Original Article

Analysis Of Microscopic Medical Images: A Case Study On Malaria

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Abstract

Malaria detection is very time consuming process, and its efficiency is impacted by the type of hardware, software used and the experience of pathologists. Deep learning has superior results in a wide range of applications, especially in data analysis. Therefore, this study gives an extensive review of malaria analysis using deep learning. To detect the images of the malaria parasite, researchers have proposed several models, such as ResNet, VGG-16, etc., to extract features. Compared to other deep learning techniques the CNN methods offer higher effectiveness and efficiency for malaria datasets for better diagnosis decisions. The main goal of this paper is to present the most popular pre trained CNN models used for analysis of microscopic malaria images and investigate the performance of each model.

Index Terms: CNN, Deep learning techniques, Machine Learning, Microscopic images, Malaria Analysis

1. INTRODUCTION

Malaria is caused by the potentially fatal plasmodium parasite and is conveyed to humas by female anopheles mosquitoes that have been infected. Several species of plasmodium, including plasmodium vivax, plasmodium ovale and plasmodium malaraia are responsible for the development of malaria (Alharbi et al.,2022). Malaria is a potentially fatal infection that mostly affects young children and pregnant women and malaria poses a huge threat to future generations, malaria may be prevented and treated if caught early. Malaria screening is a tedious and time consuming procedure of looking at slides under a microscope to identify infected erythrocytes. Light microscopy is gold standard for identifying malaria but better diagnostic tool would help prevent, manage and cure the disease more efficiently. Professional microscopists examine blood smears for signs of malaria by looking for infected erythrocytes, on the other hand malaria parasites go through many distinct life cycles in the human blood (pattanaik et al.2020), beginning with ring stage trophozoites (often referred to as “rings” in this article) as seen in figure 1.

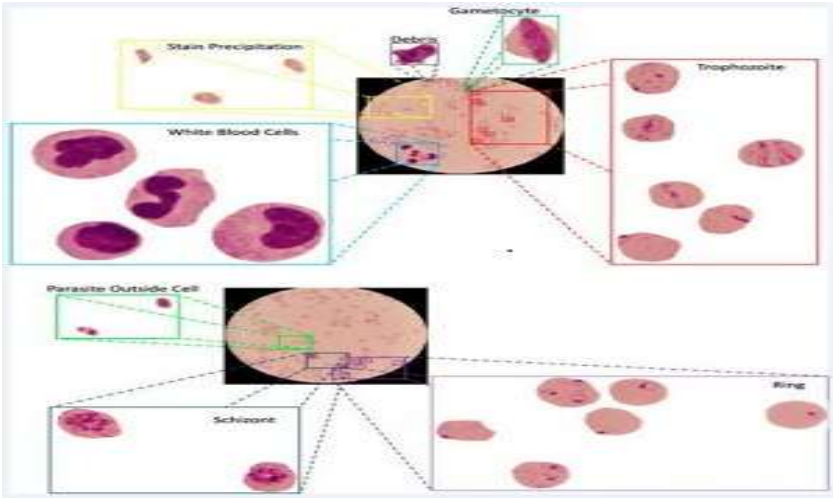

Fig. 1. Stages of Malaria in Blood Smear

Scientists from all around the globe are interested in malaria since it may be lethal, recently the majority of malaria diagnoses were made in laboratories, needing substantial human understanding about detection initially automated systems that used machine learning techniques were taken into consideration. For instance (Li et al,.2016) classified features using SVM and PCA after extracting features using architectural consideration however compared to more modern deep learning based methods, the accuracy of these model is poor. Time saving and increased diagnostic confidence are two benefits of using deep learning image analysis algorithms in diagnostics (Sinha et al.,2021). Machine learning techniques rely on layered architecture to analyze the data it is also referred as hierarchical of organized learning in other terminologies. Deep learning models may be used for categorization problems thanks to layered architecture or techniques(Hamida A et al.,) these tasks might include anything from showing connections between a variety of unstructured data and symptoms to spotting minute deviation in medical images. deep learning is better than other techniques in several ways, including the need for fewer people during training and less data pre processing. The automated quantification of parasitemia requires the successful completion of many important preprocessing processes the first step is to capture digital blood slide images, which often requires preprocessing to account for variations in lighting and staining and In the second stage, parasites and blood cells are found. To get accurate cell counts, cell segmentation is performed to identify individual cells inside cell clumps (Rosado et al,.2016)

