AUTOMATIC DETECTION OF DIABETIC RETINOPATHY USING DEEP LEARNING

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Abstract – **Diabetic retinopathy is a condition that is experienced by people who have diabetes. It affects up to 80 percent of people who have diabetes and is the leading cause of blindness for people aged from 20 to 64, Of the 415 million diabetics patients worldwide, one-third will develop retinopathy. Fifty percent of which will remain undiagnosed and would result in blindness within five years. Our aim is to make screening much more efficient and available to a broader population.**

Computer-aided diagnosis in the early detection and treatment of Diabetic Retinopathy has added advantages over traditional hand-crafted features technique due to its increased efficiency and reduced ambiguity of results. The main objective is to apply deep learning algorithms as a novel diagnostic tool for automated detection of diabetic retinopathy in retinal fundus photographs. The algorithm does binary classification of color fundus images and helps in early diagnosis of the patient. VGG-16 pretrained convolutional neural network model is used to train the network and to make the predictions. For a model trained on a small dataset, methods of fine tuning and transfer learning can help in getting favorable results. The paper shows the effect of using different network configurations with respects to training the network in order to get the best results with minimal overfitting. A comparison of improvements in the network by means of using various data augmentation techniques and pre-processing is also presented.

***Index Terms*— Diabetic Retinopathy, Image Processing, Retinal Fundus Images, Feature Extraction, Convolutional Neural Networks, Transfer Learning.**

I. INTRODUCTION

Diabetic Mellites (DM) is a series of metabolic disorders that's is associated with high levels of blood glucose over an extended period. It occurs when the body is not able to produce enough insulin or when the cells are not able to utilize the insulin produced, Insulin Is a hormone produced by pancreas. The hormone is required by cells to utilize glucose produced from food. Inadequate production or inability to use the hormone will result in high blood-glucose which over long run has many detrimental effects on the human body.

As per the latest studies, India alone is expected to have 79.4 million cases of diabetes by 2030, the largest number for any nation, of which 90% can be treated with early detection. This makes it an increasingly important disease to be diagnosed. Vision is one of the most fundamental aspects of life and the gravity of the loss of eyesight is malignant to any human. Hence, we, have come to a decision to bring about a contribution to the detection of Diabetic Retinopathy(DR) which might help doctors and other researchers in the medical field to prevent this disease from perpetuating into

humanity. Our aim is to make screening much more efficient and available to a broader population.

i. Need for Automated Grading system

Human evaluation in the diagnosis of DR is subject to erroneous results. A patient receiving two results from different graders will create a confusion within the him/her and hence, have a detrimental effect in the future treatment.

Deep nets are neural nets with multiple hidden layers, such neural nets have the ability to extract relevant features from large set of examples removing the need to specify rules for recognition explicitly. It utilizes high-level features and deviates away from traditional methods of using hand crafted features which are time-consuming and prone to errors. Deep learning develops the ability to recognize patterns which human beings could not identify. Deep learning techniques such as convoluted neural network has shown remarkable results in image recognition. The later technique has the following advantages :

- Does not rely on handcrafted features.
- Utilize the large amount of available data to identify patterns in the disease.
- Independent of segmentation.

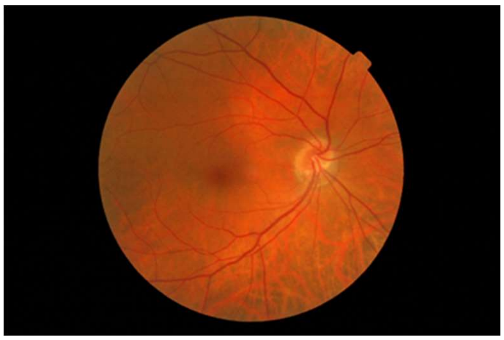

Fig 1: Fundus image with no Diabetic retinopathy

Fig 2: Fundus image with Diabetic retinopathy

ii. Deep learning as a diagnostic tool

Deep Learning networks have the ability to improve based on the data it is fed. As more data is exposed to a neural net it becomes robust. This is contrary to a conventional CAD tool that relies on hand crafted features hard coded by a human developer. Patterns that are not recognized by humans are also ignored by the static CAD system, where as a neural net can identify such patterns and improve based on previous results.

Fundus images being an extremely high-resolution image requires a large amount of time in training it. This difficulty can be mitigated by using convolutional neural networks which has shown extremely good results in image classification tasks. It eliminates ambiguities arising from human diagnosis, two doctors may give two different diagnoses.

