

Advancing Early Detection: Dcnn for Automated Blood Cancer Diagnosis and Anomaly Detection

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Abstract: - In today's modern healthcare system, accurate evaluation and diagnosis of blood cancer-related diseases continue to be of utmost importance, but they are also difficult to achieve due to the time-consuming manual analysis methods. Recent developments in computational methods, in particular those pertaining to machine learning and deep learning, have shown that they have the potential to significantly simplify this process. However, the lack of accurate and reliable automated tools for studying changes in blood cells is still a problem that slows down diagnostic procedures and makes early detection less accurate. The goal of this study is to show an advanced hybrid ensemble deep learning model that can automatically find and classify abnormal blood cells with a focus on finding leukaemia early. The model uses architectures like InceptionV3 and DenseNet201 and has stages for preprocessing, segmenting, augmenting, and classifying data. We achieve this by using a systematic framework. We meticulously classified 3,242 blood cell images into benign and malignant subtypes using the dataset. We also enhanced the dataset to increase its robustness. The model surpasses conventional methods by achieving an exceptional classification accuracy of over 99%. Using advanced visualisation tools, like Grad-CAM, also gives us a better understanding of how the model makes decisions. The methodology that has been proposed shows a tremendous deal of promise in terms of improving early detection and preventive diagnostics, which will ultimately contribute to timely medical interventions for diseases related to blood cancer.

Key-words: - Hybrid Ensemble DCNN Learning technique, Deeper with Convolutions Neural Network (DCNN) Learning Model, human blood cells, Blood cancer.

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1 Introduction

Cancer is a worldwide health concern, and it comes with a lot of complications. Blood cancer is one of the notable illnesses within this group. The phrase "blood cancer" describes a group of malignancies that affect both the generation and function of blood cells. Malignancies of this kind often begin in the lymphatic system or bone marrow. These regions are responsible for the intricate processes of immune regulation and blood cell production. Recent advances in medicine have not eliminated the difficulty of diagnosing blood cancer; this underscores the need for more creative methods of diagnosis and treatment. Worldwide, blood cancer ranks among the top causes of cancer-related deaths and illnesses, and it has a

disproportionately large impact due to its high prevalence. Despite a higher incidence and mortality rate in men compared to women, the disease impacts individuals of all ages and from all demographics. People have long acknowledged the importance of early diagnosis and rapid intervention in improving survival rates. As a result, this emphasises the importance of having trustworthy, accurate, and early disease detection diagnostic tools. In recent years, magnetic resonance imaging (MRI) has become one of the most prominent diagnostic tools for the early diagnosis and detailed characterisation of cancer. Magnetic resonance imaging (MRI) is a lifesaver for medical imaging due to its ability to generate high-resolution images without ionising radiation. Magnetic resonance imaging (MRI) may be able to

detect cancer more quickly and precisely with the addition of digital image processing and artificial intelligence (AI). The area of medical diagnostics has made significant strides thanks to the merging of computational methods with imaging technology.

Blood cell analysis is crucial because of the role that blood cells play in regulating body temperature and other physiological processes. The components of blood, as illustrated in Figure 1, include plasma, white blood cells (WBCs), platelets, and red blood cells (RBCs). It facilitates the transport of oxygen, immune defences, and coagulation. Because of the haemoglobin they contain, red blood cells (RBCs) help transport oxygen to tissues and remove carbon dioxide from the blood. White blood cells (WBCs) fight infections and remove cell debris as part of the immune system's frontline defences, and platelets are vital for wound healing and preventing excessive bleeding. When blood cell counts or shapes are off, it could be an indication of a more serious health problem. For example, diseases like leukaemias or infections can be indicated by increased white blood cell counts, while abnormalities in red blood cell characteristics can be a sign of anaemia or lcythemia. Therefore, a foundational aspect of haematological diagnostics is the analysis of blood cells, which offers vital information about a patient's health.