To distinguish between infected and uninfected blood cells, characteristics are retrieved in the final phase is determined using a trained classifier (Hung, J & Carpenter A.2017). Automation of malaria diagnostic process is crucial because doing it manually is a time consuming activity. According to Sinha et al.,(2021) automation parasite counting has several advantages over manual counting including a more accurate and consistent interpretation of the blood films, the ability to serve more patients which lessens the workload on the malaria field workers and being less expensive. Deep learning techniques, particularly convolutional networks, have been used to create a system for interpreting medical pictures. Computer-aided diagnosis has improved decision-making for illness diagnosis and prognosis by contributing to the quantitative characterisation of diagnostic indicators in the area of medical imaging. Data is transferred through many layers in deep learning models, and each succeeding layer takes the output from the one before it (Latif et al., 2019). Deep learning algorithms enhance their potential to identify relationships and connections by learning from previously processed data.

The functioning of biological neurons in the brain and how they interact to transfer information from one portion to another are the inspiration for deep learning. similar to how electrical impulses go through the cells when the succeeding layers are stimulated by the nearby neurons. Deep learning is built on top of conventional neural networks (CNNs). The data flows through the layers many times to reformat and optimise the output, with each layer handling a different portion of the overall work. Between the input and output layer there are these hidden layers (Liang ET AL., 2016)., they transform the unprocessed input into worthwhile work.

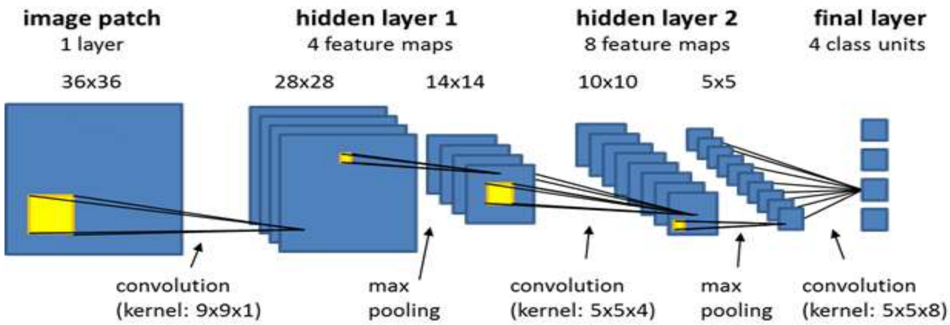

Fig. 2. An illustration of a Deep Learning Neural Network

Convolutional Neural Network (CNN) is the best method for automatically identifying malaria pathogens from microscopic pictures, according to current research. For instance, Dong et al. evaluated the performance of LeNet-5, AlexNet and GoogleNet, are three popular convolutional Neural Network . Researchers also trained an SVM classifier for comparison and came to the conclusion that CNN is better than SVM at automatically learning picture attributes. Choosing the pre-trained model layer that is most effective in extracting components from the underlying data on malaria parasites. In comparison to their custom-built model, Rajaraman et al. evaluated the performances of "lexNet, VGG-16", ResNet-50, Xception (Kumar et al. 2021), and DenseNet-121 (Maqsood et al. 2021). With their 16-layered CNN model, Liang et al. demonstrated a detection accuracy of 97.37 percent and asserted that their model beat transfer learning methods. To identify malaria parasites, Hung et al. used Imagenet to train a model before refining it with their own data.

The majority of papers that were published focused on increasing detection accuracy for malaria using deep learning-based methods. The studies by Rosado et al. and Quinn et al., both of which focused on model computational efficiency, are two notable outliers. However, the study discovered that striving for computing economy resulted in a considerable drop in model accuracy. The effectiveness of several current deep learning models for analysing malaria in microscopic blood pictures is evaluated in this paper, along with a thorough overview of malaria detection using deep learning. However, CNN models are the main focus of the study. In order to assess microscopic malaria pictures, the most common pre-trained CNN models are presented, and their respective performances are examined.

1.1 MICROSCOPIC IMAGES VERSUS NATURAL IMAGES

The use of microscopy in biomedical research is crucial. Modern microscopy technologies have opened new vistas for biological researchers as optics and computer science have evolved. Microscopy image analysis provides quantitative assistance in the improvement of disease characterizations for conditions including malaria, breast cancer, lung cancer, brain tumours, etc. Microscopy is thus essential for computer-assisted patient assessment (Liu et al., 2021). Processing picture data manually is inefficient, if not impossible, because to the enormous amount of image data that is always growing.

