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Detection of Proliferative Diabetic Retinopathy in Fundus Images Using Convolution Neural Network

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Abstract. Convolution Neural Network (CNN) is one of the techniques under Artificial Neural Network (ANN) used to develop a Deep Learning Neural Network (DLNN) algorithm for detection of Proliferative Diabetic Retinopathy (PDR) on the fundus images. About 116 PDR and 150 Non-Proliferative Diabetic Retinopathy (NPDR) of fundus images retrieved from the publicly available MESSIDOR database applied in this research. This study consisted three objectives that included the execution of two pre-processing techniques on the data-set which were resizing and normalizing the fundus images, developed deep learning operational Artificial Intelligence (AI) network of feature extraction algorithm for detection of PDR on the fundus images and determined the output classification of the network encompassing the accuracy, sensitivity and specificity. There were five different parameters carried out along this research. Here, Parameter 5 showed the best performance among the five parameters based on the value of accuracy, sensitivity, and specificity that was 73.81%, 76%, and 69% respectively.

1. Introduction

Medical topographies related to the Diabetes Mellitus (DM) has reported since three millennial years ago in the ancient Egyptians manuscript[1]. The phrase ‘Diabetes’ was first introduced by a venerable Greek Physician, Aretaeus of Cappodacia [2]–[4]. Later, in the year of 1675, Thomas Willis a Britain Physician introduced the word ‘Mellitus’ after discovered extra sugar in blood and urine of patients [5]. By the year of 1776, Dobson who is also a Britain Physician proved the cause of DM due to the presence of excess sugar[5]. While in the year of 1857, a France physician, Claude Bernard comes out with term of excess glucose [5], which is referring to the simplest form of sugar found in blood and urine. Then, two Austria physician discovered the organ in the human body, which is the pancreases [5] that responsible for controlling the level of glucose in blood and urine at the year of 1889. After that, in the year of 1921, two physicians from Canada found the hormone called insulin that in charge of restraint of the glucose level in blood and urine [5], [6].

Today, the statistics have shown that about one over hundred thousand of all over the world people are suffering DM and the number will be twice in the future[1], [2], [6], [7]. According to[8], [7], based on



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the study carried by the World Health Organization (WHO) from the year 2005 until 2011, the number of diabetic patient worldwide estimated to be increased to 366 million by the year of 2030 which is the number is double from ten years ago. Anyhow, the number of diabetic patients were overreached where the latest statistics reported about 383 million diabetic patients in year 2013 and prognosis to be 592 million in year 2035 [8]. In Malaysia, statistics on the year 2015 reported about 3.3 million cases of diabetes[6]. Mention in The Star, July 2018[9], a study showed by the National Diabetic Institute (NADI), Malaysia is at the top-notch in Asia and among the highest rank of DM cases which about 2.5 million of the adult, those are 18 years old and above are diagnosed with DM. From the data showed that the increment is very terrifying.

The NADI Chairman, Dr. Mustaffa Embong also said DM has become a silent killer in this nation due to asymptomatic condition led to others heroic health cases like heart attack, stroke, and failure of the kidney as well as diabetes retinopathy (DR), which can cause blindness[9]. As the advance state of DM, the development of DR is very progressive[10] illness. Study showed by[11], DR is the resultant of retinal vasculature destruction which affecting the loss of vision and blindness. This terrify cases not only affecting the underdeveloped and developing country but also haunting the developed country like the United State (US). The research done by Shuang Yu[12] mention that, the American Academic of Ophthalmology (AAO) did numerous study regarding to DR and had discovered two stages of DR which are the Non Proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR).

According to Deepashree [13], a patient with NPDR may suffer three phases of retinal abnormalities with are Mild NPDR, Moderate NPDR and Severe NPDR. The mild NPDR is the first phase of NPDR with an existence of at least a unit of micro-aneurysm. While the moderate NPDR is an existence of more than one unit of micro-aneurysm, hemorrhages and exudates. For the severe NPDR is a condition where the presence of large quantity of the microaneurysm, lots of hemorrhages, and many microvascular disorders.

Whilst the PDR is the advanced state or the phase after the NPDR where a new formation of blood vessel occurs. According to Shuang Yu[12], any patient diagnosed with PDR is at the most complexed conditional of a blood vessel in fundus which the occurrence of revascularization. It is parallel to Deepashree [13] and H. Aguirre[14], PDR is the late stage where the retina entered the state of neovascularization or in other words growth of new blood vessel was being triggered inside the retina. Same as Snehal[15], the PDR is the circumstances of the formation of new frangible and tenuous blood vessels which highly exposed to the occurrence of haemorrhages.

