AI-based Method for Detecting Retinal Haemorrhage in Eyes with Malarial Retinopathy

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Abstract. Cerebral Malaria (CM) as one of the most common and severe diseases in sub-Saharan Africa, claimed the lives of more than 435,000 people each year. Because Malarial Retinopathy (MR) is as one of the best clinical diagnostic indicators of CM, it may be essential to analysing MR in fundus images for assisting the CM diagnosis as an applicable solution in developing countries. Image segmentation is an essential topic in medical imaging analysis and is widely developed and improved for clinic study. In this paper, we aim to develop an automatic and fast approach to detect/segment MR haemorrhages in colour fundus images. We introduce a deep learning-based haemorrhages detection of MR inspired by Dense-Net based network called one-hundred-layers tiramisu for the segmentation tasks. We evaluate our approach on one MR dataset of 259 annotated colour fundus images. For keeping the originality of raw MR colour fundus images, 6,098 sub-images are extracted and split into a training set (70%), a validation set (10%) and a testing set (20%). After implementation, our experimental results testing on 1,669 annotated sub-images, show that the proposed method outperforms commonly mainstream network architecture U-Net.

Keywords: Malarial Retinopathy · Retinal Haemorrhage · Fundus Imaging · Deep Learning · Image Segmentation

1 Introduction

Cerebral Malaria (CM), as a form of severe malaria, is one of the most common diseases in sub-Saharan Africa, which is transmitted by the Anopheles mosquito when it feeds on previously infected humans. According to the World Malaria Report 2018 [20], malaria affected over 219 million cases of malaria in 2017 and claimed the lives of more than 435,000 people per year. 266,000 (61%) malaria deaths were children aged under 5 years. Retinopathy is clinically significant in CM because the similarity of eye and brain embryonic origins have led to shared features of the relevant microvascular systems [18]. Lewallen *et al* [15] coined the term malarial retinopathy (MR), which is one of the best clinical diagnostic indicators of CM. MR is characterized by retinal whitening, papilledema, capillary non-perfusion (CNP) and varying haemorrhage presence in the ocular fundus [2]. Therefore, screening MR may assist in improving the accuracy of diagnosis of CM by using binocular indirect ophthalmoscopy (BIO) or analysing fundus images by ophthalmic expert team [19,4]. In developing countries, however, there is a barrier to use BIO widely because of expensive equipment and technical expertise required. A fully automated analysing fundus images for MR may provide fast diagnostic assistance. MR detection methods for CM diagnosis using retinal colour images were proposed [8,9,1].

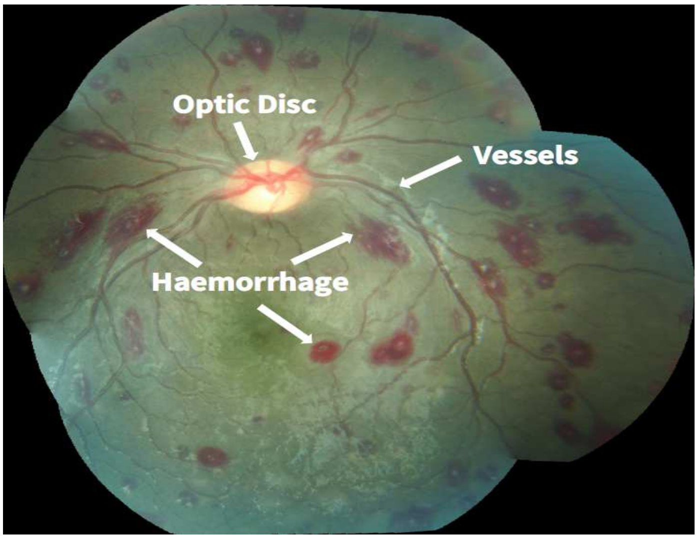

Fig. 1: An example of a montaged colour fundus image showing the presence of haemorrhages