Research in medicine and biology has effectively and extensively used machine learning methods (Esteva et al., 2019). Fluorescence microscopy methods and total internal reflection (TIRFM) have been extensively employed in research to identify subcellular structures with accurate labelling. Standard fluorescence microscopes inability to distinguish subcellular structures slightly below the diffraction limit which iabout one half the wavelength of the excitation light (200nm), is one of the crucial constraints (Paul et al., 2021). A new trend in super resolution microscopy is a recent advancement in microscope technology, thanks to these new technologies it is now possible to take a huge number of high quality photographs that include different biomedical data where breakdowns in the diffraction limit and nanometer scale biological events are documented (Sinha et al.,2021). At the same time they encountered particular difficulties with analysing the images quantitative data, as a consequences the application of computational methods to enhance microscopes performance and make it versatile in post processing is another fast expanding area in this discipline. Pictures taken with a biological microscope have been evaluated using a variety of traditional image processing methods, including morphology, feature extraction, region growth and others. However, these methods typically need computational experts who are unipolar with biomedical scientist since they sophisticated calculations (Dinesh et al., 2019)

Due to imaging and diffraction restrictions typical fluorescene microscopy images always have a low signal to noise ratio and shallow resolution (Lie et al., 2021) which makes it challenging for traditional image processing methods to work. For microscopy image processing including nuclei detection, cell segmentation, tissue segmentation, image classification and more deep learning is quickly becoming into a potent tool. In many computer vision and biological image analysis applications, convolutional neural networks (CNN), a typical deep architecture had great success (Voulodimos et al., 2018).deep learning models like Recurrent Neural Network(RNN) and Generative Adversarial Nets(GAN) are two examples that have successfully completed a range of tasks, such as image segmentation classification, object identification and super resolution reconstruction (sarker 2021). The effective use of deep neural networks (DNN) and CNN has received majority of attention for object identification and natural language processing (Gu et al.,2018).

Scientific data should be discoverable, accessible, interoperable, and reusable, according to the FAIR guiding principles (Boeckhout et al., 2018). To handle the enormous amount of photos and separate the link between a material's structure and its properties based on these images, it is critical to develop data analysis tools. Even deep learning has substantially improved tasks like object recognition, classification, prediction, etc. in natural scene picture analysis (Xing et al., 2017). The capabilities of microscopic image analysis and those of natural scene analysis still vary significantly. Microscopic imaging analysis tasks are quite diverse and difficult because materials science microscope pictures have characteristics compared to photos of natural settings (Fuhad et al., 2020).

First, raw experimental microscope images often include significant levels of noise and distortion (Ge et al., 2020). Noise is reduced by using conventional unified image pre-processing methods like the order filter and the Gaussian smooth filter. Because they depend on local information, conventional algorithms often have trouble with high-density noise. However, with a well-defined model architecture and ground truth, deep learning algorithms may overcome noise limitations. In contrast to photos of actual scenes, microscope image collections often include grayscale images. Red, Green, and Blue (RGB) or RGBD images of natural sceneries are often colour scaled and feature a variety of rich natural textures (Higaki et al. 2015). Expand the number and variety of datasets. Geometrical transformations, colour space augmentations, kernel filters, etc. are all important forms of augmentation with limited data (Shorten & Khoshgoftaar, 2019). By using simple changes like rotation, recent research on deep learning for microscopic image analysis has improved the training dataset and prevented overfitting. Additionally, most atomically resolved pictures have a characteristic lattice periodicity. Techniques for characterizing should have leaned on atom distribution.

Thirdly, since the information in a microscope image has strong relationships with physical or chemical constraints and experimental settings, the architectures of microscopy image collections are noticeably more complicated. Each microscope picture has distinct physical and chemical properties, depending on the kind of material utilised, imaging methods, technical specifications of the apparatus, ambient factors, etc. Additionally, microscopic pictures often have extremely high resolution. As a result, compared to image data of natural scenes, the size of the microscope image data is bigger and the structure of each data node is more complicated (Ge et al., 2020). Due to the abundance and variety of microscopy datasets, locating materials-specific fingerprints manually is difficult. The quantity of small image data that can be handled by deep learning algorithms depends on their proficiency in processing and mining large datasets.