2. Literature review

The time frame of the evolution of the industry is shown in Figure 2.1. According to [17], AI is the backbone of IR 4.0. The IR 4.0 consists of five main pillars as shown in Figure 2.1. The goals of 4.0 are to bring recent technology into a new era that has a higher level of operational efficiency and productivity as well as better automatization.

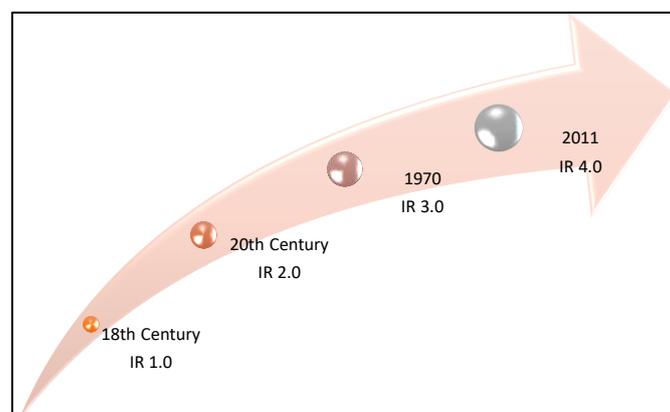


Figure 2.1: The Revolution of Industry Time Frame[16]

Whereas, in Figure 2.2 shows the five main pillars of IR 4.0. The first pillar referred to employment of the internet of thing (IoT). The IoT is the interconnection via the internet of computing devices embedded in everyday objects, enabling them to deliver and receive information [16]. The second pillar is the development of a cyber-physical system (CPS). The CPS is a mechanism that is controlled or monitored through a computer-based algorithm, firmly structured with the internet and its users. The third pillar is regarding the enhancing of digitalization approach through an enterprise architecture (EA) for the vast sector. For example in the transformation in the sector of transportation industry where an integrated digital system capable to generate robust big data analytics (BDA) that improve the decision-making and allow the intention crosswise disciplines and stakeholders[18]. The fourth pillar related to enterprise integration (EI). The IR 4.0 is urging companies to re-examine the way they do business. Hence, smart manufacturing, smart maintenance, and an endless scale of automation and integration in an overall spec of enterprise processes will change current purchase, productivity, manufacturing, sales, and maintenance processes [17]. Lastly, the fifth pillar is associated with empowering information and communication technologies (ICT). The rise of ICT in the recent era is has a strong correlation with the other pillars to cultivate the smart factory [19].

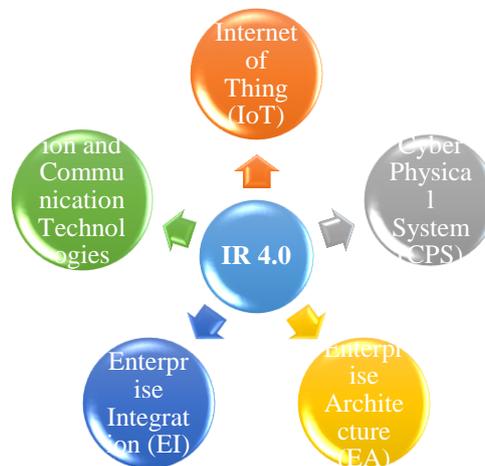


Figure 2.2: The Five Pillars of IR 4.0[17]

Nowadays, an AI used in immeasurable sectors. Especially in the manufacturing industry to operate the machinery and robotics [14]. Others, in image processing field AI plays important roles in the developments recent electronic devices like detection of DR in fundus images [17]. In the 11th Malaysia Plan, the study of AI is important to bring Malaysia close to the era of Industry 4.0[15].

AI is the knowledge and invention of computer systems to allow any mechanism performed tasks that normally demand human intelligence such as visual perception, speech recognition, decision-making, and translation between languages[20]. The development of AI is significant to the growth of recent technology. In figure 2.3 shows how AI has interrelation with the development of Industry 4.0 and some techniques of AI that commonly heard. The Artificial Neural Network are computational standards that can function similar to human nervous system and there are few types of ANN [22]. In Table 2.1 shows some prior paper that implements this method in their study.

Table 2.1: The employment of CNN technique in the prior works

Authors	Focus
[23]	Training data sampling for the detection of haemorrhages in color fundus images

[24]	To diagnose the presence of DR from digital fundus images and identify the accuracy classifying its severity.
[25]	The detection of blood vessels in fundus color images
[26]	For segmentation, detection, and classification of DR in fundus images
[27]	To evaluate the accuracy of the AI network model in the detection of DR through a screening programme of fundus images

CNN also known as Conv. Net [28] is one of the powerful methods in ANN that commonly used in images recognition. As listed in Table 2.0, all prior study that had been implementing this technique. Synonym with its name, convolution represents a multiple or numbers of layer build in a network. Figure 2.4 shows the example of a CNN architecture.