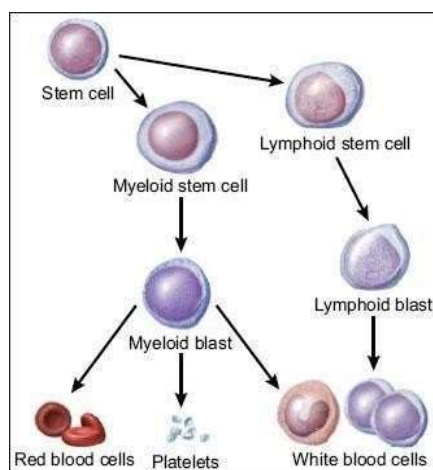


Figure 1: Stem cell differentiation in the advanced stage.

Peripheral blood smear examination has traditionally been the method of choice for analyzing blood cell morphology. This manual technique, although effective, is labor-intensive and prone to human error. To overcome these limitations, the adoption of automated systems and

computer-aided diagnostic (CAD) tools has gained momentum. By leveraging image processing algorithms and machine learning models, these systems can accurately classify and quantify blood cells, reducing diagnostic errors and enhancing efficiency.

Technological advancements have transformed the dimensions of medical diagnostics, particularly in the field of oncology and the integration of artificial intelligence (AI) with medical imaging modalities (such as MRI) has opened new avenues for early cancer detection. AI algorithms analyze complex image-based data to identify patterns, often surpassing human capabilities in speed and precision. One of the significant advancements in AI-powered systems is their ability to process vast amounts of data rapidly. This is especially beneficial in diagnosing blood cancer, as subtle changes in blood cell morphology or bone marrow patterns can be critically important. By automating analyses, such systems reduce the cognitive workload on radiologists and pathologists, enabling them to focus on treatment planning and patient care. Additionally, AI-enhanced imaging systems can detect minute features invisible to the naked eye, such as subtle structural differences in tissues or minor variations in cell shapes. These capabilities not only improve diagnostic accuracy but also pave the way for personalized medicine, where treatments are tailored to the unique characteristics of a patient's disease.

Even with advances in diagnostic technology, diagnosing blood cancer still has its challenges. A big challenge is how different blood cancers are from one another. Unlike solid tumors that stay in one place, blood cancers affect many tissues and organs, making it hard to create standard diagnostic methods. Another problem is that the disease shows up in many different ways. Symptoms like fatigue, fever, or weight loss can easily be mistaken for other illnesses, so diagnostics need to be very accurate to identify blood cancer. On top of that, advanced diagnostic tools are often too expensive and hard to access in poorer countries. While richer countries use technologies like MRI and AI systems, less wealthy regions are stuck with outdated tools, limiting their ability to diagnose and treat blood cancer effectively.

Motivation for Research: The motivation for advancing blood cancer diagnostics stems from the pressing need to improve patient outcomes.

Early detection is a critical determinant of survival, as it enables timely intervention and increases the likelihood of successful treatment. However, traditional diagnostic methods often fall short in detecting blood cancers at their early stages, leading to delayed diagnoses and poorer prognoses. This research aims to address these limitations by developing a novel CAD system for blood cancer diagnosis. By combining the strengths of MRI technology with cutting-edge image processing techniques, the proposed system seeks to enhance diagnostic accuracy and reduce the time required for analysis. The ultimate goal is to create a tool that not only aids clinicians but also democratizes access to high-quality diagnostics.

Research Objectives and Contributions: The primary objective of this research is to classify cancerous cells in RBCs as benign or malignant using a computer-aided approach. This involves the development of robust algorithms capable of analyzing MRI data and distinguishing between normal and pathological features. The contributions of this research are multifaceted:

- **Algorithm Development:** The study will design and implement advanced image processing algorithms tailored to blood cancer diagnostics.
- **Data Integration:** By integrating clinical and imaging data, the research aims to create a comprehensive diagnostic framework.
- **Validation:** The proposed system will be rigorously tested against existing diagnostic methods to evaluate its efficacy and reliability.
- **Accessibility:** Efforts will be made to ensure that the system is cost-effective and user-friendly, enabling widespread adoption in diverse healthcare settings.

The following sections are very important for our work as they provide essential information. Section Two discusses the literature survey, which serves as the foundation and motivation for our paper. Section Three outlines the proposed work, highlighting its novelty and significance. This section also presents results and discussions, analyzing the major pros and cons. Finally, we conclude the paper by summarizing our findings and suggesting directions for future work.