Fourth, analytic operations on dynamic datasets or "movies" are typically required to observe the alteration of materials. One class of deep learning model called Long Short Term Memory (LSTM) networks is used to process time sequences in a variety of tasks, including Natural Language Processing (NLP), traffic forecasting, and human action recognition. LSTM networks have the ability to "remember" information for long periods of time (Palangi et al. 2016). The detection and analysis of the dynamic processes in the materials may be aided by the use of spatial-temporal neural networks. The most essential challenge could perhaps be the illusive term "ground truth." For a supervised task, labelled data (ground truth) is necessary. It takes a long time and is inefficient to figure out the truth using human investigators and computer simulations. Additionally, a sizable quantity of accurately labelled data is required for training supervised deep learning models as well as verifying or assessing experiments.

They use software or theoretical models to build a convincing simulated dataset while taking into account the vast range of physical and chemical factors influencing the outcome. Utilizing few-shot learning techniques, which are designed to handle feeding a deep learning model with a limited training set, is an additional choice (Madsen et al., 2018; Vasudevan et al., 2018). Finally, many microscopic imaging tasks require more study or explanation since they are ambiguous.

Contrary to the bulk of functions of natural scenes or language processing, which provide clear and explicit information, many occurrences in materials science are unanticipated or unpredictable. The scientific community needs to do more study to fully understand them and their causes. Deep learning research on microscopic imaging in materials science should be carefully planned and carried out under the guidance of physical and chemical limits and understanding, taking into account all the aforementioned characteristics (Ziatdinov et al., 2017). The distinction between natural photographs and images from a versus microscopy is therefore shown in the accompanying illustration.

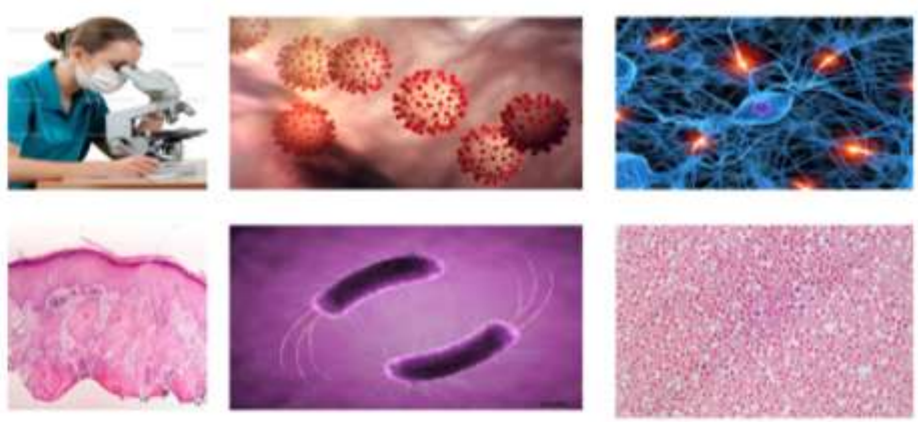

Fig. 3. Sample microscopic images

Fig. 4. Sample natural images

Algorithms for machine learning assist in automating processes that required human labour in the past. Training datasets are provided to supervised and semi-supervised classifiers so they may learn to classify input into specified categories (Latif et al., 2019). Well-known algorithms including Random Forest, Decision Tree, and Support Vector Machine Classifiers were employed in the suggested research

2. Convolutional Neural Networks (CNN)

CNNs are feed-forward neural networks that were first used in natural language processing, recommender systems, and computer vision. It is a deep neural network that feeds information to a fully connected classification layer using convolutional and pooling or subsampling layers (Liang et al., 2016). Convolution layers collect features from their inputs by filtering, and the results of several filters may be combined. Automated fluorescence microscopy, the workhorse of microscopy imaging for life sciences, generates millions of cellular pictures. CNNs outperform traditional machine learning methods in terms of understanding the spatial Organisation of image data via automated feature extraction. The distinction between the pipelines for convolutional and deep learning is seen in Figure (5).