As retinal haemorrhages are one of the visible signs on colour fundus images of MR as well as diabetic retinopathy (DR), retinal haemorrhages detection is of high importance in both MR and DR detection steps for further automated diagnosis [17]. Fig. 1 shows an example of a colour fundus image showing the presence of haemorrhages of MR. In the previous works of retinal haemorrhages detection for DR diagnosis, approaches based on splat feature classification [23] and mathematical morphology [10] were proposed. For MR haemorrhages detection, Joshi *et al* [9] developed an automated segmentation method based on splat classification for the detection of retinal haemorrhages to characterize MR. However, this work has a few limitations. the performance and running time of haemorrhages segmentation are sensitive to the size of splats so this study may not be robust for other various retinal haemorrhages case. A new deep learning network based on Dense-Net called one-hundred-layers tiramisu (Tiramisu) was proposed for meidical image semgentation by *Jégou et.al* [7]. Tiramisu model overcomes this limitation of U-Net in various medical image applications [16][7].

To the best knowledge of the authors, this is the first work that applied Deep Learning-based methods on MR. We use Tiramisu method to segment haemorrhages within colour fundus images. In this paper, we make the following contributions: (i) We develop a deep learning-based framework for segmentation in colour fundus photography. (ii) Based on this, we implement the Tiramisu model for automatic MR related haemorrhages detection and compare with general U-Net. (iii) We evaluate our segmentation performance on a supervised bio-medical segmentation setting. The remaining of the paper is organised as follows. § 2 describes the proposed method. § 3 provides a description of the experimental settings. In § 4, experimental results are presented and compared to existing methods. § 5 & § 6 gives discussion, future directions and conclusions.

2 Methodology

For many challenging tasks in computer vision, Convolutional Neural Networks (CNNs), as a branch of deep neural networks, show remarkable performance, which is able to work by extracting hierarchical features for learning. Decades later, since the power of graphical computing in the hardware field was increased through the improvements in graphical processor units (GPUs), CNNs-based methods are viable for more complex computer vision tasks, *e.g*, object segmentation, scene reconstruction, motion estimation, image restoration etc. [13]. There are many different CNNs architectures, such as LeNet-5 [14] proposed in 1995, Alex-Net [12], VGG-Net [22], ResNet [5] and Dense-Net [6] have been developed and introduced into various computer vision tasks. In terms of image segmentation, since CNNs-based models achieved state-of-the-art results, the image segmentation problem was transformed and solved as a problem of pixel-wise classification. In which, each pixel from images will be treated as single independent objects for classification [3]. On the other hand, such as U-Net proposed by Ronneberger *et al* [21] treats each image as the input and the output of neural network model as an end-to-end fashion and the performance is better when compared to pixel-wised approaches [24,16,7]. However, there are a few limitations in this image-wise method. Small objects would be segmented wrongly by U-Net framework around target annotations, because of the lack of consideration on the outside region of the object. In order to tackle this limitation, Tiramisu model makes each layer to connect with others in a feed-forward fashion for encouraging extracted features to be reused efficiently as well as strengthening feature propagation for ignoring gradually the influence from outside of targets.

2.1 CNNs architectures

In this subsection, the architectures of U-Net and Dense-Net based Tiramisu will be described respectively.

U-Net: U-Net was proposed and widely for semantic segmentation with high precise results. There are two essential paths: the down-sampling path and up-sampling path composing U-Net main architecture. In the down-sampling path of U-Net, the architecture is as similar as a typical CNNs in which each layer consists of two convolution layers with kernel size 3×3, rectified linear unit (ReLU) and pooling layers. In the other path, each layer consists of a 2×2 up-convolution layer, one concatenation operation with related feature map by skipped connections and two convolution layers with kernel size 3×3. As one of the important components in the U-Net architecture, skipped connections are designed for forwarding feature maps from down-sampling path to the up-sampling path to localize high resolution features for generating the segmentation result as final output. At the end of the last layer, a softmax classifier is attached to provide the probability distribution for each pixel. In total, the architecture of U-Net has 23 layers.

