

# CNN-Based Image Analysis for Malaria Diagnosis

Zhaohui Liang,<sup>1</sup> Andrew Powell,<sup>2</sup> Ilker Ersoy,<sup>3</sup> Mahdieh Poostchi,<sup>4</sup> Kamolrat Silamut,<sup>5</sup> Kannappan Palaniappan,<sup>4</sup> Peng Guo,<sup>6</sup> Md Amir Hossain,<sup>7</sup> Antani Sameer,<sup>8</sup> Richard James Maude,<sup>5</sup> Jimmy Xiangji Huang,<sup>1</sup> Stefan Jaeger,<sup>8\*</sup> George Thoma<sup>8</sup>

1 School of Information Technology, York University, Toronto, ON, M3J1P3, Canada

2 Computer Science Department, Swarthmore College, Swarthmore, PA 19081, USA

3 School of Medicine, University of Missouri, Columbia, MO 65212, USA

4 Computer Science Department, University of Missouri, Columbia, MO 65211, USA

5 Mahidol-Oxford Tropical Medicine Research Unit, Mahidol University, Bangkok, Thailand

6 Electrical and Computer Engineering Department, Missouri S&T, Rolla, MO 65409, USA

7 Chittagong Medical College Hospital, Chittagong, Bangladesh

8 National Library of Medicine, National Institute of Health, Bethesda, MD 20894, USA.

\*Corresponding Author: Stefan Jaeger, email: stefan.jaeger@nih.gov

**Abstract**— Malaria is a major global health threat. The standard way of diagnosing malaria is by visually examining blood smears for parasite-infected red blood cells under the microscope by qualified technicians. This method is inefficient and the diagnosis depends on the experience and the knowledge of the person doing the examination. Automatic image recognition technologies based on machine learning have been applied to malaria blood smears for diagnosis before. However, the practical performance has not been sufficient so far. This study proposes a new and robust machine learning model based on a convolutional neural network (CNN) to automatically classify single cells in thin blood smears on standard microscope slides as either infected or uninfected. In a ten-fold cross-validation based on 27,578 single cell images, the average accuracy of our new 16-layer CNN model is 97.37%. A transfer learning model only achieves 91.99% on the same images. The CNN model shows superiority over the transfer learning model in all performance indicators such as sensitivity (96.99% vs 89.00%), specificity (97.75% vs 94.98%), precision (97.73% vs 95.12%), F1 score (97.36% vs 90.24%), and Matthews correlation coefficient (94.75% vs 85.25%).

**Keywords**— convolutional neural network; deep learning; malaria; computer-aided diagnosis; machine learning

## I. INTRODUCTION

Malaria is a major infectious disease of humans. The pathogen of malaria belongs to the genus *Plasmodium*, a parasitic protozoan which can invade human erythrocytes and cause a range of symptoms. According to the WHO, 214 million people were affected by malaria in 2014 with more than 438,000 deaths [1, 2]. The economic impact has been estimated at up to 12 billion dollars per year [3].

Malaria could be prevented, controlled, and cured more effectively if a more accurate and efficient diagnostic method were available. The standard diagnostic method for malaria is the microscopic examination of blood smears for infected erythrocytes by qualified microscopists. However, this method is inefficient and the quality of the diagnosis depends on the experience and knowledge of the microscopists. Rapid diagnostic tests are also widely used but they are more expensive and provide less information than microscopy. Automatic image recognition technologies based on machine learning and big data

have been applied to both thick and thin malaria blood smears for microscopic diagnosis since 2005 [4].

In this work, we use a deep learning approach to detect parasite-infected red blood cells in thin smears on standard microscope slides prepared using routine methods. We apply a convolutional neural network (CNN) model, which is a deep learning model particularly designed for learning of two-dimensional data such as images and videos. It is inspired by experiments on the underlying physiological mechanisms in the visual cortex of felines for recognizing objects [5]. The experiments motivate a pattern recognition model to mimic the visual information processing of the brain [6]. The advantage of a CNN model is that its hierarchical structure of learning layers can be trained in a robust manner once the topology of the model fits the feature input. The model can efficiently leverage the spatial relations of the visual patterns (e.g. the edges in an image) to reduce the number of parameters that need to be learned. This improves the accuracy of the feedforward-backpropagation training procedure. Since deep learning can model very complex features, a CNN provides a general-purpose learning framework not requiring beforehand feature extraction and fine-tuning, which is an advantage over traditional classifiers.