3. Research methodology

A total of 226 fundus images retrieved from the MESSIDOR database were used for training and testing the proposed network. The fundus images consist of two classes; Proliferative Diabetic Retinopathy (PDR) and Non- Proliferative Diabetic Retinopathy (NPDR) where each class contains 116 od dataset and 150 of dataset respectively.

There are two figures; Figure 3.1 shows the block diagram of the operational of the network and Figure 3.2 shows the flowchart of the proposed network.

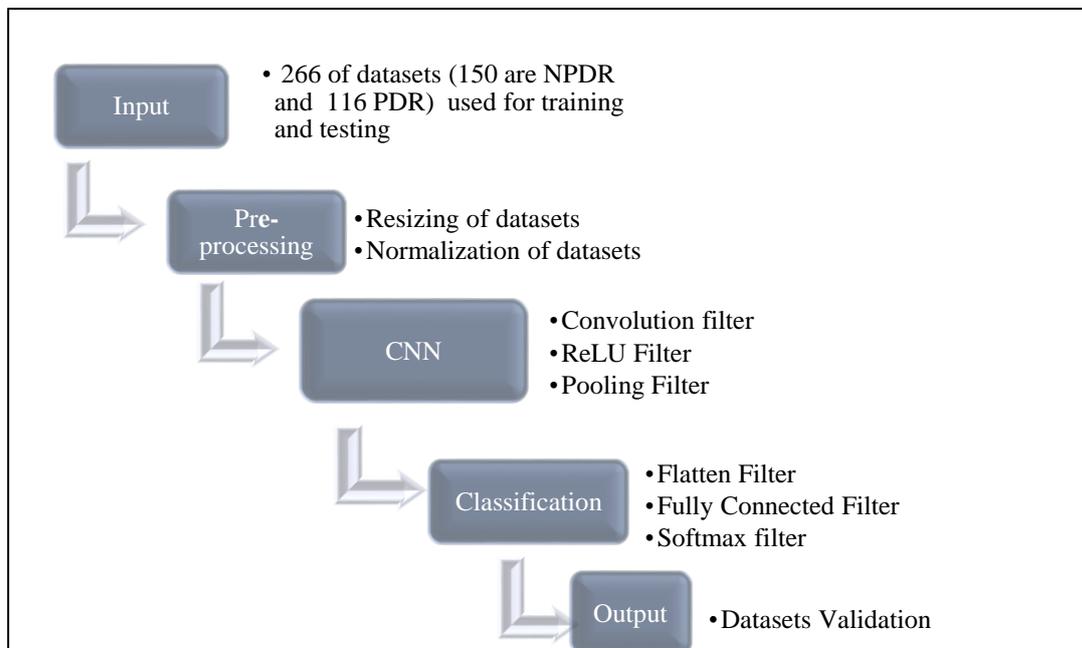


Figure 3.1: Block Diagram on the Operational of the proposed network

The Block diagram in Figure 3.1 explained the proposed method on the principle of the network operations. The first block indicated as the input for the proposed network, defined the total number of datasets used for training and testing. 150 of the datasets were diagnosed with NPDR while the other 116 datasets were diagnosed with PDR. These datasets retrieved from the MESSIDOR database.

The following block named as the pre-processing consists of two operations. The first operation was the resized of the input fundus images and the second operation was the normalization of the dataset. The convolution filter used to scale down the input dataset by 0.1 percent of the original dimensional (2240-unit width x 14880-unit height) to a new dimensional (224-unit width x 149-unit height).

The third block is the training and testing session for the proposed network named as CNN. In this block contains of three types of filters that carry out different operation on the dataset. The first filter named as convolution filter. Whereas, the second filter named as ReLU filter. And the third filter named as max-pooling filter.

The fourth block called as a classification that consists of few filters. The measurement of the network performances been carried out.

The fifth block is the output validation where analysis on the classification outputs of the network were carried out. The classification outputs for the proposed method such as sensitivity (SN), specificity (SP), and ROC were shown in the results.

Comparison on the classification outputs of the networks were carried out based on five cases. In every case, the ratio of datasets used for training and testing were different. The performance of the networks also being compared to the prior works.