Tiramisu: Compared to U-Net architecture, the most difference in the Dense-Net based

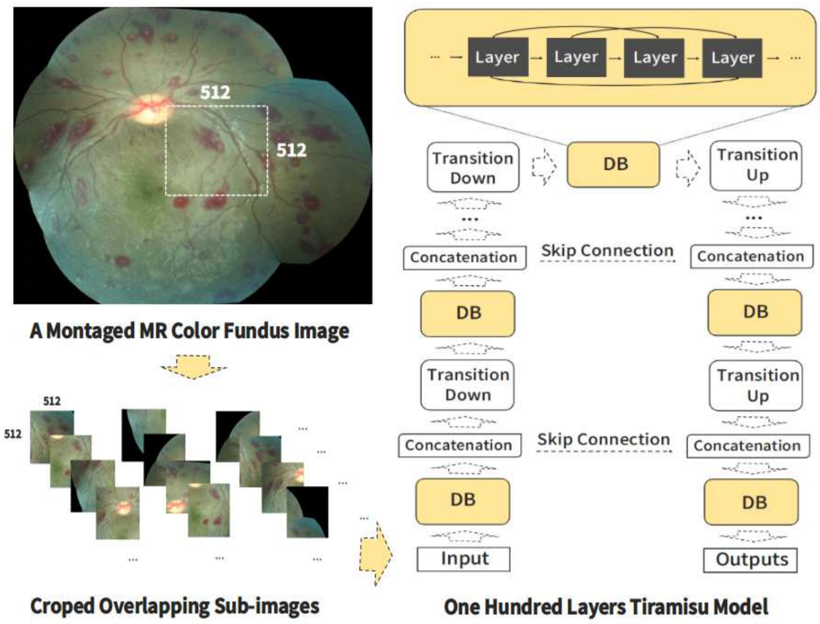

Fig. 2: Overview of our proposed method which takes the objects area and length of the boundaries into account during training.

Tiramisu architecture are: (1) Dense Block (DB) including Batch Normalization (BN) layer, ReLU, convolution layer with kernel size 3×3 and dropout layer with probability $p = 0.2$; (2) Transition down composed of BN, ReLU, 3×3 convolution and dropout with $p = 0.2$; (3) Transition up including one transposed convolution with kernel size 3×3. In each DB, every layer is connected densely with other layers. The benefits of introducing DB is for preserving the feed-forward nature and reusing extracted features more efficiently and effectively. 5 Transition Down and 5 Transition Up are introduced following DB layers. Skipped connections and concatenation operations are used as well. At the end of the last layer in Tiramisu, softmax is attached as a classification layer for generating the final probability distribution. Overall, there are 38 layers in the down-sampling path and up-sampling path, respectively. The bottleneck path consists of 15 layers. Tiramisu network has 103 layers totally including Transition Down and Transition Up blocks. In Fig 2, Tiramisu architecture is presented.

2.2 Loss functions

In order to train a CNNs-based model for achieving prediction with high accuracy, loss function could play an essential role in the machine learning field. Loss function is a measure of prediction which can be back-propagated to the previous layers for updating and optimising the weights of CNNs. As one of the most commonly used loss functions, Cross-Entropy (CE) Loss is a pixel-wise measure function. CE loss is expressed in the following Eq. 1:

$$loss_{CE}(T, P) = -\sum_{i=1}^{\Omega} [T_i \cdot \log(P_i) + (1 - T_i) \cdot \log(1 - P_i)] \tag{1}$$

where, ground truth image and the prediction are denoted as T, $P \in [0, 1]$ respectively; i indexes each pixel value in image spatial space Ω.

3 Experiments

We used Tiramisu as our MR haemorrhages segmentation framework with loss function CE. The performance will be compared with U-Net framework.

3.1 Dataset

We demonstrate our model on a sample of 259 montaged MR colour fundus images from a sample of children suffering from CM that had been admitted to the Paediatric Research Ward, Queen Elizabeth Central Hospital Malawi. Various patients who had met the WHO criteria for CM were involved, that were sampled for haemorrhage analysis. The original fundus images were captured with the use of a Nikon-E1 digital camera and produced a field view of 50 degrees. These images were derived from two groups of patients labelled died vs survived, and consist of one image per patient. After approval by the local ethics committees at the University of Malawi College of Medicine and the University of Liverpool, Nick Beare collected the representative images for the further CM analysis. The mentioned image montages were formed by stitching together multiple original images of the same eye to visualise a larger area of the retina as shown in Fig. 1. The corresponding ground truth label maps (haemorrhage regions and background) are annotated by Melissa Leak.

