Deep Learning Based Automated Extraction of Intra-Retinal Layers for Analyzing Retinal Anomalies

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Abstract

Blindness eliminates a person vision and retinal abnormalities are the second biggest reason of blindness across the globe. Each retinal abnormality affects one or more retinal layers or retinal surface. So, if we want to diagnose a particular retinal abnormality we have to extract the retinal layers to analyze the effects of that particular abnormality. Manual extraction of these retinal layers is possible but it is a cumbersome and time-consuming task. So, in our final year project we proposed a computer aided self-diagnostic system that could help the ophthalmologists in mass screening of retinal patients. In this project we have proposed the algorithms which are based on convolutional neural network (CNN). We have used two different approaches to use the CNN along with other techniques. In first method we have combined CNN with structure tensor and termed this method as convolutional neural network and structure tensor-based segmentation framework (CNN-STSF). In this method AlexNet (a pre-trained model) has been used through Transfer Learning technique. AlexNet was trained on more than 1000 patches of retinal layers and then it could successfully classify each retinal layer patch pass through it. In second approach we have used Gabor filter along with CNN to find the boundaries of each retinal layer. We have also used the flattening technique before Gabor filter to increase the horizontal shape of retina by flattening the curvature of retinal layers. And then before plotting the lines on retinal layers we have de-flattened the layers to restore their original shape and to represent the boundaries of retinal layers on original OCT scan. The proposed algorithms have been tested and validated on OCT scans which were acquired from Armed Forces Institute of Ophthalmology (AFIO) dataset and Duke University publically available dataset of OCT images.

List of Figures

List of Tables

Table of Contents

Chapter # 1

Introduction

In this chapter we are giving the project overview. Our presented thesis is the impulse for medical advancement. We select one particular part of a human eye and study it diseases and study the process of scanning. We find out that segmentation in different retinal anomalies is a complex task and consume a lot of precious time of anthropologist. We also discuss different techniques to improve already implemented systems in retinal segmentation to help and influence researchers to use their effort to improve the medical scanning process.

1.1 Project Background:

A human eye is made of different parts and components that work together for a clear vision. If any portion of the eye is damaged due to some reason it would defiantly lead towards poor eyesight and in worse case it may cause the blindness [1]. Different eye diseases affects the different parts of eye. The factors that affect the eye may be a human age, disease of the eye or any physical or chemical injuries of the eye [2]. The main visual disorders that often affect the eye are described below.

- Glaucoma
- Cataract
- Macular Edema
- Age related Macular Degeneration (AMD)
- Pterygium

Glaucoma is the name of group of diseases that causes to increases pressure of fluid of the eye [3]. This increased pressure damages the sensitive tissues of the eye; in worse case it damages the optic nerve which can disturb the transmission of visual images between eye and brain.

Cataract is the disease which cause eye lens to become opaque and cloudy, due to which the light rays cannot pass through lens easily, which result in loss of a clear vision [4]. *Cataract* most often occurs in patients above the age of 50.

Macular Edema mostly occur due to diabetes. A change in tiny, delicate retinal blood vessels of the retina occurs due to diabetes which is termed as diabetic retinopathy. In most severe case it lead patient to loss complete vision. High blood pressure and glucose level speed up the progression and development of retinal diseases.

AMD damages the Macula and is often related with the aging factor and is always bilateral i.e. occurs in both eyes [5]. Two types of AMD as listed below;

1-Dry Macular Degeneration

2-Wet Macular Degeneration

In *Dry Macular Degeneration* tiny yellowish or white deposits are formed on the retinal surface just below the Macula. These deposits are termed as Drusen. In early stage these Drusen may be small in size and number but with the passage of time the patient may begin to notice a small dark spot in his central vision. If Dry Macular Degeneration is not diagnosed and treated in its early stage it may lead towards Wet Macular Degeneration.

In *Wet Macular Degeneration* the blood vessel switch are right below the retina near Macula are started to grow abnormally that effect cause leakage of fluid between the retina layers and because of these leakage Macula is lifted up and pulled away from its base.

In *Pterygium* the white part of the eye is overlapped by noncancerous growth of thin and clear tissues [6]. The causes of this disease are unknown and its effects are painless .Surgical removal of the Pterygium is the best treatment.

1.1.1 Retinal Structure:

Retina is the innermost layer at the back of the eye. Optic nerve is located much closer to retina. The retinal structure is consisting of different layers and each layer is made of different cell to capture light and color. Macula is at the center of retina is of oval-shape and responsible for central vision [7].

The function of Retina is described as follow. Light focused by the lens is received by Photoreceptor cells of Retina. These cells are light sensitive and are capable of differentiating between different qualities like color and light-intensity. This information is further processed by the Retina and finally it is sent in the form of images to brain using optic nerve. And finally brain decides about the image i.e. what the image is. So, Retina plays an important role in the vision, any kind of damage to Retina can cause the blindness.Retinal Detachment is an eye abnormality in which the Retina is detached from its usual position. Due to this phenomena Retina is unable to receive light from lens and to process it correctly for the brain. So, brain becomes unable to receive the information form optic nerve thus leading to blindness. Retina has a layered structure. Several layers of neurons are interconnected with each other.

Inner-Limiting-Membrane (ILM) is a transparent layer separating the retina and the vitreous body. Its structure is composed of Müller cells, Collagen Fibers, Glycosaminoglycans, Laminin, and Fibronectin. Its thickness is about 10 μm.

Retinal-Pigment-Epithelium (RPE) consists ofthin layer of pigment cells which are in hexagonal shape. These cells are tightly packed together and form a single layer. The pigment of this layer protects the retinal layer from hazards of sunlight. It provides energy to choroid and some other parts of retina. Retinal Pigment Epithelium also maintains the PH balance of the fluid.

The Bruch's membrane is a boundary between RPE and the choroid layer and separates these two layers. The Bruch's membrane is made of connective tissue and choriocapillaries which carry oxygen and other nutrients for the cells. With age this layer gets thicker and it may affect the capability of capillaries to deliver oxygen to other cells of retina. A lot of oxygen is required for proper function of photoreceptor cells and this need id fulfilled by the Bruch's membrane.

The Choroid layer has a vascular structure and it is made of connective tissues and blood vessels. Outer layers of the retina get nourishment through this layer while Choroid layer gets its own blood supply from central retinal artery.

1.1.2 Deep Learning:

Deep learning is part of the big family of machine learning that is specifically used to perform different types of classification and pattern recognition in the field of computer technology. Implementation of this method is done using the art of neural network architecture which is the key element and was train to increase the probability of success. In Neural networks first a system learns about different types of data which may be images, sounds or text and then we classify that type of data using the trained model called structure network. A typical neural network has three layers: Input layer, Hidden layer and Output layer. While term “deep” is used for those Neural Networks which consist of hundreds or even thousands of neurons.

A Neural Network is inspired by human brain and a prefect copy to process information. A large number of *Neurons* are interconnected with each other. These neurons work together to solve a problem like pattern recognition or data classification. Just like a small child who learns by examples Neural Networks also learns by examples. At first we need to train Neural network. The data required for training the Neural network may be large or small depending upon the way one is using the Neural network. This training of Neural network is the most critical part of the Neural Networks for their accuracy. Once it is trained it can be considered as an "expert" to categorize the information that we present it to analyze.

The working of CNN is shown in figure 1. Using automatic algorithm it take one patch at a time from an input image and give it to Convolution layer. This patch is technically known as a filter and in our proposed system this filter size is 11x11 which is default filter size for the

AlexNet. Consider this filter as a flash light which shine on 11x11 area and we need to slide this flash area such that it shines on the entire area. In convolution layer we actually multiply the weights of filter witch a particular area of the input image and then finally these multiplications are summed up to give a final value. So we get a single number for every position of the filter on the input image. And this number is just representative of when the filter was at that position of the image. Now the filter is moved to another location and the same procedure is repeated again. The amount by which the filter shifts is called Stride. The stride is set in such a way that the output is always an integer rather than any fractional number. After sliding the filter on all possible locations of the image we get an activation map or feature map.