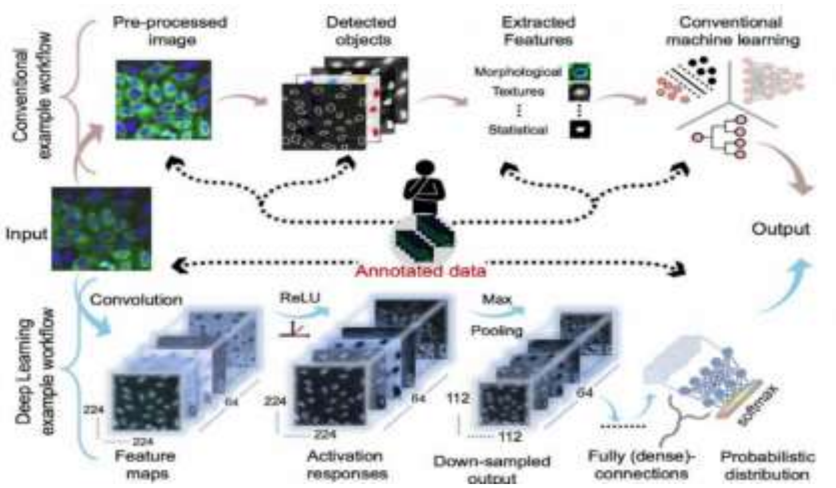

Fig.5. convolutional versus deep learning pipeline

Since the resolution of components is decreased by pooling or subsampling layers, fully connected layers are used for classification tasks. This may boost the CNN's resistance to noise and distortion. An image recognition-specific deep learning architecture is a convolutional neural network (CNN). A CNN model interprets input data using multiple layers and is characterised by four key characteristics: local connections, shared weights, pooling, and the use of many layers (Umer et al., 2020). The first CNN applications for text and voice recognition date back to the 1990s. An example of a CNN architecture is shown in Figure 6s. Pre-processing was done on the incoming data to restructure it for the embedding matrix. Four convolution layers and two max-pooling layers were used to process the input embedding matrix in Figure (6) below. The first two convolution layers use 64 and 128 filters, respectively, to train different features, and are followed by a max-pooling layer that aims to reduce output complexity and avoid overfitting the data. A max-pooling layer comes after the third and fourth convolution layers, which contain 256 and 512 filters, respectively. The last layer is a fully connected layer that will reduce the vector of height 4096 to an output vector of one since there are 1000 classes to predict (Positive, Negative).

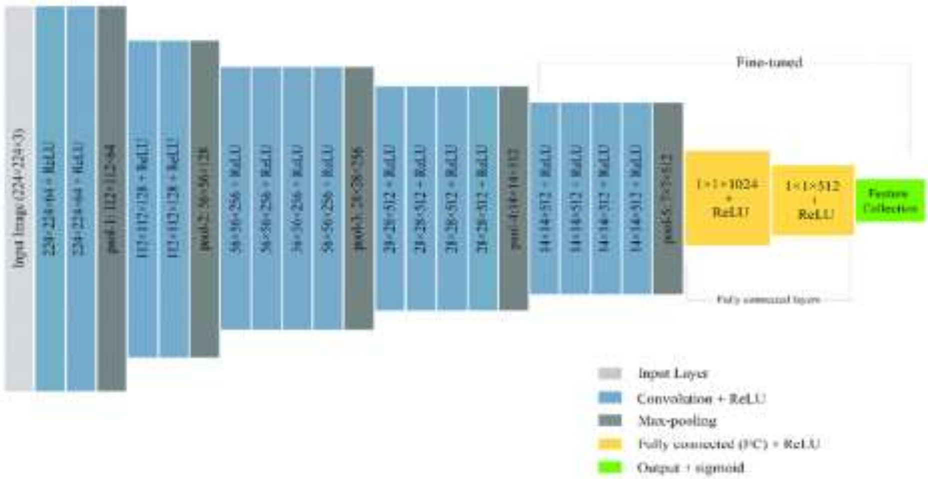

Fig. 6. Convolutional Neural Networks (CNN)

3. DEEP LEARNING TECHNIQUE ANALYSIS FOR MICROSCOPIC IMAGES

The use of microscopy in biomedical research is crucial. Modern microscopy technologies have opened new vistas for biological researchers as optics and computer science have evolved. Microscopy image analysis provides quantitative assistance for better disease characterizations for illnesses including breast cancer, malaria, lung cancer, brain tumours, etc (Saiprasath et al., 2019). Microscopy is thus essential for computer-assisted patient assessment. Manually analysing image data is inefficient or perhaps impossible because of the vast amount of image data that is always increasing. The essential phases in general picture processing and analysis are shown in figure (7).

