

Multiscale Analysis of Diagnostic Features from Color Fundus Images

A THESIS

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This thesis is dedicated

To

My Parents

for their love, support and encouragement

&

My Supervisor

for his guidance and inspiration



Certificate

This is to certify that the thesis entitled “**Multiscale Analysis of Diagnostic Features from Color Fundus Images**”, submitted by **Malaya Kumar Nath** (09610207), a research scholar in the *Department of Electronics and Electrical Engineering, Indian Institute of Technology Guwahati*, for the award of the degree of **Doctor of Philosophy**, is a record of an original research work carried out by him under my supervision and guidance. The thesis has fulfilled all requirements as per the regulations of the Institute and in my opinion has reached the standard needed for submission. The results embodied in this thesis have not been submitted to any other University or Institute for the award of any degree or diploma.

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Malaya Kumar Nath



Abstract

This thesis work is an investigation of multiscale analysis of diagnostic features of the color fundus images. Analysis of diagnostic features is done in the multiscale domain by wavelet transform. There are three major contributions. First, the different wavelet subbands are investigated for the presence of retinal features such as exudates and microaneurysms. Secondly, the pathological features are extracted. Blood vessels are extracted by using Kirsch and Gaussian matched filter (MF) based method. Inpainting is performed on the green channel image by considering the blood vessels structure as a mask for detecting the amount of blood vessels affected by pathologies. Independent component analysis (ICA) is used in multiscale for extraction of exudates and detection of changes in the retina, which occurs due to the progression of diabetes. Third, glaucoma is detected by evaluation of differential entropy in wavelet subband. The performance of different methods is analyzed by different quantitative measures such as, specificity, sensitivity, accuracy, universal quality index (UQI), Pearson correlation coefficient (PCC), and structural similarity (SSIM) etc.

The clinically important features of retinal image are the optic disc (OD), the macula and the blood vessels. The ophthalmologists examine these features for signs of various eye related diseases. The retinal image should be of sufficient quality to ensure a reliable diagnosis. Various approaches are available in the literature to study the clinical usefulness of the normal retinal features for different applications. Different features developed over the retina, such as microaneurysms, exudates, and haemorrhages, etc. due to diabetic retinopathy (DR). The analysis of the DR features is not done in the literature from the diagnostic point of view. Here, the spatial localization and multiresolution properties of discrete wavelet transform (DWT) is used for image analysis. The DWT is used to decompose the image into different subbands. The contribution of each subband towards the DR feature information is different. In the present work, the analysis is done in two ways.

First, at a particular level of wavelet decomposition, one level subband coefficients are made zero while unaltering the other level subband coefficients. The reconstructed image is analyzed. Secondly, the image is reconstructed by considering one level subband coefficients only and zeroing other level subband coefficients. From the reconstructed image, the significant information about the DR features at a particular level of subband is analyzed.

These subband information is used for extraction of features. Blood vessels and pathological features are extracted for finding the amount of blood vessel damage due to diabetic retinopathy. ICA is used in the wavelet subbands for extraction of exudates and detection of changes in the retina. ICA on multiscale improves the performance of detection of independent components, which is measured by the Amari performance index (API) and Comon test values. Detected diagnostic features are evaluated quantitatively by the Pearson correlation coefficient (PCC), universal quality index (UQI), structural similarity (SSIM), sensitivity, specificity, and accuracy etc.

The diagnostic information in wavelet subband is used for detection of glaucoma. In the literature, glaucoma is detected by the measurement of the ratio of cup area to the disc area and known as cup to disc ratio (CDR). In case of disc anomalies and inflamed disc, the disc region is not distinguished clearly. So, CDR cannot be used as a measure for glaucoma detection. Here, differential entropy and machine learning techniques are proposed for glaucoma detection. Differential entropy (DE) of the cup is calculated in wavelet subband for detection of glaucoma. The appearance of the cup changes due to glaucoma, which is used for glaucoma classification. Two classification methods are proposed, one is principal component analysis (PCA)-linear discriminant analysis (LDA) and the second is hidden Markov model (HMM)-singular value decomposition (SVD). HMM-SVD has better performance than PCA-LDA based method. DE based measure provides better performance in the detection of glaucoma from other methods.

Synopsis

Introduction

The clinical features of a normal fundus or retinal image are the optic disc (OD), the macula lutea, and the blood vessels. The development in image processing, computer vision, and pattern recognition has helped the evolution of automated diagnostic systems for diabetic retinopathy (DR), age related macular degeneration, and retinopathy of prematurity. In case of DR, fluid leaks from blood vessels into the retina and different lesions appear over the retina. Based on the appearance of pathological features such as microaneurysms (MAs), haemorrhages, larger blot haemorrhages, exudates and cupping etc., the ophthalmologists evaluate the DR condition. Various approaches have been proposed in the literature, to study the clinical importance of different DR features or lesions in the retinal image. Automated diagnostic systems require efficient detection of these DR features.

This thesis documents three investigations on pathological features using wavelet analysis. First investigation is on multiscale analysis of DR features. Multiscale or multiresolution is an invertible subband representation, which is highly tunable and have a free choice of the basis function to decompose images to subbands. Each of them contains information at a specific scale/frequency and along a specific direction. These subbands have more or less relevant information of the lesions. From the diagnostic point of view, the specific wavelet subbands are chosen. In the second investigation, multiscale ICA is proposed and evaluated for detection of DR features. Third investigation is on the analysis and detection of glaucoma using higher order statistics. Changes in the appearance optic disc region lead to glaucoma and results in peripheral vision loss. Glaucoma is generally detected by the measurement of the ratio of cup area to disc area. In some cases it fails due to misclassification of the cup and disc region. This limitation has been overcome by the measurement of negentropy in the multiscale domain. The three investigations are briefly discussed in the following sections.

0.1 Multiscale analysis of diagnostic features

First, the significance of wavelet subbands in characterizing the pathological features is investigated. The DWT separates and retains the retinal features in one or few subbands. The retinal image is

decomposed to 3-, 5-, 7-, and 9-levels using Daubechies4 (db4) wavelet in two dimensions. This generates one low frequency approximation subband and $3N$ numbers of high frequency detail subbands, where ' N ' represents the number of levels of decomposition. Different subbands represent different frequency bands of an image. They have different contributions to the image quality. Exudates, microaneurysms (MAs) and haemorrhages are the main diagnostic features due to DR. Multiscale analysis is performed by two ways. In the first case, the diagnostic importance of subbands in a particular level is examined by zeroing the coefficients of that subband and retaining all other subband coefficients. The diagnostic quality of the retinal image is observed by reconstructing the image using the altered subbands. In the second case one subband coefficients are unaltered and all other subband coefficients are made zero. These two procedures have provided the DR feature information in different subbands.

(a) *Wavelet subbands and microaneurysm information:* In 3-level wavelet decomposition all the subbands contribute equally to the feature microaneurysm (MA). In 5-level wavelet decomposition subband $L1$, subband $L2$ and subband $L3$ contain less information about the MA. Most of the information is present in subband $L4$ and subband $L5$ in 5 level wavelet decomposition. In 7-level wavelet decomposition, $L5$, $L6$, and $L7$ contribute more information towards the MA. Subband $L5$ to subband $L9$ coefficients contain higher MA information compared to other levels in 9 level wavelet decomposition. Higher subband coefficients contain more MA information compared to lower level subband coefficients.

(b) *Wavelet subbands and exudate information:* In five level decomposition of exudates $L1$ and $L2$ subbands coefficients do not contain higher information about the exudates than the other subbands. In seven level wavelet decomposition blood vessel (BV) information is reduced compared to five level wavelet decomposition. The subband coefficients $L1$, $L5$, $L6$ and $L7$ contain more exudate information compared to the other subbands. The most important subband coefficients contributing for exudate information in nine level wavelet decomposition are $L8$, $L7$, $L6$, and $L3$. Zeroing the $L1$ and $L2$ subband coefficients does not affect much in the accuracy for extraction of exudates, which are found to be 95.90% and 93.22%, respectively. The accuracy value reduces to the lowest when $L8$ subband coefficients are made to zero, and the accuracy found to be 36.95%.

0.2 Multiscale detection of DR features

At the initial stage of DR, blood vessels are affected. Various segmentation techniques such as Kirsch's method, histogram equalization approach and Gaussian based matched filter approach are merged together to get the best segmentation performance for the blood vessels. The performances of the segmentation evaluated by different performance measures and are tabulated in Table 1. Matched filter with first order Gaussian function has higher accuracy (95.46%).

Table 1: Performance measure values of different blood vessels extraction techniques.

Method	Sensitivity	Specificity	Sensibility	Accuracy	EER	Fscore	KC	KJ	KD
Kirsch	43.03	94.93	5.07	90.24	4.87	-59.06	-159.77	28.37	44.05
Modified Kirsch	42.55	93.58	6.41	90.70	4.64	-58.29	-310.15	20.80	34.15
Histogram	48.93	94.18	5.81	91.06	4.46	-63.83	-194.04	25.78	40.88
Gaussian	76.03	97.06	2.93	95.46	2.26	-85.12	21.04	56.11	71.81
KGH	49.75	97.91	2.09	91.27	4.36	-65.70	-32.17	43.67	60.62
KG	52.98	98.077	1.92	92.22	3.88	-68.64	-15.27	46.77	63.64

After segmentation of blood vessels, inpainting technique is applied to remove the effect of the blood vessels. This image only contains the pathologically affected regions along with the OD and the macula. Pathologically affected regions are separated from the inpainted image. The inpainted image is subjected to histogram equalization. The extracted pathologies are intersected with the extracted blood vessels image to obtain the blood vessels that are affected by pathology. Fig. 1(a) is the color fundus image with pathologies. The extracted blood vessels by Kirsch Gaussian matched filter method is shown in Fig. 1(b). This extracted blood vessel is used as a mask to inpaint the image. The inpainted image does not contain any blood vessels. The inpainted image is shown in Fig. 1(c). From the inpainted image the pathologies are extracted. The extracted pathologies are compared with the segmented blood vessels to find the amount of blood vessels affected by pathologies. Blood vessels affected by pathologies are shown in Fig. 1(d).

Independent component analysis is applied to the data matrix formed by the subbands of wavelet decomposition for segmentation of exudates and detection of changes in the retina due to the DR. Detection of DR features by multiscale ICA (MSICA) consists of three important blocks and they are multiscale decomposition block, formation of data matrix block, ICA block. Multiscale decomposition or transform block decomposes the signal/image into different bands depending on their frequency content. The input to the ICA model is a matrix. The data matrix is formed by combining the different bands. The performance multiscale ICA is evaluated by API and Comon test values. These values

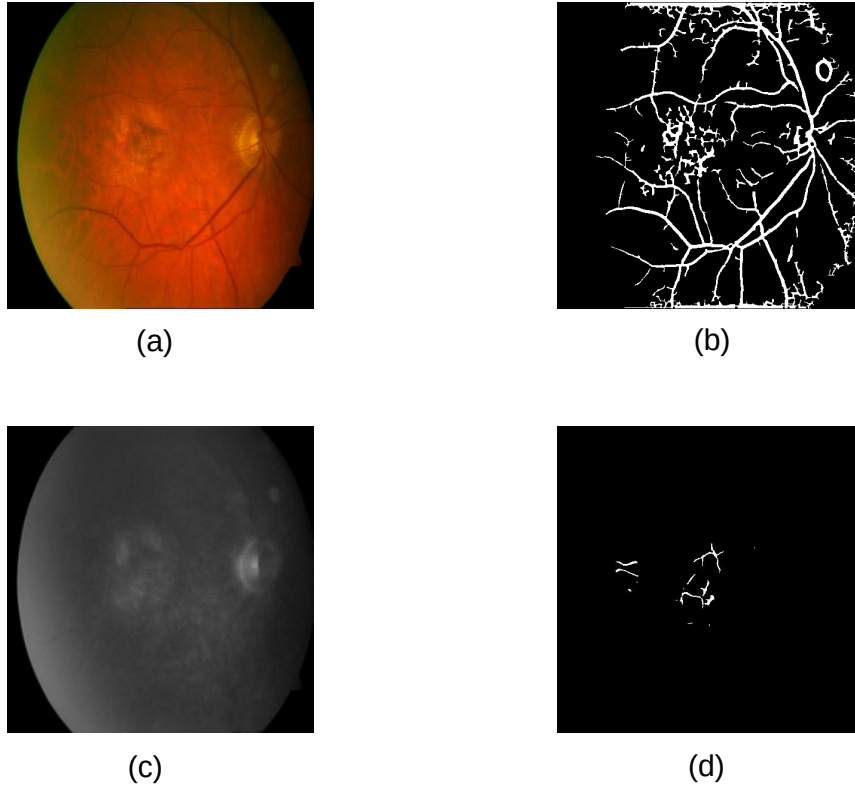


Figure 1: Assessment of pathological affected blood vessels from color fundus image: (a) color fundus image, (b) segmented blood vessels, (c) inpainted image, (d) blood vessels affected by pathology.

are calculated both in MSICA and ICA. From these values it is observed that MSICA outperforms ICA. The extracted exudates by this method are given in Fig. 2. The color fundus image with pathologies is shown in Fig. 2(a). The corresponding HSV color image is shown in Fig. 2(b). To both the color channels ICA and MSICA algorithms are applied. The extracted exudate by ICA in RGB and HSV color channels are shown in Fig. 2(c) and Fig. 2(d), respectively. Fig. 2(e) and Fig. 2(f) represent the extracted exudate by MSICA on RGB and HSV color channels, respectively. The universal quality index values for the extracted exudates is found to be 0.70 for MSICA on HSV color channel.

ICA can be used for the detection of changes from the color fundus images due to the progression of DR. In this case, the normal fundus image is compared with the DR affected image by ICA in multiscale domain. Analyzing the number of features, the retina condition can be predicted.

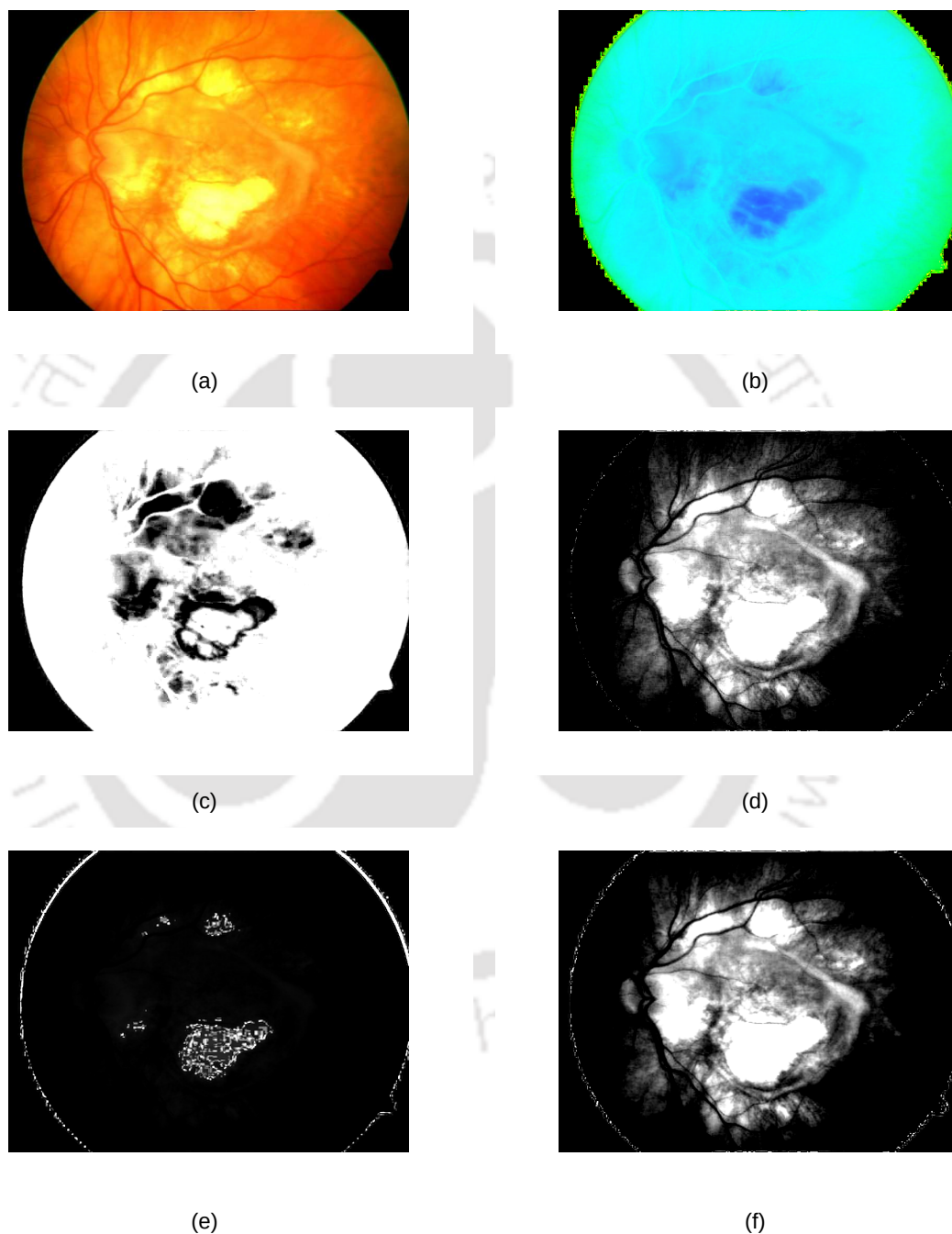


Figure 2: Extraction of exudates: (a) RGB color fundus image, (b) corresponding HSV image, (c) exudates from RGB color image by ICA, (d) exudates from the HSV color image by ICA, (e) exudates from RGB color image by multiscale ICA, (f) exudates from the HSV color image by multiscale ICA.

0.3 Assessment of Glaucoma

Glaucoma damages the optic nerve on back side of the eye. Glaucoma is assessed by measurement of intraocular pressure (IOP) and by the appearance of OD (measurement of cup-to-disc-ratio (CDR)). Measurement of CDR is treated as the most useful indicator of glaucoma and its progression. Evaluation of glaucoma requires disc evaluation with clinical experience. Analysis of the appearance of OD helps post diagnosis. Method for glaucoma detection by CDR is not possible in case of inflamed disc and disc anomalies. Here, two methods are proposed for glaucoma classification. First, is based on evaluation of differential entropy (DE) or negentropy in wavelet subband-5 for prediction of glaucoma. The second method is based on a machine learning approach for glaucoma classification.

The method based on differential entropy consists of preprocessing, wavelet decomposition, segmentation of the cup and measurement of information. True positive (TP), true negative (TN), false positive (FP) and false negative (FN) for the proposed method are found to be 0.9459, 0.8823, 0.1176, and 0.0540, respectively. The differential entropy based method is compared with two recently discussed methods in the literature. The proposed method shows the best result with an accuracy value of 92.59%.

In machine learning based glaucoma detection, the patterns of the cup are used. For normal vision, the cup looks like almost circular or elliptical. As the disease progresses, the size and the shape of the cup gradually changes. These patterns are used for glaucoma classification. Principal component analysis (PCA)-linear discriminant analysis (LDA) and hidden Markov model (HMM)-singular value decomposition (SVD) based glaucoma classification methods are used for glaucoma assessment. In PCA-LDA based method the performance of glaucoma classification depends on the number of significant eigenvalues or principal components. As the number of significant eigenvalues increases the performance also increases. Beyond four numbers of eigenvalues the performance does not increase significantly. So, 4 significant eigenvalues are considered for glaucoma classification in PCA-LDA based approach. Sensitivity and specificity for the PCA-LDA method are found to be 81.25% and 33.33%, respectively.

In HMM-SVD based method glaucoma classification singular value decomposition is used for feature extraction and 7-level HMM model is used for classification. In order to reduce the computational complexity and memory consumption, the retinal images are resized to 46×56 which results in data loss from the images. So, SVD is used for feature extraction, which compensate the data loss and

obtain a set of uncorrelated features about the cup and OD. It is used due to its stability and robust feature extraction technique for retinal images. The SVD coefficients are used as features in the sampling windows (blocks). Among the 46 singular values, only a few big singular values and their related vectors convey information about the energy and information of an image. In this case three features are considered for each block for classification by HMM. This provides an accuracy of 72.73%.

The main contributions of this thesis can be summarized as follows. DR features in the fundus image are present differently across the wavelet subband. Higher subbands contain the OD features. The MA information is present in the higher subbands of multiscale decomposition. Exudate information is present in the lower subbands. The matched filter based method for detection of blood vessels has highest the accuracy. Multiscale ICA helps find the exudate information from the fundus images with higher accuracy. This method is used for detection of changes in the fundus images due to DR. Glaucoma is detected by the measurement of CDR. CDR fails in case of disc anomalies. So differential entropy (DE) is used as a measure for assessment of glaucoma. DE value greater than 0.25 is used as a threshold for glaucoma assessment. Machine learning approach is used for glaucoma assessment. HMM-SVD based glaucoma classification performs better compared to the PCA-LDA based glaucoma classification.

0.4 Organization of the thesis

The organization of the thesis is as follows:

In **Chapter 1**, the retinal images are introduced and its clinical importance is discussed. The literature survey of retinal image analysis methods is also presented.

In **Chapter 2**, the literature review on DR feature detection are discussed. Here, the motivation for multiscale analysis of fundus image is presented for detection of features and detection of glaucoma.

In **Chapter 3**, multiscale analysis of different DR features is discussed. DR features such as MA, haemorrhages, and exudates are analyzed in different subbands of wavelet decomposition.

In **Chapter 4**, extraction of DR features from the fundus images are discussed. Here, wavelet ICA is used as a tool for extraction of exudates. This is also used as a tool for detection of the changes in the color fundus image due to DR. This may help early diagnosis of the vision loss.

In **Chapter 5**, different methods of glaucoma assessment in multiscale are presented. Here, differential entropy (DE), PCA-LDA, and HMM-SVD based glaucoma detection methods are discussed.

In **Chapter 6**, conclusions are drawn by summarizing the contributions of the work and mentioning some directions for future work.



Contents

0.1 Multiscale analysis of diagnostic features	xi
0.2 Multiscale detection of DR features	xiii
0.3 Assessment of Glaucoma	xvi
0.4 Organization of the thesis	xvii
List of Figures	xxiii
List of Tables	xxix
List of Acronyms	xxxi
List of Symbols	xxxv
1 Introduction	1
1.1 Anatomy and assessment of eye	2
1.2 Fundus image and its clinical features	6
1.2.1 Retinal diseases	9
1.3 Retinal image processing for segmentation of features	13
1.3.1 Preprocessing of retinal images	14
1.3.1.1 Non-uniform illumination correction	14
1.3.1.2 Color normalization	14
1.3.1.3 Contrast enhancement	15
1.3.2 Segmentation of normal retinal features	15
1.3.2.1 Segmentation of blood vessels	15
1.3.2.2 Segmentation of the optic disc	16
1.3.2.3 Segmentation of the macula and fovea	17
1.3.3 Detection of abnormalities	19
1.3.3.1 Detection of microaneurysms	19

Contents

1.3.3.2	Detection of exudates	20
1.3.3.3	Detection of haemorrhages	21
1.3.4	Scope for the present work	21
1.4	Organization of the thesis	22
2	Diagnostic feature analysis: A review	25
2.1	Multiscale analysis of features from fundus image	26
2.2	Wavelet filter for retinal image analysis	27
2.3	Detection of DR features	29
2.4	Detection of glaucoma	33
2.5	Motivation for the present work	39
2.6	Database	40
3	Multiscale analysis of diagnostic features of retinal images	43
3.1	Multiscale decomposition	45
3.2	DR features in wavelet subbands	47
3.2.1	Proposed method for analysis	47
3.2.2	Analysis of microaneurysms and haemorrhages	48
3.2.3	Analysis of exudates	57
3.3	Quantitative evaluation	64
3.4	Performance evaluation	68
3.5	Summary	78
4	Multiscale ICA for detection of DR features	81
4.1	Segmentation of blood vessels	83
4.1.1	Segmentation of DR features/pathologies	84
4.2	Independent component analysis for fundus image	88
4.2.1	Correlation and independence	89
4.2.2	Correlation in different color channels	90
4.2.3	Statistical evaluation of features in fundus image	91
4.2.4	Limitation of ICA	94
4.2.5	Multiscale ICA	97
4.2.6	Performance evaluation of MSICA over ICA	103

4.3	Multiscale ICA for detection of exudates	109
4.4	Detection of change in color fundus due to DR	114
4.5	Summary	116
5	Assessment of glaucoma in wavelet scale	119
5.1	Glaucoma detection by using CDR	120
5.1.1	Limitation of CDR based Glaucoma detection	122
5.1.2	Proposed method for glaucoma detection	122
5.2	Differential entropy based glaucoma detection	124
5.3	PCA-LDA based glaucoma classification	129
5.3.1	PCA and LDA representation for Glaucoma classification	130
5.3.2	Method	132
5.4	HMM-SVD based glaucoma classification	136
5.4.1	Method	138
5.5	Summary	140
6	Conclusions	143
6.1	Scope for the future work	147
A	Appendix	149
A.1	More figures for wavelet decomposition of MAS	150
A.2	Negentropy	159
	Bibliography	161
	List of Publications	171



List of Figures

1	Assessment of pathological affected blood vessels from color fundus image: (a) color fundus image, (b) segmented blood vessels, (c) inpainted image, (d) blood vessels affected by pathology.	xiv
2	Extraction of exudates: (a) RGB color fundus image, (b) corresponding HSV image, (c) exudates from RGB color image by ICA, (d) exudates from the HSV color image by ICA, (e) exudates from RGB color image by multiscale ICA, (f) exudates from the HSV color image by multiscale ICA.	xv
1.1	Cross sectional view of human eye [1].	3
1.2	Fundus fluorescein angiography [2].	5
1.3	Normal retinal photograph from Aria database.	6
1.4	Disease retinal photograph from Aria database.	7
1.5	Different stages of DR: (a) normal image, (b) glaucoma, (c) mild NPDR, (d) moderate NPDR, (e) severe NPDR, (f) mild PDR, (g) moderate PDR, and (h) severe PDR. . . .	8
2.1	(a) Original image and reconstructed images when subband coefficients of (b) L1, (c) L2, (d) L3, (e) L4 and (f) L5 are made zero.	30
2.2	Different parts of OD [3].	36
2.3	Different types of disc: (a) normal disc, (b) glaucoma disc with increase in cup size, (c) glaucoma with inflamed disc (d) glaucoma with disc anomalies.	39
3.1	Block diagram for multiscale analysis of DR features.	47
3.2	Diabetic retinopathy features (MAs and haemorrhages): (a) color fundus image, (b) red channel, (c) green channel, (d) blue channel, (e) processed image output1, (f) processed image output2.	50

3.3	Microaneurysm feature analysis in the subbands of 3-level wavelet decomposition: (a) high contrast green channel image, (b) reconstructed image, (c) approximation band, (d) $L1$ ($H1$, $V1$, $D1$) coefficients zero, (e) $L2$ ($H2$, $V2$, $D2$) coefficients zero, (f) $L3$ ($H3$, $V3$, $D3$) coefficients zero, (g) only $L1$ coefficients unaltered, (h) only $L2$ coefficients unaltered, (i) only $L3$ coefficients unaltered.	51
3.4	Microaneurysm feature analysis in the subbands of 5-level wavelet decomposition: (a-e) reconstructed image by zeroing $L1$ to $L5$ subband coefficients, respectively, (f-j) reconstructed image by keeping $L1$ to $L5$ subband coefficients, respectively and altering the coefficients of other subbands.	53
3.5	Microaneurysm feature analysis in the subbands of 7-level wavelet decomposition: (a-g) reconstructed image by zeroing $L1$ to $L7$ subband coefficients, respectively, (h-n) reconstructed image by keeping $L1$ to $L7$ subband coefficients, respectively and zeroing other coefficients.	54
3.6	Microaneurysm feature analysis in the subbands of 9-level wavelet decomposition: (a-i) reconstructed image by zeroing $L1$ to $L9$ subband coefficients, respectively, (j-r) reconstructed image by keeping $L1$ to $L9$ subband coefficients, respectively and altering other coefficients.	56
3.7	Microaneurysm and haemorrhage information in combination of wavelet subband coefficients in different level of wavelet decomposition: (a) $L4$ and $L5$ coefficients of 5-level wavelet decomposition, (b) $L5$, $L6$, and $L7$ coefficients of 7-level wavelet decomposition (c) $L5$, $L6$, $L7$, $L8$, and $L9$ coefficients of 9-level wavelet decomposition.	57
3.8	Exudate analysis in subbands of 5-level wavelet decomposition: (a-e) reconstructed image by making $L1$ to $L5$ subband coefficients zero, respectively, (f-j) reconstructed image by keeping $L1$ to $L5$ subband coefficients, respectively and altering other coefficients.	59
3.9	Exudates information in the combination of subbands in 5-level wavelet decomposition. Reconstructed image by considering (a) $L1+L2+L3$ subband coefficients, (b) $L1+L2$ subband coefficients.	60

3.10 Exudate information in subbands of 7-level wavelet decomposition: (a-g) reconstructed image by making $L1$ to $L5$ subband coefficients zero, respectively, (h-n) reconstructed image by keeping $L1$ to $L5$ subband coefficients, respectively and altering other coefficients.	61
3.11 Analysis of exudates information in a combination of wavelet subbands on 7-level decomposition. Reconstructed images by zeroing: (a) ($L2+L3$), (b) ($L3+L4$), (c) ($L2+L3+L4$), (d) ($L3+L4+L5$) subband coefficients.	62
3.12 Exudate analysis in the subbands of 9-level wavelet decomposition: (a-i) reconstructed image by making $L1$ to $L9$ subband coefficients zero, respectively, (j-r) reconstructed image by keeping $L1$ to $L9$ subband coefficients, respectively and altering other coefficients.	63
3.13 Analysis of exudates in 9-level wavelet decomposition. Reconstructed images by zeroing subband coefficients of: (a) ($L4$ and $L5$), (b) ($L4$, $L5$ and $L9$), (c) ($L3$, $L4$, $L5$, and $L9$), (d) ($L2$, $L3$, $L4$, $L5$, $L9$).	64
3.14 Boxplots for specificity, accuracy and equal error rate for different subband in 5-level wavelet decomposition (by considering one subband coefficients at a time) for sixty images	69
3.15 Boxplots for specificity, accuracy and equal error rate for different subband in 7-level wavelet decomposition (by changing one subband coefficients at a time) for sixty images	70
3.16 Extracted exudate in different band of 5-level wavelet decomposition: (a-e) reconstructed image by making $L1$ to $L5$ subband coefficients zero, respectively, (f-j) reconstructed image by keeping $L1$ to $L5$ subband coefficients, respectively and altering other coefficients.	72
3.17 ROC curve for analysis of exudates in 5-level wavelet decomposition.	74
4.1 Performance measure of blood vessel segmentation methods.	85
4.2 Detection of affected regions of BVs by DR.	86
4.3 Affected blood vessels by DR: (a) fundus image, (b) green channel image, (c) extracted blood vessels, (d) inpainted image, (e) extracted pathology, and (f) blood vessels affected by DR.	87

List of Figures

4.4	Assessment of pathology affected blood vessels from color fundus image: (a) color fundus image, (b) segmented blood vessels, (c) inpainted image, (d) blood vessels affected by pathology	88
4.5	Probability density function of kurtosis of different features: (a) pdf of OD, (b) pdf of background, (c) pdf of blood vessels, (d) pdf of exudates.	95
4.6	PDF of exudates and non exudate regions.	95
4.7	Block diagram of multiscale ICA.	98
4.8	Comparison of correlation of image in different subbands: (a) correlation between subband-5, subband-4 and subband-3, (b) correlation between original image and subband-5, (c) correlation between original image and subband-4, (d) correlation between original image and subband-3, (e) correlation between original image and subband-2, and (f) correlation between original image and subband-1.	101
4.9	Comparison of variance of image in different subbands: (a) variance between different bands and original image, (b) variance between original image and subband-5, (c) variance between original image and subband-4, (d) variance between original image and subband-3, (d) variance between original image and subband-2, and (f) variance between original image and subband-1.	102
4.10	API and Comon test values for FastICA (FICA) and efficient FastICA (EFastICA) having variation in relative amplitude and relative frequency of one test signal with respect to the other test signal.	104
4.11	API and Comon test values for multiscale ICA and ICA (having variation in amplitude and frequency of one test signal w.r.t other test signal).	105
4.12	API and Comon test values for multiscale ICA and ICA (FastICA and efficient FastICA) having variation in amplitude and frequency of one test signal w.r.t other test signal.	106
4.13	Multiscale ICA for extraction of exudates.	110
4.14	Extraction of exudates: (a) RGB color fundus image, (b) corresponding HSV image, (c) exudates from RGB color image by ICA, (d) exudates from HSV color image by ICA, (e) exudates from RGB color image by multiscale ICA, (f) exudates from HSV color image by multiscale ICA.	113
4.15	Multiscale ICA and ICA for detection of changes from color fundus images.	114

4.16	Detected changes present in color fundus image due to diabetic retinopathy: [(a), (c), (e)] green channel of the color fundus images, [(b), (d), (f)] detected changes.	115
5.1	Glaucoma detection based on CDR.	120
5.2	Evaluation of CDR, (a) fundus image, (b) green channel image, (c) extracted blood vessels, (d) inpainted image, (e) extracted cup, and (f) extracted disc.	121
5.3	Different types of disc: (a) normal disc, (b) glaucoma disc with increase in cup size, (c) glaucoma with inflamed disc, (d) glaucoma with disc anomalies.	123
5.4	Differential entropy based method for glaucoma detection.	124
5.5	Preprocessing: (a) cropped color image, (b) red channel image, (c) green channel image, (d) blue channel image, (e) illumination corrected image, (f) histogram equalized image.	125
5.6	The appearance of different features of color fundus image in different wavelet subbands and detection of the cup (a) preprocessed green channel image, (b) subband-3 image, (c) subband-5 image, (d) segmented cup.	126
5.7	Differential entropy value vs. CDR value for different size of cup.	127
5.8	ROC curve shows the segmentation performance.	129
5.9	PCA-LDA based glaucoma classification.	132
5.10	Preprocessed training images: for glaucoma and normal.	133
5.11	Eight significant eigen-images.	134
5.12	Performance values vs. number of significant eigenvalues/principal components (PCs).	135
5.13	HMM-SVD based method for glaucoma classification.	138
5.14	Output of different stages of HMM-SVD based method for glaucoma classification.	140
A.1	Reconstructed images in 5-level wavelet decomposition by considering a particular subband coefficients of image-1 from the database.	150
A.2	Reconstructed images in 5-level wavelet decomposition by zeroing a particular subband coefficients of image-1 from the database.	150
A.3	Reconstructed images in 5-level wavelet decomposition by considering a particular subband coefficients of image-2 from the database.	151

List of Figures

A.4 Reconstructed images in 5-level wavelet decomposition by zeroing a particular sub-band coefficients of image-2 from the database.	151
A.5 Reconstructed images in 5-level wavelet decomposition by considering a particular subband coefficients of image-3 from the database.	152
A.6 Reconstructed images in 5-level wavelet decomposition by zeroing a particular sub-band coefficients of image-3 from the database.	152
A.7 Reconstructed images in 5-level wavelet decomposition by considering a particular subband coefficients of image-4 from the database.	153
A.8 Reconstructed images in 5-level wavelet decomposition by zeroing a particular sub-band coefficients of image-4 from the database.	153
A.9 Reconstructed images in 5-level wavelet decomposition by considering a particular subband coefficients of image-5 from the database.	154
A.10 Reconstructed images in 5-level wavelet decomposition by zeroing a particular sub-band coefficients of image-5 from the database.	154
A.11 Reconstructed images in 7-level wavelet decomposition by considering a particular subband coefficients of image-1 from the database.	155
A.12 Reconstructed images in 7-level wavelet decomposition by zeroing a particular sub-band coefficients of image-1 from the database.	155
A.13 Reconstructed images in 7-level wavelet decomposition by considering a particular subband coefficients of image-2 from the database.	156
A.14 Reconstructed images in 7-level wavelet decomposition by zeroing a particular sub-band coefficients of image-2 from the database.	156
A.15 Reconstructed images in 7-level wavelet decomposition by considering a particular subband coefficients of image-3 from the database.	157
A.16 Reconstructed images in 7-level wavelet decomposition by zeroing a particular sub-band coefficients of image-3 from the database.	157
A.17 Reconstructed images in 7-level wavelet decomposition by considering a particular subband coefficients of image-4 from the database.	158
A.18 Reconstructed images in 7-level wavelet decomposition by zeroing a particular sub-band coefficients of image-4 from the database.	158

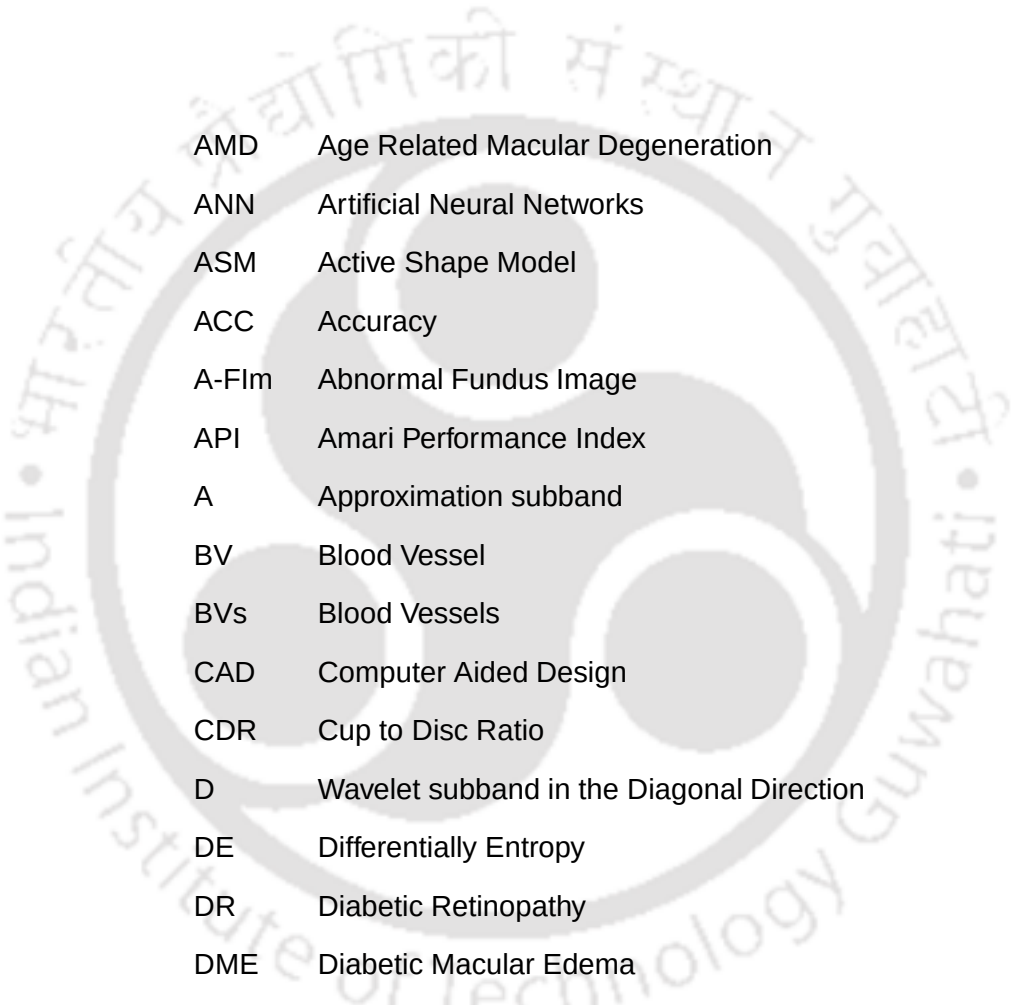
List of Tables

1	Performance measure values of different blood vessels extraction techniques.	xiii
1.1	Properties of different features in normal fundus image.	6
1.2	Characteristics of different DR features in retinal image.	10
3.1	Performance measure values of extraction of microaneurysms in different level sub-band in 5-level wavelet decomposition.	68
3.2	Performance measure values of extraction of microaneurysms in different level sub-band of 7-level wavelet decomposition.	70
3.3	Performance measure values (set-1) of extraction of exudates in different level sub-band in 5-level wavelet decomposition.	73
3.4	Performance measure values (set-2) of extraction of exudates in different level sub-band of 5-level wavelet decomposition.	73
3.5	Performance measure values (set-1) of extraction of exudates in different level sub-band of 7-level wavelet decomposition.	75
3.6	Performance measure values (set-2) of extraction of exudates in different level sub-band of 7-level wavelet decomposition.	75
3.7	Performance measure values (set-1) of extraction of exudates in different level sub-band of 9-level wavelet decomposition.	76
3.8	Performance measure values (set-2) of extraction of exudates in different level sub-band of 9-level wavelet decomposition.	76
3.9	MOS for MAs and haemorrhages in different level subbands of various levels wavelet decomposition.	77
3.10	MOS for exudates in different level subbands of various levels wavelet decomposition.	77
3.11	Cumulative metric for exudates in 5-level wavelet decomposition.	77

List of Tables

3.12 Cumulative metric for exudates in 7-level of wavelet decomposition	77
3.13 Cumulative metric for exudates in 9-level of wavelet decomposition.	77
4.1 Performance values of different blood vessels extraction techniques.	84
4.2 Performance values of different blood vessels extraction techniques in the presence of salt and pepper noise.	85
4.3 Amount of blood vessels affected by pathologies in fundus image (Im).	88
4.4 Correlation coefficient between different color channels of the images.	91
4.5 Correlation coefficient between color channels RGB and HSV.	92
4.6 Average kurtosis and negentropy values of different features in in retinal images with exudates.	93
4.7 Average kurtosis and negentropy values of different features in retinal images with haemorrhages.	93
4.8 API and Comon test values for ICA and multiscale ICA (MSICA).	108
4.9 API and Comon test values for ICA and multiscale ICA (MSICA) for variation of relative amplitude of modulated sinusoidal signal with respect to another signal. (i.e., Set-1: modulated sinusoidal signal and exponential signal, Set-2: modulated sinusoidal signal and square wave signal, Set-3: modulated sinusoidal signal and sawtooth wave signal).	109
4.10 Performance measure for extraction of exudates by ICA and MSICA.	114
5.1 Differential entropy (DE_c) value of segmented cup for glaucoma detection.	128
5.2 Performance of PCA-LDA based glaucoma classification based on the number of significant eigenvalues or principal components (PCs).	134
5.3 Comparison of performance measure for different glaucoma detection method.	140

List of Acronyms



AMD	Age Related Macular Degeneration
ANN	Artificial Neural Networks
ASM	Active Shape Model
ACC	Accuracy
A-Flm	Abnormal Fundus Image
API	Amari Performance Index
A	Approximation subband
BV	Blood Vessel
BVs	Blood Vessels
CAD	Computer Aided Design
CDR	Cup to Disc Ratio
D	Wavelet subband in the Diagonal Direction
DE	Differentially Entropy
DR	Diabetic Retinopathy
DME	Diabetic Macular Edema
DWT	Discrete Wavelet Transform
db4	Daubechies4
DRIVE	Digital Retinal Images for Vessel Extraction
EER	Equal Error Rate
EFICA	Efficient FastICA
ERG	Electroretinography
FFA	Fundus Fluorescein Angiography
FDOG	First Order Derivative of the Gaussian
FP	False Positive

List of Abbreviations

FN	False Negative
fMRI	Functional-MRI
FOV	Field of View
FICA	FastICA
GRI	Glaucoma Risk Index
GT	Ground Truth
H	Wavelet subband in the Horizontal direction
HSI	Hue Saturation Intensity
HMM	Hidden Markov Model
HRT	Heidelberg Retina Tomography
HVS	Hue Value Saturation
ICA	Independent Component Analysis
ICs	Independent Components
IOP	Intraocular Pressure
ICE	Irido Corneal Endothelial Syndrome
ISTN	Inferior Superior side to the Nasal Temporal side
KNN	K-Nearest Neighbor
KJ	Jaccard Coefficient
KC	Conformity Coefficient
KD	Dice Coefficient
KHG	Kirsch, histogram and Gaussian
KLD	Kullback-Leibler Divergence
LDA	Linear Discriminant Analysis
L1	Wavelet decomposition Level-1
L2	Wavelet decomposition Level-2
L3	Wavelet decomposition Level-3
L4	Wavelet decomposition Level-4
L5	Wavelet decomposition Level-5
L6	Wavelet decomposition Level-6
L7	Wavelet decomposition Level-7

L8	Wavelet decomposition Level-8
L9	Wavelet decomposition Level-9
MA	Microaneurysm
MAs	Microaneurysms
MLP	Multi Layer Perceptron
MV	Majority Voting
MMs	Mixture models
MRA	Multi Resolution Analysis
MSE	Mean Square Error
MAE	Mean Absolute Error
MF	Matched Filter
MSICA	Multiscale ICA
MRMR	Minimum Redundancy Maximum Relevance
MOS	Mean Opinion Score
NPDR	Non-Proliferative Diabetic Retinopathy
NN	Neural Network
N-FIm	Normal Fundus Images
OCT	Optical Coherence Tomography
OD	Optic Disc
ONH	Optic Nerve Head
PDR	Proliferative Diabetic Retinopathy
PCs	Principal Components
PCA	Principal Component Analysis
PSNR	Peak signal to Noise Ratio
PCC	Pearson Correlation Coefficient
PPV	Positive Predictive Value
PPA	Peripapillary Atrophy
RBF	Radial Basis Function
RMSE	Root Mean Square Error
RNFL	Retinal Nerve Fibre Layer

List of Abbreviations

ROC	Receiver Operating Characteristic
SVD	Singular Value Decomposition
SLO	Scanning Laser Ophthalmoscope
SVM	Support Vector Machine
SSIM	Structural Similarity
SCF	Subband Confidence Factor
SNR	Signal to Noise Ratio
TP	True Positive
TN	True Negative
3D	3-dimensional
TIF	Tagged Image File
TPR	True Positive Rate or Sensitivity
TNR	True Negative Rate or Specificity
UQI	Universal Quality Index
V	Wavelet subband in the Vertical direction

List of Symbols

A	Approximation signal
A_c	Area of cup
A_d	Area of disc
b	Wavelet subbands
BV_a	Blood vessels affected by pathologies
BV_p	Total number of blood vessels pixels
c	Number of class in LDA
C	Capacity of information
d	Number of pixels in fundus image
DE_c	Differential entropy value
G	Gain matrix
G_{api}	API value
G_{comon}	Comon test value
$H(.)$	Shannon's differential entropy
i_0	Starting level/scale
i	Resolution level
i_m	Highest pixel value in image
$I(.)$	Mutual information
K	Divergence
l	Number of samples for LDA
l_i	Distinct level of quantization
M	Mixing Matrix
n	Any number of observed signal
$\tilde{n}$	Additive white Gaussian noise

List of Symbols

N	Final decomposition level
$p(x, y)$	Image
p_{ij}	Manually marked exudate
$\hat{p}_{ij}$	Extracted exudate
$p_c(\varphi)$	Cup probability
$p_d(\varphi)$	Disc probability
$p_\phi(\varphi)$	Probability of Gaussian random variable
$\tilde{P}$	Probability distribution
q	Number of observed signals in ICA
$\tilde{Q}$	Probability distribution
s	Source signal
$\hat{s}$	Estimate of independent sources by ICA
S	Scatter matrix or covariance matrix
T	Linear transformation
U	Left orthogonal matrix in SVD
V	Right orthogonal matrix in SVD
$WT_\phi(i_0, m, n)$	Approximation coefficients
$WT_\psi^b(i, m, n)$	Detail coefficients
W	Separating matrix or un-mixing matrix in ICA
$\mathbf{x}$	Observed signal in ICA
y	Random vector
$\mathbf{z}$	Feature vector for PCA
Ω	Transformation matrix
σ	Standard deviation
σ^2	Variance
Σ	Diagonal matrix of singular values in SVD
Δ_i	Difference between two consecutive quantized values
μ	Mean value
β_2	Kurtosis proper or Pearson kurtosis
γ_2	Excess kurtosis

ξ	Error
ρ	Correlation coefficient







1

Introduction

Contents

1.1	Anatomy and assessment of eye	2
1.2	Fundus image and its clinical features	6
1.3	Retinal image processing for segmentation of features	13
1.4	Organization of the thesis	22

1. Introduction

The clinical features of a fundus or retinal image are the macula lutea, the optic disc (OD), and the blood vessels. Development in image processing, computer vision, and pattern recognition has helped the evolution of automated diagnostic systems for diabetic retinopathy (DR), age related macular degeneration (AMD), and retinopathy. In case of DR, fluid leaks from blood vessels into the retina and different lesions appear over the retina. Based on the appearance of pathological features such as microaneurysms (MAs), haemorrhages, larger blot haemorrhages, exudates and cupping etc. the ophthalmologists evaluate the DR condition. Various approaches have been proposed in the literature to study the clinical importance of different DR features or lesions in the retinal image. Automated diagnostic systems require analysis and efficient detection of these DR features.

This thesis documents three investigations on pathological features using wavelet analysis. First investigation is on multiscale analysis of DR features in different scales of wavelet decomposition. Multiscale or multiresolution is an invertible subband representation, which is highly tunable and has a free choice of the basis functions. Each of them contains specific information along a specific direction at a specific scale/frequency. These subbands have more or less relevant information of the lesions. From the diagnostic point of view, the specific wavelet subbands are chosen. In the second investigation, multiscale ICA is proposed and evaluated for detection of DR features. Third investigation is on the analysis and detection of glaucoma using higher order statistics. Changes in the appearance of an optic disc region lead to glaucoma and result in peripheral vision loss. Glaucoma is generally detected by the measurement of the ratio of cup area to disc area. In some cases it fails due to misclassification of the cup and disc region. This limitation has been overcome by the measurement of negentropy in the multiscale domain.

1.1 Anatomy and assessment of eye

The importance of medical imaging is constantly growing and making health care more effective and patient-friendly. Medical imaging is a modern health care procedure to create high resolution images of the human organs for clinical purposes, by a set of non-invasive techniques. It has become popular due to the visual documentation and its ability to extract information about many diseases for the diagnosis. These accomplishments have allowed clinicians to make accurate and efficient diagnosis in a non-invasive fashion and the therapeutic result can be closely monitored [4–6].

Fig. 1.1, shows a cross section of the human eye with important anatomical components. It is a

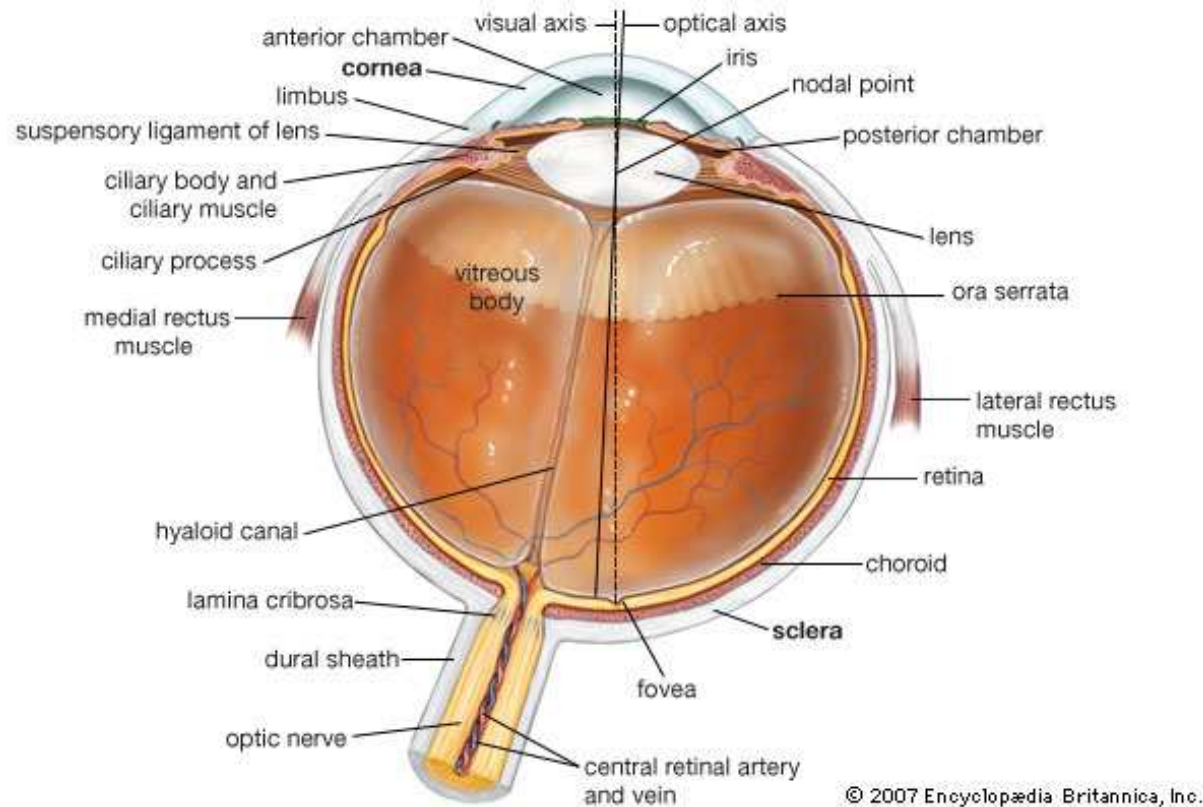


Figure 1.1: Cross sectional view of human eye [1].

precious organ, which gives the sensation of vision, including color differentiation and perception of depth due to the presence of rods and cones in the retina [4]. The visible parts of the eye include the cornea, white sclera, the colored (either green or blue or brown or a mixture of these) iris, and the pupil. The reflected light ray from the object passes through the pupil, the lens, the cornea, anterior chamber, the vitreous and is then focused on the retina. Retina consists of retinal pigment epithelium, the choroid and the sclera. The choroid is mainly responsible for blood supply of the retina. Partially blood supply through the retina occurs through the vasculature, which lies on top of the retina. The retina covers 65% on its interior surface. The neural layer present in the retina plays a direct role in vision and visual processing. Rods and cones in the retina change the reflected light rays from the object into electrical impulses and send them through the optic nerves to the occipital region of the

1. Introduction

brain where the image is perceived. The macula is a tiny area at the center of the retina, which is responsible for bright and sharp vision. The surrounding parts of the retina are called the peripheral retina and it is responsible for side or peripheral vision. The retina is damaged due to DR, which is a complication of diabetes. Diabetic retinopathy basically affects the blood vessels that nourish the retina. Fluids and blood come out from the damaged blood vessels and deposited over the retina. It leads to swelling of retinal tissue and clouding of vision. It usually affects both the eyes. Development of DR becomes more likely for a person suffering from diabetes for a longer period and causes vision loss that in many cases cannot be reversed. In the early stages of DR the visual symptoms are very rare. So, early detection and treatment can reduce the chance of the significant vision loss from DR.

A comprehensive eye examination through testing, evaluation of the retina and macula is used for diagnosis for DR. This may include:

- *Patient history* to determine difficulties in vision experienced by the patient, general condition of health affecting vision, blood pressure, and blood sugar level that may be affecting vision,
- *Visual acuity* measurements to determine the condition of central vision or bright vision,
- *Refraction* to determine the requirement for changes in an eyeglass prescription,
- *Evaluation* of retina through a dilated pupil, and
- *Measurement* of the intra ocular pressure within the eye.

These tests do not tell about anatomical changes and the status of the retina. So, retinal photography or tomography are done to know the changes in the retina. Different procedures are performed such as: (a) Ophthalmoscopy, (b) *fundus photography*, (c) *fundus fluorescein angiography (FFA)*, and (d) optical coherence tomography (OCT). Fundus photography is the photography of the retina and has the advantage of documentation for future reference. Fundus fluorescein angiography helps document current status of the retina to evaluate abnormal blood vessel growth by intravenous injection of a fluorescent dye. It increases the contrast of the retinal vasculature. Fig. 1.2 shows an example of a fluorescein angiogram in which blood vessels are more accurate than direct ophthalmoscopy [7]. This is not very common in clinical practice due to its invasive nature and side effects.

The OCT is a high-resolution, cross-sectional tomographic imaging of the internal microstructure in materials and biological systems based on interference similar to ultrasound, which produces

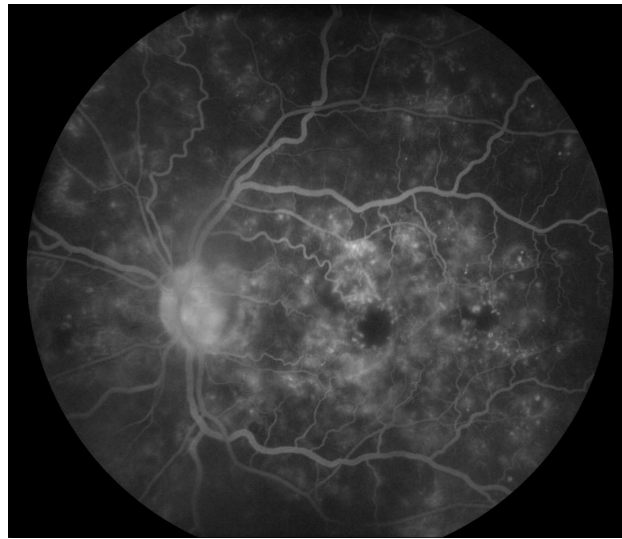


Figure 1.2: Fundus fluorescein angiography [2].

three-dimensional images within optical scattering media (e.g. biological tissue) [8–10]. It operates at near-infrared light, which uses a relatively long wavelength light to penetrate into the scattering medium. Confocal microscopy uses a similar technique, which penetrates less deeply into the sample. Microperimetry has the ability to diagnose and quantify the changes in the retinal function at a particular location over time [11]. Optos OCT scanning laser ophthalmoscope (SLO) is used to obtain structural OCT and functional microperimetry testing (<http://www.optos.com>).

One highly advanced instrument, the Optos' OCT SLO system combines the advantages of industry-leading spectral OCT imaging with a confocal SLO. Clinicians are able to both diagnose and track the smallest pathological changes in retina over time such as, assess outcomes of therapies, detect retinal functions, and capture structural changes.

Fundus photography involves the use of a retinal/fundus camera to photograph the different regions and parts of the retina. The resultant images document the patient's medical record in a photographic or digital image. The fundus camera consists of a low power microscope (such as, *mydriatic* and *non-mydriatic* [12]). In mydriatic fundus camera pupils have to be dilated, which enhance the quality of the photographic record due to a wider field of view. In non-mydriatic camera the, pupil need not be dilated. Fundus photographs are considered medically necessary as its influence the management of the patient, evaluate abnormalities in the fundus, follow the progression of a disease,

1. Introduction

plan the treatment for a disease, assess the therapeutic effect of recent surgery (e.g. photocoagulation), documentation and to establish a baseline for judgement for a disease progression.

1.2 Fundus image and its clinical features

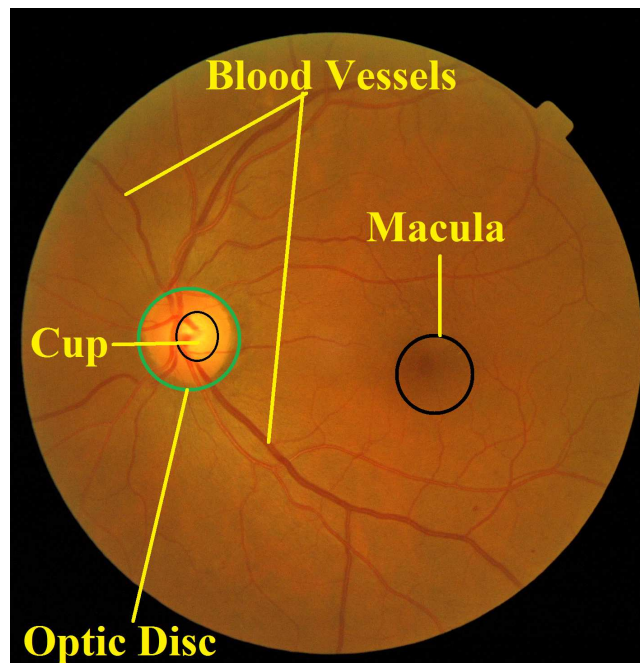


Figure 1.3: Normal retinal photograph from Aria database.