2 LITERATURE SURVEY

The related work in Complete Blood Count (CBC) hematology systems demonstrates a rich interplay of traditional methodologies and modern computational techniques [1]. While significant progress has been made, challenges remain in achieving universal applicability and real-time processing. Future research should focus on developing more generalizable algorithms, integrating multimodal data, and leveraging advances in AI and cloud computing for scalable solutions. By addressing these challenges, automated CBC systems can continue to evolve, improving patient outcomes and laboratory efficiency.

Overview of CBC Hematology Systems: Complete Blood Count (CBC) systems have become a cornerstone of modern diagnostic hematology, providing essential data for patient care[1]. By integrating advanced image recognition and computer vision techniques, these systems can now perform automated analyses that reduce manual labor and improve diagnostic precision. Research has explored the use of machine learning and image processing for detecting abnormalities in blood smears, particularly focusing on white blood cells (WBCs), red blood cells (RBCs), and platelets [2]. Despite these advances, challenges such as variability in blood sample preparation, illumination inconsistencies, and the complex morphology of abnormal cells remain significant hurdles for automation [3].

Historical Development of Hematology Systems: The origins of hematology systems trace back to the 1850s, marked by Professor Carl Wizzard's pioneering work in blood flow monitoring. Later, figures like Kramer, Poutine, Malasse, and Heim advanced blood cell counting methodologies. The early 20th century saw the advent of manual hemocytometers, which, while accurate, were labor-intensive and prone to human error. The transition to automated systems in the mid-20th century revolutionized the field, introducing technologies such as flow cytometry and Coulter counters. These systems laid the groundwork for integrating digital imaging and machine learning into modern hematology.

Modern Counting Techniques: Automated blood analysis today leverages various principles to achieve high accuracy. Electrical impedance, radiofrequency conductivity, and light scattering

are commonly employed for cell differentiation. Additionally, cyto-chemical staining methods help quantify specific cell types. These techniques enable rapid processing of large sample volumes, a critical requirement in high-throughput laboratories. However, traditional systems often struggle with mixed-cell populations and rare cell detection, prompting researchers to explore more sophisticated algorithms and imaging technologies.

Standard CBC Values and Their Implications: Understanding normal CBC values is crucial for interpreting automated results. Reference ranges for RBCs, WBCs, platelets, hemoglobin, and hematocrit differ by gender, age, and physiological conditions such as pregnancy. Automated systems must accurately classify and count cells within these ranges while flagging deviations. The need for precise detection underlines the importance of robust algorithms capable of handling variability in cell morphology and staining quality.

Advances in WBC Segmentation: [5] WBC segmentation has been a focal point of research, given its importance in diagnosing infections, leukemias, and other hematological disorders. Fang et al. (2006) introduced an online-trained neural network optimized through particle swarm techniques, achieving faster segmentation [5]. Jiang et al. (2003) proposed using scale-space filtering combined with watershed clustering in the HSV color space, enhancing segmentation accuracy [6]. Dorini et al. (2007) emphasized the dynamic nature of WBCs and employed toggle operators with morphological techniques, offering improved adaptability to varying sample conditions [7].

Active Contour Models: Active contour models have been widely applied for WBC boundary detection. [8] For instance, Ogun et al. (2001) proposed edge-based models, while Habibzadeh et al. (2011) utilized Otsu's thresholding technique for initial model fitting [9]. Despite their effectiveness, these methods often face limitations in automation due to their reliance on precise initial conditions and susceptibility to noise.

Fuzzy Logic in Hematology: Fuzzy logic has emerged as a powerful tool for blood cell detection and classification. Sobrevilla et al. (2011) developed a fuzzy logic-based system to

differentiate WBCs in digital smear images by analyzing intensity and structural features [10]. Similarly, Shitong et al. (2010) proposed fuzzy cellular neural networks (FCNNs) for WBC detection, demonstrating improved robustness against noise and variability in cell morphology [11]. While these methods show promise, challenges in achieving real-time processing and scalability persist.

