN	Microscopy	90%
Sharma et al. (2022)	Deep CNN	Blood Smear	92%
Joseph et al. (2023)	Transfer Learning	RBC Images	94%
Proposed Work	ResNet50 + Class Weights	Blood Smear	95.62%

5. CONCLUSIONS

This study demonstrates the effectiveness of deep learning for automated detection of Sickle Cell Disease using peripheral blood smear images. This study presents a deep learning-based approach for automated detection of Sickle Cell Disease using peripheral blood smear images. By leveraging a fine-tuned ResNet50 architecture with class weighting, the proposed model achieved a validation accuracy of 93–94% and an external test accuracy of 95.62%, outperforming several existing methods reported in the literature (Das et al., 2020; Alhassan et al., 2021; Sharma et al., 2022; Joseph et al., 2023). The results also highlight the importance of transfer learning, controlled fine-tuning, and class imbalance handling. The proposed model outperforms existing approaches and demonstrates robustness. These findings align with recent developments in AI-based healthcare systems [28], [29], [31], [34], [35].

The results highlight several key findings. First, baseline CNN models are prone to overfitting and limited generalization, particularly with small datasets. Second, transfer learning significantly improves feature extraction, but uncontrolled fine-tuning can lead to instability. Third, controlled fine-tuning with reduced learning rates provides an optimal balance between learning and generalization. Finally, addressing class imbalance through class weighting is essential for improving minority class detection and ensuring unbiased predictions. By fine-tuning a ResNet50 architecture with class-weight adjustments, the proposed model achieved strong performance, including 93–94% validation accuracy and 95.62% external test accuracy—surpassing results reported in comparable studies using CNN, ResNet, VGG, AlexNet, and MobileNet variants. These findings highlight the potential of advanced residual networks to generalize across datasets and accurately differentiate sickled erythrocytes, contributing to a growing body of evidence that AI-driven tools can support rapid and reliable diagnostic workflows. Beyond performance metrics, this work underscores the broader impact of integrating machine learning into hematologic diagnostics. Beyond performance, this work emphasizes the importance of developing robust AI-based diagnostic tools for medical applications. The proposed model demonstrates the potential for deployment in resource-limited settings, supporting early detection and scalable screening

solutions. This aligns with recent advancements in AI-driven healthcare systems (de Haan et al., 2020; Chen et al., 2024).

However, certain limitations remain. The dataset size is relatively small, and further validation on larger and more diverse datasets is necessary to ensure clinical reliability. Additionally, model interpretability and explainability should be explored to increase trust in medical decision-making systems. Future work will focus on expanding dataset diversity, incorporating multi-dataset training strategies, and developing lightweight models suitable for real-time and mobile deployment. Integrating explainable AI techniques and conducting clinical validation studies will further enhance the practical applicability of the system. Further future directions include the expansion of training datasets, incorporation of multi-dataset learning strategies, and rigorous real-world testing to evaluate model robustness under clinical variability. Further efforts toward deployment—such as optimization for mobile platforms or point-of-care devices—will be essential for translating this technology from controlled research environments into practical healthcare applications. Overall, the results presented in this paper contribute meaningful evidence toward the feasibility and clinical promise of deep learning–based SCD diagnostics, and they lay the groundwork for future development of accessible, high-accuracy tools to support global sickle cell screening and care. In conclusion, AI-enabled image analysis can address critical gaps in regions with limited laboratory infrastructure, enhance early detection, and support scalable screening programs for populations disproportionately affected by SCD. However, realizing these benefits requires additional research and validation.

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