Table 1.1: Properties of different features in normal fundus image.

Region Type	Size	Color	Shape	Contour
Optic Disc [13], [14]	1/30 of retina, Diameter: 1.5 to 2 mm	Orange or yellow	Round	Clear & well defined
Cup [15]	Smaller than OD, Cup is 1/3 height of disc	Pale yellow	Round	Clear edges
Macula	Diameter: 4 - 5 mm	Hazy dark	Round	-
Fovea	Diameter: 1.5 - 2.5 mm	Dark, darker than surrounding	Round	-

The Fig. 1.3 shows fundus or retinal image for normal retina. The most important parts of the normal retina are *OD*, *macula*, *fovea* and *blood vessels* [16, 17]. These features' characteristics have been tabulated in Table 1.1. Optic disc is the brightest region having an elliptical shape which appears bright orange pink with a pale center [18]. It is called blind-spot as it lacks photoreceptors. The blood vessels are emerging from the OD. Lateral to the blind spot of the eye, a hazy dark region having an oval shape with a diameter of nearly 0.4 mm is present. It is called the macula lutea (yellow spot). The

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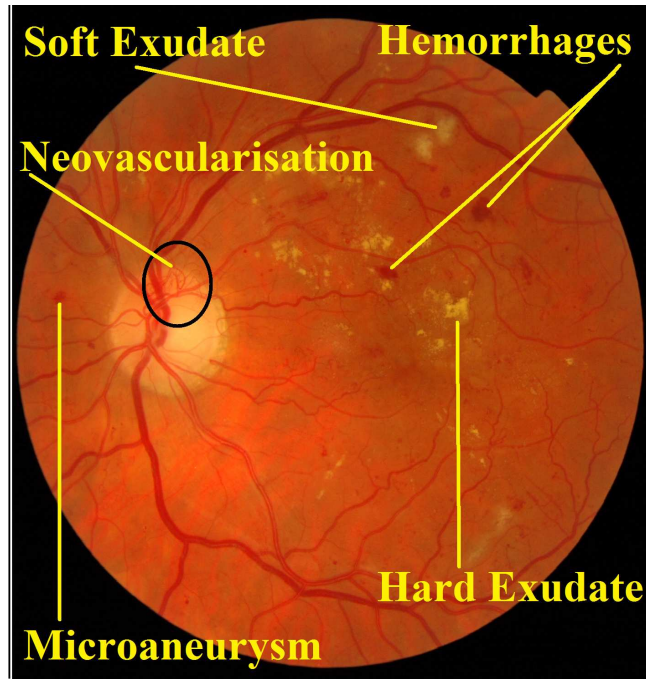


Figure 1.4: Disease retinal photograph from Aria database.

center of the macula is called fovea (having the size of a pin head), which contains only the cones and helps in acuity vision or sharp vision or bright light vision. Macula contains mostly the cones and its density declines gradually from the edge of the macula to retinal periphery. Rods are responsible for the dim light vision. The retina is nourished by the blood circulation of the blood vessels. The blood vessels give rise to a rich vascular network.

In DR, the retina is damaged due to fluid and blood leaking from the damaged blood vessels. Ophthalmologists recognize the DR, based on the features on retina, such as red lesions (*microaneurysms* (MAs), small intra retinal dot *haemorrhages*, larger blot haemorrhages), and white lesions (*exudates* and *cotton wool spots*) [19] etc. These features are tabulated in Table 1.2. Fig. 1.4 shows the different features in case of diseased retina. More number of lesions appear on the retina as the disease progresses. The appearance of the retina in different stages of DR is shown in Fig. 1.5. Fig. 1.5(a) is the normal image which does not contain any lesions. The ratio of cup area to disk area increases in Fig. 1.5(b) with some white patches on the left side. It is an image of a glaucoma affected eye. Fig. 1.5(c) is the image of mild, non-proliferative diabetic retinopathy (NPDR) which

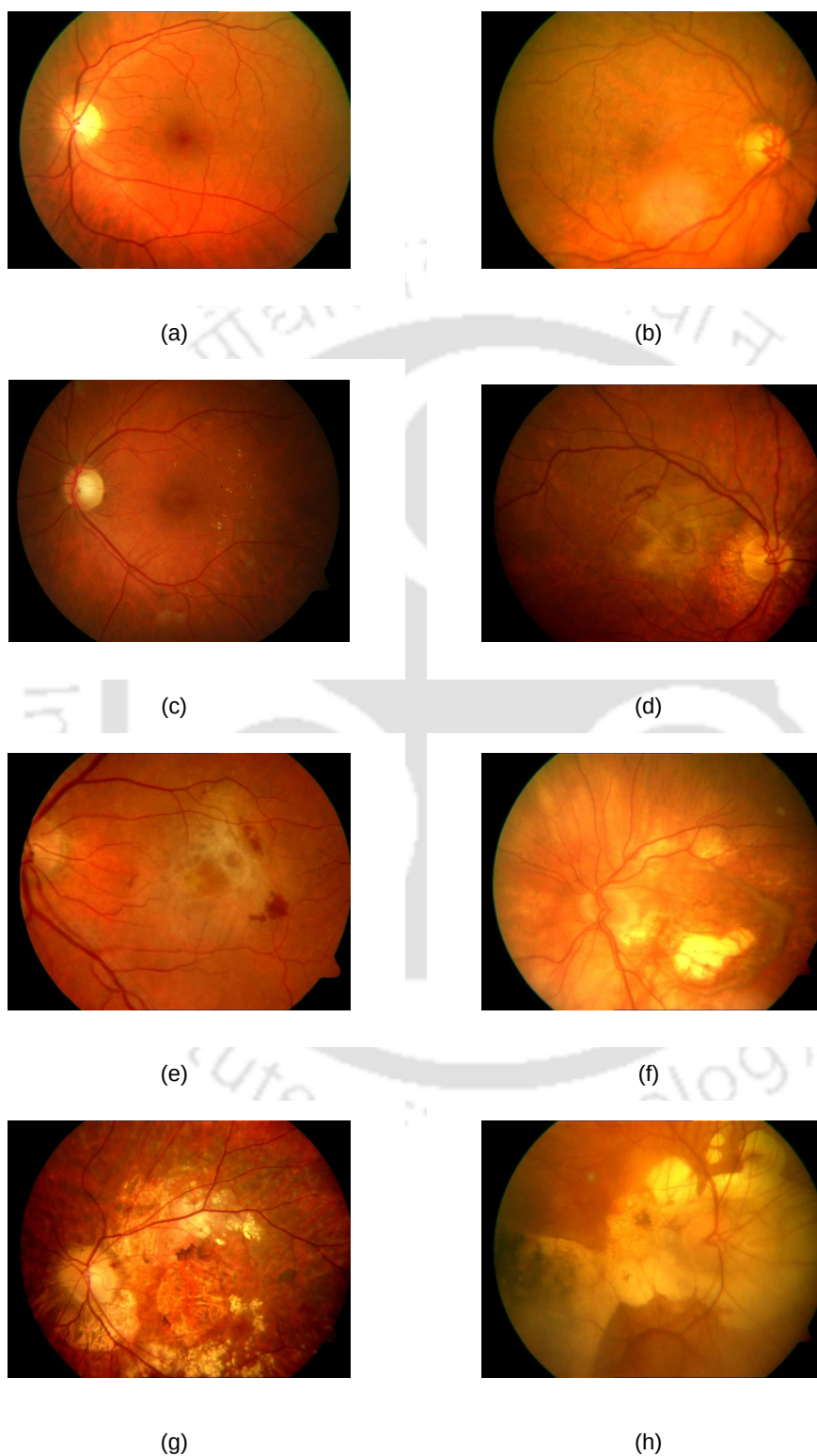


Figure 1.5: Different stages of DR: (a) normal image, (b) glaucoma, (c) mild NPDR, (d) moderate NPDR, (e) severe NPDR, (f) mild PDR, (g) moderate PDR, and (h) severe PDR.

contains microaneurysms. Microaneurysms along with exudates and haemorrhages are shown in Fig. 1.5(d). This is moderate NPDR stage. The degree of NPDR varies with the number of lesions. During severe proliferative diabetic retinopathy (PDR), exudates and haemorrhages appear in the retina. In this case, the size and the numbers are more as shown in Fig. 1.5(e). In mild PDR, the lesions appear near to the macula. It is shown in Fig. 1.5(f). During severe PDR, the lesions appear over the macula as shown in Fig. 1.5(g) and Fig. 1.5(h). In these cases, new blood vessels also appear which is called neovascularization.

Microaneurysms are the earliest indicators for the presence of DR [20]. These are saccular out pourchings of retinal capillaries. They are continually formed while the existing ones disappear. They look like isolated patterns. Microaneurysms are small red dots with sizes equal to the size of a pin head (diameter ranges from $10\mu\text{m}$ to $100\mu\text{m}$). Exudates are the protein and lipid deposits over the retina from the damaged blood vessels [21, 22]. They are found as yellowish patches with irregular borders over the retina. They appear as soft and hard exudates. Soft exudates are oval in shape, whereas hard exudates are irregular in shape. Soft exudates disappear between 4 to 12 weeks, whereas hard exudates have tended to form coalescence or macular star. During image segmentation, hard exudates are conflicted with the OD. Drusens are hyper fluorescent spots with yellowish in color, which are marks of macular degeneration [23]. They appear anywhere on the surface of the retina as soft and hard drusens. Soft drusens are dome shaped where as hard drusens have a small nodule shape. In glaucoma, the structure of the OD changes and it leads to cupping due to increase in intraocular pressure [24]. Effective treatment is possible if the conditions are detected early. So, detection of these lesions/diagnostic features is important for the diagnosis of DR and estimate of vision loss.

1.2.1 Retinal diseases

Retinal diseases occur due to diabetes for a longer period of time and affect millions of people all over the world [18]. Diabetic retinopathy and other eye diseases are characterized by structural variations in the retina. Continuous monitoring of the retina is required for effective treatment and diagnosis of the early symptoms [26–28]. Retinal images can provide necessary and important diagnostic information about diabetes, NPDR, PDR, AMD and glaucoma. Due to DR, blood vessels, OD and macula are affected and different pathological features appear over the retina. So, ophthalmologists are interested in the diagnostic features in the retina. Diabetic retinopathy is a progressive pathology

1. Introduction

Table 1.2: Characteristics of different DR features in retinal image.

Features	Size	Color	Shape	Other
Microaneurysm [20, 25]	Very small, size of a pin head, Diameter: $10\ \mu\text{m}$ - $100\ \mu\text{m}$	Reddish	Rounded	MAs are earliest unequivocal indication of DR. These are sacular outpourchings of retinal capillaries. MAs are continually forming while existing ones disappear. Looks like isolated patterns.
Soft Exudates	Small & $1/3$ of disc diameter	Whitish or pearly grey	Oval	Deposits made of lipoproteins leaking from abnormally permeable blood vessels especially MAs. Edge: Blurry or feathery Numbers: Few Onset: Rather acute Situation: Superficial, near OD No tendency of coalescence. Disappear between 4 to 12 weeks. Conflict: With OD
Hard Exudate [21, 22]	Variable, Ranging from pin point to larger than disc diameter	Waxy or yellowish white	Not regular	Deposits made of lipoproteins leaking from abnormally permeable blood vessels especially MAs. Edge: Clear & sharply defined Numbers: Usually many Onset: Very gradual Situation: Deep, underneath BVs Tendency to form coalescence. Tends to form macular star. Conflict: With OD
Soft Dursen [23]	Diameter: $\geq 125\ \mu\text{m}$	Pale yellow or grayish white	Dome shaped	These are epithelial detached pigment. Location: Any where in retina Hall mark of AMD
Hard Dursen	Diameter: $\leq 63\ \mu\text{m}$	Yellow	Small nodules	These are basal laminar deposit referred to a material located external to RPE basement membrane. Location: Any where in retina Macular degeneration.
Cotton Wool Spots	Localized	Yellowish white	Fluffy patches	Occurs due to drainage of axoplasmic content into the retina in focal ischemia that causes axoplasmic flow interruption. Causes blurry vision. Found in collagen vascular diseases, AIDS, hypertensive retinopathy.
Haemorrhage	Small or large	Red or dark red	Dot	-

and its severity can be known by the number of pathological symptoms and the types of lesions present on the retina. The different stages of DR are given below [29–31].

(i) *Non-proliferative Diabetic Retinopathy (NPDR)*: It is most common eye disease which occurs
[TH-1619_09610207](#)

due to diabetes and is a leading cause of blindness in adults. It is the earliest stage of diabetic retinopathy. It damages the blood vessels in the retina. The fluid or the blood may come out of the damaged blood vessels, causing the retina to become swollen. NPDR can cause the changes in the eye, including microaneurysms and retinal haemorrhages. It has three stages, such as

- *Mild NPDR*: This is the early stage of DR and it is manifested by the small balloon like swellings in the blood vessels known as microaneurysms.
- *Moderate NPDR*: Blood vessels are blocked in this stage.
- *Severe NPDR*: Most of the blood vessels are blocked and venous bleeding occurs in two or more quadrants of fundus image. This leads to retina haemorrhages.

(ii) *Proliferative Diabetic Retinopathy (PDR)*: This is the advanced stage of DR and a major cause of blindness over the world. It mainly occurs when many of the blood vessels in the retina are closed. This prevents enough blood flow in the retina. In order to supply blood to the area where the original vessels closed, the retina responds by growing new blood vessels. This is called neovascularization. These new vessels are fragile and abnormal in nature. They often accompanied by scar tissue that may cause the retina to wrinkle or detach. The PDR can affect both central and peripheral vision. So, PDR may cause more severe vision loss than NPDR. PDR affects vision in different ways, such as vitreous haemorrhages (new blood vessels bleed into the vitreous), traction retinal detachment (scar tissue from neovascularization shrinks, causing the retina to wrinkle and pull from its normal position) etc. PDR is progressing in three different stages.

- *Mild PDR*: New vessels (neo-vascular net) start growing to nourish the retina. These vessels are fragile and they do not cause vision loss.
- *Moderate PDR*: Fluid coming out of new fragile blood vessels and causes vision blurring.
- *Severe PDR*: Fluid deposits over the macula and causes severe vision loss.

(iii) *Diabetic Macular Edema (DME)*: It can occur at any stage of DR. It occurs due to thickening of the blood vessels near the macula or its periphery of 500 μm . Macular edema at the center causes central vision loss. This leads to distortion of visual images and may cause a significant

1. Introduction

decrease in visual acuity even in the absence of severe retinopathy. This can be further divided into three stages, such as

- *Mild DME*: Thickening of the retina occurs or hard exudates appear far from the macula.
- *Moderate DME*: Hard exudates or retinal thickening appears near macula.
- *Severe DME*: Hard exudates or retinal thickening appears over macula center (fovea).

(iv) *Age-Related Macular Degeneration (AMD)*: It generally occurs in the group of people above fifty and leads to central vision loss. AMD depends upon the smoking habits, family history, and race. Drusen and pigmentary changes in the macula are the earliest manifestations of AMD. It is of two types [32–34].

- *Dry (nonexudative) AMD*: It is most common and 90% of the AMD affected people are dry AMD, which causes blurring of central vision in the affected eye. It occurs due to slow breakdown of the light-sensitive cells in the macula. During the later stage of dry AMD, a blur spot is visible in the center of vision. Medically it is called *geographic atrophy*. It has three stages such as *early dry AMD*, *intermediate dry AMD*, and *advanced dry AMD*. Few small and medium size drusen appear in early dry AMD. Many medium size drusens or one or two large drusen appear near the macula. In advanced dry AMD light sensitive cells in the macula break down and causes blur spot in the center of the vision.
- *Wet (exudative) AMD*: About 10% of people of AMD are affected by wet AMD and this is more severe than dry AMD. In wet AMD abnormal blood vessels grow under the macula and wet the macula by the fluid coming from the blood vessels. The fluid swells the macula and damage occurs rapidly.

(v) *Glaucoma* [35, 36]: In this disease, a group of eye condition results in optic nerve damage and causes peripheral vision loss, due to increase in intraocular pressure (IOP). The noticeable vision loss cannot be seen until the disease is in advance stage. Damage to the optic nerve is not reversible. The main complications of glaucoma are blind spots in peripheral vision, tunnel vision and complete blindness. The main risk factors of glaucoma are elevated internal eye pressure, i.e., IOP, age above sixty, race, family history of glaucoma, medical conditions (like diabetics, BP and obesity), long term corticosteroid use, and other conditions (like glaucoma in one eye, eye tumors, retinal detachment, eye inflammation and lens dislocation) etc.

It can be diagnosed by measuring IOP (by tonometry), testing of optic nerve damage (by ophthalmoscopy or fundus camera), visual field (by perimetry), angle in the eye where iris meets cornea (by gonioscopy) and corneal thickness (by pachymetry). The main types of glaucoma are *open-angle* and *angle-closure* among different types of glaucoma.

- *Open-angle glaucoma*: It is the most common case of glaucoma, which occurs due to slow clogging of the drainage canals and results in increased IOP. In this case, the angle between the iris and cornea becomes wide and open. About 90% of glaucoma occurring people are suffering in primary or chronic glaucoma.
- *Angle-closure glaucoma*: It is also called as acute glaucoma or narrow-angle glaucoma and is caused by blocking drainage canals, which results in increased IOP.
- *Congenital glaucoma*: Occurs in the babies due to incomplete growth of the eye's drainage canal during perinatal period.
- *Other types* of glaucoma include secondary glaucoma, pseudo exfoliative glaucoma, pigmentary glaucoma, neovascular glaucoma, traumatic glaucoma, and irido corneal endothelial syndrome (ICE) glaucoma.

At the beginning of DR, swelling occurs in the blood vessels. PDR is signaled by the appearance of new blood vessels (i.e., neovascular net). The different features are extracted from the retina by various methods. The methods present in the literature are discussed in the next Section.

1.3 Retinal image processing for segmentation of features

In the last few decades digital retinal photography is an acceptable modality to document the retinal appearance and it plays a crucial role for diagnosis of retinal diseases. These images are important for the clinical scenarios due to easier storage, electronic transfer, quantitative analysis and for automatic diagnosis. Developing techniques for analyzing images help in the quantitative analysis, which can further help to understand the relationship between the retinal components and the eye related diseases. The retinal image analysis includes:

- preprocessing,
- segmentation of retinal landmarks such as blood vessels, OD and macula,

1. Introduction

- detection of pathological features such as: microaneurysms, haemorrhages, exudates, drusen, and neo-vascularization.

1.3.1 Preprocessing of retinal images

The main reason of preprocessing is to attenuate the image variation by normalizing the original image with the reference dataset. These variations are found to be within the same image (intra-image variability) and between images (inter-image variability). Intra image variability occurs due to differences in light diffusions, retinal pathologies, and fundus parameters (i.e., fundus thickness and reflectivity). Inter image variability occurs due to non-uniform illumination, cameras, and angle of acquisition. To achieve the above corrections, non-uniform illumination correction, color normalization and contrast enhancement are performed.

1.3.1.1 Non-uniform illumination correction

Non-uniform spatial variation in the retinal photograph occurs due to illumination component. Reflectance component causes the abrupt variation at the edges of the anatomical features. High pass filtering can overcome the non-uniform illumination [37]. Non linear point transformation proposed by Wang *et al.* for correction of non-uniform illumination [38].

1.3.1.2 Color normalization

Color helps in discriminating between the retinal features. Green channel in the RGB color space has higher contrast between the background and the features (blood vessels, haemorrhages etc.) [39]. Green channel provides more information and less subject to non-uniform illumination. Coloration in retinal images occurs due to difference in skin pigmentation, iris color, age, and macular pigment density. Color normalization reduces the inter-image and intra-image variability. The original retinal image is transformed to hue-saturation-value for color normalization [40]. A monotonic non-linear transformation function is applied for histogram equalization, which redistribute the histogram of each color channel of the input image to uniform pixel value distribution. As the normal retina reflects the blue light, histogram equalization over-emphasizes the contribution of the blue channel [41].

1.3.1.3 Contrast enhancement

Contrast (color variation or perceived brightness) enhancement alters the visual appearance that makes the object distinguishable from other objects or background. The contrast gradually reduces from the center to the periphery of the image. The center has the highest contrast and it reduces towards the periphery of the image. Histogram equalization proposed by Osareh *et al.* [41] and adaptive contrast enhancement proposed by Sinthanayothin *et al.* [40] to enhance the contrast in retinal images.

1.3.2 Segmentation of normal retinal features

In this section, various algorithms and techniques are discussed for the segmentation of different normal retinal features such as blood vessels, OD and Macula.

1.3.2.1 Segmentation of blood vessels

Basically, blood vessels are segmented by *unsupervised* and *supervised* methods. In unsupervised method matched filter, vessel tracking, morphological based method, pixel based and neural network are used, which use a predefined criteria. Matched filter employs a kernel, which has a Gaussian profile rotated to identify the cross section of vessel profile [42, 43]. So, it helps in matching the blood vessels. It has the advantage that it can reduce noise. The limitations of matched filter is that it responds not only to the vessels but also to the non vessel regions. This problem was solved by Zhang *et al.* by using a modified matched filter with double sided thresholding [44]. In this case, the mean value is not subtracted from the Gaussian filter. Modified matched filter complements the retinal image so that the vessels are brighter than the background. The image is filtered to obtain the vessel pixels. Zhang *et al.* have used a first order derivative of Gaussian for the extraction of the retinal vessels [45]. It can extract the vessels in the pathological conditions.

Morphological operators are applied for vessel segmentation due to their geometric interpolation, simplicity and efficient implementation in hardware. It has the advantage of noise reduction and better speed [46]. Mathematical morphological methods do not exploit the known vessel cross sectional shape.

Gabor wavelet transform is used for blood vessel segmentation [47–49]. The 2-D Gabor wavelet and sharpening filter enhance and sharpen the vascular pattern respectively. Vessels are extracted

1. Introduction

from the sharpened images. Vessel tracking algorithm steps along the vessels and helps in measuring width, tortuosity and provide the information about individual vessels. Unfortunately, they require a starting and ending point [50].

Some authors used classification methods for the segmentation of vessels. Artificial neural networks (ANN) have been used in the literature for the classification of vascular [51]. They use weights to decide the probability of input data to a particular class. Weights can be decided by training the data for a particular output. Sinthanayothin *et al.* [40] preprocessed the images with principal component analysis (PCA) for dimensionality reduction and neural network (NN) to identify the pathologies. Training the NN with the training data or gold standard is the major disadvantage. Staal *et al.* use a ridge based algorithm to detect vessels in a retinal image [52]. The ridges are used to partition the image into patches by assigning each image pixel to the closest line element. Feature vectors are computed for every pixel, which use the properties of the patches and the line elements. Classification of feature vectors is done by k-nearest neighbor (KNN) classifier, which classify the ridges into two different classes, the vessels and the background.

Supervised method uses prior information to decide vessel pixels from the image. In this method, each image pixel is represented by a *feature vector*. The feature vector is formed using the various filter outputs. The features consist of the output of the Gaussian filter and its derivatives up to order 2 and at five different scales augmented with the original green channel image intensity values. The KNN classifier results on a pixel probability map. A binary segmentation of the vasculature was obtained after thresholding the probability map. Then a classifier is trained with these feature vectors [13, 47, 49, 52]. Supervised method's performance is better than unsupervised methods, as the supervised methods are designed based on pre-classified data. They can produce good segmentation results, but at the cost of higher computational complexity.

Analysis of blood vessel's structure can help separate the arteries and veins, which will help measuring the arteriolar-to-venular diameter ratio (AVR) [53]. The study of relative diameters of arteries and veins shows the risk of systemic diseases such as stroke, hypertension or myocardial infarction.

1.3.2.2 Segmentation of the optic disc

Segmentation of OD is performed after determining the center of the disc. Blood vessels are crossing the OD, which distracts the segmentation. It is the brightest component in the fundus and consist of

[TH-1619_09610207](#)

high intensity pixels with high grey scale value [42]. Color space transformation and morphological filtering techniques are used by Walter and Klein for disc localization by using the luminance channel of hue-luminance-saturation color space [54]. Sinthanayothin *et al.* correctly locate the position of the OD by employing the variation of intensity between the OD and the adjacent blood vessels [40].

Niemeijer *et al.* found the anatomical structures by fitting a single point distribution model (PDM) to the image, which used a cost function that combined the local and global cues to detect the anatomical structures [55]. The authors set 16 model points within the image such that the model points lie on certain anatomical structure.

Principal component analysis (PCA) identifies the patterns in the data and express them in such a manner so that similarities and differences are highlighted. PCA was applied to project a new image to the disc space and OD center was found by calculating the minimum distance between the original image and its projection. This technique was used by Li and Chutatape to produce a training set using the brightest pixel that is firstly clustered as a candidate OD region [56]. They used PCA to locate OD as it takes the advantage of top down strategy and active shape model (ASM) for detection of shape. Pixels with highest 1% grey level in the intensity image are selected, which are mainly referring to the OD region and are clustered by single pass method to detect the candidate regions. The PCA method comprises of three steps such as obtaining the disc space, projection on disc space and calculating the distance from disc space. Active shape model builds a PDM from the training set and use iterative search procedure to find its shape.

Hough transform was used by some authors for identifying the locations and orientations of OD. Hough space tends to be sensitive to image resolution [57]. Geometrical parametric modeling (retinal vessels originating from the OD and their path follows a similar directional pattern) was used by Foracchia *et al.* for detection of OD [58]. Welfer *et al.* have used adaptive morphological approach for automatic segmentation of OD [14]. They have used image adaptive method based on vascular structure of blood vessels for detection of OD. The boundary of OD is detected by watershed transformation. Change in shape, size and depth of the OD is an indicator of various ophthalmic pathologies especially for *glaucoma* [59]. It may vary in different pathological conditions.

1.3.2.3 Segmentation of the macula and fovea

Fovea is the hazy dark region in the center of the retina and responsible for brighter vision due to high concentration of cones. Localizing the macula and fovea help diagnosing the severity of AMD.

1. Introduction

It is hard to detect the fovea as it does not have high contrast with the background. An automated method to detect the location of the optic disc and fovea is done by optimization technique [55].

Sinthanayothin *et al.* located fovea based on the location of maximum correlation between the template (size 40×40) and intensity image in HSI color space [40]. This method was tested on 112 color retinal images out of which in 78 images the fovea was detected correctly. The sensitivity of this method was found to be 99.1%. Li and Chutatape have proposed a model based approach for detection of fovea [56]. Here, the authors have used principal component analysis (PCA) to localize OD and modified active shape model to extract the main directions of blood vessels. Fovea is located based on the geometrical relation of OD and blood vessels. The method was tested on 35 images. Chutatape followed the similar procedure for detecting the fovea [60]. The modified active shape model was used for the detection of blood vessels. Fovea is determined by using the spatial relation between the OD and blood vessels. Narasimha-Iyer *et al.* determines the fovea center, based on OD center and adaptive threshold [61]. Niemeijer *et al.* used the information about the position of OD, macula center and vascular arch by using a single model (shape model and shape function) for macula detection [55]. The method reported an accuracy of 94.4% on 500 screening images and 92.0% on 100 pathological images. Singh *et al.* segments the fovea as a dark image region from color fundus images by enhancing contrast using an appearance based localization method in different image channels [62]. Kose *et al.* developed an automatic method for determining the area of macula affected in age related macular degeneration (ARMD) [63]. The location of OD and the relative distance between OD and macula were used for detecting macula.

Sagar *et al.* have identified macula by combining morphology based approach of blood vessel detection (BVD) with the property of the macula that it is the darkest area in the vicinity of OD [64]. They have reported an accuracy of 96%. Sopharak *et al.* use a similar approach to that of Sagar *et al.* for detection of fovea. They have detected fovea by using OD dimensions. Morphological operation and Hough transform are used to detect the fovea by Sekhar *et al.* by finding the spatial relation with OD [65]. Welfer *et al.* detects the fovea by using mathematical morphology techniques based on the two stages such as detection of OD location and its boundary [31]. This method achieved an accuracy of 92.13%.

1.3.3 Detection of abnormalities

The retinal image analysis provides information about vision condition due to DR. This reduces the work of trained graders. The detection of DR concentrates largely on the automated detection of *MAs, haemorrhages, drusens and exudates*.

1.3.3.1 Detection of microaneurysms

Microaneurysms appear as small, isolated patterns and typically they have low contrast. It is difficult to distinguish them from noise or pigmentation variations. Detection of microaneurysms is described by Hipwell *et al.* on angiogram images [66]. Walter *et al.* detect the microaneurysms based on diameter closing and automatic threshold scheme [25]. This method consists of four steps such as: image enhancement, shade correction, image normalization and detection of MAs. Antal and Hajdu use ensemble based microaneurysm detection, which is a simulated based search algorithm [67–69]. The accuracy of this method depends on preprocessing and candidate extractor. Watershed transform was used by Fleming *et al.* on fluorescein angiogram [70]. The dots inside the vessels are detected by vessel detection technique.

Garcia *et al.* detected the red lesions (microaneurysms and haemorrhages) and performed feature selection using logistic regression [71]. The NN based classifiers such as multi-layer perceptron (MLP), radial basis function (RBF) and support vector machine (SVM) are used to obtain the red lesions using majority voting (MV) scheme. Kose *et al.* suggested the inverse segmentation method for detections of lesions and ARMD [72]. Texture of the unhealthy fundus image is not homogeneous. Inverse method is proposed to exploit the homogeneity of the healthy area instead of unhealthy area for segmentation of lesions. First the healthy region is subtracted from the total image to obtain the unhealthy region (background image). From the background the retinal image OD and vessels are eliminated by performing the standard segmentation algorithm. Region growing approach is applied to the rest unhealthy region to obtain the different intensity regions for separations of microaneurysms, haemorrhages and exudates.

Templet matching based algorithm was used in subband of wavelet transformed image for detection of microaneurysms by Quellec *et al.* which solved the problems of high frequency noise [20]. A genetic algorithm is used for optimization of the method. Microaneurysm is modeled by a 2-D rotation symmetric generalized Gaussian function. Detection of microaneurysms still a challenging task for

1. Introduction

automatic as well as human expert system. The methods still do not reach the performance of the human expert system.

1.3.3.2 Detection of exudates

Presence of exudates within the macular region leads to diabetic macular edema. Hard exudates appear as individual streaks or in the form of clusters or in the form of circular rings surrounding the clusters of MAs. Hard and soft exudates are distinguished by their color, sharpness and borders. Exudates having high grey values appear similar to that of OD. Brightest patterns cause problems in the extraction of exudates.

Walter *et al.* [21] use local contrast to find the bright regions between the dark vessels. Candidate regions, resulting the OD are separated out. Then the contours of the exudates are found out by morphological operation. Computational intelligence technique was used by Osareh *et al.* for detection of exudates from pathological images based on color, size, edge, strength [22]. The authors used color normalization, contrast enhancement and fuzzy c-means clustering. Multi-layer NN classifier is used to classify the features.

Sopharak *et al.* proposed the mathematical morphology method for detection of exudates from color fundus images on the hue-saturation-intensity (HSI) color space as an intensity component is separated from the other two components in HSI color space [73]. Contrast enhancement was applied to the noise reduced image by median filtering on an intensity band of HSI color space. Exudates and OD show high intensity in the intensity channel of HSI color space, so contrast enhancement provides highest intensity values to exudates. OD has the similar intensity with exudates and provides limitation in exudate detection. The OD is segmented out from the contrast enhanced image by morphological closing with the disc shaped structuring element before performing exudate extraction. By applying the binary dilation operator to the vessel and OD extracted image, the exudates are separated out.

Fisher's linear discriminant analysis color information of exudates are used to classify exudates, which employs statistical recognition and color information of exudates [74]. The method consists of image processing, enhancement, feature extraction, classification and post processing. Sanchez *et al.* developed an algorithm based on statistical mixture model clustering to dynamic threshold the images to separate the exudates from the background followed by a post processing technique, which helped in demarcating the exudates from cotton wool spots [75]. Mixture models (MMs) are

statistical techniques based on probability densities such as histogram and has the advantage over nonparametric and parametric methods. It can model the pixel values to different populations. In this method first the preprocessing is applied to the green channel image of the RGB color space as green channel highlight the exudates. Dynamic threshold is set based on the statistical information, on the histogram of the enhanced image, which is modeled by using MMs. From this the OD is masked out and preprocessing is applied to detect the exudates.

1.3.3.3 Detection of haemorrhages

Detection of haemorrhages is required for early diagnosis of DR. Hatanaka *et al.* detect the haemorrhages using density analysis on the hue-saturation-value image followed by gamma correction [76]. The false positive (FP) in this method is removed by the rule based system and Mahalanobis distance. The detection method consists of image digitization, image normalization, extraction of optic nerve head, detection of haemorrhage candidates, elimination of FP in the blood vessels and the elimination of FP by feature analysis. These FP is removed by Mahalanobis distance classifiers. Different features such as - angular second moment, contrast, correlation, sum of squares, inverse difference moment, sum of average, sum variance, sum entropy, difference variance, difference entropy, information measurement for correlation, angular second moment and mean are used by each classifier for training. For diagnosis of eye diseases, this system can be applied to computer aided diagnosis (CAD) system.

1.3.4 Scope for the present work

Analysis of retinal image features is important for detecting diseases related to the retina of the human eye. The retinal image should be of sufficient quality to ensure reliable diagnosis. Various approaches have been proposed to study the clinical usefulness of the retinal image for different applications. In some cases, retinal images need to be processed for efficient diagnosis. Any such processing may cause differences in the quality of the image features. The literature related to retinal image processing focus on analysis of normal features. In wavelet domain, the normal retinal features are analyzed. In the literature the detection methods of DR features are present but these features are not sufficient to capture pathological variations. Still, there is a scope for improving the detection accuracy, and analysis of diagnostic features.

A number of retinal image analysis techniques have been discussed in the literature. They have

1. Introduction

discussed about the normal features of the retina, such as, blood vessels, macula and fovea. The normal retinal features are studied in the wavelet subbands. The study of diagnostic features in wavelet subbands are not present in the literature. In a retinal image, the features like blood vessels, optic disc and macula constitute the diagnostically important components. The diagnostic features like microaneurysms, exudates and haemorrhages are much important as they affect the vision. Early detection of these features and their analysis may delay in vision loss.

The *multiresolution analysis* (MRA) technique helps produce localized image features with good *space-frequency resolution*. This can be explored for localizing the retinal image components. The MRA property of the DWT allows improvement in the detection of diagnostic features at a specific resolution. A wavelet based analysis may be useful for preserving diagnostic information for further processing. The retinal image is decomposed into several subbands using a two dimensional DWT. The image information is spread across different subbands. Out of many subbands, a few subbands may have significant information about the diagnostic features. A detailed study in these directions for diagnostic features is not available in the literature. Hence a systematic study can be carried out to investigate diagnostic features for clinically significant information in different subbands. The subband information can also be used for detection of features and detection of changes in the retina due to diabetic retinopathy. The information in subbands can be used for detection of glaucoma. The diagnostic information in the wavelet subbands can also be used for efficient remote diagnosis.

1.4 Organization of the thesis

The organization of the rest of the thesis is as follows: In this chapter, the retinal images are introduced and their clinical importance is discussed. A literature survey of retinal image analysis is also presented.

In **Chapter 2**, the motivation for multiscale analysis of fundus image is presented for analysis of retinal features.

In **Chapter 3**, multiscale analysis of different DR features is discussed. Diabetic retinopathy features such as microaneurysms, haemorrhages, and exudates are analyzed in different subbands of wavelet decomposition.

In **Chapter 4**, extraction of DR features from the fundus images is discussed. Here, independent component analysis (ICA) is used as a tool for extraction of exudates in subbands of wavelet decom-

position. This is also used as a tool for detection of a change in the color fundus image due to DR. This may help early diagnosis of the vision loss.

In **Chapter 5**, different methods of glaucoma assessment in multiscale are presented. Here, differential entropy (DE), principal component analysis (PCA)-linear discriminant analysis (LDA), and hidden Markov model (HMM)-singular value decomposition (SVD) based methods are discussed for glaucoma detection.

In **Chapter 6**, conclusions are drawn by summarizing the contributions of the work and mentioning some directions for future work.





2

Diagnostic feature analysis: A review

Contents

2.1	Multiscale analysis of features from fundus image	26
2.2	Wavelet filter for retinal image analysis	27
2.3	Detection of DR features	29
2.4	Detection of glaucoma	33
2.5	Motivation for the present work	39
2.6	Database	40

2. Diagnostic feature analysis: A review

Color fundus images are very important tools for diagnosis of the vision loss due to diabetic retinopathy (DR) and patient treatment. The advanced digital imaging and computing methods have the full potential in modern ophthalmology as it is dependent on color fundus images [77]. As mentioned earlier, the digital fundus photography is a common procedure in ophthalmology to capture retinal images. The retinal images, thus obtained are used by medical experts to diagnose and document diseases like DR or glaucoma. Sometimes, the images are further evaluated by automatic analysis tools to support the diagnosis. Good image quality, better segmentation of DR and glaucoma features are essential to ensure a reliable diagnosis. Due to this reason, the research field of retinal image analysis has attracted a lot of interest in the automated detection of DR. Landmark detection is also an area that has received considerable interest. Landmarks consist of blood vessels, the optic disc and the fovea. This chapter will start with a brief review of analysis of the landmarks in the multiscale domain with the detection of glaucoma. Most DR detection methods use automatic blood vessel detection as a prerequisite before identifying pathological entities.

A couple of studies have been published on the analysis of features of the fundus image. It should be noted that the word feature will be used in two different contexts. The word feature refers to those components that make up a feature set used for classification. Diabetic retinopathy features on the other hand refer to pathological features such as microaneurysms, haemorrhages and exudates.

This chapter presents a review of the diagnostic feature analysis due to DR and glaucoma. Section 2.1 presents the multiscale analysis of various features in fundus images. Wavelet filter for retinal images is discussed in Section 2.2. Diabetic retinopathy feature detection is discussed in Section 2.3. A brief discussion on glaucoma and methods for detection are discussed in Section 2.4. Section 2.5 presents the motivation.

2.1 Multiscale analysis of features from fundus image

Fundus image consists of normal features (such as: blood vessels, optic disc, fovea and macula) and DR based features (such as: microaneurysms, exudates, haemorrhages, and cotton wool spots etc.). Fundus images are subjected to various processing such as compression, transmission and filtering. Separation of information by choosing suitable bands in a multiscale representation can help effective processing of the image. Significance of suitable bands can be measured using the image quality measures such as accuracy, equal error rate (EER), universal quality index (UQI), and structural

similarity (SSIM) etc. The quality measures are either subjective measures or they are objective measures. Objective quality measures are preferred. Subjective quality measures consumes more time and difficult to analyze as the experts have to examine a large number of images and rate them. Multiresolution analysis (MRA) of wavelet produces the localized image features. Different features are detected in different scales as it allows to process the frequency information separately. It has been used in image de-noising and data compression [78]. In medical imaging the diagnostic information should be preserved during the selection of subbands.

Multiscale decomposition by wavelet transform helps producing localized image features with good space frequency resolution [79–81]. This spatial localization is found to be useful in analyzing the local spectral properties of particular regions like the anatomical structures in an image. A linear transformation is used by wavelet decomposition to split an image into subbands or subimages containing different frequency information. It allows the processing of different frequency information separately. The multiresolution property of the wavelet transform has been successfully used in many applications such as image de-noising, compression, data coding [82–85] and singularity detection [86,87]. This helps localize the diagnostic information in less number of coefficients. So, processing time reduces.

2.2 Wavelet filter for retinal image analysis

Features in an image can be defined in terms of a specific structure in the image data. Image feature extraction is one of the most important applications of wavelets. One feature is distinguished from the other features in the image by the discontinuities of the intensity. Discontinuities of the intensity represent the contours. Two issues are involved in wavelets for image processing applications, i.e., selection of of an *optimum decomposition level* and an *appropriate wavelet filter*. Image quality depends on the choice of a suitable wavelet filter and level of decomposition [88]. Different mother wavelet and decomposition level highlight different features due to the frequency distribution of the features. The smoothness of the different mother wavelet is characterized by their regularity. The performance of different wavelet filters is observed by decomposing the image into various levels using a particular type of wavelet filter. The quality of the reconstructed image is evaluated at each decomposition level by using various quality measures to quantify the effect of wavelet filters [84]. For retinal image analysis, the optimum decomposition level and a better suited wavelet filter can be

2. Diagnostic feature analysis: A review

chosen from the experimental observations.

For a particular diagnostic feature, it is expected that relatively more significant information is present in certain subbands than the other subbands. The diagnostic importance of each level subband is examined by zeroing the coefficients of the subbands at one level and keeping all other level subbands coefficients unchanged. The reconstructed image with the altered subbands is analyzed to visualize information about the diagnostic features. The original and the reconstructed images are examined visually and quantitatively to assess the image quality from the point of view of the different retinal features (such as: blood vessels, the macula and the optic disc). The blood vessel information in different wavelet subband is shown in Fig. 2.1. The retinal image taken from the DRIVE database is shown in Fig. 2.1(a) and is decomposed to 5-levels using the db4 mother wavelet. The decomposition produces one approximation (A) at final level and three detail bands (horizontal (H), vertical (V), diagonal (D)) at each level. The blood vessels are characterized by high frequency subbands and are represented by changes in intensity. The image in Fig. 2.1(b) is reconstructed by zeroing the highest frequency coefficients of decomposition level-1 ($L1$) subbands, i.e., $H(1)$, $V(1)$ and $D(1)$. In this image, the vessel structure is well reconstructed and the overall image quality is close to the original image. This implies that high frequency subbands, $H(1)$, $V(1)$ and $D(1)$ do not carry significant blood vessel information. The image in Fig. 2.1(c) is reconstructed after zeroing the coefficients of $L2$ subbands $H(2)$, $V(2)$ and $D(2)$. In this image the blood vessels are slightly blurred and thin blood vessels are disappearing, but still the details of main vessels are retained. It shows that second level subband coefficients contribute more information towards the thin vessels and little information on thick vessels. Fig. 2.1(d) is the reconstructed image after zeroing the level-3 ($L3$) subbands, $H(3)$, $V(3)$ and $D(3)$ coefficients. In this image the main thick vessels are blurred and most of the thin vessels are preserved. It is visualized that the image quality is low compared to that of Fig. 2.1(c). This shows that thick vessels are more sensitive than the thin vessels to changes in the third level subband coefficients, because the thick vessels constitute the low frequency components of the image relative to the thin vessels. Fig. 2.1(e) is the reconstructed image after zeroing the coefficients of level-4 ($L4$) subbands $H(4)$, $V(4)$, $D(4)$. In this image the thin vessels are clear and has little distortion in thick vessels. The vessel pattern is well preserved in Fig. 2.1(f), which is reconstructed by zeroing the coarsest subband $H(5)$, $V(5)$ and $D(5)$ coefficients. In this image a thin ring like appearance along the circular periphery of the field of view (FOV) is seen due to the loss of global information, luminance. It

retains the diagnostic quality of the image. The subbands of lower frequency ($L3$ and $L4$) hold more of thick vessel information and high frequency ($L2$) subbands carry information about fine structures such as thin vessels.

A few research works have been reported on wavelet based retinal image analysis [89, 90] using Daubechies4 (db4) mother wavelet filters. Quellec *et al.* [20] have used wavelet transform for detection of microaneurysm. Nirmala *et al.* [88] have studied the fundus features such as blood vessels, OD and macula. They quantified blood vessels information in different wavelet subbands. Significant information about the blood vessels, OD and macula is present in few subbands. In a retinal image, vessels have different widths or resolution. The main thick vessels, branch into thin vessels and spread all over the retina. Therefore multiresolution property of the wavelets can be used to analyze the vessel features as they have the directional property. The vessel details in different orientations can be observed as the two dimensional DWT. It can decompose the image into different frequency bands in several directions. According to vessel information content, the ascending order is level-1 ($L1$), level-5 ($L5$), level-4 ($L4$), level-3 ($L3$) and level-2 ($L2$). $L2$ has highest blood vessel information. $L3$ and $L2$ subbands contain significant information about OD and macula. $L4$ and $L5$ subband has minimum information about the macula. Systematic study of pathological features such as microaneurysms, exudates, cupping in OD, and drusen are not studied in wavelet domain. Here, the pathological features are studied in multiscale. As few coefficients are associated in the wavelet subband, analysis of diagnostic features in wavelet subband will help efficient analysis, faster processing, storage and transmission. This information can be used for glaucoma estimation as well as pathological feature detection by using ICA.

2.3 Detection of DR features

Segmentation of DR features provides the progression of retinal disorders. At the initial stage of DR, blood vessels are affected. Blood vessel detection is performed prior to the detection of pathologies. Number of methods are reported for detection and extraction of exudates from color fundus images. Li and Chutatape [91] have used Kirsch's method, which uses a 3×3 image mask for extraction of exudates. Walter *et al.* [21, 25] identify the exudates by using a high grey level threshold near the macula region. The boundary is demarcated by morphological operation. This method has limitation to distinguish between the soft and the hard exudates. Fuzzy c-means clustering followed by color

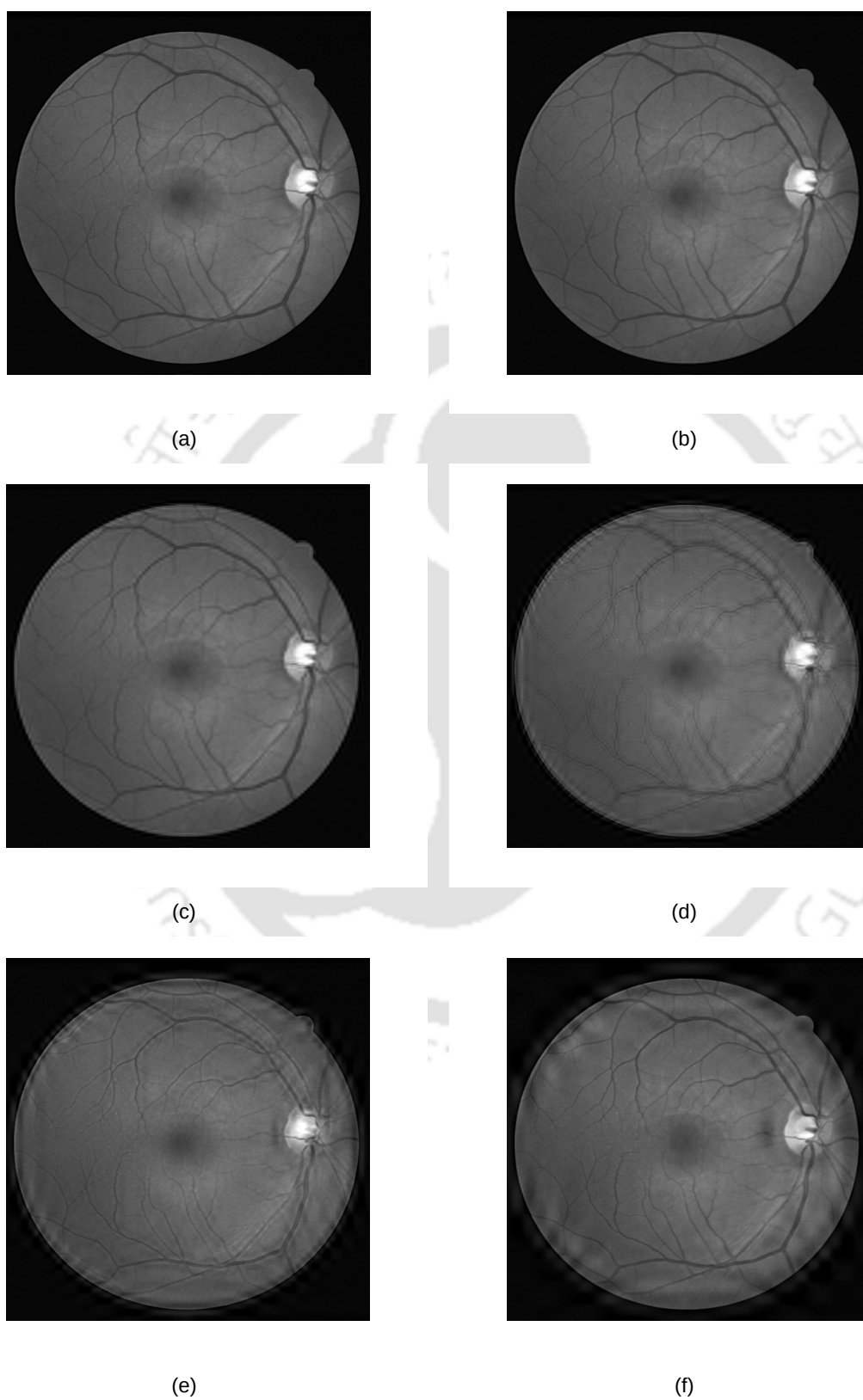


Figure 2.1: (a) Original image and reconstructed images when subband coefficients of (b) L1, (c) L2, (d) L3, (e) L4 and (f) L5 are made zero.

normalization and contrast enhancement is used by Osareh *et al.* [22] for detection of exudates.

The mathematical morphology technique is used by Spencer, Cree, Frame, and co-workers [92,93] for eliminating the blood vessels from fundus images that left the microaneurysms untouched. The mathematical morphology based method is used by Kande *et al.* for automatic detection of microaneurysms and haemorrhages [94]. They have used the morphological top hat transformation for the detection of red lesions. Sopharak *et al.* uses a hybrid method for extraction of microaneurysms from non-dilated diabetic retinopathy images [95]. They have applied the preprocessing such as median filtering, CLAHE, shade correction to the green channel image. From the preprocessed images exudates and vessels are removed. Then mathematical morphology is applied to the images for extraction of the microaneurysm candidates. Fine segmentation is obtained by the Naive Bayes classifier. The Radon Cliff Operator is used by Giancardo and co-workers for detection of microaneurysms from color fundus images [96]. Radon cliff transform has the advantages to detect single noisy Gaussian-like circular structures, regardless of their size or strength.

Presence of exudates in the macular region leads to diabetic macular edema and severe vision loss. Walter *et al.* have detected the optic disc before the extraction of exudates by mathematical morphology based method [21]. Optic disc has been extracted by applying watershed segmentation on the luminance channel. To this morphological closing is applied to find the exudate candidates. Sopharak *et al.* used mathematical morphology, along with optic disc detection for detection of exudates [97]. They have applied median filtering on the HSI image for the reduction of noise. The local contrast is enhanced by using contrast adaptive histogram equalization. The optic disc is extracted from the preprocessed image. By applying the mathematical repetitive dilation, the exudates are extracted.

Rokade and Manza extracted the exudates by using the Haar wavelet [98]. They have performed the color normalization on the green channel image. The optic disc from the processed image was extracted by mathematical erosion and dilation operation. Then contrast limited adaptive histogram equalization is applied to the image. Then by applying threshold the exudates are extracted. Haar wavelet is used for the purpose of decomposition and classification. Sanchez *et al.* used fisher discriminant analysis to classify the exudates from the color fundus image [74]. They have used color normalization followed by feature selection. A quantitative metric is defined to estimate the class separability of exudates and non-exudates pixels by using within-class and between classes scatter

2. Diagnostic feature analysis: A review

matrices. A high value of the quantitative matrix represents the classes to be separated. They have used the selection of candidates by using mathematical morphology and optic disc by using Hough transform. Sanchez et al. define a mixture model for estimating the probabilities in order to threshold the exudates dynamically from the images [74]. They have defined preprocessing followed by mixture model histogram for exudate candidate extraction.

The wavelet transform is used by Nirmala *et al.* [88] to quantify blood vessel information in different subbands. The different DR features are detected by separate segmentation algorithms. It consumes more time. No literature is available for detection of changes in the retina due to DR. The information in different wavelet subbands is assumed as independent and ICA can be used for segmentation of features. For better detection of pathological features and detection of changes in the retina due to DR, the proposed work utilizes the ICA on multiscale domain.

Independent component analysis (ICA): It is a statistical method, which is used for separating independent components or latent variables from mixture without any apriori knowledge about the independent components (ICs) [99,100]. The ICs or independent sources are independent and they are non-Gaussian in nature. The simplest ICA model can be represented by a mixing equation in which the mixture is a linear representation of independent signals given as:

$$\mathbf{x}(t) = M\mathbf{s}(t) \quad (2.1)$$

where, $\mathbf{s}(t) = s_1(t), \dots, s_q(t)$ is an $q \times 1$ column vector. The source signal, $\mathbf{x}(t) = x_1(t), \dots, x_p(t)$ collects the 'p' observed signals, mixing matrix M contains the mixture coefficients. ICA estimates a separating matrix W , which estimates the source signals $\mathbf{s}(t)$ and represented as:

$$\hat{\mathbf{s}}(t) = W\mathbf{x}(t) \quad (2.2)$$

where $\hat{\mathbf{s}}(t)$ represents the estimate of source signal. The separating matrix W is the inverse of mixing matrix M , for better separation of independent signals. In reality it is not exactly an inverse. Separating matrix W is computed by using some apriori information about the probability distribution of the inputs such that it maximizes the non-Gaussianity between the sources.

Number of sensors must be equal or greater than the number of sources which is the criteria for ICA to work. In practice, the number of sources is equal to the number of sensors. The signal coming from each sensor consists of ICs with different mixing ratios. In some practical situations,

it is difficult to arrange so many sensors to fulfill the condition of ICA. In case of functional-MRI (fMRI) data collection, it is difficult to install too many sensors in the brain. Such situations can be handled by undetermined ICA [101]. But in ECG the aim is to extract the ICs from the single channel recording. It helps detect the artifact. The detection of artifact from single channel signal can be found by single channel ICA [102]. The main limitation of single channel ICA is that the algorithm assumes the sources as stationary and disjoint. ICA has been used for images for feature extraction [103], information mining [104]. Medical signals (EEG, ECG, fMRI and fundus image) are associated with noise. So, the application of the ICA algorithm to a noisy data, making the system over-fitting for estimation of the sources. So, before applying ICA, the noise from the data needs to be removed. Low pass filtering overcomes this problem by reducing the information in the data, which leads to reduction in the independence of the sources. Wavelet transform overcomes the limitations of the low pass filter. Filtering in wavelet domain helps de-correlate the data as well as it increases the independence of the sources [45]. Multiscale decomposition by wavelet transform localized the image features with good space frequency resolution [79–81]. This spatial localization is found to be useful in analyzing the anatomical structures of an image. Multiscale ICA overcomes the problem associated with the single channel ICA. By multiscale decomposition, the single channel signal is decomposed into different spectral modes. The ICA applies to the decomposed signals/images for detection of artifacts/changes.

Independent component analysis can be used in the data matrix formed by the subbands of wavelet decomposition for segmentation of exudates and detection of changes in the retina due to DR. The process consists of three important blocks such as multiscale decomposition block, formation of data matrix block, and ICA block. ICA on wavelet scale provides the advantage of detecting changes in the retina due to DR and gives a knowledge on the progression of the disease. In case of detection of change from color fundus images the normal fundus image is compared with the DR affected image by ICA in multiscale domain. Analyzing the number of features on the retina, the condition of the retina can be predicted.

2.4 Detection of glaucoma

The disc is an inaccurate term to explain OD, as it is a 3-dimensional (3D) structure. Optic nerve lies between the retina and chiasm, which has four parts, such as: intraocular (the optic nerve head),

2. Diagnostic feature analysis: A review

intraorbital (between globe and optic canal), intra canalicular (within the optic canal), and intracranial (between optic canal and chiasm). The OD is characterized by color, contour, and a cup. The typical color of OD is orange-pink with a pale center. Due to optic atrophy (such as: glaucoma, optic neuritis, arteritic or non-arteritic ischemic optic neuropathy, or a compressive lesion) the orange pink color gradually disappears and appears pale. The healthy OD border is clear and well defined. It swells in case of papilloedema and becomes blurred in the presence of optic disc drusen. The central depression of the OD is known as the cup. It lacks of neuroretinal nerve fibres. It looks pale in color. The cup height is one third of the height of the entire disc for normal disc and gradually increases during optic atrophy. The optic nerve head is that area of the retina where nerve fibres and blood vessels exit the eye. It carries the electrical impulses to the brain for visual processing and is sensitive to the changes due to intraocular pressure (IOP) and associated with glaucoma.

Diagnosis of glaucoma is done on the basis of measurement of increased IOP, visual field test, condition of the optic nerve, and observation of a variety of possible symptoms. These symptoms decrease the ability to see objects that are not straight ahead, ability to perceive motion and to recognize color, [105] etc. Increased IOP damages the cells, which causes vision loss. IOP [106] lies between 17 millimetre of mercury (mmHg) to 21 mmHg for normal eye. Greater than 21 mmHg IOP is too high for the optic nerve cells to tolerate. It does not do any damage to the vision for entire humanity. Tonometry (Goldman Applanation Tonometry and Tonopen or non contact Tonometry) is used for measuring IOP. IOP cannot be used as a standard measure for glaucoma as tissue damage does not have a direct relation with IOP. So, detection of vision loss or glaucoma related to IOP is not always accurate.

Visual field test, which is a more specific indicator than IOP is measured by perimetry [107]. It documents the level of peripheral vision loss. In perimetry, the patient responds to a perceived flash of light by looking ahead every time. So, the accuracy of the testing of glaucoma depends on patients patience, attention and retinal sensitivity. Glaucoma cannot be guaranteed by the measurement of IOP and peripheral vision test as these measures require patient's attention and patience. The appearance of OD for assessment of glaucoma is independent of the whims of the patient, but it depends on the whims of the clinician [108, 109]. Due to these reasons, it is treated as the most useful indicator of glaucoma and its progression. Evaluation of glaucoma requires disc evaluation with a lot clinical experience. Analysis of the appearance of OD helps post diagnosis.

Optic nerve damage can be seen in the form of cupping of the OD. The size of the cup is related to the presence or absence of glaucoma. Larger the cup of the optic nerve, the greater is the likelihood that the person has glaucoma. Damages of nerve fibre occur over a longer period (10 - 30 years). So, decrease in vision loss cannot be noticed over half of the nerve fibres. The nasal side vision is lost first and peripheral vision loss occurs in the last. A thorough examination of the patient's IOP, visual field, family background and condition of the optic nerve will help the doctors to advise an appropriate treatment plan for reducing further damage of the nerve fibres. Symptoms are more important than signs. Headache during reading, blurred vision, eye aches after strong exercise, poor color perception and trouble in night are some important symptoms to be looked during the study of glaucoma. Analysis of OD is possible for the color fundus images which are taken by Heidelberg Retina Tomography (HRT) and Optical Coherence Tomography (OCT).