Figure 3.2 shows a flowchart on the operation of the proposed method. In the beginning, 266 of fundus images that include 116 of PDR dataset and 150 of NPDR dataset. All the dataset was retrieved from the MESSIDOR database.

Then, all the dataset undergoes a pre-processing procedure called 'Resizing'. During this procedure, the original size of all dataset was reduced from 2240-unit width x 1488-unit height into 224-unit width x 1488-unit height by the scale of 0.1.

After scaling down, the fundus images were normalized. The dataset with different background colour will be standardized in this procedure. For the next procedure, the PDR and NPDR dataset were randomly selected by the network to be trained. The number of training datasets for five parameters were varied starting from 50%, 55%, 60%, 65% and 70% for both PDR and NPDR dataset.

The selected datasets were used by the network for training. Whereas, for the unselected datasets were used by the network for testing. After that, the classification outcomes such as accuracy, sensitivity and specificity for five parameters were classified using CNNs technique.

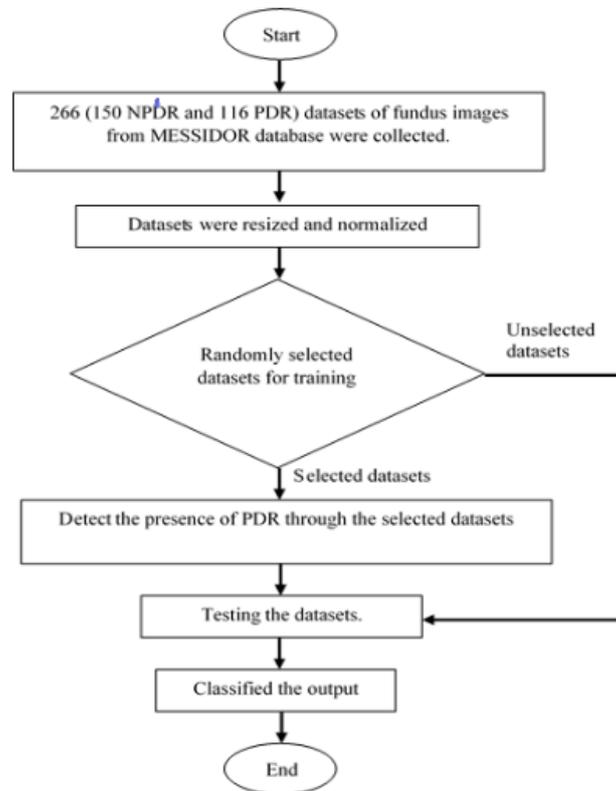


Figure 3.2: Flowchart of the Proposed Method

3.1. Input Database

The dataset of fundus images retrieved from the MESSIDOR database. This database is a research program funded by the French Ministry of Research and Defense for over 15 years, which owned numbers collection of fundus images. Furthermore, this database is the most popular used by the scientists to facilitate their studies on computer-assisted diagnoses of diabetic retinopathy (DR).

3.2. Input Dataset

The datasets refer to the fundus images consist of variety background color and fundus condition; NPDR and PDR fundus images. Not all of fundus images can be used as the input datasets for training and testing in this network. A few factors need to be considered in selecting the fundus images. Clear fundus images vision is the most significant factor to allow the network to learn the fundus images condition. Otherwise, the poor vision of the fundus images will reduce the performance of the networks and lead to defective output. Next is the condition of the fundus images where NPDR and PDR fundus images were selected for training. Figure 3.3 shows some samples of fundus images after being selected manually as the input datasets for training and testing.