## II. RELATED WORK

### A. Automatic Malaria Blood Smear Classification

Machine learning has been used to detect parasitemia in images of Giemsa-stained blood smears in [7]. This early study compared the correlation between automatic and manual parasitemia detection but did not classify infected and uninfected red blood cells. In 2009, a study by Diaz et al. applied a support vector machine (SVM) to classify preprocessed blood smear images to detect infected erythrocytes. The proposed algorithm performed well, in specificity and sensitivity, on a small dataset of 450 malaria images. Unfortunately, the model performance decreases when it is applied exclusively to blood images in the infection stage [8].

In summary, the existing approaches for automatic slide processing have only been evaluated on relatively small image sets. Although the reported outcomes are encouraging, all methods still need to prove their robustness and performance on

---

This research is supported by the HHS Ventures Fund and the Intramural Research Program of NIH, NLM, and Lister Hill National Center for Biomedical Communications.

a large set of images. It is fair to say that the current systems still leave much room for improvement in this regard. Therefore, we are proposing a new system based on deep learning, which exhibits robustness and good performance on a large and realistic image set.

### B. Convolutional Neural Network

A convolutional neural network (CNN) is a specific deep learning architecture suitable for image recognition. A CNN model processes input data by its multiple layers and is characterized by four key features: local connections, shared weights, pooling, and the use of many layers [9]. The early applications of CNN can be traced back to the 1990s for speech recognition [10] and text recognition [11]. Its use is then extended to handwriting recognition [12] and later to natural image recognition [13]. The performance of CNN models for natural image classification received another boost by the introduction of ImageNet by Alex Krizhevsky, thus also known as AlexNet, in 2012. AlexNet is considered a breakthrough application of CNNs to multi-categorical classification. In the ILSVRC-2012 competition, ImageNet composed of seven convolutional layers successfully classified the ILSVRC-2012 sets with 10,184 categories and 8.9 million images with a top-5 error of 15.3% [14]. Following this initial success, the top-5 error has been reduced to 14.8% by ZFNet in 2013 [15], then to 6.7% by GoogLeNet in 2014 [16], and to 3.6% by ResNet in 2015 [17].

### C. Challenges for CNN Applications

The idea of CNNs is to apply smaller convolutional kernels (or filters) in combination with a deep network architecture to capture the discernable image features as much as possible. However, a more complex CNN architecture will inevitably increase the demand for more powerful computing resources. New technologies such as GPU and cluster computing can effectively improve the training efficiency but they are unable to ensure the performance of classification. Other factors such as data preprocessing and size of the training dataset strongly affect the classification accuracy, however. Since the CNN classification accuracy depends on the amount of training data, small data sets such as those used in earlier approaches are not large enough for training a deep model with its many parameters. As a compromise, the method of transfer learning has been introduced where a pre-trained network model is used to extract features that a conventional classifier, such as a SVM, can use for a fine-tuned classification [18]. Transfer learning can be used as a shortcut to deep learning where time for training is saved at the cost of performance, which may be lower but still acceptable. It can be used as a temporary replacement when large training data is not immediately accessible. In this study, we will implement deep learning by both training a newly configured CNN model and applying transfer learning in order to evaluate its use for malaria blood smear classification.

## III. CONFIGURATION OF A CONVOLUTIONAL NEURAL NETWORK

The architecture of a CNN will largely determine the final net performance after training. The basic mechanism of deep learning is to apply a multi-layer network to map the input space by transforming it at the hidden nodes. Using a series of

transformations, the network tries to learn the optimal mapping of the input data through a process called back-propagation. In this process, the partial derivative or gradient of the input parameters is computed from the partial derivative of the output, given an objective function, by applying the chain rule. Thus the changes of one layer can be computed recursively by measuring the changes of the following layer connected to it.

Learning of a CNN model consists of two inverse computations: the feed-forward and the said back-propagation [19]. The feedforward propagation computes the output of all units in each layer, where for each unit a non-linear activation function  $f$  is applied to the weighted sum of all inputs from the preceding layer.

The activation function can be a rectified linear unit (ReLU), hyperbolic tangent (tanh), logistic function etc. Back-propagation is applied to train or fine-tune the deep network by optimizing the parameters/weights of each layer. By applying the above propagation mechanisms, a CNN can create a model of the input data when sufficient training data enters and propagates through the whole network.