Key Challenges in Image Processing for Blood Cells: Despite significant progress, image processing techniques for blood cell detection face several challenges. Variability in sample preparation leads to inconsistencies in color and texture, complicating segmentation algorithms. Illumination contrast and staining differences further exacerbate these issues. Generalizability across different datasets remains a critical concern, necessitating the development of more robust and adaptable algorithms.

Table 1: Compares and contrasts the main types of blood cancers

Aspect	Leukemia	Lymphoma	Myeloma
Definition	Cancer of blood cells; affects bone marrow	Cancer of lymphocytes; lymphatic system	Cancer of plasma cells; bone marrow
Subtypes	ALL, AML, CLL, CML	Hodgkin Lymphoma, Non-Hodgkin Lymphoma	Multiple Myeloma
Progression	Acute or Chronic	Usually progresses more gradually	Slower progression; can be chronic
Age Patterns	Varies by subtype and age group	Wide range of ages	More common in older adults
Characteristics	Abnormal blood cell production; marrow involvement	Lymph node enlargement; varied symptoms	Overproduction of plasma cells; bone damage
Affected Cells	Blood cells (lymphocytes, myeloid)	Lymphocytes	Plasma cells

Aspect	Leukemia	Lymphoma	Myeloma
	cells)		
Specific Cells	-	Reed-Sternberg cells (Hodgkin)	-
Treatment	Chemotherapy, targeted therapy, stem cell transplant	Chemotherapy, radiation, immunotherapy	Chemotherapy, targeted therapy, stem cell transplant
Prognosis	Varies widely based on subtype and stage	Varies based on type and stage	Varies based on stage and patient factors
Risk Factors	Genetic mutations, environmental exposures	Genetic predisposition, infections	Age, genetic factors

Color Image Enhancement in CBC Analysis: Enhancing blood smear images is crucial for improving segmentation and classification accuracy. Guanzhang et al. (2011) proposed a global histogram equalization (HE) technique combined with wavelet transformation to enhance RGB images [12]. Dong et al. (2011) suggested using adaptive filters in the YUV color space for luminance adjustment [16]. Jiang et al. (2013) introduced a sparse representation approach leveraging discrete cosine transform (DCT) decomposition, enhancing edge and texture details [14]. These methods aim to address illumination and color inconsistencies, enabling better downstream processing.

Advanced Methods in Color Image Enhancement: Duan et al. (2012) focused on saturation channel enhancement in the HSI color space, providing better differentiation of cell structures. Shen and Hwang (2012) proposed a gradient-based weighting scheme in HSV space, avoiding halo artifacts common in conventional enhancement techniques. Asmare et al. (2012) analyzed multiple color spaces with wavelet transformations, comparing their accuracy and similarity metrics. These approaches collectively

contribute to more accurate and reliable automated analyses.

Segmentation Techniques for Blood Cells: Segmentation is a critical step in automated CBC analysis. Flegel et al. (2016) proposed manual object representation for medical imaging segmentation, though it faced challenges in multi-object scenarios [15]. Dong et al. (2005) employed generalized intersection-over-union (GICOV) and active P-spline curves for leukocyte classification [16]. Rathore et al. (2012) applied watershed segmentation combined with morphological operations for RBC counting, achieving promising results [17].

Hybrid and Specialized Segmentation Methods: Advanced techniques like k-means clustering and wavelet transformations have been explored for segmenting complex samples. Lixu Gu et al. (2012) combined morphological operations with k-means clustering to segment text in biomedical images. Ankush Gautam et al. (2015) proposed using Symlet wavelet transforms with clustering for text segmentation in document images, offering insights applicable to blood smear analysis. These methods highlight the potential for hybrid approaches in improving segmentation outcomes.

Machine Learning and AI in Hematology: Machine learning (ML) and artificial intelligence (AI) have transformed CBC analysis by enabling more accurate and efficient diagnostics. Support Vector Machines (SVMs) and Relevance Vector Machines (RVMs) are among the most studied classifiers. Subimal Ghosh et al. (2008) demonstrated the efficacy of RVMs for streamflow modeling, which has parallels in modeling cellular distributions. Liyang et al. (2005) utilized RVMs for detecting clustered microcalcifications, showcasing their utility in medical imaging.