3.2 Data Preprocessing

In order to keep the originality of raw colour fundus image as well as increase the number of MR fundus images for training and validation, all 259 fundus images and the corresponding annotation are cropped into about 23 overlapped sub-images/patches

(a) An Original Image (2924 × 2623 × 3 pixels) (b) MR Related Haemorrhage Annotation

Fig. 3: An example of MR colour fundus images and the corresponding annotation of haemorrhage

for each image with relatively smaller sizes: 512 × 512 as a new dataset with 6098 sub-images. Example images and their corresponding ground truth are shown in the first left columns of Fig.3. In our experiment, the new dataset is partitioned into three subsets: training (3,543), validation (886) and testing (1,669). And then, all of the 1,669 sub-images will be recombined back to the original image size for a better demonstration.

3.3 Implementation

We implemented our networks using Keras-gpu 2.0.5 and Tensorflow-gpu 1.7 as backend. We trained our models with Adam optimizer [11] by learning rate of 10^{-5}. All the experiments were performed by using an NVIDIA K40 GPU and 32GB memory.

3.4 Evaluation Criteria

Dice Coefficient (DC) score: DC score is widely used for evaluating the performance of segmentation. DC score measures the size of overlapping regions from the ground truth reference and segmentation results. Higher DC score means better segmentation performance. DC score can be expressed as:

$$DC(T,P) = 2 \cdot \frac{\sum_{i=1}^{\Omega}(T_i \times P_i)}{\sum_{i=1}^{\Omega}(T_i + P_i)} \tag{2}$$

where, T, P are represented as the ground truth and the prediction of segmentation, respectively; i is an index of each pixel value within an image spatial space Ω.

Area under receiving operator characteristics (ROC) curve (AUC): And also, AUC is calculated as another evaluation metric. AUC is able to reflect the trade-offs between the true-positive rate (sensitivity) and the false-positive rate (specificity) at various threshold settings. Higher AUC means better performance.

4 Results

We test our MR haemorrhages segmentation framework with 1669 sub-images with manual annotation. As shown in Fig. 4, four examples from testing dataset are randomly selected to present the segmentation performance compared with one of general segmentation solutions: U-Net framework. From left to right, the example fundus image, manual annotation, segmentation results by U-Net and Tiramisu are shown respectively. DC score is introduced to quantify the segmentation performance. For MR haemorrhages segmentation, the DC scores of U-Net (0.9062) are lower than the DC scores of Tiramisu which is 0.9950. As shown in Fig.5, the segmentation framework of Dense-Net based Tiramisu model achieves better AUC results (0.9358) than U-Net segmentation framework (0.6307) under the same segmentation task.

5 Discussion

Our method based on the idea of Tiramisu is able to detect the location of MR haemorrhage. We also present one general segmentation models U-Net as the basic model to prove that our proposed method is better and more robust than U-Net in the same segmentation tasks, because of the MR haemorrhage feature reuse enabled by dense connections. However, in order to extract sub-images with the size of 512×512 for preserving the originality of raw colour fundus images, the size of training and validation datasets are increased so that it needs more memory for loading and is time-consuming also. In future work, we will investigate new strategies for optimising memory during the training process or preserving details of a dataset. And also, because in clinical practice, the number of MR haemorrhage is concerned, the function of automatically counting haemorrhage will be developed for the benefits of the clinic.

6 Conclusions

In this paper, we introduced an AI-based haemorrhages detection of MR in colour fundus images inspired by Dense-Net for the segmentation tasks. After implementation, the results showed that the proposed approach outperforms state-of-the-art U-Net approaches. It is believed that this new development will be applied to other challenging segmentation tasks. The experiment results have proved that the performance is better than commonly mainstream architectures when we test on a 1669 annotated fundus images dataset.