Appearance of OD changes during glaucoma. In the early stage of glaucoma the changes are subtle and may appear similar to that of normal OD. Gradually the cup size increases with the progression of diseases. In early 70's Armaly introduced the idea of a cup-area-to-disc-area ratio or cup to disc ratio (CDR) for assessment of glaucoma [110]. It is commonly used in clinics to classify glaucoma. For normal discs, it lies in the range of 0.3 to 0.5 and for glaucoma, it is greater than 0.5. The sight of vision is lost completely in the CDR value of 0.8. For some normal human beings CDR value lies from 0.4 to 0.6. The variation in the OD size occurs due to myopic disc and hypermetropic disc. For myopic the disc is normal, where as hypermetropic disc, there is an extensive damage of nerve-fibres. In some situations, one disc is normal and the other disc is grossly diseased but both having same CDR. So, the specific pattern of changes in the OD is used for evidence of glaucoma or progression of glaucoma with CDR. Features like focal glaucomatous optic discs, migraine, vasospasm, myopic glaucomatous discs, senile sclerotic and generalized cup enlargement are considered during assessment of glaucoma. The neuroretinal rim pattern of thickness (normal disc: inferior is thicker to superior) and areas of focal thinning (normal disc: nasal is thinner to temporal) are used for detecting glaucoma. Another characteristic of glaucoma is focal notching and during which the neuroretinal rim is absent. It is associated with peripapillary atrophy (PPA). PPA causes rim loss in case of glaucoma during the normal ageing process and high myopia. It is present with full 360 degree. Senile sclerotic discs have a shallow cup with mild sloping sides and a moth eaten neuroretinal rim. Loss of the retinal nerve fibre layer (RNFL) makes the cup to expand. The different features of the OD are shown

in Figure 2.2.

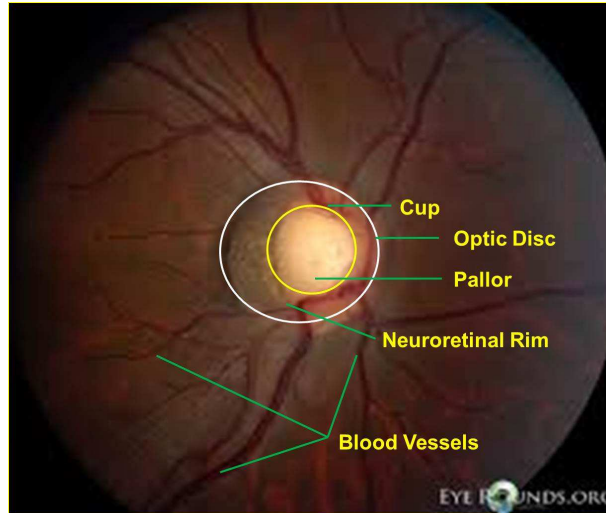


Figure 2.2: Different parts of OD [3].

Reliable method for glaucoma diagnosis is possible by investigating the retina from the fundus image and the techniques are discussed below. Gloster and Parry use the fundus image photographs for measuring the cupping in the OD for evaluation of glaucoma [111]. The degree of visual damage can be known from the appearance of OD. Parameters such as, cup horizontal diameter to disc horizontal diameter, cup diameter to disc diameter, CDR, and cup vertical diameter to disc vertical diameter etc. are used for classification of glaucoma. Correlation between neuroretinal rim area and age in normal subjects is used by Funk *et al.* [112] and Pueyo *et al.* [113] for estimation of glaucoma.

Corona *et al.* to overcome certain limitations for evaluation of glaucoma (such as: difficulty in interpretation of retinal images, intra and inter-observer variability, lack of proper standardization for evaluation of OD size and shape) generate precise metrics from the stereo OD image pairs by using a digital stereo vision system for visualization of the structure of ONH [114]. They have found the 3-D surface from the 2-D stereo images. The depth information is found out by power spectrum and zero mean normalized cross correlation.

Low order Zernike moments capture the gross features information from an image where as high order Zernike moments resolves the high frequency information. These features are used for classifying the glaucoma images from the normal images. Zernike moments are used by McIntyre

et al. for classifying the condition of the OD by using linear discriminant function derived from linear perceptron (supervised learning) [115].

Fink *et al.* used ICA for feature extraction from color fundus images and k-nearest neighbor classifier (KNN) for glaucoma classification [116]. ICA finds the OD features, which are classified by KNN classifier. ICA finds the basis images which represent the independent feature characteristic of the observed retinal images of the papilla. The corresponding coefficients of basis images have been learned from a training dataset. Then classification is done by KNN classifier.

ARGALI, an automatic cup to disc ratio measurement system is developed Wong *et al.* for glaucoma detection and analysis [117]. ARGALI technique uses color histogram analysis and level set method for detection of the cup and the disc of the color fundus images and CDR is calculated. It varies for different images due to their variability. The obtained CDR by different methods is merged by adaptive neural network for glaucoma detection.

Nayak *et al.* have used CDR, the ratio of the distance between OD center and optic nerve head to the diameter of OD, and blood vessel area in the inferior-superior side to the nasal temporal side (ISTN) for classifying the normal and glaucoma images by using neural network classifiers [118]. Jimenez *et al.* use multi-focal electroretinography (ERG) for studying the structural pattern of the retina for early diagnosis of glaucoma [119]. ERG is a recording of the bioelectric signals obtained due to summed activity of the retina cells. The authors have studied the peak amplitude and maximum latencies in wavelet domain for finding the diagnostic information.

Hatanaka *et al.* measure the CDR based online profile analysis in retinal images for early detection of glaucoma [120]. Here, blue channel of the color fundus image is used, as it has a higher contrast between the cup and rim regions. Zero crossing method is used to find the cup edge. The authors found CDR by measuring the ratio of cup diameter to disc diameter after segmenting the blood vessels erased OD from the color fundus images. Number of sliding windows (ellipse) of various sizes are used by Xu *et al.* to obtain the cup features in the OD [121]. These features are ranked by support vector machine (SVM) using radial basis function (RBF).

Information theory based method, minimum redundancy maximum relevance (MRMR) is used by Zhang *et al.* for automatic diagnosis of glaucoma from color fundus images [122]. This method uses one fourth of the features for classification. This method provides the maximum relevant and minimum redundant features based on the mutual information quotient. The classification is performed by

2. Diagnostic feature analysis: A review

adaptive boosting, SVM, linear discriminant analysis (LDA) and MRMR optimized classifiers. The authors use 23 features for glaucoma analysis, such as: vertical cup-disc ratio, ocular hypertension, alpha PPA at the optic nerve, area of the optic cup, rim inferior width, medical history of glaucoma, rim temporal width, rim thickness of inferior $\geq$ superior $\geq$ nasal $\geq$ temporal (ISNT) rule compliance, optic cup height, rim superior width, retinal nerve fibre layer defect, age of screening, right eye ocular hypertension, job category, anisometropia indication, diabetic retinopathy level, rim nasal width, eye history of retinopathy, PPA info, overall ocular hypertension, optic disc area, self reported heart attack and race category.

Bock *et al.* used PCA for data reduction and SVM classifier for glaucoma classification [15]. The images are preprocessed to have the details of the OD and the features are obtained by PCA. By using SVM classifier the images are classified into one of the class, such as glaucoma or non glaucoma. The preprocessing step consists of removal of blood vessels, illumination correction and optic head normalization. Then features of preprocessed images are obtained by PCA. Classification is done by SVM classifier. The images are classified to either glaucoma or non-glaucoma images. Bock *et al.* has found the glaucoma risk index (GRI) by combining the different feature types such as FFT, B-spline and PCA.

Joshi *et al.* have proposed a novel method for cup and OD segmentation method based on vessel bends at the cup boundary from the monocular color retinal images, which gives a 2-D projection of retinal structures [123]. It overcomes the limitations of OD segmentation. Authors segment the OD based on region based active contour model. Vessel bends and pallor information is used for segmentation of the cup.

Limitation of glaucoma detection: Measurement of CDR is most commonly used for glaucoma diagnosis in the literature. In this case, the cup and the OD are segmented for calculation of CDR and determination of glaucoma. The basic steps used in this method are preprocessing of the green channel image, illumination correction, blood vessel removal, detection of the cup and OD, calculation of CDR and detection of glaucoma. In some glaucoma cases, the cup and disc are not distinguished clearly as shown in Fig. 2.3(c) and Fig. 2.3(d). In such cases, CDR cannot be used as a measure for glaucoma. The information regarding the changes in cup size is most vital for assessment of glaucoma.

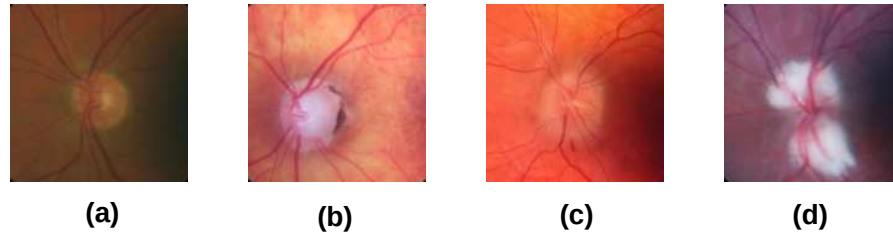


Figure 2.3: Different types of disc: (a) normal disc, (b) glaucoma disc with increase in cup size, (c) glaucoma with inflamed disc (d) glaucoma with disc anomalies.

2.5 Motivation for the present work

The medical images are subjected to different processing. The clinical utility depends on the quality of the processed images. The processing should ensure minimum loss of clinically useful information for correct and efficient assessment of medical images. In fundus image the normal features (such as blood vessels, OD and macula) are analyzed in multiscale [88]. The pathological features due to diabetic retinopathy (such as microaneurysms and exudates) are not analyzed in multiscale. It is necessary to analyze the pathological features from the diagnostic point of view. This may help with the grading of the disease due to diabetes. Different features are distributed in different scales in multiscale decomposition. The different DR features can be analyzed by MRA. Selection of wavelet subbands may be done by both objective and subjective measures.

Due to frequency localization, ICA can be used in the mixing matrix formed by the wavelet subbands of wavelet decomposition for detection of pathological features and detection of changes in the retina due to diabetes. The data matrix is formed by considering the different wavelet subbands of wavelet decomposition to which ICA is applied. Depending upon the statistical nature of the features, the DR features can be separated out. For detection of changes in the fundus image due to DR, data matrix is formed by considering the normal retina and disease retina in multiscale. The changes in the retina appeared as separate non-Gaussian signal and can be separated out by ICA.

Differential entropy (DE) finds the information present in the image. This can be used for estimation of glaucoma in multiscale. This may overcome the limitation of glaucoma estimation by calculating CDR. In this case, the cup region of the retina can be used in wavelet domain for find-

2. Diagnostic feature analysis: A review

ing the information about the cup. This can overcome the limitation of disc anomalies and inflamed disc. The patterns of the cup change in glaucoma. So, machine learning algorithms can be used for classification.

In this thesis work, the following investigations are undertaken.

- **To study and analyze the DR features in wavelet subbands**

The method uses the DWT to decompose the image into different levels. The contribution of each level subbands towards the image information is different. In the present work, two methods are proposed to examine the significance of a particular level subbands from the point of view of DR features. Here, MAs, exudates are studied in different wavelet subbands.

- In the first method, we are considering one level subband coefficients at a time by zeroing the other levels subbands coefficients.
- In the second method, the coefficients of one level wavelet subbands coefficients are made zero and all other levels of wavelet subbands coefficients are present.

- **Extraction of DR features**

Here, the following DR features are extracted.

- The blood vessels are extracted by Krisch and Gaussian matched filter method. The segmented blood vessels are used for inpainting and finding the percentage blood vessels damaged by pathologies.
- ICA is used as a tool for extraction of exudates in wavelet subbands.
- The changes in fundus image are detected by using ICA on wavelet scale.

- **Glaucoma detection**

Here, differential entropy (DE) and patterns of cup is used for detection of glaucoma. DE is calculated in wavelet subband for calculation of glaucoma. The patterns of the cup are used by machine learning approach for glaucoma classification.

2.6 Database

Methods are tested on the images of publicly available Digital retinal image for vessel extraction (DRIVE) database [124], Aria database [125], Messidor database [126] and Glaucoma database [TH-1619_09610207](#)

[16]. The databases have sufficient variation in color, illumination and quality. The DRIVE database contains 40 test images, compressed in TIF format of 768×584 pixels, 8 bits per color plane. The 40 images are divided into test set and training set, each of which contains 20 images. For each image in the test set and the training set manual segmentation data is available.

The ARIA database was collected from St. Pauls eye unit and the university of Liverpool by Zeiss-FF450+ fundus camera with 45 degree field of view (FOV). The Aria database consists of 58 pathological images with 768×576 pixels in JPEG format [125].

Forty Nine images are available from Glaucoma database obtained from an optic-disc organization. It consists of 8 normal images and 41 glaucoma images of dimension of 640×427 pixels in JPEG format. The Messidor [126] retinal images are divided into 4 zipped subsets containing each 100 images, with 1488×2240 pixels in TIF format. The images are acquired with pupil dilation and without pupil dilation.

The STARE database [43] contains 20 images, with 605×700 pixels, 8 bits per color channel. Ten of these contain pathology. These images are captured by a TopCon TRV-50 fundus camera at 35 degree field of view.



3

Multiscale analysis of diagnostic features of retinal images

Contents

3.1 Multiscale decomposition	45
3.2 DR features in wavelet subbands	47
3.3 Quantitative evaluation	64
3.4 Performance evaluation	68
3.5 Summary	78

3. Multiscale analysis of diagnostic features of retinal images

Wavelet analysis is performed by projecting the signal on the wavelet function. Complex wavelet transform with the complex-valued extension to the standard discrete wavelet transform (DWT) are the third generation wavelet transforms. This is typically two-dimensional wavelet transform deployed for the multi-resolution, sparse representation, and useful feature characterization based on the structure of an image. The major advantages of these WTs are that they do not exhibit oscillations, lack of directives, aliasing and degree of shift-variance in their magnitudes. But, the major disadvantages are that they exhibit two dimensions of the signal being transformed and yield the redundancy compared to a separable. These WTs are still under research and applied to specific applications such as human vision characterization, frequency localization, feature extraction, seismic analysis, bio-medical analysis and so on.

Multiscale analysis represents the hierarchy of structural implementation to enhance the physical characteristics of the signal (both 1D and 2D). When the wavelet decomposition stage/level of multiscale analysis is increased then it provides finer resolution from coarse resolution. In other words, it is the systematic process to analyze signal/image at the lower multiscale stage with coarse resolution and then the higher multiscale stage with fine resolution. Thus, higher stage of the multiscale analysis using wavelets provides significant multiresolution improving signal quality. It has the advantage of processes different frequencies in a different way. By using this technique, the time resolution is increased when we analyse a high frequency portion of the signal, and the frequency localization is increased when analyzing a low-frequency part of the same signal. This type of analysis is suitable for signals that have both low-frequency components with long time duration and high-frequency components with short time duration, which is the case of most signals.

Multiscale analysis helps work with less number of coefficients. It reduces the computational time and makes the algorithm efficient and faster as very few coefficients contain the information about the feature. Due to this property it is used for many applications. Multi resolution property is already used by Nirmala *et al.* [88] to study the various normal fundus image features such as blood vessels, OD and macula in wavelet scale. From their study, they concluded that very few subbands are responsible for the feature information in the fundus image. She observed that the level-2 (L_2) has the highest blood vessel information. Level-3 (L_3) and L_2 subbands contain significant information about the OD and the macula. Level-4 (L_4) and level-5 (L_5) wavelet subbands are shown to have minimum information about the macula.

Systematic study of pathological features such as microaneurysms, exudates, cupping in OD, and drusen is not carried out in wavelet domain. Diabetic retinopathy is recognized from the pathological features on the retina, such as red lesions (microaneurysms, small intra retinal dot haemorrhages, larger blot haemorrhages), white lesions (exudates and cotton wool spots) [19] etc. In the latter stage of DR, new vessels grow in order to nourish the retina. These pathological features differ not only from each other, but also from the normal anatomical features in terms of their frequency characteristics and spatial locations. Multiscale analysis of fundus images with pathological features can help provide useful information. These information can be helpful in better detection of the features and can help improve automated diagnosis of pathologies.

This chapter presents multiscale analysis of pathological fundus features. Section 3.1 discusses about the multiscale decomposition. The information of pathological features in different wavelet subbands is evaluated and analyzed in Section 3.2. Section 3.3 presents the quantitative evaluation. Various statistical measures along with subjective measure are used for evaluation of pathological features in different subbands. The significance of different subbands for the pathological features is established using the above measures. This has been discussed in Section 3.4. The summary of this chapter is given in Section 3.5.

3.1 Multiscale decomposition

The important aspect of medical images is that the information of interest is often a set of features that are spatially localized. Multiscale transform is the most popular multiresolution analysis (MRA) technique, which segregates the information of an image into a different wavelet subband matrix depending on the frequency [80]. In 2D discrete wavelet transform (DWT), the image is decomposed into one low frequency approximation (A) subband and three high frequency detail subbands such as horizontal (H) subband, vertical (V) subband, and diagonal (D) subband. The scaling and wavelet function in 2D at a resolution level i can be represented by

$$\phi_{i,m,n}(x,y) = 2^{i/2} \phi(2^i x - m, 2^i y - n) \quad (3.1)$$

$$\psi_{i,m,n}^b(x,y) = 2^{i/2} \psi^b(2^i x - m, 2^i y - n) \quad (3.2)$$

where, b represents the subbands H, V, and D. The DWT of an image $p(x,y)$ of size $(P \times Q)$ can

3. Multiscale analysis of diagnostic features of retinal images

be defined as:

$$WT_\phi(i_0, m, n) = \frac{1}{\sqrt{PQ}} \sum_{x=0}^{P-1} \sum_{y=0}^{Q-1} p(x, y) \phi_{i_0, m, n}(x, y) \quad (3.3)$$

$$WT_\psi^b(i, m, n) = \frac{1}{\sqrt{PQ}} \sum_{x=0}^{P-1} \sum_{y=0}^{Q-1} p(x, y) \psi_{i, m, n}^b(x, y) \quad (3.4)$$

where, i_0 is an arbitrary starting level/scale and the $WT_\phi(i_0, m, n)$ coefficients define approximation of $p(x, y)$ at scale i_0 . Here, (m, n) determines the position of wavelet function. The $WT_\psi^b(i, m, n)$ defines horizontal, vertical, diagonal details for scales $i \geq i_0$. Given WT_ϕ and WT_ψ^b of Eqs. (3.3) and (3.4), $p(x, y)$ is obtained via inverse DWT as:

$$p(x, y) = \frac{1}{\sqrt{PQ}} \sum_m \sum_n WT_\phi(i_0, m, n) \phi_{i_0, m, n}(x, y) + \frac{1}{\sqrt{PQ}} \sum_{b=H,V,D} \sum_{i \geq i_0} \sum_m \sum_n WT_\psi^b(i, m, n) \psi_{i, m, n}^b(x, y) \quad (3.5)$$

A N-level DWT gives rise to $(3N+1)$ subbands, one approximation band at the final level of decomposition and three detail bands (H, V, and D) at each level. The coefficients of approximation band and the detail bands of each level form the feature vector. Wavelet subbands highlight different information of features in an image [20, 88]. This information is used for finding/detecting the features.

Features in an image can be defined in terms of a specific structure in the image data. Image feature extraction is one of the most important applications of wavelets. One feature is distinguished from the other features in the image by the discontinuities of the intensity. Two issues are involved in wavelets for image processing applications, i.e., selection of an *optimum decomposition level* and an *appropriate wavelet filter* [88]. Different mother wavelets and decomposition levels highlight different features due to the frequency distribution of the features. Mother wavelets are characterized by their regularity, which describes the smoothness of the wavelet. The performance of different wavelet filters is observed by decomposing the image into various levels. The quality of the reconstructed image is evaluated at each decomposition level. Various quality measures can be used to quantify the effect of wavelet filters [84]. In this work, Daubechies4 (db4) mother wavelet is used. Subjective evaluation is based on the visual quality of reconstructed images. The optimum decomposition level and a better suited wavelet filter for retinal image analysis can be chosen from the experimental observations. The next section deals with the analysis of pathological retinal features in different wavelet subbands.

3.2 DR features in wavelet subbands

This section presents the analysis of pathological features at different decomposition levels. The wavelet decomposition of an image produces several sub-images which consist of different wavelet subband coefficients. Each wavelet subband contains information in a specific direction and along a specific scale/frequency. The advantage of using the wavelet transform is the possibility of spectral segmentation of the image features [127]. The research works related to wavelet transform based retinal image analysis focussed on the use of processed retinal image for different applications [20, 47, 88]. In this work, the importance of a wavelet subband in representing pathological features is investigated.

For analysis of pathological features in the color fundus images, different levels of decomposition are performed on the retinal images generating *detail subbands* and one *approximation subband*. The detail subbands can be put into different groups according to the levels of transformation: level-1 (L1), level-2 (L2), level-3 (L3), level-4 (L4), level-5 (L5) and so on. Each of the wavelet subband contains information about the retinal image [128]. The detail coefficients may provide vital information about the localized features of the retinal image. The approximation coefficients represent the slowly varying low frequency background of the retinal image. The proposed method for DR feature analysis in wavelet subband is discussed in subsection 3.2.1. Among the DR features exudates, microaneurysms and haemorrhages are the main diagnostic features.

3.2.1 Proposed method for analysis

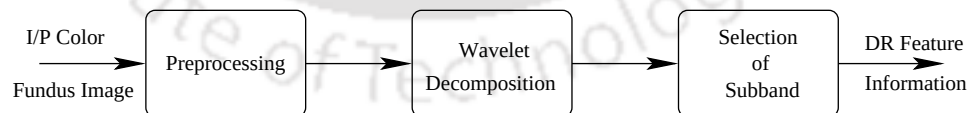


Figure 3.1: Block diagram for multiscale analysis of DR features.

The block diagram for multiscale analysis of DR features is shown in Fig. 3.1. The important steps are preprocessing, wavelet decomposition and selection of particular wavelet subband. In preprocessing, the green channel of the color fundus image is considered for the DR feature analysis as the green channel of the color fundus image has higher contrast between the DR features and the background. Illumination correction is done by subtracting the mean value of the image from the

3. Multiscale analysis of diagnostic features of retinal images

image. It provides homogeneous background. Histogram equalization is applied to the illumination corrected image to have a uniform distribution of energy.

Wavelet decomposition is applied to the preprocessed image. It is essential to know the significance of each level wavelet decomposition and in each wavelet subband from the point of view of the presence of diagnostic information or pathological feature. It is expected that certain wavelet subbands may contain relatively more diagnostic information than the other wavelet subbands. The diagnostic importance of each subband is examined by zeroing the coefficients of one level subband and retaining all other level subband coefficients. The effect of a particular level subband is analyzed by reconstructing the image with the altered subbands. The original and the reconstructed images are visually examined to assess the image quality from the point of view of pathological features. The DR features are also evaluated using different performance measures. From the appearance of the DR features and the performance measure, the significance of the wavelet subband is established.

3.2.2 Analysis of microaneurysms and haemorrhages

Microaneurysms appear as small red dots near the blood vessels. In the green channel image they appear as darker spots compared to the background. Haemorrhages appear as red cluster / patches in the retinal image. They look like a darker patch. The diagnostic importance of each wavelet subband is examined by zeroing the coefficient of one wavelet subband and keeping all other wavelet subbands undisturbed. In the literature 5-level wavelet decomposition has used Daubechies4 (db4) mother wavelet for analysis of normal retinal features [88].

The db4 is near symmetric compared to db2 and smooth. It is a compactly supported orthonormal wavelet. So, it is suitable for biomedical image and signal processing [129]. Daubechies4 mother wavelet is considered as it is closely matched with the signal to be processed. Daubechies4 mother wavelet is orthogonal and has finite vanishing moments, i.e., compact support [130]. This property ensures that the number of non-zero coefficients in the associated filter is finite. This is very useful for local analysis. Analysis of diagnostic feature is more important compared to the normal features. This is the reason we used db4 in our analysis. This mother wavelet has also been used in earlier studies. For example: Nirmala et al. have used this for the study of wavelet weighted blood vessel distortion measure for retinal images [88]. Chi et al. [131] have used Daubechies mother wavelet on hidden Markov tree model for retinal image de-noising. They have found the dependence and correlation of fundus angiography images in different wavelet scales. The edge information was preserved by the

implementation of Bayesian estimation. They have used this wavelet as this is easy to calculate. For an efficient analysis of the diagnostic features, different levels of decomposition are performed. In some cases, specific levels are selected to find the features in the band. In this study, 3-, 5-, 7- and 9- levels of wavelet decomposition are used. The experiment is performed on sixty images having microaneurysms.

Haemorrhages and microaneurysms are similar in color as that of the blood vessel. Before analyzing these features they are cropped from the other regions of the retinal image to have a detail information. Green channel image is moderately saturated compared to the blue channel and red channel images. With green channel image features like microaneurysms and haemorrhages, and the background has higher contrast. Red channel is under saturated, whereas blue channel is over saturated. In order to increase the contrast between the features and the background, the green channel image is added to the blue channel image. Fig. 3.2 shows the DR features, microaneurysms and haemorrhages, and the background. In the following discussions, the microaneurysms and the haemorrhages are referred as DR features. Cropped color fundus image having DR features is shown in Fig. 3.2(a). Red channel, green channel and blue channel images are shown in Fig. 3.2(b), Fig. 3.2(c), Fig. 3.2(d), respectively. In red and blue channels, the DR features are not visible. Good contrast is available in the green channel image as shown in Fig. 3.2(c). In order to increase the contrast between the features and the background, the pixel values of the green channel image are added to the pixel values of the blue channel image. This makes the background white, so the features can be easily visible as shown in Fig. 3.2(f). By subtracting the green channel image from the red channel image the contrast between the features and the background reduces, which is shown in Fig. 3.2(e). Wavelet transform is applied to the high contrast image for multiresolution analysis (MRA). Different levels of wavelet transform are performed on this image and the wavelet subbands are analyzed. In each level of wavelet decomposition the DR features are analyzed in two ways. In the first case, the image is reconstructed by making one level subband coefficients to zero without altering the coefficients of other level subbands. On the other way, subband coefficients are kept and all other subband coefficients are made zero. These above two methods/procedures provide the information regarding the subbands having higher information about the DR features.

Fig. 3.3 shows results for a three level wavelet decomposition. The decomposition process generates one approximation band at the third level of decomposition and three detail subbands at

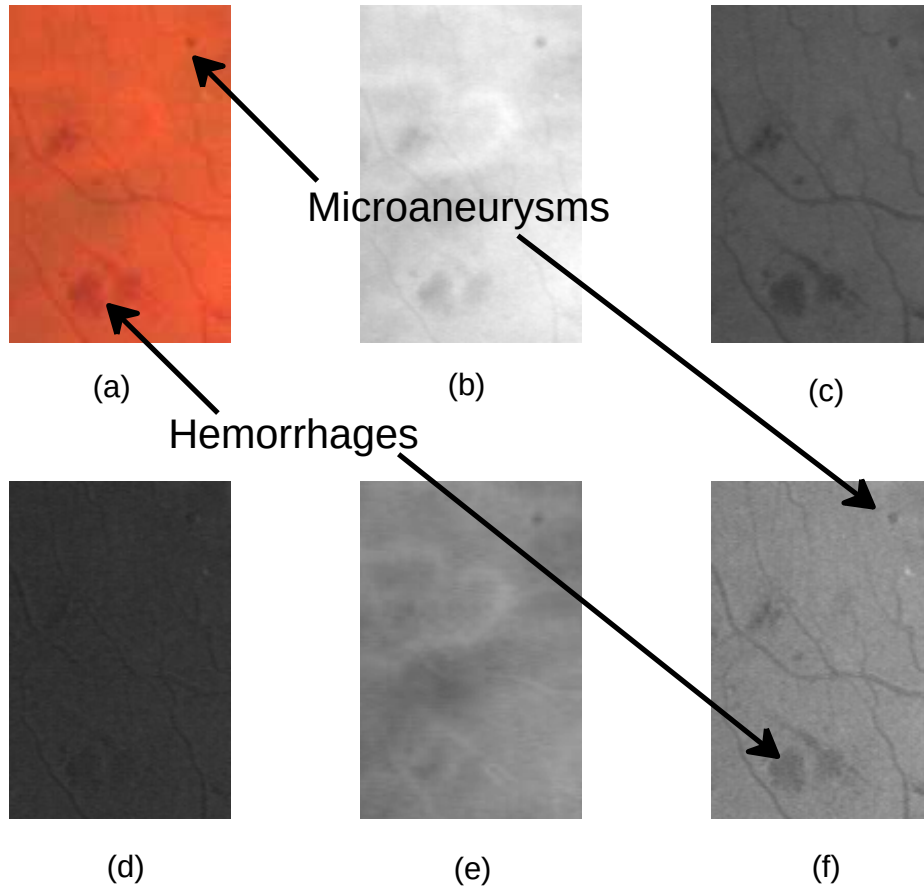


Figure 3.2: Diabetic retinopathy features (MAs and haemorrhages): (a) color fundus image, (b) red channel, (c) green channel, (d) blue channel, (e) processed image output1, (f) processed image output2.

each level ($L1$, $L2$, and $L3$). Each level coefficients are made zero systematically, and the images are reconstructed for analysis. The reconstructed images are shown in Fig. 3.3. Fig. 3.3(a) is the high contrast DR fundus image, whereas Fig. 3.3(b) is the reconstructed image. The final level approximation band image is shown in Fig. 3.3(c). The features appear similar in these images. Fig. 3.3(d), Fig. 3.3(e) and Fig. 3.3(f) are the reconstructed images after zeroing the coefficients of $L1$ ($H1$, $V1$, $D1$), $L2$ ($H2$, $V2$, $D2$), and $L3$ ($H3$, $V3$, $D3$) subband, respectively. Fig. 3.3(g), Fig. 3.3(h) and Fig. 3.3(i) are the images reconstructed after keeping the coefficients of $L1$, $L2$, and $L3$ subband, respectively, whereas the other subband coefficients are made zero. It is observed that the diagnostic features are well reconstructed in all the images, in three level wavelet decomposition and the overall image quality is good as the original image.

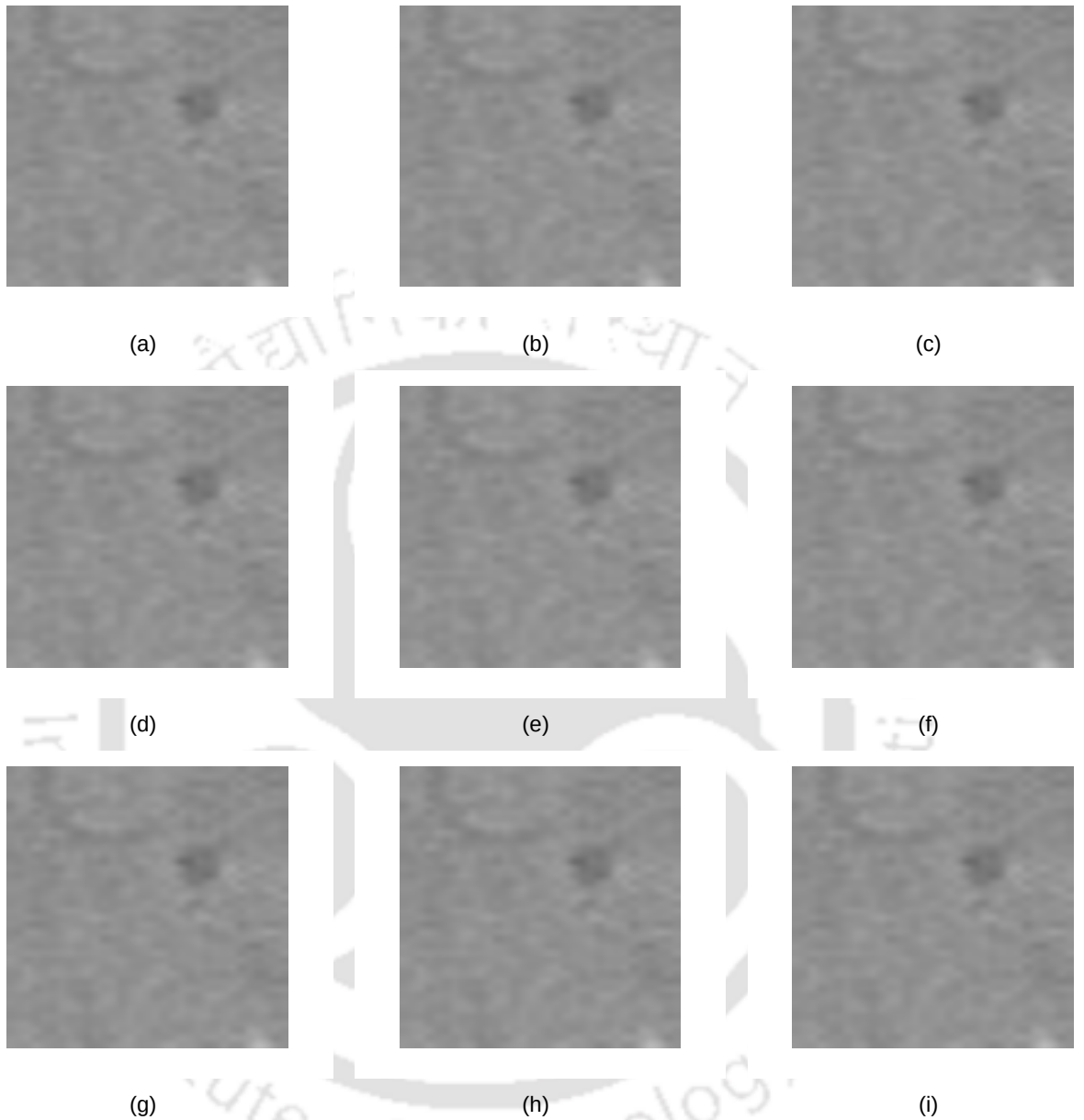


Figure 3.3: Microaneurysm feature analysis in the subbands of 3-level wavelet decomposition: (a) high contrast green channel image, (b) reconstructed image, (c) approximation band, (d) $L1$ ($H1$, $V1$, $D1$) coefficients zero, (e) $L2$ ($H2$, $V2$, $D2$) coefficients zero, (f) $L3$ ($H3$, $V3$, $D3$) coefficients zero, (g) only $L1$ coefficients unaltered, (h) only $L2$ coefficients unaltered, (i) only $L3$ coefficients unaltered.

For further analysis of the features, the level of decomposition is increased from three level to five levels. Fig. 3.4 shows analysis of different subbands in 5-level wavelet decomposition. The same procedures are performed as that of third level wavelet decomposition. Fig. 3.4(a) to Fig. 3.4(e) are the reconstructed images after zeroing the coefficients of $L1$ -subband to $L5$ -subband, respectively. Similarly, Fig. 3.4(f) to Fig. 3.4(j) are the images obtained by keeping the coefficients of $L1$ -subband

3. Multiscale analysis of diagnostic features of retinal images

to $L5$ -subband, respectively and zeroing the remaining subband coefficients. From the Fig. 3.4(a), Fig. 3.4(b) and Fig. 3.4(c) it is clear that $L1$, $L2$, and $L3$ subband coefficients are not influencing the features much. The microaneurysm and the haemorrhages are affected by the coefficients of $L4$ and $L5$ subbands. Fig. 3.4(d) and Fig. 3.4(e) are the reconstructed images obtained after making the coefficients of $L4$ and $L5$ subbands zero, respectively. It is observed that the DR features are not reconstructed properly and the overall quality of this feature is reduced. Similarly, Fig. 3.4(f) to Fig. 3.4(j) are reconstructed by retaining the coefficients of $L1$ to $L5$ subband, respectively and making the other subbands zero. This does not affect the reconstruction of the DR feature much when the coefficients of $L4$ and $L5$ subbands are present. The reconstructed images are shown in Fig. 3.4(i) and Fig. 3.4(j), respectively. The diagnostic features are affected much when the coefficients of $L4$ and $L5$ subbands are made zero. In Fig. 3.4(f) to Fig. 3.4(h), the coefficients of $L4$ and $L5$ subbands are zero. So, the feature is not reconstructed properly. Retaining the coefficients of $L4$ and $L5$ subbands the quality of the DR feature in the reconstructed image is not degraded. Fig. 3.7(a) shows the reconstructed images by the combination of coefficients in $L4$ and $L5$ subbands, respectively. It is observed that any alteration in subband coefficients of $L4$ and $L5$ will affect the DR feature in the five levels of wavelet decomposition. It is concluded that the coefficients of $L4$ and $L5$ subbands contribute more towards DR feature information in a five level wavelet decomposition.

Fig. 3.5 shows the effect of different subbands on a DR feature in a fundus image with seven level wavelet decomposition. Fig. 3.5(a) to Fig. 3.5(g) are the reconstructed images after zeroing the coefficients of $L1$ to $L7$ subband, respectively. Fig. 3.5(h) to Fig. 3.5(n) are obtained by retaining the coefficients in $L1$ to $L7$ subband and zeroing rest of the subbands coefficients. It is observed that the subband $L5$, $L6$ and $L7$ have more DR feature information compared to the other subbands as shown in Fig. 3.5(e), Fig. 3.5(f), Fig. 3.5(g), Fig. 3.5(l), Fig. 3.5(m), and Fig. 3.5(n). In the reconstructed images, shown in Fig. 3.5(h) to Fig. 3.5(k), the coefficients of $L5$, $L6$ and $L7$ subbands are zero. In these cases the quality of the DR feature is degraded to a greater extent. Fig. 3.7(b) shows the reconstructed image by combining the coefficients from $L5$, $L6$ and $L7$ subbands and zeroing the remaining subbands coefficients. These results show that the subbands of $L5$, $L6$ and $L7$ have significant microaneurysm and haemorrhages information.

The level of wavelet decomposition is increased to nine for more detail analysis of DR features in the subband. In the Fig. 3.6(a) to Fig. 3.6(i), the reconstructed images are shown by making

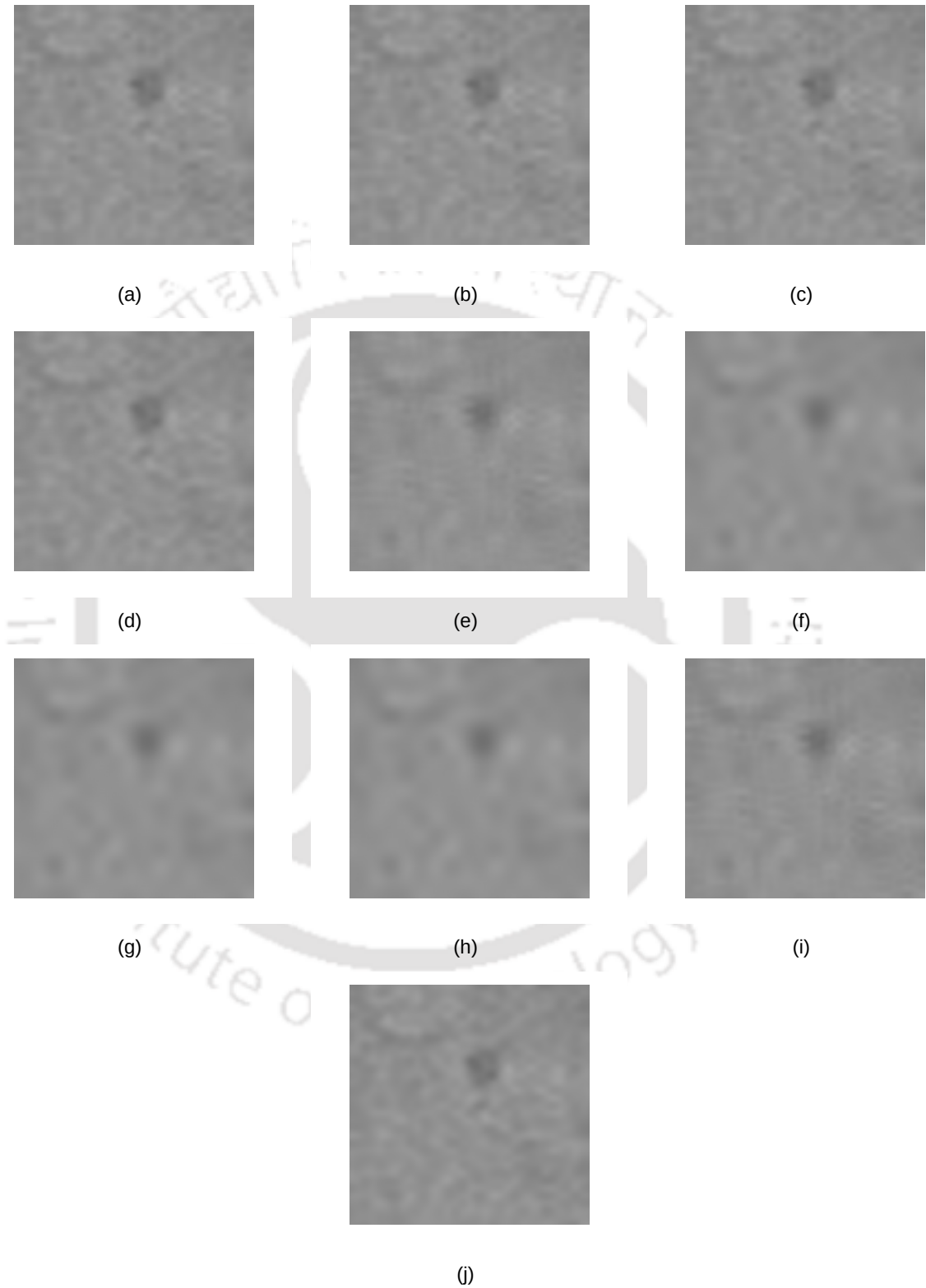


Figure 3.4: Microaneurysm feature analysis in the subbands of 5-level wavelet decomposition: (a-e) reconstructed image by zeroing $L1$ to $L5$ subband coefficients, respectively, (f-j) reconstructed image by keeping $L1$ to $L5$ subband coefficients, respectively and altering the coefficients of other subbands.

3. Multiscale analysis of diagnostic features of retinal images

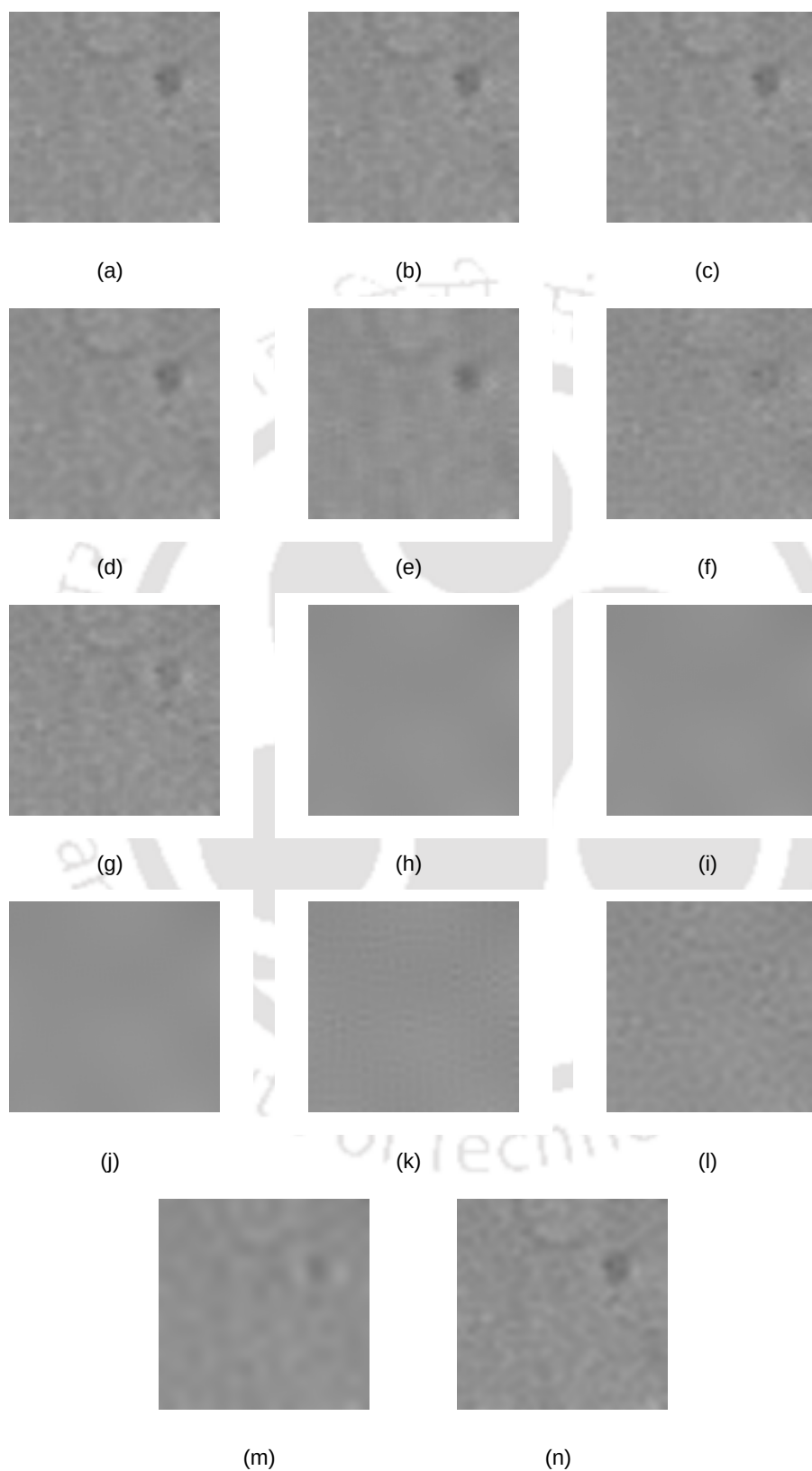


Figure 3.5: Microaneurysm feature analysis in the subbands of 7-level wavelet decomposition: (a-g) reconstructed image by zeroing $L1$ to $L7$ subband coefficients, respectively, (h-n) reconstructed image by keeping $L1$ to $L7$ subband coefficients, respectively and zeroing other coefficients.

subband coefficients of $L1$ to $L9$ zero. Similarly, subband coefficients $L1$ to $L9$ are used to reconstruct the images and the reconstructed images are shown in Fig. 3.6(j) to Fig. 3.6(r). It is observed that $L5$ to $L9$ subbands contain more microaneurysm feature information. By making subband $L5$ to $L9$ coefficients zero, the diagnostic information of DR in the reconstructed fundus image disappear, which are shown in Fig. 3.6(e) to Fig. 3.6(i). In Fig. 3.6(n) and Fig. 3.6(o) the coefficients of subband $L5$ and $L6$ are unchanged. The other subband coefficients are zero. In these two images DR feature is faintly observed. So, it may be concluded that subbands $L5$ and $L6$ contribute more for the microaneurysms feature in 9-level wavelet decomposition compared to $L7$, $L8$ and $L9$ subbands.

Fig. 3.7(c) is reconstructed by retaining the coefficients of $L5$, $L6$, $L7$, $L8$, and $L9$ subbands and zeroing the coefficients of remaining subbands. In this figure, the overall quality of the microaneurysms and haemorrhage features is as good as the original image. From the above analysis, it may be concluded that as the level of wavelet decomposition increases the higher subbands contribute more towards DR feature information.

3. Multiscale analysis of diagnostic features of retinal images

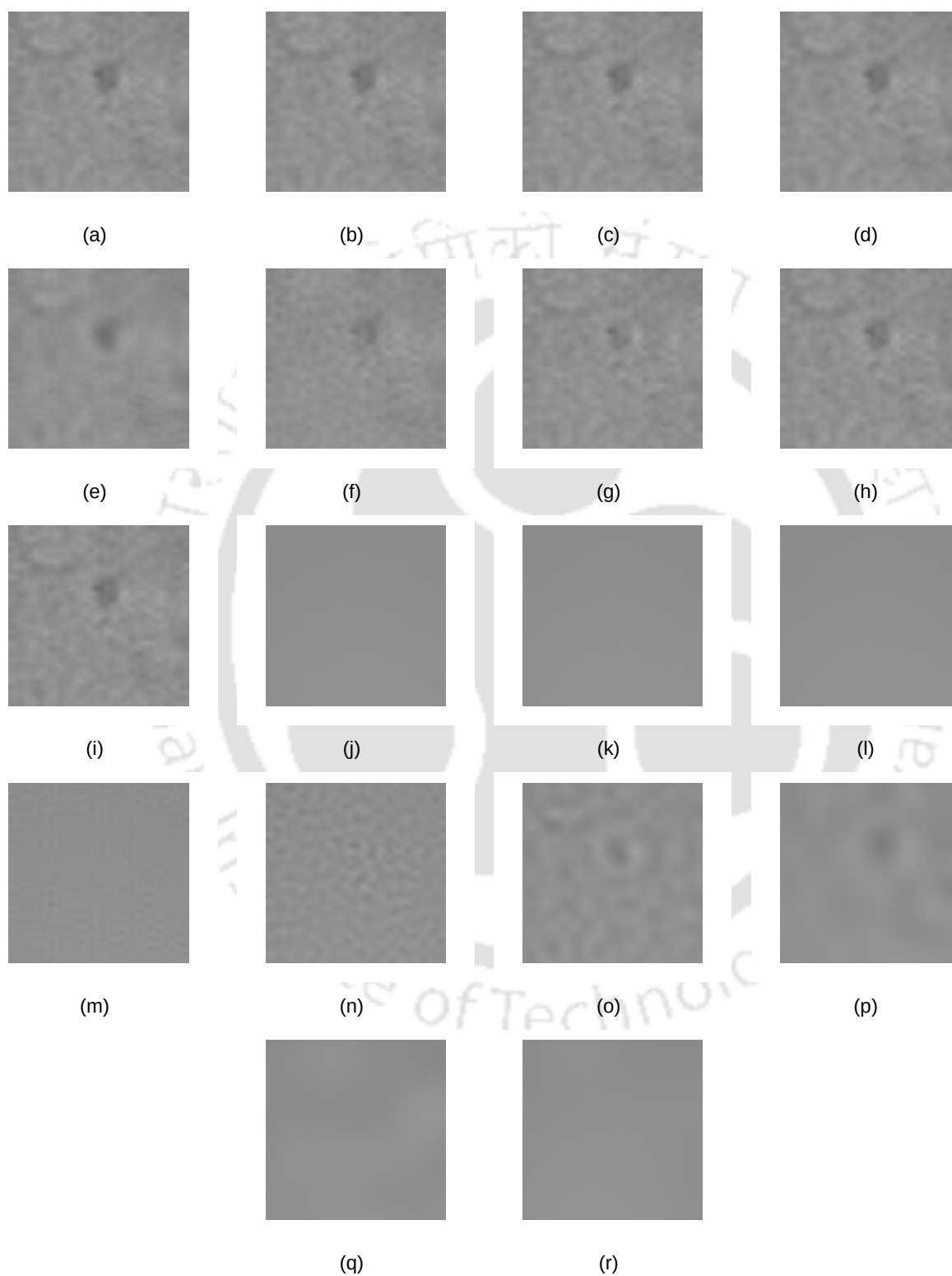


Figure 3.6: Microaneurysm feature analysis in the subbands of 9-level wavelet decomposition: (a-i) reconstructed image by zeroing $L1$ to $L9$ subband coefficients, respectively, (j-r) reconstructed image by keeping $L1$ to $L9$ subband coefficients, respectively and altering other coefficients.

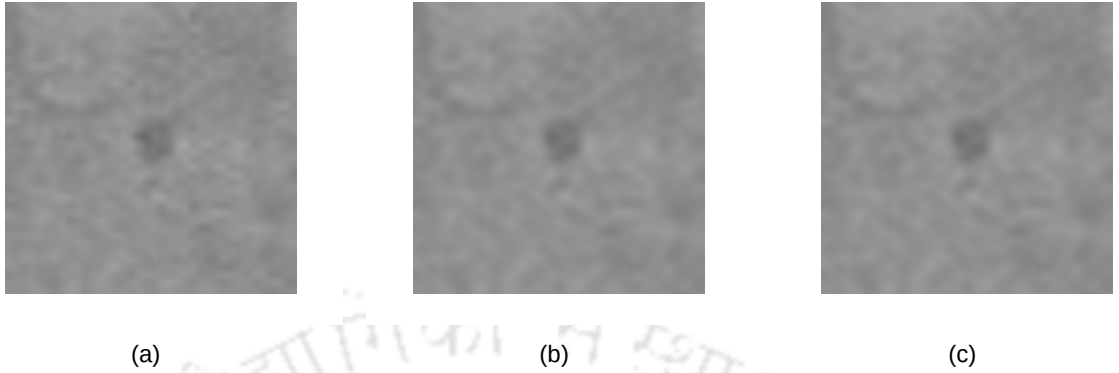


Figure 3.7: Microaneurysm and haemorrhage information in combination of wavelet subband coefficients in different level of wavelet decomposition: (a) $L4$ and $L5$ coefficients of 5-level wavelet decomposition, (b) $L5$, $L6$, and $L7$ coefficients of 7-level wavelet decomposition (c) $L5$, $L6$, $L7$, $L8$, and $L9$ coefficients of 9-level wavelet decomposition.

3.2.3 Analysis of exudates

In diabetic retinopathy, exudates are more prominent diagnostic features than the microaneurysms and the haemorrhages. The appearance of the exudates in the macular region leads to severe vision loss. Analysis of this DR feature, exudates in different wavelet subbands can provide important information which can improve the automated detection of these features. For analysis of the exudates, five, seven and nine levels of decompositions are performed. Fig. 3.8 shows the appearance of the exudates in different subbands for a five level wavelet decomposition. In this case, the subband images are reconstructed in the same way as discussed in the previous subsection. The images shown in Fig. 3.8(a) to Fig. 3.8(e) are formed by zeroing coefficients of $L1$ to $L5$ subbands, respectively. The images shown in Fig. 3.8(f) to Fig. 3.8(j) are reconstructed by retaining the coefficients of one subband at a time and changing the values of other subband coefficients to zero. Subbands $L4$ and $L5$ have the blood vessel (BV) information. By changing $L4$ and $L5$ coefficients to zero, BVs information is reduced and the reconstructed images are shown in Fig. 3.8(d) and Fig. 3.8(e). The exudate information is preserved in $L1$, $L2$ and $L3$ subbands with less information about the blood vessels. In Fig. 3.8(f), Fig. 3.8(g), and Fig. 3.8(h) only $L1$, $L2$ and $L3$ subband coefficients are present. It is observed that combining the coefficients of $L1$, $L2$ and $L3$ subbands the exudate information can be preserved and the BVs information can be suppressed. In Fig. 3.9 selective subband coefficients are combined and other subband coefficients made zero for reconstruction of the exudates. For the image shown in Fig. 3.9(a) $L4$ and $L5$ subband coefficients are reduced to zero and $L1$, $L2$ and

3. Multiscale analysis of diagnostic features of retinal images

$L3$ subband coefficients are kept unaltered. In this case blood vessels are seen with the exudates. For the image shown in Fig. 3.9(b), $L1$ subband and $L2$ subband coefficients are retained with $L3$ -subband, $L4$ -subband and $L5$ -subband coefficients as zeros. It can be observed that the exudates are preserved and the blood vessels are present with very low contrast. The quality of exudates is better compared to the other cases.

For further analysis of exudates in the wavelet subbands the decomposition level is increased from five to seven. The reconstructed images are shown in Fig. 3.10. Fig. 3.10(a) to Fig. 3.10(g) show images in which one subband coefficients at a time are made zero. The image which is obtained by zeroing the $L5$ -subband coefficients is shown in Fig. 3.10(e). In this image the blood vessel information is reduced a lot and the exudates information is preserved. In order to find the contribution of each subband towards exudates, one subband coefficients are kept and the remaining subband coefficients are made zero. The reconstructed images are shown in Fig. 3.10(h) to Fig. 3.10(n). The image in Fig. 3.10(k) is reconstructed by retaining the $L4$ -subband coefficients only. This image shows the boundaries of the BVs and parts of exudates. The exudates in this subband are blurred. In Fig. 3.10(h), Fig. 3.10(i), Fig. 3.10(j), Fig. 3.10(m), and Fig. 3.10(n) only exudates are present.

For more detailed analysis, the subband coefficients are combined. Images obtained by combining the coefficients of selective subbands are shown in Fig. 3.11. The image shown in Fig. 3.11(a) is obtained by zeroing the $L3$ and $L2$ subbands coefficients and without altering the other subband coefficients. In this image the exudates are highlighted with the blood vessels. To reduce the BV information, $L4$ and $L3$ subbands coefficients are made zero. The reconstructed image is shown in Fig. 3.11(b). In this image blood vessels information is further reduced without the degradation of exudate information. The blood vessel information should be reduced without losing the exudate information. By zeroing the coefficients of the $L4$, $L3$, and $L2$ subbands, the blood vessel information is reduced which can be seen in Fig. 3.11(c). From this result, it can be concluded that zeroing the coefficients of $L2$ and $L4$ subbands do not affect exudate information much. In this image some more blood vessel information is lost. Further reduction of blood vessel information is possible by replacing the coefficients of $L5$ -subband by zeros along with zeroing coefficients of $L4$, and $L3$ subbands. The reconstructed image is shown in Fig. 3.11(d). It is observed that information of the blood vessel reduces a lot along with little exudate information. Exudates appear little blurred in this image. From the seven level wavelet decomposition analysis, we may draw the conclusion that the coefficients of $L4$,

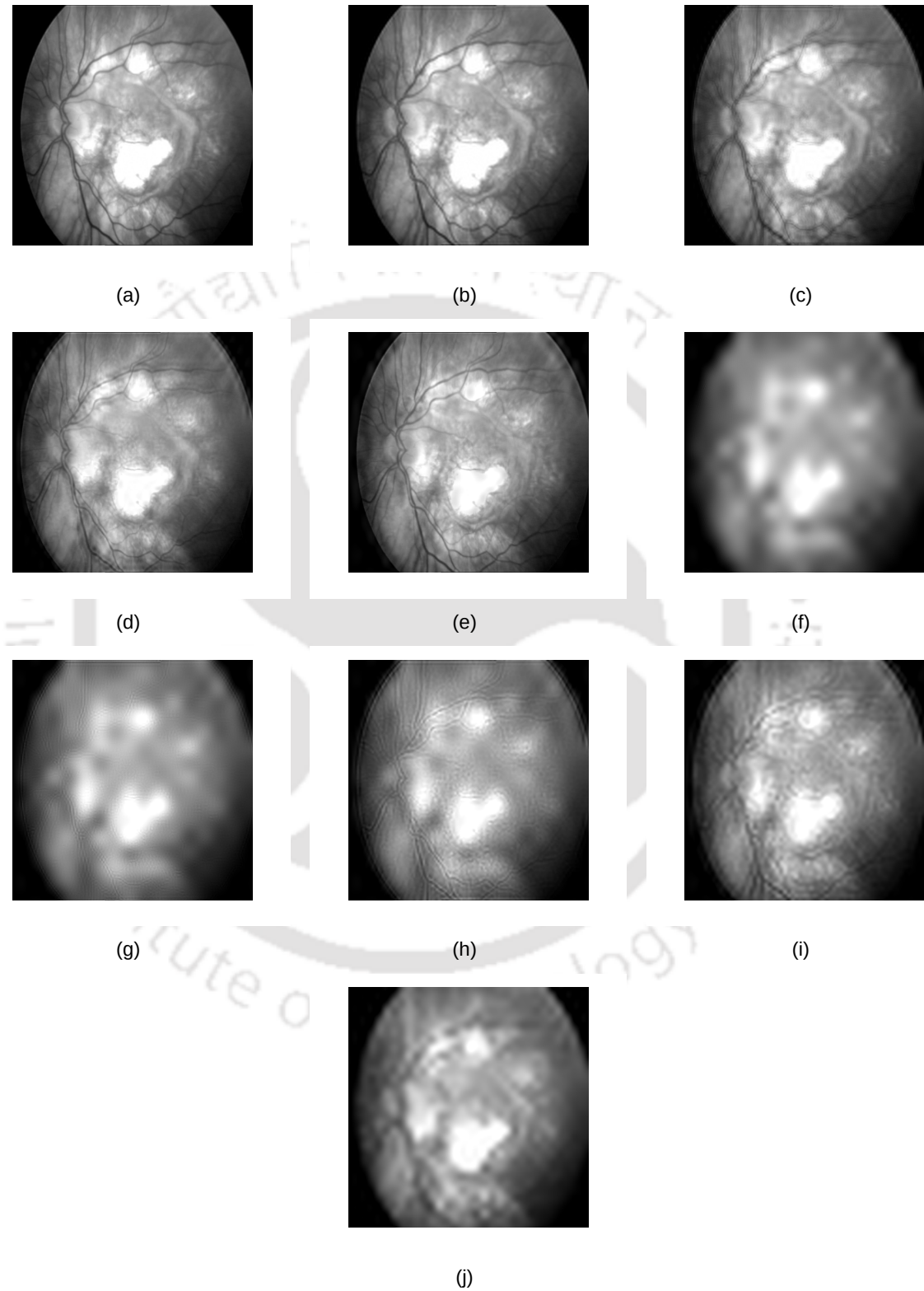


Figure 3.8: Exudate analysis in subbands of 5-level wavelet decomposition: (a-e) reconstructed image by making L1 to L5 subband coefficients zero, respectively, (f-j) reconstructed image by keeping L1 to L5 subband coefficients, respectively and altering other coefficients.