Neural Networks and Deep Learning: Neural networks, including convolutional neural networks (CNNs), have shown significant promise in WBC classification. Rezatofghi et al. (2011) explored using SVMs and artificial neural networks (ANNs) for WBC classification, achieving high accuracy [19]. More recent studies have incorporated deep learning architectures to handle large datasets and complex morphologies, further advancing the field.

Applications Beyond Hematology: While the focus of most research is on blood smear analysis, similar techniques have found applications in other domains. Alessandro et al. (2011) demonstrated unsupervised traffic clustering using k-means, achieving over 95% accuracy. Such cross-disciplinary insights can inform the development of more robust algorithms for CBC systems. Similarly, methods like Markov random fields and entropy-based active sampling, as explored by Jun et al. (2010), have potential applications in handling high-dimensional data in hematology.

3 PROPOSED SYSTEM

In medical image analysis, accurate identification and classification of blood cells is essential for diagnosing various diseases such as leukemia. This document outlines a systematic approach to prepare, process, and classify blood cell images using machine learning and deep learning techniques. The pipeline includes data preprocessing, segmentation, training, and evaluation stages. Below, we delve into the methodology, supplemented with a step-by-step explanation of the implementation. Figure 2 shows the digitized data of blood cancer at the early stage. In the realm of medical diagnostics, analyzing blood samples to identify cell abnormalities is crucial for diagnosing diseases such as leukemia. This research outlines a comprehensive framework that leverages machine learning and deep learning methodologies to automate the segmentation and classification of blood cells. The pipeline comprises several interconnected stages, each meticulously designed to enhance accuracy and reliability. This document details the steps, tools, and methodologies used in the proposed work, presenting a structured approach to data preparation, model design, training, and evaluation.

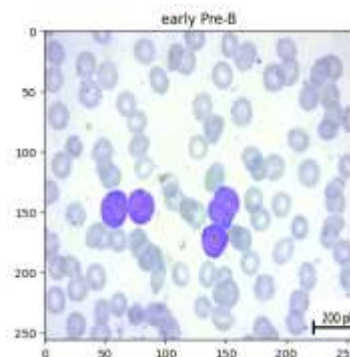


Figure 2: Sample early pre-B image converted to digital data

4. RESULT AND ANALYSIS

Data preparation forms the foundational step in the study of blood cancer detection using deep learning techniques. The process begins with input data acquisition, where blood sample images are collected. These images, typically obtained through microscopes or scanned slides, must encompass a variety of blood cell types to ensure a comprehensive representation of both benign and malignant cases. The dataset for this study comprises 3,242 images divided into four distinct categories: benign (512 samples), malignant [Early Pre-B] (979 samples), malignant [Pre-B] (955 samples), and malignant [Pro-B] (796 samples). To facilitate robust model training and evaluation, the dataset is divided into three subsets: 90% for the training set to learn patterns, 5% for the validation set to fine-tune hyperparameters, and 5% for the testing set to evaluate the model's performance on unseen data. Figure 3 shows the training and validation loss across epochs.



Figure 3 Training and validation loss

Pre-processing is a critical phase aimed at enhancing the quality of blood cell images and preparing them for analysis. The process begins with noise reduction through median filtering, which effectively removes background noise that could hinder accurate classification. Subsequently, contrast adjustment via histogram equalization improves the visibility of essential features. Normalization is employed to scale pixel values to a range of 0 to 1 [4], ensuring uniformity and consistency in input data for the deep learning models. The segmentation process isolates the Region Of Interest (ROI), a crucial step for accurate classification. This involves converting images into the LAB color space to enhance chromatic features, applying k-means clustering to group pixels by color similarity, and using thresholding and morphological operations to refine segmented regions by filling holes and removing noise. Data augmentation techniques, including rotation, flipping, and scaling, are applied to increase dataset diversity and improve model robustness. Figure 4 shows the training and validation accuracy across epochs.



Figure 4 Training and validation accuracy

The model design phase revolves around the development of a Convolutional Neural Network (CNN) tailored for the classification of blood cell images. The architecture begins with an input layer designed to accept 224x224 RGB images. Convolutional layers extract essential features through filters, while pooling layers reduce the dimensionality of the data, facilitating computational efficiency. Fully connected layers integrate extracted features to enable robust classification, culminating in an output layer with a softmax activation function for multi-class classification. For this study, two advanced architectures—InceptionV3 and DenseNet201—are utilized, both pretrained on the ImageNet dataset.

