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Improvement of the Performance of Cell Counter Devices Using a Proposed Model Combining Multilayer Perceptron Neural Networks

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ABSTRACT

In automated cell counting devices, the performance of the counting channel can be significantly affected under problematic conditions, such as platelet aggregation, leading to inaccuracies in key blood parameter measurements. Given the limitations of existing algorithms in addressing these challenges, this study proposes an enhanced algorithm to improve the counting accuracy of critical blood components, particularly platelets and hematocrit, within the counting chamber. To achieve this, a hybrid approach integrating two computational models was implemented, demonstrating an improvement in overall counting performance. Among the tested optimization techniques, the Satin Bowerbird Optimization (SBO) Algorithm yielded superior results, outperforming other methods in terms of prediction accuracy. While the Biogeography-Based Optimization (BBO) Algorithm and the Teaching-Learning-Based Optimization (TLBO) Algorithm exhibited higher accuracy for certain blood parameters compared to the SBO Algorithm, the SBO Algorithm achieved the highest number of correct predictions across all parameters. In contrast, the Particle Swarm Optimization (PSO) and Firefly (FA) Algorithms failed to produce reliable results. The findings highlight the effectiveness of the proposed algorithm in enhancing the robustness and precision of blood parameter quantification, making it a promising approach for improving automated cell counting in clinical and laboratory applications.

1. INTRODUCTION

Today, the establishment of a clinical diagnostic laboratory requires a cell counter device. Each laboratory selects the appropriate device from a plethora of available options based on budget, number of patients, required measurement parameters, device quality, accuracy, and speed. Blood tests and differential counts, which include the enumeration and morphological evaluation of red blood cells, platelets, leukocytes and their subgroups, as well as the measurement of hemoglobin, hematocrit, and erythrocyte indices, are unique [1-13]. These tests provide a quantitative and qualitative (morphological) analysis of blood cells, forming the foundation for diagnosing

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hematological abnormalities [14]. Currently, information from differential blood cell counts holds a significant place in laboratory and clinical hematology and is widely used for purposes such as screening, diagnosis, and monitoring blood and non-blood diseases. For example, in diagnosing infectious diseases, monitoring the course and response to treatment of blood diseases, and many other cases, this test plays an essential role [15].

Most laboratory specialists believe that the initial blood count test for each patient should be performed automatically. The key to this success lies in the analyzers' ability to quantitatively and qualitatively detect blood disorders and the presence of warning systems that identify samples requiring further examination. The warning symbols generated by these systems may lead to manual counting of the patient's sample or, at the very least, microscopic examination of the peripheral blood smear by the device operator. This approach ensures that patient needs are optimally met while the laboratory's potential is efficiently utilized. Factors such as the patient population served by the laboratory, the percentage of abnormal samples, the type, model, and warning criteria selected for the analyzer all influence the success of employing automatic methods. Therefore, modern hematology laboratories must consider how to routinely incorporate hematology analyzer results into their daily operations. The diagram below illustrates the optimal use of automatic and manual methods in most laboratories across the country.

Despite the efforts to enhance laboratory efficiency—whether through increased automation to reduce workload and save time, or by providing new parameters that might have clinical value—these devices still exhibit weaknesses when handling problematic samples. Manual blood testing is very time-consuming and labor-intensive, requiring highly skilled and experienced personnel, and is prone to multiple errors. Many studies have focused on manual methods or used deformable algorithms (such as snakes, watershed transform, etc.). However, these methods are impractical due to high computational costs and lengthy execution times. Consequently, there is still a need for an efficient algorithm to automate cell counting. Given the drawbacks of blood counters (in abnorma1 conditions like platelet aggregation, the presence of nucleated red blood cells in samples from oncology patients and newborns) and the shortcomings of the proposed algorithms for automated recognition of blood cells, this project aims to develop an algorithm to improve the counting process for parameters like platelets and hematocrit in a chamber called the counting channel. These blood parameters were selected because they are recognized as key or super parameters. These devices use various methods to measure and count cells, but almost all utilize one of four methods: impedance (electrical impedance method—change in electrical conductivity), optical (electro-optical), cytochemical, and hybrid. In this study, the device examined was a Sysmex model, with the researcher assessing the accuracy and precision of blood parameter counts using the impedance method. Cell counting in these types of cell counters, which is based on cell size, operates as follows: each cell counter has two apertures for blood cells to pass through, referred to as the counting bath or counting channel. Two electrodes on either side of these apertures detect changes in electrical resistance as blood cells pass through, with each change corresponding to a pulse and a count. However, in abnormal conditions like platelet aggregation, the counting channel shows weaknesses. Based on the above, the main objectives of this research are: - to examine the impact of each of these parameters on the overall performance of the device - to mathematically model the device's sensitivity to these parameters.