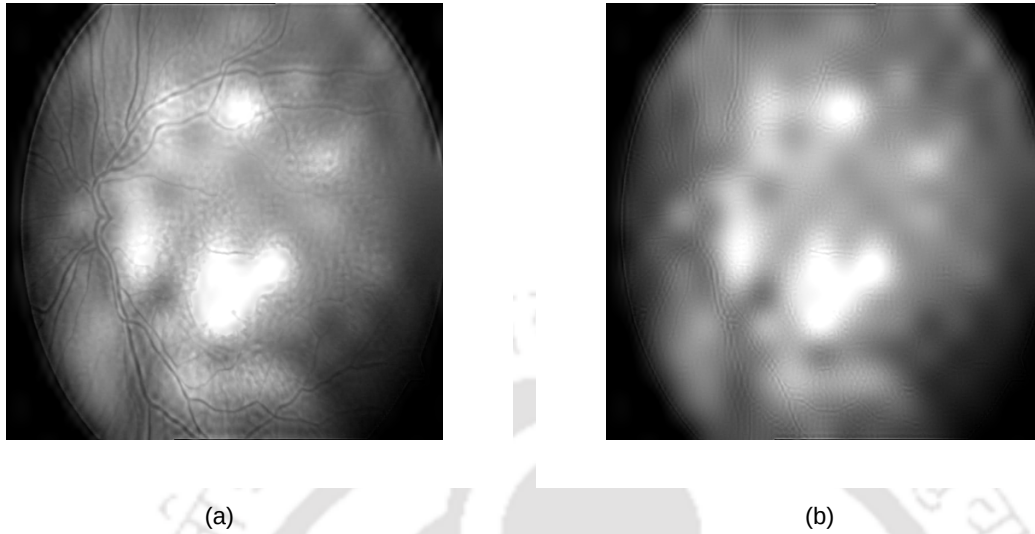


Figure 3.9: Exudates information in the combination of subbands in 5-level wavelet decomposition. Reconstructed image by considering (a) $L1+L2+L3$ subband coefficients, (b) $L1+L2$ subband coefficients.

$L3$, and $L2$ subbands do not contain significant exudate information. The most important subbands contributing for exudate information are $L7$, $L6$, $L5$, and $L1$.

Fig. 3.12 shows the reconstructed images with nine level wavelet decomposition. Fig. 3.12(a) to Fig. 3.12(i) are obtained by reducing the coefficients of subbands $L1$ to $L9$ to zero. The coefficients of $L5$ are made zero in the reconstructed image shown in Fig. 3.12(e). In this image the information of blood vessels reduces a lot. So, $L5$ -subband contains more BVs information compared to other subbands. The least amount of the BVs information is lost by zeroing the coefficients of the subbands $L4$ and $L6$. The reconstructed images corresponding to these subbands are given in Fig. 3.12(d) and Fig. 3.12(f). For a better analysis, the images are reconstructed by keeping one subband coefficients at a time and forcing all other subband coefficients to zero. The reconstructed images are shown in Fig. 3.12(j) to Fig. 3.12(r). The reconstructed images with the coefficients of $L4$ -subband and $L5$ -subbands are shown in Fig. 3.12(m) and Fig. 3.12(n), respectively. In these images blood vessels are highlighted and the exudate information is lost. So it can be concluded that $L4$ and $L5$ subbands contain the BVs information and they have little exudate information. In the Fig. 3.12(o) the BVs information is reduced to a large extent. This image is obtained by considering the $L6$ subband coefficients. Images in Fig. 3.12(j), Fig. 3.12(k), Fig. 3.12(l), Fig. 3.12(p), Fig. 3.12(q), and Fig. 3.12(r) are reconstructed by retaining the coefficients of $L1$ subband, $L2$ subband, $L3$ subband, $L7$ subband, $L8$ subband, and $L9$ subband, respectively.

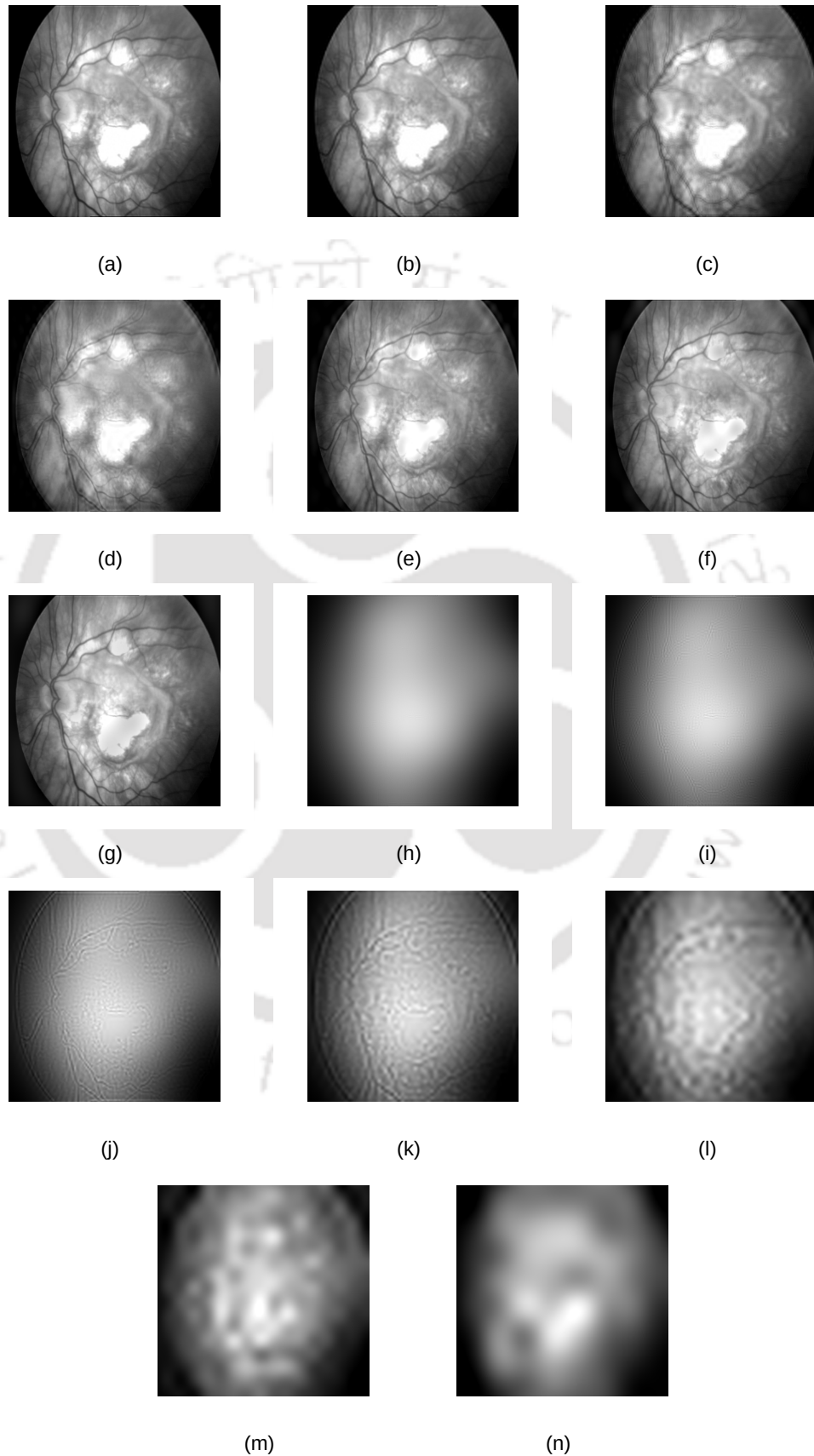


Figure 3.10: Exudate information in subbands of 7-level wavelet decomposition: (a-g) reconstructed image by making L1 to L5 subband coefficients zero, respectively, (h-n) reconstructed image by keeping L1 to L5 subband coefficients, respectively and altering other coefficients.

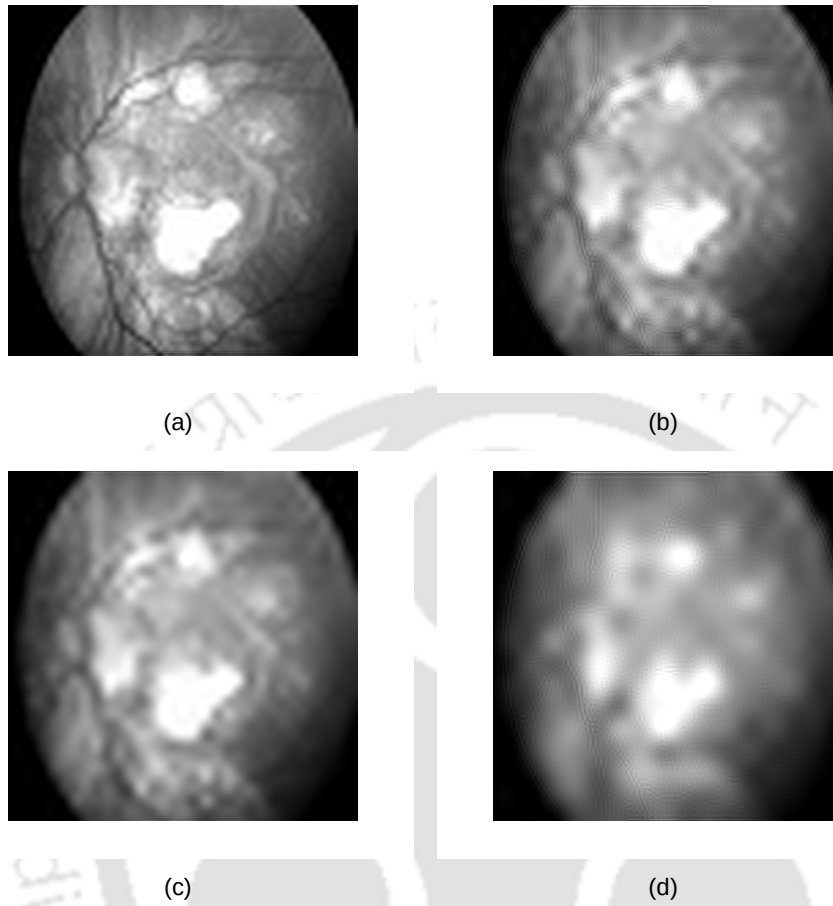


Figure 3.11: Analysis of exudates information in a combination of wavelet subbands on 7-level decomposition. Reconstructed images by zeroing: (a) ($L2+L3$), (b) ($L3+L4$), (c) ($L2+L3+L4$), (d) ($L3+L4+L5$) subband coefficients.

Suitably combining the coefficients of the different subbands in nine level wavelet decomposition, the exudate information can be preserved. The image shown in Fig. 3.13(a) is obtained by zeroing the $L5$ and $L4$ subbands coefficients. In this image, exudate information is highlighted with BVs information. Further reduction of the BVs information may be possible by making $L9$ subband coefficients zero along with the $L4$ and $L5$ subband coefficients. The reconstructed image is shown in Fig. 3.13(b). In this image blood vessels information is further reduced without the degradation of exudate information. The BVs information should be reduced without losing the information about the exudates for efficient analysis of exudates. By zeroing the coefficients of the $L9$, $L5$, $L4$ and $L3$ subbands, the BVs information are reduced to a large extent which can be seen in the image in Fig. 3.13(c). The image in Fig. 3.13(d) is reconstructed by zeroing the coefficients $L9$, $L5$, $L4$, $L3$ and $L2$ subbands. In the reconstructed image some more blood vessel information is lost. Exudates appear

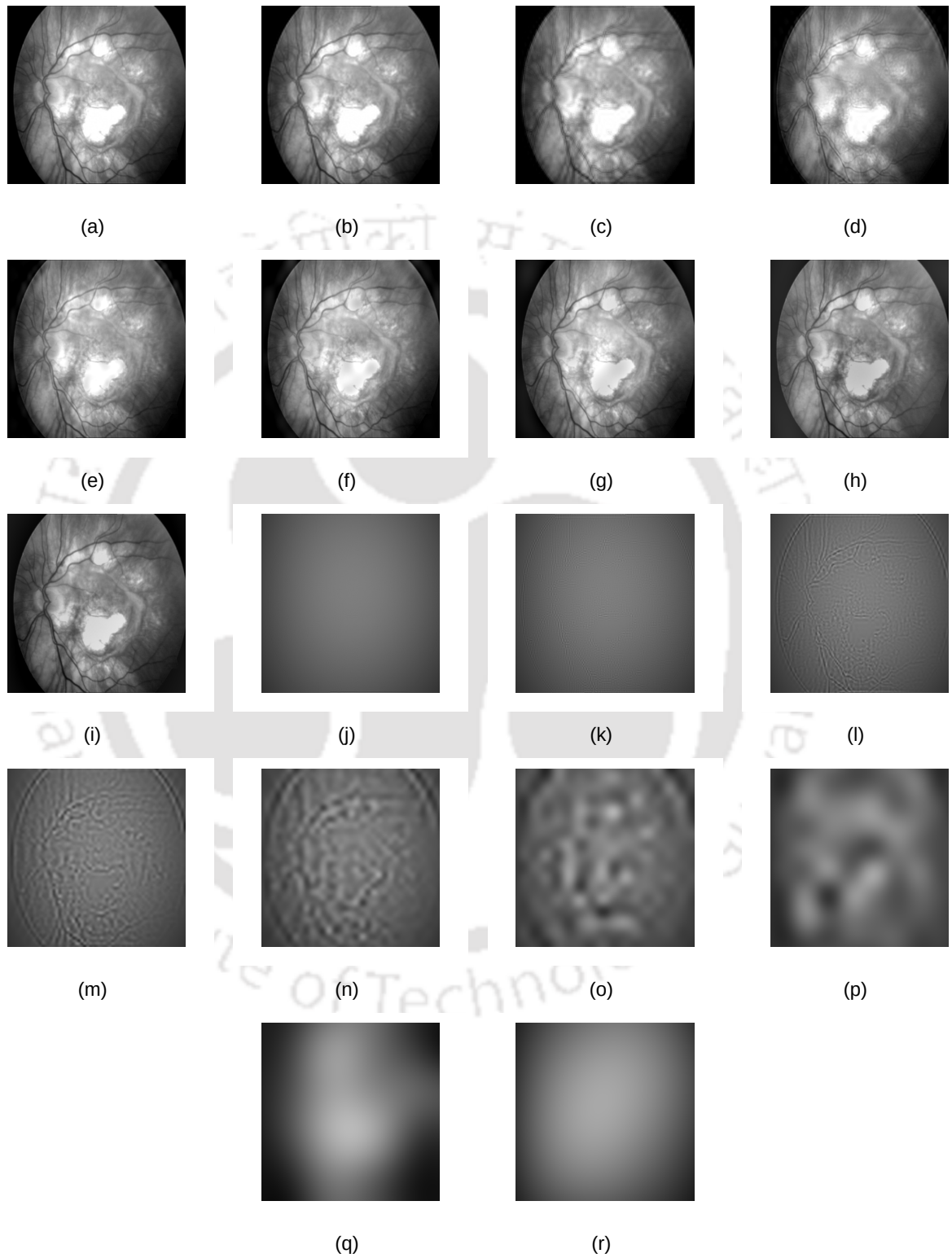


Figure 3.12: Exudate analysis in the subbands of 9-level wavelet decomposition: (a-i) reconstructed image by making L1 to L9 subband coefficients zero, respectively, (j-r) reconstructed image by keeping L1 to L9 subband coefficients, respectively and altering other coefficients.

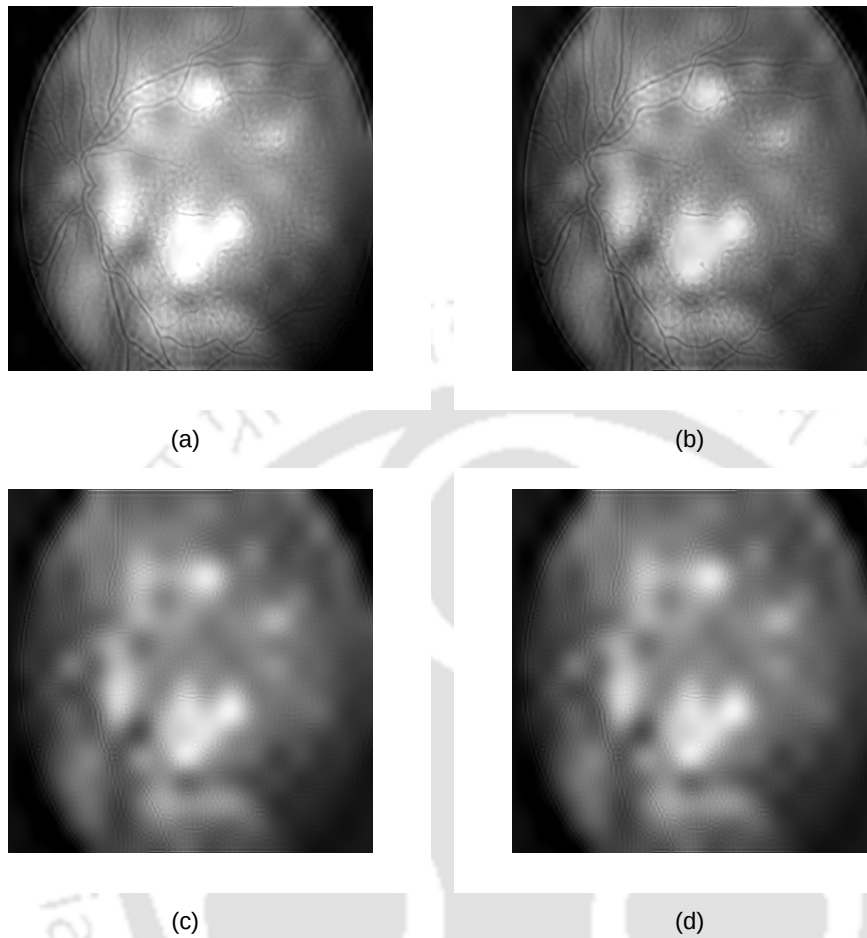


Figure 3.13: Analysis of exudates in 9-level wavelet decomposition. Reconstructed images by zeroing sub-band coefficients of: (a) ($L4$ and $L5$), (b) ($L4$, $L5$ and $L9$), (c) ($L3$, $L4$, $L5$, and $L9$), (d) ($L2$, $L3$, $L4$, $L5$, $L9$).

little blurred. In 9-level wavelet decomposition analysis, it can be concluded that the coefficients of $L9$, $L5$, $L4$, and $L2$ subbands do not contain significant exudate information. The most important subbands contributing to exudate information are $L8$, $L7$, $L6$, and $L1$.

3.3 Quantitative evaluation

The work of the multiscale analysis of DR features (microaneurysms, haemorrhages, and exudates) is studied for different databases [124, 125]. Different metrics are used to calculate the performance of the method and to justify the contribution of the different wavelet subbands towards DR features. The DR features are extracted from the original image and the subband reconstructed images by mathematical morphology and histogram based method. These measures are used to evaluate the contribution of a particular wavelet subband for the DR feature. Based on the performance measure

[TH-1619_09610207](#)

the wavelet subbands are selected for a particular DR feature.

In this work, true positive (TP), true negative (TN), false positive (FP), false negative (FN), sensitivity, specificity, sensibility, accuracy (ACC), equal error rate (EER), Conformity coefficient (KC), Jaccard coefficient (KJ), Dice coefficient (KD), mean square error (MSE), root mean square error (RMSE), peak signal to noise ratio (PSNR), mean absolute error (MSE), Pearson correlation coefficient (PCC), universal quality index (UQI), structural similarity (SSIM) are used to evaluate the performance of the feature in different wavelet subbands. The details about the measures are discussed below.

Sensitivity or true positive rate (TPR) or recall [73] is defined by:

$$\text{Sensitivity} = \left(\frac{TP}{TP + FN} \right) \times 100 \quad (3.6)$$

The sensitivity value is 100% for an ideal extraction of DR feature.

Specificity coefficient or true negative rate (TNR) measures how many pixels are correctly excluded, which involves the computation of the true negatives and is related to the dimension of the images [132, 133]. Specificity can be defined as:

$$\text{Specificity} = \left(\frac{TN}{TN + FP} \right) \times 100 \quad (3.7)$$

Sensibility [134, 135] measures how many pixels outside are included and represented by:

$$\text{Sensibility} = \left(1 - \frac{TN}{TN + FP} \right) \times 100 \quad (3.8)$$

The sensibility value should be less for better extraction of features.

Accuracy (ACC) can be defined by the total number of correctly classified to the total number of pixels in the field of view [132, 136]. Accuracy should be 100% for the best extraction of features. It can be defined as:

$$\text{ACC} = \frac{TP + TN}{TP + FN + TN + FP} \times 100 \quad (3.9)$$

Equal error rate (EER) defines the total error which is represented by:

$$\text{EER} = \left(\frac{FP + FN}{2 \times (TP + TN + FP + FN)} \right) \times 100 \quad (3.10)$$

At ERR the false match rate and false non match rate are equal. In other words, it can be stated

3. Multiscale analysis of diagnostic features of retinal images

as a condition where false acceptance rate and false rejection rate are equal. The value of EER should be zero for ideal segmentation or extraction of features.

Conformity coefficient (KC) [135] measures the ratio of miss segmented pixels and defined as:

$$KC = \left(1 - \frac{FP + FN}{TP}\right) \times 100 \quad (3.11)$$

For ideal segmentation KC is found to be 100%

Jaccard coefficients (KJ) and Dice coefficients (KD) are given by Equ. (3.12) and Equ. (3.13), respectively. They have a nonlinear response. Both are bounded between 0% to 100%. For better evaluation the performance measures should have the discriminating capacity to identify the smallest variation in the segmented image and the original image. Discrimination capacity of Jaccard coefficient is higher than the Dice coefficient and Conformity coefficient.

$$KJ = \left(\frac{TP}{TP + FP + FN}\right) \times 100 \quad (3.12)$$

$$KD = \left(\frac{2 \times TP}{2 \times TP + FP + FN}\right) \times 100 \quad (3.13)$$

Root mean square error (RMSE) [137] is defined as:

$$RMSE = \sqrt{\frac{1}{PQ} \sum_{i=1}^P \sum_{j=1}^Q (p_{ij} - \hat{p}_{ij})^2} \quad (3.14)$$

where, $P \times Q$ = image size, p_{ij} = manually marked exudate from color fundus image, $\hat{p}_{ij}$ = extracted exudate by the described algorithm in the paper. This value becomes zero when the manually marked exudate matches completely with the extracted exudate by the algorithm. Otherwise, this value will become greater than zero.

Peak signal to noise ratio (PSNR) [137] is given as:

$$PSNR = 20 \log \frac{255}{RMSE} \quad (3.15)$$

PSNR is ∞ when both the images are identical.

Mean absolute error (MAE) is expressed in the following expression [138], [137].

$$MAE = \frac{\sum_{i=1}^P \sum_{j=1}^Q (p_{ij} - \hat{p}_{ij})}{PQ} \quad (3.16)$$

MAE value is zero when both the images are identical to each other.

Pearson correlation coefficient (PCC) measures the correlation between the segmented image and the original image [137, 138]. PCC can be calculated as:

$$\text{PCC} = \frac{E((p - \mu_p)(\hat{p} - \mu_{\hat{p}}))}{\sigma_p \sigma_{\hat{p}}} \quad (3.17)$$

where, μ_p and $\mu_{\hat{p}}$ are the mean value of the images. σ_p^2 and $\sigma_{\hat{p}}^2$ are the variances. PCC approaches to a higher value when both the images are identical to each other.

Universal image quality index (UQI) combines the loss of correlation, luminance distortion and contrast distortion for measuring the image distortion [133]. The correlation coefficient measures the degree of linear correlation, whose dynamic range lies between -1 and 1 . Luminance distortion measures the closeness of mean luminances between two images. It ranges from 0 to 1 . Contrast distortion measures the similarity in contrast between the images. In equal contrast this value becomes equal to 1 . Its dynamic range is $[0, 1]$. It can be defined as:

$$\text{UQI} = \frac{4\rho_{p\hat{p}}\mu_p\mu_{\hat{p}}}{(\sigma_p^2 + \sigma_{\hat{p}}^2) \times (\mu_p^2 + \mu_{\hat{p}}^2)} \quad (3.18)$$

where, ρ_{pq} is the correlation coefficient. Its dynamic range lies $[-1, 1]$. It becomes the value 1 when both the images are identical to each other.

Structural similarity (SSIM) measures the change of luminance, contrast and symmetry of the image [139], [140]. In order to measure the SSIM it should satisfy the symmetry, bounded ness, and unique maximum. The expression of SSIM is given as:

$$\text{SSIM} = \frac{(2\mu_p\mu_{\hat{p}} + k_1)(2\sigma_{p\hat{p}} + k_2)}{(\mu_p^2 + \mu_{\hat{p}}^2 + k_1)(\sigma_p^2 + \sigma_{\hat{p}}^2 + k_2)} \quad (3.19)$$

where, k_1 and k_2 are constants. The value of k_1 and k_2 is determined as follows.

$$\begin{aligned} k_1 &= k_{11} \times L \\ k_2 &= (k_{22} \times L)^2 \end{aligned} \quad (3.20)$$

where, L is the dynamic range of pixel values of the image considered. The value k_{11} and k_{22} are less than 1 and considered to be 0.2 . In this case, the value of L is 255 as the gray scale images are eight bits. So, the value of k_1 is 51 . The value of k_2 is 2601 . The range of k_1 and k_2 is $[0, L]$ and

$[0, L^2]$, respectively.

3.4 Performance evaluation

Microaneurysms and haemorrhages are extracted by mathematical morphology based method from the original image and the reconstructed image obtained by 5-level and 7-level wavelet decomposition. The green channel of the fundus image is considered and the image is resized to 512×512 . The resized image is subjected to histogram equalization to enhance the contrast of the image. Edge detection technique by canny detector is applied for detection of the edges. Then any border of the image is removed. Then by using the mathematical erosion and dilation are performed with the disk structuring element. By using threshold the microaneurysms are extracted. The images are compared by different performance measures such as sensitivity, specificity, sensibility, accuracy and equal error rate. The values are tabulated in Table 3.1. In 5-level of wavelet decomposition the quantitative values, specificity and accuracy are higher for the L5 subband. For lower subbands these values are low.

Quantitative values (specificity and accuracy) are higher for the L5 wavelet subband. For lower subbands (i.e., L2) these values are found to be low. The accuracy value is found to be the highest for L5 subband, i.e., 76.65%. This value is the lowest in L2 subband, i.e., 58.47%. Equal error rate (ERR) is found to be least, i.e., 11.67% for L5 subband. As the accuracy and specificity values are higher in L5 wavelet subband compared to the other subbands, it may be concluded that the microaneurysm information in L5 subband is more. From this it may be concluded that the higher subband contribute more towards the microaneurysms.

Table 3.1: Performance measure values of extraction of microaneurysms in different level subband in 5-level wavelet decomposition.

Reconstructed Image	Sensitivity	Specificity	Sensibility	ACC	EER
L_1	79.96	62.80	37.20	63.42	18.29
L_2	62.78	58.45	41.55	58.47	20.76
L_3	63.08	73.71	26.29	73.22	13.39
L_4	60.61	76.63	23.37	75.90	12.05
L_5	59.28	77.44	22.56	76.65	11.67

To study the variation of different performance measures across different images, boxplots for all subbands are shown in Fig. 3.14. On each box, the central mark is the median, the edges

of the box are the 25th and 75th percentiles, the whiskers extend to the most extreme data points the algorithm considers to be not outliers, and the outliers are plotted individually. The boxplots for specificity, accuracy, and equal error rate of sixty images for different wavelet subbands in 5-level wavelet decomposition are shown in Fig. 3.14. From the boxplot it is found that the average specificity and accuracy values for L5 subband are higher compared to the other subbands. For L2 subband, these values are the least. From this, it can be concluded that more microaneurysm information is available in higher wavelet subband compared to the lower wavelet subband. The equal error rate is found to be least in L5 subband.

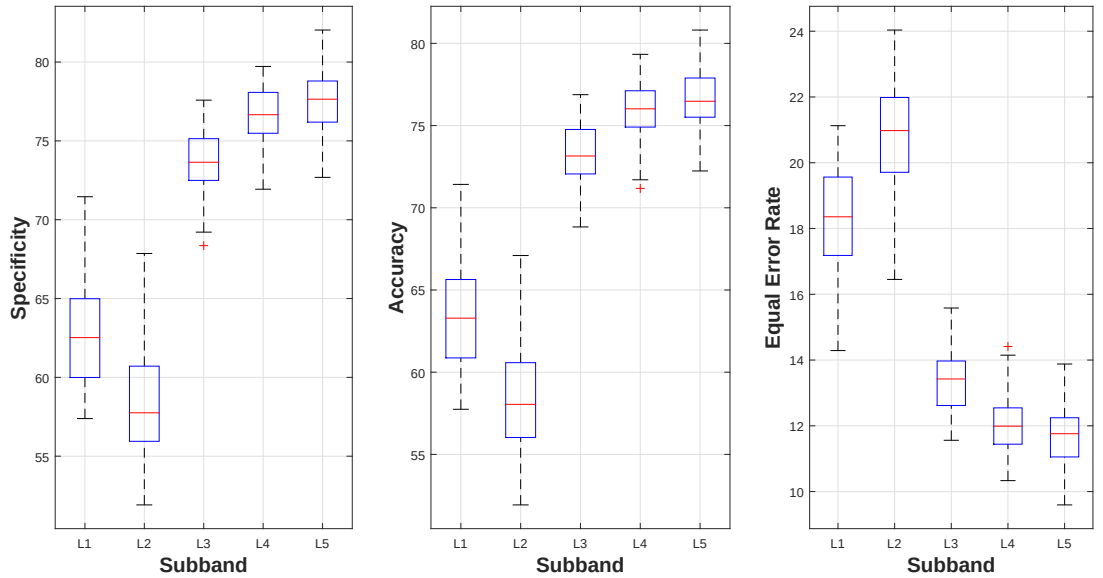


Figure 3.14: Boxplots for specificity, accuracy and equal error rate for different subband in 5-level wavelet decomposition (by considering one subband coefficients at a time) for sixty images

We have also conducted this experiment by zeroing a particular subband coefficients and considering the rest of the subband coefficients in 7-level wavelet decomposition. The performance measure values are shown in Table 3.2. The quantitative values (specificity and accuracy) are higher for the Zero L1 and Zero L2 subband reconstructed images and least for Zero L7 subband reconstructed images. The EER value is more in the Zero L7 subband reconstructed image (i.e., 6.82%) compared to the other subband reconstructed images. This shows that significant microaneurysms information is lost when higher subband coefficients are reduced to zero.

The boxplots for specificity, accuracy, and equal error rate of sixty images for different subband

3. Multiscale analysis of diagnostic features of retinal images

Table 3.2: Performance measure values of extraction of microaneurysms in different level subband of 7-level wavelet decomposition.

Reconstructed Image	STV	SPF	SEN	ACC	EER
Zero L_1	99.07	96.09	3.91	98.69	0.66
Zero L_2	99.50	93.57	6.43	98.64	0.68
Zero L_3	99.37	84.87	15.13	97.27	1.37
Zero L_4	99.36	71.16	28.84	95.27	2.37
Zero L_5	99.55	51.44	48.56	92.57	3.72
Zero L_6	99.64	37.22	62.78	90.56	4.72
Zero L_7	99.76	7.16	92.84	86.36	6.82

in 7-level wavelet decomposition (by altering one subband coefficients at a time) are shown in Fig. 3.15. From the boxplot it is found that the average specificity and accuracy values for Zero L7 and Zero L6 reconstructed subbands are lower compared to the other subbands. For Zero L1 subband these values are high. From this it may be concluded that more microaneurysm information is lost when higher subband coefficients are made zero.

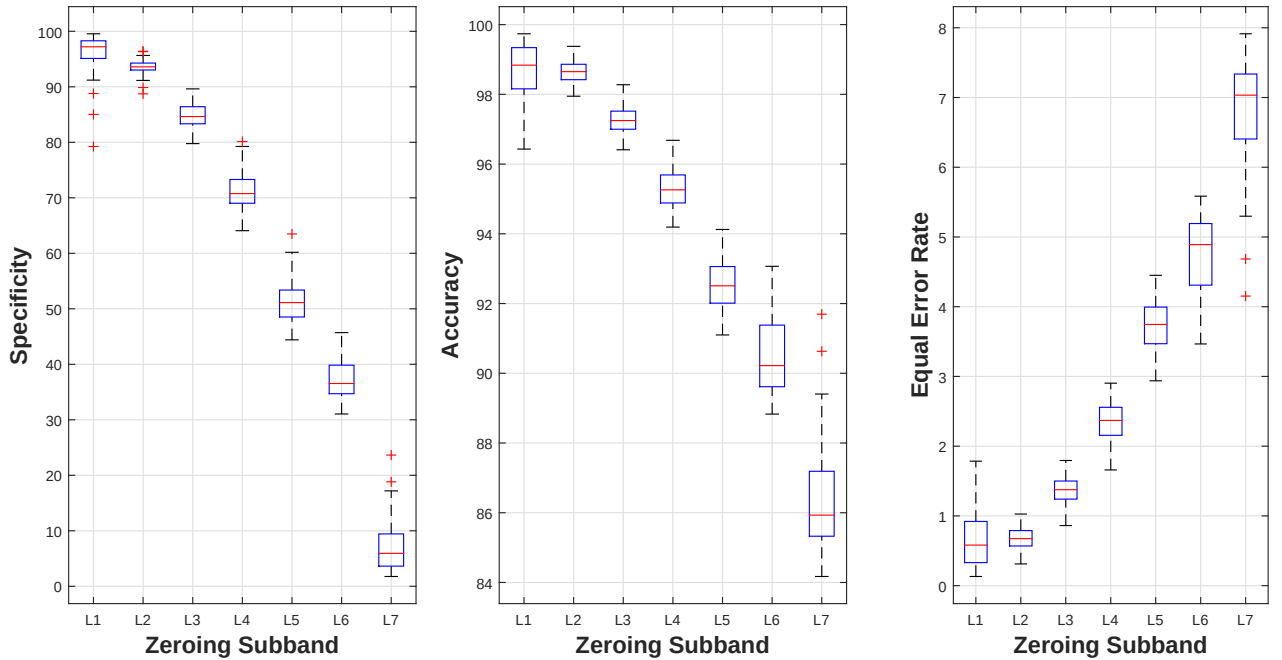


Figure 3.15: Boxplots for specificity, accuracy and equal error rate for different subband in 7-level wavelet decomposition (by changing one subband coefficients at a time) for sixty images

Extracted exudates from the original image and the reconstructed images of different level decomposition are compared by the above mentioned metrics, to know the contribution of different level

subbands towards exudates information. The metrics are divided into two sets. The Set-1 performance measurement metrics are sensitivity, specificity, sensibility, accuracy (ACC) and equal error rate (ERR). The performance measurement metrics MSE, RMSE, PSNR, MAE, PCC, UQI, and SSIM are present in Set-2. Table 3.3 shows the Set-1 performance measure values of the extraction of exudate features in different level subbands. In this table, L_1 to L_5 represent the reconstructed images by considering only one subband coefficients at a time, i.e., L_1 to L_5 subband, respectively and the rest of the subband coefficients are made zero. Similarly, 'Zero L_1 ' to 'Zero L_5 ' represent the reconstructed images by making L_1 to L_5 subband coefficients are zero, respectively and un-altering the other subband coefficients. For each case the performance is calculated. The extraction of exudate in L_4 and L_5 reconstructed image provides higher accuracy compared to the other subbands. The accuracy value is found to be highest in L_5 subband, i.e., 81.47%. But the extracted exudate in L_4 and L_5 reconstructed image highlights some blood vessels. Zeroing the L_1 subband and L_2 subbands do not affect much in the accuracy for extraction of exudates, which are found to be 95.90% and 93.22%, respectively. The accuracy value is reduced to lowest when L_5 subband coefficients are made zero, which is found to be 73.85%. The structures of extracting exudate features in different reconstructed images, considering different subbands for 5-level decomposition is shown in Fig. 3.16. Fig. 3.16 (a) to Fig. 3.16(e) are the reconstructed images obtained by altering one subband coefficients only. Fig. 3.16(f) to Fig. 3.16(j) are the reconstructed images by considering one subband coefficients and altering the rest subbands coefficients. The structural changes are calculated by MSE, RMSE, PSNR, PCC, UQI and SSIM. The values are shown in Table 3.4. Performance values in this table matches with the Table 3.3 for a particular subband. Extraction of exudates in the reconstructed image L_5 provides higher PCC and ACC values. So, any alternation in the L_5 subband coefficients, reduces the performance values in the extraction of exudates. Depending on the contribution of exudates for a particular subband, suitably subbands are combined for better exudate extraction.

To justify this technique the receiver operating characteristic (ROC) for the Table 3.3 is shown in Fig. 3.17 for higher and lower subband. It is the plot between 'sensitivity' versus '1-specificity'. The ROC plot has been shown in Fig. 3.17 for the L_5 and L_1 subband. The continuous line shows the ROC curve for L_5 subband and the dotted line shows the ROC for L_1 subband. The area under the ROC curve for L_5 subband is higher than the area under the ROC curve for L_1 subband. From the ROC curve it can be concluded that the feature information is higher in L_5 subband than in L_1

3. Multiscale analysis of diagnostic features of retinal images

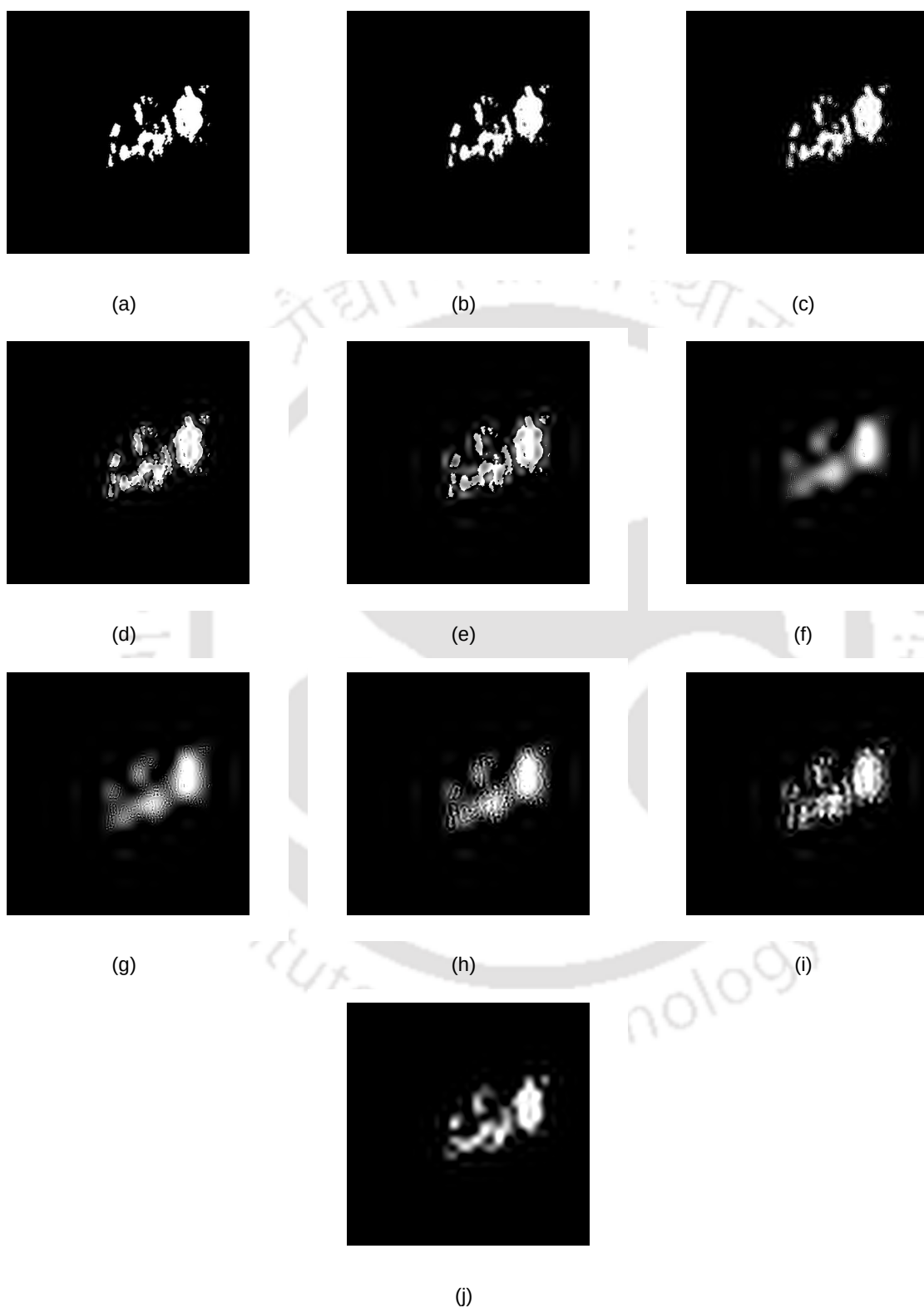


Figure 3.16: Extracted exudate in different band of 5-level wavelet decomposition: (a-e) reconstructed image by making $L1$ to $L5$ subband coefficients zero, respectively, (f-j) reconstructed image by keeping $L1$ to $L5$ subband coefficients, respectively and altering other coefficients.

Table 3.3: Performance measure values (set-1) of extraction of exudates in different level subband in 5-level wavelet decomposition.

Reconstructed Image	Sensitivity	Specificity	Sensibility	ACC	EER
L_1	98.49	70.32	29.68	71.56	14.22
L_2	98.64	70.62	29.38	71.86	14.07
L_3	99.25	71.34	28.66	72.57	13.71
L_4	99.54	71.21	28.79	72.46	13.77
L_5	99.71	80.61	19.39	81.47	9.26
Zero L_1	99.99	95.70	4.29	95.90	2.05
Zero L_2	99.99	92.89	7.10	93.22	3.39
Zero L_3	100	88.51	11.49	89.03	5.49
Zero L_4	100	82.07	17.93	82.88	8.56
Zero L_5	100	72.65	27.35	73.85	13.07

Table 3.4: Performance measure values (set-2) of extraction of exudates in different level subband of 5-level wavelet decomposition.

Reconstructed Image	MSE	RMSE	PSNRv	MAE	PCC	UQI	SSIM
L_1	0.02	0.12	66.63	0.04	206852.10	0.59	1.00
L_2	0.01	0.12	66.70	0.04	208036.17	0.59	1.00
L_3	0.01	0.12	67.06	0.04	212871.51	0.59	1.00
L_4	0.01	0.11	67.49	0.03	217995.65	0.57	1.00
L_5	0.01	0.11	67.64	0.03	218793.29	0.66	1.00
Zero L_1	0.00	0.04	75.90	0.01	256179.68	0.90	1.00
Zero L_2	0.00	0.04	75.73	0.01	256006.03	0.84	1.00
Zero L_3	0.00	0.05	73.98	0.01	253085.33	0.76	1.00
Zero L_4	0.00	0.06	72.72	0.02	250233.77	0.69	1.00
Zero L_5	0.00	0.06	72.19	0.02	248863.90	0.62	1.00

subband.

The experiment is conducted for seven level wavelet decomposition and the performance measures for the extracted exudates in different wavelet subbands are calculated and tabulated in Table 3.5 and Table 3.6. Extracted exudates in L_7 , which contains, L_7 subband coefficients has higher accuracy value compared to the extracted exudates in other reconstructed images. For this, the accuracy is found to be 56.94%. Zeroing the coefficients of one level subband and keeping other level subband coefficients, it is found that L_7 subband coefficients contribute more information towards exudate than L_1 subband coefficients. By making the coefficients of L_1 subband alone to zero, the extracted exudates have the accuracy of 95.90%. By making the coefficients of L_7 subband to zero the accuracy of extracting exudates reduces to 56.69%. Structural change of the exudates in different

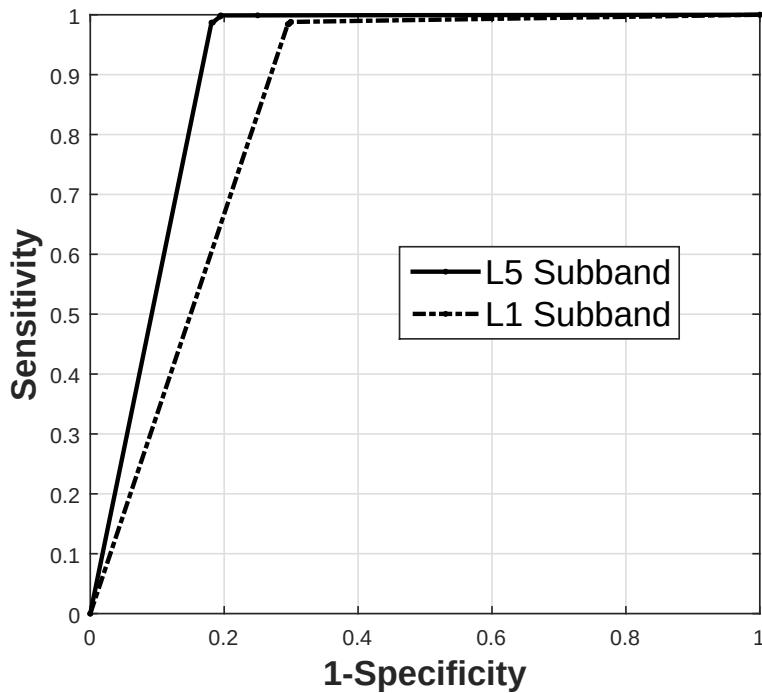


Figure 3.17: ROC curve for analysis of exudates in 5-level wavelet decomposition.

wavelet subbands is calculated by different measures and are shown in Table 3.6. The values are found to be highest for L_7 , which is reconstructed by considering the L_7 subband coefficients and making the other level subband coefficients to zero.

Similarly, the performance values of the exudate features are calculated for nine level wavelet decomposition and tabulated in Table 3.7 and Table 3.8. The value of accuracy for the extraction of exudates in the reconstructed image L_3 is found to be higher, i.e., 48.78%. It contains higher exudate information than the other reconstructed images. The L_8 reconstructed image contains less exudate information compared to L_3 reconstructed image. The accuracy value for the extraction of exudates from 'Zero L_8 ' reconstructed image is found to be very less, i.e., 36.95%. By zeroing L_8 subband coefficients and keeping other level subband coefficients reduces the accuracy of the extraction of exudates. The structure of the exudate is changed significantly when L_8 subband coefficients are made to zero. Universal quality index value is found to be 0.34 in the reconstructed image 'Zero L_8 '. Mainly the exudate information is present in L_3 and L_8 subband coefficients in nine level wavelet decomposition.

The mean opinion score (MOS) for DR features in different wavelet subbands is tabulated in the

Table 3.5: Performance measure values (set-1) of extraction of exudates in different level subband of 7-level wavelet decomposition.

Reconstructed Image	STV	SPF	SEN	ACC	EER
L_1	95.97	45.44	54.56	47.62	26.19
L_2	94.95	45.86	54.14	47.98	26.01
L_3	94.98	46.69	53.31	48.78	25.61
L_4	95.59	48.03	51.97	50.08	24.96
L_5	96.64	49.67	50.33	51.70	24.15
L_6	96.64	49.67	50.33	51.70	24.15
L_7	98.53	55.04	44.96	56.94	21.53
Zero L_1	100.00	95.70	4.30	95.90	2.05
Zero L_2	100.00	92.90	7.10	93.22	3.39
Zero L_3	100.00	88.51	11.49	89.03	5.48
Zero L_4	100.00	82.07	17.93	82.88	8.56
Zero L_5	100.00	72.65	27.35	73.85	13.07
Zero L_6	100.00	60.35	39.65	62.06	18.97
Zero L_7	100.00	54.76	45.24	56.69	21.66

Table 3.6: Performance measure values (set-2) of extraction of exudates in different level subband of 7-level wavelet decomposition.

Reconstructed Image	MSE	RMSE	PSNRv	MAE	PCC	UQI	SSIM
L_1	0.03	0.17	63.68	0.07	136355.81	0.41	1.00
L_2	0.03	0.17	63.74	0.07	138849.06	0.41	1.00
L_3	0.03	0.16	63.93	0.07	146806.74	0.41	1.00
L_4	0.03	0.16	64.13	0.06	154105.84	0.40	1.00
L_5	0.03	0.16	64.24	0.06	157636.51	0.41	1.00
L_6	0.02	0.15	64.58	0.06	168300.53	0.41	1.00
L_7	0.02	0.16	64.47	0.06	161034.30	0.46	1.00
Zero RL_1	0.00	0.04	75.90	0.01	256179.68	0.90	1.00
Zero L_2	0.00	0.04	75.73	0.01	256006.03	0.84	1.00
Zero L_3	0.00	0.05	73.98	0.01	253085.33	0.76	1.00
Zero L_4	0.00	0.06	72.72	0.02	250233.77	0.69	1.00
Zero L_5	0.00	0.06	72.19	0.02	248863.90	0.62	1.00
Zero L_6	0.01	0.07	71.19	0.03	243988.19	0.53	1.00
Zero L_7	0.01	0.07	71.57	0.03	246254.28	0.51	1.00

table by experts. From the MOS table it may be concluded that in 3-level wavelet decomposition L_3 , L_2 and L_1 subbands contains almost similar information about the microaneurysms. In 5-level wavelet decomposition L_5 , L_4 , and L_1 subbands contain more information about microaneurysms than the other subbands. In 7-level wavelet decomposition L_7 subband contains more information about MAs than the other subbands. In 9-level wavelet decomposition L_9 and L_8 subbands contain more information about the MAs.

Similarly, the MOS is tabulated for 5-level, 7-level and 9-level wavelet decomposition for exudates.

3. Multiscale analysis of diagnostic features of retinal images

Table 3.7: Performance measure values (set-1) of extraction of exudates in different level subband of 9-level wavelet decomposition.

Reconstructed Image	STV	SPF	SEN	ACC	EER
L_1	84.62	1.54	98.46	5.05	47.47
L_2	81.48	2.63	97.37	5.95	47.02
L_3	94.98	46.69	53.31	48.78	25.61
L_4	80.17	6.37	93.63	9.49	45.26
L_5	82.98	9.26	90.74	12.36	43.82
L_6	82.98	9.26	90.74	12.36	43.82
L_7	82.98	9.26	90.74	12.36	43.82
L_8	98.42	32.32	67.68	35.14	32.43
L_9	99.91	11.04	88.96	14.81	42.60
Zero L_1	100.00	95.70	4.30	95.90	2.05
Zero L_2	100.00	92.90	7.10	93.22	3.39
Zero L_3	100.00	88.51	11.49	89.03	5.48
Zero L_4	100.00	82.07	17.93	82.88	8.56
Zero L_5	100.00	72.65	27.35	73.85	13.07
Zero L_6	100.00	60.35	39.65	62.06	18.97
Zero L_7	100.00	54.76	45.24	56.69	21.66
Zero L_8	100.00	34.17	65.83	36.95	31.53
Zero L_9	100.00	54.76	45.24	56.69	21.66

Table 3.8: Performance measure values (set-2) of extraction of exudates in different level subband of 9-level wavelet decomposition.

Reconstructed Image	MSE	RMSE	PSNRv	MAE	PCC	UQI	SSIM
L_1	0.04	0.19	62.81	0.07	102485.76	0.02	1.00
L_2	0.03	0.19	62.90	0.07	111471.66	0.01	1.00
L_3	0.03	0.16	63.93	0.07	146806.74	0.41	1.00
L_4	0.03	0.18	63.33	0.07	137747.22	0.01	1.00
L_5	0.03	0.17	63.44	0.07	141187.80	0.04	1.00
L_6	0.03	0.17	63.44	0.07	141187.80	0.04	1.00
L_7	0.03	0.17	63.44	0.07	141187.80	0.04	1.00
L_8	0.03	0.18	63.21	0.07	117012.31	0.29	1.00
L_9	0.04	0.19	62.63	0.08	76913.41	0.10	1.00
Zero L_1	0.00	0.04	75.90	0.01	256179.68	0.90	1.00
Zero L_2	0.00	0.04	75.73	0.01	256006.03	0.84	1.00
Zero L_3	0.00	0.05	73.98	0.01	253085.33	0.76	1.00
Zero L_4	0.00	0.06	72.72	0.02	250233.77	0.69	1.00
Zero L_5	0.00	0.06	72.19	0.02	248863.90	0.62	1.00
Zero L_6	0.01	0.07	71.19	0.03	243988.19	0.53	1.00
Zero L_7	0.01	0.07	71.57	0.03	246254.28	0.51	1.00
Zero L_8	0.00	0.05	74.64	0.03	256225.19	0.34	1.00
Zero L_9	0.00	0.02	84.60	0.01	261542.98	0.58	1.00

Table 3.9: MOS for MAs and haemorrhages in different level subbands of various levels wavelet decomposition.

Decomposition Level	Excellent	Good	Fair	Poor	Bad
3-Level	L3, L2, L1				
5-Level	L5 Subband	L4 Subband	L1 Subband	L3 Subband	L2 subband
7-Level	L7 Subband	L6 Subband	L5 Subband	L4 Subband	L1, L2, L3 Subbands
9-Level	L9, L8 Subbands	L7, L6 Subbands	L5 Subband	L2, L3 Subbands	L1, L4 Subbands

Table 3.10: MOS for exudates in different level subbands of various levels wavelet decomposition.

Decomposition Level	Excellent	Good	Fair	Poor	Bad
5-Level	L5 Subband	L1, L2 Subbands		L3 Subband	L4 Subband
7-Level	L7, L6 Subbands	L5 Subband	L1 Subband	L4, L3 Subbands	L2 Subband
9-Level	L8, L3 Subbands	L6 Subband	L1 Subband	L2 Subbands	L9, L5, L4 Subbands

Table 3.11: Cumulative metric for exudates in 5-level wavelet decomposition.

Subband	ACC	UQI	Cumulative metric-1	Cumulative metric-2
L1	71.56	0.59	0.878	0.893
L2	71.86	0.59	0.882	0.893
L3	72.57	0.59	0.890	0.893
L4	72.46	0.57	0.889	0.864
L5	81.47	0.66	1	1

Table 3.12: Cumulative metric for exudates in 7-level of wavelet decomposition

Subband	ACC	UQI	Cumulative metric-1	Cumulative metric-2
L1	47.62	0.41	0.836	0.891
L2	47.98	0.41	0.843	0.891
L3	48.78	0.41	0.857	0.891
L4	50.08	0.41	0.880	0.891
L5	51.70	0.41	0.908	0.891
L6	51.70	0.41	0.908	0.891
L7	56.94	0.46	1	1

Table 3.13: Cumulative metric for exudates in 9-level of wavelet decomposition.

Subband	ACC	UQI	Cumulative metric-1	Cumulative metric-2
L1	5.05	0.02	0.103	0.049
L2	5.95	0.01	0.122	0.024
L3	48.78	0.41	1	1
L4	9.49	0.01	0.195	0.476
L5	12.36	0.04	0.253	0.671
L6	12.36	0.04	0.253	0.671
L7	12.36	0.04	0.253	0.671
L8	35.14	0.29	0.720	0.707
L9	14.81	0.10	0.304	0.244

3. Multiscale analysis of diagnostic features of retinal images

$L5$ subband contains higher information compared to other subbands for exudates in 5-level wavelet decomposition. In 7-level wavelet decomposition $L7$, $L6$, and $L5$ subbands contain more information about the exudates. $L8$ and $L3$ contain more exudates information about the exudates in 9-level wavelet decomposition, whereas $L4$, $L5$, and $L9$ contain less information about the exudates.

The cumulative metric is calculated from the performance measure of the extraction of the exudates by dividing the highest value with the obtained value. This measure will provide the measure for selection of wavelet subband for DR features. In this case, accuracy and UQI values are considered for the selection of subbands for the DR features. In five level decomposition, $L5$ subband contains higher exudate information. The $L7$ subband, in seven level wavelet decomposition contains higher exudate information. The $L3$ and $L8$ subbands contain higher exudate information about the DR feature in 9-level wavelet decomposition. The cumulative metric obtained for exudates matched the MOS value. For 5-level wavelet decomposition the MOS for $L5$ subband is good and it agrees with the cumulative metric value. Similarly, for 7-level wavelet decomposition the MOS for $L7$ is better compared to the other subbands. For $L7$ in 7-level wavelet decomposition the cumulative metric shows higher value. In 9-level wavelet decomposition the $L3$ and $L8$ subbands show higher cumulative metric value. The MOS for 9-level is good for $L8$ and $L3$ subbands.

3.5 Summary

In this chapter, pathological features (microaneurysms and exudates) are studied in different wavelet subbands for different level of wavelet decomposition. The fundus image is decomposed into 3-, 5-, 7- and 9-level by db4 mother wavelet. In each level microaneurysm and exudate features are studied from the view of diagnostic information. From the above study, the following conclusions can be drawn.

- (i) Analysis of MAs is done on 3-, 5-, 7-, and 9-level of wavelet decomposition with db4 mother wavelet. In 3-level wavelet decomposition, all the subbands contribute equally to the feature MAs.

In 5-level wavelet decomposition, subband $L1$, subband $L2$ and subband $L3$ contain less information about the MAs. Most of the information is present in subband $L4$ and subband $L5$ in 5-level wavelet decomposition. So, during the analysis of MAs information higher attention should be given to the coefficients of $L4$ and $L5$ subbands.

In 7-level wavelet decomposition, $L5$, $L6$, and $L7$ contribute more information towards MAs. Subband $L5$ to subband $L9$ coefficients contain higher MAs information compared to other levels. Higher subband coefficients contain more MAs information compared to lower level subband coefficients.

- (ii) In 5-level wavelet decomposition subband $L1$, $L2$ do not contain more information about exudate. The subbands $L4$ and $L5$ contain more blood vessel information. From the quantitative evaluation it is found that $L5$ subband in five level wavelet decomposition contains higher exudate information. Combining the coefficients of subbands $L1$, $L2$, and $L3$ the exudate information can be preserved and the blood vessel information can be suppressed.

In 7-level wavelet decomposition, subband $L1$, $L2$, $L3$, $L6$ and $L7$ contain the exudate information. By altering the coefficients of $L2$, $L3$, and $L4$ subbands, the blood vessel information is lost without the loss of exudate information. In 7-level wavelet decomposition, $L2$, $L3$ and $L4$ subbands do not contain significant information about the DR feature. The $L7$ subband in 7-level decomposition has higher accuracy value.