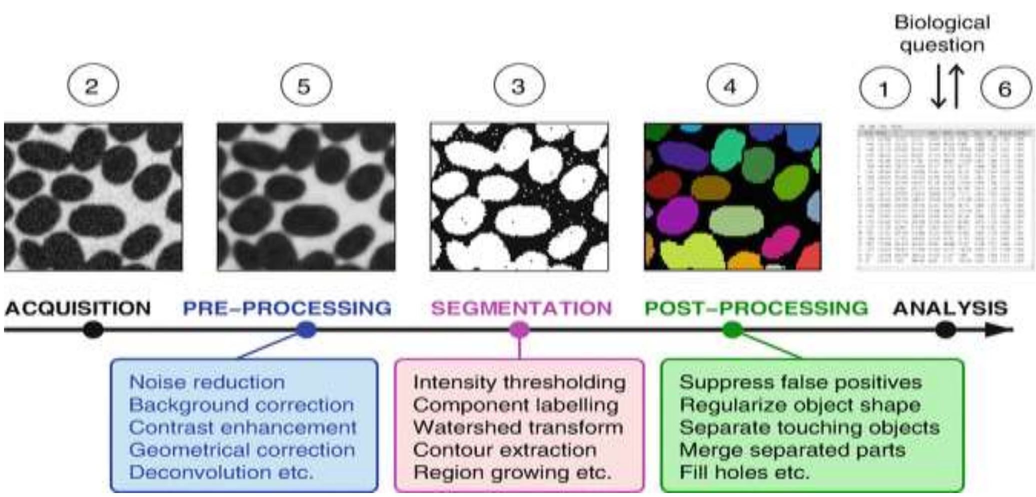

Fig. 7. Microscopic Image Anlaysis

Current computer systems employ deep learning methods to evaluate medical pictures (Anwar et al., 2018). There is a movement to automate the diagnostic system utilising different machine learning methods in order to aid human professionals in making the correct diagnosis. A deep learning-based technique was proposed by Liang et al. to discriminate malaria-infected cells from red blood cell smears. The approach they recommend is built on a 16-layer convolutional neural network that, by adopting the AlexNet architecture pretrained on the CIFAR-100 dataset, outperforms their transfer learning-based model.

A dataset of 1000 samples was used by Dong et al. just for training and testing. On the LeNet, Alex Net, and GoogleNet designs, they reported the findings from their usage of transfer learning (Rahman et al., 2019). An alternate approach based on object detection was developed by Mittal et al. They used a Faster Region-based Convolutional Neural Network (Faster R-CNN), which was pre-trained on Imagenet and then tailored using their dataset. Razzak et al. have provided an automated process that considers the responsibilities of segmenting and classifying malaria parasites. They base their classification network on an Extreme Learning Machine (ELM) and their segmentation network on a Deep Aware CNN. Through the use of a malaria blood smear imaging dataset, Pattanaik et al. (2020b) built a CAD system that showed high accuracy, sensitivity, and specificity. This study uses a cutting-edge technique for rapid processing and will help in illness detection. In multiview breast FNAC samples, Garud et al. (2017) use Google Net CNN architecture to identify malignant or benign categories. The proposed CNN achieves an accuracy of 89.71% in 8-fold validation on 37 breast cytopathology samples. A powerful 16-layer CNN-relied model was also shown by Liang et al. (2016) to automatically distinguish between single malaria-infected and non-infected cells on reliable microscopic pictures.

Yu et al. highlight that residual units are easier to adjust and can attain deep-level accuracy in a quick investigation of multiple residual networks. The paper examined substantial empirical data showing that alternative multiple-layer architectures utilised in machine learning systems fall short when compared to residual learning (ResNet). By tackling the problem of fading gradients and accuracy loss, ResNet can extract meaningful features from a picture. To strengthen the learnt representations' robustness to slight changes in the input patterns, several different forms of residual unit designs have been developed. The Google team's ResNet architecture successfully completes the ILSVRC 2015 challenge with an error rate of 3.57 percent, 152 layers, and a lower level of complexity than VGGNet (Hung and Carpenter, 2017; Das et al., 2015). ResNet connections speed up convergence while keeping the cost of computation low (Pattanaik et al. 2020).