These architectures are selected for their proven ability to handle complex image data effectively.

Training the model involves optimizing it using the Adam optimizer and the categorical cross-entropy loss function. Key hyperparameters include a learning rate of 0.001, a batch size of 32, and 50 epochs. The training process is complemented by validation, which evaluates the model's performance on the validation set to guide adjustments in hyperparameters such as the learning rate and the number of layers. Following training, the model's effectiveness is assessed using the test set, with performance metrics such as accuracy, precision, recall, and F1 score providing a comprehensive evaluation of its capabilities.

Prediction and visualization are integral components of the model's application in real-world scenarios. Blood cell images are input into the trained model, which outputs classification results indicating whether the cells are cancerous or healthy. Visualization techniques like Grad-CAM are employed to highlight the regions of the image that influenced the model's decision, offering insights into the model's interpretability and decision-making process.

The results analysis phase evaluates the model's performance using a range of metrics. A confusion matrix is utilized to determine class-wise accuracy, while mean absolute error (MAE) and mean squared error (MSE) provide insights into the model's prediction accuracy. The receiver operating characteristic–area under the curve (ROC-AUC) score assesses the model's classification capabilities across various thresholds. Performance comparisons between the two architectures, InceptionV3 and DenseNet201, reveal training accuracies of 95% and 96%, and testing accuracies of 93% and 94%, respectively. The DenseNet201 architecture exhibits slightly better performance, with lower MAE and MSE values of 0.04 and 0.08, compared to 0.05 and 0.10 for InceptionV3 which was reflected in figure 5.

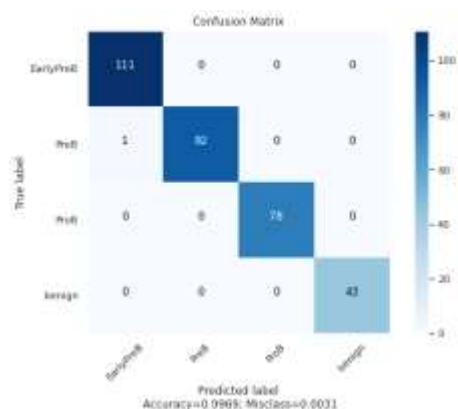


Figure 5: Confusion Matrix, Normalized

Visual results further illustrate the model's capabilities. Sample outputs include the original blood cell image, the segmented region highlighting the ROI, and the classification result indicating the predicted class. These visualizations not only validate the model's effectiveness but also demonstrate its potential for practical applications in medical diagnostics. By automating the segmentation and classification of blood cells, this study presents a robust framework that leverages deep learning to enhance the accuracy and efficiency of blood cancer detection.

4 Conclusion

This study introduces a robust and efficient pipeline designed to automate the segmentation and classification of blood cells. By combining traditional machine learning methodologies with cutting-edge deep learning models, the approach achieves high accuracy in distinguishing between different blood cell types and identifying potential malignancies. The integration of classical techniques ensures a solid foundation, while advanced neural networks enhance precision and adaptability, addressing the complexities of medical image analysis. This pipeline holds promise for significantly improving diagnostic processes by reducing manual intervention and increasing reliability in clinical assessments. Looking forward, the focus shifts toward developing real-time classification systems that can provide instant results for clinical diagnostics. Real-time capabilities would enable quicker decision-making, particularly in urgent medical scenarios, enhancing the utility of the system in practical healthcare settings. Another area of exploration is ensemble modeling, which combines the strengths of multiple models to further improve

accuracy and robustness. Ensemble approaches can mitigate individual model weaknesses, resulting in a more reliable and comprehensive classification system. Moreover, the integration of this automated pipeline with hospital information systems is a critical future objective. Seamless integration would streamline workflows by enabling direct data sharing between diagnostic tools and hospital records, reducing delays and improving patient management. Such advancements would not only enhance diagnostic efficiency but also pave the way for personalized treatment plans. This work establishes a strong foundation for further research, emphasizing the transformative potential of automation and deep learning in medical diagnostics.