In 9-level wavelet decomposition, blood vessels information is present in $L4$ and $L5$. The $L3$ and $L8$ subbands contain more exudate information, according to the performance measure values (accuracy, UQI, PCC and sensitivity etc.).



4

Multiscale ICA for detection of DR features

Contents

4.1	Segmentation of blood vessels	83
4.2	Independent component analysis for fundus image	88
4.3	Multiscale ICA for detection of exudates	109
4.4	Detection of change in color fundus due to DR	114
4.5	Summary	116

4. Multiscale ICA for detection of DR features

The distribution of clinical features (such as: microaneurysms, exudates, and haemorrhages) and normal features (such as: blood vessels, optic disc, and macula) information in different wavelet subbands of the retinal images are investigated in Chapter 3. Different wavelet subbands have different diagnostic importance. The diagnostic information of retinal features due to DR is captured by a few wavelet subbands. Different levels in five level decomposition carries different information. Extraction of DR features in wavelet scale can reduce the computation time. As different wavelet subbands contribute differently to different features, by combining two or more wavelet subbands the pathological features can be extracted by independent component analysis (ICA). Wavelet decomposition is also applied to the other color channels such as: HSV. Combining the channels of different colors and different levels of decomposition, the data matrix is formed. To the data matrix ICA is applied to find the pathological features in the color fundus images. In this chapter, extraction of blood vessels and exudates from the color fundus images is proposed in different scales of wavelet decomposition. Extraction of features is done by using ICA in multiscale domain. The ICA has the property of finding the independent components (ICs) from the mixture. The ICs are assumed to be non-Gaussian in nature. By multiscale wavelet decomposition different wavelet subbands are created. The different wavelet subbands are combined suitably to form the mixing matrix for separation of DR features from the fundus images by ICA. Applying ICA in wavelet subband can able to detect the changes occurred in the retina. This provides the progression of any disease due to DR. This is achieved by comparing a healthy/normal fundus image with the DR affected fundus images taken in the same environmental conditions. The performance of the proposed method has been compared with the existing methods in the literature.

In this chapter, ICA is used as a tool in multiscale for detection of features from fundus images. Section 4.1 discusses about the extraction of blood vessels and pathologies from the color fundus images. In this Section, the vessels affected by pathology has been calculated. Section 4.2 discusses about ICA on multiscale for fundus images. In this Section, the advantages of multiscale ICA (MSICA) over ICA are discussed. Detection of exudates is discussed in Section 4.3. Detection of changes in the retina due to DR are discussed in Section 4.4. Summary and conclusions of this chapter are presented in Section 4.5.

4.1 Segmentation of blood vessels

Various segmentation techniques are applied over the fundus images for segmentation of blood vessels (BVs). These methods include Kirsch's method [56], histogram equalization approach [141] and Gaussian based matched filter approach [45]. These techniques are merged together to obtain better segmentation performance than the individual blood vessel segmentation algorithm. The detail description of these methods is given below.

Kirsch method [56] is a template-based method which uses 8 templates in eight different possible edge directions, i.e., left-right, up-down, upper-left and lower-right, etc. For each pixel of the image, all eight templates are applied and maximum value is chosen to be compared with the threshold. The template which has been used in Kirsch's method is given below.

$$\begin{pmatrix} 5/15 & -3/15 & -3/15 \\ 5/15 & -3/15 & -3/15 \\ 5/15 & -3/15 & -3/15 \end{pmatrix}$$

The above mentioned template is slightly modified to get BV segmentation, which is given below.

$$\begin{pmatrix} 5/21 & -3/21 & -3/21 \\ 5/21 & -3/21 & -3/21 \\ 5/21 & -3/21 & -3/21 \end{pmatrix}$$

Contrast limited adaptive histogram equalization [141] method, which divides the image into a number of small non-intersecting contextual regions for processing an image. The various steps involved in this method are contrast enhancement (provide a better transform representation for subsequent image analysis steps), background exclusion (eliminates background variations), and thresholding and post filtration (produce a binary image in which the value of each pixel is either 1 (blood vessel) or 0 (background)). To remove noise from the image, morphological operations were performed on the segmented image.

Matched filter with first order Gaussian Function [45] provides good performance with comparatively low complexity. The matched filter (MF) is a zero mean Gaussian function, which uses filtering and thresholding in the original image for detecting vessels from the color fundus images. Gaussian shaped filter can be used to match the vessels for detection, as the pixel values of the cross section of a vessel can be modeled as a Gaussian function. The MF responses, both vessels and non-vessel edges. Matched filter with first order Gaussian function overcomes the limitation of MF which has the capability to reduce the noise. All the above techniques were applied to noised color fundus image

4. Multiscale ICA for detection of DR features

to check the efficiency of the segmentation process. Fundus image is associated with low contrast and non-uniform illumination and this is visible at the edge of the image. The occurrence of noise in fundus image is the impulse and Gaussian noise [142].

The above discussed methods are applied to the fundus image databases, and compared with the manually segmented images by measuring different performance measures such as sensitivity, specificity, sensibility, accuracy, equal error rate (EER), Fscore, Jaccard's coefficient (KJ), conformity coefficient (KC) and dice coefficient (KD). The Table 4.1 shows the performance of blood vessel segmentation of different methods. Above discussed methods are merged to have better segmentation of blood vessels. Merging of modified Kirsch method with the Gaussian based method (KG) provides better result compared to the merging of Kirsch, histogram and Gaussian (KHG) based method. The Gaussian based method provides higher accuracy compared to other methods. Merging Kirsch and Gaussian based methods provide higher specificity and lower sensibility compared to other methods. This method has lower accuracy than that of Gaussian based method. The performance of different methods is shown in a bar plot in Fig. 4.1. Above mentioned blood vessel segmentation methods are tested in the presence of salt and pepper noise as fundus image is affected by salt and pepper noise. The performance of different methods in the presence of noise is tabulated in Table 4.2. In the presence of noise match filter with first order Gaussian function has higher accuracy (91.01%). The KG based method is better compared to the other methods in terms of specificity (95.54%) and sensibility (4.45%) in the presence of salt and pepper noise.

Table 4.1: Performance values of different blood vessels extraction techniques.

Method	Sensitivity	Specificity	Sensibility	Accuracy	EER	Fscore	KC	KJ	KD
Kirsch	43.03	94.93	5.07	90.24	4.87	-59.06	-159.77	28.37	44.05
Modified Kirsch	42.55	93.58	6.41	90.70	4.64	-58.29	-310.15	20.80	34.15
Histogram	48.93	94.18	5.81	91.06	4.46	-63.83	-194.04	25.78	40.88
Gaussian	76.03	97.06	2.93	95.46	2.26	-85.12	21.04	56.11	71.81
KGH	49.75	97.91	2.09	91.27	4.36	-65.70	-32.17	43.67	60.62
KG	52.98	98.077	1.92	92.22	3.88	-68.64	-15.27	46.77	63.64

4.1.1 Segmentation of DR features/pathologies

The block diagram of the segmentation of DR features of the color fundus image is given in Fig. 4.2. After Gaussian based segmentation technique for extracting the blood vessels from the color fundus image, the pathologically affected regions of the fundus image are to be separated. Inpainting is used

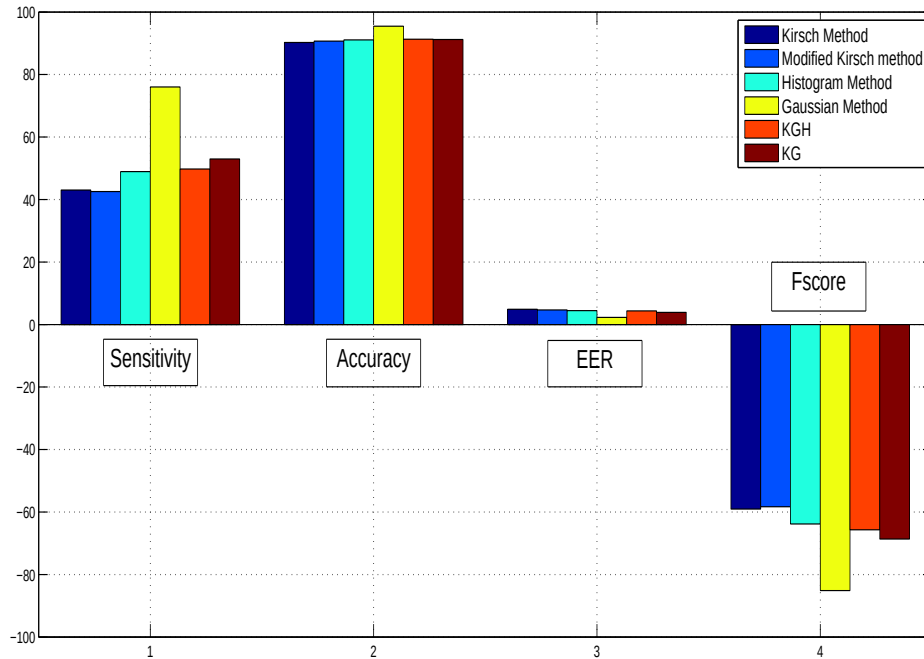


Figure 4.1: Performance measure of blood vessel segmentation methods.

Table 4.2: Performance values of different blood vessels extraction techniques in the presence of salt and pepper noise.

Method	Sensitivity	Specificity	Sensibility	Accuracy	EER	Fscore	KC	KJ	KD
Kirsch	49.37	92.09	7.90	87.21	6.39	-64.18	-132.83	30.70	46.79
Modified Kirsch	45.49	90.24	9.76	86.68	6.66	-60.25	-285.86	21.78	35.47
Histogram	52.63	90.17	9.82	87.48	6.26	-66.18	-261.37	22.06	36.05
Gaussian	70.26	93.14	6.85	91.01	4.49	-79.94	-39.81	42.04	59.09
KGH	52.66	95.24	4.75	88.19	5.90	-67.73	-37.08	42.51	59.56
KG	48.222	95.54	4.45	86.545	6.727	-63.95	-49.81	40.38	57.42

to remove the effect of the blood vessels. The fundus image contains various pathological features. The inpainted image is subjected to histogram equalization to obtain the pathologies. The extracted pathologies are intersected with the extracted blood vessel image to obtain the blood vessels that are affected by pathology. This helps determine the extent to which the pathology has affected the blood vessels. The intersection of pathologies with the blood vessels gives rise to the number of pixels of blood vessels affected by pathologies ($\%BV_a$) and represented by:

$$\%BV_a = \frac{BV_a}{BV_p} \times 100 \quad (4.1)$$

4. Multiscale ICA for detection of DR features

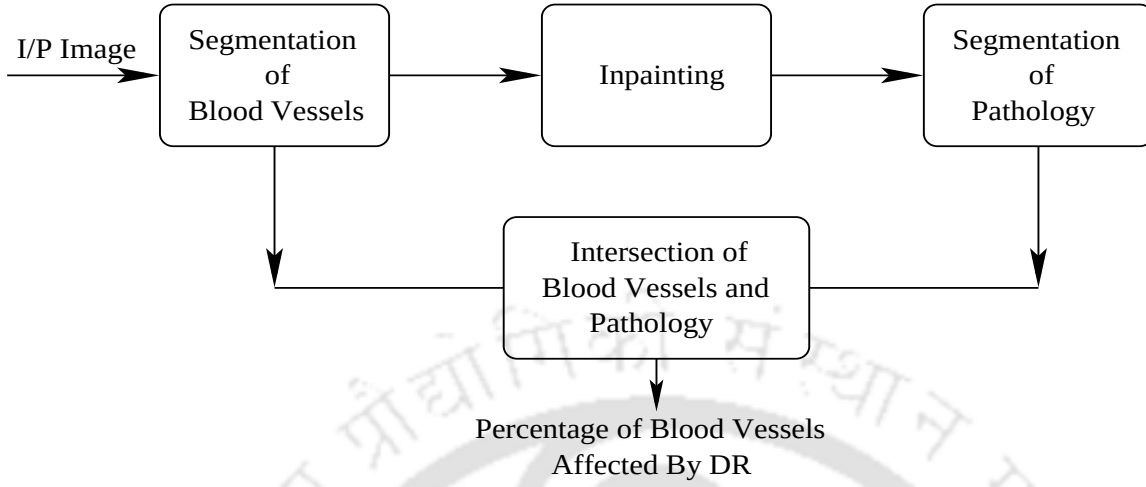


Figure 4.2: Detection of affected regions of BVs by DR.

where, BV_p represents the total number of blood vessel pixels. The pathological pixels are compared with the blood vessel pixels to find the affected blood vessels by pathologies. The output of different stages of blood vessels affected by pathologies is shown in Fig. 4.3. The color fundus image and green channel image are shown in Fig. 4.3(a) and Fig. 4.3(b), respectively. The pathologies appear as white patches in Fig. 4.3(b). Fig. 4.3(c) shows the extracted blood vessels by Kirsch Gaussian method. This image is used as a mask for inpainting technique to inpaint the green channel image. The inpainted image is shown in Fig. 4.3(d). The blood vessel information is suppressed in this image. It only highlights the pathological regions. Pathologies are extracted from the inpainted image. The extracted pathologies are shown in Fig. 4.3(e). The inpainting takes nearly 2-minutes per image. In order to overcome this problem the segmentation of blood vessels and inpainting is performed in multiscale domain. This reduces the time for inpainting. The extracted blood vessels are compared with the extracted pathologies to find the amount of blood vessels affected by pathologies. Fig. 4.3(f) shows the amount of blood vessels affected by pathologies.

Table 4.3 shows the percentage of affected blood vessels ($\%BV_a$) for 40 pathological images. In image-24 (Im-24) only 2.98% blood vessels are affected by pathologies. The Im-24 is shown in Fig. 4.4. In this case, the less amount of blood vessels are affected by pathologies. In Im-18, 68.78% of blood vessels is affected by pathologies. This is shown in Fig. 4.3. It may be concluded that, the blood vessels in Im-24 are less affected by pathologies than the blood vessels in Im-18. So, vision condition in Im-18 is poor compared to Im-24. This has been validated by the ophthalmologist in Vinayak hospital Karaikal, Puducherry.

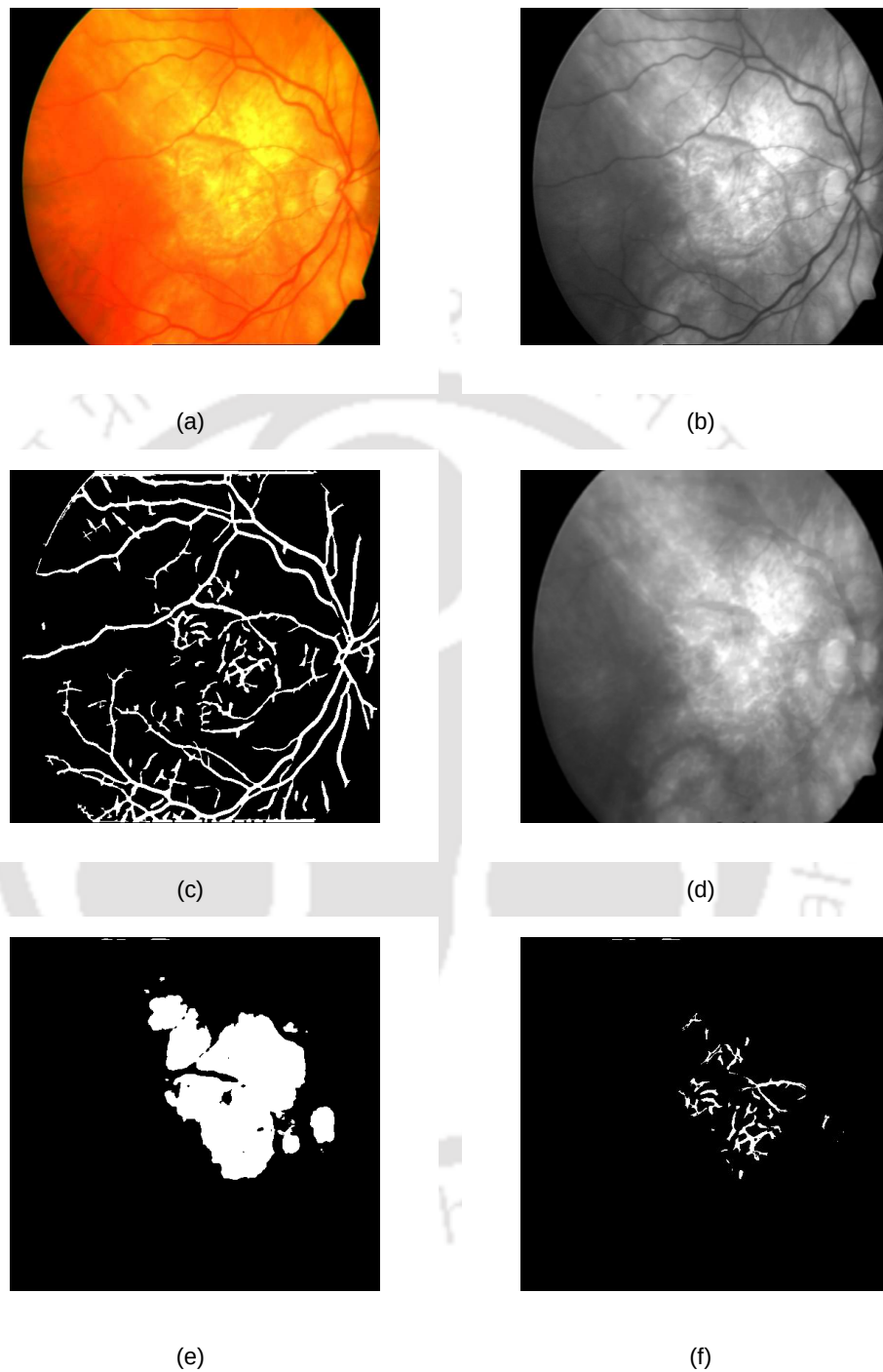


Figure 4.3: Affected blood vessels by DR: (a) fundus image, (b) green channel image, (c) extracted blood vessels, (d) inpainted image, (e) extracted pathology, and (f) blood vessels affected by DR.

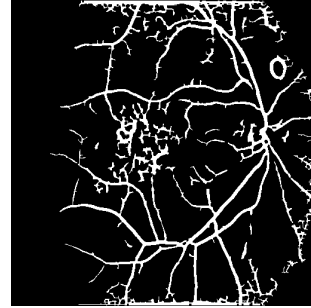
4. Multiscale ICA for detection of DR features

Table 4.3: Amount of blood vessels affected by pathologies in fundus image (Im).

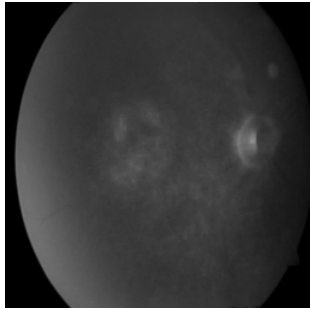
Im	BV_p	BV_a	$\%BV_a$	Im	BV_p	BV_a	$\%BV_a$	Im	BV_p	BV_a	$\%BV_a$	Im	BV_p	BV_a	$\%BV_a$
Im-1	40433	10957	27.10	Im-11	31536	3845	12.19	Im-21	29844	5510	18.46	Im-32	34123	1544	4.52
Im-2	46275	10271	22.20	Im-12	34314	6447	18.79	Im-22	33741	6975	20.67	Im-32	35348	5273	14.92
Im-3	40421	21229	52.52	Im-13	39555	3639	9.20	Im-23	29834	2923	9.80	Im-33	39577	4777	12.07
Im-4	40682	19468	47.85	Im-14	33949	5742	16.91	Im-24	30619	913	2.98	Im-34	32934	2975	9.03
Im-5	40214	4567	11.36	Im-15	37500	4980	13.28	Im-25	33325	1190	3.57	Im-35	31498	4824	15.32
Im-6	34654	1791	5.17	Im-16	32628	9571	29.33	Im-26	37377	2312	6.19	Im-36	34564	9237	26.72
Im-7	37102	5065	13.65	Im-17	35492	6470	18.23	Im-27	40034	6802	16.99	Im-37	31879	1706	5.35
Im-8	32260	4417	13.69	Im-18	32888	22619	68.78	Im-28	33266	7167	21.54	Im-38	30470	5858	19.23
Im-9	31199	6582	21.10	Im-19	34053	4550	13.36	Im-29	37333	5489	14.70	Im-39	42241	11320	26.80
Im-10	33454	10659	31.86	Im-20	37466	8825	23.55	Im-30	37132	1618	4.36	Im-40	34040	9768	28.70



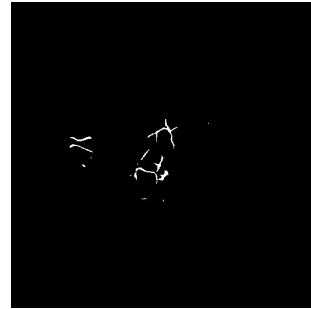
(a)



(b)



(c)



(d)

Figure 4.4: Assessment of pathology affected blood vessels from color fundus image: (a) color fundus image, (b) segmented blood vessels, (c) inpainted image, (d) blood vessels affected by pathology

4.2 Independent component analysis for fundus image

Independent component analysis (ICA) is applied to the mixing matrix formed by the subbands of wavelet decomposition to find the independent components. It can provide better performance if the features are non-Gaussian and independent. The different color channels of the fundus images, such as RGB, and HSV, etc. can be used to form the data matrix for applying ICA. RGB, and HSV

color images have different contrast as well as different information in different color channel. Due to this reason ICA is applied on color fundus images for detection of DR features. As the correlation in different color channels are not equal, so the success of DR feature detection depends on the selection of color channel. The selection of color channel for detection of DR features depends on the correlation between the color channels. This is discussed in subsection 4.2.2. The different features present in the fundus image has different distribution in terms kurtosis and negentropy, which is discussed in subsection 4.2.3. The performance evaluation of MSICA over ICA is discussed in subsection 4.2.6.

4.2.1 Correlation and independence

According to Cardoso [143] there exists a relation between maximum independence and minimum entropy. The Independent components (ICs) are calculated by minimizing the mutual information, i.e., equivalent to minimizing the sum of the entropies of all components. The connections between mutual information, entropy and non-Gaussianity are explored without imposing the somewhat arbitrary decorrelation constraint. In ICA, mutual information can be decomposed in two terms, one measures decorrelation and the other term measures Gaussianity between the components. These connections can be described in the light of information geometry.

Mutual Information or Dependence: According to Comon [144] ICA of a random vector (y) finds a basis on which the coordinates of y are as independent as possible. Statistical independence can be measured by the Kullback-Leibler divergence (KLD) from the distribution $p(y)$ of y to the product of its marginal distributions

$$I(y) = K[p(y), \prod_i p(y_i)] \quad (4.2)$$

where, the divergence $K[\tilde{P}, \tilde{Q}]$ from a probability distribution $\tilde{P}$ to another distribution $\tilde{Q}$.

$$K[\tilde{P}, \tilde{Q}] = \int \tilde{P}(y) \log \frac{\tilde{P}(y)}{\tilde{Q}(y)} dy \quad (4.3)$$

It is greater than zero when the two distributions are identical. $I(y) = 0$ if the distribution of y is the product of its marginal.

Decorrelation and Minimum Entropy: ICA is performed by two steps, (i) whiten or spear after mean removal, and (ii) rotation to maximize the independence. Whitening finds the correlation matrix, which

4. Multiscale ICA for detection of DR features

makes the components uncorrelated but not independent. Rotation is the orthogonal approach which preserves the whiteness. By the orthogonal approach, the overall transformation can be viewed as the product of a whitening matrix by an orthogonal matrix. By tuning the Equ. (4.3) into the difference of logarithm we obtain:

$$I(y) = \sum_i H(y_i) - H(y) \quad (4.4)$$

where, $H(\cdot)$ denotes Shannon's differential entropy and written as:

$$H(y) = - \int p(y) \log p(y) dy \quad (4.5)$$

By applying linear transformation T , the vectors will add a term $\log |\det T|$ to its entropy and $H(y)$ remains constant. So, dependence (mutual information) $I(y)$ in Equ. (4.4) becomes equal to a constant term $H(y)$, i.e., the sum of the marginal entropies of y . ICA is a minimum entropy method under the whiteness constraint. ICA is based on independence, but independence cannot be reduced to the simple de-correlation conditions, i.e., $E(y_i y_j) = 0$. Two random variables y_i, y_j are uncorrelated means: $E(y_i y_j) - E(y_i)E(y_j) = 0$. Two random variables y_i, y_j are independent means: $p(y_i, y_j) = p(y_i)p(y_j)$. In the next subsection correlation is calculated between different color components to determine the correlation between the color components. This may provide the information about the less correlated color channel. By applying ICA to less correlated color channel may increase the performance of independent feature detection.

4.2.2 Correlation in different color channels

In this subsection, different color channels are considered (such as: RGB, HSV, $l\alpha\beta$) [4, 37, 145]. Different images are used for the study such as Lena, mandril, normal fundus images and abnormal fundus images. Fifty four fundus images (both normal and disease fundus images) are considered for the study. Different color channels are considered and correlation between them are calculated. Table 4.4 shows the correlation coefficient values in different color component of different color channels (RGB, HSV, $l\alpha\beta$) of 10 different images such as Lena, mandril, two normal fundus images (N-FIm) and six abnormal fundus images (A-FIm). The mean correlation values for all the color channels are noted in the last row of the table. Correlation coefficients are calculated between color components of different color channels (such as: hue and saturation (HS), saturation and value (SV), value and

hue (VH), red and green (RG), green and blue (GB), blue and red (BR), I and α ($I\alpha$), α and β ($\alpha\beta$), β and I (βI). Correlation coefficients of different components of the HSV color channel are found to be less than other components of the color channels (i.e., RGB and $I\alpha\beta$). Due to this reason ICA is applied on HSV color channel to find the features as this may improve the feature detection.

Table 4.4: Correlation coefficient between different color channels of the images.

Images	Correlation(ρ)-RGB			Correlation(ρ)-HSV			Correlation(ρ)- $I\alpha\beta$		
	$\rho(RG)$	$\rho(BG)$	$\rho(BR)$	$\rho(HS)$	$\rho(SV)$	$\rho(VH)$	$\rho(I\alpha)$	$\rho(\alpha\beta)$	$\rho(\beta I)$
Lena	0.8786	0.9106	0.6764	0.5299	-0.7039	-0.6761	0.9953	0.9332	0.9012
Mandrill	0.3565	0.8071	0.1236	0.3428	0.3683	0.0304	0.9655	0.8290	0.7057
N-Flm-1	0.9846	0.9882	0.9682	-0.4606	0.8645	-0.6307	0.9993	0.9929	0.9895
N-Flm-2	0.9223	0.9852	0.9215	-0.5382	0.8800	-0.6891	0.9961	0.9890	0.9768
A-Flm-1	0.7678	0.7484	0.3239	0.3524	0.8321	0.3260	0.9889	0.8656	0.8006
A-Flm-2	0.8810	0.7945	0.5316	0.1995	0.6359	0.0779	0.9938	0.9035	0.8625
A-Flm-3	0.9102	0.4946	0.3414	0.5056	0.7779	0.2433	0.9957	0.9295	0.9098
A-Flm-4	0.7670	0.7480	0.3230	0.5050	0.7770	0.2428	0.9965	0.9337	0.9097
A-Flm-5	0.7665	0.7476	0.3235	0.5052	0.7775	0.2429	0.9929	0.8735	0.8270
A-Flm-6	0.7660	0.7470	0.3230	0.5046	0.7769	0.2423	0.9932	0.8940	0.8500
Mean	0.8000	0.7971	0.4856	0.2446	0.5986	-0.5903	0.9917	0.9143	0.8733

Table 4.5 shows the correlation coefficient values for ten images of R, G and B components of RGB color channel with the H, S, V color components of HSV color space (i.e., red and hue (RH), red and saturation (RS), red and value (RV), green and hue (GH), green and saturation (GS), green and value (GV), blue and hue (BH), blue and saturation (BS), and blue and value (BV)). The mean values of the correlation coefficients are noted in the last row. The correlation coefficient value is found to be lower between the green component of RGB and the hue component of the HSV. These different color components can be used in ICA for detection of features from the fundus images. Similarly, the correlation coefficient values of the color components are also calculated in the wavelet domain. In 5-level wavelet decomposition using db4 mother wavelet, the correlation between the green channel of RGB and hue component of HSV is found to be 0.9923 and 0.9707, respectively. For feature extraction process five level decomposition is performed using db4 mother wavelet. Based on the lower correlation coefficient values the color channels are selected for ICA application.

4.2.3 Statistical evaluation of features in fundus image

Shape, size and color of the features in the color fundus images do not provide any information about the distribution of the pixels. Statistical measures, such as kurtosis, skewness and negentropy are

4. Multiscale ICA for detection of DR features

Table 4.5: Correlation coefficient between color channels RGB and HSV.

Images	$\rho(R\text{-HSV})$			$\rho(G\text{-HSV})$			$\rho(B\text{-HSV})$		
	$\rho(RH)$	$\rho(RS)$	$\rho(RV)$	$\rho(GH)$	$\rho(GS)$	$\rho(GV)$	$\rho(BH)$	$\rho(BS)$	$\rho(BV)$
Lena	-0.6768	-0.6975	0.9993	-0.7160	-0.8943	0.8815	-0.5471	-0.9507	0.6850
Mandrill	-0.2279	0.3819	0.8377	0.1860	-0.2837	0.6066	0.5298	-0.4040	0.5299
N-FIm-1	-0.6133	0.8680	1.0000	-0.6130	0.8346	0.9846	-0.5976	0.8106	0.9682
N-FIm-2	-0.6592	0.8829	1.0000	-0.6203	-0.7587	0.9223	-0.6168	0.7581	0.9214
A-FIm-1	0.2704	0.8214	0.9997	0.4824	0.4333	0.7691	0.4197	-0.0183	0.3249
A-FIm-2	0.0524	0.6291	1.0000	0.0795	0.3162	0.8810	0.1064	0.0245	0.5317
A-FIm-3	0.1889	0.7681	0.9996	0.2850	0.6516	0.9118	0.1651	0.1324	0.3420
A-FIm-4	0.1941	0.6873	0.9998	0.2751	0.5939	0.9299	0.2121	0.1824	0.5483
A-FIm-5	-0.0108	0.6662	0.9999	0.0628	0.4424	0.8704	0.1126	0.0784	0.3254
A-FIm-6	0.1390	0.8270	1.0000	0.2109	0.6086	0.8747	0.1767	0.1499	0.4484
Mean	-0.0543	0.5834	0.9836	-0.0368	0.1944	0.8632	-0.0039	0.0763	0.5625

used to find the distribution of the data or features [146,147]. The characteristics of different features in the color fundus image are analyzed in different scales of multiscale decomposition in Chapter-2. Depending on the characteristics of the features, segmentation algorithm is proposed by multiscale ICA. Here, the statistical characteristics of different features in a fundus image are evaluated for the justification of ICA on fundus image.

Statistical characteristics (such as kurtosis and negentropy) of the features in the color fundus images are evaluated to obtain the distribution of the features in the fundus Images. Statistical independence of data is the requirement for success of ICA. Non-Gaussianity property is used to evaluate the statistical independence. Kurtosis can be used as a measure of non-Gaussianity [146]. Non-Gaussianity represents how much the higher moments differs from the value expected for the Gaussian distributed data. For Gaussian probability density function (pdf), the third moment (skewness) and fourth moment (kurtosis) are zero and $3\sigma^4$, respectively. The value, σ^2 represents the variance of Gaussian pdf. The moments of random variable y with pdf $p(y)$ are defined as:

$$\mu_i = \int_{-\infty}^{\infty} (y - \mu)^i p(y) dy \quad (4.6)$$

where, μ is the mean value of y , i.e., $\mu = \int_{-\infty}^{\infty} yp(y)dy$. The kurtosis proper or Pearson kurtosis [4] is defined as:

$$\beta_2 = \frac{\mu_4}{\mu_2^2} \quad (4.7)$$

It is normalized kurtosis value and can be equal to 3 or greater than 3 or less than 3 for Gaussian or super-Gaussian or sub-Gaussian random variable, respectively. The kurtosis excess is defined as:

$$\gamma_2 = \frac{\mu_4}{\mu_2^2} - 3 \quad (4.8)$$

The kurtosis excess is also known as, fourth order cumulant. It can be zero, negative and positive, for Gaussian, sub Gaussian and super Gaussian random variable, respectively. Fifty four color fundus images are selected from the publicly available fundus database [125] with sufficient variation of contrast. The Pearson kurtosis value is calculated for different features (optic disc, blood vessels, exudates, haemorrhages) of the color fundus images, after manual segmentation of the features of the green channel image. Here, the green channel image is considered for kurtosis evaluation as the green channel image is minimally saturated, i.e., green channel image has higher contrast between the background and the features. Similarly, for hue channel the kurtosis values are calculated. From the kurtosis values exudates and the haemorrhages are found to be super Gaussian in nature.

Table 4.6: Average kurtosis and negentropy values of different features in in retinal images with exudates.

Features	Average Kurtosis value	Average Negentropy value	Comment
Optic Disc	1.9943	0.0103	Sub Gaussian
Back ground	2.4545	0.0131	Sub Gaussian
Blood Vessels	2.3647	0.00014	Sub Gaussian
Exudate	4.5960	0.0428	Super Gaussian

Table 4.7: Average kurtosis and negentropy values of different features in retinal images with haemorrhages.

Features	Average Kurtosis value	Average Negentropy value	Comment
Optic Disc	2.2909	1.8068	Sub Gaussian
Back ground	2.2322	2.5152	Sub Gaussian
Blood Vessels	2.2384	2.2607	Sub Gaussian
Haemorrhage	3.6055	0.0743	Super Gaussian

Table 4.6 shows the average kurtosis values of different features for fifty four images with exudates as pathological features. The background is the region, excluding optic disc, blood vessels and exudates. It can be observed that, maximum kurtosis value is obtained for exudates. The kurtosis values of optic disc, blood vessels and the background are found to be less than 3 implying them as sub Gaussian in nature. For all the images, the kurtosis values of exudates are higher than 3. This shows that exudates are super-Gaussian or non-Gaussian in nature. Super Gaussianity indicates

4. Multiscale ICA for detection of DR features

statistical independence of exudates [99] from other features in the fundus image. Due to this reason, ICA can be used for separation of exudates from color fundus images.

Table 4.7 shows the average Kurtosis values of different features of fifty four fundus images with haemorrhage. From the average kurtosis value, haemorrhages are found to be super Gaussian in nature as the kurtosis value is greater than 3. Due to the non-Gaussian nature, exudates and haemorrhages can be separated out from the other features by using ICA.

The probability density function (pdf) of the kurtosis values of different features (such as OD, background, blood vessels and exudates) is plotted and shown in Fig. 4.5. Fig. 4.5 (d) shows the pdf of exudates. In this figure, the distribution is present on higher side. From the pdf plot, it may be concluded that the energy content of exudates is larger compared to the other features. Fig. 4.6 shows the pdf of exudates and the non exudates region. The non exudate region is the region in color fundus images which does not contain exudates. From this figure, we may conclude that the exudates fall on the higher side compared to the non exudate regions. Due to above mentioned reasons, ICA can be used for extraction of DR features from color fundus images. ICA can be extended to multiscale for extraction of features from fundus images as different scale contribute differently to the features as discussed in Chapter-3.

4.2.4 Limitation of ICA

Determination of suitable representation and transformation of the observed data is the central problem in biomedical signal and image processing. Unlike principal component analysis (PCA), ICA is based on higher order statistics, which decorrelates the input signal and reduces higher order statistical dependencies [148]. It is a linear transformation which transforms the multidimensional random vector into components that are statistically independent. These components are called latent variables, which are assumed to be non-Gaussian and mutually independent. The observed data ($\mathbf{x}$) is assumed to be a linear mixture of vectors of statistically independent source signals ($\mathbf{s}$), which is represented by:

$$\mathbf{x} = \mathbf{M}\mathbf{s} \quad (4.9)$$

where, 'M' represents a linear mixture called the mixing matrix ($\mathbf{M} \in \mathbb{R}^{\tilde{M} \times \tilde{N}}$). ICA recovers the independent components ($\mathbf{s}$) from the mixture ($\mathbf{x}$) by estimating the unmixing matrix ($\mathbf{W}$), which is the

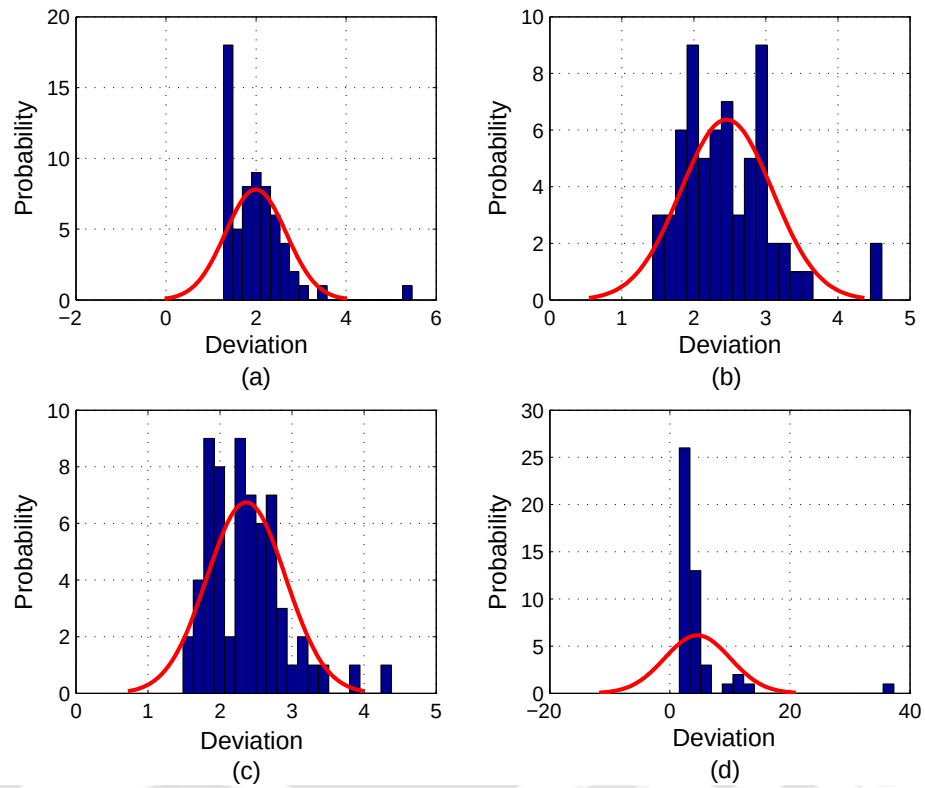


Figure 4.5: Probability density function of kurtosis of different features: (a) pdf of OD, (b) pdf of background, (c) pdf of blood vessels, (d) pdf of exudates.

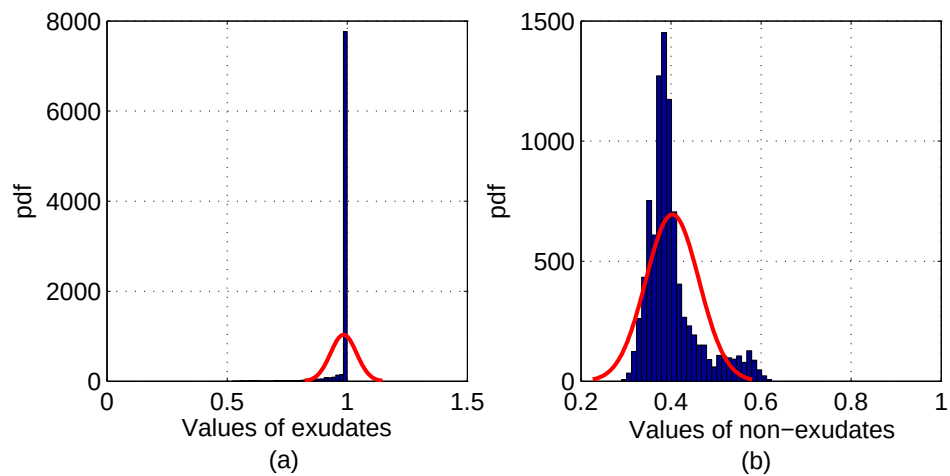


Figure 4.6: PDF of exudates and non exudate regions.

4. Multiscale ICA for detection of DR features

inverse of (M) . This can be represented as:

$$\hat{s} = Wx \quad (4.10)$$

where, $\hat{s}$ is the estimation of s . There is no direct method to obtain the unmixing matrix, as apriori information about the mixing matrix is unknown. This problem can be overcome by the central limit theorem. According to the central limit theorem the sum of two or more independent random variables has always approached towards a Gaussian distribution than the individual random variables [100]. Due to above fact non-Gaussianity can be employed for the convergence in the estimation of unmixing matrix. FastICA (FICA) algorithm estimates the independent sources ($\hat{s}$) based on measuring non-Gaussianity through negentropy or differential entropy (DE) using non-quadratic functions.

In case of practical situations (medical signals and images) the data is corrupted by noise. Suppose, the data are affected by additive white Gaussian noise ($\tilde{n} \sim \tilde{N}(0, \sigma_n^2)$). Now the observed data can be represented as:

$$x = Ms + \tilde{n} \quad (4.11)$$

Independent components can be estimated by using the unmixing matrix ($W \in R^{\tilde{M} \times \tilde{N}}$). The estimated components can be represented as:

$$\begin{aligned} \hat{s} &= Wx \\ &= W(Ms + \tilde{n}) \\ &= WMs + W\tilde{n} \end{aligned} \quad (4.12)$$

From Equ. 4.12, it is clear that the estimation of the independent component depends on WMs and influence of noise. In case of noiseless observed data ($\tilde{n} = 0$), the independent components are reconstructed perfectly. The aim is to estimate the exact independent components in the presence of noise. Optimal estimation is possible by reducing the mean square error (MSE). Error (ξ) and MSE ξ for the noisy model are given as:

$$\begin{aligned}
 \xi &= \mathbf{s} - \hat{\mathbf{s}} \\
 &= \mathbf{s} - (W M \mathbf{s} + W \tilde{\mathbf{n}}) \\
 &= (I_{\tilde{N}} - W M) \mathbf{s} - W \tilde{\mathbf{n}}
 \end{aligned} \tag{4.13}$$

$$\begin{aligned}
 MSE\xi &= \langle \xi^T \xi \rangle \\
 &= tr(\langle \xi \xi^T \rangle) \\
 &= tr\{(I_{\tilde{N}} - W M) \Sigma_s (I_{\tilde{N}} - W M)^T\} + \sigma_{\tilde{n}}^2 tr\{M M^T\}
 \end{aligned} \tag{4.14}$$

From Equ. 4.14, it is clear that the optimal error depends on the covariance of the matrix (Σ_s) and the noise variance ($\sigma_{\tilde{n}}^2$). The term $\mathbf{x}$ has limited signal to noise ratio (SNR). The SNR can be limited by fixing the variance of each unit, which is represented as:

$$SNR = \frac{\sigma_{Ms}^2}{\sigma_{\tilde{n}}^2} \tag{4.15}$$

If each unit has equal SNR the capacity of information can be given as $C = \frac{1}{2} \log_2(SNR^2 + 1)$ [149]. Limiting SNR represents limiting the capacity of the model, which is treated as capacity constraint or over fitting.

This problem can be avoided by removing the noise from the data by using a low pass filter before applying ICA. Low pass filtering in time domain reduces the information in the data, which leads to reduction of independence in the data. The limitations associated with low pass filtering can be overcome by applying wavelet transform to the observed data before applying ICA. Wavelet transform decorrelates the data which leads to increase the independency of the sources. Wavelet transform analysis is used to the local feature in the data. This makes the local region less affected by noise. So, performance of ICA algorithm may improve when applied to wavelet domain.

4.2.5 Multiscale ICA

The block diagram of multiscale ICA is given in Fig. 4.7. It consists of three important blocks such as, multiscale decomposition, formation of the data matrix, ICA. Multiscale decomposition decomposes the signal/image into different subbands depending on their frequency content. The input to the ICA model is a matrix. The data obtained from one sensor cannot be given to the ICA model as the

4. Multiscale ICA for detection of DR features

data is a vector not a matrix. Multiscale decomposition helps forming a matrix. This is due to the time invariant nature of the multiscale decomposition. All the components in the signal are present in the same phase relationship after decomposition. Then the data matrix is formed by combining the different bands to which the ICA algorithm is applied.

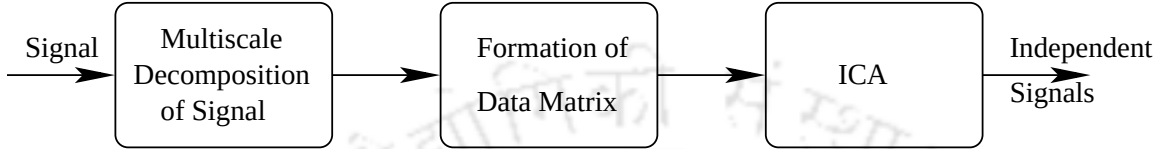


Figure 4.7: Block diagram of multiscale ICA.

The justification about multiscale ICA is discussed and it is proved that, ICA can be applied after multiscale decomposition. Suppose s_1 and s_2 are two independent components in a signal x . T_1 and T_2 are two linear transformations which are applied to x to obtain x_{T1} and x_{T2} , respectively. Suppose x has two parts x_a and x_b . We have to show that x_a and x_b are identical. Suppose s_{1a} and s_{1b} contributions of s_1 in x_a and x_b , respectively. Suppose s_{2a} and s_{2b} contributions of s_2 in x_a and x_b , respectively. ICA makes the signals as independent as possible. So, s_{1a} and s_{1b} are treated as one component as they have correlation. Similarly, s_{2a} and s_{2b} are treated as not different. But s_{1a} and s_{1b} cannot fall in same component as s_{2a} and s_{2b} as they are independent. Here, the linear transformation is used on the mixed signal before applying the ICA algorithm. The linear transformation splits the signal to different scale and ICA is applied to a suitable scale to obtain the features. Due to this reason this is called multiscale ICA. In order to prove the feasibility of multiscale ICA the following points to be proved theoretically.

(i) s_{1a} and s_{1b} are independent with s_{2a} and s_{2b} .

(ii) s_{1a} and s_{1b} or s_{2a} and s_{2b} are correlated.

Let us consider:

$$s_{1a} = \int_{-\infty}^{\infty} h_a(\lambda) s_1(t - \lambda) d\lambda \quad (4.16)$$

$$s_{1b} = \int_{-\infty}^{\infty} h_b(\lambda) s_1(t - \lambda) d\lambda \quad (4.17)$$

$$s_{2a} = \int_{-\infty}^{\infty} h_a(\lambda) s_2(t - \lambda) d\lambda \quad (4.18)$$

$$s_{2b} = \int_{-\infty}^{\infty} h_b(\lambda) s_2(t - \lambda) d\lambda \quad (4.19)$$

where, $h_a(t)$ and $h_b(t)$ are filter functions and $s_1(t)$ and $s_2(t)$ are two independent components. As $s_1(t)$ and $s_2(t)$ are two independent components, they have no correlation at any higher order moments, i.e., correlation coefficient ($\rho_{s_{1a}, s_{2a}}(t_1, t_2)$) between them is zero.

$$\rho_{s_{1a}, s_{2a}}(t_1, t_2) = \int_u \int_v h_a(u) h_a(v) \Sigma[s_1(t_1 - u) s_2(t_2 - v)] du dv \quad (4.20)$$

As $\Sigma[s_1(t_1) s_2(t_2)] = 0$. So, $\rho_{s_{1a}, s_{2a}}(t_1, t_2) = 0$. So, s_{1a} and s_{2a} are uncorrelated at higher order moments and independent. Due to the same reason s_{1b} and s_{2b} are independent.

The second condition states that s_{1a} and s_{1b} or s_{2a} and s_{2b} are correlated. The correlation between s_{1a} and s_{1b} is given by

$$\begin{aligned} \rho_{s_{1a}, s_{1b}}(t_1, t_2) &= \int_u \int_v h_a(u) h_b(v) \Sigma[s_1(t_1 - u) s_1(t_2 - v)] du dv \\ &= \rho_{s_1}(t_1 - u, t_2 - v) du dv \end{aligned} \quad (4.21)$$

This is the auto correlation function of the independent component of s_1 , which is greater than 0. $\rho_{s_{1a}, s_{1b}}(t_1, t_2)$ can be zero only when $h_a(t)$ and $h_b(t)$ are orthogonal. If the filters are orthogonal $\rho_{s_{1a}, s_{1b}}(t_1, t_2)$ is greater than zero, i.e., s_{1a} and s_{1b} are correlated.

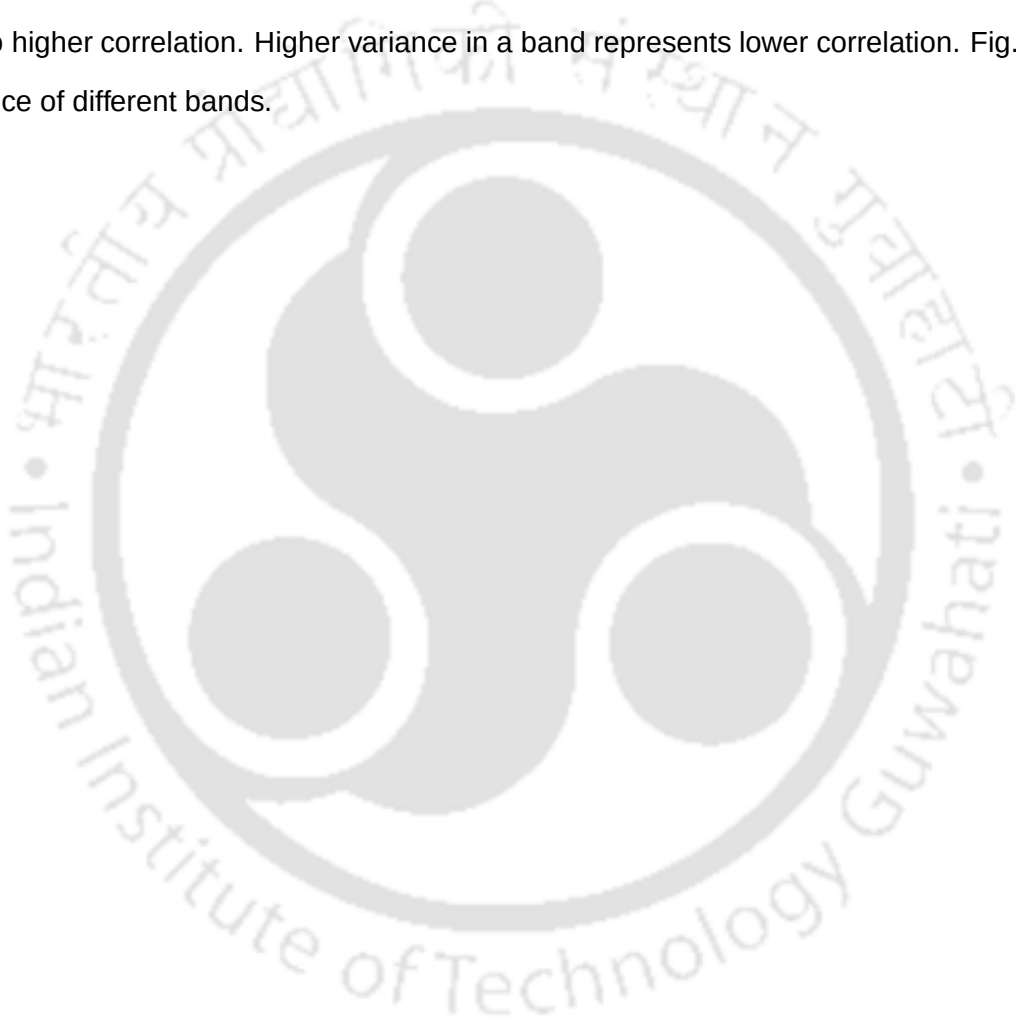
Multiscale Decomposition technique filters a signal in different frequency bands [80] as discussed in Chapter-3. *Data Matrix* is formed by combining the different bands. The different band coefficients are arranged in row wise to form the data matrix. The selection of bands depends on the calculation of the correlation coefficient between the different bands. The lesser correlation coefficient implies that the features may be more independent in nature. The correlation of different bands is given in the Fig. 4.8. Level-5, level-4 and level-3 have a lesser correlation compared to the original image. This implies that the information across the band is more independent compared to the original image. So, the data matrix is formed by combining the higher subbands. Among the band-5, band-4 and band-3 the band-3 has less correlation. The correlation between two images or signals (s_1 and s_2)

4. Multiscale ICA for detection of DR features

can be calculated as:

$$\rho_{s_1, s_2} = \frac{\text{cov}(s_1, s_2)}{\sigma_{s_1} \sigma_{s_2}} \quad (4.22)$$

The variance of the signals is related to the correlation. Correlation of signals is inversely related with variances. So, the variance of different bands is calculated to have a cross check that lower variance leads to higher correlation. Higher variance in a band represents lower correlation. Fig. 4.9 shows the variance of different bands.



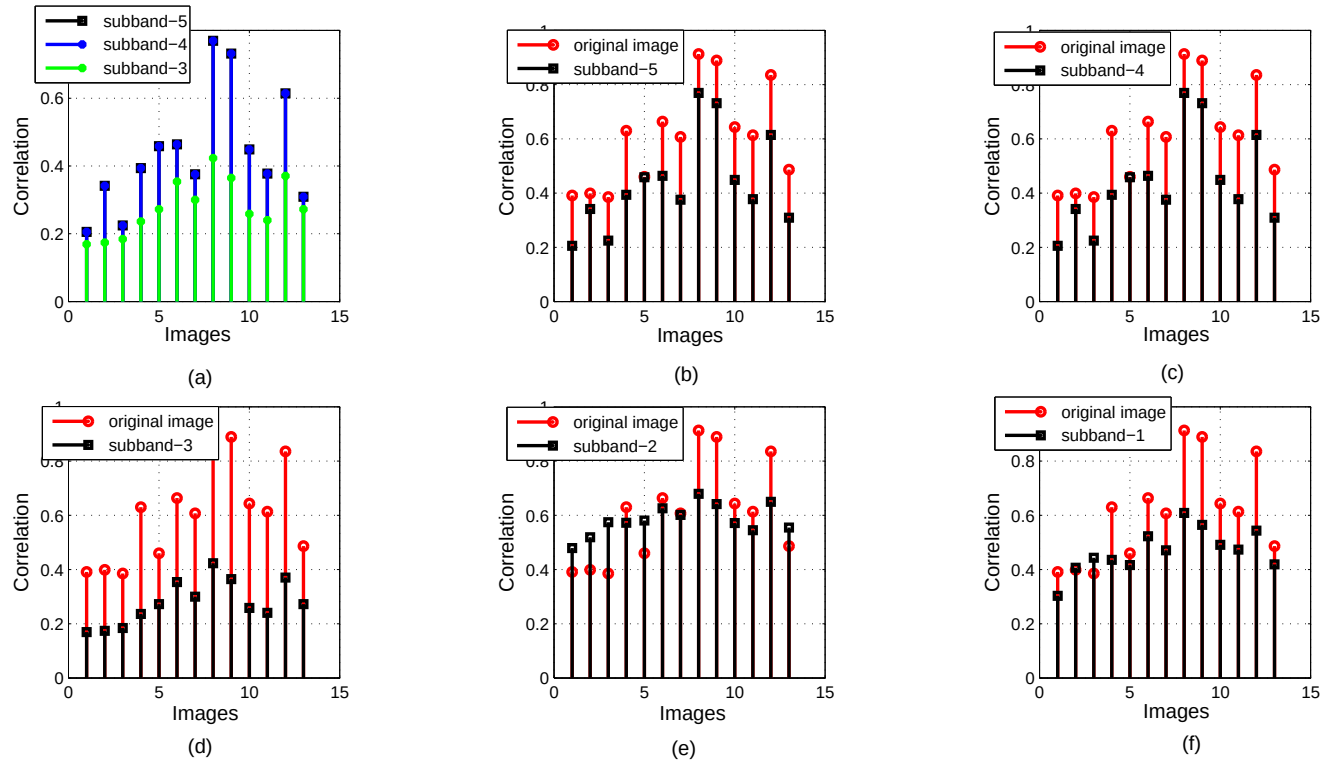


Figure 4.8: Comparison of correlation of image in different subbands: (a) correlation between subband-5, subband-4 and subband-3, (b) correlation between original image and subband-5, (c) correlation between original image and subband-4, (d) correlation between original image and subband-3, (e) correlation between original image and subband-2, and (f) correlation between original image and subband-1.

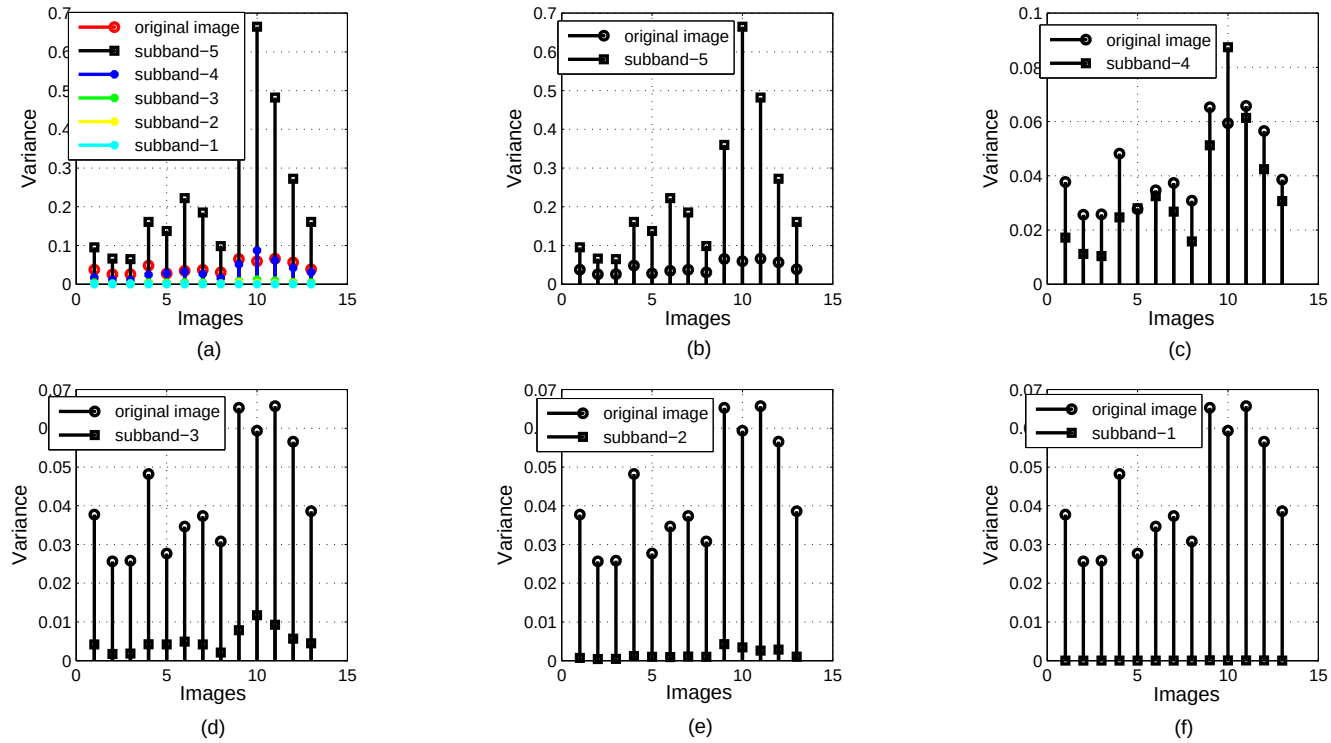


Figure 4.9: Comparison of variance of image in different subbands: (a) variance between different bands and original image, (b) variance between original image and subband-5, (c) variance between original image and subband-4, (d) variance between original image and subband-3, (d) variance between original image and subband-2, and (f) variance between original image and subband-1.