In AlexNet after every Convolution layer there is a Rectified Linear Unit Layer (ReLU). This layer uses the max(x,0) function and returns value only if the corresponding value of x is positive. So it has the property of addition.

After Rectified Linear Unit Layer (ReLU) layer the AlexNet apply a pooling layer which is also called down sampling layer. This layer takes a filter and then applies it to the input image and gives output that number which is maximum in the filter convolves around. In AlexNet there are total eight layers out of which five are convolution and three are fully connected layer. After every convolution layer there isa Linear Unit Layer (ReLU) layer, Its output is a finite dimension vector which in our case this dimension vector represent each layer of retina. The output vector contains the probability of each class. The class which has higher probability its label will be assigned to the image.

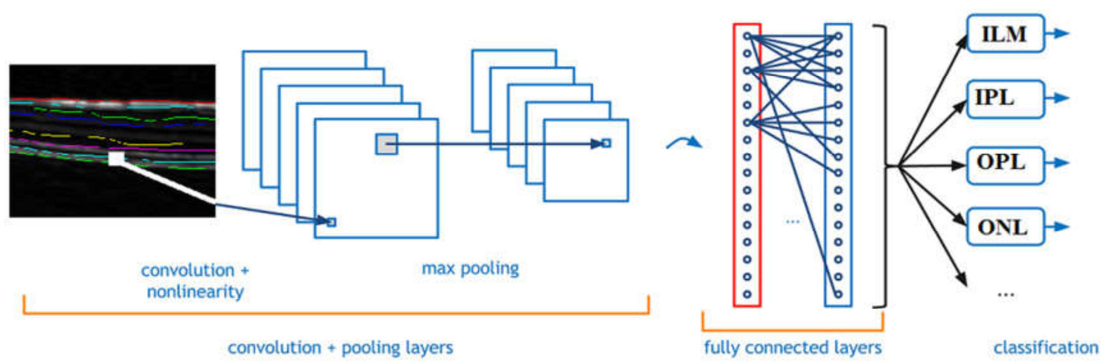

Figure 1.1: Working of Convolutional Neural Network

1.2 Problem Description:

Blindness is a pathological condition in which a person vision is completely eliminated and becomes unable to see anything. Blindness can also be partial in which person either has a blurry vision or unable to distinguish between shapes of different objects. Blindness can affect one eye or both eyes at a time. Clouding of the eye lens, any damage to the optic nerve or degradation of retina can be the reason of blurry vision. Any physical or chemical injuries to the eye may cause sudden blindness but these cases are rare and only 4% of the people around the world suffer from visual impairments as a result of anyphysical or chemical-injury. Majority cases of visual impairments are however because of eye diseases which affect the vision slowly and certain symptoms of blindness can be observed in a person who is going to blind before he completely losses his eyesight. People who are going to blind first often feel some kind of difficulty in vision which then slowly progresses into blindness. So, the immediate diagnosis and treatment can increase the chance of restoring the vision.

According to World Health Organization (WHO), 80% of blindness is avoidable however due to low ophthalmologists to patient ratio in third-world countries like Pakistan, more than 3 million people suffers from retinal diseases each year which are the leading cause of blindness. After Cataract, retinal abnormalities are the second big reason of blindness across the globe. Retinal diseases vary widely and have visual symptoms. So it is really important to pay attention to any change in vision.

1.3 Project Objectives:

As discussed earlier retinal abnormalities are the second big reason of blindness across the globe, so there is a dire need of developing computer aided self-diagnostic systems that can mass screen retinal patients in different geographical areas of the world. All the retinal diseases affect the intra-retinal layers in different ways and extracting the retinal layers is the most crucial task in evaluating retinal pathology. In our proposed algorithm we would use OCT images of retina to extract different retinal layers. Though retinal layers extraction has been done through many techniques. We are trying to improve their efficiency. The dataset that has been used in this research project is from Duke University. This dataset is publically available at Duke University website. In this project we have presented a robust algorithm for extracting retinal layers using state of the art deep CNN using AlexNet. AlexNet is the winner of 2012 competition of ILSVRC. ILSVRC is computer technology Olympics on yearly bases. Where different models compete with each other for the tasks like image classification and pattern recognition. The AlexNet was trained on 1.2 million images and could classify the objects like mouse, apple, keyboard, cats and dogs into 1000 different categories. The error rate for AlexNet is 15.4% [8].

Due to this increased efficiency we are using AlexNet model through transfer learning instead of building our model from scratch. Moreover this model requires less number of images for its training purpose and has higher accuracy [9].

Chapter # 2

Literature Review

In this chapter we are discussing different technique used by different researchers to obtain good segmentation results. We also discussed the need of segmentation and how much accuracy requires to successfully classifying healthy images from the diseased ones. There are 10 layers from which or more layers may be affected in different ways to be called diseased one. Each disease has its separate mark on OCT image. To identify the type of disease we need an anthropologist, mathematical model, image processing tool, the classifier or the deep learning program.

2.1 Characteristics of OCT Images:

Optical coherence tomography is the only feasible technique that is non-invasive to scan retina layers in 3d volume. It allows us to visualize each retina layer individually. OCTscanthe nerve fiber and other retina layer along with choroid, sclera, Prelaminar tissue, lamina cribrosa and noise. OCT have the sensitivity of 2-3mm with the resolution of 1-15 um, eachretina layer size varies from 3um to 40 um.Eye ball has the radius of 12mm, so the scan of optic nerve head of size 1.86 × 1.75 mm has a curvature of 9 ±0.5 degree.

2.2 Resolution:

Optical coherence tomography(OCT) machine has evolved in great resolutiona speed since 1997(first commercially used) it become standard for retinal imaging and care.[10] Stratus OCT has the resolution of 10 µm and can scan 400 A-scan/second, it is most affordable commercially used but its low speed prone to motion artifact and cover small area only. 3D-OCThas the resolution of 6 µm and can scan 20k A-scan/second, it has low resolution but obtain images in high speed.Cirrus HD-OCT is a spectral-domainhas a resolution of 5 µm and can scan 27k A-scans/second.The Spectralis has the resolution of 7 µm and can scan 40,000 A-scans/second.

The eye-following innovation perceives the nearness of eye development at that point repositions the output example and disposes of sweeps with movement antiquities. The Spectralis utilizes enrollment by retinal structures to takes into consideration programmed rescan of the retina at an indistinguishable area from the past visit, disposing of subjective output situating by the administrator and in this manner exact longitudinal following of different retinal maladies, for example, wet age-related macular degeneration is conceivable. Likewise, the Spectralis additionally finished examples particular focuses on the OCT filters and along these lines contrast and consolidate them with decrease dot (or irregular commotion) and upgrade particular structures. [11]

2.3 Shape of Retina:

B-scan obtained from OCT machine are consist of number of A-scans. It is the cross-section imagery of the retina. While scanning the retina machine gets A-scan and align in column to generate B-scan image. Each A-scan contain all layers of information, which obtained when laser light reflected from different layers. Every layer has some reflective index which help in differentiate one layer to another. Shape of retina disturbed when we combine A-scan images based on mathematical model of scanning which give approximation results. To get correct shape, we must find Retinal Pigment Epithelium (RPE) and adjust A-scan (columns of B-scan). Adjustment of A-scan in B-scan image also used to flatten the retina layers to improve results of filtering.