2. LITERATURE REVIEW

The first efforts to count blood cells began shortly after their discovery by van Leeuwenhoek (17th century). Following his invention of the first microscope, van Leeuwenhoek diluted chicken red blood cells in a capillary tube and counted the cells. This method evolved alongside advancements in microscopes and cell counting chambers over the next two decades. Researchers eventually developed blood cell counting devices, making cell counters one of the most widely used laboratory instruments. Yampri et al. (2006) proposed an automatic thresholding method using the green channel of images for high contrast between the nucleus and cytoplasm. Residual noise in the image was corrected using initial morphological algorithms, and the nucleus and cytoplasm were separated by an adaptive environment [16]. In this algorithm, separating the nucleus and cytoplasm is challenging because some leukocytes, such as neutrophils and eosinophils, have more than one nucleus. Sabino et al. (2004) used the green channel of a color image and selected an appropriate threshold to identify the spatial limits of leukocyte nuclei. They used simple filters such as the median filter to reduce noise during preprocessing and improved image contrast with histogram equalization [17]. Dorini et al. (2007) employed the watershed transform algorithm based on connectivity for nucleus segmentation. Information on size distribution was used to separate the cytoplasm from the background and red

blood cells [18], with morphological opening algorithms applied to enhance image areas. This method is ineffective when the cytoplasm is not spherical or red blood cells vary in size. Sadeghian et al. (2009) presented a method for differentiating the nucleus and cytoplasm in grayscale images using the snakes algorithm and Jacques thresholding [19]. Initially, a sub-image was manually selected, then the nucleus was identified using the Canny edge detection and snakes algorithms. After subtracting the nucleus from the selected sub-image and applying thresholding, the cytoplasm of the cell was determined. This method requires manual selection of the sub-image by an operator and struggles to separate the cytoplasm and nucleus in multi-nucleated cells. Moreover, since the red blood cells near the cytoplasm have similar intensities, segmenting the cytoplasm from the red blood cells using grayscale images is inefficient. This method was tested on only 20 images, and no comparative performance analysis was conducted.

Many studies have utilized deformable algorithms such as the snakes algorithm, watershed transform, etc., for separating the cytoplasm from the nucleus, differing primarily in selecting the initial boundary to avoid local minima. However, these methods are impractical due to high computational costs and long execution times. Additionally, most studies have focused on nuclear features because of segmentation algorithm limitations. However, nuclei of certain differential white blood cells are very similar, and relying solely on nuclear features increases classification errors. The obtained classification results highlight this issue. Our review found no studies specifically focused on improving cell counter performance, indicating the need for a practical algorithm to automate cell counting. Therefore, the next chapter presents the proposed approach.

3. RESEARCH METHODOLOGY

The proposed model for predicting blood parameters was implemented using MATLAB software. This model combines a multilayer perceptron neural network with various optimization algorithms, including the Firefly Algorithm, Teaching-Learning-Based Optimization (TLBO) Algorithm, Satin Bowerbird Optimization (SBO) Algorithm, Biogeography-Based Optimization (BBO) Algorithm, and Particle Swarm Optimization (PSO) Algorithm. These optimization algorithms were employed to find the optimal weights and biases for the neural network.

The TLBO Algorithm is a population-based method that uses a set of solutions to move towards a global solution. It is divided into two phases: the teacher phase, which involves learning from a teacher, and the learner phase, which involves learning through interaction among students.

The Firefly Algorithm focuses on two main issues: the difference in light intensity and the formulation of attractiveness.

The main steps of the Satin Bowerbird Optimization Algorithm include:

- Generating a random set of bowers,
- Calculating the probability for each member of the population,
- Elitism,
- Determining new position changes,
- Mutation,
- Combining the old population with the new population.

The Biogeography-Based Optimization Algorithm is population-based but does not involve reproduction, distinguishing it from reproductive strategies like genetic algorithms and evolutionary strategies. It avoids repeating solutions in the next set based on transfer probabilities aligned with solutions. It is easier to implement and requires fewer parameters to adjust. This evolutionary process models information sharing through species migration.

The Particle Swarm Optimization Algorithm retains knowledge of good solutions through all particles. Each member adjusts its position based on personal and collective experiences. This social information exchange among community members leads to evolutionary benefits, forming the basis for the development of the Particle Swarm Optimization Algorithm. The algorithm benefits from collaborative efforts among particles, sharing information to

solve problems efficiently and quickly converging on optimal solutions. The Particle Swarm Optimization Algorithm, compared to other optimization strategies, is highly adaptable to local optima problems, is easily implementable, and is widely used in solving many discrete and continuous nonlinear optimization problems. Interestingly, this algorithm only employs basic mathematical operators and yields excellent results in stable, noisy, and continuously changing dynamic environments.