4.2.6 Performance evaluation of MSICA over ICA

Performance of ICA degrades due to over-fitting problem in case of noisy data [150]. The wavelet transform has been used as a low pass filter for removal of noise and subsequent application of ICA. Multiscale ICA may help improve the segmentation of features. The effectiveness of ICA on different scales (multiscale ICA) is evaluated on simulated signals. Before applying the multiscale ICA to the fundus image, the effectiveness of multiscale ICA for the separation of signals and images are evaluated by some test signals and test images. The test signals used for the study are exponential decay signal, square wave signal, saw tooth signal and modulated sinusoidal signal. The modulated sinusoidal signal is mixed with an exponential decay signal or square wave signal or saw tooth signal linearly by a known mixing matrix (M) by two ways. One way, the signals are mixed by varying the relative amplitude of one signal keeping the amplitude of other signal constant. In another way, the modulated sinusoidal signal frequency is gradually increased with a factor of natural numbers. FastICA (FICA) [100] and efficient FastICA (EFICA) algorithms are used for separation of these signals. ICA finds the un-mixing matrix (W) which is the estimation of mixing matrix (M). For ideal separation, the un-mixing matrix is the inverse of the mixing matrix. So, multiplication of the mixing matrix and un-mixing matrix must be an identity matrix. This is known as the gain matrix (G). For practical signals the gain matrix (G) may not be an identity matrix. The deviation of the gain matrix from the identity matrix can be measured by Amari Performance Index (API) [151] and Comon test values [144]. The expression for API (G_{api}) can be given as:

$$G_{api} = \sum_{i=1}^m \left(\sum_{j=1}^m \frac{|g_{ij}|}{\max_k |g_{ik}|} - 1 \right) + \sum_{j=1}^m \left(\sum_{i=1}^m \frac{|g_{ij}|}{\max_k |g_{kj}|} - 1 \right) \quad (4.23)$$

where, $G = g_{ij} = WM$. The API is a measure of diagonality of matrix G. The API value should be very small for better separation.

The expression for computing Comon test (G_{comon}) value can be represented as:

$$G_{comon} = \sum_{i=1}^m \left(\sum_{j=1}^m |g_{ij}| - 1 \right)^2 + \sum_{j=1}^m \left(\sum_{i=1}^m |g_{ij}| - 1 \right)^2 + \sum_{i=1}^m \left| \left(\sum_{j=1}^m |g_{ij}|^2 - 1 \right) \right| + \sum_{j=1}^m \left| \left(\sum_{i=1}^m |g_{ij}|^2 - 1 \right) \right| \quad (4.24)$$

For an identity matrix API and Comon test values are zero. For real life signals, the values of these metrics are not zero, but they may approach to zero. The smaller API and Comon test values

4. Multiscale ICA for detection of DR features

indicate better performance of the algorithm.

API and Comon test values are estimated for different ICA algorithms and for different mother wavelets. Fig. 4.10 shows the API and Comon test values for FICA and EFICA algorithms for one set of mixed signals (i.e., modulated sinusoidal signal and square wave). In this case, the signals are mixed as discussed above. Fig. 4.10(a) and Fig. 4.10(b) show the API and Comon test values for FICA and EFICA for the signals which are mixed by varying the relative amplitude of one signal keeping the amplitude of other signal constant. In Fig. 4.10(a), the API values are found to be less for EFICA than FICA, whereas in Fig. 4.10(b) the Comon test values are same for both the ICA algorithms. Fig. 4.10 (c) and Fig. 4.10(d) show the API and Comon test values for FICA and EFICA for the signals which are mixed by varying the frequency of modulated sinusoidal signal in the order of natural number by keeping the frequency of other signal constant. In these sub-figures, the API and Comon test values are equal for both the ICA algorithms. From this test, it is concluded that EFICA has lower API and Comon test values compared to FICA.

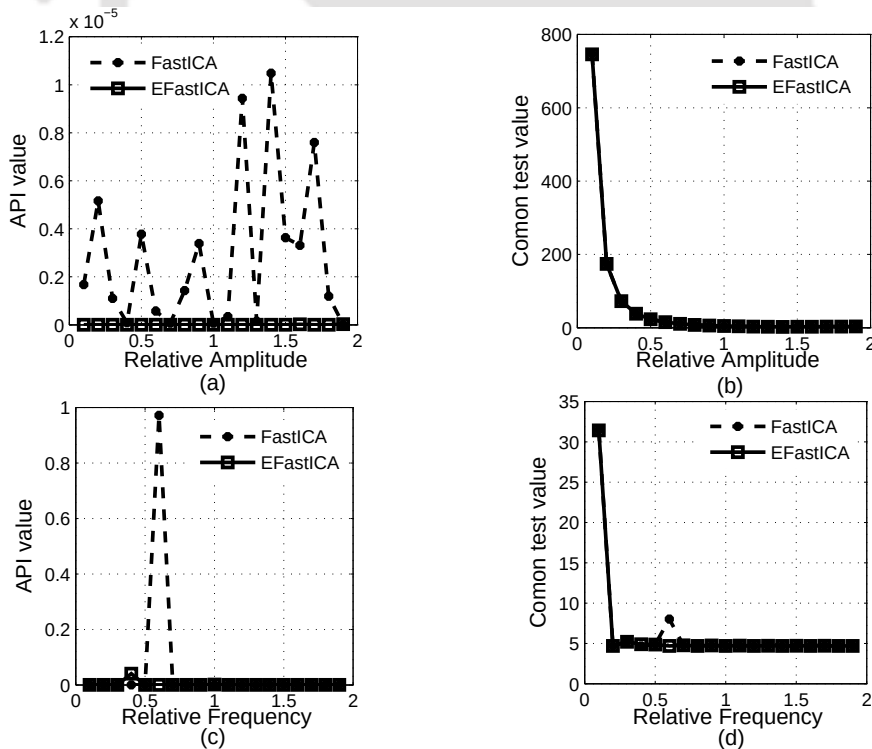


Figure 4.10: API and Comon test values for FastICA (FICA) and efficient FastICA (EFastICA) having variation in relative amplitude and relative frequency of one test signal with respect to the other test signal.

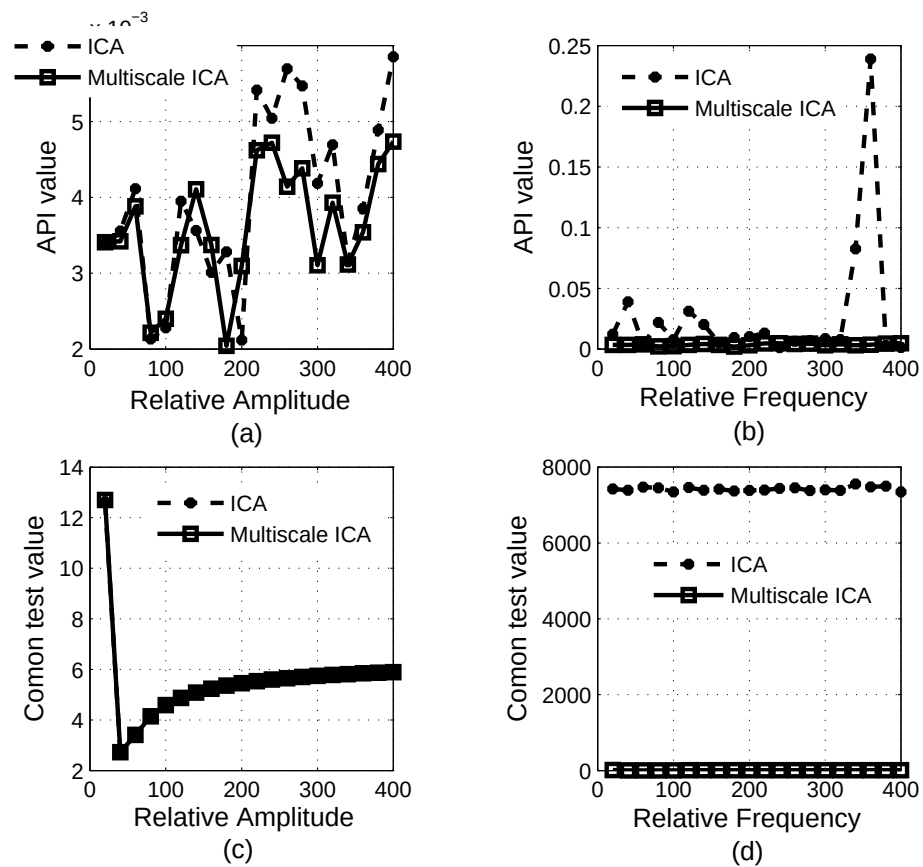


Figure 4.11: API and Comon test values for multiscale ICA and ICA (having variation in amplitude and frequency of one test signal w.r.t other test signal).

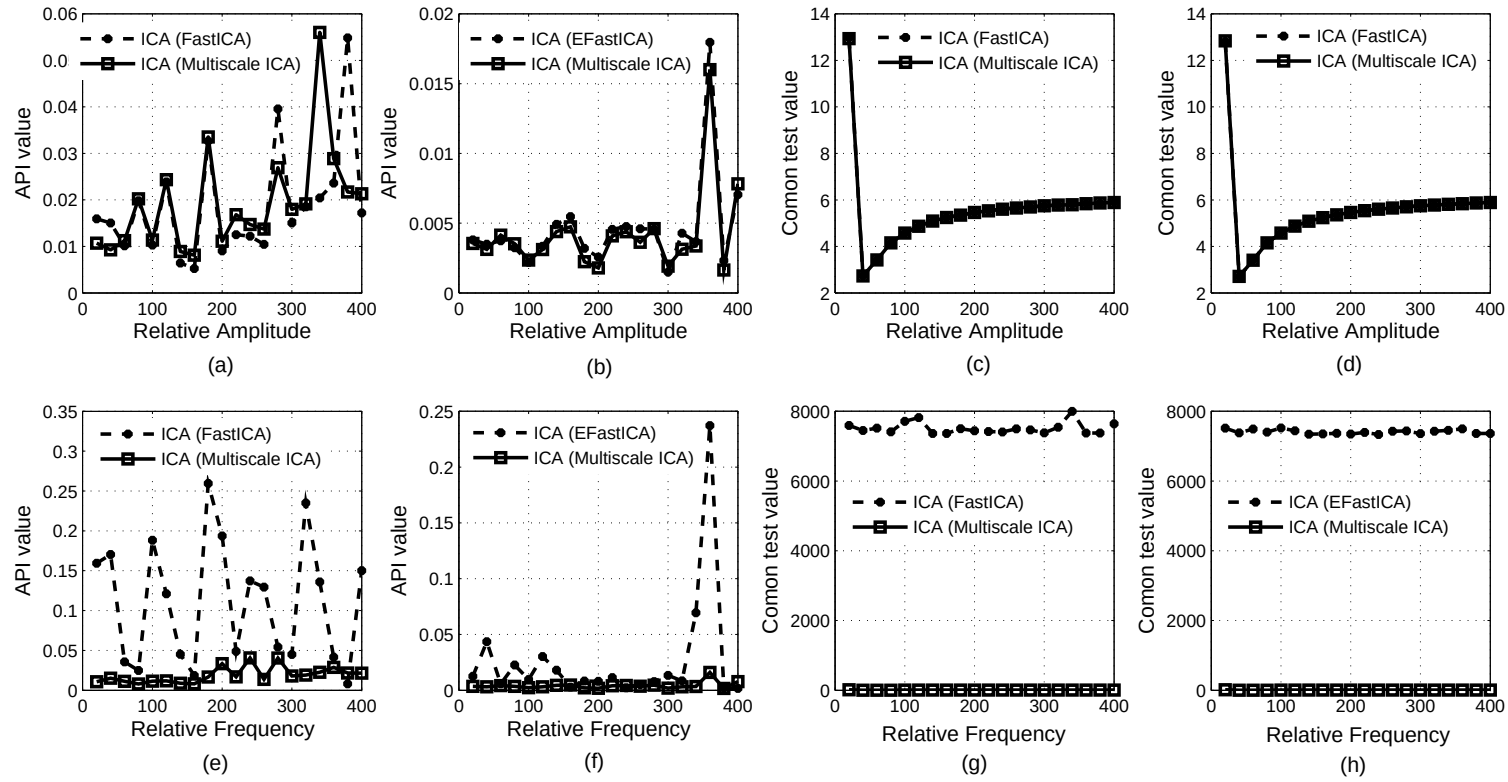


Figure 4.12: API and Comon test values for multiscale ICA and ICA (FastICA and efficient FastICA) having variation in amplitude and frequency of one test signal w.r.t other test signal.

Fig. 4.11 shows the API and Comon test values for ICA and multiscale ICA methods. In this case, the comparison is shown between the ICA and the multiscale ICA by considering the API and Comon test values for the signals as discussed above. The signals are mixed in the same way as discussed in the above paragraph. ICA is applied directly to the mixed signal to obtain the un-mixing matrix. In case of multiscale ICA the data matrix is decomposed into different wavelet subbands. Five level wavelet decomposition is performed with db4 mother wavelet. The higher subband is considered to form the new data matrix. ICA is applied to the new data matrix to obtain the un-mixing matrix. Fig. 4.11(a) and Fig. 4.11(b) show the API values for the variation of relative amplitude and frequency of one signal with respect to other signal, respectively. In both the cases, the API values are less for multiscale ICA than ICA. Fig. 4.11(c) shows the Comon test values for multiscale ICA and ICA for variation frequency of the modulated sinusoidal signal in the order of natural number. For both multiscale ICA and the ICA the Comon test values are found to be same. In Fig. 4.11(d) the Comon test values are found to be less for multiscale ICA than ICA. This test is performed for different mother wavelets. Fig. 4.12 shows the API and Comon test values for multiscale ICA (FastICA and efficient FICA) and ICA (FastICA and efficient FICA) algorithms. From the figure it is clear that most of the cases the multiscale ICA outperform than ICA.

API and Comon test values for multiscale ICA and ICA for twenty six numbers of mother wavelets are calculated. Few of the values are tabulated in Table 4.8. Most of the mother wavelets, the multiscale ICA has lower API and Comon test values than ICA. In some cases the API and Comon test values are greater in ICA than multiscale ICA. In all the twenty six mother wavelets, API and Comon test values are always less for multiscale ICA for variation of modulated sinusoidal frequency in the order of natural number. This is found to be 100%. For the variation of the relative amplitude the API and the Comon test values are found to be less for multiscale ICA than ICA for twenty and seven numbers of times, which are found to be 76.92% and 26.92%, respectively. From this study, it may be concluded that, the multiscale ICA may outperform for some mother wavelets, such as db1, db2, db5, db9, and coif1 etc. than ICA.

Table 4.9 shows API and Comon test values for ICA and multiscale ICA for variation of the relative amplitude of the modulated sinusoidal signal with respect to the other signals (i.e., either exponential signal or square wave signal or saw tooth wave signal) for twenty six numbers of mother wavelets. The amplitude of the modulated sinusoidal signal is increased in the order of natural number. The

4. Multiscale ICA for detection of DR features

Table 4.8: API and Comon test values for ICA and multiscale ICA (MSICA).

Method	Relative amplitude		Relative frequency	
	API Values	Comon test value	API value	Comon test value
ICA	0.0686	110.8627	0.5279	148.6
MSICA-db1	0.065	113.0075	0.065	113.0075
ICA	0.0654	110.8177	0.5116	148.37
MSICA-db2	0.0582	111.1856	0.0582	111.1857
ICA	0.0773	110.9456	0.5105	148.54
MSICA-db3	0.0715	111.0593	0.0714	111.0593
ICA	0.0785	110.766	0.526	148.65
MSICA-db4	0.0765	110.7988	0.0765	110.7987
ICA	0.0761	111.0079	0.4941	148.31
MSICA-db5	0.0745	111.0333	0.0745	111.0333
ICA	0.0766	111.0539	0.5186	148.62
MSICA-db6	0.0742	111.0826	0.0742	111.0826
ICA	0.0669	110.895	0.5131	148.67
MSICA-db7	0.0682	110.9167	0.0683	110.9166
ICA	0.0906	110.9674	0.5253	147.86
MSICA-db8	0.0848	110.9682	0.0848	110.9681
ICA	0.9261	110.9637	0.5196	148.23
MSICA-db20	0.0843	110.9771	0.0843	110.9771
ICA	0.0963	110.87	0.523	148.45
MSICA-sym1	0.093	113.0143	0.093	113.0143
ICA	0.08	110.9799	0.5099	148.4
MSI-sym2	0.0749	111.3477	0.0749	111.3477
ICA	0.0676	110.8941	0.5142	148.43
MSICA-sym3	0.0693	111.0077	0.0699	111.0077
ICA	0.0775	111.0978	0.5175	148.56
MSICA-sym4	0.078	111.1495	0.0779	111.1495
ICA	0.0683	110.7572	0.5277	148.51
MSICA-sym5	0.0643	110.7798	0.0643	110.7798
ICA	0.0825	110.8936	0.5216	149.17
MSICA-sym6	0.0764	110.9209	0.0763	110.921
ICA	0.0925	110.9525	0.507	148.34
MSICA-sym7	0.0888	110.9108	0.0888	110.9108
ICA	0.0818	110.8846	0.5241	148.83
MSICA-sym8	0.0858	110.899	0.0853	110.8999
ICA	0.0885	110.9399	0.518	148.53
MSICA-dmey	0.0878	110.9479	0.0878	110.9479
ICA	0.0879	110.881	0.5153	148.65
MSICA-coif1	0.0823	111.1906	0.0821	111.1906
ICA	0.0797	110.9444	0.5305	148.46
MSICA-coif2	0.072	110.985	0.072	110.985
ICA	0.0717	111.1892	0.5165	148.7
MSICA-haar	0.071	113.3678	0.0709	113.3679

Table 4.9: API and Comon test values for ICA and multiscale ICA (MSICA) for variation of relative amplitude of modulated sinusoidal signal with respect to another signal. (i.e., Set-1: modulated sinusoidal signal and exponential signal, Set-2: modulated sinusoidal signal and square wave signal, Set-3: modulated sinusoidal signal and sawtooth wave signal).

Relative amplitude and frequency	Set-1		Set-2		Set-3	
	$p(\alpha) < p(\beta)$	$p(\gamma) < p(\delta)$	$p(\alpha) < p(\beta)$	$p(\gamma) < p(\delta)$	$p(\alpha) < p(\beta)$	$p(\gamma) < p(\delta)$
20	0.7692	0.2692	0.7692	0.2692	0.7692	0.2692
40	0.7307	0.3461	0.7692	0.2692	0.7307	0.3461
60	0.6923	0.3846	0.7692	0.2692	0.8461	0.3846
80	0.8461	0.3846	0.7692	0.2692	0.7692	0.3461
100	0.7692	0.3461	0.7692	0.3461	0.7307	0.3461
120	0.7692	0.4230	0.7692	0.3461	0.7692	0.3461
140	0.7307	0.3461	0.7307	0.3461	0.7692	0.2692
160	0.7307	0.3461	0.7307	0.3461	0.6923	0.3461
180	0.6923	0.3461	0.6923	0.3461	0.6923	0.3461
200	0.7692	0.2692	0.7307	0.4230	0.7307	0.4230
Average	0.7496	0.3807	0.7538	0.3230	0.7499	0.3423

probability values for the API and Comon test are calculated for the relative variation of amplitude of the modulated sinusoidal signal for multiscale ICA and ICA for Set-1, Set-2 and Set-3 of the combinations of signals. Signals in Set-1, Set-2 and Set-3 are the combination of modulated sinusoidal signal with the exponential signal, square wave signal and saw tooth wave signal, respectively. $p(\alpha)$ and $p(\gamma)$, are the probability of API and Comon test values for multiscale ICA. Similarly, $p(\beta)$ and $p(\delta)$ are probability values for API and Comon test values for ICA algorithm. For Set-1 average value API and Comon test values are found to be 0.7496 and 0.3807, respectively. Set-2 has 0.7538 and 0.3230 average API and Comon test values. Average probability values for the API and Comon test values are found to be 0.7499 and 0.3423, respectively. From these values, it may be concluded that multiscale ICA can perform better than ICA.

4.3 Multiscale ICA for detection of exudates

The effectiveness of multiscale ICA is discussed in previous subsection. The proposed block diagram for exudate extraction is shown in Fig. 4.13. The different blocks are RGB to HSV conversation, multiscale decomposition, subband selection, and ICA. The input to this block is the color fundus

4. Multiscale ICA for detection of DR features

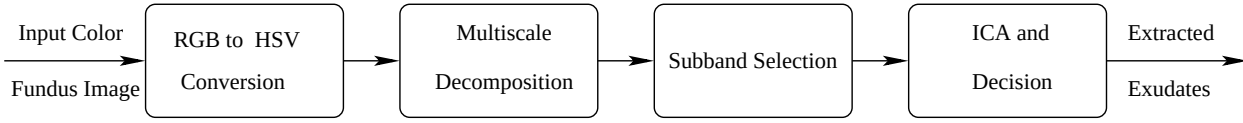


Figure 4.13: Multiscale ICA for extraction of exudates.

image and output is the extracted exudates. The description about the different blocks is given below.

RGB to HSV Conversion: The fundus image database is available in RGB format. This color channel is the mixing color channel in which the different colors are formed by the addition of 3-different primary colors [37]. The pathological feature information is more correlated in the red, green, blue channel of RGB. Since, the HSV color channel is less correlated, the input color image is converted from RGB to HSV for better feature segmentation. The HSV color space is statistically independent. The hue, saturation and value color channel are used along with the red, green and blue color channel for the further processing.

Multiscale decomposition: Wavelet decomposition is applied to the hue, saturation and value channels of HSV and red, green and blue channel of RGB. 5-level wavelet decomposition is performed on HSV and RGB color channels using db4 mother wavelet as it is found to be effective for fundus images [20]. After wavelet decomposition, the images are reconstructed by considering one subband coefficients and zeroing the rest of the subband coefficients. Five reconstructed subband images corresponding to L1, L2, L3, L4, and L5 subbands are obtained for each color channel. The wavelet decomposition distributes the feature information in different wavelet subbands. However, the DR features are not uniformly distributed across all the subbands, but present in a few of the subbands only. So, a subband selection procedure is required for capturing the exudates.

Subband selection: After wavelet decomposition the wavelet subbands are selected by the subband confidence factor and kurtosis and negentropy values for a particular color channel. Negentropy and kurtosis values are calculated for all the subbands. As the subband confidence factor for L5 subband image is higher among all other subband images, this image is selected for the creation of data matrix or mixing matrix. The rows of L5 subband image are concatenated, and the resultant vector is placed along the column of the data matrix. The rest of the columns of the data matrix are generated by following similar approach for all the color channels of RGB and HSV. Since the L5 subband contains the exudates information, so it is expected that the data or mixing matrix contains similar

information.

Subband confidence factor (SCF) for all the subbands are calculated. Typical pixel values of exudates range from $0.6i_m$ to i_m , where i_m is the highest pixel value of an image. The probability of the occurrence of pixels in the range $0.6i_m$ to i_m will help determine the effectiveness of a subband for application of ICA. The subband having higher exudate information is expected to have more probability value. The proposed subband confidence factor (SCF) is defined as the ratio of probability of the pixels in the intensity range from $0.6i_m$ to i_m , to the mean probability value. SCF for i^{th} subband is defined as:

$$SCF_i = \frac{p_i[0.6 \leq x < 1]}{P_i[x = \mu]} \quad (4.25)$$

The subband with higher exudate information and less other feature information will result in higher SCF values. In this work, the subband with the highest SCF value is chosen for ICA implementation.

For all the subband energy, entropy (information content), distribution of features (kurtosis and negentropy) and SCF are calculated. For exudates these parameters are found to be higher in fifth level subband. So, higher subband is selected for exudate extraction.

ICA: Independent component analysis (ICA) is applied to the data matrix to extract the independent components. In this case, FastICA [100] algorithm is adopted. The independent component is selected based on kurtosis values for finding the exudates. From the selected independent component exudates are extracted by threshold.

Results: ICA and MSICA methods are tested on the images of publicly available Aria and Mesidor databases. Each color image is divided into RGB and HSV color channels. Both the color channels are used to find the independent features by ICA and MSICA methods. Five level wavelet decomposition is applied to each color channel. The subband selection is based on the higher subband selection factor (SCF) and the negentropy value.

Segmentation of exudates are performed by ICA and MSICA methods on both RGB and HSV color spaces. Fig. 4.14 shows fundus image with exudates and the images with extracted exudates. Fig. 4.14(a) is the original RGB fundus image and Fig. 4.14(b) is the corresponding HSV image. This is obtained by converting RGB to HSV image. In this image the exudate region is highlighted. Due to uncorrelated nature of the HSV color channel, the exudate can be visible as different from

4. Multiscale ICA for detection of DR features

the background. The exudates are represented by the white patches in the center of the image. Fig. 4.14(c) and 4.14(d) show images with the extracted exudates by applying ICA on RGB and HSV color spaces, respectively. All the exudate regions are not clear in Fig. 4.14(c). The regions are shown clearly in the Fig. 4.14(d). It is observed that, the ICA performs better in HSV space than RGB space. Multiscale ICA is applied to both the color channels and the results are shown in Fig. 4.14(e) and 4.14(f). Fig. 4.14(e) shows the extracted exudates in RGB space. Small portion of the exudates are extracted. Extracted exudates are seen clearly Fig. 4.14(f). This is the extracted exudates, when MSICA is applied in HSV color space. From the figure, it is clear that MSICA performs better in HSV space than RGB space. This may be due to the independent nature of HSV color space and less correlation between the color components of the HSV color channel.

Performance evaluation: Performance of proposed exudate extraction method is calculated by sensitivity, conformity coefficient (KC), accuracy, PCC, and UQI etc. The ground truth image of the region of interest (ROI) is obtained by manual segmentation method. This is used for comparing the extracted exudates. Sensitivity and KC values for the proposed exudate extraction method are calculated for fifty four different images with exudates on RGB and HSV color channels. These images are taken from Aria databases. The average sensitivity and KC values for RGB color space are 88.5% and 90.3%, respectively. The average sensitivity and conformity values for HSV color space are 94.5% and 94.6%, respectively. The values are higher in HSV color channel. This shows that HSV performs better compared to RGB color space. In the literature, sensitivity values obtained by different methods are reported as 88.5% [152], 92.8% [21], and 93.5% [22]. In the proposed MSICA method in HSV color space, the average sensitivity and conformity values are found to be 94.5% and 94.6%, respectively. These values show better performance of the proposed method compared to the existing methods.

Performance factors, RMSE [137], PSNR, MSE [138], PCC [138] and UQI [133, 140] etc. are used to measure the accuracy of the proposed method. The mean values of the performance factors for fifty four images are tabulated in Table 4.10. The UQI, PCC values are high for MSICA when applied on HSV color channel. From the Table 4.10 it is clear that the MSICA over HSV color channel performs better than the other methods.

The proposed method is compared with the Walter *et al.* [21] and the Kavitha [153] methods for 54 images. The average sensitivity for the proposed method for sixty images is found to be 94.5%. The

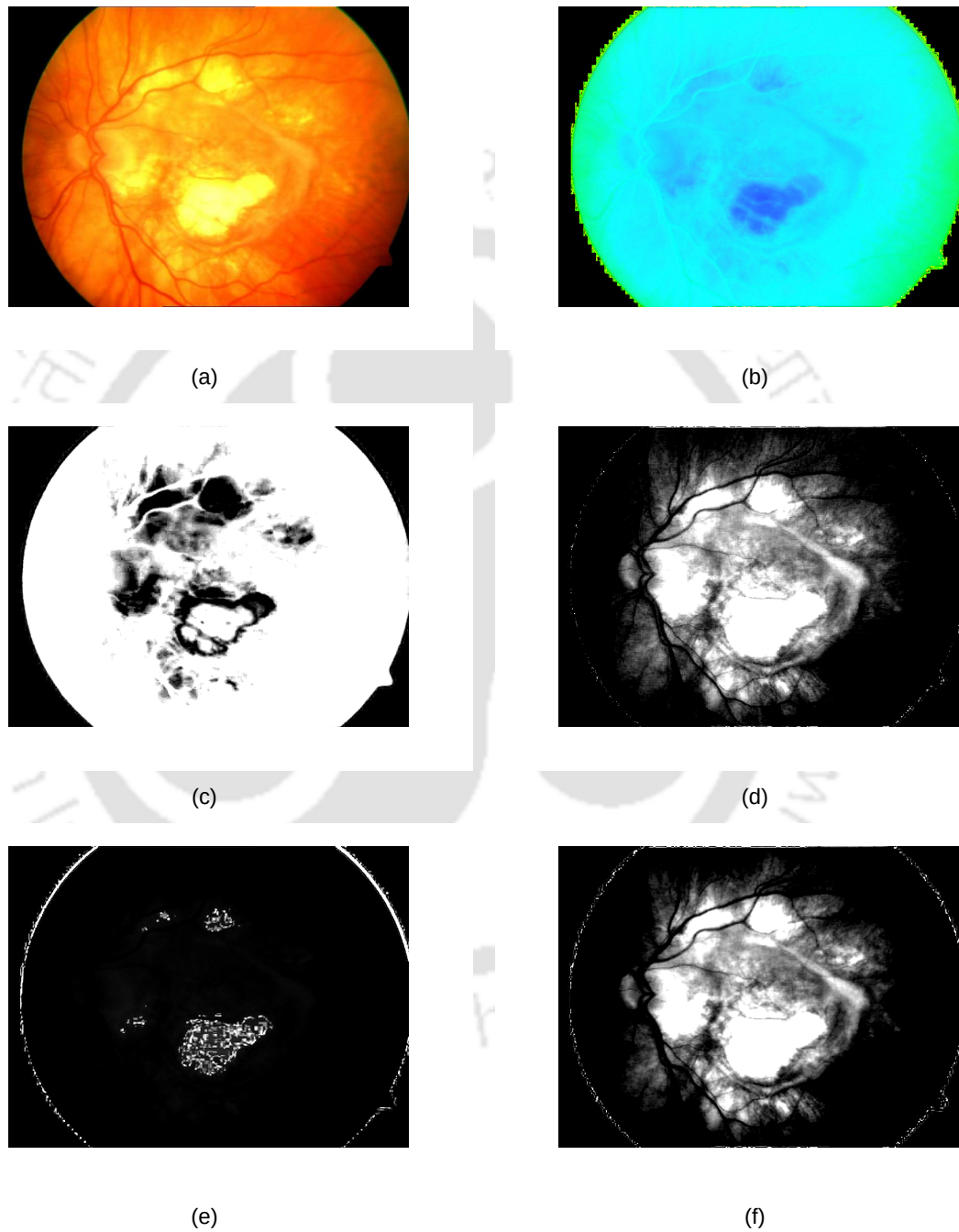


Figure 4.14: Extraction of exudates: (a) RGB color fundus image, (b) corresponding HSV image, (c) exudates from RGB color image by ICA, (d) exudates from HSV color image by ICA, (e) exudates from RGB color image by multiscale ICA, (f) exudates from HSV color image by multiscale ICA.

4. Multiscale ICA for detection of DR features

Table 4.10: Performance measure for extraction of exudates by ICA and MSICA.

Methods	Performance measures				
	RMSE	PSNR	MAE	PCC	UQI
MSICA (HSV)	0.38	56.66	0.18	23.29×10^4	0.70
MSICA (RGB)	0.41	55.82	0.18	2.01×10^4	0.60
ICA (HSV)	0.75	50.72	0.57	2.25×10^4	0.50

sensitivity for morphological based method proposed by Walter et al. and histogram based method proposed by Kavita et al. are found to be 93.06% and 81.76%, respectively. These values are found to be higher in the proposed method.

4.4 Detection of change in color fundus due to DR

ICA can be used for the detection of changes from the color fundus images due to the progression of DR. It provides the advantage of detecting changes in the retina due to DR and provides knowledge on the progression of the disease. The condition of the vision depends on the number of diagnostic features over the retina. The condition become more severe when the features appear nearer to the macula.

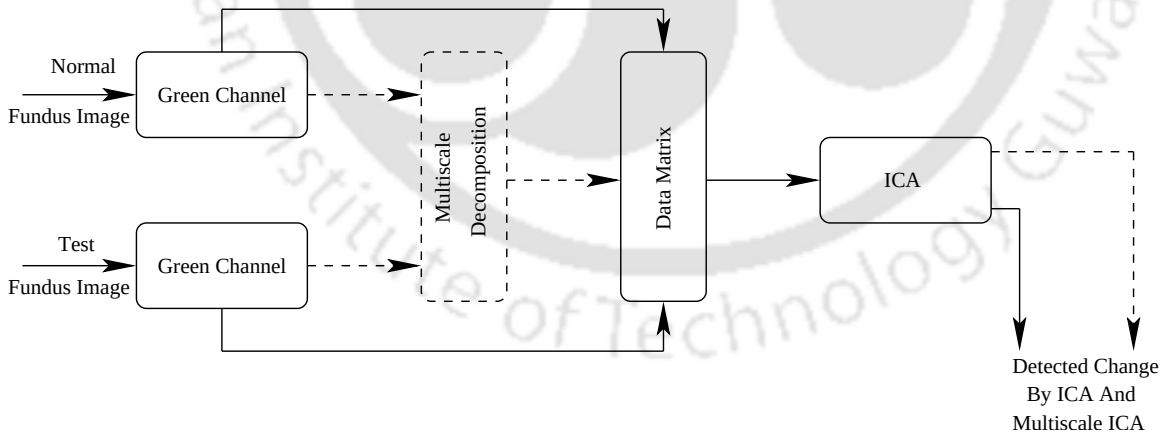


Figure 4.15: Multiscale ICA and ICA for detection of changes from color fundus images.

Method: Fig. 4.15 shows the block diagram for detection of features and changes by ICA and multiscale ICA for fundus images due to DR. The important blocks are preprocessing, multiscale decomposition, formation of mixing matrix, and ICA. In this case, two type of images are considered, i.e., normal retinal image and the image with pathology from the same datasets. In this case, both

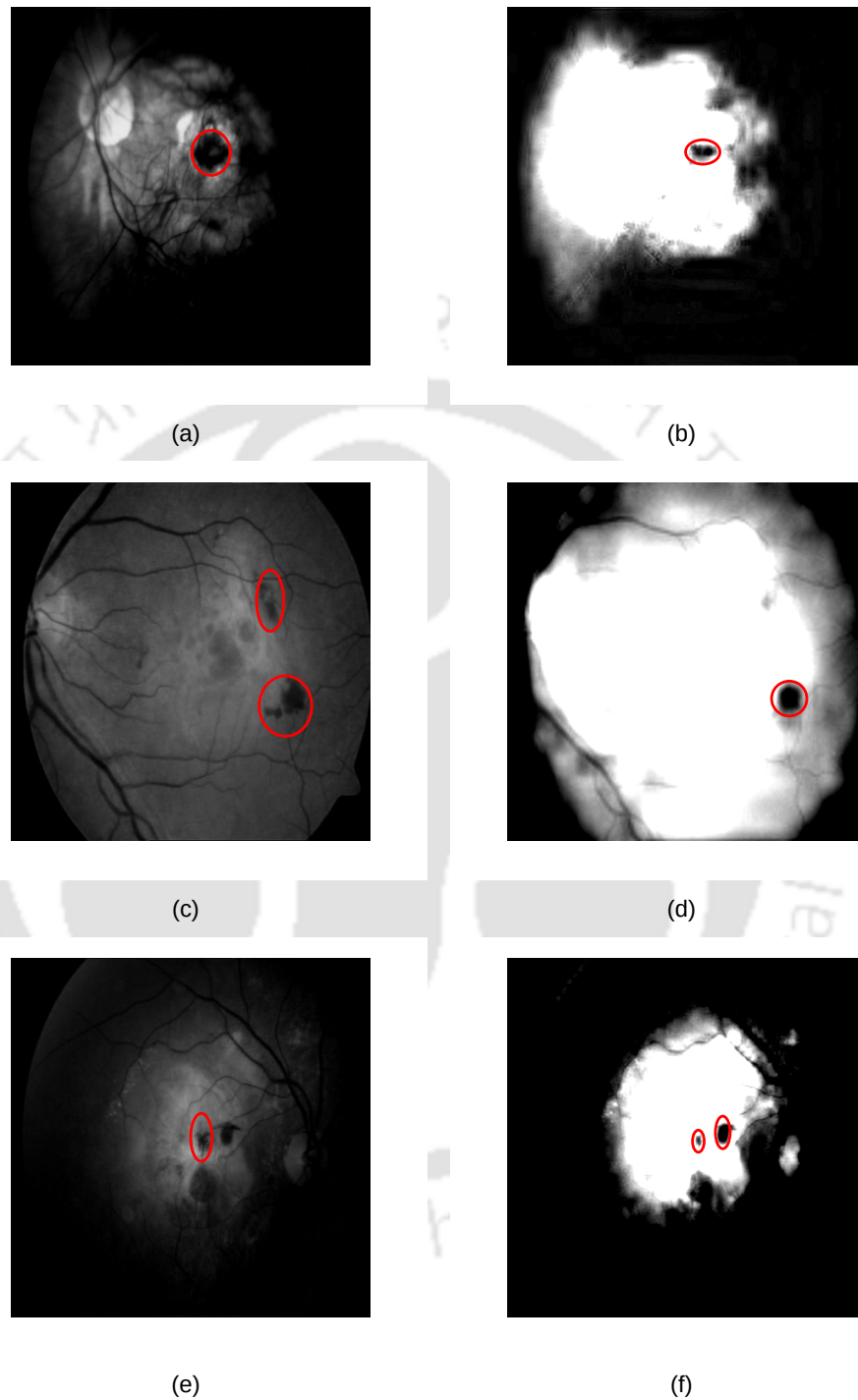


Figure 4.16: Detected changes present in color fundus image due to diabetic retinopathy: [(a), (c), (e)] green channel of the color fundus images, [(b), (d), (f)] detected changes.

the images are captured by the same camera. The green channel of both the images (normal and pathology) are considered for the further analysis as green channel has higher contrast between the

4. Multiscale ICA for detection of DR features

image features and the background. Then, the data matrix is formed. The data matrix can be formed by considering the green channel of both the images. For multiscale analysis the 5-level wavelet decomposition is applied to both the normal image and pathology image by db4 mother wavelet. In this case, the higher subbands are considered to form the data matrix. The higher subbands are more sensitive to the changes due to diabetic retinopathy. To the data matrix ICA is applied for detection of change. The extra step, which is performed in multiscale ICA is shown by dotted lines in Fig.4.15.

Results: This above discussed method for detection of change is applied to pathological images. Fig. 4.16(a) shows the green channel of the pathological image consists of haemorrhage. Haemorrhage is treated as a pathology. The detected change for the image is shown in Fig. 4.16(b). Fig. 4.16(c) and Fig. 4.16(e) are the green channel of the images consists of haemorrhages and MA. The detected changes for the above two pathological images are shown in Fig. 4.16(d) and Fig. 4.16(f), respectively. Depending on the quantity of features and size of the features the condition of retina can be estimated. This may provide the information about the condition of vision.

4.5 Summary

In this chapter, extraction of retinal features is discussed. Blood vessels are extracted by different methods such as Gaussian based match filter approach, Kirsch method and histogram method. Among these approaches Gaussian based method provides higher accuracy. The specificity value is better for the extraction of blood vessels when the Kirsch and Gaussian methods are merged. This method is applied to the pathological affected images for segmentation of the blood vessels. Then inpainting is applied to suppress the effect of the blood vessels. From the inpainted image the pathologies are segmented. Considering the overlapping regions of blood vessels and pathology the affected blood vessels by pathology is determined. This may help assessing the progression of retinal damage by assessing the number of blood vessels affected by pathological features.

Independent component analysis (ICA) and Multiscale ICA are applied to the fundus images for detection of exudates. The exudates are detected based on their statistical properties such as higher kurtosis and negentropy values compared to the other features in the color fundus images. Due to this reason, the exudates are separated out from other features, when ICA is applied. Exudates extraction is found to be better in HSV color space compared to the RGB color space. This happens due to the less correlation of the color components in the HSV color channel.

Multiscale ICA is used for detection of changes from the color fundus image that occurs due to the progression of diabetes. In this method, one normal retinal image is compared with diabetic affected retinal image by ICA and multiscale ICA. The changes in the retinal image is having non-Gaussian distribution than the normal image. This may help to assess the progression of retinal damage due to diabetes.





5

Assessment of glaucoma in wavelet scale

Contents

5.1	Glaucoma detection by using CDR	120
5.2	Differential entropy based glaucoma detection	124
5.3	PCA-LDA based glaucoma classification	129
5.4	HMM-SVD based glaucoma classification	136
5.5	Summary	140

5. Assessment of glaucoma in wavelet scale

This chapter presents the analysis and methods for detection of glaucoma. Glaucoma is an eye disease which results in peripheral vision loss, due to degeneration of optic nerves. Cup to disc ratio (CDR) is commonly used as a measure for evaluation of glaucoma. It is difficult to estimate the value of CDR if the boundaries of the cup and disc are not well defined. This problem can be overcome by finding the information present in the cup. The cup is the only region which is affected by glaucoma. The optic disc (OD) is minimally affected. Evaluation of differential entropy (DE) of the cup in wavelet subband is performed for prediction of glaucoma. The probability of pixels representing glaucoma is found to be different in different wavelet subbands. Evaluation of differential entropy, which is proportional to the probability of number of glaucoma pixels in wavelet subbands can be used as a measure of glaucoma. Another approach is based on pattern recognition. Here, the cup and disc patterns are used for detection. Principal component analysis (PCA) and linear discriminant analysis (LDA) based approaches are used for glaucoma classification from color fundus images. A method based on 7-States hidden Markov model (HMM) recognition system, which uses singular value decomposition (SVD) coefficients for feature extraction is also proposed.

In this chapter, glaucoma is detected from the color fundus images. Section 5.1 discusses about glaucoma detection using CDR. Differential entropy based glaucoma detection is discussed in Section 5.2. Section 5.3 discusses the PCA-LDA based glaucoma detection. HMM-SVD based glaucoma detection is discussed in Section 5.4. Summary of this chapter are given in Section 5.5.

5.1 Glaucoma detection by using CDR

Cup appearance changes due to glaucoma. This leads to increase in the CDR. The cup and the OD are segmented for calculation of CDR and determination of glaucoma. The block diagram for calculation of CDR is shown in Fig. 5.1. The green channel is used for preprocessing, as the red channel is saturated and the blue channel is noisy. The contrast between the blood vessels and the background is higher in the green channel.

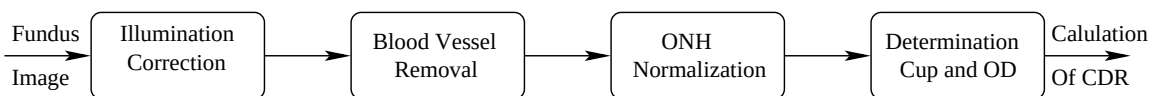


Figure 5.1: Glaucoma detection based on CDR.

The different blocks are illumination correction, blood vessel removal, detection of the cup, detec-

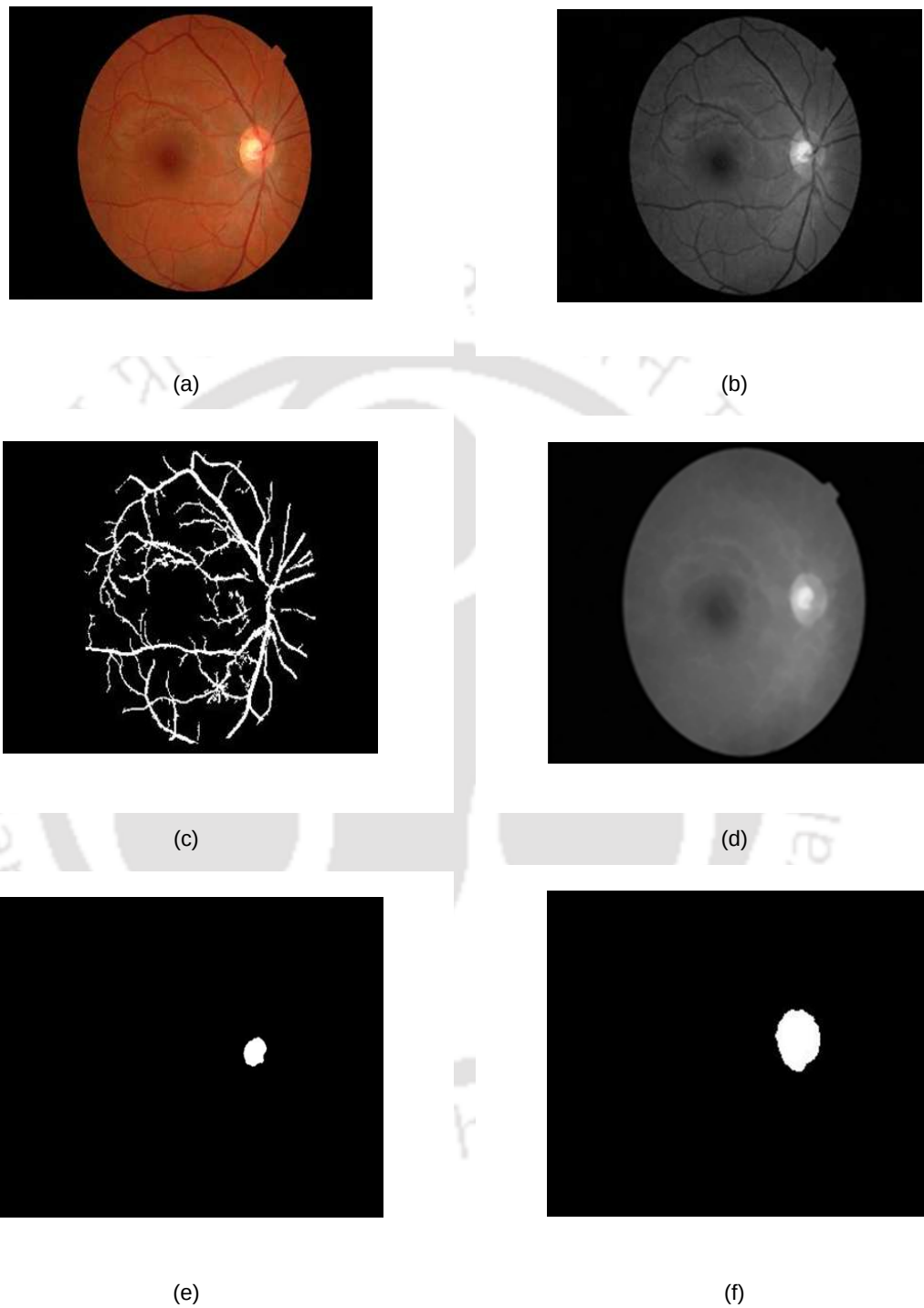


Figure 5.2: Evaluation of CDR, (a) fundus image, (b) green channel image, (c) extracted blood vessels, (d) inpainted image, (e) extracted cup, and (f) extracted disc.

tion OD, calculation of CDR and detection of glaucoma. Mathematical morphology based illumination correction corrects the non-uniformity in brightness in the image pixels, which occurs due to differ-

5. Assessment of glaucoma in wavelet scale

ent visual angles. Homogeneously corrected fundus image is obtained by subtracting the estimated background from the original image. Morphological opening is used for estimation of the background image. Blood vessel removal is performed to suppress the behaviour of vessels as they are minimally affected by glaucoma. Image inpainting [154] is used to replace the blood vessels regions of the retinal image with plausible background. The inpainted image does not contain any blood vessels. The ONH structure, which changes with glaucoma disease, is obtained by circular Hough transform [155]. Active contour method [156] is applied to the inpainted image for detection of the cup and OD. The active contour principle is based on the starting of a curve around the object to be detected, which moves inwards and stops at the boundary. After detection of the cup and the OD, CDR is calculated by taking the ratio of the area of the cup to the area of the OD. Fig. 5.2 shows the output of different stages for calculation of CDR. Fig. 5.2(a) and Fig. 5.2(b) are the color fundus image and green channel of the fundus image, respectively. The extracted blood vessels are shown in Fig. 5.2(c), which is used as a mask for inpainting. Fig. 5.2(d) is the inpainted image, which does not contain any blood vessel. The contours of the cup and the disc are shown in Fig. 5.2(e) and Fig. 5.2(f), respectively. For the above discussed image the CDR value is found to be 0.43. The CDR is calculated for seventeen normal images and thirty seven glaucoma images. Few glaucoma images are correctly detected as glaucoma by CDR method. In the presence of other DR pathologies and different conditions of disc, this method fails. Total 40 images are correctly detected by this method out of 54 images. All the normal images are detected correctly. Out of 37 glaucoma images 23 glaucoma images are detected correctly. The accuracy of glaucoma detection of CDR method is found to be 74.07%. The limitations of the CDR method are discussed in Subsection 5.1.1.

5.1.1 Limitation of CDR based Glaucoma detection

In some glaucoma cases, the cup and disc are not distinguished clearly as shown in Fig. 5.3(c) and Fig. 5.3(d). The inflamed disc is shown in Fig. 5.3(c). Fig. 5.3(d) shows the disc anomalies. In these two figures, the disc boundary is not present. In such cases, CDR cannot be used as a measure for glaucoma.

5.1.2 Proposed method for glaucoma detection

The information regarding the changes in cup size is most vital for assessment of glaucoma. In this chapter, two novel methods for glaucoma detection are proposed. First is based on evaluation of

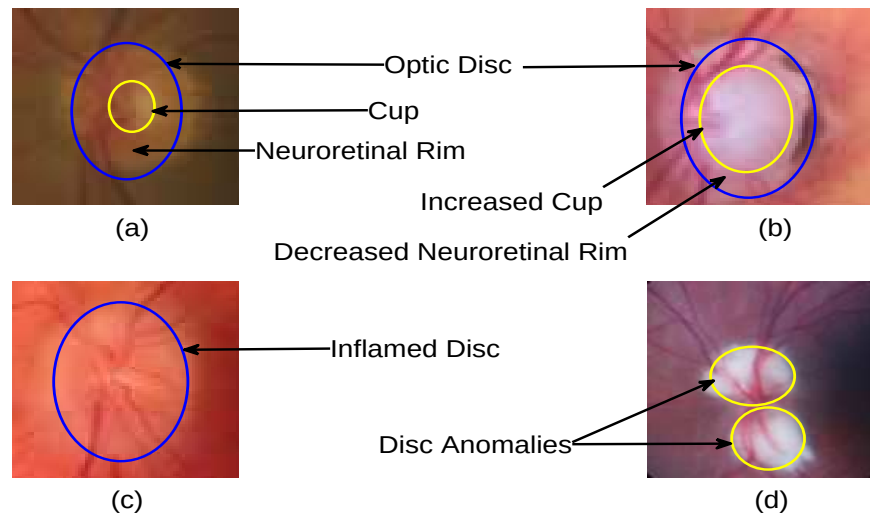


Figure 5.3: Different types of disc: (a) normal disc, (b) glaucoma disc with increase in cup size, (c) glaucoma with inflamed disc, (d) glaucoma with disc anomalies.

differential entropy (DE) in wavelet subband for detection of glaucoma. Second, machine learning approach for glaucoma classification. These methods overcome the limitations of the CDR method for glaucoma detection. The proposed DE based glaucoma detection determines the information of the cup to detect glaucoma. In this case, the DE of the cup is calculated on the wavelet scale for assessment of glaucoma. Wavelet processing enhances the performance of the glaucoma detection as the blood vessel information are suppressed in the wavelet subbands of level-5. The patterns of the cup are changed due to the glaucoma. For normal vision, the cup is looking like almost circular or elliptical. As the disease progresses, the size and shape of the cup gradually change. This pattern can be used for glaucoma classification in proposed machine learning method. Machine learning approach, trains cup and disc features for glaucoma classification. The PCA-LDA and HMM-SVD methods are discussed under the proposed machine learning approach for glaucoma classification. In PCA-LDA based method, PCA is used for feature extraction and LDA is used for class separation. The performance of this method depends on the number of principal components considered. Four numbers of principal components are sufficient to provide high performance in PCA-LDA based method. In the proposed SVD-HMM based glaucoma classification, SVD is used for feature extraction and 7-state HMM is used for classification. The proposed DE based glaucoma detection is discussed in Section 5.2. The proposed PCA-LDA and HMM-SVD based glaucoma classification methods are discussed

in Section 5.3 and Section 5.4, respectively.

5.2 Differential entropy based glaucoma detection

The proposed method, based on differential entropy for glaucoma detection is shown in Fig.5.4. It consists of preprocessing, wavelet decomposition, segmentation of the cup and measurement of information by differential entropy. The different stages are preprocessing, wavelet decomposition, segmentation of cup, calculation of negentropy and estimate of glaucoma.

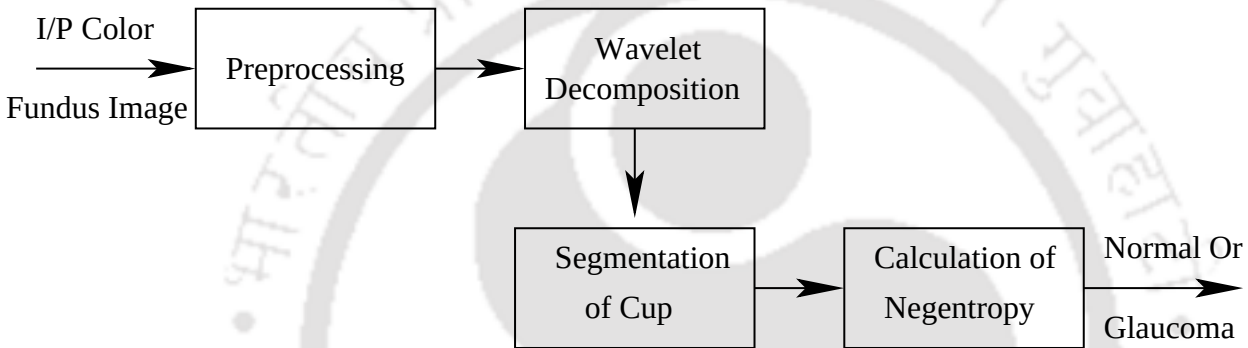


Figure 5.4: Differential entropy based method for glaucoma detection.

Preprocessing: During glaucoma, the OD appearance changes. Gradually the cup size increases with the progression of disease. Preprocessing is applied to the green channel of the color fundus image as the green channel provides higher contrast between the features and the background. Preprocessing consists of cropping, illumination correction and histogram equalization to provide the details of OD. Cropping provides the details about the OD and most of the background is removed. Illumination correction is performed to have homogeneous background, which is obtained by subtracting the mean value of the image from the original image. Histogram equalization is applied to all the images in order to spread the energy of all the pixels in the image and then normalize them to equalize the amount of energy related to each image. Fig. 5.5 shows the different preprocessing stage for glaucoma detection. Fig. 5.5(a) is the cropped, color fundus image with 128×128 pixels in bitmap format taken from the optic disc organization (<http://www.optic-disc.org>). Fig. 5.5(b), Fig. 5.5(c) and Fig. 5.5(d) show the red, green and blue channel of the cropped color fundus image, respectively. Red channel is highly saturated where as the blue channel is under saturated and noisy. Green channel image is shown in Fig. 5.5(c). This image is minimally saturated. So, green channel image is used for glaucoma detection. Fig. 5.5(e) is the illumination corrected image. It has ho-

homogeneous background. Fig. 5.5(f) shows the histogram equalized image. Histogram equalization provides uniform distribution of energy. Wavelet decomposition is applied to histogram equalized image.

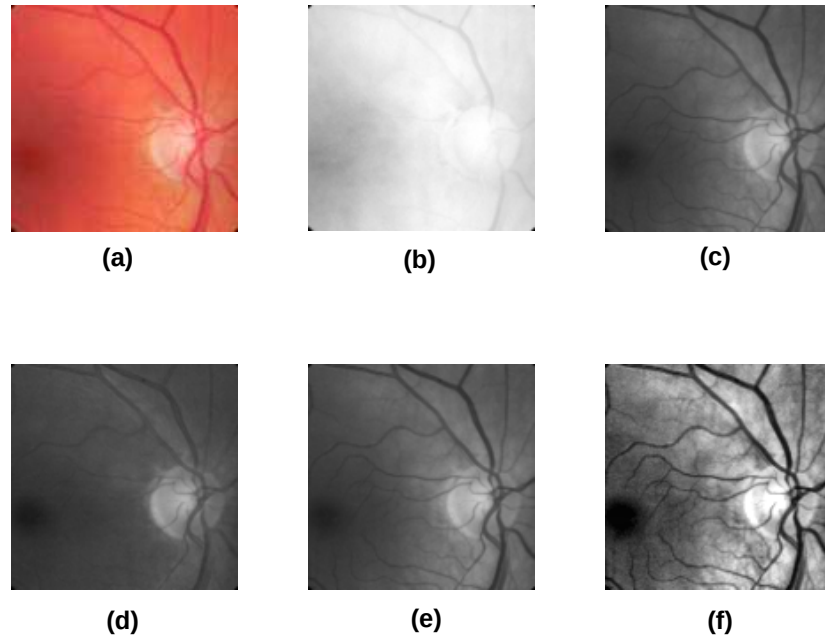


Figure 5.5: Preprocessing: (a) cropped color image, (b) red channel image, (c) green channel image, (d) blue channel image, (e) illumination corrected image, (f) histogram equalized image.

Wavelet decomposition: Wavelet subbands highlight different information of features in a fundus image (Nirmala et al. 2010; Quéllec et al. 2008). In this work, five level wavelet decomposition with Daubechies4 (db4) mother wavelet is implemented. Five level decomposition generates one approximation band at final level and fifteen detail bands. Each level generates three detail bands such as horizontal, vertical and diagonal. Five level decomposition is sufficient to highlight the OD region by suppressing the blood vessels information. Blood vessels present in OD are minimally affected by glaucoma. Fig. 5.6(a) shows the green channel of the color fundus image. The two wavelet subband images are shown in Fig. 5.6(b) and Fig. 5.6(c). It can be observed that blood vessels appear with the cup in the wavelet subband-3 image as shown in Fig. 5.6(b). The blood vessels are suppressed in wavelet subband-5 image, which is shown in Fig. 5.6(c). This image contains only the cup information. This is due to the low frequency characteristics of cup information. Different wavelet subbands for a number of fundus images are evaluated. It is observed that subband-

5. Assessment of glaucoma in wavelet scale

5 contains dominantly the cup information.

The cup appearance changes due to glaucoma. Watershed segmentation (Petrou and Petrou, 2010) is used in wavelet subband-5 for detection of the cup. Watershed segment is used for segmenting the objects that are touching each other. In this case the grey scale image can be viewed as a topographical surface, where the value of the image at each pixel represents the height. Water falling on the watershed ridge line separate the two basins. Then the watershed algorithm finds the basins and the ridge line in the image. The segmented cup is shown in Fig. 5.6(d).