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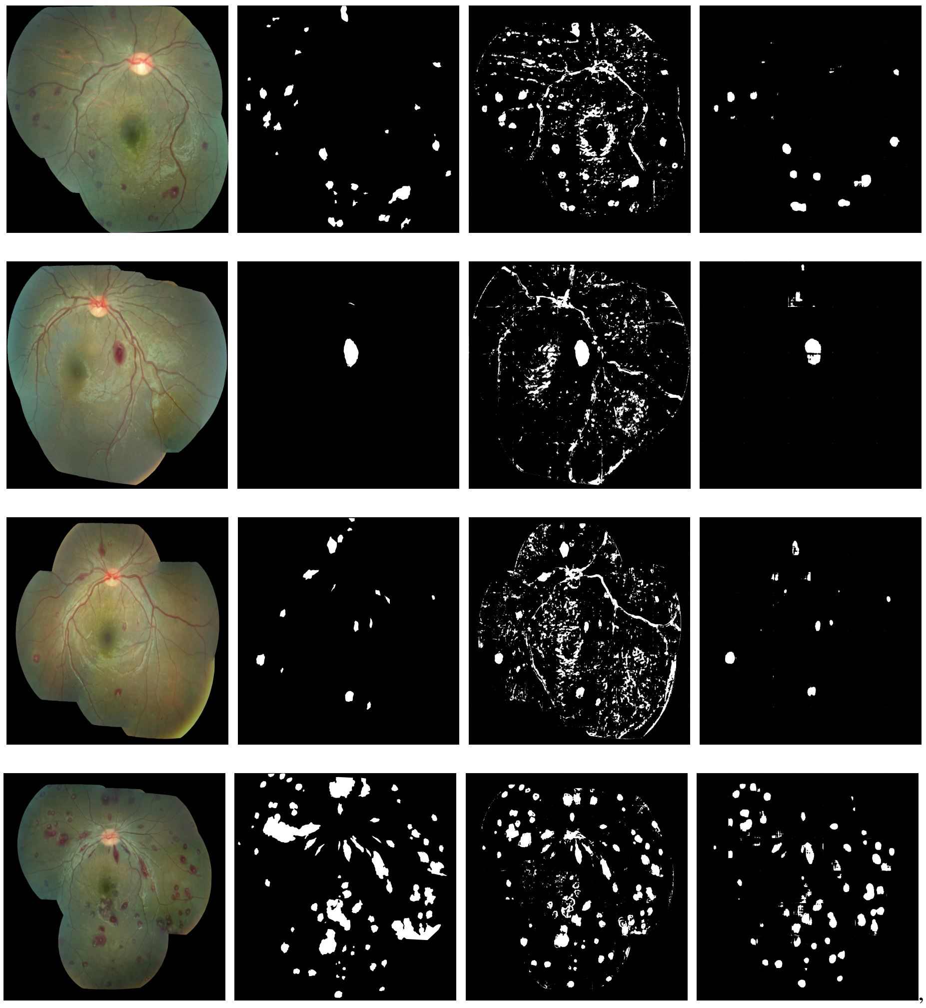
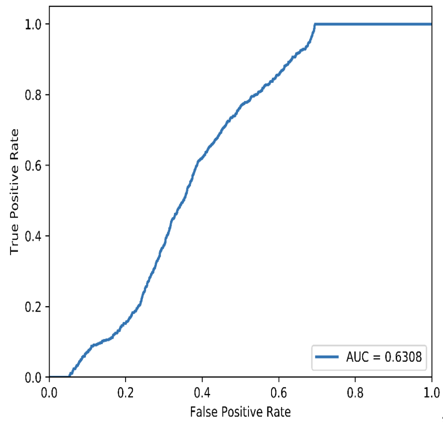
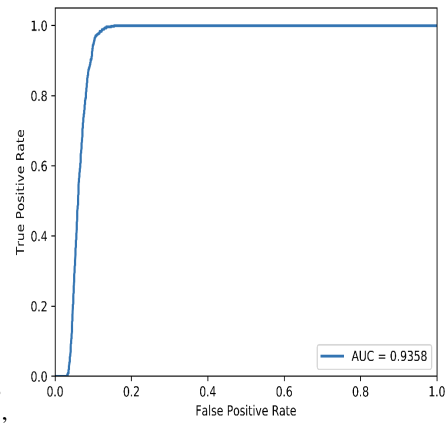


(m) Fundus Image (n) Ground Truth (o) U-Net (p) Tiramisu

Fig. 4: Haemorrhage segmentation results of four random examples images. From left to right, the original MR fundus image, ground truth, segmentation results by U-Net and Tiramisu are shown respectively.



(a) U-Net



(b) Tiramisu

Fig. 5: Performance of different segmentation methods, in terms of area under the curve (AUC) for MR haemorrhage detection with 1,669 annotated fundus sub-images

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