The primary goal of the proposed model is to precisely tune the weights and biases of the neural network using optimization algorithms for more accurate estimation. Essentially, optimization algorithms are used to suggest the most suitable weights and biases at each stage. The steps for designing the optimized neural network are as follows:

- Inputting Training and Testing Data

Initially, the input data to the neural network were normalized between zero and one. The data were then randomly divided into three equal (approximately equal) sets using a three-stage cross-validation evaluation. In each stage, one set was used as test data, and the other two sets as training data. This process continued until each set had been used as test data. The average results from the three stages were considered the final outcome.

- Creating and configuring a Neural Network

In the proposed model, a multilayer perceptron neural network was used as the base network. This network had initial parameters that needed to be specified, including:

- PR matrix: This matrix specifies the minimum and maximum for each network input.

- Determining the number of layers and neurons in each layer.

- Defining activation functions at each stage.

- Optimizing Weights and Biases

Optimizing neural network parameters is crucial in designing an optimal neural network. This stage is detailed as follows:

- Determining the number of elements in the weight matrix, input weight, and bias matrix: These matrices contain all the weights and biases of the neural network. The optimization algorithm must generate variables equal to this number at each stage.

- Generating a series of random variables between -1 and 1 for initial values using the optimization algorithm.

- Optimizing the generated variables at each stage based on the error at each step and placing them in the weight and bias matrices of the neural network.

- Returning the optimized weights and biases if termination conditions are met.

- Evaluating the optimized neural network using test data to obtain the final result.

The flowchart in Figure 1 illustrates the design steps for the optimized neural network.

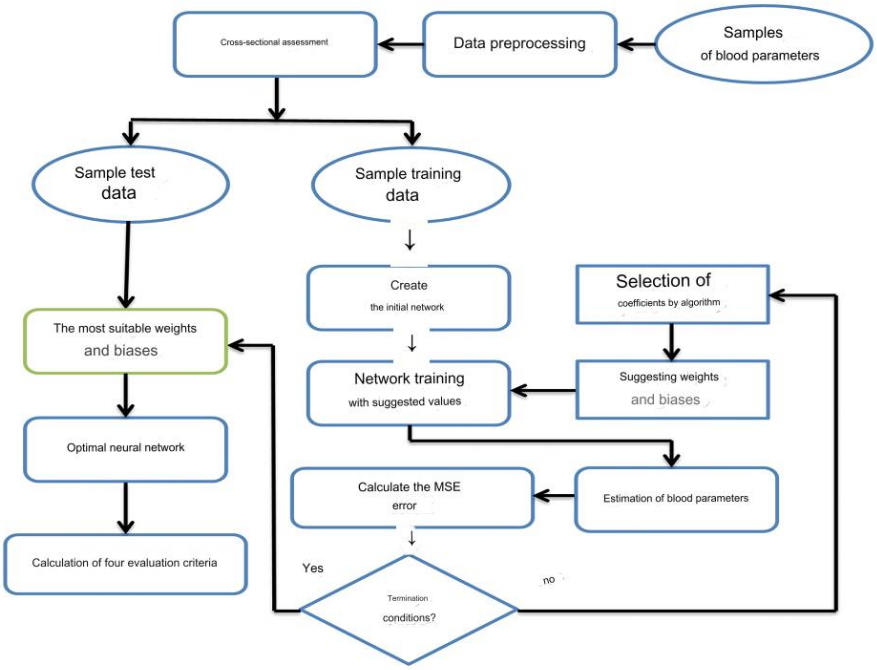

Fig.1. Flowchart of the Proposed Model Steps

Table 1 presents the results obtained from combining the multilayer perceptron neural network with various algorithms on the test dataset. As shown, the proposed multilayer perceptron neural network model with the Satin Bowerbird Optimization Algorithm achieved the best values for all evaluation criteria for both hematocrit and platelet parameters by selecting the most suitable weights and biases. The Satin Bowerbird Optimization Algorithm and the Teaching-Learning-Based Optimization Algorithm ranked second and third, respectively.

Table 1. Results from the Proposed Model on the Male Dataset

Method	Blood Parameter	MSE	RMSE	Precision	Accuracy
MLP-TLBO	HCT	0.025	0.158	77.37	79.34
	PLT	0.030	0.174	68.23	70.35
MLP-PSO	HCT	0.023	0.153	87.68	89.67
	PLT	0.029	0.170	70.24	72.38
MLP-SBO	HCT	**0.014**	**0.119**	**92.87**	**94.15**
	PLT	**0.028**	**0.167**	**72.35**	**74.19**
MLP-BBO	HCT	0.019	0.141	89.43	91.53
	PLT	0.034	0.185	58.04	59.86
MLP-FA	HCT	0.029	0.172	47.23	48.35
	PLT	0.071	0.267	49.13	50.65

The mean squared error (MSE) for the proposed multilayer perceptron neural network model with the Satin Bowerbird Optimization Algorithm for hematocrit and platelet blood parameters is lower than that of the other four models. A comprehensive analysis of the results obtained from various algorithms on this dataset reveals that the proposed multilayer perceptron neural network model with the Satin Bowerbird Optimization Algorithm is more suitable for predicting hematocrit and platelet blood parameters compared to other models.