2.4 Noise:

B-scan images not only contain layers of retina but also contain part of choroid, sclera, Prelaminar tissue, lamina cribrosa, blood Vessels, and noisy regions. These part effect the overall accuracy of the segmentation of the retina layers. Speckle noise is also common in medical images which may affect the segmentation if not address. After adjusting the shape of retina, one can also find Inner-Limiting-Membrane (ILM), Nerve-Fiber-Layer (NFL) which are most optical reflective layers remove noisy area above the retina and from Retinal-Pigment-Epithelium (RPE) remove part behind the retina of eye, so part of interest (retina layers) separated in B-scan.

2.5 Manual Segmentation:

Manual Segmentation is the golden standard in OCT images. It is time consuming as one must observe difference in shades between each layer. It is also prone to bias and require anthropologist to correctly identifying the layers.

In order to increase the probability of success we manually classify B-scan to these layers and test our program accordingly.

2.6 Image Processing:

Segmentation of layers using image processing tools is done by many researchers in past 15 years. It is a powerful tool allow to deform an image into require setup and allow us to filter the require information. B-scan images are mostly gray scaled images that mean layers have different index of pixel value. The techniques that most of the researchers used is first remove speckle noise using median fitter then find retina area by increasing contrast or using gaussian filter or using structure tensor [11] .Another method is graph search method to connect points between B-scan images and then use multiple B-scan images to create 3d segmentation and display of retina [12]. Simple image processing is fast but prone to error that's why instead of using new and fast technique researchers used this technique along with machine learning and deep learning.

2.7 Machine Learning:

Machine learning has two advantages as it not only used in segmentation but also used in classification of normal from deceased one. After some image processing technique image is enhanced to extract features and classify layers. Segmented image using structure tensor or graph search is used to automatically classify B-scan image into normal, macular edema and age-related macular degeneration [13].By combining both technique one may obtained high accuracy in segmentation and as well as classifier of normal from different diseases [14] .

2.8 Deep Learning:

It is the relative new technique used in OCT images and used for segmentation.That segmentation is used to correctly detect the deceased area from the normal one. The accuracy of this method is high and accuracy increased with the increased amount of data trained. Our purposed method is also using image processing and deep learning for segmentation of layers of retina. Our main task is to use image processing to find unknown boundary using image processing and use CNN classifier to classify the boundary point into respective boundary name like boundary between RNL and GCL layer in named as RNL, GCL .

Chapter # 3

Requirement Specifications

In this chapter different technique used to solve retinal anomalies are explained. There are equipment's used in past but due to advancement in technology new machines arrived. These machines obtained detailed information which cannot be possible before, opening the new possibilities for preventing diseases before it influence daily life of human person.OCTmachine scan 3-D retina which need to be segmented to classify each part. The method of segmenting is extensive and complex and it require special filter and multiple techniques to create a hybrid system to successfully segment each layer with precision to detect any retinal anomalies.

3.1 Existing System

Three famous techniques are used to get picture of internal side of human eye. These techniques are Fundus Fluorescein Angiography, Fundus Photography and OCT. Among these three OCT is grown popular and it is the most efficient technique to analyze retinal anomalies. This is because of two reasons: Because it is non-invasive and it gives a high resolution view of internal side of human eye as compare to Fundus Fluorescein Angiography and Fundus Photograph. So OCT has become an emerging technique for retinal imaging. And also considerable clinical literature is available for OCT imaging.

According to SHRESTHA A. ET AL[15] OCT is the best technique for both quantitative measurement as well as to determine anatomical characterization of cystoid macular edema (CME).The method proposed by this method considered 104 eyes of different people. Due to usefulness of these OCT images many researchers and ophthalmologists prefer to perform analysis on OCT images. This study also proposed a method for classification of OCT images effected with diabetic Cystoid Macular Edema.

Structure Tensor combined with smoothing filters method for segmentation of retinal layers was proposed by DELIA C. F. ET AL[16]. Due to Structure Tensor efficiency was improved to much extent.

PRATUL P. S. ET AL[17] suggested method for classification of OCT images affected with AMD and DME. This method could successfully extract retinal layers from healthy, AMD and DME effected OCT images.

3.2 Proposed System:

CNN-STSF is based on extracting retinal layers information through coherent tensors. Afterwards the extracted retinal information acts as a guide for the deep CNN model not to process all the pixel instead process only those pixels which are marked as a part of intra retinal layers. Furthermore, CNN cross verifies those pixels by computing the probabilities that whether the extracted pixels are really part of retinal layers or not based upon their neighborhood surroundings. CNN-STSF uses an AlexNet model which is trained on retinal layer patches through transfer learning. The proposed framework is presentin detail block diagram as shown in Fig 3.1.

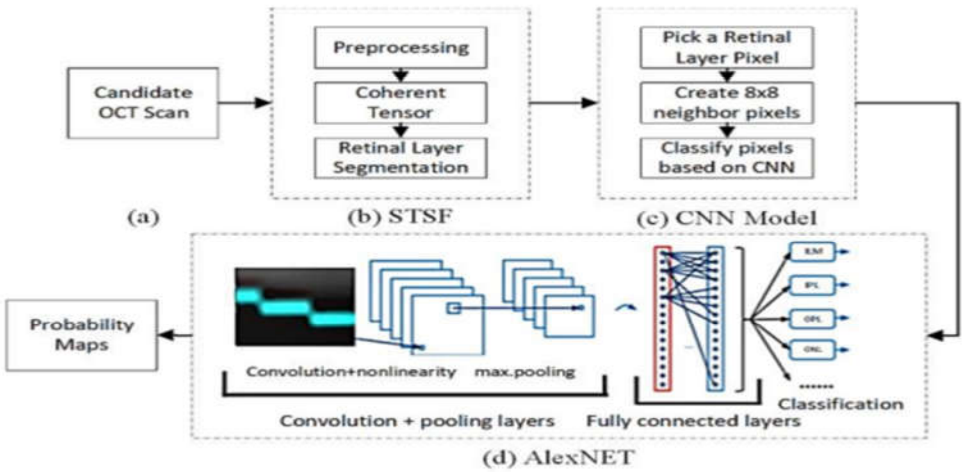

Figure 3.1 :Proposed implementation (a) input OCT scan (b) structure tensor based retinal layer segmentation (c) CNN model based retinal layer classification (d) cross verification using pre trained AlexNet

3.3 Use Cases:

The proposed system will be used by the Ophthalmologists to take decision about the retinal pathology of a patient. First a patient will need to take an Optical Coherence Tomography (OCT) scan of his eyes. This OCT image will contain all the information about the patient eyes but the Ophthalmologist is unable to take any kind of decision about the patient eye disease. As the information contained by these scan cannot be interpreted by the humans so they need to use a system which could show them all the retinal layers separately. And this separation of retinal layers will be done through our proposed system. The Ophthalmologist will need to load the OCT scans in our proposed system and then the system will take decisions about the retinal layers segmentation based on the pre-trained dataset of OCT scans. If any layer or some of its points are missing in the original OCT scan then the system will try to interpolate these layers or points to make the best approximation based on certain curve fitting methods and probability techniques. Then these layers will be mapped on the original scan so that the Ophthalmologist could observe all the layers separately. Now if all the layers are in their normal shape and none of the layer is missing or damaged then the

Ophthalmologist could classify it as a normal scan. And if any layer in the scan is missing, damaged or it is not following exactly the same shape as that of layers in the normal scan then the Ophthalmologist should classify it as an abnormal scan. Now as discussed earlier, every retinal pathology affects different retinal layer in a different way. So depending upon the layer and its shape it will become easier for the Ophthalmologist to classify this abnormality into one of the retinal pathology.