### A. CNN Architecture for Malaria Image Classification

Based on the above discussion, we apply a 17-layer CNN model for the malaria blood smear classification task (see Fig. 1).

Note that the network is organized by blocks of similar layers where the width and height of the feature maps are  $1 \times 1$  and the depth of the feature representations is 256 at the last fully connected layer. The sandwich design with one convolutional layer plus one ReLU layer allows enhanced learning [14, 20].

## IV. MODEL EVALUATION

### A. Data Source

We used archived blood smear images acquired from Chittagong Medical College Hospital, Bangladesh, and segmented the visual region of the erythrocytes from the original images [21]. Our data set contains 27,578 erythrocyte images where the ratio of infected cells to uninfected cells is 1:1. All images are normalized to the median width and height for the training and classification experiments, at  $44 \times 44$  pixels, with three color channels.

### B. Data Preprocessing

All images are read into MATLAB, resized if needed, and serialized to generate the input to the MatConvnet toolbox [22]. Before we pass the data to the CNN network for training, we apply a normalization to improve local brightness and contrast, and whiten the entire dataset using an eigenvalue decomposition (EVD) operation on the covariance matrix [22].

### C. CNN Model Training

In order to train and evaluate our CNN model, we implement a ten-fold cross-validation on the whole data set, where 90% of the images are used for training, and 10% are used for testing. In model training, 90% of the images are separated from the