Abdi and Nahavandi (2016) introduce a novel CNN multi-residual network in comparison to current models on the Image Net, CIFAR-10, and CIFAR-100 datasets using the original residual network. This method works better than others, increasing computing complexity by up to 15%. Deeper networks significantly slow down learning and the directions of overlap because of the growth in hidden layers; consequently, skip connections slightly mitigate this difficulty to a certain scope (Greenspan et al., 2016). Vijayalakshmi et al. (2020) recommended a VGG-16 model for feature extraction and a gain proportion technique for feature selection. The vector machine classifier, which distinguished between leukaemia and unaffected blood smear pictures with a 99 percent accuracy rate, was fed the chosen properties. Using several magnifications, Pattanaik et al. (2020a) created a deep residual neural network. In thin blood smear photos captured with cellphones, parasitized and uninfected erythrocytes were automatically identified. It fixed gradient difficulties and enhanced outcomes even in low-quality photos, achieving 98.08 percent accuracy.

Two methods were proposed by Yang et al. (2020): an intermittent global minimum screening (IGMS) method for quick screening of parasite-infected candidates and a customised convolutional neural network to identify malarial-infected and malaria-uninfected RBC cells in blood smear pictures. A unique stacked convolutional neural network architecture for automatically identifying the presence of malaria was proposed by Umer et al. (2020). It attained 99.96% accuracy while extracting additional characteristics. The findings demonstrate that separate abstract level characteristics may be extracted from pictures using convolutional layers with various filter sizes of filter three and depth sizes. A deep learning method designed to predict malaria quickly and accurately was proposed by Shekar et al. Three CNN models were created, and the most accurate model was selected. The Fine-Tuned CNN outperformed the other CNN models by a wide margin. From the many various methods published over the last several years, we can see that many tests were conducted to reach the present state of the art.

One of Rahman et alsuggested .'s models, TLVGG16, exceeds all other models with a hold-out test accuracy of 97.77 percent. Singh et al. employed CNN models (16 layers) in their work to provide a unique and robust machine learning strategy for automatically discriminating single cells in tiny blood smears from normal microscope slides, such as infected or non-infected for malaria cell identification. Using 27,578 images, the CNN model had an average accuracy of 97.37 percent. The learning transfer model achieved 91.99 percent on the same photos. As a result, the CNN model performs better than the transfer learning model.

The authors show that a common method in computer vision is the use of transfer learning. Contrary to other typical machine learning techniques that need rigorous feature engineering and extensive data pipelines, particular fairly excellent outcomes may be achieved, as shown in the literature. However, despite several publications, the performance numbers reported are quite disappointing from a medical standpoint (Poostchi et al., 2018). Additionally, progress has been achieved, as seen by the organic growth of machine learning and image analysis algorithms. Following the development in other sectors, this advancement has adopted essential principles and effectively applied them to malaria detection. The findings of current studies in terms of performance measures are shown in the following table (Accuracy, Sensitivity, and Specificity).

Table 1. Performance of the pre-trained CNN models in the recent works of microscopic malaria images analysis

#	CNN	Accuracy	Sensitivity	Specificity
1.	Mosquito Net (Kumar et al.)	96.60	97.60	95.8
2.	CNN-16 (Liang et al.)	97.30	97.90	97.70
3.	Inception_v3 (Huang et al.)	93.06	92.97	93.13
4.	XceptionNet (Kumar et. al)	88.9	94.10	84.10
5.	AlexNet (Vijayalakshmi et al.)	82.15	77.66	85.19
6.	AlexNet (Kumar et al.)	92.70	93.90	93.10
7.	Google Net (Vijayalakshmi et al.)	86.27	85.92	86.51
8.	A customized Pretrained-CNN (Rajaraman et al.)	98.00	98.10	99.20
9.	VGG-16 (Vijayalakshmi et al.)	95.85	95.38	96.32
10.	VGG-19 (Vijayalakshmi et al.)	95.92	95.29	96.55
11.	Resnet-50 (Kumar et al.)	95.17	92.37	97.27
12.	Resnet-101 (Alharbi et al.)	95.62	94.19	97.10
13.	Resnet-152 (Das et al.)	95.05	92.15	97.25
14.	ResNet-146 (Sinha et al.)	99.23	99.52	99.17
15.	A customized CNN model (Maqsood et al., 2021)	97.37	96.99	97.75