Chapter # 4

System Design

In this chapter we discussed complete process of performing OCT scan for retinal anomalies. These procedures are done for every eye patient whose eye visualization is affected. We explain how new and old methods are affected in studying retina anomalies. And we also explain our contribution in this process and restrain in other part of OCT scan process which can be overcome to further improve this system.

4.1 System Architecture:

For our proposed system first a candidate will need to capture OCT images of his retina. The candidate will sit in front of the OCT machine and to keep his head still he should rest his chin on the support attached to the OCT machine. This OCT machine captures the retina images without touching your eyes. It can take up to 5 to 10 minutes to complete the scans. Sometimes the ophthalmologist may need to put dilating eye drops in candidate eyes. This will make easier to examine the retina asdilating eye drops helps to widen the pupil. In general blue, green and hazel color eyes are dilated faster than brown color eyes. If the ophthalmologist uses the dilating drops for candidate's eyes his vision may become blurry. His eyes may become sensitive to light rays or he feels difficulty to focus on the objects that are close to him. The duration of these two effects will depend upon the type of dilating drops used and how a candidate's eyes react to these dilating eye drops.

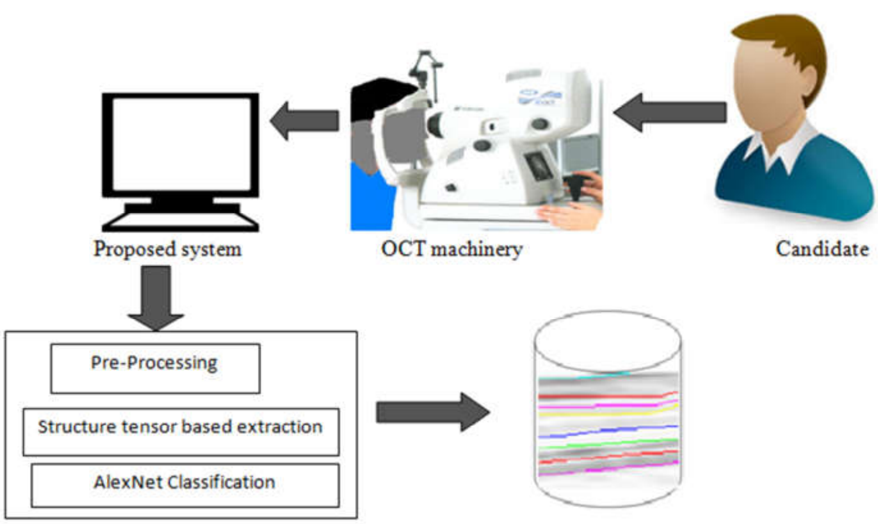

Figure 4.1: System Architecture

Multiple scans are taken using the above mentioned steps and finally an ophthalmologist will select the best taken scan of OCT image of retina layers. These multiple scans are saved in one folder in computer. The next step is to upload these all images in our proposed system.

The folder is read by the system and all OCT images are processed one by one and will extract all retinal layers. During this process if any layer is missing the proposed system will use the some estimation technique to approximate the retinal layers in a best possible way.
When all retinal layers are extracted then this finally extracted image is mapped on a scan which is a healthy OCT scan. Now depending upon the kind of pathology one or maybe more retina layers will not be same as that of layers in the original healthy OCT scans. So ophthalmologist will classify it as an abnormal scan. In other case if all the layers that are extracted are exactly same as that of original healthy OCT scans the ophthalmologist will classify it as a normal OCT scan as none of the retinal pathology has affected any of the retinal layer.
The proposed system objectives have been achieved by using two different ways. In both methods first we have used some image processing techniques in order to refine the OCT images and then we have used the state of the art of Deep Learning to accomplish the desired tasks.

4.2 Design Constraints:

The key elements that are responsible for the performance of our proposed system are MATLAB latest versions, Graphics Processing Unit and central processing unit of a computer. As our project is software based so we have no constraint of budget or cost for our system. The thing that we need to implement our project was to update our MATLAB version to latest one which is in our case MATLAB 2017-a.
The CNN model which we have used in our proposed project is AlexNet. This model is supportable only in MATLAB 2017. Moreover this version has many other new features which are used in the Deep Learning theory.
Graphics Processing Unit is important hardware component in the field of Image processing and deep learning. As for our proposed system first we need some Image Processing technique for pre-processing of OCT scans to be used by our system. To perform image processing operations on GPU we need to shift data from CPU to GPU. Also GPU is also needed to train and test deep learning program. We have used three computers with no dedicated GPU. So it was a constraint for our project to slow down its computations. Due to this limitation our proposed system took more time to be trained on the retinal layer patches as compared to that if we used a dedicated GPU along with a CPU.
SSD is the type of data storage device. It is the replacement of hard disk drive to increase the speed of data flow from hard disk to the RAM. In order train AlexNet large amount of data is

trained in number of iterations and each iteration load image from the hard disk by using SSD we can train more images and also observe the behavior of trained network on different dataset. We try to train the neural network from the scratch but when we increase dataset and layers of neural network we face difficulty in observing the behavior due to the constrain of time. Beside these limitations we try our best to successfully train the model in limited shots.

In our proposed system it is the only CPU that performs operations on the images and training on the retinal layer patches through AlexNet model of Convolutional Neural Network. CPU works in sequence. To start any second operation it should finish operation it is performing earlier. Some specifications of the Computers used in our system are listed in table 4.1

Table 4.1 Hardware specification

Serial No.	Computer Name and Model	RAM Size	Clock Speed	Core
1	Desktop PC	8GB	3.4GHz	i7
2	HP R205NE	6GB	2.2GHz	i5
3	HP Elitebook6930	2GB	2.4GHz	Core2Duo

4.3 Design Methodology:

The proposed system objectives have been achieved by using two different ways. In both methods first we have used some image processing techniques in order to refine the OCT images and then we have used Deep Learning to accomplish the desired tasks. In last few years many different researches had been proposed for automated extraction of retinal layers from OCT scans [18-28].

In first method we have used the Structure Tensor for segmentation purpose of the OCT images and then Deep Learning technique to cross verify the retinal layers extraction points. The original OCT image is first loaded into the system to acquire only the high intensity contributing channel instead of the entire image. This is done by normalizing the input image to a resolution of 720 × 1280. A 2D adaptive low pass wiener filter is used to suppress noise [18]. This denoising causes to increase the sparsity of intra-retinal pathology. The response of wiener filter is based on average intensity of surrounding pixels. After this, the segmentation is performed using a second-order structure tensor. A localized Gaussian window is then used in order to smooth each tensor. From these four tensors only, a high coherent tensor is used further to compute a binary map. Edge of retinal layers is computed by applying canny edge detection technique on binary map.

Fig 4.2 shows the steps involved in segmenting all retinal layers. The results acquired using tensors are further verified through AlexNet model. For a retinal layer pixel in coherent tensor, an 8x8 neighborhood patch is computed centered at.The patch is then resized to resolution of 227x227x3 to make it compatible for the input size of tuned AlexNet model. AlexNet then computes the probabilities of against eight retinal layers classes and the ninth no layer class. Then becomes part of that class for which it has the highest probability and is placed on the respective class probability map . The architectural description of AlexNet is presented in Table-I whereas the training of AlexNet was conducted on 1,200 retinal layers patches with epochs, initial learning rate and batch size is set prior to our knowledge to 20,0.001 and 64 respectively.