The paper shows how a pre-trained model can be used to train a network for a new task and be deployed quickly for the problem of classifying DR in fundus imagery. This is a task with increasing diagnostic relevance, discussed earlier, and one that has been subject to many studies in the past. We then analyze the performance and dissect the capabilities of our network.

The rest of the paper is organized as follows. Section II presents an overview of related work, section III describes the architecture of the CNN and the training methods used in this work, section IV presents the results from our experiments, section V concludes the paper with discussion on the results and future work.

II. Related work

At present, diagnosis of DR is a slow and strenuous process that requires ophthalmologists to analyse color photographs of retinas. They then categorize the damage to the subject's eyes into four grades. The manual grading though effective is cumbersome. On an average, it takes more than 48 hours for the reports of the patient to come on record. Furthermore, in inaccessible areas where there are insufficient clinicians and resources, patients are left without any aid.

The motivation for the project was stimulated by the base paper by Zhang et al, which reviews research and development on computer-aided ocular disease diagnosis with three data type repositories. Each database is coupled with an algorithm for various ocular diseases. The paper realizes a statistical approach towards image-based studies conducted on various ocular diseases. From the diverse ocular disease types, diabetic retinopathy is a familiar ocular disease which occurs in higher probability than the rest. From the survey of works on DR, a majority of the work has been targeted on detecting lesions associated with DR. Less work has gone into converting lesion detection to DR detection.

A large amount of research has been done by the research community in the field of binary classification of DR. Gardner et al., achieved an accuracy of 88.4% for a binary classification using SVM on a small dataset of 200 images. Methods for classification into three grades were proposed by Nayak et al., By methodology of the research, the neural network had been trained on the fed data. Comparative analysis of the results was done based on the manual grading made by ophthalmologists.

In terms of the approach used, only a few works used non-clinical features for DR diagnosis. Non-clinical features are intrinsic details in funduscopic images and they can be detected by using Deep Learning techniques. A need for an automated grading system brought through deep learning can provide a substantial improvement in this domain.

i. Traditional Handcrafted Features

The base paper (Zhuo Zhang, et al) is reviewed to correlate detection of ocular diseases without the deep learning techniques being implemented. Traditionally, detection of ocular diseases was carried by using image processing techniques like histogram equalization, shade correction, convolution with a Gaussian mask, median filtering. Histogram equalization and shade correction is used for contrast enhancement and illumination normalization respectively. The use of gaussian mask and median filter is a common practice for elimination of noise. More extreme techniques involve elimination of blood vessels as its often misinterpreted as a red lesion or a microaneurysm and results in false positives. The choice of a suitable pre-processing method depends on the desired effect. The selection of pre-processing method depends on the desired result. Experimentally, CLAHE effectively improves local contrast but it is susceptible to noise. Since there is a subjective tendency for the pre-processing methods, it was decided to select the best combination of pre-processing and segmentation methods. Although there have been researches in development of an automated system for the detection of DR, most of them dealt with the usage of hand crafted features. The problem with handcrafted features is that they are unreliable, un-generalized and require large amount of human effort which nullifies the concept of automated grading system.

ii. Computer Aided Diagnostics

Diabetic Retinopathy (DR) is the result of excess glucose in the blood stream for a prolong period of time. This causes the tiny blood vessels to get clogged, forcing the body to develop new blood vessels which are weak and often ruptures; leading to leakage of fluids into the retina resulting in Microaneurysms, haemorrhages and Hard Exudates.
Miniscule details in a DR image can be identified by implementing trivial deep learning and image processing techniques such as feature extraction and convolution. Two papers Gulshan et al, Meindert Niemeijer et al, were extensively reviewed to provide guidance towards classifying DR images. For algorithm development, macula-centred retinal fundus images were obtained from fundus image repositories in India and abroad. In the first dataset from EyePACS, there were a random sample of macula-centred images. The second one is a Messidor-2 dataset which was used as a benchmark for testing performance of automated detection algorithm [23]. The second one was Messidor-2 data set which was used as a benchmark for testing performance of automated detection algorithm. For algorithm training, input images were scale normalized by detecting the circular mask of the fundus image and resizing the diameter of the fundus to be 299 pixels wide. To speed up the training, batch normalization was implemented on the ImageNet dataset.

Two traits were noticeably observed from the two papers:

(1) Increase in Relative performance is independent of the number of grades per image.