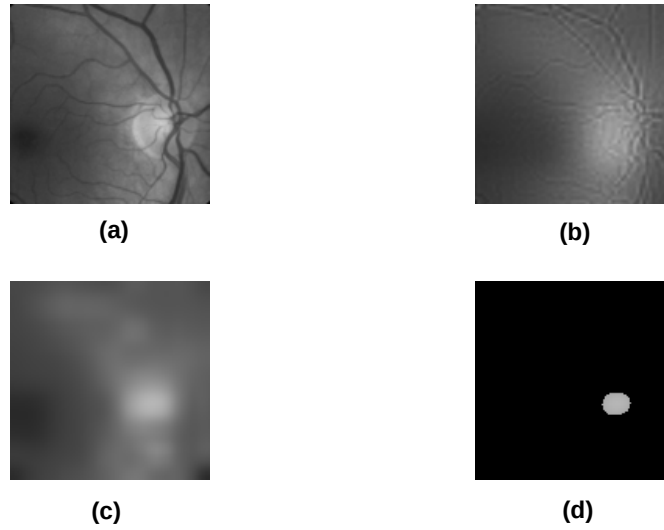


Figure 5.6: The appearance of different features of color fundus image in different wavelet subbands and detection of the cup (a) preprocessed green channel image, (b) subband-3 image, (c) subband-5 image, (d) segmented cup.

Differential entropy as a measure for glaucoma: Parameter CDR is the ratio of cup area (A_c) to disc area (A_d). The cup area and disc area are proportional to the number of cup pixels and the number of disc pixels, respectively. If the cup probability ($p_c(\varphi)$) is defined as the ratio of number of cup pixels to the total number of pixels in the image then the cup area is proportional to the cup probability. Similarly, the disc area is proportional to the disc probability ($p_d(\varphi)$). So, CDR can be written as:

$$CDR = \frac{A_c}{A_d} = \frac{p_c(\varphi)}{p_d(\varphi)} \quad (5.1)$$

The cup size increases with the progression of glaucoma. Normally, the disc size does not

change. So, the change in CDR value will be proportional to the probability of the cup. The relative change in the cup probability can be used as a measure of glaucoma in place of CDR. The change of cup probability can be estimated by the differential entropy (DE_c) [146] of the cup as:

$$DE_c = \int p_c(\varphi) \log_2 \frac{p_c(\varphi)}{p_\phi(\varphi)} d\varphi \quad (5.2)$$

where, $p_\phi(\varphi)$ is the probability of the Gaussian random variable with same mean and variance as that of $p_c(\varphi)$. This measure does not require the evaluation of disc size which is difficult to estimate in some glaucoma cases. By choosing a suitable threshold, the normal and glaucoma images can be separated. The optimum threshold value for DE_c is calculated by the simulated cup and disc. Fig. 5.7 shows DE_c value vs. CDR value for different sizes of cup. The DE_c value of cup lies below 0.26 for the CDR value ranges from 0.3 to 0.5. DE_c value is higher than 0.26 for glaucoma images. The linear relationship between CDR and DE_c values suggests that DE_c can be used not only for detection of glaucoma, but also for evaluation and progression of glaucoma. So, $DE_c = 0.25$ can be used as a threshold for detection of glaucoma.

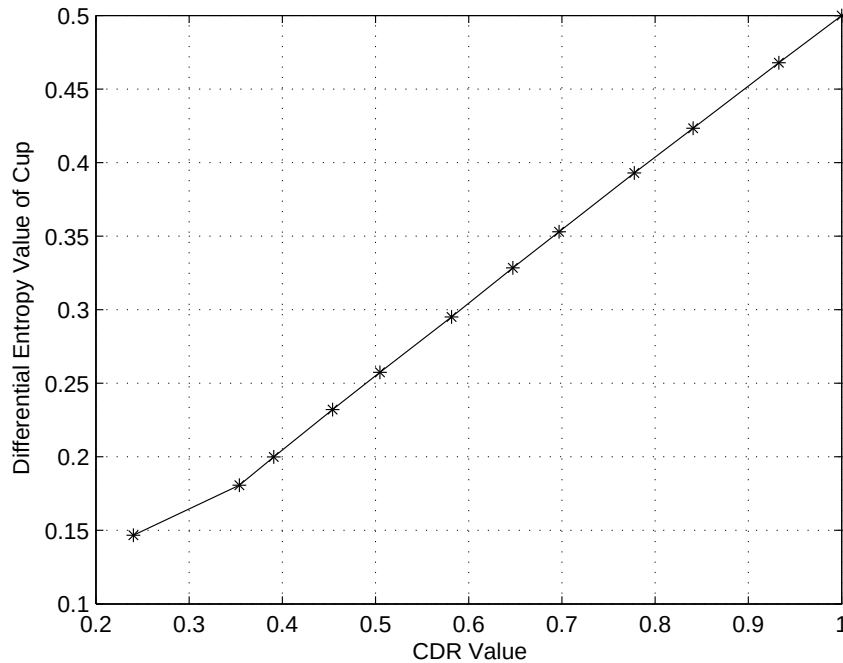


Figure 5.7: Differential entropy value vs. CDR value for different size of cup.

Results: This method is applied on 45 images (37 glaucoma images and 8 normal images) ob-

5. Assessment of glaucoma in wavelet scale

tained from the optic-disc organization [16] and 9 normal images from DRIVE database. This dataset consists of 17 normal images and 37 glaucoma images. Five level wavelet decomposition is performed on the preprocessed image by Daubechies4 (db4) mother wavelet. Watershed segmentation is performed in wavelet subband-5 and DE_c values for the segmented cup is calculated. Table 5.1 shows the results for 54 images. Out of 37 glaucoma images 35 glaucoma images are detected correctly. Out of 17 normal images 15 normal images are detected correctly. For normal images the DE_c value is found to be less than 0.25. For glaucoma images the value is found to be greater than 0.25. Im-7 and Im-49 are normal images but detected as glaucoma. Im-14 and Im-15 are glaucoma images and detected as normal images. In this case, all types of glaucoma having different types of disc appearance are classified. The performance of the method is calculated by true positive (TP), true negative (TN), false positive (FP) and false negative (FN) values [21, 135]. TP, TN, FP and FN for the proposed method are found to be 0.9459, 0.8823, 0.1176, and 0.0540, respectively.

Table 5.1: Differential entropy (DE_c) value of segmented cup for glaucoma detection.

Images	DE_c	Images	DE_c	Images	DE_c	Images	DE_c	Images	DE_c	Images	DE_c
Im-1	0.12	Im-10	0.88	Im-19	0.80	Im-28	0.74	Im-37	0.89	Im-46	0.10
Im-2	0.20	Im-11	0.90	Im-20	0.52	Im-29	0.27	Im-38	0.69	Im-47	0.17
Im-3	0.24	Im-12	0.85	Im-21	0.50	Im-30	0.32	Im-39	0.79	Im-48	0.11
Im-4	0.22	Im-13	0.73	Im-22	0.37	Im-31	0.49	Im-40	0.87	Im-49	0.26
Im-5	0.06	Im-14	0.19	Im-23	0.84	Im-32	0.69	Im-41	0.79	Im-50	0.17
Im-6	0.05	Im-15	0.17	Im-24	0.37	Im-33	0.54	Im-42	0.59	Im-51	0.15
Im-7	0.28	Im-16	0.27	Im-25	0.89	Im-34	0.56	Im-43	0.90	Im-52	0.17
Im-8	0.22	Im-17	0.30	Im-26	0.99	Im-35	0.58	Im-44	0.88	Im-53	0.87
Im-9	0.60	Im-18	0.94	Im-27	0.36	Im-36	0.90	Im-45	0.87	Im-54	0.87

In this method, sensitivity and specificity are found to be 94.59% and 88.23%, respectively. Sensitivity and specificity should be a high value for best performance. Fig. 5.8 shows the receiver operating characteristic (ROC) for the proposed DE based glaucoma detection method. It is the plot between the sensitivity versus (1-specificity) [157]. The accuracy becomes maximum if the ROC curve runs from (0, 0) coordinate to (1, 1) coordinate through the (0, 1) coordinate. Accuracy becomes 50%, when the ROC curve passes through the diagonal. In the proposed method the ROC curve lies towards the higher accuracy side. Fig. 5.8 shows the ROC curve. In this curve, the plot is more inclined towards the sensitivity axis. So, the method can perform better classification.

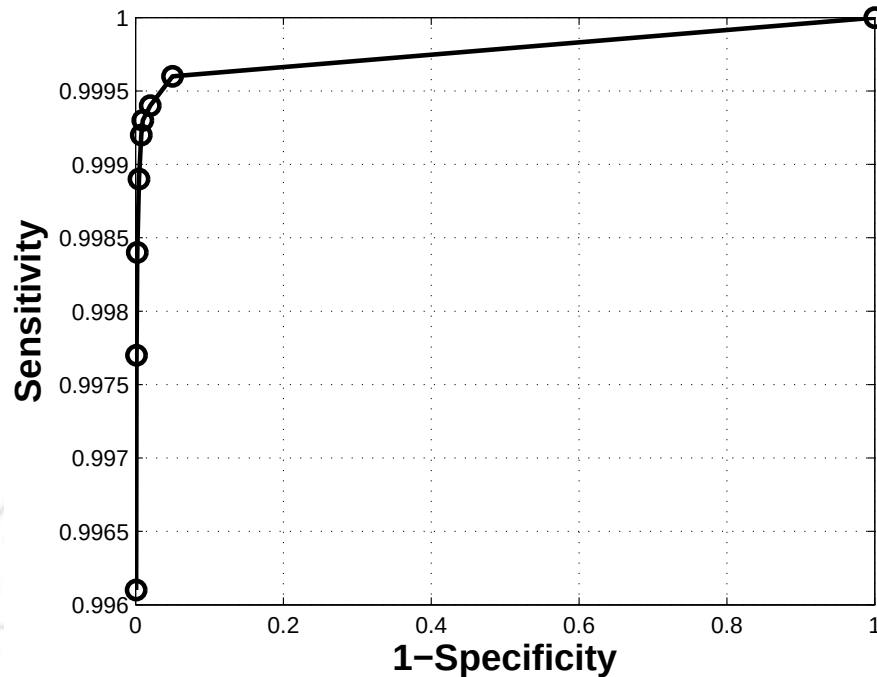


Figure 5.8: ROC curve shows the segmentation performance.

5.3 PCA-LDA based glaucoma classification

Appearance-based approaches of classification generally operate directly on images and process the image as two dimensional patterns. These methods extract features to optimally represent images which belong to a class and to separate images from different classes. Ideally, it is desirable to use only features having high separability power, while ignoring the rest. Most effort in the literature has been focused mainly on developing feature extraction methods and employing powerful classifiers such as hidden Markov models (HMMs), neural networks (NNs) and support vector machine (SVM) [158]. The main trend in feature extraction has been representing the data in a lower dimensional space computed through a linear or non-linear transformation satisfying certain properties. Statistical techniques have been widely used for recognition and in analysis to extract the abstract features of the patterns. Principal component analysis (PCA), linear discriminant analysis (LDA) and discrete cosine transform (DCT) are three main techniques used for data reduction and feature extraction in the appearance based approaches. DCT removes some high frequency details and in this way reduce the size of images. LDA algorithm selects features that are most effective for class

5. Assessment of glaucoma in wavelet scale

separability, while PCA selects features important for class representation. PCA might outperform LDA when the number of samples per class is small and in the case of the training set with a large number of samples. Compared to the PCA method, the computation of the LDA is much higher and PCA is less sensitive to different training data sets. LDA is not applicable, when the dimensionality of images is high. To resolve this problem PCA and LDA methods are combined. By applying PCA to preprocessed images, low dimensionality images are obtained. These images are now ready for applying LDA.

PCA and LDA are two classical tools used in the appearance based approaches for dimensionality reduction and feature extraction [159, 160]. LDA based algorithms outperform the PCA-based ones in solving the pattern classification problems, since the former takes the between class variations into account [161]. The LDA is a powerful feature extraction tool for pattern recognition in general and for face recognition. It was introduced to this application area by 1997 [160].

Many recognition systems have been proposed in the literature. In the appearance-based approaches, the images are viewed as a feature vector. Appearance based recognition methods try to reduce the dimensionality of the original image space with respect to a certain criterion. Because of the huge dimensions of an image, it may contain redundant or noisy information, and its processing requires a high computational cost. A feature reduction is performed by applying some standard algorithms of pattern recognition. The most known approach is the PCA representation, proposed by Turk and Pentland [159] in which the image is projected in a space in which the correlation among the components is zero. Another appearance based approach is the LDA representation proposed by Kriegmann et al. [160] where the image is projected in the Fisher space, in which the variability among the vectors of the same class is minimized and the variability among the vectors of different classes is maximized.

5.3.1 PCA and LDA representation for Glaucoma classification

The features of the cup are used in PCA [151, 162] and LDA [163] based glaucoma classification. Principal component analysis finds a direction along which maximum variation of data occurs. Due to the above reason, PCA is used for data reduction and finds the OD features by finding a direction along which maximum variation of data occurs. The LDA finds class separability and decision regions among the classes for glaucoma classification.

Let Z be a d -dimensional feature vector. Here, d is equal to the number of pixels of each fundus

image. The high dimensionality of the related image space is a well-known problem for the design of a good verification algorithm. Therefore, methods for reducing the dimensionality of such image space are required. It can be achieved by PCA. PCA is defined by:

$$o_i = \Omega^T z_i \quad (5.3)$$

where, $z_i \in \mathbf{z} \subseteq R^d, i = 1, 2, \dots, n$. $\mathbf{z}$ be a d-dimensional feature vector. The number of pixels in each fundus image is represented by 'd'. 'n' represents number of samples. Ω is a d-dimensional transformation matrix, whose columns are the eigenvectors related to the eigenvalues. Eigenvalues computed according to the formula given below.

$$\lambda e_i = S e_i \quad (5.4)$$

where, 'S' is the scatter matrix (i.e., the covariance matrix). It defines the d-dimensional space in which the covariance among the components is zero. In this way, it is possible to consider a small number of principal components exhibiting the highest variance (the most expressive features).

The Linear Discriminant Analysis (also called Fisher Discriminant Analysis) is defined by the transformation:

$$o_i = \tilde{\Omega}^T z_i \quad (5.5)$$

The columns of $\tilde{\Omega}$ being the eigenvectors of within-class scatter matrix and between-class scatter matrix. The eigenvectors of LDA are called fishers. LDA transformation is strongly dependent on the number of classes (c), the number of samples (n) and the original space dimensionality (d). There are almost 'c - 1' nonzero eigenvectors. The 'c - 1' being the upper bound of the discriminant space dimensionality. We need 'd + c' samples at least to have a non-singular within-class scatter matrix. It is impossible to guarantee this condition in many real applications. Consequently, an intermediate transformation is applied to reduce the dimensionality of the image space. In order to prevent within-class scatter matrix to become singular, PCA is used as a preprocessing step and the final transformation is $\Omega_{opt}^T = \tilde{\Omega}^T \Omega^T$.

5.3.2 Method

The different steps of this method are shown in Fig.5.9. The proposed PCA-LDA based glaucoma classification consists of following steps such as, preprocessing, dimensionality reduction using PCA, feature extraction for class separability using LDA and classification.

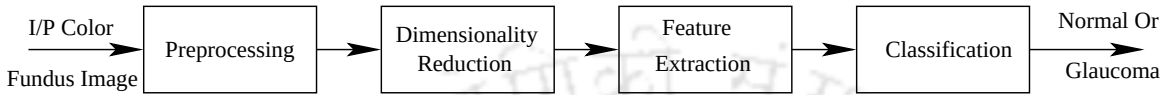


Figure 5.9: PCA-LDA based glaucoma classification.

Preprocessing: This step is same as that of the preprocessing step discussed in Section 5.2, which consists of cropping, illumination correction and histogram equalization. The color images are resized and manually cropped to 64×64 pixels to have only details of OD. After Illumination correction and histogram equalization the image is changed to an image vector of dimension 4096×1 .

Dimensionality Reduction: The vectors obtained in the preprocessing stage are used for estimating the covariance matrix. Significant eigenvectors are computed from the covariance matrix. For reducing computational complexity, few eigenvectors are considered depending upon the accuracy. Computational cost directly depends on the number of eigenvectors computed. Here, PCA is used for dimensionality reduction. By this method each glaucoma image is converted to an image vector. Then all the glaucoma images are arranged to form the image matrix. Eigenvectors and covariance matrix are calculated by applying PCA on the image matrix.

LDA Feature Extraction: LDA calculates the class-scatter matrix and covariance matrix of the significant eigenvectors. As mentioned earlier, significant eigenvectors (within a class scatter matrix and between class scatter matrix) can be used for separability of classes in addition to dimension reduction. This is used to select the eigenvectors related to the greater eigenvalues.

Classification: Classification is based on the similarity score. The input color fundus images are classified as either normal or glaucoma class. The feature vector of testing image is compared to the feature vector of normal and abnormal images by considering the minimum distance.

Results: This method is tested on 54 images (37 glaucoma images and 17 normal images) obtained from the optic-disc organization [16] and DRIVE database. For each class five images are used for training purpose. The rest 44 images are used for testing purpose. Before applying PCA and LDA, all the images are preprocessed. The input fundus images are resized to a standard size

of 64×64 . The cropped images highlight the information about OD. After preprocessing, the image is converted to a row vector. Fig. 5.10 shows some of the selected preprocessed images. Then, PCA is applied to construct a class scatter matrix and covariance matrix. The significant eigenvectors are used for separability of class. In this case, only one significant eigenvector is available due to two classes, i.e., normal and glaucoma.

In PCA-LDA method, eight significant eigen-images are computed and shown in Fig. 5.11. Four most significant eigenvalues are sufficient for the optimum performance in most of the cases (shown in Table 5.2). These significant eigenvectors are used for separability of classes and dimensionality reduction. The higher eigenvalues are selected. These are called principal components. Two classes are considered, so there is only one major eigenvector associated with major eigenvalues, which has the class separable capability. So, extracting only one LDA feature can increase the discriminatory power of the method. The feature vector of testing image is compared with the calculated feature vectors of both the classes, i.e., normal and glaucoma. The minimum distance from the testing image to one of the classes, determines its class. Increase in number of selected PCA features decreases error classification. Increase in LDA features increase separability power.

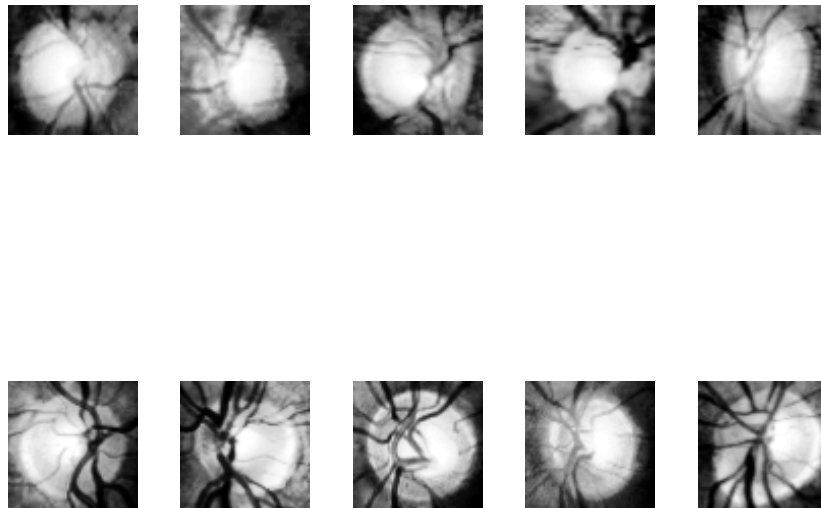


Figure 5.10: Preprocessed training images: for glaucoma and normal.

The performance of the proposed glaucoma classification algorithm is calculated by accuracy,

5. Assessment of glaucoma in wavelet scale

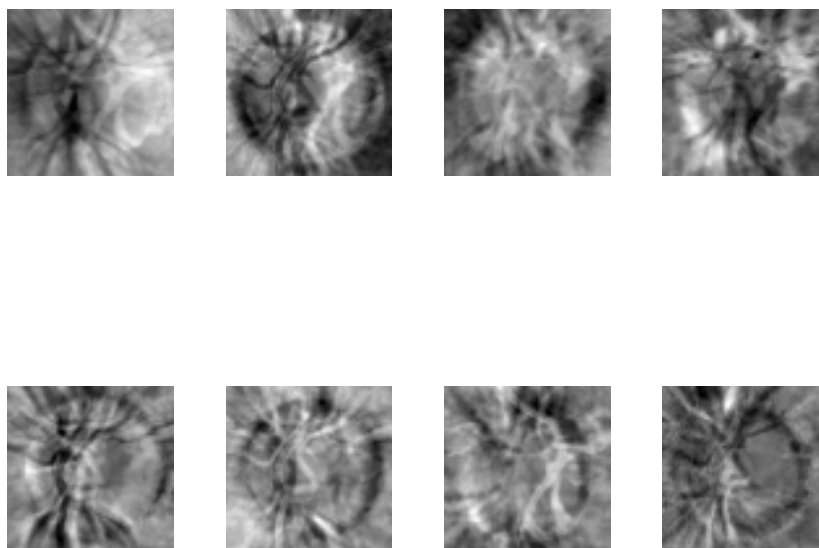


Figure 5.11: Eight significant eigen-images.

Table 5.2: Performance of PCA-LDA based glaucoma classification based on the number of significant eigen-values or principal components (PCs).

No of PCs	Classified	Misclassified	Accuracy%	Sensitivity%
1	30	14	68.18	78.13
2	25	19	56.82	59.38
3	27	17	61.36	65.63
4	30	14	68.18	81.25
5	30	14	68.18	81.25
6	26	18	59.09	59.38
7	26	18	59.09	59.38
8	27	17	61.36	65.63
9	26	18	59.09	62.50
10	15	29	34.09	15.63

sensitivity, and specificity [44], [135]. Sensitivity is the measure for classifying glaucoma images as glaucoma. Sensitivity is defined as the ratio of correctly classified glaucoma images to the total number of glaucoma images. Specificity measures the number of normally classified fundus images from the total number of normal fundus images. Accuracy is defined as the ratio of the total number of correctly classified images (i.e., glaucoma images classified as glaucoma and non glaucoma images classified as non glaucoma) to the total number of images. Sensitivity, specificity and accuracy are

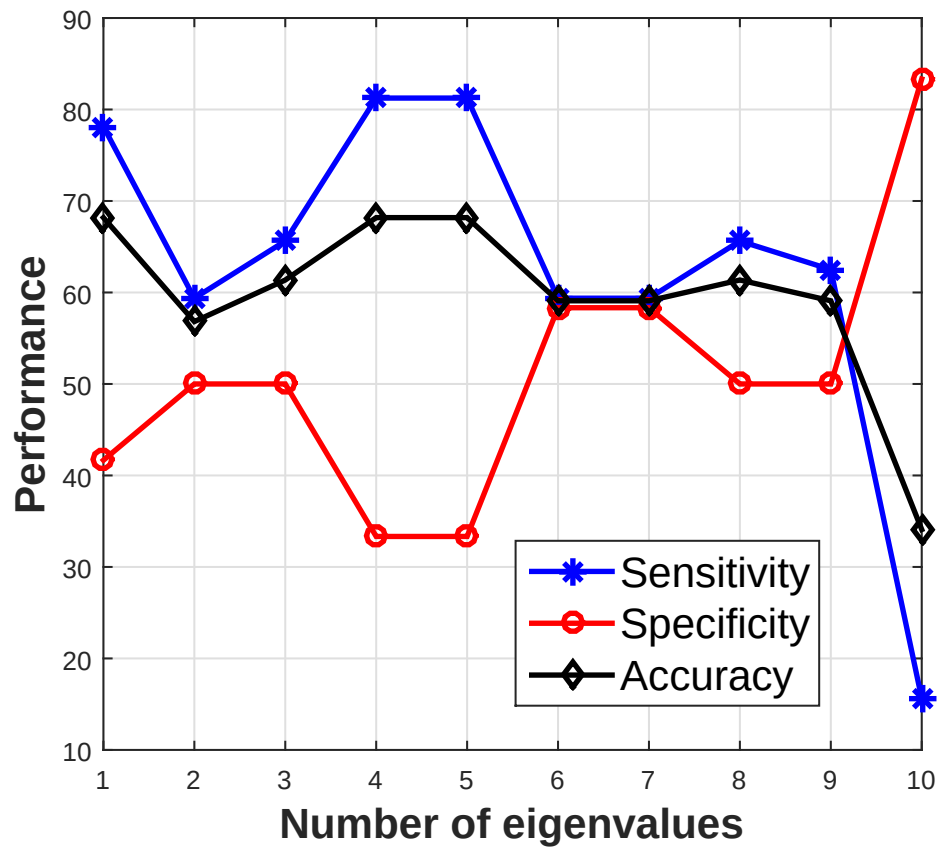


Figure 5.12: Performance values vs. number of significant eigenvalues/principal components (PCs).

found to be 81.25%, 33.33% and 68.18%, respectively for this method. Higher values represent better classification. Fig. 5.12 shows the variation of sensitivity, specificity and accuracy versus the number of significant eigenvalues or principal components. Sensitivity and specificity increase with increase in the number of eigenvalues. The optimum performance is obtained by considering four numbers of significant eigenvalues for the considered dataset. Table 5.2 shows the variation of accuracy and sensitivity with the number of principal components (PCs) considered. Accuracy increases with increasing the number of significant eigenvalues. It attains highest value with 4 numbers of principal components. Significant change in accuracy does not occur for classification of glaucoma, beyond 4 number of PCs. But it increases the computation time for classification.

5.4 HMM-SVD based glaucoma classification

The method employs a 7-State one-dimensional discrete Hidden Markov Model (HMM) to model the retina image along with singular value decomposition (SVD) for feature extraction. Hidden Markov Models are generally used for modeling 1-D datasets, but it has also been used to model 2-D datasets based applications such as texture segmentation, object recognition and face recognition [164]. A discrete-time HMM, can be viewed as a Markov Model whose states cannot be explicitly observed. Every HMM is related to non-observable states called the hidden states and an observable emission sequence generated by each of the hidden states individually. The entities of HMM are the number of states in the model, the number of different observation symbols, transition probability, observation symbol probability and initial state distribution. HMMs generally work on sequences of symbols called the observation vectors, while an image is represented in a 2-D matrix form. Thus, in the case of recognition problem using one dimensional discrete HMM, recognition is based on frontal view, where the retinal image is divided into 7-regions such as upper terminal, upper secondary, upper primary, optic disc region, lower primary, lower secondary, lower terminal in their natural order from top to bottom. Each of these portioned retinal regions is assigned to a state in a left to right one dimensional HMM model. The major advantage of the above model is its simple structure and a small number of parameters to adjust. The mentioned retinal regions have been featured using SVD.

The observation sequence is generated by dividing the retina image of width w and height h into overlapping blocks of width w and height $\tilde{h}$. A $w \times \tilde{h}$ sliding window is moved from top to bottom of the image which creates a sequence of overlapping sub-image blocks. Here, the successive sub-image blocks are the referred interpretation. The number of blocks B_L extracted from each retina image is given by:

$$B_L = \frac{h - \tilde{h}}{\tilde{h} - o} + 1 \quad (5.6)$$

where, o is overlap between two successive blocks. A high percentage of overlap between successive blocks significantly boosts the performance of the system, it also increases the computational complexity. From the study, it has been observed that as long as o is significantly large ($o \leq \tilde{h} - 1$) and $\tilde{h} \approx h/10$, the recognition rate is not very sensitive to the variations of $\tilde{h}$.

Singular Value Decomposition (SVD) transforms correlated variables into a set of uncorrelated

ones that better expose the various relationships between the original data elements [165]. Singular values of given data matrix bears information regarding the noise level, energy and the rank of the matrix, etc. As singular vectors of a matrix are orthonormal span bases of the matrix, they can exhibit some features of the patterns embedded in the image [164]. SVD provides an efficient way of extracting features from an image, in an algebraic form. Singular value decomposition matrix generates two mutually orthogonal matrices, and a diagonal matrix of singular values. Evidently the first two singular values are very much bigger than remaining ones and consequently, have more significance.

Coefficients obtained from SVD form continuous valued sequence, which shape the observation vectors. If considered in the same continuous form, infinite possible observation vectors will be encountered that cannot be modeled using discrete HMM. So, there is a need to quantize the features described above. This is normally handled by a process of rounding, truncation, flooring or other irreversible, nonlinear processes which causes information loss. Here, quantization is done by using the following algorithm. Assume a vector $w = (w_1, w_2, \dots, w_n,)$ with continuous elements. Suppose w_i is to be quantized into l_i distinct levels. So the difference between two consecutive quantized values will be given by:

$$\Delta_i = \frac{w_{imax} - w_{imin}}{l_i} \quad (5.7)$$

where, w_{imax} and w_{imin} are the maximum and minimum values that w_i can assume in all possible observation vectors, respectively. Knowing Δ_i , element w_i will be replaced by its quantized value computed as:

$$w_{iquantized} = \frac{w_i - w_{imin}}{\Delta_i} \quad (5.8)$$

Thus all the elements of w_i would be quantized. At the end, each quantized vector is linked with a label, i.e., an integer value. So, each of the sub-image block is mapped to an integer. Considering all the blocks of an image, the retina is mapped into a series of integer values that is considered as an observation vector. Now the images are interpreted as a 1-D sequence of numbers and the sequence can be easily modeled using HMM [164, 166] for classification.

After representing each retinal image in the form of observation vectors, they are modeled using a 7-State HMM model. The HMM model is then trained using Baum-Welch algorithm. After

5. Assessment of glaucoma in wavelet scale

representing the retina images by observation vectors, the HMM parameters are estimated using the Baum-Welch algorithm which maximizes the probability of the observation associated with the training image. This gives the final estimated HMM for a given training image.

5.4.1 Method

The block diagram for glaucoma classification by HMM-SVD is shown in Fig. 5.13. The different steps for HMM-SVD based glaucoma classification are Gaussian based segmentation, inpainting, manual cropping, SVD, HMM, and glaucoma classification. The preprocessing is same to that of the PCA-LDA based method. In this case the image is resized to the 46×56 .

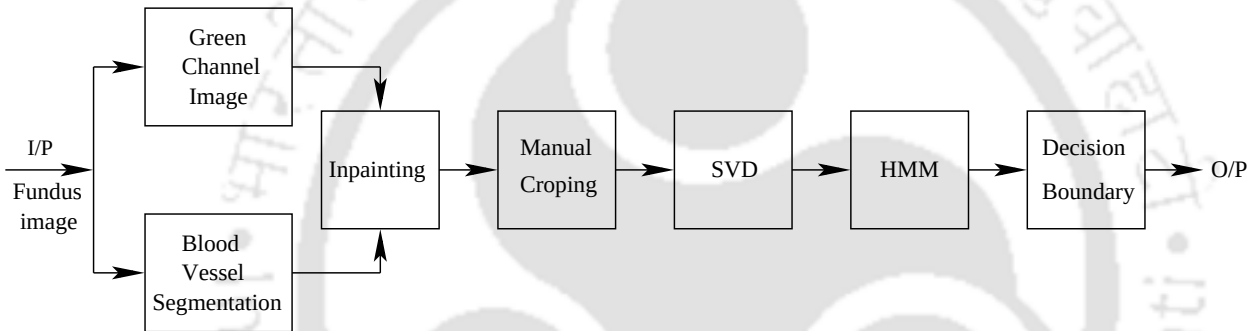


Figure 5.13: HMM-SVD based method for glaucoma classification.

Gaussian based segmentation: The pixel values of the cross section of blood vessel have the shape of a Gaussian function and it has an intrinsic property of noise reduction. Due to this, the Gaussian matched filter is used for extraction of the blood vessel patterns from the fundus image as it provides better segmentation with comparatively low complexity. Then image inpainting is applied to remove the blood vessels from the fundus image, as glaucoma affects the OD region only. The observation sequence is generated by dividing the retina image into overlapping blocks.

In order to reduce the computational complexity and memory consumption, the retinal images are resized to 46×56 which results in data loss from the images. *Singular value decomposition* (SVD) [165] is used for feature extraction which compensate the data loss and obtain a set of uncorrelated features about the cup and OD. It is used due to its stability and robust feature extraction technique for retinal images. The SVD coefficients are used as features in the sampling windows (blocks). A sampling window of 46×5 pixels have been used with an overlap of 80% in vertical direction ($\tilde{h} = 5, o = 4$). Observation vector is composed of a large number of $w \times h$ blocks ($w = 46, h = 5$), each containing 230 pixels. The number of blocks of a 46×56 image is 52. The SVD coefficients

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of each block are computed and used as features. A sub-image block of size 46×5 generates a Σ matrix with the same dimensions, which implies that there are 46 distinct singular values present for each of the 52 blocks. Among the 46 singular values, only a few big singular values and their related vectors convey information about the energy and information of an image. The SVD of a $m \times n$ matrix X is given by:

$$X = U\Sigma V^T \quad (5.9)$$

where, $U_{m \times m}$ and $V_{n \times n}$ are mutually orthogonal matrices, and Σ is a $m \times n$ diagonal matrix of singular values with components $\sigma_{\hat{i}\hat{j}} = 0$ for $\hat{i} \neq \hat{j}$ and $\sigma_{\hat{i}\hat{j}} > 0$ for $\hat{i} = \hat{j}$. Further, there exist non-unique matrices U and V such that $\sigma_1 \geq \sigma_2 \geq \dots \geq \sigma_n$.

Coefficients obtained from SVD are quantized. At the end, each quantized vector is linked with a label, i.e., an integer value. So, each of the sub-image block maps to an integer. Considering all the blocks of an image, the retina is mapped into a series of integer values that is considered as an observation vector. Now the images are interpreted as a 1-D sequence of numbers, the sequence can be easily modelled using HMM for classification.

Thus, in the case of glaucoma classification problem using one dimensional discrete HMM, recognition is based on frontal view, where the retina image is divided into seven regions. Each of these partitioned retinal regions is assigned to a state in a left to right one dimensional HMM model. The major advantage of the above model is its simple structure and a small number of parameters to adjust. The HMM model is then trained using Baum-Welch algorithm. After representing the retina images by observation vectors, the HMM parameters are estimated using the Baum-Welch algorithm which maximizes the probability of the observation associated with the training image. This gives the final estimated HMM for a given training image. The output of different stages is shown in Fig. 5.14.

Results: The system was tested on 54 images, which contains 17 healthy retina images and 37 glaucoma images. Five retinal images from each class are used for training and remaining 44 images are used for testing. Out of 44 images 32 images are correctly classified and 12 images are misclassified. Accuracy, sensitivity and specificity values are found to be 72.73%, 78.13%, and 58.33%, respectively. Table 5.3 shows the comparison of performances of different glaucoma detection methods.

5. Assessment of glaucoma in wavelet scale

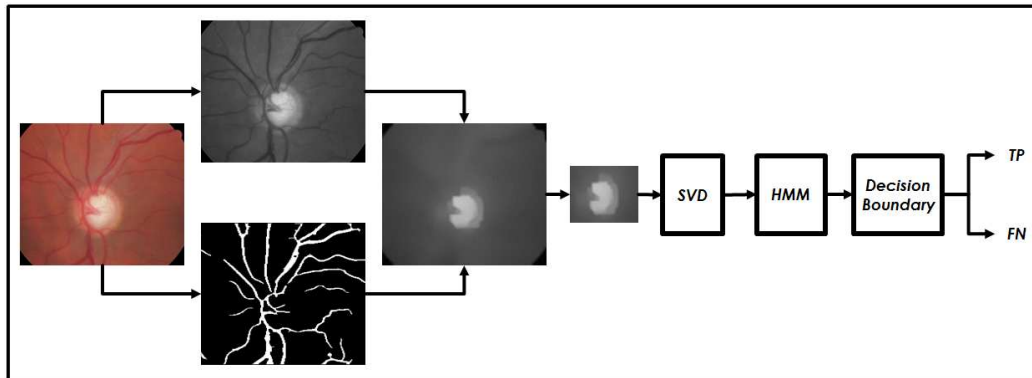


Figure 5.14: Output of different stages of HMM-SVD based method for glaucoma classification.

Table 5.3: Comparison of performance measure for different glaucoma detection method.

Method	Accuracy	Sensitivity	Specificity
CDR	74.07%	62.16%	100%
DE	92.59%	94.59%	88.23%
PCA-LDA	68.18%	81.25%	33.33%
HMM-SVD	72.73%	78.13%	58.33%

5.5 Summary

In this chapter, glaucoma is detected from the color fundus images by using four different methods. The first method is the calculation of CDR for assessment of glaucoma. This method fails in case of disc anomalies. Differential entropy based glaucoma assessment can overcome the limitations of CDR based method. This method finds the information present in the cup as the parameters of the cup changes during the progression of glaucoma and other regions are minimally affected. Differentially entropy based method can be able to predict/identify the stages of glaucoma as in case of CDR based method. An accuracy of 92.59% is obtained by DE based glaucoma detection.

Machine learning techniques such as, PCA-LDA and HMM-SVD based approach are also used for glaucoma classification. In PCA-LDA based method, PCA is used for data reduction and LDA to find within the class and between class scatter matrix. In this case 68.18% images are classified correctly. As the number of significant eigenvalues or principal components increases the accuracy and sensitivity of the method increases up to certain number then decreases. The best result is

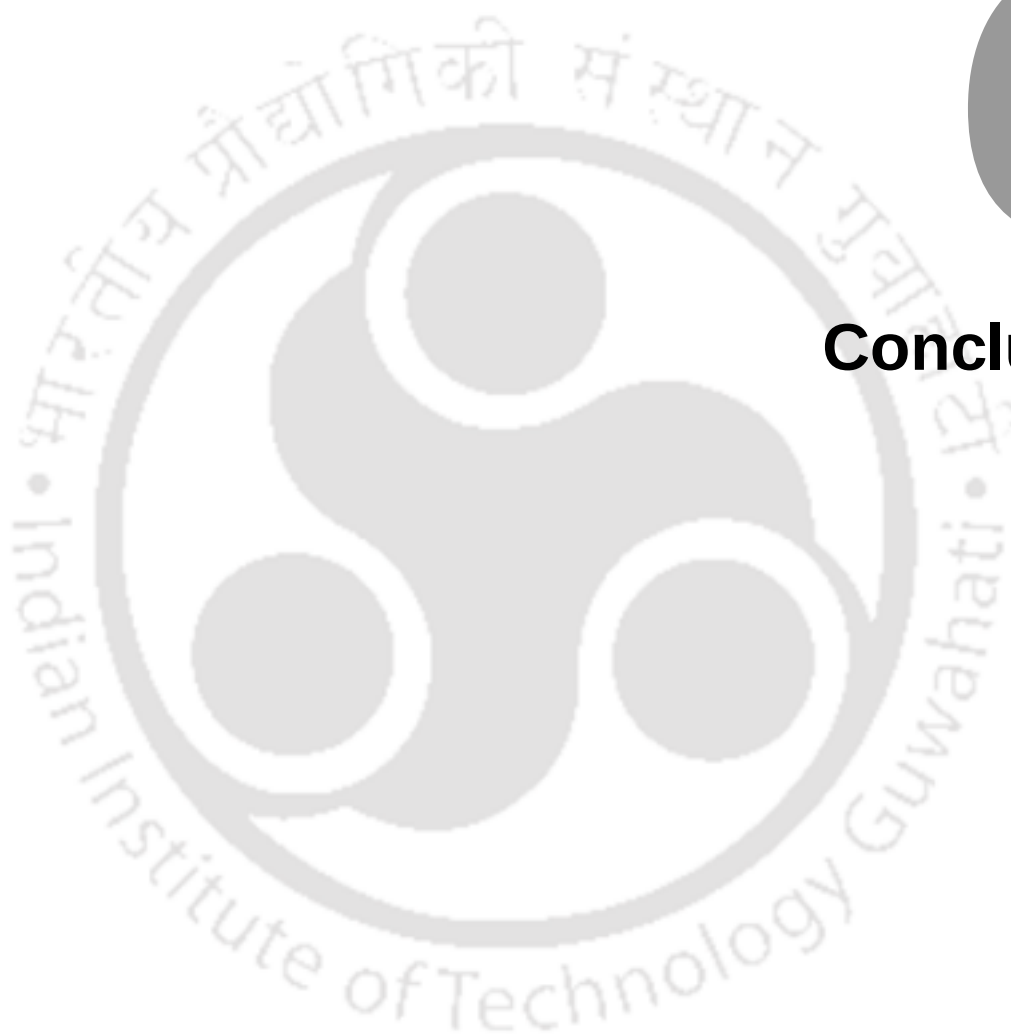
obtained when four number of eigenvalues are considered. In case of HMM-SVD based method SVD is used for glaucoma feature detection, whereas HMM is used as a classifier. This method provides an accuracy of 72.73%.





6

Conclusions



Contents

6.1 Scope for the future work	147
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6. Conclusions

In this thesis, we have analyzed and investigated the diagnostic features of the fundus images in the different scales of multiscale decomposition. This chapter includes the justification of the project, main contributions, results, final conclusions and future work. Diabetic retinopathy (DR) is a sight threatening disease. The DR screening process allows for the early detection of the disease and therefore allows for timely intervention in order to prevent vision loss. Retinal images have the potential for early detection of retinal pathologies due to DR and increased intra ocular pressure. The ophthalmologists examine the clinically/diagnostically important features (such as exudates, microaneurysms, blood vessels, and cupping of the cup etc.) for signs of various eye related diseases. Better detection of these pathological features and determination of their location can help predict the physicians about the condition of vision and prevent further damages.

From the literature review and the initial investigations, the best course of action was to build a framework based on vessel segmentation followed by the analysis of features in multiscale. This analysis was used for segmentation of the diagnostic features' exudates and detection of glaucoma. By multiscale decomposition, the fundus images are decomposed into different subbands. In each subband, the features are highlighted differently due to their different frequency contents. Higher subbands highlight the exudate and OD by suppressing the blood vessel. Glaucoma affects the optic disc (OD) and other features are minimally affected. During glaucoma the size of cup increases and the area of rim decreases. So, for detection of glaucoma the segmentation algorithm is used in higher subband to find the cup size. Exudates in higher subbands are highlighted by suppressing the macula and blood vessels. Normally, the exudates are non-Gaussian in nature. But other features (blood vessels, macula etc.) are sub Gaussian in nature. Independent component analysis (ICA) is applied to the data matrix formed by the subbands of multiscale decomposition and the different features are extracted. These features have the clinical importance for grading of diabetic retinopathy. Multiscale analysis is used for detection of glaucoma. The work in this thesis can be summarized as follows:

In **Chapter 1**, different clinical features' characteristics of retinal image and their importance were discussed. The literature survey on the analysis of clinically important normal features of a retinal image such as: OD, the macula and the blood vessels were presented. The characteristics of abnormal features, such as: microaneurysms, exudates, and haemorrhages were discussed. Different methods to segment the features were presented in this chapter.

In **Chapter 2**, the state-of-art methods for segmentation of diagnostic features in retinal image were discussed. The limitations of these methods were discussed. The different methods for glaucoma classification were explained. The motivation for the study of retinal features in wavelet subbands was presented.

In **Chapter 3**, the diagnostic features (microaneurysms and exudates) of the fundus image in different scales of wavelet decomposition were analyzed. The fundus image was decomposed into 3-, 5-, 7-, and 9-levels using db4 mother wavelet. In each level microaneurysm and exudates features were studied from the point view of diagnostic information. Following conclusions were drawn from the study.

- (i) Analysis of microaneurysm is performed on 3-, 5-, 7-, and 9-level of wavelet decomposition with db4 mother wavelet. In 3-level wavelet decomposition all the subbands contribute equally to the feature microaneurysm. In 5-level wavelet decomposition, subband $L1$, subband $L2$ and subband $L3$ contain less information about the MAs. Most of the information are present in subband $L4$ and subband $L5$ in 5-level wavelet decomposition. So, during the transmission or storage more attention should be given to the coefficients of $L4$ and $L5$ subbands. In 7-level wavelet decomposition, $L5$, $L6$, and $L7$ contribute more information towards MAs. Subband $L5$ to subband $L9$ coefficients contain higher MAs information compared to other levels in 9-level wavelet decomposition. Higher subband coefficients contain more MAs information compared to lower level subband coefficients.
- (ii) In 5-level wavelet decomposition the $L1$ and $L2$ subbands do not contain higher information about the exudates. The subbands $L4$ and $L5$ contain more blood vessels information. In 7-level wavelet decomposition subband $L1$, $L2$, $L3$, $L6$ and $L7$ contain the exudate information. By making $L2$, $L3$, and $L4$ subbands coefficients zero, the blood vessel information is lost without the loss of exudate information. In 7-Level wavelet decomposition $L2$, $L3$ and $L4$ subbands do not contain significant information about the DR feature. In 9-level wavelet decomposition blood vessels information is present in $L4$ and $L5$ subbands. The significant exudates information is not present in $L2$, $L4$, $L5$, and $L9$ subbands of 9-level decomposition. Significant exudate information is present in $L3$ and $L8$ subbands.
- (iii) The DR features in different wavelet subbands of various levels of wavelet decomposition were

6. Conclusions

compared quantitatively by different performance measures such as accuracy, specificity, universal quality index (UQI), Pearson correlation coefficient (PCC) and structural similarity (SSIM) etc.

In **Chapter 4**, the percentage of blood vessels affected by pathology and the extraction of exudates were discussed along with the detection of changes in the retina due to DR. The outcomes are summarized below.

- (i) Blood vessels were extracted by different methods such as Gaussian based match filter approach, Kirsch method and histogram method. Among these approaches, the Gaussian based method provides higher accuracy. Combined Kirsch and Gaussian method provides better performance in terms of sensitivity. This method is applied to the pathological images for segmentation of the blood vessels. Then the image inpainting operation is applied to suppress the effect of the blood vessels. From the inpainted image, the pathologies were segmented. Taking the overlapping regions of blood vessels and pathology, the affected blood vessels by pathology were determined. This helps assess the progression of retinal damage by assessing the number of blood vessels affected by pathological features.
- (ii) Independent component analysis on multiscale performs better compared to the ICA for separation of independent components and signals. This was tested by Amari performance index (API) and Comon test values for simulated signals and images. These values are found to be less in multiscale ICA than ICA. The ICA and multiscale ICA are applied to the fundus images for detection of exudates. The exudates are detected based on their statistical properties such as kurtosis and negentropy values. These values are found higher for exudates compared to the other features in the color fundus images. Due to this reason, the exudates are separated out from other features when ICA is applied. Extraction of exudates is found to be better in HSV color space compared to the RGB color space. This happens due to the less correlation of the color components in the HSV color channel.
- (iii) ICA on multiscale was extended for detection of changes from the color fundus image due to DR. In this method, one normal retinal image was compared with diabetic affected retinal image. The independent components were determined from both the images for detection of the changes in the retina. This may help assess the progression of retinal damage due to

[TH-1619_09610207](#)

diabetes.

In **Chapter 5**, assessment of glaucoma from the retinal images were discussed. In this chapter, two methods were discussed for glaucoma estimation, i.e., differential entropy (DE) based method and pattern recognition based method. In DE based method differential entropy value of the segmented cup was used for glaucoma detection. This method is able to detect the glaucoma in different disc condition. The second approach was based on pattern recognition. Here, the patterns of the cup and disc were used for detection of glaucoma. Principal component analysis (PCA)-linear discriminant analysis (LDA) and hidden Markov model (HMM)-singular value decomposition (SVD) approaches were used for glaucoma classification from color fundus images. The conclusions of this chapter are summarized below.

- (i) Differential entropy based glaucoma assessment overcame the limitations of glaucoma detection by CDR based method. In this method, cup information was used as a parameter for progression of glaucoma. An accuracy of 92.59% was obtained by DE based glaucoma detection.
- (ii) In PCA-LDA based method, PCA was used for data reduction and LDA was used to determine the class between the class scatter matrix. In this case, 68.18% images were classified correctly. As the number of principal components increases the specificity and sensitivity of the method increases till certain number then decreases. The best result was obtained by considering four numbers of principal components. In case of HMM-SVD based method, feature extraction is done using SVD, whereas HMM was used for classification. An accuracy of 72.73% was obtained by this method.

6.1 Scope for the future work

The thesis points to some interesting future work.

- Wavelet provides the resolution of the features based on their frequency content. Making the mathematical model for the features will help to analyze the features efficiently.
- This technique can be further used in telemedicine applications for automatic systems. This could have a positive impact on the diminution of the necessary resources in terms of specialists and examination time in diagnostic centers.

6. Conclusions

- ICA performance may improve if the statistical characteristics are known aprior to the application of ICA. This statistical information about the features may be used in the data matrix formed by the subbands of wavelet decomposition for the efficient detection of changes due to DR. This approach can be modified for finding the changes going to occur in the retina due to the DR by capturing the images of the same patients over time. These changes may have the direct relationship with the stress in the eye, intraocular pressure, blood pressure and diabetes. By quantifying the features according to certain rule in a rule based system, the automatic grading of DR is possible.
- The patterns of blood vessels in the optic disc is the unique feature of the retina. These retinal features are unique to each individual. So, features may be used to compute the disparity of the image features and to find the best matched retinal image pair.



A

Appendix

Contents

A.1 More figures for wavelet decomposition of MAs	150
A.2 Negentropy	159

A.1 More figures for wavelet decomposition of MAs

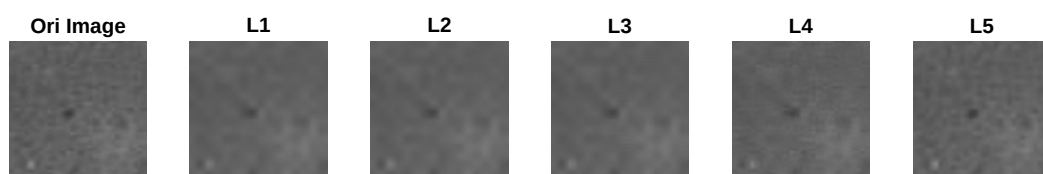


Figure A.1: Reconstructed images in 5-level wavelet decomposition by considering a particular subband coefficients of image-1 from the database.

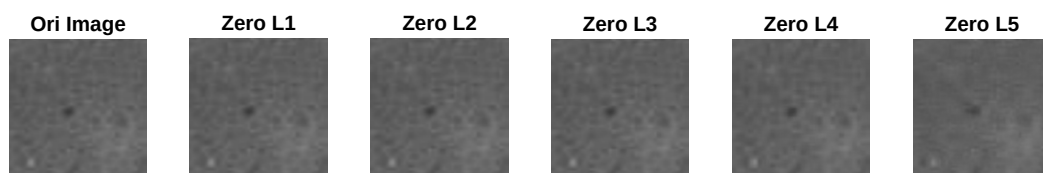


Figure A.2: Reconstructed images in 5-level wavelet decomposition by zeroing a particular subband coefficients of image-1 from the database.

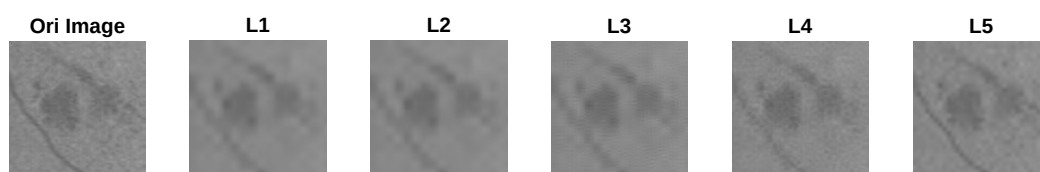


Figure A.3: Reconstructed images in 5-level wavelet decomposition by considering a particular subband coefficients of image-2 from the database.



Figure A.4: Reconstructed images in 5-level wavelet decomposition by zeroing a particular subband coefficients of image-2 from the database.

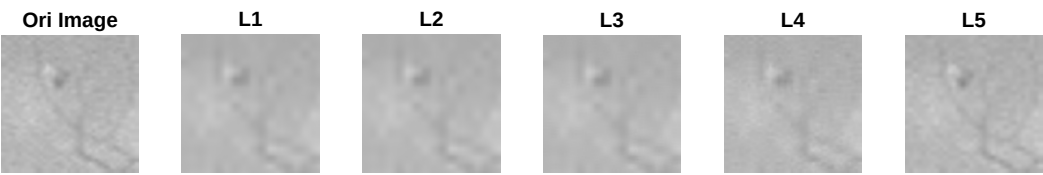


Figure A.5: Reconstructed images in 5-level wavelet decomposition by considering a particular subband coefficients of image-3 from the database.

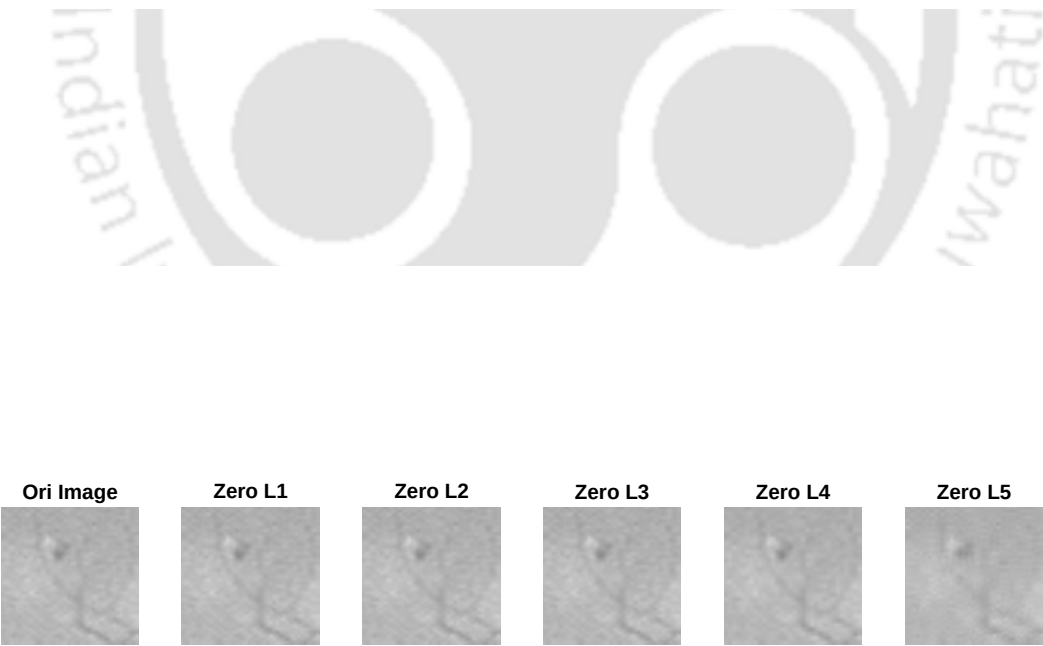


Figure A.6: Reconstructed images in 5-level wavelet decomposition by zeroing a particular subband coefficients of image-3 from the database.

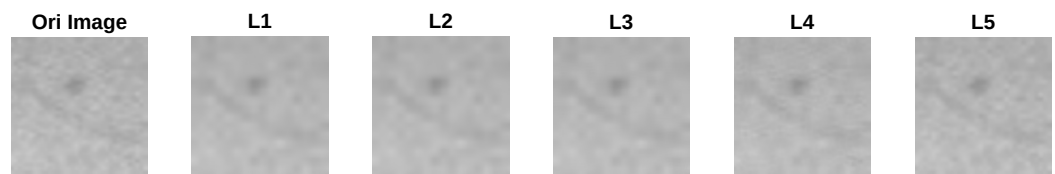


Figure A.7: Reconstructed images in 5-level wavelet decomposition by considering a particular subband coefficients of image-4 from the database.



Figure A.8: Reconstructed images in 5-level wavelet decomposition by zeroing a particular subband coefficients of image-4 from the database.

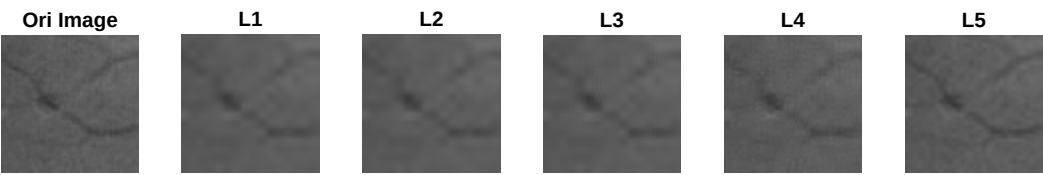


Figure A.9: Reconstructed images in 5-level wavelet decomposition by considering a particular subband coefficients of image-5 from the database.

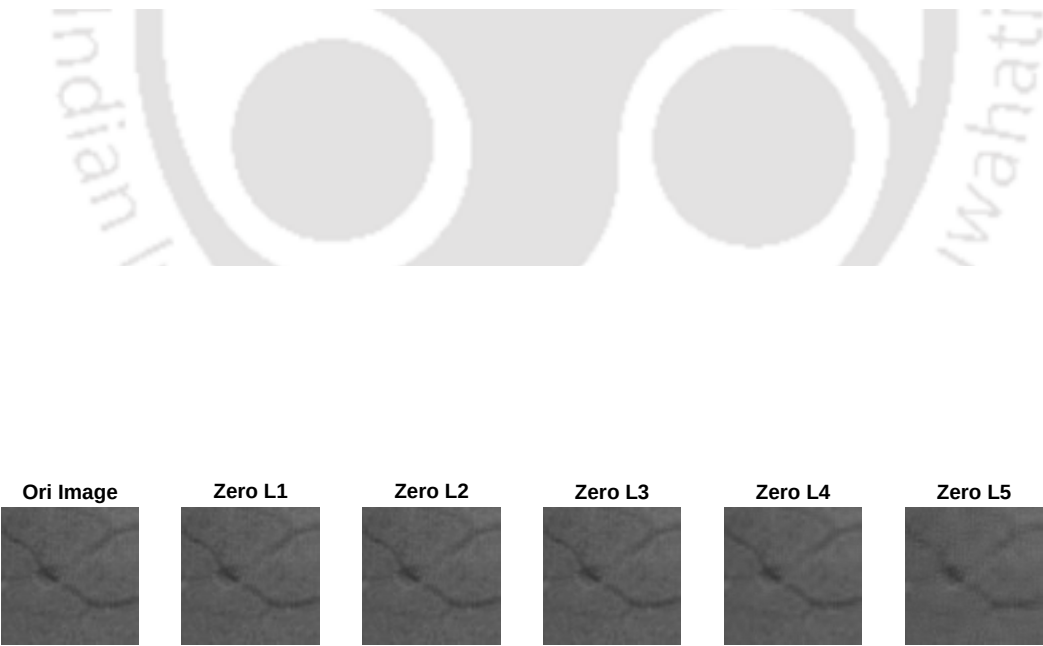


Figure A.10: Reconstructed images in 5-level wavelet decomposition by zeroing a particular subband coefficients of image-5 from the database.

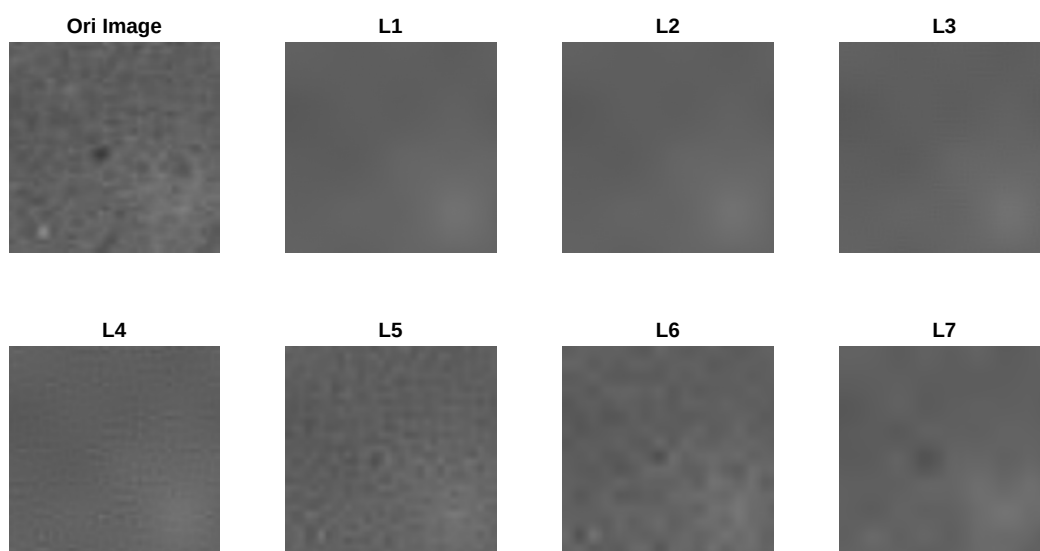


Figure A.11: Reconstructed images in 7-level wavelet decomposition by considering a particular subband coefficients of image-1 from the database.