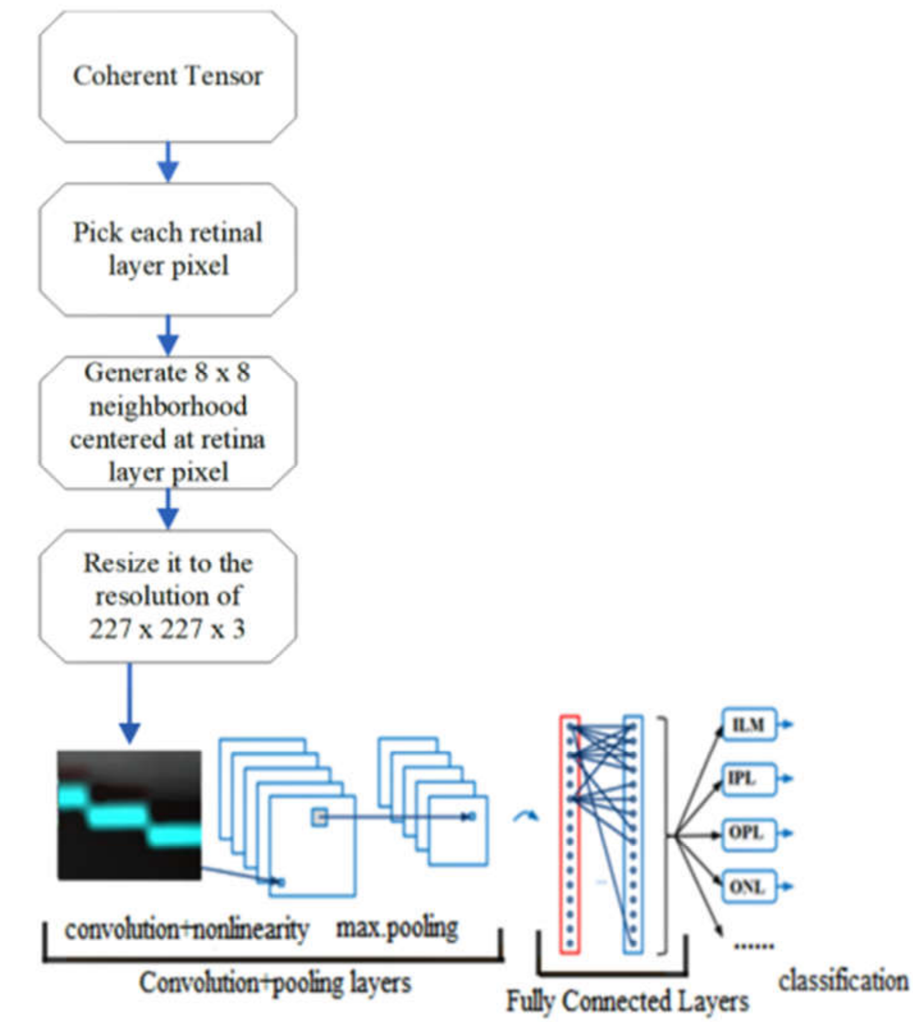

Figure 2.2 : AlexNet Retinal Layer Classification

Chapter # 5

System Implementation

In this chapter we discussed different kind of methods and technique which we used throughout this project. We also discuss the prone and cons of each technique when applied on OCT images. Some of our achieved methodologies use one or more filtering techniques to make a hybrid system.

5.1 System Architecture:

The overall system architecture has been described in the previous chapter here we will discusshow different algorithm work in a group to create a hybrid system. First we get images of a patient in folder as used in DUKE data set or in video containing frames that represent B-scans as used in AFIO data set. Then using each B-scan we extract all the boundary layers in the form of lines and combine all layer lines to create a 3D structure of retina layers surfaces
Each B-scan images contain information of all layers in that cross-section area of retina. In our project we extract each layer form all the B-scan images and create a surface of that layer we programed to extract all layers and display the surface together in 3-d view. Each surface that isformed by the layers from each B-scan are done in parallel.
We used structure tensor to filter the layers and separate each layer from one to another by using hysteresis3d. The found lines are then checked by AlexNet deep learning program.

5.2 Tools and Technology used

In this project we utilize our laptops and latest MATLAB software. We utilize our knowledge of math and way on imagination in image processing to solve complex medical problem. The tools we use may not be the best for this project but we didn't relay and failed by the limitation of hardware as discussed in limitation. Most of the tools we used are work in series to reduce computational space.

5.2.1 Hardware

MATLAB minimum requirement using Intel processor has to be 64-bit processor and at least 2GB of RAM. Graphic card is not mandatory for this project but it really speed up the process of testing and hence debugging. In image processing most of the variables has to be optimized based on experience that require human intervention that's why it recommended that hardware should be sound and equipped with latest technology.
In this project we use laptops to write codes of each module separately and test it using main program. By dividing task in small modules the problem of slow hardware can be managed. Another problem that we face is training AlexNet, it trains using images of size 272x272 and

these images are color images so in order to train on large number of data set you need a hardware that can handle large data and number of iteration. Final training is done on Desktop PC provided by university to train AlexNet and it took around 12 hours to complete. Final versions of all methods that's we used can be tested and displayed utilizing minimum hardware requirements of MATLAB. We also tested our algorithms on HP Elitebook6930. It work with 10% more time on execution. Each hardware specification is shown in table 5.1.

5.2.2Curve fitting

There are many ways to apply curve fitting to improve layer boundaries. In order to decrease error with respect to manual segmentation we have to segment the lines to reach the level of human accuracy. In our project we used three type of curve fitting

1. Polynomial curve fitting.
2. Median line filter.
3. Linear Interpolation.

Linear Interpolation is used in small gaps and we didn't prefer to fill large gaps using interpolation due to its inability to generate line curve. The curvature of retinal layers can be compromised using linear interpolation in order to retain the curvature we use polynomial curve fitting. In *Polynomial curve fitting* we used 3^{rd} order polynomial to fill small gaps and in large gaps we used 8^{th} order of polynomial curve fitting. *Median filter* are used to remove points that are fail to detect correctly. It uses the size of each layer and removes any abnormal distant point that may lie on other layer. This technique in used in semantic to correct the clusters of points or used in CNN if it fail to detect in actual system.

5.3 Language Used

MATLAB is the programing language. It is proprietary for commercial used .It is best used in educational purposes. MATLAB can interact with C# or with other programing languages.

5.4 Algorithms

Many algorithms are used in order to accomplished the task of automation. As the OCT scan contain B-scan images so 2-D filters are used such as Gabor and ST filters and 1-D filers are used to normalize A-scans.

5.4.1 Wiener Filter:

The Weiner Filter was proposed by Norbert Weiner in 1940.This filter is used in order to minimize the noise of an image. It actually makes the noise smooth by taking overall man square error in the filtering [29].

The Weiner Filter actually estimates the mean and variance of each pixel and then it performs smoothing action. It performs a very little smoothing when variance is large and vice versa. This adaptive filtering technique is better than that of linear filtering technique but one disadvantage is that it takes more time for computations purpose than that of a linear filter. Following are the mathematical expressions that describe how does a Weiner Filter performs its calculations,

$$\mu = \frac{1}{\mathrm{NM}} \sum_{\mathrm{n1,n2} \in \eta} \mathrm{a}\ (\mathrm{n1}, \mathrm{n2}) \tag{1}$$

$$\sigma^2 = \frac{1}{NM} \sum_{n1,n2 \in \eta} a\ (\mathrm{n1}, \mathrm{n2}) \tag{2}$$

Ifv^2=Noise Variance Then,

$$b(n1, n2) = \boldsymbol{\mu} + \frac{\sigma^2 - v^2}{\sigma^2} (a(n1, n2) - \boldsymbol{\mu}) \tag{3}$$

5.4.2 Structure Tensor:

In mathematics the Structure Tensor is used in order to find a pre-dominant direction based on the gradient for a specific point .In our proposed system we have used a second order Structure Tensor which is computed at the orientation of 0 and π/2 radians. The four possible generated tensors are mathematically expressed as follow,

$$I_D(x, y) = \begin{bmatrix} I_{xx} & I_{xy} \\ I_{yx} & I_{yy} \end{bmatrix} I_{xx} = \sum_{x_i \epsilon W_x} \sum_{y_i \epsilon W_j} W(x_i, y_j) \left(\frac{\partial I_D(x - x_i, y - y_j)}{\partial x} \right)^2 \tag{4}$$

$$I_{xy} = \sum_{x_i \epsilon W_x} \sum_{y_i \epsilon W_j} W(x_i, y_j) \left(\frac{\partial I_D(x - x_i, y - y_j)}{\partial x} \right) \left(\frac{\partial I_D(x - x_i, y - y_j)}{\partial y} \right) \tag{5}$$

$$= I_{yx}$$

$$I_{yy} = \sum_{x_i \epsilon W_x} \sum_{y_i \epsilon W_j} W(x_i, y_j) \left(\frac{\partial I_D(x - x_i, y - y_j)}{\partial y} \right)^2 \tag{6}$$

A localized Gaussian window is used in order to smooth each Tensor [8]. The computed Tensors are shown in figure 5.1. From these four tensors only a high coherent tensor is used further to compute a binary map.