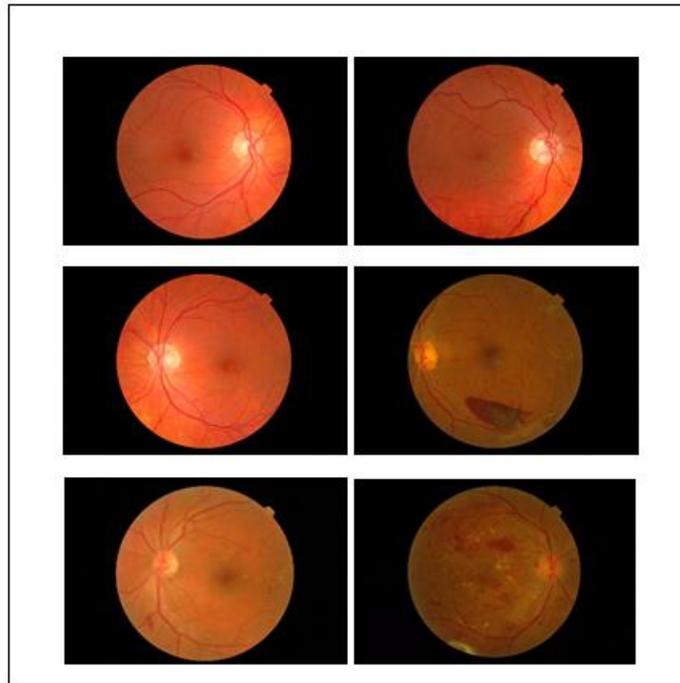


Figure 3.3: Sample of various fundus images from MESSIDOR database

3.3. Pre-Processing

This section consists of two parts; resizing and normalization. Both were crucial to generate precise output of the networks. The resizing of the input datasets in this procedure referring to change the size of the fundus images while the normalization of the datasets referring to standardize the background red green blue (RGB) color of the fundus images.

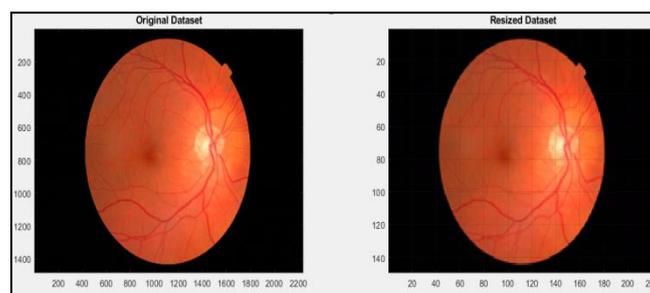


Figure 3.4: Before and after resized of sample dataset.

The dataset from the MESSIDOR came with variation sizes. Then, all the fundus images were resized into a standard scale. This was due to variation scale of dataset that may affecting the networks to operate. A dataset with a large scale may increase the processing time and requires higher performance of central processing unit (CPU) to perform the desired method.

However, if the scale of the dataset was resized to a very small size, it may reduce the information and resolution of the fundus image. Also, the compatibility of the CPU performance needs to be identified to allow the networks to operate at optimum range. Figure 3.4 shows a sample of a dataset before and after being resized. Here, the original size of the dataset was 1488 unit wide and 2240 unit height and after resized on scale of 0.1%, its became 149 unit wide and 224 unit height.

Next, since the fundus images that retrieved from the MESSIDOR database were variety in color background as shown in Figure 3.4 as the RGB color of each datasets defer to one another, normalization was done to standardize the color of the fundus images.

3.4. Classification using CNNs Techniques

Convolution Neural Networks (CNNs) also known as Conv.Net or comp.net is an artificial neural network that is so far been most popularly used for analyzing images. Although image analysis has been the widespread use of CNNs, they can also be used for other data analysis or classification problems as well. Most generally, CNNs can be illustrated as an ANN that has some types of specialization for being able to pick out or detect patterns and make sense of them.

This pattern detection is what makes CNNs so useful for image analysis. CNNs has hidden layers called convolutional layers and these layers are precisely differentiates CNNs with a standard multilayer perceptron (MLP). These convolutional layers do just like any other layer, a convolutional layer receives input then transform the input in some way and then outputs the transform input to the next layer. With a convolutional layer operation;

i. Function of Convolution Layer in Feature Learning

Convolution layer is the main layer in feature learning that does most of the computational dense stimulating. The convolution layer consists of a cluster of learnable filters. Every filter is small spatially with three-dimensional which is the width and height as well as the depth ($w \times h \times d$).

In the proposed network, three set of convolution layer with a different size were designed. The first set has a dimensional of $3 \times 16 \times 1$. The second set has a dimensional of $3 \times 32 \times 1$ and the third set has a dimensional of $3 \times 64 \times 1$.

ii. Function of ReLU Layer in Feature Learning

The ReLU layer applied an elementwise activation function. For example the $\max(0, x)$ thresholding at zero. Commonly, this layer present at every set of convolution layer and pooling layer. This layer ensure the size and the volume of the dataset unchanged after being filter.

iii. Function of Pooling Layer in Feature Learning

The next layer present in feature learning is the pooling. Its function is to reduce the spatial size of the fundus images representation to decrease the amount of parameters and computation in the network. A pooling layer operates on each feature map independently. There are two kinds of pooling layer types, which are the max pooling, and the sum or mean pooling.