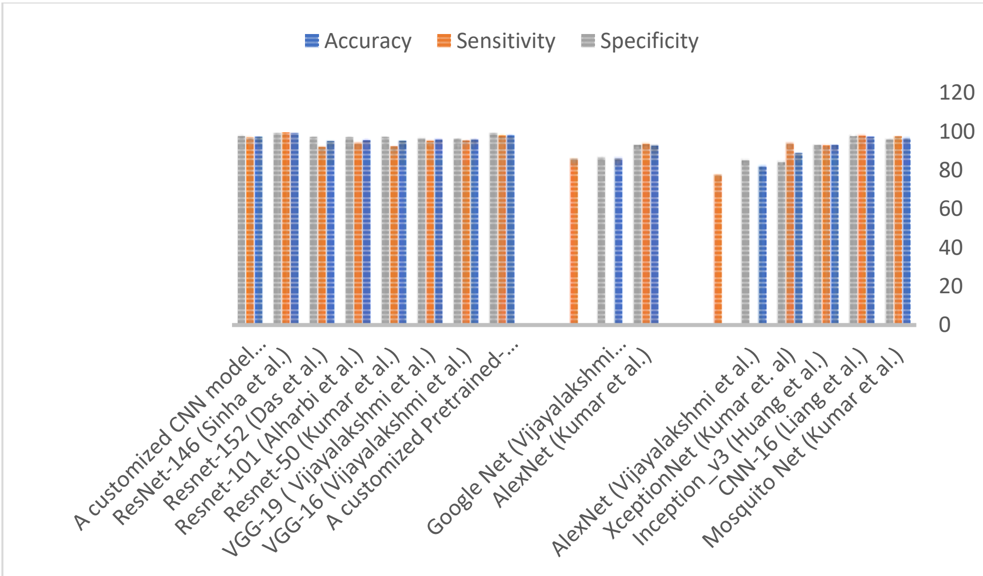

Fig. 8. Performance of the pre-trained CNN models in the recent works of microscopic malaria images analysis

The vast majority of research show that the CNN method delivers improved efficacy and efficiency for malaria data sets when compared to other deep learning methods, allowing for better diagnostic analysis. The table lists the most common CNN architectures and how well they function while analysing microscopic malarial picture data. ResNet-146 outscored other pre-trained CNNs in every performance indicator, as shown in (Table 1). The second-best result is obtained by a customised Pre-trained-CNN; as shown in table (1), the majority of the approaches have so far been successful in diagnosing malaria sickness with high accuracy.

4. Public Malaria Datasets

Research on microscopic pictures, particularly images of malaria, may make use of many publicly accessible databases. Several examples of available public malaria datasets are provided in Table 2.

Table 2. Characteristics of the public malaria datasets

#	Dataset	Total of images	Resolution	Total of parasites
1	Dataset, a (Pattanaik etval., 2020)	1182	750×750	7245
2	Dataset, b (Rahman et al., 2019)	27,558	Heterogeneous	13,779
3	Dataset c (Kittichai et al., 2021)	12,761	448×448	-
4	Dataset, d (Liang et al., 2016)	27,578	44×44	13,789
5	Dataset, e (Loddo et al., 2018)	210	2592 x 1944	1437
6	Dataset, f (Yang et al., 2021)	883	1382 x 1030	3586
7	Dataset, g (Delgado et al., 2020)	331	2400 x 1800	-

It's important to keep in mind that the larger the number of samples, the better the accuracy of deep learning. High-resolution photos are readily available, but processing them incurs a significant computer cost, thus scientists often downsize the images to better fit their computing needs.

5.CONCLUSION

Malaria analysis is a time-consuming procedure that may be improved with better machinery, more advanced software, and more seasoned pathologists. Many researchers in the area of digital pathology have lately turned their focus to computational microscopic imaging technologies as a means of resolving the analytical problems. The identification of malaria has therefore been a major focus of study in the field of digital image analysis and computer vision technology during the last decade. Since deep learning has become so popular, large collections of tagged images for use in training are a must. More people will be able to be checked out, and more thorough, widespread field testing will be possible. Traditional methods of malaria detection, which include collecting samples and analyzing cell growth, are time consuming. Therefore, a deep learning model has been developed to rapidly and accurately predict malaria. Accordingly, the majority of the research summarized aimed to enhance the precision of deep learning-based approaches for malaria diagnosis. The suggested CNN method has been shown to be more successful and efficient for malaria data sets than existing deep learning methods, leading to more accurate diagnoses. Researchers have suggested many models, including ResNet, VGG-16, etc., to extract features for malaria parasite image detection. Organizing ways for locating COVID-19 smears in human lungs, as well as creating CNN-based procedures for diagnosing disorders including pneumonia and breast cancer, will be the primary areas of attention for future study.

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