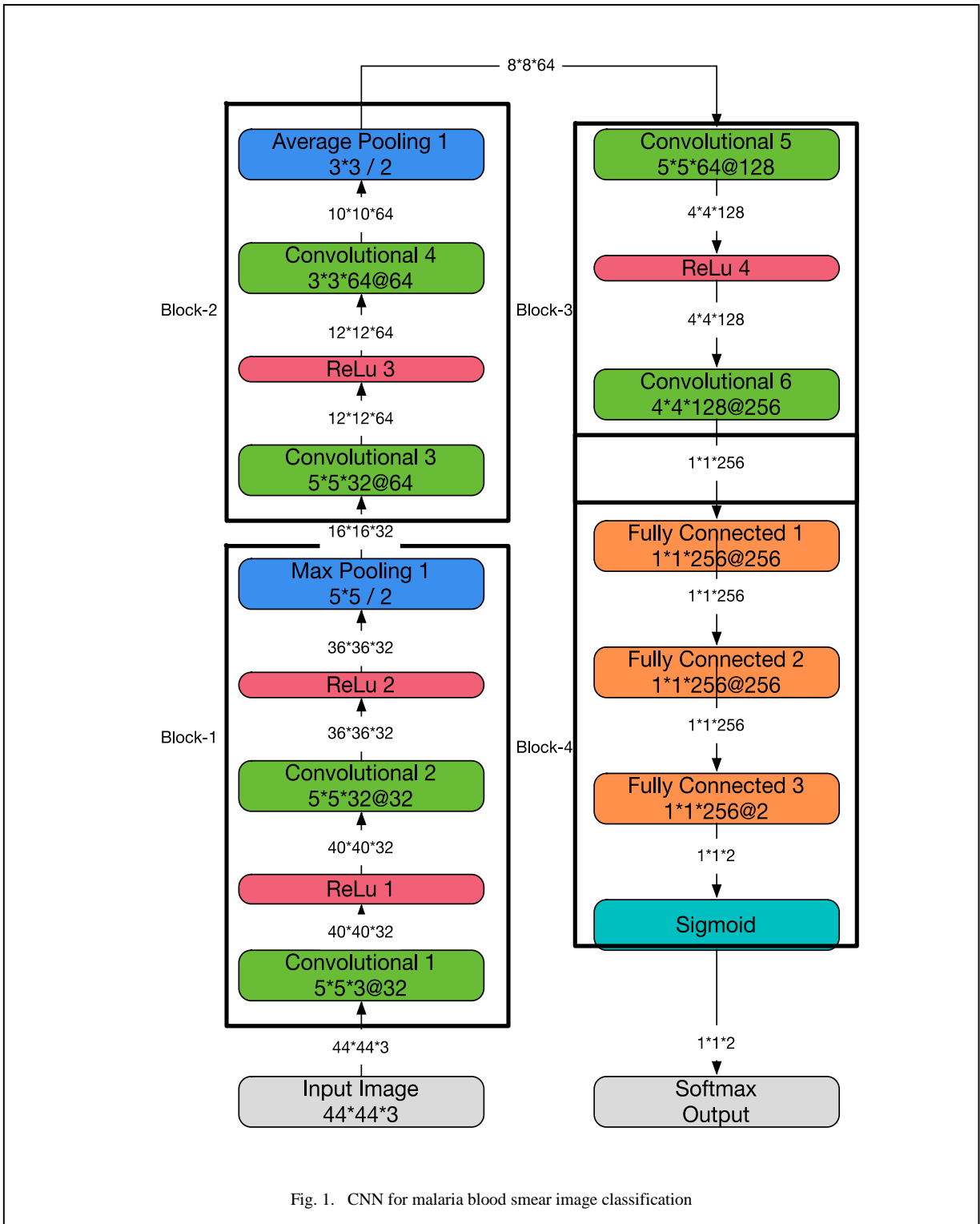


Fig. 1. CNN for malaria blood smear image classification

training set for the actual training and the remaining 10% are used for back-propagation validation.

The performance evaluation criteria are the average accuracy, sensitivity, specificity, precision, F1 score, and Matthews correlation coefficient over the ten-fold cross-validation. A pre-trained AlexNet based on the CIFAR-100 data set is applied as the feature extractor for transfer learning. It is

linked to a conventional SVM classifier to implement transfer learning as a comparison to our CNN model.

#### D. Result

Table I presents the results of the two ten-fold cross-validations:

TABLE I. OUTCOMES OF CROSS-VALIDATION

Measure	CNN model	Transfer Learning
Accuracy	97.37%	91.99%
Sensitivity	96.99%	89.00%
Specificity	97.75%	94.98%
Precision	97.73%	95.12%
F1 Score	97.36%	90.24%
Matthews correlation coefficient	94.75%	85.25%

The results show that the new CNN model has a superior performance compared to the transfer learning model. The average classification accuracy of the CNN model is 97.37%, and the model sensitivity, specificity, and precision all reach the 97% level. The F1 score and the Matthews correlation coefficient (MCC) of the trained CNN model are both more than 7% larger than the transfer learning model. This shows that the trained CNN model is a much better representation of the training images than the transfer learning model, which relies on feature extraction from a pre-trained model trained on an entirely different image set.

## V. CONCLUSIONS AND DISCUSSIONS

Based on the above experiment, we conclude that our newly designed convolutional neural network model is a suitable solution for blood smear classification. Compared to transfer learning and other similar studies [7, 8, 23], the CNN model shows much better classification performance after training with more than 27,000 images. Its performance is affected by both the architecture and the volume of training data.

We expect that deep learning will significantly improve the working efficiency and accuracy of malaria diagnosis and other health-related applications, following our previous studies on deep learning for genomics [24].

## ACKNOWLEDGMENT

We would like to acknowledge all the patients in Bangladesh. Mahidol-Oxford Tropical Medicine Research Unit is funded by the Wellcome Trust of Great Britain. Other support includes the NSERC CREATE award, the ORF-RE award in BRAIN Alliance of Canada, and the National Natural Science Foundation of China (No.81573827).