3.5. Classification Outcomes

Basically, a classification outcome consists of few categories;

i. Accuracy;

Accuracy = No. of Predicted/Total no dataset [13].

ii. Sensitivity, S_n ;

Sensitivity defined as the proportion of datasets with a positive index test among all the datasets that is have the PDR;

$$S_n = (TP) / (TP + FN) [13]$$

iii. Specificity, S_p ;

Specification, S_p defined as of the proportion of all datasets index test among the datasets that do not have the PDR;

$$S_p = (TN) / (TN + FP) [13]$$

4. Result and discussions

Experimental analysis and testing are running on a Toshiba Satellite laptop Intel Core i7 Central Processing Unit (CPU), 2.1 (GHz) with 4 GB of Random-Access Memory (RAM). Window 7 was installed as the operating system.

4.1. Summary of Training Progress Graph for All Parameters

The training progress graph provided three important information during the network undergo training session. Firstly, it provides the percentages of training accuracy validation of the network carry out deep learning on the dataset. Second, it shows the pattern on data loss over iteration and epoch. Epoch referred to one forward pass and one backward pass of all training dataset while iteration is one forward and one backward pass of each batch size of dataset [25]. The third significant information that can gain from this graph is the duration time of the network used to complete the training session.

For this study, the number of iteration and epoch was remained the same for five different parameters. Table 4.1 shows the summary for the testing accuracy for every parameter. From Figure 4.1, the configuration indicated by the blue line showed an increased pattern form. However, due to some feature information on the dataset that had been loss during the resized session, the pattern did not rise rapidly. Therefore, mean value for every increment were counted, as shown by the dotted line.

Then, the rate amount of data loss during the training was shown by the red line. The pattern of the rate loss showed decreasing because of the epoch and number of iterations allowed the network to retrain the dataset repeatedly. Noticed that, the faint color of blue and red line at these graphs represented the actual progress of the network while the brighter color was after smoothed by the three filters; soft filter layer, flatten filter layer and fully connected filter layer. As the result, the line with the brighter color almost closed to the dotted line.

It was noticed that, as the percentage of information loss reduced, the percentage of accuracy increased. It means the network able to capture features information on the dataset and filtered out noise on the dataset during training session. Therefore, the more the percentage of information loss, the higher the accuracy of the network.

Table 4.1: Summary of Training Progress for All Parameters

Parameters	No of dataset (batch size of dataset)		Testing Accuracy (%)	Training Time (s)
	Training	Testing		
1	50 PDR: 50	66 PDR: 100	71.08	30
	NPDR	NPDR		
	Total = 100	Total = 166		
2	55 PDR : 55	61 PDR : 95	71.15	19
	NPDR	NPDR		
	Total = 110	Total = 156		
3	60 PDR : 60	56 PDR : 90	71.23	13
	NPDR	NPDR		
	Total = 120	Total = 146		
4	65 PDR : 65	51 PDR : 85	71.32	15
	NPDR	NPDR		
	Total = 130	Total = 136		
5	70 PDR : 70	45 PDR : 80	73.81	15
	NPDR	NPDR		
	Total = 140	Total = 126		

4.2. Summary of Confusion Matrix for All Parameters

The output class represented the actual number of the dataset while the target class represented the predicted number of the dataset. Both output class and target class have two classes that are denoted as ‘0’ represented the NPDR dataset and ‘1’ represented PDR dataset.

Table 4.2 shows the summary for all parameters that consists of number of dataset used for both training and testing as well as the number of dataset in each class that named as True Positive (TP), True Negative (TN), False Positive (FP), and False Negative (FN).

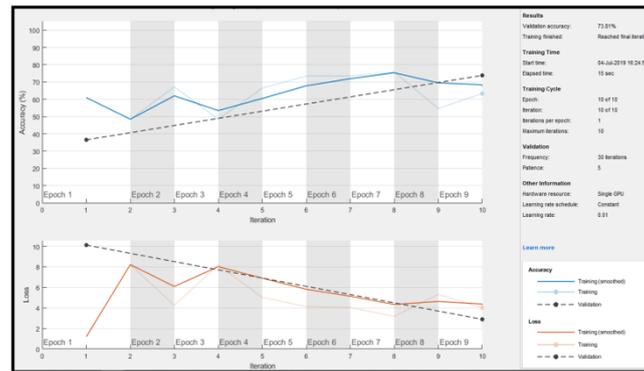


Figure 4.1: Sample of Training Progress Graph for Parameter 5

Table 4.2: Summary of Classes Based on the Confusion Matrix of All Parameters

Parameters	No of dataset		Classes			
	Training	Testing	TP	TN	FP	FN
1	50 PDR : 50 NPDR	66 PDR : 100 NPDR	100	18	0	48
	Total = 100	Total = 166	Total = 166			
2	55 PDR : 55 NPDR	61 PDR : 95 NPDR	95	16	0	45
	Total = 110	Total = 156	Total = 156			
3	60 PDR : 60 NPDR	56 PDR : 90 NPDR	76	28	14	28
	Total = 120	Total = 146	Total = 146			
4	65 PDR : 65 NPDR	51 PDR : 85 NPDR	80	17	5	34
	Total = 130	Total = 136	Total = 136			
5	70 PDR : 70 NPDR	45 PDR : 80 NPDR	68	25	12	21
	Total = 140	Total = 126	Total = 126			