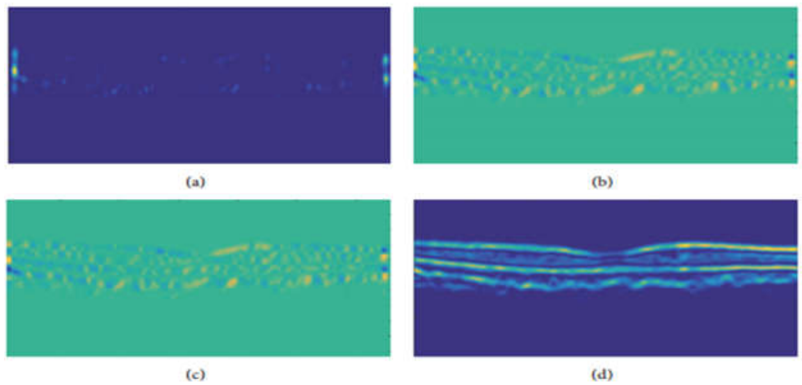

Figure 3.1: Second-order structure tensor grid: : (a) tensor computed through the dot product of horizontal gradient, (b) tensor computed through the dot product of horizontal and vertical gradients, (c) tensor computed through the dot product of vertical and horizontal gradients, and (d) tensor computed through the dot product of vertical gradient

5.4.3 Canny edge detection:

Canny Edge detection is used to detect edges in an image.It returns a binary image in which 1s and 0s are distributed in such a way that where it finds an edge it will have a1 and if it does not find an edge it will have 0 at that point [30].The default method used by this technique to find the edges in a image is Sobel Edge detection method. But while using the canny edge detection technique we can also specify to use other methods which are supportable with this emthod like Laplacian of Gaussian and Zero-crossings. The emthod that we wan to use can be choosen by specifying the parameters that are availabe for each method.

5.4.4 AlexNet Model:

AlexNet can classify objects into 1000 different catageroies but we have used it as a classifier only to classify 9 different objects. In our case the 8 different objects are actually retinal layer patches and one is actually a no layer object. The architectural description of AlexNet is presented in Table-5.1 whereas the training of AlexNet was conducted on 1,200 retinal layers patches for 20 epochs with an initial learning rate of 0.001 and the batch size is 64.

Table 5.1 ALEXNET architecture for CNN-STSF

Sr. No.	Layers	Description
1	Input	Resolution of 227x227x3
2	Convolution	96 convolutions
3	3 Rectified Linear Unit	Values less than 0 are clamped to 0
4	Cross Channel Normalization	With 5 channels per element
5	Max Pooling	3x3 max pooling
6	Convolution	256 convolutions
7	7 Rectified Linear Unit	Values less than 0 are clamped to 0
8	Cross Channel Normalization	With 5 channels per element
9	Max Pooling	3x3 max pooling
10	Convolution	384 convolutions
11	Rectified Linear	Unit Values less than 0 are clamped to 0
12	Convolution	384 convolutions
13	Rectified Linear Unit	Values less than 0 are clamped to 0
14	Convolution	256 convolutions
15	Rectified Linear Unit	Values less than 0 are clamped to 0
16	Max Pooling	3x3 max pooling
17	Fully Connected	4096 fully connected layers
18	Rectified Linear Unit	Values less than 0 are clamped to 0
19	Dropout	0.5 threshold
20	Fully Connected	4096 fully connected layers
21	Rectified Linear Unit	Values less than 0 are clamped to 0
22	Dropout	0.5 threshold
23	Fully Connected	8 fully connected layers
24	Softmax Activation	Softmax activation with final class probabilities
25	Classification Output	ILM, IPL, OPL, ONL, IS, RPE, BMand CH classes

5.4.5 Gabor Filter:

In computer vision and image processing the Gabor transfor is used in order to extract feature of an image, texture analysis and for estimation of disparity map. In order to tune Gabor filter for an image we need to adjust its frequency and orientation. Then it would be helpful in order to find a specific frequency content in that image. Mathematical explanation for a 2D Gabor filter is described as follow,

$$f(x, y, \omega, \theta, \sigma_x, \sigma_y) = \frac{1}{2\pi\sigma_x\sigma_y} . exp[\frac{-1}{2}\{\left(\frac{x}{\sigma_x}\right)^2 + \left(\frac{y}{\sigma_y}\right)\}^2 + j\,\omega(xcos\theta + ysin\theta)] \tag{7}$$

Where,

σ is the spatial extent i.e the bonding box of the filter

θ is the orientation of the filter

ω is the radial frequency of the sinusoid

In our purposed method our program tuned the Gabor filter for an orientation based on angle find by ILM and a frequency(f) of 0.1 while keeping the spatial extent σ_x and σ_y to be equal. In our proposed method, the system automatically adjusts the orientation of Gabor Filter. When the Gabor Filter window is moved after every four pixels then depending upon the orientation of the ILM layer points the angle is adjusted to create a cluster on every layer. In OCT images layer direction from ILM changed form some angle to the acheivedhorzantal RPE layer . So if we need to extract the layers we should tune our filter accroding to that direction. We use gabor filter to get normalize A-scan to differentiate eash layer. Due to the use of Gabor Filter it becomes easy for the create cluster of layers and also to create patches to classify using CNN. In cluster of layer sequence of image is used to classify this work on normal images called semantic classification. In AMD and DME decease part more efficient approch of CNN used to classify layers afficently.

5.4.6 Semantic Classifier:

This classification is used with Gabor filter to classify each a-scan column by column in a b-scan image. In order to classify correctly we select only those column that have only 5 clusters and use those cluster to identify whole column. This type of classification work best for normal patient because there is no distortion in there layers. Gabor filter and samentic classification that we used is also used is decease patient as the region of the covered area by decease is usually very smaller than normal region. The speed of this type of classification is very high and the result of each a-scan generated by this method is either 100% correct or automatically requested to use other method that's why we prioritize this method. For reference in figure 5.2 we show that using this method we classify 87.5% column in five cluster and remove region will be further processed and by filtering each line we are able to plot boundary lines of each layer.