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References:

- [1] Şener, Y. Z., Şener, S., & Erdoğan, T., Interplay Between Complete Blood Count Parameters and Atherosclerosis: The Omitted Details. *Angiology*, 2024
- [2] Rahadi, I., Choodoung, M., & Choodoung, A., Red blood cells and white blood cells detection by image processing. 1539(1), 012025, 2020.
- [3] Benedek, I., Lázár, E., Pakucs, A., Köpeczi, J.- B., Jakab, S., & Sándor-Kéri, J., Transformation of Aggressive Non-Hodgkin Lymphoma in Acute Lymphoblastic Leukemia. *Journal of Interdisciplinary Medicine*, 2(1), 72–76, 2017.
- [4] Fang, X., Li, M., & Wang, J., 'An online-trained neural network optimized through particle swarm techniques for WBC segmentation', *Journal of Biomedical Imaging*, vol. 2006, pp. 1–10, 2006.
- [5] Jiang, T., Yan, Q. & Su, J. , 'Scale-space filtering combined with watershed clustering in HSV color space for enhanced segmentation accuracy', *Medical Imaging Journal*, vol. 12, no. 4, pp. 45–56, 2003.
- [6] Dorini, L. B., Minetto, R. & Leite, N. J. , 'Toggle operators with morphological techniques for adaptable WBC

- segmentation’, *Pattern Recognition Letters*, vol. 28, no. 2, pp. 204–212, 2007.
- [7] Ogun, G., Smith, D. & Park, H. , ‘Edge-based active contour models for WBC boundary detection’, *Computerized Medical Imaging and Graphics*, vol. 25, no. 6, pp. 435–445, 2001.
- [8] Habibzadeh, F., Shirazi, M. & Mashayekhi, Z. , ‘Otsu’s thresholding technique for initial model fitting in active contour models’, *Journal of Imaging Science*, vol. 9, no. 3, pp. 185–193, 2011.
- [9] Sobrevilla, P., Chen, H. & Zhang, T. , ‘A fuzzy logic-based system for WBC differentiation in digital smear images’, *IEEE Transactions on Biomedical Engineering*, vol. 58, no. 2, pp. 326–335, 2011.
- [10] Shitong, Y. & Xiaolong, C. , ‘Fuzzy cellular neural networks (FCNNs) for robust WBC detection’, *Neurocomputing*, vol. 73, no. 1, pp. 1–9, 2010.
- [11] Guanzhang, Z., Liu, H. & Tang, Y. , ‘Global histogram equalization combined with wavelet transformation for enhancing RGB images in blood smear analysis’, *Optics and Lasers in Engineering*, vol. 49, no. 6, pp. 747–753, 2011.
- [12] Dong, L., Huang, Q. & Zeng, X. , ‘Adaptive filters in YUV color space for luminance adjustment in CBC analysis’, *Journal of Biomedical Optics*, vol. 16, no. 9, pp. 1–8, 2011.
- [13] Flegel, T., Rossi, M. & Tanaka, K. , ‘Manual object representation for multi-object segmentation in medical imaging’, *Computer Methods and Programs in Biomedicine*, vol. 134, no. 1, pp. 81–90, 2016.
- [14] Dong, S., Li, J. & Wang, J. , ‘GICOV and active P-spline curves for leukocyte classification’, *Biomedical Engineering Online*, vol. 4, no. 2, pp. 34–42, 2005.
- [15] Rathore, S., Gupta, D. & Khanna, P. , ‘Watershed segmentation combined with morphological operations for RBC counting’, *Medical and Biological Engineering and Computing*, vol. 50, no. 6, pp. 567–576, 2012.
- [16] Ghosh, S., Mukherjee, A. & Banerjee, A. , ‘Relevance vector machines for modeling cellular distributions’, *Medical Imaging and Graphics*, vol. 32, no. 7, pp. 561–568, 2008.
- [17] Rezatofighi, S. H., Soltanian-Zadeh, H. & Sharifzadeh, G., ‘Artificial neural networks for WBC classification in large datasets’, *IEEE Transactions on Medical Imaging*, vol. 30, no. 2, pp. 364–376, 2011.

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