4.3. Summary of Receiver Operating Characteristic (ROC) for All Parameters

Table 4.3 shows the summary of information from all ROC graph for all parameters. To get a better performance, the value of the Specificity and Sensitivity should closer to 100%. The ROC graphs for Parameter 1 until Parameter 5 were shown in Figure 4.3(i), Figure 4.3(ii), Figure 4.3(iii), Figure 4.3(iv), and Figure 4.3(v) respectively.

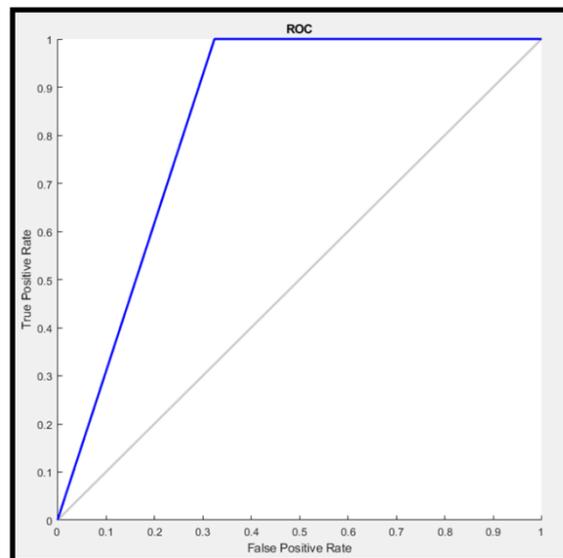
The y-axis of the ROC graph represented the True Positive Rate (TPR) that also indicated the sensitivity (Sn) of the network during testing session. Whereas, on the x-axis of the ROC graph represented the False Positive Rate (FPR) that also used to indicate the value of specificity of the network but the value of the FPR need to deduct by value of 1.

For Figure 4.3 (i), the value of the specificity is 100%, whereas the value for sensitivity is 67% (1-0.33). This showed large gap percentage values between sensitivity and specificity. The possible reason that lead to this are the poor resolution of the dataset used for testing. Others possible reason like under train also may led to this performance.

Then, Figure 4.3 (iii) shows the value of specificity 67% whereas the value for sensitivity is 73% (1-0.27)

Table 4.3: Summary of Information of All ROC Graph

Parameters	Specificity, S_p (%) ($S_p=1-FPR$)	Sensitivity, S_n (%) ($S_n=TPR$)
1	100	67.00
2	100	68.00
3	68.00	72.00
4	78.00	70.00
5	69.00	76.00

**Figure 4.3(i):** Receiver Operating Characteristic (ROC) Graph for Parameter 1

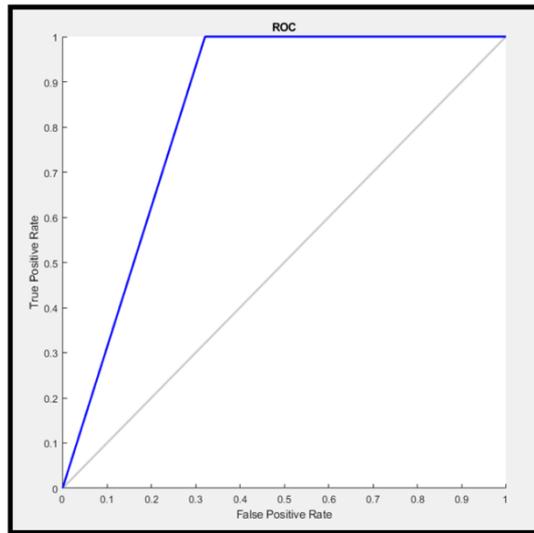


Figure 4.3(ii): Receiver Operating Characteristic (ROC) Graph for Parameter 2

Like Parameter 1, Figure 4.3(ii) shows the value for specificity is 100% whereas the value for sensitivity is 68.0% (1-0.32).