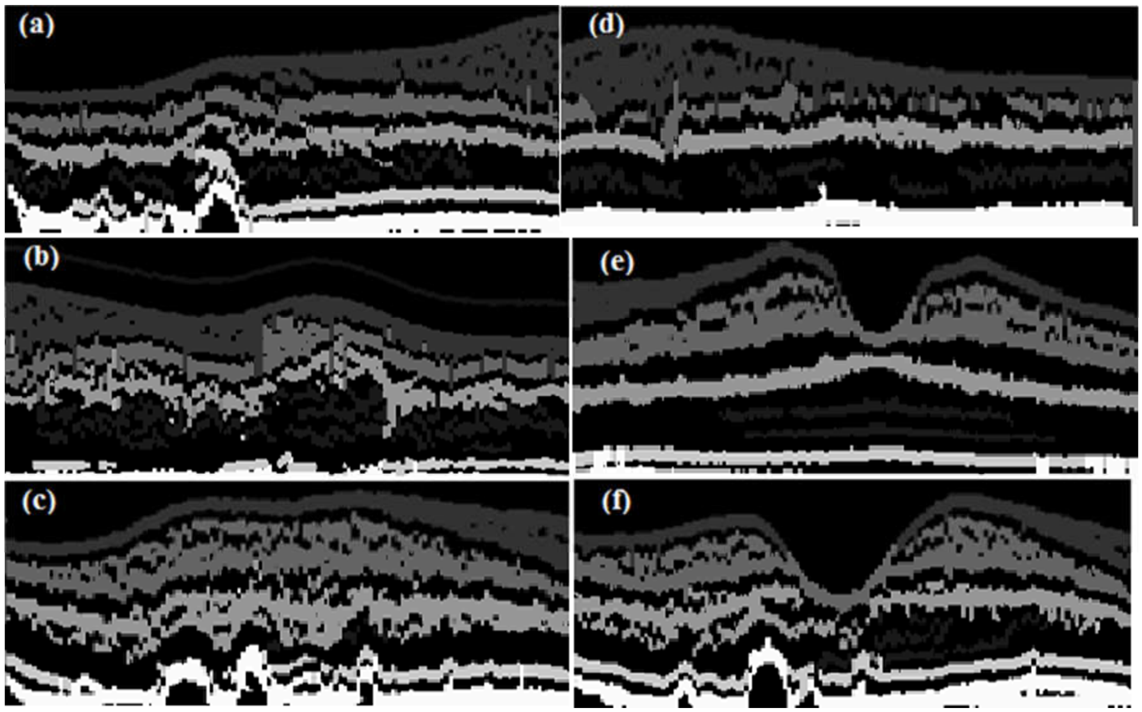

Figure 5.2 Gabor filter images of flattened B-scan with semantic classifier

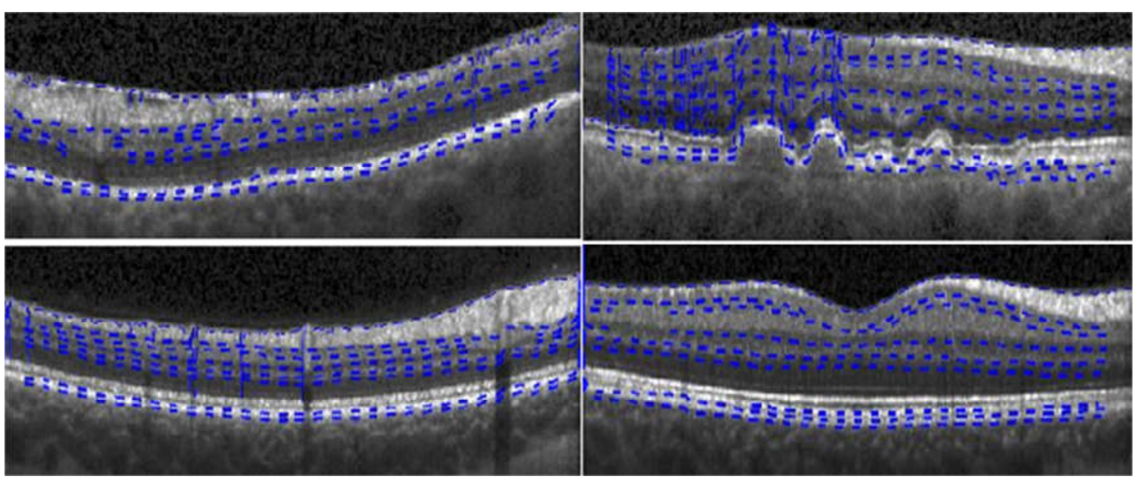

Figure 5.3: Semantic Segmentation on Original Image

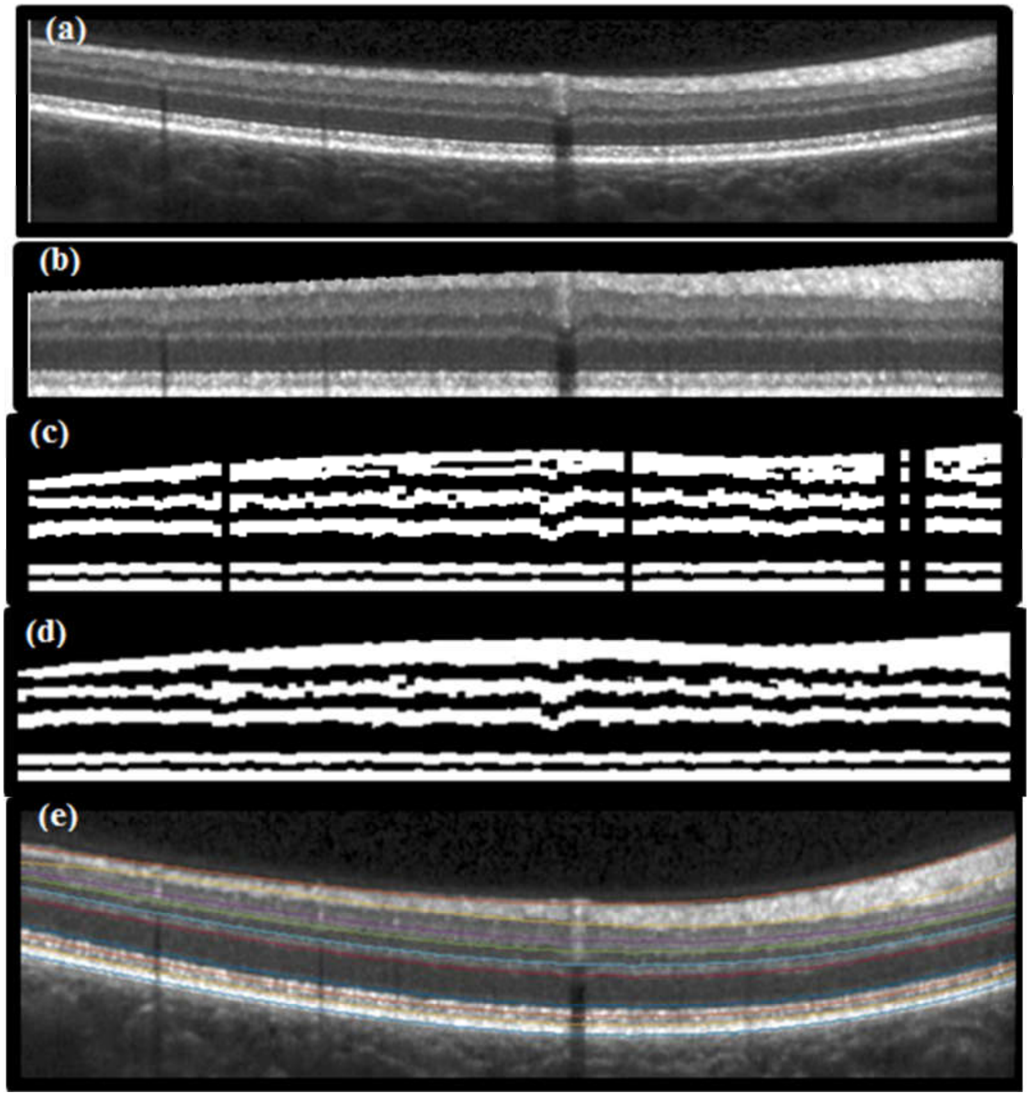

Figure 5.4 : Semantic method results (a) Non processed B-scan image (b) Flattened curvature of B-scan image (c) image is classify using Semantic classifier (d) Image further use Semantic filter with median filter (e) B-scan Image with boundary line plotting on non-processed B-scan image.