(2) The comparison between the usage of single or multiple grades per image in the tuning set showed that former had a better overall performance.

iii. Hardware dependencies and libraries

While dealing with CNN, the computational complexity heavily depends on the hardware resources. As better throughput can be achieved with GPUs because of their parallel processing power, going ahead with such a hardware architecture is the most viable option. Dynamic hardware resource management is not possible with personal computers; Hence, going ahead with cloud platform for the hardware resources is a more viable option. The cuDNN library of NVIDIA was used which enables the maximum utilization if the hardware therefore yielding better performance.

Summary of the survey is as follows:

- Deep learning techniques can be employed in research of medical image analysis.
- Identify the challenges involved with training the CNN diagnostic tool and also realize the hardware dependencies and computational complexities.
- Come up with a solution to decide the best configuration of the CNN in order to get

the best results with the given dataset of fundus images.

III. METHODOLOGY

A. Datasets

For algorithm development, macula-centred retinal fundus images were obtained from three different sources:
Kaggle retinopathy challenge, Messidor- A open database from three clinics from France and Centre for diabetics and endocrine diseases, Kanpur.

The Kaggle dataset is the most comprehensive dataset with 35,000 images. Kaggle dataset is prone to extreme noise in both images and labels and contains artefacts with many images being overexposed, underexposed or out of focus using the entire dataset alone will result in a poor network. The Messidor dataset is around 1200 in total while the dataset from the private clinic comes to 800 images. The dataset is divides into 4 grades as there are four stages for diabetic retinopathy they are:

0-No DR
1-Mild DR
3 and 4- Proliferative DR

Upon analysing the dataset, it was found that most of the Images do not contain any disease, Kaggle dataset alone has

22000 images without any indication of DR likewise images with mild DR was found to be difficult for network to train as there was not any prominent consistent features in the dataset. With regards to this, bucketing of the images into two classes was done- NO DR images, DR images (which is combination of stage 4 and 3 images from all dataset)
This is done to ensure that the network recognizes all the distinct features during initial training.

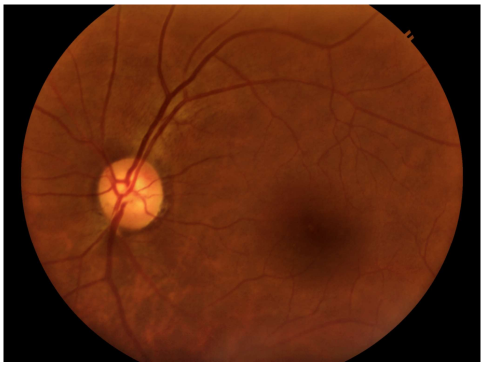

Fig.3 Clinical data

Fundus images from three sources are taken from three different types of cameras hence have different shades, lighting and colour to eliminate such ambiguities shade correction has been carried out by taking Green colour channel correction, this in addition to above corrections also eliminates the ambiguities in colour of retinal images of people from different ethnicity.

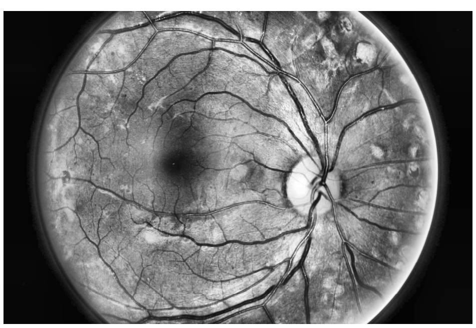

Fig.4 shade corrected Green channel Non-DR

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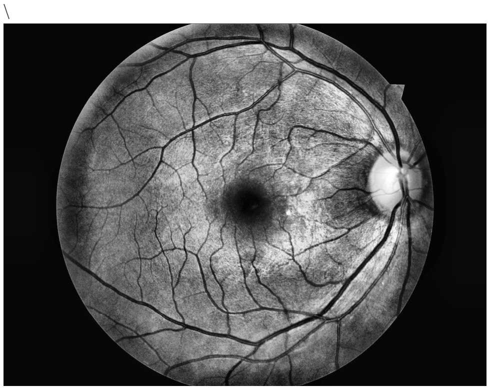

Fig.5 shade corrected Green channel DR

B. Grading

All the DR images were graded manually by ophthalmologists. From the given datasets, images which were found to overexposed, underexposed and those which were not able to provide any useful deductions were removed. The final dataset was made in such a way that there was an equal representation of both classes; this is to avoid the network from being biased towards a certain class. For the CNN network, the dataset is conventionally split into parts- 80 percent for training and 20 percent for validation.