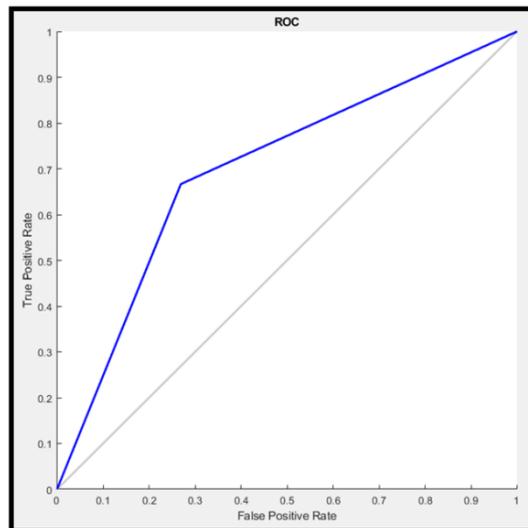


Figure 4.3(iii): Receiver Operating Characteristic (ROC) Graph for Parameter 3

This showed that, during the testing session, the proposed network only able to clarify the dataset with PDR with value of 67% correct. The reason that led to this output due to the poor resolution of dataset used for tested.

Based on Figure 4.3(iv), the value of specificity is 77% whereas the value for sensitivity is 70%. This value was higher than the Parameter 3 but lower than Parameter 1 and Parameter 2.

Meanwhile, Parameter 5 in Figure 4.3(v) shows the value of specificity closer to Parameter 4 which is 68% and the value of sensitivity is 76%.

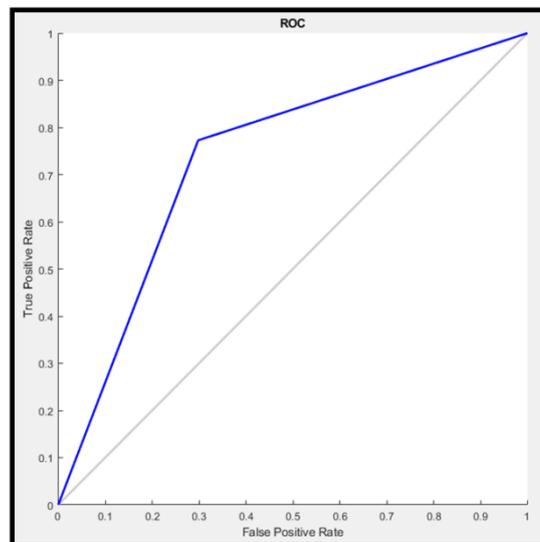


Figure 4.3(iv): Receiver Operating Characteristic (ROC) Graph for Parameter 4

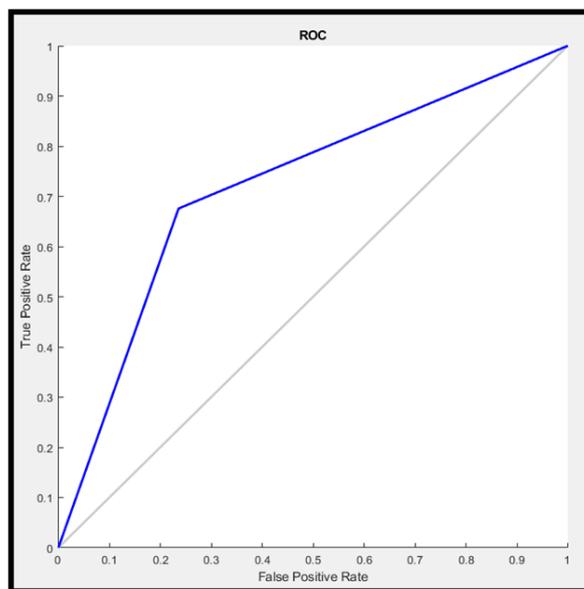


Figure 4.3(v): Receiver Operating Characteristic (ROC) Graph for Parameter 5

5. Conclusions

Based on this research, all the objectives which mention earlier were achieved. As a conclusion, Parameter 5 showed the best performance among five parameters by having the highest accuracy, which was 73.81%. In addition, the percentage value of sensitivity and specificity for parameter 5 were 76% and 69% respectively. The values of parameter 5 from this study were not as good as the prior work due to several constraints that were faced during this research. Firstly, it was due to the low of specification of the computer that used to run the proposed network where only limited numbers of dataset could be used for training and testing. Other than that, the low resolution of dataset image also had influenced the network to detect the presence of PDR. This is because, during the resizing procedure, some information

on the original dataset may diminished and made the network unable to detect that information which will affect the percentage of output value. As for future study, higher specification of computer is highly recommended to allow greatest numbers of dataset to be used for training and testing as well as increase the performance of the network to detect the presence of PDR in the dataset.

6. References

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