Chapter # 6

System Testing and Evaluation

Our proposed system was tested on OCT images of two datasets. One was acquired from Armed Forces Institute of Ophthalmology (AFIO) and other one was downloaded from Duke university website that is publically available on following URLs:

http://people.duke.edu/~sf59/RPEDC_Ophth_2013_dataset.htm

http://people.duke.edu/~sf59/Chiu_BOE_2014_dataset.htm.

In our case the system accuracy was checked by comparison of manually extracted retinal layers by ophthalmologists with extracted layers of proposed algorithms. The table 6.1 shows the mean error which is calculated between manually segmented retinal layers and that of automatically segmented layers by proposed algorithms in term of pixel points.

Table 6.1 Mean error between manual and automated lines pixel points

Patient Number	1	2	3	4	5	6
ILM	0.547337	0.748521	0.963116	0.80572	0.342209	0.452663
NFL-GCL	0.71499	1.04931	1.135108	0.820513	0.687377	0.936884
GCL-ONL	0.939152	1.031686	0.906257	0.882233	0.67147	0.76101
ONL-IPL	1.085799	1.045365	0.937788	1.072978	1.253452	1.20217
OPL-INL	0.909297	1.104591	1.119513	1.246123	0.872739	1.019433
INL-RPE	0.975276	0.789347	0.834361	0.643804	0.554345	0.748513
RPE-BM	0.621577	0.857304	0.926243	0.895154	0.878195	0.905858
BM-chroid	1.19E-14	1.19E-14	1.19E-14	1.19E-14	1.19E-14	1.19E-14

To test our proposed system, we load an OCT scan in our proposed system and then it extracts the retinal layers. We have used the color lines to highlight each retinal layer. As shown in figure 6.1 ILM is plotted in red color, IS is in yellow, ONL is in blue, OPL and choroid are in green, IPL and BM are in cyan and RPE is shown in purple. We have tested our proposed algorithms on both health and diseased OCT scans but till now we have not targeted any specific retinal abnormality to be detected by our proposed system. Our main goal in this project was only the correct extraction of retinal layers. The next figures show the final output of our proposed system in term of all layers are extracted.

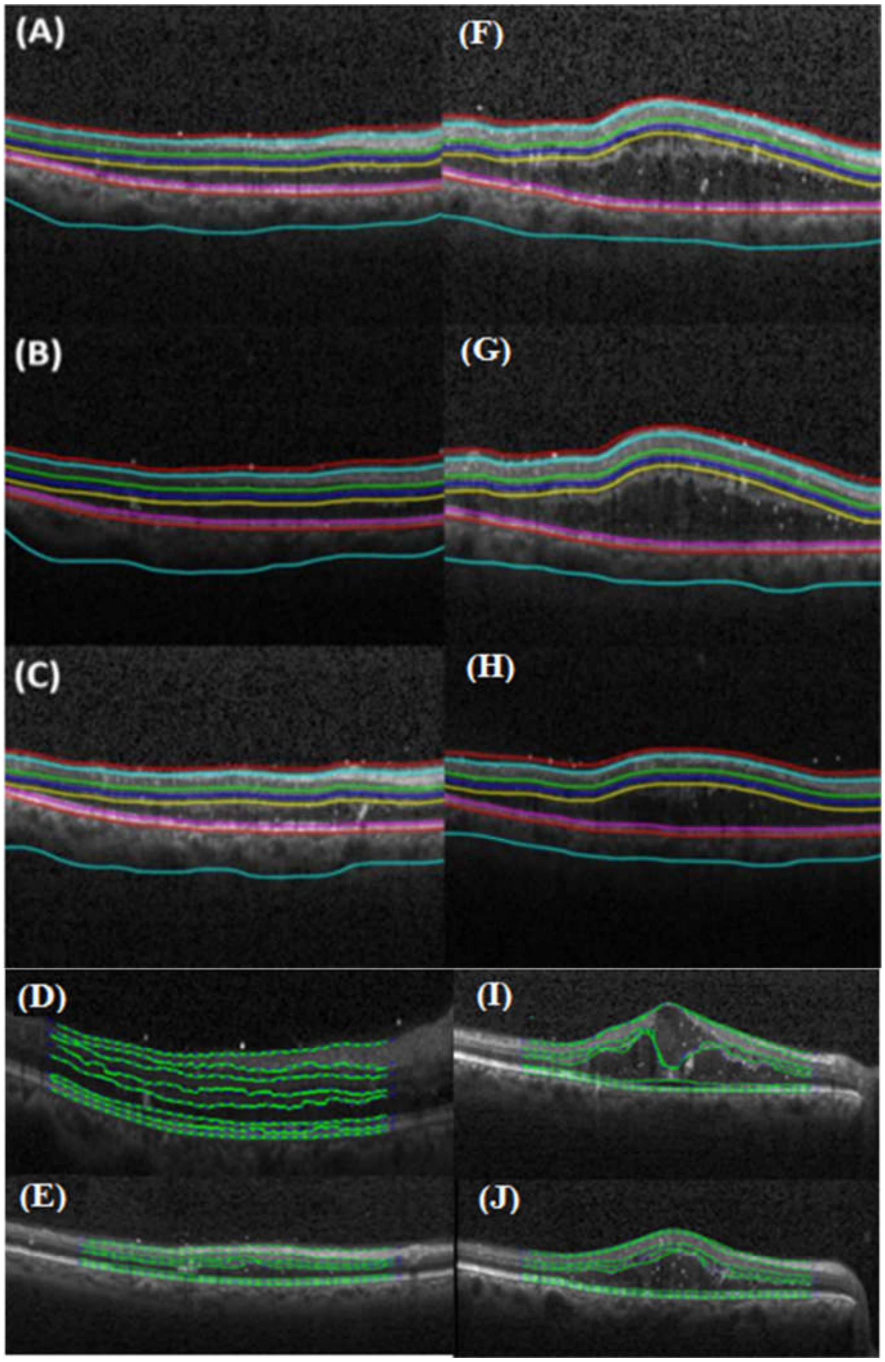

Figure 6.1Auto-segmented retinal layers: (A)-(E) eight layers extracted from healthy scans, (F)- (J) eight layers extracted from diseased scans

Chapter # 7

Conclusion

This thesis proposes an automatic system for extraction of retinal layers for analyzing retinal anomalies. We have used the state of the art deep Convolutional Neural network (CNN) along with other techniques to improve the reliability and efficiency of the proposed system.

CNN works like a human brain and learns like a child so now it depends upon us how do we provide the training dataset to CNN for its fine tuning. Before the CNN performs the classification of data we needed to refine it so that CNN could easily learns about the desired features of the provided data. In our case this data was the patches of retinal layers obtained from OCT images. These patches were obtained from the Structure Tensor based segmentation of retinal layers and then CNN was trained using these patches. After CNN has been trained it could successfully classify each retinal patch into one of the category specified in its fully connected layer.

In the whole process of developing and completing the project we learn a lot. We try our best in creating best methods and combine them together to make a hybrid approach.

In our experience of creating a best solution for one type of images may not good enough for all images and by testing on lot of image we can improve the accuracy. That's why we didn't focus on one algorithm instead we use different algorithm and combine the best parts of all the system to make a program that automatically gave results with high accuracy.

This is the high potential subject and lot of improvement always possible. We are honored that our solution is presented for IEEE conference and we also want to utilize our work in practical life by implementing these algorithms along with OCT machines.

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