4. CONCLUSION

One of the most critical sections of a clinical diagnostic laboratory is hematology, where blood cell analysis can play a significant role in disease diagnosis. Various tests are performed on patients' blood samples in the hematology section, most of which involve a complete blood cell count and differential leukocyte count. These tests form the cornerstone of diagnosing hematologic abnormalities.

The initial attempts to count blood cells occurred shortly after their discovery by van Leeuwenhoek in the 17th century. Following the invention of his first microscope, he diluted chicken red blood cells in a capillary glass tube to count the cells. This method evolved over the next two decades alongside the development of microscopes and cell counting chambers. After years of effort, researchers were able to introduce blood cell counting devices. In general, cell counters are one of the most widely used and essential laboratory instruments. A cell counter comprises various units, each affecting the device's overall performance. Hematology analyzers or cell counters are fully automated machines used for quantitative measurement of blood parameters in medical laboratories. In other words, these devices count the number of blood cells in a specified volume of blood. The main components of a cell counter typically consist of three main systems: hydraulic, pneumatic, and electronic.

Hydraulic System Functions: The hydraulic system's functions include drawing the necessary solutions and blood samples, discharging the drawn solutions or blood, diluting the sample, mixing the sample with solutions, and adding lysing solution to the sample.

Pneumatic System Functions: The primary function of the pneumatic system is to generate a vacuum or constant pressure to control valves and regulate the movement of solutions and samples within the hydraulic system.

Electronic System Functions: This system is controlled by a microprocessor and is responsible for the following tasks:

1. Measuring and processing signals resulting from impedance changes.
2. Calculating and transmitting results to the printer or any desired output.
3. Plotting graphs of main parameters.
4. Controlling measurement timing and test sequences.
5. Executing the Q.C. program and system calibration.
6. Storing and retrieving results.

Principles of Blood Cell Counting: In conventional cell counters, based on cell size, there are two apertures or orifices: one for red blood cells and platelets and the other for white blood cells. The diluted sample is suctioned into the red and white blood cell orifices by negative pressure. Two electrodes are placed on either side of these orifices, and when a blood cell passes through them, the electrical resistance between the electrode’s changes. Each change is considered a pulse and a count. Conventional cell counters typically directly measure the number of white blood cells, red blood cells, platelets, and hematocrit, plot histograms for them, and calculate other blood indices based on these measurements. Some cell counters can approximately differentiate normal white blood cells based on cell size. All these devices use an optical system similar to a spectrophotometer to measure hemoglobin at a wavelength of 520 nanometers. Additionally, these devices can distinguish normal white blood cells from abnormal ones using peroxidase staining.

The impedance method is more commonly used due to its relative ease and benefits. Optical cell counters report hematology indices using light and the principles governing it. Cytochemistry, a method exclusively used in Bayer devices, is also employed. Various companies worldwide offer different types of these devices with different methods, with Sysmex being one of the most prominent.

In the proposed model, different optimization algorithms produced varying results by suggesting different weights and biases. In this model, as in the previous one, using the Satin Bowerbird Optimization Algorithm resulted in better outcomes than other algorithms, with the highest number of correct predictions. The Particle Swarm

Optimization and Firefly Algorithms failed to produce any acceptable results. For further studies, the following suggestions are proposed:

- In this study, platelet and hematocrit parameters were counted in the counting bath (counting channel); hence, hardware implementation is necessary to automate all counting stages with minimal error, improving the performance of the counting channel and relevant orifices.

- Feature selection of blood parameters using optimization algorithms instead of using all parameters for the prediction process.

- Performing feature selection of blood parameters in a fuzzy manner (a percentage of each feature).

- Reporting other identified cell parameters such as area, granule staining intensity, and leukocyte perimeter to assist the treating physician significantly. Evaluating these indices may also help diagnose specific diseases, which requires conducting tests to match program results with a particular group of patients.

- Implementing the proposed algorithm using the C or C++ programming language instead of MATLAB to improve the algorithm's speed. Additionally, using a user interface will facilitate user interaction with the program.

Transparency Statement

The data supporting this study are available upon reasonable request to the corresponding author, subject to ethical and confidentiality considerations.

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Declaration of Interest

The authors declare that they have no competing interests.

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