C. Preprocessing Techniques

Pre-processing is done over these images to enhance the features and highlight minimalistic components such as the microaneurysms. Adaptive Histogram Equalization(AHE) is an image pre-processing technique used to ameliorate the contrast of images. However, an excessive amount of AHE can overamplify the noise in areas where the image is homogenous. Hence, a technique called Contrast Limited Adaptive Histogram Equalization(CLAHE) is used to combat such issues and effectively enhance features in an image. In this context, CLAHE is applied across all the DR images and this serves as a prerequisite for the process of differentiating the images during classification. This was implemented using the OpenCV packages [24].
Further pre-processing was done to carry out shade correction as images from different dataset were obtained from different cameras with different levels of exposure. The green channel correction also eliminates the problem of difference in color of retina of people from different ethnicity. Passing image to VGG network involves subtracting the mean value and normalizing the pixel values in the range of 0 to 1.

D. Data Augmentation

Techniques such as deep learning require a large amount of dataset to properly generalize a problem, utilization of small number of data for training a net result in the problem of over fitting, over fitting is the phenomenon where a model learns for the given data and is not able to get a generalized function such models give poor result when an external input is given. The problem of overfitting due to less number of data can be avoided by means of augmenting the available data. Augmentation is defined as deriving new dataset from available data, an efficient method to increase the dataset, , is by flipping the images with 90^0 and 270^0 rotation, left-right and top-bottom mirroring, random crop, zoom ,sheer and by introducing random noise. Another important augmentation technique employed was changing contrast I of an images in following format $I=\alpha I+\beta$ where α and β vary from 0 to standard deviation of Intensities. Utilizing such techniques dramatically increase the dataset size and reduces the chance of overfitting to a considerable extend.

Fig. 6 Fundus image without CLAHE performed

Fig. 7 Fundus image with CLAHE performed

E. Algorithm

VGG 16 pretrained model is used for classification process VGG 16 is a network developed by the Visual Geometry Group, Department of Engineering Science, University of Oxford. It was trained on the famous ImageNet subset for ILSVRC challenge 2015.the network was trained on a million images and therefor has learned a rich set of features for most of the common images. The original network is trained for 1000 classes. From practical point of view developing a convolutional neural network from scratch which includes randomly generated weights would require an extremely large dataset hence for most scenarios at hand the practice of transfer learning is employed.

Transfer Learning

Transfer Learning involves the usage of two main methods-
Net as fixed feature extractor and Fine-tuning of neural net.

Fixed feature extractor- In this scenario the fully connected layer is removed, and the remaining part of the net is considered as feature extractor for the new dataset to be trained. In the case of VGG, a vector is computed for the batch of images which also consists of an activation for each hidden layer just before the final classifier layer. Once all the vectors have been extracted from all the images it can fed to a traditional machine learning classifier such as SoftMax classifier or an SVM. The vectors extracted from the net are usually called bottleneck features. This is advisable if dataset is extremely small.

F. Fine Tuning

The practice implemented in this paper involves removing the original fully connected layers and implementing custom layers based on the requirement. The weights of the model are fine-tuned by means of backpropagation using very low learning rate. Fine tuning can be extended to all layers of the model but a network like VGG which is trained on 1.2 million images the top layers will be configured to recognize more generic features such as edges or colour blobs therefore leaving the top layers frozen while fine tuning is advisable. We remove the original fully connected layer and adds a custom layers and fine tunes the network up to final convolution block of VGG 16. Fine tuning more than that would result in problem of overfitting if the dataset is small.

As a rule of thumb if the dataset is extremely low then its best to train a linear classifier only.

Fine tuning on small dataset usually results in overfitting, if dataset is large fine tuning can be done on entire net without having much concern of overfitting. A medium size dataset as in the case used in this project fine tuning of fully-connected layers is advisable, a more aggressive approach for fine tuning can be done where more and more layers are unfrozen and fine-tuned, but the network must be monitored for overfitting.

While fine-tuning extremely small learning rate must be applied hence use of Stochastic Gradient Descent (SGD) is preferred over ADAM optimizer.