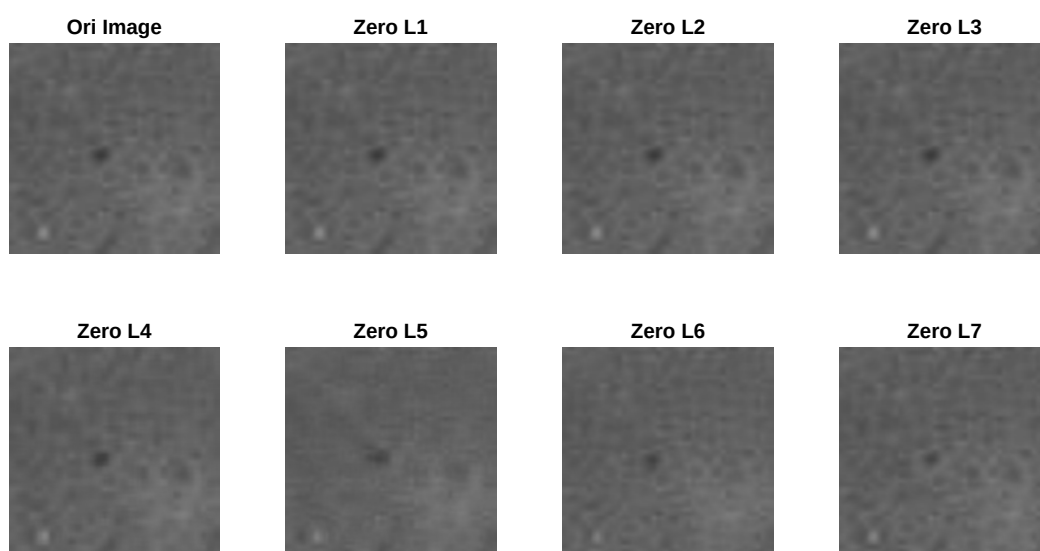


Figure A.12: Reconstructed images in 7-level wavelet decomposition by zeroing a particular subband coefficients of image-1 from the database.

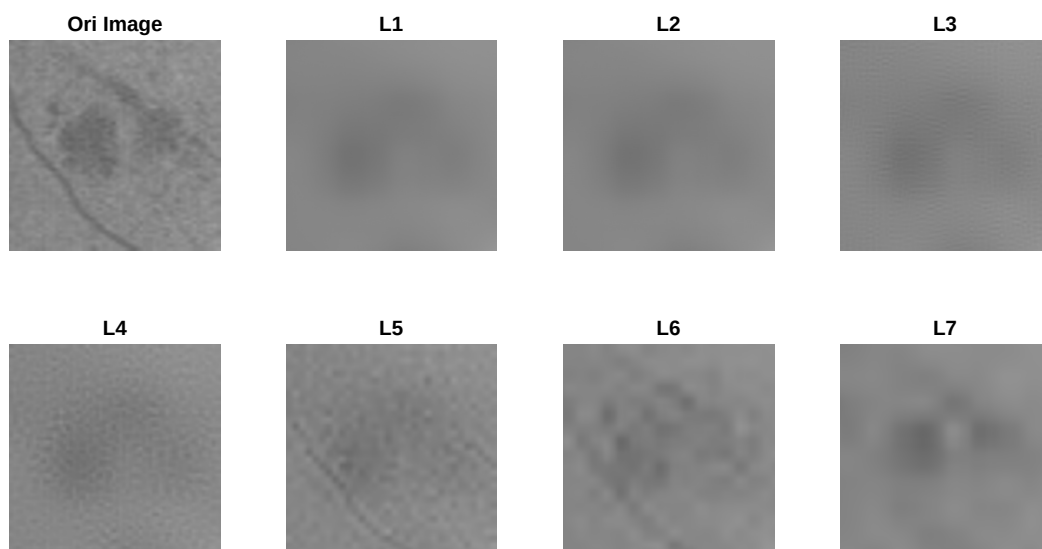


Figure A.13: Reconstructed images in 7-level wavelet decomposition by considering a particular subband coefficients of image-2 from the database.

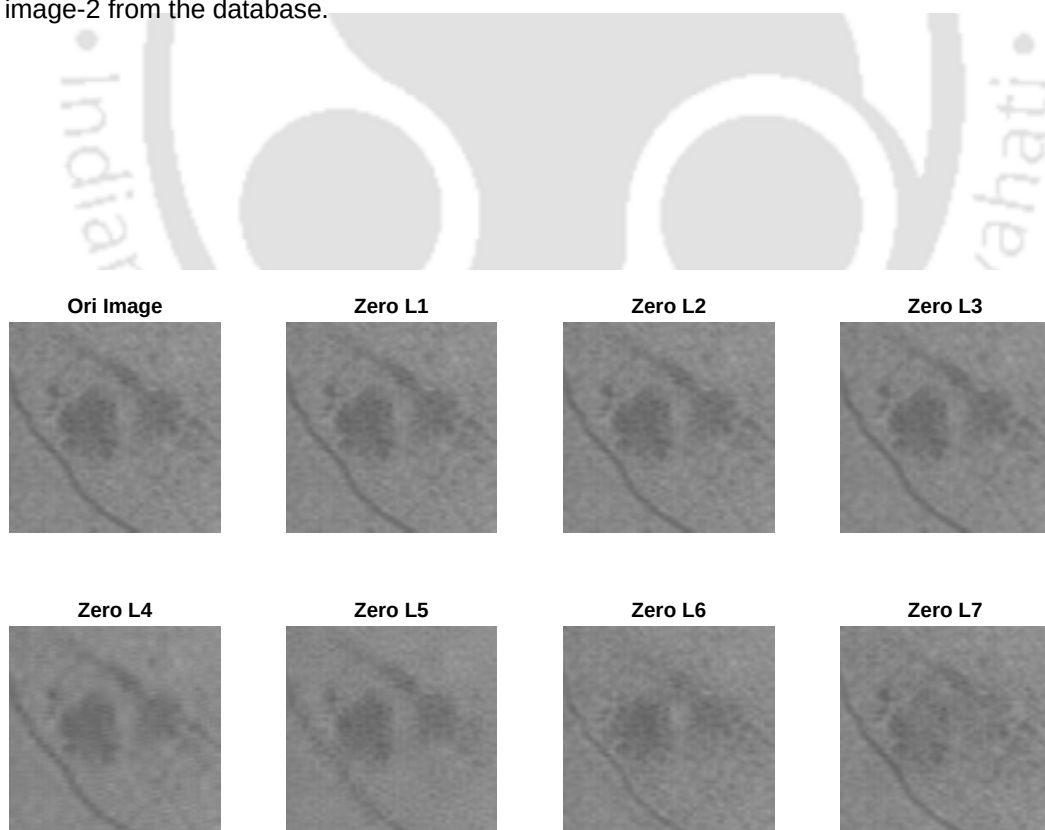


Figure A.14: Reconstructed images in 7-level wavelet decomposition by zeroing a particular subband coefficients of image-2 from the database.

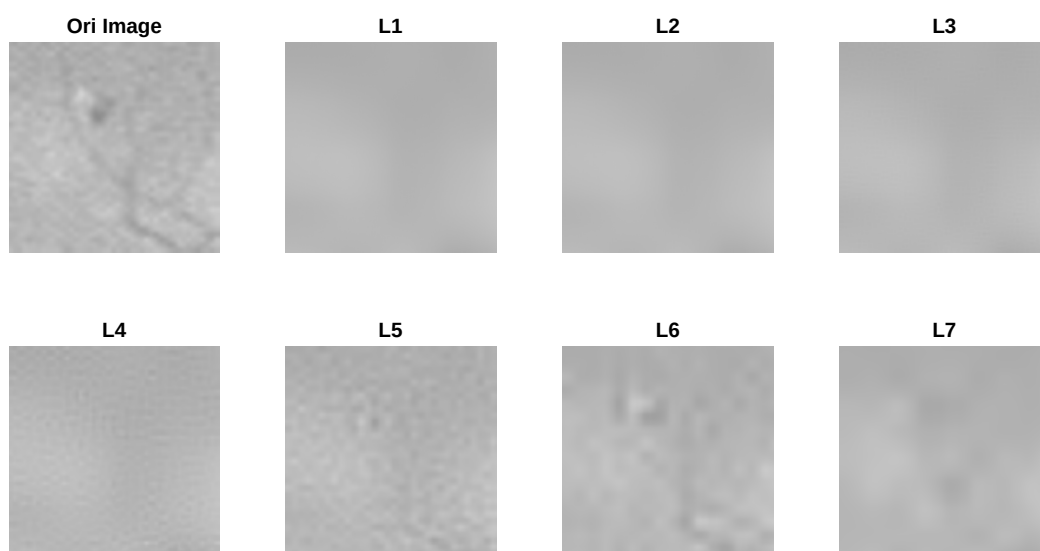


Figure A.15: Reconstructed images in 7-level wavelet decomposition by considering a particular subband coefficients of image-3 from the database.

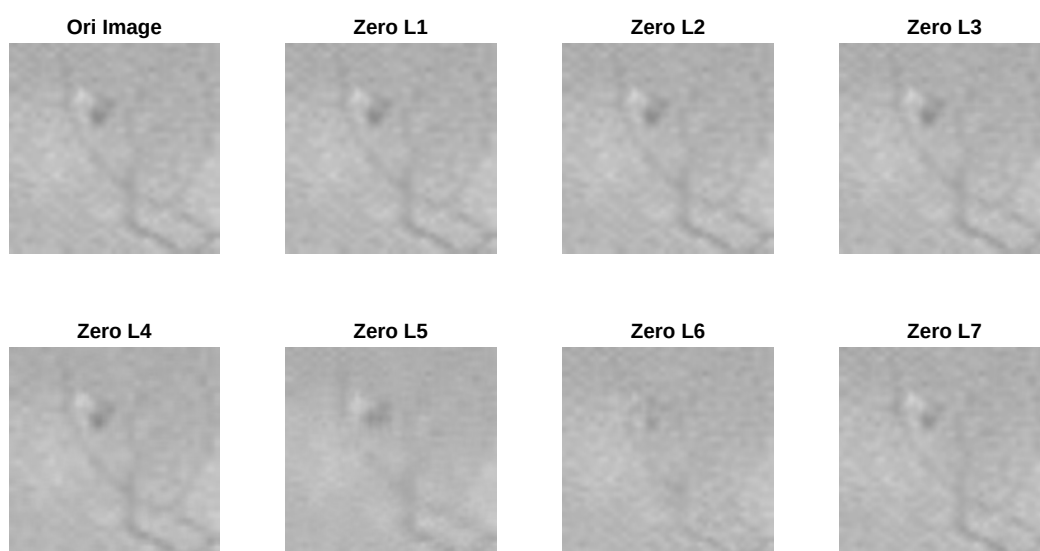


Figure A.16: Reconstructed images in 7-level wavelet decomposition by zeroing a particular subband coefficients of image-3 from the database.

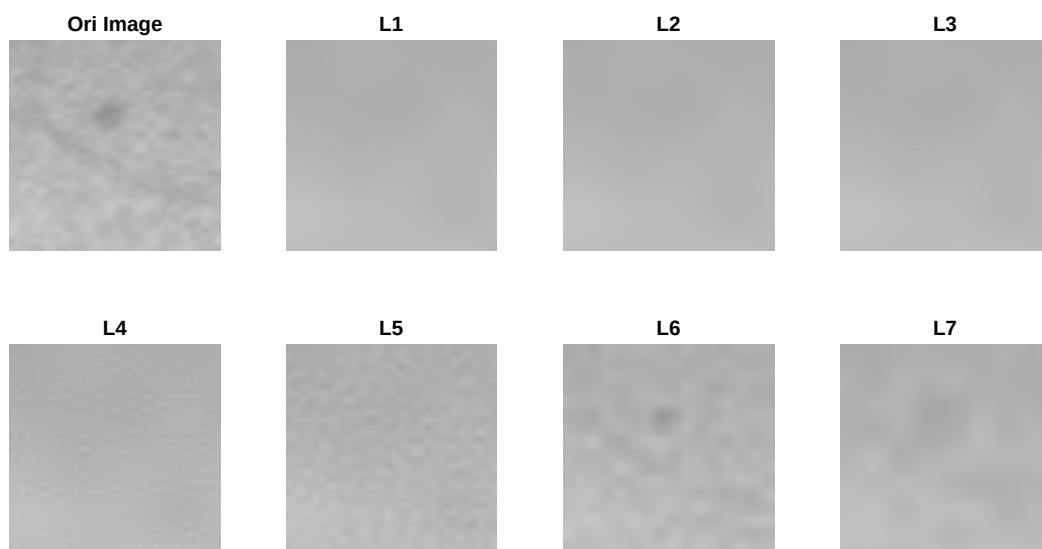


Figure A.17: Reconstructed images in 7-level wavelet decomposition by considering a particular subband coefficients of image-4 from the database.

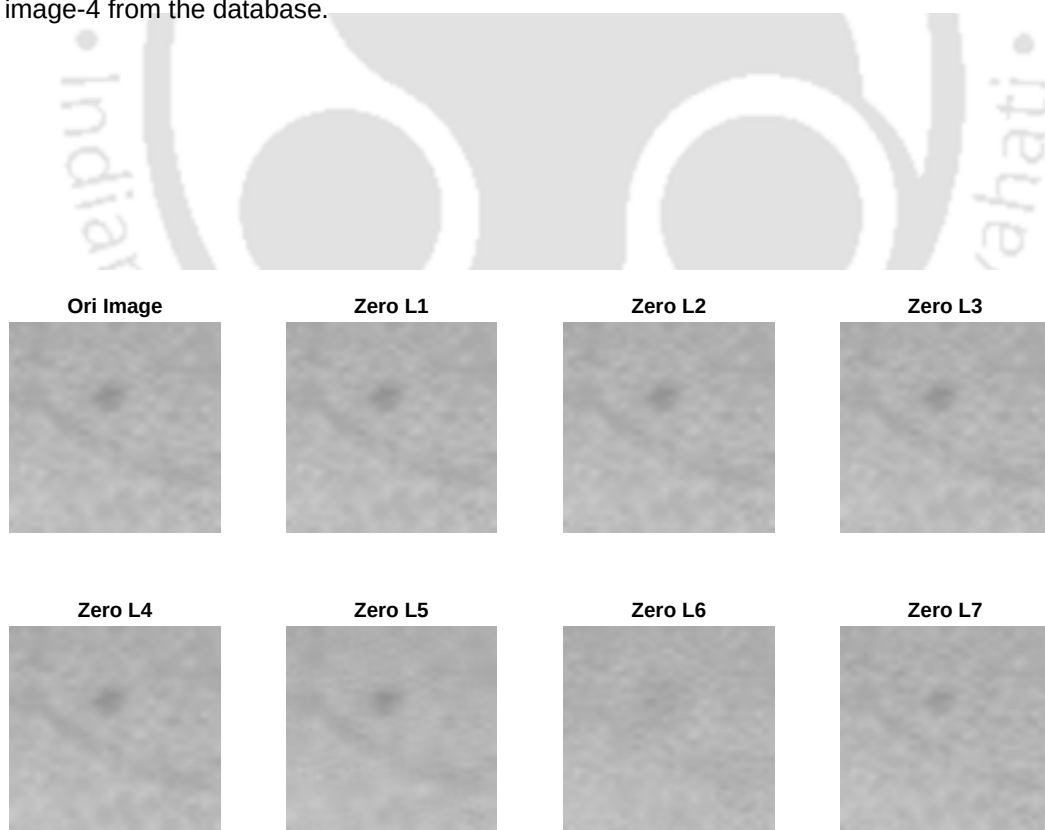


Figure A.18: Reconstructed images in 7-level wavelet decomposition by zeroing a particular subband coefficients of image-4 from the database.

A.2 Negentropy

Negentropy is defined as the differential entropy. It can be calculated as finding the difference of the entropy of a random variable from the Gaussian random variable having same mean and variance. It can take the value zero or positive. For Gaussian random variable it is zero and for non-Gaussian random variable it is positive. Negentropy of a random variable ' y ' can be represented by the following expression [146].

$$J(y) = H(y_{gauss}) - H(y) \quad (A.1)$$

where y_{gauss} is a Gaussian random variable of same covariance matrix as y . $H(y)$ is defined as the entropy and can be defined as

$$H(y) = - \int P_y(\xi) \log P_y(\xi) d\xi \quad (A.2)$$

Negentropy can be found by the approximations. The classical method for approximating Negentropy can be defined as

$$J(y) \approx \frac{1}{12} E\{y^3\}^2 + \frac{1}{48} kurtosis(y)^2 \quad (A.3)$$

The above expression can be equivalently represented by using the Kullback-Leibler divergence as given below. The proof is based on the fact that only the first and second order moment of the Gaussian densities are nonzero [144].

$$J(y) = D_{KL}(P_y \| P_{y_{gauss}}) = \int P_y \log \frac{P_y(\xi)}{P_{y_{gauss}}(\xi)} d\xi \quad (A.4)$$



References

- [1] <http://www.britannica.com>.
- [2] "<http://www.retinabatonrouge.com/>."
- [3] "<http://webeye.ophth.uiowa.edu/eyeforum/>."
- [4] E. N. Marieb, *Human Anatomy and Physiology*, Ninth ed., E. N. Marieb, Ed. San Francisco: Pearson Education, 2006.
- [5] J. S. Duncan and N. Ayache, "Medical image analysis: progress over two decades and the challenges ahead," *IEEE Transactions on Pattern Analysis and Machine Intelligence*, vol. 22, no. 1, pp. 85–106, January 2000.
- [6] E. Magdy, M. Ibrahim, and A. S. F. Quan D. Nguyen, "Computer aided analysis of fluorescein angiograms using color leakage maps," *IET Image Processsing*, vol. 9, no. 6, pp. 486–495, 2015.
- [7] A. Agarwal, *Fundus Fluorescein and Indocyanine Green Angiography*, First ed., A. Agarwal, Ed. 6900 Grove Road, Thorofare, NJ 08086 USA: Slack Incorporated, 2008.
- [8] J. G. Fujimoto, C. Pitris, S. A. Boppart, and M. E. Brezinski, "Optical coherence tomography: An emerging technology for biomedical imaging and optical biopsy," *Neoplasia*, vol. 2, no. 1-2, pp. 9–25, January-April 2000.
- [9] W. Drexler and J. G. Fujimoto, *Optical Coherence Tomography: Technology and Applications*, First ed., W. Drexler and J. G. Fujimoto, Eds. Springer Berlin Heidelberg New York: Springer, March 2008.
- [10] A. F. Fercher, W. Drexler, C. K. Hitzenberger, and T. Lasser, "Optical coherence tomography principles and applications," *Institute of Physics Publishing*, vol. 66, pp. 239–303, January 2003.
- [11] E. Midea, "Microperimetry," *Arch Soc Esp Oftalmol*, vol. 81, pp. 183–184, 2006.
- [12] S. C. Siu, T. C. Ko, K. W. Wong, and W. N. Chan, "Effectiveness of non-mydratic retinal photography and direct ophthalmoscopy in detecting diabetic retinopathy," *Hong Kong Medical Journal*, vol. 4, no. 4, pp. 367–370, December 1998.
- [13] M. Niemeijer, B. van Ginneken, M. J. Cree, A. Mizutani, G. Quellec, C. I. Sánchez, B. Zhang, R. Hornero, M. Lamard, C. Muramatsu, X. Wu, G. Cazuguel, J. You, A. Mayo, Q. Li, Y. Hatanaka, B. Cochener, C. Roux, F. Karray, M. García, Hiroshi Fujita, and M. D. Abrámo, "Retinopathy online challenge: Automatic detection of microaneurysms in digital color fundus photographs," *IEEE Transactions on Medical Imaging*, vol. 29, no. 1, pp. 185–195, January 2010.
- [14] D. Welfer, J. Scharcanski, C. M. Kitamura, M. M. D. Pizzol, L. W. Ludwig, and D. R. Marinho, "Segmentation of the optic disk in color eye fundus images using an adaptive morphological approach," *Elsevier: Computers in Biology and Medicine*, vol. 40, no. 2, pp. 124–137, February 2010.
- [15] R. Bock, J. Meier, L. G. Nyl, J. Hornegger, and G. Michelson, "Glaucoma risk index: automated glaucoma detection from color fundus images," *Elsevier: Medical Image Analysis*, vol. 14, no. 3, pp. 471–481, June 2010.
- [16] "<http://www.optic-disc.org>."
- [17] J. Sun, F. Luan, and H. Wu, "Optic disc segmentation by balloon snake with texture from color fundus image," *International Journal of Biomedical Imaging: Hindawi Publishing Corporation*, pp. 1–14, February 2015.

REFERENCES

- [18] "<http://www.nei.nih.gov>."
- [19] O. Faust, U. R. Acharya, E. Y. K. Ng, K. H. Ng, and J. S. Suri, "Algorithms for the automated detection of diabetic retinopathy using digital fundus images: A review," *Journal of Medical Systems*, vol. 36, no. 1, pp. 145–157, February 2012.
- [20] G. Quellec, M. Lamard, P. M. Josselin, G. Cazuguel, B. Cochener, and C. Roux, "Optimal wavelet transform for the detection of microaneurysms in retina photographs," *IEEE Transactions on Medical Imaging*, vol. 27, no. 9, pp. 1230–1241, September 2008.
- [21] T. Walter, J. C. Klein, P. Massin, and A. Erginay, "A contribution of image processing to the diagnosis of diabetic retinopathy detection of exudates in color fundus images of the human retina," *IEEE Transactions on Medical Imaging*, vol. 21, no. 10, pp. 1236–1243, October 2002.
- [22] A. Osareh, B. Shadgar, and R. Markham, "A computational intelligence based approach for detection of exudates in diabetic retinopathy images," *IEEE Transactions on Information Technology in Biomedicine*, vol. 13, no. 4, pp. 535–545, July 2009.
- [23] E. Ahmed, *A Textbook of Ophthalmology*, Second ed., Ahmed, Ed. New Delhi, India: PHI, 2001.
- [24] P. N. Schacknow and J. R. Samples, *The Glaucoma Book*, First ed., P. N. Schacknow and J. R. Samples, Eds. Portland, USA: Springer, 2010.
- [25] T. Walter, P. Massin, A. Erginay, R. Ordonez, C. Jeulin, and J. C. Klein, "Automatic detection of microaneurysms in color fundus images," *Elsevier: Medical Image Analysis*, vol. 11, no. 6, pp. 555–566, December 2007.
- [26] C. I. Sánchez, R. Hornero, M. I. López, and J. Poza, "Retinal image analysis to detect and quantify lesions associated with diabetic retinopathy," in *26th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (IEMBS)*. San Francisco, CA: IEEE, September 2004, pp. 1624–1627.
- [27] S. Roychowdhury and D. D. Koozekanani, "DREAM: diabetic retinopathy analysis using machine learning," *IEEE Journal of Biomedical and Health Informatics*, vol. 18, no. 5, pp. 1717–1728, September 2014.
- [28] R. Richa, R. Linhares, E. Comunello, A. V. Wangenheim, J. Y. Schnitzler, B. Wassmer, C. Guillemot, G. Thuret, P. Gain, G. Hager, and R. Taylor, "Fundus image mosaicking for information augmentation in computer-assisted slit-lamp imaging," *IEEE Transaction on Medical Imaging*, vol. 33, no. 6, pp. 1304–1312, June 2014.
- [29] N. Silberman, K. Ahrlich, R. Fergus, and L. Subramanian, "Case for automated detection of diabetic retinopathy," *Association for the Advancement of Artificial Intelligence (AAAI) Spring Symposium Series, North America*, March 2010.
- [30] T. A. Ciulla, A. G. Amador, and B. Zinman, "Diabetic retinopathy and diabetic macular edema," *Diabetes Care*, vol. 26, no. 9, pp. 2653–2664, September 2003.
- [31] D. Welfer, J. Scharcanski, and D. R. Marinho, "Fovea center detection based on the retina anatomy and mathematical morphology," *Computer Methods and Programs in Biomedicine*, vol. 104, no. 3, pp. 397–409, December 2011.
- [32] T. A. R. E. D. S. R. Group, "The age-related eye disease study system for classifying age-related macular degeneration from stereoscopic color fundus photographs: the age-related eye disease study report number 6," *American Journal of Ophthalmology*, vol. 132, no. 5, pp. 668–681, November 2001.
- [33] G. Querques, F. Coscas, R. Forte, N. Massamba, M. Sterkers, and E. H. Souied, "Cystoid macular degeneration in exudative age-related macular degeneration," *American Journal of Ophthalmology*, vol. 152, no. 1, pp. 100–107, July 2011.
- [34] J. W. Miller, "Age-related macular degeneration revisited piecing the puzzle: The LXIX Edward Jackson Memorial Lecture," *American Journal of Ophthalmology*, vol. 155, no. 1, pp. 1–35, January 2013.
- [35] "<http://www.glaucomafoundation.org>."

- [36] "http://www.glaucoma.org."
- [37] R. C. Gonzalez and R. E. Woods, *Digital Image Processing*, Third ed. Prentice Hall: Prentice Hall of India, August 2007.
- [38] H. Wang, W. Hsu, K. G. Goh, and M. L. Lee, "An effective approach to detect lesions in color retinal images," in *Proceedings, IEEE Conference on Computer Vision and Pattern Recognition*, vol. 2, Hilton Head Island, SC, June 2000, pp. 181–186.
- [39] K. Rapantzikos, M. Zervakis, and K. Balas, "Detection and segmentation of drusen deposits on human retina: Potential in the diagnosis of age-related macular degeneration," *Elsevier: Medical Image Analysis*, vol. 7, no. 1, pp. 95–108, March 2003.
- [40] C. Sinthanayothin, J. F. Boyce, H. L. Cook, and T. H. Williamson, "Automated localisation of the optic disc, fovea, and retinal blood vessels from digital colour fundus images," *British Journal of Ophthalmology*, vol. 83, no. 8, pp. 902–910, August 1999.
- [41] A. Osareh, M. Mirmehdi, B. Thomas, and R. Markham, "Automated identification of diabetic retinal exudates in digital colour images," *British Journal of Ophthalmology*, vol. 87, no. 10, pp. 1220–1223, October 2003.
- [42] S. Chaudhuri, S. Chatterjee, N. Katz, M. Nelson, and M. Goldbaum, "Detection of blood vessels in retinal images using two-dimensional matched filters," *IEEE Transactions on Medical Imaging*, vol. 8, no. 3, pp. 263–269, September 1989.
- [43] A. Hoover, V. Kouznetsova, and M. Goldbaum, "Locating blood vessels in retinal images by piecewise threshold probing of a matched filter response," *IEEE Transactions on Medical Imaging*, vol. 19, no. 3, pp. 203–210, March 2000.
- [44] L. Zhang, Q. Li, J. You, and D. Zhang, "A modified matched filter with double-sided thresholding for screening proliferative diabetic retinopathy," *IEEE Transactions on Information Technology in Biomedicine*, vol. 13, no. 4, pp. 528–534, July 2009.
- [45] B. Zhang, L. Zhang, L. Zhang, and F. Karray, "Retinal vessel extraction by matched filter with first-order derivative of gaussian," *Elsevier: Computers in Biology and Medicine*, vol. 40, no. 4, pp. 438–445, April 2010.
- [46] F. Zana and J. C. Klein, "A multimodal registration algorithm of eye fundus images using vessels detection and hough transform," *IEEE Transactions on Medical Imaging*, vol. 18, no. 5, pp. 419–428, May 1999.
- [47] J. V. B. Soares, J. J. G. Leandro, R. M. C. Jr., H. F. Jelinek, and M. J. Cree, "Retinal vessel segmentation using the 2-D Gabor wavelet and supervised classification," *IEEE Transactions on Medical Imaging*, vol. 25, no. 9, pp. 1214–1222, September 2006.
- [48] M. U. Akram, A. Tariq, S. Nasir, and S. A. Khan, "Gabor wavelet based vessel segmentation in retinal images," in *IEEE Symposium on Computational Intelligence for Image Processing (CIIP)*, IEEE, Ed., Nashville, TN, March–April 2009, pp. 116–119, 10.1109/CIIP.2009.4937890.
- [49] D. Selvathi and P. L. Vaishnavi, "Gabor wavelet based blood vessel segmentation in retinal images using kernel classifiers," in *International Conference on Signal Processing, Communication, Computing and Networking Technologies (ICSCCN)*, IEEE, Ed. Thuckafay, July 2011, pp. 830–835, 10.1109/ICSCCN.2011.6024665.
- [50] T. Teng, M. Lefley, and D. Claremont, "Progress towards automated diabetic ocular screening: a review of image analysis and intelligent systems for diabetic retinopathy," *IEEE Medical and Biological Engineering and Computing*, vol. 40, pp. 2–13, 2002.
- [51] K. Akita and H. Kuga, "A computer method of understanding ocular fundus images," *Pattern Recognition*, vol. 15, no. 6, pp. 431–443, 1982.
- [52] J. Staal, M. D. Abrámoﬀ, M. Niemeijer, M. A. Viergever, and B. van Ginneken, "Ridge-based vessel segmentation in color images of the retina," *IEEE Transactions on Medical Imaging*, vol. 23, no. 4, pp. 501–509, April 2004.

REFERENCES

- [53] C. Muramatsu, Y. Hatanaka, T. Iwase, T. Hara, and H. Fujita, "Automated selection of major arteries and veins for measurement of arteriolar-to-venular diameter ratio on retinal fundus images," *Elsevier: Computerized Medical Imaging and Graphics*, vol. 35, no. 6, pp. 472–480, September 2011.
- [54] T. Walter and J. C. Klein, "Segmentation of color fundus images of the human retina: Detection of the optic disc and the vascular tree using morphological techniques," *Medical Data Analysis Lecture Notes in Computer Science: Springer-Verlag Berlin Heidelberg*, vol. 2199, pp. 282–287, 2001.
- [55] M. Niemeijer, M. D. Abràmoff, and B. van Ginneken, "Segmentation of the optic disc, macula and vascular arch in fundus photographs," vol. 26, no. 1, pp. 116–127, January 2007.
- [56] H. Li and O. Chutatape, "Automated feature extraction in color retinal images by a model based approach," *IEEE Transactions on Biomedical Engineering*, vol. 51, no. 2, pp. 246–254, February 2004.
- [57] A. Hoover and M. Goldbaum, "Locating the optic nerve in a retinal image using the fuzzy convergence of the blood vessels," *IEEE Transactions on Medical Imaging*, vol. 22, no. 8, pp. 951–958, August 2003.
- [58] M. Foracchia, E. Grisan, and A. Ruggeri, "Detection of optic disc in retinal images by means of a geometrical model of vessel structure," *IEEE Transactions on Medical Imaging*, vol. 23, no. 10, pp. 1189–1195, October 2004.
- [59] P. Mitchell, H. Leung, J. J. Wang, E. Rochtchina, A. J. Lee, T. Y. Wong, and R. Klein, "Retinal vessel diameter and open-angle glaucoma: the blue mountains eye study," *Elsevier: Ophthalmology*, vol. 112, no. 2, pp. 245–250, February 2005.
- [60] O. Chutatape, "Fundus foveal localization based on vessel model," in *Proceedings of the 28th IEEE EMBS Annual International Conference*, 2006, pp. 4440–4444.
- [61] H. Narasimha-Iyer, A. Can, B. Roysam, C. V. Stewart, H. L. Tanenbaum, A. Majerovics, and H. Singh, "Robust detection and classification of longitudinal changes in color retinal fundus images for monitoring diabetic retinopathy," *IEEE Transactions on Biomedical Imaging*, vol. 53, no. 6, pp. 1084–1098, June 2006.
- [62] J. Singh and J. Sivaswamy, "Fundus foveal localization based on image relative subtraction-ires approach," in *IEEE Conference*, 2008.
- [63] C. Kose, U. Sevik, and O. Genalioglu, "Automatic segmentation of age-related macular degeneration in retinal fundus images," *Elsevier: Computers in Biology and Medicine*, vol. 38, p. 611619, 2008.
- [64] A. V. Sagar, S. Balasubramanian, and V. Chandrasekaran, "Automatic detection of anatomical structures in digital fundus retinal images," in *IAPR Conference on Machine Vision Applications*, Tokyo, JAPAN, May 2007, pp. 483–486.
- [65] S. Sekhar, W. Al-Nuaimy, and A. Nandi, "Automated localisation of optic disk and fovea in retinal fundus images," in *European Signal Processing Conference*, Switzerland, August 2008.
- [66] J. H. Hipwell, F. Strachan, J. A. Olson, K. C. McHardy, P. F. Sharp, and J. V. Forrester, "Automated detection of microaneurysms in digital red-free photographs: A diabetic retinopathy screening tool," *Wiley: Diabetic Medicine*, vol. 17, no. 8, pp. 588–594, August 2000.
- [67] B. Antal and A. Hajdu, "An ensemble-based microaneurysm detector for retinal images," in *18th IEEE International Conference on Image Processing (ICIP)*, IEEE, Ed., Brussels, September 2011, pp. 1621–1624.
- [68] B. Antal, I. Lázár, A. Hajdu, and T. P. Zsolt Török, Adrienne Csutak, "Evaluation of the grading performance of an ensemble-based microaneurysm detector," in *Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*. Boston, MA: IEEE, August-September 2011, pp. 5943–5946, 10.1109/IEMBS.2011.6091469.
- [69] B. Nagy, B. Antal, B. Harangi, and A. Hajdu, "Ensemble-based exudate detection in color fundus images," in *7th International Symposium on Image and Signal Processing and Analysis (ISPA)*, IEEE, Ed., Dubrovnik, Croatia, September 2011, pp. 700–703.

- [70] A. D. Fleming, S. Philip, K. A. Goatman, J. A. Olson, and P. F. Sharp, "Automated microaneurysm detection using local contrast normalization and local vessel detection," *IEEE Transactions on Medical Imaging*, vol. 25, no. 9, pp. 1223–1232, September 2006.
- [71] M. García, M. I. López, D. Álvarez, and R. Hornero, "Assessment of four neural network based classifiers to automatically detect red lesions in retinal images," *Medical Engineering and Physics*, vol. 32, no. 10, pp. 1085–1093, December 2010.
- [72] C. Köse, U. Sevik, C. Ikibas, and H. Erdol, "Simple methods for segmentation and measurement of diabetic retinopathy lesions in retinal fundus images," *Elsevier: Computer Methods and Programs in Biomedicine*, vol. 107, no. 2, pp. 274–293, August 2012.
- [73] A. Sopharak, B. Uyyanonvara, S. Barman, and T. H. Williamson, "Automatic detection of diabetic retinopathy exudates from non-dilated retinal images using mathematical morphology methods," *Elsevier: Computerized Medical Imaging and Graphics*, vol. 32, no. 8, pp. 720–727, December 2008.
- [74] C. I. Sánchez, R. Hornero, M. I. López, M. Aboy, J. Poza, and D. Abásolo, "A novel automatic image processing algorithm for detection of hard exudates based on retinal image analysis," *Elsevier: Medical Engineering and Physics*, vol. 30, no. 3, pp. 350–357, April 2008.
- [75] C. I. Sánchez, M. García, A. Mayo, M. I. López, and R. Hornero, "Retinal image analysis based on mixture models to detect hard exudates," *Elsevier: Medical Image Analysis*, vol. 13, no. 4, pp. 650–658, August 2009.
- [76] Y. Hatanaka, T. Nakagawa, Y. Hayashi, T. Hara, and H. Fujita, "Improvement of automated detection method of hemorrhages in fundus images," in *30th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBS)*, IEEE, Ed., Vancouver, British Columbia, Canada, August 2008, pp. 5429–5432, 10.1109/IEMBS.2008.4650442.
- [77] N. Patton, T. M. Aslam, T. MacGillivray, I. J. Deary, B. Dhillon, R. H. Eikelboom, K. Yogesan, and I. J. Constable, "Retinal image analysis: concepts, applications and potential," *Elsevier: Progress in retinal and eye research*, vol. 25, no. 1, pp. 99–127, January 2006.
- [78] F. Murtagh, "Multidimensional clustering algorithms," *Physica-Verlag*, 1985.
- [79] M. Unser and A. Aldroubi, "A review of wavelets in biomedical applications," *Proceeding of the IEEE*, vol. 84, no. 4, pp. 626–638, April 1996.
- [80] S. Mallat, *A Wavelet Tour to Signal Processing*, Third ed. Elsevier: Academic Press, 2009.
- [81] M. Unser, A. Aldroubi, and A. Laine, "Guest editorial: Wavelets in medical imaging," *Proceeding of the IEEE*, vol. 22, no. 3, pp. 285–288, March 2003.
- [82] M. Antonini, M. Barlaud, P. Mathieu, and I. Daubechies, "Image coding using wavelet transform," *IEEE Transactions on Image Processing*, vol. 1, no. 2, pp. 205–220, April 1992.
- [83] A. Munteanu, J. Cornelis, G. V. der Auwera, and P. Cristea, "Wavelet image compression - the quadtree coding approach," *IEEE Transactions on Information Technology in Biomedicine*, vol. 3, no. 3, pp. 176–185, September 1999.
- [84] S. Grgic, M. Grgic, and B. Zovko-Cihlar, "Performance analysis of image compression using wavelets," *IEEE Transactions on Industrial Electronics*, vol. 48, no. 3, pp. 682–695, June 2001.
- [85] M. Penedo, W. A. Pearlman, P. G. Tahoces, M. Souto, and J. J. Vidal, "Region-based wavelet coding methods for digital mammography," *IEEE Transactions on Medical Imaging*, vol. 22, no. 10, pp. 1288–1296, October 2003.
- [86] S. Mallat and W. L. Hwang, "Singularity detection and processing with wavelets," *IEEE Transactions on Information Theory*, vol. 38, no. 2, pp. 617–643, March 1992.
- [87] D. P. K. Lun, T. C. Hsung, and Y. F. Ho, "Wavelet singularity detection for image processing," in *45th Midwest Symposium on Circuits and Systems (MWSCAS)*, IEEE, Ed., Department of Electronics and Information Engineering, The Hong Kong Polytechnic University, Hung Ham. Kowloon, Hong Kong: IEEE, August 2002, pp. II.156–II.159.

REFERENCES

- [88] S. R. Nirmala, S. Dandapat, and P. K. Bora, "Wavelet weighted blood vessel distortion measure for retinal images," *Biomedical Signal Processing and Control: Elsevier*, vol. 5, no. 4, pp. 282–291, October 2010.
- [89] P. Hänsen, P. E. Undrill, and M. J. Cree, "The application of wavelets to retinal image compression and its effect on automatic microaneurysm analysis," *Computer Methods and Programs in Biomedicine*, vol. 56, no. 1, pp. 1–10, April 1998.
- [90] R. H. Eikelboom, K. Yogesan, C. J. Barry, I. J. Constable, M. L. Tay-Kearney, and P. H. H. L. Jitskaia, "Methods and limits of digital image compression of retinal images for telemedicine," *Investigative Ophthalmology and Visual Science*, vol. 41, no. 7, pp. 1916–1924, June 2000.
- [91] H. Li and O. Chutatape, "Fundus image feature extraction," in *Proceedings of the 22ND Annual EMBS International Conference*, Chicago, July 2000, pp. 23–28.
- [92] T. Spencer, K. M. H. J. Olson, P. Sharp, and J. Forrester, "An image processing strategy for the segmentation and quantification in fluorescein angiograms of the ocular fundus," *Computer Biomedical Research*, vol. 29, pp. 284–302, 1996.
- [93] M. Cree, J. Olson, K. M. Hardy, P. Sharp, and J. Forrester, "A fully automated comparative microaneurysm digital detection system," *Eye*, vol. 11, pp. 622–628, 1997.
- [94] G. B. Kande, T. S. Savithri, and P. V. Subbaiah, "Automatic detection of microaneurysms and hemorrhages in digital fundus images," *Journal of Digital Imaging*, vol. 23, no. 4, pp. 430–437, 2010.
- [95] A. Sopharak, B. Uyyanonvara, and S. Barman, "Simple hybrid method for fine microaneurysm detection from non-dilated diabetic retinopathy retinal images," *Computerized Medical Imaging and Graphics*, vol. 37, pp. 394–402, 2013.
- [96] L. Giancardo, F. Meriaudeau, T. P. Karnowski, K. W. Tobin, Y. Li, and E. Chaum, "Microaneurysms detection with the radon cliff operator in retinal fundus images," *Medical Imaging*, vol. 7623, 2010.
- [97] A. Sopharak, B. Uyyanonvara, and S. Barman, "Fine exudate detection using morphological reconstruction enhancement," *International Journal of Applied Biomedical Engineering*, vol. 1, no. 1, pp. 45–50, 2010.
- [98] P. M. Rokade and R. R. Manza, "Automatic detection of hard exudates in retinal images using haar wavelet transform," *International Journal of Application or Innovation in Engineering and Management (IJAEM)*, vol. 4, no. 5, 2015.
- [99] A. Hayvarinen, "Survey on ICA," *Neural Computing Surveys*, vol. 2, pp. 94–128, 1999.
- [100] A. Hyvärinen and E. Oja, "Independent component analysis: Algorithms and applications," *Neural Networks*, vol. 13, no. 4-5, pp. 411–430, 2000.
- [101] L. D. Lathauwer and J. Castaing, "Fourth-order cumulant-based blind identification of underdetermined mixtures," *IEEE Transactions on Signal Processing*, vol. 55, no. 6, pp. 2965–2973, June 2007.
- [102] M. E. Davies and C. J. James, "Source separation using single channel ICA," *Elsevier: Signal Processing*, vol. 87, no. 8, pp. 1819–1832, August 2007.
- [103] W. Zou, Y. Li, K. C. Lo, and Z. Chi, "Improvement of image classification with wavelet and independent component analysis (ICA) based on a structured neural network," *IEEE, Ed., Hong Kong Polytechnic University, Kowloon. Sheraton Vancouver Wall Centre Hotel, Vancouver, BC, Canada: IEEE*, July 2006, pp. 3949–3954.
- [104] V. P. Shah, N. H. younan, S. S. Durbha, and R. L. King, "Feature identification via a combined ICA wavelet method for image information mining," *IEEE Geoscience and Remote Sensing Letters*, vol. 7, no. 1, pp. 18–22, January 2010.
- [105] P. N. Schacknow and J. R. Samples, *The Glaucoma Book: A Practical, Evidence-Based Approach to Patient Care*, First ed., P. N. Schacknow and J. R. Samples, Eds. 233 Spring Street, New York, NY 10013, USA: Springer, April 2010.
- [106] L. Xu, Y. Wang, J. Li, and J. B. Jonas, "Single intraocular pressure measurement for glaucoma detection: Beijing eye study," *Wiley: Acta Ophthalmologica*, vol. 86, no. 2, p. 229, March 2008.

- [107] I. Dersu, M. N. Wiggins, R. H. Anne Luther, and J. Chacko, "Understanding visual fields, Part I: Goldmann perimetry," *Journal of Ophthalmic Medical Technology*, vol. 2, no. 2, 2006.
- [108] R. A. A. Ghafar, T. Morris, T. Ritchings, and I. Wood, "Detection and characterisation of the optic disk in glaucoma and diabetic retinopathy," in *Annual Conference in Medical Image Understanding*, London, UK, 2004, pp. 23–24.
- [109] "<http://www.moorfields.nhs.uk/>."
- [110] "<http://www.willsglaucoma.org/>."
- [111] J. Gloster and D. G. Parry, "Use of photographs for measuring cupping in the optic disc," *British Journal of Ophthalmology*, vol. 58, pp. 850–862, 1974.
- [112] J. Funk, T. Dieringer, and F. Grehn, "Correlation between neuroretinal rim area and age in normal subjects," *Springer Verlag: Graefe's Archive for Clinical Experimental Ophthalmology*, vol. 227, no. 6, pp. 544–548, 1989.
- [113] V. Pueyo, J. M. Larrosa, V. Polo, A. Pérez-Inigo, A. Ferreras, and F. M. Honrubia, "Sector-based analysis of the distribution of the neuroretinal rim by confocal scanning laser in the diagnosis of glaucoma," *Arch Soc Esp Oftalmol*, vol. 81, pp. 135–140, 2006.
- [114] E. Corona, S. Mitra, M. Wilson, T. Krile, Y. H. Kwon, and P. Soliz, "Digital stereo image analyzer for generating automated 3-D measures of optic disc deformation in glaucoma," *IEEE Transactions on Medical Imaging*, vol. 21, no. 10, pp. 1244–1253, October 2002.
- [115] A. R. McIntyre, M. I. Heywood, P. H. Artes, and S. S. R. Abidi, "Toward glaucoma classification with moment methods," in *First Canadian Conference on Computer and Robot Vision 2004 (CRV04)*, 2004. London, ON, Canada: IEEE, May 2004, pp. 265–272.
- [116] F. Fink, K. Wörle, P. Gruber, A. M. Tomé, J. M. G. Sáez, C. G. Puntonet, and E. W. Lang, "ICA analysis of retina images for glaucoma classification," in *30th Annual International IEEE EMBS Conference*, IEEE, Ed. Vancouver, British Columbia, Canada: IEEE, August 2008, pp. 4664–4667.
- [117] J. Liu, D. W. K. Wong, J. H. Lim, H. Li, N. M. Tan, Z. Zhang, T. Y. Wong, and R. Lavanya, "ARGALI: An automatic cup-to-disc ratio measurement system for glaucoma analysis using level-set image processing," in *13th International Conference on Biomedical Engineering IFMBE Proceedings*, vol. 23, 2009, pp. 559–562.
- [118] J. Nayak, U. R. Acharya, P. S. Bhat, N. Shetty, and T. C. Lim, "Automated diagnosis of glaucoma using digital fundus images," *Journal of Medical Systems: Springer*, vol. 33, no. 5, pp. 337–346, October 2009.
- [119] J. M. M. Jiménez, S. Ortega, L. Boquete, J. M. Rodríguez-Ascariz, and R. Blanco, "Multi-focal electroretinography: structural pattern analysis and early glaucoma detection," *IEEE Electronics Letters*, vol. 45, no. 22, pp. 1113–1115, October 2009.
- [120] Y. Hatanaka, A. Noudo, C. Muramatsu, A. Sawada, T. Hara, T. Yamamoto, and H. Fujita, "Automatic measurement of cup to disc ratio based on line profile analysis in retinal images," in *33 Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBS)*, IEEE, Ed. Boston, Massachusetts USA: IEEE, August–September 2011, pp. 3387–3390.
- [121] Y. Xu, D. Xu, S. Lin, J. Liu, J. Cheng, C. Y. Cheung, T. Aung, and T. Y. Wong, "Sliding window and regression based cup detection in digital fundus images for glaucoma diagnosis," *Springer-Verlag*, pp. 1–8, 2011.
- [122] Z. Zhang, C. K. Kwok, J. Liu, F. Yin, A. Wirawan, C. Cheung, M. Baskaran, T. Aung, and T. Y. Wong, "MRMR optimized classification for automatic glaucoma diagnosis," in *33 Annual International Conference of the IEEE Engineering in Medicine and Biology Society, (EMBS)*. Boston, Massachusetts USA: IEEE, August–September 2011, pp. 6228–6231.
- [123] G. D. Joshi, J. Sivaswamy, and S. R. Krishnadas, "Optic disk and cup segmentation from monocular colour retinal images for glaucoma assessment," *IEEE Transactions On Medical Imaging*, vol. 30, no. 6, pp. 1192–1205, June 2011.

REFERENCES

- [124] M. Niemeijer and B. V. Ginneken, "DRIVE database," 2002, [online] Available: <http://www.isi.uu.nl/Research/Databases/DRIVE/results.php>.
- [125] D. Farnell, "Aria database," [online] Available: www.eyecharity.com.
- [126] Jean-Claude, "Messidor database," [online] Available: <http://messidor.crihan.fr>.
- [127] A. Lame and S. Song, "Multiscale wavelet representations for mammographic feature analysis," *Mathematical Methods in Medical Imaging, Proceedings of SPIE*, vol. 1768, pp. 306–316, 1992.
- [128] C. W. Chen, Y. Q. Zhang, and K. J. Parker, "Subband analysis and synthesis of volumetric medical images using wavelet," in *Visual Communications and Image processing*, W. SPIE, Bellingham, Ed., vol. 2308, Chicago, IL, USA, 1994, pp. 1544–1555.
- [129] S. Lahmiri, "Features extraction from high frequency domain for retina digital images classification," *Journal of Advances in Information Technology*, vol. 4, no. 4, pp. 194–198, November 2013.
- [130] Daubechies, *Ten lectures on wavelets*. SIAM, 1992.
- [131] L. H. K. L. Y. G. Dong Cui, Minmin Liu and Q. Jiao, "The application of wavelet-domain hidden markov tree model in diabetic retinal image de-noising," *Biomedical Engineering Journal*, vol. 9, pp. 194–198, August 2015.
- [132] B. Antal and A. Hajdu, "An ensemble-based system for microaneurysm detection and diabetic retinopathy grading," *IEEE Transactions on Biomedical Engineering*, vol. 59, no. 6, pp. 1720–1726, June 2012.
- [133] Z. Wang and A. C. Bovik, "A universal image quality index," *IEEE Signal Processing Letters*, vol. 9, no. 3, pp. 81–84, March 2002.
- [134] A. M. Mendonca and A. Campilho, "Segmentation of retinal blood vessels by combining the detection of centerlines and morphological reconstruction," *IEEE Transaction on Medical Imaging*, vol. 25, no. 9, pp. 1200–1213, September 2006.
- [135] H. H. Chang, A. H. Zhuang, D. J. Valentino, and W. C. Chu, "Performance measure characterization for evaluating neuroimage segmentation algorithms," *Elsevier: NeuroImage*, vol. 47, no. 1, pp. 122–135, August 2009.
- [136] C. Kose, U. Sevik, and O. Genalioglu, "Simple methods for segmentation and measurement of diabetic retinopathy lesions in retinal fundus images," *Elsevier: Computer Methods and Programs in Biomedicine*, vol. 107, no. 2, pp. 274–293, August 2012.
- [137] A. M. Eskicioglu and P. S. Fisher, "Image quality measures and their performance," *IEEE Transactions on Communications*, vol. 43, no. 12, pp. 2959–2965, December 1995.
- [138] A. M. Grigoryan and M. Grigoryan, *Brief Notes in Advanced DSP Fourier Analysis with MATLAB*, 1st ed. Taylor and Francis, CRC Press, February 2009.
- [139] Z. Wang, A. C. Bovik, H. R. Sheikh, and E. P. Simoncelli, "Image quality assessment: From error visibility to structural similarity," *IEEE Transactions on Image Processing*, vol. 13, no. 4, pp. 600–612, April 2004.
- [140] D. Rousseau, A. Delahaies, and Fran, "Structural similarity measure to assess improvement by noise in nonlinear image transmission," *IEEE Signal Processing Letters*, vol. 17, no. 1, pp. 36–39, January 2010.
- [141] S. P. Meshram and M. S. Pawar, "Extraction of retinal blood vessels from diabetic retinopathy imagery using contrast limited adaptive histogram equalization," *International Journal on Advanced Computer Theory and Engineering*, vol. 2, no. 3, pp. 2319–2526, 2013.
- [142] A. F. M. Hani and H. A. Nugroho, "Retinal vasculature enhancement using independent component analysis," *Journal of Biomedical Science and Engineering*, vol. 2, pp. 543–549, November 2009.
- [143] J. F. Cardoso, "Blind signal separation: statistical principles," *Proceedings of the IEEE*, vol. 86, no. 10, pp. 2009–2025, October 1998.
- [144] P. Comon, "Independent component analysis, a new concept?" *Elsevier: Signal Processing*, vol. 36, no. 3, pp. 287–314, 1994.

- [145] G. A. Baxes, *Digital Image Processing: Principles and Applications*, First ed. Professional, Reference and Trade Group, 605 Third Avenue, New York, N.Y. 10158-0012: John Wiley and Sons, Inc., 1994.
- [146] A. Hyvarinen, J. Karhunen, and E. Oja, *Independent Component Analysis*, First ed., S. Haykin, Ed. John Wiley and Sons, Inc, New York, U.S.A: John Wiley and Sons, 2001.
- [147] B. Gabrys, R. J. Howlett, and L. C. Jain, Eds., *Knowledge-based Intelligent Information and Engineering Systems*, vol. 2. Bournemouth, UK: Springer, October 2006.
- [148] A. J. Bell and T. J. Sejnowski, "An information-maximization approach to blind separation and blind deconvolution," *Neural Computation*, UCSD, vol. 7, no. 6, pp. 1129–1159, February 1995.
- [149] T. M. Cover and J. A. Thomas, *Elements of Information Theory*, First ed., T. M. Cover, Ed. New York: John Wiley and Sons, 1991.
- [150] V. P. Shah, N. H. Younan, S. S. Durbha, and R. L. King, "Feature identification via a combined ICA wavelet method for image information mining," *IEEE Geoscience and Remote Sensing Letters*, vol. 7, no. 1, pp. 18–22, January 2010.
- [151] S. Haykin, *Neural Networks: A Comprehensive Foundation*, Second ed. Prentice Hall, Inc., New Jersey, U.S.A: PHI, 2006.
- [152] C. Sinthanayothin, "Image analysis for automatic diagnosis of diabetic retinopathy," Ph.D. dissertation, Kings College of London, London, U.K., 1999.
- [153] S. Kavitha and K. Duraiswamy, "Automatic detection of hard and soft exudates in fundus images using color histogram thresholding," *European Journal of Scientific Research*, vol. 48, no. 3, pp. 493–504, 2011.
- [154] A. Criminisi, P. Prez, and K. Toyama, "Region filling and object removal by exemplar-based image inpainting," *IEEE Transactions on Image Processing*, vol. 13, no. 9, pp. 1200–1212, September 2004.
- [155] M. Petrou and C. Petrou, *Image Processing The Fundamentals*, Second ed., M. Petrou, Ed. Singapore: Wiley, 2010.
- [156] T. F. Chan and L. A. Vese, "Active contours without edges," *IEEE Transactions on Image Processing*, vol. 10, no. 2, pp. 266–277, February 2001.
- [157] A. Oprea and C. Vertan, "A quantitative evaluation of the hip prosthesis segmentation quality in x-ray images," *Proceedings of IEEE International Symposium on Signals, Circuits and Systems*, pp. 1–4, July 2007.
- [158] A. H. Sahoolizadeh, B. Z. Heidari, and C. H. Dehghani, "A new face recognition method using pca, lda and neural network," *International Journal of Electrical and Electronics Engineering*, pp. 507–512, Nov 2008.
- [159] M. Turk and A. Pentland, "Eigenfaces for recognition," *Journal of Cognitive Neuroscience*, vol. 3, no. 1, pp. 71–86, 1991.
- [160] P. N. Belhumeur, J. P. Hespanha, and D. J. Kriegman, "Eigenfaces vs. fisherfaces: recognition using class specific linear projection," *IEEE Transactions on Pattern Analysis and Machine Intelligence*, vol. 19, no. 7, pp. 711–720, 1997.
- [161] M. Sadeghi, M. Samiei, and J. Kittler, "Fusion of PCA-based and LDA-based similarity measures for face verification," *EURASIP Journal on Advances in Signal Processing*, pp. 12–19, July 2010.
- [162] H. Anton, *Elementary Linear Algebra*, Fifth ed., H. Anton, Ed. John Wiley and Sons Inc.
- [163] M. T. Sadeghi, M. Samiei, and J. Kittler, "Fusion of PCA-based and LDA-based similarity measures for face verification," *EURASIP Journal on Advances in Signal Processing*, pp. 1–12, 2010.
- [164] H. M. Naimi and P. Davari, "A new fast and efficient HMM-based face recognition system using a 7-state HMM along with SVD coefficients," *Iranian Journal of Electrical and Electronic Engineering*, vol. 4, no. 1, pp. 46–57, April 2008.
- [165] K. Baker, "Singular value decomposition tutorial," pp. 1–24, March 2005.
- [166] L. R. Rabiner, "A tutorial on hidden markov models and selected application in speech recognition," *In proceedings of the IEEE*, vol. 77, no. 2, pp. 257–286, February 1989.



LIST OF PUBLICATIONS

Journals:

1. **M. K. Nath** and S. Dandapat, "Multiscale ICA for Fundus Image Analysis, *International Journal of Imaging Systems and Technology*, vol. 23, no. 4, pp. 327-337, November 2013. DOI: 10.1002/ima.22067.
2. **M. K. Nath** and S. Dandapat, "Techniques of Glaucoma Detection from Color Fundus Images: A Review, *I.J. Image, Graphics and Signal Processing*, vol. 9, pp. 44-51, September 2012. DOI: 10.5815/ijigsp.2012.09.07.
3. **M. K. Nath** and S. Dandapat, "Differential Entropy in Wavelet Subband for Assessment of Glaucoma, *International Journal of Imaging Systems and Technology*, vol. 22, no. 3, pp. 161-165, September 2012. DOI: 10.1002/ima.22017.
4. M. Mishra, **M. K. Nath**, and S. Dandapat, "Glaucoma Detection from Color Fundus Images, *International Journal of Computer and Communication Technology (IJCCT)*, vol. 2, no. 6, pp. 7-10, 2011.
5. S. R. Nirmala, **M. K. Nath**, and S. Dandapat, "Retinal Image Analysis: A Review, *International Journal of Computer and Communication Technology (IJCCT)*, vol. 2, no. 6, pp. 11-15, 2011.
6. M. Mishra, **M. K. Nath**, S. R. Nirmala, and S. Dandapat, "Image Processing Techniques for Glaucoma Detection, *Communications in Computer and Information Science: Advances in Computing and Communications: Springer*, vol. 192, pp. 365-373, July 2011.

Conferences:

1. Rohan Prasad, **M. K. Nath** and Samarendra Dandapat "Rule Based Expert System for Automatic Diagnosis of DR from Color Fundus Images, in *Proceedings of the AISC-2012*, (IIT BHU, India), December 2012.
2. J. P. Medhi, **M. K. Nath** and Samarendra Dandapat "Automatic Grading of Macular Degeneration From Color Fundus Images, in *Proceedings of the 2012 World Congress on Information*

List of Publications

and Communication Technologies (WICT), (Trivandrum, India), pp. 511-514, IEEE, October-November 2012.

3. **M. K. Nath** and S. Dandapat, "Detection of Changes in Color Fundus Images due to Diabetic Retinopathy, in *2nd National Conference on Computational Intelligence and Signal Processing (CISP)*, 2012, (Guwahati, Assam, India), pp. 81-85, IEEE, March 2012.
4. **M. K. Nath**, M. Mishra, and S. Dandapat, "PCA and LDA based Approach to Glaucoma Classification from Color Fundus Images, in *35Th National Systems Conference*, (IIT Bhubaneswar, India), pp. 186-191, Macmillan Advanced Research Series, December 2011.
5. **M. K. Nath** and S. Dandapat, "Segmentation of Retinal Blood Vessels from Color Fundus Images by using Morphological Approach, in *National Conference on Computational Intelligence and Signal Processing (CISP)*, (Don Bosco University Guwahati, Assam, India), 2011.
6. **M. K. Nath** and S. Dandapat, "Feature Detection from Color Fundus Images by Wavelet ICA, in *MedImage*, (IIT Delhi, India), December 2010.