## REFERENCES

- [1] World Malaria Report, World Health Organization, 2015.
- [2] C.J.L. Murray, L.C. Murray, S.S. Lim, K.G. Andrews, K.J. Foreman, D. Haring, N. Fullman, M. Naghavi, R. Lozano and A.D. Lopez, "Global malaria mortality between 1980 and 2010: a systematic analysis." *The Lancet*, 2012, 379(9814), pp. 413-431.
- [3] S. Mali, S.P. Arguin, and P.M. Arguin, "Malaria surveillance—United States, 2010." *MMWR Surveillance Summary*, 2012, 61(2), pp. 413-431.
- [4] F. Tokumasu, R.M. Fairhurst and G.R. Ostera, "Band 3 modifications in *Plasmodium falciparum*-infected AA and CC erythrocytes assayed by autocorrelation analysis using quantum dots." *Journal of Cell Science*, 2005, 118(5), pp. 1091-1098.
- [5] D.H. Hubel and T.N. Wiesel, "Receptive fields of single neurones in the cat's striate cortex." *The Journal of physiology*. 1959 Oct 1;148(3), pp. 574-91.
- [6] I. Arel, D.C. Rose and T.P. Karnowski, "Deep machine learning—a new frontier in artificial intelligence research [research frontier]." *IEEE Computational Intelligence Magazine*. 2010 Nov;5(4), pp.13-8.
- [7] S.W. Sio, W. Sun, S. Kumar, W.Z. Bin, S.S. Tan, S.H. Ong, H. Kikuchi, Y. Oshima and K.S. Tan, "MalariaCount: an image analysis-based program for the accurate determination of parasitemia." *Journal of microbiological methods*. 2007 Jan 31;68(1), pp. 11-8.
- [8] G. Díaz, F.A. González and E. Romero, "A semi-automatic method for quantification and classification of erythrocytes infected with malaria parasites in microscopic images." *Journal of Biomedical Informatics*. 2009 Apr 30;42(2), pp. 296-307.
- [9] Y. LeCun, Y. Bengio, G. Hinton, "Deep learning." *Nature*. 2015 May 28;521(7553), pp. 436-44.
- [10] A. Waibel, T. Hanazawa, G.E. Hinton, K. Shikano and K. Lang, "Phoneme recognition using time-delay neural networks." *IEEE Trans. Speech Signal Process*, 1989 37, pp. 328-339.
- [11] Y. LeCun, L. Bottou, Y. Bengio and P. Haffner, "Gradient-based learning applied to document recognition." *Proceedings of the IEEE*. 1998 Nov;86(11), pp. 2278-324.
- [12] P.Y. Simard, D. Steinkraus and J.C. Platt, "Best practices for convolutional neural networks applied to visual document analysis." *In ICDAR 2003 Aug 3, Vol. 3, pp. 958-962.*
- [13] R. Vaillant, C. Monrocq and Y. LeCun, "Original approach for the localisation of objects in images." *IEEE Proceedings-Vision, Image and Signal Processing*. 1994 Aug, 141(4), pp. 245-50.
- [14] A. Krizhevsky, I. Sutskever and G.E. Hinton. "Imagenet classification with deep convolutional neural networks." *Advances in neural information processing systems*. 2012, pp. 1097-1105.
- [15] M.D. Zeiler and R. Fergus, "Visualizing and understanding convolutional networks." *European Conference on Computer Vision*. 2014, Sep 6, pp. 818-833.
- [16] C. Szegedy, W. Liu, Y. Jia, P. Sermanet, S. Reed, D. Anguelov, D. Erhan, V. Vanhoucke and A. Rabinovich, "Going deeper with convolutions." *IEEE Conference on Computer Vision and Pattern Recognition*, 2015, pp. 1-9.
- [17] K. He, X. Zhang, S. Ren and J. Sun, "Deep residual learning for image recognition." *arXiv preprint, arXiv: 1512.03385*, 2015 Dec.
- [18] Mathworks, Deep learning, 2016, Access on August 24, URL: <http://www.mathworks.com/discovery/deep-learning.html>
- [19] K. Jarrett, K. Kavukcuoglu, M.A. Ranzato and Y. LeCun, "What is the best multi-stage architecture for object recognition?" In *International Conference on Computer Vision, IEEE*, 2009, pp. 2146-2153.
- [20] A. Hyvarinen and E. Oja, "Independent component analysis: algorithms and applications," *Neural networks*, 2000 Jun 30, 13(4), pp.411-430.
- [21] I. Ersoy, F. Bunyak, J. M. Higgins, and K. Palaniappan, "Coupled edge profile active contours for red blood cell flow analysis," in *9th IEEE International Symposium on Biomedical Imaging (ISBI)*, 2012, pp. 748–751.
- [22] A. Vedaldi, K. Lenc and A. Gupta, "MatConvNet - Convolutional Neural Networks for MATLAB," URL: [www.vlfeat.org](http://www.vlfeat.org), access on Aug 24, 2016.
- [23] D.K. Das, A.K. Maiti, and C. Chakraborty, "Automated system for characterization and classification of malaria-infected stages using light microscopic images of thin blood smears." *Journal of Microscopy*, 2015, 257(3), pp. 5140-5144.
- [24] Z. Liang, J.X. Huang, X. Zeng, G. Zhang, "DL-ADR: a novel deep learning model for classifying genomic variants into adverse drug reactions," *BMC Medical Genomics*, 2016 Aug 10, 9(2): pp. 48.