ConvNet Configuration					
A	A-LRN	B	C	D	E
11 weight layers	11 weight layers	13 weight layers	16 weight layers	16 weight layers	19 weight layers
input (224 × 224 RGB image)					
conv3-64	conv3-64 **LRN**	conv3-64 **conv3-64**	conv3-64 conv3-64	conv3-64 conv3-64	conv3-64 conv3-64
maxpool					
conv3-128	conv3-128	conv3-128 **conv3-128**	conv3-128 conv3-128	conv3-128 conv3-128	conv3-128 conv3-128
maxpool					
conv3-256 conv3-256	conv3-256 conv3-256	conv3-256 conv3-256	conv3-256 conv3-256 **conv1-256**	conv3-256 conv3-256 **conv3-256**	conv3-256 conv3-256 conv3-256 **conv3-256**
maxpool					
conv3-512 conv3-512	conv3-512 conv3-512	conv3-512 conv3-512	conv3-512 conv3-512 **conv1-512**	conv3-512 conv3-512 **conv3-512**	conv3-512 conv3-512 conv3-512 **conv3-512**
maxpool					
conv3-512 conv3-512	conv3-512 conv3-512	conv3-512 conv3-512	conv3-512 conv3-512 **conv1-512**	conv3-512 conv3-512 **conv3-512**	conv3-512 conv3-512 conv3-512 **conv3-512**
maxpool					
FC-4096					
FC-4096					
FC-1000					
soft-max					

Fig. 8 VGG16 Pre-trained network Layer configuration (Image Courtesy- Simonyan et al.,)

IV. Result and Discussion

Training of a neural net from scratch has shown unfavorable results, with large amount of resources and time being utilized without getting satisfactory results, in fact the network was a poor classifier which only performed slightly better than random guessing. The practice of boosting can be utilized in such cases where in combination of number of weak learners outperform a strong learner, but this is found to be computationally expensive with respect to the task at hand and utilization of a CNN type neural network becomes redundant.

With respect to above mentioned statements transfer learning and fine tuning were employed on VGG 16.

In order to measure the performance of the VGG 16 network for the given dataset, we perform a comparative evaluation of multiple layer configurations. For a pretrained neural network like VGG 16, the accuracy and validation depend on utilization of various hyper parameters. By comparing the configurations, one can choose the best set of hyper parameters for the dataset on which the classification needs to be done.

Choosing the hyper parameters is a tedious process and involves trial and error to a certain extend.

i. As the dataset is small having large number of parameters would result in problem of overfitting hence configurations which has lower number of parameter is preferred.
ii. Hence, only two fully connected layers are used, training the fully connected layer was found to contain the maximum number parameters therefor the following configurations for the fully connected layers are used 64 to 16, 32 to 8 and 16 to 8 fully connected configurations, final layer is a two class SoftMax predictor.
iii. All the above configurations have been trained using normal CLAHE images samples, Shade corrected Green channel images and finally all the above-mentioned networks are also fine-tuned aggressively by including final convolution layer of VGG 16. All the above configurations have been trained using normal CLAHE on the images samples, Shade corrected Green channel images and finally all the above-mentioned networks are also fine-tuned aggressively by including final convolution layer of VGG 16.

V. Conclusion

The following conclusions can be drawn from the observations-

- Smaller datasets require training of network with lesser number of parameters. This can be observed from the fact that the 64 to16 fully connected network configuration performed poorly compared to the other two networks.
- Configuration which was smaller than 16 to 8 fully connected layers were found to underfit.
- In the case where there is limited sample the employment of data augmentation techniques has significantly improved the trainability of network.
- The pre-processing of data has given an observable improvement in accuracy. The use of adaptive contrast enhancements technique enabled the network to detect finer details such as micro aneurisms, the use of green channel for shade correction combined with CLAHE has shown maximum improvements. Thus, the need for multiple types of pre-processing suggest that current systems are yet to generalize features for learning without human intervention.
- Fine tuning of a pre-trained network was found to be extremely effective method to train the network. Initially the VGG 16 was trained by freezing all the convolutional blocks and training just the fully connected layers which has given satisfactory results but more aggressive method of fine tuning by unfreezing the final convolutional layer was able to yield better accuracy.

Thus, by utilizing the practice of fine tuning we were able to achieve higher accuracies than network trained from scratch with minimal time and resources. Further improvements in detection requires larger dataset with lower noise in annotations.

VI. Future Scope

With ever increasing number of database both in terms of size and variety the utilization of neural nets in the field of medical imagining is becoming more and more prominent. Neural nets have shown its ability to highly generalize a task with high accuracy and have started rivalling human graders at certain tasks thus use of Artificial Intelligence (AI) in field of bio medical imaging is expected to rise at an exponential rate, the use of such proposed methods reduces the need for human intervention thus making grading of diseases fast, reliable and free from human errors. Future developments must be aimed at creating neural nets that are able to recognize and generalize a class with minimal number of images such a concept is known as One Shot Learning, achieving such fast learning with minimal number of data will require more advanced nets and would help in increasing the areas in which neural nets can be employed as not all fields of medicine have such large number of datasets.

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